of pK_{BH^+} values. The data in Table III therefore seem concordant with our view that the H_C scale is more appropriate to the protonation of carbon bases of the type discussed in this paper than the $H_{R'}$ scale, or any acidity scale that has been presented to date.

Acknowledgment. I wish to thank Professor F. A. Long for suggesting this project, for providing his laboratory facilities, and for very many helpful discussions. This work was supported by a grant from the Atomic Energy Commission to Cornell University.

Quantitative Comparison of Nucleophilic Substitution at Sulfonyl *vs.* Sulfinyl Sulfur. The Hydrolysis of Aryl α-Disulfones in Aqueous Dioxane[1a]

John L. Kice and George J. Kasperek[1b]

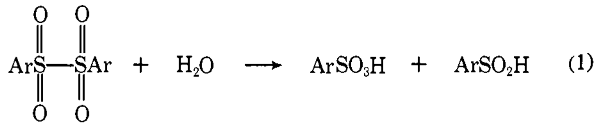
Contribution from the Department of Chemistry, Oregon State University, Corvallis, Oregon 97331. Received April 21, 1969

Abstract: The spontaneous (uncatalyzed) hydrolysis of aryl α-disulfones (eq 1) has been studied kinetically in acidic aqueous dioxane. Because this reaction differs from the previously investigated[2] spontaneous hydrolysis of aryl sulfinyl sulfones (eq 2) only in that eq 1 involves nucleophilic substitution at sulfonyl ($>SO_2$) sulfur while eq 2 involves substitution at sulfinyl ($>SO$) sulfur, the data for the two reactions (Table II) provide a *quantitative* comparison of the influence of various important reaction variables on nucleophilic substitution at sulfonyl *vs.* sulfinyl sulfur. This comparison reveals that, despite the fact that the substitution at sulfinyl sulfur is 10^4 times faster than the one at sulfonyl sulfur, the two reactions show a remarkable similarity in (1) dependence of rate on aryl group structure, (2) increase in rate with water content of the solvent, (3) solvent isotope effect, and (4) $\Delta S^{\ddagger}$. The large difference in rate arises solely as a result of a 6.0-kcal/mole difference in activation energy. The conclusion is that analogous nucleophilic substitutions at sulfonyl and sulfinyl sulfur do not differ significantly in their detailed mechanism: nucleophilic substitution at sulfonyl sulfur is much slower merely because of a less favorable activation energy. The large solvent isotope effect ($k_{H_2O}/k_{D_2O} = 2.3$) for α-disulfone hydrolysis indicates that a proton transfer is part of the rate-determining step of that reaction. Various mechanisms including this feature are discussed, and it is concluded that a mechanism (eq 8) involving a concerted proton transfer from the attacking water molecule to the departing $ArSO_2$ group is the most satisfactory one on the basis of presently available evidence. Finally, comparison of the spontaneous hydrolysis of α-disulfones with that of aryl sulfonic anhydrides (eq 3) shows that in reactions of the type under consideration a change in the character of the leaving group is apparently much more likely to lead to a significant change in mechanism than is a change in the site where substitution occurs from sulfonyl to sulfinyl sulfur.

Quantitative comparison of various important characteristics of nucleophilic substitution reactions occurring at different oxidation states of sulfur should contribute much to a better understanding of some of the general principles governing such processes. One pair of oxidation states that it is of great interest to compare in this way is sulfinyl sulfur ($>S{=}O$) and sulfonyl sulfur ($>SO_2$).

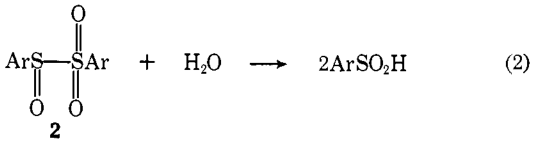
For such a comparison to be truly meaningful one must take pains to select two reactions which differ *only* in the oxidation state of the sulfur being attacked, and where all else, such as the nature of the group being displaced, nature of the attacking nucleophile, solvent medium, etc., is identical. The principal deterrent which has prevented such a study in the past has undoubtedly been the fact that most sulfinyl compounds undergo substitution so much faster than their sulfonyl counterparts that it is not easy to find a pair of reactions where the rates for both sulfinyl and sulfonyl compound are accurately measurable under the same conditions.

We have now been able to make the first such quantitative comparison of substitution at sulfinyl and sulfonyl sulfur by obtaining data on the spontaneous hydrolysis of aryl α-disulfones (eq 1) in aqueous dioxane and comparing it with the extensive results already available[2] on the spontaneous hydrolysis of aryl sulfinyl sulfones (eq 2) in the same medium. As is readily evident the two



$$\mathrm{Ar\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}Ar + H_2O \longrightarrow ArSO_3H + ArSO_2H} \qquad (1)$$

1



$$\mathrm{Ar\underset{\underset{O}{\|}}{S}{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}Ar + H_2O \longrightarrow 2ArSO_2H} \qquad (2)$$

2

reactions meet our requirements that the leaving group ($ArSO_2$), the solvent medium, and the substituting nucleophile (H_2O) should be exactly the same for both reactions and differ only in that eq 1 involves substitution at sulfonyl sulfur while eq 2 involves substitution at sulfinyl sulfur.

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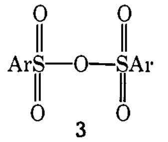
[1] (a) This research supported by the National Science Foundation Grant GP-6952; (b) NDEA Fellow, 1966–1969.

[2] J. L. Kice and G. Guaraldi, *J. Am. Chem. Soc.*, **89**, 4113 (1967).

It is also of interest to compare certain characteristics of the spontaneous hydrolysis of **1** with those of other aryl sulfonyl derivatives possessing different leaving groups, such as sulfonic anhydrides[3] (**3**) and sulfonyl chlorides[4] (**4**). This comparison reveals that changes in the character of the leaving group can lead to quite significant alterations in certain important details of the mechanisms of these substitutions at sulfonyl sulfur.


