for the hydrolysis of the aryl sulfate ion to be somewhat less than would otherwise be the case. Since no such resonance stabilization of the transition state is possible in the case of the hydrolysis of alkyl sulfate ions, we can see why aryl sulfate ions should hydrolyze considerably faster than their alkyl counterparts.

Experimental Section

Preparation and Purification of Materials. Sodium phenyl sulfate was prepared by the procedure of Burkhardt and Lapworth.[12] It was purified by several recrystallizations from ethanol and after each recrystallization was triturated with diethyl ether. Analysis indicated that the product so obtained is a hydrate, $C_6H_5OSO_3Na \cdot 0.5H_2O$. *Anal.* Calcd for $C_6H_5OSO_3Na \cdot 0.5H_2O$: C, 35.13; H, 2.95. Found: C, 35.20; H, 3.14.

Pyridinium p-Nitrophenyl Sulfate. This was prepared by a modification of the procedure of Burkhardt and Lapworth.[12] A mixture of 20 g (0.125 mole) of pyridiniumsulfonic acid[13] and 100 ml of dry benzene was placed in a three-necked flask which had been fitted with a reflux condenser and drying tube and a stirrer. After the mixture had been brought to 70°, 10 g (0.072 mole) of p-nitrophenol was added, and the reaction mixture was stirred for 4 hr at reflux.

The pyridinium p-nitrophenyl sulfate was then filtered off and recrystallized twice from water. After each recrystallization the dried salt was triturated with a small amount of ether. The salt was finally dried under reduced pressure over calcium chloride; mp 76°. *Anal.* Calcd for $C_{12}H_{10}N_2O_6S$: C, 44.29; H, 3.38. Found: C, 44.23; H, 3.29.

Solvents. Dioxane was purified by the procedure suggested by Wiberg.[14]

Procedure for Kinetic Runs. The reaction vessel was of a type previously described[15] in connection with kinetic study of the disproportionation of sulfinic acids. Its construction is such that an aliquot may be withdrawn without exposing the remainder of the solution to the atmosphere.

To initiate a run a weighed amount of the aryl sulfate salt was dissolved in a measured volume of the proper solvent containing the desired amount of perchloric or hydrochloric acid. The resulting solution was placed in the reaction vessel and deaerated for 5 to 10 min with prepurified nitrogen. While being deaerated the solution was cooled in an ice bath. After the solution was deaerated, the reaction vessel was placed in a constant temperature bath. The reaction was then followed by removing 1- or 2-ml aliquots, diluting these aliquots to 50 ml with 95% ethanol, and measuring the optical density of the resulting solutions at either 277 mμ (for the phenyl sulfate ion hydrolysis) or 320 mμ (for the p-nitrophenyl sulfate ion hydrolysis).

(12) G. N. Burkhardt and A. Lapworth, *J. Chem. Soc.*, 684 (1926).
(13) P. Baumgarten, *Ber.*, **59**, 1166 (1926).

(14) K. B. Wiberg, "Laboratory Technique in Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, p 245.
(15) J. L. Kice and K. W. Bowers, *J. Am. Chem. Soc.*, **84**, 605 (1962).

The Mechanism of the Acid Hydrolysis of Bunte Salts (S-Alkyl and S-Aryl Thiosulfates)[1]

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Abstract: The rates of acid-catalyzed hydrolysis (eq 1) of a series of S-aryl and S-alkyl thiosulfates (Bunte salts) have been measured under a variety of reaction conditions in water and various dioxane–water mixtures. The data on the variation of the hydrolysis rate with the acidity of the medium and on the increase in rate accompanying an increase in the dioxane content of dioxane–water mixtures have been compared with corresponding data for two closely related acid-catalyzed hydrolyses: (1) that of sodium aryl sulfates (a reaction thought to proceed by an A-1 mechanism) and (2) that of sodium methyl selenate (a reaction presumably proceeding by an A-2 mechanism). This comparison shows that the response of the Bunte salt hydrolysis to these particular reaction variables is very closely comparable to that of the sulfate hydrolysis and very different from that of the selenate hydrolysis, and it strongly suggests that the Bunte salt hydrolysis proceeds by an A-1 mechanism. It is shown that the observed solvent isotope effect for the Bunte salt hydrolysis ($k_{D_2O}/k_{H_2O} = 1.4$) and the variation of rate with Ar for $ArSSO_3^-$ ($\rho \cong -0.5$) are also compatible with the particular A-1 mechanism shown in eq 3. This mechanism involves an initial reversible protonation of the Bunte salt on the divalent sulfur followed by rate-determining unimolecular dissociation of the zwitterion intermediate to thiol and sulfur trioxide. It is thus the same type of mechanism proposed for the sulfate hydrolysis. A tentative explanation is advanced to explain why the Bunte salt and sulfate hydrolyses, although proceeding by the same basic mechanism, show somewhat different response of rate to changes in alkyl or aryl group structure.

