

# AN ABSTRACT OF THE THESIS OF

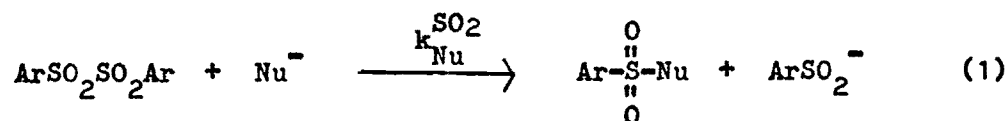
George James Kasperek for the Ph. D.  
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 in Chemistry presented on July 29, 1969  
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Title: The Mechanism of Some Reactions of Aryl  $\alpha$ -Disulfones

Abstract approved *Redacted for Privacy*

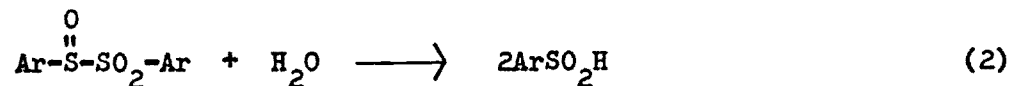
*Dr. John L. Kice*

The relative reactivity of 12 common nucleophiles, including water, in a displacement reaction at sulfonyl sulfur (equation 1) in 60% aqueous dioxane (v/v) has been determined kinetically.



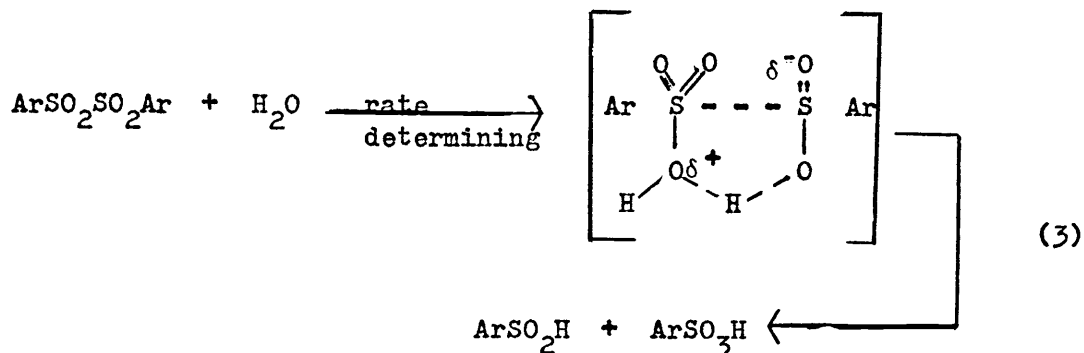
These data were obtained either from studies of the spontaneous and nucleophile-catalyzed hydrolyses of aryl  $\alpha$ -disulfones, or, in the case of primary and secondary amines and azide, from direct measurement of the rate of reaction of nucleophile and  $\alpha$ -disulfone.

The spontaneous (uncatalyzed) hydrolysis of the aryl  $\alpha$ -disulfones (equation 1,  $\text{Nu} = \text{H}_2\text{O}$ ) was the most thoroughly studied. This reaction differs from the previously investigated spontaneous hydrolysis of aryl sulfinyl sulfones (equation 2) only in that equation 1 involves



nucleophilic substitution at sulfonyl ( $>\text{SO}_2$ ) while equation 2 involves substitution at sulfinyl ( $>\text{SO}$ ) sulfur. Comparing the data of these two reactions provides a quantitative measure of the

influence of various important reaction variables on nucleophilic substitutions at sulfonyl versus sulfinyl sulfur. This comparison reveals that, although substitution at sulfinyl sulfur is  $10^4$  times faster than at sulfonyl sulfur, the two reactions are quite similar in (1) dependence of rate on aryl group structure, (2) increase in rate with water content of the solvent, (3) solvent isotope effect, and (4)  $\Delta S^\ddagger$ . The difference in rate arises solely as a result of the 6.0 kcal/mole difference in activation energy. The conclusion is that nucleophilic substitutions at sulfonyl and sulfinyl sulfur do not differ much in their detailed mechanisms, and that nucleophilic substitution is faster at sulfinyl sulfur only because of a more favorable activation energy. The large solvent isotope effect ( $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} = 2.3$ ) for the  $\alpha$ -disulfone hydrolysis indicates that a proton transfer is part of the rate-determining step of that reaction. A mechanism (equation 3) consistent with this fact and the dependence



of the rate on the other reaction variables is presented. Also comparison of the spontaneous hydrolysis of  $\alpha$ -disulfones with that of other sulfonyl derivatives shows that in reactions involving attack at sulfonyl sulfur a change in the character of the leaving group is apparently much more likely to lead to a significant change in

mechanism than changing the site where substitution occurs from sulfonyl to sulfinyl sulfur.

The data obtained for various nucleophiles in equation 1 revealed that the order of nucleophilic reactivity toward sulfonyl sulfur is  $\text{OH}^- \gg \text{n-BuNH}_2 > \text{Et}_3\text{N} > \text{N}_3^- > \text{F}^- > \text{t-BuNH}_2 > \text{NO}_2^- > \text{AcO}^- > \text{Cl}^- > \text{Br}^- \gg \text{H}_2\text{O}$ . This order is almost the exact reverse of the order found for nucleophilic substitution at sulfinyl sulfur. Interpretation of these results in terms of the theory of hard and soft acids and bases (HSAB) indicates that sulfonyl sulfur is a much harder electrophilic center than sulfinyl sulfur, just as HSAB would have predicted it should be. Comparison of the data for sulfonyl sulfur with analogous data on nucleophilic reactivity for a substitution at another hard electrophilic center, carbonyl carbon, reveals that both substitutions exhibit essentially the same order of nucleophilic reactivity. Thus sulfonyl sulfur is at least as hard an electrophilic center as carbonyl carbon.

The solvolysis of aryl  $\alpha$ -disulfones was also carried out in a very strongly acidic medium - - acetic acid - water containing varying amounts of sulfuric acid. The rate of solvolysis was found to increase with increasing concentration of acid, and the solvent isotope effect for the acid-catalyzed reaction was ( $k_{\text{H}}/k_{\text{D}} = 1.45$ ). A mechanism consistent with these results is presented and its implications regarding the correct mechanism of the acid-catalyzed solvolysis of aryl sulfinyl sulfones in this same medium are discussed.

The Mechanism of Some Reactions  
of Aryl  $\alpha$ -Disulfones

by

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A THESIS

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APPROVED:

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Date thesis is presented July 29, 1969

Typed by Judith Kasperek for George Kasperek

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To Judith

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# THE MECHANISM OF SOME REACTIONS OF ARYL $\alpha$ -DISULFONES

## INTRODUCTION

One of the most fascinating areas of research in both organic and biochemistry is the nature of the sulfur-sulfur bond (37). A large variety of compounds containing the sulfur-sulfur bond are possible because the sulfur atom contains unshared electron pairs which can be utilized in the formation of covalent bonds with oxygen.

Compounds of the type  $\begin{array}{c} \text{O} \quad \text{O} \\ \parallel \quad \parallel \\ \text{R}-\text{S}-\text{S}-\text{R} \\ \parallel \quad \parallel \\ \text{O} \quad \text{O} \end{array}$  are referred to in the literature

as S,S,S',S' tetroxides, sulfonyl sulfones,  $\alpha$ -disulfones, or simply disulfones. The latter names are used by most authors and also by Chemical Abstracts. This thesis will refer to these compounds as  $\alpha$ -disulfones.

Several methods for the preparation of  $\alpha$ -disulfones have been described. Historically  $\alpha$ -disulfones were first prepared by Kohler and MacDonald (43) in 1899. Their method consisted of reacting the sodium salt of a sulfinic acid with a sulfonyl chloride, equation 1.

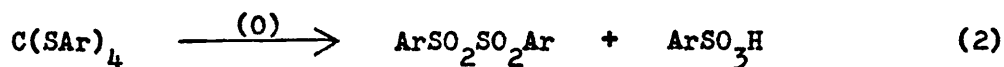


This method was quite general in application, and was used to make not only a symmetrical  $\alpha$ -disulfone, p-tolyl  $\alpha$ -disulfone, but also an unsymmetrical  $\alpha$ -disulfone, phenyl p-tolyl  $\alpha$ -disulfone. Hinsberg (30) carried out similiar experiments and confirmed this work.

A few years later, Smiles and Hilditch (29,53) found that  $\alpha$ -disulfones could be prepared by oxidizing either alkyl or aryl sulfinic acids with potassium permanganate.

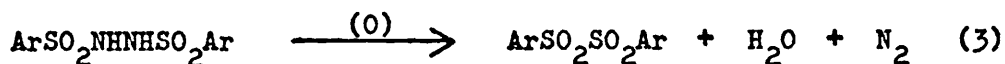
In 1938 Karrer and coworkers (36) found that in addition to the thiol-sulfonate, a small amount of  $\alpha$ -disulfone was formed by the action of copper powder on p-toluenesulfonyl chloride in anhydrous pyridine. Subsequently Pearl, Evans, and Dehn (46) discovered that a better yield of  $\alpha$ -disulfone could be obtained if potassium were used instead of copper.

Backer (4) was able to obtain some  $\alpha$ -disulfone by the oxidation of tetrathioorthocarbonates in anhydrous chloroform with perbenzoic acid, equation 2.



Barnard (6) found the action of ozone on disulfides produced small amounts of  $\alpha$ -disulfone. Other oxidizing agents can also be utilized to prepare  $\alpha$ -disulfone from their corresponding disulfides, thiosulfinates, and thiosulfonates (1, 25).

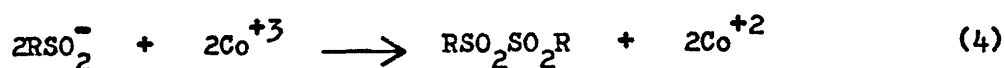
All of the methods described thus far give very poor yields of the  $\alpha$ -disulfone (4 - 16%). In 1966 Flemming and Fahr (23) were able to prepare aromatic  $\alpha$ -disulfones in much better yield (13 - 50%). Their method consisted of oxidizing the appropriate diarylsulfonylhydrazine with mercuric oxide or N-bromosuccinimide, equation 3.





The chief drawback of this reaction was that it was difficult to scale up, and like the others, product purification was difficult.

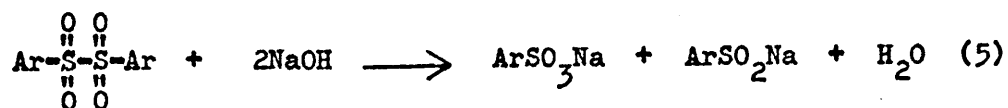
Allen and coworkers (17), also in 1966, found many  $\alpha$ -disulfones could be prepared quite expeditiously by the oxidation of either the aryl or alkyl sulfinic acids or their salts with an acidic solution of cobaltic sulfate, equation 4. The cobaltic oxidation procedure



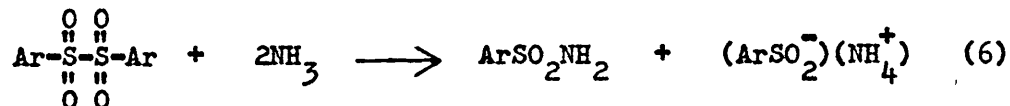
produces an  $\alpha$ -disulfone not only in relatively high yield (35 - 56%), but also in an easily purifiable form, since the other major product is the water soluble sulfonic acid.

Aromatic  $\alpha$ -disulfones are crystalline solids which melt with decomposition at high temperatures. They are quite insoluble, but they do dissolve in aromatic solvents, alcohols, and ethers to the extent of about  $10^{-3}$  M. The substituted phenyl  $\alpha$ -disulfones all have fairly strong absorbances in the ultraviolet region with a  $\lambda_{\text{max}}$  in the range of 244 - 286 m $\mu$  ( $\log \epsilon \approx 4$ ). The  $\alpha$ -disulfones have strong bands at 7.5  $\mu$  and 8.8  $\mu$  in the infrared. These are ascribed to the asymmetric and symmetric O=S=O stretch respectively (8).

Even though  $\alpha$ -disulfones have been known for over 70 years, their chemistry has received practically no attention. The alkaline hydrolysis of  $\alpha$ -disulfones to yield the corresponding sulfinic and sulfonic acids has been reported, equation 5 (43, 52). Recently the



kinetics of this reaction have been measured (2). Similarly the reaction of  $\alpha$ -disulfones with ammonia, equation 6 (53) or piperidine

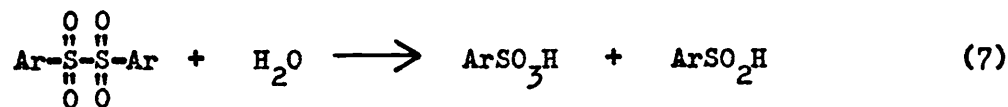


(4) gave sulfonamides and sulfinate salts. Recently the thermal decomposition of several  $\alpha$ -disulfones has been carried out in diglyme and bromobenzene (21).

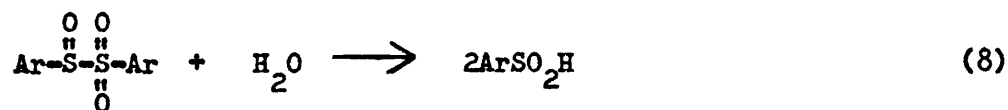
One of the most important questions yet unanswered in organic sulfur chemistry is the differences in the characteristics of nucleophilic substitution reactions occurring at different oxidation states of sulfur. One pair of oxidation states that is of great interest to compare is that of sulfinyl sulfur ( $>\text{S}=\text{O}$ ) and sulfonyl sulfur ( $>\text{SO}_2$ ). The only difference in the sulfur atoms is that while sulfinyl sulfur has a lone pair of electrons, sulfonyl sulfur utilizes these electrons to form a bond with another oxygen atom.

In order to make such a comparison truly meaningful, one must take care to compare two reactions which are identical in all respects except for the oxidation state of the sulfur being attacked. That is, the group being displaced, the attacking nucleophile, solvent medium, etc., must be the same in both cases. Probably the main reason such a study has not been made in the past is that most sulfinyl compounds undergo substitution so much faster than their sulfonyl counterparts that it is difficult to find a pair of reactions where the rate for both sulfinyl and sulfonyl compounds can be accurately measured under the same conditions.

It is now possible to make the first quantitative comparison of substitution at sulfinyl and sulfonyl sulfur by obtaining data on the spontaneous hydrolysis of aryl  $\alpha$ -disulfones (equation 7) in



aqueous dioxane and comparing them to the extensive results already available (39) on the spontaneous hydrolysis of aryl sulfinyl sulfones (equation 8) in the same medium. It is clear that the two



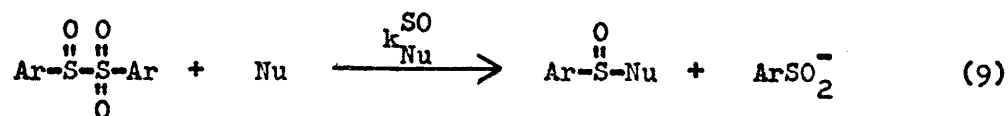
reactions meet the requirements in that the leaving group ( $\text{ArSO}_2$ ), the solvent medium, and the substituting nucleophile ( $\text{H}_2\text{O}$ ) are exactly the same for both reactions and differ only in that equation 7 involves substitution at sulfonyl sulfur while equation 8 involves substitution at sulfinyl sulfur.

In their extensive study of the mechanism of the hydrolysis of aryl sulfinyl sulfones (equation 8), Kice and Guaraldi (39) found the solvent isotope effect ( $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} = 2.7$ ) to be quite large, the rate of reaction to increase as the amount of water in the solvent increased, the activation parameters to be  $E_a = 8.8$  kcal/mole and  $\Delta S^\ddagger = -37.1$  e.u., and that the rate was accelerated by electron withdrawing groups in the aromatic rings and slowed by electron releasing groups. It will be interesting and certainly of great value to obtain similar data for the hydrolysis of aryl  $\alpha$ -disulfones so that a detailed comparison between reactions at sulfinyl and sulfonyl can be made.

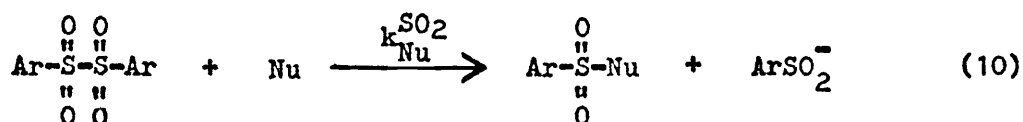
It is also interesting to compare the relative nucleophilicity of various nucleophiles at sulfinyl versus sulfonyl sulfur, since the relative reactivity of a group of nucleophiles in a substitution reaction can change quite markedly with a change in the nature of the electrophilic center at which substitution occurs (18).

In general "hard bases" (20), nucleophiles which are of low polarizability and high electronegativity, have an advantage over other nucleophiles in substitution at centers such as carbonyl carbon (31) or tetracoordinate phosphorus (18). Nucleophiles which are of high polarizability and low electronegativity, the "soft bases" (20), react best in substitutions involving centers such as  $\text{Pt}^{\text{II}}$  (48) or peroxide oxygen (19). Pearson and Songstad (49) made a thorough analysis of these effects and have shown that the data can be nicely rationalized using the theory of hard and soft acids and bases (HSAB).

In a study by Kice and Guarnaldi (38), the relative reactivity of a series of common nucleophiles towards sulfinyl sulfur was determined by obtaining the rates of a series of nucleophilic substitutions involving aryl sulfinyl sulfones (equation 9). Similar

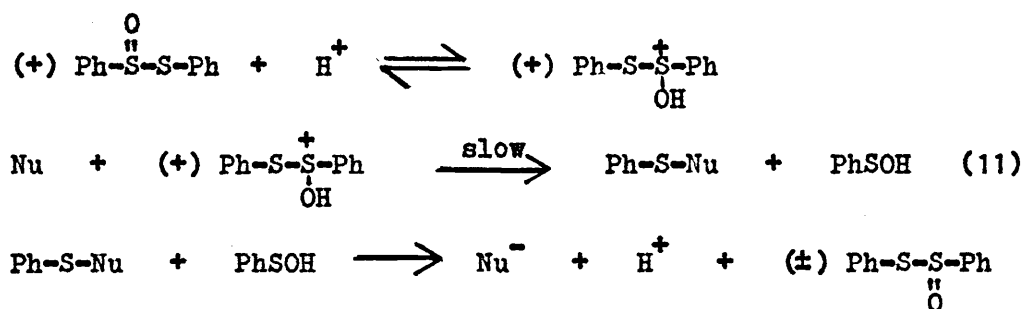


data for nucleophilic substitution at sulfonyl sulfur can be obtained from measurement of the rates of analogous substitution of aryl  $\alpha$ -disulfones (equation 10). Notice once more that equations 9 and 10



involve the same leaving group ( $\text{ArSO}_2$ ) and have been studied in the same solvent (60% aqueous dioxane (v/v)). Thus a comparison of the results for the two systems allows one to evaluate in an unequivocal manner what effect a change in substitution site from sulfinyl to sulfonyl sulfur has on the relative reactivity of various nucleophiles.

The rates of the acid and nucleophile catalyzed racemization of aryl thiosulfonates, equation 11, have been determined by Kice and



and Large (42). Since equations 10 and 11 differ in that substitution occurs at sulfonyl (equation 10) versus sulfenyl sulfur (equation 11), a comparison of the reactivity of sulfenyl versus sulfonyl sulfur can be made. This comparison is not as unequivocal as that between sulfinyl and sulfonyl sulfur because, even though all reactions concerned were run in 60% aqueous dioxane, the reactions involving sulfenyl sulfur have a different leaving group. However a comparison of the rates of the reactions shown in equations 10 and 11 with various nucleophiles will at least give an estimate of the relative reactivities of different nucleophiles toward sulfenyl versus sulfonyl sulfur.

HSAB theory (18) would predict that sulfonyl sulfur should be a significantly harder electrophilic center than either sulfinyl or sulfenyl sulfur. This means that the basicity and electronegativity,

rather than the polarizability, of a series of nucleophiles should be the more important factor in determining their order of relative reactivity toward sulfonyl sulfur, in contrast to the situation with sulfinyl (39) and sulfenyl sulfur (42) where polarizability, electronegativity, and basicity are all important. Measuring the relative reactivity of a series of nucleophiles towards aryl  $\alpha$ -disulfones (equation 10) can be used to test this theory (1) by suitable comparison of the results for sulfenyl, sulfinyl, and sulfonyl sulfur from equations 9, 11, and 10; and (2) by comparing the behavior of sulfonyl sulfur with that of other centers like carbonyl carbon, where basicity and electronegativity are thought to be the main factors determining relative reactivity of a series of nucleophiles in substitution at that center.

It is also of interest and importance to the understanding of the mechanisms involved in organic sulfur chemistry to determine the effect of leaving groups on substitution reactions. Other nucleophilic substitution reactions at sulfonyl sulfur have been studied, and they are of interest in connection with the studies of aryl  $\alpha$ -disulfones to be discussed in this thesis. Christensen has studied the hydrolysis of some aryl sulfonic anhydrides in aqueous dioxane (11, 12), and the hydrolyses of aryl sulfonyl chlorides have also been studied (24, 50, 56). Since these compounds differ from aryl  $\alpha$ -disulfones only in containing a different leaving group, the study allows the effect of different leaving groups to be determined. This comparison reveals that changes in the character of the leaving group can lead to quite

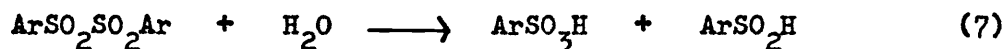
significant alterations in certain important details of the mechanism of these substitutions at sulfonyl sulfur.

Until the present study, no one had systematically studied the mechanisms of reactions of aryl  $\alpha$ -disulfones. About all that was known of the reactions of  $\alpha$ -disulfones were their products. The purpose of this thesis is to provide data on reactions of aryl  $\alpha$ -disulfones that can be compared to the data already available on reactions at other centers, specifically different oxidation states of sulfur. A further purpose is to investigate the effect of different leaving groups on the reactivity and mechanism of nucleophilic substitutions at sulfonyl sulfur. The importance of obtaining this information to organic sulfur chemistry in general and to sulfone chemistry in particular, prompted us to investigate in detail the mechanism of some reactions of aryl  $\alpha$ -disulfones.

## RESULTS

Spontaneous Hydrolysis of Aryl  $\alpha$ -Disulfones

The first reaction of the  $\alpha$ -disulfones studied was their spontaneous hydrolysis, equation 7. This hydrolysis involves the



nucleophilic substitution of water on one of the sulfonyl sulfur atoms, and the cleavage of a sulfur-sulfur bond.

The  $\alpha$ -disulfones used in this study were prepared by the oxidation of the sodium salt of the corresponding sulfinic acid with an acidic solution of cobaltic sulfate as described by Denzer, et al. (17).

The solvent of choice was 60% aqueous dioxane (v/v). The primary reason for this was to allow comparison of the data for the  $\alpha$ -disulfones with the data for the spontaneous hydrolysis of the aryl sulfinyl sulfones obtained by Kice and Guaraldi (40) in this same solvent medium.

Stoichiometry

Aryl  $\alpha$ -disulfones have been reported (52) to undergo a slow spontaneous hydrolysis into a molecule each of sulfonic and sulfinic acid. Thus the stoichiometry shown in equation 7 is correct.

Kinetics of the Hydrolysis

Since the solubility of  $\alpha$ -disulfones is low, it was necessary



to select a method of following the kinetics of their hydrolysis which would not require the use of large amounts of material. Because  $\alpha$ -disulfones have a strong absorption maximum in the region 244 - 286  $m\mu$  ( $\log \epsilon \approx 4$ ), and the sulfonic and sulfinic acids produced in this hydrolysis do not, the use of ultraviolet spectroscopy suggested itself as a means of following the progress of this reaction. It was found that the kinetics of this reaction could be followed satisfactorily by this method.

The kinetic data were obtained by plotting the logarithm of  $(A - A_{\infty})$  or the logarithm of  $(A - A_{\infty}/A_0 - A_{\infty})$  versus time. Figures 1 and 2 show typical first order plots of several  $\alpha$ -disulfones in 60% aqueous dioxane (v/v). From these one can see that clean first order kinetics are obtained for the hydrolysis in all cases.

The spontaneous hydrolysis of all the aryl  $\alpha$ -disulfones studied was carried out under a nitrogen atmosphere in a specially designed apparatus (see Experimental section) which permitted easy removal of aliquots for ultraviolet measurement.

Dependence of the Rate on Acidity. Table 1 lists the first order rate constants ( $k_h$ ) for the hydrolysis of diphenyl  $\alpha$ -disulfone in 60% aqueous dioxane (v/v) containing varying concentrations of added perchloric acid. From this table it is evident that varying the concentration of added perchloric acid from 0.001 M to 2.0 M leads to no significant variation in the rate of hydrolysis of diphenyl  $\alpha$ -disulfone. Thus the hydrolysis of  $\alpha$ -disulfones is not subject to detectable acid catalysis.

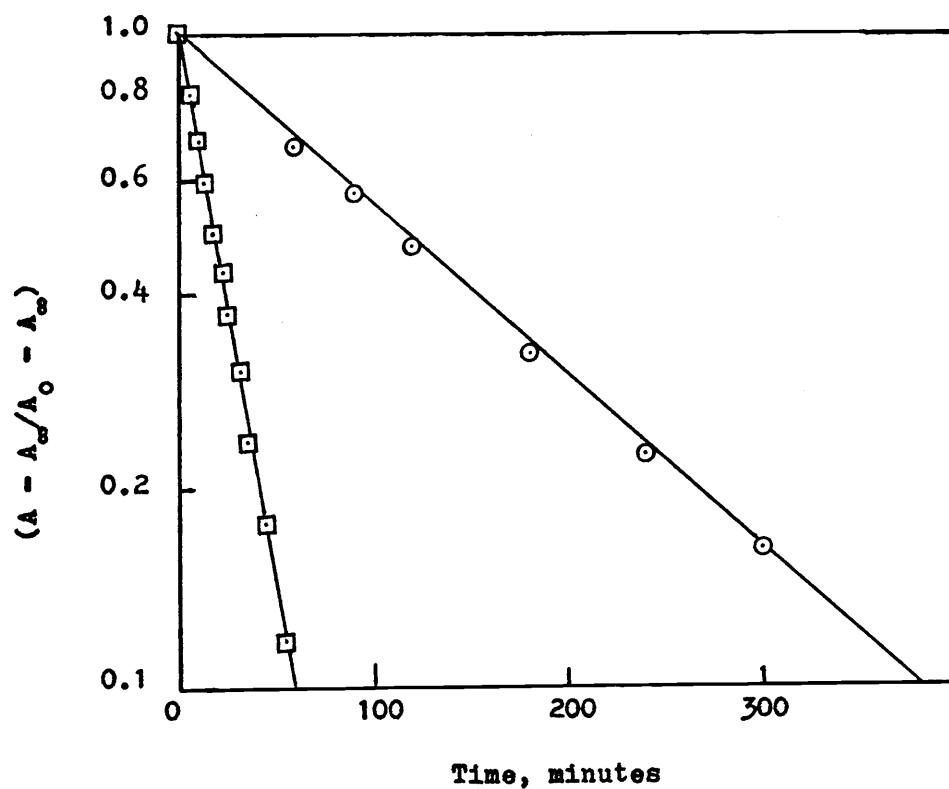


Figure 1. Rate of spontaneous hydrolysis of  $\text{ArSO}_2\text{SO}_2\text{Ar}$  at  $80.3^\circ \text{C}$ ., in 60% aqueous dioxane (v/v) containing  $0.01 \text{ M HClO}_4$ .

○,  $\text{Ar} = \text{C}_6\text{H}_5$

□,  $\text{Ar} = \text{p-BrC}_6\text{H}_4$

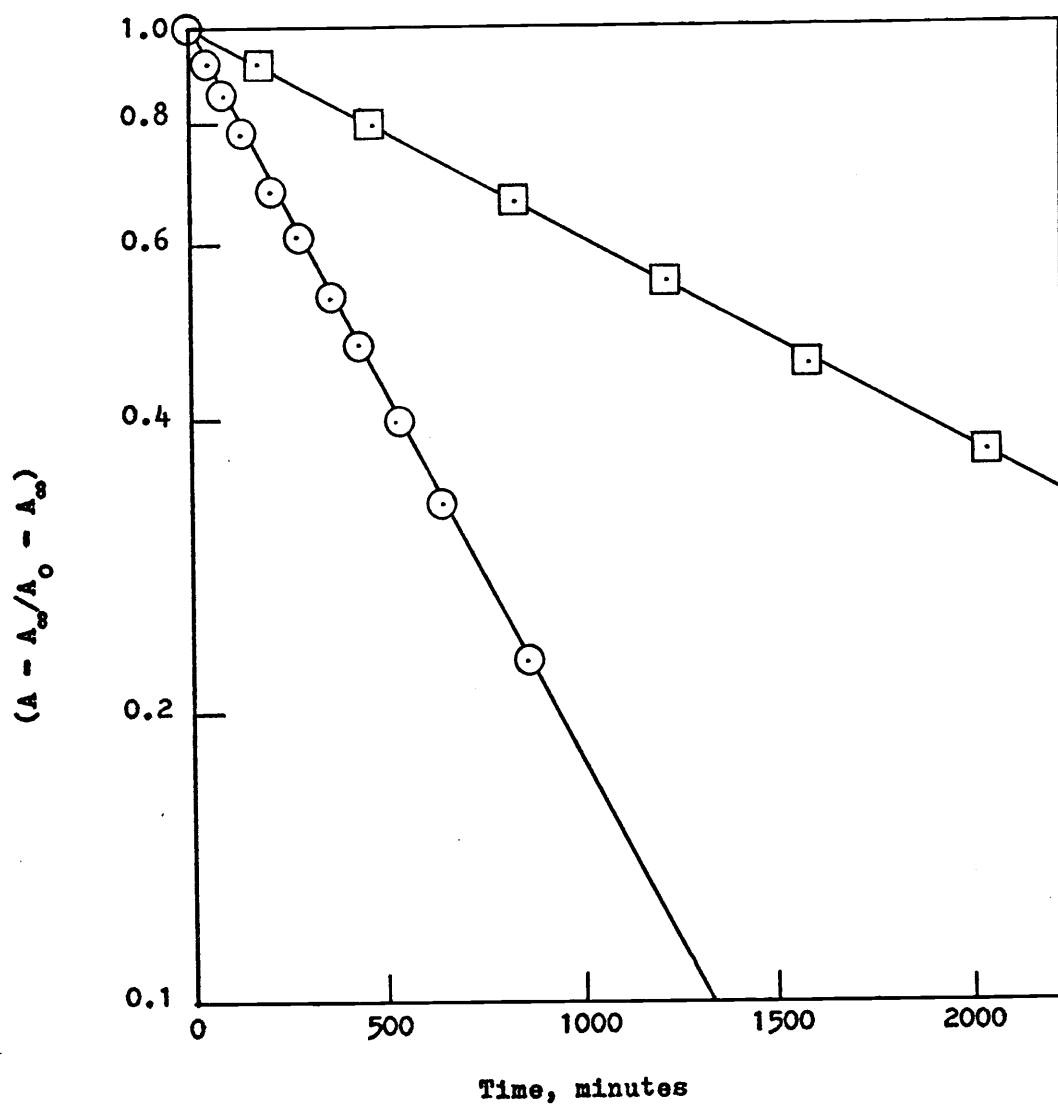


Figure 2. Rate of spontaneous hydrolysis of  $\text{ArSO}_2\text{SO}_2\text{Ar}$  at  $80.3^\circ \text{C}$ . in 60% aqueous dioxane(v/v) containing  $0.01 \text{ M HClO}_4$

○, Ar =  $\text{p-CH}_3\text{C}_6\text{H}_4$

□, Ar =  $\text{p-CH}_3\text{OC}_6\text{H}_4$

Table 1. Dependence of the rate of hydrolysis of diphenyl  $\alpha$ -disulfone on acidity.<sup>a</sup>

$[\text{HClO}_4], \text{ M}$	$k_h \times 10^4, \text{ sec}^{-1}$
0.001	1.05
0.01	1.00
0.10	0.89
1.00	1.09
2.00	0.93

<sup>a</sup>All runs in 60% aqueous dioxane (v/v) at 80.3° C. with the initial concentration of diphenyl  $\alpha$ -disulfone  $5 \times 10^{-5} \text{ M}$ .

Dependence of the Rate on Ionic Strength. The dependence of the rate of the spontaneous hydrolysis of diphenyl  $\alpha$ -disulfone on ionic strength was determined by adding varying amounts of lithium perchlorate to the reaction mixture. Examination of Table 2 shows that the rate of spontaneous hydrolysis of diphenyl  $\alpha$ -disulfone is not affected greatly by the concentration of lithium perchlorate. Thus the rate of hydrolysis of diphenyl  $\alpha$ -disulfone is not subject to any large salt effect.

