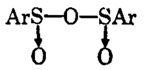
Mechanisms of Substitution Reactions at Sulfinyl Sulfur. IV. The Hydrolysis of Sulfinyl Sulfones (Sulfinic Anhydrides) in Aqueous Dioxane[1]

John L. Kice and Giancarlo Guaraldi

Contribution from the Department of Chemistry, Oregon State University, Corvallis, Oregon. *Received March 20, 1967*

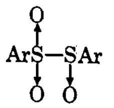
Abstract: The hydrolysis of a series of aryl sulfinyl sulfones (II) has been investigated under a variety of reaction conditions in acidic aqueous dioxane. The results are compared where appropriate to the hydrolytic behavior of the corresponding carboxylic anhydrides and/or sulfite esters. In the absence of nucleophilic additives, the hydrolysis of II occurs almost exclusively by a spontaneous (or uncatalyzed) pathway, even in quite acidic aqueous dioxane. This contrasts with the hydrolysis of II in acetic acid–water and also with the hydrolysis of the corresponding sulfite esters in aqueous dioxane, where, in both cases, an acid-catalyzed pathway accounts for virtually the entire rate. Reasons for these differences in behavior are outlined. The spontaneous hydrolysis of II exhibits a large solvent isotope effect, $k_{H_2O}/k_{D_2O} = 2.7$, and is markedly accelerated by both an increase in the percentage water in the solvent and by the presence of electron-withdrawing substituents in the aryl groups. A mechanism consistent with all the experimental facts is shown in eq 6. The hydrolysis of II can be catalyzed by such nucleophilic additives as halide ions or alkyl sulfides. The halide ion catalyzed hydrolysis has been studied and a mechanism proposed (eq 9 and 10), and the results are compared with the halide ion catalyzed hydrolysis of sulfite esters. The alkyl sulfide catalyzed hydrolysis of II has also been studied, and the results are compared with those previously obtained for the same reaction in acetic acid–1% water. The comparison indicates that eq 11 is the correct mechanism for the sulfide-catalyzed reaction.

The anhydrides of aromatic sulfinic acids do *not* have a structure (I) analogous to a carboxylic anhydride but rather possess the sulfinyl sulfone structure II.[2]



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

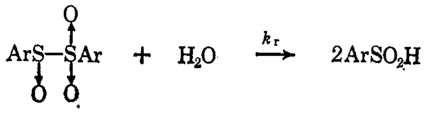
I



$$\mathrm{Ar\underset{\downarrow\atop O}{S}{-}\overset{O\atop\uparrow}{\underset{\downarrow\atop O}{S}}Ar}$$

IIa, Ar = $p\text{-}CH_3OC_6H_4$
b, Ar = $p\text{-}CH_3C_6H_4$
c, Ar = C_6H_5
d, Ar = $p\text{-}ClC_6H_4$

Like a carboxylic anhydride, however, the sulfinyl sulfones hydrolyze readily to the corresponding sulfinic acid (eq 1). This facile hydrolysis is, of course, a substitution reaction occurring at sulfinyl sulfur, and it has been our belief that study of its mechanism can contribute to a better general understanding of substitution reactions at sulfinyl sulfur, a subject in which there has been considerable recent interest.[3-6]



$$\mathrm{Ar\underset{\downarrow\atop O}{S}{-}\overset{O\atop\uparrow}{\underset{\downarrow\atop O}{S}}Ar} + H_2O \xrightarrow{k_r} 2ArSO_2H \qquad (1)$$

II

Our previous investigations[7] of the solvolysis of II in acetic acid–1% water as solvent, while providing considerable information about the mechanisms of both the normal[7a] and the alkyl sulfide catalyzed[7b] reactions, left a number of important questions unresolved. We were hopeful that some of these might be answered by studying the solvolysis of II in a very different solvent medium and for that reason undertook the investigations of the hydrolysis of sulfinyl sulfones in aqueous dioxane described in the present paper. We find that the current results do indeed supplement and complement our earlier studies[7] in an informative way, with the result that we can now formulate mechanisms for the hydrolysis of II under a variety of conditions with considerably increased precision.

The use of aqueous dioxane as the solvent has the important added advantage of allowing us to make a detailed comparison of the hydrolysis of II with the hydrolytic behavior in this same medium of (a) alkyl[8] and aryl[8b,9] sulfites and (b) carboxylic anhydrides.[10,11] As we shall see in the Discussion, consideration of the differences and similarities exhibited by the several reactions is both interesting and enlightening.

Results

Hydrolysis of II in 60% Dioxane. The hydrolyses of the various sulfinyl sulfones were investigated kinetically in 60% dioxane (v/v) containing varying amounts of added perchloric acid (0.01–2.0 *M*). Some runs were also made in the presence of both lithium perchlorate and perchloric acid. The disappearance of II followed clean first-order kinetics in each instance. Rate constants (k_r) are tabulated in Table I.

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[1] This research supported by the Directorate of Chemical Sciences, Air Force Office of Scientific Research, under Grant AF-AFOSR-106-65.

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Table I. Hydrolysis of Sulfinyl Sulfones in 60% Dioxane

Sulfinyl sulfone	Temp, °C	($LiClO_4$), *M*	($HClO_4$), *M*	$k_r \times 10^2$, sec^{-1}
IIa	21.4	0.00	0.10	0.20
			0.20	0.19
			0.40	0.21
			1.00	0.19
			1.62	0.24
			2.00	0.44
		0.25	0.10	0.22
		1.00	0.10	0.24
		1.50	0.10	0.22
		2.00	0.10	0.20
IIb	21.4	0.00	0.01	0.46
			0.12	0.48
			0.12 (D_2O)	0.18
			0.50	0.49
			1.00	0.50
	20.1	0.00	0.01	0.41
	26.6	0.00	0.01	0.58
	32.8	0.00	0.01	0.77
	37.9	0.00	0.01	1.03
IIc	21.4	0.00	0.10	1.5
			0.20	1.6
			0.40	1.6
			1.00	1.7
			2.00	1.2
		0.50	0.10	1.8
		1.00	0.10	1.7
		2.00	0.10	1.3
IId	21.4	0.00	0.02	11
			0.40	10
			0.80	11
			1.60	6.3
			2.00	4.4
		1.50	0.10	10
		2.00	0.10	7.1

The most striking feature of these data, particularly when compared with our earlier results[7a] in acetic acid–1% water, is the almost complete absence of any acid-catalyzed contribution to k_r. Only for the *p*-anisyl compound (IIa), and then only at high perchloric acid concentration (1.5 *M*), is there any increase in k_r with increasing concentration of strong acid. In contrast, in acetic acid–1% H_2O the rate of hydrolysis in solutions containing 1.0 *M* H_2SO_4 was, depending on the structure of the Ar group in II, from 9 to 50 times faster than the rate in solutions 0.1 *M* in H_2SO_4.

The decrease in k_r with increasing perchloric acid concentration observed for IIc and IId at high acid concentration would appear to be a salt effect, since a similar decrease in k_r is brought about by the addition of comparable concentrations of lithium perchlorate to solutions 0.1 *M* in $HClO_4$.

Measurement of k_r for IIb in dioxane–D_2O reveals that the sulfinyl sulfone hydrolysis in 60% dioxane has a large solvent isotope effect, $k_{H_2O}/k_{D_2O} = 2.7$.

From the data in Table I on the hydrolysis of IIb at five different temperatures, one calculates the following activation energy and entropy: $E_a = 9.4$ kcal; $\Delta S^{\ddagger} = -37.1$ eu. We see that, while the activation energy is rather small, $\Delta S^{\ddagger}$ is very large and negative.

Variation in Hydrolysis Rate with Solvent Composition. Table II summarizes data on the change in the hydrolysis rate of IIa and IIb with changes in the water content of the solvent. It is apparent that for both sulfinyl sulfones k_r increases markedly with increasing water content of the medium, the rate increasing about 130-fold on going from 80% dioxane to 30% dioxane.