On being heated in aqueous acid Bunte salts (S-alkyl or S-aryl thiosulfates) are hydrolyzed to bisulfate and the appropriate mercaptan (eq 1).[2-4] The reaction

$$R\text{-}S\text{-}SO_3^- + H_2O \xrightarrow{H^+} R\text{-}SH + HSO_4^- \qquad (1)$$
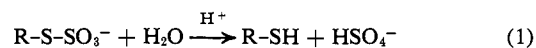
is one of a sizeable group of hydrolyses of sulfate derivatives (eq 2) which involve replacement of the group Y

$$Y\text{-}SO_3^- + H_2O \longrightarrow HO\text{-}SO_3^- + Y\text{-}H \qquad (2)$$
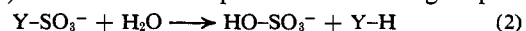
originally bonded to the sulfate sulfur by OH. Some other members of the group are the following hydrolyses: sulfamic acid[5] (eq 2, Y = NH_2); aryl sulfates[6]

(2) T. S. Price and D. F. Twiss, *J. Chem. Soc.*, **95**, 1725 (1909).
(3) (a) Z. El-Heweki and E. Taeger, *J. Prakt. Chem.*, **7**, 191 (1958); (b) P. Baumgarten, *Ber.*, **63**, 1330 (1930).
(4) (a) H. E. Westlake and G. Dougherty, *J. Am. Chem. Soc.*, **63**, 658 (1941); (b) H. Z. Lecher and E. M. Hardy, *J. Org. Chem.*, **20**, 475 (1955); (c) U. Weiss and S. Sokol, *J. Am. Chem. Soc.*, **72**, 1687 (1950); (d) B. Saville, *J. Chem. Soc.*, 1730 (1960).

(5) J. P. Candlin and R. G. Wilkins, *ibid.*, 4236 (1960).
(6) (a) G. N. Burkhardt, W. G. K. Ford, and E. Singleton, *ibid.*, 17 (1936); (b) J. L. Kice and J. M. Anderson, *J. Am. Chem. Soc.*, **88**, 5242 (1966).

Table I. Kinetics of the Acid-Catalyzed Hydrolysis of Bunte Salts in 60% Dioxane at 69.7°

Bunte salt,[a] $RSSO_3^-M^+$, R	M^{+b}	$k_\psi \times 10^4$, sec^{-1c}					
		0.24 M	0.40 M	0.60 M	0.81 M	1.20 M	1.81 M
C_6H_5	$C_5H_5NH^+$	0.69	0.92	1.33	1.81	2.95	5.65
C_6H_5	Na^+	0.66	0.90	1.25	1.73	2.77	5.20
$p\text{-}CH_3C_6H_4$	$C_5H_5NH^+$	0.66	1.00	1.29	1.61	2.78	5.22
$p\text{-}(CH_3)_3CC_6H_4$	$C_5H_5NH^+$	0.72	0.93	1.45	1.82	2.96	4.68
$p\text{-}ClC_6H_4$	$C_5H_5NH^+$	0.45	0.66	1.07	1.31	2.09	3.98
$p\text{-}BrC_6H_4$	$C_5H_5NH^+$	0.47	0.62	0.98	1.18	2.04	3.75
$p\text{-}O_2NC_6H_4$	$C_5H_5NH^+$	0.17	0.34	0.48	0.81	1.65	4.0
$m\text{-}O_2NC_6H_4$	Na^+	0.19	0.29	0.44	0.65	1.19	2.61
$C_6H_5CH_2$	Na^+	0.79	1.08	1.52	1.91	3.33	5.9
CH_3CH_2	Na^+	1.01	1.41	2.22	2.82	4.54	8.82

[a] All runs at an initial Bunte salt concentration of 0.05 M. [b] $C_5H_5NH^+$ equals pyridinium ion. [c] At molarities of $HClO_4$ shown.

(Y = OAr); alkyl sulfates[7] (Y = OR); thiosulfate[8] (Y = S$^-$); hydroxylamine O-monosulfate[9,10] (Y = ONH$_2$); and N-monosulfate[9] (Y = NHOH).

A detailed knowledge of the mechanism of the Bunte salt hydrolysis is of interest for several reasons. First, and most important, it can contribute to further understanding of the type of mechanisms involved in the hydrolysis of sulfate derivatives. Second, since the pharmaceutical activity and radiation-protective properties of certain Bunte salts may actually be due to the mercaptan liberated by their hydrolysis,[11] knowledge of the mechanism is of considerable pharmacological importance.

Several years ago we reported[12] the results of a kinetic study of the acid-catalyzed hydrolysis of a Bunte salt (EtSSO$_3^-$Na$^+$) in aqueous hydrochloric and perchloric acids. These data, however, were not sufficient to allow any extensive conclusions about the mechanism of the reaction or even to permit a definite decision as to whether the hydrolysis was of the A-1 or A-2 mechanistic type. In order to answer this question and to obtain a reasonably detailed picture of the hydrolysis mechanism we have now carried out a more extensive study of the hydrolysis of a variety of Bunte salts in which we have determined: (1) the dependence of the rate of hydrolysis of $RSSO_3^-$ on the structure of R; (2) the solvent isotope effect; (3) the variation of the rate and the activation parameters with water content in dioxane–water mixtures; and (4) the dependence of the rate on the concentration of strong acid catalyst in 60% dioxane as solvent. These results are combined with the earlier data[12] on the dependence of the rate on acidity in aqueous acid and are then compared with appropriate data for the acid-catalyzed hydrolyses of sodium phenyl sulfate[6b] (a known A-1 reaction) and sodium methyl selenate[13] (an A-2 reaction).

