AN ABSTRACT OF THE THESIS OF

Charlene Ann Walters for the degree of Doctor of Philosophy

in Chemistry presented on March 2, 1977

Title: Kinetic Studies of Some Reactions of Sulfinate and Sulfonate Esters

Redacted for Privacy

Abstract approved: _____

Dr. P. K. Freeman

Redacted for Privacy

_____

Dr. John L. Kice (In absentia)

Kinetic Studies of the Methanolysis of Methyl p-Toluenesulfinate

The kinetics of the symmetrical exchange reaction, shown in Equation 1, have been studied using NMR techniques.

Eq. 1

Acetate ion was 10^3 times more effective at catalyzing the transesterification than was the hindered base 2,6-lutidine, and was therefore more thoroughly investigated.

Reaction rates, determined in methanol-d_3 and d_4 solutions containing sodium acetate and acetic acid, showed first order dependence upon acetate ion concentration. The acetate catalysis constant, k_{OAc}, changed systematically with the buffer ratio, but the variations noted in CD_3OD were greater than those in CD_3OH. The solvent isotope effects measured for the two buffer ratios were thus slightly different -- $k^H_{OAc}/k^D_{OAc} = 1.3$ for the 2:1 acetate buffers and $k^H_{OAc}/k^D_{OAc} = 1.5$ for the 1:1 solutions. Methoxide ion also contributes to the overall reaction rate, giving a solvent isotope effect $k^H_{OMe}/k^D_{OMe} = 1.5$.

These observations suggest that the overall exchange process consists of two routes -- (a) a small specific base catalyzed reaction by methoxide ion, and (b) a larger acetate ion catalyzed contribution proceeding through a general acid, specific base pathway. A kinetically significant pre-equilibrium step provides a rationale for the fact that k_{OAc} decreases with acetate buffer ratio. The similarity of the solvent isotope effects for k_{OMe} and k_{OAc} is accounted for by the ultimate attack by methoxide ion at sulfinyl sulfur in both cases.

The data is consistent with either a symmetrical intermediate or a transition state on the reaction coordinate. A "skewed" transition state with HOAc hydrogen-bonded to the methoxyl group of the ester is considered

less likely, but cannot be excluded. The issue of metastable intermediates in reactions at sulfinyl sulfur is therefore not resolved in this study.

Kinetic Studies of the Hydrolysis of p-Toluenesulfonic Acid Esters

p-Nitrophenyl p-toluenesulfonate was hydrolyzed in 20% aqueous acetonitrile and 60% glyme-40% water solutions containing tertiary amine buffers (Equation 2).

$$ArSO_3Ar' + H_2O \xrightarrow{R_3N/R_3N\text{-}H^+} ArSO_3H + Ar'OH \qquad \text{Eq. 2}$$

Ar = tolyl Ar' = p-nitrophenyl

Hydroxide ion catalysis was easily detected in both solvents. There was no rate dependence upon triethylamine concentration in acetonitrile, but the observation of a minimal effect in 2:1 and 1:1 amine buffers in glyme suggests some catalysis by TEA in the latter solvent. The maximum estimated catalysis constant was $k_{TEA} = 5 \times 10^{-6} M^{-1} sec^{-1}$.

By contrast, N-ethylpyrrolidine was quite effective in accelerating the hydrolysis reaction in glyme. The reactions with this amine obeyed first order kinetics and provided a catalysis constant $k^{II}_{NEP} = 6.1 \times 10^{-5} M^{-1} sec^{-1}$ for all the buffer ratios studied in isotopically normal solvent. In 60% glyme - 40% D_2O, k^{D}_{NEP} was 4.1×10^{-5} $M^{-1} sec^{-1}$. These experimental observations support a

nucleophilic catalysis mechanism for the hydrolysis of p-nitrophenyl p-toluenesulfonate in NEP-buffered glyme solutions.

Rates of reaction due to NEP were at least 12 times greater than those estimated for TEA. This is consistent with a nucleophilic attack by TEA at the sulfur atom, greatly slowed by the steric hindrance of three freely-rotating ethyl groups in the amine, or with a slower general base catalysis route. The data do not distinguish between the two possibilities.

While this study demonstrates a great difference in catalytic behavior between TEA and NEP, it cannot be stated that an actual mechanism change was observed, such as that seen in Campbell's work with sulfinyl sulfones (18). However, the results do suggest that a delicate sterically-controlled balance between nucleophilic and general base catalyzed routes may exist in sulfonyl sulfur substitution reactions.

Kinetic Studies of Some Reactions of Sulfinate and Sulfonate Esters

by

Charlene Ann Walters

A THESIS

submitted to

Oregon State University

in partial fulfillment of
the requirements for the
degree of

Doctor of Philosophy

June 1977

APPROVED:

Redacted for Privacy

Professors of Chemistry in charge of major

Redacted for Privacy

Redacted for Privacy

Chairman of the Department of Chemistry

Redacted for Privacy

Dean of the Graduate School

Date thesis is presented March 2, 1977

Typed by Bobbie Smith for Charlene Walters.

ACKNOWLEDGEMENT

I want to thank Dr. John Kice, Dr. P. K. Freeman and the members of my doctoral committee for their help and guidance of my studies at O.S.U.

Financial assistance through the National Defense Education Act is also gratefully acknowledged.

TABLE OF CONTENTS

II. Kinetic Studies of the Hydrolysis of p-Toluenesulfonic Acid Esters

LIST OF TABLES

LIST OF FIGURES

KINETIC STUDIES OF SOME REACTIONS OF SULFINATE AND SULFONATE ESTERS

I. Kinetic Studies of the Methanolysis of Methyl p-Toluenesulfinate

INTRODUCTION

Alkyl arenesulfinates were described as early as 1885 (58) and since then synthetic methods have been devised to produce them in good yields. These esters may be prepared in five general ways:

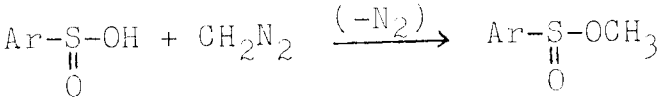
(1) most commonly, by reaction of arylsulfinyl chloride with alcohols, using pyridine or potassium carbonate as an HCl-acceptor (59);

$$Ar-\underset{\underset{O}{\|}}{S}-Cl + EtOH \xrightarrow[\text{pyridine/ether}]{(-HCl)} Ar-\underset{\underset{O}{\|}}{S}-OEt$$

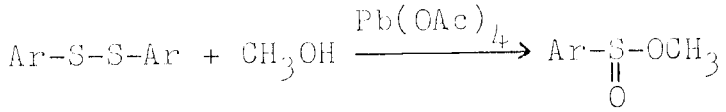
(2) by the action of alkyl chlorocarbonates upon arylsulfinic acid salts in alcohol solvents (37,58);

$$Ar-\underset{\underset{O}{\|}}{S}-ONa + C(=O)(Cl)(OEt) + CH_3OH \xrightarrow[(-NaCl)]{(-CO_2)} Ar-\underset{\underset{O}{\|}}{S}-OCH_3 + EtOH$$

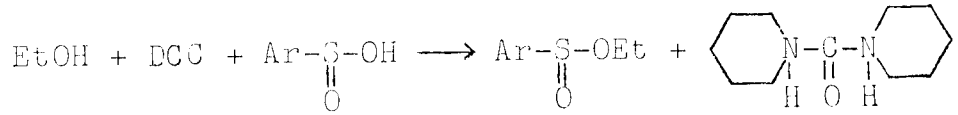
(3) by treatment of arylsulfinic acids with diazomethane (2);



(4) by the oxidation of aromatic disulfides or thiols with lead tetraacetate (73);



(5) and most recently, by the coupling of sulfinic acids and alcohols using dicyclohexylcarbodiimide (DCC) (52).



In each case, the reactions take place under moderate conditions, attendant side reactions can be minimized, and the desired ester easily separated from the product mixtures.

Upon examining chemical formulae for sulfinic acid esters, one notes a striking similarity to those of carboxylic acid esters. By purely formal analogy, each contains a central atom doubly-bonded to oxygen, and two other groups -- an alcoholic moiety and an alkyl or aryl function. However, the two classes of compounds

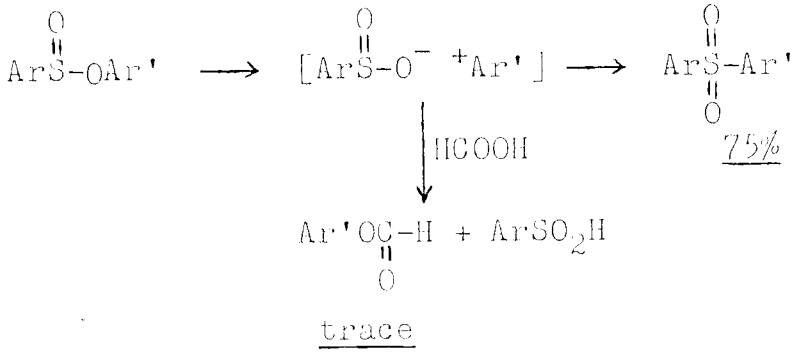
differ markedly in structure and hybridization state. Carboxylic acid esters involve the carbonyl carbon in a sp_2-planar arrangement; in sulfinic acid esters, sulfur assumes an sp_3-pyramidal configuration.

Substitution reactions of acetates and benzoates have been studied extensively and their mechanistic pathways clearly delineated. The analogous reactions of sulfinates have received much less attention, but some significant research has been published on this topic.

Only a few papers, dealing with the preparation of arenesulfinate esters, had appeared in the literature prior to 1925. Henry Phillips (59) then published his classic studies of the preparation, properties, reactions and structure of n-alkyl p-toluenesulfinates. He reported that these esters can be resolved into enantiomers which possess optical activity and postulated a pyramidal structure with asymmetric sulfur atom at the apex. This structure was later confirmed by other investigators (84). Alcoholysis of these compounds showed that alkoxyl group exchange occurred with Walden inversion at sulfur. The sulfur-oxygen bond was cleaved in all cases.

Groups headed by Phillips and Joseph Kenyon continued to study various sulfinate ester reactions during the next two decades (1,5,33-35). Some of the more complex

esters, such as phenylmethylcarbinyl p-toluenesulfinate, rearranged during solvolysis to the corresponding sulfones (1). These products arose from ionic reactions involving carbon - oxygen bond fission.

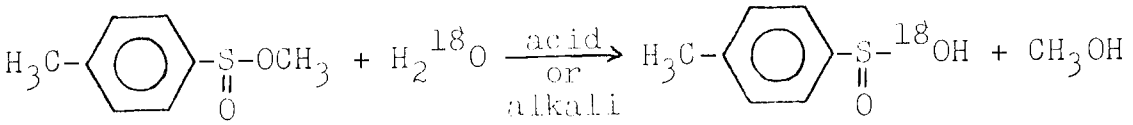


Ar = p-tolyl

Ar' = phenylmethylcarbinyl

In 1958, Wragg, McFadyen and Stevens (83) carried out related studies of the rearrangement of aralkyl arenesulfinates to their corresponding sulfones. Esters in which the alcohol moiety can stabilize a developing positive charge were noted to undergo C-O bond cleavage, ion pair formation and ultimate collapse of the intermediates to sulfones. Simple n-alkyl esters could not react in this way and thus showed exclusive S-O bond breaking.

Bunton and Hendy (15) used the following reaction to determine bond cleavage sites in substrates such a methyl p-toluenesulfinate:

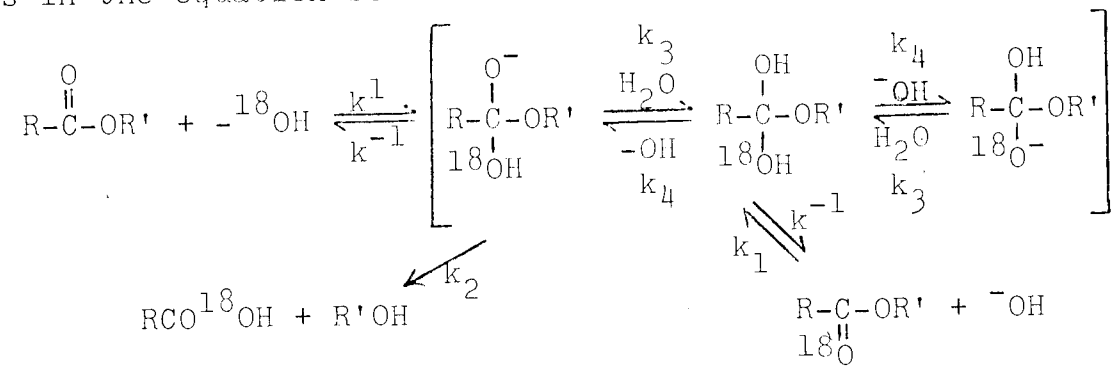


The methanol product contained no oxygen-18, indicating that substitution was occurring exclusively at sulfur, with ensuing S-O bond scission. In related work with the diphenylmethyl p-toluenesulfinate, products from both types of bond cleavage were observed (16).

Darwish and Noreyko (21) investigated the effects of substituents, solvents and bases upon aralkyl benzenesulfinates. They showed that in systems which can undergo C-O or S-O bond cleavage, the attack site can be controlled by proper selection of base and solvent. They also noted that the benzenesulfinates solvolyzed only 35 times more rapidly than 2,6-dimethylbenzenesulfinates. Unsubstituted ethyl benzoate hydrolyzes 10^5 times faster than ethyl 2,6-dimethylbenzoate. On the basis of the small rate decrease seen in substituted sulfinates, Darwish and Noreyko concluded that in steric behavior sulfinates more closely resemble sulfonates than they do carboxylic acid esters. Bunnett and Bassett had already reported that ortho methyl group substitution in benzenesulfonic acid esters produced only slight or "miserable" rate effects (13).

These studies, while nicely defining stereochemistry and the cleavage sites within the molecule, revealed only limited information about the nature of reaction intermediates. Since tetrahedral intermediates have been shown to exist in carboxylic acid ester reactions, it seemed reasonable to investigate the possible occurence of metastable species in comparable reactions of sulfinic acid esters.

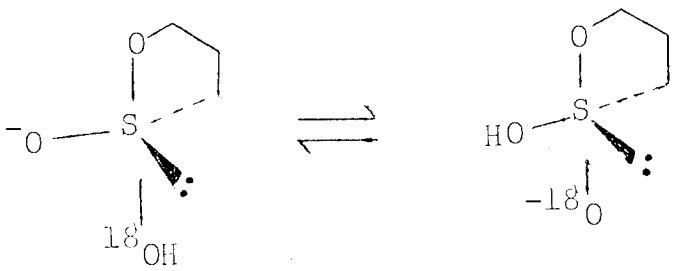
Bender's classic test for metastable intermediates was that of ^{18}O incorporation into acetates during partial hydrolysis (6). Mechanistically this can be depicted as in the equation below.



Unhydrolyzed ester can be found to contain ^{18}O, clearly requiring the formation of a finite-lived intermediate capable of oxygen equilibration. This test, while unambiguous in reactions of acetates and alkyl benzoates, fails to show ^{18}O incorporation accompanying hydrolysis of aryl benzoates. Rather than assume that a tetrahedral

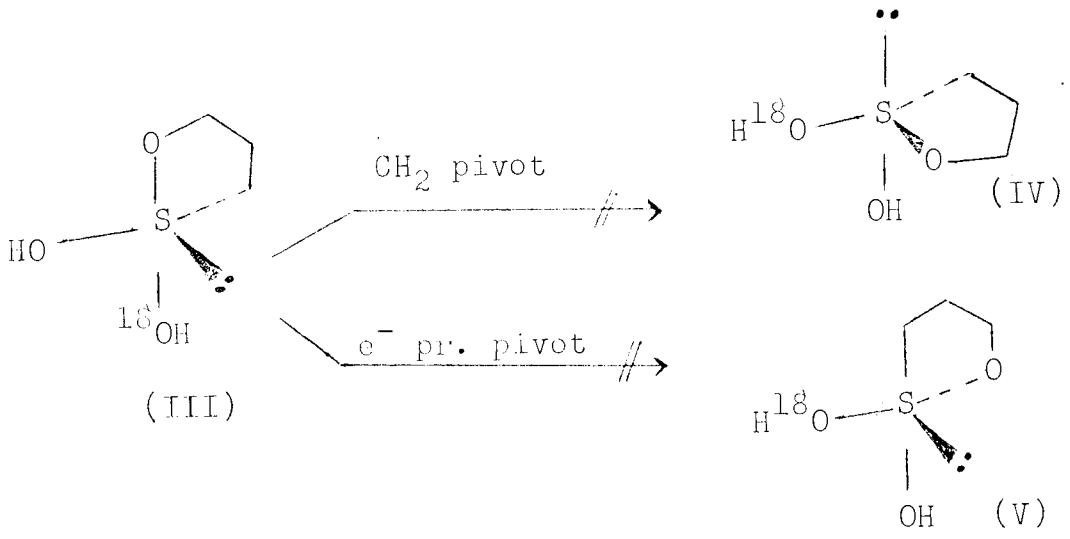
intermediate is not formed in the latter case, one should consider the total process. Bender (7) argues that for aryl benzoates the protonation-deprotonation steps occur slowly enough to be kinetically significant. Hydrolysis is thus much faster than the processes of ^{18}O equilibration and return to the starting ester. No ^{18}O incorporation into the unhydrolyzed substrate is observed, although the intermediate is most probably formed.

This test of ^{18}O incorporation has been tried for several sulfinic acid esters. The tracer experiments with five and six-membered cyclic sulfinates have shown no oxygen-18 exchange into the unhydrolyzed starting material (55). It has been suggested that such compounds may react via trigonal bipyramidal intermediates with the ring spanning one apical and one equatorial position.



(I) (II)

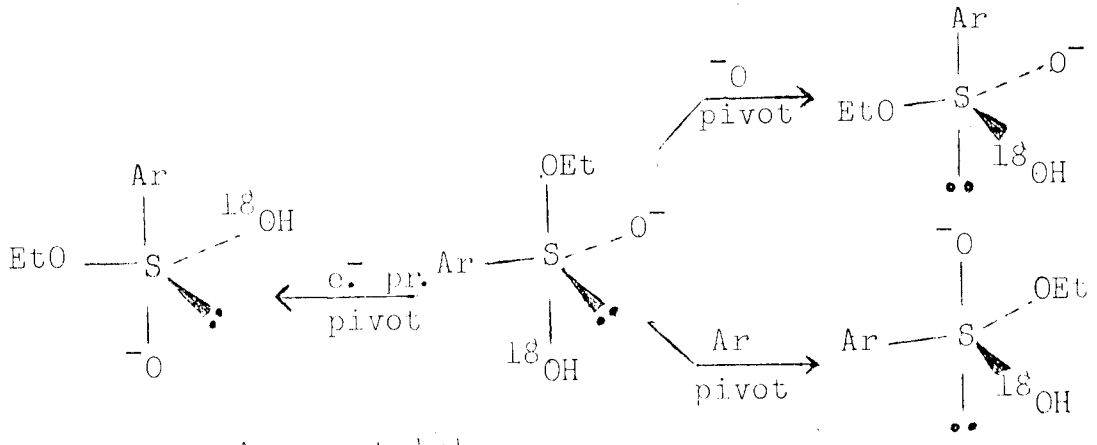
Proton transfer leading from (I) to (II) and ultimate ^{18}O equilibration is probably quite slow. According to Mutterties rules, the most electronegative substituents prefer to occupy the apical sites in the intermediate (81). Since ^{-}OH is more electronegative than the sulfinyl oxygen, a structure such as (II) would place both groups into energetically unfavorable positions. Another process could lead to ^{18}O incorporation -- that of protonation to III followed by pseudorotation.



But there are reasons to believe that pseudorotation of intermediate (III) might be rather slow. Pivot about the equatorial methylene group to produce (IV) would force the ring to span two equatorial positions, intro-

ducing strain energy and forcing the electron pair into a disallowed apical position. In forming (V), pivot about the electron pair while interchanging the $-^{18}OH$ and -OH groups, simultaneously places a methylene group into an unfavorable position. Considering the constraints upon the molecule in either process, it is not at all unreasonable that collapse of III to unhydrolyzed ester or the ring opening to product could occur far faster than equilibration of oxygens.

This lack of ^{18}O exchange has been observed for the open chain analogs also (36). The non-cyclic esters are not restricted in the same manner as the oxathiolanes and oxathianes. However, the energy considerations of pseudorotating <u>any</u> radial substituent of a trigonal bipyramidal intermediate into a higher energy apical position should favor the hydrolysis or return process over ^{18}O incorporation.



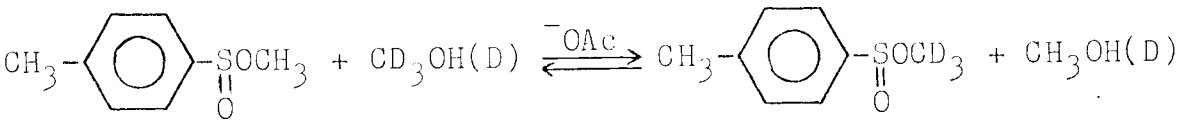
Ar = p-tolyl

The idea of trigonal bipyramidal intermediates in sulfur systems was first suggested in 1960 (8). These species have been invoked extensively in reactions of phosphorus compounds and various researchers have indeed reported evidence for these intermediates in sulfur systems (4,45,47,67). It must be noted that much of the body of information relating to the sulfur compounds is still inconclusive and often controversial.

Given the factors disfavoring ^{18}O equilibration in trigonal bipyramidal intermediates, it is not possible to use tracer evidence to argue for or against their occurence in sulfinate ester solvolyses. The geometry of an intermediate and that of an S_N2 transition state should be identical -- so that the question remains one of the timing of bond breaking and bond formation during substitution at the sulfur center.

The failure of ^{18}O tracer studies in determining the existence of intermediate in sulfinate ester solvolyses reactions requires one to look for alternative techniques. The kinetic method used by S.L. Johnson seems quite suited to this study (29). She was able to show in the case of ethyl trifluoroacetate the probable existence of tetrahedral intermediates. Ethanolysis of this carboxylic acid ester was carried out in amine-buffered heavy ethanol

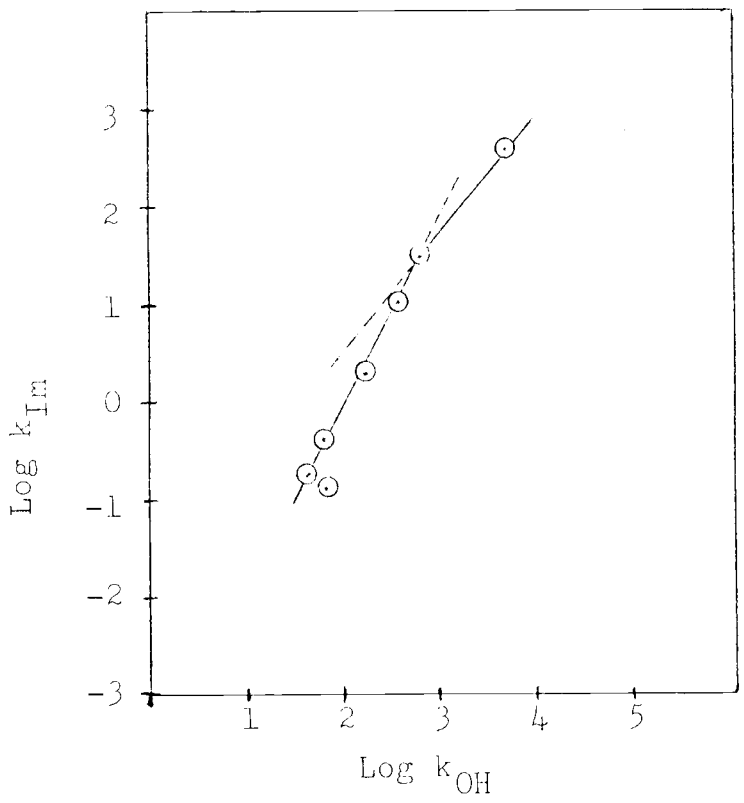
(C_2D_5OH). The observation of general base catalysis of the ethoxyl exchange reaction was deemed consistent only with a symmetrical mechanism proceeding through a tetrahedral intermediate. Other suggested routes such as S_N2 displacements and nucleophilic catalysis were seen to violate microscopic reversibility or were inconsistent with observed kinetics. This same type of test could be applied to an analogous sulfur system, methyl p-toluenesulfinate.



