Conformational Equilibria of Six-membered Ring Sulphoxides: the Effect of β-Electron-withdrawing Groups [1]

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^{1}H N.m.r. parameters are reported for various six-membered ring sulphoxides. Chemical shift and coupling constant data reveal that the oxides of thian-3-one and 3-dicyanomethylenethian adopt preferentially the axial S=O conformer. Introduction of a sulphur atom into these ring systems at the remaining position β to the sulphinyl group increases the amount of equatorial S=O conformer. Orbital–orbital interactions in these and related systems are considered.

EQUILIBRATION studies of 4-substituted thian 1-oxides [2] and a low temperature n.m.r. study of thian 1-oxide [3] (1) have shown that in these systems the sulphinyl S=O bond exhibits a preference for the axial site. Rationalisations of this preference have included a suggestion that attractive interactions between the bond and *syn*-axial protons are important [2a] and some tentative evidence in support of this view has been obtained.[4] More recently, Zefirov [5] suggested that the equatorial S=O conformer (1eq) may be destabilised by induced charge at H-4eq, whilst molecular mechanics calculations by Allinger's group [6] have focused attention on repulsions between the S=O bond and vicinal hydrogens.

Introduction of a heteroatom β to the sulphoxide function modifies the S=O bond preference.[7] Previously we showed that at equilibrium, *trans*-2-t-butyl-1,3-dithian 1-oxide predominates over the *cis*-isomer,[8] and n.m.r.[9] and dipole moment measurements [8,9] demonstrated that 1,3-dithian 1-oxide (2) and its 2,2-dimethyl analogue exist predominantly with the S=O bond equatorial. Low temperature n.m.r. measurements made by other groups quantified the result for (2),[10,11] and showed that 1,3,5-trithian 1-oxide (3) probably exists exclusively as the equatorial S=O conformer.[11] In contrast, however, 1,3-oxathian 3-oxide (4) shows no significant preference for either conformer at room temperature [12] and indeed exists predominantly as (4ax) at low temperature.[10,12]

In the present paper we turn our attention towards the sulphoxides (5)—(8) which, in contrast to (2)—(4), contain an electron deficient group at the β-position. The study also includes an examination of (9) and (10) in which the S=O bond experiences effects from

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[1] Preliminary communication, K. Bergesen, B. M. Carden, and M. J. Cook, *Tetrahedron Letters*, 1975, 4479.

[2] (*a*) C. R. Johnson and D. McCants, jun., *J. Amer. Chem. Soc.*, 1965, **87**, 1109; 1964, **86**, 2935; (*b*) J. C. Martin and J. J. Uebel, *ibid.*, p. 2936.

[3] J. B. Lambert and R. G. Keske, *J. Org. Chem.*, 1966, **31**, 3429; see also J. B. Lambert, D. S. Bailey, and C. E. Mixan, *ibid.*, 1972, **37**, 377.

[4] C. R. Johnson, H. Diefenbach, J. E. Keiser, and J. C. Sharp, *Tetrahedron*, 1969, **25**, 5649; N. L. Allinger, J. A. Hirsch, M. A. Miller, and I. J. Tyminski, *J. Amer. Chem. Soc.*, 1969, **91**, 337.

[5] N. S. Zefirov, *Tetrahedron Letters*, 1975, 1087.

[6] N. L. Allinger and J. Kao, *Tetrahedron*, 1976, **32**, 529.

[7] For a survey see M. J. Cook, *Kemia-Kemi*, 1976, **3**, 16.

[8] M. J. Cook and A. P. Tonge, *Tetrahedron Letters*, 1973, 849.

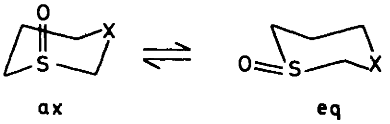
[9] M. J. Cook and A. P. Tonge, *J.C.S. Perkin II*, 1974, 767.

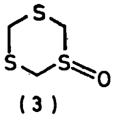
[10] L. Van Acker and M. Anteunis, *Tetrahedron Letters*, 1974, 225.

[11] S. A. Khan, J. B. Lambert, O. Hernandez, and F. A. Carey, *J. Amer. Chem. Soc.*, 1975, **97**, 1468.

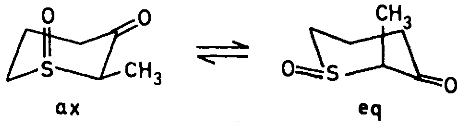
[12] K. Bergesen, M. J. Cook, and A. P. Tonge, *Org. Magnetic Resonance*, 1974, **6**, 127.

both a β-electron-withdrawing group and a β-sulphur atom.

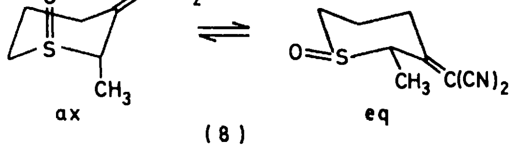



(3)

(1) X = CH$_2$
(2) X = S
(4) X = O
(5) X = C=O
(7) X = C=C(CN)$_2$



(6)

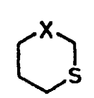


(8)

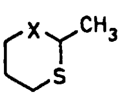
(9) X = C=O
(10) X = C=C(CN)$_2$

RESULTS

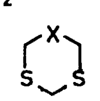
Preparation of Compounds.—Thian-3-one (11), 2-methylthian-3-one (12), and 1,3-dithian-5-one (13) were prepared by Dieckmann cyclisation of the appropriate diesters. Reaction with malononitrile afforded the dicyanomethylene



(11) X = C=O
(14) X = C=C(CN)$_2$



(12) X = C=O
(15) X = C=C(CN)$_2$



(13) X = C=O
(16) X = C=C(CN)$_2$

derivatives (14)—(16). Oxidation of (11)—(16) to the corresponding sulphoxides was achieved using either sodium metaperiodate or *m*-chloroperbenzoic acid. Compounds (6) and (8) were obtained as the major components of mixtures from which the minor component in each, presumed to be the other isomer, could not be isolated because of insufficient quantities. Attempts to obtain the *cis*-isomer of (8) by treating (6) with malononitrile merely yielded (8) itself.

