AN ABSTRACT OF THE THESIS OF

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Title: STUDIES OF SOME REACTIONS OF SULFINYL SULFONES AND SULFINIC ANHYDRIDES

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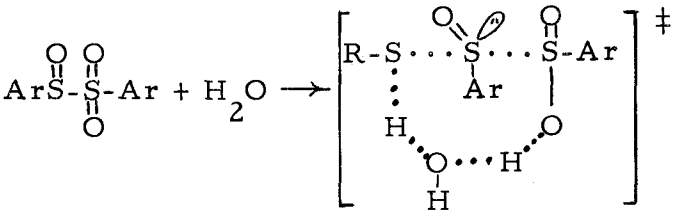
Abstract approved: John L. Kice

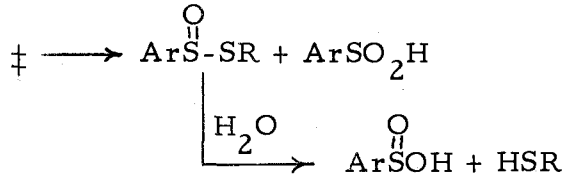
The Reaction of n-Butyl Mercaptan with p-Toluenesulfinyl p-tolyl Sulfone

n-Butyl mercaptan has been found to react with p-toluenesulfinyl p-tolyl sulfone in acidified 60% dioxane. The reaction is first order in the mercaptan. The reaction with mercaptan, $k_M[RSH]$, combined with normal (spontaneous) hydrolysis, k_r^o, accounts for the observed rate of disappearance of the sulfinyl sulfone where $k_{obs} = k_r^o + k_M[RSH]$.

Except for a salt effect, the rate of the mercaptan reaction is independent of the acid concentration between 0.01 and 0.4 M H^+. Of the two possible acid-independent reactions that might be thought to contribute to the value of k_M, evidence is discussed which supports direct interaction of the mercaptan with the sulfinyl sulfone, $k_{RSH}[RSH]$, as the only one of consequence. The lack of acid

catalysis substantiates the notion of Kice and Guaraldi (28) that a nucleophile such as HOH or RSH transfers its proton to the leaving group in the rate-determining step. The proton transfer probably occurs via a chain of one or more water molecules (eq. 1).

(1) 



At acid concentrations smaller than 0.01 M H^+ in 60% dioxane, the mercaptan is ionized to such an extent that the powerful nucleophile mercaptide ion, $RS^{\ominus}$, contributes significantly to the rate of disappearance of p-toluenesulfinyl p-tolyl sulfone. A plot of k_M vs $[H^+]^{-1}$ where $k_M = k_{RSH} + k_{RS^{\ominus}} K_a^{RSH} [H^+]^{-1}$ is satisfactorily linear. K_a^{RSH} is the acid dissociation constant of the mercaptan.

The Reactions of p-Methoxybenzenesulfinyl p-Anisyl Sulfone with Tertiary Amines

The catalysis of the hydrolysis of p-methoxybenzenesulfinyl p-anisyl sulfone in aqueous dioxane or aqueous glyme by a variety of buffered tertiary amines has been observed. Depending on the steric requirements and pK_b of the particular amine being used as the catalyst the mechanism follows either a nucleophilic or general

base-catalyzed pathway.

The small solvent isotope effect ($k^{H_2O}/k^{D_2O} = 1.4$) and a detectable common ion effect indicate that pyridine, pK_b 8.75, catalyzes the hydrolysis of the title compound in 60% dioxane at 21.4°C as a nucleophile. That all of the catalysis is due to the amine under these conditions is demonstrated by plotting $k_{obs}-k_{un}$ *vs* the pyridine concentration where k_{obs} is the observed first order rate constant and k_{un} is the first order rate constant for the spontaneous hydrolysis of the title compound. The plot is satisfactorily linear (for H_2O as well as D_2O) and intercepts the origin.

Diethylbenzylamine (DEBA), pK_b 4.44, is strong enough as a base that reaction of hydroxide ion with the sulfinyl sulfone plays a significant role in addition to amine catalysis in the hydrolysis of the title compound in 60% glyme in DEBA/$DEBAH^+$ buffers at 21.4° C. The rate constant, k_{OH}, for hydroxide ion attack at the sulfinyl sulfur of the title compound was estimated from the data obtained for 1/1 DEBA/DEBA·H^+ buffers to be 7×10^6 $M^{-1}sec^{-1}$. Rate studies providing information on the rate constant for the amine catalysis, k_A, revealed that DEBA catalyzes the reaction by the general base mechanism. The solvent isotope effect, $k_A^{H_2O}/k_A^{D_2O}$, was 2.4. The reaction constitutes the first known example of general base catalysis for substitution at sulfinyl sulfur.