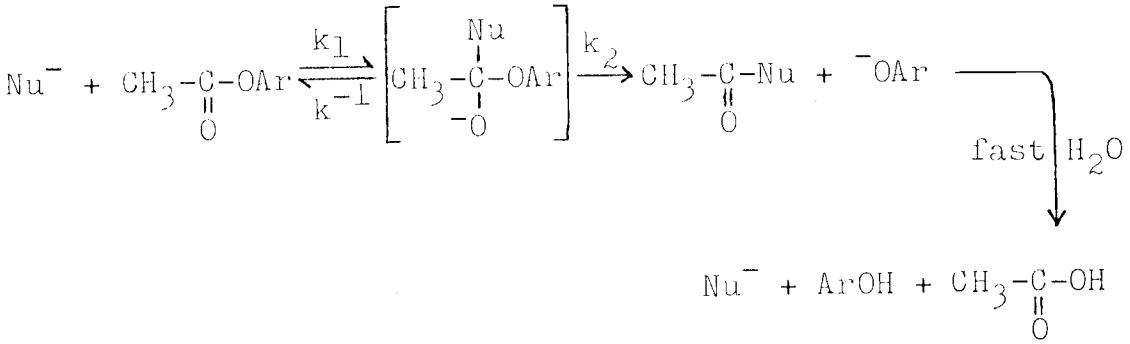
Since the entering and leaving groups differ only in isotopic substitution and are otherwise nearly chemically equivalent, the forward and reverse reactions must proceed in the same manner. If general base catalysis could be observed in this system, it would provide strong evidence for an intermediate existing along a symmetrical exchange pathway.

Kirsch and Jencks' studies (44) of substituted aryl acetates suggests still another tool to detect the metastable species. If one plots the rates of imidazole catalysis of hydrolysis versus the rates obtained in media containing hydroxide ion, it can be seen that a

"break" in the correlation line occurs.



Mechanistically this break is explained by a change in the rate determining step, indicating that an intermediate exists along the reaction pathway.



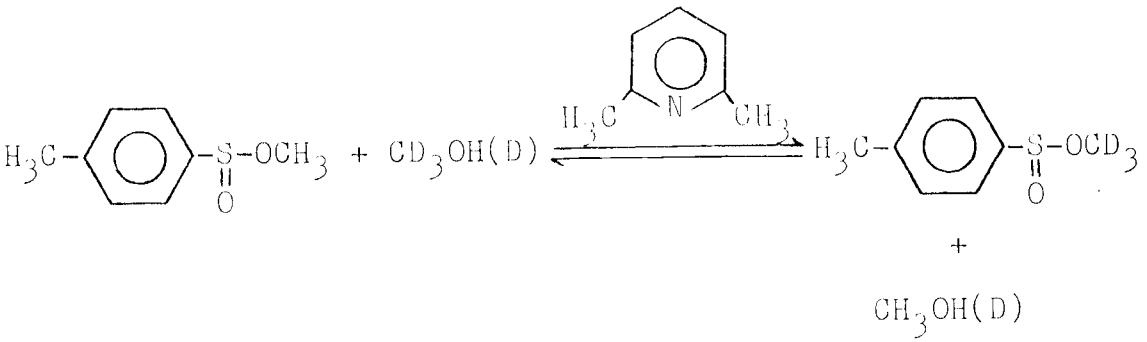
For all cases of hydroxide catalyzed hydrolysis, the -OAr is a better leaving group than -OH and k_1 is the rate determining step. When imidazole is employed as a catalyst, the rate determining step depends upon the pKa of the substituted -OAr group. If the pKa of -OAr is greater than that of imidazole, k_2 becomes rate determining. For the nitro- substituted moieties only, the pKa is less than that of the attacking nucleophile and k_1 becomes the rate determining step.

Two groups have reported syntheses of aryl arenesulfinates (48,83). It was hoped that a series of substituted aryl benzenesulfinates or p-toluenesulfinates could be synthesized and the imidazole versus -OH rate test applied to a sulfinyl sulfur system. This test coupled with the methyl group exchange reaction should then provide more definitive evidence for, or against, intermediates in substitutions at sulfur.

RESULTS

Exchange of Methanol-d_4 with Methyl p-toluenesulfinate in the Presence of Added 2,6-Lutidine

Catalysis of the exchange by 2,6-lutidine was the first reaction studied.

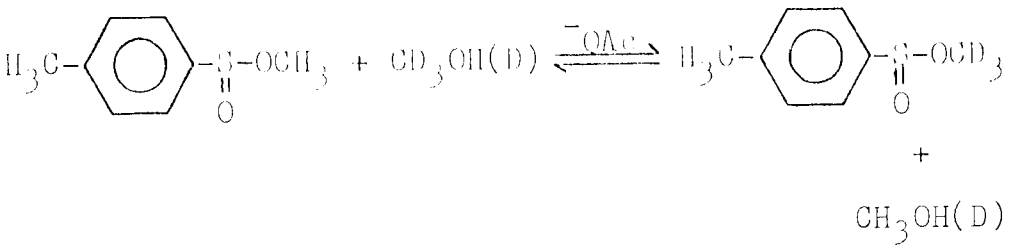


The reaction was carried out at 62°C in CD_3OD with 0.210 M. lutidine, 0.105 M. lutidinium perchlorate added to the ester solution. The exchange was extremely slow, with an estimated k_{obs} in the range of 10^{-8} to 10^{-9} second $^{-1}$.

Darwish and Noreyko (21) had reported lutidine-catalysis of methoxyneophyl arenesulfinate solvolyses, but they used lutidine contaminated with traces of picolines. Lutidine used in this study was free of picolines as indicated by vpc checks. Catalysis of the ester exchange was indeed effected by the 2,6-lutidine, but at rates too slow for convenient study.

Acetate-catalyzed Exchange of Methanol-d_4 with Methyl p-toluenesulfinate

The remainder of the kinetic studies with methyl p-toluenesulfinate involved the following reaction:



The exchange proceeds very slowly without acetate added to the reaction medium. Methoxyl interchange is significantly faster when sodium acetate and acetic acid are present in solution.

Several groups have reported that substitution reactions of n-alkyl arenesulfinates are accelerated by acetate without defining the operative mechanisms (21,59). Data of Darwish and Noreyko showed acetate to be a much more effective catalyst than lutidine. Rates obtained in acetate solutions were 100 to 1000 times faster than for lutidine and could thus be determined more facilely.

Cleavage site in the molecule

Studies of Phillips (59), Bunton and Hendy (15), and Wragg, McFadyen and Stevens (83) all have shown that

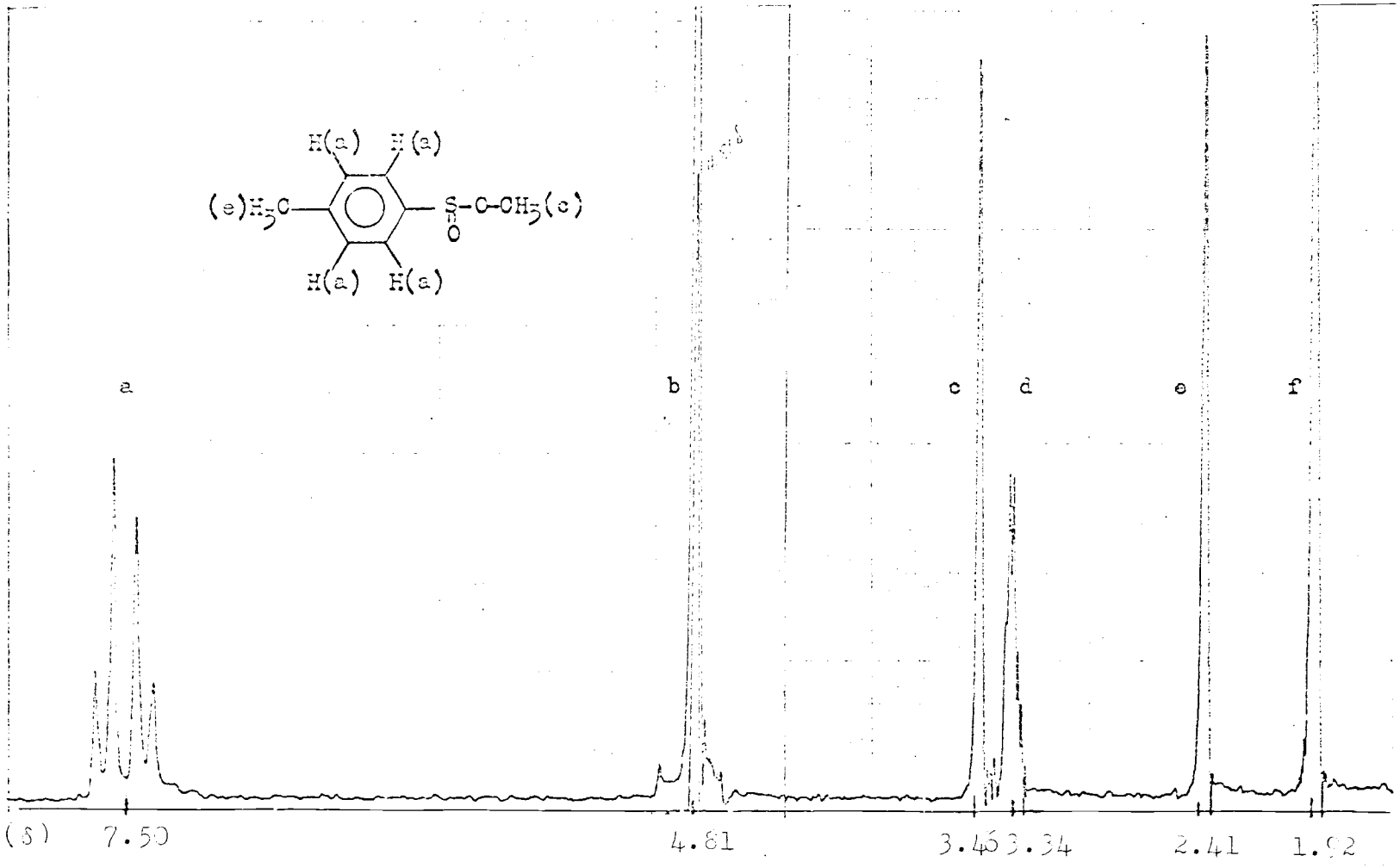
the substitution reactions of n-alkyl arenesulfinates proceed with sulfur - oxygen bond scission. Therefore one can be sure that the exchange reaction shown on page 15 will proceed by S-O rather than C-O bond cleavage. The possibility of C-O cleavages was also excluded in the experimental study by showing that there were no detectable side reactions leading to products resulting from C-O bond scission.

NMR procedure for the kinetic determinations

The NMR spectrum of methyl p-toluenesulfinate in acetate-buffered CD_3OD is shown in Figure 1, along with appropriate assignments for each of the sulfinate ester protons. Singlet b (4.81 δ) is the alcohol hydroxyl proton resulting from the 1% non-deuteration in the solvent. Multiplet d (centered at 3.34 δ) is deemed to arise from traces of CHD_2-, CH_2D-, and CH_3- in the deuterated methanol. Signal f (1.92 δ) is due to the methyl group in the sodium acetate or acetic acid.

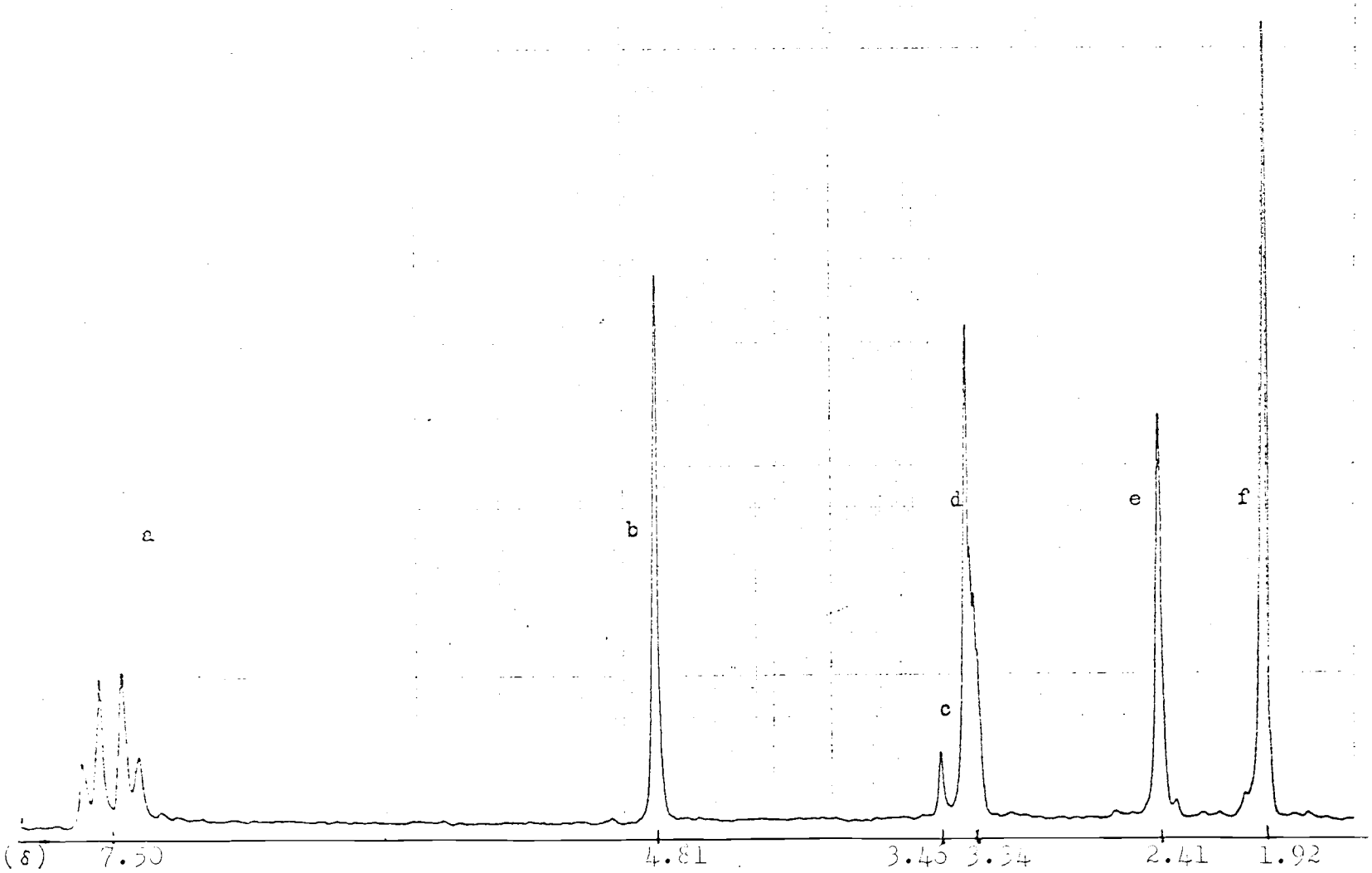
The NMR spectrum of the acetate-buffered solutions will have the appearance of signals in Figure 1 at time zero of the reaction. As the reaction proceeds, the singlet c and multiplet d are altered in shape and magnitude. Figure 2 shows the appearance of these signals at

FIGURE I. NMR spectrum of methyl p-toluenesulfinate in acetate-buffered CD_3OD



peak assignments and appearance of the NMR spectrum at time zero

FIGURE 2. NMR spectrum of methyl p-toluenesulfinate in acetate buffered CD_3OD



NMR peak appearance at approximately three to four half lives

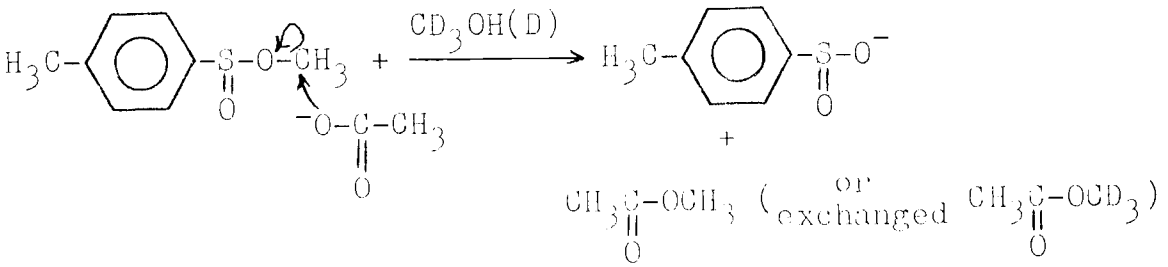
approximately three to four half-lives of the reaction. By monitoring the rate of decrease in the ester $-OCH_3$ signal c relative to either tolyl-CH_3, signal e, or acetate-CH_3, signal f -- both of which remain constant throughout the reaction -- it was possible to obtain data to calculate the observed rate constant for the ester exchange reaction. The ester methoxyl signal c is separated from the adjacent multiplet (signal d) of the solvent by 12 Hz, and can be integrated quite accurately.

NMR checks for potential side reactions

Two side reactions were deemed possible in the exchange reaction between methanol-d_3 and methyl p-toluenesulfinate.

1. Competing hydrolysis, arising from inadvertent traces of moisture, would lead to formation of p-toluenesulfinic acid. Addition of a small amount of sodium p-toluenesulfinate to the kinetic solution produced the NMR spectrum shown in Figure 3. The A_2B_2 quartet (centered at 7.50 δ) in the aromatic proton region has been replaced by a more complex multiplet. A second tolyl-CH_3 peak is noted adjacent to the tolyl-CH_3 peak of the ester, but separated by at least 8 Hz. Formation of this side product is thus easily detected.

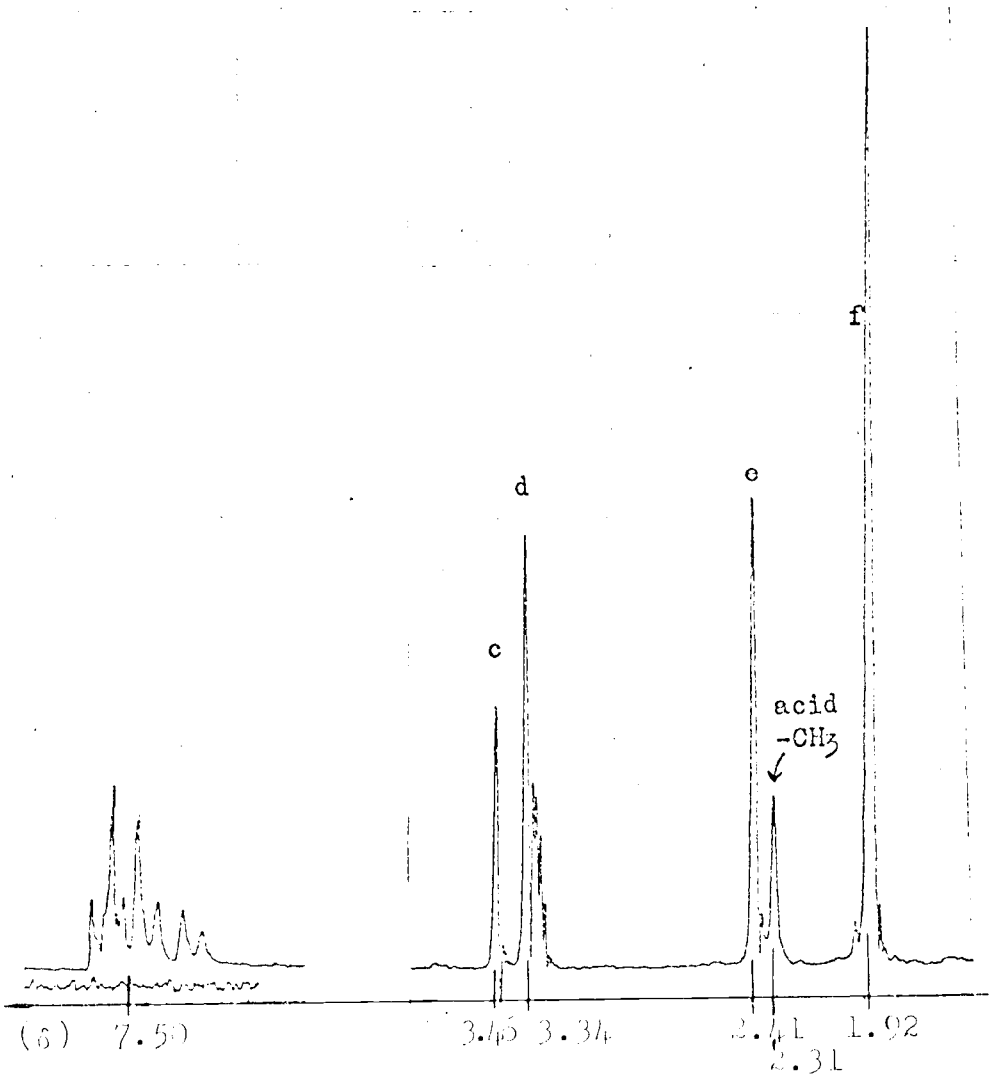
2. A second possible side reaction is shown in the equation below:



Attack at carbon, rather than sulfur, would give the C-O cleavage product methyl-d_3 acetate. Possibility of this reaction is remote from literature reports, but was excluded for completeness of the investigation. Methyl acetate added to reaction solutions produced the NMR spectrum in Figure 4. A second peak due to the methyl acetate is separated from the acetate catalyst peak by 8.0 Hz. Moreover the trace amounts of p-toluenesulfinic acid liberated during such an attack would give the additional peak changes noted in Figure 3. These were not observed.

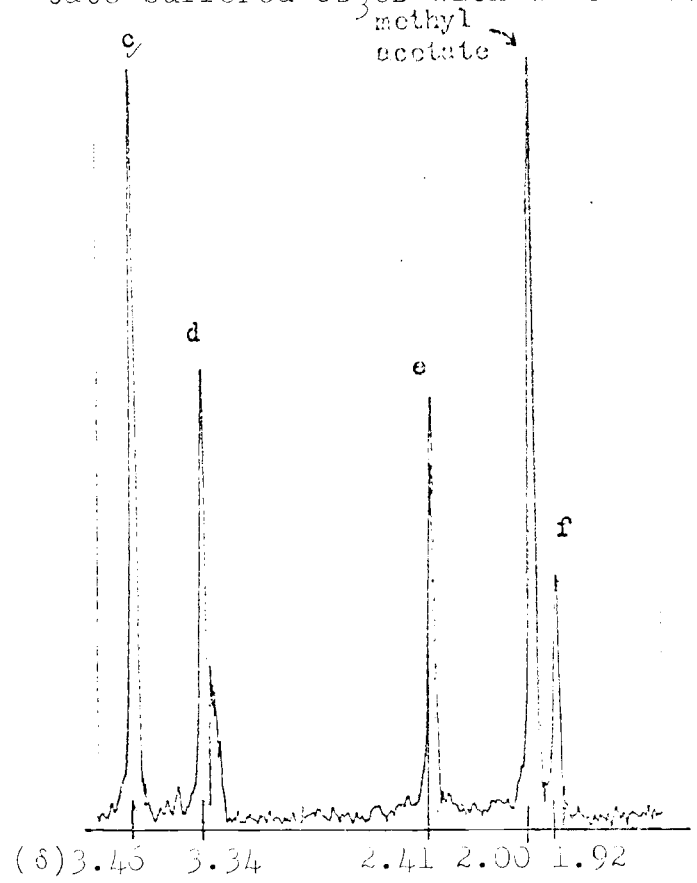
The complete disappearance of methoxyl protons (signal c) in the NMR scans taken at eight to ten half-lives (t_∞) and the lack of extraneous peaks in the scans indicated that all kinetic runs proceeded cleanly to completion.

