# Nucleophilic Substitution at Sulphur. Part 3.[1] The Alkaline Hydrolysis of Some Cyclic and Open-chain Sulphonate Esters

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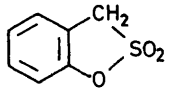
The rates of alkaline hydrolysis of a number of aryl cyclic and open-chain sulphonate esters have been studied at various temperatures. The enthalpies and entropies of activation have been determined. The difference in reactivity between the five-membered sultone and other cyclic and open-chain analogues is shown to arise from a combination of both enthalpy and entropy strain. The detailed mechanism of alkaline hydrolysis of sulphonate esters and the cause of ring strain in sultones are discussed in some detail.

SEVERAL examples have been reported of extraordinary differences between the rates of alkaline hydrolysis of esters of five-membered cyclic esters of inorganic oxy-acids of phosphorus and sulphur and their six-membered and open-chain analogues. The five-membered cyclic phosphates [2-6] and phosphonates [7] hydrolyse $10^5$—$10^8$ times faster than their open-chain analogues. Similarly the five-membered aromatic sulphate, *o*-phenylene sulphate hydrolyses $2 \times 10^7$ times faster than diphenyl sulphate [8] and *o*-hydroxytoluene-α-sulphonic acid sultone shows a rate enhancement of $7 \times 10^6$ over its open-chain analogue, phenyl toluene-α-sulphonate.[9,10]

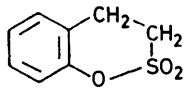
The cause of kinetic acceleration in cyclic esters has been the subject of much speculation and was originally thought to be associated principally with some form of ring strain. Thermochemical measurements showed [11] that ethylene phosphate is indeed strained relative to open-chain phosphates by *ca.* 21—25 kJ $mol^{-1}$, and that this enthalpy strain is one of the major factors responsible for kinetic acceleration in cyclic phosphates. This has been further confirmed by *X*-ray crystallographic structure determinations on five-membered cyclic phosphates which indicate considerable angle strain in the ring arising from small O–P–O bond angles, *e.g.* for *o*-phenylene cyclic phosphate the endocyclic O–P–O bond angle is 98.4°.[12] It has been suggested that angle strain is the dominant part of the overall strain energy of such systems.[13]

The important observation [5,14] that kinetic acceleration is observed for five-membered cyclic phosphates, not only for ring-opening saponification but also for reactions not involving ring cleavage such as oxygen exchange and hydrolysis of groups external to the ring, led to the suggestion that such reactions proceed through a trigonal bipyramidal intermediate which can undergo pseudorotation.[15] Thus ring strain in the five-membered ring is reduced, without ring opening, in a transition state that has a naturally small O–P–O bond angle.

In recent years, the importance of entropy contributions to the increased rates of reaction of five-membered cyclic esters has been recognised. Thus determination of the Arrhenius parameters for the alkaline hydrolysis of cyclic and open-chain phosphonyl compounds shows that the high reactivity of the five-membered oxaphospholan ring is due to a combination of both enthalpy and entropy strain.[16] On the other hand, entropy strain is the main cause of the observed kinetic acceleration in the alkaline hydrolyses of cyclic sulphite and sulphinate esters.[17,18] It has been assumed, however, that the major cause of the high reactivity of cyclic sulphonates is due to ring strain.[19]



(1)



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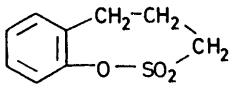


(3)

$PhCH_2 \cdot SO_2 \cdot OPh$

(4)

$PhSO_2 \cdot OPh$

(5)

In an attempt to examine the relative importance of entropy and enthalpy strain on kinetic acceleration in cyclic sulphonates, we now report a detailed study of the activation parameters for the alkaline hydrolysis of a number of cyclic and open-chain aromatic sulphonates (1)—(5).

## EXPERIMENTAL

*Materials.*—The sulphonates were prepared by standard methods. *o*-Hydroxytoluene-α-sulphonic acid sultone (1), recrystallised from ethanol, had m.p. 86—87° (lit.,[20] 86°), β-2-hydroxyphenylethanesulphonic acid sultone (2), recrystallised from ether, had m.p. 110—111° (lit.,[21] 111—112°), γ-2-hydroxyphenylpropanesulphonic acid sultone (3), recrystallised from ether, had m.p. 132—133° (lit.,[22] 132°), phenyl toluene-α-sulphonate (4), recrystallised from light petroleum (b.p. 40—60°) had m.p. 86.5—87.5° (lit.,[9] 86.7—87.1°), and phenyl benzenesulphonate (5) had b.p. 118—120° at 0.5 mmHg (lit.,[23] 191—192° at 10 mmHg).