$\mathrm{Ar\overset{O}{\underset{O}{S}}{-}O{-}\overset{O}{\underset{O}{S}}Ar}$

3


$\mathrm{Ar\overset{O}{\underset{O}{S}}Cl}$

4

Results

Kinetics of Hydrolysis of Aryl α-Disulfones in Acidic Aqueous Dioxane. Aryl α-disulfones (**1**) had been reported[5] to undergo a slow spontaneous hydrolysis (eq 1) into a molecule each of sulfonic and sulfinic acid. Actually we find that their spontaneous hydrolysis in acidic aqueous dioxane at temperatures in the neighborhood of 80° is considerably faster than one might have gathered from the fragmentary statements in the earlier literature[5] and that it can be followed very conveniently by ultraviolet spectrophotometry in the region 240–290 mμ.[6] Plots of log $(A - A_\infty)$ *vs.* time showed excellent linearity in all cases, demonstrating that the hydrolysis of **1** in acidic aqueous dioxane follows clean first-order kinetics.

Table I lists the first-order rate constants (k_h) observed for the hydrolysis of different **1** in aqueous dioxane under the various reaction conditions investigated. A number of aspects of these results merit brief comment.

(1) It is evident (section A, Table I) that variation of the concentration of added perchloric acid from 0.001 to 2.0 *M* leads to no significant variation in the rate of hydrolysis of phenyl α-disulfone. Thus the hydrolysis of α-disulfones is not subject to detectable acid catalysis, and the values of k_h in Table I may be equated in each instance with the rate of spontaneous (or uncatalyzed) hydrolysis of **1**. The experiments with added lithium perchlorate indicate that the spontaneous hydrolysis rate is not subject to any large salt effects.

(2) A plot of log k_h *vs.* $1/T$ for the data in section B of Table I gives $E_a = 14.6$ kcal/mole and $\Delta S^{\ddagger} = -37.7$ eu for the spontaneous hydrolysis of phenyl α-disulfone. Large negative entropies of activation have been observed before for other spontaneous hydrolyses in aqueous dioxane.[2,4a,7]

(3) The spontaneous hydrolysis of phenyl α-disulfone shows a rather large solvent isotope effect, $(k_{H_2O}/k_{D_2O}) = 2.3$, being considerably faster in 60% dioxane–40% H_2O than in 60% dioxane–40% D_2O.

Table I. Kinetics of Hydrolysis of Aryl α-Disulfones in Acidic Aqueous Dioxane

Ar in **1**[a]	Solvent	Temp °C	$HClO_4$, *M*	Li-ClO_4, *M*	$k_h \times 10^4$, sec^{-1}
	A. Effect of Acidity and Ionic Strength				
C_6H_5	60% dioxane (v/v)	80.3	0.001	0.00	1.05
			0.01	0.00	1.00
			0.10	0.00	0.89
			1.00	0.00	1.09
			2.00	0.00	0.93
			0.001	0.01	1.10
			0.001	0.10	1.21
			0.01	0.40	1.13
	B. Effect of Temperature				
C_6H_5	60% dioxane (v/v)	94.3	0.01	0.00	1.92
		88.9	0.01	0.00	1.48
		80.3	0.01	0.00	1.00
		70.5	0.01	0.00	0.55
		58.8	0.01	0.00	0.26
		49.2	0.01	0.00	0.12
	C. Solvent Isotope Effect				
C_6H_5	60% dioxane–40% D_2O	80.3	0.001	0.00	0.466
	D. Effect of Solvent Composition				
C_6H_5	70% dioxane (v/v)	80.3	0.01	0.00	0.44
	60% dioxane (v/v)	80.3	0.01	0.00	1.00
	50% dioxane (v/v)	80.3	0.01	0.00	2.60
	40% dioxane (v/v)	80.3	0.01	0.00	4.87
	E. Effect of Aryl Group Structure				
p-$CH_3OC_6H_4$	60% dioxane (v/v)	80.3	0.01	0.00	0.084
p-$CH_3C_6H_4$	60% dioxane (v/v)	80.3	0.01	0.00	0.29
C_6H_5	60% dioxane (v/v)	80.3	0.01	0.00	1.00
p-ClC_6H_4	60% dioxane (v/v)	80.3	0.01	0.00	5.54
p-BrC_6H_4	60% dioxane (v/v)	80.3	0.01	0.00	6.40

[a] Initial concentration of **1**, 5×10^{-5} *M*.

(4) The rate of hydrolysis increases markedly with an increase in the water content of the solvent medium (section D, Table I), being slightly over 10 times faster in 40% dioxane than it is in 70% dioxane.

(5) The rate of spontaneous hydrolysis of **1** is strongly dependent on the structure of the aryl group (section E, Table I), electron-releasing substituents like *p*-MeO or *p*-Me retarding the rate markedly and electron-attracting ones like *p*-Cl or *p*-Br accelerating it. A plot of log k_h *vs.* σ_p for the *para* substituent in the aromatic ring indicates that ρ for the spontaneous hydrolysis of **1** is +3.5. (One should, of course, remember that since going from one α-disulfone to another means a change in the substituent in both rings of **1**, this ρ value is really not as large as it may at first appear.)

Discussion

This section will be divided into three parts. The first will deal with a quantitative comparison of nucleophilic substitution at sulfinyl (>S=O) and sulfonyl sulfur (>SO_2), making use of data on the spontaneous hydrolyses of aryl α-disulfones (eq 1) and aryl sulfinyl sulfones[2] (eq 2). The second will outline our view of the probable mechanism of the spontaneous hydrolysis of α-disulfones (**1**). The third will examine the effect of a change in leaving group on the spontaneous hydrolysis of sulfonyl derivatives in aqueous dioxane by comparing our data for **1** with those for aryl sulfonic anhydrides (**3**) recently reported by Christensen,[3] and to a

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[3] N. H. Christensen, *Acta Chem. Scand.*, **20**, 1955 (1966); **21**, 899 (1967).

[4] (a) R. V. Vizgert, *Russ. Chem. Rev.*, **32**, 1 (1963); (b) G. Geissler, P. Hermann, K. H. Reps, and R. Wustner, *Z. Phys. Chem.* (Liepzig), **221**, 185 (1962); (c) R. E. Robertson and P. M. Laughton, *Can. J. Chem.*, **35**, 1319 (1957).

[5] Houben-Weyl, "Methoden der organischen Chemie," Vol. 9, 4th ed, Georg Thieme Verlag, Stuttgart, 1955, p 255.