Activation Parameters. The effect of temperature on the spontaneous hydrolysis of diphenyl  $\alpha$ -disulfone was determined by running the reaction at six different temperatures over a 50° range (Table 3). A plot of  $\log k_h$  versus  $1/T$  (Figure 3) is linear and an activation energy,  $E_a$ , of 14.6 kcal/mole was determined from the slope.

Table 2. Dependence of the rate of hydrolysis of diphenyl  $\alpha$ -disulfone on ionic strength.<sup>a</sup>

$[\text{HClO}_4], \text{ M}$	$[\text{LiClO}_4], \text{ M}$	$k_h \times 10^4, \text{ sec}^{-1}$
0.001	0.00	1.05
0.001	0.01	1.10
0.001	0.10	1.21
0.01	0.40	1.13

<sup>a</sup>All runs in 60% aqueous dioxane (v/v) at 80.3° C. with the initial concentration of diphenyl  $\alpha$ -disulfone  $5 \times 10^{-5} \text{ M}$ .

Table 3. Dependence of the rate of hydrolysis of diphenyl  $\alpha$ -disulfone on temperature.<sup>a</sup>

$T, ^\circ\text{C.}$	$k_h \times 10^4, \text{ sec}^{-1}$
94.3	1.92
88.9	1.48
80.3	1.00
70.5	0.55
58.8	0.26
49.2	0.12

<sup>a</sup>All runs in 60% aqueous dioxane (v/v) containing 0.01 M  $\text{HClO}_4$  with the initial concentration of diphenyl  $\alpha$ -disulfone  $5 \times 10^{-5} \text{ M}$ .

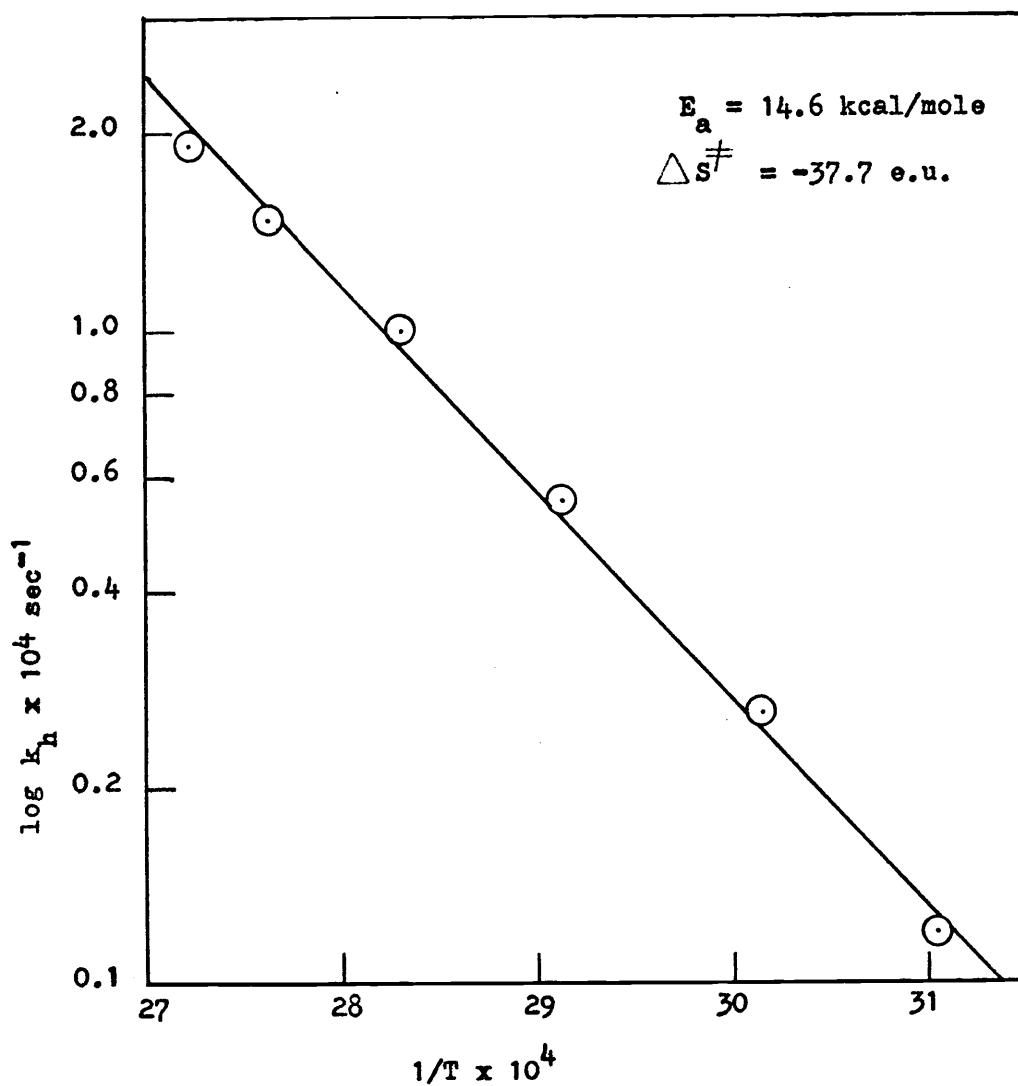


Figure 3. Plot of  $\log k_h$  versus  $1/T$  for the hydrolysis of phenyl  $\alpha$ -disulfone in acidic 60% aqueous dioxane (v/v).

The entropy of activation was also calculated,  $\Delta S^\ddagger = -37.7$  e.u. Entropies of activation this large and negative are frequently encountered for spontaneous hydrolysis in dioxane-water (39) and indicate a highly ordered transition state.

Deuterium Solvent Isotope Effect. The rate of hydrolysis of diphenyl  $\alpha$ -disulfone in 60% dioxane - 40%  $D_2O$  containing 0.001 M  $HClO_4$  at  $80.3^\circ$  C. was found to be  $0.466 \times 10^{-4} \text{ sec}^{-1}$ . Comparing this to the rate in 60% dioxane - 40%  $H_2O$  under identical conditions ( $1.05 \times 10^{-4} \text{ sec}^{-1}$ ), an isotope effect ( $k_{H_2O}/k_{D_2O}$ ) of 2.3 is obtained. This is a rather large solvent isotope effect indicating that the rate of hydrolysis of diphenyl  $\alpha$ -disulfone is considerably faster in 60% dioxane - 40%  $H_2O$  than in the corresponding  $D_2O$  system.

Dependence of the Rate on Solvent Composition. The rate of hydrolysis of diphenyl  $\alpha$ -disulfone increases markedly with an increase in the water content of the solvent medium (Table 4) being just over 10 times faster in 40% dioxane than in 70% dioxane.

Table 4. Dependence of the rate of hydrolysis of diphenyl  $\alpha$ -disulfone on solvent composition.<sup>a</sup>

Solvent Composition	$k_h \times 10^4, \text{ sec}^{-1}$
70% dioxane (v/v)	0.44
60%	1.00
50%	2.60
40%	4.87

<sup>a</sup>All runs at  $80.3^\circ$  C. with 0.01 M  $HClO_4$  and initial concentration of diphenyl  $\alpha$ -disulfone  $5 \times 10^{-5}$  M.

Dependence of the Rate on Aryl Group Structure. The rate of spontaneous hydrolysis of aryl  $\alpha$ -disulfones shows a strong dependence on aryl group structure. Table 5 shows that electron releasing substituents such as p-MeO or p-Me retard the rate markedly while electron attracting ones like p-Cl and p-Br accelerate it. A plot of  $\log k_h$  versus  $\sigma$  (Figure 4) for the p-substituent in the aromatic ring gives a  $\rho$  for the spontaneous hydrolysis of aryl  $\alpha$ -disulfones of +3.5. This seem quite large. However, one should remember than in going from one  $\alpha$ -disulfone to another, the substituent in both rings is changed. Thus this  $\rho$  value is not as large as it appears at a cursory glance.

Table 5. Dependence of the rate of hydrolysis of aryl  $\alpha$ -disulfones on aryl group structure.<sup>a</sup>

Ar	$k_h \times 10^4, \text{sec}^{-1}$
<u>p</u> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	0.084
<u>p</u> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	0.29
C <sub>6</sub> H <sub>5</sub>	1.00
<u>p</u> -ClC <sub>6</sub> H <sub>4</sub>	5.54
<u>p</u> -BrC <sub>6</sub> H <sub>4</sub>	6.44

<sup>a</sup>All runs were carried out in 60% aqueous dioxane (v/v) at 80.3° C. with 0.01 M HClO<sub>4</sub> added. The initial concentration of aryl  $\alpha$ -disulfone was  $5 \times 10^{-5}$  M.



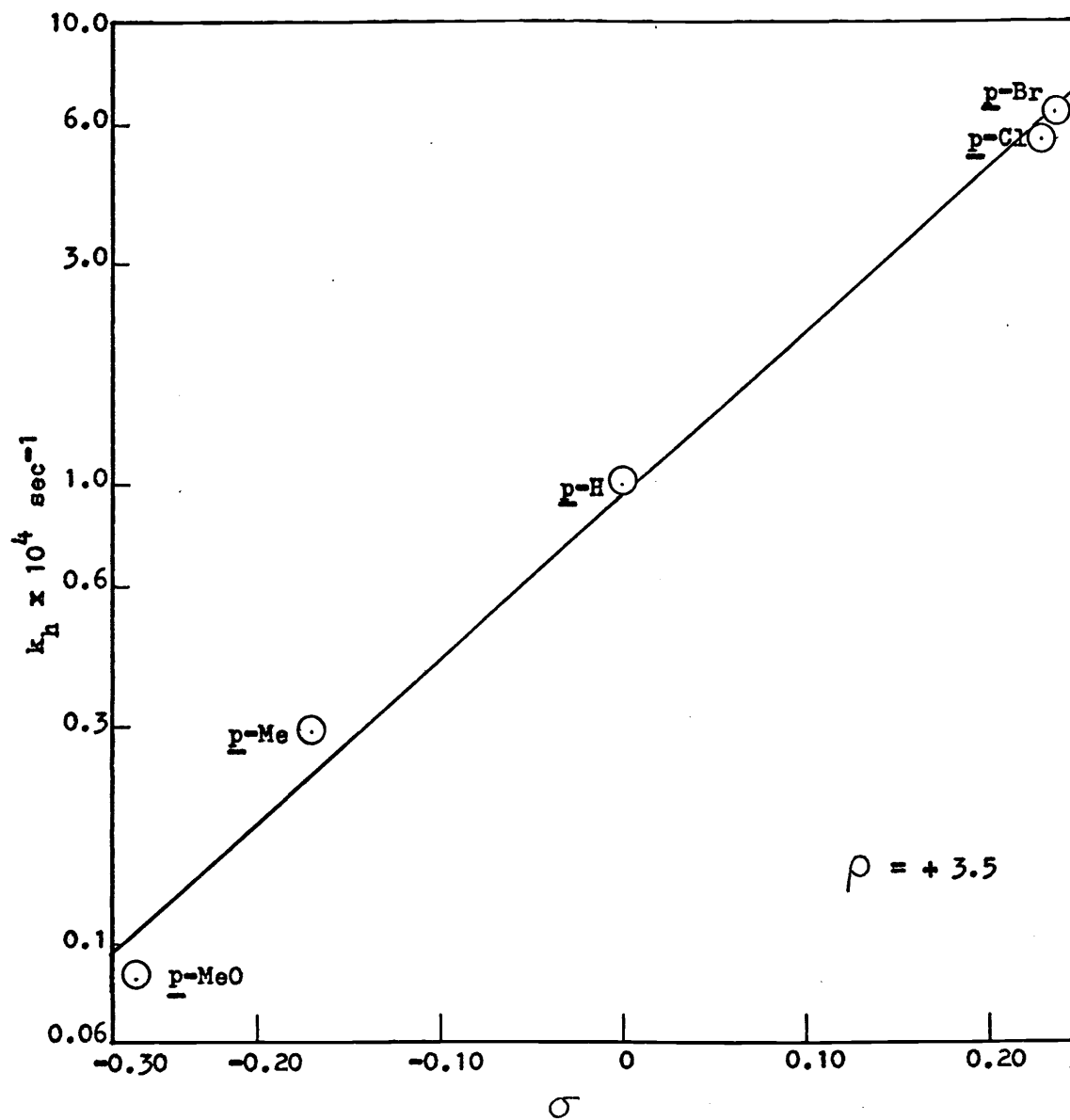


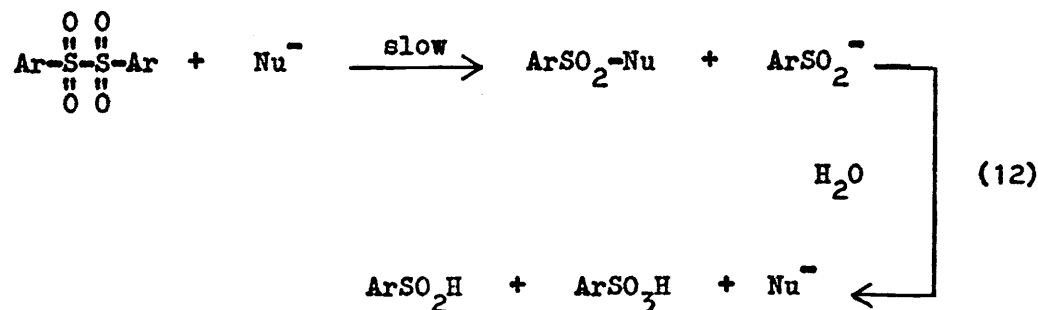
Figure 4. Plot of  $k_h$  versus  $\sigma$  for various  $\alpha$ -disulfones.

### Nucleophile Catalyzed Hydrolysis of Aryl $\alpha$ -Disulfones

The procedure for obtaining data on the reactivity of nucleophiles in the reaction shown in equation 10 was essentially the same as that used in the spontaneous hydrolysis.

#### Stoichiometry

The stoichiometry of these nucleophile catalyzed hydrolyses is quite simple (equation 12). The nucleophile reacts with the  $\alpha$ -disulfone in a slow step to form  $\text{ArSO}_2\text{-Nu}$  which is rapidly hydrolyzed to give back the nucleophile and sulfonic acid.



#### Acetate Ion Catalysis

Acetate ion was the first nucleophile used to catalyze the hydrolysis of the  $\alpha$ -disulfones. Since an acetate - acetic acid buffer system was used in the studies of catalysis by the other nucleophiles, a detailed study of its effect on the hydrolysis of aryl  $\alpha$ -disulfones was made. That acetate ion is indeed a catalyst is shown in Figure 5 where it is observed that adding just 0.005 M sodium acetate leads to a rate of hydrolysis which is 10 fold faster

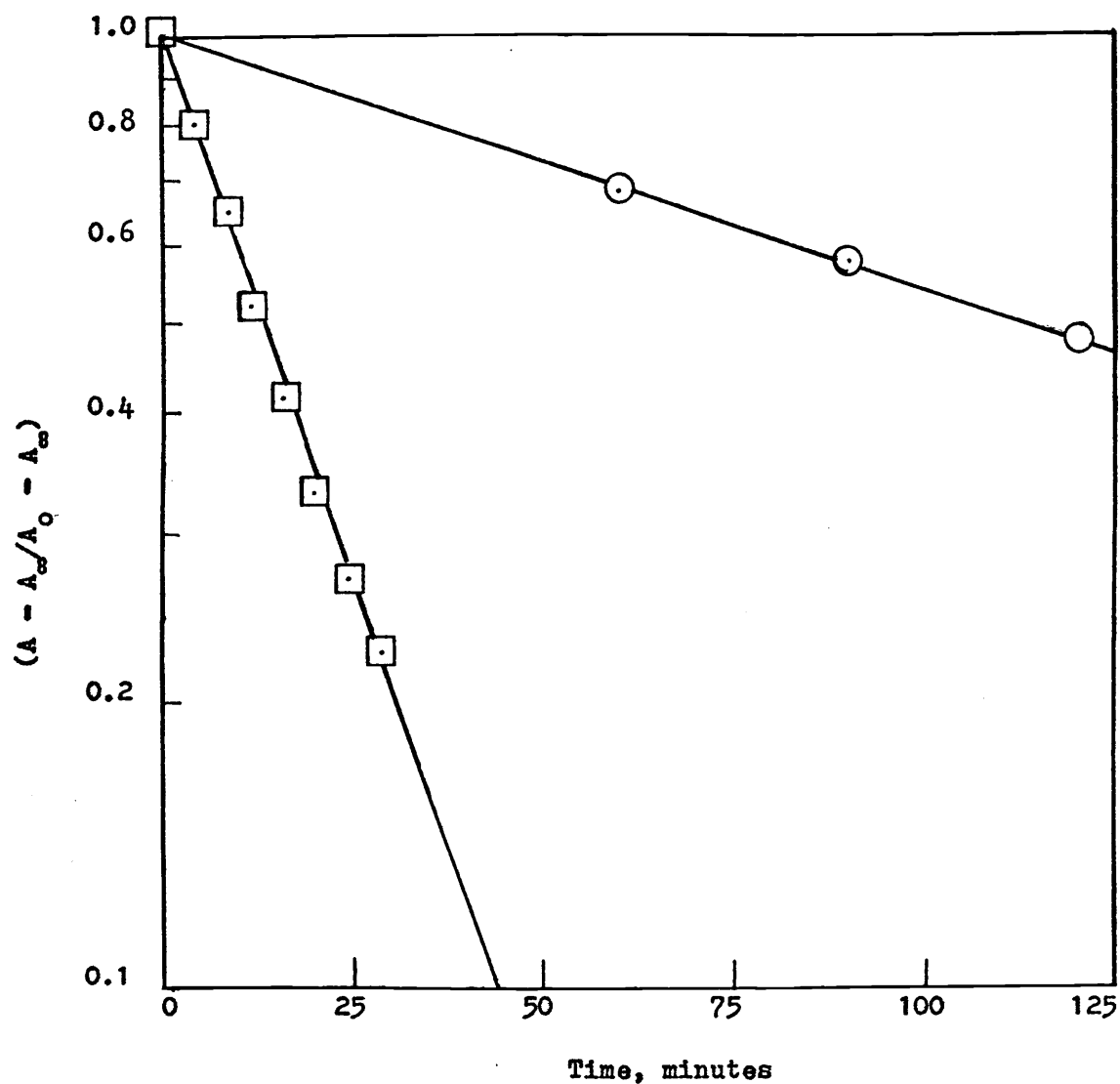


Figure 5. Hydrolysis of  $5 \times 10^{-5}$  M phenyl  $\alpha$ -disulfone in 60% aqueous dioxane (v/v) at  $80.30^\circ \text{C}$ .

○ = Uncatalyzed, 0.01 M  $\text{HClO}_4$ .

□ = Acetate Catalyzed (0.005 M NaOAc, 0.005 M HOAc).

than the rate of the uncatalyzed hydrolysis at this temperature.

### Kinetics of Acetate Ion Catalysis

Kinetic Order with Respect to Acetate Ion. Plots of  $k_h$  versus  $(\text{AcO}^-)$ , see Figure 6 for an example, are linear in all cases, showing that the rate of acetate catalyzed reactions is proportional to the first power of acetate ion concentration. Thus this reaction is first order in acetate ion, and  $k_{\text{OAc}}$ , the actual second order rate constant for the acetate ion catalyzed hydrolysis is equal to the slope of such plots.

Dependence of Rate on Buffer Ratio. The rate of hydrolysis of phenyl  $\alpha$ -disulfone was measured in a variety of acetate buffers in 60% aqueous dioxane at  $80.3^\circ \text{C}$ . The results are found in Table 6.

Table 6. Effect of acetate buffer ratio on acetate ion catalyzed hydrolysis of phenyl  $\alpha$ -disulfone.<sup>a</sup>

$[\text{AcO}^-] \times 10^3, \text{M}$	$[\text{HOAc}] \times 10^3, \text{M}$	$k_h \times 10^4, \text{sec}^{-1}$
4.0	40.0	7.6
4.0	4.0	7.7
4.0	0.40	8.2
1.0	1.0	2.9
1.0	10.0	3.1

<sup>a</sup>Initial concentration of phenyl  $\alpha$ -disulfone  $5 \times 10^{-5} \text{M}$ . All runs in 60% aqueous dioxane (v/v) at  $80.3^\circ \text{C}$ .

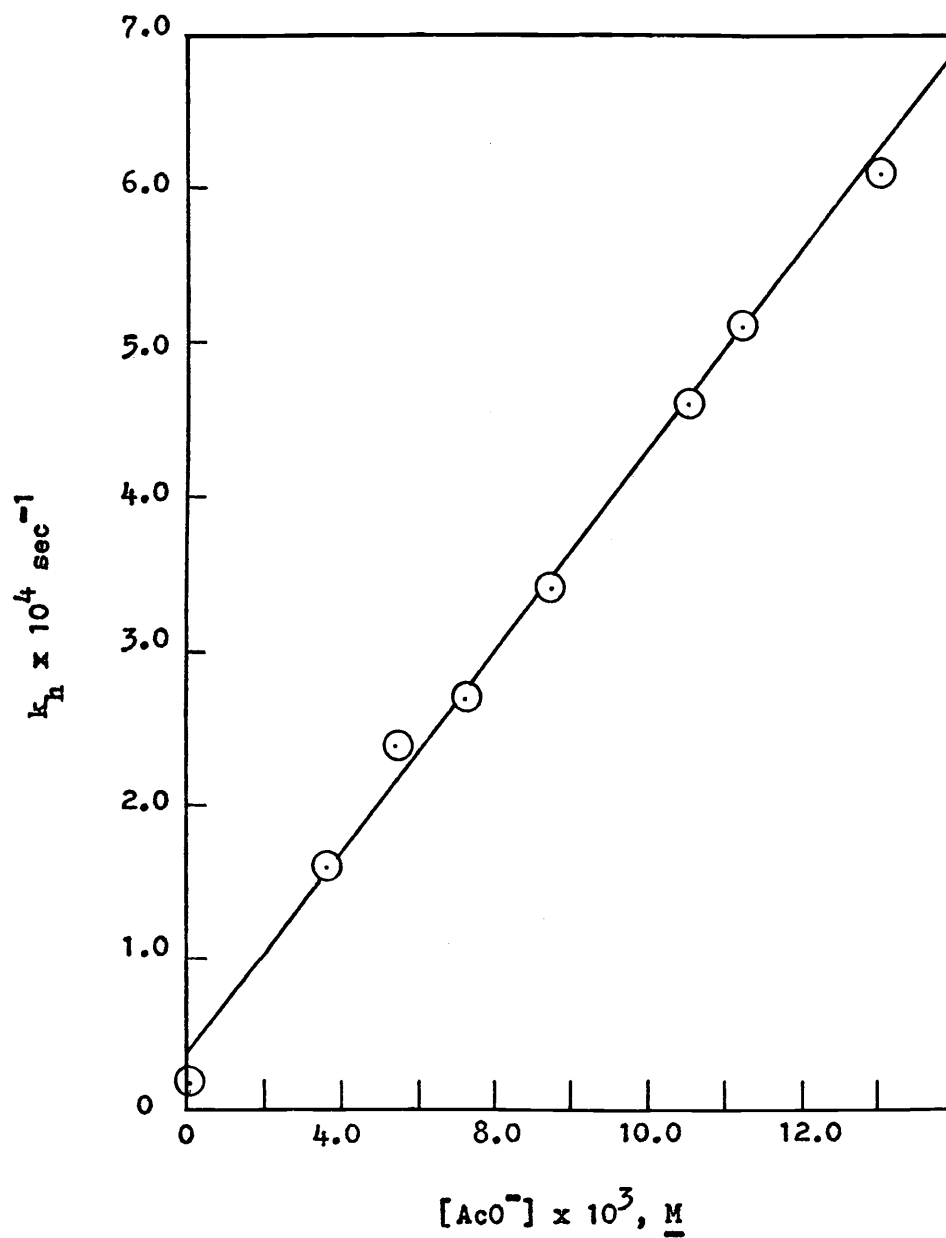


Figure 6. Acetate ion catalyzed hydrolysis of phenyl  $\alpha$ -disulfone in 60% aqueous dioxane at 54.9° C. Plot of  $k_h$  versus  $[AcO^-]$ . All runs in 1:1 HOAc: $AcO^-$  buffer.

It should be noted that even though the buffer ratios vary from  $(\text{HOAc})/(\text{AcO}^-) = 10$  to  $(\text{HOAc})/(\text{AcO}^-) = 0.10$  there is no significant change in  $k_h$  as long as the concentration of acetate ion is kept constant. This demonstrates that it is acetate ion, not hydroxide ion, which is responsible for all the increase in the rate of hydrolysis which is observed.

Activation Parameters. The activation parameters were determined by studying the acetate ion catalyzed hydrolysis at four different temperatures, Table 7. Figure 7 shows a plot of  $\log k_{\text{OAc}}$  versus  $1/T$ . From this one calculates the following activation parameters for the acetate ion catalyzed hydrolysis:  $E_a = 15.6$  kcal/mole;  $\Delta S^\ddagger = -19.8$  e.u.

Deuterium Solvent Isotope Effect. The rate constant  $k_h$  for the acetate catalyzed hydrolysis of phenyl  $\alpha$ -disulfone with  $0.1 \text{ M}$   $\text{NaOAc}$  and  $0.1 \text{ M}$   $\text{HOAc}$  in  $60\%$  dioxane -  $40\%$   $\text{H}_2\text{O}$  at  $54.9^\circ \text{C}$ . is  $33.5 \times 10^4 \text{ sec}^{-1}$ . When the same reaction is run in  $60\%$  dioxane -  $40\%$   $\text{D}_2\text{O}$ , the rate constant is  $30.8 \times 10^4 \text{ sec}^{-1}$ . Thus the acetate ion catalyzed hydrolysis of  $\alpha$ -disulfones exhibits only a very small solvent isotope effect,  $k_{\text{OAc}}^{\text{H}_2\text{O}}/k_{\text{OAc}}^{\text{D}_2\text{O}} = 1.1$

### Fluoride Ion Catalysis

Fluoride ion is an excellent catalyst for the hydrolysis of aryl  $\alpha$ -disulfones, as is shown in Figure 8, where it is observed that addition of only  $5 \times 10^{-5} \text{ M}$  sodium fluoride causes the rate to increase by a factor of two over the rate of hydrolysis observed without added fluoride.

Table 7. Catalysis of the hydrolysis of phenyl  $\alpha$ -disulfone by acetate ion.<sup>a</sup>

T, °C.	[AcO <sup>-</sup> ] x 10 <sup>3</sup> <u>M</u>	[HOAc] x 10 <sup>3</sup> <u>M</u>	k <sub>h</sub> x 10 <sup>4</sup> sec <sup>-1</sup>	k <sub>OAc<sup>-</sup></sub> <sup>(b)</sup> M <sup>-1</sup> sec <sup>-1</sup>
90.8	0.43	0.43	3.8	0.34
	0.72	0.72	4.6	
	1.08	1.08	5.7	
	1.44	1.44	7.1	
	1.80	1.80	8.0	
	2.17	2.17	9.0	
80.3	1.0	1.0	2.9	0.18
	2.0	2.0	4.2	
	3.0	3.0	5.5	
	4.0	4.0	7.7	
	5.0	5.0	9.2	
67.9	3.6	3.6	3.2	0.076
	7.2	7.2	6.0	
	10.8	10.8	8.4	
54.9	0.0	0.0	0.19	0.033
	3.6	3.6	1.6	
	5.8	5.8	2.4	
	7.2	7.2	2.7	
	9.4	9.4	3.4	
	13.0	13.0	4.6	
	14.4	14.4	5.1	
	18.0	18.0	6.1	

<sup>a</sup>All runs in 60% aqueous dioxane (v/v). Initial concentration of phenyl  $\alpha$ -disulfone  $5 \times 10^{-5}$  M.

<sup>b</sup>Evaluated from slope of plot of k<sub>h</sub> versus [AcO<sup>-</sup>]; see Figure 6 for an example.

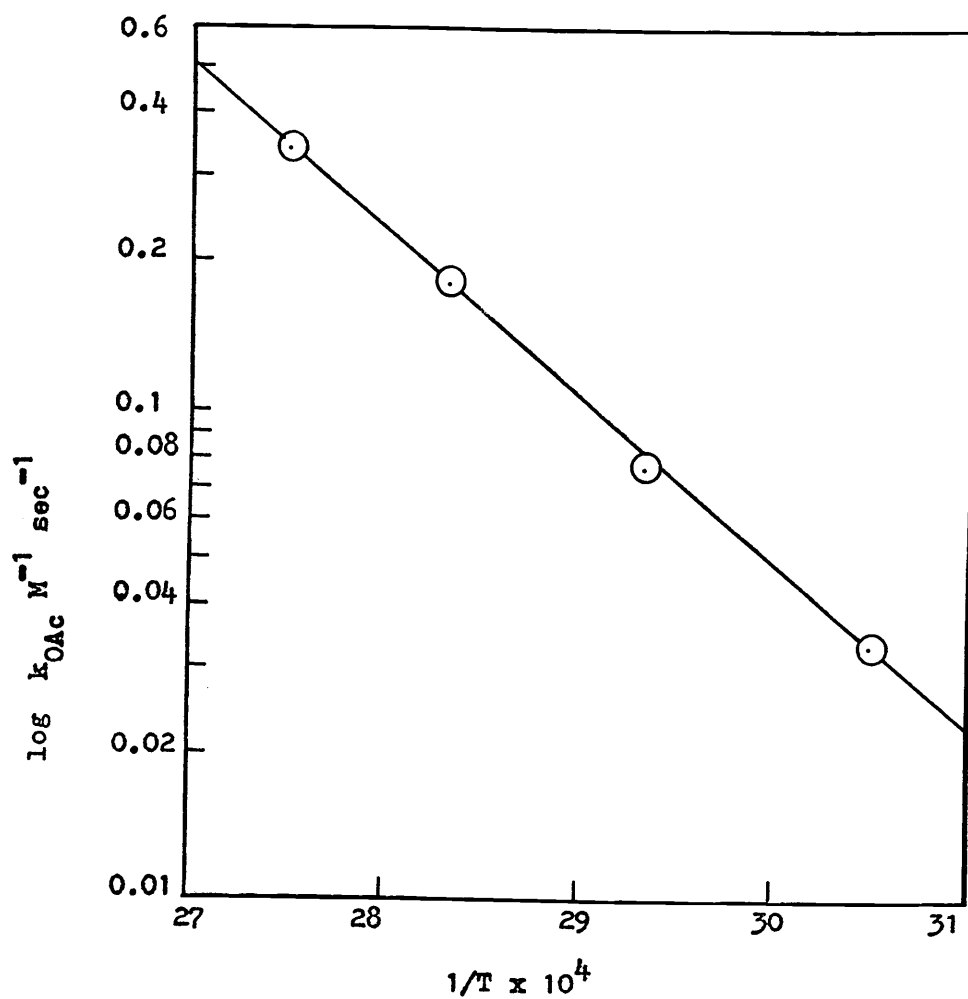


Figure 7. Plot of  $k_{\text{OAc}}$  versus  $1/T$  for acetate ion catalyzed hydrolysis of phenyl  $\alpha$ -disulfone in 60% aqueous dioxane (v/v).



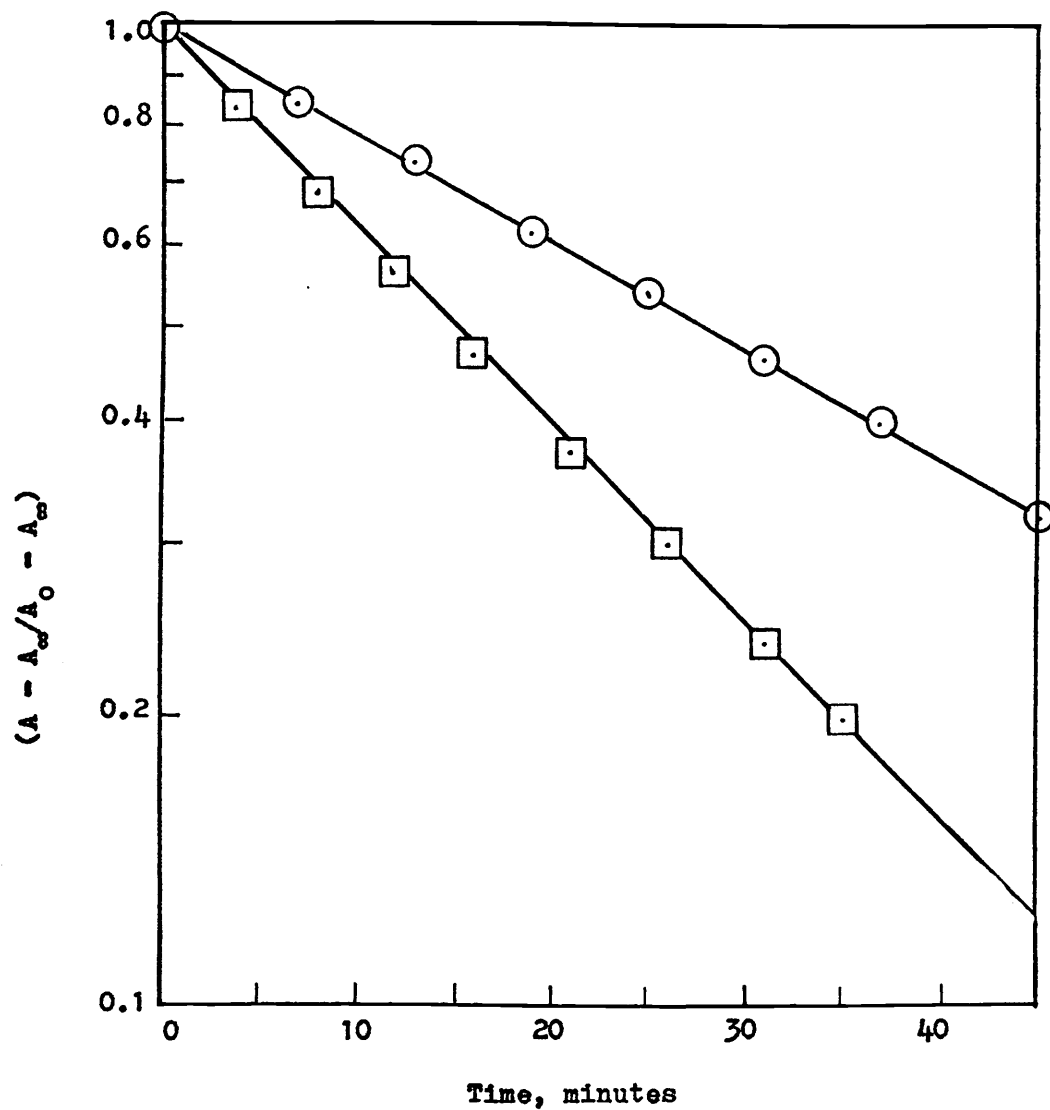


Figure 8. Hydrolysis of  $5 \times 10^{-5}$  M phenyl  $\alpha$ -disulfone in 60% aqueous dioxane (v/v) at  $80.3^\circ \text{C}$ .