*Kinetic Measurements.*—The rates of alkaline hydrolysis

were determined spectrophotometrically by following the characteristic absorption of the phenolic products; 2-hydroxytoluene-α-sulphonic acid sultone 280 nm; β-2-hydroxyphenylethanesulphonic acid sultone 290 nm; γ-2-hydroxyphenylpropanesulphonic acid sultone 290 nm; phenyl α-toluenesulphonate 287 nm; phenyl benzenesulphonate 235 nm. Spectrophotometric measurements were made on a Unicam SP 800 spectrometer operating on a constant wavelength scan mode and fitted with an external recorder and a thermostat-controlled cell holder (±0.1°). Alkaline hydrolyses were carried out in either sodium hydroxide solutions containing a small amount (*ca.* 4%) of organic solvent to increase solubility or, in the case of the more reactive five-membered sultone (1), in boric acid buffer solution. It was assumed that the amount of organic solvent present did not affect the determination of the hydroxide-ion concentration from the apparent pH values for experiments carried out in buffer solutions. Furthermore, it was assumed that at this low level of organic solvent, the rate of hydrolysis and hence Arrhenius parameters are unaffected by variation in the organic solvent used. This was confirmed for the hydrolysis of (1) in both acetonitrile and DMSO.

The first-order rate coefficients, $k_1$, were determined at a number of different pH values for each compound studied at each temperature. Values of $k_1$ were calculated graphically and values of the second-order rate coefficients, $k_2$, were calculated numerically using values of [$OH^-$] or

TABLE 1

Alkaline hydrolysis of *o*-hydroxy-α-toluenesulphonic acid sultone at 39.1°

| pH | 9.32 | 8.85 | 8.48 |
|---|---|---|---|
| $10^5$[$OH^-$]/M | 5.75 | 1.95 | 0.507 |
| $10^3k_1/s^{-1}$ | 5.88 | 2.14 | 1.00 |
| $k_2$/l mol$^{-1}$ s$^{-1}$ | 104 | 110 | 118 |

graphically from plots of $k_1$ *versus* [$OH^-$]. For runs carried out in buffer solutions, values of [$OH^-$] were derived from measured pH values, the activity coefficient, $\gamma_{OH^-}$, of the hydroxide ion being taken as unity. Runs were carried out at least in duplicate and gave consistent results (Table 1).

*Influence of Temperature.*—The entropies ($\Delta S^\ddagger$) and enthalpies ($\Delta H^\ddagger$) of activation were calculated from the equation $k = kT/h \exp(\Delta S^\ddagger/R) \exp(-\Delta H^\ddagger/RT)$ by a least-squares procedure from data at various temperatures (Table 2).

TABLE 2

Second-order rate coefficients $k_2$/l mol$^{-1}$ s$^{-1}$ for the alkaline hydrolysis of sulphonate esters (1)—(5)

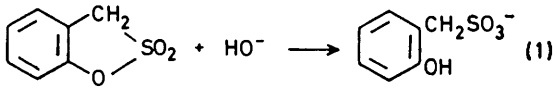
| *T*/°C | 24.6 | 32.7 | 36.8 | 39.1 | 45.2 |
|---|---|---|---|---|---|
| $k_2$ (1) [a] | 49 | 76 | 100 | 110 | 157 |
| *T*/°C | 24.5 | 30.6 | 33.0 | 37.9 | 45.0 |
| $10^3k_2$ (2) [a] | 1.61 | 2.83 | 3.38 | 5.22 | 10.0 |
| *T*/°C | 40.0 | 44.9 | 49.5 | 54.5 | 58.0 |
| $10^5k_2$ (3) [b] | 5.10 | 7.65 | 11.8 | 18.5 | 25.1 |
| *T*/°C | 32.0 | 40.0 | 42.5 | 51.0 | 56.0 |
| $10^4k_2$ (4) [c] | 1.60 | 3.92 | 5.41 | 15.2 | 28.4 |
| *T*/°C | 34.6 | 41.1 | 45.4 | 50.3 | 55.6 |
| $10^4k_2$ (5) [d] | 5.40 | 10.2 | 14.8 | 22.9 | 35.5 |

[a] 4% MeCN. [b] 4% DMSO. [c] 4% DME. [d] 4% Dioxan.