FIGURE 3. NMR spectrum of methyl p-toluenesulfinate in acetate-buffered CD_3OD with added sodium p-toluenesulfinate

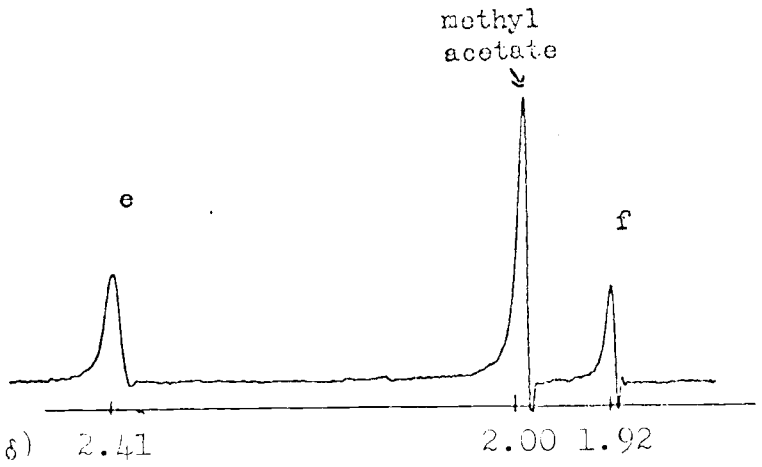


peak appearances on 100 Hz sweepwidth (alcohol hydroxyl proton not shown)

FIGURE 4. NMR spectra of methyl p-toluenesulfinate in acetate-buffered CD_3OD with added methyl acetate



(a) buffer acetate, methyl acetate peak separation shown on 1000 Hz sweepwidth spectrum



(b) peak appearance on 250 Hz sweepwidth spectrum

Kinetic plots to obtain k_{obs}

The first order rate constants, k_{obs}, were determined by graphing the logarithm of ($-OCH_3/-OAc$) or the logarithm of ($-OCH_3$/tolyl-CH_3) versus time. The slopes, k_{obs}, were also verified by least squares computer analysis. Figure 5 shows a typical first order rate plot for the reaction. It can also be noted that the slopes are identical regardless of the ratio used in plotting. No deviation from linearity is seen after six to seven half-lives so the reaction order is verified.

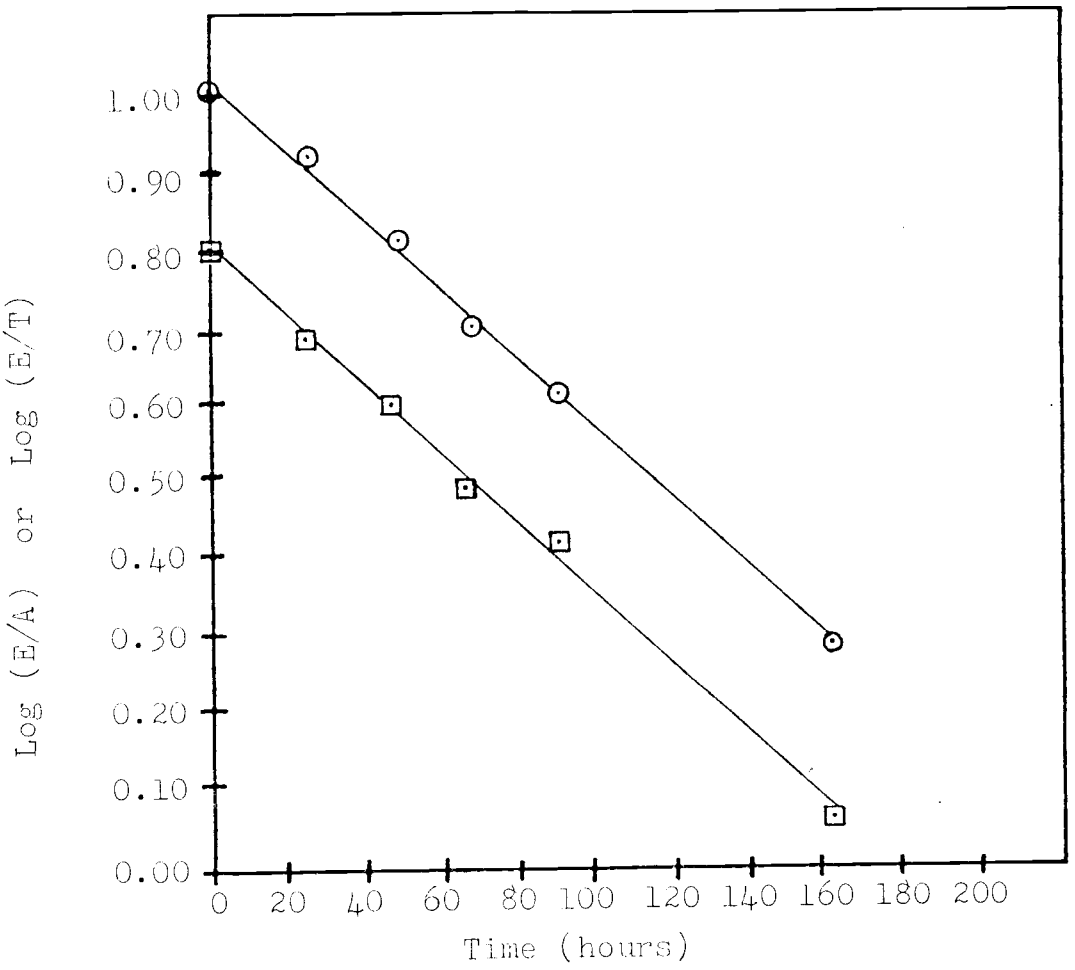
Reactions were carried out in two different solvents, CD_3OH and CD_3OD, at constant ionic strength maintained by lithium perchlorate. Several buffer ratios of sodium acetate/acetic acid were used, with acetate ion concentrations varied systematically.

The rates obtained for the various reactions in CD_3OH are shown in Table 1. Similar reactions in CD_3OD are summarized in Table 2.

Kinetic plots for k_{OAc} the second order catalytic constant

The second order rate constant for acetate catalysis, k_{OAc}, was obtained from plots of k_{obs} versus acetate ion concentrations. A series of k_{obs} for buffer ratios of 2/1, 1/1, and 0.735/1 were obtained for the acetate-catalyzed runs in CD_3OH. These are shown in Figure 6.

FIGURE 5 Typical first order rate of exchange of 0.20 M. methyl p-toluenesulfinate with acetate buffered methanol-d_3 at 62°C.



a) Data obtained from the NMR integration of ester-OCH_3 and acetate-CH_3. Ratio plotted (E/A) ⊡

b) Data obtained from the NMR integration of ester-OCH_3 and tolyl-CH_3. Ratio plotted (E/T) ⊙

c) Solution components: sodium acetate 0.21 M., acetic acid 0.105 M.

TABLE 1. Kinetics of the exchange between 0.20 M. methyl p-toluenesulfinate and methanol-d_3 solvent at 62.0°C.*

$[^-OAc]/[HOAc]$	$[^-OAc] \times 10^1$ M.	$[HOAc] \times 10^1$ M.	$k_{obs} \times 10^6$ sec^{-1}
2:1	2.10	1.05	2.78
2:1	2.10	1.05	2.74
2:1	1.58	0.79	2.42
2:1	1.40	0.70	2.27
2:1	1.05	0.53	1.92
2:1	1.05	0.53	1.96
2:1	0.70	0.35	1.76
2:1	0.70	0.35	1.72
1:1	2.10	2.10	1.85
1:1	2.10	2.10	1.83
1:1	1.40	1.40	1.41
1:1	1.05	1.05	1.17
0.735:1	2.10	2.86	1.68
0.735:1	1.40	1.91	1.21
0.735:1	1.05	1.43	1.05
0.735:1	0.70	0.96	0.85

*Ionic strength held constant at 0.21 M. by addition of lithium perchlorate

TABLE 2. Kinetics of the exchange between 0.20 M. methyl p-toluenesulfinate and methanol-d_4 solvent at 62.0°C.*

$[^-OAc]/[HOAc]$	$[^-OAc] \times 10^1$ M.	$[HOAc] \times 10^1$ M.	$k_{obs} \times 10^6$ sec^{-1}
2:1	2.10	1.05	1.96
2:1	2.10	1.05	2.00
2:1	1.58	0.79	1.68
2:1	1.58	0.79	1.69
2:1	1.40	0.70	1.54
2:1	1.40	0.70	1.54
2:1	1.05	0.53	1.34
2:1	1.05	0.53	1.35
2:1	0.70	0.35	1.16
1:1	2.10	2.10	1.20
1:1	1.40	1.40	0.91
1:1	1.05	1.05	0.74
1:1	0.70	0.70	0.65

*Ionic strength held constant at 0.21 M. by addition of lithium perchlorate

TABLE 3. Rate constants for the exchange of methyl p-toluenesulfinate[a] with acetate-buffered methanol-d_3 and methanol-d_4[b] solvents

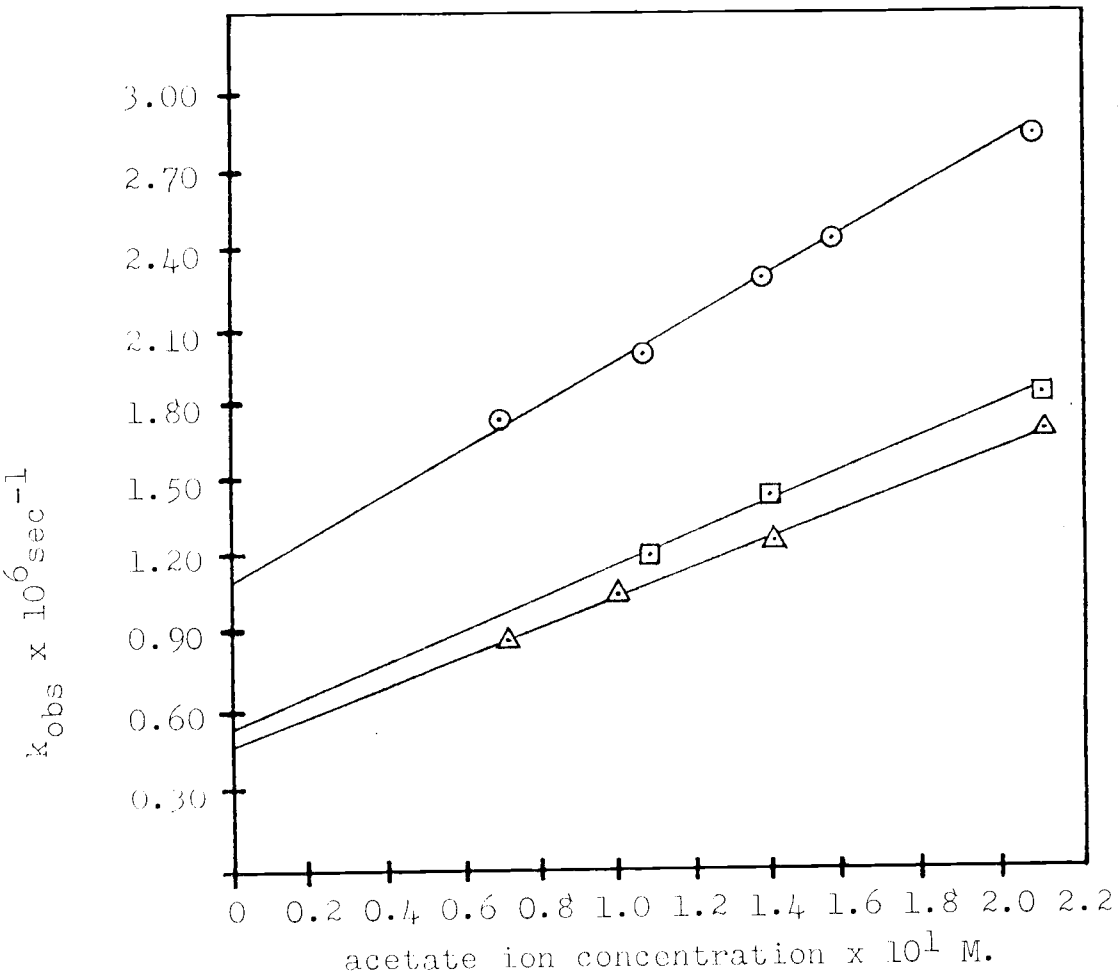
Solvent	$[^-OAc]/[HOAc]$	Slope = k_{OAc^-} ($\times 10^6 M^{-1} sec^{-1}$)	Intercept = k'_{OMe}[c] ($\times 10^6 sec^{-1}$)
CD_3OH	2/1	7.85	1.14
CD_3OH	1/1	6.20	0.54
CD_3OH	0.735/1	6.05	0.42
CD_3OD	2/1	5.97	0.72
CD_3OD	1/1	4.03	0.35

a) concentration of ester 0.20 M. for all runs

b) all data obtained at constant ionic strength 0.21 M. at 62°C.

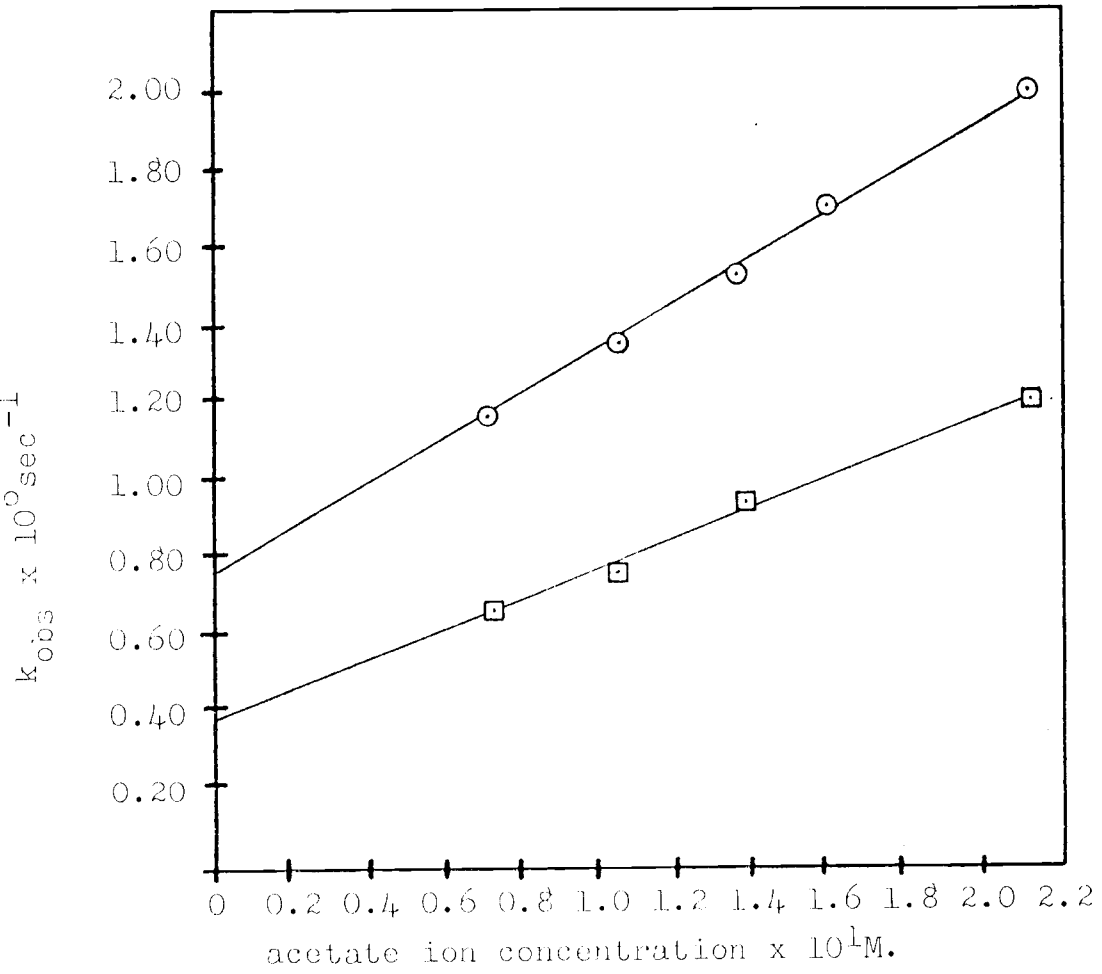
c) k'_{OMe} is equivalent to $k_{OMe}[^-OMe]$

FIGURE 6. Exchange of methanol-d_3 with methyl p-toluene-sulfinate in acetate - acetic acid buffered solutions at 62°C.



a) Ester concentration 0.20 M. for all runs
b) Ionic strength maintained at 0.21 M. with lithium perchlorate
c) Sodium acetate/acetic acid buffer ratio:
   2/1 ⊙
   1/1 ⊡
   0.735/1 △
d) Slope = k_{OAc} for exchange reaction in CD_3OH

FIGURE 7. Exchange of methanol-d_4 with methyl p-toluene-sulfinate in acetate - acetic acid buffered solutions at 62°C.



a) Ester concentration 0.20 M. for all runs
b) Ionic strength maintained at 0.21 M. with lithium perchlorate
c) Sodium acetate/acetic acid buffer ratio:
⊙ 2/1
⊡ 1/1
d) Slope = k_{OAc} for exchange reaction in CD_3OD

Similarly a series of runs in buffer ratios 2/1 and 1/1 were carried out in CD_3OD and are shown in Figure 7. All rates were also verified with least squares computer calculations. A summary of the rates obtained is given in Table 3.

The intercepts in all cases are different from zero and will be shown later to result from methoxide ion contribution to the rate.

Solvent isotope effects

Solvent isotope effects for the acetate-catalyzed exchange reactions in methanol-d_3 and methanol-d_4 are given in Table 4 (below).

TABLE 4. Solvent isotope effects for the rate constants shown in Table 3.

$^-OAc/HOAc$	$k_{OAc}^{CD_3OH}/k_{OAc}^{CD_3OD}$	$k'_{OMe}^{CD_3OH}/k'_{OMe}^{CD_3OD}$
2/1	1.31 ± 0.1	1.58 ± 0.1
1/1	1.54 ± 0.1	1.54 ± 0.1

The solvent isotope effect on the second order rate constant k_{OAc} is seen to vary with the buffer ratio. The effect on the methoxide term k'_{OMe} remains constant however. Closer examination of the rates given in Table 3 and Figures 6 and 7 show that the slopes for plots of k_{obs} versus acetate concentration, giving k_{OAc}, are varying with the buffer ratio. Normally one should expect the slopes to remain the same and give the same k_{OAc} for all the buffer ratios. The observed variations occur to a greater degree in CD_3OD than in CD_3OH, leading to the greater solvent isotope effect noted in the 1/1 buffers.

The intercepts change as predicted. These are decreasing by the same magnitude as the buffer ratios in both solvents, so that the solvent isotope effect for the methoxide ion term remains constant.

Possible reasons for the changes in k_{OAc} and the meaning of the solvent isotope effects will be discussed later in this chapter.

Attempted synthesis of aryl arenesulfinates

Several techniques to synthesize either phenyl p-toluenesulfinate or phenyl benzenesulfinate were tried without success. These methods are described in the

Experimental section of this chapter. The phenyl ester would be needed, along with a series of substituted aryl benzene- or p-toluenesulfinates, in order to apply the imidazole versus hydroxide catalyzed hydrolysis test for intermediates.

The literature reports of these compounds are incomplete and contradictory. One group (83) reported phenyl benzenesulfinate to be a crystalline compound and gave a melting point for the "unstable needles". They cited no spectral or analytical data. A Russian group (48) described this ester as an oil and published a sulfur analysis consistent with the expected percentages. Both groups stated that they were unable to purify the product.

The phenyl ester should presumably be one of the more stable ones of its series. Since it appeared to be so unstable and resistant to purification techniques, further work in this line of research seemed unwarranted.

DISCUSSION

Exchange of Methanol-d_4 with Methyl p-toluenesulfinate in the Presence of 2,6-Lutidine

The exchange reaction of methyl p-toluenesulfinate with CD_3OD was seen to be catalyzed by lutidine, but the rates were extremely slow. The observed catalysis could be consistent with at least three general mechanisms -- nucleophilic displacement of $-OCH_3$ by lutidine, general base catalysis by lutidine, and specific base catalysis by methoxide.

The Darwish and Noreyko studies (21) with p-methoxyneophyl benzenesulfinates in anhydrous ethanol determined solvolysis rates, under identical conditions, for the two catalysts 2,6-lutidine and acetate ion. Acetate was much more effective than lutidine in catalyzing the ethanolysis of the esters by a factor of 10^3.

In these studies with methyl p-toluenesulfinate in deuterated methanol, the observed rates of exchange follow a similar pattern. The acetate reactions lie in the range of 10^{-6} sec^{-1} while lutidine rates are only 10^{-8} or 10^{-9} sec^{-1}. This rate difference of 10^2 or 10^3 is in

superficial agreement with those values noted by Darwish and Noreyko. Further data is needed before any mechanism can be defined for the reaction.

Acetate Catalyzed Exchange of Methanol-d_3 and -d_4 with Methyl p-toluenesulfinate

Three major questions require detailed consideration in this discussion -- the various species contributing to the overall reaction rate, the meaning of the solvent isotope effect and the mechanism(s) consistent with the data.

Rate expression for the exchange reaction

The reaction of methyl p-toluenesulfinate with methanol-d_3 and -d_4 in acetate-buffered solutions is most definitely catalyzed by acetate ion. Graphs of k_{obs} versus ($^-$OAc) extrapolated to zero concentration of acetate ion are seen to give intercepts that are different from zero. This indicates that another species is also contributing to the overall rate of the reaction, logically this would be methoxide ion present in the solvent. The total methoxyl exchange rate can thus be expressed as in Equation 1.

$$k_{obs} = k_{OAc}(^{-}OAc) + k_{OMe}(^{-}OMe) \qquad \text{Equation 1}$$

(Tables in the Results section designate the intercepts as k'_{OMe}; $k'_{OMe} = k_{OMe}(^{-}OMe)$.)

Rate-concentration plots show good linearity and first order dependence upon acetate ion concentration is observed for all the buffer ratios studied. This confirms the first term in Equation 1 and the graphical slopes of the plots directly provide values for k_{OAc}, the acetate catalysis constant. (Table 3 shows the k_{OAc} values measured in the two solvents. All lie between 4 and 8 x $10^{-6} M^{-1} sec^{-1}$.)

Analysis of the second term, k_{OMe} (^{-}OMe), is not so straightforward. There is no way to measure the methoxide ion concentrations in the solutions, so they must be found by calculation. Methoxide is produced in the solvent by autoprotolysis of methanol and by the solvent interaction with acetate ion. Its generation might be represented simplistically by the following equilibrium reaction:

$$(^{-}OAc) + MeOH \overset{K1}{\rightleftharpoons} HOAc + (^{-}OMe)$$

Methoxide ion concentration can then be related to an equilibrium constant K_1 and the acetate buffer ratio.

$$(^{-}OMe) = K_1 \left(\frac{^{-}OAc}{HOAc}\right)$$

If such an expression is correct, the rate of the methoxide ion catalyzed reaction should vary proportionally with the acetate buffer ratio. Stated another way, the intercept rate k'_{OMe}, when divided by the buffer ratio, should give a constant value. Such behavior is indeed noted. Table 5 (below) summarizes these relationships for the reactions in CD_3OH.

TABLE 5. Methoxide Catalyzed Rates in CD_3OH

Buffer Ratio	Graph Intercept k'_{OMe} ($\times 10^{5} sec^{-1}$)	Experimental Rel. Intercepts	Calc. Rel. Intercepts	$\frac{k'_{OMe}}{B/BH^+}$
2	1.14	2.72	2.71	0.57
1	0.54	1.36	1.28	0.54
0.735	0.42	1.00	1.00	0.57

One might next assess whether the data will provide a reasonable value for k_{OMe}, the methoxide catalysis constant. K_1 can be defined in another way as being equal to the ratio of two <u>known</u> equilibrium constants, K_{MeOH} the autoprotolysis constant for methanol and K_{HOAc}

the acid dissociation constant for acetic acid in methanol. The final form for term 2 of Equation 1 then becomes $k_{OMe}(K_{MeOH}/K_{HOAc})(^{-}OAc/HOAc)$. Deuteration probably does not alter these equilibrium constants appreciably, so that assigning pK values of 16.7 (22) and 9.6 (20) respectively seems appropriate. Using the experimental buffer ratios in the calculations, the rate constant k_{OMe} is found to be 7 $M^{-1}sec^{-1}$.