Results

The kinetics of the various Bunte salt hydrolyses (eq 1) were all studied by following the rate of formation of mercaptan. The exact experimental procedure (see Experimental Section) varied somewhat depending on

(7) (a) R. L. Burwell, J. Am. Chem. Soc., 74, 1462 (1952); (b) S. Burstein and S. Liberman, ibid., 80, 5235 (1958).
(8) W. A. Pryor, ibid., 82, 4794 (1960).
(9) J. P. Candlin and R. G. Wilkins, ibid., 87, 1490 (1965).
(10) P. A. S. Smith, H. R. Alul, and R. L. Baumgarten, ibid., 86, 1139 (1964).
(11) B. Milligan and J. M. Swan, Rev. Pure Appl. Chem., 12, 72 (1962)
(12) J. L. Kice, J. Org. Chem., 28, 957 (1963).
(13) C. A. Bunton and B. N. Hendy, J. Chem. Soc., 3130 (1963).

the Bunte salt and solvent medium. In every case, though, good first-order kinetics were observed.

Effect of Bunte Salt Structure on Rate of Hydrolysis. Table I summarizes the variation in experimental first-order hydrolysis rate constant, k_ψ, with changes in Bunte salt structure and acid concentration for 60% dioxane as solvent. Two points are worth noting initially. First, from the top two rows of data it is clear that the nature of the cation M$^+$ accompanying the anion $RSSO_3^-$ has no significant effect on the rate of hydrolysis. Second, the data for the S-phenyl, S-benzyl, and S-ethyl thiosulfates reveal that simple alkyl and aryl Bunte salts hydrolyze at very similar rates. This is in contrast to the behavior of the corresponding sodium alkyl and aryl sulfates, $ROSO_3^-Na^+$, where the aryl sulfates hydrolyze much faster than the alkyl compounds.[6b]

As far as the various aryl Bunte salts are concerned, the data in Table I indicate that the presence of electron-withdrawing substituents in the aromatic ring leads to a decrease in the rate of hydrolysis. Figure 1 shows a plot of log k_ψ for $YC_6H_4SSO_3^-$ vs. σ for the hydrolyses in 0.40 M perchloric acid. While the correlation is not particularly good, ρ appears to be about -0.6. Actually, quantitative assessment of the effect of structure on hydrolysis rate is somewhat further complicated by the fact that the nitro-substituted compounds, particularly the p-nitrophenyl Bunte salt, exhibit a more pronounced dependence on acidity than do the other Bunte salts.[14] This means that the nitro compounds will appear more reactive relative to the other salts at higher perchloric acid concentrations. Thus a plot similar to Figure 1 for the data for 1.20 M perchloric acid solutions gives an apparent ρ of -0.4.

Effect of Dioxane Content on Rate of Hydrolysis in Dioxane–Water Mixtures. The rate of hydrolysis of sodium S-benzyl thiosulfate was measured at a fixed perchloric acid concentration in three different dioxane–water mixtures at several temperatures. The results are shown in Table II. From these it is apparent that the rate of hydrolysis is markedly increased by an increase in the dioxane content of the medium. The effect is similar to the one observed in the acid hydrolysis of sodium aryl sulfates[6b] but is somewhat larger in magnitude. The data show that it is entirely due to a more favorable entropy of activation.

(14) Just why the nitro compounds show a somewhat different dependence of rate on acid concentration than the other Bunte salts is not known at present. However, we doubt that it is indicative of a different mechanism of hydrolysis for these compounds and suspect that it may be due to solvation phenomena involving the nitro group.

Table II. Effect of Solvent Composition on the Rate of
Acid-Catalyzed Hydrolysis of Sodium S-Benzyl Thiosulfate

[HClO$_4$], M	Solvent	Temp, °C	$k_\psi \times 10^4$, sec^{-1}	E_a, kcal/mole
0.495	40% dioxane–60% H$_2$O (v/v)	70.0	0.243	
		85.0	1.58	
		90.0	2.79	30.0
	60% dioxane–40% H$_2$O (v/v)	60.0	0.36	
		70.0	1.45	
		80.0	4.98	30.4
	80% dioxane–20% H$_2$O (v/v)	40.1	0.37	
		50.0	1.70	
		60.0	7.20	30.4
		70.0	(27)[a]	

[a] Calculated from data at 40, 50, and 60°.

Solvent Isotope Effect. The solvent isotope effect associated with a typical Bunte salt hydrolysis was determined by measuring the rate of acid-catalyzed hydrolysis of sodium S-ethyl thiosulfate in heavy and light water. The results, which are shown in Table III, indicate $(k_{D_2O}/k_{H_2O}) = 1.4$ for the hydrolysis of this Bunte salt.

Table III. Solvent Isotope Effect for the Acid-Catalyzed
Hydrolysis of Sodium S-Ethyl Thiosulfate

Temp, °C	Solvent	[HCl], M	[DCl], M	$k_\psi \times 10^4$, sec^{-1}
95	H$_2$O	1.00		0.78[a]
	D$_2$O		1.00	1.08[a]
	$(k_{D_2O}/k_{H_2O}) = 1.4$			

[a] Average of two runs.