## DISCUSSION

It is unlikely that alkaline hydrolysis of aryl sulphonates would involve nucleophilic attack at the aromatic carbon atom. Using oxygen-18 tracer techniques, Bunton and Frei showed that the alkaline hydrolysis of phenyl toluene-*p*-sulphonate involved attack at sulphur with fission of the sulphur–oxygen bond.[24] Similar results were found for the hydrolysis of sulphate esters. Thus the five-membered *o*-phenylene cyclic sulphate hydrolyses in alkaline solution to the half-ester with sulphur–oxygen bond fission.[25]

Our kinetic results (Table 1) are consistent with those of earlier workers [9,24] who showed that the alkaline hydrolyses of both cyclic and open-chain aryl sulphonates, *e.g.* of *o*-hydroxytoluene-α-sulphonic acid sultone (1) and phenyl toluene-*p*-sulphonate follow second-order kinetics consistent with the overall reactions shown in equations (1) and (2). The kinetic and bond-fission




(1)

$$p\text{-}MeC_6H_4SO_2\cdot OPh + HO^- \longrightarrow p\text{-}MeC_6H_4SO_3^- + PhOH \quad (2)$$

studies suggest that the hydrolyses of phenyl arenesulphonates proceed *via* nucleophilic attack of hydroxide ion at sulphur. For the cyclic sulphonates studied in the present work and phenyl toluene-α-sulphonate (5), however, other mechanisms not involving direct attack of hydroxide ion at sulphur are possible. Two such mechanisms involving the formation of carbanions and/or sulphenes as intermediates are shown in equations (3) and (4) for the hydrolysis of (1).

From a study of the hydrolysis of sultone (1) in $D_2O$–$OD^-$ solution, Kaiser and his co-workers showed that a carbanion is formed rapidly and reversibly from the sultone in basic solution.[26] They were able to eliminate the concerted mechanism [equation (3)] as a major reaction pathway and furthermore, concluded that a carbanion–sulphene mechanism as shown in equation (4) does not provide an important pathway for the hydrolysis of the five-membered sultone.

More recently Williams and his co-workers have shown [27,28] that the hydrolysis and aminolysis of aryl toluene-α-sulphonates proceeds *via* a stepwise elimination–addition mechanism (*E*1cB) involving a sulphene intermediate (Scheme 1). Evidence for the formation

$$PhCH_2SO_2OAr + B \rightleftharpoons Ph\bar{C}HSO_2OAr + BH^+$$

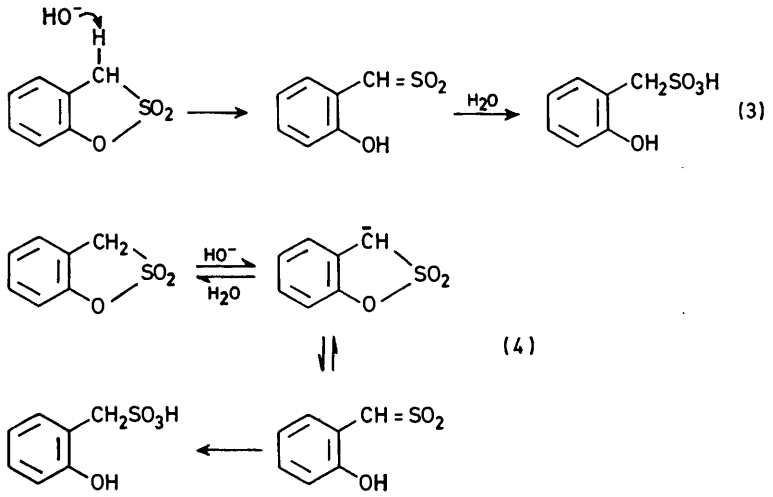
$$Ph\bar{C}HSO_2OAr \longrightarrow PhCH{=}SO_2 + ArO^-$$

$$PhCH{=}SO_2 + H_2O + B \longrightarrow PhCH_2SO_3^- + BH^+$$

SCHEME 1

of a sulphene intermediate *via* an *E*1cB mechanism has also been reported by King and Beatson.[29] Williams also proposed [27,28] that the *E*1cB mechanism for the hydrolysis of five-membered cyclic sulphonate esters is sterically suppressed. Thus molecular orbital calculations using the CNDO/2 program suggest that the