^{1}H *N.m.r. Spectra and Conformational Analysis of Thian Derivatives*.—Spectra of (5)—(8), (12), and (15) in CDCl$_3$ and of (5) in pyridine were recorded at 220 MHz. All show signals characteristic of protons in predominantly equatorial and axial sites indicative of biased conformational equilibria. Attempts to obtain spectra of the sulphoxides at temperatures below coalescence were thwarted by solubility problems.

Assignments followed from the usual considerations of signal multiplicity and known shielding and deshielding effects of particular atoms or groups. Chemical shifts (Table 1) were refined by trial and error simulation experiments using the LAOCOON 3 program,[13] with iterative matching of experimental and calculated spectra in regions where lack of serious overlap rendered such an approach meaningful. Data for certain of the vicinal *trans* coupling constants, important for assessing conformational equilibria, were also obtained by this treatment (Table 2). Omissions in Table 2 indicate that the values were considered unreliable. Thus, spectra of (5) and (6) in CDCl$_3$ show the geminal protons H$_c$ and H$_d$ as deceptively simple absorptions and coupling constants involving these protons are difficult to evaluate with confidence; the same problem arises for H$_g$ and H$_h$ in the spectrum of (5) in pyridine. Partial signal overlap for non-geminal protons in the spectra of (7) and (8) increases uncertainties in one or two $^3J_{trans}$ values in these compounds. Errors quoted in Table 2 refer to the ranges of values which do not significantly affect the fit between the simulated and experimental spectra.

The 2-methyl group in the keto-sulphoxide (6), as well as in the parent sulphide (12), exists predominantly in the equatorial site as adjudged from the narrow lines of the quartet for the C-2 methine proton. The orientation of the S=O bond in the major conformer of (6) follows from the chemical shifts of H$_e$ and H$_f$. The deshielding of the former and shielding of the latter is characteristic of an axial S=O bond;[14,15] thus δ (H$_e$) − δ(H$_f$) = 0.48 p.p.m., compared with −0.17 p.p.m. in the parent sulphide (12). The small low frequency shift of H$_h$ and large high frequency shift of H$_g$ on oxidation of the sulphide is a further manifestation of an axial S=O bond.[15] Accordingly we assign the *cis*-configuration to (6).

The keto-sulphoxide (5) in CDCl$_3$ shows the protons of the CH$_2$CH$_2$CH$_2$ fragment absorbing at similar chemical shifts to those of (6) and we conclude that the predominant conformer of (5) is also the one having the S=O bond axial. Here δ (H$_e$) − δ (H$_f$) = 0.53 p.p.m., marginally larger than the value found for (6). In (6), the combination of the axial preference of the S=O bond [evident in (5)] with an equatorial 2-methyl group will render the system sufficiently highly biased for it to be considered a model for conformer (5ax).* Comparison of values for $^3J_{trans}$ in (5) and (6) shows that in the former, $J_{e.h}$ is smaller and $J_{f.g}$ larger which is consistent with the presence of small but significant amounts of conformer (5eq). Taking $J_{ax.ax}$ = 13.4 and $J_{eq.eq}$ = 3.7 Hz for

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* Interestingly, an attempt to epimerise (6) into the *trans*-isomer, in which at any time one functionality adopts its less stable orientation, produced an equilibrium mixture containing only 12% of material presumed to be the *trans*-isomer (for details see Experimental section and ref. 16).

[13] S. Castellano and A. A. Bothner-By, *J. Phys. Chem.*, 1964, **41**, 3863.

[14] K. W. Buck, A. B. Foster, W. D. Pardoe, M. H. Qadir, and J. M. Webber, *Chem. Comm.*, 1966, 759.

[15] R. Lett and A. Marquet, *Tetrahedron*, 1974, **30**, 3379.

[16] For details see B. M. Carden, Ph.D. thesis, University of East Anglia, 1977.

both (5ax) and (5eq), the equation $J_{obs.} = n\,J_{ax.ax} + (1 - n)$ indicates that in $CDCl_3$ (5) exists as (5ax) to the extent of $86 + 4\%$; $-\Delta G°_{293} = 3.7$—5.3 kJ mol^{-1}. In the spectrum of (5) in pyridine, from which reliable values for $J_{e.h}$ and $J_{f.g}$ were not obtained (see above), the band width at half-height for H_f is *ca.* 29 Hz. In $CDCl_3$ the value is 32 Hz whereas for (6) it is only 22.5 Hz from which we estimate that in pyridine the ratio of (5ax) to (5eq) is *ca.* 90 : 10.