When N-benzylpyrrolidine (NBP), pK_b 4.49, was tested as a catalyst in the hydrolysis of the title compound, it was found to be at

least ten times more effective than diethylbenzylamine. The rates were too fast to measure accurately, but the fact that NBP, with a pK_b nearly identical to that for DEBA, is so much more effective than DEBA as a catalyst in this reaction implies that NBP is acting as a nucleophilic catalyst rather than a general base. The result suggests that there is, in this instance, a very delicate, sterically controlled balance between the two catalytic mechanisms.

Studies on the Anhydride of 2-Methyl-2-Propanesulfinic Acid

The synthesis of the first authentic sulfinic acid anhydride by Kice and Ikura (31) has been shown to be the result of thermodynamic control where the potential steric strain due to having two large t-butyl groups in close proximity to one another in the hypothetical 2-methyl-2-propanesulfinyl t-butyl sulfone is avoided by formation of the less compact sulfinic anhydride. That the rather abrupt switch from sulfinyl sulfone formation, which is the end result for similar reactions of other alkanesulfinic acid salts and halides studied by Kice and Ikura, to anhydride formation in the t-butyl case is not related to the switch from the usual sodium to the silver salt of 2-methyl-2-propanesulfinic acid for one of the starting materials was established when the silver salt of methanesulfinic acid reacted with methanesulfinyl chloride to give the sulfinyl sulfone.

Attempts to initiate and observe the isomerization of

2-methyl-2-propanesulfinic anhydride to the corresponding sulfinyl sulfone were frustrated by the fact that the sulfinyl bromide that was formed when LiBr was introduced into a dry acetonitrile solution of the anhydride is thermodynamically much more stable than either the anhydride or the sulfinyl sulfone. Evidence for the unexpected stability of the sulfinyl bromide was obtained from kinetic studies involving bromide attack on the sulfinic anhydride in acidified 95% acetonitrile. When the concentration of bromide ion was doubled from five to ten times the molar concentration of the anhydride, the first order rate of decrease in the absorbance at 238 nm was identical to the previous bromide run. The anhydride was completely converted to the sulfinyl bromide and lithium sulfinate salt in a period of less than ten seconds, the approximate amount of time that elapsed between the initial combination of the reaction mixture and the beginning of the recorded portion of the run. The process monitored by uv was merely that of the hydrolysis of the sulfinyl bromide. Infrared evidence was obtained which also supports the contention that in the case of t-butyl as the alkyl group the sulfinyl bromide is substantially more stable thermodynamically than either the sulfinic anhydride or its hypothetical isomer, 2-methyl-2-propanesulfinyl t-butyl sulfone.

Studies of Some Reactions of Sulfinyl Sulfones and Sulfinic Anhydrides

by

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Typed by Nancy Kerley for John Douglas Campbell

To my wife, Kay

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I would like to thank Dr. John L. Kice for his unwavering help and inspiration in guiding my graduate and thesis work at Oregon State University.

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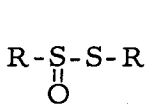
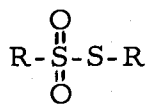
Introduction

The stimulus for current interest in the nature of sulfur-sulfur bonding is derived in large part from recent advances in the field of biochemistry. Physical organic chemists and enzymologists, for example, have found common ground in their efforts to study the mechanisms of the chemical transformations of biochemically important compounds. The role played by the sulfur-sulfur linkage in a number of bioorganic reactions is not well understood.

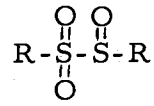
One of the significant chemical features of sulfur atoms participating in S-S bonds is the availability of the nonbounded pairs of electrons on each sulfur atom for covalent bonding with oxygen. The possible combinations are illustrated by structures I-V.



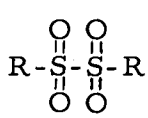
I
thiolsulfinate



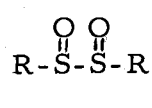
II
thiolsulfonate



III
sulfinyl sulfone



IV
α-disulfone



V
disulfoxide
(as yet unisolated)