Table II. Variation in Hydrolysis Rate of II with Solvent Composition in Aqueous Dioxane[a]

Sulfinyl sulfone	($HClO_4$), *M*	% dioxane (v/v)	$k_r \times 10^2$, sec^{-1}
IIa	0.10	80	0.026
		70	0.063
		60	0.20
		50	0.53
		40	1.55
		30	3.7
		20	8.4
IIb	0.10	80	0.062
		70	0.15
		60	0.46
		50	1.43
		40	2.8
		30	8.5

[a] All data are for 21.4°.

Alkyl Sulfide Catalyzed Hydrolysis of II. The solvolysis of II in acetic acid–1% water can be markedly accelerated by the addition of small amounts of alkyl sulfides.[7b] This sulfide-catalyzed reaction is first order in both sulfinyl sulfone and sulfide and strongly acid catalyzed, a plot of log k_r *vs.* the Hammett acidity function, H_0, being linear with a slope of approximately one. Because of the lack of acid catalysis of the ordinary hydrolysis in aqueous dioxane and the fact that 60% dioxane containing 0.10–2.0 *M* $HClO_4$ represents a much less acidic medium[12] than the acetic acid–water–sulfuric acid solutions used in the earlier study,[7b] we were interested in determining whether an alkyl sulfide catalyzed hydrolysis of II could even be observed in 60% dioxane, and, if it could, whether or not it was still subject to acid catalysis.

We find that an alkyl sulfide catalyzed hydrolysis of II can indeed be observed in 60% dioxane. Rate data for the hydrolyses of the various sulfinyl sulfones in the presence of *n*-butyl sulfide are shown in Table III.

Table III. *n*-Butyl Sulfide Catalyzed Hydrolysis of II in 60% Dioxane[a]

Sulfinyl sulfone	(R_2S) × 10^2, *M*	($HClO_4$), *M*	$k_r \times 10^2$, sec^{-1}	$k_S = [(k_r - k_r^0)/(R_2S)]$[b]
IIa	1.08	0.067	0.28	0.08
		0.20	0.58	0.36
		0.27	0.84	0.60
		0.40	1.3	1.04
		0.81	6.3	5.6
IIb	1.80	0.07	0.74	0.15
	1.08	0.10	0.73	0.24
	1.14	0.12	0.92	0.39
		0.12 (D_2O)	0.50	0.28
	0.88	0.20	1.1	0.70
		0.40	2.0	1.7
		0.60	3.8	3.8
	0.175	0.80	1.7	6.9
IIc	0.44	0.20	2.1	1.2
		0.40	3.1	3.4
		0.60	4.8	7.3

[a] All runs at 21.4°. [b] k_r^0 equals the rate of hydrolysis in the absence of sulfide under otherwise identical conditions. Values of k_r^0 for IIa–c assumed to be independent of ($HClO_4$) in the range of acid concentrations employed. Values used ×10^2: IIa, 0.19; IIb, 0.47 (in D_2O), 0.18; IIc, 1.6.

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In the presence of the sulfide the rate constant for hydrolysis is given by

$$k_r = k_r^0 + k_S(R_2S)$$

where k_r^0 equals the rate constant in the absence of sulfide under otherwise identical conditions. Values of k_S

$$k_S = (k_r - k_r^0)/(R_2S)$$

for the various reaction conditions are given in the last column of Table III.

Examination of the variation of k_S with perchloric acid concentration shows that, unlike the normal hydrolysis of II, the sulfide-catalyzed hydrolysis is still strongly acid catalyzed in 60% dioxane. A plot of log k_S for IIb *vs.* $-H_0$[12] is linear with a slope of 0.95. The less extensive data for IIa and IIc also give linear plots of log k_S *vs.* $-H_0$ with slopes close to unity. Although one thus has the same formal dependence of k_S on H_0 in 60% dioxane as was observed[7b] in acetic acid–1% water, it is important to point out that the k_S values for a given H_0 in 60% dioxane are about 100-fold larger than would be predicted from the earlier results in acetic acid–1% water, given the difference in H_0 values for the two media. Thus at $H_0 = -1.13$ in acetic acid–1% water, k_S for the *n*-butyl sulfide catalyzed solvolysis of IIb is 7.5.[7b] From this result the expected k_S in 60% dioxane containing 0.40 *M* $HClO_4$ ($H_0 = +1.57$) would be 7.5/500, or 0.015. We see from Table III that the actual value is 1.7, almost 100 times larger. Clearly, then, for a given acidity as measured by H_0, the rate of the sulfide-catalyzed reaction is much faster in 60% dioxane than in acetic acid–1% water. The proper interpretation of this result will be considered in the Discussion.

We have also measured the solvent isotope effect associated with the *n*-butyl sulfide catalyzed hydrolysis of IIb in 60% dioxane. The value found, $k_{H_2O}/k_{D_2O} = 1.4$, is somewhat larger than the value of 1.15 observed for the benzyl sulfide catalyzed solvolysis of the same sulfinyl sulfone in acetic acid–1% water.[7b]

Halide Ion Catalyzed Hydrolysis of II. Other nucleophiles besides alkyl sulfides can catalyze the hydrolysis of II in 60% dioxane. Because they have been previously studied[8] as catalysts for the hydrolysis of sulfite esters, we were particularly interested in examining the effect of chloride and bromide ions on the hydrolysis of II. Our results for chloride ion are summarized in Table IV. Table V lists the results with bromide ion and the even more potent nucleophilic catalyst, iodide ion.

Table IV. Chloride Ion Catalyzed Hydrolysis of II in 60% Dioxane

Sulfinyl sulfone	Temp, °C	$(Cl^-) \times 10^4$, *M*	$(HClO_4)$, *M*	$k_r \times 10^2$, sec^{-1}	$k_{Cl} = [(k_r - k_r^0)/(Cl^-)]$[a]
IIb	20.1	1.32	0.01	0.78	28
	21.4	1.32	0.01	0.87	30
		2.67	0.01	1.3	32
			0.032	1.4	34
			0.04[b]	1.5	37
			0.08	1.5	37
		1.24	0.32	0.98	41
			0.48	1.0	45
			0.80	1.1	51
	26.6	1.32	0.01	1.1	37
	32.8	1.32	0.01	1.5	52
	37.9	1.32	0.01	1.9	67
IIa	21.4	2.97	0.04	0.54	12
			0.08	0.58	13
			0.20	0.64	15
			0.40	0.76	19

[a] k_r^0 equals the rate of hydrolysis in the absence of chloride ion under otherwise identical conditions. Values of k_r^0 for IIa and IIb taken from Table I assuming k_r^0 independent of $(HClO_4)$ in the range of acid concentrations employed. [b] $ArSO_2H$ added initially, 6.4×10^{-4} *M*.

Table V. Bromide and Iodide Ion Catalyzed Hydrolyses of II in 60% Dioxane[a]

Sulfinyl sulfone	Catalyst	$(X^-) \times 10^4$, *M*	$(HClO_4)$, *M*	$k_r \times 10^2$, sec^{-1}	$k_X = [(k_r - k_r^0)/(X^-)]$[b]
IIb	Br^-	0.75	0.02	1.6	1.5×10^2
			0.08	1.7	1.6×10^2
			0.40	2.3	2.4×10^2
		3.74	0.40	9.6	2.4×10^2
		0.75	0.60	2.8	3.2×10^2
			0.80	3.2	3.6×10^2
		0.374	0.90	1.9	3.8×10^2
	I^-	0.106	0.10	4.4	3.7×10^3
			0.20	5.0	4.2×10^3
			0.40	6.0	5.2×10^3
			0.60	7.6	6.7×10^3
IIa	Br^-	1.27	0.04	1.05	71
			0.08	1.1	73
			0.20	1.4	93
			0.40	1.7	117
	I^-	0.28	0.04	4.0	1.3×10^3
		0.14	0.10	2.3	1.5×10^3
		0.28	0.20	6.2	2.1×10^3
			0.40	8.6	3.0×10^3

[a] All runs at 21.4°. [b] k_r^0 equals rate of hydrolysis of II in the absence of halide ion under otherwise identical conditions. Values used $\times 10^2$; IIa, 0.19; IIb, 0.47.

