Studies on the Oxidation of 1,3-Dithiane and 5,5-Disubstituted Analogues Including X-Ray Crystal Structure, Equilibration Studies and pK_a Measurements on Selected Oxides

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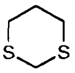
Oxidation of 1,3-dithiane has been carried out using eight different oxidants under several different reaction conditions. The most favourable conditions for obtaining the required *trans*-1,3-dithiane 1,3-dioxide were to use either MCPBA in Et_2O or $NaIO_4$ in $MeOH-H_2O$. Other 5,5-disubstituted-1,3-dithianes were also prepared and subjected to similar oxidations. For these compounds the best oxidant for obtaining the *trans*-dioxides was O_3. A rationalisation for the stereochemical outcome of the oxidations is presented and requires that *trans*-1,3-dithiane 1,3-dioxide is more stable than *cis*-1,3-dithiane 1,3-dioxide. This is borne out by equilibration studies of the two diastereoisomeric sulfoxides using N_2O_4. A rationalisation for the greater stability of the *trans* compared to the *cis* isomer is also presented and fits with the pK_a values and melting points of the two compounds.

Metallated 1,3-dithianes are very useful, practical, acyl anion equivalents.[1] In some of the higher oxidation states of 1,3-dithiane **2–6** such compounds as **2**,[2] **3** and **5** can act as potential chiral acyl anions. Of these, structure **3** possesses C_2 symmetry and this feature has additional advantages in asymmetric synthesis. In reactions of metallated-**3** with trigonal electrophiles only one new stereocentre will be generated and this greatly simplifies analysis and separation. In addition, higher selectivity is often found in reactions of C_2 symmetric compounds, presumably due to the reduced number of competing transition states.[3] Indeed, we have previously shown that Na-**3** reacts with very high diastereoselectivity (20–25:1) with aromatic aldehydes.[4] One of the challenges in the preparation of **3** from 1,3-dithiane was to limit the extent of oxidation to the sulfoxide oxidation level and to control the relative stereochemistry of the product to favour the (±) structure **3** over the *meso* isomer **4**. The only previous reports on the oxidation of 1,3-dithiane have been by Carey[5] and more recently by Bien.[6] Carey isolated the *cis* dioxide from oxidation of 1,3-dithiane using *m*-chloroperbenzoic acid) (MCPBA) but did not report the ratio of products obtained[5] whilst Bien used MCPBA, $NaIO_4$ and O_3 and his results are discussed alongside ours.[6]



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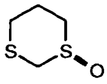

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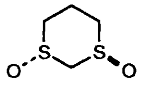

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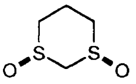

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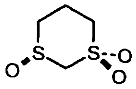

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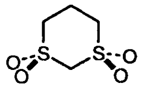

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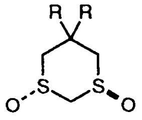
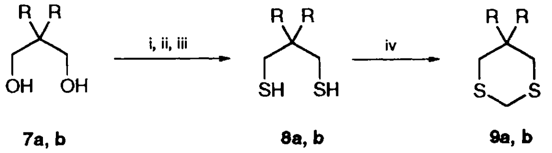
5,5-Disubstituted analogues of **3** can similarly act as chiral acyl anions and may have beneficial physical properties. However, such compounds suffer from the same preparative challenges confronted in the preparation of *trans*-1,3-dithiane 1,3-dioxide itself. In this paper we describe, in full, the stereoselective syntheses of the *trans* dioxides **3**, **3a** and **b** and discuss some of the surprising physical properties of such compounds.



3a R = Me
3b R = Et

Results

The substituted six-membered ring cyclic sulfides were prepared as shown in Scheme 1.The starting diols **7a**, **b** were converted into the dithiols[7] **8a**, **b**, using the procedure described by Eliel, and subsequently converted into the corresponding 1,3-dithianes **9a**, **b** using BF_3·OEt_2.[8] Unsubstituted 1,3-dithiane was obtained commercially.