This value of k_{OMe} is a reasonable one in comparison to other reported oxyanion catalysis constants. Najam and Tillet reported a rate constant of 16.2 $M^{-1}sec^{-1}$ for the hydroxide ion catalyzed hydrolysis of methyl benzenesulfinate at 61°C. (55) Bunton and Hendy determined a k_{OH} value of 4 $M^{-1}sec^{-1}$ for methyl p-toluenesulfinate hydrolysis in alkaline 40% dioxane at 0°C (15).

The total rate expression may thus be given by Equation 2 in which all quantities and constants are definable.

$$k_{obs} = k_{OAc}(^{-}OAc) + k_{OMe}\left(\frac{K_{MeOH}}{K_{HOAc}}\right)\left(\frac{^{-}OAc}{HOAc}\right) \qquad \text{Equation 2}$$

Solvent isotope effects

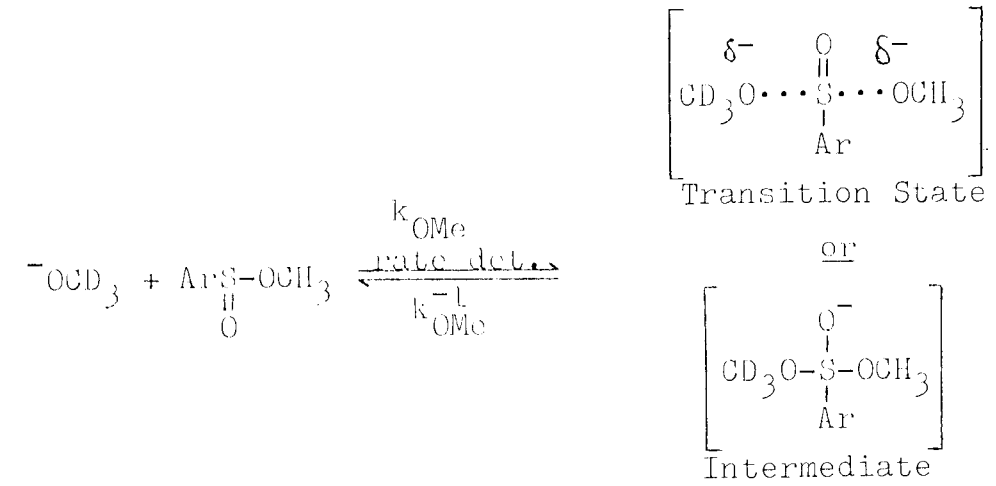
The solvent isotope effect has become a useful tool to distinguish between nucleophilic displacement and

general base catalyzed mechanisms. If a nucleophile attacks at a reaction center in a molecule without concurrent transfer of a solvent proton in the rate determining step, nearly identical rates of reaction in normal and deuterated solvents are observed. S. L. Johnson (30) has reported solvent isotope effects ranging 0.8 - 1.5 for oxygen anions reacting in nucleophilic catalysis routes. Reactions which involve transfer of a deuterium or hydrogen atom during the rate determining step commonly exhibit solvent isotope effects of 2 and above. The region of 1.5 - 2.0 thus remains one of ambiguity and overlap between the two mechanistic pathways.

The solvent isotope effects for the acetate-catalyzed exchange reaction of methyl p-toluenesulfinate and methanol-d_3 and -d_4 are 1.3 and 1.4 for the 2/1 and 1/1 buffer ratios respectively. Unfortunately these values lie on the borderline region between the two mechanistic types.

The solvent isotope effect for methoxide ion catalysis was found to be 1.5 for both buffer ratios. The reaction shows a direct dependence upon buffer ratio and consequently the pH of the medium, and can therefore be described by a specific base mechanism. This is outlined in Scheme I.

Scheme I



$$^{-}OCD_3 + ArS(=O)-OCH_3 \underset{k^{-1}_{OMe}}{\overset{k_{OMe}\ \text{rate det.}}{\rightleftharpoons}}$$

Transition state or Intermediate $\underset{k_{OMe}}{\overset{k^{-1}_{OMe}}{\rightleftharpoons}}$ $ArS(=O)-OCD_3 + {}^{-}OCH_3$,

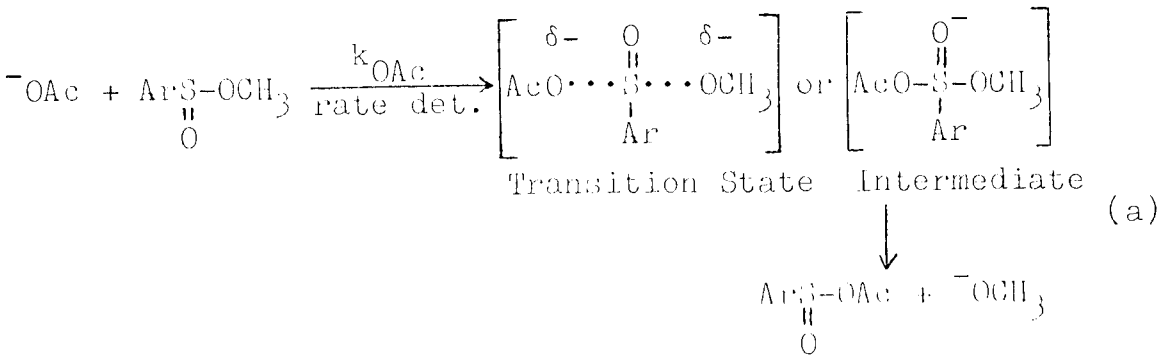
Ar = p-tolyl

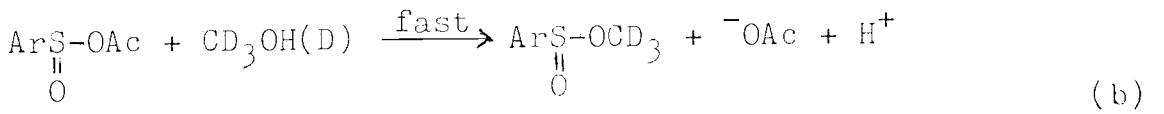
Assignment of a mechanism for the acetate catalyzed-reaction requires more consideration.

Possible mechanisms of acetate ion catalysis

Considering only the magnitude of the solvent isotope effect, the most defensible mechanism for the exchange reaction would appear to be a direct nucleophilic displacement of a leaving group by acetate, according to Scheme II.

Scheme II



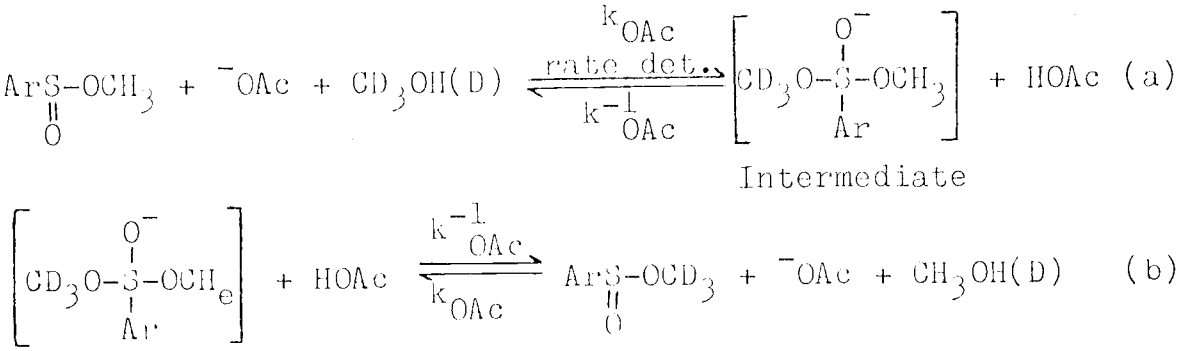


Ar = p-tolyl

However, it does not seem sensible to expect acetate to effect a direct substitution of methoxide since acetate is a much weaker nucleophile and a much weaker base than methoxide. A comparison of the second order rate constants calculated for the two species shows that methoxide is 10^6 times more effective than acetate as a catalyst.

Another possible mechanism, still under consideration because of the inconclusive solvent isotope effect, is one of general base catalysis depicted by Scheme III.

Scheme III



Ar = p-tolyl

Several facts exclude immediate acceptance of this alternative. The measured solvent isotope effect of 1.3 - 1.5 is certainly much smaller than expected for these types of reactions. Moreover, the usual behavior of k_{gb}, a general base catalysis constant, is to remain unchanged over a range of differing buffer ratios. Instead k_{OAc} is increasing with decreasing buffer ratio.

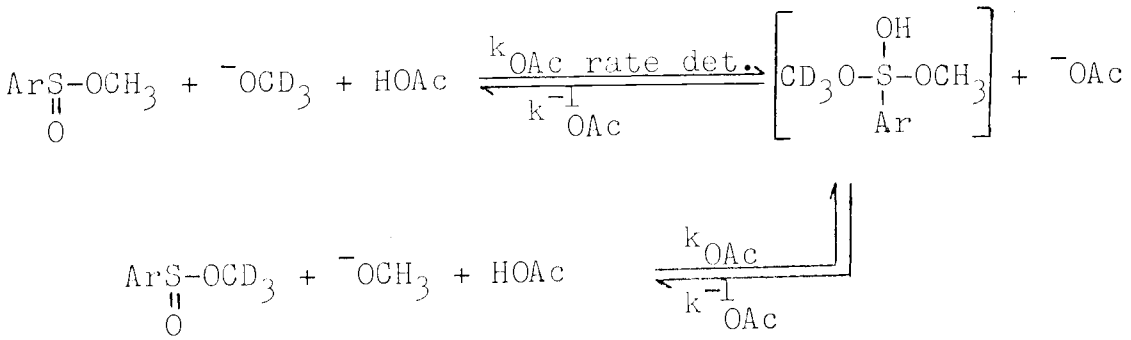
Oakenfull, Riley and Gold (24) found that acetate ion was the "crossover point" in reactions of substituted acetates and concluded that the total rate was a combination of both nucleophilic and general base catalysis. In this system with the sulfinate ester, it might be possible to describe the term in rate Equation 1, k_{OAc} ($^{-}$OAc), as being composed of two reactions -- k^{nu}_{OAc} ($^{-}$OAc) + k^{gb}_{OAc} ($^{-}$OAc). The contribution of the nucleophilic route

should still be quite small. Such an explanation suffers from the same objections as either individual route. True, it might lead to a small solvent isotope effect than a pure general base reaction, and a higher one than most nucleophilic routes. It cannot however offer rationale for the catalysis constants k_{OAc} differing with buffer ratio to give slightly different solvent isotope effects.

Is there perhaps yet another mechanism which can account for the similarity of the solvent isotope effects for acetate and methoxide and also account for the changing values of k_{OAc}?

A reaction pathway that is kinetically indistinguishable from general base catalysis is one of combination general acid and specific base catalysis. Scheme IV outlines such a route.

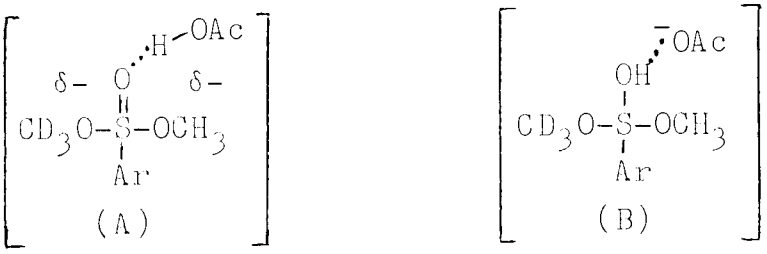
Scheme IV



Ar = p-tolyl

Several facets of this scheme seem more reasonable in accommodating the experimental results than other mechanisms. First, the ultimate species which attacks at sulfur is $^{-}OCD_3$, leading to displacement of $^{-}OCH_3$ from the molecule. This can account for the fact that the solvent isotope effect upon k_{OAc} and k_{OMe} are nearly identical. The reverse reaction still differs only in isotopic composition of the methoxyl group, symmetry of the reaction is preserved, and microscopic reversibility is not violated.

Secondly, the solvent isotope effect can be explained in light of the function of HOAc. The most probable placement of HOAc in the transition state (A) or intermediate (B) is in a hydrogen-bonded orientation to the sulfinyl oxygen.



(A) (B)

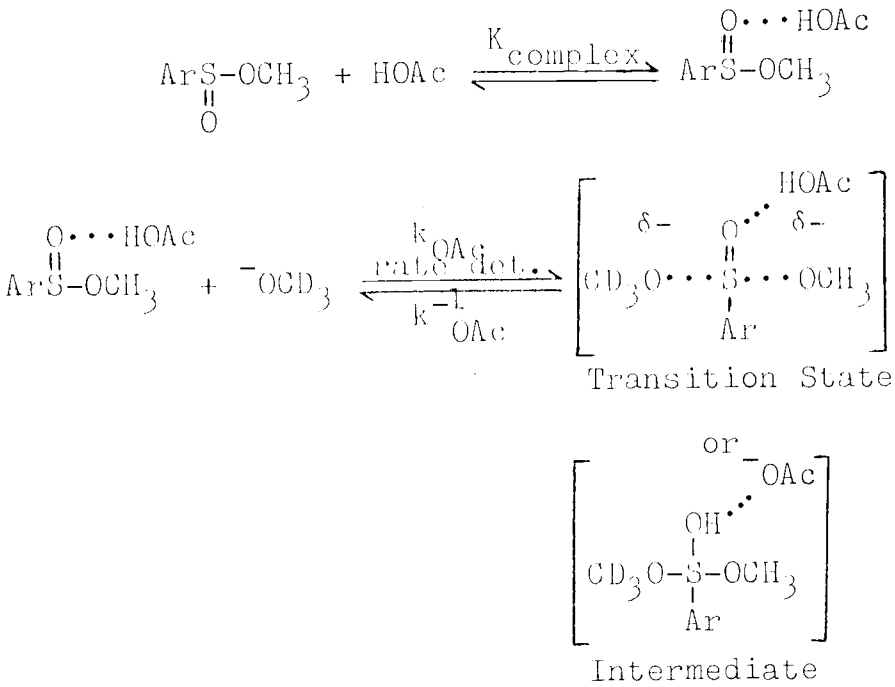
Ar = p-tolyl

One must remember that the solvent isotope effect is at a maximum when the hydrogen or deuterium atom lies midway between the acetic acid molecule and the ester. If the

hydrogen or deuterium atom is more closely bound to either the sulfinyl oxygen or the acetate group in the transition state or intermediate, the effect will be less. Jencks (28) has discussed proton transfer reactions to and from oxygen and sulfur and noted that they often exhibit abnormally low solvent isotope effects. These lowered values result because the highest energy barrier of the principal reaction does not always correspond to the energy barrier for proton transfer.

On first consideration, one might not like the idea of a termolecular transition state or intermediate, but Bruice and Benkovic (11) argue that this need not be unreasonable. Termolecular collisions are quite probable when reactant concentrations are "high". Moreover, this type of collision cannot be distinguished from a two-step reaction involving the formation of a complex in a rapid preequilibrium step and subsequent reaction with another reactant in a slow step. The acetate catalyzed reaction would then be given by Scheme V.

Scheme V



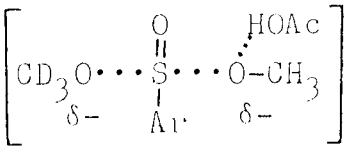
Another puzzling aspect of the data can be rationalized by Scheme V. Why is k_{OAc} changing so much with the buffer ratio in both solvents? If the value of $K_{complex}$ is large enough so that a significant concentration of the acid-ester complex is formed, then the amount of HOAc could be expected to have an effect upon the value of k_{OAc}.

The rate expression would require modification to include the preequilibrium step. The actual acetate rate constant now becomes k'_{OAc} and is defined in Equation 3 below.

$$k_{obs}(1 + K_{complex}(HOAc)) = k'_{OAc} \cdot K_{complex}\left(\frac{K_{MeOH}}{K_{HOAc}}\right)(^{-}OAc) + k_{OMe}(^{-}OMe) \qquad \text{Equation 3}$$

Although the rate constant for the acetate reaction by this analysis, k'_{OAc}, is different from the k_{OAc} previously noted, the value for k_{OMe} and the intercepts remain the same. Certainly for some values of $K_{complex}$, the plots by Equation 3 should be linear and might also provide more similar k'_{OAc} results for the different buffer ratios. Unfortunately, there is no method to accurately determine the correct value for $K_{complex}$, so proof of this hypothesis is unavailable.

Although the acetic acid molecule has been represented to be hydrogen-bonded to the sulfinyl oxygen in the transition state (or intermediate), it could assist the reaction in another fashion. Bonding with the methoxyl oxygen in the ester would make a better leaving group for the substitution reaction. This would appear to invoke an unsymmetrical transition state along the reaction pathway.



Ar = p-tolyl

Burwell and Pearson (17) have pointed out that microscopic reversibility is not violated by this type of skewed transition state if the reverse pathway is a mirror image of the forward reaction. The total reaction would then occur 50% by each pathway crossing one energy maximum. The same considerations for the transfer of a proton in the transition state should apply.

Summary

Considering the possible routes, it seems most logical to assume that the correct mechanism for acetate-catalyzed exchange of methanol-d_3 and -d_4 with methyl p-toluenesulfinate must be one of general acid, specific base catalysis. The solvent isotope effect is lower than normally expected for the reasons advanced in this discussion. However the data does not indicate any stronger support for the existence of an intermediate than for a transition state on the reaction pathway. Thus the question of metastable intermediates in sulfinyl sulfur reactions remains frustratingly unanswered in the current study.

EXPERIMENTAL

Preparation and Purification of Materials

Methyl p-toluenesulfinate

Methyl p-toluenesulfinate was prepared by reacting p-toluenesulfinyl chloride with methanol in pyridine, in the manner described by Bunton and Hendy (15). The crude product was purified by distillation under reduced pressure to afford a colorless oil, b.p. 68.5-69.5°C./ 0.2 torr, n_D^{25} 1.541 (literature values, b.p. 70°C/0.01 torr (15), n_D^{20} 1.5436 (27)).

Lithium perchlorate

Reagent grade lithium perchlorate (K and K Instruments) was used without further purification.

Sodium acetate

Sodium acetate was recrystallized from anhydrous methanol, dried for several hours at 125°C., and stored in a dessicator until use.

Acetic acid

Acetic acid was dried by distillation from acetyl borate, as described by Wiberg (82), b.p. 117-118°C.

2,6-Lutidine

2,6-lutidine was separated from traces of picolines by distillation from the boron trifluoride adduct, as recommended by Brown, Johnson and Podall (10). A vpc check showed the distillate to be free of 2- and 3-picolines.

Methanol-d_4 (99% D)

Commercially available methanol-d_4 (Brinkman Instruments) was rendered anhydrous by distillation from magnesium methoxide-d_3 (82).

Methanol-d_3

Methanol-d_3, CD_3OH, was prepared from methanol-d_4 in the following manner. Methanol-d_4, 7.5 ml. (0.185 mole) was added to 56 ml. (3.1 moles) distilled water and the resulting solution distilled using a spinning-band column. The recovered methanol, b.p. 63-65°C., 6.9 ml. (0.175 mole), was added to a second 56 ml. quantity of distilled water, and this solution was again fractionally

distilled through the spinning-band column (54). The methanol-d_3 distillate, b.p. 63-65°C., 6.4 ml., was then dried by the same procedure used for methanol-d_4.

Acetate buffer solutions

Sodium acetate and acetic acid in the requisite amounts were weighed into a volumetric flask and the contents brought to volume with either methanol-d_3 or methanol-d_4.

Stock lithium perchlorate solutions

Methanol-d_3 and methanol-d_4 solutions containing 0.21 M. lithium perchlorate were prepared for use in maintaining constant ionic strength in the various kinetic runs.

Procedure for Kinetic Runs

For a typical kinetic run, methyl p-toluenesulfinate was weighed into a volumetric flask and appropriate volumes of sodium acetate-acetic acid buffer and stock lithium perchlorate solution introduced by micropipet. The resultant solution was then brought to volume with solvent, transferred to an NMR tube, and placed in a constant temperature oil bath set at 62.0°C. ± 0.5°C. At suitable

intervals, the sample was removed from the bath and spectra obtained on a Varian HA-100 NMR spectrometer. Since the NMR sample probe was at a much lower temperature than 62°C., no discernable reaction occurred during scanning operations. Time corrections were made for the period spent out of the oil bath.

For methanol-d_3 samples, the hydroxyl proton at 4.81 δ was used as an internal reference. For methanol-d_4 runs, a benzene-filled capillary external reference (7.20 δ) was employed. NMR scans covered a 250 Hz. sweep width and three to five integrations were taken for each peak of interest. The average integration value was then used in subsequent rate calculations. At the beginning and end of each reaction, a TMS external reference was used and 1000 Hz. sweepwidth spectra obtained in order to rule out side reactions. No extraneous peaks were observed.

Attempted synthesis of phenyl p-toluenesulfinate and phenyl benzenesulfinate

The procedure used by Wragg, McFadyen and Stevens (83) was followed. A solution of benzenesulfinyl chloride or p-toluenesulfinyl chloride in dry ether was added to phenol in ether-pyridine at 0°C. After appropriate stirring, the ether layer was removed, washed with dilute

perchloric acid, sodium bicarbonate and water. After drying over sodium sulfate, the ether layer was evaporated in vacuo to yield a mushy residue. Attempts to purify the product by sublimation, recrystalization, column or thin layer chromatography were not successful. Thin layer chromatograms showed three components, one with an Rf value suggestive of an ester. Elution and subsequent chromatographic checks showed the ester-like component to be decomposing into the same components observed on the primary TLC plate.

Another attempt was the method used by the Russian group (48). Sodium phenoxide was prepared by adding metallic sodium to phenol in dry ether under a nitrogen atmosphere. The p-toluenesulfinyl chloride was then added to this solution, the sodium chloride precipitate removed and the ether layer evaporated in vacuo. Phenoxide was also prepared from phenol and methyl lithium and utilized in the same way. Both trials met with failure, yielding unstable amorphous crystalline products which resisted purification.

Further attempts at synthesis of aryl arenesulfinates were therefore abandoned.

II. Kinetic Studies of the Hydrolysis of p-Toluenesulfonic Acid Esters

INTRODUCTION

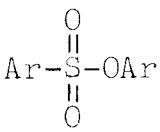
One of the most common oxidation states of sulfur is tetracoordinate sulfonyl sulfur. In these compounds, the sulfur atom is bonded to four other groups -- two of which are oxygen. This center may be represented in several ways (I-IV).

(I) (II) (III) (IV)

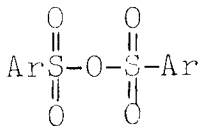
The structure and exact electronic configuration of this group is far more complex than any of these representations indicate. The sulfur bonds to oxygen certainly do not have double-bond reactivity comparable to that found in carbonyl carbon, but neither is the semi-polar coordinate covalent designation (II) entirely accurate. Studies of the bond lengths in sulfonic acid esters indicate that the S=O distance is 1.43 Å, close to that expected for a

double bond and significantly different from the value 1.7 Å measured for the S-O bond in the compounds. (77) This has been attributed to the availability of vacant 3d orbitals in the sulfur atom, making possible p-dπ bonding with oxygen (53). Addition of reagents to the S=O bond does not take place, in contrast to the numerous addition-type reactions described for carbonyl compounds. Thus it is currently thought that the resonance structures (III) and (IV) are the best representation of the sulfonyl group (70).