If the halide ion catalyzed reactions are first order in halide, k_r in the presence of halide ion will be given by

$$k_r = k_r^0 + k_X(X^-) \tag{2a}$$

and

$$k_X = \frac{k_r - k_r^0}{(X^-)} \tag{2b}$$

so that for a given halide ion and a given set of reaction conditions $(k_r - k_r^0)/(X^-)$ should be a constant independent of halide ion concentration. A pair of runs with IIb and chloride ion (lines 2 and 3 of Table IV) and another pair with IIb and bromide (lines 3 and 4 of Table V) indicate this is true for both the chloride and bromide ion catalyzed reactions. We assume it is also so for the iodide ion catalyzed reaction. Values of k_X computed according to eq 2b for the various halide ions and reaction conditions are shown as the last column of both Tables IV and V.

For each of the halide ion–sulfinyl sulfone combinations studied k_X is seen to increase with increasing perchloric acid concentration, and, in each case, as can be seen from some typical plots in Figure 1, the dependence of k_X on acid concentration is of the form

$$k_X = k_X^0 + k_X'(H^+) \tag{3}$$

Values of k_X^0 and k_X' (obtained from plots of the type shown in Figure 1) for the various halide ion catalyzed hydrolyses studied are shown in Table VI. An examination of these data and eq 3 shows that the situation in

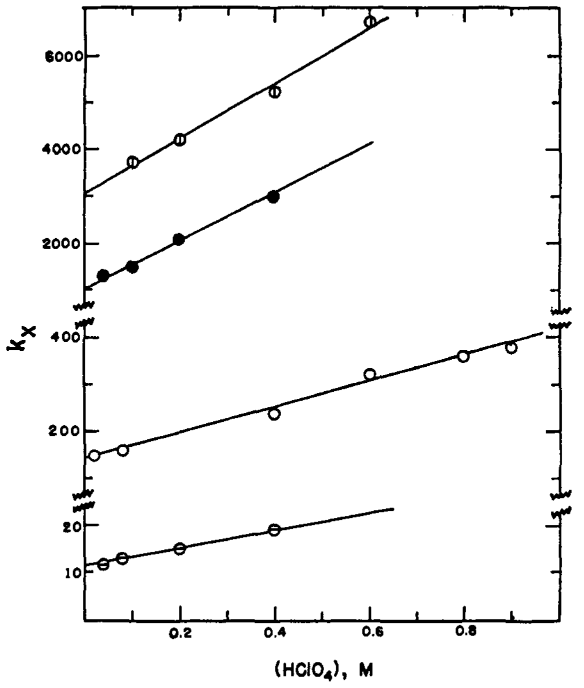


Figure 1. Dependence of k_X for the halide ion catalyzed hydrolysis of II on perchloric acid concentration in 60% dioxane: IIa, chloride ion, ⊖; IIb, bromide ion, ○; IIa, iodide ion, ●; IIb, iodide ion, ⦶.

the halide ion catalyzed hydrolyses differs from the alkyl sulfide catalyzed hydrolysis in the following important ways: (1) an H$^+$-independent component ($k_X{}^0$) makes a large contribution to the over-all rate constant for the nucleophile-catalyzed reaction; (2) the acid-catalyzed portion of the rate depends on the stoichiometric concentration of acid rather than on H_0.

Table VI. Rate Constants for Halide Ion Catalyzed Hydrolyses of Sulfinyl Sulfones[a]

Sulfinyl sulfone	Halide ion	$k_X{}^0 \times 10^{-3}$, M^{-1} sec^{-1}	$k_X{}' \times 10^{-3}$, M^{-2} sec^{-1}
IIa	Cl$^-$	0.012	0.02
	Br$^-$	0.065	0.14
	I$^-$	1.0	5
IIb	Cl$^-$	0.032	0.025
	Br$^-$	0.15	0.3
	I$^-$	3.0	6

[a] All data at 21.4° in 60% dioxane.

In Table IV are listed values of k_{Cl} for IIb for runs in the presence of only 0.01 M HClO$_4$ at several different temperatures. Because the acid-catalyzed component contributes effectively nothing to k_{Cl} at these low acid concentrations, we can use these data to estimate the activation energy and entropy associated with $k_{Cl}{}^0$ for IIb. These are found to be E_a = 8.5 kcal and $\Delta S^{\ddagger} = -22$ eu. Interestingly, E_a is not much less than that for the uncatalyzed hydrolysis, but the entropy of activation is much less negative.

Discussion

We shall divide the Discussion into four main sections. The first will deal with the uncatalyzed hydrolysis of II in dioxane–water, while the second will be concerned with the halide ion catalyzed hydrolysis. In each case comparisons with the behavior of carboxylic anhydrides and/or sulfite esters will be made. In the third section we will discuss the sulfide-catalyzed hydrolysis and show how the present results allow us to make a decision between previously suggested[7b] mechanistic alternatives for this reaction. The fourth section will show that the present data can also be used to clarify certain details regarding the mechanism of the normal acid-catalyzed solvolysis of II in acetic acid–1% water.[7a]

Mechanism of the Uncatalyzed Hydrolysis of II in Dioxane–Water. The following facts regarding the hydrolysis of II in dioxane–water seem particularly noteworthy. First, except for the *p*-anisyl compound, there is no indication of any acid catalysis of the hydrolysis, and even in the case of IIa such catalysis is of no importance except at high perchloric acid concentrations (>1.5 M). This is in marked contrast to the behavior of both the halide ion and sulfide catalyzed hydrolyses where an acid-catalyzed component is either readily evident or, as in the case of the R$_2$S-catalyzed reaction, completely dominant even at relatively low acid concentrations. Second, the uncatalyzed (or spontaneous) hydrolysis of II shows a large solvent isotope effect, $k_{H_2O}/k_{D_2O} = 2.7$, and is markedly accelerated by an increase in the per cent of water in the solvent. Third, there is a sizeable effect of aryl group structure on the rate of hydrolysis of II, and this effect on k_r is almost exactly *inversely* proportional to the effect the same change in aryl group structure has on the equilibrium constant (K_e) for the ArSO$_2$H–II equilibrium, as measured in acetic acid–1% water solvent.[7a] Interestingly, as the comparison in Table VII shows, the response of the spontaneous hydrolysis of II to these various reaction variables is very similar to that exhibited by the spontaneous hydrolysis of arylcarboxylic anhydrides.[10c,11]

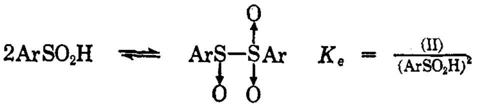
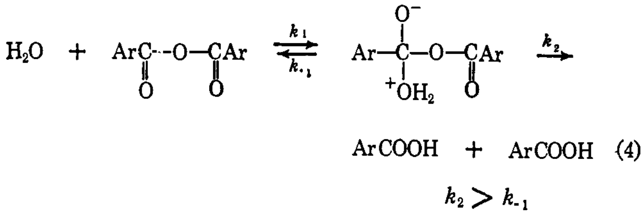

$$2\mathrm{ArSO_2H} \rightleftharpoons \mathrm{Ar}\underset{\downarrow\atop \mathrm{O}}{\mathrm{S}}-\overset{\mathrm{O}\atop\uparrow}{\underset{\downarrow\atop \mathrm{O}}{\mathrm{S}}}\mathrm{Ar} \qquad K_e = \frac{(\mathrm{II})}{(\mathrm{ArSO_2H})^2}$$

Table VII. Effect of Reaction Variables on the Spontaneous Hydrolyses of Aryl Sulfinyl Sulfones and Carboxylic Anhydrides in Dioxane–Water

	Spontaneous hydrolysis of	
Reaction variable	ArS(O)-SO$_2$Ar	ArC(O)-OCOAr
Solvent isotope effect[a] (k_{H_2O}/k_{D_2O})	2.7	3.4
Aryl group,[b] relative rate		
p-CH$_3$OC$_6$H$_4$	0.13	0.12
p-CH$_3$C$_6$H$_4$	0.32	0.35
C$_6$H$_5$	(1.0)	(1.0)
p-ClC$_6$H$_4$	6.7	5.2
Solvent composition,[c] relative rate		
50% dioxane	(1.0)	(1.0)
60% dioxane	0.38	. . .
75% dioxane	. . .	0.15
80% dioxane	0.05	0.10

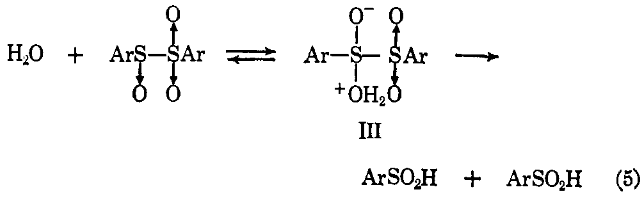
[a] Data for II from Table I; those for anhydride are for benzoic anhydride (ref 10c); both sets of results for 60% dioxane. [b] Data for II are for 60% dioxane (Table I). Those for the anhydrides are for 75% dioxane (ref 11). [c] Data for II are for IIb at 21.4° (Table II). Those for anhydride are for benzoic anhydride at 25° (ref 11).