Scheme 1 *Reagents:* i, MsCl, py; ii, Na_2S, S, DMF; iii, $LiAlH_4$, Et_2O; iv, $(MeO)_2CH_2$, BF_3·OEt_2

The results from the oxidation[9] of 1,3-dithiane and the corresponding 5,5-disubstituted analogues with various oxidising reagents are summarised in Tables 1 and 2, respectively. The most extensive studies in this oxidation were carried out on the parent 1,3-dithiane itself and several points are worthy of note. Oxidation of 1,3-dithiane to the monoxide **2** occurred rapidly but subsequent oxidation of the second sulfide to the bis oxide **3**/**4** was much slower. In fact, if reactions were conducted using only 2 equiv. of oxidant, monoxide was invariably left over at the end of the reaction, together with sulfone–sulfoxide and the desired bis oxide, but if reactions were allowed to proceed to complete consumption of the monoxide (using an excess of oxidant) a significant amount of over oxidation to the sulfone–

Table 1 Oxidation of 1,3-dithiane

Entry	Oxidant	Solvent	Temp	Ratio of products 2	3	4	5
1	$Bu_4N^+IO_4^-$	CH_2Cl_2	room temp.	100	0	0	0
2	$KHSO_5$	acetone–H_2O	room temp.	0	66	34	0
3	$NaBO_3$	$MeCO_2H$	55 °C	20	49	31	0
4	$NaBO_3$	MeOH–H_2O	room temp.	49	39	27	20
5	O_3	MeOH	−40 °C	*a*	57	43	*a*
6[b]	O_3	CH_2Cl_2	−40 °C	*a*	75	25	*a*
7	H_2O_2	MeOH	room temp.	*a*	78	22	*a*
8	Bu^tOCl	*c*	*c*	—	—	—	—
9	N_2O_4	*c*	*c*	—	—	—	—
10	MCPBA	CH_2Cl_2	0 °C	0	33	52	15
11	MCPBA	Et_2O	0 °C	0	55	45	0
12[b]	MCPBA	$CHCl_3$	0–5 °C	*a*	65	35	*a*
13	$NaIO_4$	MeOH–H_2O	room temp.	6	74	14	6
14	$NaIO_4$	MeOH–H_2O	room temp.	0	82	8	10
15	$NaIO_4$	MeOH–H_2O	room temp.	0	71	Trace	29
16[b]	$NaIO_4$	MeOH–H_2O	20–65 °C	*a*	70	30	*a*

[a] Only *trans*:*cis* ratios determined. [b] Taken from Bien.[6] [c] A variety of solvents and reaction conditions were tried.

sulfoxide **5** occurred. In practise, reactions were carefully monitored by TLC and quenched when only faint spots representing the monoxide and sulfone–sulfoxide could be seen. This shows that the presence of the monoxide markedly retards the rate of oxidation of the second sulfide. No bis sulfone or sulfone–sulfide were obtained in any of the reactions.

In the oxidation of 1,3-dithiane, tetrabutylammonium periodate[10] was found to be a weak oxidant only giving the monoxide (entry 1) and neither Bu^tOCl[11] (entry 8) nor N_2O_4[12,13] (entry 9) gave isolable products. These results were particularly disappointing as previous work in the literature indicated that the latter two reagents gave sulfoxides with the highest ratios in favour of the thermodynamic isomer[14,15] (see later for why this is desirable in our case). All other oxidants ($NaBO_3$,[16] oxone,[17] H_2O_2) worked well but either MCPBA in Et_2O or $NaIO_4$ were the reagents of choice for formation of the *trans* dioxide **3**. The other reagents suffered either from lower ratios of *trans*:*cis* isomers or problematic separation of the products from the inorganic residues. Oxidation of 1,3-dithiane with MCPBA in Et_2O was a very clean reaction as the product dioxides **3** and **4** precipitated out of solution, completely preventing over oxidation. Simple filtration followed by flash chromatography* gave diastereoisomerically pure samples of the *cis* and *trans* dioxides. Conducting the same oxidation in CH_2Cl_2 was less clean, as some over oxidation occurred presumably because of incomplete precipitation of the dioxides, but a different ratio of **3**:**4** was obtained. Since the *trans* isomer **3** is very much more soluble than the *cis* isomer **4** it is expected that as the reaction proceeds the *trans* isomer will be oxidised preferentially to the sulfone-sulfoxide and the mixture will become enriched with the *cis* diastereoisomer. Oxidation of 1,3-dithiane using $NaIO_4$ gave a preponderance of the *trans* dioxide but different runs gave different ratios of *trans*:*cis* isomers. It was noted that higher ratios of *trans*:*cis* sulfoxides were accompanied by greater amounts of the sulfone–sulfoxide **5**. As both *cis* and *trans* sulfoxides **3** and **4** are completely soluble in MeOH–H_2O, the increased ratios of **3**:**4** with increasing levels of sulfone–sulfoxide **5** indicates that the *cis* diastereoisomer oxidises at a faster rate than the *trans* diastereoisomer. It is difficult to compare our results with those obtained by Bien since the reaction conditions used were quite different and the ratios of monoxide and sulfoxide–sulfone were not indicated. If limited or over oxidation occurred in his experiments this would give quite different ratios of *trans*:*cis* products due to the different solubilities and different rates of over oxidation of the two isomers.

