AN ABSTRACT OF THE THESIS OF

<u>James Morley Anderson</u>   for the   <u>Ph. D.</u>
        (Name of student)   (Degree)

in   <u>Chemistry</u>   presented on <u>April 28, 1967</u>
        (Major)   (Date)

Title: MECHANISMS OF REACTIONS OF BUNTE SALTS AND
       RELATED COMPOUNDS
       I. THE ACID HYDROLYSIS OF SODIUM ARYL SULFATES
       II. THE ACID HYDROLYSIS OF BUNTE SALTS (S-ALKYL
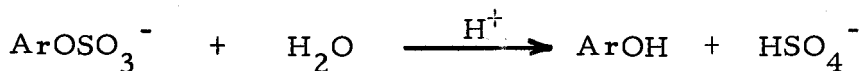   AND S-ARYL THIOSULFATES)

Abstract approved: _____Redacted for Privacy_____
                            John L. Kice

I. THE ACID HYDROLYSIS OF SODIUM ARYL SULFATES

The mechanism of the acid hydrolysis of sodium aryl sulfates
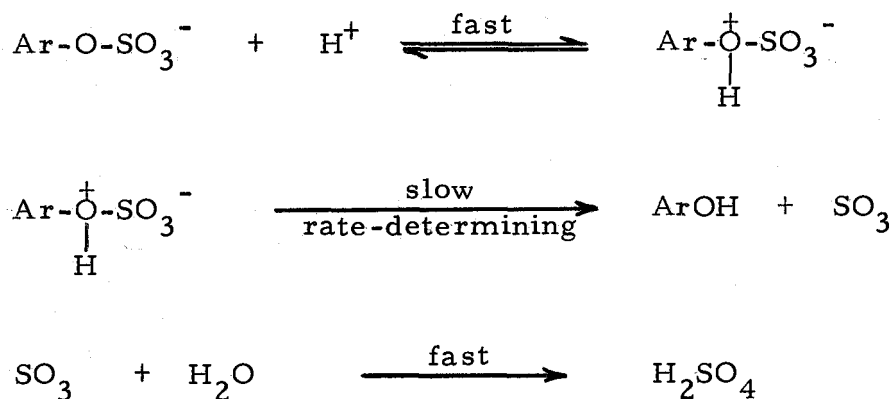
has been investigated.

$$ArOSO_3^- \ + \ H_2O \ \xrightarrow{\ H^+\ } \ ArOH \ + \ HSO_4^-$$

Data obtained by earlier workers have indicated that the rate of

hydrolysis of a series of aryl sulfates is best correlated by σ_- con-

stants with a ρ of about +0.5.

The present study has involved determination of (1) the solvent

isotope effect, (2) the dependence of hydrolysis rate on acidity of the

medium, and (3) the response of rate to changes in dioxane content

in dioxane-water mixtures for the acid-catalyzed hydrolysis of sodium

phenyl sulfate. The experimentally determined solvent isotope effect,

$k_{D_2O}/k_{H_2O} = 2.43$, lies in the range, $k_{D_2O}/k_{H_2O} = 1.9-2.6$, of val-

ues normally associated with A-1 hydrolysis mechanisms. A plot

of the logarithm of k_ψ for the hydrolysis of sodium phenyl sulfate

in aqueous hydrochloric acid solutions versus the Hammett acidity

function, $-H_o$, gives a linear plot with a slope of 0.99. The effect

of dioxane content on the rate of hydrolysis of sodium phenyl sulfate

was determined at a fixed strong acid concentration for 40, 60, and

80 percent dioxane-water mixtures. An increase in the dioxane con-

tent from 40 percent to 80 percent increased the rate of hydrolysis

by a factor of 67.

The above experimental results for the acid-catalyzed hydroly-

sis of sodium phenyl sulfate are compared with those for a closely

related reaction, the acid-catalyzed hydrolysis of sodium methyl

selenate. This latter reaction is known to proceed by an A-2 mech-

anism. In each case the data suggest that the mechanisms of the two

hydrolyses are different and that the hydrolysis of the aryl sulfate

involves an A-1 mechanism. The following A-1 mechanism is sug-

gested.

$$Ar-O-SO_3^- \ + \ H^+ \ \underset{}{\overset{fast}{\rightleftharpoons}} \ Ar-\overset{+}{\underset{H}{O}}-SO_3^-$$

$$Ar-\overset{+}{\underset{H}{O}}-SO_3^- \ \xrightarrow[\text{rate-determining}]{slow} \ ArOH \ + \ SO_3$$

$$SO_3 \ + \ H_2O \ \xrightarrow{fast} \ H_2SO_4$$

An explanation is offered as to how the hydrolysis of sodium aryl sulfates can occur <u>via</u> this A-1 mechanism and yet still exhibit the dependence of rate on aryl group structure which is observed. This same explanation also accounts for the fact that aryl sulfate ions hydrolyze much faster than alkyl sulfate ions.

II. THE ACID HYDROLYSIS OF BUNTE SALTS (S-ALKYL AND S-ARYL THIOSULFATES)

Seven different substituted aryl Bunte salts have been prepared and kinetic studies of their acid hydrolysis have been carried out in
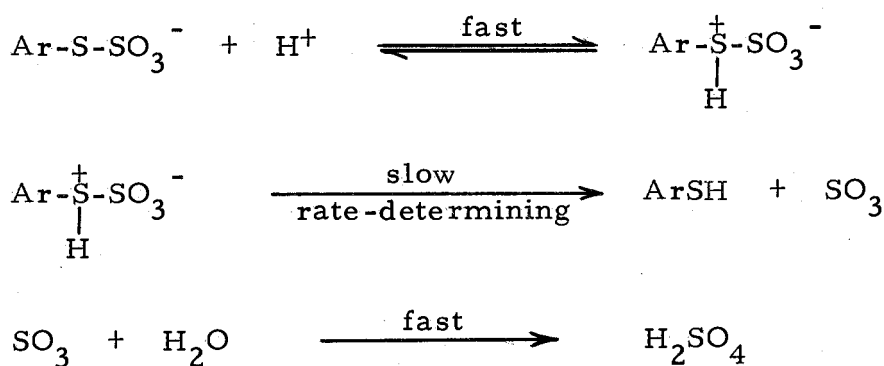
$$ArSSO_3^- + H_2O \xrightarrow{H^+} ArSH + HSO_4^-$$
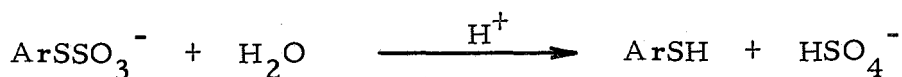
dioxane-water perchloric acid mixtures. Kinetic studies of the hydrolysis of two alkyl Bunte salts, the benzyl and ethyl compounds, were also carried out.

The hydrolysis rates of the aryl Bunte salts are best correlated by σ constants with a ρ of about -0.6. This indicates that the electron density on the sulfenyl sulfur, Ar-S-, is somewhat lower in the transition state of the rate-determining step than in the starting Bunte salt. The alkyl Bunte salts hydrolyze at essentially the same rate as does the phenyl Bunte salt.

The dependence of rate on the acidity of the medium and the response of rate to changes in dioxane content in dioxane-water

mixtures for the Bunte salt hydrolysis are compared with those

from the acid-catalyzed hydrolyses of sodium methyl selenate, a

known A-2 hydrolysis, and sodium phenyl sulfate, a known A-1

hydrolysis, and on the basis of this comparison the following A-1

mechanism is suggested for the Bunte salt hydrolysis. The previ-

ously determined solvent isotope effect for the Bunte salt hydrolysis

is discussed and shown to be consistent with the suggested A-1

mechanism.

$$\text{Ar-S-SO}_3^- + \text{H}^+ \xrightleftharpoons{\text{fast}} \overset{+}{\text{Ar-}\underset{\underset{\text{H}}{|}}{\text{S}}}\text{-SO}_3^-$$

$$\overset{+}{\text{Ar-}\underset{\underset{\text{H}}{|}}{\text{S}}}\text{-SO}_3^- \xrightarrow[\text{rate-determining}]{\text{slow}} \text{ArSH} + \text{SO}_3$$

$$\text{SO}_3 + \text{H}_2\text{O} \xrightarrow{\text{fast}} \text{H}_2\text{SO}_4$$

The fact that the Bunte salt hydrolysis and the aryl sulfate ion

hydrolysis occur via the same A-1 type mechanism yet exhibit differ-

ent structural effects is also discussed and an explanation is pre-

sented to account for the fact that they show this somewhat different

response of rate to changes in structure.

Mechanisms of Reactions of Bunte Salts
and Related Compounds

I. The Acid Hydrolysis of Sodium
    Aryl Sulfates

II. The Acid Hydrolysis of Bunte Salts
     (S-Alkyl and S-Aryl Thiosulfates)

by

James Morley Anderson

A THESIS

submitted to

Oregon State University

in partial fulfillment of
the requirements for the
degree of

Doctor of Philosophy

June 1967

APPROVED:

Redacted for Privacy

Professor of Chemistry
                    (in charge of major

Redacted for Privacy

Chairman of Department of Chemistry

Redacted for Privacy

Dean of Graduate School

Date thesis is presented _____ April 28, 1967 _____

Typed by Opal Grossnicklaus for _____ James Morley Anderson _____

To my parents,

Arnold S. and Evelyn Anderson.

Acknowledgement

I would like to thank Dr. John L. Kice for his interest, encouragement, and patience. His guidance has been invaluable and is sincerely appreciated.

Also, I would like to thank the Public Health Service for financial support during the course of this work.

My thanks are also extended to my friend Anne for whose help I am extremely grateful.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

MECHANISMS OF REACTIONS OF BUNTE SALTS
AND RELATED COMPOUNDS

I. THE ACID HYDROLYSIS OF SODIUM ARYL SULFATES

INTRODUCTION

The second part of this thesis is concerned with a study of the acid-catalyzed hydrolysis of S-aryl and S-alkyl thiosulfates, the so-called Bunte salts (Eq. 1).

$$RSSO_3^- \ + \ H_2O \ \xrightarrow{H^+} \ RSH \ + \ HSO_4^- \qquad (Eq. 1)$$

During this work it became evident that a detailed knowledge of the mechanism of the acid-catalyzed hydrolysis of sodium aryl sulfates (Eq. 2) would be helpful to the interpretation of the Bunte salt data, and it was for this reason that the present study was primarily undertaken.

$$ArOSO_3^- \ + \ H_2O \ \xrightarrow{H^+} \ ArOH \ + \ HSO_4^- \qquad (Eq. 2)$$
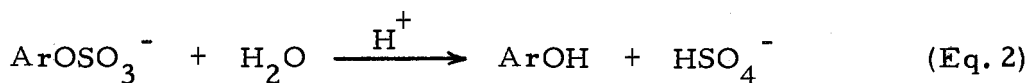
In 1936 Burkhardt and co-workers (16, 17, 18) conducted a kinetic study of the hydrolysis of sodium aryl sulfates in dilute hydrochloric acid. This study established the rate law (Eq. 3) for the reaction.

$$Rate \ = \ k_2 \ (H^+)(ArOSO_3^-) \qquad (Eq. 3)$$

These workers also found that the rate was accelerated by the

presence of electron-withdrawing substituents on the aromatic

ring. Specifically, a plot of the logarithm of the rate constant

versus the logarithm of the ionization constant of the correspond-

ing phenol, ArOH, was linear with a slope of about 0.25. The effect

of added salt was studied, and it was shown that the addition of po-

tassium chloride up to a concentration equal to that of sodium phenyl

sulfate produced only a slight increase in rate. The fact that the

rate is accelerated by the presence of electron-withdrawing substi-

tuents on the aromatic ring of the aryl sulfates (17, 18) indicates the

electron density on the phenolic oxygen is greater in the transition

state of the hydrolysis reaction than in $ArOSO_3^-$ itself.

At first this observation seems somewhat surprising when
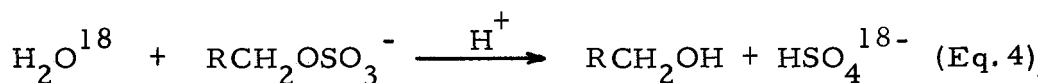
one recalls the mechanism which has generally been suggested for

the acid-catalyzed hydrolysis of sodium alkyl sulfates, $ROSO_3Na$.

A number of studies have shown that the acid-catalyzed hydrolysis

of a sodium n-alkyl sulfate (Eq. 4) involves oxygen-sulfur bond

cleavage (20, 21).

$$H_2O^{18} + RCH_2OSO_3^- \xrightarrow{H^+} RCH_2OH + HSO_4^{18-} \quad (Eq.\,4)$$

The fact that the rate of hydrolysis correlates with the Hammett

acidity function and that the entropy of activation is small and

positive has led workers (3, 4, 11, 21, 29) to suggest the following

A-1 type mechanism for the reaction (Eq. 5). At first glance it seems unlikely that the aryl sulfate reaction could involve this

$$RCH_2OSO_3^- + H^+ \xrightleftharpoons{\text{fast}} RCH_2\overset{+}{\underset{H}{O}}-SO_3^- \qquad \text{(Eq. 5a)}$$

$$RCH_2\overset{+}{\underset{H}{O}}-SO_3^- \xrightarrow[\text{rate-determining}]{\text{slow}} RCH_2OH + SO_3 \qquad \text{(Eq. 5b)}$$

$$SO_3 + H_2O \xrightarrow{\text{fast}} H^+ + HSO_4^- \qquad \text{(Eq. 5c)}$$
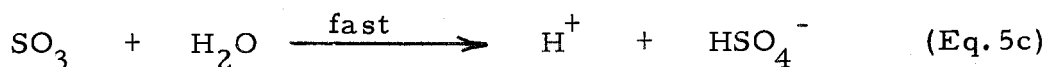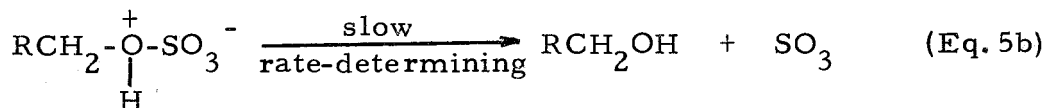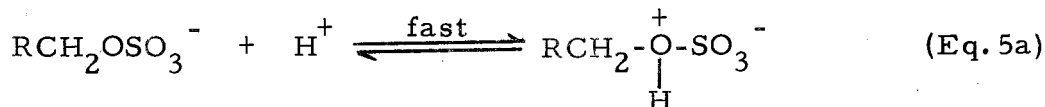
same mechanism (Eq. 5) because one would expect that in such a mechanism the electron density on the phenolic oxygen would be less, not greater, in the transition state than it is in $ArOSO_3^-$ itself.

One possible explanation could be that the hydrolysis of the aryl sulfate proceeds by a different mechanism, specifically the following A-2 mechanism (Eq. 6).

$$ArOSO_3^- + H^+ \xrightleftharpoons{\text{fast}} ArOSO_3H \qquad \text{(Eq. 6a)}$$

$$ArOSO_3H + H_2O \xrightarrow[\text{rate-determining}]{\text{slow}} ArO^- + H_2\overset{+}{O}SO_3H \qquad \text{(Eq. 6b)}$$

$$ArO^- + H_2\overset{+}{O}SO_3H \xrightarrow{\text{fast}} ArOH + H^+ + HSO_4^- \qquad \text{(Eq. 6c)}$$
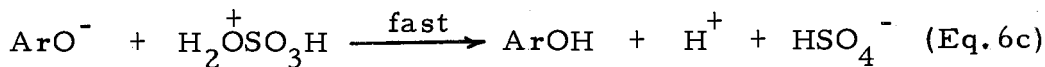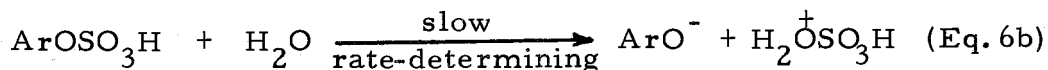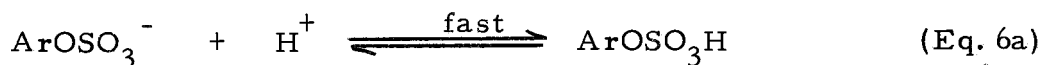
A mechanism of this type could account for the acceleration of rate by the presence of electron-withdrawing substituents of the aromatic ring as noted by Burkhardt and co-workers (17, 18). Also a mechanism of this type, A-2, could be much faster for the aryl sulfate,

$ArOSO_3^-$, hydrolysis than for the alkyl sulfate, $ROSO_3^-$, hydrolysis because ArO^- would be a much better leaving group than RO^-. The fact that for a given acid concentration, the hydrolysis rate of sodium phenyl sulfate (17) is indeed several hundred times larger than the hydrolysis rate of ethyl hydrogen sulfate (4) is also suggestive of this mechanism.

Ideally, the comparison of the solvent isotope effect, the dependence of rate on acidity of the medium, and the response of rate to changes in reaction solvent for the acid-catalyzed hydrolysis of sodium phenyl sulfate with those reaction variables of a known A-1 or A-2 type hydrolysis would be most helpful in deciding this matter and in determining the correct mechanism of the hydrolysis of sodium aryl sulfates.

Fortunately, such a comparison is possible as Bunton and Hendy (11) have determined, with a rather high degree of certainty, the exact mechanism of the acid-catalyzed hydrolysis of methyl hydrogen selenate. The structural similarity between sodium methyl selenate, I, and sodium phenyl sulfate, II, is very close and this favors the reliability of such a comparison.

$$CH_3\text{-}O\text{-}SeO_3^-Na^+ \qquad\qquad C_6H_5\text{-}O\text{-}SO_3^-Na^+$$
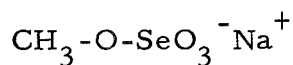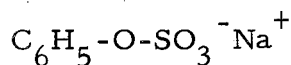
$$\text{I} \qquad\qquad\qquad\qquad\qquad \text{II}$$

For the acid-catalyzed hydrolysis of methyl hydrogen selenate, Bunton and Hendy (11) found that the entropy of activation was large and negative, $\Delta S = -23$ e.u., and that the activation energy was small, $E_a = 17.6$ kcal./mole. The solvent isotope effect, k_{D_2O}/k_{H_2O}, was 1.36. These facts suggest an A-2 mechanism in which either there is a direct displacement by water on CH_3OSeO_3H or an initial addition of water to this species occurs, and the resulting adduct then decomposes (42). The rate of hydrolysis increases as the dielectric constant of the medium is reduced. Plots of the logarithm of the first-order rate constant against the stoichiometric concentration of acid are linear with slopes ranging from 0.8 to 0.9. This also indicates that a water molecule is playing an active role as a nucleophile in the rate-determining step (33). From these experimental facts, Bunton and Hendy (11) concluded that the hydrolysis of methyl hydrogen selenate involves an A-2 mechanism in which water attacks the selenium atom of methyl hydrogen selenate (Eq. 7).

$$CH_3OSeO_3^- + H^+ \xrightleftharpoons{\text{fast}} CH_3OSeO_3H \qquad \text{(Eq. 7a)}$$

$$CH_3OSeO_3H + H_2O \xrightarrow[\text{rate-determining}]{\text{slow}} CH_3OH + H_2SeO_4 \qquad \text{(Eq. 7b)}$$
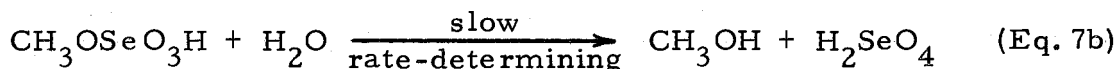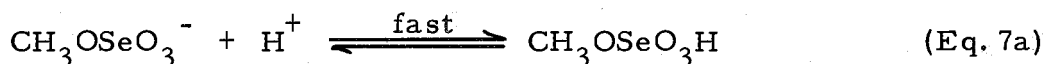
Therefore, if the acid-catalyzed hydrolysis of aryl sulfates occurs via an A-2 type mechanism one might expect its (1) solvent

isotope effect, (2) dependence of rate on acidity of the medium, and (3) response of rate to changes in dioxane content in dioxane-water mixtures to be similar to those observed by Bunton and Hendy (11) for the selenate system. On the other hand, if the hydrolysis of the sulfates involves an A-1 mechanism it will: (1) exhibit a considerably larger value of k_{D_2O}/k_{H_2O} that that found for the selenate system, (2) show a more pronounced increase in rate with increasing acidity, and (3) probably give a greater acceleration of rate with increasing dioxane content in dioxane-water mixtures.