TABLE 1

^1H Chemical shifts for thian and thian oxide derivatives at 220 MHz (20°)

Compound					Ring protons [a]							
No.	Y	a	b	Solvent	H_a	H_b	H_c	H_d	H_e	H_f	H_g	H_h
(5)	O	H	H	$CDCl_3$	3.64	3.69	2.59	2.59	2.85	2.32	3.14	3.01
				C_5H_5N	3.82	4.08	2.52	2.64	2.89	2.12	3.07	3.07
(6)	O	CH_3	H	$CDCl_3$	*b*	3.61	2.60	2.59	2.88	2.40	3.20	2.99
(12)	O	CH_3	H	$CDCl_3$	*c*	3.61	2.55	2.37	2.34	2.51	2.68	3.03
(7)	$C(CN)_2$	H	H	$CDCl_3$	4.22	3.66	3.12	2.58	2.75	2.34	3.12	2.88
(8)	$C(CN)_2$	H	CH_3	$CDCl_3$	4.46	*d*	3.00	2.66	2.71	2.30	2.98	2.91
(15)	$C(CN)_2$	H	CH_3	$CDCl_3$	3.96	*e*	2.93	2.54	2.14	2.49	2.49	3.11

[a] In p.p.m. downfield from tetramethylsilane as internal standard; H_a, H_c, H_f, and H_g give rise to signals for protons predominantly or exclusively equatorial; H_b, H_d, H_e, and H_h give signals for protons occupying predominantly or exclusively acid sites. [b] Me at δ 1.44. [c] Me at δ 1.25. [d] Me at δ 1.56. [e] Me at δ 1.67.

In the dicyanomethylene derivatives (8) and (15) the 2-methyl group, when equatorial, will suffer $A^{1,3}$ strain [17] with the cyano function. Indeed for both compounds the signal for the methine proton at C-2 is broadened by planar W coupling indicating that the methyl group is axial in the predominant conformer. This conclusion is confirmed by the characteristic deshielding of the *syn*-axial protons H_d and H_h and shielding of the equatorial protons H_c and H_g[18] *e.g.* δ (H_h) − δ (H_g) = 0.62 p.p.m. in (15) but only 0.35 in (12). These effects account partly for the main differences in the spectra of (8) and (7); in (8), δ (H_h) − δ (H_g) = −0.07 and δ (H_d) − δ (H_c) = −0.34 p.p.m. which contrast with values of −0.24 and −0.54 p.p.m. respectively in (7). Both compounds, however, show H_e absorbing at higher frequency than H_f, [δ (H_e) − δ (H_f) = 0.41 p.p.m. in each, *cf.* −0.35 p.p.m. in the sulphide (15)], demonstrating that in each the S=O bond is axial in the major conformer. Thus in (8) the configuration of the S=O and C–Me bonds is *trans*.

TABLE 2

trans Vicinal coupling constants for thian oxide derivatives at 220 MHz (20°)

Compound					Coupling constant (*J*/Hz) [a]			
No.	Y	a	b	Solvent	$J_{c.f}$	$J_{d.e}$	$J_{e.h}$	$J_{f.g}$
(5)	O	H	H	$CDCl_3$			12.2 ± 0.2	5.2 ± 0.2
				C_5H_5N	4.0 ± 0.4	12.8 ± 0.4		
(6)	O	CH_3	H	$CDCl_3$			13.4 ± 0.2	3.7 ± 0.2
(7)	$C(CN)_2$	H	H	$CDCl_3$	4.6 ± 0.3	12.2 ± 0.2	12.5 ± 0.3	
(8)	$C(CN)_2$	H	CH_3	$CDCl_3$	3.4 ± 0.2	13.1 ± 0.2		

[a] For identification of *J* values see key in Table 1.

We surmise that the sole formation of (8) from (6) involves epimerisation at C-2 of the initially formed *cis*-isomer of (8). Such isomerisation would relieve $A^{1,3}$ strain and accommodate a marked axial preference of the S=O bond in the presence of the β-dicyanomethylene function. Relief of a destabilising *gauche* S=O • • • C–Me interaction could be an additional factor.

As above, we believe the combination of two stabilising conformational features will cause (8) to adopt very predominantly, if not exclusively, the axial S=O conformer (8ax). Using (8) as a 'fixed model' providing limiting values for $J_{ax.ax}$ and $J_{eq.eq}$, data for $J_{d.e}$ and $J_{c.f}$ in (7) show that (7ax) is present to the extent of $89 + 4\%$; $-\Delta G°_{293}$ 4.2—6.9 kJ mol^{-1}.

^1H *N.m.r. Spectra and Conformational Analysis of Dithian Oxide Derivatives.*—The 100 MHz spectrum of (9) was obtained in $CDCl_3$ but that of (10), which is insufficiently soluble in this solvent, was run in deuterioacetone. As for the thian oxide derivatives low solubility precluded low temperature measurements. The spectra are simple in appearance showing three AB patterns in which some lines are split further by coupling through four bonds. Assignments (Table 3) were verified by deuterium exchange at C-4 and -6. For (7) this was achieved *via* base catalysed H–D exchange on the precursor (13), and for (8) by direct exchange using D_2O and one drop of pyridine in [$^2H_6$]acetone.[16] All parameters were refined using the LAOCOON 3 program treating the spectra as ABCDEF systems.