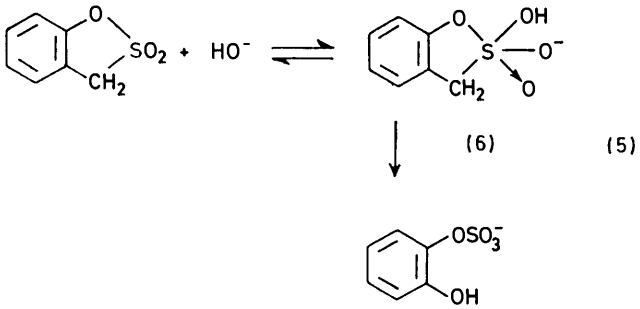
planar configuration of the parent sulphene $CH_2SO_2$ with all bond angles fixed at 120° is 147 kJ $mol^{-1}$ more stable than the perpendicular form [30,31] in which the OSO plane is perpendicular to the $H_2CS$ plane. The transition state for the elimination of the phenoxide ion from an acylic sulphonyl carbanion would therefore be expected to resemble the planar form of the sulphene. On the other hand, for the five-membered cyclic sulphonate, although the benzylic proton is labile and the phenoxide ion is a good leaving group, the *E*1cB




mechanism is suppressed because the transition state for this reaction can only lead to the high-energy perpendicular sulphene.[27,28] Thus any differences in the rates of alkaline hydrolysis of sultones and of phenyl benzenesulphonate which does not possess a labile hydrogen atom and cannot hydrolyse by an *E*1cB mechanism, should reflect the differences in the rate of attack at sulphonyl sulphur in cyclic and acyclic esters.

*Mechanism of Nucleophilic Attack.*—There has been considerable speculation as to whether nucleophilic substitution at sulphonyl sulphur proceeds *via* an $S_N2$-type mechanism with synchronous bond-forming and -breaking, or whether bond formation is complete before bond-breaking starts to occur. The latter situation would imply the existence of a pentaco-ordinate intermediate. Attempts to detect the presence of such chemical species in nucleophilic substitution reactions have been unsuccessful. No oxygen-18 exchange could be detected in the unhydrolysed sulphonate recovered after partial hydrolysis in alkaline solution of either phenyl toluene-*p*-sulphonate,[24-32] 2-hydroxytoluene-α-sulphonic acid sultone (1), or β-2-hydroxyphenylethanesulphonic acid sultone (2).[25] These results show that in such reactions, *e.g.* in the hydrolysis of (1), it is not possible to detect the reversible formation of intermediates such as (6), in which the exocyclic oxygen atoms have become equilibrated [equation (5)].

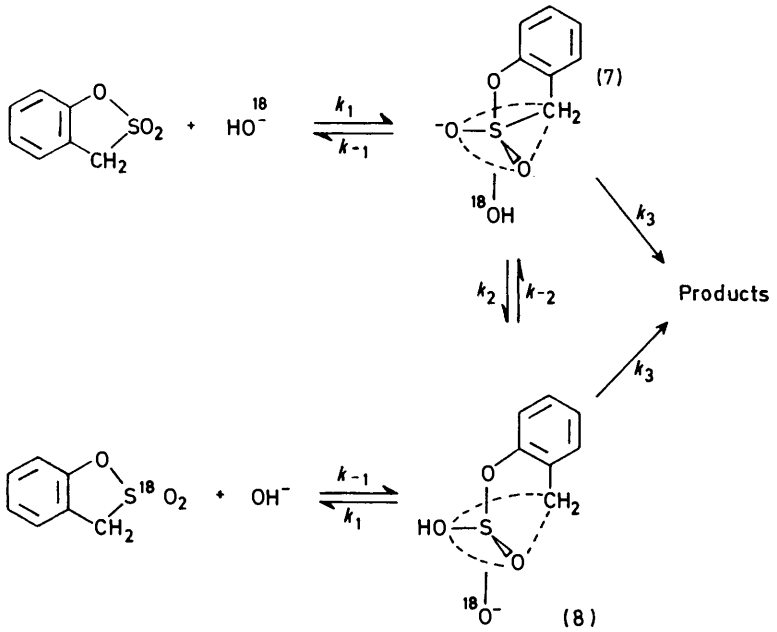
As originally pointed out by Bender,[33] however, the lack of back exchange does not rule out the existence of an intermediate since the rate of oxygen equilibration of an intermediate might be much slower than its rate of decomposition and hence no oxygen exchange would be observed. If an intermediate were formed in the hydrolysis of sulphonates it seems reasonable to suppose, by analogy with substitution reactions at phosphorus, that it would have trigonal bipyramidal geometry. Kaiser and Kézdy pointed out [34] that the failure to observe oxygen exchange in the hydrolysis of sultones can be predicted if the preference rules which apply to the pseudorotation of intermediates in phosphate ester hydrolysis can be applied to pentaco-ordinate sulphur intermediates. Thus since negatively charged groups would be expected to occupy equatorial positions, equilibration of oxygen atoms in a trigonal bipyramidal intermediate *via* a simple proton transfer as in (7) ⟶ (8), which would place an $O^-$ group in an apical position,




