Ring-size Effects in the Oxidation and Reduction of Some Cyclic Sulphoxides

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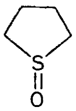
The oxidation rates of thietan 1-oxide (1), tetrahydrothiophen 1-oxide (2), and 2*H*-tetrahydrothiopyran 1-oxide (3) by perbenzoic acid in acidic and alkaline media have been measured in 40 : 60 dioxan–water. The effect of ring size is small, suggesting no major changes in rehybridization at the reaction centre in going from the ground to the transition state. The reduction rates of (1)–(3) and of *cis*-(4) and *trans*-4-t-butyl-2*H*-tetrahydrothiopyran 1-oxide (5) by iodide ion in aqueous perchloric acid solution have also been determined. As the reduction rates show a different dependence on acid concentration for the compounds examined, the interpretation of the ring-size effect is complex. The analysis of reduction rates of compounds (3)—(5) shows that the sulphinyl oxygen atom preferentially occupies the axial position.

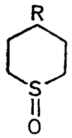
THE effect of ring size on rates has proved to be a useful tool to investigate the characteristics and magnitude of hybridization changes occurring at the reaction centre on going from the ground to the transition state.[1] In this respect, known reactions of organosulphur compounds are envisaged to occur either with little variation of co-ordination at sulphur or with the intervention of reactive intermediates with expanded co-ordination. Organic sulphoxides have a tetrahedral structure[2] which is described as being sp^3-like with superimposition of *d* orbitals. Electrophilic peroxyacid oxidation to sulphones should not bring about dramatic changes in bond angles and steric compression. On the other hand both alkaline oxidation[3] and acid-catalysed reduction[4,5] of sulphoxides have been proposed to proceed *via* a mechanism involving sp^3d hybridized intermediates, which bear some resemblance to recently reported sulphuranes.[6]

Therefore we thought it interesting to investigate the changes in rate brought about by varying the ring size of some simple sulphoxides. The four-, five-, and six-membered ring sulphoxides were chosen, as model substrates, since variation in reaction rates in these systems should arise as a result of changes in angle strain and steric compression effects.

(1)



(2)



(3) R = H
(4) R = *cis*-Bu^t
(5) R = *trans*-Bu^t

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[1] R. W. Alder, R. Baker, and J. M. Brown, 'Mechanism in Organic Chemistry,' Wiley–Interscience, London, 1971, and references therein.

[2] H. H. Szmant, in 'Sulfur in Organic and Inorganic Chemistry,' ed. A. Senning, Dekker, New York, 1971.

[3] R. Curci and G. Modena, *Tetrahedron*, 1966, **22**, 1227, 1235.

[4] D. Landini, G. Modena, F. Montanari, and G. Scorrano, *J. Amer. Chem. Soc.*, 1970, **92**, 7168.

[5] G. Scorrano, *Accounts Chem. Res.*, 1973, **6**, 132.

[6] J. C. Martin and E. F. Perozzi, *J. Amer. Chem. Soc.*, 1974, **96**, 3155 and previous papers.

RESULTS

Oxidation.—The rates of oxidation of thietan 1-oxide (1), tetrahydrothiophen 1-oxide (2), and 2*H*-tetrahydrothiopyran 1-oxide (3) to the corresponding 1,1-dioxides have been measured in 40 : 60 dioxan–water at 25°. The oxidations were carried out with perbenzoic acid both in acidic (apparent pH 3·6—3·2) and alkaline media (apparent pH 11·85), where the oxidizing agent is $PhCO_3^-$.

As previously reported,[3] all reactions conform to a second-order rate law, first order in each reactant. The rate coefficients are shown in Table 1.

TABLE 1

Rates of oxidation for cyclic sulphoxides in 40 : 60 dioxan–water at 25°

Compound	pH	10^2k/l mol^{-1} s^{-1}
(1)	3·6—3·2	4·07
	11·85	41·5
(2)	3·6—3·2	2·85
	11·85	26·9
(3)	3·6—3·2	7·81
	11·85	40·1

Reduction.—Reductions of sulphoxides (1)—(3) were carried out in aqueous perchloric acid in the presence of 0·3M-iodide ion, and were found to follow stoicheiometry (1).

$$>SO + 2H^+ + 2I^- \longrightarrow >S + I_2 + H_2O \quad (1)$$

The rates of reduction of *cis*- (4) and *trans*-4-t-butyl-2*H*-tetrahydrothiopyran 1-oxide (5) have also been measured in 6·35M-$HClO_4$. The progress of the reaction can be conveniently followed by titration of the iodine formed,[4] except in the case of thietan 1-oxide (1). For the latter compound in fact, we found that the reduction product (thietan) decomposes in the acidic solutions employed, most likely by ring opening. The decomposition product, probably a thiol, in turn reacts with iodine. Since reduction of the sulphoxide and reaction with iodine are of comparable rates, the iodometric method gives incorrect results. This problem seems to have been overlooked by other authors who have investigated this reaction.[7] We bypassed this experimental difficulty by following the disappearance of the thietan 1-oxide by g.l.c. (see Experimental section).