[6] The exact wavelength used depends on the nature of the Ar group in **1** (see Experimental Section).

[7] (a) C. A. Bunton and S. G. Perry, *J. Chem. Soc.*, 3070 (1960); C. A. Bunton, N. A. Fuller, S. G. Perry, and I. H. Pitman, *ibid.*, 4478 (1962); C. A. Bunton, N. A. Fuller, S. G. Perry, and V. J. Shiner, *ibid.*, 2918 (1963); (b) E. Berliner and L. H. Altschul, *J. Am. Chem. Soc.*, **74**, 4410 (1952).

Table II. Comparison of Spontaneous Hydrolyses of Aryl α-Disulfones and Aryl Sulfinyl Sulfones in Aqueous Dioxane

Reaction variable	Spontaneous hydrolysis of $ArSO_2SO_2Ar$	 $ArS(O)SO_2Ar$[a]
(k_{H_2O}/k_{D_2O}) in 60% dioxane[b]	2.3	2.7
Solvent composition, relative rate[b]		
40% dioxane	4.9	6.1
50% dioxane	2.6	3.1
60% dioxane	(1.0)	(1.0)
70% dioxane	0.44	0.33
Aryl group, relative rate[c]		
p-$CH_3OC_6H_4$	0.084	0.13
p-$CH_3C_6H_4$	0.29	0.31
C_6H_5	(1.0)	(1.0)
p-ClC_6H_4	5.5	6.7
ρ (from plot of log k *vs.* σ)	+3.5	+3.4
Rates and activation parameters for Ar = C_6H_5 in 60% dioxane		
Rate constant at 21.4°	1.5×10^{-6} sec^{-1}	1.6×10^{-2} sec^{-1}
E_a	14.6 kcal	8.8 kcal[d]
$\Delta S^{\ddagger}$	−37.7 eu	−37.1 eu[d]

[a] Data from ref 2. [b] Data for **1** are for Ar = C_6H_5 at 80.3°; those for **2** are for Ar = p-$CH_3C_6H_4$ at 21.4°. [c] Data for both **1** and **2** in 60% dioxane, at 80.3° for **1** and 21.4° for **2**. [d] Activation parameters for **2**, Ar = C_6H_5, estimated from those for **2** with Ar = p-$CH_3C_6H_4$ (E_a = 9.4 kcal; $\Delta S^{\ddagger}$ = −37.1 eu) by assuming all $k_{p\text{-H}}/k_{p\text{-CH}_3}$ due to a difference in E_a.

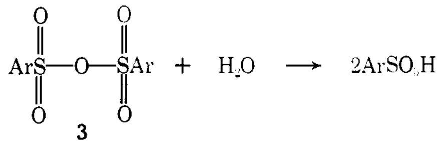
lesser extent with certain results[4] for aryl sulfonyl chlorides (**4**).

Comparison of Substitution at Sulfonyl and Sulfinyl Sulfur. Table II gives a tabular summary of the pertinent data on the spontaneous hydrolyses of α-disulfones (**1**) and sulfinyl sulfones (**2**). On examination of the table one is immediately struck by the very close similarity in the response of the two reactions to so many of the reaction variables, despite the fact that the substitution at sulfinyl sulfur (hydrolysis of **2**) occurs much faster than the one at sulfonyl sulfur (hydrolysis of **1**). Thus, the two reactions show almost the same dependence of rate on aryl group structure ($\rho = +3.5$ for the hydrolysis of **1** and $+3.4$ for the hydrolysis of **2**), approximately the same increase in rate with an increase in the water content of the solvent, and are characterized by almost identical large negative entropies of activation (−37.1 and −37.7 eu) in 60% dioxane. In this same solvent both are subject to quite large solvent isotope effects, k_{H_2O}/k_{D_2O} being 2.7 for the hydrolysis of the sulfinyl sulfone and only somewhat smaller, 2.3, for the hydrolysis of the α-disulfone. *The only truly significant differences between the two reactions are that the rate of spontaneous hydrolysis of the α-disulfone is about 10,000 times slower than the rate of spontaneous hydrolysis of the sulfinyl sulfone and that this large difference in hydrolysis rates arises* solely *from the fact that the activation energy for hydrolysis of* **1** *is about 6 kcal/mole larger than that for* **2**.

We conclude from this that analogous nucleophilic substitutions at sulfonyl and sulfinyl sulfur probably do not differ at all significantly as regards their detailed mechanism. Nucleophilic substitution at sulfonyl sulfur is merely much slower because of a significantly higher activation energy.

We have seen that for the two substitutions at sulfonyl and sulfinyl sulfur represented by eq 1 and 2 the one at sulfonyl sulfur is the slower by a factor of 10^4. From the data in an accompanying paper,[8] one finds $(k_{Nu}^{SO}/k_{Nu}^{SO_2})$ is also about 10^4 for acetate ion, a nucleophile which, according to the theory of hard and soft acids and bases,[9,10] is a base of hardness comparable to water, but that $(k_{Nu}^{SO}/k_{Nu}^{SO_2})$ is much larger ($\sim 10^7$) for nucleophiles like chloride or bromide ions which are softer bases than acetate or water. The rate ratio $(k_h^{SO}/k_h^{SO_2})$ of 10^4 which we have observed for eq 1 and 2 is thus representative only of substitutions at $>SO$ and $>SO_2$ involving nucleophiles of a hardness comparable to water, acetate, etc. With nucleophiles which are harder bases $(k_{Nu}^{SO}/k_{Nu}^{SO_2})$ will be smaller; with those which are softer bases it will be much larger.

