Basic Properties of Cyclic Sulphides and Sulphoxides

By **Ruggero Curci, Fulvio Di Furia, Arrigo Levi, Vittorio Lucchini, and Gianfranco Scorrano,*** Centro C.N.R. Meccanismi di Reazioni Organiche, Istituto di Chimica Organica dell'Universita', 35100 Padova, Italy

The pK_{BH^+} values of four-, five-, and six-membered ring sulphides and sulphoxides have been estimated in aqueous sulphuric acid by using an n.m.r. technique. The protonation behaviours of tetrahydrothiophen and tetrahydrofuran have been compared. No appreciable influence of ring size on basicity has been found except in the case of thietan 1-oxide, which is observed to be less basic than the corresponding acyclic sulphoxide. The pK_{BH^+} values of the *cis*- and *trans*-4-t-butyl derivatives of the six-membered ring sulphoxide indicate that the oxygen atom of the SO group is more basic in the axial than in the equatorial position.

THE relative basicities of cyclic sulphides have been estimated by determining the stability of their iodine complexes,[1,2] or by studying their ability to hydrogen bond with phenol.[3] Similarly, the stability constants of hydrogen bonded complexes of cyclic sulphoxides with methanol[4] or phenol[5] have been used to estimate the change of S=O group basicity with ring size. These measurements were carried out in organic solvents, and therefore the estimated basicities have no direct relationship with the thermodynamic pK_{BH^+} values, which refer to dilute solutions in water. The only direct measurements in water–sulphuric acid solutions are those reported by Arnett *et al.*[6] and Horak *et al.*[7] These authors used either a u.v.[6] or an extraction[7] technique to estimate the ionization ratios ($I = c_{BH^+}/c_B$, where c_{BH^+} and c_B represent the concentration of the protonated and free base, respectively) of tetrahydrothiophen. However, the u.v. spectra were difficult to analyse[6] and the extraction technique fails to give reliable results for acyclic dialkyl sulphides,[8] ethers,[9] and alcohols.[9,10] Information on the effect of ring size on protonation equilibria of functional groups is of general interest in conformational analysis. Moreover, knowledge of the protonation behaviour of cyclic sulphides and sulphoxides was needed to analyse correctly spectroscopic and reactivity data obtained from other research. Therefore, we decided to apply to this problem an n.m.r. technique extensively used in our laboratory and successfully employed for the determination of pK_{BH^+} values of various compounds.[8-11]

RESULTS

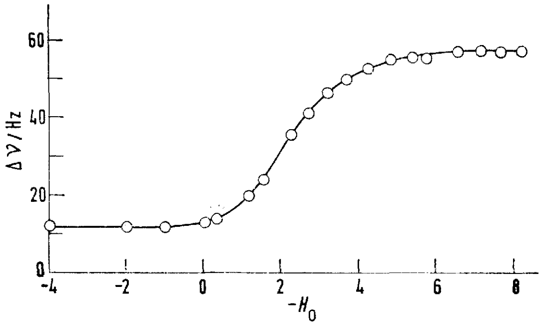
We have studied the protonation equilibrium ($BH^+ \rightleftharpoons B + H^+$) in aqueous sulphuric acid solutions for thietan (1), tetrahydrothiophen (2), tetrahydrothiopyran (3), their corresponding oxides (4)—(6), and *trans*- (7) and *cis*-4-t-butyl tetrahydrothiopyran 1-oxide (8). The n.m.r. technique used[8-11] involves the measurement of changes in chemical shifts of protons on the carbon atom α to the group undergoing protonation relative to those of the trimethylammonium ion as a function of the acidity of the medium. The use of Me_3NH^+ as internal standard was found advantageous[8,11] in minimizing solvent effects. The n.m.r. spectra of compounds (1)—(8) are quite complex; however, on monitoring the peak of highest intensity in the multiplet from the α-CH_2 group, and plotting $\Delta\nu$ (*i.e.*, $\nu - \nu_{ref}$) against $-H_0$, excellent sigmoid curves were obtained (see Figure). The chemical shifts of the free ($\Delta\nu_B$) and protonated ($\Delta\nu_{BH^+}$) bases can be estimated either from the curves or, more accurately, through statistical analysis of $\Delta\nu$ values (see Experimental section). The data are summarized in Table 1.