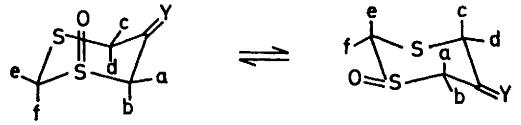
In the keto derivative (9) only one set of *cis*-protons experiences four bond coupling which shows that these are equatorial in the major conformer of a highly biased equilibrium. Here, of course, there are no β-CH_2 functions to assist assignment of S=O orientation. Furthermore an alternative criterion, *viz.* the chemical shift difference between axial and equatorial protons α to a sulphinyl group, is

[17] F. Johnson, *Chem. Rev.*, 1968, **68**, 375.

[18] D. Daneels and M. Anteunis, *Org. Magnetic Resonance*, 1974, **6**, 617.

TABLE 3

^{1}H N.m.r. parameters for 1,3-dithian oxide derivatives at 100 MHz (35°)



Parameter [a,b]	(9) in $CDCl_3$ (Y = O)	(10) in $(CD_3)_2CO$ [Y = $C(CN)_2$] [b,c]
δH_a	3.60	4.41
δH_b	4.15	4.09
δH_c	3.35	4.01
δH_d	3.15	3.73
δH_e	3.79	4.55
δH_f	4.17	4.02
$J_{a,b}$	−11.2	−12.0
$J_{c,d}$	−13.5	−13.0
$J_{e,f}$	−13.7	−13.1
$J_{a,c}$	0.0	0.9
$J_{b,d}$	1.5	1.0
$J_{c,e}$	0.0	0.9
$J_{d,f}$	1.6	0.9
$J_{a,e}$	0.0	0.8
$J_{b,f}$	1.7	1.0
$J_{a,d}$	0.0	−0.1
$J_{b,c}$	−0.1	−0.1
$J_{c,f}$	−0.1	0.0
$J_{d,e}$	0.0	−0.1
$J_{a,f}$	0.0	0.1
$J_{b,e}$	0.3	0.0

[a] Chemical shift δ in p.p.m. downfield from tetramethylsilane as internal standard. Coupling constant *J* in Hz. [b] For (10), the configuration of the S=O bond relative to the protons cannot be assigned (see text). Thus the assignment for geminal pairs of protons could equally well be reversed. [c] For (9), ABCDEF analysis: 107 lines matched to within ±0.26 Hz; root mean square error of fit 0.083. Calculated 'probable error' for each parameter <0.05 Hz. For (10), ABCDEF analysis: 170 lines matched to within ±0.16 Hz; root mean square error 0.068. 'Probable error' for each parameter <0.03 Hz. However the accuracy with which individual experimental lines could be measured limits reliability of *J* values to ±0.1 Hz.

now considered unreliable;[15] indeed in the present case the parameter δ (H_b) − δ (H_a) is particularly suspect because of local effects of the C=O bond. However, the composite term [δ (H_b) − δ (H_a)] − [δ (H_d) − δ (H_e)] should cancel these effects to a large extent, and indeed cancel those of any other function incorporated at the 5-position of the 1,3-dithian 1-oxide ring system. *trans*-2-t-Butyl-1,3-dithian 1-oxide [9] (in $CDCl_3$) and 1,3,5-trithian 1-oxide [11] (in $CHClF_2$), both of which have an equatorial S=O bond give values of 0.66 and 0.78 p.p.m. respectively, whereas *cis*-2-t-butyl-1,3-dithian 1-oxide [9] gives a value of −0.05 p.p.m. Accordingly we believe this parameter provides a useful probe for conformational assignments in 5-substituted 1,3-dithian 1-oxide derivatives; for (9), which gives a value of 0.75 p.p.m., we conclude the predominant conformer is (9eq). However, quantitative evaluation of the equilibrium constant from the data does not seem appropriate.

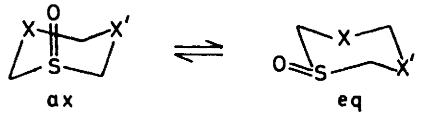
In contrast with (9) the dicyanomethylene sulphoxide (10) gives a spectrum which shows that both sets of *cis*-protons experience coupling through four bonds. One set of couplings is marginally larger than the other but the differences are small (Table 2) and clearly both conformers are populated approximately to the same extent. Because of this situation, and because chemical shifts may be affected by the solvent acetone, it is difficult to apply criteria for assigning the S=O bond configuration relative to the ring protons.

DISCUSSION

Conformational equilibrium data for six-membered ring sulphoxides having various atoms or groups at the β-position are collected in Table 4. Rigorous comparisons are not possible because of the different conditions of measurement. However, assuming that the $\Delta G°$ values for (1), (5), and (7) are dominated by ΔH rather than ΔS, it is evident at least on a qualitative basis that the replacement of a β-CH_2 unit by a C=O or a $C=C(CN)_2$ group enhances the axial S=O preference. Such a change in preference reflects the summed contributions of various conformational effects and these will be considered in turn. In terms of steric factors, replacement of CH_2 by an sp_2 carbon atom has long been considered to lead to a reduction in 1,3-steric repulsions. However this is an over simplification which has become particularly evident from Lambert and Clikeman's recent study of (17ax) ⇌ (17eq) where X = OH, OCD_3, SCH_3, *etc.*[19] The 'steric' effect of the system, where steric is used in the most general sense, apparently can either be attractive or repul-