One's first reaction might be that this value for k_{D_2O}/k_{H_2O} was indicative of an A-2 mechanism for the Bunte salt hydrolysis since it is in the range (1.3–1.7) normally associated[15,16] with such a mechanism. However, one must remember that the usual rules for relating solvent isotope effects to A-1 and A-2 mechanisms are derived for protonation of the substrate on oxygen and that an A-1 mechanism for the Bunte salt hydrolysis such as

$$R-S-SO_3^- + H^+ \underset{fast}{\overset{}{\rightleftharpoons}} R-\overset{+}{\underset{|}{S}}-SO_3^- \overset{slow}{\longrightarrow}$$
$$H$$

$$\begin{bmatrix} R-\overset{\delta+}{\underset{|}{S}}\cdots SO_3^{\delta-} \\ H \end{bmatrix} \longrightarrow R-SH + SO_3 \quad (3)$$
transition state
I

involving protonation of the substrate on sulfur could exhibit a considerably smaller solvent isotope effect because of the considerably lower vibrational stretching frequency associated with an S–H bond as compared to an analogous O–H bond.

As a matter of fact we can make a reasonable rough estimate of what k_{D_2O}/k_{H_2O} should be for the mechanism in eq 3. We know from other work[6b] that the acid-catalyzed hydrolysis of sodium phenyl sulfate takes

(15) J. G. Pritchard and F. A. Long, *J. Am. Chem. Soc.*, **78**, 6008 (1956); **80**, 4162 (1958).
(16) C. A. Bunton and V. J. Shiner, Jr., *ibid.*, **83**, 3207 (1961).

Figure 1. Log (k/k_0) vs. σ for the hydrolysis of *meta*- and *para*-substituted S-phenyl thiosulfates in 60% dioxane containing 0.40 M perchloric acid.

place by the following A-1 mechanism

$$Ph\text{-}O\text{-}SO_3^- + H^+ \underset{}{\overset{fast}{\rightleftharpoons}} Ph\text{-}\overset{+}{\underset{|}{O}}\text{-}SO_3^- \overset{slow}{\longrightarrow}$$
$$H$$

$$\begin{bmatrix} Ph\text{-}\overset{\delta+}{\underset{|}{O}}\cdots SO_3^{\delta-} \\ H \end{bmatrix} \longrightarrow PhOH + SO_3 \quad (4)$$
transition state
II

and that at 60° it exhibits a solvent isotope effect of $(k_{D_2O}/k_{H_2O}) = 2.4$. The considerably lower stretching frequency of the S–H bond in I as compared with the O–H bond in II should cause (k_{D_2O}/k_{H_2O}) for eq 3 to be smaller than that for eq 4. If we assume, as is a reasonable approximation, that this difference in vibrational stretching frequency is the only significant factor responsible for a difference in k_{D_2O}/k_{H_2O} for the two reactions, then the solvent isotope effect for eq 3 should be given by

$$\left(\frac{k_{H_2O}}{k_{D_2O}}\right)_{eq\ 3} = \left(\frac{k_{H_2O}}{k_{D_2O}}\right)_{eq\ 4} \times$$
$$\text{antilog}\left[\frac{\nu_{OH}{}^{II} - \nu_{SH}{}^{I}}{12.53 \times T}\right] \quad (5)$$

As a reasonable estimate for $\nu_{OH}{}^{II} - \nu_{SH}{}^{I}$ we have taken the difference between ν_{OH} for phenol in water, calculated from the equation of Bunton and Shiner[17] as 3225 cm^{-1}, and ν_{SH} for an aliphatic mercaptan,[18] 2575 cm^{-1}.[19] This leads to a predicted solvent isotope effect for eq 3 at 60° of

$$\left(\frac{k_{H_2O}}{k_{D_2O}}\right)_{eq\ 3} = \frac{1}{2.4} \times \text{antilog}\left[\frac{3225 - 2575}{12.53 \times 333}\right] =$$
$$\frac{1.43}{2.4} = 0.60$$

Using the equation given by Bunton and Shiner[17] for the predicted dependence of solvent isotope effect on

(17) C. A. Bunton and V. J. Shiner, Jr., *ibid.*, **83**, 42 (1961).
(18) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958, pp 350–351.
(19) The effects of substituents on the rates of the two reactions indicate that there is probably not a large amount of positive charge on the sulfur and oxygen atoms of I and II. Therefore the use of the mercaptan and the phenol as models for the state of the S–H and O–H bonds in I and II, respectively, while not ideal, is probably satisfactory.

temperature, at 95° this would be

$$\left(\frac{k_{H_2O}}{k_{D_2O}}\right)_{eq\ 3} = 0.63, \text{ or } \left(\frac{k_{D_2O}}{k_{H_2O}}\right)_{eq\ 3} = 1.6$$
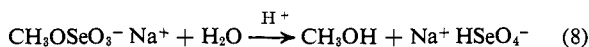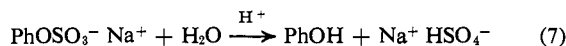
From this analysis we can see that an A-1 mechanism of the type shown in eq 3 can easily exhibit a solvent isotope effect whose magnitude is in the range normally associated with A-2 mechanisms for substrates involving protonation on oxygen. For this reason the value of 1.4 found for k_{D_2O}/k_{H_2O} for the Bunte salt hydrolysis is just as consistent with the A-1 mechanism shown in eq 3 as it is with the A-2 mechanism shown in eq 6.