With this in mind we accordingly undertook to determine the response of the sulfate hydrolysis to these changes in reaction conditions, in order that we might compare our results with those of Bunton and Hendy for the selenate system.

RESULTS

Synthesis of Sodium Aryl Sulfates

The first synthesis of an alkaline earth aryl sulfate was by

Baumann (5) who prepared potassium phenyl sulfate by heating an

alkaline solution of potassium pyrosulfate with phenol (Eq. 8). A

considerable number of years later Burkhardt and Lapworth (19)

$$\phi OH + K_2S_2O_7 \xrightarrow{\text{KOH}} \phi OSO_3K + KHSO_4 \qquad \text{(Eq. 8)}$$
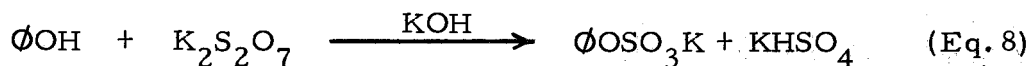
prepared sodium phenyl sulfate by reacting a mixture of

N, N-dimethylaniline and chlorosulfonic acid with phenol (Eq. 9).

$$\phi OH + (CH_3)_2 N\phi + ClSO_3H \longrightarrow \phi OSO_3H + (CH_3)_2(\phi)NHCl \quad \text{(Eq. 9a)}$$

$$\phi OSO_3H + NaOH \longrightarrow \phi OSO_3Na + H_2O \qquad \text{(Eq. 9b)}$$
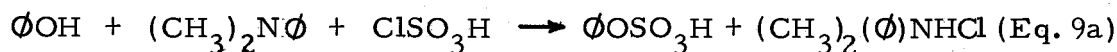
Our own synthesis of sodium phenyl sulfate followed Burkhardt

and Lapworth's procedure. The other sulfate whose hydrolysis we

have investigated was pyridinium p-nitrophenyl sulfate. This was

prepared by reacting the complex that is formed between pyridine

and sulfur trioxide with p-nitrophenol in refluxing benzene. The

product is pyridinium p-nitrophenyl sulfate (Eq. 10).

$$p\text{-}O_2NC_6H_4OH + C_5H_5N{:}SO_3 \longrightarrow p\text{-}O_2NC_6H_4OSO_3{}^- \overset{+}{H}NC_5H_5 \quad \text{(Eq. 10)}$$
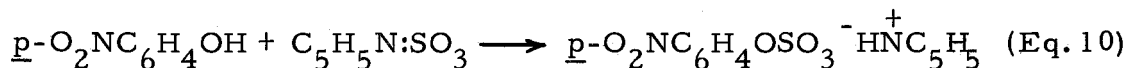
Kinetic Study of the Hydrolysis Reaction

The reaction vessel used, Figure 3, allowed an aliquot to be withdrawn without exposing the remainder of the reaction solution to the atmosphere. A run was initiated by dissolving a weighed amount of the aryl sulfate salt 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 five to ten minutes with pre-purified 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 one or two milliliter aliquots, diluting these aliquots with 95 percent ethanol, and measuring the optical density of the resulting solutions at 277 millimicrons for the phenyl sulfate ion hydrolysis or 320 millimicrons for the p-nitrophenyl sulfate ion hydrolysis. Since the extinction coefficient for the aryl sulfate ion is much smaller than that for the aryl phenol, the rate of the acid-catalyzed hydrolysis can be followed conveniently by observing the increase with time of the absorbance of the solution. An infinity time point was taken after eight to ten half-lives and the first-order rate constant, k_ψ, was calculated from a plot of the logarithm of $(A_\infty - A)$ versus time.

The rates of hydrolysis of sodium phenyl sulfate and

pyridinium-p-nitrophenyl sulfate were measured under a variety
of reaction conditions and the experimental first-order rate con-
stants for the acid-catalyzed hydrolysis, k_ψ, as studied at different
acid concentrations are tabulated in Tables 1 and 2.

Table 1. Kinetics of the acid-catalyzed hydrolysis of sodium phenyl
sulfate.

Temperature, °C	Solvent	Acid, $\underline{M}$		$k_\psi \times 10^{+4}$, sec.$^{-1}$
40.1	H_2O	HCl,	5.81	17.4
			4.97	9.08
			4.36	5.93
			2.91	1.63
			2.00	0.87
			1.00	0.32
30.1	60% dioxane- 40% water (v/v)	$HClO_4$,	1.81	10.3
			1.21	6.06
			0.81	3.80
			0.60	3.43
			0.50	2.47
			0.40	2.19
			0.24	1.57

Table 2. Kinetics of the acid-catalyzed hydrolysis of pyridinium
p-nitrophenyl sulfate.

Temperature °C	Solvent	Acid, $\underline{M}$	$k_\psi \times 10^{+4}$, sec.$^{-1}$
39.7	H_2O	HCl, 4.39	25.9
		2.92	6.98
		1.98	3.36
		1.00	1.28
30.1	60% dioxane- 40% water (v/v)	$HClO_4$, 0.81	14.3
		0.61	10.3
		0.40	7.57
		0.24	5.39

Figure 1 shows a plot of the logarithm of k_ψ for the hydrolysis of sodium phenyl sulfate and pyridinium p-nitrophenyl sulfate in aqueous hydrochloric acid solutions versus the Hammett acidity function (35), $-H_o$, for the same media. For sodium phenyl sulfate and pyridinium p-nitrophenyl sulfate the plots are linear with slopes of 0.99 for both compounds.

Figure 2 shows a plot of the logarithm of k_ψ for the hydrolysis of sodium phenyl sulfate and pyridinium p-nitrophenyl sulfate in 60 percent dioxane-40 percent water (volume/volume) perchloric acid solutions versus the Hammett acidity function (1, 12), $-H_o$, for the
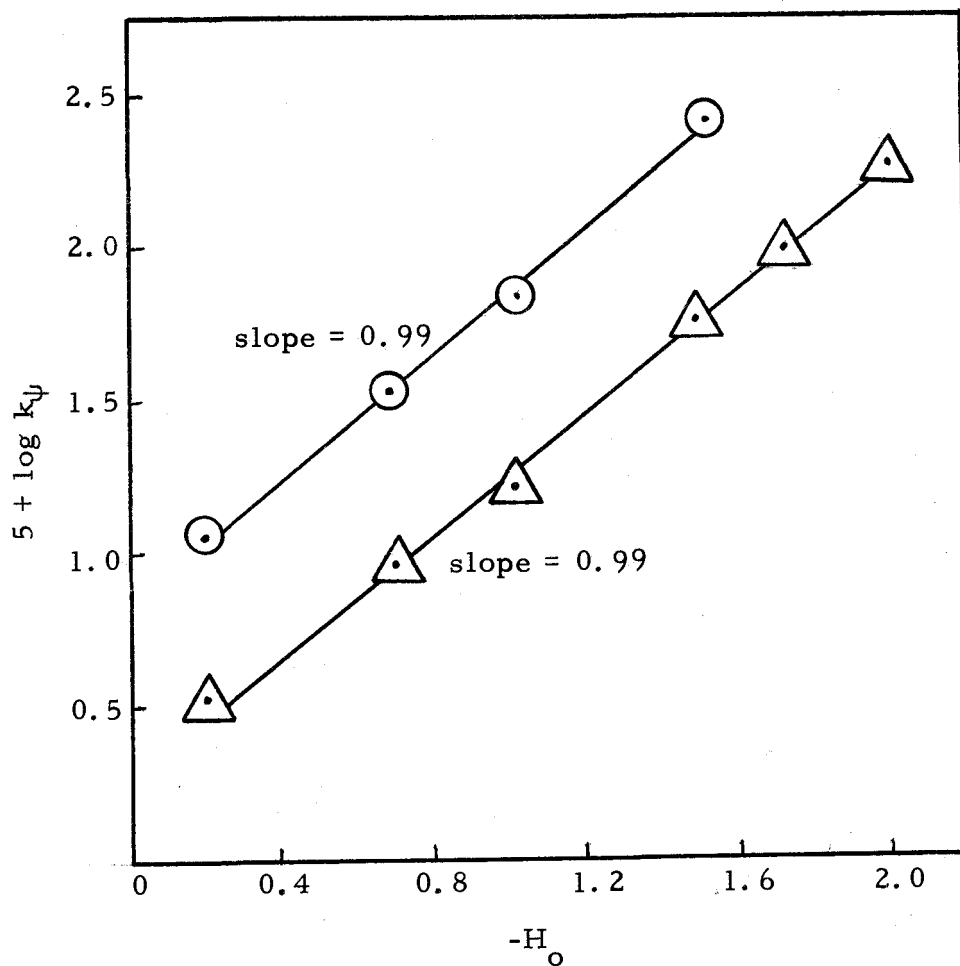
Figure 1. Logarithm of k_ψ versus the Hammett acidity function, $-H_o$, in aqueous hydrochloric acid.

△ – sodium phenyl sulfate at 40.1 °C.

◯ – pyridinium p-nitrophenyl sulfate at 39.7 °C.
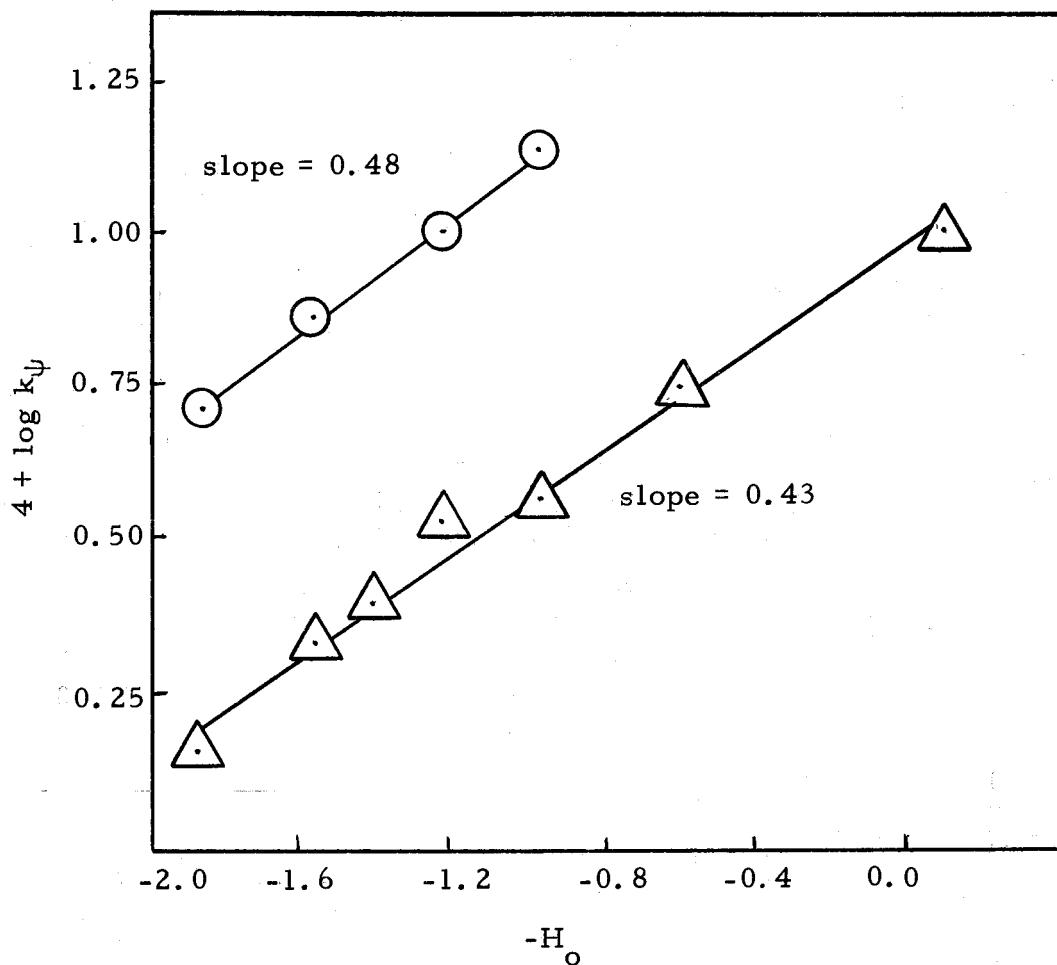
Figure 2. Logarithm of k_ψ versus the Hammett
acidity function, $-H_o$, in 60% dioxane-
40% water (v/v) perchloric acid solu-
tions at 30.1 °C.

$\triangle$ - sodium phenyl sulfate.

$\bigcirc$ - pyridinium p-nitrophenyl sulfate.

same media. The plots are linear with slopes of 0.43 and 0.48, respectively.

The p-nitrophenyl compound was prepared and hydrolyzed in order to check that the substituent effect on rate reported by Burkhardt was correct. Our average value of $k_\psi \, (\underline{p}\text{-NO}_2)/k_\psi \, (\underline{p}\text{-H})$ in water as solvent at 39.7° C is 4.3. The value previously obtained by Burkhardt and co-workers (17, 18) at 48.6° in water was 5.0. Although we seem to find somewhat less rate enhancement for the p-nitro compound than they did, the results are still closely comparable and their data on the effects of substituents on hydrolysis rate are basically reliable.

The kinetic data for the solvent isotope effect, k_{D_2O}/k_{H_2O}, is found in Table 3. It is obvious from Table 3 that the acid-catalyzed hydrolysis proceeds more rapidly in deuterium oxide than in water, $k_{D_2O}/k_{H_2O} = 2.43$. This furnishes evidence that the conjugate acid of the reactant is an intermediate in an equilibrium prior to the rate-determining step.

Table 3. Kinetics of the acid-catalyzed hydrolysis of sodium phenyl sulfate in water and deuterium oxide at 60.7° C.

Acid, $\underline{M}$	Solvent	$k_{\psi} \times 10^{+4}$, sec.$^{-1}$
DCl, 0.859	D_2O	6.79
		6.78
		6.82
HCl, 0.857	H_2O	2.82
		2.78

$$k_{D_2O}/k_{H_2O} = 2.43$$

The effect of dioxane content on the rate of hydrolysis of sodium phenyl sulfate in dioxane-water mixtures is shown in Table 4. All kinetic runs were made at a perchloric acid concentration of 0.495 $\underline{M}$ and the value of k_{ψ} in 80 percent dioxane-20 percent water (volume/volume) at 30.1° C was obtained by extrapolation. From Table 4, it is apparent that increasing the dioxane content from 40 percent to 80 percent increases the rate of hydrolysis by a factor of 67.

Table 4.   Effect of dioxane content on the kinetics of the acid-catalyzed hydrolysis of sodium phenyl sulfate.

Temperature °C	Dioxane, percent	$k_\psi \times 10^{+4}$, sec.$^{-1}$
30.1	40	0.494
		0.486
30.1	60	2.47
30.1	80	33
20.2	80	8.28
		9.97
		8.86
15.1	80	4.83
		4.88

DISCUSSION

A priori several possible mechanisms can be suggested for the acid-catalyzed hydrolysis of aryl sulfates. Two possibilities, both of the A-1 mechanistic type, are shown in equations 11 and 12. In an A-1 type mechanism one has a rapid and reversible protonation of the substrate which is then followed by a rate-determining

Mechanism A-1a

$$Ar-O-SO_3^- \ + \ H^+ \ \underset{}{\overset{fast}{\rightleftharpoons}} \ Ar-\overset{+}{\underset{H}{O}}-SO_3^- \qquad \text{(Eq. 11a)}$$

$$Ar-\overset{+}{\underset{H}{O}}-SO_3^- \ \xrightarrow{\underset{\text{rate-determining}}{\text{slow}}} \ ArOH \ + \ SO_3 \qquad \text{(Eq. 11b)}$$

$$SO_3 \ + \ H_2O \ \xrightarrow{\text{fast}} \ H_2SO_4 \qquad \text{(Eq. 11c)}$$

Mechanism A-1b

$$Ar-O-SO_3 \ + \ H^+ \ \underset{}{\overset{fast}{\rightleftharpoons}} \ Ar-O-SO_3H \qquad \text{(Eq. 12a)}$$

$$Ar-O-SO_3H \ \xrightarrow{\underset{\text{rate-determining}}{\text{slow}}} \ ArO^- \ + \ ^+SO_3H \qquad \text{(Eq. 12b)}$$

$$ArO^- \ + \ ^+SO_3H \ + \ H_2O \ \xrightarrow{\text{fast}} \ ArOH \ + \ H_2SO_4 \qquad \text{(Eq. 12c)}$$
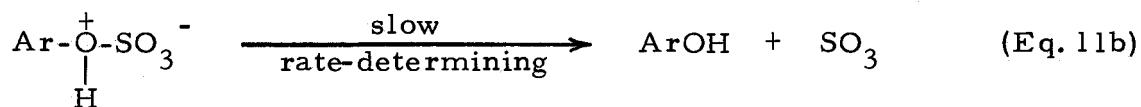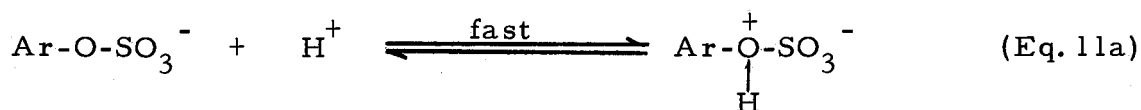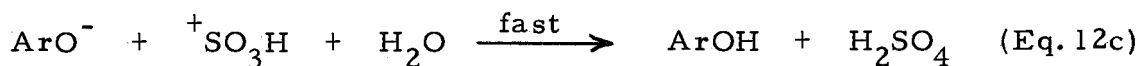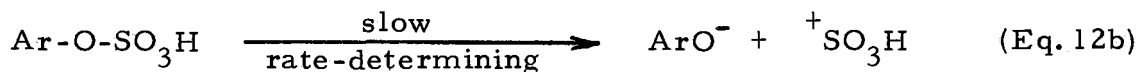
unimolecular decomposition of the protonated substrate, as in

equations 11b and 12b. These two A-1 mechanisms differ only in

the site of the protonation of the aryl sulfate. The phenolic oxygen,

Ar-O-, is protonated in equation 11 whereas a sulfonate oxygen,

$-SO_3^-$, is protonated in equation 12.

The A-1a mechanism, equation 11, involving phenolic oxygen

protonation is equivalent to the mechanism most commonly suggested

for the acid-catalyzed hydrolysis of alkyl sulfates (3, 4, 11, 29). The

A-1b mechanism, equation 12, seems a most unlikely and unrealistic

possibility for the following reasons. Heterolysis of the oxygen-

sulfur bond and expulsion of ArO^- should actually be easier in the

anion $Ar-O-SO_3^-$ than in the sulfonate protonated form, III. On the

other hand, protonation on the phenolic oxygen as in IV should clearly

assist the cleavage of the oxygen-sulfur bond by converting Ar-O-

to a better leaving group, $Ar-\overset{+}{O}(H)-$. Thus the need for acid

$$Ar-O-SO_3H \qquad\qquad Ar-\overset{+}{\underset{H}{O}}-SO_3^-$$
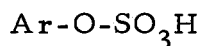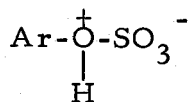
$$III \qquad\qquad\qquad IV$$

catalysis makes sense for the A-1a mechanism (Eq. 11), but makes

no sense for the A-1b mechanism (Eq. 12).