TABLE 4

Conformational equilibrium data for selected cyclic sulphoxides



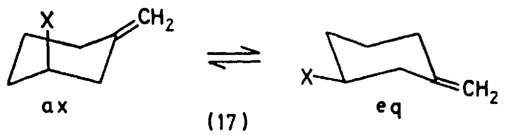
Compound							
No.	X	X′	Solvent	T/°C	% Conformer ax	$\Delta G°$ [a]/kJ mol^{-1}	Ref.
(1)	CH_2	CH_2	CH_2Cl_2	−90	62	−0.75	3
(2)	S	CH_2	$CHCl_2F$	−92	15.4	2.56	10
			$CHClF_2$	−81.5	16	2.64	11
(4)	O	CH_2	$CHCl_2F$	−98	83.5	−2.36	10
(5)	C=O	CH_2	$CDCl_3$	20	86 ± 4	−3.7 to −5.3	Present work
(7)	$C=C(CN)_2$	CH_2	$CDCl_3$	20	89 ± 4	−4.2 to −6.9	Present work
(3)	S	S	$CHClF_2$	−70° to ambient	*ca.* 0 [b]	Large	11
(9)	S	C=O	$CDCl_3$	35	Minor species		Present work
(10)	S	$C=C(CN)_2$	$(CD_3)_2CO$	35	*ca.* 50	*ca.* 0	Present work

[a] Negative value denotes axial conformer predominates. [b] Only one conformer present, presumed to be (3 eq).[11]

[19] J. B. Lambert, and R. R. Clikeman, *J. Amer. Chem. Soc.*, 1976, **98**, 4203; J. B. Lambert, R. R. Clikeman, and E. S. Magyar, *ibid.*, 1974, **96**, 2265.

sive depending on solvent. In CF_2Cl_2, substituents exhibit a larger equatorial preference than in the corresponding cyclohexyl derivative. On the other hand, in the more polar hydrogen bonding solvent $CHFCl_2$, the substituents exhibit smaller equatorial preferences than are found in the fully saturated ring analogues.[19] Data for (1), (5), and (7), all obtained in relatively polar hydrogen bonding solvents, clearly follow the latter trend. However, the analogy between series (17) and the sulphoxide derivatives is confused somewhat by the long C–S bond in thian derivatives, which may well reduce the importance of 1,3-steric interactions.

Dipole interactions between the sulphinyl function and the C=O and $C{=}C(CN)_2$ groups are predicted to favour the equatorial S=O conformer, but electrostatic factors could well favour the axial conformer. Recently Eliel *et al.*[20] postulated that electrostatic effects, involving ring oxygen atoms and a side chain sulphinyl sulphur atom, govern the axial preference of the 5-methylsulphinyl group on the 1,3-dioxan ring. Application of the principle of electrostatic interactions to the present systems suggests that in (5eq) and (7eq), effects are repulsive, but in (5ax) and (7ax) they are less so or are even attractive [see (18) and (19)].



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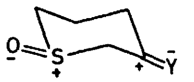
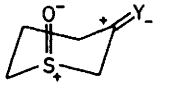


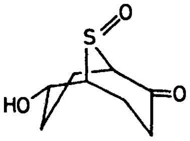
(18)



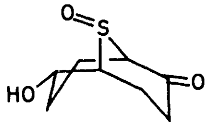
(19)

A remaining effect to be considered is an orbital–orbital interaction between the S=O group and the β π system. Of interest to the present study are u.v. data for compounds (20) and (21) [21] which indicate that electronic interactions in β-keto-sulphoxides depend upon the spatial relationship of the two chromophores. The u.v. spectrum of (20), in which the spatial arrangement of the S=O and C=O functions compares with that in (5ax), shows a more structured absorption pattern than that of (21) with bands absorbing at longer $\lambda_{max.}$ and higher extinction coefficient. The type of interaction is unclear, although charge transfer from the non-bonding electrons on sulphur is precluded from solvent shift studies. However, through space orbital overlap (22) of the type proposed by Zefirov [22,23] and referred to as the ' hockey sticks ' effect does not appear to be ruled out. In analogy with interactions described for certain substituted benzodioxans, type (22) overlap should be stabilising.[22,*] Such an effect, however, requires certain assumptions about the hybridisation of the sulphinyl oxygen atom.

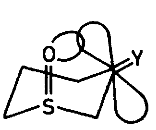
Data for the dithian 1-oxides (2), (9), and (10) when compared with those for (1), (5), and (7) show that introduction of a β-sulphur atom consistently increases the amount of equatorial S=O conformer present. For the simplest 1,3-dithian 1-oxide system, (2), we suggested earlier [8] that dipole–dipole interactions may contribute in some measure and lately this view has received support from calculations by Allinger's group.[6] Nevertheless it is disconcerting to find that 1,3-oxathian 3-oxide does not exhibit a similar equatorial preference. For these systems it is attractive to invoke a *n–d* overlap which is conformationally dependent and which favours the equatorial S=O conformer. On this basis the difference between the conformational behaviour of (2) and (4) can be ascribed to the greater degree of overlap in (2), arising from the more diffuse orbitals of the β-sulphur atom. Evidence in favour of *n–d* orbital overlap accrues from a photoelectron spectroscopic study of 1,3,5-trithian 1-oxide which strongly indicates charge transfer.[24] *X*-Ray data for (23) [25] and (24) [26] reveal short S · · · S internuclear distances and these may be a further manifestation of orbital–orbital interactions: it is likely, though, that electrostatic effects are also involved here. There is however an alternative model to *n–d* overlap, provided by the application of the ' hockey sticks ' effect hypothesis. By analogy with substituted 1,4-dioxans and 1,4-oxathians,[22] overlap of type (25) should destabilise the axial S=O conformer more so when $X = S$ than when $X = P$. As above, the argument depends upon assumptions regarding hybridisation.