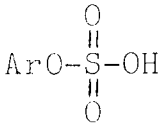
No less than eight different classes of sulfur compounds contain the sulfonyl grouping in the molecule. These are shown below:

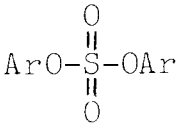


Sulfonic Acid Ester

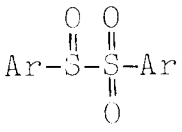


Sulfonic Anhydride

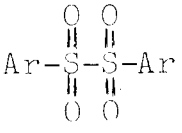




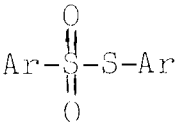
Esters of Sulfuric Acid



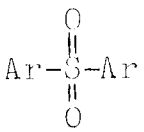
Sulfinyl Sulfone



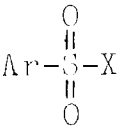
α-Disulfone



Thiolsulfonate



Sulfone



Sulfonyl Halides

Of these compounds, the sulfonate esters are one of the most widely known. These esters have great utility in industry in the manufacture of dyes, drugs, surfactants, insecticides and numerous other types of organic products. They can also serve as alkylating and arylating agents in synthetic schemes (77). A complete list of their applications in commercial and theoretical chemistry would demand the space of several volumes.

In the previous Chapter, it was noted that phenyl esters of arylsulfinic acids are unknown. By contrast, such esters of arylsulfonic acids are easily prepared. There are numerous reports in the literature dealing with their syntheses. Two general methods for synthesis have traditionally been used.

1. The sulfonyl chloride and appropriate phenol are stirred in solutions containing pyridine, aniline or sodium carbonate.

$$ArSO_2Cl + Ar'OH \xrightarrow[(-HCl)]{\text{pyridine}} Ar\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-OAr'$$

This scheme has the disadvantage of side reaction to ethers and amine salts (72,73).

2. Sulfonyl chlorides may be treated with sodium phenoxides in anhydrous solvents as in (a) (12). Phenol in aqueous sodium hydroxide may also be brought to react with the sulfonyl chloride as in (b) (9).

$$ArSO_2Cl + Ar'ONa \xrightarrow[\text{alcohol}]{\text{anhydrous}} Ar\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-OAr' + NaCl \quad (a)$$

$$ArSO_2Cl + Ar'OH \xrightarrow[(-HCl)]{\text{aq. NaOH}} Ar\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-OAr' \quad (b)$$

More recently the reactions have been improved by the use of different solvents. Hoffman for example has used dimethylformamide in a reaction generally applicable to aryl arenesulfonates (25).

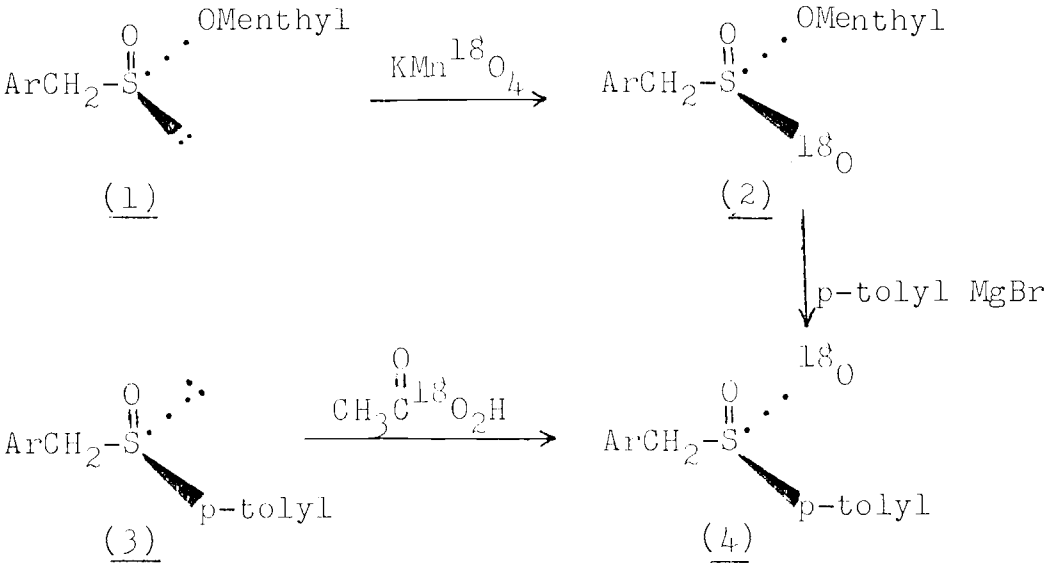
$$ArSO_2Cl + Ar'OH \xrightarrow[(-HCl)]{\text{DMF, aq. NaOH}} Ar\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-OAr'$$

This reaction has the advantages of short preparation times, ambient temperature conditions, and ease of product separation. Similarly, Wentworth and Sciaraffa claimed good yields (above 90%) with reactions in acetone. By their method, CF_3-, p-nitro-, and halide-substituted phenyl toluenesulfonates were prepared (80).

The polarity of the S=O bond in these compounds renders the sulfonyl sulfur positive and thus quite susceptible to nucleophilic attack. The sulfonyl group is coordinatively saturated so substitution products are derived from these reactions with nucleophilic agents.

Since these tetracoordinate compounds contain two equivalent S=O bonds, the sulfonyl center is achiral. The stereochemistry of substitution reactions is thus not

easily determined. The only direct way to introduce asymmetry into the sulfonyl group is to use isotopic substitution of one of the oxygen atoms, a procedure complicated by the fact that the measured optical rotations are quite small. This approach was used by Andersen and Sabol (66) in the reaction sequence given below.



They oxidized (R)-menthylphenyl methanesulfinate (1) to the corresponding sulfonate (2) with ^{18}O-labelled potassium permanganate. Sulfonate (2), subjected to Grignard reaction, gave sulfone (4), which was of (S)-configuration. The stereochemistry of the benzyl p-tolylsulfone had previously been established by Stirling (69) by oxidation of sulfoxide (3). This sequence confirmed that the substitution reaction occurring at the sulfur atom in the

sulfonate ester proceeded with inversion of configuration. Sulfinate esters are likewise known to undergo inversion during substitution.

Kice and coworkers carried out extensive quantitative comparisons between reactions at sulfinyl centers in sulfinyl sulfones and sulfonyl centers in α-disulfones. They found that the two centers differ primarily in the activation energy required for nucleophilic substitution, but otherwise appear to react by analogous mechanisms (38). In light of this statement, one might well expect that the nucleophilic displacement reactions of the sulfinates and sulfonates both involve the same stereochemistry.

Substitution reaction of sulfonate esters have received the attention of a number of research groups during the last two decades in attempts to improve syntheses, define mechanisms and measure reaction kinetics.

Aryl benzenesulfonates have been hydrolyzed under acid, neutral and basic conditions in a variety of solvent systems. Vizgert reported that phenyl benzenesulfonates were not susceptible to hydrolysis in weakly acidic media (77). One used 3.5 - 10 N HCl solutions and found that phenyl and p-nitrophenyl benzenesulfonates were hydrolyzed sluggishly in these quite acidic solutions.

Oxygen-18 studies confirmed the mechanism involved an S_N2 attack by water at the sulfur atom, and showed no ^{18}O-incorporation into unreacted ester (56,57).

The spontaneous or neutral hydrolysis reaction has been shown to be significant only in the case of the highly activated esters 2,4-dinitrophenyl and 2-nitrophenyl benzenesulfonate. Again ^{18}O studies show that S-O bond cleavage, arising from substitution at sulfonyl sulfur, is the reaction pathway. The nitro groups promote neutral hydrolysis only when located in the phenolic portion of the molecule. Phenyl 2,4-dinitrobenzenesulfonate, for example, is resistant to this reaction.

Vizgert's group has conducted solvolyses using aryl sulfonate esters substituted in nearly every conceivable manner. Isotope studies have established that the alkaline hydrolysis reaction occurs by S-O bond scission (77). More current studies by Oae and Kiritani indicate that a certain amount of reaction may take place by C-O bond scission, at least in the case of phenyl and p-nitrophenyl esters. They found that the S-O and C-O type reactions compete during the alkaline hydrolysis in 1% potassium hydroxide, but interpretation of their data was hampered by the tendency of p-nitrophenol itself to incorporate ^{18}O from the solvent. Accordingly, the S-O reaction was judged to be the predominant pathway (at least 80%) (57).

Recent studies using other nucleophiles such as amines, alkoxides, or thiophenoxides have been aimed almost exclusively at the dinitrophenyl arylsulfonates. These substrates can undergo either S-O or C-O bond cleavage and thus are the target of investigations seeking to clarify the conditions affecting each type of reaction.

Vizgert has looked at reactions of aliphatic and aromatic amines with the 2,4-dinitrophenyl ester of benzenesulfonic acid. The majority of these involve attack at the phenolic C_1-carbon rather than at sulfur (75,78). Oae (71) and Bunnett and Bassett (13) have done studies with the p-nitrophenyl ester and found dual fission there also. One notable distinction between the mono-nitro and dinitrophenyl esters was that the relative percentages of the two cleavage products were quite different. While piperidine catalysis led to nearly complete C-O cleavage with 2,4-dinitrophenyl benzene-sulfonate, it gave 90% S-O products with the p-nitrophenyl ester.

The literature contains only a few examples of tertiary amine catalyzed substitution reactions at tetracoordinate sulfur. Studies of the pyridine-catalyzed hydrolysis of benzenesulfonyl chloride have been reported

by Rogne (62,63) and Ciuffarin, Senatore and Stangeland (68). Kirkien-Konasiewicz, Sammy and Maccoll investigated the methanolysis of 2,4-dinitrophenyl p-toluenesulfonate catalyzed by pyridine and its methyl derivatives (43). Kaiser's work with cyclic sulfonates demonstrated that N-methylimidazole catalyzes the hydrolysis reaction by a general base mechanism (31).

Some information is available concerning primary and secondary amine reactions with sulfonates, but aliphatic tertiary amine data is nearly non-existent. Primary and secondary amines theoretically can react with sulfonic acid esters to form sulfonamides and phenols. Tertiary amines however require the formation of quaternary amine salts. The alkyl amine salts are unstable in aqueous solution and rapidly hydrolyze to release sulfonic acid, phenol and to regenerate the amine. The overall reaction could thus be represented by the following equation:

$$ArS(=O)_2-OAr' + H_2O \xrightarrow[k_H]{R_3N} ArS(=O)_2-OH + Ar'OH$$

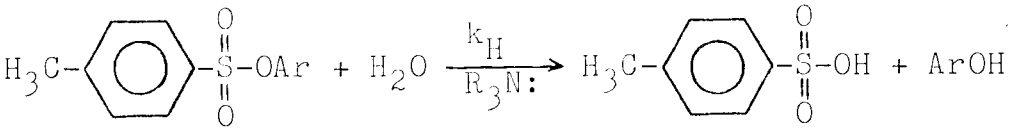
Since Kice and Kasperek (41) reported that triethylamine catalyzes the hydrolysis of aryl α-disulfones, it seemed of interest to investigate tertiary amine

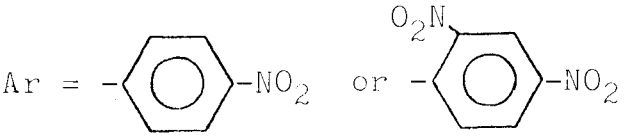
reactions at another type of sulfonyl sulfur center -- namely aryl p-toluenesulfonates.

Thus the goals of this research were (a) to demonstrate catalysis of arylsulfonate hydrolyses by several tertiary amines, (b) to elucidate their modes of reactivity, and (c) to see if increased steric effects in the amine could induce changes in the reaction mechanism.

RESULTS

The p-toluenesulfonic acid esters of p-nitrophenol and 2,4-dinitrophenol are sufficiently activated to hydrolyze at convenient rates. These compounds were thus subjected to studies of tertiary amine catalyzed reactions, as shown in the following equation:





Spectrophotometric method for monitoring hydrolysis rates of p-toluenesulfonic acid esters

The p-nitrophenol or 2,4-dinitrophenol released upon hydrolysis of the esters can be monitored by spectrophotometric means. The phenolate forms of both compounds absorb strongly in the visible region of the spectrum -- p-nitrophenolate at 400 nm ($\log \varepsilon = 4.26$) and 2,4-dinitrophenolate at 360 nm ($\log \varepsilon = 4.17$) (60). These peaks are well-separated from those of the ester

itself. Absorbance changes at the appropriate λ_{max} thus conveniently provide data for calculation of k_H, the rate constant for the hydrolysis reaction.

Hydrolysis of 2,4-Dinitrophenyl p-Toluenesulfonate in Triethylamine (TEA)-Buffered 20% Acetonitrile

The first reaction studied was the hydrolysis of 2,4-dinitrophenyl p-toluenesulfonate in the presence of TEA and TEA-H^+. Table 6 shows the rates obtained for 4:1 amine buffers in 20% acetonitrile. There is no detectable dependence of the rate upon the concentration of TEA.

This ester has been reported to undergo spontaneous hydrolysis (74,76), so the rate represents a combination of spontaneous and hydroxide ion catalysis. Study of this compound is further complicated by its tendency to undergo both C-O and S-O bond cleavage (12). Emphasis was therefore shifted to p-nitrophenyl p-toluenesulfonate and all subsequent hydrolysis reactions were carried out using this ester.

TABLE 6. Kinetics of the hydrolysis of 2,4-dinitrophenyl p-toluenesulfonate[a] in 20% aqueous acetonitrile-triethylamine buffer at 40°C.[b]

TEA/TEA-H^+	TEA x 10^2M.	TEA-H^+ x 10^2M.	k_H, x 10^3 sec^{-1}
4:1	10.0	2.50	1.24
4:1	10.0	2.50	1.23
4:1	5.0	1.25	1.28
4:1	5.0	1.25	1.31
4:1	2.5	0.63	1.28

a) concentration of ester at 10^{-4}M. for all runs.

b) ionic strength maintained at 0.10 M. with lithium perchlorate.

Hydrolysis of p-Nitrophenyl p-Toluenesulfonate in TEA-Buffered 20% Acetonitrile

p-Nitrophenyl p-toluenesulfonate was hydrolyzed in TEA-buffered 20% acetonitrile at 70°C. The rates of hydrolysis, k_{II}, obtained for buffer ratios of 4:1, 2:1 and 1:1 are given in Table 7. These rates are seen to be independent of concentration of TEA, but the dependence of k_{II} on buffer ratio shows that the hydrolysis that is observed is due to reaction of ^{-}OH with the ester rather than to spontaneous hydrolysis.

Hydrolysis of p-Nitrophenyl p-Toluenesulfonate in TEA-Buffered 60% Aqueous Glyme

The solvent system was changed from 20% acetonitrile to 60% glyme in order to slow the rate of hydroxide ion catalyzed hydrolysis. It was hoped that this might then allow for detection of catalysis by triethylamine. Since the rates were very slow, for more facile measurement, the temperature of reaction was increased to 115°C. This required the use of sealed glass ampoules. Data from kinetic runs using TEA buffers of 4:1, 2:1 and 1:1 in 60% glyme solutions are summarized in Table 8. Unfortunately, any evident catalysis by TEA is again obscured by the faster hydroxide reaction.

TABLE 7. Kinetics of the hydrolysis of p-nitrophenyl p-toluenesulfonate[a] in 20% aqueous acetonitrile-triethylamine buffer at 70.0°C.[b]

TEA/TEA-H^+	TEA x 10^2 M.	TEA-H^+ x 10^2 M.	k_H, x 10^5 sec^{-1}	ave. k_H, x $10^5 sec^{-1}$
4:1	10.00	2.50	8.15	
4:1	10.00	2.50	8.21	
4:1	5.00	1.25	8.58	
4:1	5.00	1.25	8.48	
4:1	2.50	0.68	8.15	
4:1				8.31
2:1	10.00	5.00	4.28	
2:1	10.00	5.00	4.23	
2:1	5.00	2.50	4.42	
2:1	2.50	1.25	4.24	
2:1	1.25	0.68	4.38	
2:1				4.31
1:1	10.00	10.00	1.97	
1:1	5.00	5.00	1.97	
1:1	2.50	2.50	2.02	
1:1	1.25	1.25	2.07	
1:1				2.01

a) concentration of ester at 10^{-4}M. for all runs
b) ionic strength maintained at 0.10 M. with lithium perchlorate

TABLE 8. Kinetics of the hydrolysis of p-nitrophenyl p-toluenesulfonate[a] in 60% aqueous glyme-triethylamine buffer at 115°C.[b]

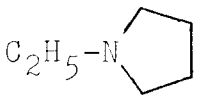
TEA/TEA-H^+	TEA x 10^2 M.	TEA-H^+ x 10^2 M.	k_H, x 10^6 sec^{-1}
4:1	8.00	2.00	6.98
4:1	6.00	1.50	7.03
4:1	4.00	1.00	6.93
4:1	4.00	1.00	6.98
4:1	2.00	0.50	6.98
2:1	8.00	4.00	4.14
2:1	6.00	3.00	4.03
2:1	4.00	2.00	3.90
2:1	2.00	1.00	3.86
1:1	5.00	5.00	2.34
1:1	5.00	5.00	2.44
1:1	3.75	3.75	2.22
1:1	2.50	2.50	2.08
1:1	2.50	2.50	2.21
1:1	1.25	1.25	1.99

a) concentration of ester 5 x 10^{-5}M. for all kinetic runs

b) all runs carried out at constant ionic strength of 0.05 M.

Hydrolysis of p-Nitrophenyl p-Toluenesulfonate in N-ethyl pyrrolidine (NEP)-Buffered 60% Glyme Solutions

Because of the surprising lack of significant catalysis by TEA, it was decided to investigate reactions with the chemically equivalent, but less sterically-hindered amine, N-ethylpyrrolidine:



Hydrolysis of p-nitrophenyl p-toluenesulfonate is indeed accelerated by this tertiary amine. Table 9 lists the rates obtained for the three buffer ratios in 60% aqueous glyme. In order to clarify the mechanism of catalysis, a similar series of kinetic runs were carried out for a 4:1 amine buffer in 60% glyme - 40% D_2O. These results are found in Table 10.

Spontaneous hydrolysis of p-nitrophenyl p-toluenesulfonate

Prolonged heating of the ester in 60% aqueous glyme solution of 0.05 M. ionic strength but lacking in amine showed the neutral or spontaneous hydrolysis reaction to be negligible under the conditions of this study. These results agree with other research information, indicating no neutral hydrolysis for p-nitrophenyl p-

toluenesulfonate in related aqueous dioxane solvent systems (76,79).

Calculation of k_H, the hydrolysis rate constant

All hydrolysis rate constants, k_H, were determined from the graphical slopes of plots of 1 + log $(A_\infty - A)$ versus time. Figure 8 is a typical plot for the reaction of the p-nitrophenyl ester in NEP-buffered 60% aqueous glyme.

Calculation of k_{NEP}, the second order catalysis constant

The second order catalysis constants for NEP, k_{NEP}, were determined from plots of k_H versus concentration of NEP. These values of k_{NEP} for reactions in 60% aqueous glyme and 60% glyme- 40% D_2O are listed in Table 11. For both solvents, a small hydroxide reaction is occurring. See for example k'_{OH}, the intercepts noted in Table 11.

The value for k_{NEP} is the same for all three buffer ratios studied. Figure 9 depicts this clearly with three parallel lines representing the 4:1, 2:1 and 1:1 buffer series.

TABLE 9. Kinetics of the hydrolysis of p-nitrophenyl p-toluenesulfonate[a] in 60% aqueous glyme - N-ethylpyrrolidine buffer at 115.0°C.[b]

NEP/NEP-H^+	NEP x 10^2 M.	NEP-H^+ x 10^2 M.	k_H, x 10^6 sec^{-1}
4:1	8.00	2.00	14.10
4:1	8.00	2.00	14.20
4:1	6.00	1.50	12.80
4:1	6.00	1.50	12.90
4:1	4.00	1.00	11.80
4:1	4.00	1.00	11.70
4:1	2.00	0.50	10.20
4:1	2.00	0.50	10.70
2:1	8.00	4.00	9.74
2:1	6.00	3.00	8.18
2:1	4.00	2.00	6.91
2:1	2.00	1.00	5.95
1:1	5.00	5.00	5.68
1:1	4.00	4.00	5.12
1:1	3.00	3.00	4.35
1:1	1.25	1.25	3.11
1:1	1.00	1.00	3.00

a) concentration of ester 5 x 10^{-5}M. for all runs

b) ionic strength held constant at 0.05 M. with lithium perchlorate

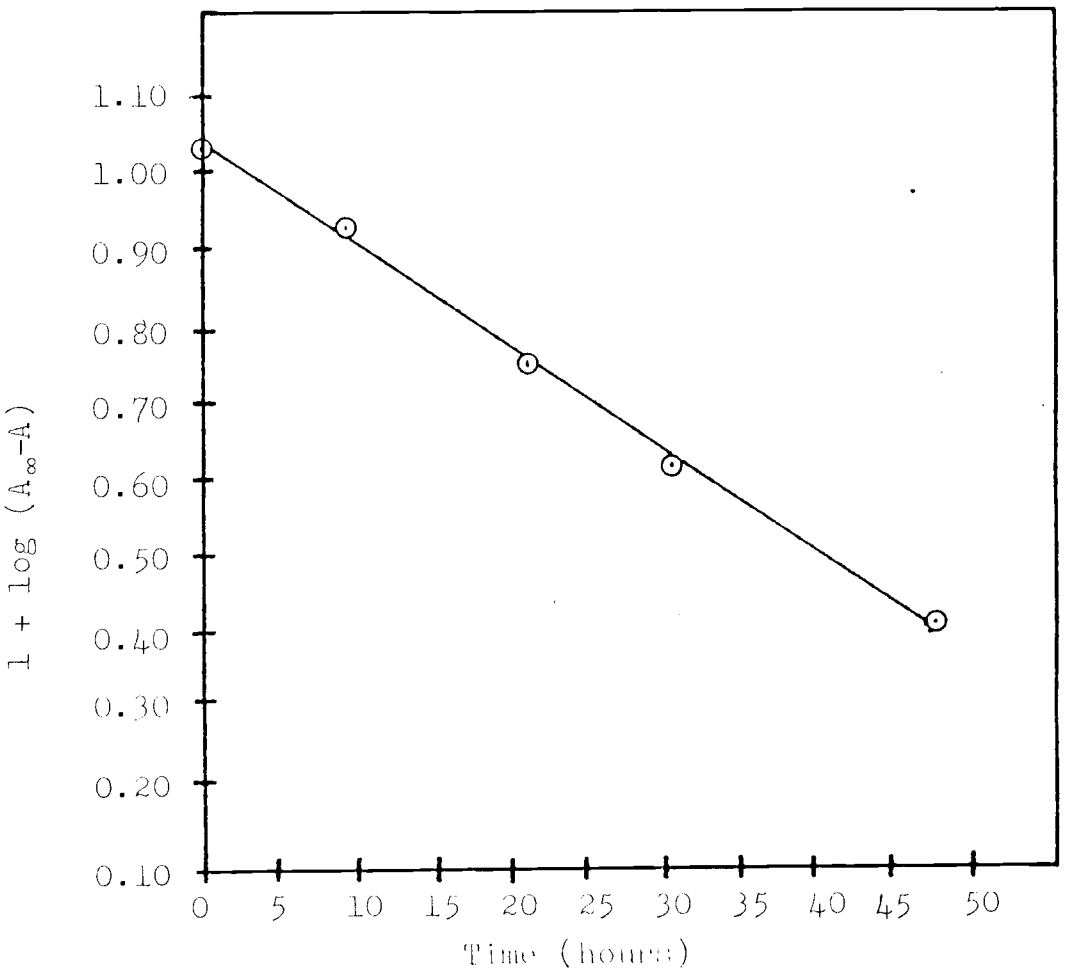
TABLE 10. Kinetics of the hydrolysis of p-nitrophenyl p-toluenesulfonate[a] in 60% glyme - 40% D_2O[b] and N-ethylpyrrolidine buffer at 115°C.