The rate coefficients for the reduction of the sulphoxides used in this study are reported in Table 2.

As with other sulphoxides,[4] compounds (1)—(5) were found to react at convenient rates in a range of acidity 1·7—8·1M-$HClO_4$, where they are substantially protonated. Therefore, the rate coefficients of interest are those estimated on the basis of the actual fraction of protonated sulphoxide. These rate coefficients (k_1) have been evaluated from the experimental k_{obs} values on the basis of the rate equation * $k_{obs}[SO]_{st} = k_1[SOH^+]$ (see also Experimental section). Values of $[SO]_{st}/[SOH^+]$ and log k_1 at the various acidities are reported in Table 2. In Table 3 correlations between log k_1 and acidity functions are presented for compounds (1)—(3), dimethyl sulphoxide,[4] and (+)-phenyl isopropyl sulphoxide.[8]

TABLE 2

Rates of reduction for cyclic sulphoxides in aqueous perchloric acid in the presence of 0·3M-NaI at 25°

Compound	c_{H^+}/ mol l^{-1}	$-H_0$ [a]	10^5k_{obs}/ s^{-1}	$[SO]_{st}$/ $[SOH^+]$	5+ log k_1
(1)	2·59	1·19	1·42	17·9 [b,c]	1·41
	3·42	1·56	4·84	11·9 [b,c]	1·76
	4·05	1·85	14·2	8·34 [b,c]	2·07
	4·12	1·88	18·1	8·08 [b,c]	2·16
	4·97	2·32	90·4	5·35 [b,c]	2·68
(2)	1·73	0·76	5·58	8·44 [b,d]	1·67
	2·59	1·19	28·6	4·86 [b,d]	2·14
	3·42	1·56	103	3·26 [b,d]	2·53
	4·27	1·95	358	2·34 [b,d]	2·92
	5·03	2·35	1170	1·81 [b,d]	3·33
(3)	4·27	1·95	1·25	2·78 [b,e]	0·54
	5·22	2·46	2·89	1·91 [b,e]	0·74
	6·35	3·11	13·0	1·41 [b,c]	1·26
	7·47	3·81	55·5	1·18 [b,e]	1·82
	8·10	4·31	198	1·10 [b,e]	2·34
(4)	6·35	3·11	44·9	1·63 [b,f]	1·86
(5)	6·35	3·11	4·71	1·38 [b,g]	0·81

[a] Corrected for salt effect.[4] [b] Evaluated (see text) with the aid of equation (7), by using the appropriate pK_{BH^+} and ϕ values. [c] $pK_{BH^+} = -1·92$; $\phi = 0·64$. [d] $pK_{BH^+} = -1·34$, $\phi = 0·56$. [e] $pK_{BH^+} = -1·48$, $\phi = 0·54$. [f] $pK_{BH^+} = -1·73$, $\phi = 0·51$. [g] $pK_{BH^+} = -1·49$, $\phi = 0·51$.

TABLE 3

Correlations between rate coefficients for reduction [a] of cyclic sulphoxides and acidity functions [b]

Compound	log k_1 against $-H_0$ s (r)	log $k_1 + H_0$ against H_0 + log c_{H^+} s (= ϕ) [c]
(1)	1·13 (0·997)	−0·17
(2)	1·04 (0·999)	−0·05
(3)	0·77 (0·992)	+0·26
Dimethyl sulphoxide [d]	1·02	−0·03
(+)-Isopropyl phenyl sulphoxide [e]	0·74	+0·30

[a] In aqueous perchloric acid in the presence of 0·3M-NaI at 25°. [b] The slopes (s) and correlation coefficients (r) were evaluated by least-square analysis. [c] The correlation coefficients have in this case low values, as expected for slopes near zero. They are not listed. [d] Data of ref. 4 at 0·3M-NaI were treated according to the new pK_{BH^+} (−1·54) and ϕ (+0·58) values evaluated by us for dimethyl sulphoxide using the H_0 values recently reported by C. D. Johnson, A. R. Katritzky, and S. A. Shapiro, *J. Amer. Chem. Soc.*, 1969, **91**, 6654. Therefore the s and ϕ values here reported are slightly different from those in ref. 4. [e] Ref. 8. These data refer to the chloride ion-induced racemization.