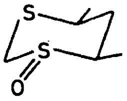
(20)



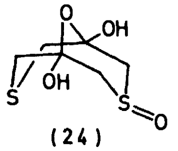
(21)



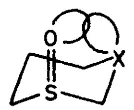
(22)



(23)



(24)



(25)

Orbital–orbital interactions probably also account largely for the position of the conformational equilib-

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* We thank Professor Zefirov for drawing our attention to the application of this effect to the present system.

[20] M. K. Kaloustian, N. Dennis, S. Mager, S. A. Evans, F. Alcudia, and E. L. Eliel, *J. Amer. Chem. Soc.*, 1976, **98**, 956; E. L. Eliel, D. Kandasamy, and R. C. Sechrest, *J. Org. Chem.*, 1977, **42**, 1533.

[21] C. Ganter and J.-F. Moser, *Helv. Chim. Acta*, 1971, **54**, 2228.

[22] N. S. Zefirov, V. S. Blagoveshchensky, I. V. Kazimirchik, and N. S. Surova, *Tetrahedron*, 1971, **27**, 3111.

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[25] A. T. McPhail, K. D. Onan, and J. Koskimies, *J.C.S. Perkin II*, 1976, 1004. Further *X*-ray data have been reported by F. A. Carey, P. M. Smith, R. J. Maher, and R. F. Bryan, *J. Org. Chem.*, 1977, **42**, 961.

[26] S. Abrahamsson and G. Rehnberg, *Acta Chem. Scand.*, 1972, **26**, 3309. For a discussion of the data see N. S. Zefirov, *Russ. Chem. Rev.*, 1975, **44**, 196.

brium of (9) and (10), but here the β π system will perturb the interaction. However the perturbation is difficult to assess, either in character or in degree, and it does not seem meaningful to speculate on it at the present time.

Conclusions.—A C=O or a $C=C(CN)_2$ group at the position β to a sulphoxide group enhances the axial preference of the S=O bond. In contrast, introduction of a β-sulphur atom increases the amount of equatorial S=O conformer. The conformational preference of the S=O bond is thus particularly susceptible to the atom or group at the β-position and the origins of this susceptibility lay beyond simple steric and dipolar effects. Orbital–orbital interactions may well be dominant factors in these systems. Before a definitive conclusion can be made, however, a systematic study of the role of solvent on these equilibria is necessary; such an investigation is planned for the future.

EXPERIMENTAL

I.r. spectra were recorded as liquid films or as mulls in Nujol as appropriate using a Perkin-Elmer 257 spectrometer. N.m.r. spectra measured at 100 MHz were obtained using a Varian Associates HA 100 spectrometer operating at 35°. Spectra were obtained at 250 Hz sweep width with calibrations at 10 Hz intervals. Spectra at 220 MHz (250 Hz sweep width, calibrations at 25 Hz intervals) were measured at 20° by the Physico-chemical Measurements Unit (PCMU), Harwell.

Computations were carried out by means of a local version of the LAOCOON 3 program using a UNIVAC 1110 computer. Graphical output was obtained from a Calcomp plotter.

Materials.—The following compounds were prepared using published routes: thian-3-one [27] (11), b.p. 60° at 2.2 mmHg (lit.,[27] 77—80° at 5 mmHg); 1,3-dithian-5-one [28] (13), m.p. 102—104° (lit.,[28] 103.5—104.5°); 5-dicyanomethylene-1,3-dithian [29] (16), m.p. 177—179° (lit.,[29] 179—180.5°).

Thian-3-*one* 1-*Oxide* (5).—Thian-3-one (1.93 g) in methanol (100 ml) was refluxed with a solution of sodium metaperiodate (3.56 g) in water (10 ml) for 0.5 h and then cooled to room temperature. The precipitated sodium iodate was filtered off and the filtrate evaporated to near dryness *in vacuo*. The colourless semi-solid residue was extracted with chloroform (50 ml) and the extract dried ($MgSO_4$), and evaporated to give *thian*-3-*one* 1-*oxide* (1.95 g, 89%) as a liquid which crystallised on trituration with diethyl ether. Recrystallisation from ethyl acetate–hexane afforded needles, m.p. 85—88° (Found: C, 45.65; H, 6.1. $C_5H_8O_2S$ requires C, 45.5; H, 6.1%), $\nu_{max.}$ 1 700, 1 060, 1 030br, and 1 003 cm^{-1}.

3-*Ethoxycarbonylpropyl* 1-*Ethoxycarbonylethyl Sulphide*.—To a solution of sodium (23 g) in absolute ethanol (970 ml) was added ethyl 2-mercaptopropionate (134 g), sodium iodide (1 g), and ethyl 4-chlorobutyrate (151 g). The resulting mixture was stirred under reflux for 2 h and allowed to cool to room temperature. After 12 h the salt was filtered off and the residue evaporated under pressure to remove excess of ethanol. Chloroform (600 ml) was added and the solution washed several times with water (6 × 50 ml), dried ($MgSO_4$), evaporated under reduced pressure and the residue distilled to yield 3-*ethoxycarbonylpropyl* 2-*ethoxycarbonylethyl sulphide* (195 g, 79%) as an oil, b.p. 128—130° at 2.0 mmHg (Found: C, 52.9; H, 8.1. $C_{11}H_{20}O_4S$ requires C, 53.2; H, 8.1%).