○ =  $2 \times 10^{-3}$  M HOAc and  $2 \times 10^{-3}$  M NaOAc added.

□ = Fluoride catalyzed ( $2 \times 10^{-3}$  M HOAc,  $2 \times 10^{-3}$  M NaOAc,  $5 \times 10^{-5}$  M NaF).

### Kinetics of Fluoride Ion Catalysis

The rate of the fluoride-catalyzed hydrolysis of aryl  $\alpha$ -disulfones was studied in 60% aqueous dioxane (v/v) which contained a 1:1 HOAc:AcO<sup>-</sup> buffer, to keep the pH constant and on the acid side of neutrality. The effect of fluoride ion on the hydrolysis was determined by varying the amount of sodium fluoride added.

Order with Respect to Fluoride Ion. Figure 9 shows a plot of  $k_h$  versus ( $F^-$ ) for the hydrolysis of phenyl  $\alpha$ -disulfone in 60% aqueous dioxane (v/v) at 80.3° C. Since this plot is linear, the reaction is first order in fluoride. The second order rate constant  $k_F$  is equal to the slope of this plot. The other cases of fluoride catalyzed hydrolysis of aryl  $\alpha$ -disulfones studied also gave linear plots of  $k_h$  versus ( $F^-$ ). Their second order rate constants were evaluated from the slopes.

Dependence of Rate on Added Benzenesulfinic Acid. The effect of adding benzenesulfinic acid to the fluoride catalyzed hydrolysis of phenyl  $\alpha$ -disulfone was determined at 21.3° C. in 60% aqueous dioxane (v/v) containing a 1:1 buffer of HOAc:AcO<sup>-</sup>, which was 0.002 M in (AcO<sup>-</sup>). The reaction was catalyzed by 0.005 M NaF. The reaction without added benzenesulfinic acid had a rate constant of  $0.66 \times 10^{-3} \text{ sec}^{-1}$ , while the reaction with 0.001 M benzenesulfinic acid has a rate constant of  $0.64 \times 10^{-3} \text{ sec}^{-1}$ . Thus adding benzenesulfinic acid, one of the products of the reaction, in a much greater quantity than produced by the reaction has no significant effect on the rate of

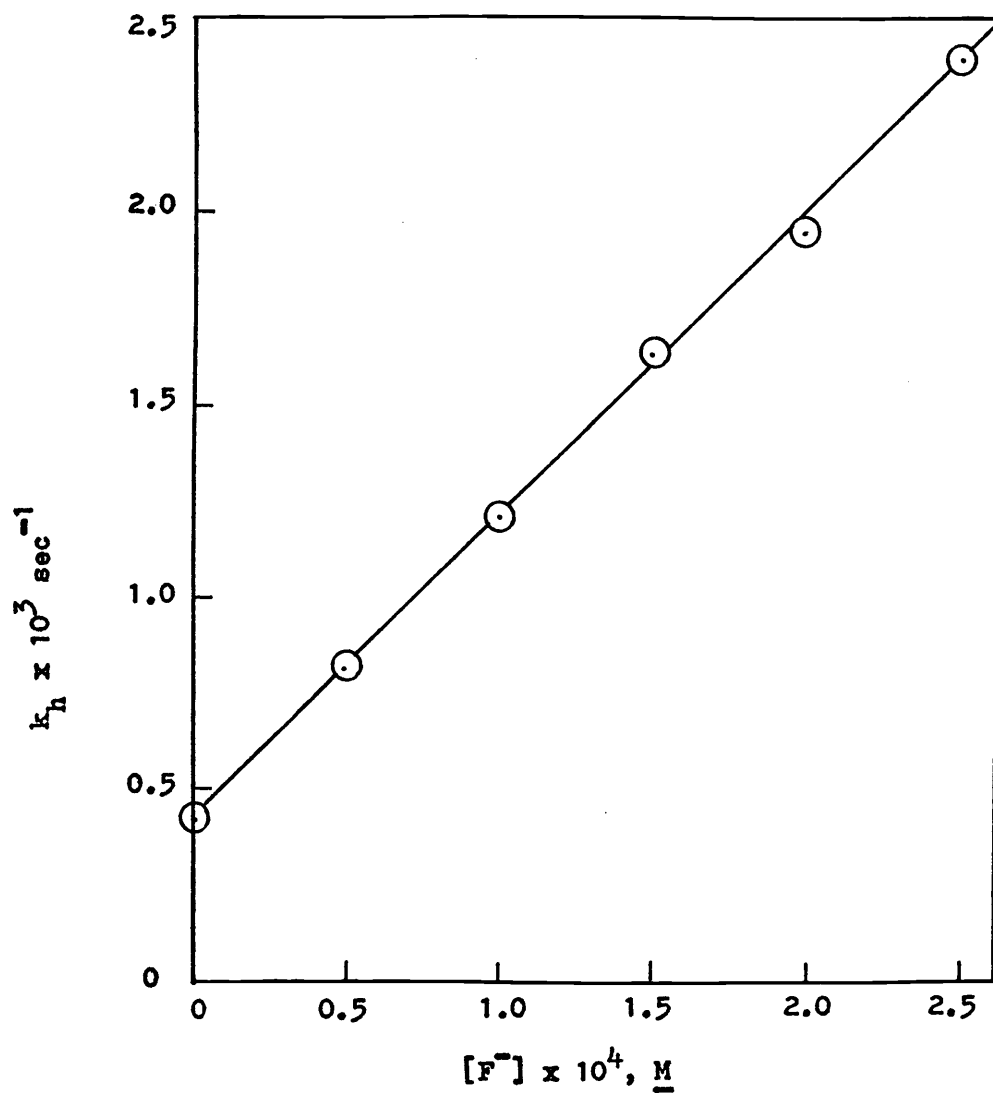


Figure 9. Fluoride ion catalyzed hydrolysis of phenyl  $\alpha$ -disulfone in 60% aqueous dioxane (v/v) at 80.3° C. Plot of  $k_h$  versus  $[F^-]$  for a series of runs in a 1:1 HOAc:AcO<sup>-</sup> buffer 0.002 M in AcO<sup>-</sup>.

fluoride ion catalyzed hydrolysis of aryl  $\alpha$ -disulfones. In the  $\text{AcO}^-:\text{HOAc}$  buffer the added benzenesulfinic acid is of course actually present as the benzenesulfinate ion,  $\text{PhSO}_2^-$ .

Activation Parameters. Phenyl  $\alpha$ -disulfone was hydrolyzed at four different temperatures in 60% aqueous dioxane (v/v) in the presence of varying amounts of sodium fluoride in a 1:1  $\text{HOAc}:\text{AcO}^-$  buffer, Table 8. The second order rate constants  $k_F$  were obtained by taking the slopes of plots of  $k_h$  versus  $(\text{F}^-)$  (for an example see Figure 9). The activation parameters were determined in the usual manner, i.e. by plotting  $k_F$  versus  $1/T$  as shown in Figure 10. From the slope of this plot one estimates  $E_a = 14.4$  kcal/mole and  $\Delta S^\ddagger = -15.9$  e.u. for the fluoride catalyzed reaction of phenyl  $\alpha$ -disulfone.

Dependence of Rate on Aryl Group Structure. The variation of  $k_F$  with changes in the structure of the aryl group of the  $\alpha$ -disulfones was investigated at  $21.3^\circ \text{C}$ . using  $\text{Ar} = \text{C}_6\text{H}_5$ ,  $\text{Ar} = \text{p-CH}_3\text{C}_6\text{H}_4$ ,  $\text{Ar} = \text{p-ClC}_6\text{H}_4$  and  $\text{Ar} = \text{p-CH}_3\text{OC}_6\text{H}_4$ . The data for  $\text{Ar} = \text{C}_6\text{H}_5$  are in Table 8 while the data for the latter three are found in Table 9. A plot of the  $\log k_F$  values for these aryl  $\alpha$ -disulfones versus  $\sigma$  (Figure 11) gives a good straight line with a slope,  $\rho$ , of  $+5.0$ . This is a large  $\rho$  but it should be remembered that the spontaneous hydrolysis of aryl  $\alpha$ -disulfones also had a large positive  $\rho$  of  $+3.5$ .

#### Chloride Ion Catalysis

In contrast to the marked catalysis of the hydrolysis of phenyl  $\alpha$ -disulfone by very small concentrations ( $\sim 10^{-4} \text{ M}$ ) of added fluoride

Table 8. Effect of temperature on the fluoride catalyzed hydrolysis of phenyl  $\alpha$ -disulfone.<sup>a</sup>

T, °C.	[AcO <sup>-</sup> ] in 1:1 HOAc:AcO <sup>-</sup> buffer	[F <sup>-</sup> ] x 10 <sup>4</sup> , M	k <sub>h</sub> x 10 <sup>3</sup> , sec <sup>-1</sup>	k <sub>F</sub> , M <sup>-1</sup> sec <sup>-1</sup> (b)
80.3	0.002 M	0.50	0.82	7.8
		1.0	1.21	
		1.5	1.64	
		2.0	1.95	
		2.5	2.40	
54.9	0.002	2.0	0.43	1.8
		3.0	0.60	
		4.0	0.79	
		5.0	0.99	
36.0	0.020	4.0	0.27	0.39
		12.0	0.65	
		20.0	0.94	
		28.0	1.20	
		40.0	1.68	
21.3	0.020	8.0	0.13	0.126
		16.0	0.23	
		24.0	0.34	
		32.0	0.43	
		40.0	0.54	
		50.0	0.66	

<sup>a</sup>Initial concentration of phenyl  $\alpha$ -disulfone  $5 \times 10^{-5}$  M in 60% aqueous dioxane (v/v).

<sup>b</sup>Evaluated from slope of plot of k<sub>h</sub> versus [F<sup>-</sup>], see Figure 9 for an example.

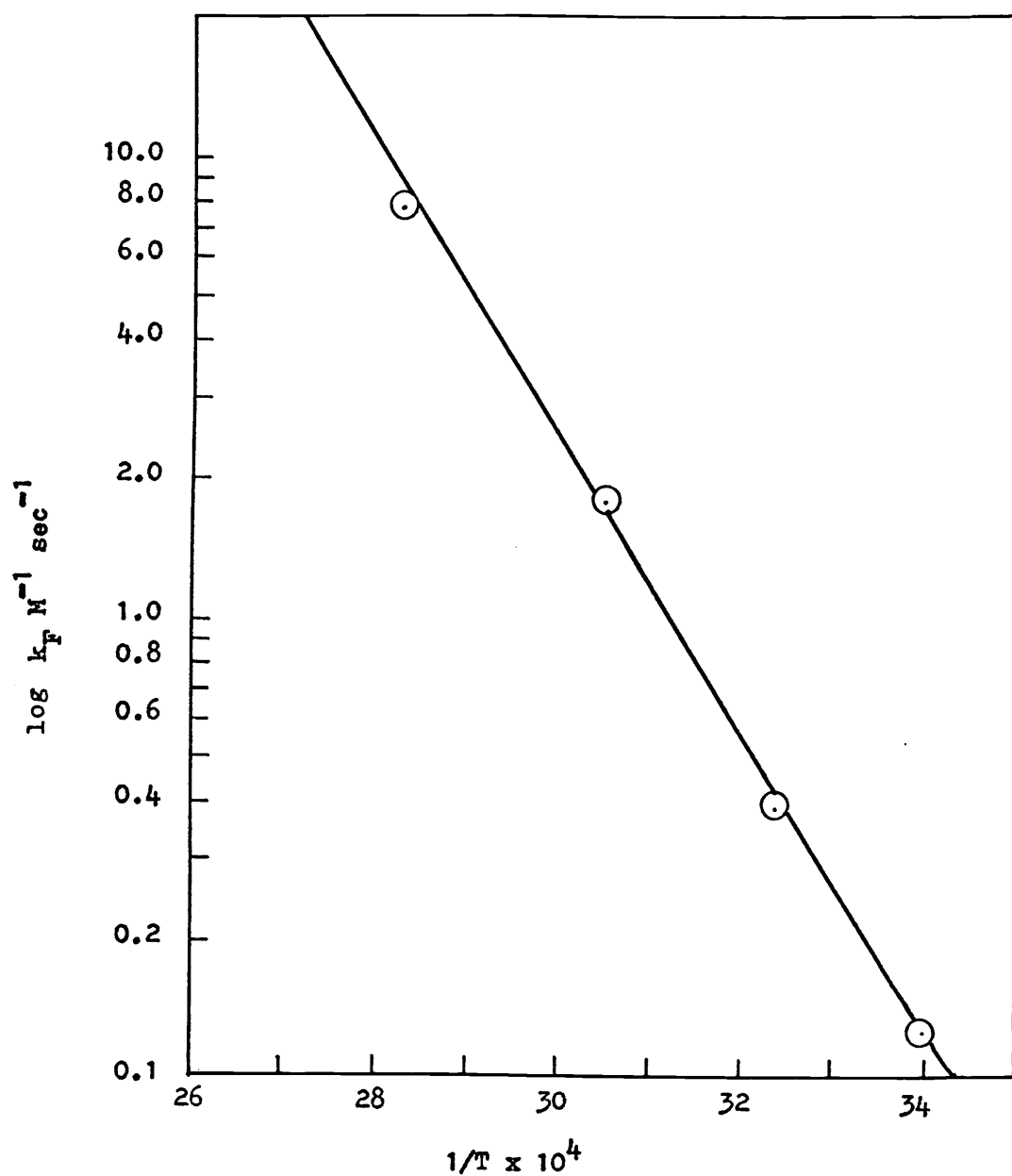


Figure 10. Plot of  $k_F$  versus  $1/T$  for fluoride ion catalyzed hydrolysis of phenyl  $\alpha$ -disulfone in 60% aqueous dioxane (v/v).

Table 9. Effect of aryl group structure on the fluoride ion catalyzed hydrolysis of aryl  $\alpha$ -disulfones.<sup>a</sup>

$\text{ArSO}_2\text{SO}_2\text{Ar}$ , Ar =	$[\text{F}^-] \times 10^4$ , M	$k_h \times 10^3$ , $\text{sec}^{-1}$	$k_F$ , $\text{M}^{-1}\text{sec}^{-1}$ (b)
$\text{p-ClC}_6\text{H}_4$	3.2	0.95	
	6.4	1.33	
	9.6	1.65	1.20
	12.8	2.16	
	16.0	2.45	
$\text{p-CH}_3\text{C}_6\text{H}_4$	20.0	0.053	
	40.0	0.092	
	60.0	0.13	0.018
	80.0	0.17	
	100.0	0.19	
$\text{p-CH}_3\text{OC}_6\text{H}_4$	16.0	0.0073	
	40.0	0.016	
	60.0	0.022	0.0034
	80.0	0.029	
	100.0	0.034	

<sup>a</sup>All runs at 21.3° C. with an initial concentration of aryl  $\alpha$ -disulfone of  $5 \times 10^{-5}$  M in 60% aqueous dioxane (v/v) containing a 1:1 HOAc:AcO<sup>-</sup> buffer 0.020 M in AcO<sup>-</sup>.

<sup>b</sup>Evaluated from slope of plot of  $k_h$  versus  $[\text{F}^-]$ , see Figure 9 for an example.

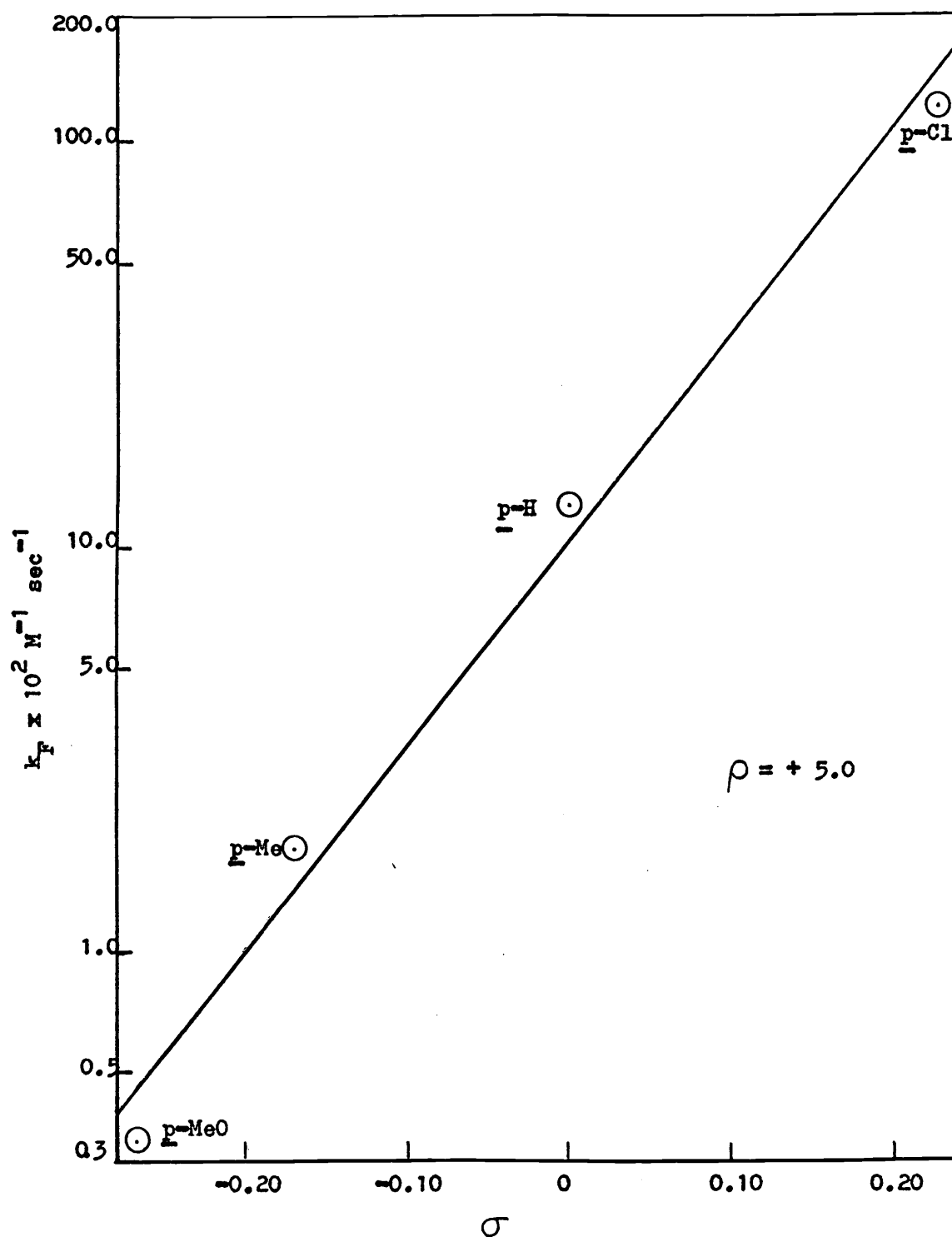


Figure 11. Effect of aryl group structure on the fluoride catalyzed hydrolysis of aryl  $\alpha$ -disulfones in 60% dioxane at 21.3° C. Plot of  $k_F$  versus  $\sigma$ . All runs in 1:1 HOAc:AcO<sup>-</sup> buffer.



ion, even quite large concentrations of chloride ion have only a small effect on the hydrolysis rate (see Figure 12).

Kinetics of Chloride Ion Catalysis. The rate of hydrolysis of phenyl  $\alpha$ -disulfone has been determined in 60% aqueous dioxane (v/v) at 80.3° C. as a function of chloride ion concentration, and the results are shown in Table 10.

Table 10. Hydrolysis of phenyl  $\alpha$ -disulfone in the presence of added chloride.<sup>a</sup>

$[\text{LiClO}_4], \text{ M}$	$[\text{Cl}^-], \text{ M}$	$k_h \times 10^4, \text{ sec}^{-1}$	$k_{\text{Cl}}, \text{ M}^{-1} \text{ sec}^{-1}(\text{b})$
0.40	0.00	1.13	
0.30	0.10	1.42	
0.20	0.20	1.72	0.00030
0.10	0.30	2.05	
0.00	0.40	2.36	

<sup>a</sup>All runs at 80.3° C. in 60% aqueous dioxane (v/v), 0.01 M  $\text{HClO}_4$ . Initial concentration of phenyl  $\alpha$ -disulfone  $5 \times 10^{-5}$  M.

<sup>b</sup>Calculated from slope of a plot of  $k_h$  versus  $[\text{Cl}^-]$ , see Figure 13.

That the chloride catalyzed hydrolysis is first order in chloride ion can be seen from the linearity of a plot of  $k_h$  versus  $[\text{Cl}^-]$ . This plot is shown in Figure 13. The slope of this plot is equal to  $k_{\text{Cl}}$ , the second order rate constant of chloride ion catalysis of phenyl  $\alpha$ -disulfone at 80.3° C. This rate constant is  $3 \times 10^{-4} \text{ sec}^{-1}$

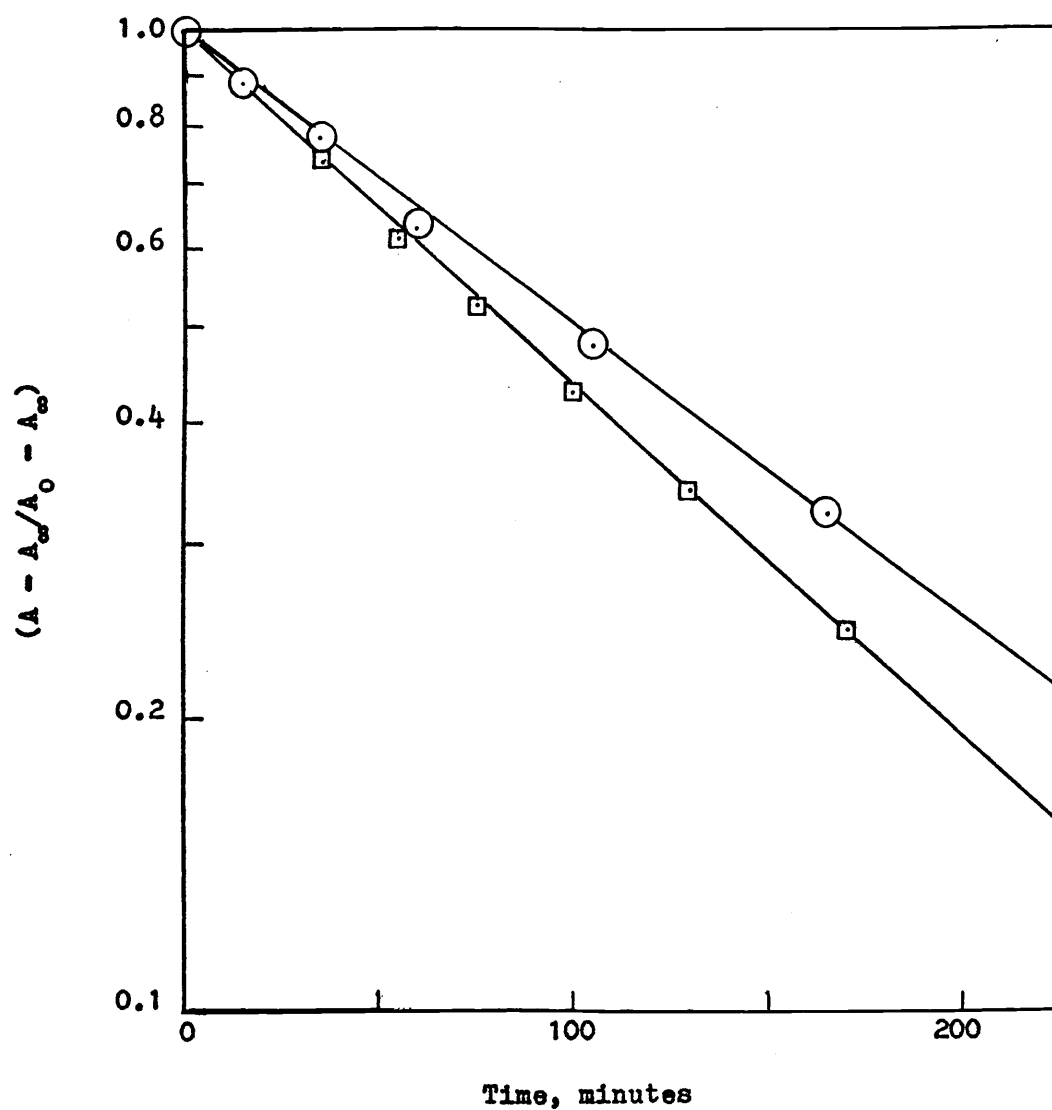


Figure 12. Effect of chloride ion on the hydrolysis of phenyl  $\alpha$ -disulfone at 80.3° C. in 60% aqueous dioxane (v/v) containing 0.01 M  $\text{HClO}_4$

○ = Uncatalyzed, 0.40 M  $\text{LiClO}_4$

□ = Chloride catalyzed, 0.10 M  $\text{LiCl}$ , 0.30 M  $\text{LiClO}_4$

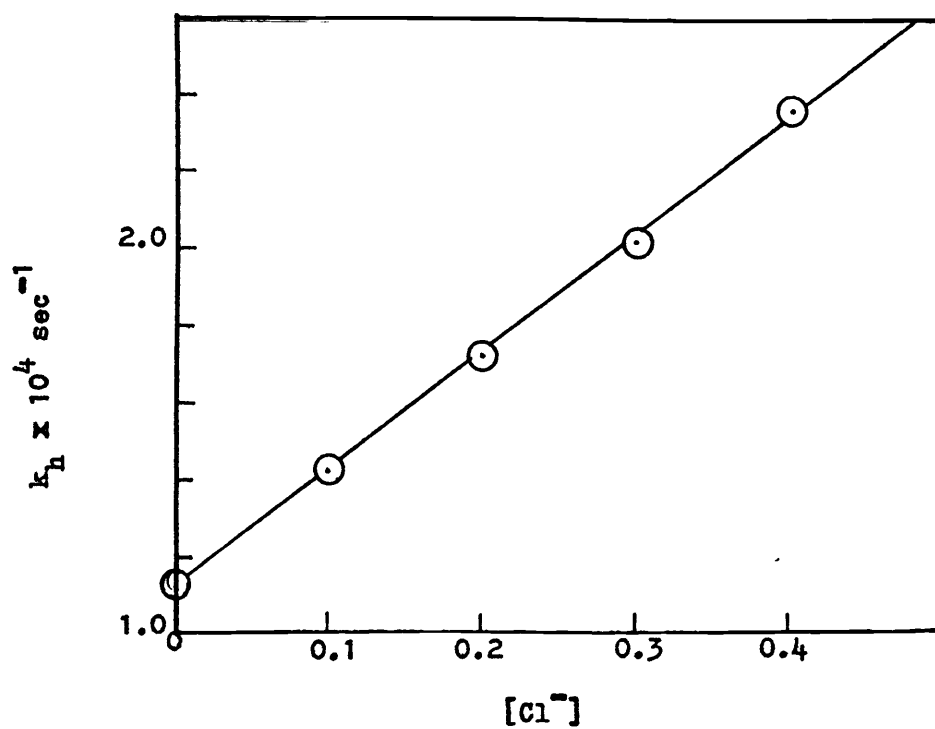


Figure 13. Chloride ion catalyzed hydrolysis of phenyl  $\alpha$ -disulfone at  $80.3^\circ \text{C}$ . in 60% aqueous dioxane (v/v). Plot of  $k_h$  versus  $[Cl^-]$  for a series of runs with the ionic strength held constant at 0.4 with  $LiClO_4$ .

which is quite small indeed, being only about 4/100,000ths the rate constant for the fluoride ion catalyzed reaction at the same temperature.

### Bromide Ion Catalysis

Bromide ion was also found to have only a small catalytic effect on the hydrolysis of phenyl  $\alpha$ -disulfone at 80.3° C. in aqueous dioxane.

Kinetics of Bromide Ion Catalysis. The effect of varying the concentration of added bromide ion on the rate of hydrolysis of phenyl  $\alpha$ -disulfone is shown in Table 11. A plot (Figure 14) of

Table 11. Effect of bromide ion on the hydrolysis of phenyl  $\alpha$ -disulfone.<sup>a</sup>

$[\text{LiClO}_4], \text{ M}$	$[\text{Br}^-], \text{ M}$	$k_h \times 10^4, \text{ sec}^{-1}$	$k_{\text{Br}}, \text{ M}^{-1} \text{ Sec}^{-1}(\text{b})$
0.40	0.00	1.13	
0.20	0.20	1.47	
0.10	0.30	1.63	0.00017
0.00	0.40	1.80	

<sup>a</sup>Initial concentration of phenyl  $\alpha$ -disulfone  $5 \times 10^{-5} \text{ M}$ . All runs at 80.3° C. in 60% aqueous dioxane containing 0.01  $\text{M}$   $\text{HClO}_4$ .

<sup>b</sup>Evaluated from the slope of Figure 14.

$k_h$  versus  $(\text{Br}^-)$  is linear indicating that the reaction is first order in bromide ion. The slope of this plot is  $k_{\text{Br}}$ , the second order rate

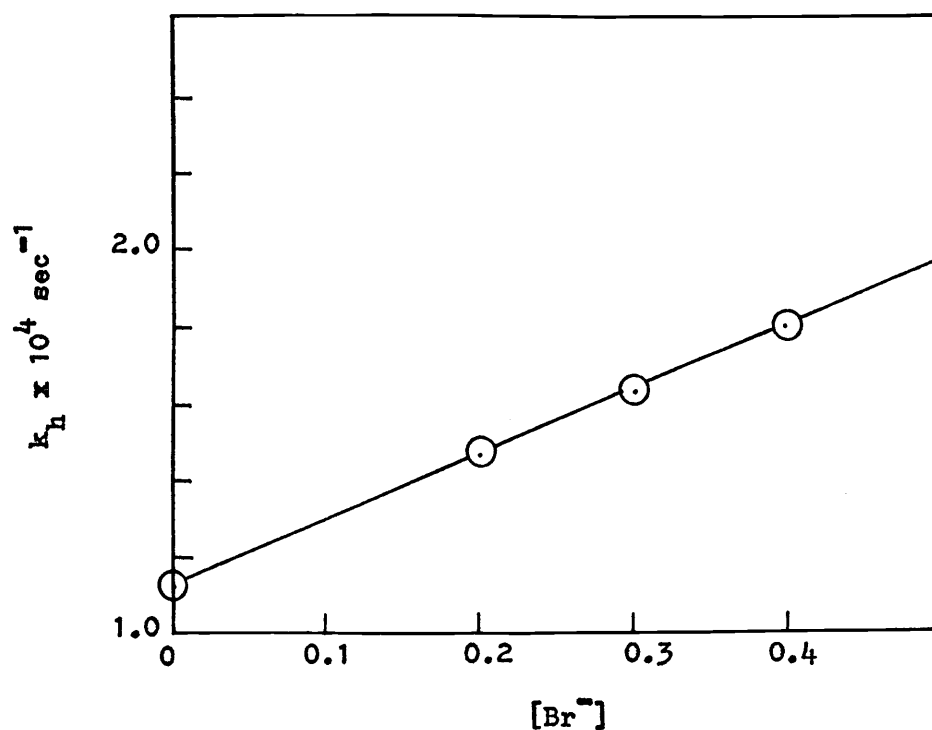


Figure 14. Bromide ion catalyzed hydrolysis of phenyl  $\alpha$ -disulfone at 80.3° C. in 60% aqueous dioxane (v/v) 0.01 M in  $\text{HClO}_4$ . Plot of  $k_h$  versus  $[\text{Br}^-]$  for a series of runs with the ionic strength held constant at 0.4 with  $\text{LiClO}_4$ .

constant for the bromide ion catalyzed hydrolysis. The rate constant determined in this manner is  $1.7 \times 10^{-4} \text{ M}^{-1} \text{ sec}^{-1}$ , which is even smaller than that for chloride ion at the same temperature.