TABLE 1

Chemical shifts of unprotonated ($\Delta\nu_B$) and protonated ($\Delta\nu_{BH^+}$) bases in aqueous sulphuric acid [a]

Compound	$\Delta\nu_B$/Hz	$\Delta\nu_{BH^+}$/Hz
(1)	−28·7	*b*
(2)	7·9	−54·8
(3)	31·0	−32·9
(4)	−42·1	−110·7
(5)	−11·4	−56·7
(6)	−3·2	−43·0
(7)	14·8	−32·1
(8)	−13·2	−57·0

[a] Chemical shifts (at 90 MHz) are relative to Me_3NH^+ and measured at 25°. Positive values indicate upfield shifts. [b] Decomposition of this compound prevents any evaluation of the chemical shift of the protonated base.



Correlation of $\Delta\nu$ with $-H_0$ for tetrahydrothiophen 1-oxide in aqueous sulphuric acid

In the case of thietan, however, acid-catalysed decomposition of the substrate takes place before significant changes

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in chemical shift can be measured. This reaction is quite fast at 8·5M-H_2SO_4 (H_0 −4·03).

From the $\Delta\nu$ values in media of varying acidity, ionization ratios were evaluated as $I = (\Delta\nu - \Delta\nu_B)/(\Delta\nu_{BH^+} - \Delta\nu)$. As discussed in detail elsewhere,[8-11] thermodynamic pK_{BH^+} values were obtained from the Bunnett–Olsen equation (1).[12] This also allows the estimation of ϕ values, a parameter which gives information concerning solvation requirements of the protonation equilibria.[10,13] In Table 2 pK_{BH^+} and ϕ values for compounds (2)—(8) are reported together with $(H_0)_{\frac{1}{2}}$ (H_0 at half protonation) and m values (from the equation $\log I = -mH_0 + \text{constant}$)

$$\log I + H_0 = \phi(H_0 + \log c_{H^+}) + pK_{BH^+} \qquad (1)$$

TABLE 2

Protonation equilibria of cyclic sulphides and sulphoxides [a]

Compound	pK_{BH^+} [b]	ϕ [b]	$(H_0)_{\frac{1}{2}}$ [c]	m [c]
(2)	−6·84	−0·32	−5·42	1·30
	(0·15)	(0·03)	(0·01)	(0·03)
(3)	−6·74	−0·35	−5·26	1·32
	(0·32)	(0·08)	(0·03)	(0·07)
(4)	−1·92	0·64	−3·78	0·42
	(0·03)	(0·006)	(0·1)	(0·05)
(5)	−1·34	0·56	−2·26	0·57
	(0·05)	(0·02)	(0·16)	(0·03)
(6)	−1·48	0·54	−2·41	0·52
	(0·07)	(0·03)	(0·05)	(0·02)
(7)	−1·73	0·51	−2·76	0·58
	(0·05)	(0·02)	(0·12)	(0·03)
(8)	−1·49	0·51	−2·37	0·596
	(0·05)	(0·03)	(0·18)	(0·03)

[a] In aqueous sulphuric acid at 25°. [b] Evaluated as slope (ϕ) and intercept (pK_{BH^+}) from least square analysis of $\log I + H_0$ against $H_0 + \log c_{H^+}$ plots; $r > 0{\cdot}99$. Values in parentheses are standard deviations. [c] Evaluated from least-square analysis of $\log I$ against $-H_0$ plots; m values are slopes and $(H_0)_{\frac{1}{2}}$ the values for $\log I = 0$. Values in parentheses are standard deviations.