NEP/NEP-H^+	NEP x 10^2 M.	NEP-H^+ x 10^2 M.	k_H, 10^6 sec^{-1}
4:1	8.00	2.00	10.20
4:1	8.00	2.00	10.20
4:1	6.00	1.50	9.65
4:1	6.00	1.50	9.79
4:1	4.00	1.00	8.75
4:1	4.00	1.00	8.78
4:1	2.00	0.50	7.95
4:1	2.00	0.50	7.95

a) concentration of ester 5 x 10^{-5}M. for all runs

b) ionic strength held constant at 0.05 M. with lithium perchlorate

FIGURE 8. Typical first order rate of hydrolysis of p-nitrophenyl p-toluenesulfonate in NEP-buffered 60% aqueous glyme



a) ester concentration 5 x 10^{-5}M.

b) reaction at 115°C. at ionic strength 0.05 M.

TABLE 11. Rate constants for the NEP-catalyzed hydrolysis of p-nitrophenyl p-toluenesulfonate[a] in 60% glyme - 40% water and in 60% glyme - 40% D_2O

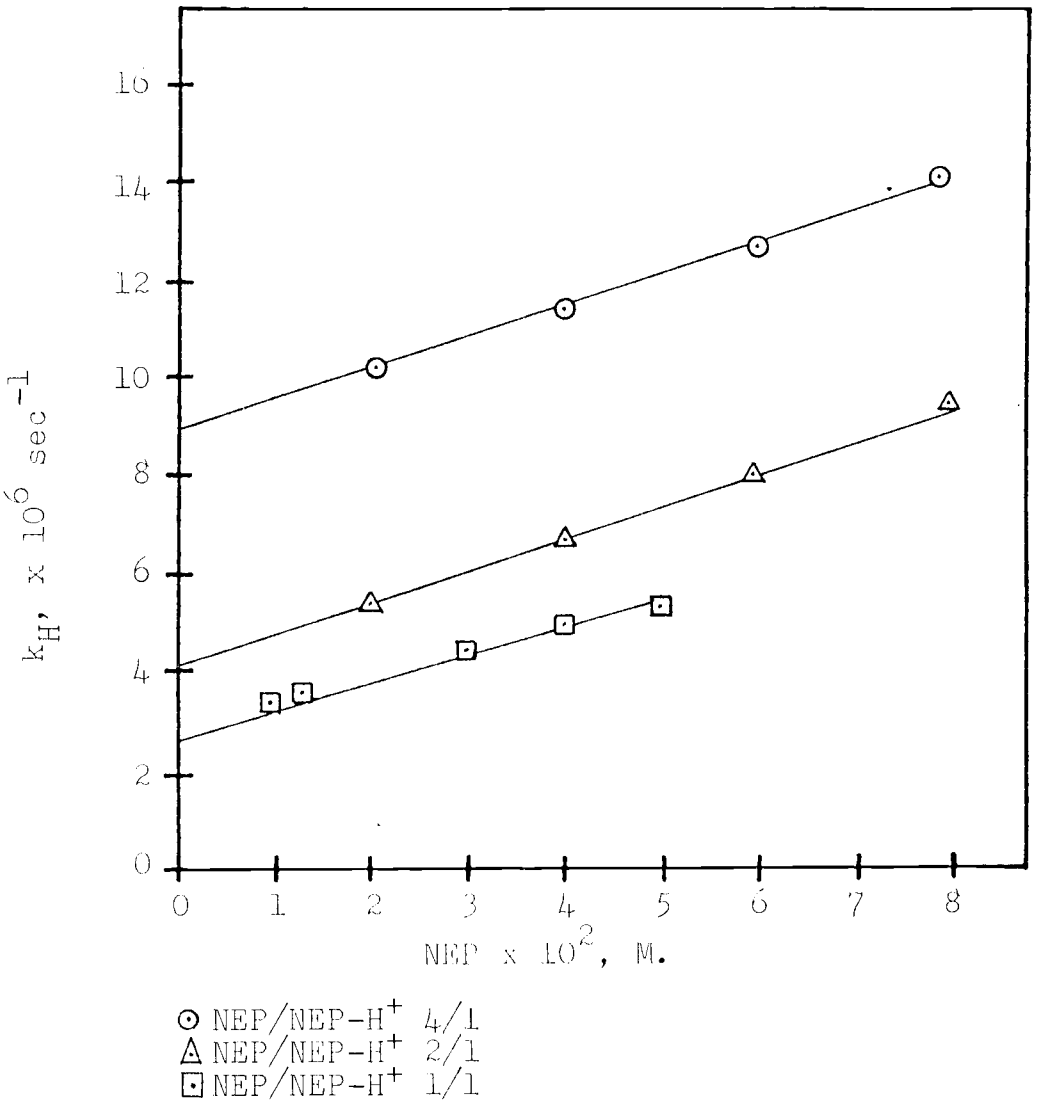
Solvent	NEP/NEP-H^+	k_{NEP}, ($\times 10^5$ $M^{-1}sec^{-1}$)	intercept rate k'_{OH}($\times 10^5 sec^{-1}$)	k'_{OH}/buffer ratio ($\times 10^5 sec^{-1}$)
60% glyme-	4:1	6.13	0.92	0.23
40% H_2O	2:1	6.06	0.45	0.23
	1:1	6.20	0.24	0.24
60% glyme- 40% D_2O	4:1	4.10	0.71	0.18

a) ester concentration 5×10^{-5} M. for all runs
b) all data obtained at constant ionic strength 0.05 M. at 115.0°C.

TABLE 12. Comparison of Intercept rates for TEA and NEP reactions in 60% aqueous glyme solutions.

Buffer Ratio	k'_{OH} for NEP ($\times 10^5 sec^{-1}$)	k'_{OH} for TEA ($\times 10^5 sec^{-1}$)	k'_{OH} ratio NEP/TEA
4:1	0.92	0.70	1.31
2:1	0.45	0.37	1.22
1:1	0.24	0.19	1.26

FIGURE 9. Rate, concentration graph showing the dependence of the hydrolysis of p-nitrophenyl p-toluenesulfonate upon NEP buffer ratio in 60% aqueous glyme*



*All runs carried out at 115°C. with ionic strength constant at 0.05 M.

Solvent isotope effect for NEP-catalyzed hydrolysis

The NEP-catalyzed hydrolysis of p-nitrophenyl p-toluenesulfonate was carried out in 60% glyme - 40% H_2O and 60% glyme - 40% D_2O in order to determine the solvent isotope effect upon the reaction rate. In isotopically normal solvent, k_{NEP} was found to be $6.13 \times 10^{-5} M^{-1} sec^{-1}$ for the 4:1 buffer ratio. The corresponding k_{NEP} measured in D_2O was $4.10 \times 10^{-5} M^{-1} sec^{-1}$. Thus a solvent isotope effect $k_{NEP}^{H_2O}/k_{NEP}^{D_2O} = 1.5 \pm 0.1$ is noted.

The hydroxide catalyzed rates yield a solvent isotope effect of $k_{OH}^{,H_2O}/k_{OH}^{,D_2O} = 1.3 \pm 0.1$.

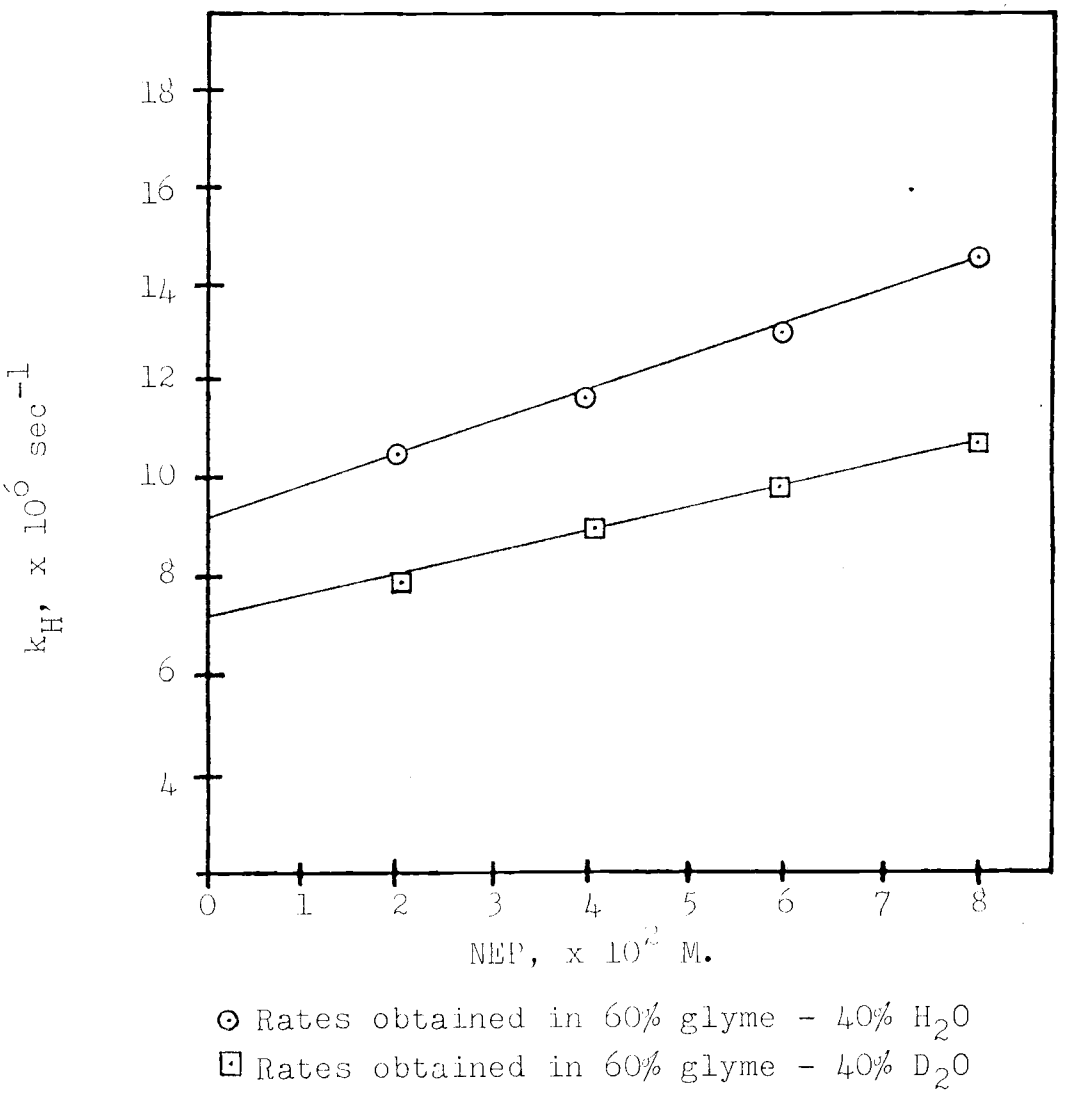
Figure 10 shows a comparison of the rates obtained in the two solvents using the 4:1 amine buffer series.

Comparison of the catalytic behavior of TEA and NEP

Variations of TEA concentration are seen to have no measurable effect upon the rates of hydrolysis of the p-nitrophenyl ester in 60% glyme or in 20% acetonitrile. In contrast to this, NEP can effectively catalyze the hydrolysis in 60% glyme. Figure 11 illustrates this difference in behavior of the two amines.

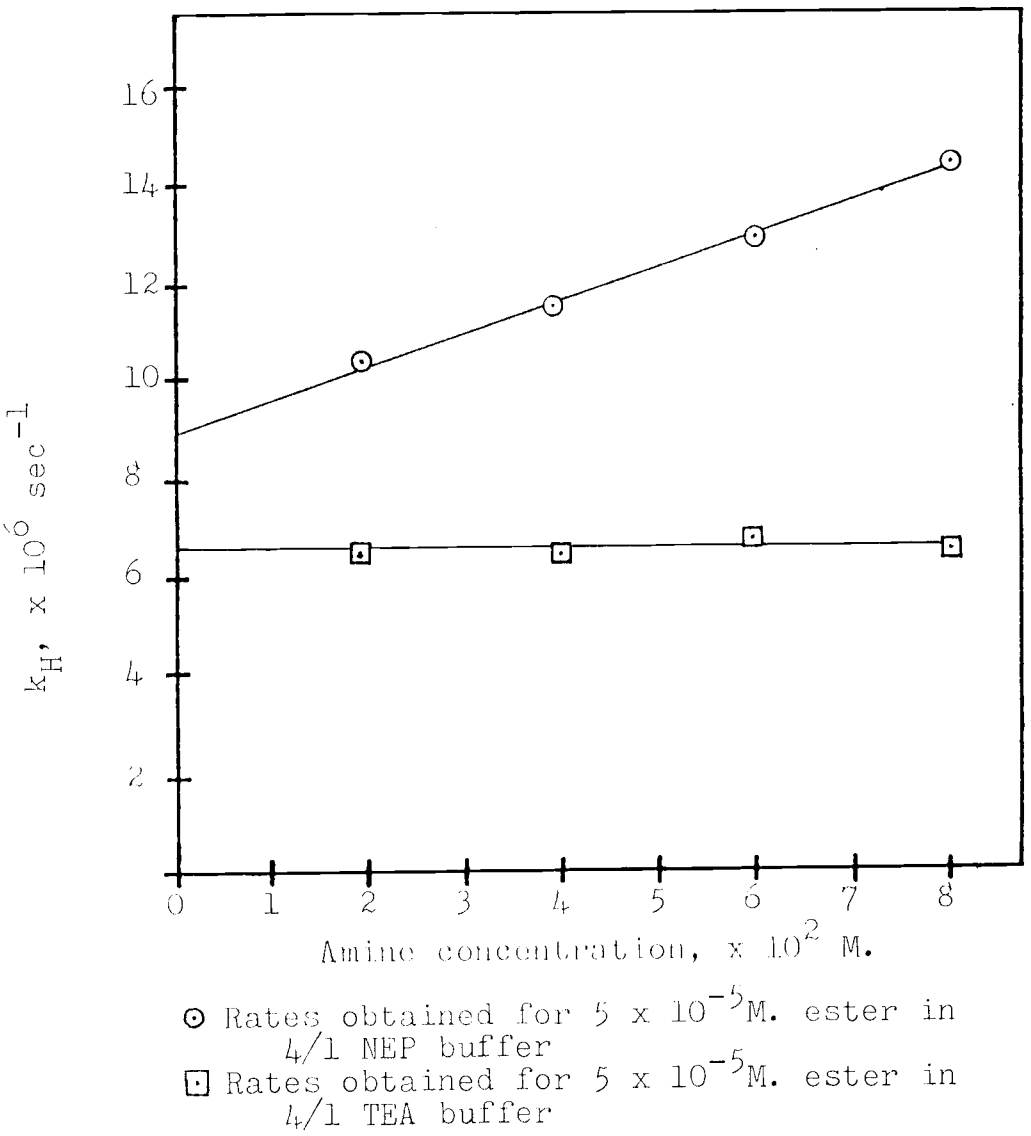
The rates of hydroxide ion reaction are slightly faster in NEP solutions than in TEA buffered ones. Table 12 shows that NEP is a stronger base than TEA by a factor of 1.3. Translated into pKa values, the pKa

FIGURE 10. Solvent isotope effect upon the rate of hydrolysis of p-nitrophenyl p-toluenesulfonate in 4:1 NEP-buffered solutions at 115°C.*



*Ionic strength held constant at 0.05 M. for all runs. Initial concentration of ester 5 x 10^{-5} M. in all runs.

FIGURE 11. Hydrolysis of p-nitrophenyl p-toluenesulfonate in amine-buffered 60% aqueous glyme at 115°C.*



*Ionic strength held constant at 0.05 M. for all runs.

for NEP is about 0.2 greater than that of TEA.

The possible reasons for these differences in catalysis by the two amines, the meaning of the solvent isotope effect and the mechanism(s) consistent with the observations will be handled in the Discussion.

Catalysis by other amines

Hydrolysis reactions of p-nitrophenyl p-toluenesulfonate were also carried out in 60% aqueous glyme solutions containing the following amine buffer components: pyridine and pyridinium perchlorate, imidazole and imidazolium perchlorate, and N-methylimidazole and N-methylimidazolium perchlorate. The reaction of interest -- the uncomplicated hydrolysis of ester to release p-nitrophenol -- was not observed.

No further studies were conducted to elucidate the modes of reaction for these amines.

DISCUSSION

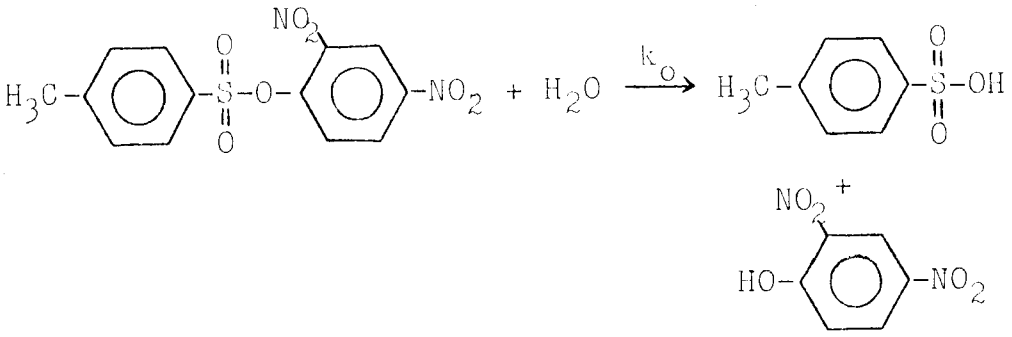
Hydrolysis of 2,4-Dinitrophenyl p-Toluenesulfonate in Triethylamine-Buffered 20% Aqueous Acetonitrile

When hydrolysis of 2,4-dinitrophenyl p-toluenesulfonate was carried out in 20% aqueous acetonitrile, changes in the triethylamine concentration had no effect upon the rates of the reaction.

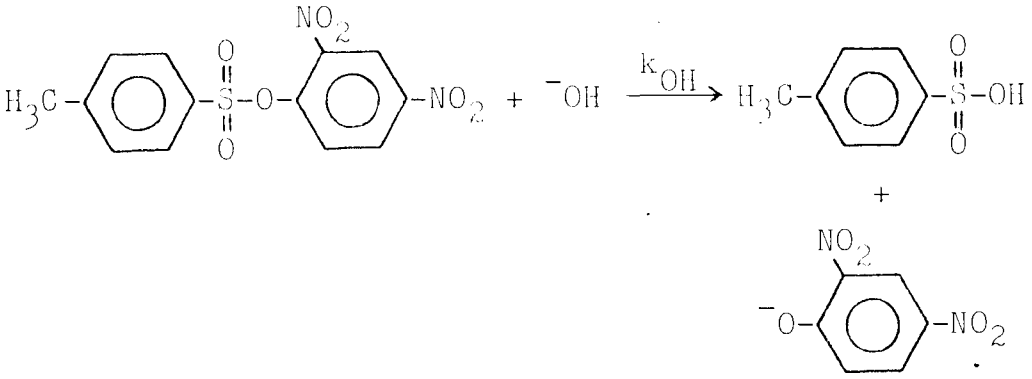
Vizgert has reported that this ester undergoes both neutral and alkaline hydrolysis reactions (77). The observed rates of hydrolysis can thus be described by the expression:

$$k_H = k_o + k_{OH}(^-OH)$$

The rate of spontaneous (neutral) hydrolysis, k_o, arises from attack of water at the sulfonyl sulfur, as shown in the following equation.

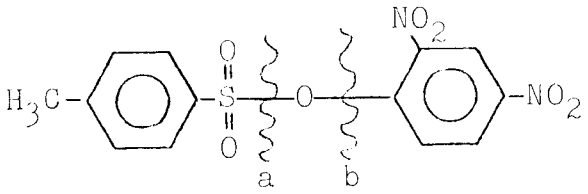


The second term in the rate expression, $k_{OH}(^{-}OH)$, defines the contribution of the hydroxide ion catalyzed reaction.



Although the ^{18}O-labelling studies have shown that neutral and hydroxide ion catalyzed hydrolyses take place by attack at sulfur with ensuing S-O bond scission (57,79), other nucleophilic reagents do not react so straightforwardly.

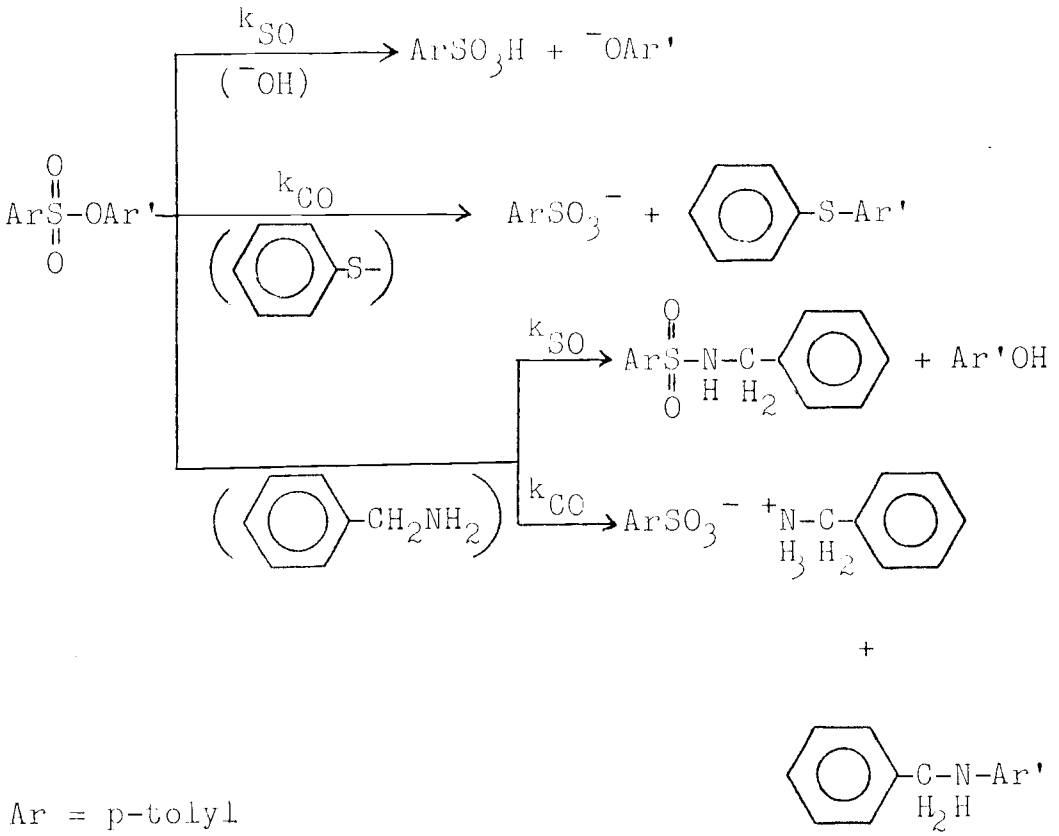
The 2,4-dinitrophenyl ester is an example of a sulfonate which contains two electrophilic centers.



The sulfonyl sulfur is highly positive because of the polarity of the S=O bonds, and nucleophilic attack at this site yields products of S-O bond cleavage (path a). In the phenolic moiety, the electron withdrawing nitro

groups render the aryl-Cl carbon very positive. Nucleophilic attack at this carbon leads to path b products.

Frequently both types of compounds are noted in the product mixture, with the relative percentages dependent upon the nucleophile and the solvent system. Hydroxide ion gives only S-O products, but thiophenoxide ion leads to formation of C-O products exclusively. Amines yield mixtures of both types of compounds (12,78).