Bunton, *et al.*,[10c] have concluded from data in Table VII and other known facts about the spontaneous hydrolysis of anhydrides that the mechanism of that reaction is as shown in eq 4, with the rate-determining step being k_1, the nucleophilic addition of water to a carbonyl group of the anhydride. Given the similar response of the hydrolysis of II to all the variables in Table VII, an analogous mechanism for its spontaneous hydrolysis (eq 5) is an obvious possibility. The same arguments presented by Bunton, *et al.*,[10] for the anhydride reaction can be used in the present case to explain how the mechanism in eq 5 could account for the large solvent isotope effect, the pronounced dependence of rate on water content of the solvent, and the large negative $\Delta S^{\ddagger}$ observed for the uncatalyzed hydrolysis of II.



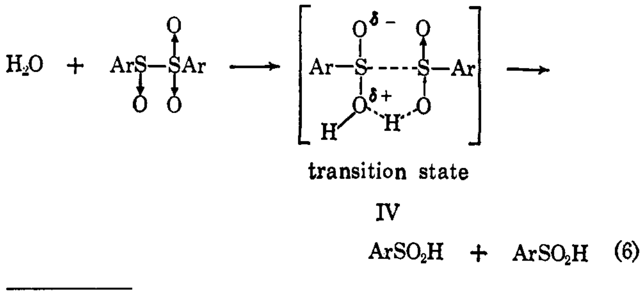
$$H_2O + Ar\underset{\underset{O}{\|}}{C}{-}O{-}\underset{\underset{O}{\|}}{C}Ar \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Ar{-}\overset{\overset{O^-}{|}}{\underset{\underset{^+OH_2}{|}}{C}}{-}O{-}\underset{\underset{O}{\|}}{C}Ar \xrightarrow{k_2} ArCOOH + ArCOOH \quad (4)$$

$$k_2 > k_{-1}$$



$$H_2O + Ar\underset{\underset{O}{\downarrow}}{S}{-}\overset{\overset{O}{\uparrow}}{\underset{\underset{O}{\downarrow}}{S}}Ar \rightleftharpoons \underset{\text{III}}{Ar{-}\overset{\overset{O^-}{|}}{\underset{\underset{^+OH_2}{|}}{S}}{-}\overset{\overset{O}{\uparrow}}{\underset{\underset{O}{\downarrow}}{S}}Ar} \longrightarrow ArSO_2H + ArSO_2H \quad (5)$$

While the mechanism in eq 5 is in accord with the data, we believe that the various results are in equally good accord with a very closely related alternative mechanism (eq 6) in which the formation of III as an actual intermediate is by-passed by making nucleophilic attack of water on the sulfinyl group concerted with scission of the S–S bond and transfer of a proton from $-OH_2^{\delta+}$ to the departing $ArSO_2$ group.[13] Because we feel that this latter mechanism can be more easily integrated conceptually with the probable mechanisms of the halide ion and sulfide catalyzed hydrolyses, we prefer to use it, rather than eq 5, as the basis for our further discussion.



$$H_2O + Ar\underset{\underset{O}{\downarrow}}{S}{-}\overset{\overset{O}{\uparrow}}{\underset{\underset{O}{\downarrow}}{S}}Ar \longrightarrow \left[Ar{-}\overset{\overset{O^{\delta-}}{|}}{\underset{\underset{\underset{H\quad H}{O^{\delta+}}}{|}}{S}}{\cdots\cdots}\overset{\overset{O}{\uparrow}}{\underset{\underset{O}{\downarrow}}{S}}{-}Ar\right] \longrightarrow ArSO_2H + ArSO_2H \quad (6)$$

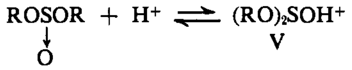
transition state

IV

Consideration of eq 6 reveals a simple explanation for the fact that the normal hydrolysis of II is not acid catalyzed whereas the sulfide-catalyzed reaction requires an acid catalyst. Specifically, we suggest that uncharged weak nucleophiles, such as water or an alkyl sulfide, are unable to displace sulfinate ion ($ArSO_2^-$) as such from II. If these nucleophiles are to effect a substitution on the sulfinyl group of II, a proton must be transferred to the $ArSO_2$ group coincident with the scission of the $S(O)$–SO_2 bond, so that the $ArSO_2$ group is effectively displaced as the sulfinic acid.[15] When water is the attacking nucleophile it can supply this required proton itself, since its two protons become increasingly acidic as the new O–S bond is formed. The alkyl sulfide, on the other hand, has no such proton that it can transfer to the $ArSO_2$ group, with the result that when it performs an analogous substitution on the sulfinyl sulfur the required proton must be donated by some strong acid present in the solution.

With nucleophiles such as halide ions, substitution of II can apparently occur both *via* an acid-catalyzed route and by direct displacement of $ArSO_2^-$ as such. This point will be discussed in detail in the next section.

One further point regarding the uncatalyzed hydrolysis of II seems worthy of comment. In contrast to II, one finds[8,9] for either simple alkyl or aryl sulfites in 60% dioxane containing 0.10–1.0 *M* $HClO_4$ that their hydrolysis *via* an acid-catalyzed, A2-type mechanism (eq 7) is many times faster than their spontaneous (or uncatalyzed) hydrolysis. Several factors probably contribute to the very different behavior observed with II. First, the change from OR to $ArSO_2$ as the group to be displaced results in a much more rapid rate of spontaneous hydrolysis. Second, the unfavorable inductive effect of the adjacent sulfonyl group means that the amount of sulfinyl-protonated II which will be present at equilibrium in a solution of a given acidity will be orders of magnitude smaller than the equi-



$$RO\underset{\underset{O}{\downarrow}}{S}OR + H^+ \rightleftharpoons \underset{\text{V}}{(RO)_2SOH^+} \quad (7a)$$

$$H_2O + V \xrightarrow{\text{rate determining}} ROH + ROSO_2H \quad (7b)$$

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[13] That eq 6 could exhibit essentially the same solvent isotope effect etc. as eq 5 is suggested by the following considerations. First, the solvent isotope effect in eq 5 would presumably arise from changes in vibrational frequencies attending the formation of III which involve (1) the hydrogens of the attacking water molecule and (2) the hydrogens in water molecules hydrogen bonded to the negatively charged oxygen.[14] A decrease in both the negative character of the latter oxygen and the positive character of the other oxygen, as in eq 6, would be expected to decrease k_{H_2O}/k_{D_2O} markedly.[14] However, in eq 6 the *primary* isotope effect associated with the transfer of one of the $-OH_2^{\delta+}$ protons to the $ArSO_2$ group could easily counterbalance this and lead to an over-all solvent isotope effect of the same magnitude as for eq 5. Second, the pronounced dependence of rate on water concentration and the large negative $\Delta S^{\ddagger}$ would be ascribed in eq 5 to the need for extensive solvation of the zwitterionic intermediate III by solvent water. Decreased dipolar character, as in eq 6, might therefore seem to demand a decreased dependence of rate on water concentration and a less negative $\Delta S^{\ddagger}$. However, one should remember that the proton transfer depicted in eq 6 may actually take place *via* a chain of intervening water molecules (a so-called Grotthus chain). This would almost certainly be so if the entering (OH_2) and leaving ($ArSO_2$) groups occupy the apical positions of a trigonal bipyramid. The need for the cooperation of a number of solvent water molecules in the depicted proton transfer could easily counterbalance any decreased water requirement due to decreased dipolar character of the transition state. Third, in view of the relationship between k_r and $1/K_s$, the mechanism in eq 6 is obviously also compatible with the observed effects of aryl group structure on k_r.