would be very slow compared to the breakdown of the intermediate in either the forward or reverse directions, *i.e.* $k_1$ and $k_2 \gg k_3$ (Scheme 2).

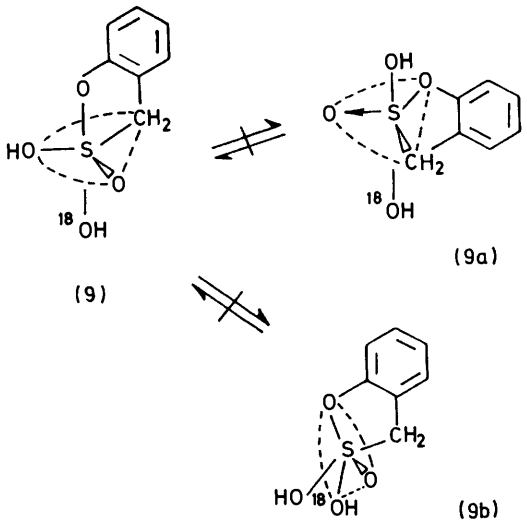
It is possible to envisage an alternative route for oxygen exchange of (7) involving first protonation of $O^-$, then pseudorotation followed by deprotonation (Scheme 3). Such a mechanism is, however, not possible for *o*-hydroxytoluene-α-sulphonic acid sultone. The trigonal bipyramidal intermediate (9) derived from (7) by protonation cannot readily undergo pseudorotation [(9) ⟶ (9a)] which would expand the ring angle to 120°, whereas pseudorotation about O would push the ring

methylene group into an unfavourable apical position. The conjugate acid of (7) is therefore frozen in the trigonal bipyramid form (9). The situation is similar to that observed for the methyl ester of propylphosphoric acid which hydrolyses with 99.8% ring-opening but with




SCHEME 2

<0.2% exocyclic cleavage [35] and for the hydrolysis of cyclic sulphinates.[18] Even if a mechanism were available for pseudorotation of an intermediate in the alkaline hydrolysis of sulphonates, it has been suggested

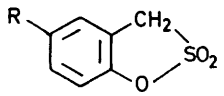


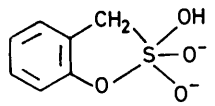

SCHEME 3

that such a process would be much slower than at phosphorus.[36]

Kaiser and Zaborsky have studied [37] the alkaline hydrolysis of a series of 5-substituted 2-hydroxytoluene-α-sulphonic acid sultones (10). The rates of hydrolysis are fairly sensitive to substituent effects but the ρ value obtained (+1.23) does not provide a method of distinguishing between addition–elimination and $S_N2$-type mechanisms.

If pentaco-ordinate intermediates are involved in the hydrolysis of sulphonate esters, then a formal possibility is that species like (6) might ionize in basic media to give the corresponding dianion, such as (11). A kinetic term second-order in hydroxide-ion on concentration has been found for the alkaline hydrolysis of anilides.[38] This was interpreted in terms of the ionization of a tetrahedral intermediate formed by addition of hydroxide ion to the carbonyl carbon. Kaiser and his co-workers observed [39] only a first-order dependence on hydroxide-ion concentration in strongly basic solutions for the hydrolyses of β-2-hydroxyphenylethane- and γ-2-hydroxyphenylpropane-sulphonic acid sultones (2) and (3), indicating




that if pentaco-ordinate intermediates are involved in the hydrolysis of sulphonate esters, reaction will occur through a monoanionic species.