### Nitrite Ion Catalysis

The catalytic effectiveness of nitrite ion on the hydrolysis of phenyl  $\alpha$ -disulfone was found to be intermediate between acetate and fluoride.

### Kinetics of Nitrite Ion Catalysis

Order with Respect to Nitrite Ion. The dependence of the rate on the concentration of added nitrite ion was determined in the same manner as for fluoride ion. Figure 15 shows a plot of  $k_h$  versus  $(\text{NO}_2^-)$  at  $67.9^\circ \text{ C.}$  in 60% aqueous dioxane (v/v). Since this plot is linear, the reaction is first order with respect to nitrite ion.

Activation Parameters. The rate of the nitrite catalyzed hydrolysis of phenyl  $\alpha$ -disulfone was studied as a function of temperature in 60% aqueous dioxane (v/v) containing a 1:1 HOAc:AcO<sup>-</sup> buffer ratio, 0.002 M in AcO<sup>-</sup>. The data from this study are found in Table 12. A plot of  $\log k_{\text{NO}_2}$  versus  $1/T$  (Figure 16) yields  $E_a = 12.9 \text{ kcal/mole}$  and  $\Delta S^\ddagger = -24.6 \text{ e.u.}$  for the activation parameters of the nitrite catalyzed hydrolysis of phenyl  $\alpha$ -disulfone.

Dependence of the Rate on Aryl Group Structure. A series of runs with p-tolyl  $\alpha$ -disulfone at  $80.3^\circ \text{ C.}$  (Table 13) showed that  $k_{\text{NO}_2}$  for that compound was only  $0.26 \times k_{\text{NO}_2}$  for phenyl  $\alpha$ -disulfone under

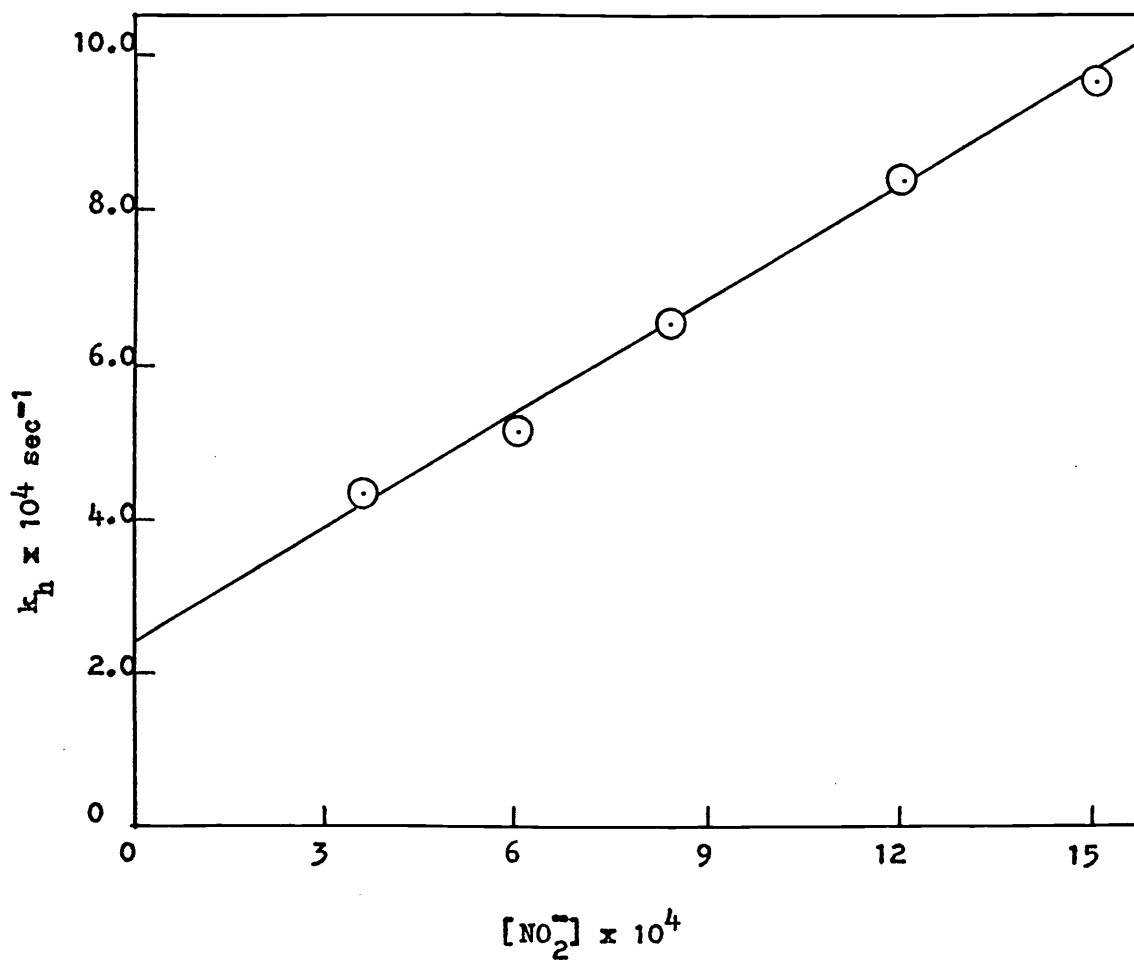


Figure 15. Nitrite ion catalyzed hydrolysis of phenyl  $\alpha$ -disulfone in 60% aqueous dioxane (v/v) at 67.9° C. Plot of  $k_h$  versus  $[\text{NO}_2^-]$  for a series of runs in 1:1 HOAc:AcO<sup>-</sup> buffer, 0.002M in AcO<sup>-</sup>.

Table 12. Effect of temperature on the catalysis of the hydrolysis of phenyl  $\alpha$ -disulfone by nitrite ion.<sup>a</sup>

T, °C.	$[\text{NO}_2^-] \times 10^3, \text{ M}$	$k_h \times 10^4, \text{ sec}^{-1}$	$k_{\text{NO}_2}, \text{ M}^{-1} \text{ sec}^{-1}(\text{b})$
80.3	0.50	8.7	
	1.0	12.3	0.79
	1.5	16.5	
67.9	0.30	4.3	
	0.60	5.1	
	0.90	6.5	0.47
	1.20	8.4	
	1.50	9.2	
54.9	0.60	2.3	
	0.90	2.9	
	1.20	3.5	0.20
	1.50	4.0	
39.7	0.60	0.84	
	0.90	1.10	
	1.20	1.32	0.082
	1.50	1.55	

<sup>a</sup>All runs made in 60% aqueous dioxane (v/v) containing a 1:1 HOAc:AcO<sup>-</sup> buffer, 0.002 M in AcO<sup>-</sup>. Initial concentration of phenyl  $\alpha$ -disulfone  $5 \times 10^{-5}$  M.

<sup>b</sup>Calculated from the slope of plots of  $k_h$  versus  $[\text{NO}_2^-]$  at each temperature, see Figure 15 for an example.



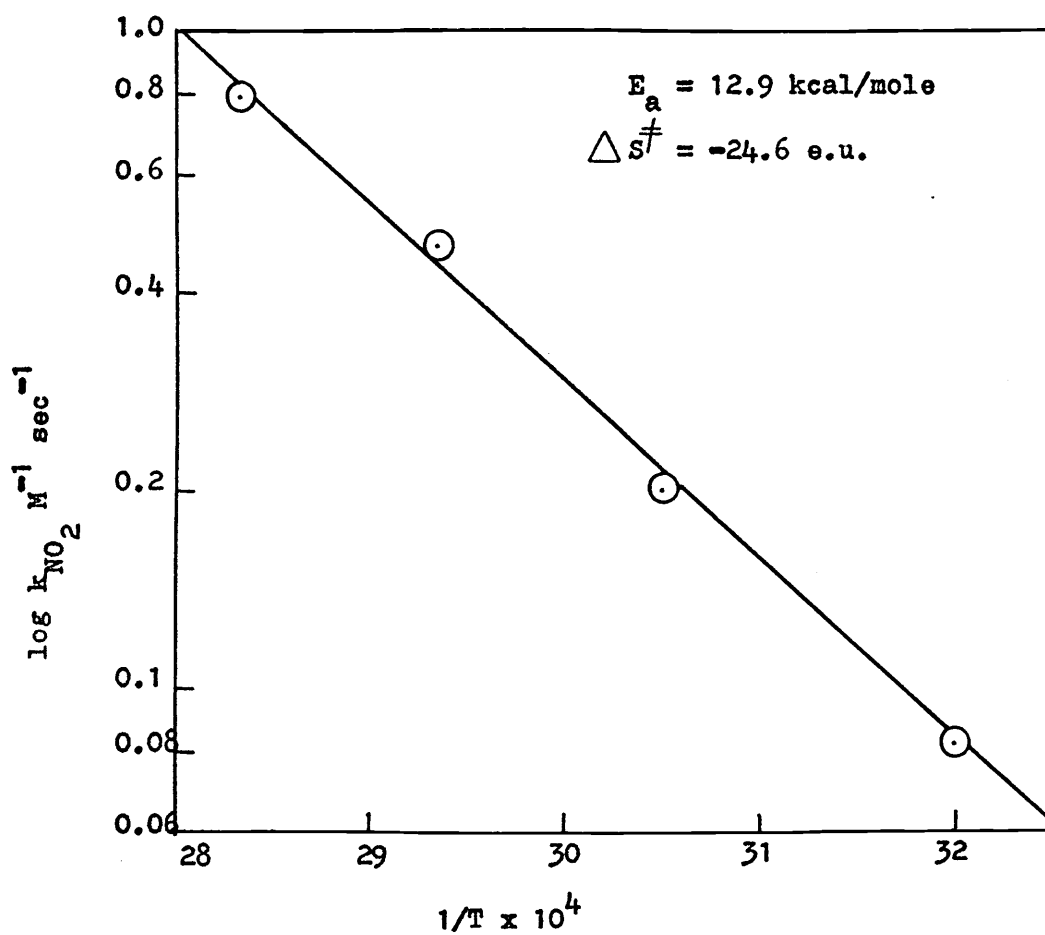


Figure 16. Nitrite ion catalyzed hydrolysis of phenyl  $\alpha$ -disulfone in 60% aqueous dioxane (v/v). Plot of  $k_{\text{NO}_2}$  versus  $1/T$ .

Table 13. Hydrolysis of *p*-tolyl  $\alpha$ -disulfone in the presence of added nitrite ion.<sup>a</sup>

$[\text{NO}_2^-] \times 10^3, \text{ M}$	$k_h \times 10^4, \text{ sec}^{-1}$	$k_{\text{NO}_2}, \text{ M}^{-1} \text{ sec}^{-1}(\text{b})$
0.00	1.24	
0.50	2.28	
1.00	3.3	0.20
1.50	4.2	

<sup>a</sup>All runs at 80.3° C. in 60% aqueous dioxane (v/v) containing a 1:1 HOAc:AcO<sup>-</sup> buffer, 0.002 M in AcO<sup>-</sup>. Initial concentration of *p*-tolyl  $\alpha$ -disulfone  $5 \times 10^{-5}$  M.

<sup>b</sup>Calculated from slope of plot of  $k_h$  versus  $[\text{NO}_2^-]$ .

the same conditions, thereby further demonstrating what was previously seen from the uncatalyzed and fluoride catalyzed reactions, i.e.

that the rate constants are very sensitive to changes in the structure of the aryl group and electron-donating substituents in the para positions slow the rate of hydrolysis.

#### Triethylamine Catalysis

The effectiveness of triethylamine as a catalyst in the hydrolysis of aryl  $\alpha$ -disulfones was determined in 60% aqueous dioxane (v/v) at 21.3° C. It was hoped that by studying this catalysis information about the rate of the hydroxide ion catalyzed hydrolysis could be obtained. Unfortunately this could not be done due to a trace of some impurity in the dioxane.

### Kinetics of Triethylamine Catalysis in Aqueous Dioxane

The kinetics of the triethylamine catalyzed hydrolysis of aryl  $\alpha$ -disulfones were determined directly in the spectrophotometer in a specially designed cell by the direct method (see Experimental section).

The reaction rates were determined by plotting  $k_h$  versus  $(Et_3N)$ . The slope of such plots is the second order rate constant,  $k_{Et_3N}$ . The intercept, at zero amine concentration, of such plots should be equal to  $k_{OH}(OH^-)$  since the hydroxide ion concentration is held constant by keeping the  $(Et_3N):(Et_3NH^+)$  buffer ratio constant. However, it was found that due to some impurity, whose effect can be noticed only in basic aqueous dioxane, the intercepts at zero amine concentration changed considerably from one set of runs to another, although the slopes stayed virtually the same. A more detailed discussion of this is contained in the section on the reactions of aryl  $\alpha$ -disulfones with t-butylamine.

Table 14 contains data on the triethylamine catalyzed hydrolysis of phenyl  $\alpha$ -disulfone at two different  $(Et_3N):(Et_3NH^+)$  buffer ratios. It is evident from looking at this table that increasing the  $(Et_3N):(Et_3NH^+)$  buffer ratio by a factor of three does not increase the intercept by a factor of three. Since increasing the hydroxide ion concentration has not changed the intercept at all, it can only be concluded that the rate at the intercept is due to something besides hydroxide. This is unfortunate, but as will be seen later this

Table 14. Triethylamine catalyzed hydrolysis of phenyl  $\alpha$ -disulfone.<sup>a</sup>

$[\text{Et}_3\text{N}] \times 10^2$	$[\text{Et}_3\text{NH}^+] \times 10^2$	$k_h \times 10^4$	$k_{\text{Et}_3\text{N}}^{(b)}$	Intercept $\times 10^4(c)$
<u>M</u>	<u>M</u>	<u>sec<sup>-1</sup></u>	<u>M<sup>-1</sup>sec<sup>-1</sup></u>	<u>sec<sup>-1</sup></u>
6.0	6.0	19.7		
4.0	4.0	14.8		
3.0	3.0	12.3	0.027	4.8
2.0	2.0	9.1		
6.0	2.0	18.1		
4.8	1.6	15.8		
3.6	1.2	12.4	0.023	4.8
2.4	0.8	10.2		
1.2	0.4	7.6		

<sup>a</sup>Initial concentration of phenyl  $\alpha$ -disulfone  $5 \times 10^{-5}$  M. Ionic strength held at 0.1 with lithium perchlorate. Runs at 21.3° C. in 60% aqueous dioxane (v/v).

<sup>b</sup>Calculated from slope of plot of  $k_h$  versus  $[\text{Et}_3\text{N}]$ .

<sup>c</sup>Intercept at zero amine concentration.

problem can be overcome by changing to another solvent system. However, despite the fact that the intercepts cannot be used to determine  $k_{OH}$ , the slopes can be used to get  $k_{Et_3N}$  with considerable accuracy.

Dependence of Rate on Aryl Group Structure. The effect of aryl group structure was determined at  $21.3^\circ$  C. in 60% aqueous dioxane (v/v) with a 1:1 ( $Et_3N$ ):( $Et_3NH^+$ ) buffer ratio. The data for phenyl  $\alpha$ -disulfone are found in Table 14. The data for  $Ar = p\text{-CH}_3C_6H_4$ ,  $Ar = p\text{-ClC}_6H_4$ , and  $Ar = p\text{-MeOC}_6H_4$  are tabulated in Table 15. A look at this data shows that the rate of the triethylamine catalyzed hydrolysis of aryl  $\alpha$ -disulfones is markedly dependent on aryl group structure. Figure 17 shows a plot of  $k_{Et_3N}$  versus  $\sigma$ . A  $\rho$  of +4.4 is estimated from the slope of this plot. It should be noted again that both the spontaneous hydrolysis and the fluoride ion catalyzed hydrolysis had large positive  $\rho$ 's.

Deuterium Solvent Isotope Effect. The rates of the triethylamine catalyzed hydrolysis of phenyl and  $p$ -chloro  $\alpha$ -disulfone were determined in 60% dioxane - 40%  $D_2O$  in exactly the same manner as in 60% dioxane - 40%  $H_2O$ . The data for the determination in the deuterated media are given in Table 16.

The second order rate constants,  $k_{Et_3N}$ , were found to be markedly smaller in the deuterated medium for both of the aryl  $\alpha$ -disulfones studied. The solvent isotope effect ( $k_{Et_3N}^{H_2O}/k_{Et_3N}^{D_2O}$ ) was 2.0 in both cases. This indicates that a proton transfer is occurring in the rate determining step and that unlike the other catalysts

Table 15. Effect of aryl group on the triethylamine catalyzed hydrolysis of aryl  $\alpha$ -disulfones.<sup>a</sup>

ArSO <sub>2</sub> SO <sub>2</sub> Ar, Ar =	[Et <sub>3</sub> N] x 10 <sup>2</sup> , M	[Et <sub>3</sub> NH <sup>+</sup> ] x 10 <sup>2</sup> , M	k <sub>h</sub> , sec <sup>-1</sup>	k <sub>Et<sub>3</sub>N</sub> , M <sup>-1</sup> sec <sup>-1</sup> (b)
p-ClC <sub>6</sub> H <sub>4</sub>	6.0	6.0	11.58	0.17
	5.0	5.0	10.30	
	4.0	4.0	8.35	
	3.0	3.0	6.76	
	2.0	2.0	4.85	
p-MeC <sub>6</sub> H <sub>4</sub>	6.0	6.0	0.400	0.0055
	5.0	5.0	0.339	
	3.0	3.0	0.234	
	2.0	2.0	0.177	
p-MeOC <sub>6</sub> H <sub>4</sub>	6.0	6.0	0.0786	0.00105
	5.0	5.0	0.0745	
	4.0	4.0	0.0633	
	3.0	3.0	0.0481	
	2.0	2.0	0.0420	

<sup>a</sup>Initial concentration of aryl  $\alpha$ -disulfone  $5 \times 10^{-5}$  M. All runs at 21.3° C. in 60% aqueous dioxane (v/v) with the ionic strength held constant at 0.1 with lithium perchlorate.

<sup>b</sup>Calculated from the slope of a plot of k<sub>h</sub> versus [Et<sub>3</sub>N].

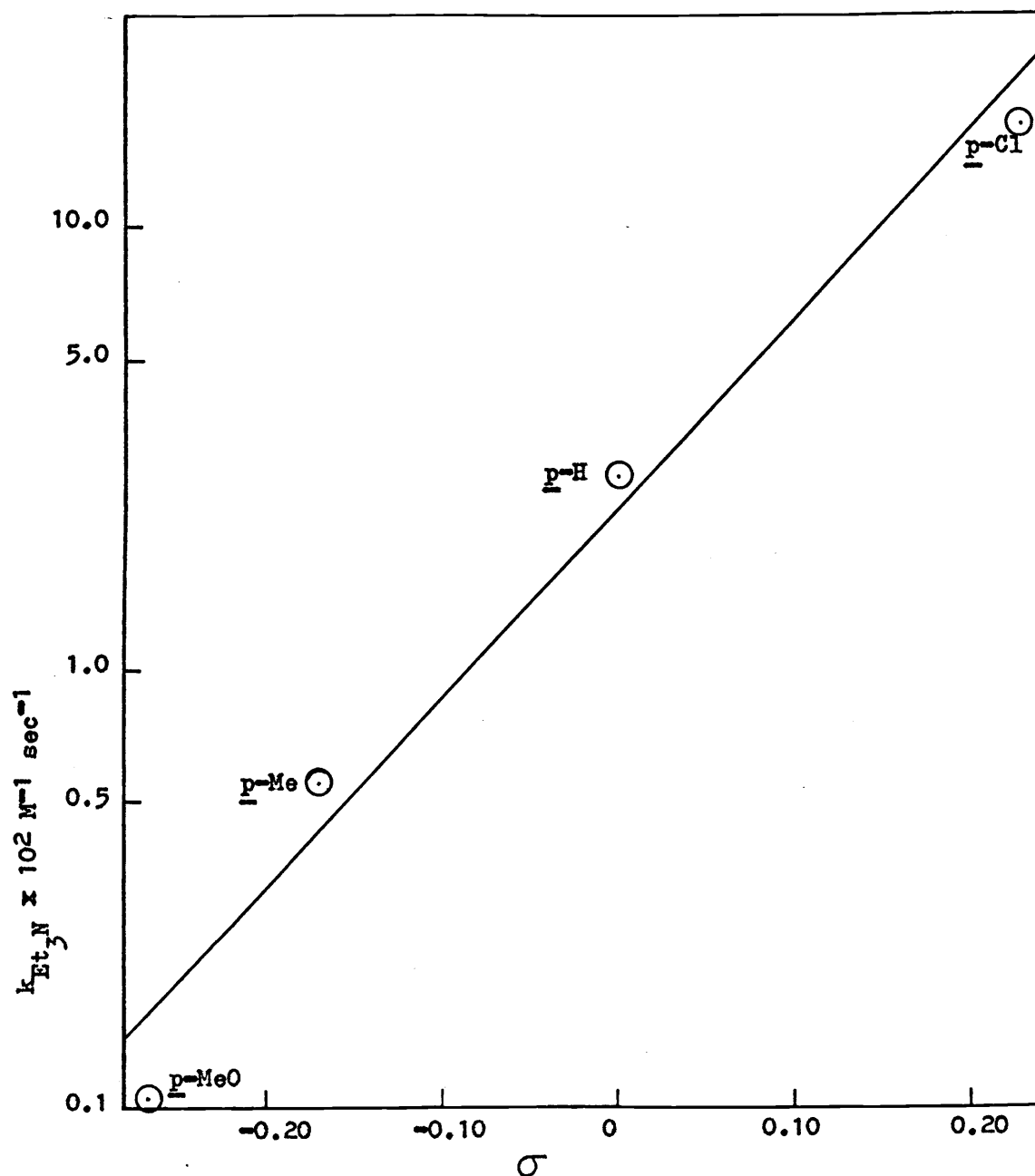


Figure 17. Effect of aryl group structure on the rate of triethylamine catalyzed hydrolysis of aryl  $\alpha$ -disulfones at 21.3° C. in 60% aqueous dioxane (v/v) with a 1:1  $[\text{Et}_3\text{N}]:[\text{Et}_3\text{NH}^+]$  buffer ratio and the ionic strength held at 0.1 with lithium perchlorate. A plot of  $k_{\text{Et}_3\text{N}}$  versus  $\sigma$ .

Table 16. Hydrolysis of aryl  $\alpha$ -disulfones in 60% dioxane-40% D<sub>2</sub>O (v/v).<sup>a</sup>

ArSO <sub>2</sub> SO <sub>2</sub> Ar, Ar =	[Et <sub>3</sub> N] x 10 <sup>2</sup> , M	[Et <sub>3</sub> NH <sup>+</sup> ] x 10 <sup>2</sup> , M	k <sub>h</sub> x 10 <sup>3</sup> , sec <sup>-1</sup>	k <sub>Et<sub>3</sub>N</sub> , M <sup>-1</sup> sec <sup>-1</sup> (b)
p-ClC <sub>6</sub> H <sub>4</sub>	6.0	6.0	5.70	0.086
	5.0	5.0	4.54	
	4.0	4.0	3.64	
	3.0	3.0	2.96	
	2.0	2.0	2.13	
C <sub>6</sub> H <sub>5</sub>	6.0	6.0	0.920	0.0134
	5.0	5.0	0.784	
	4.0	4.0	0.627	
	3.0	3.0	0.492	
	2.0	2.0	0.384	

<sup>a</sup>All runs at 21.3°C. Ionic strength held at 0.1 with lithium perchlorate. Initial concentration of aryl  $\alpha$ -disulfone 5 x 10<sup>-5</sup> M.

<sup>b</sup>Calculated from slope of plots of k<sub>h</sub> versus [Et<sub>3</sub>N].



studied, triethylamine is acting as a general base rather than as a nucleophile in catalyzing the hydrolysis of aryl  $\alpha$ -disulfones. This point will be taken up in more detail in the Discussion.

#### Kinetics of Triethylamine Catalysis in Aqueous Glyme

As noted, the intercepts at zero amine concentration in aqueous dioxane were neither very reproducible nor dependent on the  $(\text{Et}_3\text{N}):(\text{Et}_3\text{NH}^+)$  buffer ratio. A likely cause of the intercept under these conditions is catalysis by the anion of some peroxidic impurity present in the dioxane, this impurity being completely converted to the anion in a 1:1  $(\text{Et}_3\text{N}):(\text{Et}_3\text{NH}^+)$  buffer, but not converted to the anion at all in the 1:1 or 10:1  $(\text{HOAc}):(\text{AcO}^-)$  buffers used in the other work. If so, it seemed possible that the use of 60% aqueous glyme (v/v) might get around this difficulty and allow us to measure  $k_{\text{OH}}$ , since glyme is much less prone to form peroxidic impurities than dioxane.

The rate of triethylamine catalyzed hydrolysis of p-chlorophenyl  $\alpha$ -disulfone was determined at  $21.3^\circ \text{C}$ . in 60% aqueous glyme (v/v) using the same kinetic procedure previously used for such measurements in 60% aqueous dioxane. The results of this study are shown in Table 17. In this new solvent system, the intercepts at zero amine concentration are not only quite reproducible but also vary with the  $(\text{Et}_3\text{N}):(\text{Et}_3\text{NH}^+)$  buffer ratio. Figure 18 shows a plot of  $k_h$  versus  $(\text{Et}_3\text{N})$  at a 1:1 and 4:1 buffer ratio. It can be seen that the intercept increases by a factor of 4.2 while the slopes are

Table 17. Triethylamine catalyzed hydrolysis of p-chlorophenyl  $\alpha$ -disulfone in 60% aqueous glyme.<sup>a</sup>

$[\text{Et}_3\text{N}] \times 10^2$	$[\text{Et}_3\text{NH}^+] \times 10^2$	$k_h \times 10^3$	$k_{\text{Et}_3\text{N}}^{(b)}$	intercept $\times 10^4$ (c)
<u>M</u>	<u>M</u>	$\text{sec}^{-1}$	$\text{M}^{-1} \text{sec}^{-1}$	$\text{sec}^{-1}$
6.4	6.4	1.57		
4.8	4.8	1.23		
3.2	3.2	0.86	0.022	1.6
1.6	1.6	0.50		
6.40	1.60	2.44		
5.12	1.28	2.06		
3.84	0.96	1.76	0.028	6.7
2.56	0.64	1.35		
1.28	0.32	1.03		

<sup>a</sup>Initial concentration of p-chlorophenyl  $\alpha$ -disulfone  $5 \times 10^{-5}$  M. All runs at 21.3° C. with the ionic strength held constant at 0.08 with lithium perchlorate.

<sup>b</sup>Evaluated from slope of line in Figure 18.

<sup>c</sup>Intercept at zero amine concentration.

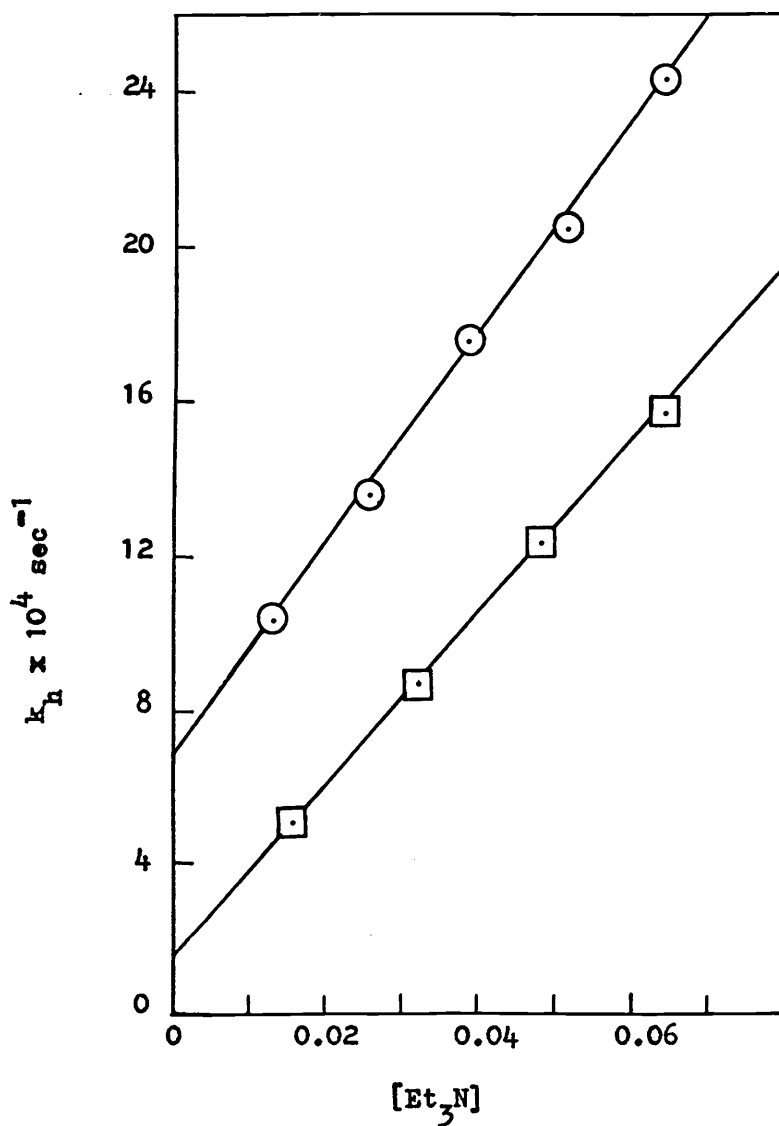


Figure 18. Triethylamine catalyzed hydrolysis of p-chloro-phenyl  $\alpha$ -disulfone in 60% aqueous glyme (v/v) at 21.3° C. Ionic strength held at 0.08 with added lithium perchlorate. Plot of  $k_h$  versus  $[\text{Et}_3\text{N}]$ .

□ = 1:1  $[\text{Et}_3\text{N}]:[\text{Et}_3\text{NH}^+]$  buffer ratio

○ = 4:1  $[\text{Et}_3\text{N}]:[\text{Et}_3\text{NH}^+]$  buffer ratio.

essentially unchanged. This is good evidence that the rate at the intercept is due to the reaction of hydroxide ion with the  $\alpha$ -disulfone. However, since the dissociation constant of triethylamine is not known in 60% glyme, the second order rate constant  $k_{OH}$  can not be calculated exactly. We shall consider how to estimate this quantity from the data in the Discussion.

Dependence of Rate on Aryl Group Structure. The variation of  $k_{Et_3N}$  with changes in the structure of the aryl group was investigated at 21.3° C. in 60% aqueous glyme (v/v) using phenyl  $\alpha$ -disulfone, p-tolyl  $\alpha$ -disulfone, and p-methoxyphenyl  $\alpha$ -disulfone. The data for these aryl  $\alpha$ -disulfones are shown in Table 18. A plot of  $\log k_{Et_3N}$  versus  $\sigma$  for the p-substituent (Figure 19) gives a straight line with a slope  $\rho$ , of +4.8. This is quite similar to the one obtained ( $\rho = +4.4$ ) for the same compounds in 60% aqueous dioxane (v/v). Thus although the rates are about ten times slower in aqueous glyme than in aqueous dioxane, the effect of aryl group structure on the hydrolysis is about the same in both solvent systems.

Attempts to measure the kinetics of the hydroxide ion- $\alpha$ -disulfone reaction directly failed because this reaction was too fast to study by the methods being used, i.e. the reaction of a solution of  $5 \times 10^{-5}$  M p-methoxyphenyl  $\alpha$ -disulfone with 0.05 M NaOH appeared to be instantaneous at 21.3° C. However, since the intercepts at zero amine concentration of the plots of  $k_h$  versus  $(Et_3N)$  (Tables 17 and 18) have been shown to be due to hydroxide ion catalysis, one can get a measure of the effect of aryl group structure on the rate of the

Table 18. Triethylamine catalyzed hydrolysis of aryl  $\alpha$ -disulfones in 60% aqueous glyme (v/v).<sup>a</sup>

$\text{ArSO}_2\text{SO}_2\text{Ar}$	$[\text{Et}_3\text{N}] \times 10^2$	$[\text{Et}_3\text{NH}^+] \times 10^2$	$k_h \times 10^4$	$k_{\text{Et}_3\text{N}} \times 10^3(\text{b})$	Intercept $\times 10^6(\text{c})$
Ar =	<u>M</u>	<u>M</u>	$\text{sec}^{-1}$	$\text{M}^{-1}\text{sec}^{-1}$	$\text{sec}^{-1}$
$\text{C}_6\text{H}_5$	6.4	6.4	1.79	2.5	22.0
	4.8	4.8	1.49		
	3.2	3.2	1.30		
	1.6	1.6	0.59		
$\text{p-CH}_3\text{C}_6\text{H}_4$	6.4	6.4	0.367	0.44	7.4
	4.8	4.8	0.270		
	3.2	3.2	0.206		
	1.6	1.6	0.150		
$\text{p-CH}_3\text{OC}_6\text{H}_4$	6.4	6.4	0.0695	0.078	2.0
	4.8	4.8	0.0580		
	3.2	3.2	0.0456		
	1.6	1.6	0.0330		

<sup>a</sup>All runs at 21.3° C. with the ionic strength held constant at 0.08 with lithium perchlorate.