Oxidations of 1,3-dithiane with all reagents always gave a preponderance of the *trans* diastereoisomer but in varying degrees of excess depending on the oxidant used. This was surprising in light of the fact that the spectrum of oxidants used includes those that work under reagent approach control, product development control and thermodynamic product control. Before discussing which oxidants fitted into which class we needed to determine which isomer, **3** or **4**, was the thermodynamic isomer and this is discussed in the following section.

In contrast to the oxidation of 1,3-dithiane, where all reagents gave a preponderance of the *trans* diastereoisomer, oxidation of 5,5-disubstituted 1,3-dithianes using the same reagents gave mainly the *cis* dioxides **4a**/**b**. Table 2 summarises the results for oxidation of 5,5-dimethyl-1,3-dithiane but both the dimethyl and diethyl analogues behaved similarly. Ozone, a small electrophilic oxidant, gave the highest ratio of the desired *trans* diastereoisomer **3a**/**b**.

Equilibration Studies.—Attempted equilibration[18] studies with HCl–dioxane[19] on the *trans* and *cis* dithiane dioxides **3** and **4** caused only decomposition. Attempted equilibration by heating resulted in no reaction at moderate temperature (150 °C) and only decomposition at higher temperatures (refluxing decalin 191 °C). However, equilibration did occur with N_2O_4[20] (Scheme 2) and the results obtained are shown in Table 3. It should be noted that N_2O_4 forms a 1:1 addition complex with sulfoxides and so equilibration studies with N_2O_4 can only give thermodynamic ratios of the sulfoxide–N_2O_4 complex.[13] However, the results obtained using N_2O_4 are often closely related to thermodynamic ratios obtained by other means.[13] A further complication in the analysis of these results was the observation of slow formation of the sulfoxide–sulfone **5**, possibly *via* disproportionation of the bis sulfoxide to the sulfide–sulfone[12] followed by oxidation. Nevertheless, the results obtained show that the *trans* dioxide **5** is thermodynamically more stable than the *cis* isomer **4**. This finding was corroborated using molecular mechanics calculated[21] and the

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* We initially encountered problems in the separation of the *cis* and *trans* dioxides by flash chromatography (Bien also reported similar difficulties[6]). However, Merck silica gel gives very much better separation than Spherisorb silica gel.

Table 2 Oxidation of 5,5-dimethyl-1,3-dithiane[a]

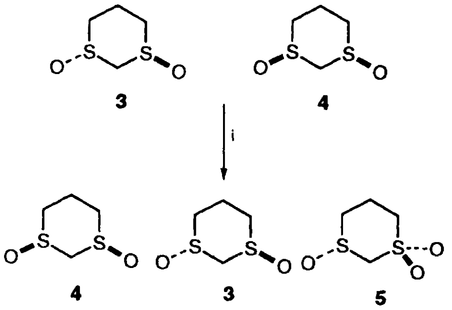
Entry	Oxidant	Solvent	Temp.	Ratio of products[b] 3a	4a
1	O_3	MeOH	−40 °C	58	42
2	H_2O_2	CH_2Cl_2	0 °C–room temp.	27	73
3	Bu^tOCl	*c*	*c*	0	0
4	MCPBA	CH_2Cl_2	0 °C	23	77
5	$NaIO_4$	MeOH-H_2O	room temp.	20	80

[a] Oxidation of 5,5-diethyl-1,3-dithiane gave similar results. [b] Only *trans*:*cis* ratios determined. [c] A variety of solvents and reaction conditions were tried but without success.

Table 3 Equilibration studies on 1,3-dithiane-1,3-dioxides using N_2O_4

t/h	3	4	5
0	100	0	0
0.58	86	12	2
9	84	12	4
72	74	8	18
0	0	100	0
0.58	5	87	8
9	56	34	10
18	59	23	18
72	19	0	81

trans sulfoxide was 0.8 kcal mol^{-1} more stable than the *cis* isomer.



Scheme 2 *Reagents and conditions:* i, N_2O_4, 0 °C

Discussion

The generally accepted mechanism for the oxidation by peroxy reagents (Table 1; entries 2–4, 7 and 10–12) involves nucleophilic attack by sulfur on an electrophilic oxygen atom and the stereochemical outcome of such oxidations is governed by reagent approach control.[15] In analysing the stereochemical outcome of the oxidation one needs to consider the two conformers of the monoxide $\mathbf{2}_{ax}$ and $\mathbf{2}_{eq}$. These conformers are in rapid equilibrium (Fig. 1) and even though conformer $\mathbf{2}_{eq}$ is favoured,[22–24] both conformers need to be considered because of the Curtin–Hammett principle.[25] Considering $\mathbf{2}_{ax}$, both lone pairs may be less reactive than the lone pairs of $\mathbf{2}_{eq}$: the axial lone pair suffers from incipient dipole repulsions with the axial sulfoxide and the equatorial lone pair may be involved in anomeric stabilisation reducing its nucleophilicity.[26,27] Considering $\mathbf{2}_{eq}$, again the equatorial lone pair may be involved in anomeric stabilisation reducing its nucleophilicity and this leaves the axial lone pair to attack the peroxy reagent. These factors may be responsible for the preferential formation of the *trans* isomer **3**.

