The Stereoisomers of 1,3-Dithiane 1,3-Dioxides. Preparation, Configuration and Some Conformational Aspects

Shlomo Bien,* Sol K. Celebi† and Moshe Kapon
Department of Chemistry, Technion, Israel Institute of Technology, Haifa 32000, Israel

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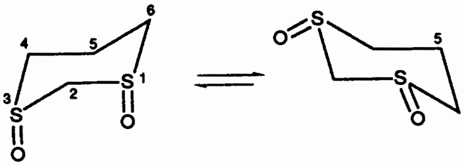
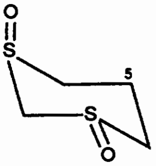
Oxidation of 1,3-dithiane with different oxidizing agents gave the 1,3-dithiane *cis*- and *trans*-1,3-dioxides **1** and **2**. Their configuration and the conformational preferences of the sulphinyl oxygen atom have been determined by NMR spectroscopy and by X-ray analyses.

In connection with synthetic studies we needed to prepare the two configurational isomers, 1,3-dithiane *cis*- and *trans*-1,3-dioxides **1** and **2**, as starting materials.



1a **1e**



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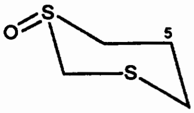

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Although cyclic sulphoxides including substituted 1,3-dithiane derivatives have been the target for numerous studies of different aspects,[1] data were found in the literature for the *cis*-isomer **1** only. Mild oxidation of 1,3-dithiane 1-oxide **3**[2] with *m*-chloroperbenzoic acid in CH_2Cl_2 gave a mixture of the *cis*- and *trans*-1,3-dioxides, from which the *cis*-isomer was separated by crystallization.[1c] On repeating this procedure, and from additional experiments on the oxidation of 1,3-dithiane or 1,3-dithiane 1-oxide with different oxidizing agents, we found some difficulty in separating satisfactorily pure isomers by fractional crystallization. Separation and purification was, however, possible by careful and tedious column chromatography on silica gel followed by crystallization.‡ After our work was complete, we became aware of a recent communication[3] reporting the preparation of the *trans*-isomer by oxidation of dithiane with sodium metaperiodate (no experimental conditions or physical data given).§

With the pure isomers in our hand, their structures could then be investigated by NMR spectroscopy and X-ray crystallography. In the ^{1}H NMR spectrum the *cis*- and *trans*-isomers were expected to show a completely different pattern for the resonance of the C-2 methylene protons. Indeed, the spectrum of the higher melting isomer (m.p. 239–240 °C) showed an AB system, centred at δ 4.58 due to $C(2)\text{–}H_2$. On the other hand, the spectrum of the lower melting isomer (m.p. 182–183 °C) displayed a singlet at δ 4.78 due to these protons. An AB spectrum can only be attributed to a symmetrical dioxide, *e.g.* the *cis*-isomer **1e** or **1a**. If ring inversion in the dioxides is fast on the ^{1}H NMR time scale at room temperature (as it was shown for the monoxide[1c]) the lower melting compound which exhibits a singlet for the C-2 protons, must be the *trans*-isomer **2**.

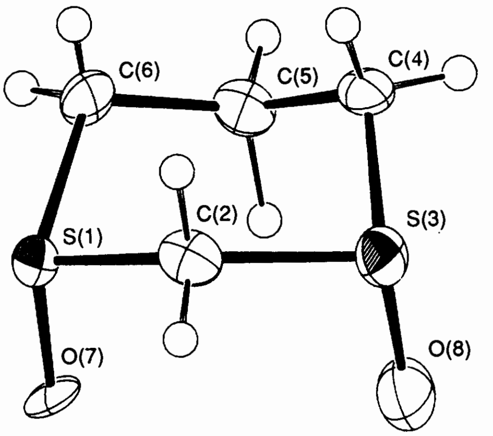

Fig. 1. ORTEP[8] perspective drawing of **1** showing atom labels. Ellipsoids are of 50% probability.

Further information was obtained from ^{13}C NMR spectroscopy. An axial oxygen substituent on the sulphur in the chair conformation is known to exert a shielding effect on the β-carbons as compared with an equatorial sulphinyl oxygen atom (S–O).[1b,4] This 'γ-*gauche* effect'[5] is clearly recognized in the chemical shifts we observed at room temperature for C-5 in the dioxides **1** and **2** and in the monoxide **3**: δ 7.9, 16.6 and 28.5, respectively. Thus, the unusually high shielding of this carbon in the *cis*-isomer might be suggestive, but not definitive for the diaxial conformation **1a**.