Initial concentration of aryl  $\alpha$ -disulfone  $5 \times 10^{-5}$  M.

<sup>b</sup>Calculated from slope of plot of  $k_h$  versus  $[\text{Et}_3\text{N}]$ .

<sup>c</sup>Intercept at zero amine concentration.

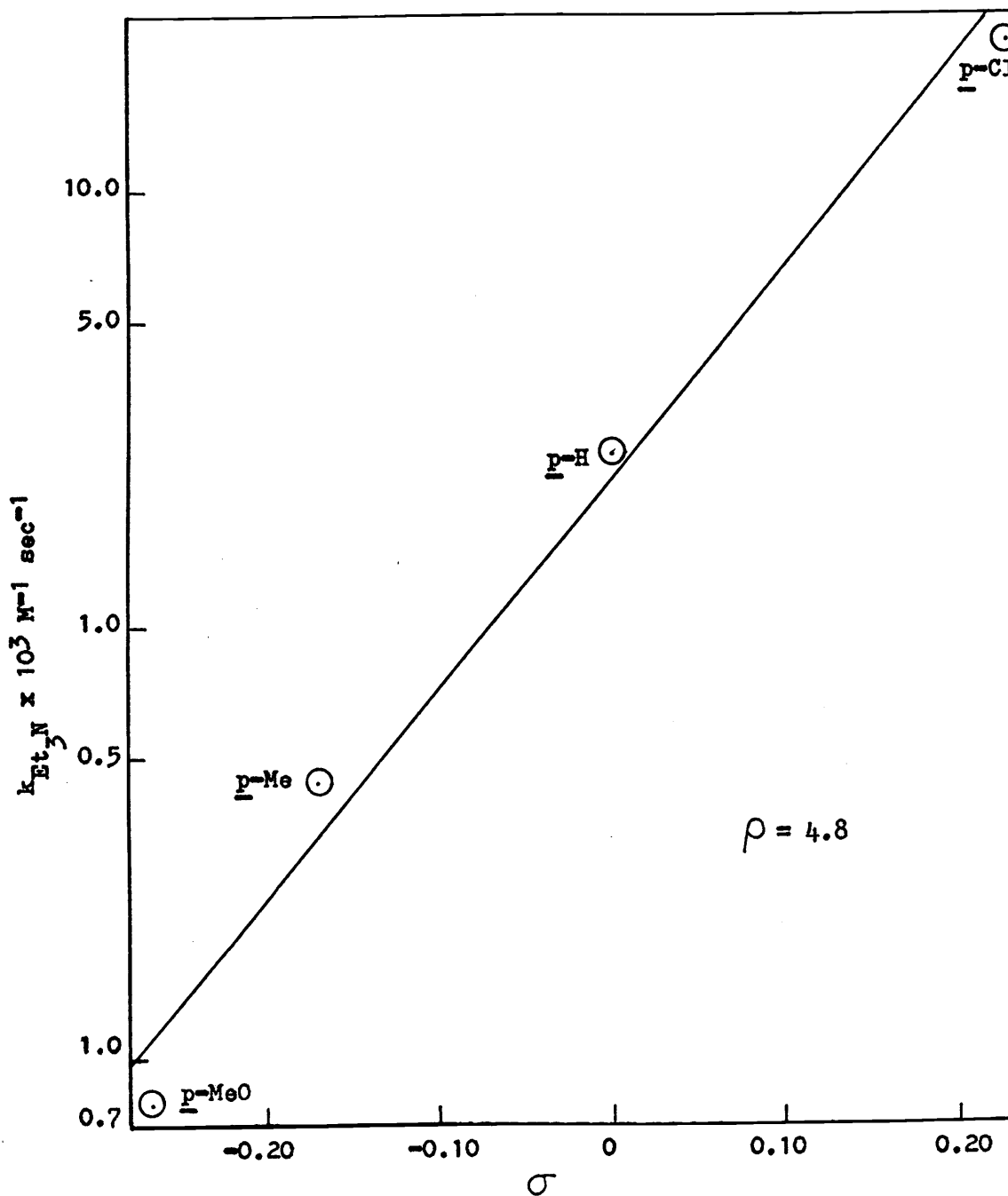


Figure 19. Effect of aryl group structure on the rates of triethylamine catalyzed hydrolysis of aryl  $\alpha$ -disulfones in 60% glyme (v/v) with a 1:1  $[\text{Et}_3\text{N}]:[\text{Et}_3\text{NH}^+]$  buffer ratio. A plot of  $k_{\text{Et}_3\text{N}}$  versus  $\sigma$ .

reaction of hydroxide with aryl  $\alpha$ -disulfones by plotting these intercepts versus  $\sigma$  for the p-substituents. Such a plot is shown in Figure 20. The slope of this plot,  $\rho$ , is +3.5. Although this value of  $\rho$  was determined in 60% aqueous glyme, one would expect its value to be quite similar in 60% aqueous dioxane just as the  $\rho$ 's for the triethylamine-catalyzed reactions were similar. Thus, the effect of aryl group structure on the hydroxide- $\alpha$ -disulfone reaction is quite large in aqueous glyme and most probably also quite large in aqueous dioxane. Actually this would be expected since both the fluoride and nitrite ion catalyzed hydrolyses of aryl  $\alpha$ -disulfones show a large effect of aryl group structure on their rate.

#### Reaction of Aryl $\alpha$ -Disulfones with Sodium Azide

The reaction of sodium azide with p-tolyl  $\alpha$ -disulfone (equation 14) was studied in 60% aqueous dioxane (v/v) at 21.3° C. so that the reactivity of the azide nucleophile towards sulfonyl sulfur could



be determined. p-Tolyl  $\alpha$ -disulfone was used rather than phenyl  $\alpha$ -disulfone because of the azide ion's absorption at the wave length maximum for the latter.

#### Stoichiometry

Reaction of sodium azide (0.0125 M) with p-tolyl  $\alpha$ -disulfone

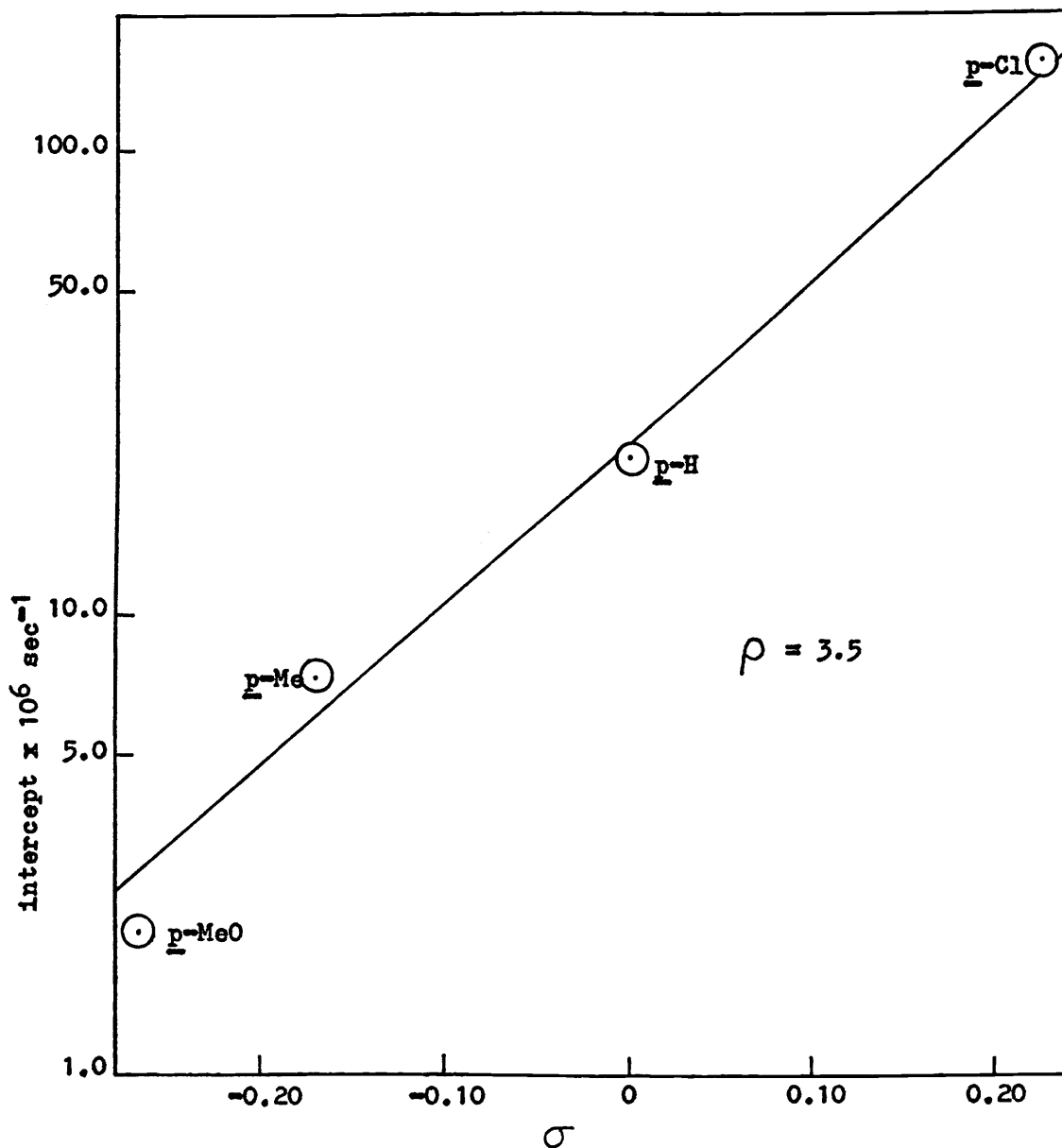


Figure 20. Effect of aryl group structure on the hydroxide ion catalyzed hydrolysis of aryl  $\alpha$ -disulfones in 60% aqueous glyme (v/v). Plot of the intercepts at zero amine concentration for the runs in 1:1  $[\text{Et}_3\text{N}]:[\text{Et}_3\text{NH}^+]$  buffer versus  $\sigma$ .



(0.005 M) in 60% aqueous dioxane (v/v) gave a 90% yield of p-toluenesulfonyl azide, indicating that the stoichiometry shown in equation 14 is correct and that the azide formed is stable under the reaction conditions. Thus this reaction differs from the previously mentioned catalyzed hydrolyses in that  $\text{ArSO}_2\text{Nu}$  is stable once it is formed.

#### Kinetics of the Azide p-Tolyl $\alpha$ -Disulfone Reaction

The kinetics of this reaction (equation 14) can be followed spectrophotometrically by the same procedure used to follow the triethylamine-catalyzed hydrolysis of aryl  $\alpha$ -disulfones. A slightly smaller overall change in absorbance is observed, due to the absorption of sodium azide and the product p-toluenesulfonyl azide. The results of such a kinetic study in 60% aqueous dioxane (v/v) at 21.3° C. are given in Table 19. A large excess of azide ion over

Table 19. Reaction of azide ion with p-tolyl  $\alpha$ -disulfone.<sup>a</sup>

$[\text{N}_3^-] \times 10^2, \text{ M}$	$k_1 \times 10^3, \text{ sec}^{-1}(\text{b})$	$k_{\text{N}_3}, \text{ M}^{-1} \text{ sec}^{-1}(\text{c})$
2.0	2.24	
1.6	1.96	
1.2	1.41	0.115
0.80	0.97	
0.40	0.47	

<sup>a</sup>Initial concentration of p-tolyl  $\alpha$ -disulfone  $7 \times 10^{-5}$  M. All runs at 21.3° C. in 60% aqueous dioxane (v/v) with ionic strength maintained at 0.04 by addition of lithium perchlorate.

<sup>b</sup>Experimental first order rate constant for disappearance of p-tolyl  $\alpha$ -disulfone. <sup>c</sup>Evaluated from slope of Figure 21.

p-tolyl  $\alpha$ -disulfone was employed so that the disappearance of p-tolyl  $\alpha$ -disulfone followed first order kinetics. Figure 21 shows a plot of  $k_1$ , the experimental first order rate constant, versus  $(N_3^-)$ . From its slope,  $k_{N_3^-}$ , the second order rate constant due to azide for p-tolyl  $\alpha$ -disulfone is found to be  $0.114 \text{ M}^{-1} \text{ sec}^{-1}$  at  $21.3^\circ \text{ C}$ .

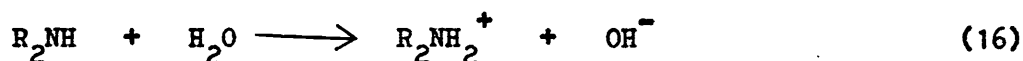
#### Reactions of $\alpha$ -Disulfones with Primary and Secondary Amines

Primary and secondary amines are known (4) to react with aryl  $\alpha$ -disulfones to give sulfonamides (equation 15). In neutral or



weakly alkaline 60% dioxane, the sulfonamides do not themselves hydrolyze at an appreciable rate.

Although one might think that the hydroxide ion formed by the ionization of amine in this medium (equation 16) would be able to



compete with the amine for the  $\alpha$ -disulfone, this is not the case.

With the possible exception of t-butylamine, the primary and secondary n-alkylamines are sufficiently reactive that in a 1:1 amine:alkylammonium salt buffer containing 0.01 M or more amine, the reaction with amine (equation 15) is the only process of importance.

#### Reaction with n-Butylamine, Diethylamine, and iso-Butylamine

These amines react with aryl  $\alpha$ -disulfones to form sulfonamides

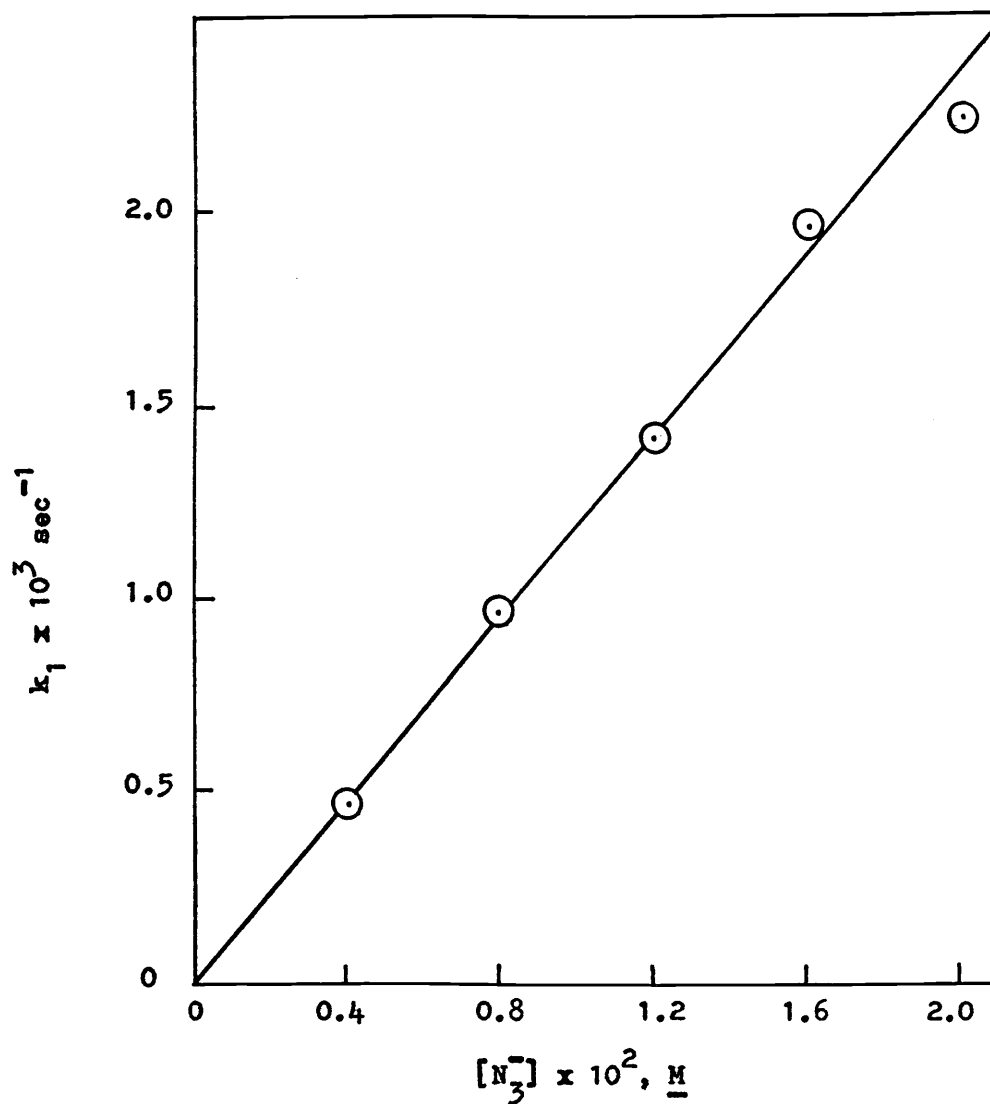


Figure 21. Rate of reaction of azide ion with p-tolyl  $\alpha$ -disulfone in 60% aqueous dioxane (v/v) at 21.3 ° C. Plot of  $k_1$  for the disappearance of p-tolyl  $\alpha$ -disulfone versus  $[N_3^-]$ . All runs at an ionic strength of 0.04

as shown in equation 15. They are so reactive that in a 1:1 amine: alkylammonium salt buffer containing 0.01 M or more amine, no reaction but that shown in equation 15 can be detected.

Kinetics of the Reaction of *n*-Butylamine, Diethylamine, and iso-Butylamine with *p*-Tolyl  $\alpha$ -Disulfone. The kinetics of this reaction can be followed spectrophotometrically in the same general way as used for the reaction of *p*-tolyl  $\alpha$ -disulfone with azide ion. All these reactions of *p*-tolyl  $\alpha$ -disulfone with amine were studied under conditions where the amine was present in at least a 100 fold excess over the  $\alpha$ -disulfone, so that the disappearance of the  $\alpha$ -disulfone followed first order kinetics. The results are summarized in Table 20. Plots of the experimental first order rate constants for the disappearance of *p*-tolyl  $\alpha$ -disulfone,  $k_1$ , versus (amine) were linear for all the amines. The slope of the plot of  $k_1$  versus (amine),  $k_{\text{amine}}$ , is in each case equal to the second order rate constant for the attack of an amine at the sulfonyl sulfur of an aryl  $\alpha$ -disulfone.

#### Reaction with *t*-Butylamine

The reaction of *t*-butylamine with aryl  $\alpha$ -disulfones was investigated in 60% aqueous dioxane (v/v) at 21.3° C. It was found to be reasonably reactive, but not as much as the other primary and secondary amines investigated.

Kinetics of the *t*-Butylamine Aryl  $\alpha$ -Disulfone Reaction. The kinetics of the reaction of *t*-butylamine with *p*-tolyl  $\alpha$ -disulfone were measured at 21.3° C. in 60% aqueous dioxane (v/v) by the same procedure used to follow the reaction of azide ion with aryl  $\alpha$ -

Table 20. Reaction of primary and secondary amines with p-tolyl  $\alpha$ -disulfone in 60% aqueous dioxane at 21.3° C.<sup>a</sup>

Amine	[amine] x 10 <sup>2(b)</sup> <u>M</u>	[amine-H <sup>+</sup> ] x 10 <sup>2</sup> <u>M</u>	k <sub>1</sub> x 10 <sup>3(c)</sup> sec <sup>-1</sup>	k <sub>amine</sub> (d) M <sup>-1</sup> sec <sup>-1</sup>
n-Butylamine	2.4 2.0 1.6 1.2 0.8	2.4 2.0 1.6 1.2 0.8	79 67 48 37 26	3.3
Diethylamine	4.0 3.6 2.8 2.0 0.8	4.0 3.6 2.8 2.0 0.8	10.2 8.6 6.9 5.1 2.2	0.24
iso-Butylamine	3.2 2.8 2.0 0.8	3.2 2.8 2.0 0.8	51 45 33 13.2	1.6

<sup>a</sup>Ionic strength maintained at 0.04 in all runs by the addition of lithium perchlorate.

Initial concentration of p-tolyl  $\alpha$ -disulfone 5 x 10<sup>-5</sup> M.

<sup>b</sup>Solution prepared by adding calculated amount of HCl to solution of the amine.

<sup>c</sup>Experimental first order rate constant for the disappearance of p-tolyl  $\alpha$ -disulfone.

<sup>d</sup>Evaluated from slope of plot of k<sub>1</sub> versus [amine]. See Figure 22 for an example.

disulfones. The data for runs carried out on three consecutive days with 1:1 (t-butyl-NH<sub>2</sub>):(t-butyl-NH<sub>3</sub><sup>+</sup>) and p-tolyl  $\alpha$ -disulfone are given in Table 21. These data are plotted in Figure 22. From this figure one can see that although the plots of  $k_1$  versus (t-butyl-NH<sub>2</sub>) are linear and the slope remains constant, the intercepts at zero amine concentration increase on each successive day. Since the aqueous amine solution was made up fresh each day, the cause of this increasing intercept must be in the dioxane  $\alpha$ -disulfone solution. This impurity in the dioxane was most probably a peroxide of some sort because the t-butylamine  $\alpha$ -disulfone reaction was run with freshly distilled dioxane and then run again after bubbling air through the dioxane for five minutes. The rates were essentially the same. However, 24 hours later, while the rate in the freshly distilled dioxane increased only a little (see Figure 22), the reaction was too fast to measure with the dioxane that had previously had the air bubbled through it. It should be pointed out that this phenomenon occurs only in basic solution, and that the slopes of the plots of  $k_1$  versus (amine) are not effected. Since the intercepts do change, no attempt was made to correlate them with anything.

#### Effect of Aryl Group Structure on the t-Butylamine Aryl

$\alpha$ -Disulfone Reaction. The effect of aryl group structure on the t-butylamine aryl  $\alpha$ -disulfone reaction was determined in 60% aqueous dioxane (v/v) at 21.3° C. The results for p-tolyl  $\alpha$ -disulfone are given in Table 21 and those for p-chlorophenyl  $\alpha$ -disulfone, phenyl  $\alpha$ -disulfone, and p-methoxyphenyl  $\alpha$ -disulfone are found in Table 22.

Table 21. Kinetics of the t-butylamine p-tolyl  $\alpha$ -disulfone reaction at 21.3° C. as a function of time.<sup>a</sup>

Time (days) <sup>(b)</sup>	[ <u>t</u> -butyl-NH <sub>2</sub> ] <sup>(c)</sup> <u>M</u>	[ <u>t</u> -butyl-NH <sub>3</sub> <sup>+</sup> ] <u>M</u>	k <sub>1</sub> x 10 <sup>3(d)</sup> sec <sup>-1</sup>	k <sub><u>t</u>-butyl-NH<sub>2</sub></sub> <sup>(e)</sup> M <sup>-1</sup> sec <sup>-1</sup>
0	0.40 0.32 0.24 0.16 0.08	0.40 0.32 0.24 0.16 0.08	3.04 2.54 1.93 1.63 0.93	0.0066
1	0.40 0.32 0.24 0.16	0.40 0.32 0.24 0.16	3.77 3.27 2.59 2.24	0.0066
2	0.40 0.32 0.16 0.08	0.40 0.32 0.16 0.08	4.66 4.30 3.21 2.41	0.0066

<sup>a</sup>All runs in 60% aqueous dioxane (v/v). Initial concentration of p-tolyl  $\alpha$ -disulfone  $5 \times 10^{-5}$  M. Ionic strength held at 0.4 with lithium perchlorate.

<sup>b</sup>A fresh dioxane  $\alpha$ -disulfone solution was made up on day 0 and used again on day 1 and 2.

<sup>c</sup>Solution prepared by adding calculated amount of HClO<sub>4</sub> to solution of the amine.

<sup>d</sup>Experimental first order rate constant for the disappearance of p-tolyl  $\alpha$ -disulfone.

<sup>e</sup>Calculated from the slope of Figure 22.

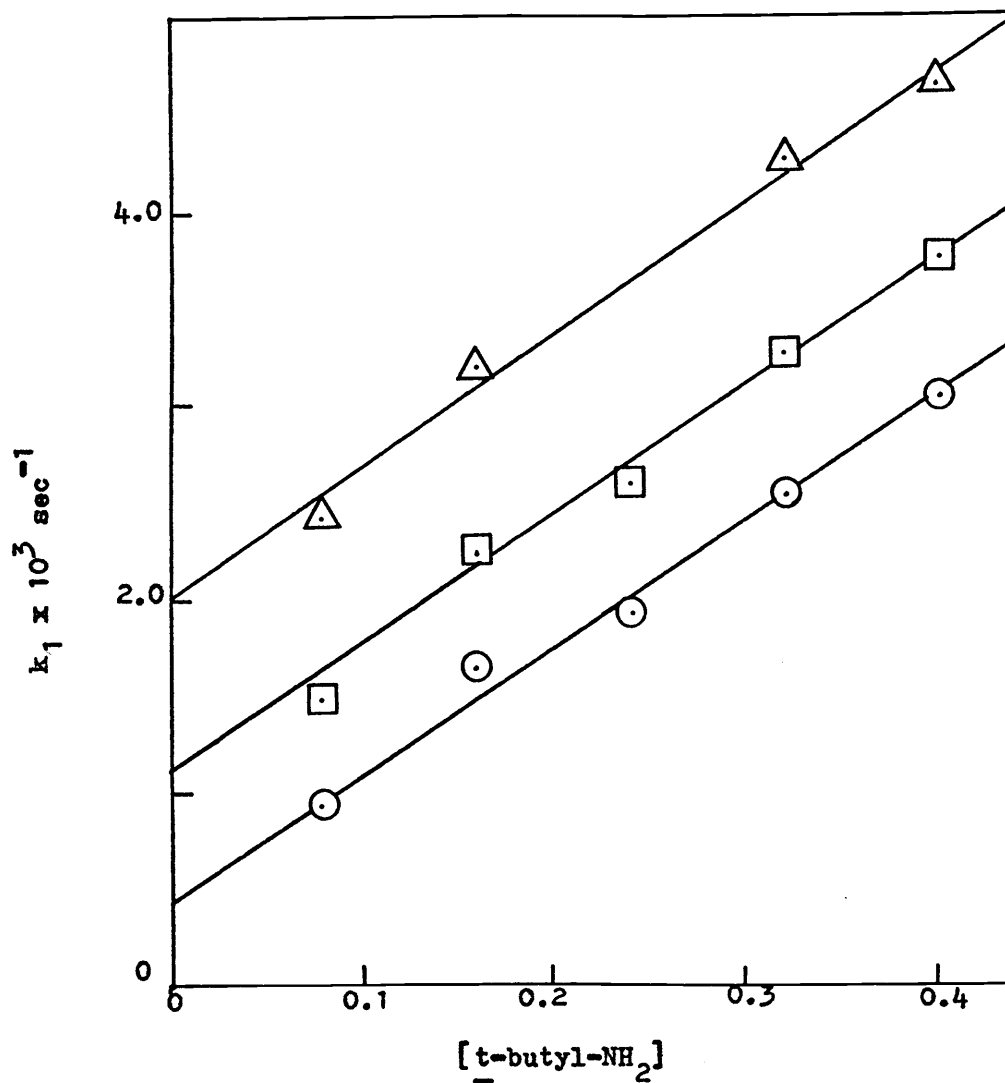


Figure 22. Rate of reaction of  $t\text{-butylamine}$  with  $p\text{-tolyl } \alpha\text{-disulfone}$  in 60% aqueous dioxane (v/v) at  $21.3^\circ \text{C}$ . For runs on three consecutive days.

○ = Day 0,    □ = Day 1,    △ = Day 2



Table 22. Effect of aryl group structure on the t-butylamine aryl  $\alpha$ -disulfone reaction.<sup>a</sup>

ArSO <sub>2</sub> SO <sub>2</sub> Ar	[ <u>t</u> -butyl-NH <sub>2</sub> ] <sup>(b)</sup>	[ <u>t</u> -butyl-NH <sub>3</sub> <sup>+</sup> ]	k <sub>1</sub> x 10 <sup>3(c)</sup>	k <sub><u>t</u>-butyl-NH<sub>2</sub></sub> <sup>(d)</sup>
Ar =	<u>M</u>	<u>M</u>	sec <sup>-1</sup>	M <sup>-1</sup> sec <sup>-1</sup>
<u>p</u> -ClC <sub>6</sub> H <sub>4</sub>	0.080	0.080	32.7	0.335
	0.064	0.064	28.5	
	0.048	0.048	22.1	
	0.032	0.032	16.5	
	0.016	0.016	11.9	
	0.0064	0.0064	8.1	
C <sub>6</sub> H <sub>5</sub>	0.40	0.40	14.51	0.033
	0.32	0.32	12.21	
	0.16	0.16	6.97	
	0.08	0.08	4.31	
<u>p</u> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	0.40	0.40	0.730	0.0012
	0.32	0.32	0.645	
	0.16	0.16	0.475	
	0.08	0.08	0.366	

<sup>a</sup>All reactions in 60% aqueous dioxane (v/v) at 21.3° C. Initial concentration of aryl  $\alpha$ -disulfone 5 x 10<sup>-5</sup> M. Ionic strength held at 0.4 with lithium perchlorate.

<sup>b</sup>Solution prepared by adding calculated amount of HClO<sub>4</sub> to the solution of amine.

<sup>c</sup>Experimental first order rate constant for the disappearance of aryl  $\alpha$ -disulfone.

<sup>d</sup>Evaluated from the slopes of plots of k<sub>1</sub> versus [t-butyl-NH<sub>2</sub>].

The second order rate constants,  $k_{\text{t-butyl-NH}_2}$ , were calculated from the slopes of plots of  $k_1$  versus  $(\text{t-butyl-NH}_2)$ . If these second order rate constants are plotted versus  $\sigma$  for the para substituents on the aromatic ring (Figure 23), a slope,  $\rho$ , of +5.0 is obtained. This  $\rho$  is about the same size as those found for substitution of other nucleophiles at the sulfonyl sulfur of aryl  $\alpha$ -disulfones.

#### Solvolysis of Aryl $\alpha$ -Disulfones in Strong Acid

As discussed at the beginning of the Results section, no acid catalysis of the rate of hydrolysis of aryl  $\alpha$ -disulfones could be detected in aqueous dioxane. (One will recall that the rate of hydrolysis was virtually the same in aqueous dioxane containing 0.001 M  $\text{HClO}_4$  as it was when 2.0 M  $\text{HClO}_4$  was used.) However, in going to acetic acid - 0.56 M water containing sulfuric acid, a much more acidic medium, acid catalysis was detectable.

#### Kinetics of the Solvolysis of Aryl $\alpha$ -Disulfones in Acetic Acid

p-Chlorophenyl  $\alpha$ -disulfone and p-tolyl  $\alpha$ -disulfone were solvolyzed at 80.3° C. in acetic acid - 0.56 M water containing varying amounts of sulfuric acid. The kinetic procedure was quite simple and involved mixing the appropriate solutions and taking aliquots at various time intervals.