DISCUSSION

Oxidation.—Previous work carried out in this and other laboratories has suggested that the oxidation of sulphoxides by peroxyacids in acidic media involves nucleophilic attack by the sulphur lone-pair on the peroxyacid O–O bond[9] [equation (2)]. Electrophilic

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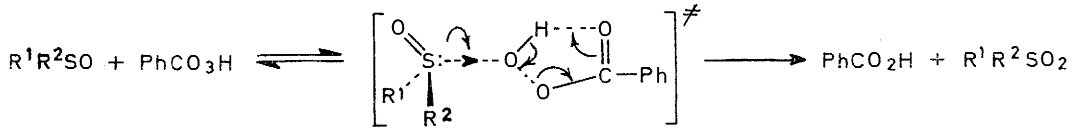
* [SO] and $[SOH^+]$ represent the concentration of free and protonated base, and $[SO]_{st}$ stands for stoicheiometric concentration of sulphoxide.

[7] S. Tamagaki, M. Mizino, H. Yoshida, H. Hirota, and S. Oae, *Bull. Chem. Soc. Japan*, 1971, **44**, 2456.

[8] D. Landini, G. Modena, U. Quintily, and G. Scorrano, *J. Chem. Soc.* (*B*), 1971, 2041.

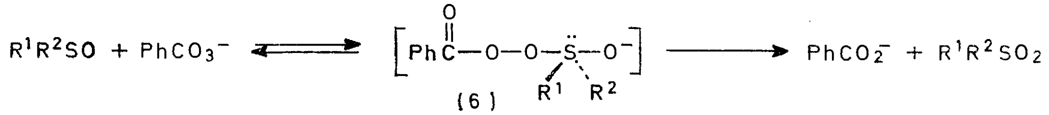
[9] R. Curci, R. A. Di Prete, J. O. Edwards, and G. Modena, in 'Hydrogen-bonded Solvent Systems,' eds. A. K. Covington and P. Jones, Taylor and Francis, London, 1968, pp. 303 *et seq.* and references therein.

oxidation of sulphoxides[9] (like the oxidation of sulphides[10]) would involve only a small change in molecular geometry on going from the reactants to the transition state; therefore, no significant effects of ring size on rates would be expected here, consistent with observation. This is parallel to the results of Modena *et al.*[11] in the oxidation of cyclic sulphides by H_2O_2, the relative rates being 1·0 : 2·1 : 1·2 for four-, five-, and six-membered ring sulphides.[11]



(2)

On the other hand, oxidation by $PhCO_3^-$ has been proposed to occur *via* a two step mechanism, involving an intermediate adduct (6) formed by nucleophilic attack by the peroxy-anion on the SO bond [equation (3)].



$$R^1R^2SO + PhCO_3^- \rightleftharpoons \left[PhC(=O){-}O{-}O{-}\ddot{S}(R^1)(R^2){-}O^-\right] \longrightarrow PhCO_2^- + R^1R^2SO_2 \qquad (3)$$

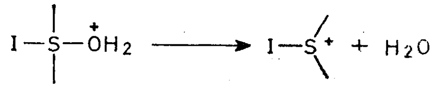
(6)

The acidic and alkaline oxidations show opposite (although small) substituent effects on rates.[3] Steric effects were also found to be small for both reactions. although the alkaline oxidation is more sensitive than the acidic.

Inspection of the data in Table 1 reveals that in either acidic or alkaline oxidation by perbenzoic acid, the effects of ring size on rates are small, with the five-membered ring showing in both cases the lowest rate.