Besides these A-1 mechanisms, of which we have now elimin-

ated the A-1b mechanism (Eq. 12) from further serious consideration,

there are several A-2 type mechanisms which need to be considered.

An A-2 mechanism differs from an A-1 mechanism in the fact that

the rate-determining step involves the reaction of the protonated

substrate with water, rather than a unimolecular decomposition of

this species as in equations 11b and 12b.

The first A-2 mechanism, designated A-2a, involves a rapid

reversible protonation to form IV followed by a rate-determining

nucleophilic displacement of $Ar-\overset{+}{O}(H)-$ by water (Eq. 13). The other

possible A-2 mechanisms would involve initial protonation to give

III. The first of these A-2 mechanisms, designated A-2b (Eq. 14),

Mechanism A-2a

$$Ar-O-SO_3^- \; + \; H^+ \; \underset{}{\overset{fast}{\rightleftharpoons}} \; Ar-\underset{\underset{H}{|}}{\overset{+}{O}}-SO_3^- \qquad \text{(Eq. 13a)}$$

$$Ar-\underset{\underset{H}{|}}{\overset{+}{O}}-SO_3^- \; + \; H_2O \; \xrightarrow[\text{rate-determining}]{\text{slow}} \; ArOH + H_2\overset{+}{O}SO_3^- \qquad \text{(Eq. 13b)}$$

$$H_2\overset{+}{O}SO_3^- \; \xrightarrow{\text{fast}} \; H_2SO_4 \qquad \text{(Eq. 13c)}$$
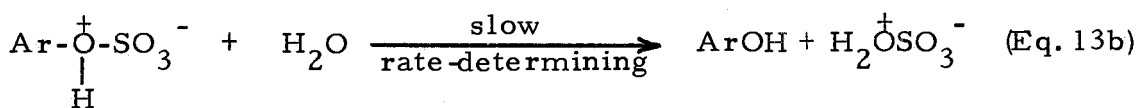
involves protonation followed by a nucleophilic displacement of ArO^-

by water from III. The second, designated A-2b' (Eq. 15), differs

from the first in that an adduct with water is formed. This adduct

may decompose as in equation 15c, or, more likely, it may transfer

a proton to form the zwitterion, $Ar-\overset{+}{O}(H)-SO_4H_2{}^-$ which decomposes (Eq. 15d).

Mechanism A-2b

$$Ar-O-SO_3{}^- \ + \ H^+ \ \underset{}{\overset{fast}{\rightleftharpoons}} \ Ar-O-SO_3H \qquad \text{(Eq. 14a)}$$

$$Ar-O-SO_3H \ + \ H_2O \ \xrightarrow[\text{rate-determining}]{\text{slow}} \ \left[H_2\overset{\Delta+}{O}\cdots \underset{OH}{SO_2}\cdots \overset{\Delta-}{O}Ar \right]$$

$$\xrightarrow{\hspace{2cm}} \ H_2\overset{+}{O}SO_3H \ + \ ArO^- \qquad \text{(Eq. 14b)}$$

$$ArO^- \ + \ H_2\overset{+}{O}SO_3H \ \xrightarrow{\text{fast}} \ ArOH + H_2SO_4 \qquad \text{(Eq. 14c)}$$

Mechanism A-2b'

$$Ar-O-SO_3{}^- \ + \ H^+ \ \overset{fast}{\rightleftharpoons} \ Ar-O-SO_3H \qquad \text{(Eq. 15a)}$$

$$Ar-O-SO_3H \ + \ H_2O \ \overset{fast}{\rightleftharpoons} \ Ar-O-\underset{O}{\overset{OH}{\underset{|}{S}}}\big\langle {}^{OH}_{OH} \ \overset{fast}{\rightleftharpoons}$$

$$Ar-\underset{H}{\overset{O^-}{\underset{|}{\overset{+}{O}}}}-\underset{O}{\overset{}{S}}\big\langle {}^{OH}_{OH} \qquad \text{(Eq. 15b)}$$

$$Ar-O-\underset{O}{\overset{OH}{\underset{\|}{S}}}\big\langle {}^{OH}_{OH} \ \xrightarrow[\text{rate-determining}]{\text{slow}} \ ArO^- \ + \ H_3\overset{+}{S}O_4 \ \overset{fast}{\rightleftharpoons}$$

$$ArOH \ + \ H_2SO_4 \qquad \text{(Eq. 15c)}$$

$$Ar-\underset{H}{\overset{O^-}{\underset{|}{\overset{+}{O}}}}-\underset{O}{\overset{}{\underset{\|}{S}}}\big\langle {}^{OH}_{OH} \ \xrightarrow[\text{rate-determining}]{\text{slow}} \ ArOH + H_2SO_4 \qquad \text{(Eq. 15d)}$$
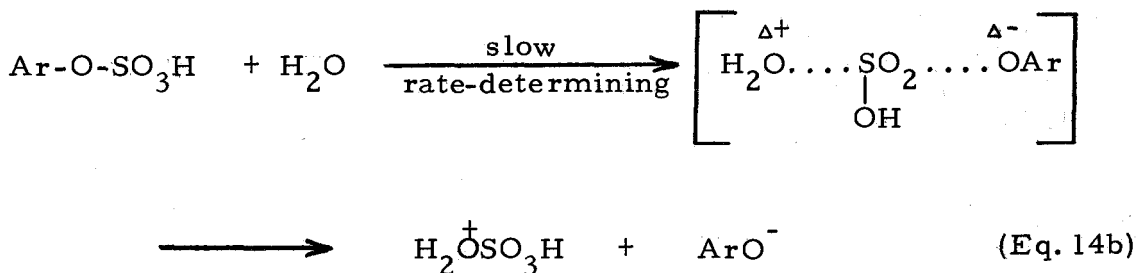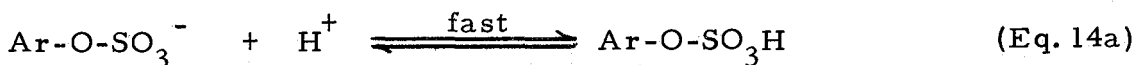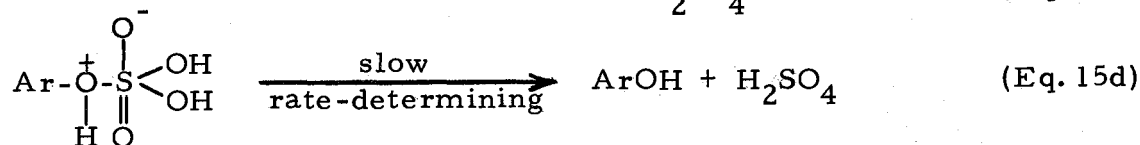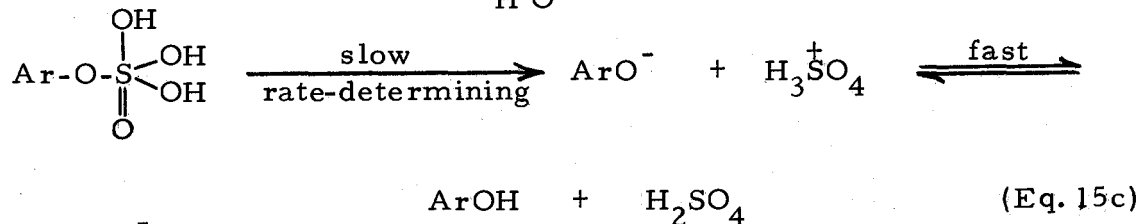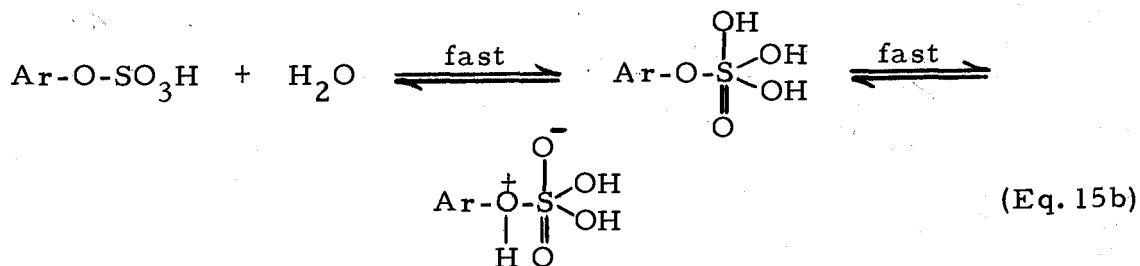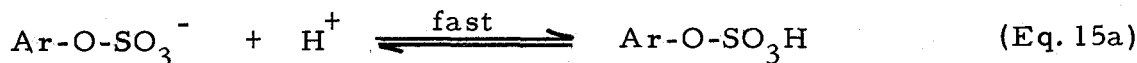
If the sodium phenyl sulfate hydrolysis occurs via an A-2 mechanism, as pointed out in the Introduction, the solvent isotope effect, the dependence of rate on acidity of the medium, and the response of rate to changes in dioxane content in dioxane-water mixtures for the acid-catalyzed hydrolysis of sodium phenyl sulfate should be similar to the changes in these same reaction parameters found for the acid-catalyzed hydrolysis of methyl hydrogen selenate. On the other hand, if it takes place via an A-1 mechanism the response of the rate of the sulfate hydrolysis to these variables will be quite different from that found for the hydrolysis of sodium methyl selenate.

Table 5. Reaction parameters for general A-1 and A-2 hydrolyses.

Mechanism	Acidity dependence of rate	Solvent isotope effect, k_{D_2O}/k_{H_2O}
A-1	$\propto -H_o$ (35)	1.9-2.6 (14, 38, 39)
A-2	$\propto [HX]$ (35)	1.3-1.7 (14, 38, 39)
$CH_3OSeO_3^-$	$\propto [HX]$ (11)	1.36 (11)

Each of the reaction parameters found for the sodium phenyl sulfate hydrolysis will now be compared with those values in Table 5 in an attempt to determine whether the sulfate hydrolysis occurs through an A-1 or an A-2 mechanism.

The acid-catalyzed hydrolysis of sodium phenyl sulfate shows a considerable solvent isotope effect, $k_{D_2O}/k_{H_2O} = 2.43$. Bunton and Shiner (14) and others (38, 39) have shown that the solvent isotope effect for A-1 type hydrolyses is usually higher, $k_{D_2O}/k_{H_2O} = 1.9$-2.6, than that found for A-2 type hydrolyses, $k_{D_2O}/k_{H_2O} = 1.3$-1.7. Since the selenate hydrolysis (11), $k_{D_2O}/k_{H_2O} = 1.36$, is most certainly an A-2 type, the solvent isotope effect found for the acid-catalyzed hydrolysis of sodium phenyl sulfate, Table 3, $k_{D_2O}/k_{H_2O} = 2.43$, supports an A-1 mechanism. After this work was completed, Benkovic (9) reported the solvent isotope effect for potassium p-carboxyphenyl sulfate as being 2.32. On the basis of this solvent isotope effect, $k_{D_2O}/k_{H_2O} = 2.32$, and the entropy of activation, $\Delta S = +3.2$, Benkovic also suggests an A-1 mechanism for alkali aryl sulfate hydrolyses.

A plot of the logarithm of k_ψ for the hydrolysis of sodium phenyl sulfate in aqueous hydrochloric acid solutions versus the Hammett acidity function, $-H_o$, for the same media gives a linear plot with a slope of 0.99, Figure 1. However, a plot of the logarithm of the observed rate constant for the hydrolysis of sodium methyl selenate versus the Hammett acidity function, $-H_o$, gives a smooth curve whose slope decreases with increasing acidity (11). In contrast, a plot of the logarithm of the observed rate constant for the selenate system versus the stoichiometric concentration of

acid is linear with a slope of about 0.9 (11). The above data show

that the hydrolysis of sodium phenyl sulfate is dependent upon H_o

whereas the hydrolysis of sodium methyl selenate is dependent upon

the concentration of the added acid. This difference in the response

of the rates of hydrolysis of the aryl sulfate ion and the methyl selen-

ate ion to changes in acidity in strongly acid solutions suggests con-

siderably less involvement of water in the transition state for the

hydrolysis of the aryl sulfate ion. Given the results of Fuller,

Hughes and Ingold (25) which show that the H_- acidity function calcu-

lated from the protonation of aryl sulfonate ions by hydrochloric

and perchloric acids is parallel to the Hammett acidity function,

$-H_o$, for acid concentrations between 1.5 and 6.0$\underline{M}$ in aqueous solu-

tion, the dependence of rate on acidity observed for the hydrolysis

of the aryl sulfate ion is that expected for an A-1 type hydrolysis

(35).

A plot of the logarithm of k_ψ for the hydrolysis of sodium

phenyl sulfate in 60 percent dioxane solutions containing 0.24-1.81$\underline{M}$

perchloric acid versus the Hammett acidity function, $-H_o$, for these

same solutions is linear but with a slope of only 0.43, Figure 2. It

is obvious that the parallel between H_o and H_- which is observed for

1.5-6.0$\underline{M}$ aqueous perchloric and hydrochloric acid solutions (23)

does not extend to solutions of the same acids in 60 percent dioxane

solutions. This is hardly surprising, however.

Table 6 shows the effect of dioxane content on the rates of
hydrolysis in dioxane-water mixtures for the aryl sulfate ion and
the methyl selenate ion. The dissociation constant, K_a, of any
neutral acid HA decreases with increasing dioxane content of a
dioxane-water mixture. As the dioxane content is increased, the
dielectric constant of the medium is decreased and neutral or zwit-
terion species are favored over ionic species in the solution. This
means that for a given hydrogen ion concentration the fraction of aryl
sulfate ion present at equilibrium as either the neutral species, III,
or the zwitterion, IV, should increase with increasing dioxane content
of the medium (Eq. 16). The same would also be true for the fraction
of methyl selenate ion present as CH_3OSeO_3H or $CH_3\overset{+}{O}(H)SeO_3^-$.

Table 6. Effect of dioxane content on relative rate of hydrolysis
in dioxane-water mixtures.

Percent dioxane (v/v)	$k/k_{40\% \text{ dioxane}}$	
	Aryl sulfate hydrolysis[1,2]	Methyl selenate hydrolysis[3,4]
40	(1.0)	(1.0)
60	5.0	1.6
80	67[5]	6.3

1. Table 4.
2. Data are for 0.5$\underline{M}$ perchloric acid solutions at 30.1 °C.
3. Reference 11.
4. Data are for 0.1$\underline{M}$ perchloric acid solutions at 25.1 °C.
5. Extrapolated from data at lower temperatures.

$$Ar-O-SO_3^- + H^+ \rightleftharpoons Ar-\overset{+}{\underset{H}{O}}-SO_3^- \rightleftharpoons Ar-O-SO_3H \qquad (Eq.\ 16)$$

IV   III
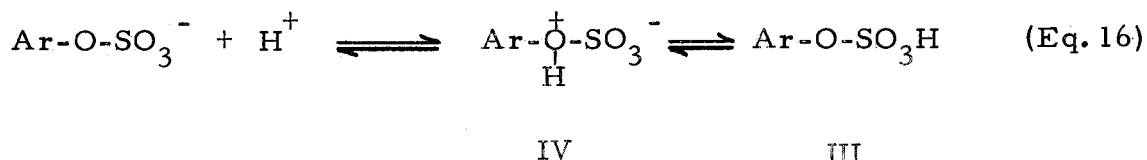
Since the concentration of the conjugate acid of the aryl sulfate ion increases with increasing dioxane content, the rate of an A-1 type hydrolysis would also be expected to rise accordingly. The rate of an A-2 type hydrolysis for the same change in dioxane content would also increase, but the increase would be less than that for the A-1 type hydrolysis, since increasing the dioxane content would decrease the activity and concentration of water, which acts as a nucleophile in the A-2 hydrolysis. Since the methyl selenate hydrolysis almost certainly occurs via an A-2 mechanism, the observed difference in the rate enhancement found in Table 6 is further support for an A-1 mechanism for the hydrolysis of aryl sulfates.

A comparison of the solvent isotope effect, the dependence of rate on acidity of the medium, and the response of rate to changes in dioxane content in dioxane-water mixtures for the acid-catalyzed hydrolysis of the aryl sulfate ion with similar data for the hydrolysis of the methyl selenate ion points toward an A-1 mechanism for the aryl sulfate hydrolysis. As already noted the only reasonable A-1 mechanism is the one (Eq. 11) involving the zwitterion, IV.

In current terminology one would say that the observation of Burkhardt, Ford and Singleton (17) concerning the relationship

between the hydrolysis rate of $ArOSO_3^-$ and the acidity of ArOH, is
equivalent to saying that the rate of hydrolysis of $ArOSO_3^-$ is corre-
lated better by σ_- constants than by σ constants and that the reaction
has a ρ of about +0.5 (Appendix 1). This means that the electron
density on the phenolic oxygen is slightly greater in the transition
state of the rate-determining step than in the aryl sulfate ion and
that there is a greater resonance interaction in the transition state
between the phenolic oxygen and an electron-withdrawing para sub-
stituent than in the starting aryl sulfate ion.

Bell and co-workers (2, 8) and others (28) have shown that the
sulfonate group, $-SO_3^-$, can act as a strong electron-withdrawing
group when immediately adjacent to a reaction site. This strong
electron-withdrawing tendency is due to the decreased electron
density on the sulfur atom as a result of the contribution of structure
Vb to the resonance hybrid. The contribution of structure Vb de-
creases the electron density on the phenolic oxygen in the aryl
sulfate ion and also prohibits any important resonance interaction

Va   Vb
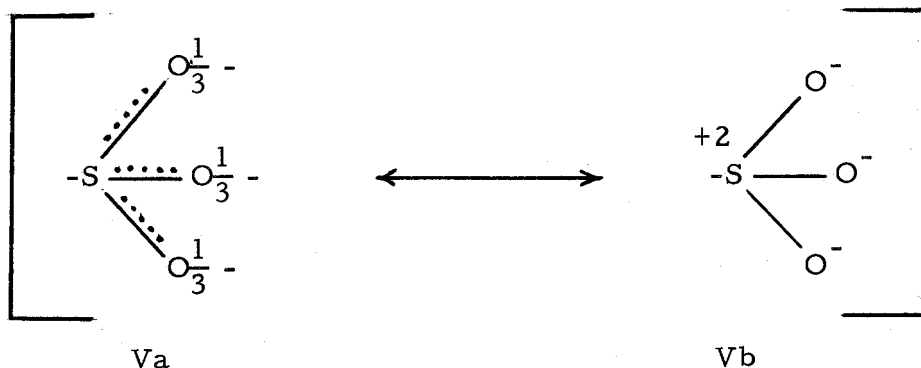
with a _para_ substituent in the aryl sulfate ion, such as the nitro group,

$-NO_2$. This is due to the unfavorable energetics associated with the

contributing structure VI in which both the adjacent sulfur and
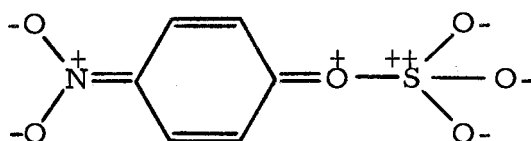
VI

oxygen atom are positively charged.