DISCUSSION

Sulphides.—As mentioned above, thietan was found to undergo decomposition in acid solution;[14] this prevented any accurate measurement of the extent of its protonation. Therefore, the only useful information obtained is that (1) is not significantly protonated in <8·5M-sulphuric acid (H_0 −4·03). This result may be compared with the H_0 values at which compounds (2) and (3) are 1% protonated, *i.e. ca.* −3·9 and −3·7, respectively, suggesting that (1) is probably less basic than (2) and (3).

The five- and six-membered ring sulphides (2) and (3) have almost the same basicity, *i.e.* pK_{BH^+} −6·84 and −6·74, respectively; these values are also very similar to those of non-cyclic compounds [*cf.* Me_2S: pK_{BH^+} −6·99; ϕ −0·27; $(H_0)_{\frac{1}{2}}$ −5·71; m 1·26 [8,15]]. Therefore, it appears that the basicity of the sulphur atom does not change appreciably when it is part of a ring. A similar situation seems to hold for the corresponding oxygen compounds. Indeed by treating the n.m.r. data recently reported by Lee and Cameron [16] for tetrahydrofuran in a way similar to that adopted by us for acyclic ethers [9] the following results are obtained: [15] pK_{BH^+} −2·32; ϕ 0·78; $(H_0)_{\frac{1}{2}}$ −6·69; m 0·25. The corresponding values for diethyl ether are pK_{BH^+} −2·39; ϕ 0·78; $(H_0)_{\frac{1}{2}}$ −6·94; m 0·27. Again, no major difference in the pK_{BH^+} values (nor in the ϕ and m parameters), is observed between the cyclic and open-chain compounds.

On comparing the protonation behaviour of tetrahydrothiophen and tetrahydrofuran, it can be observed, as in the case of acyclic ethers and sulphides,[9] that the oxygen compound is much more basic than the sulphur analogue in dilute aqueous solutions (ΔpK_{BH^+} *ca.* 4). However, the ionization ratio for the former increases with acid concentration much less rapidly than that for the latter (m 0·25 and 1·3, respectively). The sulphur compound is half-protonated at lower acidity than its oxygen analogue. Moreover, the log I value for tetrahydrothiophen is higher than the corresponding values for tetrahydrofuran in >10·9M-sulphuric acid; thus the former is more basic than the latter in these media. This represents another example of the powerful effect of solvent on acid–base equilibria and on relative basicities. Indeed, compared with tetrahydrofuran, tetrahydrothiophen has a similar heat of protonation in FSO_3H (tetrahydrofuran 19·6 ± 0·2, tetrahydrothiophen 19·7 ± 0·2 kcal mol^{-1}),[17] although the latter gives the stronger complexes with $SbCl_5$ [18] and with iodine [14,19] in hydrocarbon solvents.

Thus, the importance of evaluating how protonation equilibria are modified by changing the solvent composition is again emphasized. The quantity which gives pertinent information on this question is ϕ [equation (1)]. As discussed elsewhere,[9,13] the meaning of the ϕ parameter is better understood by expressing the Bunnett–Olsen equation (1) in terms of activity coefficients * as in equation (2), where X is the base under investigation and B is the reference Hammett base.

$$\log f_{H^+} - \log(f_{XH^+}/f_X) = (1 - \phi)[\log f_{H^+} - \log(f_{BH^+}/f_B)] \qquad (2)$$

From the definition of activity coefficients,[21-23] log f is proportional to the free energy change in transferring one mole of the indicated species from its solution in water to that in acid. Therefore, in equation (2), ϕ reflects the effect of changing medium on the equilibrium protonation of base X compared with the effect on the similar equilibrium involving the reference base B.

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* Equation (2) may be easily derived from the equation $H_X + \log c_{H^+} = (1 - \phi)(H_0 + \log c_{H^+})$ suggested by Hammett [20] as the general form of the Bunnett–Olsen equation.