A large number of sulphuranes, compounds of sulphur(IV) in which four ligands are attached to sulphur, and sulphurane oxides have been prepared and isolated by Martin and his co-workers.[40] Such compounds have been shown to have a trigonal bipyramidal structure. Evidence for the occurrence of pseudorotation of such structures has been adduced from $^{19}F$ n.m.r. and other studies.[41–44] In the absence of definite evidence to the

contrary we assume that nucleophilic substitution reactions at sulphur occur *via* a trigonal bipyramidal intermediate.

*Kinetic Acceleration in Sultones.*—The relative reactivity (at 39°) towards hydroxide ion attack on going from the five-, six-, and seven-membered sultones to the open-chain phenyl benzenesulphonate change in the order $110 : 5.2 \times 10^{-3} : 5.1 \times 10^{-5} : 1 \times 10^{-3}$ (Table 3). This data compares fairly closely with that of Kaiser and his co-workers who, however, did not determine Arrhenius parameters. Thus $k_{(1)}/k_{(2)} \sim 2 \times 10^4$ (*cf.*[9] $2.3 \times 10^4$) and $(k_{(1)}/k_{(2)} \sim 4.5 \times 10^5$ (*cf.*[9] $6.8 \times 10^5$). Our values obtained for activation parameters are shown in Table 3. The differences in reactivity between the

TABLE 3

Arrhenius parameters and relative rates for the alkaline hydrolysis of sulphonate esters

| Sulphonate | $k_{rel.}$ | $\Delta H^{\ddagger}$/ kJ mol$^{-1}$ | $\Delta S^{\ddagger}$/ J K$^{-1}$ mol$^{-1}$ * |
|---|---|---|---|
| (1) [a] | 110 | 45.3 ± 0.8 | −61.2 ± 29 |
| (1) [b] | 106 | 43.6 ± 0.8 | −67.0 ± 2.1 |
| (2) | $5.2 \times 10^{-3}$ | 67.0 ± 1.3 | −72.5 ± 4.3 |
| (3) | $5.1 \times 10^{-5}$ | 74.2 ± 1.3 | −90.1 ± 3.8 |
| (4) | $3.9 \times 10^{-4}$ | 98.0 ± 2.6 | +2.89 ± 4.2 |
| (5) | $1 \times 10^{-3}$ | 72.5 ± 0.4 | −71.2 ± 2.1 |

* Calculated at 30 °C.

[a] 4% MeCN. [b] 4% DMSO.

five-membered sultone and other sulphonate esters are seen to arise from a combination of both enthalpy and entropy strain. This is unexpected since it has previously been assumed that enthalpy strain was the main cause of kinetic acceleration in the hydrolysis of the five-membered sultone.

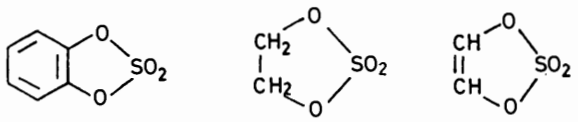
As the ring size decreases from seven to five, the entropy of activation becomes more favourable. The effect on the entropy of activation is explicable in terms of the 'entropy-strain' principle.[45] In the transition state for hydrolysis, the molecule takes up a more ordered structure and the molecular motions of the six- and seven-membered and open-chain sulphonates are suppressed. This loss of entropy increases the free energy of activation. For the relatively rigid five-membered sultone (1), the molecule is already constrained and there is relatively small loss of entropy in reaching the transition state and hence (1) has the smallest negative entropy of activation, resulting in a lower free energy of activation.

The reactivity and Arrhenius parameters of phenyl benzenesulphonate are somewhat anomalous because of the use of this compound with one $CH_2$ group less than sultone (1) as the open-chain reference compound, although the value of $\Delta S^{\ddagger}$ is likely to provide a good indication of the value to be expected for an open-chain diaryl sulphonate. The different mechanism of hydrolysis (*E*1cB) of phenyl toluene-α-sulphonate shows up clearly in the value of the entropy of activation, $\Delta S^{\ddagger} \sim 2.9$ J K$^{-1}$ mol$^{-1}$ (30°), which is dramatically different from that of any of the other sulphonates studied.