The rate-determining step in the A-la hydrolysis mechanism

(Eq. 11) is the dissociation of the zwitterion, IV, to phenol and sulfur

trioxide. If the phenolic oxygen-sulfur bond is almost completely

broken by the time the transition state is reached in this reaction,

the electron density on the phenolic oxygen will be essentially the

same as in phenol itself and could be somewhat greater than in the

starting aryl sulfate ion (Eq. 17). Furthermore, _para_ substituents
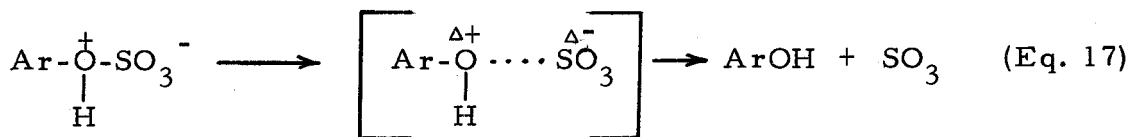
such as the nitro group could contribute to the mesomeric stabiliza-

tion of this transition state in the same way they stabilize the phenol,
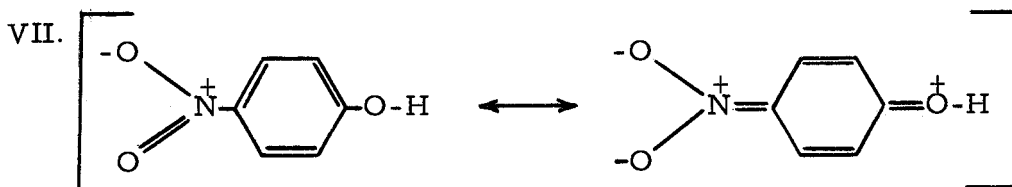
VII

Therefore, both the small positive ρ value, $\rho = +0.5$, and the fact that the rates of hydrolysis are correlated better by σ_- than by σ constants are accounted for if the structure of the transition state for the aryl sulfate ion hydrolysis is assumed to be considerably closer to the products, phenol and sulfur trioxide, than to the starting aryl sulfate ion.

The fact that aryl sulfate ions hydrolyze much faster than alkyl sulfate ions can also be accounted for by the A-la mechanism in Equation 11 and the above considerations. Since there is no stabilization of the aryl sulfate ion through resonance interaction of an unshared pair of electrons on the phenolic oxygen with the aromatic ring, the resonance interaction previously described for the transition state would cause the activation energy for the hydrolysis of the aryl sulfate ion to be somewhat less than would otherwise be the case. As no such resonance stabilization of the transition state is possible in the case of the hydrolysis of alkyl sulfate ions, the aryl sulfate ions would be expected to hydrolyze much faster than the alkyl sulfate ions, as is indeed the case.

After this work had been completed, Batts (3, 4) reported results of a kinetic study of the hydrolysis of alkyl hydrogen sulfates in moist dioxane and aqueous acid solutions. Batts found that the rate of hydrolysis in aqueous acid correlated with $-H_o$ and that the entropy of activation was +7.2 e.u. in 5.0$\underline{M}$ perchloric acid, +1.0

e.u. in 1.0$\underline{M}$ perchloric acid and +5.3 e.u. in water for the hydrolysis of methyl hydrogen sulfate. This evidence along with previous studies (3, 4, 11, 20, 21, 29) support an A-1 mechanism (Eq. 18) for the acid-catalyzed hydrolysis of alkyl hydrogen sulfates. This A-1 mechanism is the same as that which has been suggested for the acid-catalyzed hydrolysis of sodium aryl sulfates in this thesis, mechanism A-1a (Eq. 11).

$$R\text{-}O\text{-}SO_3^- + H^+ \xrightleftharpoons{\text{fast}} R\overset{+}{\underset{\underset{H}{|}}{O}}\text{-}SO_3^- \qquad \text{(Eq. 18a)}$$

$$R\overset{+}{\underset{\underset{H}{|}}{O}}\text{-}SO_3^- \xrightarrow[\text{rate-determining}]{\text{slow}} ROH + SO_3 \qquad \text{(Eq. 18b)}$$

$$SO_3 + H_2O \xrightarrow{\text{fast}} H_2SO_4 \qquad \text{(Eq. 18c)}$$
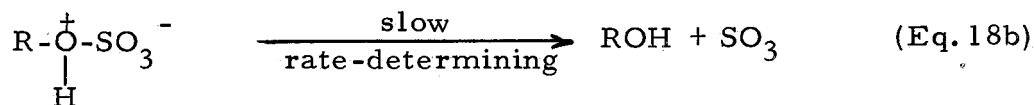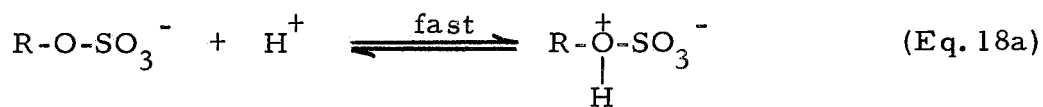
EXPERIMENTAL

Materials

Phenol. (Baker and Adamson Chemical Company, Inc.)
Phenol was dried over phosphorus pentoxide in a vacuum desiccator
at a pressure of 0.5 mm.

Sodium Phenyl Sulfate. Sodium phenyl sulfate was prepared
by the procedure of Burkhardt and Lapworth (19). A solution of 100
grams (0.82 moles) of N, N-dimethylaniline in 100 ml. of carbon
disulfide was placed in a three-necked flask which had been fitted
with a reflux condenser and drying tube, a dropping funnel, and a
stirrer. After the solution had been cooled to -10°C in a salt-ice
bath, 34 grams (0.21 moles) of chlorosulfonic acid was added, with
stirring, at a rate maintaining the temperature below 0°C. A solu-
tion of 25 grams (0.27 moles) of phenol in 50 ml. of carbon disulfide
was then added and the mixture stirred for an hour.

The carbon disulfide was removed with a Büchi rotary evapo-
rator and the cold viscous residue poured cautiously into a solution
of 22 grams of potassium hydroxide, 10 grams of hydrated barium
hydroxide, and 200 ml. of water, keeping the temperature below 30°C.

The resulting precipitate was filtered off and the remaining
solution extracted with benzene and diethyl ether to remove the

N, N-dimethylaniline and remaining phenol, respectively. The benzene and ether layers were discarded and the aqueous layer evaporated with a Büchi rotary evaporator to yield sodium phenyl sulfate.

The sodium phenyl sulfate was recrystallized twice from 100% ethanol and after each recrystallization trituated with diethyl ether. It was then dried over calcium chloride in a vacuum desiccator at 1.0 mm. pressure.

$$C_6H_5OSO_3Na \cdot \frac{1}{2}H_2O \qquad m.p. > 300°C$$

Calculated	C 35.13%	H 2.95%
Found	C 35.20%	H 3.14%

Ultraviolet $\qquad \lambda_{max.} = 262.4\ m\mu\ \log \epsilon = 2.64$

Infrared (Nujol) $\qquad 1200\ cm.^{-1}$

$\qquad\qquad\qquad\qquad 1206\ cm.^{-1} \quad \nu_s SO_2$

$\qquad\qquad\qquad\qquad 1238\ cm.^{-1}$

N.M.R. (D$_2$O, external TMS standard)

$\qquad$ singlet $\qquad 2.7\ \mathcal{T} \qquad$ aromatic protons

$\qquad$ singlet $\qquad 5.5\ \mathcal{T} \qquad$ water

p-Nitrophenol. (Aldrich Chemical Company, Inc.)

p-Nitrophenol was recrystallized from water and dried over calcium chloride in a vacuum desiccator at 0.5 mm. pressure. The melting point was 120-124°C (Literature Value, m.p. 114°C).

Pyridinium <u>p</u>-Nitrophenyl Sulfate. Pyridinium <u>p</u>-nitrophenyl sulfate was prepared by a modification of the procedure of Burkhardt and Lapworth (19). Pyridinium sulfonic acid was prepared using the procedure of Baumgarten (6).

A mixture of 20 grams (0.125 moles) of pyridinium sulfonic acid 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° C on a water bath, 10 grams (0.072 moles) of <u>p</u>-nitrophenol was added and the reaction mixture stirred for four hours with refluxing.

The benzene was filtered off and the pyridinium <u>p</u>-nitrophenyl sulfate was recrystallized from water twice and after each recrystallization trituated with diethyl ether. It was then dried over calcium chloride in a vacuum desiccator at 1.0 mm. pressure.

$C_{12}H_{10}N_2O_6S$ m. p. 76° C (uncorrected)

Calculated C 44.29% H 3.38%

Found C 44.23% H 3.29%

Ultraviolet λ_{max} = 287 mμ log ε = 3.97

Infrared (Nujol) 1193 cm.$^{-1}$

1222 cm.$^{-1}$ $\nu_s SO_2$

N.M.R. None

Deuterium Chloride. (Carl Roth Karlsruhe, Germany) ca. 20 percent DCl in D_2O.

Deuterium Oxide. (Bio-Rad Laboratories). 99.85 percent D_2O.

Solvents

Dioxane. Reagent grade dioxane was purified by the method suggested by Wiberg (41, p. 245). It was distilled under nitrogen from the sodium ketyl of benzophenone, b.p. 101°C.

Perchloric Acid. A 70 percent stock solution of reagent grade perchloric acid was diluted with water and the normality of the resulting solutions was determined by titration with standard base to a phenolphthalein endpoint.

These solutions were then used in a further dilution to obtain solutions of desired acidities for the kinetic runs.

Deuterium Chloride - Deuterium Oxide. Ten grams of approximately 20 percent deuterium chloride were diluted to 54 ml. with deuterium oxide. Three one milliliter samples were titrated with 0.100N sodium hydroxide from a microburet. The resulting solution was determined to be 0.859N. The hydrochloric acid solution used for comparison in the kinetic isotope effect study was made up in the same manner with a resulting acidity of 0.857N.

Hydrochloric Acid. Reagent grade hydrochloric acid was used

and its solutions were prepared in the same manner as those of perchloric acid.

Procedures

Dioxane-Water Solution Procedure. In the preparation of the dioxane-water-perchloric acid reaction solutions, the amount of water in the volume of perchloric acid solution necessary to give the desired acidity of the reaction solution was calculated. The amount of water calculated was then taken into account when calculating the volume of water to be added to the dioxane to give a solution 60 percent dioxane-40 percent water by volume.

Dioxane-Water-Perchloric Acid Solution Procedure. Dioxane, water, and perchloric acid were pipetted separately into a beaker to give the desired reaction solution.

Kinetic Procedures. A weighed amount of the aryl sulfate was dissolved in a measured volume of the desired dioxane-water-acid mixture or the water-acid mixture. The solution was then placed in the reaction vessel.

The reaction vessel is a 100 ml. round-bottom flask fitted with a gas inlet tube, a condenser, and a buret. A series of three-way stop-cocks, one between the buret and condenser and one between the buret and flask, allowed samples of a known volume to be withdrawn without exposing the solution to the atmosphere, Figure 3.

After the solution had been placed in the reaction vessel, it was deaerated from five to ten minutes with pre-purified nitrogen while it was cooled in an ice bath. The reaction vessel was then placed in a constant temperature bath. After temperature equilibration, approximately two minutes, the initial sample (time equal to zero) was taken. At appropriate time intervals aliquots were removed and diluted with 95 percent ethanol. An infinity time point was taken after eight to ten half-lives and the first-order rate constant was calculated from plots of $\log(A_\infty - A)$ versus time. The kinetics were determined by following the change in optical density of the diluted sample solutions on a Cary Model 15 spectrophotometer using 95 percent ethanol in the reference beam.

For the sodium phenyl sulfate kinetics, two ml. aliquots of the 0.0285$\underline{M}$ sodium phenyl sulfate (zero time) reaction solutions were diluted to 50 ml. and the appearance of phenol was measured at 277 mμ.

For the pyridinium $\underline{p}$-nitrophenyl sulfate kinetics, one ml. aliquots of the 0.00856$\underline{M}$ pyridinium $\underline{p}$-nitrophenyl sulfate (zero time) reaction solutions were diluted to 50 ml. and the appearance of $\underline{p}$-nitrophenol was measured at 320 mμ.

three-way
stopcocks

nitrogen
inlet
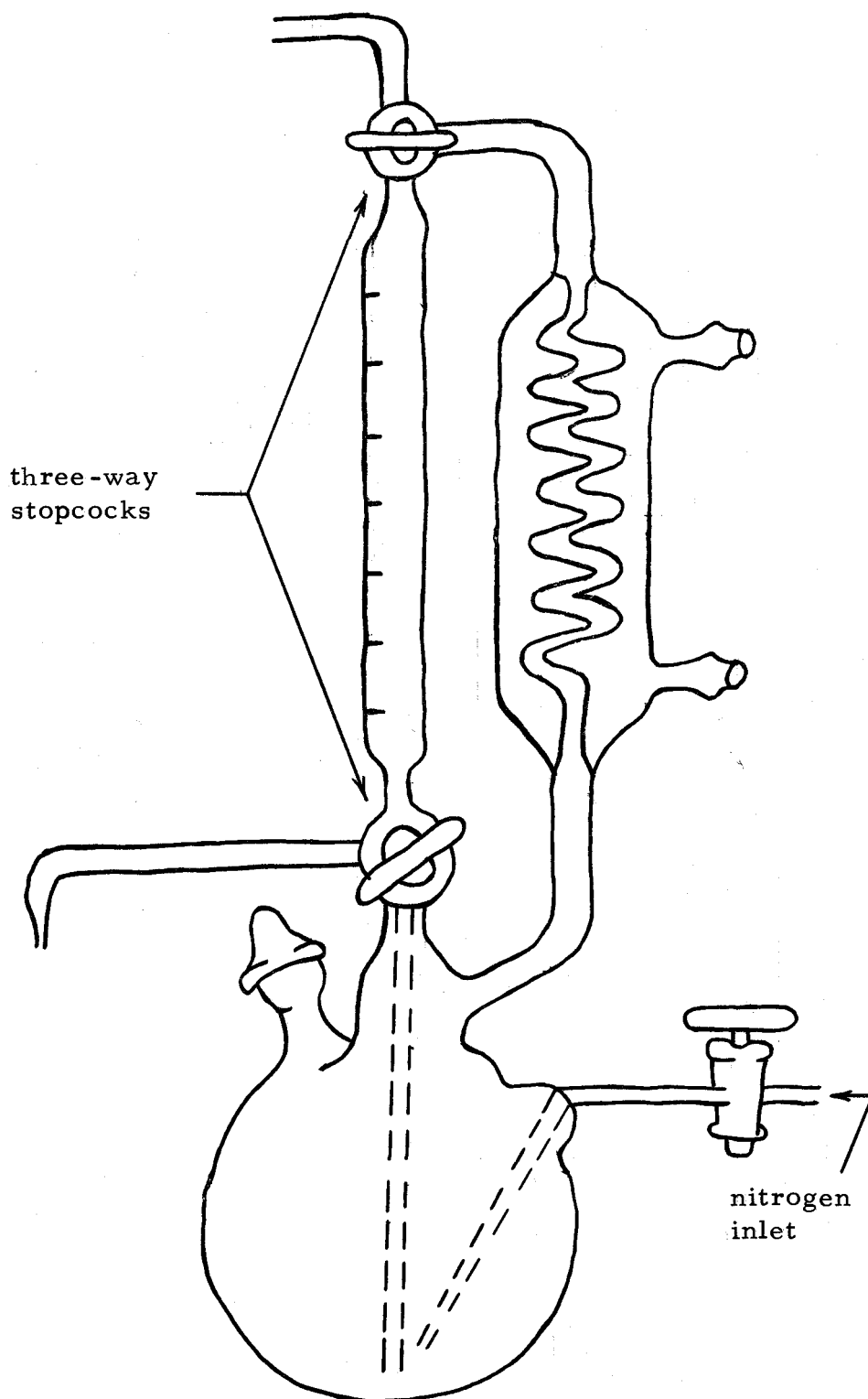
Figure 3. Reaction vessel.

II. THE ACID HYDROLYSIS OF BUNTE SALTS
(S-ALKYL AND S-ARYL THIOSULFATES)

INTRODUCTION

A detailed knowledge of the acid-catalyzed hydrolysis of S-alkyl and S-aryl thiosulfates (Eq. 19)(34), the so-called Bunte salts (10), is of interest for several reasons. First, and most important, it can

$$R\text{-}S\text{-}SO_3^- + H_2O \xrightarrow{\text{H}^+} RSH + HOSO_3^- \qquad (Eq. 19)$$
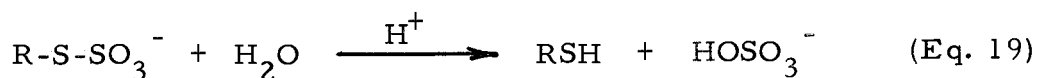
contribute to further understanding of the type of mechanisms involved in the hydrolysis of sulfate derivatives (Eq. 20). Table 7 includes a

$$Y\text{-}SO_3^- + H_2O \xrightarrow{\text{H}^+} Y\text{-}H + HOSO_3^- \qquad (Eq. 20)$$
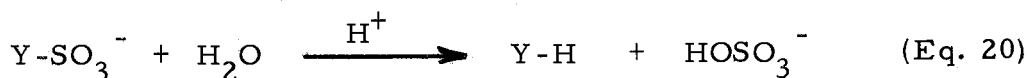
number of sulfate derivatives with suggested mechanisms for their respective acid-catalyzed hydrolyses. Second, a knowledge of the mechanism of the acid-catalyzed hydrolysis of Bunte salts is of considerable pharmacological importance since pharmaceutical activity and radiation protective ability has been attributed to certain Bunte salts and/or the mercaptan liberated by their hydrolysis (30, 32, 41).

Rosenthal and Citarel (41) felt that the radiation protective ability was due to two mechanisms. The radicals and peroxides formed during irradiation are scavenged by the thiols, thereby preventing the destruction of vital thiol-containing enzymes. These

thiol-containing enzymes are also protected by their reaction

with the thiosulfates to form an unsymmetrical disulfide. Subse-

quent regeneration of the thiol group is accomplished by cellular

reducing agents. Bunte salts are also favored over thiols as radia-

tion protecting agents because of their ready solubility in aqueous

solutions and their much lower toxicity.

Table 7. Sulfate derivative hydrolyses.

Y-	Suggested mechanism	References
$^=(O_3S)_2N-O-$	A-1	23
$^-(O_3S)NH-O-$	A-1	23, 24
$^-(O_3S)N(OH)-O-$	A-1	24
H_2N-O-	A-1	22, 24
R-O-	A-1	3, 4, 11, 21, 29
Ar-O-	A-1	17, 18, [1]/
$^-S-$	A-1 or A-2	40
HO-NH-	A-2	24

[1]/ This thesis, Part I.