The first order rate constants,  $k_s$ , for these solvolyses were determined by plotting the logarithm of  $A - A_\infty$  versus time, just as

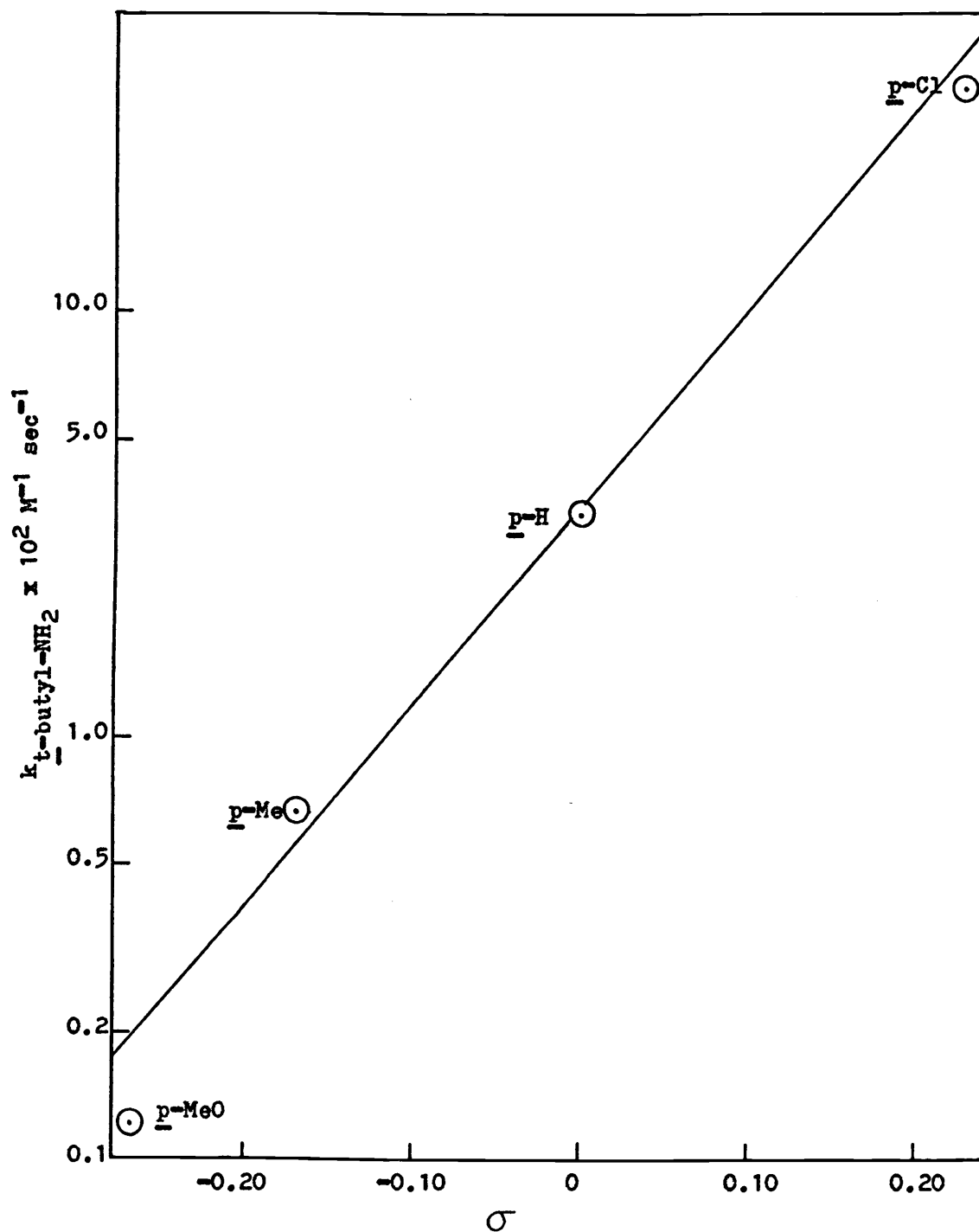


Figure 23. Effect of aryl group structure on the *t*-butylamine aryl  $\alpha$ -disulfone reaction at 21.3° C. in 60% aqueous dioxane (v/v). A plot of  $k_{t\text{-butyl-NH}_2}$  versus  $\sigma$ .

for the spontaneous hydrolysis of the aryl  $\alpha$ -disulfones. These plots showed excellent linearity in all cases. The results of these studies are found in Table 23. Although the rates of disappearance of these  $\alpha$ -disulfones in acetic acid were much slower than in aqueous dioxane, acid catalysis was easily detected. Figure 24 shows a plot of  $-H_o$  versus the logarithm of  $k_s$ . From this Figure it can be seen that p-tolyl  $\alpha$ -disulfone, the more stable in aqueous dioxane, showed a greater acidity dependence than did p-chlorophenyl  $\alpha$ -disulfone.

The deuterium solvent isotope effect was also determined for the solvolysis of p-tolyl  $\alpha$ -disulfone in DOAc - 1% water. At 80.3° C. in DOAc containing 0.56 M  $D_2O$  and 1.0 M  $D_2SO_4$ , the rate,  $k_s$ , was  $17.7 \times 10^7 \text{ sec}^{-1}$ . This compares to a rate of  $24.6 \times 10^7 \text{ sec}^{-1}$  for the solvolysis of the same compound under the same conditions in a protium solvent. This gives a solvent isotope effect ( $k_{H_2O}/k_{D_2O}$ ) of 1.45. This is not a large deuterium solvent isotope effect but does tend to indicate that a proton transfer is involved in the rate determining step.

Table 23. Dependence of the rate of solvolysis of p-chlorophenyl and p-tolyl  $\alpha$ -disulfone on acidity in acetic acid.<sup>a</sup>

ArSO <sub>2</sub> SO <sub>2</sub> Ar, Ar =	[H <sub>2</sub> SO <sub>4</sub> ], M	k <sub>s</sub> x 10 <sup>7</sup> , sec <sup>-1</sup>
<u>p</u> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	1.00	24.6
	0.80	15.5
	0.48	6.1
	0.20	1.12
	0.10	0.82
	1.00 (D <sub>2</sub> SO <sub>4</sub> )	17.0 <sup>(b)</sup>
<u>p</u> -ClC <sub>6</sub> H <sub>4</sub>	1.00	12.8
	0.75	10.0
	0.50	8.0
	0.25	4.7

<sup>a</sup>Initial concentration of aryl  $\alpha$ -disulfone  $5 \times 10^{-5}$  M. All reactions ran in acetic acid-0.56 M in H<sub>2</sub>O at 80.3°C.

<sup>b</sup>This reaction was run in DOAc-0.56 M in D<sub>2</sub>O.

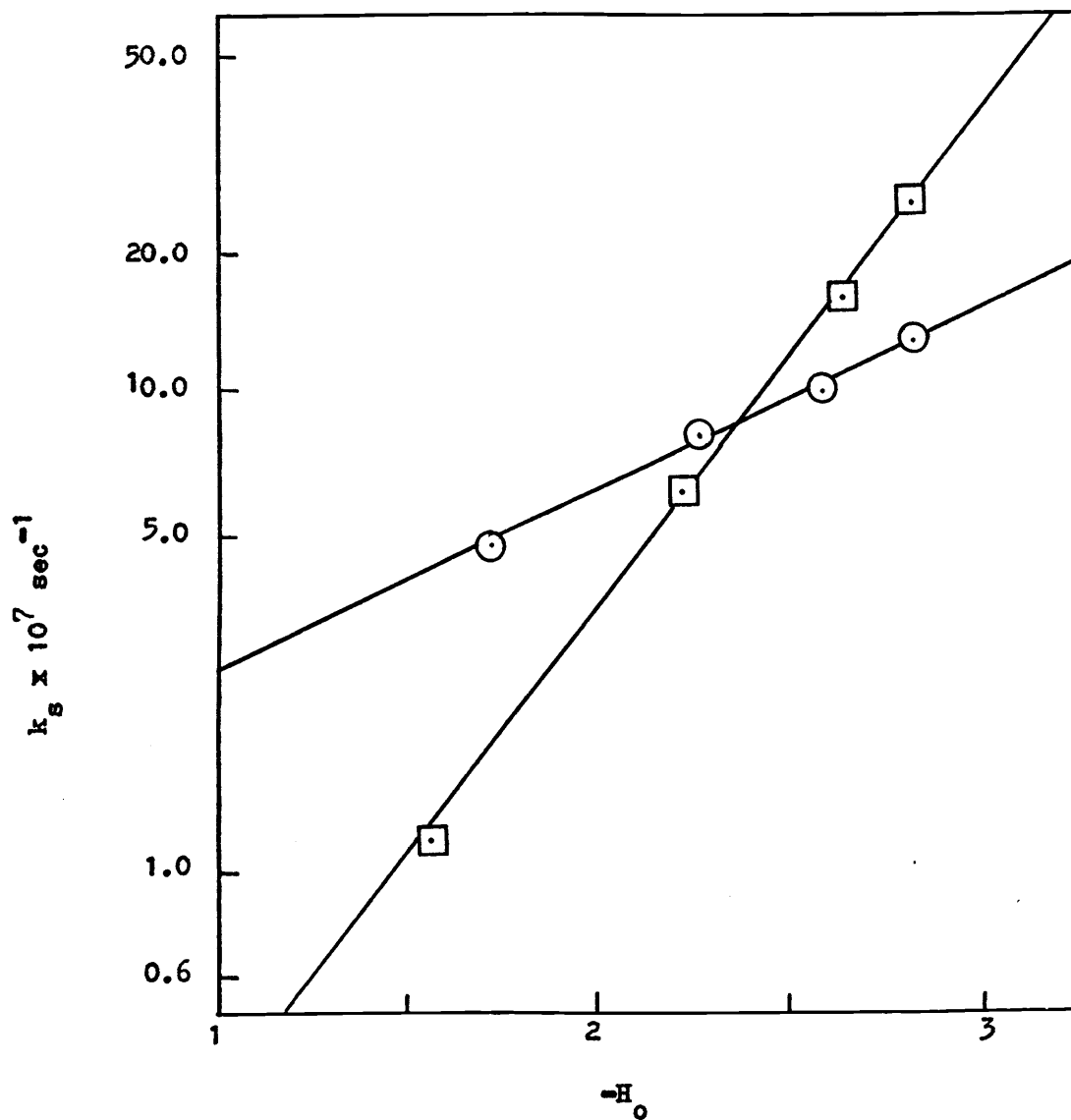


Figure 24. Dependence of solvolysis rate ( $k_s$ ) of aryl  $\alpha$ -disulfones on acidity ( $-H_0$ ) in acetic acid - 0.56 M water.

○ = p-Chlorophenyl  $\alpha$ -disulfone

□ = p-Tolyl  $\alpha$ -disulfone

## DISCUSSION

Spontaneous Hydrolysis of Aryl  $\alpha$ -Disulfones

This section of the discussion will be divided into three parts. The first of these will deal with a quantitative comparison of nucleophilic substitutions at sulfinyl ( $>\text{S}=\text{O}$ ) and sulfonyl sulfur ( $>\text{SO}_2$ ). The data on the spontaneous hydrolysis of aryl  $\alpha$ -disulfones (equation 7) and aryl sulfinyl sulfones (39) (equation 8) will be used in making this comparison. The second section will discuss the possible mechanisms of spontaneous hydrolysis of aryl  $\alpha$ -disulfones and present the most probable one. The third section will examine the effect of a change in the leaving group on the spontaneous hydrolysis of sulfonyl derivatives in aqueous dioxane by comparing the data for aryl  $\alpha$ -disulfones with those for aryl sulfonic anhydrides (11, 12), and aryl sulfonyl chlorides (24, 50, 56).

Comparison of Substitution at Sulfonyl and Sulfinyl Sulfur

Table 24 contains a tabular summary of the pertinent data on the spontaneous hydrolyses of aryl  $\alpha$ -disulfones and aryl sulfinyl sulfones. Examination of this table reveals that these two reactions show a very similar response to most reaction variables, despite the fact that substitution at sulfinyl sulfur (hydrolysis of the sulfinyl sulfones) occurs much faster than the substitution at sulfonyl sulfur (hydrolysis of the  $\alpha$ -disulfones). In particular, the two reactions show about the same dependence of rate on aryl group structure

Table 24. Comparison of spontaneous hydrolysis of aryl  $\alpha$ -disulfones and aryl sulfinyl sulfones in aqueous dioxane.

Reaction Variable	Spontaneous Hydrolysis of	
	$\text{ArSO}_2\text{SO}_2\text{Ar}$	$\text{ArS(O)SO}_2\text{Ar}^{(a)}$
$(k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}})$ in 60% dioxane <sup>(b)</sup>	2.3	2.7
Solvent Composition <sup>(b)</sup> (relative rate)		
40% dioxane	4.9	6.1
50% dioxane	2.6	3.1
60% dioxane	(1.0)	(1.0)
70% dioxane	0.44	0.33
Aryl Group (relative rate) <sup>(c)</sup>		
$\text{p-CH}_3\text{OC}_6\text{H}_4$	0.084	0.13
$\text{p-CH}_3\text{C}_6\text{H}_4$	0.29	0.31
$\text{C}_6\text{H}_5$	(1.0)	(1.0)
$\text{p-ClC}_6\text{H}_4$	5.5	6.7
$\rho$	+3.5	+3.4
Rates and Activation Parameters for $\text{Ar} = \text{C}_6\text{H}_5$ in 60% Dioxane		
Rate constant at 21.4° C.	$1.5 \times 10^{-6} \text{ sec}^{-1}$	$1.6 \times 10^{-2} \text{ sec}^{-1}$
$E_a \neq$	14.6 kcal	8.8 kcal <sup>(d)</sup>
$\Delta S^\ddagger$	-37.7 e.u.	-37.1 e.u. <sup>(d)</sup>

<sup>a</sup>Data from reference 39.

<sup>b</sup>Data for  $\text{C}_6\text{H}_5\text{SO}_2\text{SO}_2\text{C}_6\text{H}_5$  at 80.3° C.; those for  $\text{p-CH}_3\text{C}_6\text{H}_5\text{S(O)SO}_2\text{-p-CH}_3\text{C}_6\text{H}_5$  at 21.4° C.

<sup>c</sup>Data for both in 60% dioxane; at 80.3° C. for the  $\alpha$ -disulfone and 21.4° C. for the sulfinyl sulfone.

<sup>d</sup>Activation parameters for  $\text{C}_6\text{H}_5\text{S(O)SO}_2\text{C}_6\text{H}_5$  estimated from those for  $\text{p-CH}_3\text{C}_6\text{H}_4\text{S(O)SO}_2\text{-p-CH}_3\text{C}_6\text{H}_5$  ( $E_a = 9.4 \text{ kcal}$ ,  $\Delta S^\ddagger = -37.1 \text{ e.u.}$ ) by assuming all  $k_{\text{p-H}}/k_{\text{p-CH}_3}$  due to difference in  $E_a$ .



( $\rho = +3.5$  for the hydrolysis of the  $\alpha$ -disulfones and  $+3.4$  for the hydrolysis of the sulfinyl sulfones), almost identical large negative entropies of activation ( $-37.1$  and  $-37.7$  e.u.) in 60% dioxane, and approximately the same increase in rate with an increase in the water content of the solvent. In 60% aqueous dioxane, both are subject to quite large solvent isotope effects,  $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}}$  being 2.7 for the hydrolysis of the sulfinyl sulfones and only somewhat smaller, 2.3, for the hydrolysis of the  $\alpha$ -disulfones. The only truly significant differences between the two reactions are that the rate of spontaneous hydrolysis of the  $\alpha$ -disulfones is about 10,000 times slower than the rate of spontaneous hydrolysis of the sulfinyl sulfones. This large difference in hydrolysis rate arises solely from the fact that the activation energy for the hydrolysis of  $\alpha$ -disulfones is about 6 kcal/mole larger than that for the sulfinyl sulfones.

From these facts one concludes that analogous nucleophilic substitutions at sulfonyl and sulfinyl sulfur probably do not differ at all significantly with regards to their detailed mechanism. Nucleophilic substitution at sulfonyl sulfur is merely much slower because the process has a significantly higher activation energy.

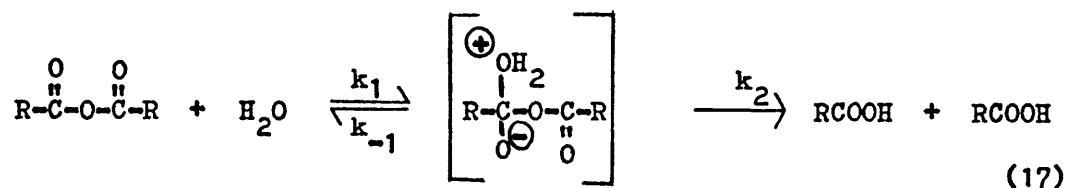
When water is the attacking nucleophile, substitution at sulfonyl sulfur (equation 7) is slower by a factor of  $10^4$  than substitution at sulfinyl sulfur (equation 8). The question arises as to whether the same difference in rates of substitution at  $>\text{SO}_2$  and  $>\text{SO}$  will be observed when other nucleophiles are the attacking agents. The nucleophile catalyzed hydrolysis of aryl  $\alpha$ -disulfones (equation 10) has also been studied, and although this hydrolysis will be discussed

later, a few pertinent points brought out now will serve to answer the questions raised above. If the rates of the nucleophile-catalyzed hydrolyses of the  $\alpha$ -disulfones are compared to the rates (27) for attack of the same nucleophiles on the sulfinyl sulfones (equation 9), the relative nucleophilicity of these nucleophiles towards sulfinyl versus sulfonyl sulfur can be obtained. Such a comparison reveals that for acetate ion, which is an oxygen nucleophile like water,  $k_{\text{Nu}}^{\text{SO}}/k_{\text{Nu}}^{\text{SO}_2}$  is also about  $10^4$ . However, with fluoride ion, which according to the Theory of Hard and Soft Acids and Bases (49) is probably a harder base than acetate or water,  $k_{\text{Nu}}^{\text{SO}}/k_{\text{Nu}}^{\text{SO}_2}$  is only about 250, and for chloride ion, a softer base than acetate or water, the same ratio is very much larger, being about  $10^7$ . Therefore, one should recognize that while, even in the most favorable cases, substitution at sulfonyl sulfur will always be much slower than substitution at sulfinyl sulfur, the exact magnitude of the rate factor will depend on the character of the attacking nucleophile. The rate ratio ( $k_{\text{Nu}}^{\text{SO}}/k_{\text{Nu}}^{\text{SO}_2}$ ) of  $10^4$  observed for substitution of water at sulfinyl and sulfonyl sulfur is thus presumably representative only of substitutions at  $>\text{S}=\text{O}$  and  $>\text{SO}_2$  involving nucleophiles of a hardness comparable to water, acetate, etc. With nucleophiles which are softer bases ( $k^{\text{SO}}/k^{\text{SO}_2}$ ) will be much larger; and those which are harder bases will have a smaller ratio.

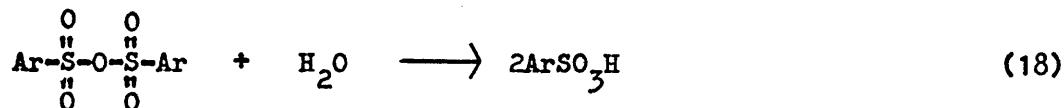
#### Mechanism of the Spontaneous Hydrolysis of Aryl $\alpha$ -Disulfones

The large solvent isotope effect ( $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} = 2.3$ ) strongly indicates that a proton transfer is involved as a part of the rate-

determining step of the spontaneous hydrolysis of aryl  $\alpha$ -disulfones. On the other hand, Bunton and Shiner (10) have presented arguments that solvent isotope effects of this magnitude for carboxylic anhydride hydrolysis could be associated with a mechanism (equation 17)



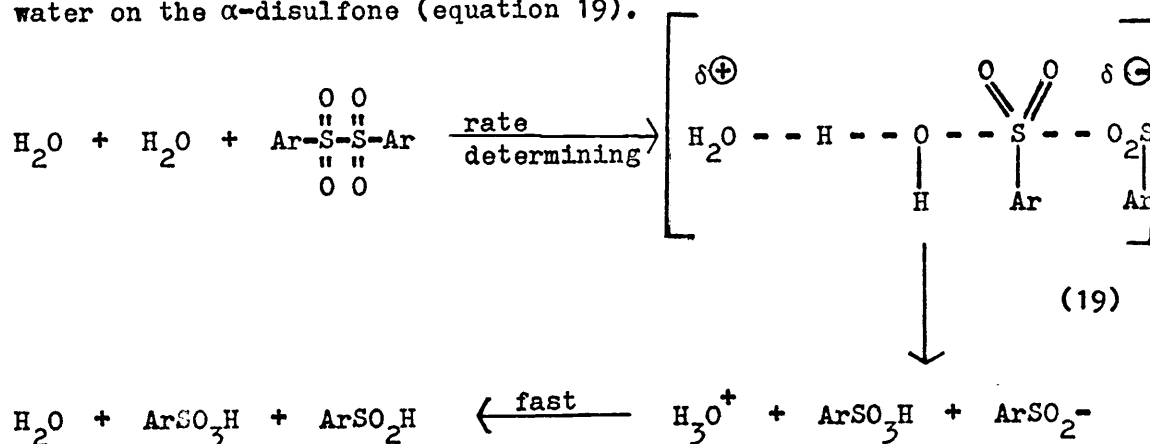
for the reaction where the rate-determining step was attack by water (step  $k_1$ ) rather than the breakdown of the intermediate (step  $k_2$ ). However, if an analogous type of mechanism were proposed to explain the hydrolysis of aryl  $\alpha$ -disulfones, it would require that the spontaneous hydrolysis of aryl sulfonic anhydrides (equation 18)



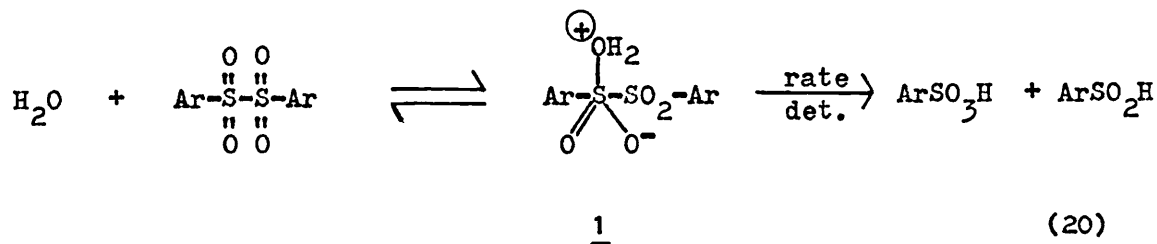
in aqueous dioxane should show a solvent isotope effect of the same magnitude as that for the  $\alpha$ -disulfones. In actual fact, the spontaneous hydrolysis of aryl sulfonic anhydrides shows only a very small solvent isotope effect under such conditions (11, 12) ( $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} = 1.2$ ). Thus the only explanation left for the large solvent isotope effect in the spontaneous hydrolysis of the aryl  $\alpha$ -disulfones is that the proton transfer is involved as part of the rate-determining step of the reaction.

At first glance there are three plausible possible mechanisms for the spontaneous hydrolysis of aryl  $\alpha$ -disulfones which incorporate a proton transfer into the rate-determining step. The first of

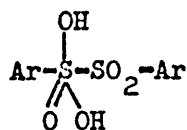
these involves general base catalysis by water on the attack of water on the  $\alpha$ -disulfone (equation 19).



The second possible mechanism (equation 20) postulated reversible formation of an intermediate 1, followed by a rate-determining step in which the scission of the S-S bond is accompanied by a transfer of one of the protons in the intermediate to the departing  $\text{ArSO}_2$  group.

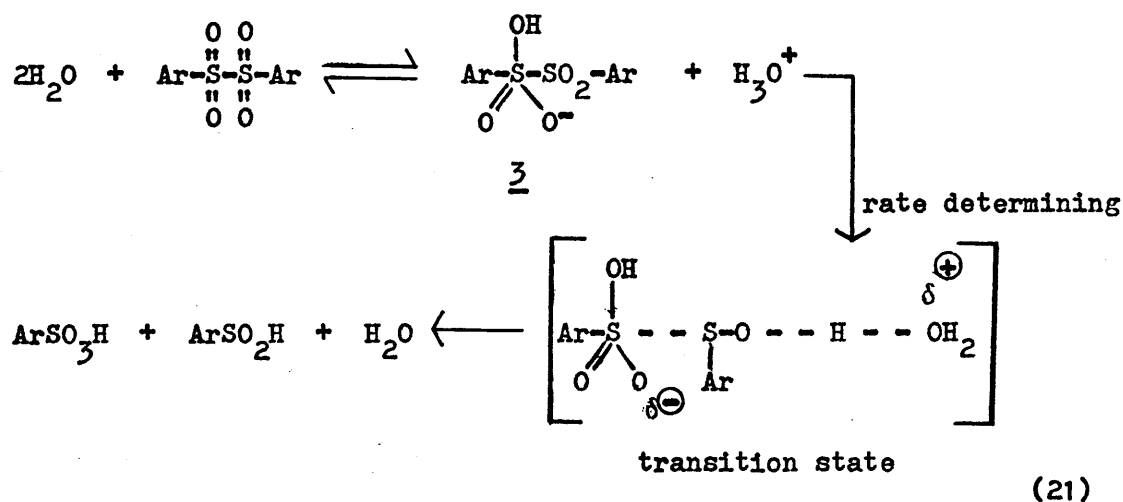


Of course the intermediate could also be pictured as having structure 2 rather than 1. The difference being that while 1 has charge separation, 2 is a neutral species.

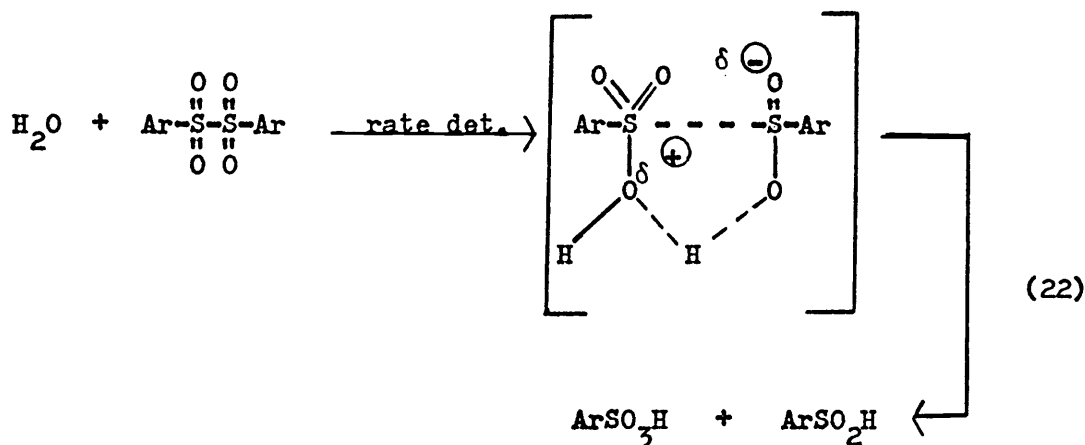


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Another alternative on this same theme would be the reversible formation of intermediate 3 and its subsequent rate-determining breakdown in the manner shown in equation 21. In the mechanism shown in equation 21 it is essential that the breakdown of 3 be rate-determining. Otherwise the mechanism is not distinguishable in any significant way from the general base catalysis by water of the attack of water as shown in equation 19.



The third possible mechanism (equation 22) once again has a proton transfer to the leaving  $\text{ArSO}_2$  group as part of the rate-determining step, but this time the formation of an intermediate such as 1, 2, or 3 is by-passed by making nucleophilic attack of water on the sulfonyl group concerted with the scission of the  $\text{S}-\text{S}^{\delta+}$  bond and transfer of a proton from the incoming water molecule ( $-\text{OH}_2$ ) to the departing  $\text{ArSO}_2$  group. It should be pointed out that this proton transfer may actually take place through a chain of water molecules. This certainly seems necessary if the entering ( $-\text{OH}_2$ ) and leaving ( $\text{ArSO}_2$ ) groups occupy apical positions of a trigonal bipyramid.



The mechanism in equation 19 is rendered unattractive by the observation that acetate ion, a considerably stronger base than water, catalyzes the hydrolysis of the aryl  $\alpha$ -disulfones by a mechanism involving nucleophilic catalysis (equation 10,  $\text{Nu} = \text{AcO}^-$ ) and not by one in which it functions as a general base. If the spontaneous hydrolysis were to have as its rate-determining step, a reaction involving general base catalysis by water on the attack of  $\text{H}_2\text{O}$  on the  $\alpha$ -disulfone, the acetate ion catalyzed hydrolysis ought to take place via general base catalysis by acetate of the attack of water on the  $\alpha$ -disulfone, which it clearly does not because it exhibits a solvent isotope effect ( $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}}$ ) of very close to unity.

This leaves only the mechanisms shown in equations 20, 21, or 22, which all involve a proton transfer to the departing  $\text{ArSO}_2$  group as part of the rate-determining step of the spontaneous hydrolysis of aryl  $\alpha$ -disulfones, as possible alternatives. Both the mechanism shown in equation 20 and the one in equation 21, involve a discrete intermediate species where one has had the addition of either water (1)

or a hydroxyl group (3) to one of the sulfone groups of the  $\alpha$ -disulfone. Such intermediates are, of course, formally analogous to the tetra-

hedral addition intermediate  $\text{R}-\overset{\text{O}^-}{\underset{\text{OH}}{\text{C}}}-\text{Y}$  whose existence has been repeat-

edly demonstrated (7, 9 pp. 22-24, 59-60, 102-103) in the mechanism of hydrolysis reactions of carboxylic acid derivatives,  $\text{RC(O)Y}$ .

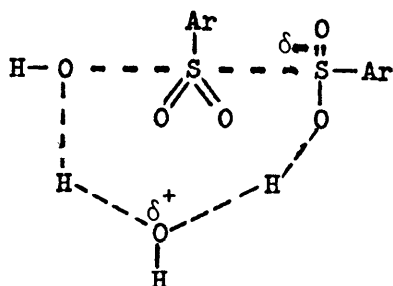
However, in the case of substitution reactions involving sulfonyl derivatives, no definite evidence for the existence of analogous intermediates exists despite experimental efforts (56, 35) to find positive evidence for such intermediates. Until such time as there is definite proof that species of the type represented by 1 or 3 are actual intermediates in the hydrolysis of sulfonyl derivatives, it is preferable to avoid writing mechanisms involving them for such reactions. For this reason, the mechanism shown in equation 22 for the spontaneous hydrolysis of aryl  $\alpha$ -disulfones is currently favored.

The mechanism (equation 22) for the spontaneous hydrolysis of  $\alpha$ -disulfones is identical, except that substitution occurs at sulfonyl rather than sulfinyl sulfur, with the one proposed by Kice and Guaraldi (39) for the spontaneous hydrolysis of aryl sulfinyl sulfones. This is in accord with the many striking similarities shown in Table 24 in the response of these two reactions to the various reaction variables.

The mechanism (equation 22) for the spontaneous hydrolysis of aryl  $\alpha$ -disulfones is also consistent with the large, negative  $\Delta S^\ddagger$ ,

because the key transition state for this mechanism is highly ordered, requiring a large negative  $\Delta S^\ddagger$ . This mechanism is also consistent with the sizeable positive  $\rho$  for the reaction. Since the sulfur atoms which are joined by the original S-S bond carry a partial positive charge and repel each other, electron-withdrawing groups on the aromatic rings tend to intensify this repulsion and cause the hydrolysis to proceed faster. Electron donating groups on the aromatic ring have the opposite effect in that they tend to alleviate the repulsion caused by the like charges on the sulfur atoms.

Since the transfer of the proton from the incoming water molecule to the departing  $\text{ArSO}_2$  group in equation 22 probably actually involves the assistance of at least one additional water molecule, i.e.

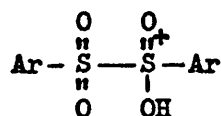


it can be thought of, in effect, as a mechanism involving both general base catalysis of the attack of water and general acid catalysis of the departure of the  $\text{ArSO}_2$  group, but with these two phenomena occurring as a concerted process. Mechanisms of this type have been observed before and were termed "one encounter" proton transfers (33). Although some people are skeptical of mechanisms of this sort, the lack of any positive evidence for intermediates



akin to 3 in the hydrolyses of sulfonyl derivatives leads one to prefer equation 22 to the equivalent "two-encounter" transfer represented by equation 21.

Finally one might ask why an acid catalyzed mechanism involving attack of water on the protonated  $\alpha$ -disulfone 4 doesn't make at least

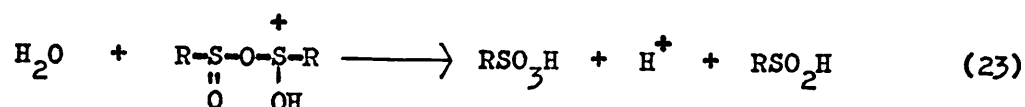


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some contribution to the overall rate of hydrolysis of the  $\alpha$ -disulfone, since proton transfer to the departing  $\text{ArSO}_2$  group is apparently important in the spontaneous hydrolysis. The reason it does not is most likely due to the fact that sulfone groups have a very low basicity (27, 3). In fact the pKa of the conjugate acid of dimethyl sulfone is -12.3. The pKa of 4 would be even more negative because of the electron withdrawing effect of the  $\text{ArSO}_2$  group. This low basicity keeps the equilibrium concentration of 4 so infinitesimal even in solutions containing 2.0 M  $\text{HClO}_4$  that a mechanism featuring attack of water on this intermediate simply cannot compete effectively with the spontaneous hydrolysis under these conditions. The same sort of phenomenon was also observed by Kice and Guaraldi (39) in the hydrolysis of aryl sulfinyl sulfones in aqueous dioxane. This explanation seems quite logical since recently Kice and Ikura (41) have shown that an acid-catalyzed term does make a significant contribution to the over all rate of hydrolysis of a true sulfinic anhydride (5) in the same solvent medium. Sulfinyl groups are much



more basic than sulfone groups. For example, the pKa of the conjugate acid of dimethyl sulfoxide is -2.7 (26), so that a given sulfinyl function is about  $10^{10}$  more basic than the corresponding sulfone group. It is this much great basicity of the sulfinyl function which allows the concentration of 6 to be large enough to allow a mechanism involving nucleophilic attack of water on 6 (equation 23) to compete



effectively with the spontaneous hydrolysis in the case of 5. The extremely low basicity of sulfone groups prevents an analogous mechanism from operating in the hydrolysis of the sulfinyl sulfones and  $\alpha$ -disulfones.