2-*Ethoxycarbonyl*-2-*methylthian*-3-*one*.—To a suspension of sodium (4.6 g) in dry toluene (500 ml) was added absolute alcohol (50 ml), from which excess of ethanol was removed azeotropically. When the still-head temperature reached 106°, the bis-ester above (50 g) in dry toluene (175 ml) was added over 5 min with efficient stirring. The mixture was refluxed with stirring for a further 3 h during which time it turned from colourless through yellow to brown. The solution was then left overnight at room temperature. The mixture was distilled to remove ethanol until the temperature of the distilling fraction reached 106°. The mixture was then cooled and poured onto a mixture of ice (250 g) and hydrochloric acid (12N; 40 ml). The organic layer was removed and the aqueous layer extracted with ether (4 × 150 ml). The combined organic extracts (and toluene portion) were dried ($MgSO_4$), filtered, and evaporated *in vacuo* to yield a yellow liquid which solidified on cooling (31 g). Recrystallisation from light petroleum (b.p. 60—80°) afforded 2-*ethoxycarbonyl*-2-*methylthian*-3-*one*, m.p. 79—82°, as needles (Found: C, 53.2; H, 6.9. $C_9H_{14}O_3S$ requires C, 53.4; H, 7.0%), $\nu_{max.}$ 1 690 and 1 727 cm^{-1}.

2-*Methylthian*-3-*one* (12).—The above β-keto-ester (12 g) was heated under reflux with sulphuric acid (2N; 100 ml) for 9 h. The mixture was cooled to room temperature and extracted with methylene chloride (5 × 30 ml). The organic extract was dried ($MgSO_4$), filtered, and evaporated *in vacuo*. The residue was distilled yielding 2-*methylthian*-3-*one* (4.0 g, 52%) as a liquid, b.p. 60—62 ° at 2.0 mmHg (Found: C, 55.05; H, 7.8. $C_6H_{10}OS$ requires C, 55.35; H, 7.7%), $\nu_{max.}$ 1 705 cm^{-1}.

cis-2-*Methylthian*-3-*one* 1-*Oxide* (6).—2-Methylthian-3-one (4.1 g) in methanol (175 ml) was heated under reflux with a solution of sodium metaperiodate (6.7 g) in water (20 ml) for 1 h. The mixture was cooled to room temperature and the precipitated sodium iodate filtered off. The filtrate was evaporated *in vacuo*, and the residue treated with chloroform (75 ml). The solution was dried ($MgSO_4$), and evaporated to give an orange oily residue, which was treated with diethyl ether and immediately cis-2-*methylthian*-3-*one* 1-*oxide* crystallised as needles (1.6 g, 35%), m.p. 95—105°. Purification using preparative t.l.c. (silica using ethyl acetate as eluent) afforded only one isomer (R_F 0.1). Recrystallisation (cyclohexane–ethyl acetate) afforded a pure sample, m.p. 95—105° (Found: C, 48.9; H, 6.7. $C_6H_{10}O_2S$ requires C, 49.3; H, 6.9%), $\nu_{max.}$ 1 705, 1 077, 1 037, and 990 cm^{-1}.

3-*Dicyanomethylenethian* (14).—Thian-3-one (1.9 g) in ethanol (40 ml) and water (25 ml) at 50° was treated with malononitrile (1.1 g) and the mixture heated at 100° for 20 min during which time a green colour developed. The solution was maintained at −5° for 2 h after which time trituration liberated crystals (2.2 g) which on recrystallisation (ethyl acetate–cyclohexane) afforded 3-*dicyanomethylenethian*, m.p. 84—85°, as needles (Found: C, 58.3; H, 5.0; N, 16.8. $C_8H_8N_2S$ requires C, 58.5; H, 4.9; N, 17.1%), $\nu_{max.}$ 2 230 and 1 590 cm^{-1}.

3-*Dicyanomethylenethian* 1-*Oxide* (7).—To a solution of 3-dicyanomethylenethian (0.3 g) in methylene chloride (30 ml) at 0° was added a solution of *m*-chloroperbenzoic acid (0.3 g) in methylene chloride (10 ml) over 10 min. The mixture was stirred at 0° for 1 h and evaporated *in vacuo*. The resulting residue was washed with dry ether (3 × 10

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[27] E. A. Fehnel, *J. Amer. Chem. Soc.*, 1952, **74**, 1569.

[28] A. Lüttringhaus and H. Prinzbach, *Annalen*, 1959, **624**, 79.

[29] E. G. Howard and R. V. Lindsey, jun., *J. Amer. Chem. Soc.*, 1960, **82**, 158.

ml) and a portion of the remaining solid was chromatographed using preparative t.l.c. to afford 3-*dicyanomethylenethian* 1-*oxide* as needles (from ethyl acetate), m.p. 138—141° (Found: C, 53.45; H, 4.4; N, 15.5. $C_8H_8N_2OS$ requires C, C, 53.5; H, 4.5; N. 15.5%), $\nu_{max.}$ 2 225, 1 590,. 1 055, 1 030, and 1 003 cm^{-1}.