Mechanism of the Spontaneous Hydrolysis of Aryl α-Disulfones. In contrast to the spontaneous hydrolysis of α-disulfones, the spontaneous hydrolysis of aryl sulfonic anhydrides[3] in 60% dioxane (eq 3) shows only



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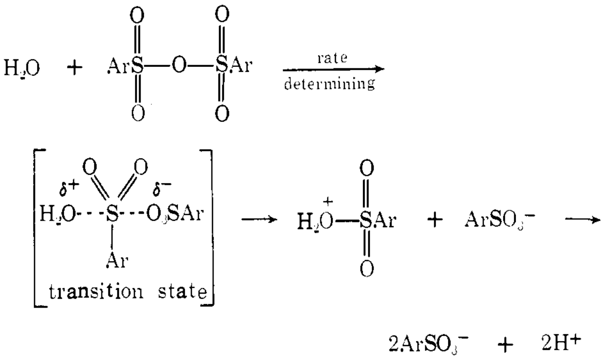
$$ArSO_2{-}O{-}SO_2Ar + H_2O \longrightarrow 2ArSO_3H \qquad (3)$$

a very small solvent isotope effect, $(k_{H_2O}/k_{D_2O}) = 1.2$. From this and the response of eq 3 to other reaction variables Christensen[3] has concluded that the rate-determining step of the spontaneous hydrolysis of **3** involves a simple attack of water on the sulfonyl group of **3** (eq 4). In particular, *no proton transfer is involved as part of the rate-determining step of the hydrolysis of* **3**.



$$H_2O + ArSO_2{-}O{-}SO_2Ar \xrightarrow[\text{determining}]{\text{rate}} \left[\overset{\delta+}{H_2O}\cdots S(O_2)(Ar)\cdots \overset{\delta-}{O_3SAr}\right] \longrightarrow H_2\overset{+}{O}{-}SO_2Ar + ArSO_3^- \longrightarrow 2ArSO_3^- + 2H^+ \qquad (4)$$

Since a large solvent isotope effect, $(k_{H_2O}/k_{D_2O}) = 2.3$, is observed for the spontaneous hydrolysis of α-disulfones, it is quite clear that the spontaneous hydrolysis of **1** does not proceed by a mechanism analogous to eq 4 in which a simple attack of water on the sulfonyl group constitutes the rate-determining step. Instead the large solvent isotope effect strongly suggests that *a proton transfer is involved as part of the rate-determining step of the hydrolysis of* **1**.

A priori, there are three plausible possible mechanisms for the spontaneous hydrolysis of **1** which involve a proton transfer as part of the rate-determining step. In the first of these one has general base catalysis by water of the attack of water on **1** (eq 5). The second possible mechanism (eq 6) postulates the reversible formation of an intermediate **5**, followed by a rate-determining step in which the scission of the S–S bond is accompanied by

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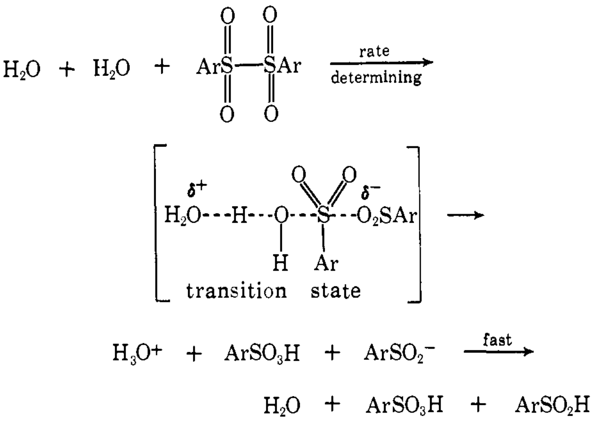
(8) J. L. Kice, G. J. Kasperek, and D. Patterson, *J. Am. Chem. Soc.*, **91**, 5516 (1969).

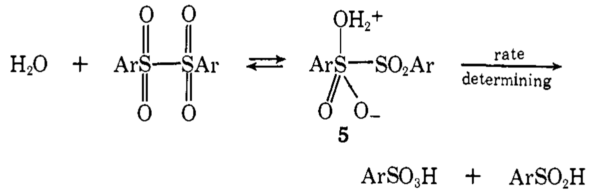
(9) R. G. Pearson and J. Songstad, *ibid.*, **89**, 1837 (1967).

(10) R. G. Pearson, *ibid.*, **85**, 3533 (1963).



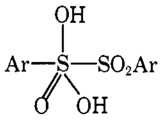
(5)

transfer of one of the protons in the intermediate to the departing $ArSO_2$ group.



(6)

One may, of course, also picture the intermediate as having structure **6**, rather than **5**. Another alternative would be the reversible formation of intermediate **7** (eq 7a) and its subsequent rate-determining breakdown in the manner shown in eq 7b.



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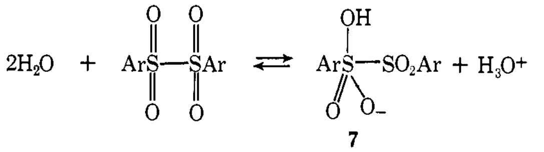
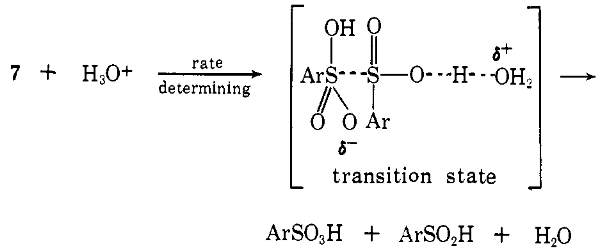


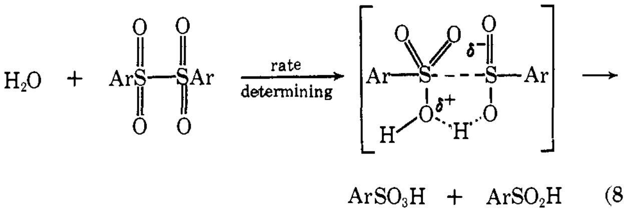
(7a)



(7b)

In the mechanism shown in eq 7a and 7b it is, however, of course *essential* that step 7b be rate determining. Otherwise the mechanism is not distinguishable in any significant way from that in eq 5.