#### Comparison of the Spontaneous Hydrolysis of $\alpha$ -Disulfones and Other Sulfonyl Derivatives.

Christensen (12, 11) has recently made an extensive study of the spontaneous hydrolysis of aryl sulfonic anhydrides in aqueous dioxane and aqueous acetone. Since the only difference in the hydrolysis of  $\alpha$ -disulfones and sulfonic anhydrides is that the former has  $\text{ArSO}_2$  and the latter  $\text{ArSO}_2\text{O}$  as leaving groups, it is interesting to compare the aryl sulfonic anhydride results (Table 25) with the analogous data for the spontaneous hydrolysis of the  $\alpha$ -disulfones

Table 25. Spontaneous hydrolysis of aryl sulfonic anhydrides.<sup>a</sup>

Reaction Variable	Spontaneous Hydrolysis of $\text{ArSO}_2\text{OSO}_2\text{Ar}$
$(k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}})$ in 60% dioxane	1.25
Solvent Composition (relative rate) <sup>(b)</sup>	
40% dioxane	7.5
50% dioxane	3.0
60% dioxane	(1.0)
70% dioxane	0.35
Aryl group (relative rate) <sup>(c)</sup>	
$\text{p-CH}_3\text{OC}_6\text{H}_4$	—
$\text{p-CH}_3\text{C}_6\text{H}_4$	0.47
$\text{C}_6\text{H}_5$	(1.0)
$\text{p-ClC}_6\text{H}_4$	5.2
$\rho$ (from plot of above data plus that for $\text{m-NO}_2$ and $\text{p-Br}$ )	+ 2.5
Rates and Activation Parameters Estimated for $\text{Ar} = \text{C}_6\text{H}_5$ in 64.7% Dioxane <sup>(d)</sup> .	
Rate constant at 21.4° C.	$7.4 \times 10^{-2} \text{ sec}^{-1}$
$E_a$	12.7 kcal/mole
$\Delta S^\ddagger$	-20.4 e.u.

<sup>a</sup>Data from references (12, 11). In some cases graphical interpolation was necessary to get the specific data shown in this table.

<sup>b</sup>Data are for  $\text{Ar} = \text{p-CH}_3\text{C}_6\text{H}_4$  at 22.5° C.

<sup>c</sup>Data are for 70% acetone as a solvent at 20° C.

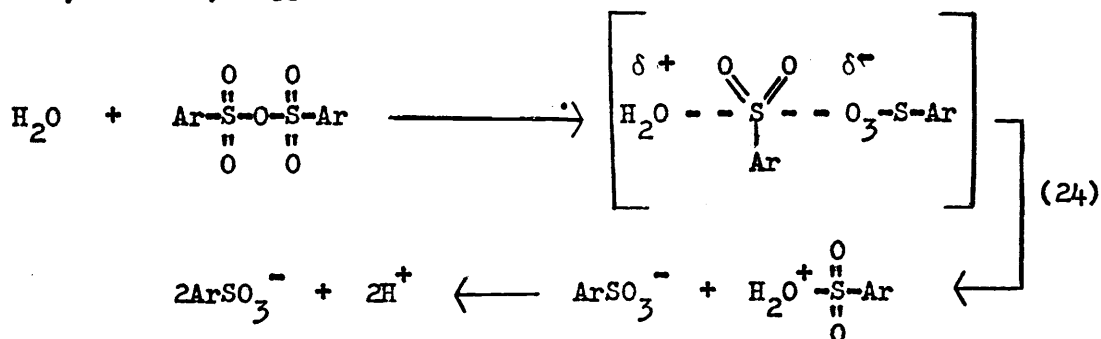
<sup>d</sup>Since actual data are available only for  $\text{Ar} = \text{p-CH}_3\text{C}_6\text{H}_4$  in this solvent, the results for  $\text{Ar} = \text{C}_6\text{H}_5$  were estimated assuming that  $k_{\text{p-H}}/k_{\text{p-CH}_3}$  is the same in this solvent as in the others and that the entire difference in  $(k_{\text{p-H}}/k_{\text{p-CH}_3})$  is due to a difference in  $E_a$ .

(first column of Table 24). On making such a comparison, one finds that  $\rho$  for the hydrolysis of the anhydride, while still positive, is somewhat smaller (+2.5) than that for the hydrolysis of the  $\alpha$ -disulfones (+3.5). One also notes that the rate of hydrolysis of sulfonic anhydride increases somewhat more rapidly with an increase in the percentage of water in the solvent than does the rate for the  $\alpha$ -disulfones. However, both these differences in behavior are really quite small. The two truly large and significant differences between the two hydrolyses are: (1) the solvent isotope effect, which is much smaller for the sulfonic anhydride than for the  $\alpha$ -disulfone; and (2) the much faster rate of hydrolysis of the sulfonic anhydride, which turns out to be due almost entirely to a more favorable  $\Delta S^\ddagger$  for that reaction than for the hydrolysis of the  $\alpha$ -disulfone.

These large differences in  $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}}$  and  $\Delta S^\ddagger$  for the two reactions most probably indicate that there are some significant differences in the detailed mechanisms for the hydrolyses of these two sulfonyl compounds. This is quite different from the results observed for the hydrolyses of the sulfinyl sulfones and  $\alpha$ -disulfones, where the much faster rate for sulfinyl sulfones resulted solely from a difference in the activation energy for the two reactions. Also both hydrolyses showed comparable solvent isotope effects, and the conclusion was that even though one reaction involved substitution at sulfinyl sulfur and the other substitution at sulfonyl sulfur, the same type of mechanism was involved in both cases. Taken together

these various results indicate that in substitution at sulfinyl and sulfonyl sulfur the nature of the leaving group is much more important in determining the mechanism than is the site at which substitution occurs.

The very small solvent isotope effect for the spontaneous hydrolysis of sulfonic anhydrides indicates that no proton transfer is involved as part of the rate-determining step. Christensen (12, 11) has, in fact, suggested a mechanism (equation 24) which consists of a



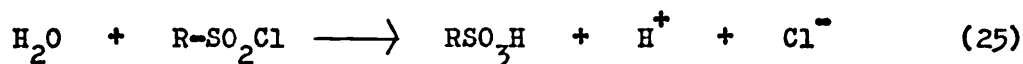
simple  $S_N2$  type displacement by water of  $\text{ArSO}_3^-$ . This mechanism seems quite reasonable and would certainly be in accord with the observed solvent isotope effect of  $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}}$  of 1.25 and with the fact that its value seems to be effectively independent of the percent dioxane in the solvent.

In comparing the mechanism for the spontaneous hydrolysis of  $\alpha$ -disulfones (equation 22) and that for sulfonic anhydrides (equation 24), one notices that when the leaving group is changed from  $\text{ArSO}_2^-$  to one like  $\text{ArSO}_3^-$ , which is the conjugate base of a much stronger acid, then (a) one no longer needs to assist the departure of the leaving group with a proton transfer of the sort shown in equation 22

and (b) one also does not need to aid the nucleophilic attack of water by removing a proton from it concurrent with the formation of the new O-S bond.

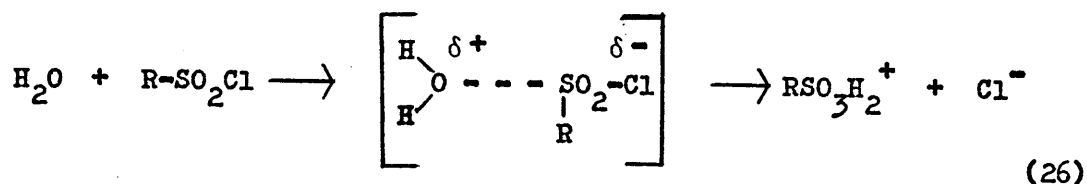
The large difference in the value of  $\Delta S^\ddagger$  for the hydrolyses of the sulfonic anhydrides, and  $\alpha$ -disulfones can also be satisfactorily rationalized in terms of the mechanistic differences between equation 22 and equation 24. Thus the concerted proton transfer from the incoming water molecule to the departed  $\text{ArSO}_2$  group shown in the mechanism in equation 22 for the spontaneous hydrolysis of the  $\alpha$ -disulfones is the type of process which should involve a highly ordered transition state and have a very large negative  $\Delta S^\ddagger$ . In contrast the mechanism for the spontaneous hydrolysis of the sulfonic anhydrides in equation 24 is merely a simple bimolecular displacement. In bimolecular displacements of this type involving two neutral molecules which react to form a pair of oppositely charged ions, one expects the value of  $\Delta S^\ddagger$  to be about -20 e.u. For example,  $\Delta S^\ddagger$  for the reaction  $\text{Et}_2\text{S} + \text{MeI} \longrightarrow \text{Et}_2\text{S}^+\text{Me} + \text{I}^-$  is about -25 e.u. (55).

If the suggestion that a proton transfer is involved in the rate-determining step of the spontaneous hydrolysis of sulfonyl derivatives only when the leaving group is a weak acid is correct, the spontaneous hydrolysis of sulfonyl chlorides (equation 25)



should also not have a proton transfer as part of its rate-determining

step, because chloride ion is also the conjugate base of a strong acid. This hydrolysis should accordingly exhibit a relatively small value of  $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}}$ . Those cases that have been studied (24, 50) do indeed show a considerably smaller  $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}}$  of 1.5 - 1.6 than does  $\alpha$ -disulfone hydrolysis, although one which is, to be sure, somewhat larger than for the hydrolysis of sulfonic anhydrides. It is small enough, however, to be consistent with a mechanism of the same type involved in the hydrolysis of the sulfonic anhydride (10). This mechanism is shown in equation 26.

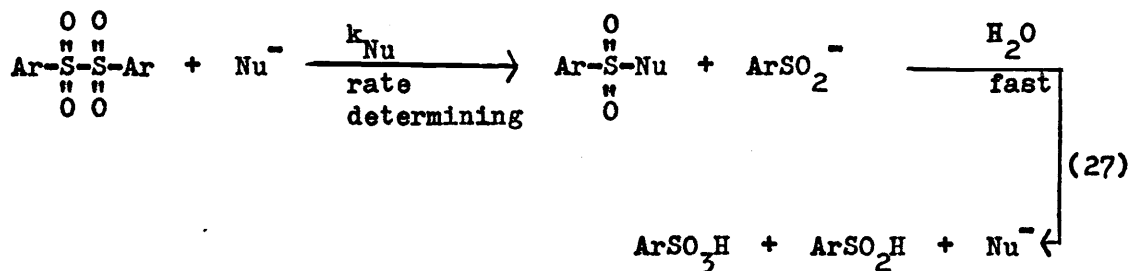


Interestingly, although no proton transfer appears to be involved in the rate-determining step of the hydrolysis of the sulfonyl chlorides, the reaction shows (56) a considerably more negative  $\Delta S^\ddagger$  than the hydrolysis of the sulfonic anhydrides. At this stage the reason for this difference in  $\Delta S^\ddagger$  is hard to rationalize. However, Whalley (57) has pointed out that conclusions based on entropies of activation are often subject to uncertainty. This may well be the case with the sulfonyl chlorides especially since the conclusions derived from  $\Delta S^\ddagger$  differ with those arrived at by other means of probing the mechanism such as the solvent isotope effect.

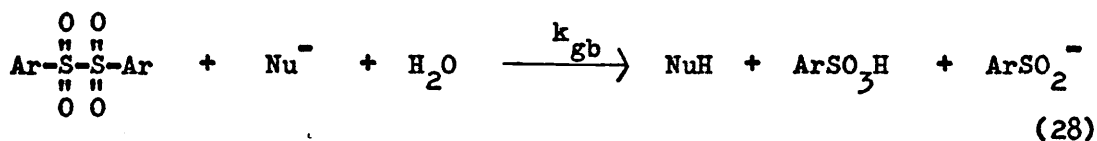
Nucleophile Catalyzed Hydrolysis and Other Nucleophilic  
Substitution Reactions of Aryl  $\alpha$ -Disulfones

Mechanisms of the Nucleophile Catalyzed Hydrolysis of Aryl  
 $\alpha$ -Disulfones.

There are two possible mechanisms that can be proposed to explain the nucleophile-catalyzed hydrolysis of aryl  $\alpha$ -disulfones. The first mechanism is nucleophilic catalysis and is shown in equation 27.



The other mechanism is general base catalysis by the nucleophile of the attack of water on the  $\alpha$ -disulfone (equation 28).



These two mechanism can easily be differentiated by measuring the solvent isotope effect. One would expect the solvent isotope effect ( $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}}$ ) to be close to one for the nucleophile catalyzed mechanism (equation 27) but much larger, around two, for the general base mechanism. The solvent isotope effect for the acetate ion-catalyzed hydrolysis ( $k_{\text{H}_2\text{O}}^{\text{OAc}}/k_{\text{D}_2\text{O}}^{\text{OAc}}$ ) was only 1.1. This isotope effect is in the



range expected for nucleophilic catalysis, and serves to exclude the general base mechanism (equation 28) from consideration, since all previous examples where acetate ion functions as a general base catalyst, as in equation 28, have considerably larger solvent isotope effects associated with them (34, p. 281).

Both fluoride and nitrite ions are weaker bases than acetate ion, and yet they are much better catalysts for the hydrolysis of  $\alpha$ -disulfones. They must therefore both be acting as nucleophilic catalysts, since were they acting as general base catalysts they could not be better catalysts than the stronger base, acetate ion. Chloride and bromide ion have never been observed to act as general base catalysts for hydrolysis reactions, and so their weak catalytic effect on the present reaction is also undoubtedly due to nucleophilic catalysis.

The triethylamine-catalyzed hydrolysis of aryl  $\alpha$ -disulfones appears to be quite different however. The solvent isotope effect measured and found to be  $(k_{\text{H}_2\text{O}}^{\text{Et}_3\text{N}}/k_{\text{D}_2\text{O}}^{\text{Et}_3\text{N}} = 2.0)$ . This is entirely inconsistent with a nucleophilic catalysis mechanism and totally consistent with a general base mechanism such as equation 28. The most probable reason triethylamine acts as a general base rather than a nucleophilic catalyst is its considerable steric bulk. Since it can only approach the sulfonyl sulfur with great difficulty, it catalyzes the hydrolysis by functioning as a general base, pulling a proton off a water molecule and thus facilitating the attack of that water molecule on the  $\alpha$ -disulfone, as shown in equation 28.

The conclusion is that all of the nucleophiles studied as catalysts, with the exception of triethylamine, catalyze the hydrolysis via nucleophilic catalysis, as shown in equation 27. That the attack of the nucleophile on the  $\alpha$ -disulfone is the rate-determining step is demonstrated by the fact that the initial addition of varying amounts of  $\text{ArSO}_2^-$  to the fluoride ion catalyzed hydrolysis of the  $\alpha$ -disulfone at  $21.3^\circ \text{C}$ . did not decrease the rate of hydrolysis. This shows that the rate of the reaction  $\text{ArSO}_2^- + \text{ArSO}_2\text{F} \longrightarrow \text{ArSO}_2\text{SO}_2\text{Ar} + \text{F}^-$  is slow compared to the rate of hydrolysis of  $\text{ArSO}_2\text{F}$  under these conditions ( $\text{ArSO}_2\text{F} + \text{H}_2\text{O} \longrightarrow \text{ArSO}_2\text{H} + \text{H}^+ + \text{F}^-$ ). That being the case the rate-determining step of the nucleophile catalyzed hydrolysis is the attack of the nucleophile on the  $\alpha$ -disulfone. Thus the second order rate constants ( $k_{\text{OAc}}$ ,  $k_{\text{F}}$ , etc) for the different nucleophile-catalyzed hydrolyses are the rate constants ( $k_{\text{Nu}}^{\text{SO}_2}$  of equation 10) for the attack of nucleophiles on the sulfonyl sulfur of the  $\alpha$ -disulfones.

The second order rate constants ( $k_{\text{N}_3}$ ,  $k_{\text{amine}}$ ) for the reaction of nucleophiles like azide ion and primary and secondary amines with the  $\alpha$ -disulfones are obviously also equal to  $k_{\text{Nu}}^{\text{SO}_2}$ , since they form stable products,  $\text{ArSO}_2\text{Nu}$ , on reaction with the  $\alpha$ -disulfones.

#### Relative Reactivity of Nucleophiles Towards Sulfonyl Sulfur.

Table 26 contains the values of  $k_{\text{Nu}}^{\text{SO}_2}$  for the reaction of phenyl  $\alpha$ -disulfone in 60% aqueous dioxane (v/v) with all of the nucleophiles

Table 26. Reactivity of nucleophiles toward phenyl  $\alpha$ -disulfone.

Nucleophile	$k_{\text{Nu}}^{\text{SO}_2}$ (eq. 10) $\text{M}^{-1} \text{sec}^{-1}(\text{a})$	$k_{\text{Nu}}^{\text{SO}_2}/k_{\text{OAc}}^{\text{SO}_2}$
$\text{OH}^-$	$1.2 \times 10^4(\text{b})$	$5.4 \times 10^6$
$n\text{-BuNH}_2$	13	$5.9 \times 10^3$
$\text{iso-BuNH}_2$	6.4	$2.9 \times 10^3$
$\text{Et}_3\text{NH}$	0.96	$4.4 \times 10^2$
$\text{N}_3^-$	0.72	$3.3 \times 10^2$
$\text{F}^-$	0.13	59
$t\text{-BuNH}_2$	0.033	15
$\text{NO}_2^-$	0.022	10
$\text{AcO}^-$	0.0022	(1.0)
$\text{Cl}^-$	$3.5 \times 10^{-6}(\text{c})$	$0.0016(\text{d})$
$\text{Br}^-$	$2.0 \times 10^{-6}(\text{c})$	$0.0009(\text{d})$

<sup>a</sup>All data are at 21.3° C. in 60% aqueous dioxane (v/v) as a solvent.

<sup>b</sup>Calculated from intercept of plot of  $k_h$  versus  $(\text{Et}_3\text{N})$  in 60% aqueous glyme assuming  $k_{\text{Et}_3\text{N}}$  and  $k_{\text{OH}}$  show the same dependence on solvent.

<sup>c</sup>Calculated from data at 80.3° C. assuming  $k_{\text{Cl}^-}^{\text{SO}_2}$  and  $k_{\text{Br}^-}^{\text{SO}_2}$  show the same dependence on temperature at  $k_{\text{OAc}}^{\text{SO}_2}$ .

<sup>d</sup>Measured at 80.3° C.

studied. (The values for  $n\text{-BuNH}_2$ ,  $\text{iso-BuNH}_2$ , and  $\text{Et}_3\text{NH}$  are calculated from the rate constants for the reactions of these nucleophiles with  $p\text{-tolyl } \alpha\text{-disulfone}$  assuming  $k_{\text{Nu}}^{\text{SO}_2}$  shows the same dependence on Ar as does the spontaneous hydrolysis of phenyl  $\alpha\text{-disulfone}$ , another reaction involving attack of an uncharged nucleophile on the  $\alpha\text{-disulfone}$ . In the case of azide ion, the assumption was made that  $k_{\text{N}_3}$  would increase just as much as  $k_{\text{F}}$  did in going from  $p\text{-tolyl}$  to phenyl  $\alpha\text{-disulfone}$ .) Calculating  $k_{\text{OH}}$  the rate constant for the reaction of hydroxide ion with the  $\alpha\text{-disulfone}$  (equation 10,  $\text{Nu} = \text{OH}^-$ ) was a little more difficult because hydroxide ion was found to be too reactive to measure directly without the aid of special equipment. The method used to obtain  $k_{\text{OH}}$  involved running the triethylamine catalyzed hydrolysis of the  $\alpha\text{-disulfone}$  at different amine concentrations and keeping the  $(\text{Et}_3\text{N}/\text{Et}_3\text{NH}^+)$  buffer ratio constant. The values of  $k_{\text{h}}$  for such runs were then plotted versus  $(\text{Et}_3\text{N})$ , the slope of such a plot being equal to the second order rate constant,  $k_{\text{Et}_3\text{N}}$ , and the intercept being equal to  $k_{\text{OH}}(\text{OH})$ . This method could not be used reliably in aqueous dioxane to get  $k_{\text{OH}}$  because of the formation of peroxides which led to erratic values of the intercepts (see Figure 22). To get  $k_{\text{OH}}(\text{OH})$  aqueous glyme was used instead as this solvent is known to be much less prone to form peroxides. This solvent system was quite satisfactory, and that the intercept of a plot of  $k_{\text{h}}$  versus  $(\text{Et}_3\text{N})$  was entirely due to  $k_{\text{OH}}(\text{OH})$  was easily demonstrated by changing the  $(\text{Et}_3\text{N}/\text{Et}_3\text{NH}^+)$  buffer ratio from 1:1 to 4:1 and observing the expected increase in the intercept of a factor of four (see Figure 18).

Since  $k_{\text{OH}}(\text{OH})$  is equal to the intercept of plots of  $k_h$  versus (amine), all that is necessary in order to be able to calculate  $k_{\text{OH}}$  is a knowledge of  $(\text{OH}^-)$  for the particular  $\text{Et}_3\text{N}:\text{Et}_3\text{NH}^+$  buffer used. However this is no easy task because the data necessary to calculate  $(\text{OH}^-)$  in aqueous glyme are not available, i. e.  $(\text{OH}^-) = (K_w/K_a)(\text{Et}_3\text{N}/\text{Et}_3\text{NH}^+)$  and neither the autoprotolysis constant of water,  $K_w$ , nor the acid dissociation constant,  $K_a$ , for  $\text{Et}_3\text{NH}^+$  is known in this solvent. However, since glyme and dioxane are really quite similar solvents, both being diethers and miscible with water in all proportions, the data available for  $K_w$  and the  $K_a$  of triethylamine in 60% aqueous dioxane can probably be used without causing any serious error. In 60% aqueous dioxane,  $K_w = 64 \times 10^{-19}$  (28) and the  $K_a$  for  $\text{Et}_3\text{NH}^+$  is  $3.16 \times 10^{-10}$  (47). The only other assumption made was that  $k_{\text{OH}}$  showed the same solvent dependence as  $k_{\text{Et}_3\text{N}}$  on going from 60% aqueous dioxane to 60% aqueous glyme. With all of these assumptions, the value of  $k_{\text{OH}}$  is subject to more uncertainty than the other second order rate constants but should be correct within a factor of 10.

Looking at Table 26 one sees that the spread in reactivity between the most reactive nucleophile studied, hydroxide ion, and the least reactive, bromide ion, is about  $10^{10}$ . Also noteworthy is the fact that fluoride ion is over  $10^4$  more reactive toward sulfonyl sulfur than either chloride or bromide ion. Azide ion is even more reactive than fluoride ion by a factor of six.

In order to compare these data with the data on the relative reactivity of various nucleophiles towards other centers, it is advantageous to express the data for sulfonyl sulfur in terms of the relative reactivity of each nucleophile compared to that of some other nucleophile as the standard. In this instance acetate ion was chosen as the standard and the values of  $(k_{\text{Nu}}^{\text{SO}_2}/k_{\text{OAc}}^{\text{SO}_2})$  are given in the last column of Table 26.

Comparison of the Reactivity of Nucleophiles Toward Sulfonyl, Sulfinyl, and Sulfenyl Sulfur.

As a result of a study of the nucleophile-catalyzed hydrolysis of aryl sulfinyl sulfones by Kice and Guaraldi (40), the reactivity of a series of nucleophiles in substitution reactions at the sulfinyl sulfur of these compounds ( $k_{\text{Nu}}^{\text{SO}}$  of equation 9) is known. This is precisely the data needed to compare the reactivity of various nucleophiles in substitutions at sulfinyl and sulfonyl sulfur, because both the nucleophile-catalyzed hydrolysis of the sulfinyl sulfones (equation 9) and that of the  $\alpha$ -disulfones (equation 10) were carried out in the same solvent (60% aqueous dioxane) and both involve the same leaving group ( $\text{ArSO}_2^-$ ). Thus comparing  $(k_{\text{Nu}}^{\text{SO}}/k_{\text{OAc}}^{\text{SO}})$  for equation 9 with  $(k_{\text{Nu}}^{\text{SO}_2}/k_{\text{OAc}}^{\text{SO}_2})$  for the same nucleophiles in equation 10, allows one to assess the change in relative reactivity of the various nucleophiles caused by changing the substitution site from sulfinyl to sulfonyl sulfur. Table 27 lists the data for those nucleophiles for which data are available for both equations

Table 27. Nucleophilicity toward sulfinyl versus sulfonyl sulfur.<sup>a</sup>

Nucleophile	Sulfinyl Sulfur ( $k_{\text{Nu}}^{\text{SO}}/k_{\text{OAc}}^{\text{SO}}$ ) in eq. 9	Sulfonyl Sulfur ( $k_{\text{Nu}}^{\text{SO}_2}/k_{\text{OAc}}^{\text{SO}_2}$ )
$\text{Br}^-$	7.2	0.0009
$\text{Cl}^-$	1.3	0.0016
$\text{AcO}^-$	(1.0)	(1.0)
$\text{F}^-$	0.49	59
$\text{H}_2\text{O}$	$1.1 \times 10^{-5(b)}$	$3.0 \times 10^{-5}$

<sup>a</sup>All data are for 60% aqueous dioxane (v/v) as the solvent.  
For equation 9,  $\text{Ar} = \text{p-MeOC}_6\text{H}_4$ , for equation 10,  $\text{Ar} = \text{C}_6\text{H}_5$ .

<sup>b</sup> $k_{\text{H}_2\text{O}}^{\text{SO}}$  is the rate of spontaneous hydrolysis of  $\text{ArSOSO}_2\text{Ar}$  from reference 40.

9 and 10. A glance at this table reveals that the order of nucleophilic reactivity of these nucleophiles is strikingly different toward sulfinyl and sulfonyl sulfur. One finds an almost complete reversal in the reactivity order when going from substitution at sulfinyl sulfur to sulfonyl sulfur. The order of relative reactivity of these nucleophiles towards sulfinyl sulfur is  $\text{Br}^- > \text{Cl}^- \approx \text{AcO}^- \gg \text{H}_2\text{O}$ . This order of nucleophilicity is very similar to that observed (31) for  $\text{S}_{\text{N}}2$  substitution at  $\text{sp}^3$  carbon. The order of relative reactivity towards sulfonyl sulfur is quite different,

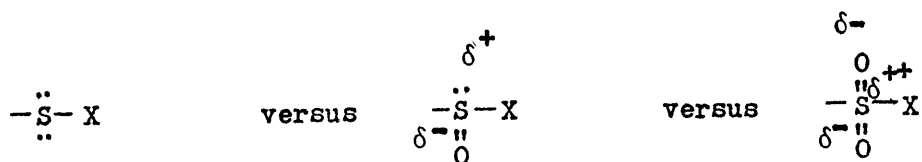
however, being  $F^- \gg AcO^- \gg Cl^- > Br^- > H_2O$ . In this case fluoride and acetate are now much more reactive than chloride or bromide. An important thing to note, however, is that the two oxygen nucleophiles, water and acetate, have about the same value of  $(k_{H_2O}/k_{OAc})$  for both sulfinyl and sulfonyl sulfur, despite the fact that acetate ion is much more reactive than water in each instance.

According to HSAB theory (47), nucleophiles like acetate ion, fluoride ion, or water are much harder bases than chloride or bromide ion. The application of HSAB to nucleophilic substitution reactions (49) leads to the conclusion that hard nucleophiles should react particularly readily with hard electrophilic centers and soft nucleophiles with soft electrophilic centers. Thus the HSAB interpretation of the results in Table 27 would be that sulfonyl sulfur represents a much harder electrophilic center than sulfinyl sulfur.

Kice and Large (42) have determined the relative reactivity of a series of nucleophiles at sulfenyl sulfur by studying the racemization of optically active phenyl benzenethiolsulfinate (equation 11). They found sulfenyl sulfur to be significantly softer than sulfinyl sulfur, as is evidenced by the  $(k_{Br}^S/k_{Cl}^S)$  ratio of 35. The ratio for sulfinyl sulfur,  $(k_{Br}^{SO}/k_{Cl}^{SO})$  is much less, 5.4 (40), and for the presumably harder sulfonyl sulfur  $(k_{Br}^{SO_2}/k_{Cl}^{SO_2})$  is only 0.56. The HSAB interpretation of all these results is that as an electrophilic center sulfonyl sulfur is harder than sulfinyl sulfur which is harder than sulfenyl sulfur.



This is just what HSAB theory would have predicted in advance about these centers. According to HSAB, the three principal factors which tend to make an electrophilic center hard are: (1) the absence of unshared pairs of easily excited outer shell electrons on the atom being attacked; (2) a high positive charge on the atom; (3) small size of the atom. The third criterion is not important here because in all three cases under discussion=sulfenyl, sulfinyl, and sulfonyl sulfur-attack of the nucleophile occurs at a sulfur atom. However, sulfenyl sulfur has two unshared pairs of outer shell electrons on sulfur, sulfinyl sulfur has one such pair, and sulfonyl sulfur has none. Because of the dipolar character of the  $\overset{\delta^+}{\text{S}}=\overset{\delta^-}{\text{O}}$  bond, sulfinyl sulfur also has a higher positive charge on sulfur than does sulfenyl sulfur, and sulfonyl sulfur has more positive charge on the sulfur than does sulfinyl sulfur, i.e.

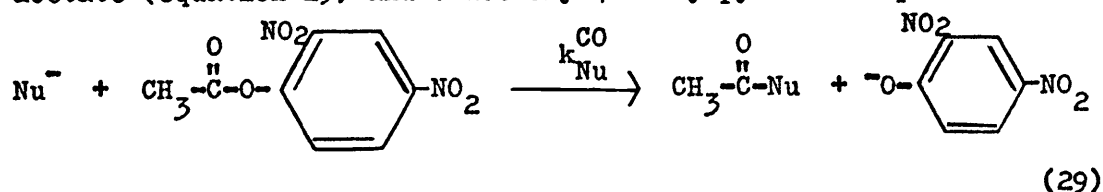


Thus HSAB would have predicted that the combination of these two effects should make sulfonyl sulfur a harder electrophilic center than sulfinyl sulfur, which is harder than sulfenyl sulfur, and this is just what is found experimentally.

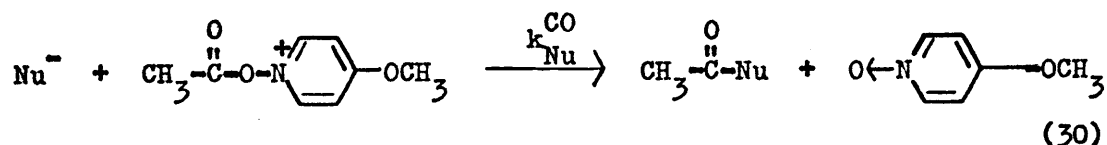
#### Comparison of the Reactivity of Nucleophiles Toward Sulfonyl Sulfur and Carbonyl Carbon

Jencks and Gilchrist (32) have provided data on the reactivity

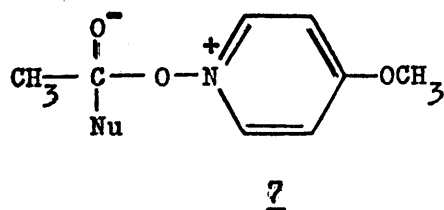
of a wide range of nucleophiles towards both 2,4 dinitrophenyl acetate (equation 29) and 1-acetoxy-4-methylpyridinium perchlorate



(equation 30). They showed that the rate-determining step in



equation 30 is that attack of the nucleophile on the carbonyl carbon, not the breakdown of the tetrahedral intermediate 7. The



same is almost certainly true for most nucleophiles in equation 29. Thus this data of Jencks and Gilchrist (32) gives a measure of the relative reactivity of various nucleophiles towards carbonyl carbon, another hard electrophilic center.

Table 28 contains values of  $(k_{\text{Nu}}^{\text{CO}}/k_{\text{OAc}}^{\text{CO}})$  for equations 29 and 30 for all the nucleophiles for which  $(k_{\text{Nu}}^{\text{SO}_2}/k_{\text{OAc}}^{\text{SO}_2})$  is also available for equation 10. Inspection of this table reveals that the relative reactivity of the nucleophiles studied is roughly the same for sulfonyl sulfur and carbonyl carbon. The relative reactivity of the various nucleophiles towards sulfonyl sulfur is in the order

Table 28. Relative nucleophilicity towards sulfonyl sulfur versus carbonyl carbon.

Nucleophile	Sulfonyl Sulfur <sup>(a)</sup>	Carbonyl Carbon <sup>(b)</sup>	
	$(k_{\text{Nu}}^{\text{SO}_2}/k_{\text{OAc}}^{\text{SO}_2})$ in eq. 10	$(k_{\text{Nu}}^{\text{CO}}/k_{\text{OAc}}^{\text{CO}})$ eq. 29	$(k_{\text{Nu}}^{\text{CO}}/k_{\text{OAc}}^{\text{CO}})$ eq. 30
$\text{OH}^-$	$5.4 \times 10^6$ (c)	$9.5 \times 10^4$	$8.6 \times 10^3$
$n\text{-BuNH}_2$	$5.9 \times 10^3$	$2.1 \times 10^5$ (d)	$3.1 \times 10^3$ (d)
$\text{N}_3^-$	$3.3 \times 10^2$	$1.7 \times 10^3$	$3.5 \times 10^2$
$\text{F}^-$	59	5.6	3.3
$\text{NO}_2^-$	10	15	7.7
$\text{AcO}^-$	(1.0)	(1.0)	(1.0)
$\text{H}_2\text{O}$	$3 \times 10^{-5}$ (e)	$3.5 \times 10^{-4}$	$2 \times 10^{-4}$

<sup>a</sup> Solvent, 60% aqueous dioxane (v/v); temperature 21.3° C.; Ar = C<sub>6</sub>H<sub>5</sub>.