$$R-S-SO_3^- + H^+ \underset{}{\overset{fast}{\rightleftharpoons}} R-S-SO_3H \tag{6a}$$

$$RSSO_3H + H_2O \xrightarrow{slow} R\overset{\displaystyle OH}{\underset{\displaystyle OH}{S}}SO_2H \xrightarrow{fast} RSH + H^+ + HSO_4^- \tag{6b}$$
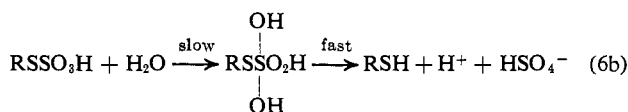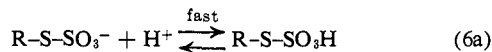
The decision between such mechanisms will accordingly have to be based on other experimental results than the solvent isotope effect.

Discussion

Two reactions which are closely related to the Bunte salt hydrolysis are the acid-catalyzed hydrolyses of sodium phenyl sulfate (eq 7) and sodium methyl selenate (eq 8). As already noted, the hydrolysis of the sulfate presumably proceeds by the A-1 mechanism

$$PhOSO_3^- Na^+ + H_2O \xrightarrow{H^+} PhOH + Na^+ HSO_4^- \tag{7}$$

$$CH_3OSeO_3^- Na^+ + H_2O \xrightarrow{H^+} CH_3OH + Na^+ HSeO_4^- \tag{8}$$

shown in eq 4.[6b] On the other hand, Bunton and Hendy[13] have shown that the hydrolysis of the selenate almost certainly proceeds by an A-2 mechanism involving attack of water on the selenium atom of methyl hydrogen selenate (eq 9).

$$CH_3OSeO_3^- + H^+ \underset{}{\overset{fast}{\rightleftharpoons}} CH_3OSeO_3H \tag{9a}$$

$$CH_3OSeO_3H + H_2O \xrightarrow{slow} CH_3OH + H^+ + HSeO_4^- \tag{9b}$$
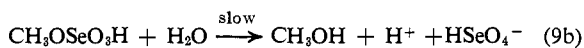
As might be expected from the fact that one is an A-1 reaction while the other is A-2, the sulfate and selenate hydrolyses differ markedly in: (1) their change in rate with changing acid concentration in concentrated aqueous acid; (2) their change in rate with changing dioxane content in aqueous dioxane solutions containing a fixed amount of strong acid; and (3) their solvent isotope effect. It was our hope, therefore, that comparison of suitable experimental data for the Bunte salt hydrolysis with the results just cited for the sulfate and selenate hydrolyses might rather clearly indicate whether the Bunte salt reaction involves an A-1 or A-2 mechanism.

Unfortunately, for reasons outlined in some detail in the preceding section, the solvent isotope effect for the Bunte salt hydrolysis is not helpful in defining mechanism, being just as consistent with an A-1 mechanism involving protonation on sulfur (eq 3) as with an A-2 mechanism involving protonation on oxygen (eq 6). The data on the dependence of rate on acidity and dioxane content are, however, of value.

Log k_ψ for the acid-catalyzed hydrolysis of sodium phenyl sulfate in aqueous acid plots linearly vs. the Hammett acidity function, $-H_0$, with a slope of 0.99.[6b] An earlier study[12] showed that log k_ψ for the hydrolysis of the Bunte salt $CH_3CH_2SSO_3Na$ exhibits exactly the same dependence on $-H_0$ in aqueous acid. In contrast, Bunton and Hendy[13] found for the hydrolysis of sodium methyl selenate that a plot of log k_ψ vs. $-H_0$ was far from linear, being a smooth curve whose slope decreased with increasing $-H_0$. The dependence of the rate of hydrolysis of the Bunte salt on H_0 in aqueous acid is thus identical with that exhibited by the known A-1 reaction —the sulfate hydrolysis (eq 7)—and very different from that for the A-2 reaction—the selenate hydrolysis (eq 8). It is also interesting that in 60% dioxane the rates of hydrolysis of $PhSSO_3Na$ and $PhOSO_3Na$[6b] increase by the same magnitude for a given change in strong acid concentration.[20] This also suggests that the two hydrolyses probably proceed by quite similar mechanisms.