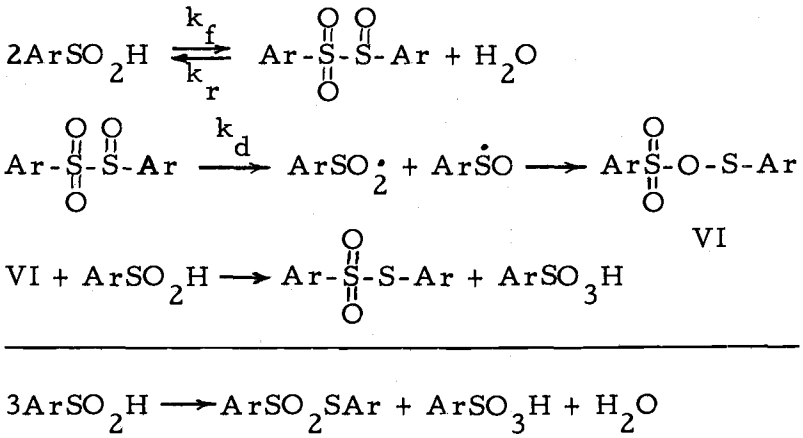
With the exception of type V, a substantial amount of chemistry is known for several examples of these substances (18). The work described in this thesis employed various sulfinyl sulfones, type III, as the substrates of interest.

The first discovery of sulfinyl sulfones occurred in 1866 when Otto and Ostrop reacted phosphorus pentachloride with benzenesulfinic acid in order to prepare benzenesulfinyl chloride (44). They isolated a side product of the formula $C_{12}H_{10}S_2O_3$, but had little idea of its structure at the time. In 1908, Knoevenagel and Polack (34) developed a general process for preparing a variety of such compounds and since their method consisted of dehydrating the parent sulfinic acid they assumed that the product, a sulfinic acid anhydride, possessed a structure analogous to the anhydrides of carboxylic acids. It was not until 1960 that Brederick and coworkers elucidated by means of infrared analysis the true structure of such products as III, the sulfinyl sulfones (2, 5).

Sulfinyl sulfones are much less stable thermally than disulfides, thiolsulfinates, thiolsulfonates or α-disulfones. In anhydrous dioxane at 50°, for instance, p-toluenesulfinyl p-tolyl sulfone decomposes with a half life of about 30 minutes (33). This easy thermal decomposition has been shown in the case of aromatic sulfinyl sulfones to involve an initial homolytic fission of the S-S bond (33).

Aromatic sulfinyl sulfones have been shown to be the key

intermediate in the disproportionation of aromatic sulfinic acids to thiolsulfonates and sulfonic acids (30). The studies that led to this conclusion were carried out in acidic media of low water activity. At 30° C the amount of sulfinyl sulfone in equilibrium with the sulfinic



$$3ArSO_2H \longrightarrow ArSO_2SAr + ArSO_3H + H_2O$$

acid is small but can be as much as several percent. The fact that the sulfinyl sulfones have a strong ultraviolet maximum at about 300 nm and that the solvent is transparent at that wave length makes it possible to detect very small concentrations of III (e. g. 10^{-4} - 10^{-5} M) (26). This feature has been utilized in measuring the individual rate constants for the formation and hydrolysis of sulfinyl sulfones as well as their equilibrium concentrations. At temperatures below 70° C and at acidities greater than 0. 1 M the rate determining step in the disproportionation is usually the homolytic cleavage of the S-S bond (k_d). At higher temperatures and acidities below 0. 1 M in a chloride

free system[1] k_d can become enough faster than k_r so that the formation of the sulfinyl sulfone (k_f) is effectively rate controlling.

Kice and Guaraldi have carried out extensive studies on the nucleophilic substitution reactions of aromatic sulfinyl sulfones, $ArS(O)SO_2Ar$ (26, 27, 28, 29). In acetic acid-1% water (27) or in 60% dioxane (28) at 21°, a temperature low enough to prevent any significant contribution to the disappearance of the sulfinyl sulfone by k_d, the hydrolysis of $ArS(O)SO_2Ar$ can be catalyzed by added sulfides, R_2S. The sulfide-catalyzed reaction is further catalyzed by acid in both solvent systems.

There is ample evidence which indicates that the catalytic role of the sulfide in the hydrolysis of $ArS(O)SO_2Ar$ is that of a nucleophile. In the first place the reaction is first order in sulfide as well as sulfinyl sulfone. First order kinetics for the sulfide is

$$\text{rate} = k_r[\text{sulfinyl sulfone}]$$

$$k_r = k_r^o + k_s[R_2S]$$

substantiated by the constant value obtained for $(k_r - k_r^o)[R_2S]^{-1} = k_s$ when the concentration of R_2S is changed (27). The constant k_r^o equals k_r in the absence of sulfide under otherwise identical conditions and has been determined experimentally for several sulfinyl

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[1] Traces of chloride ion have a profound positive catalytic effect on both k_r and k_f at low sulfinic acid concentration (30).

sulfones (26, 30).