In 1963 Kice (31) conducted a kinetic study of the acid-catalyzed

hydrolysis of sodium S-ethyl thiosulfate, the ethyl Bunte salt, in

aqueous acid solutions. Plots of the logarithm of the observed first-

order rate constants versus the Hammett acidity function, $-H_o$, were

linear and gave slopes ranging from 0.99 to 1.04. Comparison of the observed rate constants at low acid concentration with those calculated by extrapolation from the data at much higher H_o values showed that the rate at low hydrogen ion concentration was that predicted by extrapolation from the rates at high acidities. Therefore, the dependence of rate on acidity does not change in the manner that would be expected if the conjugate acid of the Bunte salt had an ionization constant smaller than or equal to unity. Kice (31) therefore concluded that $C_2H_5SSO_3H$ was a strong acid and the Bunte salt existed in all the aqueous solutions almost exclusively as $C_2H_5SSO_3^-$. The data presented by Kice (31) were not sufficient to allow any extensive conclusions about the mechanism of the reaction to be made 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 determine whether the Bunte salt hydrolysis occurs via an A-1 or A-2 mechanism, one would like to compare experimental results from the Bunte salt hydrolysis with those from known A-1 and known A-2 hydrolyses of closely related compounds. Fortunately two reactions which are closely related to the Bunte salt hydrolysis have been studied. The acid-catalyzed hydrolysis of sodium phenyl sulfate (This thesis, Part I) proceeds via an A-1 mechanism (Eq. 21) whereas the acid-catalyzed hydrolysis of sodium methyl selenate (11) proceeds via an A-2 mechanism (Eq. 22).

$$\text{Ar-O-SO}_3^- + \text{H}^+ \;\underset{}{\overset{\text{fast}}{\rightleftharpoons}}\; \text{Ar-}\overset{+}{\underset{H}{\text{O}}}\text{-SO}_3^- \qquad \text{(Eq. 21a)}$$

$$\text{Ar-}\overset{+}{\underset{H}{\text{O}}}\text{-SO}_3^- \;\xrightarrow[\text{rate-determining}]{\text{slow}}\; \text{ArOH} + \text{SO}_3 \qquad \text{(Eq. 21b)}$$

$$\text{SO}_3 + \text{H}_2\text{O} \;\xrightarrow{\text{fast}}\; \text{H}_2\text{SO}_4 \qquad \text{(Eq. 21c)}$$

$$\text{CH}_3\text{OSeO}_3^- + \text{H}^+ \;\underset{}{\overset{\text{fast}}{\rightleftharpoons}}\; \text{CH}_3\text{OSeO}_3\text{H} \qquad \text{(Eq. 22a)}$$

$$\text{CH}_3\text{OSeO}_3\text{H} + \text{H}_2\text{O} \;\xrightarrow[\text{rate-determining}]{\text{slow}}\; \text{CH}_3\text{OH} + \text{H}_2\text{SeO}_4 \qquad \text{(Eq. 22b)}$$
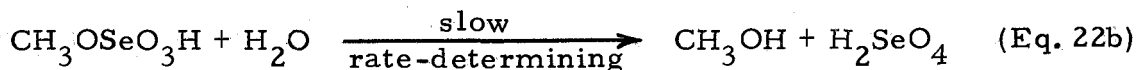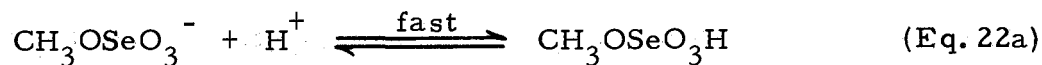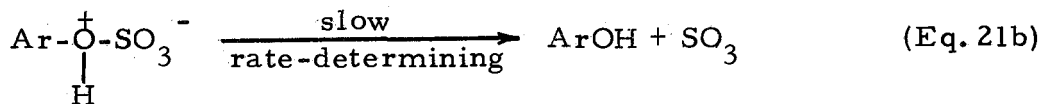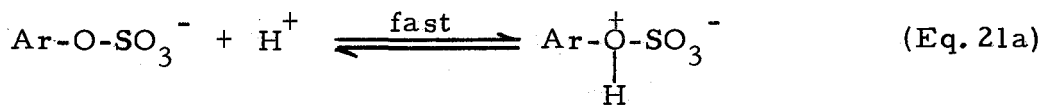
As might be expected from the fact that the sulfate hydrolysis is an A-1 reaction while the selenate hydrolysis is an A-2 reaction, they differ markedly in their change in rate with changing acid concentration in concentrated aqueous acid, their change in rate with changing dioxane content in aqueous dioxane solutions containing a fixed amount of strong acid, and their solvent isotope effect.

With this in mind we accordingly undertook to determine the response of the Bunte salt hydrolysis to these changes in reaction conditions, in order that we might compare our results with those of Bunton and Hendy (11) for the selenate system and our results for the sulfate system (This thesis, Part I). This comparison of the response of the Bunte salt hydrolysis to the responses of the sulfate hydrolysis, A-1, and the selenate hydrolysis, A-2, for similar changes in the reaction conditions would be most helpful in deciding

the correct mechanism of the acid-catalyzed hydrolysis of Bunte

salts. The reliability of this comparison is favored by the struc-

tural similarity between sodium phenyl sulfate, VIII, sodium methyl

selenate, IX, and sodium S-phenyl thiosulfate, X, the phenyl Bunte

salt.

$$\text{C}_6\text{H}_5\text{-O-SO}_3^{\,-}\text{Na}^+ \qquad\qquad \text{CH}_3\text{-O-SeO}_3^{\,-}\text{Na}^+$$

VIII   IX

$$\text{C}_6\text{H}_5\text{-S-SO}_3^{\,-}\text{Na}^+$$
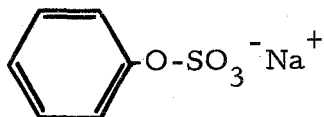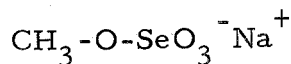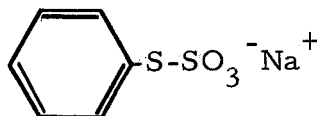
X

Determination of the effect of changes in structure on the rate

of hydrolysis of Bunte salts would also be most helpful in determin-

ing their mechanism of hydrolysis. It is apparent from the work of

Burkhardt and co-workers (18, Appendix 1) that the rate of aryl

sulfate ion hydrolysis is increased by the presence of electron-

withdrawing para substituents. Also, the hydrolysis rate of aryl

sulfate ions (17) is several hundred times larger than the hydrolysis

rate of ethyl hydrogen sulfate (4). If the Bunte salt hydrolysis occurs

via the same A-1 mechanism as does the aryl and alkyl sulfate ion

hydrolysis, it might be expected that the effect of structure on the

rate of hydrolysis would be similar for the aryl sulfate ions and the aryl Bunte salts. On the other hand, if the Bunte salt hydrolysis were occurring <u>via</u> a different mechanism this might also be reflected in the effect of structure on the rate of Bunte salt hydrolysis. Whatever the case, the effect of <u>para</u> substituents and a corresponding Hammett $\rho\sigma$ plot could provide information regarding the change in electron density at the reaction site, the sulfenyl sulfur, between the starting Bunte salt and the transition state.

RESULTS

Synthesis of Bunte Salts

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 (7). The complex between pyridine and sulfur trioxide, $\underline{N}$-pyridinium sulfonic acid (6), was heated with the appropriate aromatic thiol in carbon tetrachloride to give the corresponding pyridinium S-aryl thiosulfate (Eq. 23).

$$ArSH \ + \ C_5H_5NSO_3 \ \longrightarrow \ ArSSO_3^- \ H\overset{+}{N}C_5H_5 \qquad (Eq. 23)$$
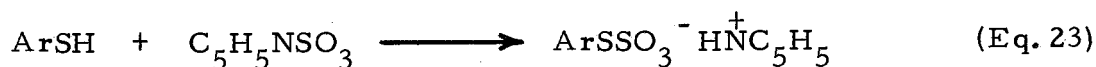
Pyridinium S-phenyl thiosulfate is a known compound (7), but the other pyridinium S-aryl thiosulfates had not been previously prepared and their respective analytical data and melting points are summarized in Table 8.

Sodium S-phenyl thiosulfate was prepared as its monohydrate from pyridinium S-phenyl thiosulfate by an ion-exchange procedure using the sodium form of the Dowex 50W-X4 resin. Its analytical data and melting point are found in Table 8.

Sodium S-($\underline{m}$-nitrophenyl) thiosulfate was prepared as its monohydrate by the method of Lecher and Hardy (32), which involves the reaction of bis-(3-nitrophenyl) disulfide with sodium $\underline{meta}$-bisulfite,

Table 8. Properties of Bunte salts.

$ArSSO_3^-H\overset{+}{N}C_5H_5$ Ar-	Melting Point, °C[1]	Formula	Calculated, %		Found, %	
			C	H	C	H
$\underline{p}\text{-}CH_3C_6H_4$	115-117	$C_{12}H_{13}NO_3S_2$	50.86	4.62	50.80	4.72
$\underline{p}\text{-}ClC_6H_4$	123-124	$C_{11}H_{10}ClNO_3S_2$	43.49	3.32	43.18	3.41
$p\text{-}BrC_6H_4$	129	$C_{11}H_{10}BrNO_3S_2$	37.94	2.89	37.91	3.01
$\underline{p}\text{-}(CH_3)_3CC_6H_4$	139	$C_{15}H_{19}NO_3S_2$	55.36	5.88	54.94	5.87
$\underline{p}\text{-}O_2NC_6H_4$	155-156	$C_{11}H_{10}N_2O_5S_2$	42.03	3.21	41.83	3.23
$ArSSO_3^-Na^+$ Ar-						
C_6H_5	180-182	$C_6H_5NaO_3S_2 \cdot H_2O$	31.30	3.06	31.26	3.33
$\underline{m}\text{-}O_2NC_6H_4$	105	$C_6H_4NNaO_5S_2 \cdot H_2O$	26.18	2.19	26.42	2.28

[1] (uncorrected)

$Na_2S_2O_5$. The analytical data and melting point are found in Table 8.

Kinetic Study of the Hydrolysis Reaction

All kinetic 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 the sodium aryl sulfates, Figure 3. 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 the hydrolysis of the Bunte salt with 0.10$\underline{N}$ iodine solution. After ten half-lives an infinity mercaptan titer was determined, and the first-order rate constant was determined from a plot of the logarithm of $[1-(RSH)/(RSH)_\infty]$ versus time. The infinity mercaptan titer in each case corresponded satisfactorily to that expected from the amount of Bunte salt hydrolyzed and good first-order plots were obtained.

In the case of the nitro-substituted S-aryl thiosulfates it was difficult to detect the end point of the titration visually. Therefore, with these compounds, the end point was detected potentiometrically.

The hydrolysis of the ethyl Bunte salt was carried out in sealed tubes. The tubes, containing aliquots of the reaction solution, were deaerated using a freeze-thaw procedure before being sealed. The

reaction was followed by removing tubes at appropriate time inter-

vals, cooling and opening them, and then titrating the contents for

mercaptan in the usual manner with 0.10$\underline{N}$ iodine solution.

The rates of hydrolysis of the Bunte salts were measured under

a variety of reaction conditions. The experimental first-order rate

constants for the acid-catalyzed hydrolysis, k_ψ, as studied at differ-

ent acid concentrations are tabulated in Table 9.

It is obvious from a comparison of the rate constants for pyr-

idinium S-phenyl thiosulfate, Table 9, row 1, and sodium S-phenyl

thiosulfate, Table 9, row 2, that the nature of the cation, pyridinium

or sodium, has no significant effect on the rate of hydrolysis.

Figure 4 shows a plot of the logarithm of the observed rate

constant for the acid-catalyzed hydrolysis of pyridinium S-phenyl

thiosulfate, sodium S-($\underline{m}$-nitrophenyl) thiosulfate, and pyridinium

S-($\underline{p}$-nitrophenyl) thiosulfate in 60% dioxane-40% water (volume/

volume) perchloric acid solutions versus the Hammett acidity func-

tion, $-H_o$, for the same media (1, 12).

It is apparent from Figure 4 and Table 9 that the nitro-substi-

tuted Bunte salts exhibit a greater dependence on acidity than do the

other Bunte salts. 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

Table 9. Kinetics of the acid-catalyzed hydrolysis of Bunte salts in 60% dioxane at 69.7°C.

Bunte salt, [1] RSSO$_3^-$M$^+$		$k_\psi \times 10^4$, sec^{-1} [3]					
R	M$^+$ [2]	0.24M	0.40M	0.60M	0.81M	1.20M	1.81M
C$_6$H$_5$	C$_5$H$_5$NH$^+$	0.69	0.92	1.33	1.81	2.95	5.65
C$_6$H$_5$	Na$^+$	0.66	0.90	1.25	1.73	2.77	5.20
p-CH$_3$C$_6$H$_4$	C$_5$H$_5$NH$^+$	0.66	1.00	1.29	1.61	2.78	5.22
p-(CH$_3$)$_3$CC$_6$H$_4$	C$_5$H$_5$NH$^+$	0.72	0.93	1.45	1.82	2.96	4.68
p-ClC$_6$H$_4$	C$_5$H$_5$NH$^+$	0.45	0.66	1.07	1.31	2.09	3.98
p-BrC$_6$H$_4$	C$_5$H$_5$NH$^+$	0.47	0.62	0.98	1.18	2.04	3.75
p-O$_2$NC$_6$H$_4$	C$_5$H$_5$NH$^+$	0.17	0.34	0.48	0.81	1.65	4.0
m-O$_2$NC$_6$H$_4$	Na$^+$	0.19	0.29	0.44	0.65	1.19	2.61
C$_6$H$_5$CH$_2$	Na$^+$	0.79	1.08	1.52	1.91	3.33	5.9
CH$_3$CH$_2$	Na$^+$	1.01	1.41	2.22	2.82	4.54	8.82

[1] All runs at an initial Bunte salt concentration of 0.05M.
[2] C$_5$H$_5$NH$^+$ equals pyridinium ion. [3] At molarities of HClO$_4$ shown.
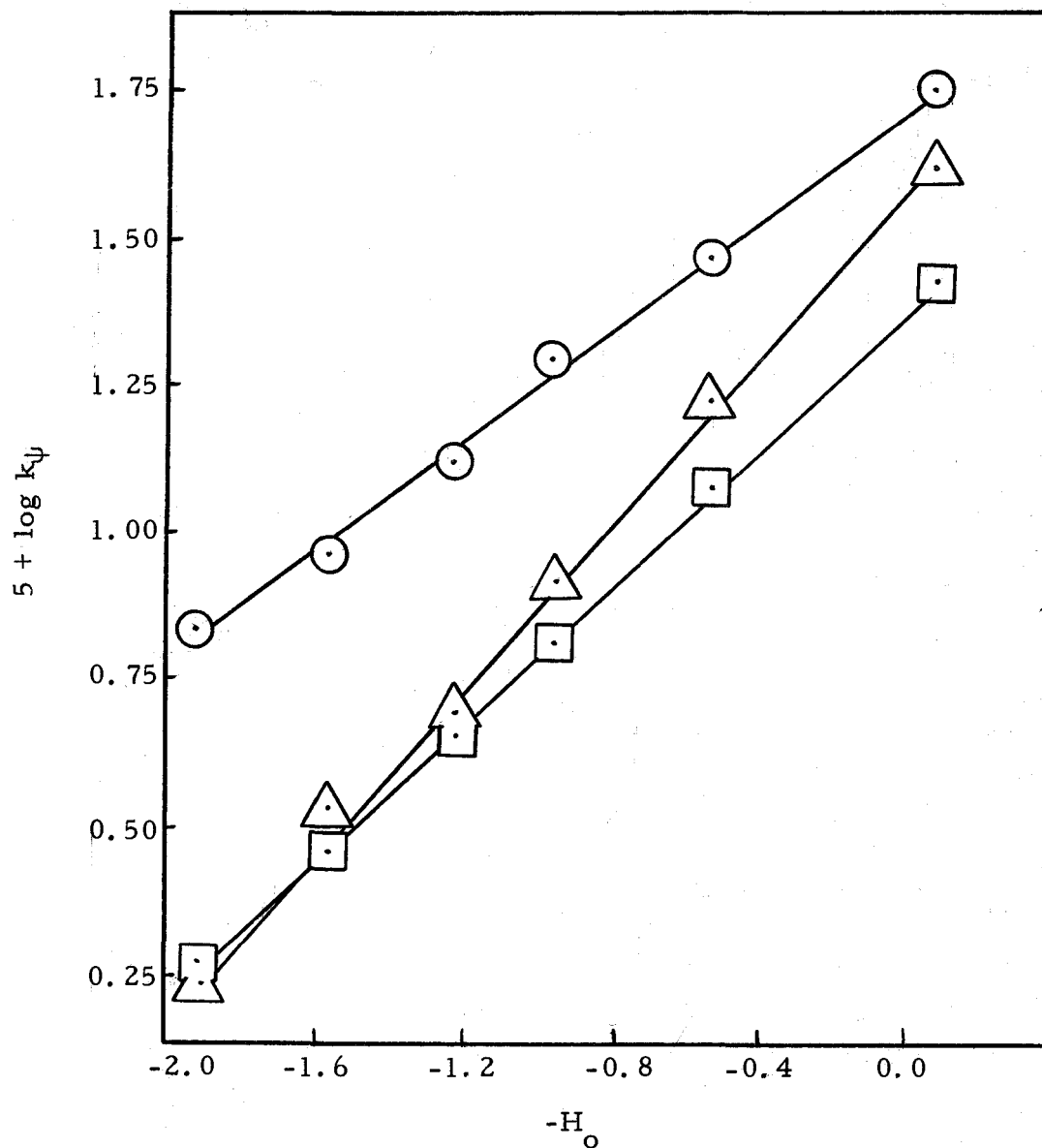
Figure 4.   Logarithm of k_ψ versus the Hammett acidity
function, $-H_o$, in 60% dioxane-40% water
perchloric acid solutions at 69.7° C.

○ - pyridinium S-phenyl thiosulfate

□ - sodium S-(m-nitrophenyl) thiosulfate

△ - pyridinium S-(p-nitrophenyl) thiosulfate

and suspect that it may be due to solvation phenomena involving the nitro group.

Figure 5 shows a plot of the logarithm of (k_{ψ}/k_o), where k_o is the rate constant of the phenyl Bunte salt, versus σ for the hydrolysis of meta- and para-substituted S-phenyl thiosulfates in 60% dioxane containing 0.40$\underline{M}$ perchloric acid. The slope of the plot, ρ, is about -0.6.

The solvent isotope effect and the variation of the rate with dioxane content in dioxane-water mixtures were carried out by Pawlowski (36) and his results as well as those of Kice's (31) will be included in the discussion of the mechanism of the acid-catalyzed hydrolysis of Bunte salts.

Table 10. Effect of acidity on the Bunte salt hydrolysis.

Bunte salt $RSSO_3^-M^+$		Slope of log k_ψ versus $-H_O$ plot for 60% dioxane- 40% water (v/v)
R	M^+	perchloric acid solutions
C_6H_5	$C_5H_5NH^+$	0.48
C_6H_5	Na^+	0.46
$\underline{p}$-$CH_3C_6H_4$	$C_5H_5NH^+$	0.47
$\underline{p}$-$(CH_3)_3CC_6H_4$	$C_5H_5NH^+$	0.48
$\underline{p}$-ClC_6H_4	$C_5H_5NH^+$	0.47
$\underline{p}$-BrC_6H_4	$C_5H_5NH^+$	0.46
$C_6H_5CH_2$	Na^+	0.47
CH_3CH_2	Na^+	0.49
$\underline{m}$-$O_2NC_6H_4$	Na^+	0.60
$\underline{p}$-$O_2NC_6H_4$	$C_5H_5NH^+$	0.72
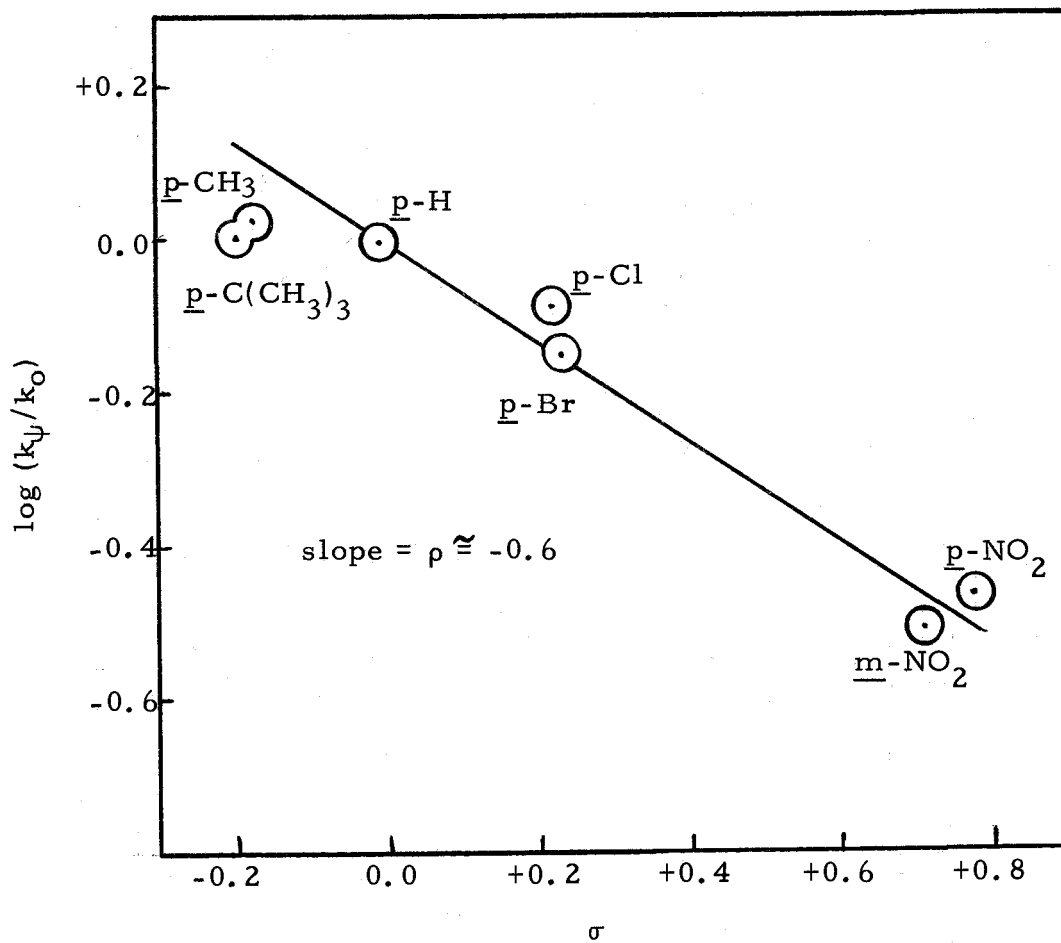
Figure 5. Logarithm of (k_ψ / k_o) versus σ for the hydrolysis of meta- and para-substituted S-phenyl thiosulfates in 60% dioxane containing 0.40M perchloric acid.