In aqueous dioxane the rates of both the A-1 hydrolysis of sodium phenyl sulfate[6b] (eq 4) and the A-2 hydrolysis of sodium methyl selenate[13] (eq 9) increase with an increase in the dioxane content of dioxane-water mixtures containing a fixed concentration of perchloric acid. However, for the reasons outlined in the preceding paper,[6b] the rate of the A-1 hydrolysis proceeding via eq 4 should, and does, show a considerably larger increase for a given increase in dioxane content than that found for the A-2 hydrolysis of the selenate (eq 9). Comparison of the effect of dioxane content on the rate of the Bunte salt hydrolysis in aqueous dioxane with the results for the sulfate and selenate hydrolyses can therefore provide a further indication whether the Bunte salt hydrolysis involves an A-1 or an A-2 mechanism. Such a comparison is presented in Table IV. From it one can see that the Bunte salt

Table IV. Effect of Per Cent Dioxane on Relative Rate of Hydrolysis in Dioxane-Water Mixtures

| Solvent | $k/k_{40\%\ diox}$, hydrolysis of | | |
	$PhCH_2SSO_3Na^a$	$PhOSO_3Na^b$	$CH_3OSeO_3Na^c$
40% dioxane	(1.0)	(1.0)	(1.0)
60% dioxane	6.0	5.0	1.6
80% dioxane	110[d]	67[d]	6.3

[a] Data are for 70° for solutions 0.5 M in perchloric acid. [b] Data are for 30.1° for solutions 0.5 M in perchloric acid.[6b] [c] Data are for 25.1° for solutions 0.1 M in perchloric acid.[13] [d] Extrapolated from data at lower temperatures.

hydrolysis shows rate increases which are quite similar to those found for the sulfate hydrolysis and much larger than those found for the selenate hydrolysis. These results would therefore seem to provide further indication that the Bunte salt hydrolysis proceeds by an A-1 mechanism.

(20) A plot of log k_ψ for the hydrolysis rate of either $PhSSO_3Na$ (Table I) or $PhOSO_3Na$[6b] in 60% dioxane containing 0.24-1.81 M HClO$_4$ vs. $-H_0$ for these same solutions,[21] while linear, has a slope of only $+0.45$. Obviously the parallel between H_0 and H_- which has been observed for 1.0-6.0 M aqueous perchloric or hydrochloric acid solutions[22] does not extend to solutions of the same acids in 60% dioxane. This is hardly surprising, however.

(21) C. A. Bunton, J. B. Ley, A. J. Rhind-Tutt, and C. A. Vernon, J. Chem. Soc., 2327 (1957).

(22) Unpublished results of Fuller, Hughes, and Ingold (Fuller, Thesis, London, 1961) quoted by Bunton and Hendy.[13]

The only reasonable A-1 mechanism that can be written for the Bunte salt hydrolysis is the one shown in eq 3.[23] One must then ask whether the observed effect of substituents on the rate of hydrolysis of $ArSSO_3^-$ ($\rho = -0.5$) is compatible with this mechanism. The answer is clearly in the affirmative, since for the mechanism shown in eq 3 it is perfectly reasonable that the electron density on the sulfide sulfur could be somewhat lower in the transition state (I) than it is in the Bunte salt itself.

Accordingly, we feel that an A-1 mechanism is strongly indicated for the Bunte salt hydrolysis by the data on the dependence of rate on acidity and dioxane content and that the particular A-1 mechanism shown in eq 3 is one which is completely compatible with both the solvent isotope effect and the effect of changes in Bunte salt structure on reaction rate.

Comparison of Structural Effects in the Hydrolysis of Bunte Salts and Sodium Aryl Sulfates.

The rates of the Bunte salt and sulfate hydrolyses respond somewhat differently to changes in alkyl or aryl group structure. Thus the hydrolysis of aryl Bunte salts is somewhat retarded by electron-withdrawing substituents in the aromatic ring ($\rho \cong -0.5$, rate correlated by σ) while the hydrolysis of sodium aryl sulfates[6] is accelerated by the same substituents ($\rho = +0.5$, rate correlated by $\sigma-$). Also sodium phenyl sulfate apparently hydrolyzes much faster than its alkyl counterparts while there is practically no difference in the rates of hydrolysis of phenyl and alkyl Bunte salts. Since the A-1 mechanism (eq 3) that we are advocating for the Bunte salt hydrolysis is exactly the same type of mechanism proposed[6b] for the sulfate hydrolysis (eq 4), we need to explain how the two reactions can have the same basic mechanism and yet exhibit somewhat different response of rate to alkyl and and aryl group structure. The succeeding paragraphs outline a tentative explanation.

For the sulfate hydrolysis we have shown[6b] that both the faster rate for aryl sulfates and the positive ρ value and correlation of rates by $\sigma-$ constants can be explained by assuming that, although there is no significant resonance interaction between an unshared pair on oxygen and the aromatic ring in $ArOSO_3^-$ itself, there is significant stabilization of the transition state for its hydrolysis by an interaction of this sort, just as there is stabilization of the product phenol, i.e.
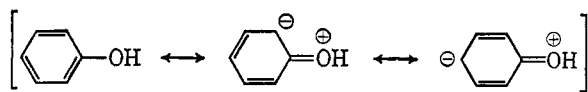
(23) The alternate A-1 mechanism (eq 10), involving the oxygen-protonated conjugate acid of the Bunte salt (III) as an intermediate, seems unacceptable for several reasons. First, in contrast to eq 3 where