[14] C. A. Bunton and V. J. Shiner, Jr., *J. Am. Chem. Soc.*, **83**, 3207 (1961).

[15] The extremely low basicity associated with sulfonyl groups in organic molecules[16] means that the equilibrium concentration of sulfonyl-protonated II in the present solutions will be incredibly small.[7b] This is presumably the reason why a mechanism involving conversion of $ArSO_2$ to the better leaving group ArS^+O_2H by transfer of the proton in an equilibrium *prior* to the scission of the S–S bond is not competitive with eq 6.

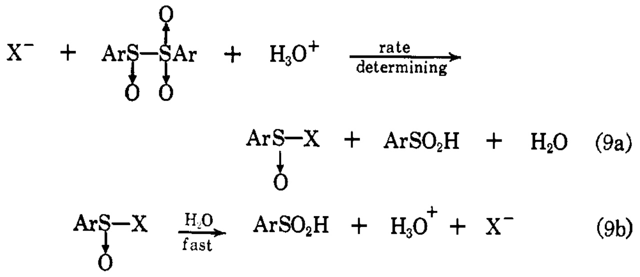
[16] S. K. Hall and E. A. Robinson, *Can. J. Chem.*, **42**, 1113 (1964); E. M. Arnett and C. Douty, *J. Am. Chem. Soc.*, **86**, 409 (1964).

librium concentration of protonated sulfite (V).[17] This could serve to make a reaction analogous to eq 7b a much less important contributor to the total rate of hydrolysis than is the case for the sulfites.

Mechanism of the Halide Ion Catalyzed Hydrolysis. The kinetics of all the halide ion catalyzed hydrolyses of IIa and IIb are of the form

$$-\mathrm{d}\ln(\mathrm{II})/\mathrm{d}t = k_X{}^0(X^-) + k_X{}'(X^-)(H^+) \qquad (8)$$

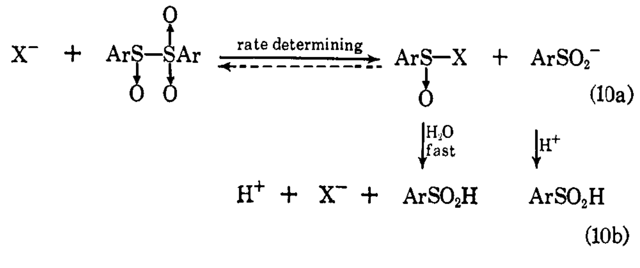
There are thus two halide ion catalyzed pathways for hydrolysis, one of which is also acid catalyzed. In both the relative efficacy (Table VI) of the various halide ions as catalysts ($I^- > Br^- > Cl^-$) parallels their order of nucleophilic reactivity in other reactions,[18] making it seem essentially certain that the role of the halide ion must be to perform a displacement of the $ArSO_2$ group by nucleophilic attack on the sulfinyl sulfur of II. The sulfinyl halide, ArS(O)X, so formed then hydrolyzes very rapidly to sulfinic acid and HX. From the discussion in the preceding section regarding the mechanisms of the spontaneous and sulfide-catalyzed reactions it seems reasonable to conclude that in the acid-catalyzed portion of the halide-assisted hydrolysis the function of the acid is to assist the displacement of the $ArSO_2$ group by transferring a proton to it coincident with the scission of the S–S bond. For the acid-catalyzed reaction a mechanism of the type shown in eq 9 thus seems indicated.



$$X^- + Ar\underset{O}{S}-\overset{O}{\underset{O}{S}}Ar + H_3O^+ \xrightarrow[\text{determining}]{\text{rate}} Ar\underset{O}{S}-X + ArSO_2H + H_2O \qquad (9a)$$

$$Ar\underset{O}{S}-X \xrightarrow[\text{fast}]{H_2O} ArSO_2H + H_3O^+ + X^- \qquad (9b)$$

For the H^+-independent reaction (the $k_X{}^0$ term in eq 8) we propose a closely analogous mechanism (eq 10), the only difference being that the halide ion in this case effects the displacement of $ArSO_2^-$ directly without the need for the accompanying proton transfer of eq 9a.



$$X^- + Ar\underset{O}{S}-\overset{O}{\underset{O}{S}}Ar \xrightarrow{\text{rate determining}} Ar\underset{O}{S}-X + ArSO_2^- \qquad (10a)$$

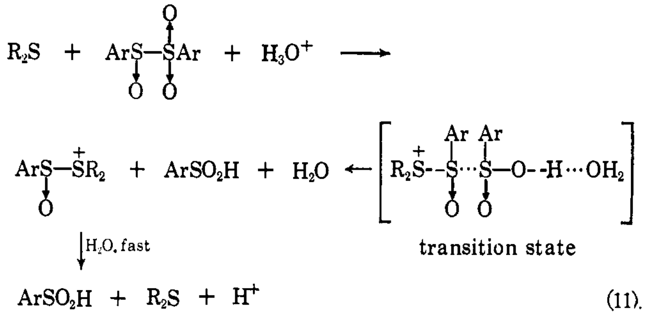
$$Ar\underset{O}{S}-X \xrightarrow[\text{fast}]{H_2O} H^+ + X^- + ArSO_2H \qquad ArSO_2^- \xrightarrow{H^+} ArSO_2H \qquad (10b)$$

One additional important aspect of the mechanism in eq 10 is revealed by experiments reported elsewhere.[19] These show that when the pH of the medium is not sufficiently acidic to convert the initially formed $ArSO_2^-$ ion to the sulfinic acid, $ArSO_2H$, the reverse of step 10a can become an important reaction. (This is what the dashed arrow in eq 10 is meant to imply.) Thus, even though transfer of a proton to the $ArSO_2$ group is not required in the rate-determining step of eq 10, it is required in a rapid subsequent step if one is to avoid the incursion of the ArS(O)X + $ArSO_2^-$ reaction and a concomitant decrease in the catalytic effectiveness of a given concentration of halide ion.

In contrast to the present results, the chloride and bromide ion catalyzed hydrolyses of either alkyl[8] or aryl[8b,9] sulfites show no H^+-independent term. This is true even for catechol sulfite,[3b] which, unlike the other sulfites, but like II, exhibits a much faster rate of spontaneous hydrolysis than of acid-catalyzed hydrolysis in 60% dioxane. Undoubtedly the fact that an H^+-independent term is a major contributor to the rate of chloride or bromide ion catalyzed hydrolysis of II can be traced to the fact that $ArSO_2^-$ is much less basic, and, therefore, much more easily displaced than ArO^- or RO^-.

Mechanism of the Alkyl Sulfide Catalyzed Hydrolysis. A previous study[7b] of the sulfide-catalyzed solvolysis of II in acetic acid–1% water has already clearly established a number of points about the mechanism of the sulfide-catalyzed reaction. These are: (1) the reaction is strongly acid catalyzed; (2) it involves a nucleophilic attack of the alkyl sulfide, R_2S, on the sulfinyl group of II which results in the displacement of the $ArSO_2$ group; (3) the displacement of the $ArSO_2$ group is assisted by the transfer of a proton to it in the rate-determining step. This latter conclusion is now further confirmed by the solvent isotope effect, $k_{H_2O}/k_{D_2O} = 1.4$, found in the present work.