The conformation of the isomeric sulphoxides in the solid state has been determined by X-ray structure analysis which also allowed a study of the geometrical changes in the dithiane ring with the mutual disposition of the S–O bonds in the two isomers. Good single crystals were easily obtained from the *trans*-isomer, but much work was needed in order to obtain a few crystals suitable for X-ray from the *cis*-isomer.

Both isomers, as depicted in Figs. 1 and 2, adopted the more stable chair conformation. Final fractional co-ordinates are

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† *Present address:* Dokuz Eylul University, Faculty of Engineering and Architecture, Department of Environmental Engineering, Bornova, Izmir, Turkey.

‡ By using this method the *cis*-isomer had a m.p. 25 °C higher than the reported value.[1c]

§ We are more grateful to one of the referees for drawing our attention to this recent publication relevant to our work.

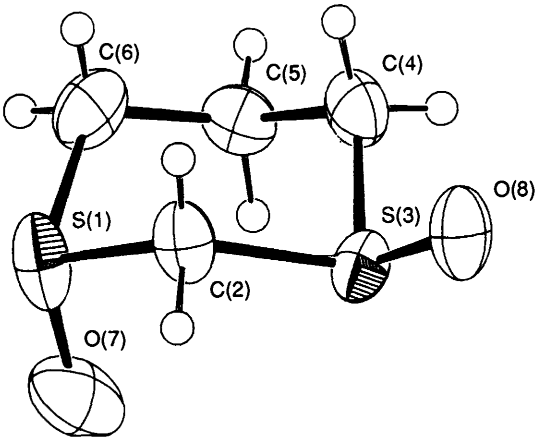

Fig. 2. ORTEP[8] perspective drawing of **2** showing atom labels. Ellipsoids are of 50% probability.

Table 1. Final fractional co-ordinates ($\times 10^4$) for **1**. Esds are in parentheses.

Atom	*x*	*y*	*z*
S(1)	4258(2)	−2821(3)	2175(4)
C(2)	3390(10)	−628(15)	3402(19)
S(3)	1677(2)	−180(3)	2221(5)
C(4)	902(10)	−2581(15)	3183(20)
C(5)	1589(9)	−4363(15)	1866(20)
C(6)	2978(10)	−4721(15)	3083(25)
O(7)	4302(6)	−2800(10)	−927(11)
O(8)	1669(7)	−108(11)	−926(14)

Table 2. Final fractional co-ordinates ($\times 10^4$) for **2**. Esds are in parentheses.

Atom	*x*	*y*	*z*
S(1)	4224(2)	181(2)	2086(2)
C(2)	3389(7)	−1248(7)	3296(9)
S(3)	2075(2)	−376(2)	4378(2)
C(4)	938(6)	146(8)	2519(9)
C(5)	1587(6)	1376(7)	1444(8)
C(6)	2746(7)	703(8)	626(8)
O(7)	4543(4)	1615(5)	3207(6)
O(8)	1440(4)	−1764(5)	5165(6)

Table 3. Selected bond lengths/Å and angles/° for **1**.

S(1)–C(2)	1.80(1)	S(3)–C(4)	1.81(1)
S(1)–C(6)	1.82(1)	S(3)–O(8)	1.509(7)
S(1)–O(7)	1.487(5)	C(4)–C(5)	1.51(1)
C(2)–S(3)	1.817(9)	C(5)–C(6)	1.52(1)
C(2)–S(1)–C(6)	98.4(4)	C(2)–S(3)–O(8)	109.0(4)
C(2)–S(1)–O(7)	108.4(4)	C(4)–S(3)–O(8)	107.3(4)
C(6)–S(1)–O(7)	106.2(4)	S(3)–C(4)–C(5)	113.2(6)
S(1)–O(2)–S(3)	120.2(5)	C(4)–C(5)–C(6)	113.5(8)
C(2)–S(3)–C(4)	97.9(4)	S(1)–C(6)–C(5)	113.8(7)

Table 4. Selected bond lengths/Å and angles/° for **2**.