$$R\text{-}S\text{-}SO_3^- + H^+ \underset{}{\overset{\text{fast}}{\rightleftharpoons}} RSSO_3H \overset{\text{slow}}{\longrightarrow}$$
$$\text{III}$$
$$RS^- + HSO_3^+ \overset{H_2O}{\underset{\text{fast}}{\longrightarrow}} RSH + H_2SO_4 \quad (10)$$
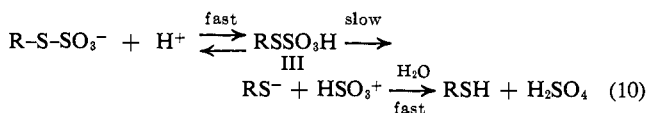
protonation on sulfur assists cleavage of the S-S bond by converting $RS-$ to the better leaving group $\overset{+}{R}S(H)-$, we can assign no reasonable role for the proton in eq 10, since heterolysis of the S-S bond and expulsion of RS^- should be easier for $RS\text{-}SO_3^-$ than for $RS\text{-}SO_3H$. Second, eq 10 should exhibit a considerably larger value of k_{D_2O}/k_{H_2O} than 1.4. Third, the observed effects of changes in the structure of R on rate indicate that the sulfide sulfur has a slightly lower electron density in the transition state than it has in the Bunte salt itself; eq 10 would seem to require the opposite, i.e., an increase in the electron density on the sulfide sulfur on going from Bunte salt to transition state.

This implies that in the sulfate hydrolysis the transition state is considerably closer in structure to (phenol + sulfur trioxide) than it is to $Ar\overset{+}{O}(H)\text{-}SO_3^-$ and that the O-S bond is almost entirely severed by the time the transition state is reached.

We suggest two factors are responsible for the different response of rate to structural change observed for the Bunte salt hydrolysis. First, we think the S-S bond is probably broken to a lesser extent in the Bunte salt transition state than is the O-S bond in the sulfate transition state. This would mean that, compared to the sulfate reaction, the transition state for the Bunte salt hydrolysis is further from the products (ArSH + $\overset{+}{S}O_3$) and closer to the zwitterion intermediate (ArS-$(H)\text{-}SO_3^-$) in structure.[24] As a result, the electron density on the sulfide sulfur in the transition state can be significantly lower than the electron density on the analogous oxygen atom in the transition state for the hydrolysis of the sulfate. Second, both because the structure of the transition state for the Bunte salt reaction is not as close to products and because resonance of an unshared pair with the aromatic ring is less important for thiophenol than for phenol,[26] any stabilization of the transition state for hydrolysis of an aryl Bunte salt via resonance of an unshared pair on sulfur with the aromatic ring is so small as to be of no consequence. This explains why, unlike the sulfates, where resonance stabilization of this sort in the transition state leads to a much faster rate of hydrolysis for the aryl compounds, the aryl and alkyl Bunte salts hydrolyze at essentially the same rate.

Experimental Section

Preparation of Bunte Salts. Pyridinium S-Aryl Thiosulfates. The various pyridinium S-aryl thiosulfates were all prepared by the same general procedure, which was a slight modification of the one described by Baumgarten.[3b] It consisted of heating together in carbon tetrachloride for 1-2 hr on the steam bath equimolar amounts of the appropriate aromatic thiol and N-pyridinium-sulfonic acid.[27] After cooling the mixture, the Bunte salt was filtered off and purified by being recrystallized several times from ethanol. After each recrystallization the Bunte salt was triturated with a small amount of ether. It was finally dried in a vacuum desiccator at 1-mm pressure.

Pyridinium S-phenyl thiosulfate, mp 89-91° (lit.[3b] 89-91°), was a known compound. The other pyridinium S-aryl thiosulfates had not been previously prepared. Their analytical data and melting points are summarized in Table V.

Sodium S-phenyl thiosulfate was prepared from pyridinium S-phenyl thiosulfate by an ion-exchange procedure. Dowex 50W-X4 resin was converted to the sodium form by treatment with 10% sodium chloride solution. After being treated with sodium chloride solution the resin was washed with distilled water until the eluent gave a negative test for chloride ion with silver nitrate.

Pyridinium S-phenyl thiosulfate (15 g, estimated as equivalent to 38% of the total resin wet-volume exchange capacity) was dissolved in 200 ml of water, and the solution was allowed to stand in contact with the column of ion-exchange resin for 1 hr. The column of resin was then allowed to drain and was subsequently washed with

(24) According to Hammond's principle[25] this postulate that the transition state occurs somewhat earlier along the reaction coordinate in the Bunte salt case is only tenable if the free energy change for $Ar\overset{+}{S}(H)\text{-}SO_3^- \longrightarrow ArSH + SO_3$ is considerably more favorable than that for $Ar\overset{+}{O}(H)\text{-}SO_3^- \rightarrow ArOH + SO_3$. Whether this is in fact true or not cannot be determined with certainty, but it at least seems reasonable such a difference might exist.

(25) G. S. Hammond, J. Am. Chem. Soc., 77, 334 (1955).

(26) Compare, for example, $\sigma_p - \sigma_m$ for CH_3O (-0.38) with that for CH_3S (-0.15).

(27) P. Baumgarten, Ber., 59, 1166 (1926).