The stereochemical outcome of periodate reactions is thought to be governed by product development control.[15] Such a scenario exists when the same factors that influence the stability of the product also operate in the transition state but not necessarily to the same degree. Periodate oxidation of 1,3-dithiane gave largely the *trans* dioxide and from equilibration studies with N_2O_4, this isomer was found to be thermodynamically more stable than the *cis* isomer. Our results are therefore in keeping with the literature.[15]

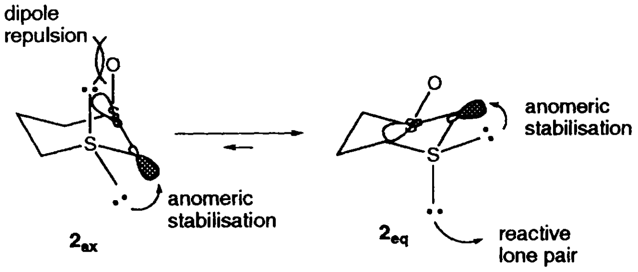


Fig. 1

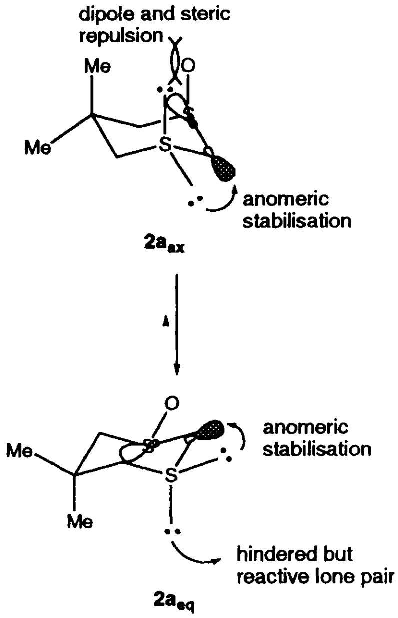
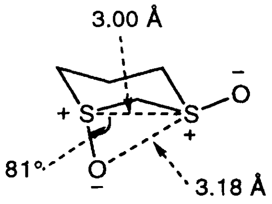


Fig. 2

Steric effects probably dominate the oxidation of 5,5-disubstituted 1,3-dithianes. There is likely to be an even greater preponderance of the $\mathbf{2a}_{eq}$ over the $\mathbf{2a}_{ax}$ conformer than in the non-substituted case and in this conformation the axial lone pair is particularly hindered and only the equatorial lone pair is accessible (Fig. 2). However, small highly electrophilic oxidants may not be as susceptible to steric hindrance and may allow attack of the hindered but more nucleophilic axial lone pair and this would give a preponderance of the *trans* isomer. Ozone is a small highly electrophilic oxidant and did give a preponderance of the *trans* isomer (Table 2; entry 1). These arguments account for the stereochemical outcomes observed.



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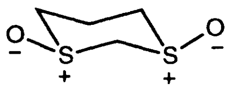

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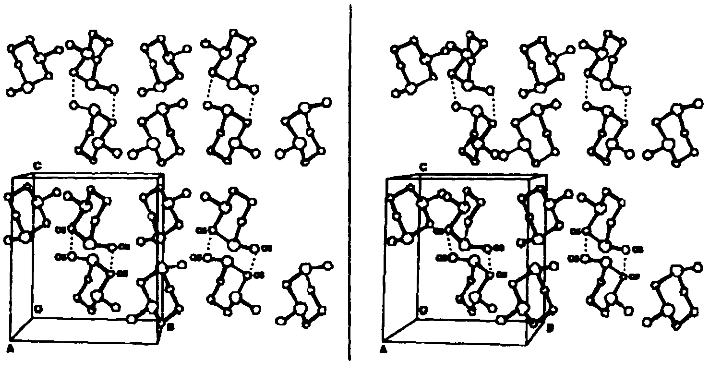

Fig. 3

X-Ray Structure.—The X-ray crystal structure of **3**[6,28] reveals a shorter than expected O(1)–S(2) distance (3.18 Å) and this suggests the possibility of favourable dipole–dipole interactions from the axial sulfoxide to the equatorial sulfoxide. Such interactions could account for the greater thermodynamic stability of compound **3** over the *cis* isomer **4**, in which no such dipole stabilisation is possible.