In the third possible mechanism (eq 8) one once again has proton transfer to the leaving $ArSO_2$ group as part of the rate-determining step, but this time the formation of an intermediate such as **5**, **6**, or **7** is by-passed by making nucleophilic attack of water on the sulfonyl group concerted with the scission of the S–S bond and transfer of a proton from the incoming water molecule to the departing $ArSO_2$ group.[11]



(8)

In our opinion the mechanism in eq 5 is rendered unattractive by the observation[8] that acetate ion, a considerably stronger base than water, catalyzes the hydrolysis of **1** by a mechanism involving *nucleophilic* catalysis and *not* by one in which it functions as a general base. We feel that if the spontaneous hydrolysis were to have as its rate-determining step a reaction involving general base catalysis by water of the attack of H_2O on **1** the acetate ion catalyzed hydrolysis ought to take place *via* general base catalysis by acetate of the attack of water, which it clearly does not.[8]

We thus believe that a proton transfer to the departing $ArSO_2$ group is involved as part of the rate-determining step of the spontaneous hydrolysis of **1**, and the question then becomes which of the several mechanisms incorporating that feature (eq 6, eq 7a plus 7b, or eq 8) is the correct one. Both the mechanism shown in eq 6 and the one in eq 7a plus 7b involve as discrete intermediates species where one has had the addition of either water (**5**) or a hydroxyl group (**7**) to one of the sulfone groups of **1**. Such intermediates are, of course, formally analogous to the tetrahedral addition intermediates whose existence has been repeatedly demonstrated[12,13] in mechanisms of hydrolysis reactions of carboxylic acid derivatives, RC(O)Y. However, in the case of substitution reactions involving sulfonyl derivatives, no definite evidence for the existence of analogous intermediates yet exists. All experimental efforts,[4a] including recent work by Kaiser and Zaborsky,[14] to find *positive* evidence for such intermediates in hydrolyses involving sulfonyl derivatives have been unsuccessful. Until such time as there is definite proof that species of the type represented by **5** or **7** are actual intermediates in hydrolyses of sulfonyl derivatives, we feel it is preferable to avoid writing mechanisms involving them for such reactions. For this reason we currently favor the mechanism shown in eq 8 for the spontaneous hydrolysis of **1**.

The mechanism (eq 8) for the spontaneous hydrolysis of **1** is identical, except that substitution occurs at sulfonyl rather than sulfinyl sulfur, with the one proposed earlier[2] for the spontaneous hydrolysis of **2**. This is in accord with the many striking similarities in the response of the two reactions to the reaction variables in Table II. The arguments given by Kice and Guaraldi[2] to show that the mechanism proposed for the spontaneous hydrolysis of **2** is consistent with a large negative $\Delta S^{\ddagger}$ and a sizable positive ρ for that reaction are also applicable to explaining why the mechanism in eq 8 for the hydrolysis of **1** will have a similar negative $\Delta S^{\ddagger}$ and positive value of ρ.

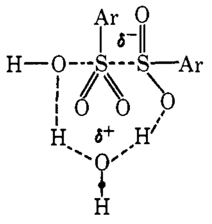
(11) The proton transfer depicted in eq 8 may actually take place through a chain of water molecules. This would almost certainly seem required if the entering ($-OH_2$) and leaving ($ArSO_2$) groups occupy apical positions of a trigonal bipyramid.

(12) The original demonstration of their involvement was the classic work of Bender.[13] For further examples of experiments demonstrating their existence see T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms," Vol. I, W. A. Benjamin, Inc., New York, N. Y., 1966, pp 22–24, 59–60, 102–103.

(13) M. L. Bender, *J. Am. Chem. Soc.*, 73, 1626 (1951).

(14) E. T. Kaiser and O. R. Zaborsky, *ibid.*, 90, 4626 (1968).

Finally, we would stress that, since the transfer of the proton from the incoming water molecule to the departing $ArSO_2$ group in eq 8 probably actually involves the assistance of *at least* one additional water molecule, *i.e.*



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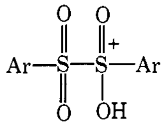
it can be thought of, in effect, as a mechanism where one has both general base catalysis of the attack of water and general acid catalysis of the departure of the $ArSO_2$ group, but with these two phenomena occurring as a concerted process.[15,16]

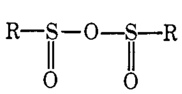
Since proton transfer to the departing $ArSO_2$ group is apparently important in the spontaneous hydrolysis, some may wonder why an acid-catalyzed mechanism involving attack of water on the protonated α-disulfone (9) does not make at least some contribution to the over-



$$\mathrm{Ar-\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{S}}-\underset{\underset{OH}{|}}{\overset{\overset{O}{\|}}{S}}{}^{+}-Ar}$$

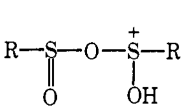
9

all rate hydrolysis of 1, particularly at high perchloric acid concentration. The reason it does not is almost certainly due to the fact that the extremely low basicity of sulfone groups[17] keeps the equilibrium concentration of 9 so infinitesimal even in solutions containing 2.0 *M* $HClO_4$ that a mechanism featuring attack of water on this intermediate simply cannot compete effectively with the spontaneous hydrolysis under these conditions. The same sort of phenomenon was also observed[2] in the hydrolysis of 2 in aqueous dioxane. The recent demonstration[18] that an acid-catalyzed term *does* make a significant contribution to the over-all rate of hydrolysis of a true sulfinic anhydride (10) in the same solvent medium provides strong evidence for the validity of this explanation.



$$\mathrm{R-\underset{\underset{O}{\|}}{S}-O-\underset{\underset{O}{\|}}{S}-R}$$

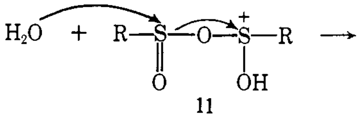
10



$$\mathrm{R-\underset{\underset{O}{\|}}{S}-O-\overset{+}{\underset{\underset{OH}{|}}{S}}-R}$$

11

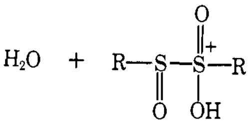
Sulfinyl groups are so much more basic than sulfone groups[19,20] that the equilibrium concentration of 11 is large enough so that a mechanism involving nucleophilic attack of water on 11 (eq 9) can compete effectively with the spontaneous hydrolysis in the case



11

$$RSO_2H + H^+ + RSO_2H \qquad (9)$$

of 10, whereas the extremely low basicity of sulfone groups prevents an analogous mechanism (eq 10) from doing so in the case of 2.



$$\mathrm{H_2O + R-\underset{\underset{O}{\|}}{S}-\underset{\underset{OH}{|}}{\overset{\overset{O}{\|}}{S}}{}^{+}-R} \not\rightarrow \text{not important,}$$