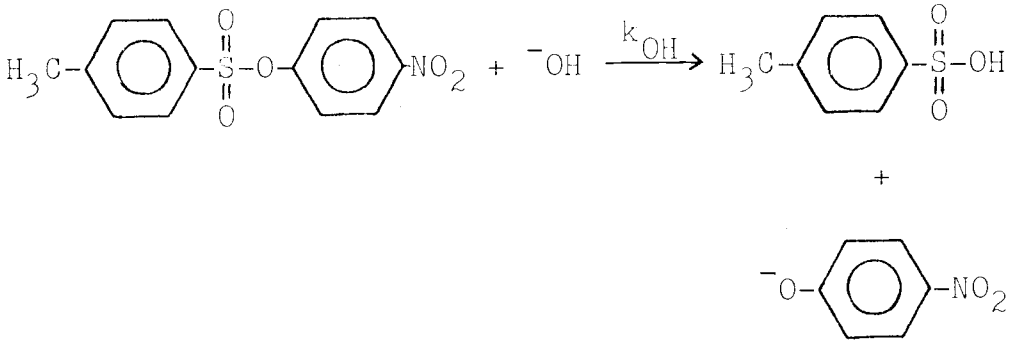
Ar = p-tolyl

Ar' = 2,4-dinitrophenyl

This activation of the ester by the nitro groups is helpful in that it speeds the reaction to convenient rates for measurement, but it also confuses the issue of the nucleophilic attack site quite badly. For this reason, the p-nitrophenyl ester of p-toluenesulfonic acid was selected as a better candidate for accomplishing the intended goals of this research effort.

Hydrolysis of p-Nitrophenyl p-Toluenesulfonate in Amine-Buffered Solutions

The hydrolysis of p-nitrophenyl p-toluenesulfonate in 20% aqueous acetonitrile, like the 2,4-dinitrophenyl ester, was not catalyzed by triethylamine. Since this mono-nitro ester is not susceptible to spontaneous (neutral) hydrolysis (77), the reaction is catalyzed only by the hydroxide ion present at the pH of the amine buffer.



This contention is further supported if one examines the rates obtained for the different TEA-TEA-H^+ buffer ratios as shown in Table 13.

TABLE 13. Intercept rates for p-nitrophenyl p-toluene-sulfonate in amine and acetonitrile solutions

TEA/TEA-H^+	k'_{OH} x $10^5 sec^{-1}$	Expt. Rel. Intercepts	Calc. Rel. Intercepts.
4:1	8.30	4.15	4.00
2:1	4.30	2.15	2.00
1:1	2.00	1.00	1.00

a) all rates obtained in 20% aq. acetonitrile at 70°C.
b) ionic strength 0.1 M. for all runs.
c) initial concentration of ester 10^{-4} M.

The measured relative intercept rates are very close to those expected if one assumes that the rates of the hydroxide ion catalyzed hydrolysis reaction, k'_{OH}, vary linearly with the buffer ratio of the amine.

As a means of suppressing this hydroxide ion reaction, a solvent system of 60% glyme - 40% water was next employed. With this solvent change, the hydroxide ion rate was reduced by at least a factor of 10. Considering the different temperatures of reaction (70°C. vs. 115°C.), the actual deceleration in glyme solutions is of course considerably greater than that.

Even in the glyme solutions, catalysis of the solvolysis by TEA is not readily apparent. Data for

the 2:1 and 1:1 amine buffer ratios suggests that slight catalysis by TEA may be occurring. At the pH of these buffers, the hydroxide ion reaction may be just slow enough that the TEA reaction can begin to compete, but the magnitude of this effect approaches the lower detection limits of the measurement method itself. Since no such rate variations are seen in 20% aqueous acetonitrile and very slight ones are noted in the 60% aqueous glyme solvent system, the TEA catalysis may indeed be real. However, the catalysis constant for TEA, k_{TEA}, can certainly be no larger than $5 \times 10^{-6} M^{-1} sec^{-1}$. This value was too imprecise to warrant further experimental clarification of the reaction mechanism.

Kice and Campbell were able to observe marked mechanistic differences among the reactions of sulfinyl sulfones with sterically hindered and non-hindered tertiary amines of similar structures (40). It thus seemed valuable to look at the effect of N-ethylpyrrolidine upon this sulfonate ester system to see whether such differences also occur at sulfonyl sulfur. This amine is structurally comparable to TEA, except that two ethylene groups are constrained in a 5-membered heterocyclic ring. This allows for less steric interaction at the nitrogen atom of the reagent, but should not greatly affect the basicity or inherent nucleophilic reactivity of the amine.

Results for the various kinetic runs carried out in 60% glyme solutions containing NEP show that catalysis by NEP is clearly observable. From the slopes of graphical plots of k_H versus amine concentration, the second order rate constant for the catalysis, k_{NEP}, was easily determined to be $6.1 \pm 0.1 \times 10^{-5} M^{-1} sec^{-1}$. This value for k_{NEP} was essentially the same for all three buffer series and is at least 12 times larger than the maximum estimated catalysis constant for TEA, k_{TEA}.

The NEP-catalyzed reaction is not the only one taking place during the hydrolysis of the ester, since the rate-concentration graphs do not pass through the origin. It has already been established that no spontaneous hydrolysis reaction is operative for this ester, so the other contribution to the overall hydrolysis rate must then arise solely from hydroxide ion influence.

The total rate for the hydrolysis reaction is thus given by the following equation:

$$k_H = k_{NEP} (NEP) + k_{OH} (^{-}OH)$$

Hydroxide ion concentration (^{-}OH) can be expressed in terms of two equilibrium constants, K_w, the autoprotolysis constant for water, and K_{NEP-H^+}, the acid dissociation constant for the N-ethylpyrrolidinium ion, and the buffer

ratio of the amine. The last term in the equation accordingly becomes:

$$k'_{OH} = k_{OH}(^{-}OH) = k_{OH}\left(\frac{K_w}{K_{NEP-H^+}}\right)\left(\frac{NEP}{NEP-H^+}\right)$$

intercept
rate

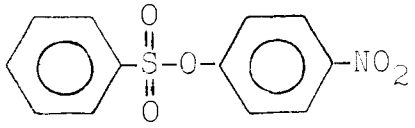
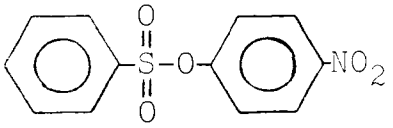
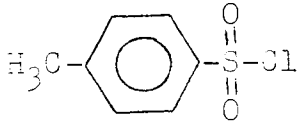
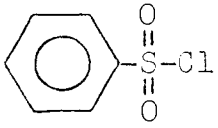
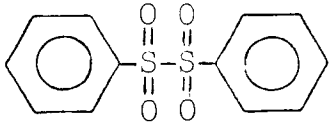
Intercept rates corresponding to the hydroxide ion catalyzed reaction, k'_{OH}, should therefore change in direct proportion to the amine buffer ratios and division of k'_{OH} by the buffer ratio should give a constant. This is exactly what one sees in the results listed in Table 11.

Having determined a suitable rate expression for the hydroxide ion reaction, one might next wish to extract a value for k_{OH}, the actual second order hydroxide ion catalysis constant. This is not a simple task however. Although the equilibrium constants K_w and K_{amine} in water and in dioxane-water solutions are known, they have not been measured in aqueous glyme. An approximation can be made using the calculation technique devised by Kice and Kasperek (32). Glyme and dioxane are solvents of similar composition in that they both are completely miscible with water and have very low dielectric constants. Thus ionization data for aqueous dioxane can probable be applied to glyme solutions without drastic error.

K_w in 60% dioxane - 40% water has been reported to be 64×10^{-19} and K_{TEA-H^+}, 3.16×10^{-10}. The rates for the hydroxide ion reaction given in Table 12 showed that the basicity of triethylamine and N-ethylpyrrolidine differ by just 0.2 pKa unit. From this comparison a K_{NEP-H^+} value of 2×10^{-10} is derived. One more assumption is required -- that k_{OH} show the same solvent dependence as k_{NEP} in changing from dioxane-water to glyme-water solutions. On this basis, k_{OH} is calculated to be approximately 75 $M^{-1}sec^{-1}$.

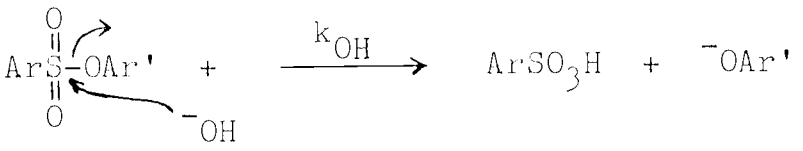
Second order rate constants for hydroxide ion catalyzed solvolyses at sulfonyl sulfur cover a wide range of values. Table 14 lists a few of these compiled from literature references. The k_{OH} value estimated for the p-nitrophenyl p-toluenesulfonate reaction, 75 $M^{-1}sec^{-1}$, lies well within established limits, but admittedly does not compare too favorably with these rate constants reported for sulfonate esters. In this study the temperature of measurement is much higher than those used in any of the reactions noted in Table 14, and the solvent system is different. Moreover, the calculation provides only an approximate value for k_{OH} and well may be in error by a factor of 10.

TABLE 14. Hydroxide ion catalysis constants for hydrolysis reactions of sulfonyl sulfur compounds

Compound	Temp. °C.	Solvent	$k_{OH}M^{-1}sec^{-1}$	Reference
	50	50% aq. dioxane	0.079	57
	30	70% aq. dioxane	0.016	74
	50	70% aq. dioxane	0.076	74
	30	water	24.4	61
	30.8	50% aq. acetonitrile	21.0	19
	48	50% aq. acetonitrile	83.5	19
	21.3	60% aq. glyme	75	42

Having defined the catalytic species involved in the ester hydrolysis, one needs to look next at the mechanisms involved. For this purpose, the solvent isotope effect was measured for the hydrolysis reaction in 4:1 NEP-buffered glyme solutions. The solvent isotope effect was $k_{NEP}^{H_2O}/k_{NEP}^{D_2O} = 1.5 \pm 0.1$ for the amine reaction. The intercept rates were noted to give a ratio $k_{OH}^{'H_2O}/k_{OH}^{'D_2O} = 1.3 \pm 0.1$.

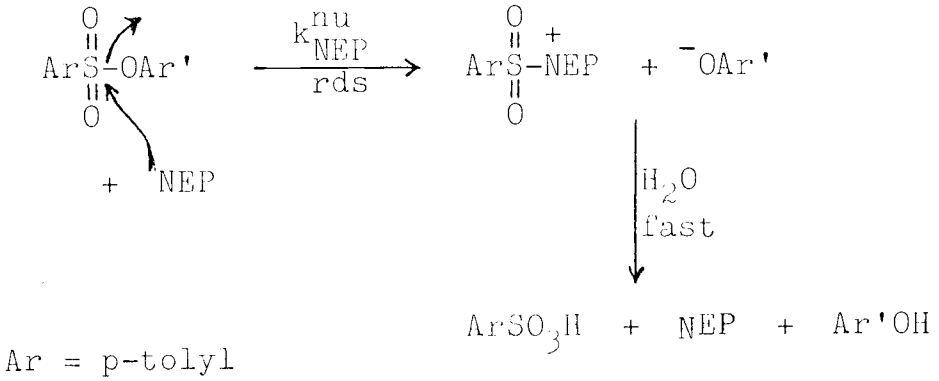
The magnitude of the solvent isotope effect for the hydroxide ion reaction is consistent with a nucleophilic or specific base mechanism, proceeding by direct displacement at sulfur. Oxyanions reacting by this route quite consistently have solvent isotope effects ranging from 0.9 to 1.5 (30).



Ar = p-tolyl Ar'= p-nitrophenyl

Reaction of the NEP could however be described by two mechanisms -- direct nucleophilic substitution as in Scheme I or general base catalyzed hydrolysis depicted by Scheme II.

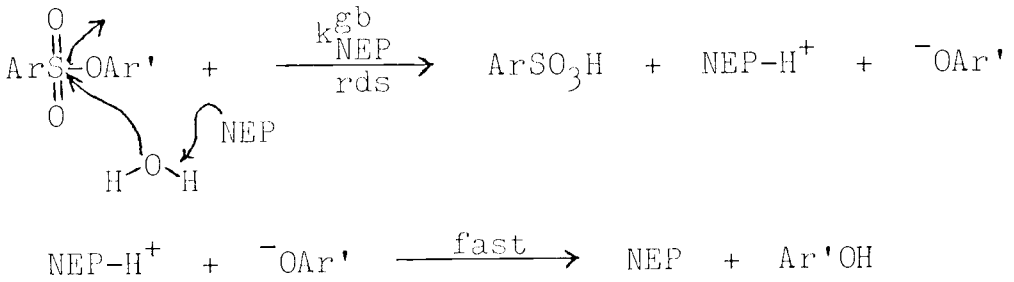
Scheme I



Ar = p-tolyl

Ar' = p-nitrophenyl

Scheme II

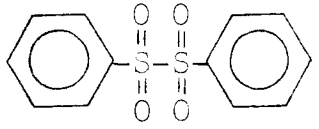
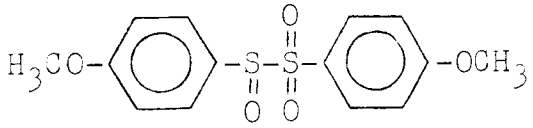
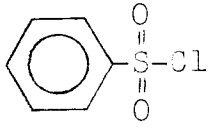
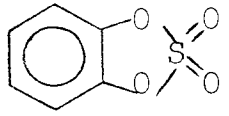
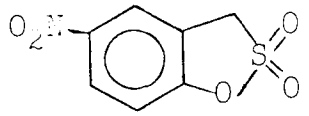


Ar= p-tolyl Ar' = p-nitrophenyl

Two observations strongly support the nucleophilic displacement mechanism, shown in Scheme I, as the correct one for the NEP-catalyzed hydrolysis of p-nitrophenyl p-toluenesulfonate. First, the solvent isotope effect $k^{H_2O}_{NEP}/k^{D_2O}_{NEP} = 1.5$ is compatible with such a route. Table

15 shows a number of solvent isotope effects which have been measured for solvolyses reactions of sulfur compounds using nitrogen nucleophiles. Nucleophilic catalysis mechanisms are seen to produce solvent isotope effects of 1.1 to 1.4 while general base routes give considerably larger values of 2.4 to 3.5. The one result 2.0 measured for tertiary amine catalyzed hydrolysis of α-disulfones was originally thought to represent general base catalysis. It was later reexamined and is now felt to result from competing nucleophilic and general base pathways. A second fact that confirms the nucleophilic mechanism is the large difference in behavior of NEP and TEA. These amines possess nearly identical basicity, yet NEP is at least 12 times more effective in catalyzing the solvolysis of the ester than is TEA. This is logical if one considers that TEA is more sterically hindered than its cyclic counterpart. The ethyl groups are free to rotate and inhibit approach of the nitrogen atom to the sulfonyl sulfur. NEP however, having two ethylene groups restricted in a ring structure, has less crowding about the nitrogen atom and is less hindered during nucleophilic attack. If a general base pathway were being used by NEP, it would be extremely difficult to explain why TEA, an equally good base, is so much poorer at catalyzing the hydrolysis.

TABLE 15. Solvent isotope effects for reactions of sulfur substrates with nitrogen nucleophiles

Substrate	Nucleophile	k_{H_2O}/k_{D_2O}	Mechanism	Reference
	triethylamine	2.0	general base & nucleophilic	32,39
	N-ethylpyrrolidine	1.4	nucleophilic	39
	pyridine	1.4	nucleophilic	18
	diethylbenzylamine	2.4	general base	18
	pyridine	1.1	nucleophilic	62
	N-methylimidazole	3.5	general base	31
	N-methylimidazole	3.5	general base	31

If one considers that the slight catalysis measured for TEA is valid, then several explanations are feasible for the reaction. (a) The hydrolysis might proceed by simple nucleophilic catalysis which is greatly decelerated by the steric effect in the amine, so that the reaction due to TEA is slower than the hydroxide ion one -- i.e. $k_{OH}(^{-}OH) >> k^{nu}_{TEA}(TEA)$. (b) TEA because of steric hindrance by its three ethyl groups may be forced to react by a general base mechanism. Approach of a hydrogen atom to nitrogen would be far less restricted than that of the ester sulfur atom, but this route might still be much slower than the hydroxide reaction. Similar to case (a), the situation is $k_{OH}(OH) >> k^{gb}_{TEA}(TEA)$. (c) TEA could be acting by both routes, as in Kice and Kasperek's studies with phenyl α-disulfone -- $k_{OH}(^{-}OH) >> k^{nu}_{TEA}(TEA) + k^{gb}_{TEA}(TEA)$. Unfortunately, this point was not resolved. While this study demonstrates a great difference in behavior between the two amines, it cannot be stated that an actual mechanism change was noted, such as that seen in Campbell's work with sulfinyl sulfones.

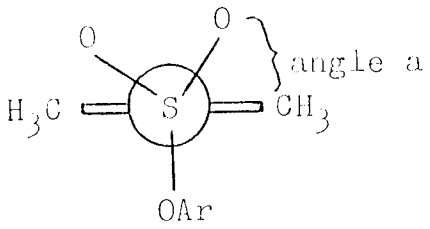
The reaction mechanism for NEP-catalyzed hydrolysis of p-nitrophenyl p-toluenesulfonate is clearly nucleophilic. Does it then proceed concertedly through an S_N2 transition state or stepwise through an intermediate? Substitution

reactions at sulfonyl centers such as esters have often been represented as passing through a transition state rather than an intermediate. It would be helpful to summarize just what is known about this supposed transition state and also to consider if there is not also a strong possibility of intermediates in reactions of sulfonate esters.

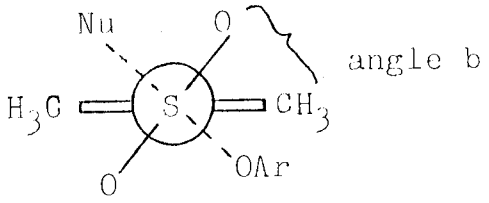
Vizgert has determined the Hammett ρ values for substituted phenyl benzenesulfonates and for the phenyl esters of substituted benzenesulfonates. These were found to be large and positive ρ = +2.7 and ρ = +2.2 respectively (77). These values are quite similar to the large (ρ = +2.6) Hammett ρ values noted in ethyl benzoate hydrolyses for which intermediates are described. For the sulfonate esters, this was taken to indicate that the bond making process was advanced over the bond breaking one, and would also seem to be suggestive of a mechanism with an intermediate on the reaction coordinate.

Vizgert has also claimed that highly activated esters, such as the 2,4-dinitrophenyl benzenesulfonate, can produce isolable compounds with aliphatic amines. He argues that less active esters may too form analogous intermediates that are simply not stable enough to characterize (75).

Another significant contribution toward describing the transition state of intermediate in sulfonyl sulfur reactions has been the study of rate effects in sterically hindered esters. Using aryl esters of p-toluenesulfonic acid and mesitylenesulfonic acid, Bunnett and Bassett found that alpha methyl groups in the acidic moiety did little to retard the solvolysis rates. In contrast to the great rate decreases caused by ortho methyl substituents in benzoates, the rate of hydrolysis for p-nitrophenyl p-toluenesulfonate was only eight times faster than that of p-nitrophenyl mesitylenesulfonate. Bunnett and Bassett explained this in terms of the geometry of the transition state. In mesitylenesulfonates, the bond angle between sulfonyl oxygen and the ortho methyl group is essentially the same in the reactant (I--angle a) and the transition state or intermediate (II -- angle b). Some steric interaction occurs from nucleophile-CH_3 and OAr-CH_3 compressions, so slight rate differences between p-toluenesulfonate and mesitylenesulfonate reactions are seen.



I - Reactant



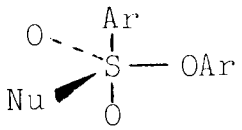
II - Transition State

Bunnett and Bassett point out that an intermediate would also be subject to the same considerations as a transition state, and thus do not attempt to support either species by their argument (12,13).

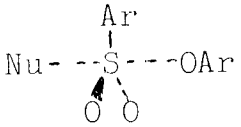
Rogne, in related work with arylsulfonyl halides, however, is more definitely in favor of a transition state. He has studied reactions of a group of substituted aromatic sulfonyl chlorides with substituted anilines. He first established the Brønsted plot for a series of sulfonyl chlorides reacting with 3,4-substituted anilines. Then he determined the reaction rates for the same series of compounds using 2-methylaniline and 2,6-dimethylaniline. For the latter two series, the difference between the observed methanolysis rates and those predicted by using the 3,4-substituted aniline plot were designated Δk and attributed to steric effects. As the positive charge at sulfur was diminished by electron donating substituents in the sulfonyl halide, the steric effect became less pronounced. Rogne finds this consistent with a transition state in which bond formation, nucleophile to sulfur, becomes "looser" or less advanced as compared to bond breaking. In other work with these substrates, he has demonstrated that the extent of bond formation relative to bond cleavage is altered both by the groups in aniline

and by the substituents introduced into the sulfonyl halide (64,65).

Although no real kinetic or spectral evidence exists for true intermediates, one really can't say that the reactions of arylsulfonate esters definitely proceed through transition states. The successful isolation by J. C. Martin and co-workers (3,49-51) of various stable sulfuranes and related compounds certainly suggests that intermediates analogous to I and II below should be energetically accessible. Whether one has an intermediate or merely a transition state, suggested geometry places the nucleophile (Nu) and leaving group (OAr) either in the same plane as the sulfonyl group, as in I below, or opposite each other and perpendicular to the O-S-O plane, as in II (14,46). Structure II is generally preferred.



I

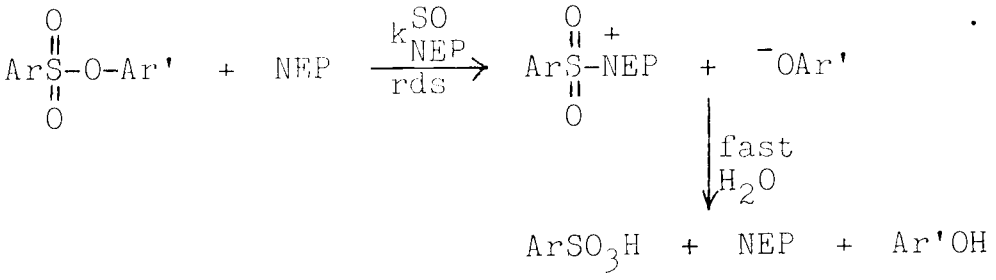


II

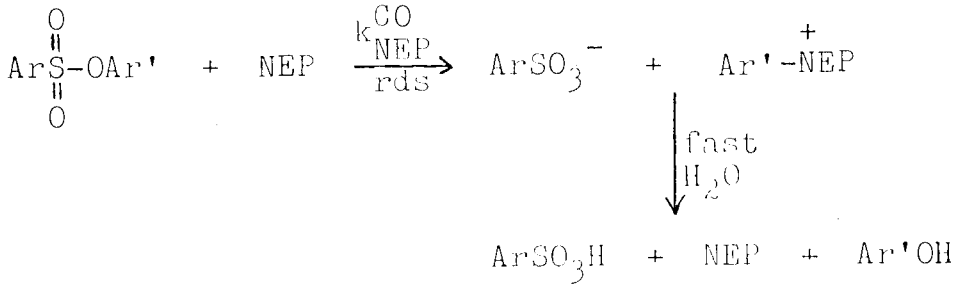
One further question regarding the hydrolysis reaction of p-nitrophenyl p-toluenesulfonate needs to be resolved. Can one be certain that attack of the nucleophiles TEA and NEP is occurring at sulfur rather than at

the phenolic C_1-carbon of the ester? The p-nitro group exerts an electron withdrawing effect to make that carbon quite positive. A C-O type side reaction would not be detected in this study without concurrent use of ^{18}O labelling. Rate determining attack of the nucleophile at carbon or sulfur would rapidly proceed to yield identical hydrolysis products.

S-O Attack



C-O Attack



Ar = p-tolyl Ar' = p-nitrophenyl

Several facts support the S-O cleavage route for the TEA- and NEP-catalyzed reactions. The studies of Bunnett and Bassett using this ester and a series of nucleophiles showed that at least 90% of the reaction with piperidine

occurred with S-O bond scission (12). Vizgert has noted that the arylation reaction is greatly disfavored with strong bases (78). Certainly TEA and NEP can be considered very basic amines, with pKa's comparable to that of piperidine. If one wishes to discount the slight effect by TEA upon the hydrolysis and say that only hydroxide ion catalysis is operative, then the attack site is unambiguously sulfur.

Other nucleophiles such as the imidazoles and pyridine failed to react with the p-nitrophenyl ester under the conditions of this study. It is possible that C-O type reactions could be more favorable for these reactants and that the products are more complex than those from simple hydrolysis. This point was not further resolved.