DISCUSSION

A priori several possible mechanisms can be suggested for the acid-catalyzed hydrolysis of Bunte salts. These mechanisms differ from each other in two principal ways. First, certain ones are of the A-1 mechanistic type while the rest are of the A-2 type. In an A-1 mechanism the rate-determining step is a unimolecular decomposition of the protonated substrate, while in an A-2 mechanism the rate-determining step involves a bimolecular reaction of water with the protonated substrate. The second way in which they differ is in the site of protonation of the substrate. Certain of the mechanisms involve protonation of the Bunte salt on the sulfenyl sulfur, Ar-S-, the remainder, protonation at one of the sulfonate oxygens, $-SO_3^-$.

Two possible A-1 mechanisms can be written. The first of these, mechanism A-1a (Eq. 24), involves protonation of the sulfenyl sulfur. The second, mechanism A-1b (Eq. 25), involves protonation of the Bunte salt on a sulfonate oxygen. Mechanism A-1b can be rather quickly eliminated from further consideration on the basis of the following arguments. Heterolytic cleavage of the sulfur-sulfur bond and expulsion of ArS^- should actually be easier in the anion $Ar-S-SO_3^-$ than in the sulfonate protonated form, XI. On the other hand, protonation on the sulfenyl sulfur as in XII should clearly assist the cleavage of the sulfur-sulfur bond by converting

Mechanism A-1a

$$Ar\text{-}S\text{-}SO_3^- \quad + \quad H^+ \quad \underset{\xrightarrow{\hspace{1.5cm}}}{\overset{\text{fast}}{\rightleftharpoons}} \quad Ar\text{-}\overset{+}{\underset{H}{S}}\text{-}SO_3^- \qquad \text{(Eq. 24a)}$$

$$Ar\text{-}\overset{+}{\underset{H}{S}}\text{-}SO_3^- \quad \xrightarrow[\text{rate-determining}]{\text{slow}} \quad ArSH \quad + \quad SO_3 \qquad \text{(Eq. 24b)}$$

$$SO_3 \quad + \quad H_2O \quad \xrightarrow{\text{fast}} \quad H_2SO_4 \qquad \text{(Eq. 24c)}$$

Mechanism A-1b

$$ArSSO_3^- \quad + \quad H^+ \quad \underset{\xrightarrow{\hspace{1.5cm}}}{\overset{\text{fast}}{\rightleftharpoons}} \quad ArSSO_3H \qquad \text{(Eq. 25a)}$$

$$ArSSO_3H \quad \xrightarrow[\text{rate-determining}]{\text{slow}} \quad ArS^- \quad + \quad {}^+SO_3H \qquad \text{(Eq. 25b)}$$

$$ArS^- \quad + \quad {}^+SO_3H \quad + \quad H_2O \quad \xrightarrow{\text{fast}} \quad ArSH \quad + \quad H_2SO_4 \qquad \text{(Eq. 25c)}$$
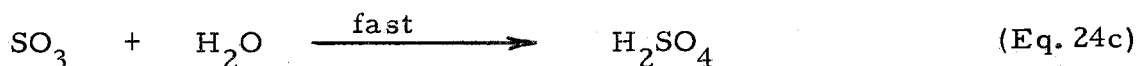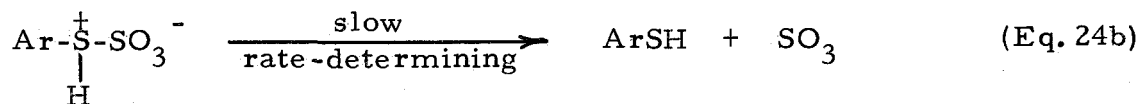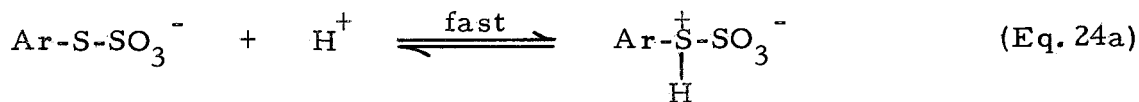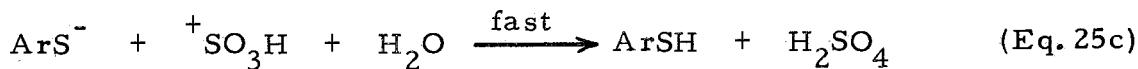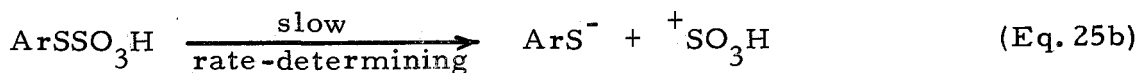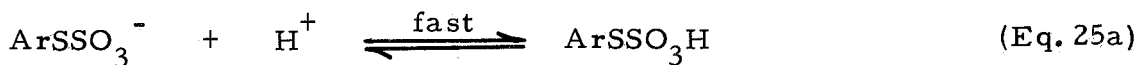
$Ar\text{-}S\text{-}$ to a better leaving group $Ar\text{-}\overset{+}{S}(H)\text{-}$. Therefore, the need for

acid catalysis makes sense for the A-1a mechanism (Eq. 24), but

makes no sense for the A-1b mechanism (Eq. 25). Mechanism A-1b

is therefore eliminated from further serious consideration.

$$Ar\text{-}S\text{-}SO_3H \qquad\qquad\qquad Ar\text{-}\overset{+}{\underset{H}{S}}\text{-}SO_3^-$$
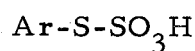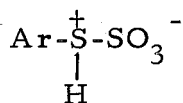
$$XI \qquad\qquad\qquad\qquad XII$$

We shall now outline the several possible A-2 mechanisms that one can write for the Bunte salt hydrolysis. The first A-2 mechanism, designated A-2a (Eq. 26), involves a rapid reversible protonation on the sulfenyl sulfur, XII, followed by a rate-determining nucleophilic displacement of $Ar-\overset{+}{S}(H)-$ by water.

Mechanism A-2a

$$Ar-S-SO_3^- + H^+ \underset{fast}{\overset{fast}{\rightleftharpoons}} Ar-\underset{\underset{H}{|}}{\overset{+}{S}}-SO_3^- \qquad (Eq. 26a)$$

$$Ar-\underset{\underset{H}{|}}{\overset{+}{S}}-SO_3^- + H_2O \xrightarrow[\text{rate-determining}]{slow} ArSH + H_2\overset{+}{O}SO_3^- \qquad (Eq. 26b)$$

$$H_2\overset{+}{O}SO_3^- \xrightarrow{fast} H_2SO_4 \qquad (Eq. 26c)$$
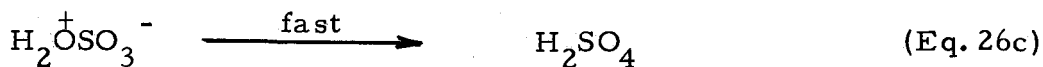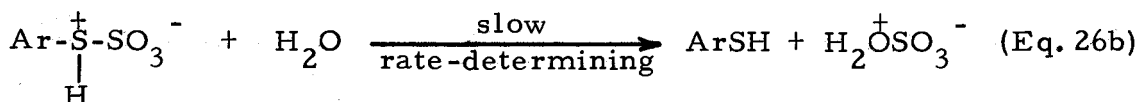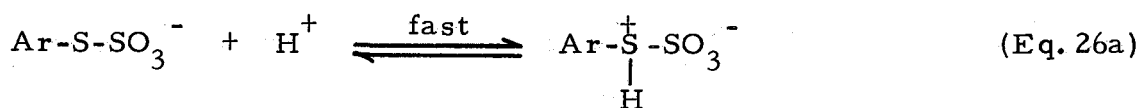
The other possible A-2 mechanisms would involve initial protonation of a sulfonate oxygen, XI. The first of these A-2 mechanisms, designated A-2b (Eq. 27), involves protonation followed by a nucleophilic displacement of ArS^- by water from $ArSSO_3H$. The second, designated A-2b' (Eq. 28), differs from the first in that an adduct with water is formed. This adduct may decompose as in equation 28c, hereafter referred to as mechanism A-2b'(1), or, more likely, it may transfer a proton to form a zwitterion which then decomposes (Eq. 28e). This latter possibility will be referred to as mechanism A-2b'(2).

Mechanism A-2b

$$ArSSO_3^- + H^+ \xrightleftharpoons{fast} ArSSO_3H \qquad \text{(Eq. 27a)}$$

$$ArSSO_3H + H_2O \xrightarrow[\text{rate-determining}]{\text{slow}} \left[H_2\overset{\Delta+}{O} \cdots \underset{OH}{SO_2} \cdots \overset{\Delta-}{S}Ar \right]^- \longrightarrow$$

$$H_2\overset{+}{O}SO_3H + ArS^- \qquad \text{(Eq. 27b)}$$

$$ArS^- + H_2\overset{+}{O}SO_3H \xrightarrow{fast} ArSH + H_2SO_4 \qquad \text{(Eq. 27c)}$$

Mechanism A-2b'

$$ArSSO_3^- + H^+ \xrightleftharpoons{fast} ArSSO_3H \qquad \text{(Eq. 28a)}$$

$$ArSSO_3H + H_2O \xrightleftharpoons{fast} Ar-S-\underset{\underset{O}{\|}}{\overset{\overset{OH}{|}}{S}}\!\!-\!\!\begin{smallmatrix}OH\\OH\end{smallmatrix} \xrightleftharpoons{fast}$$

$$Ar-\overset{+}{\underset{\underset{H}{|}}{S}}\!\!-\!\!\underset{\underset{O}{\|}}{\overset{\overset{O^-}{|}}{S}}\!\!-\!\!\begin{smallmatrix}OH\\OH\end{smallmatrix} \qquad \text{(Eq. 28b)}$$

Mechanism A-2b'(1)

$$\text{Ar-S-}\overset{\overset{\displaystyle OH}{|}}{\underset{\underset{\displaystyle O}{\|}}{S}}\overset{\displaystyle \diagdown OH'}{\diagup OH} \quad \xrightarrow[\text{rate-determining}]{\text{slow}} \quad ArS^- \ + \ H_3\overset{+}{S}O_4 \qquad \text{(Eq. 28c)}$$

$$ArS^- \ + \ H_3\overset{+}{S}O_4 \quad \xrightarrow{\text{fast}} \quad ArSH \ + \ H_2SO_4 \qquad \text{(Eq. 28d)}$$

Mechanism A-2b'(2)

$$\text{Ar-}\overset{\overset{\displaystyle O^-}{|}}{\underset{\underset{\displaystyle H}{|}}{\overset{+}{S}}}\text{-}\overset{\diagup OH}{\underset{\underset{\displaystyle O}{\|}}{S}\diagdown OH} \quad \xrightarrow[\text{rate-determining}]{\text{slow}} \quad ArSH \ + \ H_2SO_4 \qquad \text{(Eq. 28e)}$$
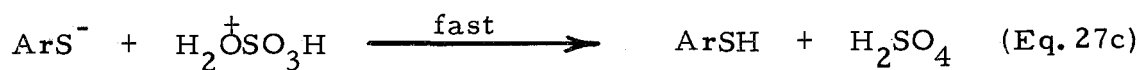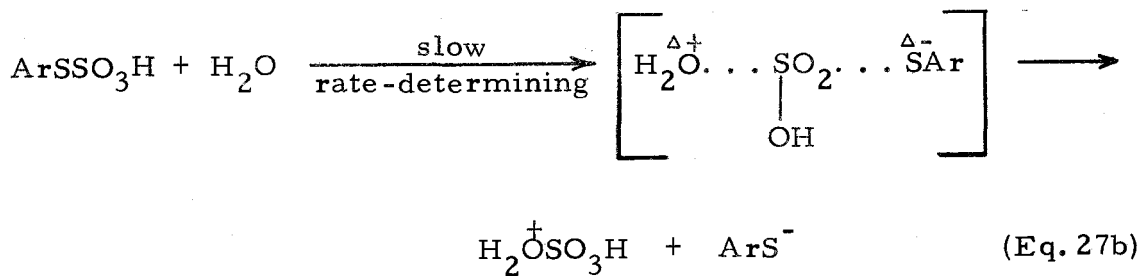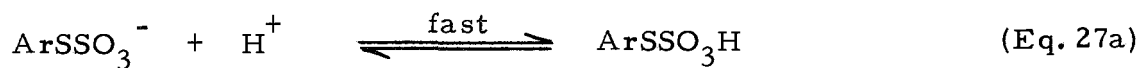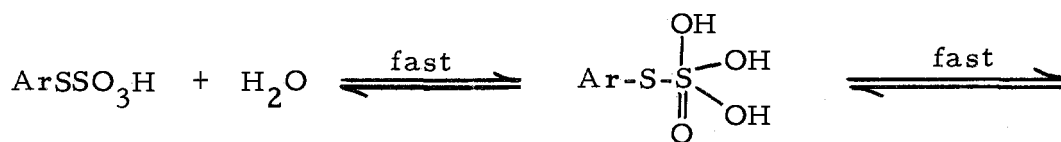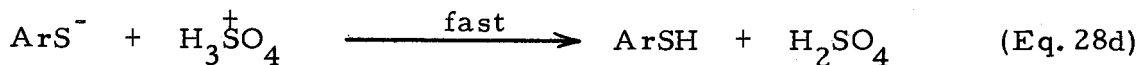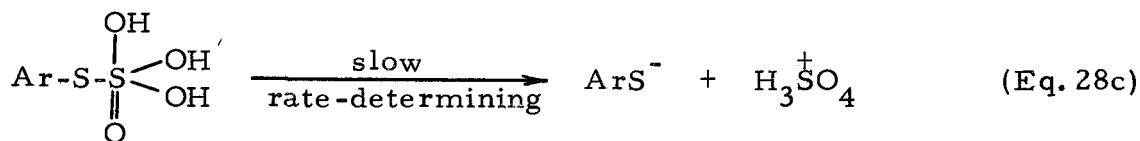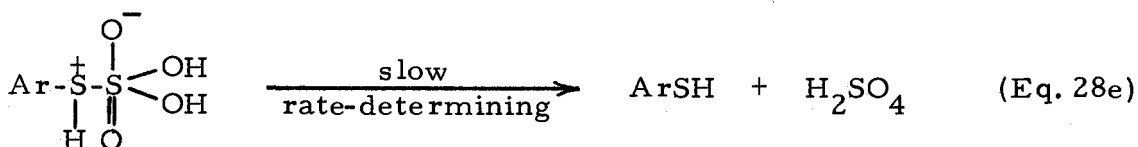
The possible A-2 mechanisms may be divided into two classes

on the basis of the products of their rate-determining step. The

rate-determining steps in mechanisms A-2a and A-2b'(2) give the

aryl mercaptan, ArSH, as a product whereas the rate-determining

steps of mechanisms A-2b and A-2b'(1) give the aryl mercaptide

ion, ArS^-, as a product. It is apparent from Table 9 that for a

given acid concentration the rate of hydrolysis of the p-nitrophenyl

Bunte salt is smaller than that for the unsubstituted phenyl Bunte

salt. A closer inspection of Table 9 reveals that electron-withdraw-

ing para substituents retard the hydrolysis rate whereas electron-

donating para substituents accelerate the hydrolysis rate. This

structural effect is not that expected for mechanisms A-2b and

A-2b'(1). If either of these mechanisms were operating, one would

expect electron-withdrawing para substituents to accelerate the rate of hydrolysis because of increased stabilization of the aryl mercaptide ion. Also, the rate of Bunte salt hydrolysis is best correlated by σ constants, Figure 5, not σ_- constants, as would be expected if the aryl mercaptide ion were being formed in the rate-determining step. It is also obvious from Table 9 that the aryl and alkyl Bunte salts hydrolyze at about the same rate, with the ethyl and benzyl Bunte salts, for a given acid concentration, actually hydrolyzing at a somewhat faster rate than does the p-nitrophenyl Bunte salt. This also argues against the formation of the mercaptide ion in the rate-determining step as it would be expected that the p-nitrophenyl mercaptide ion would be much more stable than either the benzyl mercaptide ion or the ethyl mercaptide ion. This increased stability should result in a faster rate of hydrolysis and it is obvious that this is not the case. Therefore, those mechanisms, A-2b and A-2b'(1), which produce the aryl mercaptide ion in the rate-determining step are eliminated from further serious consideration.

Those mechanisms which now remain for consideration are the A-1a (Eq. 24), the A-2a (Eq. 26), and the A-2b'(2) (Eq. 28).

The solvent isotope effect for the acid-catalyzed hydrolysis of sodium S-ethyl thiosulfate, the ethyl Bunte salt, has been determined, $k_{D_2O}/k_{H_2O} = 1.4$ (36). Because this value for the solvent

isotope effect is in the range, $k_{D_2O}/k_{H_2O} = 1.3-1.7$, normally

associated with an A-2 mechanism (14, 38, 39) it might at first seem

to be evidence against the A-1a mechanism. However, a calcula-

tion (Appendix 2) using the Bunton-Shiner approach (13, 14, 15) for

solvent isotope effects, shows that, because of the fact that the A-1a

mechanism for the Bunte salt hydrolysis involves protonation on

sulfur, the value of 1.4 found for k_{D_2O}/k_{H_2O} is that which one

would expect for the A-1a mechanism. The Bunton-Shiner ap-

proach (13, 14, 15) relating solvent isotope effects to A-1 and A-2

mechanisms is based on the changes in the stretching frequencies

associated with various bonds involving hydrogen atoms. More

precisely, the solvent isotope effect is related to the difference in

the summation of the hydrogen stretching frequencies in the initial

and transition states divided by the absolute temperature.

Since the special circumstances of the Bunte salt hydrolysis

conspire to make the solvent isotope effect a less unequivocal

indicator of mechanism than usual, the burden of discerning by

which mechanism the Bunte salt hydrolysis takes place falls upon

the dependence of rate on the acidity of the medium and the response

of rate to changes in dioxane content in dioxane-water mixtures.

Fortunately, as will be pointed out, these reaction variables are

quite helpful in deciding between an A-1 or an A-2 mechanism for

the Bunte salt hydrolysis. If the Bunte salt hydrolysis takes place

via an A-1 mechanism, the response of rate of the Bunte salt

hydrolysis to these reaction variables should be similar to the

changes in these same reaction variables found for the acid-catalyzed

hydrolysis of sodium phenyl sulfate. On the other hand, if the Bunte

salt hydrolysis takes place via an A-2 mechanism, the response of

rate of the Bunte salt hydrolysis to these reaction variables should

parallel those for the hydrolysis of sodium methyl selenate.