In other systems, *e.g.* the BH_4^- reduction of cycloalkanones, large variations in rates occur on going from cyclobutanone to cyclopentanone to cyclohexanone, the relative rates being 38 : 1 : 23.[12] In the latter reaction $sp^2 \longrightarrow sp^3$ rehybridization at the reaction centre occurs on going from the ground to the transition state, and the observed trend in relative rates results from changes in relief of angle strain and from steric compression effects. Furthermore, in the alkaline hydrolysis of sulphites, $(RO)_2SO$, Tillett *et al.*[13] found that the five-membered ring compound reacts *ca.* 250-fold faster than the six-membered analogue. No such large difference in rates is found for cyclic sulphoxides; some rehybridization change at the reaction centre should occur on going from the ground to the transition state but the rate constants suggest that they are relatively small. Thus, an interesting difference seems to exist between alkaline hydrolysis of sulphites and alkaline oxidation of sulphoxides, since in both cases nucleophilic attack at the sulphenyl sulphur should produce a d^2sp^3 bipyramidal intermediate or transition state.

Reduction.—The intervention of several penta-coordinate sulphur intermediates has been suggested in the reduction of sulphoxides in acidic media.[4,5] The reaction involves[4,5] nucleophilic attack by I^- on the protonated sulphoxide, further protonation of the intermediate, and formation of an halogenosulphonium ion in a slow step [equation (4)]. The dependence of the reduction rates of four- and five-membered ring sulphoxides on the acidity of the medium is quite similar to that observed for dimethyl sulphoxide (Table 3); on the other hand, k_1 values for the six-membered ring compound are found to increase with medium acidity less steeply (see Figure). Clearly, the different dependence of reduction rates on medium acidity calls for some caution in comparing the reactivity of these three sulphoxides at a single acid concentration.[7,14] A meaningful comparison can be made among the rates of (1), (2), and dimethyl sulphoxide as these compounds show a similar dependence of k_1 on acid concentration.



$$I{-}\overset{|}{\underset{|}{S}}{-}\overset{+}{O}H_2 \longrightarrow I{-}S^{+}\!\!\lessgtr + H_2O \qquad (4)$$

Thietan 1-oxide reacts *ca.* 4 and tetrahydrothiophen 1-oxide *ca.* 19 times faster than dimethyl sulphoxide, The groups linked to the sulphur in the four- and five-membered ring sulphoxides are oriented in such a way as to require a minimum of reorganization to reach the geometry of the pentacovalent intermediate upon attack by iodide ion. The easy formation[15] of difluorosulphuranes from reaction of thietan and tetrahydrothiophen with trifluoromethyl hypofluorite also testifies to the inclination of sulphur atoms in four- and five-membered rings to give rise to pentacovalent intermediates. It is interesting that the difluorosulphurane produced from tetrahydrothiophen is less stable than that from thietan.[15] This might explain the higher rate of reduction of (2) relative to (1).

The six-membered ring sulphoxide is less reactive than the other cyclic sulphoxides by an extent which depends on the acidity of the solution. A correct treatment of

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[10] G. Modena and L. Maioli, *Gazzetta*, 1957, **87**, 1306 and following papers.

[11] A. Cerniani, G. Modena, and P. E. Todesco, *Gazzetta*, 1960, **90**, 382.

[12] H. C. Brown and K. Ichilawa, *Tetrahedron*, 1957, **1**, 221.

[13] P. B. D. de la Mare, J. G. Tillett, and H. F. van Woerden, *J. Chem. Soc.*, 1962, 4888; J. G. Tillett, *Mechanisms of Reactions of Sulfur Compounds*, 1969, **4**, 129.

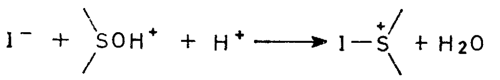
[14] L. Sagramora, A. Garbesi, and A. Fava, *Helv. Chim. Acta*, 1972, **55**, 675.

[15] D. B. Denney, D. Z. Denney, and Y. F. Hsu, *J. Amer. Chem. Soc.*, 1973, **95**, 4064.

reduction rates involves the adoption of the Bunnett–Olsen equation [16] in the form (5).[5] This gives ϕ values

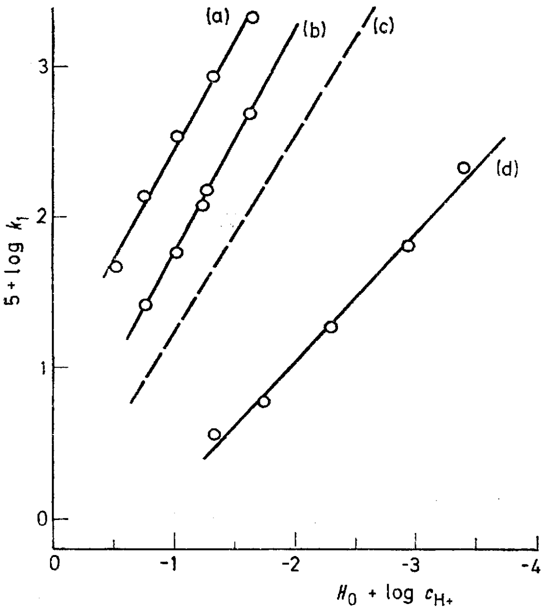
$$\log k_1 + H_0 = \phi(H_0 + \log c_{H^+}) + \text{constant} \quad (5)$$