The X-ray structure also reveals intermolecular attractions (Fig. 3), not between the sulfoxide groups as might be expected, but rather between a sulfoxide group and one of the C-2 protons (conventional numbering of dithiane, but C-5 in Fig. 3). It is thus hydrogen bonding (involving C–H bonds) that is responsible for the high lattice energy, high melting point (170 °C) and poor solubility of **3**. If hydrogen bonding is also important in crystal packing of **4** then, as the C-2 protons of **4** are even more acidic than those of **3** (see below), a higher melting point (216 °C) and poorer solubility can be expected. This is exactly what is observed. It is highly unusual to observe H-bonding from C–H groups.

Acidity.—The pK_as of compounds **3** and **4** were determined to be 24.9 and 22.0 respectively.* The large difference between the two is probably a reflection of the reduced dipole moment of **3**, compared to **4**, as a result of the dipole stabilisation observed in the X-ray structure of **3**. Both of the C-2 protons of **3** underwent rapid deuterium exchange in D_2O with $t_{1/2}$ = 4 h at room temp. and neutral pH. The C-2 protons are evidently kinetically very labile even though they have relatively low thermodynamic acidity.

Conclusion

We have developed a practical synthesis of *trans*-1,3-dithiane 1,3-dioxide **3** and other C_2 symmetric analogues. The X-ray crystal structure shows (1) dipole stabilisation in the *trans* dioxide and (2) intramolecular H-bonds between sulfinyl oxygens and the C-2 protons. The former effect is manifested in a higher pK_a of the *trans* relative to the *cis* dioxide and the latter effect is manifested in a lower melting point of the *trans* relative to the *cis* isomer.

Experimental

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. Proton and ^{13}C NMR spectra were recorded on a Jeol 270 MHz or a Bruker 250 MHz instrument. All coupling constants are given in Hertz. Mass spectra were obtained on a Kratos MS 25 instrument operating in EI, CI mode and on a Kratos MS 80 in +ve FAB mode. Infrared spectra were recorded in the range 4000–600 cm^{-1} using a Perkin Elmer 157G Grating Infrared Spectrophotometer. Solvents and reagents were dried and purified prior to use according to standard procedures. Petrol refers to light petroleum, boiling range 60–80 °C. Diethyl ether (referred to as ether) was pre-dried over sodium wire and then refluxed over sodium benzophenone ketyl under a nitrogen atmosphere until anhydrous. Thin layer chromatography (TLC), used routinely to monitor the progress and purity of compounds, was performed on Merck DC-alufolien Kieselgel 60 F_{254} sheets containing fluorescent indicator. TLC plates were visualised when possible by wavelength of 356 nm ultraviolet light and by treatment with either a solution of phosphomolybdic acid (5 g in 100 cm^3 95% absolute ethanol) or 0.5% (*m*/*v*) aqueous solution of potassium permanganate, followed by warming of the TLC plate. Purification of compounds was achieved by medium pressure chromatography using Sorbsil C60 40/60H silical gel or Merck 40/60 silica gel.

2,2-Dimethylpropane-1,3-diol dimesylate,[29,7] 2,2-diethylpropane-1,3-diol dimesylate,[29] 2,2-dimethylpropane-1,3-dithiol[7] and 5,5-dimethyl-1,3-dithiane[30] are all known compounds but no literature data have been reported on them.

Purification of MCPBA.—A buffer solution was prepared by adding NaOH soln. (0.1 mol dm^{-3}; 136 cm^3) and KH_2PO_4 (0.2 mol dm^{-3}; 82 cm^3) to H_2O (112 cm^3). MCPBA (50–60% purity; 31.7 g, 91.9 mmol) was dissolved in diethyl ether (250 cm^3). The ether solution was washed four times with buffer, dried and filtered.

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* We thank Professor Bordwell for carrying out the pK_a measurements. These were measured in Me_2SO.

Oxidation of 1,3-*Dithiane*.—Oxidation of 1,3-dithiane using $NaIO_4$ has been previously described.[28] Dithiane (5.0 g, 41.7 mmol) was dissolved in dry ether (100 cm^3) and the solution cooled to −40 °C. To this was added the MCPBA solution prepared above, dropwise. Stirring was continued for 1 h at −40 °C, after which the precipitate was filtered off. The ^1H NMR spectrum of the precipitate indicated a mixture of *cis* and *trans* dithiane dioxide in a 1:1.27 ratio. Flash column chromatography on Merck silica gel using 5% EtOH–acetone as the eluent afforded *trans* dithiane dioxide **3** (3.31 g, 52.3%), m.p. 170–172 °C, lit.,[29] m.p. 170–171 °C. Continued elution of the column gave some of the *cis* dioxide **4** (2.44 g, 39%), m.p. 217–218 °C, lit[5] m.p. 215–216 °C.