12

concentration of 12 too small (10)

Comparison of the Spontaneous Hydrolysis of α-Disulfones and Other Sulfonyl Derivatives. Christensen[3] has recently conducted an extensive study of the spontaneous hydrolysis of aryl sulfonic anhydrides (3), eq 3, in aqueous dioxane and aqueous acetone. Since the hydrolysis of 3 differs formally from that of 1 only in that the leaving group has been changed from $ArSO_2$ to $ArSO_2O$, it is very interesting to compare Christensen's results with 3 (Table III) with the analogous data for the spontaneous hydrolysis of 1 (first column of Table II). Such a comparison reveals that ρ for the hydrolysis of 3, while still positive, is somewhat smaller (+2.5) than that for the hydrolysis of 1 (+3.5). It also shows that the rate of hydrolysis of 3 increases somewhat more rapidly with an increase in the percentage water in the solvent than does the rate for 1. Both these

Table III. Spontaneous Hydrolysis of Aryl Sulfonic Anhydrides[a]

Reaction variable	Spontaneous hydrolysis of $ArSO_2OSO_2Ar$
(k_{H_2O}/k_{D_2O}) in 60% dioxane[b]	1.25
Solvent composition, relative rate[b]	
40% dioxane	7.5
50% dioxane	3.0
60% dioxane	(1.0)
70% dioxane	0.35
Aryl group, relative rate[c]	
p-$CH_3C_6H_4$	0.47
C_6H_5	(1.0)
p-ClC_6H_4	5.2
ρ (from plot of above data plus those for m-NO_2 and p-Br)	+2.5
Rates and activation parameters estimated for Ar = C_6H_5 in 64.7% dioxane[d]	
Rate constant at 21.4°	7.4×10^{-2} sec^{-1}
E_a	12.7 kcal/mole
$\Delta S^{\ddagger}$	−20.4 eu

[a] Data from ref 3. In some cases graphical interpolation from data in ref 3 was necessary to get the specific data shown in this table. [b] Data are for Ar = p-$CH_3C_6H_4$ at 22.5°. [c] Data are for 70% acetone as solvent at 20°. [d] Since actual data are available only for Ar = p-$CH_3C_6H_4$ in this solvent, the results for Ar = C_6H_5 were estimated assuming that $(k_{p\text{-H}}/k_{p\text{-CH}_3})$ is the same in this solvent as in others and that the entire difference in $(k_{p\text{-H}}/k_{p\text{-CH}_3})$ is due to a difference in E_a.

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(15) Such mechanisms have been termed by Jencks[16] "one-encounter" proton transfers. Some persons find them attractive; others regard them with a somewhat jaundiced eye. In the present case it is only the lack of any positive evidence for intermediates akin to 7 in hydrolyses of sulfonyl derivatives which causes us to prefer eq 8 to the equivalent "two-encounter" transfer represented by eq 7a plus 7b.

(16) W. P. Jencks and E. G. Sander, *J. Am. Chem. Soc.*, **90**, 4377 (1968).

(17) S. K. Hall and E. A. Robinson, *Can. J. Chem.*, **42**, 1113 (1964); E. M. Arnett and C. Douty, *J. Am. Chem. Soc.*, **86**, 409 (1964). The pK_a of the conjugate acid of dimethyl sulfone, for example, is −12.3. Because of the electron-withdrawing effect of the $ArSO_2$ group the pK_a of 9 would be even more negative.

(18) J. L. Kice and K. Ikura, *J. Am. Chem. Soc.*, **90**, 7378 (1968).

(19) The pK_a of the conjugate acid of dimethyl sulfoxide is −2.7,[20] so that a given sulfinyl function is about 10^{10} more basic than the corresponding sulfone group.

(20) P. Haake and R. D. Cook, *Tetrahedron Letters*, 427 (1968).

differences in behavior are relatively modest, however. The two really large and significant differences between the two hydrolyses are (a) the solvent isotope effect, which is much smaller for **3** than for **1**; and (b) the much faster rate of hydrolysis of **3**, which turns out to be due almost entirely to a much less negative $\Delta S^{\ddagger}$ for that reaction than for the hydrolysis of **1**.

As noted earlier these large differences in (k_{H_2O}/k_{D_2O}) *and* $\Delta S^{\ddagger}$ *for the two reactions indicate that there are some significant differences in the detailed mechanisms of the hydrolyses of* **3** *and* **1**. The situation thus contrasts sharply with that observed for the hydrolyses of **1** and **2**. There the much faster rate for **2** resulted solely from a difference in the activation energy for the two reactions, both hydrolyses showed comparable solvent isotope effects, and the conclusion was that, even though one reaction involved substitution at sulfinyl sulfur and the other substitution at sulfonyl sulfur, the same type of mechanism was involved in both cases. Taken together these various results indicate that *in substitutions at* $>S{=}O$ *and* $>SO_2$ *a change in the nature of the leaving group is much more likely to lead to a significant change in mechanism than is a change in the site where substitution occurs from sulfinyl to sulfonyl sulfur.*

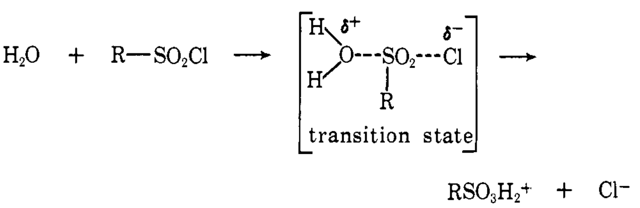
The difference between the mechanism for the spontaneous hydrolysis of **1** (eq 8) and that for **3** in eq 4 suggests that, when the leaving group is changed from $ArSO_2^-$ to one, like $ArSO_3^-$, which is the conjugate base of a much stronger acid, then (a) one no longer needs to assist the departure of the leaving group with a proton transfer of the sort shown in eq 8 and (b) one also does not need to aid the nucleophilic attack of water *via* the expedient of removing a proton from it concurrent with the formation of the new O–S bond (as in **8**).