One final statement in conclusion -- the complexity of the reactions at sulfur centers cannot be overemphasized. Kice and Campbell found that steric changes in a nucleophile, which was otherwise equivalent to another, led to profound differences in their reaction mechanisms. The work of Kice and Kasperek demonstrated that solvent isotope effects can often be misleading. A value of k_{H_2O}/k_{D_2O} = 2.0 that seemed clearly indicative of general base catalysis was instead found to represent a combination of two mechanisms, nucleophilic and general base (32,39). Thus it

seems necessary to confirm such data by comparisons between closely related nucleophiles. Campbell's work and the use of the dual studies of triethylamine and N-ethylpyrrolidine in this investigation represent such an approach.

EXPERIMENTAL

Preparation and Purification of Materials

p-Nitrophenyl p-toluenesulfonate

To prepare p-nitrophenyl p-toluenesulfonate, 13.3 g. (0.096 mole) p-nitrophenol was dissolved in 50 ml. N,N-dimethylformamide, then treated with 12.5 ml. of 7.6 M. sodium hydroxide, followed by 18.1 g. (0.098 mole) p-toluenesulfonyl chloride in 50 ml. N,N-dimethylformamide. The solution was stirred for one-half hour, and then poured over 100 g. ice. The sulfonate ester precipitated immediately. The product was suction-filtered, washed with copious quantities of cold water and dried (25). Recrystallization was effected from ethanol, product m.p. 95-96°C. (literature value m.p. 96-97°C.) (12).

2,4-Dinitrophenyl p-toluenesulfonate

This ester was prepared using 2,4-dinitrophenol and p-toluenesulfonyl chloride in aqueous carbonate solution, according to the instructions of Ullman and Nadai (73). After appropriate isolation, the product was purified from methanol to yield colorless crystals melting at 123-124°C. (literature m.p. 121-122°C) (72).

Amines

As suggested by Wiberg (82), triethylamine and N-ethylpyrrolidine (Adams Chemical Co.) were purified by distilling from barium oxide under nitrogen immediately before use.

Reagent grade pyridine was treated first with potassium hydroxide pellets, and then distilled from barium oxide under nitrogen just prior to use (82).

Imidazole (Aldrich Chemical Co.) was purified by recrystallizing two times from acetone and petroleum ether, product m.p. 87-89 C. (literature value m.p. 88-89°C.) (26).

Commercially available N-methylimidazole (Aldrich Chemical Co.) was distilled at 2.7 torr immediately before use, b.p. 54-55°C./2.7 torr.

Lithium perchlorate

Reagent grade lithium perchlorate (K and K Instruments) was used without further purification. Stock solutions of lithium perchlorate in water or deuterium oxide were made for use in maintaining constant ionic strength in kinetic runs.

Perchloric acid

Reagent grade perchloric acid was used to prepare a solution of 1.236 M. perchloric acid. Standardization was accomplished by titration with sodium hydroxide of known normality. For runs carried out in deuterium oxide, 1.155 M. perchloric acid in D_2O was similarly prepared and standardized.

Deuterium oxide

Deuterium oxide (99.8% D) was obtained from Diaprep. Inc. and used without further treatment.

Acetonitrile

Reagent grade acetonitrile was dried by distillation from phosphorus pentoxide under a nitrogen atmosphere (82).

Glyme

Commercially available glyme (Ansul Co.) was rendered anhydrous by distilling it first from sodium and then from lithium aluminum hydride immediately before use.

Buffer Solutions

Aqueous buffer solutions were prepared by weighing the requisite quantity of amine into a volumetric flask and diluting part way with distilled water. Standard perchloric acid was added from a microburette, lithium perchlorate introduced if needed, and the entire solution brought to volume. Since the aqueous buffer solutions were to be mixed with acetonitrile or glyme containing the ester, compensation was made for this final dilution step.

Procedure for Kinetic Runs

For a typical kinetic run, the appropriate amounts of buffer solution and stock lithium perchlorate were pipetted into a volumetric flask, and all but 1.0 ml. of glyme or acetonitile added. The solution was allowed to cool to room temperature whereupon the final 1.0 ml. volume of solvent, containing the ester was added. The flask was then brought to volume with either 20% aqueous acetonitrile (v/v) or 60% aqueous glyme (v/v) as appropriate. The final solution was divided into six to eight aliquots.

For runs of p-nitrophenyl p-toluenesulfonate in 20% aqueous acetonitrile, stoppered vials were used, and the constant temperature oil bath set at 70.0°C. Kinetic runs

in 60% aqueous glyme required the use of sealed ampoules. A constricted pyrex tube was loaded with three to four ml. of solution, fitted with a stopper and stopcock assembly, and placed in a pentane slush bath (-131°C.) for freezing. The cooled ampoule was then evacuated, one atmosphere of nitrogen introduced and the contents allowed to thaw. The tube was next placed into liquid nitrogen, evacuated and sealed using an oxygen flame. After all tubes sealed in this manner had thawed and come to room temperature, they were mixed and placed in a constant temperature silicone oil bath set at 115.0°C.

At appropriate intervals, vials or ampoules were removed and the solution absorbances read at the applicable wavelengths on a Cary Model 15 recording spectrophotometer. The infinity absorbance was determined after 8 to 10 half-lives had elapsed.

Hydrolysis of the 2,4-dinitrophenyl ester was significantly faster so these runs were carried out directly in the Cary 15 in a cuvet thermostatted at 40.0°C.

First order rate constants were obtained from graphical plots of $1 + \log (A_\infty - A)$ versus time. Second order catalysis constants were calculated from ordinary hydrolysis rate versus amine-concentration graphs. All results were further verified by least squares computer analyses.

The absorbances of buffered solutions, containing p-nitrophenol or 2,4-dinitrophenol instead of the ester, were compared to the experimental A_∞ values. If the measured A_∞ was not within two to three percent of the expected value, the run was discarded. Spectral absorbance scans were run on the final solutions and at least one other point during the reaction to determine if any extraneous side reactions were occurring. These were not seen.

It should be stressed that all of the amine reactions were highly susceptible to contamination, presumably by amine oxidation products. Thus it was imperative that all components of the kinetic solutions be purified directly before use. Purified amines kept for even one day under inert atmosphere in the dark gave data that was inconsistent and non-reproducible.

BIBLIOGRAPHY

1. Arcus, C. L., M. P. Balfe and J. Kenyon. The molecular rearrangement of (-)-phenylmethylcarbinyl dl-p-toluene-sulphinate. Journal of the Chemical Society, 485 (1938).

2. Arndt, F. and H. Scholz. Beziehungen zwischen Acidität und Tautomerie Amidgruppe, Hydroxamsäuren, Sulfinsäuren, und Sulfhydroxamsäuren. Annalen der Chemie, 510, 62 (1934).

3. Astrologes, Gary W. and J. C. Martin. An aryltrialkoxysulfurane prepared from a cyclic sulfenate. Polarity rules and sulfurane reactivity. Journal of the American Chemical Society, 97, 6909 (1975).

4. Astrologes, Gary W. and J. C. Martin. Pseudorotation and fragmentation of perfluoropinacol orthosulfite. A tetraoxysulfurane. Journal of the American Chemical Society, 98, 2895 (1976).

5. Balfe, Michael P., Joseph Kenyon and Andras L. Tarnoky. Alkyl-oxygen fission in sulphinic esters. Journal of the Chemical Society, 446 (1943).

6. Bender, Myron L. and Robert J. Thomas. The concurrent alkaline hydrolysis and isotopic oxygen exchange of a series of p-substituted methyl benzoates. Journal of the American Chemical Society, 83, 4189 (1961).

7. Bender, Myron, Hideo Matsui, Robert J. Thomas and Stephen W. Tobey. The concurrent alkaline hydrolysis and isotopic oxygen exchange of several alkyl benzoates and lactones. Journal of the American Chemical Society, 83, 4193 (1961).

8. Berry, R. Stephen. Correlation of rates of intramolecular tunneling processes, with application to some group V compounds. Journal of Chemical Physics, 32, 933 (1960).

9. Borrows, E. T., J. C. Clayton, B. A. Hems and A. G. Long. The synthesis of thyroxine and related substances. Part II. The preparation of dinitrodiphenyl ethers. Journal of the Chemical Society, S190 (1949).

10. Brown, Herbert C., Sidney Johnson and Harold Podall. Purification and physical properties of 2,6-lutidine and 2,4,6-collidine. Journal of the American Chemical Society, 76, 5556 (1954).

11. Bruice, Thomas C. and Stephen Benkovic. Bioorganic mechanisms. Vol. I. New York, W. A. Benjamin (1966). 362 p.

12. Bunnett, J. F. and J. Y. Bassett, Jr. Sulfur-Oxygen scission versus carbon-oxygen scission in reactions of 2,4-dinitrophenyl p-toluenesulfonate and related esters with nucleophilic reagents. Journal of the American Chemical Society, 81, 2104 (1959).

13. Bunnett, J. F. and J. Y. Bassett, Jr. Kinetics of reactions of piperidine with nitrophenyl esters of p-toluenesulfonic and mesitylenesulfonic acids. The miserable effect of ortho-methyl groups. Journal of Organic Chemistry, 27, 2345 (1962).

14. Bunton, C. A. and (Mrs.) Y. F. Frei. The hydrolysis of aryl sulphonates. Part I. Journal of the Chemical Society, 1872 (1951).

15. Bunton, C. A. and B. N. Hendy. Tracer studies in ester hydrolysis. Part X. The hydrolysis of methyl toluene-p-sulphinate. Journal of the Chemical Society, 2562 (1962).

16. Bunton, C. A. and B. N. Hendy. Tracer studies in ester hydrolysis. Part XI. The hydrolysis of diphenylmethyl toluene-p-sulphinate. Journal of the Chemical Society, 627 (1963).

17. Burwell, Robert L., Jr. and Ralph G. Pearson. The principle of microscopic reversibility. Journal of Physical Chemistry, 70, 300 (1966).

18. Campbell, John Douglas. Studies of some reactions of sulfinyl sulfones and sulfinic anhydrides. Ph.D. thesis. Corvallis, Oregon State University (1972). 105 numb. leaves.

19. Ciuffarin, Ennio, Lucio Senatore and Mauro Isola. Nucleophilic substitution at four-co-ordinate sulphur. Mobility of the leaving group. Journal of the Chemical Society Perkin II, 468 (1972).

20. Clare, B. W., D. Cook, E. C. F. Ko, Y. C. Mac and A. J. Parker. Solvation of ions. IX. The effect of anion solvation on acid dissociation constants in methanol, water, dimethylformamide, and dimethyl sulfoxide. Journal of the American Chemical Society, 88, 1911 (1966).

21. Darwish, David and John Noreyko. The solvolysis of arenesulfinates, sulfur-oxygen versus carbon-oxygen bond fission. Canadian Journal of Chemistry, 43, 1366 (1965).

22. Dondon, Marie-Louise. Etudes sur les constantes d'autoprotolyse de solvants hydroxyles. Journal de Chimie Physique, 59, 1151 (1962).

23. Field, Lamar, Charles B. Hoelzel and J. Michael Locke. Organic disulfides and related substances. VI. A one-step synthesis of aromatic sulfinic esters from lead tetraacetate and aromatic disulfides or thiols. Journal of the American Chemical Society, 84, 847 (1962).

24. Gold, V., D. G. Oakenfull and T. Riley. The acetate-catalysed hydrolysis of aryl acetates. Journal of the Chemical Society (B), 515 (1968).

25. Hoffman, Reinhard, W. Protonierung und Halogenidabspaltung der 2-halogen-phenyl-anionem in äthanol. Chemische Berichte, 98, 222 (1965).

26. Holmquist, Barton and Thomas C. Bruice. Electrostatic Catalysis. II. A comparison of spontaneous and alkaline hydrolytic rate constants for α-substituted o-nitrophenyl esters. Journal of the American Chemical Society, 91, 2982 (1969).

27. Housa, Armand Joseph Henri, Joseph Kenyon and Henry Phillips. The relative configurations of d-β-octanol and its dextrorotatory halides. The interconversion of the optically active β-octanols by a new method. Journal of the Chemical Society, 1708 (1929).

28. Jencks, William P. Catalysis in Chemistry and Enzymology. New York, McGraw-Hill (1969). 644 p.

29. Johnson, S. L. General base catalyzed ethanolysis of ethyl trifluoroacetate. Journal of the American Chemical Society, 86, 3819 (1964).

30. Johnson, S. L. General base and nucleophilic catalysis of ester hydrolysis and related reactions. Advances in Physical Organic Chemistry, 5, 237 (1967).

31. Kaiser, Emil Thomas. Enzymatic and nonenzymatic reactions of cyclic sulfonate and sulfate esters. Accounts of Chemical Research, 3, 145 (1970).

32. Kasperek, George James. The mechanism of some reactions of aryl α-disulfones. Ph.D. thesis. Corvallis, Oregon State University (1970). 125 numb. leaves.

33. Kenyon, Joseph and Henry Phillips. The optical instability of tercovalent carbonium kations. The transformation of 1-phenyl-methylcarbinyl dl-p-toluenesulphinate into optically inactive p-tolyl-α-phenylethylsulfone. Journal of the Chemical Society, 1676 (1930).

34. Kenyon, Joseph, Henry Phillips and Gerald R. Shutt. Walden inversion reactions of the p-toluenesulphinic and the p-toluenesulphonic esters of ethyl-d-β-phenyl propionate. Journal of the Chemical Society, 1663 (1935).

35. Kenyon, Joseph, Henry Phillips and Frank M. H. Taylor. Some Walden inversion reactions of the p-toluenesulphonic and p-toluenesulphinic esters of 1-phenylmethylcarbinol. Journal of the Chemical Society, 173 (1933).

36. Kobayashi, Michio, Ritsuko Nishi and Hiroshi Minato. Kinetic studies on the hydrolysis of ethyl benzenesulfinates. Bulletin of the Chemical Society of Japan, 47, 888 (1974).

37. Kobayashi, Michio and Miki Terao. Organic sulfur compounds. VI. The reactions of arylsulfinic acids with alkyl chlorocarbonates. Bulletin of the Chemical Society of Japan, 39, 1292 (1966).

38. Kice, John L. Aspects of nucleophilic substitution at different oxidation states of sulfur. International Journal of Sulfur Chemistry (C), 6, 3 (1971).

39. Kice, John L. and S. A. Burton. Private communication (1976).

40. Kice, John L. and J. Douglas Campbell. Mechanisms of substitution reactions at sulfinyl sulfur. VII. General base catalysis by a tertiary amine of the hydrolysis of an aryl sulfinyl sulfone. Journal of Organic Chemistry, 36, 2291 (1971).

41. Kice, John L. and George J. Kasperek. Mechanisms of substitution reactions at sulfonyl sulfur. III. General base catalysis of the hydrolysis of aryl α-disulfones. Journal of the American Chemical Society, 92, 3393 (1970).

42. Kice, John L. and Eugenia Legan. Relative nucleophilicity of common nucleophiles toward sulfonyl sulfur. II. Comparison of the relative reactivity of twenty different nucleophiles toward sulfonyl sulfur vs. carbonyl carbon. Journal of the American Chemical Society, 95, 3912 (1973).

43. Kirkien-Konasiewicz, Alicja, G. M. Sammy and Allan Maccoll. The methanolysis of nitrophenyl esters. Part III. The kinetics of the base-catalysed methanolysis and pyridinolysis of 2,4-dinitrophenyl toluene-p-sulphonate. Journal of the Chemical Society (B), 1364 (1968).

44. Kirsch, Jack F. and William P. Jencks. Non-linear structure-reactivity correlations. The imidazole-catalyzed hydrolysis of esters. Journal of the American Chemical Society, 86, 837 (1964).

45. Klemperer, Walter G., Jeanne K. Krieger, Michael D. McCreary, E. L. Mutterties, Daniel D. Traficante and George M. Whitesides. A dynamic nuclear magnetic resonance study of fluorine exchange in liquid sulfur tetrafluoride. Journal of the American Chemical Society, 97, 7023 (1975).

46. Laird, R. M. and M. J. Spence. The mechanism of acyl sulphonate reactions. Part III. The solvolyses of acyl sulphonates and sulphonic anhydrides, both cyclic and acyclic, in hydroxylic solvents, and the reaction of acetyl benzenesulphonates with a series of 3- and 4-substituted anilines. Journal of the

Chemical Society (B), 1434 (1971).

47. LaFochelle, Ronald W. and Barry M. Trost. Reactions of organolithiums with arylsulfonium salts. Journal of the American Chemical Society, 93, 6077 (1971).

48. Levchenko, E. S., N. Ya. Derkach and A. V. Kirsanov. Esters of N-arylsulfonylareneiminosulfonic acids. Zhurnal Organicheskoi Khimii, 1, 947 (1965). English translation p. 952.

49. Martin, J. C. and R. J. Arhart. Sulfuranes I. A stable tetracoordinate tetracovalent sulfur compound in solution. Journal of the American Chemical Society, 93, 2339 (1971).

50. Martin, J. C. and R. J. Arhart. Sulfuranes. II. The isolation and characterization of a crystalline dialkoxydiarylsulfurane. Journal of the American Chemical Society, 93, 2341 (1971).

51. Martin, J. C. and Michael M. Chau. Simultaneous participation of three neighboring groups in the transition state for a radical-forming perester decomposition. A new route to hypervalent compounds of sulfur and iodine. Journal of the American Chemical Society, 96, 3319 (1974).

52. Miyaji, Yoshiko, Hiroshi Minato and Michio Kobayashi. Syntheses of alkyl p-toluenesulfinates by use of N,N'-dicyclohexylcarbodiimide. Bulletin of the Chemical Society of Japan, 44, 862 (1971).

53. Moffitt, W. The nature of the sulfur-oxygen bond. Royal Society of London Proceedings, Series A, Mathematical and Physical Sciences, 200, 409 (1950).

54. Murray, A. III, and D. L. Williams. Organic Synthesis with Isotopes. Part II. New York, Interscience (1958). 1338 p.

55. Najam, Aziz A. and John G. Tillett. Nucleophilic substitution at sulphinyl sulphur. Kinetics and oxygen-18 tracer studies of the alkaline hydrolysis of some sulphinate esters. Journal of the Chemical Society Perkin II, 858 (1975).

56. Oae, Shigeru, Tsugio Fukumoto and Reiko Kiritani. Non-oxygen exchange reaction of sulfone group of phenyl benzenesulfonate in acid hydrolysis. Bulletin of the Chemical Society of Japan, 36, 346 (1963).

57. Oae, Shigeru and Reiko Kiritani. Acid and basic hydrolyses of p-nitrophenyl benzenesulfonate. Bulletin of the Chemical Society of Japan, 38, 765 (1965).

58. Otto, Robert and Adelbert Rössing. Beiträge zur Lösung der Frage nach der Constitution der Sulfinsäuren. Chemische Berichte, 18, 2493 (1885).

59. Phillips, Henry. Investigations on the dependence of rotatory power on chemical constitution. Part XXVII. The optical properties of n-alkyl p-toluenesulphinates. Journal of the Chemical Society, 2552 (1925).

60. Phillips, John P., Robert E. Lyle and Paul R. Jones, eds. Organic Electronic Spectral Data. Vol. V. 1960-1961. New York, Interscience (1969). 1019 p.

61. Rogne, O. Kinetics of the neutral and alkaline hydrolysis of aromatic sulphonyl chlorides in water. Journal of the Chemical Society (B), 1294 (1968).

62. Rogne, O. Kinetics of the reaction of benzenesulphonyl chloride with pyridines in aqueous solution. Journal of the Chemical Society (B), 727 (1970).

63. Rogne, O. Rates of reaction of benzenesulphonyl chloride with some nucleophiles in aqueous solution. Journal of the Chemical Society (B), 1056 (1970).

64. Rogne, O. The kinetics and mechanism of the reactions of aromatic sulphonyl chlorides with anilines in methanol: Brønsted and Hammett correlations. Journal of the Chemical Society (B), 1856 (1971).

65. Rogne, O. Steric hindrance in the reaction of aromatic sulphonyl chlorides with anilines. Effect of 2-methyl and 2,6-dimethyl substituents in aniline. Journal of the Chemical Society Perkin II, 472 (1972).

66. Sabol, Michale A. and Kenneth K. Andersen. Nucleophilic substitution at tetracoordinate hexavalent sulfur. The reaction of (-)-menthyl phenylmethanesulfonate with p-tolylmagnesium bromide. Journal of the American Chemical Society, 91, 3603 (1969).

67. Sheppard, William A. Tetraarylsulfuranes. Journal of the American Chemical Society, 93, 5597 (1971).

68. Stangeland, L. J., L. Senatore and E. Ciuffarin. Solvent effects and Brønsted coefficients in nucleophilic substitutions at tetracoordinate sulphur. Journal of the Chemical Society Perkin II, 852 (1972).

69. Stirling, C. J. M. (-)-Benzyl p-tolyl [$^{16}O^{18}O$] sulphone: A new example of optical activity due to isotopic dissymmetry. Journal of the Chemical Society, 5741 (1963).

70. Strating, J. The sulfonyl group and its effects in organic compounds. In: Organic Sulfur Compounds, ed. by N. Kharasch. Vol. I. New York, Pergammon Press (1961). 624 p.

71. Tagaki, Waichiro, Takehiko Kurusu and Shigeru Oae. Reaction of p-nitrophenyl benzenesulfonates with thiophenoxides. Bulletin of the Chemical Society of Japan, 42, 2894 (1969).

72. Tipson, R. Stuart. On esters of p-toluenesulfonic acid. Journal of Organic Chemistry, 9, 235 (1944).

73. Ullman, Fritz and Geza Nadai. Über die Herstellung von o-nitrierten Aminen aus den entsprechenden Phenolderivaten. Chemische Berichte, 41, 1870 (1908).

74. Vizgert, R. V. The hydrolysis of esters of aromatic sulfonic acids. V. The hydrolysis of esters of benzenesulfonic acid and substituted phenols. Journal of General Chemistry of the USSR, 28, 1873 (1958).

75. Vizgert, R. V. Reactions of esters of aromatic sulfonic acids. IX. Reaction of 2,4-dinitrophenyl benzenesulfonate with aliphatic amines. Journal of General Chemistry of the USSR, 30, 3405 (1960).

76. Vizgert, R. V. Mechanisms of hydrolysis of phenyl esters of substituted benzenesulfonic acids. XIII. Journal of General Chemistry of the USSR, 32, 624 (1962).

77. Vizgert, R. V. Mechanisms of the hydrolysis of aromatic sulphonyl chlorides and of alkyl and aryl arenesulphonates. Russian Chemical Reviews, 32, 1 (1963).

78. Vizgert, R. V., I. M. Ozdrovskaya, and E. N. Ozdrovskii. Kinetics of the reaction of dinitrophenyl benzenesulfonate with aliphatic amines. Zhurnal Organicheskoi Khimii, 4, 1812 (1968). English tranlation p. 1749.

79. Vizgert, R. V., E. K. Savchuk and M. P. Ponomarchuk. Investigation of the mechanism of the hydrolysis of nitro-substituted aryl sulfonates by means of O^{18}. Akademiia Nauk SSR Proceedings, Chemistry Section, 125, 306 (1959).

80. Wentworth, Stanley E. and Patrick L. Sciaraffa. Preparation of tosylates of phenols and acidic alcohols. Organic Preparations and Procedures, 1, 225 (1969).

81. Westheimer, F. H. Pseudo-rotation in the hydrolysis of phosphate esters. Accounts of Chemical Research, 1, 70 (1968).

82. Wiberg, Kenneth. Laboratory Technique in Organic Chemistry. New York, McGraw-Hill (1960). 262 p.

83. Wragg, A. H., J. S. McFadyen, and T. S. Stevens. The rearrangement of sulphinic esters. Journal of the Chemical Society, 3603 (1958).

84. Ziegler, von K. and A. Wenz. Stereochemische Studien: I. Die Racemisation optisch aktiver Sulfinsaureester. Annalen der Chemie, 511, 109 (1934).