S(1)–C(2)	1.804(6)	S(3)–C(4)	1.794(6)
S(1)–C(6)	1.794(6)	S(3)–O(8)	1.498(4)
S(1)–O(7)	1.511(4)	C(4)–C(5)	1.534(9)
C(2)–S(3)	1.799(7)	C(5)–C(6)	1.495(9)
C(2)–S(1)–C(6)	97.4(3)	C(2)–S(3)–O(8)	104.4(2)
C(2)–S(1)–O(7)	106.5(2)	C(4)–S(3)–O(8)	107.0(2)
C(6)–S(1)–O(7)	106.2(3)	S(3)–C(4)–C(5)	111.8(4)
S(1)–C(2)–S(3)	113.0(3)	C(4)–C(5)–C(6)	112.7(5)
C(2)–S(3)–C(4)	96.1(3)	S(1)–C(6)–C(5)	113.7(4)

Table 5. Selected torsion angles/° for **1** and **2**.

	1	**2**
S(1)–C(2)–S(3)–C(4)	54.3	65.9
C(2)–S(3)–C(4)–C(5)	−56.7	−63.6
S(3)–C(4)–C(5)–C(6)	71.4	69.6
C(4)–C(5)–C(6)–S(1)	−70.2	−67.2
C(5)–C(6)–S(1)–C(2)	54.8	59.6
C(6)–S(1)–C(2)–S(3)	−53.4	−63.7

presented in Tables 1 and 2 and important bond lengths and angles are shown in Tables 3 and 4.* The most interesting finding was the *syn*-diaxial conformation **1a** in the *cis*-isomer with remarkable distortion in the dithiane ring. This conformation introduces a local crowded environment on the ring due to the repulsive interactions between the polarized S–O bonds. The strain is relieved by an elongated S(1) ••• S(3) distance of 3.140 Å across the ring as compared with the normal value of 3.005 Å in the unstrained *trans*-isomer **2**. Also, the bond angle S(1)–C(2)–S(3) is more opened in the *cis* than in the *trans* isomer, the angles being 120.2° and 113.0° respectively. The ring in the *cis* isomer is more flattened in the crowded region as indicated by the smaller absolute torsion angles around the bonds S(1)–C(6), S(1)–C(2), C(2)–S(3) and S(3)–C(4) (see Table 5). The overall geometry of the unstrained *trans*-isomer **2** is similar to that found in a number of substituted 1,3-dithiane-1,3-dioxides[1b,g,h] none of them having the *syn*-diaxially disposed S–O bonds.

It is important to note the similarity between our *cis*-isomer **1** and 2,2-diphenyl-1,3-dithiane *cis*-1,3-dioxide, the structure of which has been determined earlier by Bryan *et al.*[6] This highly strained molecule was found to be diaxial in the crystal with an elongated S(1) ••• S(3) distance of 3.171 Å and also exhibited a high shielding (δ 9.37) of C-5 in the ^{13}C NMR spectrum. On the other hand, in the 2-phenyl-1,3-dithiane *trans*-1,*trans*-3-dioxide (having also a *syn* alignment of the S–O groups), C-5 was significantly less shielded (δ 13.8) and in the crystal, the molecule showed the diequatorial dioxide conformation.[1g]

In spite of these and some other supporting examples,[4c] it would, however, be mistaken to decide about the conformational preferences of 1,3-dithiane-1,3-dioxides in solution simply by comparing their conformation in the crystal and the chemical shift values of C-5 in their ^{13}C NMR spectra measured at room temperature. The ultimate decision between the *e,e* or *a,a* conformations **1e** or **1a** in solution is theoretically possible both by ^{1}H and ^{13}C NMR studies at low temperature. Although solubility problems prevented us from performing these measurements, the recent observation[3] regarding the solubility of the *trans*-isomer in mixtures of pyridine and THF might be helpful in future studies.