More important, there is the observed relationship between the structure of the sulfide and the rate of hydrolysis (27). The correlation between log k_s and $\Sigma\sigma^*$ for a series of sulfides is very good with $\rho^* = -1.6$. This result shows that the sulfide sulfur has a significantly lower electron density in the transition state than it has in the original state.

As noted earlier the sulfide-catalyzed hydrolysis of $ArS(O)SO_2Ar$ is also influenced by the acid concentration. A correlation between the rate and the Hammett acidity function, H_o, over a limited acidity range has been examined by Kice and Guaraldi for several sulfide-sulfinyl sulfone combinations. In acetic acid-1% water (27) as well as in 60% dioxane (28) plots of log k_s *vs* $-H_o$ were all satisfactorily linear with slopes close to 1. A solvent isotope effect was measured for the benzyl sulfide catalyzed hydrolysis of p-toluene-sulfinyl p-tolyl sulfone in acetic acid-1% water ($k_s^H/k_s^D = 1.15$) (27) and for the *n*-butyl sulfide catalyzed reaction of the same substrate in 60% dioxane ($k_s^H/k_s^D = 1.4$) (28).

A few years ago a correlation between log k and $-H_o$ such as that indicated in the preceding paragraph might have been interpreted as indicating that the reaction involved specific lyonium ion rather than general acid catalysis (52). This hypothesis has more recently been shown to be invalid (36, 37) and several examples of

general acid catalyzed reactions that exhibit a linear correlation for log k *vs* $-H_o$ have now been documented (38, 40).

In the present example the aforementioned solvent isotope effects ($k_s^H/k_s^D > 1$) definitely suggest that general acid catalysis, rather than specific H^+ catalysis, is what is involved in the sulfide-catalyzed sulfinyl sulfone hydrolysis. In other words, the displacement of the $ArSO_2$ group by the sulfide is assisted by the transfer of a proton to the $ArSO_2$ group in the rate determining step.

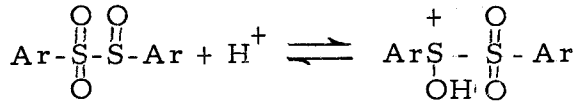
There are two mechanisms that are compatible with the foregoing data and discussion (eqs. 1 and 2).

(1) $R_2S + ArS(=O)_2\text{-}S(=O)\text{-}Ar + H_3O^+ \longrightarrow [R_2\overset{+}{S}\text{--}\overset{Ar}{\underset{O}{\overset{|}{S}}}\cdots\overset{Ar}{\underset{O}{\overset{|}{S}}}\text{-O--H}\cdots OH_2]^{\ddagger}$

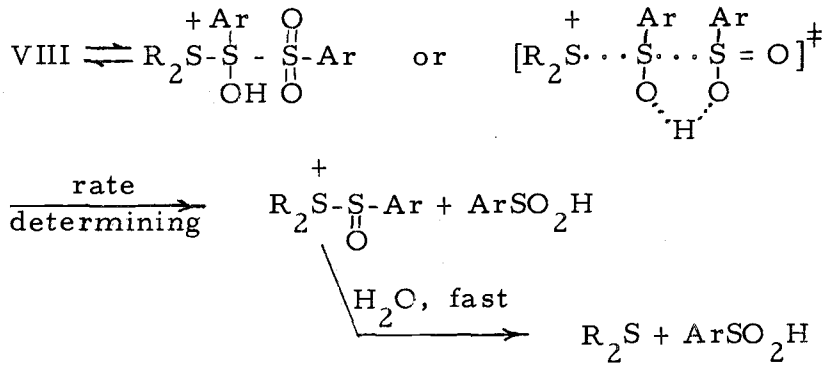
$$\xrightarrow[\text{determining}]{\text{rate}} ArS(=O)\text{-}\overset{+}{S}R_2 + ArSO_2H + H_2O$$

VII

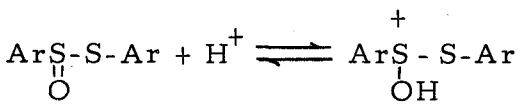
$$\xrightarrow{H_2O,\ \text{fast}} ArSO_2H + R_2S + H^+$$

(2) 

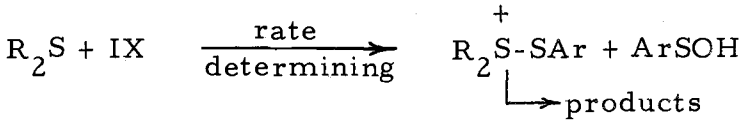
VIII



The latter mechanism (eq. 2) has, however, been pronounced unlikely on the basis of the following argument. First, the sulfide catalyzed hydrolysis of aryl thiolsulfinates, ArS(O)SAr, in either the acetic acid - 1% water system or 60% dioxane has been shown to follow the path outlined in eq. 3 (19, 20, 21, 22, 23). The