Izbicka and Bolen have recently determined the enthalpy changes accompanying the alkaline hydrolysis of the five- and six-membered sultones (1) and (2) by calorimetry.[46] The values obtained were −181.8 and −83.7 kJ mol$^{-1}$ respectively. The larger heat of hydrolysis for (1) is consistent with the larger ring strain present in the five-membered ring. The actual value of the differences in $\Delta H_{hyd}$ of the two systems is, however, surprisingly large and suggests a much greater strain difference than that predicted by the difference in rates of alkaline hydrolysis.

*Ring Strain in Cyclic Sulphonates.*—The origin of ring strain in five-membered cyclic esters has been the subject of much speculation which has centred around three possible causes, *viz.* (*a*) angle strain,[47] and (*b*) strain-induced changes in the 2*p*–3*d* π-character of the endocyclic heteroatom bonds [7,48] and 1,3-non-bonding interactions between the oxygen atoms.[49]

The presence of considerable ring strain in five-membered cyclic sulphates and sulphonates has been confirmed by *X*-ray structure analysis. The six-membered sultone (2) which undergoes hydrolysis only some ten times faster than its open-chain analogue (4) is much less strained than the five-membered ring (1) having a much larger internal C–S–O bond angle of 101.4° and a larger C–O–S bond angle of 116.5° (compared to 108.9°).[50] Thus much less perturbation of the ring angle at sulphur is required to achieve a transition state geometry favourable to reaction at sulphur in the five-membered sultone. Similarly Boer and Flynn have



(12) (13) (14)

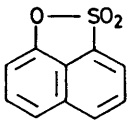
shown [51] that all the angles in *o*-phenylene sulphate (12) are strained. The O–S–O bond angle of 97.1° is well below that of the tetrahedral angle, the O–C–C angles are distorted to values of 112.5 and 110.7°, well below the normal angle for $sp^2$-hybridised carbon. The two S–O–C angles (108.6°) are also considerably lower than expected for an acyclic diester.[51] Kaiser and his co-workers [52] detected considerable ring strain in ethylene sulphate (13) with an internal O–S–O bond angle of 98.4°, similar to that found in *o*-phenylene sulphate. A related compound of considerable interest is the very reactive vinylene sulphate (14). This has [52] an O–S–O bond angle of 93.6°, very close to that required for a trigonal bipyramidal intermediate for alkaline hydrolysis. Another interesting feature of (14) is that the C–O bond distance is only 1.24 Å compared with 1.46 Å in (13), and the internal S–O bond length is 1.62 Å compared with 1.53°.

The earlier proposal that 2*p*–3*d* π-bonding between the endocyclic oxygen atoms and the heteroatom could induce ring strain in cyclic phosphate esters has now been largely discarded. Although n.m.r. studies have

shown that phosphorus nuclei in strained cyclic phosphoranes are more shielded than their unstrained alicyclic analogues,[48] this effect does not appear to originate from ring strain because *X*-ray studies could detect no difference in the corresponding endo- and exo-cyclic P–OC bond lengths.[53] Boer and Flynn have suggested [51] that any changes in multiple-bond character of sulphur and phosphorus cyclic esters are more likely to be electronic in origin.

*X*-Ray studies [51] of *o*-phenylene sulphate (12) have shown that the five-membered ring is unexpectedly distorted to a non-planar envelope structure where the sulphur atom lies 0.249 Å above a plane through the six carbon and two oxygen atoms. It was suggested that the most likely cause of such an effect was 1,3-interactions between the lone pairs of the ring oxygen and the exocyclic oxygen atoms. Such interactions could be minimised in the five-membered ring by bending into a non-planar conformation. Davis predicted [54] on theoretical grounds that whereas such interactions are negligible in the five-membered ring of ethylene sulphite with only one exocyclic oxygen atom, they could be larger in a cyclic ester with four oxygen atoms attached to phosphorus or sulphur as in phosphates or sulphates.

It seems likely, therefore, that although the major cause of enthalpy strain observed in the alkaline hydrolyses of sulphate and sulphonate esters arises from angle strain, lone-pair–lone-pair repulsions may also contribute to the observed destabilization of the five-membered ring. In this connection it is interesting to note that in contrast to the behaviour of the sultone (15) which hydrolyses $10^7$ times faster than its open-chain analogue,[9] the α-disulphone (16) which contains no ring oxygen atoms shows a similar reactivity to that of phenyl α-disulphone.[55]

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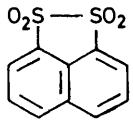


(16)

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