The possible influence of the oxidizing agent on the *cis*, *trans*

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* Complete listings of bond lengths and bond angles, hydrogen atom co-ordinates and displacement parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details, see 'Instructions for Authors' (1990), *J. Chem. Soc., Perkin Trans. 2*, in the January issue. Lists of structure factor tables are available on request from the authors.

ratio of the dioxides was investigated by using *m*-chloroperbenzoic acid, sodium metaperiodate and ozone. Examination of the ^1H NMR spectrum of the crude product (before chromatography) by area measurement of the $C(2)H_2$ signal at δ 4.58 (AB system) *versus* δ 4.78 (singlet) showed the preferential formation of the *trans*-isomer (65–75%) with all three oxidizing agents. Aggarwal, in his communication, reports that detailed studies of the oxidation of dithiane with sodium metaperiodate led to a selectivity of 95:5 in favour of the *trans*-isomer (details will be published elsewhere).[3] Different reaction conditions (solvent, temperature, etc.) might be responsible for the discrepancy in the *cis*, *trans* ratios observed by us and those reported by Aggarwal. After our aim of separating the pure isomers had been achieved, no further attempt was made either to improve stereoselectivity or change the isomer ratio.

Experimental

M.p.s were measured in sealed capillaries and are uncorrected. IR spectra were recorded with a Perkin-Elmer Infracord spectrophotometer. ^1H NMR spectra were taken on a Varian T-60 spectrometer for solutions in trifluoroacetic acid, with tetramethylsilane as internal reference. ^{13}C NMR spectra were measured in the Fourier transform mode at 25.2 MHz on Varian XL-100 spectrometer.

Oxidation of 1,3-*Dithiane with* m-*Chloroperbenzoic Acid.*—A solution of *m*-chloroperbenzoic acid (85%; 20.3 g, 0.10 mol) in chloroform (300 cm^3) was added dropwise during *ca.* 1 h to a stirred solution of 1,3-dithiane (6.0 g, 0.05 mol) in chloroform (400 cm^3), keeping the temperature at 0–5 °C. Stirring was continued for 15 min at the same temperature, then dry ammonia was bubbled through the solution for 2 h at 0 °C. The precipitate which formed was removed by filtration and the solvent was evaporated to yield a white solid (6.78 g), m.p. 150–156 °C. TLC on silica with chloroform–methanol (6:1) showed two major and one minor spots.

An aliquot (4.0 g) of the mixture was column chromatographed on silica gel (Woelm, deactivated with 10% water; 440 g). Elution with chloroform–methanol (40:1) gave small amounts (75 mg) of a solid, m.p. 202–204 °C, with IR absorption bands typical of a sulphone; this was not investigated further. Further elution afforded a mixture (610 mg) of the sulphone and the *trans*-dioxide **2** followed by 1,3-*dithiane* trans-1,3-*dioxide* **2** itself (800 mg), m.p. 182–183 °C (from absolute EtOH) (Found: C, 31.7; H, 5.30; S, 42.2. $C_4H_8O_2S_2$ requires C, 31.55; H, 5.29; S, 42.12); ν_{max}(KBr) 1000, 1020 and 1030 cm^{-1}; δ_H 2.90 (2 H, m), 3.50 (4 H, m), and 4.78 (2 H, s); $\delta_C(H_2O)$ 16.6 (C-5), 48.3 (C-4, 6) and 61.7 (C-2).

Elution was then continued with chloroform–methanol (40:2) to yield a mixture (740 mg) of the *trans*- and *cis*-dioxides followed by a fraction of 1,3-dithiane-*cis*-1,3-dioxide **1** (980 mg), m.p. 239–240 °C (from absolute MeOH) (lit.,[1c] 215–216 °C) (Found: C, 31.6; H, 5.3; S, 41.9. Calc. for $C_4H_8O_2S_2$: C, 31.55; H, 5.3; S, 42.1); ν_{max}(KBr) 1000, 1025 and 1035 cm^{-1}; δ_H 2.25 (1 H, m), 3.46 (5 H, m), and 4.58 (2 H, AB, *J* 13.0 Hz); $\delta_C(H_2O)$ 7.9 (C-5), 46.6 (C-4, 6) and 56.8 (C-2).

In the crude reaction mixture (before the chromatography) the *cis*-and *trans*-dioxides were present in the ratio (NMR spectroscopy) of 35:65, respectively.

Oxidation of 1,3-*Dithiane with Sodium Metaperiodate.*—A solution of sodium metaperiodate (7.1 g, 0.03 mol) in water (52 cm^3) was added dropwise over 1 h to a stirred solution of dithiane (2.0 g, 0.017 mol) in methanol (250 cm^3) at 20 °C. After being stirred for an additional hour at room temperature, the reaction was filtered and evaporated to give a product (5.40 g) contaminated with inorganic materials. Continuous extraction of an aliquot (2.84 g) of this product with chloroform for 5 days and evaporation of the solvent gave the mixture (0.86 g; m.p. 168–172 °C) of the *cis*- and *trans*-dioxides **1** and **2** in the ratio (NMR spectroscopy) 30:70, respectively.