An earlier study (31) of the hydrolysis of the ethyl Bunte salt

in aqueous acid has shown that a plot of the logarithm of the first-

order rate constant versus the Hammett acidity function, $-H_o$, gives

a slope of 0.99. It is apparent from Figure 1 (Part I) that the hydrol-

ysis of sodium phenyl sulfate in aqueous acid also exhibits the same

dependence on the Hammett acidity function, $-H_o$. In contrast, a

plot of the logarithm of the rate constant for the acid-catalyzed

hydrolysis of sodium methyl selenate (11) versus $-H_o$ is far from

linear, being a smooth curve whose slope decreases with increasing

$-H_o$. The dependence of the rate of hydrolysis of the Bunte salt on

$-H_o$ in aqueous acid is identical with that exhibited by the known A-1

sulfate hydrolysis (Part I) and very different with that exhibited by

the known A-2 selenate hydrolysis (11).

It is also interesting that in 60 percent dioxane the rates of

hydrolysis of sodium phenyl sulfate and sodium S-phenyl thiosulfate

increase by the same magnitude for a given change in strong acid

concentration. Plots of the logarithm of the rate constant versus
$-H_o$ for the hydrolysis of sodium phenyl sulfate and sodium S-phenyl
thiosulfate in 60 percent dioxane-40 percent water (v/v) perchloric
acid solutions give slopes of 0.43 and 0.46, respectively. This
also suggests that the two hydrolyses probably proceed by similar
mechanisms.

It must be remembered that the Hammett acidity function,
$-H_o$ (Eq. 29), applies only to equilibria involving uncharged bases,
B, and their conjugate acids, BH^+. There is no reason that the
Hammett acidity function, $-H_o$, should correlate the change in

$$-H_o = \log \frac{a_{H^+} f_B}{f_{BH^+}} \qquad \text{(Eq. 29)}$$

$\left[Ar\overset{+}{\underset{H}{S}}SO_3^- \right] \Big/ \left[ArSSO_3^- \right]$ with acid concentration in strongly acidic
solutions, since this ratio should be dependent on $a_{H^+} f_{A^-} / f_{HA}$; and
it is certainly unlikely that f_{A^-}/f_{HA} will change with acid concen-
tration in the same manner as f_B/f_{BH^+}.

Obviously the parallel between H_o and H_- which happens to be
observed for 1.0-6.0M aqueous perchloric or hydrochloric acid
solutions (25) does not extend to solutions of the same acids in 60
percent dioxane. This is not at all surprising, however.

In aqueous dioxane the rates of both the A-1 hydrolysis of
sodium phenyl sulfate and the A-2 hydrolysis of sodium methyl

selenate increase with an increase in the dioxane content of dioxane-water mixtures containing a fixed concentration of perchloric acid. However, for the reasons outlined earlier (Part I, page 23), the rate of hydrolysis of the sulfate, a reaction proceeding by an A-1 mechanism analogous to equation 24 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. A comparison of the effect of dioxane content on the rate of the Bunte salt hydrolysis in aqueous dioxane is found in Table 11.

Table 11. Effect of dioxane content on relative rate of hydrolysis in dioxane-water mixtures.

Percent dioxane (v/v)	$k/k_{40\%\ dioxane}$		
	ϕCH_2SSO_3Na [1] Hydrolysis	ϕOSO_3Na [2] Hydrolysis	CH_3OSeO_3Na [3] Hydrolysis
40	(1.0)	(1.0)	(1.0)
60	6.0	5.0	1.6
80	110 [4]	67 [4]	6.3

[1] Data are for $0.5\underline{M}$ perchloric acid solutions at 70° C. Reference 36.

[2] Data are for $0.5\underline{M}$ perchloric acid solutions at 30.1° C. Table 4.

[3] Data are for $0.1\underline{M}$ perchloric acid solutions at 25.1° C. Reference 11.

[4] Extrapolated from data at lower temperatures.

It is obvious that the Bunte salt hydrolysis shows rate increases which are similar to those found for the sulfate hydrolysis and much larger than those found for the selenate hydrolysis. These results provide further evidence that the Bunte salt hydrolysis proceeds by an A-1 mechanism.

The data on the dependence of rate on the acidity of the medium and on its dioxane content strongly indicate an A-1 mechanism for the Bunte salt hydrolysis. As pointed out earlier, the only reasonable A-1 mechanism is the A-1a mechanism (Eq. 24).

It is obvious that the A-1 mechanism suggested for the Bunte salt hydrolysis, mechanism A-1a (Eq. 24), is the same type as that suggested for the sodium aryl sulfate hydrolysis, mechanism A-1a (Eq. 11). That being the case, an explanation is needed as to how these two reactions can exhibit a somewhat different response of rate to alkyl and aryl group structure and yet have the same type of mechanism. First, a summary of the structural effects of each reaction is in order.

The hydrolysis of aryl Bunte salts is somewhat retarded by electron-withdrawing substituents ($\rho \cong -0.6$, rate correlated by σ) while the hydrolysis of sodium aryl sulfates is accelerated by electron-withdrawing substituents ($\rho = +0.5$, rate correlated by σ_-). Also, sodium phenyl sulfate hydrolyzes much faster than the sodium alkyl sulfates while there is essentially no difference in the rates of

hydrolysis of phenyl and alkyl Bunte salts.

The fact that the sodium aryl sulfate hydrolysis rates were accelerated by electron-withdrawing substituents and correlated by σ_- constants was explained (Part I) by assuming a greater resonance interaction in the transition state between the phenolic oxygen and an electron-withdrawing para substituent than in the starting aryl sulfate ion. The lack of resonance interaction in the starting aryl sulfate ion was attributed to the very strong electron-withdrawing tendency of the sulfonate group, $-SO_3^-$, which is bonded directly to the phenolic oxygen, Ar-O-. It was also shown in Part I that the enhanced resonance interaction in the transition state between the aromatic ring and an unbonded pair of electrons on the phenolic oxygen, suggested by the correlation of rates with σ_- constants, implies that the transition state is closer in structure to the products, phenol and sulfur trioxide, than to the starting aryl sulfate ion. The fact that sodium aryl sulfate ions hydrolyzed several hundred times faster than sodium alkyl sulfate ions was easily explained by the lack of any analogous resonance interaction in the transition state for the alkyl case.

The fact that the aryl Bunte salt rates are slightly accelerated by electron-donating groups and that the rates are correlated by σ constants must mean that this same sort of resonance interaction is not important in the transition state for the Bunte salt hydrolysis.

This is also suggested by the fact that, unlike the sulfate case, the rates of hydrolysis of the alkyl and aryl Bunte salts are effectively the same. There are two factors that probably combine to make this the case.

Resonance between an unshared pair of electrons on sulfur and the aromatic ring is known to be much less significant for thiophenol, XIII, X = S, than similar resonance for phenol, XIII, X = O.

XIII
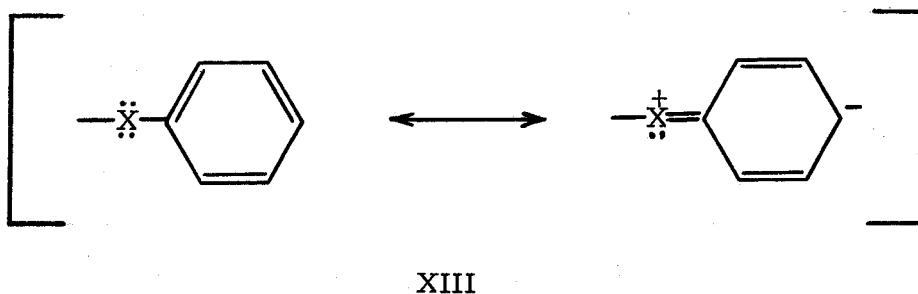
This is evident from the fact that $\sigma_p - \sigma_m$ for CH_3S- is only -0.15 while it is -0.38 for CH_3O- (44, p. 410). This occurs because overlap of the 3p orbital holding the unshared pair of electrons on sulfur with the 2p orbital of the ring carbon to which it is attached is less effective than the overlap of the same 2p orbital of the ring carbon with an electron-rich 2p orbital on oxygen. Because of this, even if the structure of the Bunte salt transition state involved as great a degree of breaking of the sulfur-sulfur bond as that of the oxygen-sulfur bond in the sulfate hydrolysis, one would expect any rate enhancement by electron-withdrawing *para* substituents in the

aromatic ring to be considerably smaller than for the sulfate reac-
tion. Also, one would expect only a modest acceleration of the
hydrolysis rate for the aryl Bunte salts over that observed for their
alkyl counterparts.

In addition it seems quite likely, since $Ar\text{-}\overset{+}{\underset{H}{S}}\text{-}SO_3^{-}$ is presum-
ably a higher energy intermediate than $Ar\text{-}\overset{+}{\underset{H}{O}}\text{-}SO_3^{-}$, that the transi-
tion state for the Bunte salt hydrolysis actually occurs earlier along
the reaction coordinate (27), that is, that it involves a lesser degree
of breaking of the sulfur-sulfur bond, than does the transition state
for the sulfate reaction. This means that the structure of the Bunte
salt transition state is closer to that of the reactants ($Ar\text{-}\overset{+}{\underset{H}{S}}\text{-}SO_3^{-}$)
and further from that of the products ($ArSH + SO_3$) than the analogous
transition state for the sulfate reaction. This will serve to decrease
even further the importance of any resonance interaction of the type
previously outlined (XIII), and it is not hard to imagine that the struc-
ture of the Bunte salt transition state could be such that an interaction
of this type becomes effectively non-existent. For this reason, the
lack of acceleration of hydrolysis rate for aryl Bunte salts as com-
pared to alkyl Bunte salts is perfectly reasonable even though such
an acceleration is observed for the sulfates. It also seems perfectly
possible that the structure of the transition state for the Bunte salt
reaction will be close enough to $Ar\text{-}\overset{+}{\underset{H}{S}}\text{-}SO_3^{-}$ so that there is actually

a slight decrease in electron density on sulfur on going from Bunte

salt to transition state, thereby explaining the small negative ρ

observed for this hydrolysis.

EXPERIMENTAL - BUNTE SALT

Materials

Pyridine. Reagent grade pyridine was allowed to stand over potassium hydroxide pellets for several days and then refluxed for a day with barium oxide. It was then distilled under anhydrous conditions.

Sulfur Trioxide. (Sulfan, Baker and Adamson Chemical Company, Inc.) The sulfur trioxide was used directly from the container.

N-Pyridinium Sulfonic Acid. N-Pyridinium sulfonic acid was prepared using the procedure of Baumgarten (6). The reaction was carried out in a three-necked flask fitted with a dropping funnel, a reflux condenser and drying tube, and a stirrer. After 250-300 ml. of anhydrous carbon tetrachloride had been added to the flask and cooled to below 0°C in an ice-salt bath, 80.1 grams (1.0 mole) of sulfur trioxide was added and the mixture allowed to cool. Pyridine, 79.1 grams (1.0 mole), was then added cautiously via the dropping funnel. Care was taken to keep the reaction mixture cold during the pyridine addition.

After the pyridine addition was completed, the reaction mixture was stirred for an additional 15 minutes; the N-pyridinium

sulfonic acid was filtered from the carbon tetrachloride and the by-
product, pyridinium sulfate, was removed by washing with ice water.
The N-pyridinium sulfonic acid was then filtered using a fritted disc
Büchner funnel and kneaded to take off as much water as possible.

The N-pyridinium sulfonic acid was then dried over phosphorus
pentoxide at 0.5 mm. pressure. The yield was greater than 90 per-
cent. The melting point was 160-170° C (uncorrected)(Literature
value 175° C).

Pyridinium S-Phenyl Thiosulfate. Pyridinium S-phenyl thio-
sulfate was prepared using the procedure of Baumgarten, sulfonation
of thiophenol (7). A mixture of 22 grams (0.2 moles) of thiophenol
and 32 grams (0.2 moles) of N-pyridinium sulfonic acid was placed
in a three-necked flask fitted with a reflux condenser and drying tube,
and a stirrer. The mixture was heated on a water bath until one
clear phase was observed and then rapidly poured into a beaker.

After the pyridinium S-phenyl thiosulfate crystallized, it was
recrystallized from ethanol twice and after each recrystallization
trituated with diethyl ether. It was then dried over calcium chloride
in a vacuum desiccator at 1.0 mm. pressure.

$C_{11}H_{11}NO_3S_2$ m.p. 88.5-91° C (uncorrected)

(Literature value 89-91° C)

Sodium S-Phenyl Thiosulfate. Sodium S-phenyl thiosulfate was

prepared by ion-exchange from pyridinium S-phenyl thiosulfate

using Dowex 50W-X4 resin. (Wet volume exchange capacity 1.31

meq./ml.) The resin was converted to the sodium form with ten

percent sodium chloride solution. Batches of the ten percent sodium

chloride were added until no change in the pH of the eluent was ob-

served. The resin was then washed thoroughly with distilled water

until the eluent gave a negative test for chloride ion using silver

nitrate solution.

The water level in the column was brought to the level of the

resin and 15 grams (55.6 meq. -38 percent of total resin wet volume

exchange capacity) of pyridinium S-phenyl thiosulfate dissolved in

200 ml. of water added to the column. The column was allowed to

stand for one hour and then it was drained. The column was washed

with distilled water and the wash water collected. The wash water

was removed with a Büchi rotary evaporator but not completely.

The removal of the wash water was completed in a vacuum desiccator

at 1.0 mm. pressure.

$C_6H_5NaO_3S_2 \cdot H_2O$ m.p.   86-88° C (uncorrected)

Calculated   C   31.30% H   3.06%

Found   C   31.26% H   3.33%

Pyridinium S-(p-tolyl) Thiosulfate.   Pyridinium S-(p-tolyl)

thiosulfate was prepared using a modification of the procedure of

Baumgarten, sulfonation of p-toluenethiol (7). Carbon tetrachloride

was used as the solvent for the reaction. The reaction mixture was

heated on a water bath at 55-60° C for about 45 minutes.

The pyridinium S-(p-tolyl) thiosulfate was recrystallized from

ethanol twice and after each recrystallization trituated with diethyl

ether. It was then dried over calcium chloride in a vacuum desic-

cator at 1.0 mm. pressure.

$C_{12}H_{13}NO_3S_2$ m.p.   115-117° C (uncorrected)

           Calculated   C 50.86%   H 4.62%

           Found   C 50.80%   H 4.72%

Pyridinium S-(p-Chlorophenyl) Thiosulfate. Pyridinium

S-(p-chlorophenyl) thiosulfate was prepared using a modification of

the procedure of Baumgarten, sulfonation of p-chlorothiophenol (7).

Carbon tetrachloride was used as the solvent for the reaction.

The pyridinium S-(p-chlorophenyl) thiosulfate was recrystal-

lized from ethanol twice and after each recrystallization trituated

with diethyl ether. It was then dried over calcium chloride in a

vacuum desiccator at 1.0 mm. pressure.

$C_{11}H_{10}ClNO_3S_2$ m.p.   123-124° C (uncorrected)

           Calculated   C 43.49%   H 3.32%

           Found   C 43.18%   H 3.41%

Pyridinium S-(p-Bromophenyl) Thiosulfate. Pyridinium

S-(p-bromophenyl) thiosulfate was prepared and recrystallized in

the same manner as pyridinium S-(p-chlorophenyl) thiosulfate.

$C_{11}H_{10}BrNO_3S_2$ m. p.   129° C   (uncorrected)

Calculated   C   37.94%   H   2.89%

Found   C   37.91%   H   3.01%

Pyridinium S-(p-Butylphenyl) Thiosulfate.   Pyridinium

S-(p-t-butylphenyl) thiosulfate was prepared and recrystallized in

the same manner as pyridinium S-(p-tolyl) thiosulfate.   The reac-

tion mixture was heated on a water bath at 50-55°C for two hours.

$C_{15}H_{19}NO_3S_2$ m. p.   139° C   (uncorrected)

Calculated   C   55.36%   H   5.88%

Found   C   54.93%   H   5.87%

p-Nitrothiophenol.   p-Nitrothiophenol was prepared using the

method of Price and Stacy (37).   The reaction was carried out in

a three-necked flask to which was fitted a reflux condenser with a

drying tube, a stirrer, and a dropping funnel.

To a solution of 10 grams (0.0635 moles) of p-nitrochloro-

benzene in 30 ml. of boiling alcohol, an alcoholic solution of sodium

disulfide was added portionwise over a period of ten minutes.   The

sodium disulfide was prepared by dissolving 10.8 grams (0.0447

moles) of sodium sulfide nonahydrate and 1.43 grams (0.0447 moles)

of sulfur in ethanol.   The undissolved material was added to the re-

action flask gravimetrically.

After the sodium disulfide solution had been added, an alcoholic

solution of 2.54 grams (0.0635 moles) of sodium hydroxide was

added from the dropping funnel over a period of 20 minutes and the

reaction mixture refluxed over a water bath. The mixture was then cooled and poured onto 60 grams of ice and 90 ml. of water. A precipitate was removed by filtration.

The filtrate was acidified with 1N hydrochloric acid and the crude p-nitrothiophenol collected by filtration and washed with 30 ml. of water. The p-nitrothiophenol was dissolved in 15 ml. of ethanol and after the addition of 2.54 grams of sodium hydroxide in 90 ml. of water, the solution was filtered and the p-nitrothiophenol was reprecipitated with hydrochloric acid. The p-nitrothiophenol was then collected by filtration and dried over calcium chloride in a vacuum desiccator at 1.0 mm. pressure. The yield was 47 percent (Literature value 60%). The melting point was 77-79° C (uncorrected) (Literature value 75-76° C).

Pyridinium S-(p-Nitrophenyl) Thiosulfate. Pyridinium S-(p-nitrophenyl) thiosulfate was prepared and recrystallized in the same manner as pyridinium S-(p-tolyl) thiosulfate. The reaction mixture was heated on a water bath at 60-64° C for two hours.

$C_{11}H_{10}N_2O_5S_2$ m.p.   155-156° C (uncorrected)

Calculated   C   42.03%   H   3.21%

Found   C   41.83%   H   3.23%

Sodium S-(m-Nitrophenyl) Thiosulfate. Sodium S-(m-nitrophenyl) thiosulfate was prepared using the method of Lecher and Hardy, the reaction of bis-(3-nitrophenyl) disulfide with sodium meta-bisulfite (32).

The reaction was carried out in a three-necked flask fitted with a reflux condenser and a stirrer. A mixture of 28.5 grams (0.30 moles) of sodium meta-bisulfite, $Na_2S_2O_5$, 25 ml. of water, 23.0 grams (0.075 moles) of bis-(3-nitrophenyl) disulfide, and 375 ml. of methanol was refluxed for three hours with stirring. Sodium hydroxide, 3.0 grams (0.075 moles), was then added to convert the excess meta-bisulfite to sulfite. The reaction mixture was allowed to cool for 15 minutes after the addition of the sodium hydroxide and then placed in an ice-bath.

The resulting slurry was filtered and the residue washed with 125 ml. of methanol. The methanol used for washing was evaporated and the resulting crystalline material was alternately washed with anhydrous methanol and the methanol evaporated until it gave the carbon and hydrogen analysis values reported in the literature.

$C_6H_4NNaO_5S_2 \cdot H_2O$ m.p.   105° C (uncorrected)

	Calculated	C 26.18%	H 2.19%

Calculated   C 26.18%   H 2.19%

Found   C 26.42%   H 2.28%

Sodium S-Ethyl Thiosulfate. The sodium S-ethyl thiosulfate was prepared by Pawlowski (36, p. 123).

Sodium S-Benzyl Thiosulfate. The sodium S-benzyl thiosulfate was prepared by Pawlowski (36, p. 123)

Solvents

Dioxane. Reagent grade dioxane was purified by the method
suggested by Wilberg (41, p. 245). It was distilled under nitrogen
from the sodium ketyl of benzophenone, b. p. 101° C.