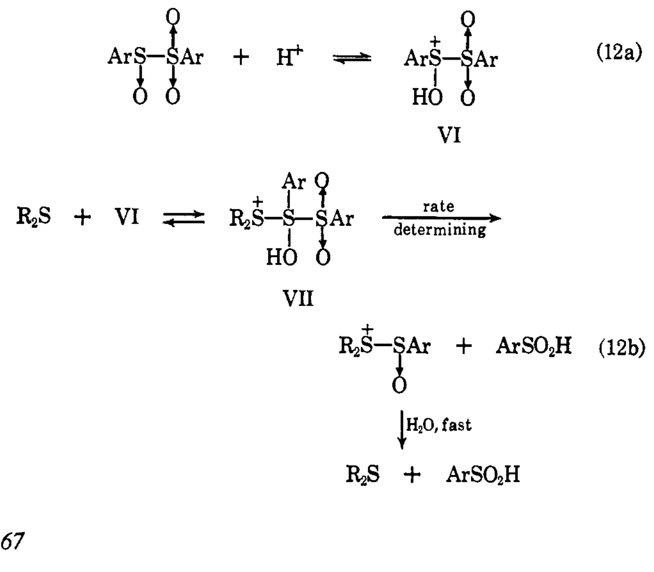
These various data are compatible with either of two mechanisms for the reaction. In the first of these (eq 11) the attack of R_2S is concerted with the scission of the $S(O)-SO_2$ bond and the donation of a proton to the departing $ArSO_2$ group by H_3O^+. The second mechanism (eq 12) involves attack of the sulfide on the



$$R_2S + Ar\underset{O}{S}-\overset{O}{\underset{O}{S}}Ar + H_3O^+ \longrightarrow \left[R_2\overset{+}{S}\text{--}\overset{Ar}{\underset{O}{S}}\cdots\overset{Ar}{\underset{O}{S}}\text{—O--H}\cdots OH_2\right] \longrightarrow Ar\underset{O}{S}-\overset{+}{S}R_2 + ArSO_2H + H_2O$$

transition state

$$Ar\underset{O}{S}-\overset{+}{S}R_2 \xrightarrow{H_2O,\ \text{fast}} ArSO_2H + R_2S + H^+ \qquad (11)$$



$$Ar\underset{O}{S}-\overset{O}{\underset{O}{S}}Ar + H^+ \rightleftharpoons Ar\overset{+}{\underset{HO}{S}}-\overset{O}{\underset{O}{S}}Ar \qquad (12a)$$

VI

$$R_2S + \text{VI} \rightleftharpoons R_2\overset{+}{S}-\overset{Ar}{\underset{HO}{S}}-\overset{O}{\underset{O}{S}}Ar \xrightarrow[\text{determining}]{\text{rate}} R_2\overset{+}{S}-\underset{O}{S}Ar + ArSO_2H \qquad (12b)$$

VII

$$R_2\overset{+}{S}-\underset{O}{S}Ar \xrightarrow{H_2O,\ \text{fast}} R_2S + ArSO_2H$$

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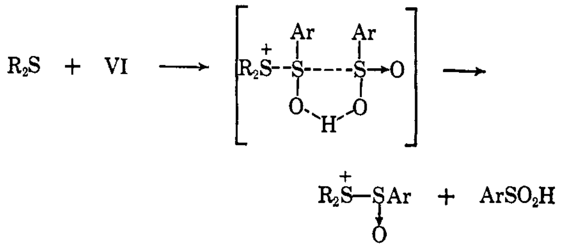
(17) Because of the extremely low basicity of sulfonyl groups,[16] the equilibrium concentration of *sulfonyl*-protonated II will, of course, be much smaller than the concentration of sulfinyl-protonated II.

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

(19) J. L. Kice and G. Guaraldi, *Tetrahedron Letters*, 6135 (1966).

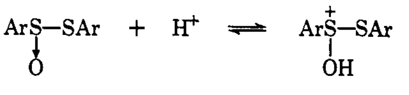
protonated sulfinyl sulfone (VI). This is then followed by the expulsion of $ArSO_2H$ from the resulting intermediate.[20] The data we have so far discussed do not



(12b′)

permit a distinction between the two possibilities. We believe, however, that the additional considerations which we will now outline do allow us to decide between these two mechanisms and that they favor eq 11 as the mechanism for the sulfide-catalyzed hydrolysis.

Certain sulfide- and acid-catalyzed reactions of aryl thiolsulfinates, ArS(O)SAr, have been studied[21,22] in this laboratory in the same solvent media (acetic acid–1% water and 60% dioxane) used to study the sulfide-catalyzed hydrolysis of II. The experimental evidence, including solvent isotope effects ($k_{H_2O}/k_{D_2O} = 0.5–0.7$), indicates that these sulfide-catalyzed thiolsulfinate reactions proceed by the mechanism shown in eq 13. This involves rate-determining nucleophilic



$$ArS(\rightarrow O)—SAr + H^+ \rightleftharpoons Ar\overset{+}{S}(OH)—SAr \quad (13a)$$

VIII

$$R_2S + VIII \xrightarrow{\text{rate determining}} R_2\overset{+}{S}—SAr + ArSOH \quad (13b)$$

attack of R_2S on the protonated thiolsulfinate (VIII). The experimental rate constant, k_S, for one particular *n*-butyl sulfide catalyzed thiolsulfinate reaction has been found to be about 150 times smaller in 60% dioxane containing 0.40 M $HClO_4$ ($H_0 = +1.57$) than it is in acetic acid–1% water containing 0.10 M H_2SO_4 ($H_0 = -1.13$). Thus, in this reaction which other experimental evidence indicates involves the rate-determining reaction of the sulfide with the protonated thiolsulfinate, a decrease in the acidity of the medium leads to a decrease in rate of approximately the magnitude that would be predicted by assuming that (1) the rate of eq 13b is not strongly solvent dependent and (2) the equilibrium concentration of VIII depends on H_0. Since the equilibrium concentration of VI should presumably depend on H_0 in essentially the same manner as that of VIII does, and since the rate of eq 12b (or 12b′) should not be any more dependent on the solvent than that of eq 13b, we would expect, if the mechanism of the sulfide-catalyzed hydrolysis were as shown in eq 12, that k_S for the butyl sulfide catalyzed hydrolysis of IIb in 60% dioxane–0.40 M $HClO_4$ should be about 150 times smaller than k_S for the same reaction in acetic acid–1% water–0.10 M H_2SO_4. *In actual fact it is only 4.5 times slower.* Because of this we feel that eq 12 is not a satisfactory mechanism for the sulfide catalyzed hydrolysis of II, and we are therefore led to favor eq 11 as the mechanism for this reaction.

We have seen that over a limited acidity range in either 60% dioxane or acetic acid–1% water that log k_S for the R_2S-catalyzed hydrolysis of II does plot linearly *vs.* $-H_0$ with a slope close to unity. In view of the discussion in the previous paragraph, however, we do not think this fact has its usual supposed mechanistic significance. Rather we consider it is simply another example of the fact that some general acid catalyzed reactions are known which give behavior of this type.[23] The observed solvent isotope effect of $k_{H_2O}/k_{D_2O} = 1.4$ is, of course, entirely compatible with a general acid catalyzed mechanism of the type shown in eq 11.

The Present Results and the Mechanism of Solvolysis of II in Acetic Acid–1% Water. In acetic acid–1% water containing 0.10–1.00 M H_2SO_4 the rate of the normal[24] hydrolysis of II is given[7a] by

$$k_r = k + k'h_0^a \quad (14)$$

where a = 0.8–1.0 depending on aryl group in II. Although k and k' vary with aryl group structure in markedly different ways (*vide infra*), for IIa–d their relative magnitudes in each case are such that for sulfuric acid concentrations of 0.40 M or greater the acid-catalyzed term in eq 14 ($k'h_0^a$) is the only important contributor to k_r. Thus in acetic acid–1% water–0.40 M H_2SO_4 the hydrolysis of II occurs almost exclusively by an acid-catalyzed pathway, in marked contrast to 60% dioxane–0.40 M $HClO_4$, where it occurs entirely by an uncatalyzed (or spontaneous) pathway.