<sup>b</sup> Solvent, water; temperature 25° C.

<sup>c</sup> Calculated from data in glyme by assuming the same solvent dependence in  $k_{\text{Et}_3\text{N}}^{\text{SO}_2}$  and  $k_{\text{OH}}^{\text{SO}_2}$ .

<sup>d</sup> Data are for  $n\text{-PrNH}_2$  rather than for  $n\text{-BuNH}_2$ .

<sup>e</sup>  $k_{\text{H}_2\text{O}}^{\text{SO}_2}$  is the spontaneous rate of hydrolysis of phenyl  $\alpha$ -disulfone.

$\text{OH}^- \gg \text{n-BuNH}_2 \gg \text{N}_3^- > \text{F}^- > \text{NO}_2^- > \text{AcO}^- \gg \text{H}_2\text{O}$ . The reactivity for carbonyl carbon in equation 30 is  $\text{OH}^- > \text{n-BuNH}_2 \gg \text{N}_3^- \gg \text{NO}_2^- > \text{F}^- > \text{AcO}^- \gg \text{H}_2\text{O}$ . This same order is found for equation 29 except that hydroxide ion and n-butylamine are reversed. Seemingly the only significant differences in the nucleophilic order at sulfonyl sulfur and carbonyl carbon are that fluoride and nitrite ion are reversed and that hydroxide is more reactive relative to the amines at sulfonyl sulfur than it is at carbonyl carbon. Fluoride ion is more reactive towards sulfonyl sulfur while nitrite ion is more reactive towards carbonyl carbon. Since fluoride ion is considered a harder base than nitrite or acetate ion, this difference can be taken to mean that sulfonyl sulfur is a somewhat harder electrophilic center than carbonyl carbon. This fact may also be supported by the observation that hydroxide ion, which is a harder base than an amine, is more reactive, relative to the amines, in the substitution at sulfonyl sulfur than in the one at carbonyl carbon. However, because the leaving group in equation 10 is different from the ones in equations 29 and 30, and the latter two reactions were studied in water while the former was investigated in 60% aqueous dioxane (v/v), the conclusions reached are subject to some uncertainty.

Finally, the high reactivity of azide ion towards sulfonyl sulfur and carbonyl carbon needs to be rationalized. Azide ion with its  $\pi$  electrons is usually classified by HSAB as a borderline base, and is considered by most to be about as soft as chloride ion. Since azide is this soft, its high reactivity toward hard

electrophilic centers like sulfonyl sulfur and carbonyl carbon is at first sight surprising. This is a difficult dilemma to solve, but perhaps the answer lies in considering basicity as well as hardness, since azide ion is a much stronger base than chloride ion. This can be done by utilizing the oxibase scale equation (equation 31)

$$\log (k/k_0) = \alpha E + \beta H \quad (31)$$

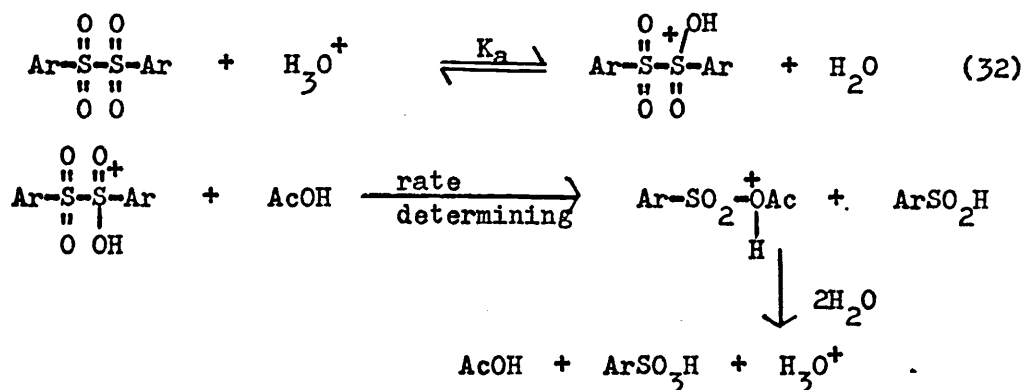
proposed by Davis (15, pp. 311-328, 14, pp. 189-238). In equation 31, E is related to the polarizability of the nucleophile and  $\alpha$  is the sensitivity of the substrate to this polarizability. On the other hand H, which is given by the equation  $H = pK_a + 1.74$ , is directly related to the basicity of the nucleophile and  $\beta$  is the sensitivity of the substrate to this basicity. At hard electrophilic centers like sulfonyl sulfur, the  $\beta H$  term should be quite important as is evidenced by the much greater reactivity of hydroxide ion over bromide ion. Both these ions have about the same E value, 1.51 for bromide and 1.65 for hydroxide, but the H values are quite different being -6 for bromide ion and 17.48 for hydroxide ion. It is evident that the much greater reactivity of hydroxide ion toward sulfonyl sulfur must be due to this difference in the value of H. If the value of E for bromide ion and azide ion are compared, it is found that they are quite similar, with E for azide being 1.58. Thus these two nucleophiles are of about the same softness. However, if the H values are compared, one finds the value of H for azide to be 6.46 which is much larger than the -6 for bromide ion. Thus on

the basis of equation 31, one would expect that azide ion would be much more reactive than either bromide ion or chloride ion (the latter has  $E = 1.24$  and  $H = -3.0$ ). Besides one should be careful when applying the principles of HSAB, because as Edwards points out (personal communication) any nucleophile that has  $\pi$  electrons is potentially likely to give trouble in selected cases. In this case, one can conclude that at hard centers such as sulfonyl sulfur and carbonyl carbon both hardness and basicity are important factors in determining reactivity.

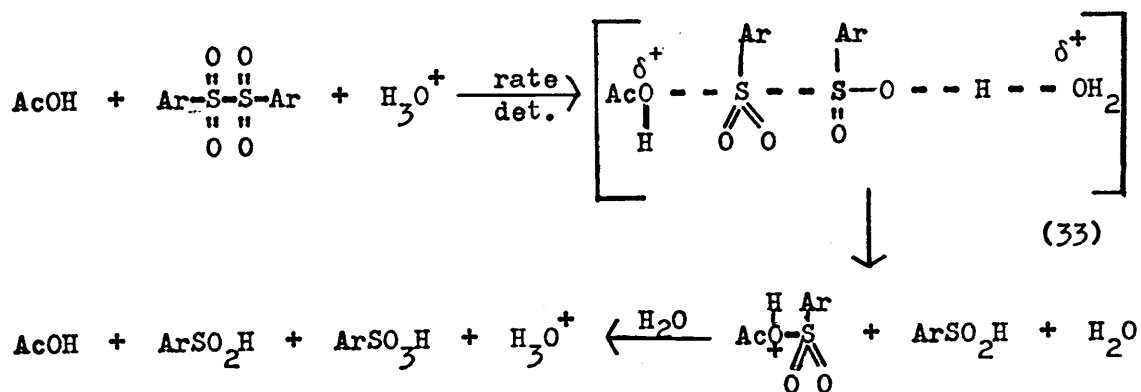
#### Solvolysis in Acetic Acid - Water

The solvolysis of both p-chlorophenyl  $\alpha$ -disulfone and p-tolyl  $\alpha$ -disulfone was studied in acetic acid - 1% water containing varying amounts of added sulfuric acid. The rate of solvolysis of both these compounds increased as the acidity of the medium was increased in the manner shown in Figure 24.

This dependence of solvolysis rate on acidity in the strongly acidic acetic acid - water mixture could be explained by either of the following two mechanisms. The first, equation 32, involves



preequilibrium protonation and subsequent breakdown of the protonated species to form products. The second possible mechanism, equation 33 involves the attack of acetic acid concerted with a proton transfer.

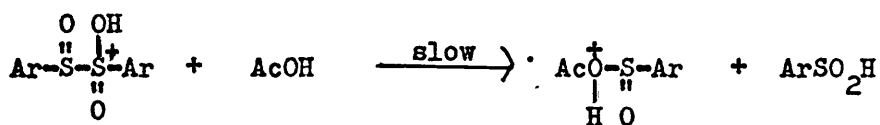
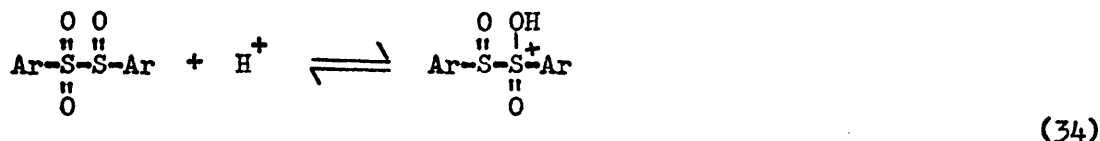


The observed isotope effect ( $k_{\text{H}}/k_{\text{D}}$ ) for the acid-catalyzed solvolysis is 1.45. This is definitely not in accord with mechanism 32. The first step of mechanism 32 would be expected to have a solvent isotope effect of ( $k_{\text{H}}/k_{\text{D}} \approx 0.5$ ) and  $k_{\text{H}}/k_{\text{D}}$  for the rate determining step of equation 32 would be expected to be about unity. Therefore, mechanism 32 would be predicted to exhibit a solvent isotope effect ( $k_{\text{H}}/k_{\text{D}}$ ) of less than one. This is clearly not the case and so this mechanism is eliminated.

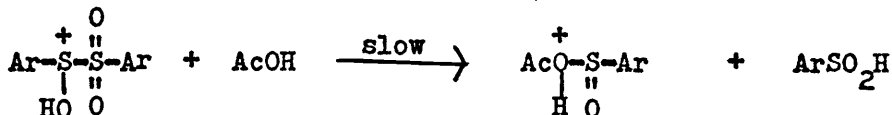
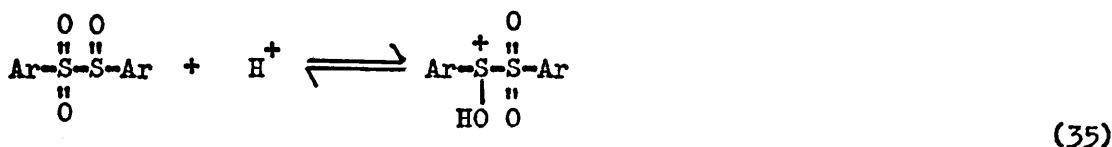
On the other hand, mechanism 33 does agree with the experimental facts. Since a proton is transferred in the rate-determining step, the solvent isotope effect ( $k_{\text{H}}/k_{\text{D}}$ ) would be expected to be greater than one, as is observed. Thus 33 is the preferred mechanism.

This demonstration that mechanism 32 cannot be correct leads to an important conclusion regarding the mechanism of the acid-catalyzed solvolysis of aryl sulfinyl sulfones in acetic acid -

1% water. In a previous study, Kice and Guaraldi (38) measured the solvent isotope effect ( $k_H/k_D$ ) for the acid catalyzed solvolysis of p-methoxybenzenesulfinyl p-methoxybenzenesulfone in acetic acid - 1% water and found it to be 0.72. Two mechanisms are consistent with this solvent isotope effect. The first mechanism (equation 34)



involves preequilibrium protonation of the sulfinyl sulfone on the sulfonyl oxygen. The second mechanism (equation 35) is identical



to the one shown in equation 34 except that preequilibrium protonation occurs at the oxygen on the sulfinyl sulfur. That both mechanisms are consistent with the solvent isotope effect, is apparent if one considers that the expected solvent isotope effect ( $k_H/k_D$ ) for the first step in each case is expected to be less than one. In the first mechanism (equation 34), the second step does not involve a proton transfer so the solvent isotope effect should remain less



than one. In the second mechanism (equation 35) the solvent isotope effect ( $k_H/k_D = 0.72$ ) can be explained by using ( $k_H/k_D \approx 0.4$  to  $0.5$ ) for the preequilibrium step, and ( $k_H/k_D \approx 1.4$  to  $1.8$ ) for the second step (38). Of these two mechanisms, the one involving protonation of sulfinyl sulfur (equation 35) is now to be preferred since the other mechanism (equation 34) involves protonation of the oxygen on the sulfonyl sulfur and this is not observed in the acid catalyzed solvolysis of the  $\alpha$ -disulfones in the same medium. One would expect that if the sulfonyl protonated species were important in the sulfinyl sulfone reaction, it would also be important in the  $\alpha$ -disulfone reaction, which it clearly is not. Thus the mechanism involving sulfonyl protonated sulfinyl sulfone is highly unlikely. The reason that the sulfonyl group is not protonated is presumably due to its low basicity as discussed on page 83.

## EXPERIMENTAL

Preparation of MaterialsSodium Benzenesulfinate

Sodium benzenesulfinate was obtained from the Aldrich Chemical Company, Inc., and was used without further purification.

Sodium p-Toluenesulfinate

The commercially available dihydrate of sodium p-toluenesulfinate (Aldrich Chemical Company, Inc.) was used without further purification.

Sodium p-Chlorobenzenesulfinate

The hydrate of the salt was prepared by the reduction of the commercially available p-chlorobenzenesulfonyl chloride (Waterloo Chemical Company, Inc.) with sodium sulfite in basic solution according to the procedure described by Bäder and Herman (5).

Sodium p-Bromobenzenesulfinate

Sodium p-bromobenzenesulfinate was prepared in the same manner as sodium p-chlorobenzenesulfinate, using p-bromobenzenesulfonyl chloride (Aldrich Chemical Company, Inc.)

Sodium p-Methoxybenzenesulfinate

p-Methoxybenzenesulfonyl chloride was prepared by the reaction of anisole with chlorosulfonic acid in chloroform at  $-5^{\circ}$  to  $5^{\circ}$  C.,

according to the procedure described by Morgan and Cretcher ( ). The crude sulfonyl chloride was recrystallized from boiling hexane and then reduced with sodium sulfite according to the direction of Overberger and Godfrey (45).

#### Preparation of $\alpha$ -Disulfones

The  $\alpha$ -disulfones were prepared by the oxidation of the sodium salts of the respective sulfinic acids with an acidic solution of cobaltic sulfate according to the directions of Denzer, Allen, Conway, and van der Veen (17).

#### Preparation of Cobalt (III) Sulfate

The cobaltic sulfate solution was prepared by electrolysis of a saturated solution of cobaltous sulfate in 10 N  $\text{H}_2\text{SO}_4$  at  $0^\circ \text{C}$ . as described by Swann and Xanthakos (54). A platinum anode  $45 \text{ cm}^2$  in area and a copper cathode were used. A current of 4.5 amperes at 4.2 volts was passed through the cell for four to five hours. Enough 10 N  $\text{H}_2\text{SO}_4$  was added at  $0^\circ \text{C}$ . to dissolve the suspension of cobaltic sulfate. The resulting solution was filtered through a coarse sintered glass funnel with the aid of suction and used immediately in the oxidation of sulfinic acid salts.

#### Oxidation of Sulfinic Acid Salts

A solution or slurry of sulfinic acid salt in 50 ml of 10 N  $\text{H}_2\text{SO}_4$  and 50 ml of t-butyl alcohol was made up in a one liter

Erlenmeyer flask. The chilled solution of cobaltic sulfate, as prepared above, was run into this with vigorous stirring until the blue color of Co (III) persisted for one minute. The mixture was immediately poured into four times its volume of cold water, and the insoluble  $\alpha$ -disulfone was isolated by filtration. The crude  $\alpha$ -disulfone was dried, and recrystallized from benzene - ethanol until a constant melting point was reached. All the  $\alpha$ -disulfones showed infrared absorptions in the  $7.5\mu$  and  $8.8\mu$  regions (KBr pellet). The following  $\alpha$ -disulfones were prepared by the cobaltic sulfate oxidation method.

#### Diphenyl $\alpha$ -Disulfone

Yield 66%, m.p.  $193 - 195^\circ \text{C.}$ ,  $\lambda_{\text{max}}$  (dioxane)  $244 \text{ m}\mu$  ( $\log \epsilon$ , 4.412). (Literature values (17), m.p.  $196 - 196.5^\circ \text{C.}$ ,  $\lambda_{\text{max}}$   $237 \text{ m}\mu$  ( $\log \epsilon$ , 4.30).)

#### Di-p-tolyl $\alpha$ -Disulfone

Yield 58%, m.p.  $220 - 223^\circ \text{C.}$ ,  $\lambda_{\text{max}}$  (dioxane)  $258 \text{ m}\mu$  ( $\log \epsilon$ , 4.428). Literature values (17), m.p.  $222^\circ \text{C.}$ ,  $\lambda_{\text{max}}$   $250 \text{ m}\mu$  ( $\log \epsilon$ , 4.36).)

#### Di-p-chlorophenyl $\alpha$ -Disulfone

Yield 56%, m.p.  $230 - 231^\circ \text{C.}$ ,  $\lambda_{\text{max}}$  (dioxane)  $263 \text{ m}\mu$  ( $\log \epsilon$ , 4.518). (Literature values (6), m.p.  $230^\circ \text{C.}$ ) Anal.  
Calculated for  $\text{C}_{12}\text{H}_8\text{Cl}_2\text{O}_4\text{S}_2$ : C, 41.04; H, 2.39. Found: C, 41.08; H, 2.29

Di-p-bromophenyl  $\alpha$ -Disulfone

Yield 50%, m.p.  $233 - 234^{\circ}$  C.,  $\lambda_{\max}$  (dioxane)  $267 \text{ m}\mu$   
 (log  $\epsilon$  , 4.498). (Literature values (17), m.p.  $205^{\circ}$  C.,  $\lambda_{\max}$   
 $262 \text{ m}\mu$  (log  $\epsilon$  , 4.29).) Anal. Calculated for  $\text{C}_{12}\text{H}_8\text{Br}_2\text{O}_2\text{S}_2$ :  
 C, 32.75; H, 1.83. Found: C, 33.06; H, 1.86.

Di-p-methoxyphenyl  $\alpha$ -Disulfone

Yield 68%, m.p.  $192 - 193^{\circ}$  C.,  $\lambda_{\max}$  (dioxane)  $286 \text{ m}\mu$   
 (log  $\epsilon$  , 4.319). (Literature values (17), m.p.  $232^{\circ}$  C.,  $\lambda_{\max}$   
 $277 \text{ m}\mu$  (log  $\epsilon$  , 4.45).) Anal. Calculated for  $\text{C}_{14}\text{H}_{14}\text{O}_6\text{S}_2$ :  
 C, 49.11; H, 4.12. Found: C, 49.01; H, 4.18.

p-Toluenesulfonyl Azide

p-Toluenesulfonyl azide was prepared by the reaction of  
 p-toluenesulfonyl chloride with sodium azide in 10% water - 90%  
 dioxane as described by Curtius (13). The recrystallized azide  
 melted at  $22^{\circ}$  C., (Literature value (13), m.p.  $22^{\circ}$  C.)

Purification of Solvents and Other ReagentsInorganic Salts

Lithium perchlorate was analytical, reagent grade and was used  
 without further purification. Sodium acetate, sodium azide, sodium  
 bromide, lithium chloride, sodium fluoride, and sodium nitrite were  
 reagent grade and were recrystallized from distilled water and dried  
 before using.

### Inorganic Acids

Hydrochloric acid, sulfuric acid, and perchloric acid were analytical, reagent grade and were used without further purification. Deuterated sulfuric acid ( $D_2SO_4$ ) was obtained from Diaprep Incorporated, and was used without further purification.

### Deuterium Oxide

Commercially available deuterium oxide was used without further purification since it was certified by the manufacturer (Stohler Isotope Chemicals) to contain 99.8 atom % D.

### Amines

Diethylamine, triethylamine, iso-butylamine, and tert-butylamine were reagent grade and were distilled from barium oxide under nitrogen before use.

### Dioxane

Reagent grade dioxane was further purified by the method described by Fieser (22, p. 234) and distilled under a nitrogen atmosphere on a sixty centimeter, glass helices -packed, fractionating column, b.p.  $101^{\circ}C$ .

### Glyme

Commercially available glyme ( Ansul Company) was further

purified by distilling it first from sodium, and then from  $\text{LiAlH}_4$  directly before use.

### Acetic Acid

Commercially available acetic acid (Baker and Adamson) was further purified as suggested by Wiberg (58, p. 249) by distilling it from acetyl borate on an Oldershaw column, b.p.  $118^\circ \text{C}$ .

### Acetic Acid-d

Acetyl chloride was distilled from N,N-dimethylaniline. Deuterium oxide was added to the purified acetyl chloride according to the procedure described by De la Mare (16). The resulting acetic acid-d was distilled through a 10 cm, silvered, vacuum-jacketed, Vigreux column, b.p.  $117 - 117.5^\circ \text{C}$ .

### Acetic Acid Stock Solutions

Sulfuric acid was titrated with 1.00 N sodium hydroxide and found to be 95.2% sulfuric acid. The remaining 4.8% was assumed to be water. A 100 ml volumetric flask containing 20.6 g of this sulfuric acid and 1.01 g of water was made up to volume with acetic acid at  $20^\circ \text{C}$ . The resulting solution was 2 M in sulfuric acid and contained 2% water. The stock solutions for the kinetic runs in deuterated solvents were made up in the same manner using acetic acid-d, deuterium oxide, and sulfuric acid-d<sub>2</sub>.

### Dioxane Stock Solutions

Enough  $\alpha$ -disulfone was added to freshly distilled dioxane to make the resulting solution about  $5 \times 10^{-5}$  M on dilution with water to 60/40 dioxane-water. The water used to make these dilutions contained the appropriate amount of nucleophile and acid to give the desired concentrations.

### Procedure for Kinetic Runs

#### Procedure in Acetic Acid

In each run, 25 ml of a solution of the  $\alpha$ -disulfone in acetic acid was pipetted into a 100 ml volumetric flask. To this, 25 ml of the acetic acid - 2% water solution, containing the appropriate amount of sulfuric acid, was added. The resulting solution was deaerated by passing prepurified nitrogen through the solution for five minutes. The deaerated solution was placed in a constant temperature bath. After thermal equilibrium was reached, approximately five minutes, the initial sample was taken. The samples were removed by pipetting out about three ml of the solution and immediately cooling it to zero degrees. This solution was then placed in a cuvette, and the concentration of the  $\alpha$ -disulfone was determined spectrophotometrically with a Cary Model 15 ultraviolet spectrophotometer. The wavelengths used were  $270 \text{ m}\mu$  for the p-tolyl  $\alpha$ -disulfone, and  $275 \text{ m}\mu$  for the p-chlorophenyl  $\alpha$ -disulfone. The absorbance,  $A$ , of the solution was used as a measure of concentration. More points were taken at the appropriate time intervals. Since



these runs were quite slow, the infinity value was assumed to be zero. This assumption is warranted because the plots of  $\log A$  versus time, used to obtain the rate constants, showed excellent linearity.

#### Aliquot Procedure in Aqueous Dioxane

In each run, 30 ml of the dioxane solution which contained the  $\alpha$ -disulfone, and 20 ml of an aqueous solution containing the appropriate combination of perchloric acid, lithium perchlorate, and nucleophile (if any was being used) were pipetted into the apparatus shown in Figure 25. The reaction vessel was deaerated by passing prepurified nitrogen through the solution for about five minutes. After deaeration, the reaction vessel was placed in a constant temperature bath. When the reaction vessel and its contents reached bath temperature, approximately five minutes, the initial sample was taken.

Samples were removed by the following procedure. Stopcock A was turned  $180^\circ$  from the position shown in Figure 25. This allowed the nitrogen coming in the nitrogen inlet to force some of the solution up into the graduated tube C. This solution was trapped there by turning stopcock B  $45^\circ$  clockwise, and returning stopcock A to its original position. The trapped sample was then allowed to run out the delivery tube D by turning stopcock B another  $45^\circ$  clockwise. About one-half ml was run through the delivery tube and into a waste beaker, thus rinsing the tube. The remainder was run

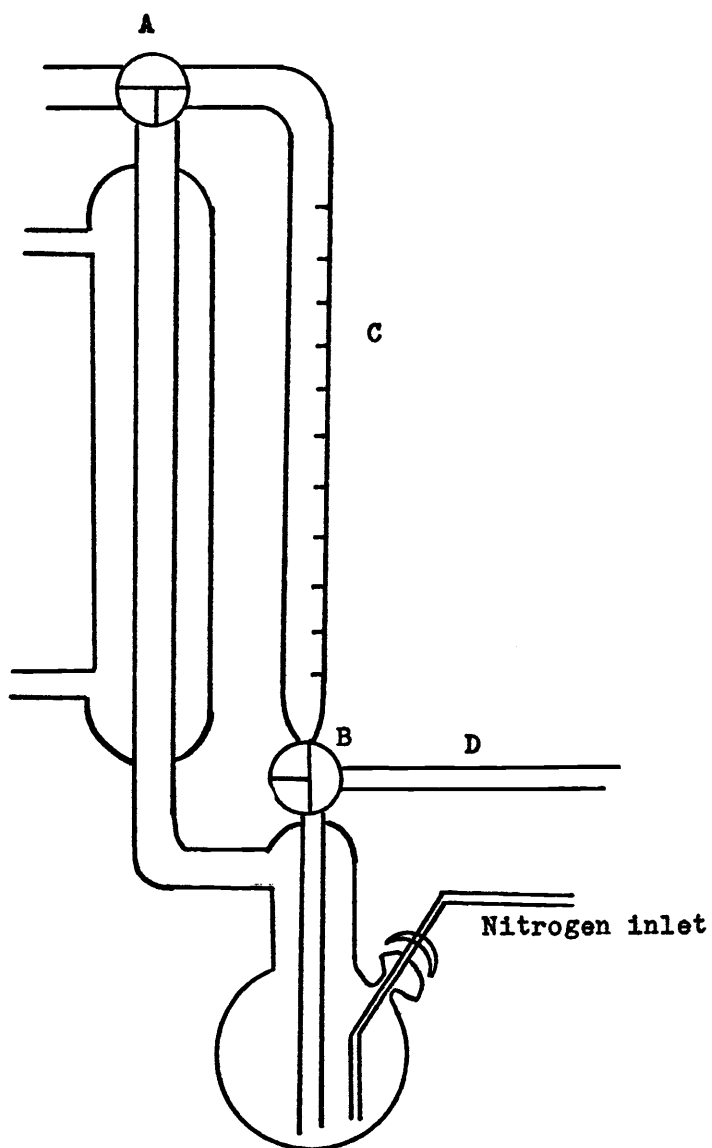


Figure 25. Reaction vessel for aliquot method

into a 10 ml beaker surrounded by ice water. Stopcock B was returned to its original position and the nitrogen pressure was turned off. The solution was allowed to stand in the ice water for about 30 seconds. It was then poured into a cuvette and its absorbance read on a Beckmann Model DB or a Cary Model 15 ultraviolet spectrophotometer. This allowed the concentration of the  $\alpha$ -disulfone to be determined. The wavelength, corresponding to the  $\lambda_{\text{max}}$  of the  $\alpha$ -disulfone, was used for this purpose. The reaction was followed by taking additional samples at appropriate intervals in the same manner for two to three half-lives. An infinity value was taken after eight to ten half-lives. The absorbance of the infinity values varied from close to zero to about 0.20, depending on the  $\alpha$ -disulfone, but in most cases it was near zero. The pseudo-first-order rate constants were determined by plotting  $\log(A_t - A_\infty)$  versus time.

This procedure was used for all the kinetics studied in aqueous dioxane with the exception of those studied by the direct method. The same procedure was also used in the solvent effect studies, but in these reactions the amounts of dioxane and water were varied.

#### Direct Procedure in Aqueous Dioxane

All the reaction rates measured at 21.3° C., and the solvent isotope effect for the acetate catalyzed reaction were determined using a somewhat different procedure in which the progress of the reaction was followed directly in the spectrophotometer. The

temperature was held constant by thermostating the cell holder in the instrument. The special cell shown in Figure 26 was used for these studies. Two ml of water containing all of the reactants except the  $\alpha$ -disulfone was pipetted into chamber C. Three ml of a dioxane solution which contained the  $\alpha$ -disulfone was pipetted into chamber A. Stopcock B was then closed, and chamber C was stoppered with a ground glass stopper. The reaction vessel was then set in a constant temperature bath for five minutes. After thermal equilibrium was reached, the reaction vessel was removed from the bath and the contents thoroughly mixed. The cell was then inserted into the jacketed cell holder of the Cary Model 15 ultraviolet spectrophotometer, and the absorbance recorded as a function of time. The wavelengths used were the same as in the aliquot procedure with the following exception. In the reaction of azide with p-tolyl  $\alpha$ -disulfone, 275 m $\mu$  was used, because of the absorption of sodium azide in the 240 m $\mu$  range.

#### Procedure for Aminolysis in Aqueous Dioxane

The general procedure for aminolysis was exactly the same as the direct procedure. The disappearance of the  $\alpha$ -disulfones was followed spectrophotometrically at the following wavelengths: p-chlorophenyl  $\alpha$ -disulfone, 270 m $\mu$  ; phenyl  $\alpha$ -disulfone, 255 m $\mu$  ; p-tolyl  $\alpha$ -disulfone, 270 m $\mu$  ; and p-methoxyphenyl  $\alpha$ -disulfone, 286 m $\mu$  . The 1:1 RNH<sub>2</sub>:RNH<sub>3</sub><sup>+</sup> buffer solutions were prepared by adding the calculated amount of standard hydrochloric acid or perchloric acid to a standard solution of the amine in water.

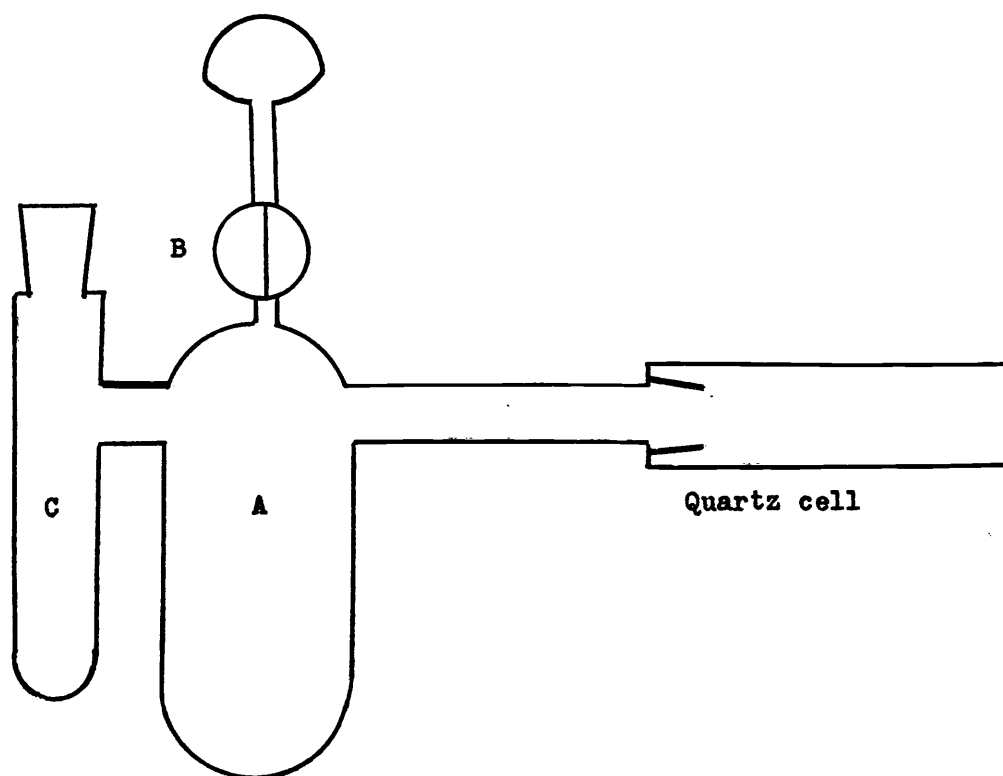


Figure 26. Reaction vessel for direct method.

### Procedure for Aminolysis in Aqueous Glyme

The same kinetic procedure as described above for the aminolysis reactions in aqueous dioxane was used to follow the disappearance of the  $\alpha$ -disulfones in aqueous glyme.

### Procedure for Azide Product Study

p-Tolyl  $\alpha$ -disulfone (0.62 g) and sodium azide (0.33 g) were dissolved in 400 ml of 60% dioxane. The resulting solution was heated at 60° C. for five hours. The solution was then rotary evaporated to dryness. The resulting white solid was dissolved in water and extracted with ether. The ether solution was washed with dilute sulfuric acid, dilute sodium hydroxide, and finally with water. The washed ether solution was then dried with magnesium sulfate. The ether was evaporated off leaving the azide as an almost colorless oil which crystalized on standing in the cold. The azide melted at 22° C. (literature value (13), 22° C.), and had an identical infrared spectrum when compared to an authentic sample of p-toluene-sulfonyl azide.

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