Perchloric Acid. A 70 percent stock solution of reagent grade
perchloric acid was diluted with water and the normality of the re-
sulting solutions were determined by titration with standard base to
a phenolphthalein endpoint. These solutions were then used in a
further dilution to obtain solutions of desired acidities for the kinetic
runs.

Iodine Solutions. The iodine solutions were prepared in the
usual manner and titrated with standard arsenious oxide solution to
the starch endpoint.

Procedures

Aryl and Alkyl Thiosulfates. All of the aryl and alkyl thio-
sulfates were subjected to the following kinetic procedure except
the ethyl thiosulfate.

A weighed amount of the desired thiosulfate was dissolved in
a measured volume of the desired dioxane-water-acid mixture.
The solution was then placed in the reaction vessel.

The reaction vessel is a 100 ml. round-bottom flask fitted

with a gas inlet tube, a condenser, and a buret. A series of three-way stop-cocks, one between the buret and condenser and one between the buret and flask, allowed samples of a known volume to be withdrawn without exposing the solution to the atmosphere (Figure 3).

After the solution had been placed in the reaction vessel, it was deaerated from five to 15 minutes with pre-purified nitrogen while it was cooled in an ice-bath. The reaction vessel was then placed in a constant temperature bath. After temperature equilibration, approximately two minutes, the initial sample (time equal to zero) was taken. At appropriate time intervals aliquots were removed and titrated with the standard iodine solution to the visual endpoint determined by excess iodine. An infinity time point was taken after eight to ten half-lives and the first-order rate constant was calculated from plots of log $(1-I_2/I_2 \infty)$ versus time. The milliequivalents of iodine solution required to titrate the mercaptan, the product of the acid hydrolysis of the thiosulfate, in the reaction solution is represented by I_2. The usual procedure was to withdraw a 5 ml. aliquot from the 0.050$\underline{M}$ Bunte salt reaction solution and titrate it with 0.10$\underline{N}$ iodine solution.

Because of the difficulty in determining the endpoint, the nitro-substituted phenyl thiosulfate kinetics were followed by a potentiometric titration using a Beckman model #72 pH meter with a combined platinum-calomel Beckman electrode (26).

Ethyl Thiosulfate. The ethyl thiosulfate kinetics were followed by the use of sealed tubes as the product of the acid hydrolysis of the ethyl thiosulfate, ethyl mercaptan, was gaseous at the temperature at which the kinetics were determined.

A weighed amount of the ethyl thiosulfate was dissolved in a measured volume of the desired dioxane-water-acid mixture to give a 0.050$\underline{M}$ ethyl Bunte salt reaction solution. Five ml. aliquots were then pipetted into reaction tubes. The reaction tubes were constructed from 8 mm. pyrex tubing and four inch test tubes.

The reaction tubes were then connected to a vacuum manifold and frozen in dry ice-acetone baths. The reaction tubes, i.e., individual kinetic samples, were then pumped down, the vacuum system closed, the samples allowed to warm, refrozen, and pumped down again. The vacuum system was closed and pre-purified nitrogen bled into the manifold. The reaction tubes were submitted to a pressure of 700 mm. Hg. The reaction tubes were allowed to warm and then closed off with an oxygen-gas torch. The tubes were then placed in a rack which was immediately placed into a constant temperature bath. After temperature equilibration, approximately two minutes, the initial sample (time equal to zero) was taken. Points were taken by withdrawing the tube from the constant temperature bath, cooling it, smashing the end, and pouring the liquid into a beaker for the iodimetric titration.

BIBLIOGRAPHY

1. Banthorpe, D. V., E. D. Hughes, Sir Christopher Ingold and Jyotibhushan Roy. Mechanism of the benzidine and semidine rearrangements. Part VIII. Some acidity functions in aqueous dioxan. Kinetics of the rearrangement of hydrazobenzene at high acidities. Journal of the Chemical Society, 1962, p. 3294-3299.

2. Bascombe, K. N. and R. P. Bell. Acidity functions of some aqueous acids. Journal of the Chemical Society, 1959, p. 1096-1104.

3. Batts, B. D. Alkyl hydrogen sulphates. Part I. Hydrolysis in moist dioxan solution. Journal of the Chemical Society, 1966, Section B, p. 547-551.

4. _____. Alkyl hydrogen sulphates. Part II. The hydrolysis in aqueous acid solution. Journal of the Chemical Society, 1966, Section B, p. 551-555.

5. Baumann, E. Ueber die Aetherschwefelsäuren Phenole. Berichte der Deutschen Chemischen Gesellschaft 11:1907-1916. 1878.

6. Baumgarten, Paul. Über N-pyridinium-sulfonsäure. Berichte der Deutschen Chemischen Gesellschaft 59:1166-1171. 1926.

7. _____. Zur Kenntnis der Phenylthioschwefelsäure. Berichte der Deutschen Chemischen Gesellschaft 63:1330-1335. 1930.

8. Bell, R. P. and D. J. Rawlinson. Kinetics of the acid and alkaline hydrolysis of potassium ethoxycarbonylmethanesulphonate. Journal of the Chemical Society, 1958, p. 4387-4390.

9. Benkovic, Stephen. Studies on sulfate esters. II. Carboxyl group catalysis in the hydrolysis of salicyl sulfate. Journal of the American Chemical Society 83:5511-5515. 1966.

10. Bunte, Hans. Zur Constitution der unterschwefligen Säure. Berichte der Deutschen Chemischen Gesellshaft 7:646-648. 1874.

11. Bunton, C. A. and B. N. Hendy. Tracer studies in ester hydrolysis. Part XII. Dimethyl selenate. Journal of the Chemical Society, 1963, p. 3130-3137.

12. Bunton, C. A., J. B. Ley, A. J. Rhind-Tutt and C. A. Vernon. The H_O acidity function in aqueous dioxan and in methanol. Journal of the Chemical Society, 1957, p. 2327-2334.

13. Bunton, C. A. and V. J. Shiner, Jr. Isotope effects in deuterium oxide solution. I. Acid-base equilibria. Journal of the American Chemical Society 83:42-47. 1961.

14. _____. Isotope effects in deuterium oxide solution. Part II. Reaction rates in acid, alkaline and neutral solution, involving only secondary solvent effects. Journal of the American Chemical Society 83:3207-3214. 1961.

15. _____. Isotope effects in deuterium oxide solution. Part III. Reactions involving primary effects. Journal of the American Chemical Society 83:3214-3220. 1961.

16. Burkhardt, George Norman, Alwyn G. Evans and Ernest Warhurst. The hydrolysis of arylsulphuric acids. Part II. Kinetic considerations. Journal of the Chemical Society, 1936, p. 25-26.

17. Burkhardt, George Norman, W. G. Kenneth Ford and Eric Singleton. The hydrolysis of arylsulphuric acids. Part I. Journal of the Chemical Society, 1936, p. 17-25.

18. Burkhardt, George Norman, Charles Horrex and Doreen I. Jenkins. The hydrolysis of aryl sulphuric acids. Part III. Journal of the Chemical Society, 1936, p. 1649-1653.

19. Burkhardt, George Norman and Arthur Lapworth. Arylsulphuric acids. Journal of the Chemical Society, 1926, p. 684-690.

20. Burstein, Shlomo and Seymour Lieberman. Kinetics and mechanism of solvolysis of steroid hydrogen sulfates. Journal of the American Chemical Society 80:5235-5239. 1958.

21. Burwell, Robert L., Jr. The hydrolysis of optically active secondary butyl hydrogen sulfate. Journal of the American Chemical Society 74:1462-1466. 1952.

22. Candlin, J. P. and R. G. Wilkins. Sulphur-nitrogen compounds. Part I. The hydrolysis of sulphamate ion in perchloric acid. Journal of the Chemical Society, 1960, p. 4236-4241.

23. _____. Sulphur-nitrogen compounds. Part II. The hydrolysis of hydroxylaminetrisulphonate and hydroxylamine-NO-disulphonate ions in perchloric acid. Journal of the Chemical Society, 1961, p. 3625-3633.

24. _____. Sulfur-nitrogen compounds. III. The acid hydrolysis of hydroxylamine-N, N-disulfonate and hydroxylamine N- and O-monosulfonates. Journal of the American Chemical Society 87:1490-1494. 1965.

25. Fuller, Hughes and Ingold. Unpublished results; Fuller, thesis, London, 1961. (Cited in: Bunton, C. A. and B. N. Hendy. Tracer studies in ester hydrolysis. Part XII. Dimethyl selenate. Journal of the Chemical Society, 1963, p. 3130-3137. Reference 11)

26. Gringras, L. and G. Sjöstedt. Potentiometric determination of arylsulfinic acids. Acta Chemica Scandinavia 15:433-434. 1961.

27. Hammond, George S. A correlation of reaction rates. Journal of the American Chemical Society 77:334-338. 1955.

28. Ingold, C. K. Structure and mechanism in organic chemistry. Ithaca, New York, Cornell University Press, 1953. 828 p.

29. Kaiser, E. T., Manuel Panar and F. H. Westheimer. The hydrolysis of some cyclic esters of sulfuric acid. Journal of the American Chemical Society 85:602-607. 1963.

30. Kaluszyner, A., P. Czerniak and Ernst D. Bergmann. Thiozolidines and aminoalkylthiosulfuric acids as protecting agents against ionizing radiation. Radiation Research 14:23-28. 1961.

31. Kice, John L. A kinetic study of the acid hydrolysis of a Bunte salt. Journal of Organic Chemistry 28:957-961. 1963.

32. Lecher, Hans Z. and Elizabeth M. Hardy. Some new methods for preparing Bunte salts. Journal of Organic Chemistry 20: 475-487. 1955.

33. Long, F. A. and M. A. Paul. Application of the H_o acidity function to kinetics and mechanisms of acid catalysis. Chemical Reviews 57:935-1010. 1957.

34. Milligan, Brian and J. M. Swan. Bunte salts ($RSSO_3Na$). Reviews of Pure and Applied Chemistry 12:72-94. 1962.

35. Paul, M. A. and F. A. Long. H_o and related indicator acidity functions. Chemical Reviews 57:1-45. 1957.

36. Pawlowski, Norman Edward. The mechanisms of the scission of some sulfur-sulfur bonds. III. The acid hydrolysis of Bunte salts. Ph. D. thesis. Corvallis, Oregon State University, 1965. 134 numb. leaves.

37. Price, Charles C. and Gardner W. Stacy. p-Nitrophenyl disulfide, p-nitrophenyl sulfide and p-nitrothiophenol. Journal of the American Chemical Society 68:498-500. 1946.

38. Pritchard, J. G. and F. A. Long. Hydrolysis of ethylene oxide derivatives in deuterium oxide-water mixtures. Journal of the American Chemical Society 78:6008-6013. 1956.

39. _____. The kinetics of the hydrolysis of trimethylene oxide in water, deuterium oxide, and 40% aqueous dioxane. Journal of the American Chemical Society 80:4162-4165. 1958.

40. Pryor, William A. The kinetics of the disproportionation of sodium thiosulfate to sodium sulfide and sulfate. Journal of the American Chemical Society 82:4794-4797. 1960.

41. Rosenthal, Norman A. and L. Citarel. Radioprotective properties of aminoalkyl Bunte salts. In: Abstracts of Papers, 141st Meeting, American Chemical Society, Washington, D. C., March, 1962. p. 29N.

42. Schaleger, L. L. and F. A. Long. Entropies of activation and mechanisms of reactions in solution. In: Advances in physical organic chemistry, by V. Gold. ed. Volume 1. New York, Academic Press, 1963. p. 1-33.

43. Wiberg, Kenneth B. Laboratory techniques in organic chemistry. New York, McGraw-Hill, 1960. 262 p.

44. _____. Physical organic chemistry. New York, John Wiley and Sons, 1964. 591 p.

APPENDICES

APPENDIX 1

Table 12. Kinetics of the acid-catalyzed hydrolysis aryl sulfate
ions in aqueous solution (18).

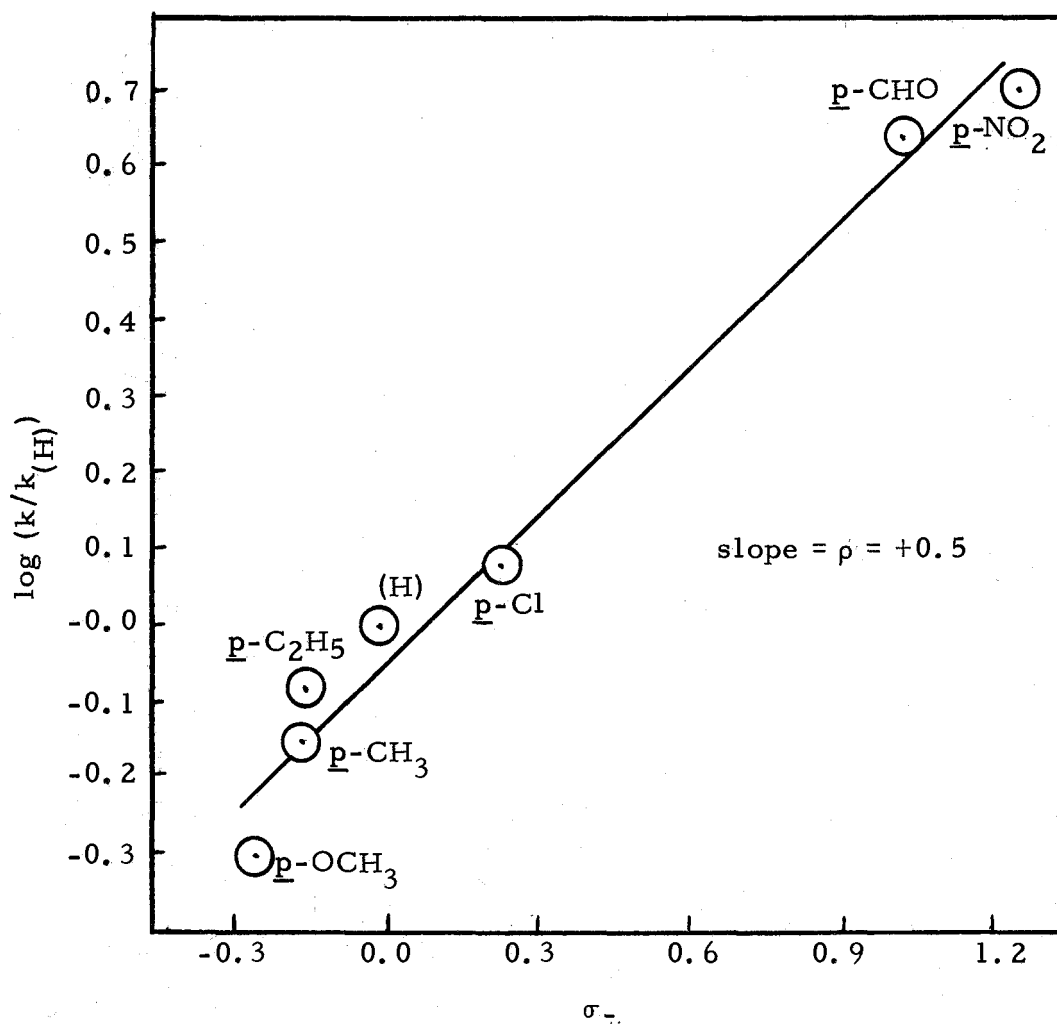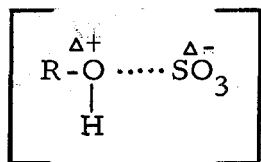| Substituent	$k \times 10^{+4}$ $M^{-1}sec.^{-1}$ at 48.7° C	$k \times 10^{+2}$ $M^{-1}sec.^{-1}$ at 78.7° C
$p\text{-}NO_2$	4.50	1.20
$p\text{-}CHO$	3.87	1.01
$p\text{-}OCOCH_3$	3.32	0.77
$m\text{-}NO_2$	2.05	0.578
$m\text{-}CHO$	1.52	0.453
$m\text{-}OCOCH_3$	1.40	0.418
$p\text{-}Cl$	1.08	0.362
$m\text{-}OCH_3$	1.02	0.340
(H)	0.89	0.335
$m\text{-}CH_3$	0.88	0.320
$p\text{-}C_2H_5$	0.74	0.251
$p\text{-}CH_3$	0.687	0.238
$p\text{-}OCH_3$	0.450	0.180

Figure 6. Logarithm of $[k/k_{(H)}]$ versus σ_- (44, p. 410)
for the hydrolysis of para-substituted aryl
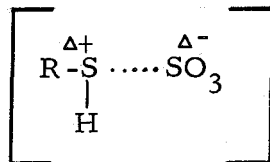sulfates at 48.7°C (18).

APPENDIX 2

CALCULATED SOLVENT ISOTOPE EFFECT
FOR THE BUNTE SALT HYDROLYSIS

The usual rules (13, 14, 15, 38, 39) which apply solvent isotope effects to A-1 and A-2 mechanisms are derived for substrates which are protonated on oxygen. However, the A-1a mechanism (Eq. 24) for the Bunte salt hydrolysis involves protonation on sulfur and could show a smaller isotope effect because of the considerably lower vibrational stretching frequency associated with a sulfur-hydrogen bond as compared to an analogous oxygen-hydrogen bond.

The solvent isotope effect for the acid-catalyzed hydrolysis of sodium phenyl sulfate has been determined, $k_{D_2O}/k_{H_2O} = 2.4$, at 60°C (Table 3, Part I). The hydrolysis of aryl sulfates (Part I) and Bunte salts (Part II) proceed through similar A-1 mechanisms, equations 11 and 24, respectively, and it also has been shown that the transition states for the two reactions (XIV and XV) are quite similar in structure.

$$\left[\begin{array}{c} \overset{\Delta+}{R-O} \cdots \overset{\Delta-}{SO_3} \\ | \\ H \end{array} \right] \qquad \left[\begin{array}{c} \overset{\Delta+}{R-S} \cdots \overset{\Delta-}{SO_3} \\ | \\ H \end{array} \right]$$

XIV   XV

As a good approximation, therefore, it is reasonable to assume

that the considerably lower sulfur-hydrogen stretching frequency

in XV will be the only significant factor responsible for a difference

in k_{D_2O}/k_{H_2O} for the two reactions and to use appropriate stretching

frequencies to calculate k_{D_2O}/k_{H_2O} for the Bunte salt hydrolysis,

using the general principles and equations outlined by Bunton and

Shiner (13, 14). The estimated solvent isotope effect for the Bunte

salt hydrolysis would thus be given by equation 30.

$$\left[\frac{k_{H_2O}}{k_{D_2O}}\right]_{\substack{Bunte \\ salt}} = \left[\frac{k_{H_2O}}{k_{D_2O}}\right]_{\substack{Aryl \\ sulfate}} \times antilog\left[\frac{\nu_{OH}^{XIV} - \nu_{SH}^{XV}}{12.53 \times T}\right] \quad (Eq.\ 30)$$

As a reasonable estimate for $\nu_{OH}^{XIV} - \nu_{SH}^{XV}$, we have taken the

difference between ν_{OH} for phenol in water, calculated from the

equation of Bunton and Shiner (13) as 3225 cm.$^{-1}$, and ν_{SH} for an

aliphatic mercaptan, 2575 cm^{-1}. 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 atom of XV or the oxygen

atom of XIV. Therefore, the use of the mercaptan and the phenol

as models for the state of the sulfur-hydrogen bond in XV and the

oxygen-hydrogen bond in XIV is probably satisfactorily, although

certainly not ideal.

Equation 30 gives a predicted solvent isotope effect for the

Bunte salt hydrolysis, proceeding through the A-1a mechanism,

at 60° C of 0. 60. At 95° C, the predicted solvent isotope effect,

k_{H_2O}/k_{D_2O}, would be 0. 63, or k_{D_2O}/k_{H_2O} = 1. 6.

From this analysis we can see that an A-1 mechanism involv-

ing protonation on sulfur 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.