2,2-*Dimethylpropane*-1,3-*diol Dimesylate*.—To a solution of methanesulfonyl chloride (21.99 g, 0.192 mol) in dry pyridine (50 cm^3) at 0 °C was added dropwise, over 5 min, a solution of 2,2-dimethylpropane-1,3-diol **7a** (10 g, 0.096 mol) in dry pyridine (30 cm^3). The mixture was allowed to warm slowly to room temperature and stirring was continued overnight. The reaction mixture was then poured onto a mixture of ice (250 g), water (50 cm^3) and conc. HCl (100 cm^3). The resulting mixture was extracted with dichloromethane (3 × 150 cm^3). The combined organic extracts were washed with 10% aq. HCl (2 × 100 cm^3), water (100 cm^3) and brine (100 cm^3), dried ($MgSO_4$) and evaporated to dryness to leave a pale yellow solid. This was recrystallised from ethyl acetate–light petroleum to yield white crystals 14.63 g, 59%), m.p. 67 °C; δ(270 MHz; $CDCl_3$) 1.07 (6 H, s), 3.05 (6 H, s) and 4.02 (4 H, s); ν_{max}/cm^{-1} 1440, 1340, 1160, 940 and 830.

2,2-*Diethylpropane*-1,3-*diol Dimesylate*.—By the same method as above the dimesylate was prepared from 2,2-diethylpropane-1,3-diol **7b** (10 g, 0.076 mol). The product was recrystallised from ethyl acetate to yield white crystals, (14.44 g, 69%), m.p. 93 °C; δ_H(270 MHz; $CDCl_3$) 0.89 (6 H, t, *J* 7.5), 1.39 (4 H, q, *J* 7.5), 3.05 (6 H, s) and 4.05 (4 H, s); ν_{max}/cm^{-1} 1450, 1340, 1170, 930 and 830.

2,2-*Dimethylpropane*-1,3-*dithiol* **8a**[7].—2,2-Dimethylpropane-1,3-diol dimesylate (10 g, 0.038 mol), sodium sulfide nonahydrate (9.23 g, 0.038 mol) and sulfur (1.23 g, 0.038 mol) were dissolved in dry *N*,*N*-dimethylformamide (DMF) (100 cm^3) and the solution stirred at 100 °C for 72 h. The reaction mixture was then poured onto a mixture of water (250 cm^3) and ice (100 g) and extracted into ether (3 × 100 cm^3). The aqueous layer was acidified by addition of conc. HCl and extracted with ether (2 × 50 cm^3). The combined organic extracts were washed with water (50 cm^3) and brine (50 cm^3), dried ($MgSO_4$) and evaporated to leave a yellow oil. This was then dissolved in dry ether (20 cm^3) and the solution added dropwise to a slurry of lithium aluminium hydride (1.44 g, 0.038 mol) in dry ether (40 cm^3), under nitrogen, over 10 min. Stirring was continued at room temperature for 3 h. The mixture was then cooled to 0 °C and water (10 cm^3, at 0 °C) was added to it cautiously, followed by an excess of 10% aqueous sulfuric acid. The mixture was extracted with ether (3 × 100 cm^3) and the combined organic extracts were washed with water (50 cm^3) and brine (50 cm^3), dried ($MgSO_4$) and evaporated to yield a pale yellow oil. This was distilled under reduced pressure (20 mmHg) using a Kugelrohr (150 °C) to leave a pale yellow oil (3.24 g, 63%); δ_H (270 MHz; $CDCl_3$) 1.00 (6 H, s), 1.21 (4 H, t, *J* 8.8) and 2.53 (2 H, d, *J* 8.8).

2,2-*Diethylpropane*-1,3-*dithiol* **8b**.—Compound **8b** was prepared in the same way as **8a** from 2,2-diethylpropane-1,3-diol dimesylate (10 g, 0.035 mol). Kugelrohr distillation (20 mmHg, 180 °C) gave a pale yellow oil (3.98 g 69%); δ_H(270 MHz; $CDCl_3$) 0.78 (6 H, t, *J* 7.5), 1.10 (2 H, t, *J* 8.6), 1.36 (4 H, q, *J* 7.5) and 2.52 (4 H, d, *J* 8.6).