The acetic acid–1% water–sulfuric acid solutions differ from the 60% dioxane–perchloric acid solutions in two important ways: (1) they represent a much less nucleophilic solvent medium; (2) they are much more strongly acidic (as measured by their H_0 values). The first factor should, and does, cause the rate of spontaneous hydrolysis of II to be much slower than in 60% dioxane. For example, k for IIb in acetic acid–1% water is 50 times smaller than its rate of spontaneous hydrolysis in 60% dioxane. How much the second factor will increase the rate of acid-catalyzed reaction over what it is in 60% dioxane will depend on (a) how sensitive the acid-catalyzed reaction itself is to the nucleophilicity of the solvent and (b) the exact nature of the dependence of its rate on the acidity of the medium.

Previously we suggested[7a] that acid catalysis of the normal and sulfide-catalyzed hydrolyses in acetic acid–1% water involved the same mechanism as regards the details of the timing, etc. of the proton transfer. Now we must reexamine that hypothesis most carefully. Table III shows that the rate of the sulfide-catalyzed reaction is effectively the same in 60% dioxane–0.80 M $HClO_4$ as it is in acetic acid–1% water–0.10 M H_2SO_4. If our previous hypothesis were true, this would require that in every case the rate of the normal acid-catalyzed hydrolysis of II in 60% dioxane–0.80 M $HClO_4$ should

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[20] As noted in the earlier paper,[7b] a mechanism involving attack of R_2S on VI, but not involving VII as an actual intermediate, is also possible. In that case one simply assumes that the transfer of the proton to the $ArSO_2$ group is concerted with the attack of R_2S, as in eq 12b′.

[21] J. L. Kice and C. G. Venier, *Tetrahedron Letters*, 3629 (1964); J. L. Kice, C. G. Venier, and L. Heasley, *J. Am. Chem. Soc.*, **89**, 3557 (1967).

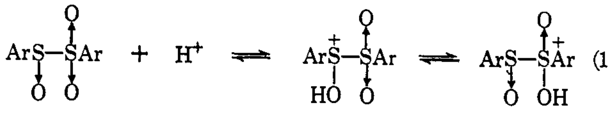
[22] J. L. Kice and G. B. Large, unpublished results.

[23] H. G. Kuivila and K. V. Nahabedian, *J. Am. Chem. Soc.*, **83**, 2159 (1961); F. A. Long and M. A. Paul, *Chem. Rev.*, **57**, 935 (1957).

[24] By "normal" we mean not catalyzed by alkyl sulfides or halide ions.

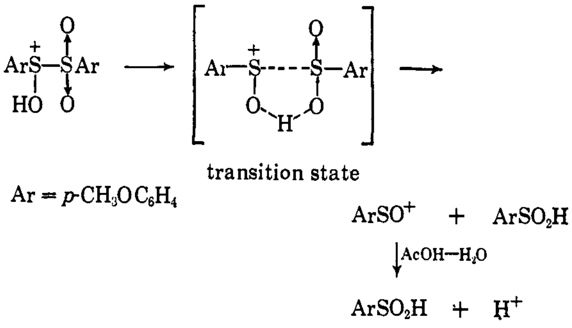
be *at least equal*[25] to its rate in acetic acid–1% water–0.10 M H_2SO_4. Consider then the data for IIa. Its rate constant for acid-catalyzed hydrolysis in acetic acid–1% water–0.10 M H_2SO_4 is 2.1×10^{-3} sec^{-1}.[7a] Since its rate of spontaneous hydrolysis in 60% dioxane is 2×10^{-3} sec^{-1}, our previous hypothesis would then require that the over-all rate of hydrolysis of IIa in 60% dioxane–0.80 M $HClO_4$ should be at least twice its rate of spontaneous hydrolysis. This is most certainly *not* what is observed (Table I). Even in the more strongly acidic 60% dioxane–1.0 M $HClO_4$ the rate of hydrolysis of IIa is still no greater than its rate of spontaneous hydrolysis. Only when we go to solutions like 60% dioxane–2.0 M $HClO_4$, which on an H_0 basis are about 20 times more acidic than 60% dioxane–0.80 M $HClO_4$,[12] do we get an acid-catalyzed contribution to the over-all rate of this magnitude, *i.e.*, 2×10^{-3} sec^{-1}. We conclude from this that our previous hypothesis was wrong, and that, in actual fact, the normal and sulfide-catalyzed hydrolyses do differ in a significant way as regards the mechanisms involved in their catalysis by acids.

Granted this fact, what then is the mechanism of the acid-catalyzed hydrolysis of II in acetic acid–1% water? In attempting an answer to this question one must keep in mind two other significant features of this reaction. The first is that it shows a dependence of rate on the nature of the aryl group in II which is *completely different from that which is exhibited by the other reactions of II that we have studied.* These latter reactions (the spontaneous hydrolysis, the sulfide-catalyzed reaction, etc.) all show a rate pattern of the type p-Cl > p-H > p-Me > p-MeO. The acid-catalyzed hydrolysis of II, on the other hand, is characterized by a particularly fast rate for the p-anisyl compound and an over-all rate pattern of the type, p-MeO >> p-Me ≅ p-Cl > p-H. The second interesting feature is that, in contrast to the sulfide-catalyzed reaction, the acid-catalyzed hydrolysis of IIa is *faster* in deuterated medium, $k_{\mathrm{HOAc}}/k_{\mathrm{DOAc}} = 0.72$.


$$\mathrm{Ar\underset{O}{S}-\overset{O}{\underset{O}{S}}Ar + H^+ \rightleftharpoons Ar\overset{+}{\underset{HO}{S}}-\overset{O}{\underset{O}{S}}Ar \rightleftharpoons Ar\underset{O}{S}-\overset{O}{\underset{OH}{\overset{+}{S}}}Ar} \quad (15)$$

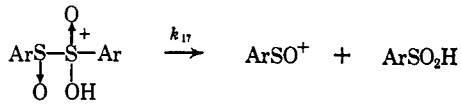
VI IX

We feel that the simplest explanation of these various facts is to assume that, unlike the other reactions of II, the normal acid-catalyzed hydrolysis does, in fact, involve a protonated form of the sulfinyl sulfone as the key intermediate. We further suggest that the rate-determining step of the reaction involves dissociation of the S–S bond in this conjugate acid of II. The more electron-withdrawing the aryl group in II the more this dissociation is accompanied by nucleophilic participation of the solvent at the sulfinyl sulfur. On the other hand, when the aryl group is an electron-donating one like p-anisyl which can effectively stabilize a positive charge on the sulfinyl sulfur, then the dissociation of the S–S bond in protonated II is not accompanied by much nucleophilic participation by solvent, and the rate-determining step effectively results in the formation of $ArSO^+ + ArSO_2H$. Whether such a mechanism for IIa is best represented as involving the sulfinyl-protonated form VI, with transfer of the proton from the sulfinyl group to the departing $ArSO_2$ group accompanying the scission of the S–S bond (eq 16), or as a simple dissociation (eq 17) of the sulfonyl-protonated form IX, cannot be decided from presently available data.[26] When the aryl group is one such as p-chlorophenyl, as in IId, we suggest that the mechanism in eq 16 (or 17) is modified in such a way as to have much more nucleophilic participation by solvent.


$$\mathrm{Ar\overset{+}{\underset{HO}{S}}-\overset{O}{\underset{O}{S}}Ar \longrightarrow \left[Ar-\overset{+}{\underset{O}{S}}{\cdots}\overset{O}{\underset{O}{S}}-Ar\right] \longrightarrow ArSO^+ + ArSO_2H \xrightarrow{AcOH-H_2O} ArSO_2H + H^+} \quad (16)$$

transition state

Ar = p-$CH_3OC_6H_4$


$$\mathrm{Ar\underset{O}{S}-\overset{O}{\underset{OH}{\overset{+}{S}}}-Ar \xrightarrow{k_{17}} ArSO^+ + ArSO_2H} \quad (17)$$

Ar = p-$CH_3OC_6H_4$

Experimental Section

Preparation and Purification of Materials. The preparation and purification of the various sulfinyl sulfones have been described in earlier papers,[7,27] as has the purification of the n-butyl sulfide[7b] and potassium chloride[27] used. Dioxane was purified by the method of Wiberg.[28] Lithium perchlorate (Gallard-Schlesinger Chem.) was recrystallized from water and dried under vacuum at 140°. Potassium bromide and iodide (B & A Reagent) were recrystallized twice from water. The perchloric acid used (Baker Analyzed Reagent) contained less than 5×10^{-4}% chloride ion as an impurity.