Oxidation of 1,3-*Dithiane with Ozone.*—Ozone was bubbled into a stirred solution of 1,3-dithiane (1.20 g, 0.01 mol) in methylene dichloride (130 cm^3) at −40 °C. The reaction was monitored by TLC (silica; $CHCl_3$–MeOH, 6:1) and was complete in 40 min. The mixture was allowed to warm to room temperature, the solvent was evaporated under reduced pressure and the oily product (1.40 g) was dissolved in $CHCl_3$–MeOH, 10:1 and filtered through a dry deactivated silica gel column. Evaporation of the solvent gave a solid residue (0.98 g; m.p. 173–175 °C) which consisted of the dioxides **1** and **2** in the ratio (NMR spectroscopy) of 25:75, respectively.

Crystal Structure Determinations

Crystal Data for **1**.—$C_4H_8S_2O_2$, M_r = 152.2, triclinic, a = 9.861(3), b = 6.650(2), c = 4.790(2) Å, α = 91.16(5), β = 89.99(5), γ = 91.91(5)°, V = 313.9 Å^3 (from 2θ values of 25 reflections $6.1 \leqslant 2\theta \leqslant 17.6°$), Z = 2, D_c = 1.611 g cm^{-3}, $F(000)$ = 160, μ(Mo-Kα) = 0.69 mm^{-1}, λ = 0.7107 Å, space group $P\bar{1}$, T = 20 °C.

Data collection and processing. Philips PW 1100/20 four-circle diffractometer: graphite monochromatized Mo-Kα radiation, ω/2θ scan mode, 2θ max 50°, index ranges h −11 to 11, k −7 to 7, l 0 to 5, scan speed 1° ω min^{-1}, scan width 1.2° ω, no significant variations observed for three standard reflections, no absorption corrections; 1097 reflections measured, 1072 unique, 820 with $F_0 \geqslant 3\sigma(F_0)$ [$\sigma(F_0)$ from counting statistics only].

Structure solution and refinement. Direct methods,[7] full-matrix refinement on *F*, weighting scheme $w = 2.626/[\sigma^2(F_0) + 0.0008F_0{}^2]$, R = 0.079, wR = 0.077, 105 parameters, max shift/esd 0.1, final difference electron density within ±0.7 e Å^{-3}.

Crystal Data for **2**.—$C_4H_8S_2O_2$, M_r = 152.2, monoclinic, a = 9.802(3), b = 8.399(3), c = 8.007(3) Å, β = 97.46(5)°, V = 313.9 Å^3 (from 2θ values of 25 reflections $6.8 \leqslant 2\theta \leqslant 20.6°$), Z = 4, D_c = 1.547 g cm^{-3}, $F(000)$ = 320, μ(Mo-Kα) = 0.69 mm^{-1}, λ = 0.7107 Å, space group $P2_1/c$, T = 20 °C.

Data collection and processing. Philips PW1100/20 four-circle diffractometer, graphite monochromatized Mo-Kα radiation, ω/2θ scan mode, 2θ max 50°, index ranges h −11 to 11, k 0 to 9, l 0 to 9, scan speed 1.5° ω min^{-1} scan width 1.2° ω, no significant variations observed for three standard reflections, no absorption corrections; 1318 reflections measured, 1112 unique, 797 with $F_0 \geqslant 3\sigma(F_0)$ [$\sigma(F_0)$ from counting statistics only].

Structure solution and refinement. Direct methods,[7] full-matrix refinement on *F*, weighting scheme $w = 2.045/[\sigma^2(F_0) + 0.0009F_0{}^2]$, R = 0.057, wR = 0.056, 105 parameters, max shift/esd 0.4 final difference election density ±0.4 e Å^{-3}.

Acknowledgements

The authors thank Professor Dr. W. V. Philipsborn of the University of Zürich, Switzerland, for recording and help with interpretation of the ^{13}C NMR spectra. We are also grateful to Professor F. A. Carey of the University of Virginia, USA for some unpublished ^{13}C NMR data on substituted 1,3-dithiane oxides.

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Paper 0/02344B
Received 25th *May* 1990
Accepted 1st *August* 1990