of $-0{\cdot}17$ and $-0{\cdot}05$ for (1) and (2), respectively, and these are similar to the ϕ value estimated for dimethyl sulphoxide (ϕ $-0{\cdot}03$). For compound (3) the estimated ϕ value ($+0{\cdot}26$) is close to that for the acid-catalysed racemization of (+)-isopropyl phenyl sulphoxide by Cl^- ($+0{\cdot}30$).[8] Since we have shown [4,5] that the same reaction scheme holds for both racemization and reduction of sulphoxides by halide ions, the change in ϕ value should have the same meaning.[8] A positive ϕ value may be taken to indicate the incursion of a reaction path characterized by general acid catalysis [equation (6)]. The incursion of this additional path is



$$I^- + \rangle SOH^+ + H^+ \longrightarrow I{-}\overset{+}{S}\langle + H_2O \quad (6)$$

shown when the attack by iodide ion on sulphur is made difficult by steric crowding. Steric hindrance by the isopropyl group is present in $PhSOPr^i$, and in the case of the six-membered compound the axial hydrogens at C-3 and -5 may be oriented in such a way as to hinder formation of pentaco-ordinate sulphur intermediates.



Correlations between reduction rates and acidity of the medium for (a) thietan 1-oxide, (b) tetrahydrothiophen 1-oxide, (c) dimethyl sulphoxide, and (d) 2*H*-tetrahydrothiopyran 1-oxide

The *trans*-4-t-butyl-2*H*-tetrahydrothiopyran 1-oxide (5) is reduced *ca.* 10 times faster than the *cis*-isomer (4) in $6{\cdot}35\text{M-}HClO_4$. As isomer (5) is thermodynamically less stable than (4) [17] this implies that the steric crowding in the transition state is almost the same, irrespective of whether the attack by I^- occurs from the *endo*- or *exo*-side. This result is not unexpected since the axial : equatorial ratio in cyclohexane systems does not differ significantly for I and OH substituents.[18] Assuming the polar effect of the 4-t-butyl group to be small,[19] the rates of reduction of (4) and (5) can be taken to represent, respectively, those of the axial (k_A) and of the equatorial (k_E) forms. Knowing the rate of reduction of (3), these figures can be used [18] to estimate * roughly an axial : equatorial ratio of 82 : 18 for the six-membered ring sulphoxide (3). This is consistent with n.m.r. evidence indicating that the sulphinyl oxygen shows a preference for the axial position.[20]

EXPERIMENTAL

Materials and Solvents.—All chemicals employed not described below are reagent grade commercial samples. The sulphoxides [10] and perbenzoic acid [21] samples have been described previously. Dioxan was purified by standard methods.[22] 40 : 60 Dioxan–water was made up at 25° by weighing the proper amount of distilled water into volumetric flasks, which were then filled to the mark with dioxan. Perchloric acid solutions were prepared by dilution of the concentrated acid with distilled water and titrated with standard NaOH solutions. H_0 Values have been obtained by interpolation of published data,[23] and corrected for salt effect by NaI, as in a previous paper.[4]

Oxidation Reactions.—Aliquot portions of perbenzoic acid standard solutions in the mixed solvent were added at zero time to known volumes of standard solutions of the sulphoxides in the same mixed solvent, unbuffered (acidic oxidation) or buffered ($0{\cdot}1\text{M-}NaHCO_3$–$0{\cdot}2\text{M-}NaOH$). For runs in alkaline media the apparent pH of the reaction mixture was constant to $\pm 0{\cdot}05$ unit, as monitored by a standard glass–calomel electrode chain (Radiometer pH meter PHM-26c). Aliquot portions were withdrawn at time intervals and the perbenzoic acid concentration was determined following a reported iodometric procedure.[21] The rate coefficients reported in Table 1 are averages ($\pm 3\%$) from two or more independent runs.