5,5-*Dimethyl*-1,3-*dithiane* **9a**.—A solution of $BF_3{\cdot}OEt_2$ (1.32 cm^3) and glacial acetic acid (2.7 cm^3) in chloroform (5 cm^3) was stirred under nitrogen and refluxed. A solution of 2,2-dimethylpropane-1,3-dithiol **8a** (1.5 g, 0.011 mol) and methylal (dimethoxymethane) (0.73 g, 0.012 mol) in chloroform (15 cm^3) was then added dropwise over 15 min. The mixture was refluxed for a further 30 min. The mixture was then allowed to cool to room temp. when it was washed with water (20 cm^3), 10% aqueous potassium hydroxide (20 cm^3) and brine (20 cm^3), dried (K_2CO_3) and evaporated to yield a yellow oil (1.63 g, 100%); ν_{max}/cm^{-1} 1730, 1450, 1380, 1360, 1290, 1170, 750 and 710; δ_H(270 MHz; $CDCl_3$) 1.18 (6 H, s), 2.56 (4 H, s) and 3.63 (2 H, s); *m*/*z* 148 (100%, M^+) 101 (25), 87 (30), 69 (75), 56 (65) and 41 (40).

5,5-*Diethyl*-1,3-*dithiane* **9b**.—**9b** was prepared in the same way as **9a** from 2,2-diethyl-propane-1,3-dithiol (2.0 g, 0.012 mol) to give an oil (2.1 g, 100%), ν_{max}/cm^{-1} 1730, 1440, 1370, 1300, 1180, 1040, 980, 750, 710 and 710; δ_H(270 MHz; $CDCl_3$) 0.80 (6 H, t, *J* 7.5), 1.60 (4 H, q, *J* 7.5), 2.57 (4 H, s) and 3.64 (4 H, s); *m*/*z* 176 (80%, M^+), 97 (45), 69 (45), 55 (100) and 41 (40) (Found: M^+, 176.0673. $C_8H_{16}S_2$ requires *M*, 176.0692).

Oxidation of 5,5-*Dimethyl*-1,3-*dithiane*.—5,5-Dimethyl-1,3-dithiane, **9a** (0.91 g, 6.15 mmol) was dissolved in methanol (40 cm^3) and the solution cooled to −78 °C. Ozone was bubbled through the stirred solution for 6 h. The methanol was evaporated off and the residue purified by flash chromatography on silica gel eluting with 30% ether–acetone. Early fractions yielded 5,5-dimethyl-1,3-dithiane monosulfoxide as colourless crystals (0.29 g, 29%), m.p. 95–97 °C; ν_{max}/cm^{-1} 720 and 1025; δ_H(270 MHz; $CDCl_3$) 1.81 (3 H, s), 1.33 (3 H, s), 2.20 (1 H, ddd, *J* 14.1, 2.01, 1.46), 2.40 (1 H, d, *J* 12.1), 2.64 (1 H, d, *J* 14.1), 3.14 (1 H, ddd, *J* 12, 2.7, 2.0), 3.44 (1 H, d, *J* 12.3) and 4.02 (1 H, ddd, *J* 12.3, 2.7, 1.46); *m*/*z* 164 (60%, M^+) 134 (40) and 69 (100) (Found: M^+, 164.0322. $C_6H_{12}OS_2$ requires *M*, 164.0330). Later fractions yielded a mixture of the *cis* and *trans* bissulfoxides. The *trans* isomer was crystallised from acetone to yield colourless crystals **3a** (0.28 g, 25%), m.p. 148–150 °C, ν_{max}/cm^{-1} 1440, 1370 and 1010; δ_H(270 MHz; $[^2H_6]Me_2SO$) 1.24 (6 H, s), 2.95 (2 H, d, *J* 13.4), 3.02 (2 H, d, *J* 13.4) and 4.39 (2 H, s); *m*/*z* 180 (60%, M^+) 131 (100), 69 (50) (Found: M^+, 180.0258. $C_6H_{12}O_2S_2$ requires *M*, 180.0277).The mother liquor was evaporated, the residue dissolved in hot acetone–ether and the solution cooled to yield white crystals of the *cis* isomer **3b** (0.164 g, 15%), m.p. 168 °C; ν_{max}/cm^{-1} 1440, 1370 and 1015; δ_H(270 MHz; $[^2H_6]Me_2SO$) 1.00 (3 H, s), 1.15 (3 H, s), 2.90 (2 H, d, *J* 11.9), 3.27 (2 H, dd, *J* 11.9, 2.3), 3.98 (1 H, d, *J* 9.5) and 5.07 (1 H, dt, *J* 9.5, 2.3); *m*/*z* 180 (50%, M^+), 131 (100) and 69 (40) (Found: M^+, 180.0263. $C_6H_{12}O_2S_2$ requires *M*, 180.0277).