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Direct measurements of activity coefficients [21-23] show that they decrease in the series $f_{H^+} > f_{XH^+} > f_X$. The order of activity coefficients above is that expected on the basis of chemical intuition; the charged species XH^+, in fact, has greater solvation requirements than uncharged X, and specific interactions with solvent molecules should become stronger as the size of the ion decreases.[9,13,21-23] As a consequence of the order of activity coefficients, both sides of equation (2) are >0, with the relative magnitude of the differences of the logarithms depending on the ratio f_{acid}/f_{base}. When $f_{XH^+}/f_X < f_{BH^+}/f_B$, $[\log f_{H^+} - \log (f_{XH^+}/f_X)] > [\log f_{H^+} - \log (f_{BH^+}/f_B)]$ and ϕ is negative. Therefore, as the ϕ value gives information on the relative magnitude of the ratio f_{XH^+}/f_X, it is to be considered a useful tool in estimating the differences in specific interactions with solvent molecules of the free base and of its conjugate acid.[9,13]

For instance, when a large and polarizable cation is obtained upon protonation as, *e.g.*, in the case of Ar_3C^+ from $Ar_3COH + H^+$, the ratio f_{XH^+}/f_X measured experimentally is small and negative ϕ values are found; this suggests that the differences in solvent specific interactions of XH^+ and of X are small, probably because of the effective dispersal of positive charge in triarylmethylium ions.[9,13] The opposite situation (f_{XH^+}/f_X large, ϕ positive) is found in the case of protonation of oxygen bases, *e.g.* ethers or amides, where the positive charge in the conjugate acid is more localized.[9,13]

The different ϕ values observed in the protonation of ethers and sulphides (*ca.* +0·8 and *ca.* −0·3, respectively) indicate that sulphonium ions (R_2SH^+) are less solvated than oxonium ions (R_2OH^+). This is not surprising, since the presence of the large and polarizable sulphur atom makes the dispersion of the positive charge more effective in R_2SH^+ than in R_2OH^+.[9] It is then obvious that the relative ease in formation of the cation, *i.e.* the relative basicity of the two compounds, changes with the solvating ability of the water–acid solutions.

This discussion emphasizes, once again, the point that pK_{BH^+} values, which refer to dilute aqueous solutions, represent meaningful indexes of basicity *towards the proton in that particular medium only*. The complete description of the protonation behaviour of a weak base in aqueous acids may be, however, achieved by the use of both ϕ and pK_{BH^+} parameters.[13]

Sulphoxides.—Inspection of Table 2 reveals that the four-membered ring compound (4) is the least basic among the cyclic sulphoxides, the pK_{BH^+} values of the five- and six-membered sulphoxides being little different from those of the open-chain compounds [*cf.* Me_2SO: pK_{BH^+} −1·54; ϕ 0·58; $(H_0)_{\frac{1}{2}}$ −2·69; *m* 0·52].[15] Moreover compound (4) has a ϕ value of 0·64, which is significantly greater than those observed for the other cyclic sulphoxides (0·51—0·56). As discussed above, positive ϕ values are associated with strong interactions with water, which occurs when the charge on the 'onium ion is more localized. Hence, the conjugate acid of (4) is apparently less capable of dispersing the charge through the sulphur atom than the other cyclic sulphoxides.