It would appear that one can also rationalize the large difference between $\Delta S^{\ddagger}$ for the hydrolyses of **1** and **3** satisfactorily in terms of the mechanistic difference between eq 8 and eq 4. Thus the concerted proton transfer from the incoming water molecule to the departing $ArSO_2$ group shown in the mechanism in eq 8 for the spontaneous hydrolysis of **1** is the type of process which should involve a very highly ordered transition state and have a very large negative $\Delta S^{\ddagger}$. In contrast the mechanism for the spontaneous hydrolysis of **3** in eq 4 is merely a simple bimolecular displacement. When of the type $Nu^- + R\text{–}Y \rightarrow R\text{–}Nu + Y^-$ such reactions often have entropies of activation in the range -8 to -12 eu in protic solvents similar to 65% dioxane.[21] However, since eq 4 is a case where two neutral molecules react to form a pair of oppositely charged ions, one would expect its $\Delta S^{\ddagger}$ to be somewhat more negative than this. The observed value of -20 eu is not unreasonable.[22–24]

If our suggestion is correct that a proton transfer is involved in the rate-determining step of the spontaneous hydrolyses of sulfonyl derivatives only when the leaving group is the anion of a weak acid, the spontaneous hydrolysis of sulfonyl chlorides (**4**) (eq 11) should also not

$$H_2O + RSO_2Cl \longrightarrow RSO_3H + H^+ + Cl^- \qquad (11)$$

have a proton transfer as part of its rate-determining step and should, accordingly, exhibit a relatively small value of k_{H_2O}/k_{D_2O}. Those cases that have been studied[4b,c] do indeed show a considerably smaller k_{H_2O}/k_{D_2O} (1.5–1.6) than does α-disulfone hydrolysis, although one which is, to be sure, somewhat larger than for the hydrolysis of **3**. It is still small enough, however, to be consistent with a mechanism of the type



according to the estimates of Bunton and Shiner.[25]

Interestingly, although no proton transfer appears to be involved in the rate-determining step of the hydrolysis of **4**, the reaction shows[4a] a considerably more negative $\Delta S^{\ddagger}$ than the hydrolysis of **3**. At this stage any suggestion regarding the reasons for this difference in $\Delta S^{\ddagger}$ would be highly speculative. However, it does seem to point up the potential dangers in placing too much reliance on $\Delta S^{\ddagger}$ as an indicator of mechanism, particularly when it leads to conclusions at variance with those derived from other means of probing mechanism.

Experimental Section

Preparation and Purification of Aryl α-Disulfones. Cobaltic sulfate was prepared by the method of Swann and Xanthakos.[26] This was then used to oxidize the appropriate arylsulfinic acid ($ArSO_2H$) to the corresponding α-disulfone (**1**) using the procedure described by Denzer, Allen, Conway, and van der Veen.[27] All of the aryl α-disulfones **1** except the compound where Ar = p-ClC_6H_4 were reported previously by these workers.[27] For both Ar = C_6H_5 and Ar = p-$CH_3C_6H_4$ the melting points of our purified α-disulfones agreed closely with the values given in ref 27. However, in the case of both Ar = p-$CH_3OC_6H_4$ (mp 192–193°; lit.[27] mp 232°) and Ar = p-BrC_6H_4 (mp 233–234°; lit.[27] mp 205°) the melting points of our purified α-disulfones were drastically different from those reported by Denzer, *et al.*[27]; and yet the infrared spectra of these two compounds, when compared with those of the α-disulfones where Ar = C_6H_5 or p-$CH_3C_6H_4$, showed clearly that our compounds were α-disulfones. We are at a loss to explain the difference between our melting points and those reported for these same substances by Denzer, *et al.*,[27] but, to verify the purity of our p-MeO and p-Br α-disulfones, we have subjected them, as well as the p-Cl compound, to elemental analysis.

p-Anisyl-α-disulfone (1, Ar = p-$CH_3OC_6H_4$) had mp 192–193°. *Anal.* Calcd for $C_{14}H_{14}O_6S_2$: C, 49.11; H, 4.12. Found: C, 49.10; H, 4.18. Its ultraviolet spectrum (dioxane) showed λ_{max} 286 mμ (log ε 4.319).

p-Bromophenyl α-disulfone (1, Ar = p-BrC_6H_4) had mp 233–234°. *Anal.* Calcd for $C_{12}H_8Br_2O_4S_2$: C, 32.75; H, 1.83. Found: C, 33.06; H, 1.86. Its ultraviolet spectrum (dioxane) showed λ_{max} 267 mμ (log ε 4.498).

p-Chlorophenyl α-disulfone (1, Ar = p-ClC_6H_4) had mp 230–231°. *Anal.* Calcd for $C_{12}H_8Cl_2O_4S_2$: C, 41.04; H, 2.29. Found: C, 41.08; H, 2.29. Its ultraviolet spectrum (dioxane) showed λ_{max} 263 mμ (log ε 4.518).

Purification of Solvents and Other Reagents. Dioxane was purified using the method described by Fieser.[28] Analytical reagent grade perchloric acid and lithium perchlorate were used without further purification.

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[21] For some typical values, see A. Streitweiser, *Chem. Rev.*, **56**, 571 (1956).

[22] In ethanol, for example, $\Delta S^{\ddagger}$ for the reaction $Et_2S + MeI \rightarrow Et_2S^+Me + I^-$ is -25 eu.[23] (Ethanol is a solvent of about the same dielectric constant but appreciably smaller Y value[24] than 60–65% dioxane.)

[23] J. K. Syrkin and I. T. Gladischew, *Acta Physiochim. USSR*, **2**, 291 (1935).

[24] S. Winstein and A. H. Fainberg, *J. Am. Chem. Soc.*, **78**, 2770 (1956).

[25] C. A. Bunton and V. J. Shiner, Jr., *ibid.*, **83**, 3207 (1961).

[26] S. Swann, Jr., and T. S. Xanthakos, *ibid.*, **53**, 400 (1931).

[27] G. C. Denzer, Jr., P. Allen, Jr., P. Conway, and J. M. van der Veen, *J. Org. Chem.*, **31**, 3418 (1966).

[28] L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co. Boston, Mass., 1957, p 284.