Reduction Reactions.—The reduction of all compounds studied, except thietan 1-oxide, was followed by an iodometric technique described elsewhere.[4] At zero time, a thermostatted NaI aqueous solution (*ca.* 2·7 g in 10 ml) was added under nitrogen to thietan 1-oxide in aqueous perchloric acid (50 ml) of known concentration. Portions (5 ml) were withdrawn at intervals and poured into water (50 ml) containing $Na_2S_2O_3$ (10 ml; $0{\cdot}02\text{N}$). The aqueous solution was extracted with $CHCl_3$ (3 × 50 ml), the organic fraction dried (Na_2SO_4), and the solvent distilled off

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* The equation $k = N_Ak_A + N_Ek_E$ was used, where N_A and N_E are molar fractions of the axial and equatorial isomers, respectively.

[16] J. F. Bunnett and F. P. Olsen, *Canad. J. Chem.*, 1966, **44**, 1917.

[17] C. R. Johnson and D. McCants, *J. Amer. Chem. Soc.*, 1965, **87**, 1109.

[18] E. L. Eliel, 'Stereochemistry of Carbon Compounds,' McGraw-Hill, New York, 1962.

[19] J. McKenna, J. M. McKenna, and B. G. Hutley, *J.C.S. Chem. Comm.*, 1974, 522 and references therein.

[20] J. B. Lambert and R. G. Keske, *J. Org. Chem.*, 1966, **31**, 3429.

[21] R. Curci and A. M. Piepoli, *Boll. sci. Fac. Chim. ind. Bologna*, 1969, **23**, 237.

[22] L. F. Fieser and M. Fieser, 'Reagents for Organic Synthesis,' Wiley, New York, 1967.

[23] K. Yates and H. Wai, *J. Amer. Chem. Soc.*, 1964, **86**, 5408.

under reduced pressure. The oily residue was quantitatively transferred to a volumetric flask containing a known amount of acetophenone (internal standard) in $CHCl_3$. *G.l.c. analyses* were performed using a HP 5750G instrument equipped with an 8 ft × 1/8 in column (5% FFAP on 80/100 Chromosorb G DMCS) and the concentration of (1) was evaluated at various times. Pseudo-first-order rate coefficients (k_{obs}) were obtained on plotting log c_{SO} against time.

The stability of thietan 1-oxide in $HClO_4$ solutions was checked. Some decomposition was found to occur (k_d $5{\cdot}7 \times 10^{-7}$ s^{-1} at $4{\cdot}8$M-$HClO_4$). The rate of disappearance of (1) increased in the presence of chloride ion (k_d $1{\cdot}5 \times 10^{-6}$ at $4{\cdot}8$M-$HClO_4$ in the presence of $0{\cdot}3$M-NaCl); this may be due to attack by halide ion on the carbon α to the protonated SO group. This reaction is similar to the halide ion-promoted ring opening of β-propiolactone.[24] Following this hypothesis a rate constant of $2{\cdot}5 \times 10^{-5}$ s^{-1} can be estimated for ring opening of thietan 1-oxide by $0{\cdot}3$M-NaI in $4{\cdot}8$M-$HClO_4$. The rate constant for disappearance of (1) under these conditions is $9{\cdot}0 \times 10^{-4}$ s^{-1}, which is 36 times faster than the estimated rate for attack on carbon. From these figures it can be concluded that the experimental rate of disappearance of (1) in the presence of I^- truly represents the rate of reduction of thietan 1-oxide to thietan.

To correlate the experimental rate constants with medium acidity, the protonation fraction $[SO]_{st}/[SOH^+]$ has been estimated for each substrate.[4,5] Bearing in mind that $[SO] + [SOH^+] = [SO]_{st}$, this was done evaluating the ionization ratios $I = [SOH^+]/[SO]$ at each acid concentration by using the Bunnett–Olsen equation [25] in the form (7); the necessary pK_{BH^+} and ϕ values for the same compounds were determined by an independent study.[26]

$$\log I + H_0 = \phi(H_0 + \log c_{H^+}) + pK_{BH^+} \qquad (7)$$

[4/1670 *Received*, 8*th August*, 1974]

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[24] P. D. Bartlett and G. Small, jun., *J. Amer. Chem. Soc.*, 1950, **72**, 4867.

[25] J. F. Bunnett and F. P. Olsen, *Canad. J. Chem.*, 1966, **44**, 1899.

[26] R. Curci, F. Di Furia, A. Levi, V. Lucchini, and G. Scorrano, *J.C.S. Perkin II*, 1975, 341.