Procedure for Kinetic Runs. The apparatus used has already been described.[27] In the present work a carefully measured amount of a solution of the sulfinyl sulfone in anhydrous dioxane was placed in chamber A of the apparatus while a measured amount of an aqueous dioxane solution of perchloric acid and any other additives such as lithium perchlorate, n-butyl sulfide, etc. was placed in chamber B. The amounts of the solutions in A and B were chosen so that on mixing the final solution would have the desired dioxane content. The two solutions in A and B were then brought to temperature in the constant-temperature bath. They were then rapidly mixed, and the resulting solution was quickly transferred to chamber C of the apparatus, a 1-cm spectrophotometer cell. The apparatus was immediately placed in a previously described[27] thermostated cell holder inside a Cary Model 15 spectrophotometer, and the disappearance of the sulfinyl sulfone was followed by recording the decrease in the optical density with time at 300–306 mμ, the exact wavelength used depending on the sulfinyl sulfone.[7a,27] With

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[25] This assumes no dependence of the acid-catalyzed rate on solvent nucleophilicity. To the extent that there was also a dependence of the acid-catalyzed rate on solvent nucleophilicity the rate would be that much *larger* than the rate in acetic acid–1% water–0.10 M H_2SO_4.

[26] Our previous view[7a] that IX could not be an intermediate in the normal acid-catalyzed hydrolysis was based on (1) a demonstration[7b] that IX could not be involved in the sulfide-catalyzed reaction and (2) our earlier belief[7a] that the mechanism of acid catalysis of the normal and sulfide-catalyzed hydrolyses was the same. Now that we have shown that the latter is *not* the case, we can no longer eliminate IX as a possible intermediate, because, despite the very low concentrations of IX which would presumably be present at equilibrium,[15,16] the over-all rates of acid-catalyzed hydrolysis are all slow enough so that the value of k_{17} need not exceed reasonable values.

[27] J. L. Kice, G. Guaraldi, and C. G. Venier, *J. Org. Chem.*, **31**, 3561 (1966).

[28] K. B. Wiberg, "Laboratory Technique in Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, p 245.

proper preparation and practice it was possible to begin rate measurements within a few seconds after mixing so that quite rapid rates of hydrolysis could be followed. However, it should be pointed out that in the fastest rates in Tables I-V ($k_r = 10^{-1}$ sec^{-1}) we were able to follow only the last 25-30% of the hydrolysis of II. Since all the reactions followed good first-order kinetics this did not really make any difference, however, particularly since by using a larger initial concentration of II we could still follow the hydrolysis over essentially the same over-all change in optical density.

The initial sulfinyl sulfone concentrations used in the kinetic runs were in the range 0.9-1.8 $\times 10^{-4}$ M, except for the very fast runs where initial concentrations of 1.8-3.5 $\times 10^{-4}$ M were used. The per cent dioxane in our solutions was calculated after the fashion of Bunton, *et al.*[12]

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Mechanism of the Pyridoin Condensation

John P. Schaefer and James L. Bertram

Contribution from the Department of Chemistry, University of Arizona, Tucson, Arizona. *Received February 17, 1967*

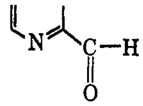
Abstract: When pyridine-2-aldehyde (**1**) is dissolved in acetic acid, 2,2′-pyridoin is formed. The reaction is second order in aldehyde and is catalyzed by acids and metal ions. At 70° an isotope effect ($k_{\mathrm{RCHO}}/k_{\mathrm{RCDO}}$) of 2.52 was measured which indicates that the aldehydic hydrogen bond is being broken in the rate-determining step. A mechanism which involves nucleophilic addition of **1** to the conjugate acid of **1** followed by a rate-determining removal of a proton, cyclization, and elimination is proposed.

From a classical viewpoint, the benzoin condensation is of importance since it represents one of the first organic reactions whose mechanism was defined using the now commonplace tools of physical organic chemistry.[1,2] For a number of years the reaction was thought to be specifically catalyzed by cyanide ion,[3] but recent work on the mechanism of thiamine action has shown that similar reactions in biological systems and in the laboratory can be accomplished through the catalytic action of thiazolium salts.[4-6] Less well known is the fact that in certain circumstances acid-catalyzed condensations leading to benzoins are also possible; this paper attempts to elucidate the mechanism of such a reaction.

Results and Discussion

The dimerization of pyridine-2-aldehyde (**1**) to 2,2′-pyridoin (**2**), hereafter referred to as the pyridoin condensation, was first reported in 1953 by Hensel.[7] He found that orange crystals of **2** precipitated when equal volumes of **1** and glacial acetic acid were stirred together for a few hours; it was also observed that the 3- and 4-aldehydes failed to undergo condensation under similar conditions. Also, Marvel and Stille[8] have noted that **2** was a by-product which they obtained during some boron trifluoride catalyzed condensation reactions of **1** with other substrates.

To define the scope of this reaction in greater detail, we studied the behavior of furfural, thiophene-2-aldehyde, pyrrole-2-aldehyde, imidazole-4(5)a-ldehyde, 8-acetoxyquinoline-2-aldehyde, and quinoline-2-aldehyde under similar conditions; of these compounds only quinoline-2-aldehyde underwent condensation. These observations suggest that the minimum structural factors which are required for reaction are



and that secondary factors, such as steric effects and basicity, play an important role in determining the ease with which condensation occurs.

A preliminary investigation of the ultraviolet spectrum of **2** showed that in the presence of acid the strong absorption maximum at 380 mμ (ε 18,000) quickly disappeared with the concurrent appearance of two maxima at 233 and 260 mμ (ε ~3000). Since **1** has two maxima in the ultraviolet at 233 and 260 mμ (ε 3460 and 2950, respectively) it appeared either (a) that the condensation was reversible and, under dilute conditions, **2** was reverting to **1**, (b) that a disproportionation reaction was taking place giving 2,2′-pyridil (**3**) and 2,2′-dihydropyridoin (**4**), or (c) that **2** was simply being oxidized to **3** by air. Compounds **3** and **1** should have similar spectral properties in the ultraviolet region of the spectrum.

Thin layer chromatography (tlc) using RSC silica gel G and developing with a 50:50 mixture of chloroform–ethyl acetate gave a clean separation of authentic individual and mixed samples of **1** (R_f 0.79), **2** (R_f 0.21), **3** (R_f 0.63), and **4** (R_f 0.10). Using a 1:9 mixture of concentrated ammonium hydroxide and ethanol, a good separation of **4** (R_f 0.58) and picolinic acid (**5**) (R_f 0.24) was obtained. Regardless of the reaction conditions used, only 2,2′-pyridoin and 2,2′-pyridil were observed as products.

Further product analysis was carried out by vapor phase chromatography (vpc) utilizing a 10 ft $\times$ 0.25

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(1) A. Lapworth, *J. Chem. Soc.*, **83**, 995 (1903).
(2) A. Lapworth, *ibid.*, **85**, 1206 (1904).
(3) For an excellent summary of the scope and a historical review, see W. S. Ide and J. S. Buck, *Org. Reactions*, **4**, 269 (1948).
(4) T. Ugai, S. Tanaka, and S. Dokawa, *J. Pharm. Soc. Japan*, **63**, 269 (1943).
(5) T. Ugai, S. Tanaka, and S. Dokawa, *ibid.*, **64**, 605 (1944).
(6) R. Breslow, *J. Am. Chem. Soc.*, **80**, 3719 (1958), and other papers in this series.
(7) H. Hensel, *Angew. Chem.*, **65**, 491 (1953).
(8) C. S. Marvel and J. K. Stille, *J. Org. Chem.*, **21**, 1313 (1956).