2-*Methyl*-3-*dicyanomethylenethian* (15).—To a solution of 2-methylthian-3-one (3.55 g) in ethanol (60 ml) and water (35 ml) was added malononitrile (1.21 g) and the mixture heated on a steam-bath for 4 h during which time a violet colour developed. When cold, colourless crystals precipitated out of solution on trituration, which on recrystallisation (aqueous EtOH) afforded 3-*dicyanomethylene*-2-*methylthian* (3.4 g, 70%) as needles, m.p. 72—73° (Found: C, 60.4; H, 5.7; N, 15.8. $C_9H_{10}N_2S$ requires C, 60.4; H, 5.7; N, 15.7%), $\nu_{max.}$ 2 230 and 1 590 cm^{-1}.

trans-3-*Dicyanomethylene*-2-*methylthian* 1-*Oxide* (8).—(a) 2-Methyl-3-dicyanomethylenethian (0.4 g) in methylene chloride (20 ml) at room temperature was treated with *m*-chloroperbenzoic acid (0.4 g). The mixture was stirred for 1 h and evaporated *in vacuo* to dryness. The residue was washed with dry ether (3 × 10 ml) and t.l.c. of the residue indicated the presence of two components. A portion of the mixture was subjected to preparative t.l.c. and the major component was isolated. However the minor component was present in insufficient quantities to enable isolation. Recrystallisation (ethyl acetate) of the isolated portion yielded trans-3-*dicyanomethylene*-2-*methylthian* 1-*oxide* as microcrystals, m.p. 138—140° (Found: C, 55.8; H, 5.2; N, 14.5. $C_9H_{10}N_2OS$ requires C, 55.65; H, 5.2; N, 14.4%), $\nu_{max.}$ 2 225, 1 585, 1 085, 1 050, 1 038, and 1 008 cm^{-1}.

(b) *cis*-2-Methylthian-3-one 1-oxide (1.0 g) in ethanol (7 ml) and water (3 ml), was treated with malononitrile (0.5 g) and the mixture kept at 30° for 15 h. The resulting solution was evaporated *in vacuo* to dryness from which *trans*-3-dicyanomethylene-2-methylthian 1-oxide was isolated as above, identical in all respects with the previous sample.

1,3-*Dithian*-5-*one* 1-*Oxide* (9).—To a warm solution of 1,3-dithian-5-one (0.14 g) in methanol (100 ml) was added sodium metaperiodate (0.23 g) in water (5 ml) and the solution heated under reflux for 1 h. The solution was filtered and the filtrate evaporated to near dryness *in vacuo*. The residue was extracted with methylene chloride (3 × 10 ml) and the organic extract dried ($MgSO_4$) and evaporated. The yellow residue (0.15 g) was recrystallised (acetonitrile) to afford 1,3-*dithian*-5-*one* 1-*oxide* as needles, m.p. 159—162° (Found: C, 31.65; H, 4.0. $C_4H_6O_2S_2$ requires C, 32.0; H, 4.0%), ν_{max} 1 695, 1 035br, and 865 cm^{-1}.

[4,4,6,6-$^2H_4$]-1,3-*Dithian*-5-*one*.—1,3-Dithian-5-one (1.5 g) in dry methylene chloride (25 ml) was shaken for 0.5 h with a solution of sodium (0.4 g) in deuterium oxide (25 g). The organic layer was separated and the aqueous fraction acidified (D_2O–D_2SO_4) and extracted with methylene chloride (3 × 25 ml). The organic fractions were combined, dried ($MgSO_4$), and evaporated to yield [4,4,6,6-$^2H_4$]-1,3-dithian-5-one (0.6 g, 35%), m.p. 160—162°.

[4,4,6,6-$^2H_4$]-1,3-*Dithian*-5-*one* 1-*Oxide*.—4,4,6,6-Tetradeuterio-1,3-dithian-5-one (0.5 g) was converted into [4,4,6,6-$^2H_4$]-1,3-*dithian*-5-*one* 1-*oxide*, needles, m.p. 160—162°, $\nu_{max.}$ *ca.* 2 200 cm^{-1}, by the method used for the protio-analogue.

5-*Dicyanomethylene*-1,3-*dithian* 1-*Oxide* (10).—To a solution of 5-dicyanomethylene-1,3-dithian (0.6 g) in methylene chloride (60 ml) at 0° was added *m*-chloroperbenzoic acid (0.6 g) in methylene chloride (25 ml) over 0.5 h. The solution was left to stand for 10 h, then evaporated. The residue was washed with dry ether (3 × 10 ml) and the remaining solid (0.62 g) was recrystallised (CH_3CN with activated charcoal) to afford 5-*dicyanomethylene*-1,3-*dithian* 1-*oxide* as needles, m.p. 167—169° (Found: C, 42.3; H, 3.0; N, 14.25. $C_7H_6N_2OS_2$ requires C, 42.4; H, 3.05; N, 14.1%), $\nu_{max.}$ 2 230, 1 590, 1 050br, and 918 cm^{-1}.

Attempted Epimerisation of cis-2-*Methylthian*-3-*one* 1-*Oxide* (6).—A solution of (6) (50 mg) in [$^2H_6$]acetone (0.5 ml), pyridine (3 drops), and D_2O (3 drops) was maintained at room temperature. The n.m.r. spectrum was run at intervals. H–D Exchange occurred at C-2 and the 2-methyl signal [δ 1.32 (d)] collapsed to a singlet; a new methyl singlet appeared at δ 1.42. The system reached equilibrium within 45 h and the ratio of the areas of the 2-methyl group signal in (6) and the new methyl group signal was 88 : 12.

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