A comparison of the pK_{BH^+} values of the six-membered ring sulphoxides allows one to evaluate the importance of conformational effects. It is known [24] that a t-butyl group in the 4-position in a substituted cyclohexane does not influence significantly the charge density at C-1. It seems safe to assume that the same holds in the sulphoxide series. The difference in pK_{BH^+} values observed for compounds (7) and (8) can then be attributed to conformational effects indicating that the oxygen of the S=O group is more basic in the axial than in the equatorial position. Several pieces of evidence support the preference for a sulphoxide oxygen to reside in the axial position in cyclic compounds.[25-27] It was reported that in tetrahydrothiopyran 1-oxide the 1-axial conformation is favoured by some 175 cal mol^{-1} at −90°.[26] The errors in the estimate of pK_{BH^+} are rather large (±0·07) and therefore an accurate evaluation of the axial : equatorial ratio is precluded. However, a rough estimate can be made comparing the actual pK_{BH^+} value for tetrahydrothiopyran 1-oxide (6) (−1·48 ± 0·07) with the value of −1·58 ± 0·05 which can be calculated [28] on the basis of the pK_{BH^+} values for compounds (7) (equatorial oxygen) and *cis*-(8) (axial oxygen), and of the published [26] value of the axial : equatorial ratio (68 : 32) for compound (6). The fair agreement found suggests that in the cyclic compounds examined the sulphinyl oxygen atom also prefers the axial position in aqueous solutions at 25°.

The results obtained for the 4-t-butyl derivatives are easier to interpret. Here the *cis*-isomer is more stable than the *trans* [25] by 1·3 kcal mol^{-1}. Our data indicate that for protonated sulphoxides the preference for the substituent to remain in the axial position is retained. The difference in stability between axial and equatorial forms is in fact enhanced by some 0·3 kcal mol^{-1} on protonation.

This calls for some comment concerning the reasons for the 1-axial preference in cyclic sulphoxides. It is commonly accepted [26,27] that in tetrahydrothiopyran 1-oxide the sulphinyl oxygen atom has a van der Waals interaction with the axial 3- and 5-H. Our finding that the axial position is preferred even in the case of the conjugate acid, where, owing to S=O protonation, such interactions might be greatly diminished, casts some doubt on this interpretation. Although we have no definite answer on the reasons for the axial preference, we feel that attention should be drawn to the possibility of positive interactions between the equatorial lone-pair and the adjacent bonds. This hypothesis is now being investigated.

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EXPERIMENTAL

Materials.—The sulphides and sulphoxides employed were either commercial products or were synthesized by literature methods. They were purified by fractional distillation or crystallization and gave the anticipated physical and spectral data.

pK_{BH^+} *Measurements*.—Sulphuric acid solutions were prepared by dilution and titrated with standard aqueous NaOH solutions. The H_0 values were obtained by interpolation of literature data.[29] The n.m.r. spectra were recorded on a Bruker HFX-10 instrument at 90 MHz with trimethylammonium ion as internal standard and internal lock on the acid–water band. The temperature was checked by the methanol method and chemical shifts were read at ±0·1 Hz with a frequency difference counter.

Protonation was monitored by following the highest peak of the α-CH_2 multiplet which undergoes the largest shift. On plotting $\Delta\nu(\nu - \nu_{ref})$ of the more intense peak in the multiplet against $-H_0$ sigmoid curves were obtained (Figure). From these sigmoids $\Delta\nu_B$ and $\Delta\nu_{BH^+}$ values could be obtained. They may also be computed by using equation (1) and expressing $\Delta\nu$ as a function of H_0, log c_{H^+}, $\Delta\nu_B$, $\Delta\nu_{BH^+}$, ϕ, and pK_{BH^+}. By using a computer the last four terms were varied until the best fit between calculated and experimental $\Delta\nu$ values was found through the least-square analysis method of Sillén.[30] The $\Delta\nu_B$ and $\Delta\nu_{BH^+}$ values so obtained agree within experimental error (±0·1 Hz) with those obtained from sigmoid plots and are reported in Table 1. Ionization ratios were then evaluated between 5 and 95% protonation and used [9] to compute the pK_{BH^+}, ϕ, $(H_0)_{\frac{1}{2}}$, and m values which appear in Table 2. In the case of tetrahydrofuran the $\Delta\nu$ values reported by Lee and Cameron [16] were adopted: these were evaluated as the difference between the chemical shifts of the α- and β-CH_2 groups. The computed $\Delta\nu_B$ and $\Delta\nu_{BH^+}$ values are 112·4 and 140·2 Hz respectively.

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