Procedure for Kinetic Runs. A standard solution of the α-disulfone in dioxane was prepared and the proper volume of this solution was pipetted into the reaction flask of an apparatus of the same type as that used previously to follow the kinetics of the disproportionation of sulfinic acids,[29] or the thiolsulfinate-sulfinic acid reaction.[30] The proper volumes of standard aqueous solutions of perchloric acid and lithium perchlorate were then pipetted into the same reaction vessel, and the solutions were thoroughly mixed. The final solution was deaerated by bubbling nitrogen through it and the apparatus for 5 min. The reaction vessel was then immersed in a constant-temperature bath, and after 5 min, to allow the solution to reach bath temperature, an initial aliquot was removed and quickly cooled to room temperature by chilling it in ice-water. The absorbance of this aliquot was then measured at the wavelength corresponding to the λ_{max} of the α-disulfone in dioxane. (These wavelengths have already been listed for three of the α-disulfones used. For the remaining two, they were 244 mμ for Ar = C_6H_5 and 258 mμ for Ar = p-$CH_3C_6H_4$.) Other aliquots were removed at appropriate time intervals over 2–3 reaction half-lives and an infinity point was taken after 8–10 half-lives. The absorbances of these various samples were determined in the same way as for the initial point. The absorbance of the infinity point was close to zero for every α-disulfone except the p-MeO compound. In that case a solution having an initial optical density of 0.75 gave an optical density for the infinity point of 0.16. In all cases plots of log $(A - A_\infty)$ *vs.* time showed excellent linearity.

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(29) J. L. Kice and K. W. Bowers, *J. Am. Chem. Soc.*, **84**, 605 (1962).

(30) J. L. Kice, C. G. Venier, and L. Heasley, *ibid.*, **89**, 3557 (1967).

The Relative Nucleophilicity of Some Common Nucleophiles toward Sulfonyl Sulfur. The Nucleophile-Catalyzed Hydrolysis and Other Nucleophilic Substitution Reactions of Aryl α-Disulfones[1a]

John L. Kice, George J. Kasperek,[1b] and Dean Patterson[1c]

Contribution from the Department of Chemistry, Oregon State University, Corvallis, Oregon 97331. *Received April 21, 1969*

Abstract: The relative reactivity of nine common nucleophiles in a displacement reaction at sulfonyl sulfur (eq 2) in 60% dioxane has been determined from either kinetic data on their catalysis of the hydrolysis of aryl α-disulfones (**2**) or, in the case of primary and secondary amines and azide ion, from direct measurement of their rate of reaction with **2**. These data for sulfonyl sulfur (Table VII) are compared in Table VIII with data for some of these same nucleophiles in an exactly analogous displacement at sulfinyl sulfur (eq 1). The substitution at sulfonyl sulfur shows an entirely different pattern of nucleophile reactivity ($F^- \gg AcO^- \gg Cl^- > Br^- > H_2O$) than the one at sulfinyl sulfur ($Br^- > Cl^- \cong AcO^- > F^- \gg H_2O$). Interpreted in terms of the theory of hard and soft acids and bases (HSAB) these results indicate that sulfonyl sulfur is a much harder electrophilic center than sulfinyl sulfur, exactly as HSAB would have predicted it should be. Comparison of the data for sulfonyl sulfur with analogous data on nucleophilic reactivity in a substitution at another hard electrophilic center, carbonyl carbon (Table IX), reveals that the order of reactivity of the various nucleophiles toward sulfonyl sulfur ($RNH_2 > N_3^- > F^- > NO_2^- > AcO^-$) is about the same as toward carbonyl carbon.

In protic solvents the relative reactivity of a group of nucleophiles in a substitution reaction can change quite markedly with a change in the nature of the electrophilic center at which the substitution takes place.[2] In general, nucleophiles which are of low polarizability and high electronegativity, so-called "hard" bases,[3] enjoy an advantage over other nucleophiles in substitutions at centers such as carbonyl carbon[4] or tetracoordinate phosphorus.[5] Nucleophiles which are of high polariazability and low electronegativity, so-called "soft" bases,[3] react particularly readily in substitutions involving centers such as Pt^{II} [6] or peroxide oxygen.[7] A thoughtful and thorough analysis of these effects was first given by Edwards and Pearson.[8] More recently, Pearson and Songstad[9] have shown that the data can also be nicely rationalized using the concepts of the theory of hard and soft acids and bases (HSAB).

In an earlier study[10] the relative reactivity of a series of common nucleophiles toward sulfinyl sulfur was determined by measurement of the rates of a series of nucleophilic substitutions involving aryl sulfinyl sulfones (eq 1). The present paper shows that similar data for nucleophilic substitution at sulfonyl sulfur can be obtained from measurement of the rates of analogous substitutions of aryl α-disulfones (eq 2). Since eq 1 and 2 involve the same leaving group ($ArSO_2$) and have been studied in the same solvent (60% dioxane), comparison of the results for the two systems allows one to evaluate in a completely unequivocal manner what effect a change in substitution site from sulfinyl to sulfonyl sulfur has on the relative reactivity of various nucleophiles.

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(1) (a) This research supported by the National Science Foundation, Grant GP-6952; (b) NDEA Fellow, 1966–1969; (c) NSF Summer Undergraduate Research Participant, 1968.

(2) J. O. Edwards, "Inorganic Reaction Mechanisms," W. A. Benjamin, Inc., New York, N. Y., 1965, pp 51–72.

(3) R. G. Pearson, *J. Am. Chem. Soc.*, **85**, 3533 (1963); *Science*, **151**, 172 (1966).

(4) W. P. Jencks and J. Carruiolo, *J. Am. Chem. Soc.*, **82**, 1778 (1960).

(5) Reference 2, pp 59–63, 177–180.

(6) R. G. Pearson, H. Sobel, and J. Songstad, *J. Am. Chem. Soc.*, **90**, 319 (1968).

(7) J. O. Edwards, "Peroxide Reaction Mechanisms," J. O. Edwards, Ed., Interscience Publishers, New York, N. Y., 1962, pp 67–106.

(8) J. O. Edwards and R. G. Pearson, *J. Am. Chem. Soc.*, **84**, 16 (1962).

(9) R. G. Pearson and J. Songstad, *ibid.*, **89**, 1827 (1967).

(10) J. L. Kice and G. Guaraldi, *ibid.*, **90**, 4076 (1968).