Oxidation of 5,5-*Diethyl*-1,3-*dithiane*.—5,5-Diethyl-1,3-dithiane, **12** (2.0 g, 0.011 mol) was dissolved in methanol (75 cm^3) and the solution cooled to −78 °C. Ozone was bubbled through the stirred solution for 5 h. The methanol was evaporated off and the product purified by flash chromatography on silica gel eluting with 30% ether–acetone. Early fractions yielded 5,5-diethyl-1,3-dithiane monosulfoxide as an oil (0.54 g, 25%); ν_{max}/cm^{-1} 1650, 1440, 1370, 1300, 1245 and 1020; δ_H(270 MHz; $CDCl_3$) 0.87 (6 H, q, *J* 7.2), 1.38–1.52 (2 H, m), 1.69–1.95 (2 H, m), 2.31 (2 H, d, *J* 12.6), 2.58 (1 H, d, *J* 14.3), 2.58 (1 H, d, *J* 14.3), 3.22 (1 H, d, *J* 12.6), 3.44 (1 H, d, *J* 12.3) and 4.02 (1 H, d, *J* 12.3); *m*/*z* 192 (30%, M^+) 175 (50), 97 (100), 84 (40) and 55 (95) (Found: M^+, 192.0640. $C_8H_{16}OS_2$ requires *M*, 192.0641). Later fractions yielded a mixture of *cis* and *trans* bissulfoxides. These were separated by flash chromatography on silica gel eluting with a gradient of 2–5% isopropyl alcohol–dichloromethane. Earlier fractions contained the *cis* bissulfoxide **3b** (0.44 g, 19%), m.p. 145–147 °C; ν_{max}/cm^{-1} 1440, 1370 and 1020; δ_H(270 MHz; CDCl$_3$) 0.95 (6 H, t, *J* 7.4), 1.40 (2 H, q, *J* 7.4), 1.57 (2 H, q, *J* 7.5), 2.66 (2 H, d, *J* 12.8), 3.35 (2 H, dd, *J* 12.8, 2.4), 3.63 (1 H, d, *J* 10.4) and 4.89 (1 H, dt, *J* 10.4, 2.4); *m/z* 208 (10%, M$^+$) 195 (25), 97 (75) and 55 (100) (Found: M$^+$, 208.0582. $C_8H_{16}O_2S_2$ requires *M*, 208.0590). Later fractions contained predominantly the *trans* bissulfoxide **3a**. Crystallisation from toluene–ether yielded white crystals (0.4 g, 16%), m.p. 122–123 °C; ν_{max}/cm^{-1} 1445, 1370 and 1030; δ_H(270 MHz; CDCl$_3$) 0.94 (6 H, t, *J* 7.3), 1.67 (4 H, q, *J* 7.5), 2.88 (2 H, d, *J* 13.9), 2.95 (2 H, d, *J* 13.9) and 4.07 (2 H, s); *m/z* 208 (25%, M$^+$) 159 (20), 97 (100) and 55 (90) (Found M$^+$, 208.0603. $C_8H_{16}O_2S_2$ requires *M*, 208.0590).

General Procedure For N_2O_4 *Equilibration Studies.*—All glassware was dried and flushed with nitrogen prior to use. Dinitrogen tetraoxide was passed through a drying tube packed with phosphorus/sand, condensed onto a solid CO$_2$ condenser cooled with CCl$_4$–CO$_2$ and dripped onto the dithiane dioxide at 0 °C. The solution was stirred for the described period of time, after which the N_2O_4 was evaporated with a stream of nitrogen. The resulting oil was subjected to a vaccum of 5 Torr for *ca.* 4 h. The residue was dissolved in [$^2H_6$]Me$_2$SO and its composition determined by NMR. For reaction times greater than 180 min, after 10 min the flask was stoppered and placed in a refrigerator at 4 °C. After the described period the flask was cooled in an ice bath and the N_2O_4 maintained at reflux using a heat gun. N_2O_4 was evaporated at ambient temperature.

General Procedure For Equilibration Studies By NMR.—Dry N_2O_4 was condensed into a two-necked flask at −78 °C, equipped with balloon and inlet, to yield a colourless solid which was melted as required. To the dithiane dioxide (10 mg), cooled in an ice bath, was added the deuteriated solvent (0.5 cm^3) followed by N_2O_4 (1.5 cm^3). The suspension was stirred at ambient temperature (1–2 min) to cause dissolution and then added to an NMR tube at −30 °C. The tube was sealed at this temperature and then brought to ambient temperature just before running the NMR spectrum. Both methods gave similar results.

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