Table V. Properties of Pyridinium S-Aryl Thiosulfates

ArSSO₃⁻ C₅H₅NH⁺ Ar =	Mp, °C	Formula	Calcd, %		Found, %	
			C	H	C	H
p-CH₃C₆H₄	115–117	C₁₂H₁₃NO₃S₂	50.86	4.62	50.80	4.72
p-ClC₆H₄	123–124	C₁₁H₁₀ClNO₃S₂	43.49	3.32	43.18	3.41
p-BrC₆H₄	129	C₁₁H₁₀BrNO₃S₂	37.94	2.89	37.91	3.01
p-(CH₃)₃CC₆H₄	139	C₁₅H₁₉NO₃S₂	55.36	5.88	54.94	5.87
p-O₂NC₆H₄	155–156	C₁₁H₁₀N₂O₅S₂	42.03	3.21	41.83	3.23

distilled water. The wash water was collected. Evaporation of the wash water under reduced pressure yielded pure sodium S-phenyl thiosulfate as its monohydrate, mp 180–182° dec. *Anal.* Calcd for C₆H₅S₂O₃Na·H₂O: C, 31.30; H, 3.06. Found: C, 31.26; H, 3.33.

Sodium S-(*m*-nitrophenyl) thiosulfate was prepared by the method of Lecher and Hardy.[4b] This involves the reaction of bis(3-nitrophenyl) disulfide with sodium bisulfite. The only modification that was made in their procedures was to wash the final product a number of times with anhydrous methanol instead of only once.

Sodium S-Ethyl Thiosulfate. This was prepared as described in an earlier paper.[12]

Sodium S-benzyl thiosulfate was synthesized by the method of Milligan and Swan.[28]

p-Nitrothiophenol was prepared by the procedure of Price and Stacy.[29] All the other aromatic thiols required for preparation of the various pyridinium S-aryl thiosulfates were purchased from commercial sources.

Solvents. Dioxane was purified by the same method used in the accompanying paper.[6b]

Procedure for Kinetic Runs. All runs except those involving the ethyl Bunte salt were carried out in the same type of reaction vessel

used for kinetic studies of the hydrolysis of sodium aryl sulfates.[6b] The procedure for preparing and deaerating the reaction solutions was also the same as that employed in the sulfate studies. The course of the reactions was followed by removing aliquots at appropriate time intervals and titrating the mercaptan which had been produced by hydrolysis of the Bunte salt with 0.1 N iodine solution. After 10 half-lives an infinity mercaptan titer was determined, and the first-order rate constant for the run was determined from a plot of log {1 − [(RSH)/(RSH)∞]} *vs.* time. The infinity mercaptan titer in each case corresponded satisfactorily to that expected from the amount of Bunte salt taken and the stoichiometry of eq 1.

In the case of the nitro-substituted S-aryl thiosulfates it was difficult to detect the end pont of the titration visually. With these compounds the end point was detected potentiometrically using a Beckman Model 72 pH meter with a combined platinum–calomel Beckman electrode.[30]

The runs with the ethyl Bunte salt in either water or deuterium oxide were carried out using a previously described procedure.[12] The runs with the same Bunte salt in 60% dioxane were carried out in sealed tubes. These tubes, containing aliquots of the reaction solution, were degassed in the usual manner before being sealed. The reaction was followed by removing tubes at appropriate time intervals, cooling and opening them, and then titrating the contents for mercaptan in the usual way with 0.1 N iodine solution.

(28) B. Milligan and J. M. Swan, *J. Chem. Soc.*, 2172 (1962).
(29) C. C. Price and G. W. Stacy, *J. Am. Chem. Soc.*, 68, 498 (1946).

(30) L. Gringas and G. Sjostedt, *Acta Chem. Scand.*, 15, 433 (1961).

Orientation, Reactivity, and Mechanism in the Addition of Methanol to 4-Chlorobenzyne[1]

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Abstract: 4-Chlorobenzyne adds methanol to form *p*- and *m*-chloroanisole in different ratios depending on the sodium methoxide concentration. The observed *para/meta* ratio is between 4.2 and 6.3 in neutral methanol and between 1.8 and 2.6 in 2 *M* methanolic sodium methoxide. The change in ratio shows that methoxide ion is more reactive than methanol toward 4-chlorobenzyne. The greater reactivity of methoxide ion and the fact that a stronger orienting effect prevails in methanol than in methoxide addition indicate that methanol addition is stepwise rather than a concerted, four-center process.

A n aryne generated in an alcoholic solvent usually adds the alcohol to form an aryl alkyl ether.[3−5] Addition of alcohol to a 4-substituted benzyne leads

to a mixture of isomeric ethers of *meta* and *para* orientation.
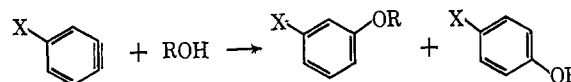
We have generated 4-chlorobenzyne in methanol solution by several routes, both in the presence and in the absence of sodium methoxide, and we have found

(3) M. Stiles, R. G. Miller, and U. Burckardt, *J. Am. Chem. Soc.*, 85, 1792 (1963).
(4) G. Wittig and R. W. Hoffmann, *Chem. Ber.*, 95, 2718, 2729 (1962).
(5) R. W. Hoffmann, G. E. Vargas-Nunez, G. Guhn, and W. Sieber, *ibid.*, 98, 2074 (1965).