(3) 

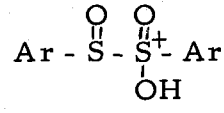
IX



experimental rate constant, k_s, for the n-butyl sulfide catalyzed reaction of the thiolsulfinate was found to be about 150 times smaller in 60% dioxane, 0.40 M $HClO_4$ (H_o = +1.57) than it was in acetic acid-1% water, 0.10 M H_2SO_4 (H_o = -1.13). The large difference in the

value of k_s for eq. 3 in the two solvents is almost certainly primarily a result of the large difference in the acidity of the two media as reflected in the sizable difference of their H_o values. If eq. 2 were the proper mechanism for the sulfide-catalyzed hydrolysis of sulfinyl sulfones, its general similarity to the mechanism in eq. 3 would lead one to predict that k_s for the n-butyl sulfide catalyzed hydrolysis of sulfinyl sulfones should also be a great deal smaller in 60% dioxane than it is in acetic acid-1% water. When the relative rates for the latter reaction were measured, however, k_s was only 4.5 times smaller in 60% dioxane, 0.40 M $HClO_4$, than it was in acetic acid-1% water, 0.10 M H_2SO_4 (28). Therefore, eq. 2 is regarded as the less likely of the two mechanisms outlined in eqs. 1 and 2.

One may wonder why a route involving initial protonation of the sulfone moiety to form the intermediate X followed by nucleophilic attack of R_2S at the sulfinyl center to displace $ArSO_2H$ is not important in the sulfide-catalyzed solvolysis of sulfinyl sulfones. The answer is found in the extremely weak basic character of sulfone



X

groups ($pK_a \leqq -12$). Even in solutions containing 2.0 M $HClO_4$ the equilibrium concentration of X is much too low to make any

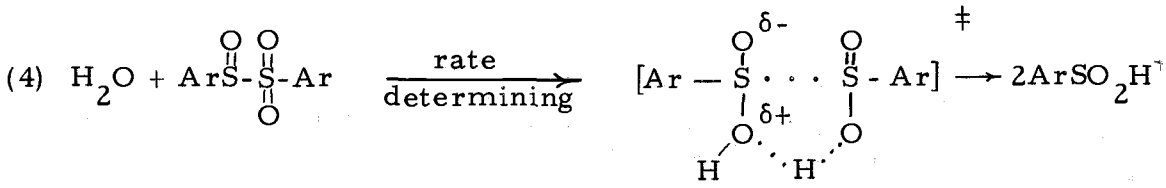
significant contribution to the rate (25).

Kice and Guaraldi discovered that, unlike the sulfide catalyzed hydrolysis, the simple hydrolysis of $ArS(O)SO_2Ar$ in 60% dioxane is not subject to significant acid catalysis (28). When sulfide is not present, the only important reaction at 21°C is the spontaneous hydrolysis.

The uncatalyzed (spontaneous) hydrolysis of aryl sulfinyl sulfones is characterized by a large solvent isotope effect (e.g. $k_{H_2O}/k_{D_2O} = 2.7$ for p-toluenesulfinyl p-tolyl sulfone, XI), a large negative entropy ($\Delta S^{\ddagger} = -37.1$ e.u. for XI) and by a marked acceleration in rate when the percent of water in the solvent is increased. When the aryl groups contain electron-donating substituents in the para position, the reaction rate is retarded; electron-withdrawing para substituents enhance the rate relative to para-H ($\rho = +3.4$).

The large solvent isotope effect strongly suggests that a proton transfer is involved as part of the rate-determining step. Several mechanisms that incorporate such a proton transfer as well as accommodate the rest of the data can be considered (eqs. 4 through 7).

The mechanism depicted in eq. 4 was favored by Kice and Guaraldi for the spontaneous hydrolysis of sulfinyl sulfones (28).



In it nucleophilic attack of water on the sulfinyl group is concerted with the scission of the S-S bond and transfer of a proton from the incoming water molecule to the outgoing $ArSO_2$ group. This proton transfer could actually take place through a chain of one or more intervening water molecules (see eq. 7 below).

The other possible mechanisms (eqs. 5-7) for the spontaneous hydrolysis are analogous to the reaction pathways presented by Kice and Kasperek as mechanistic possibilities for the spontaneous hydrolysis of aryl α-disulfones (25). From the similar response of the spontaneous hydrolyses of sulfinyl sulfones and α-disulfones to various reactions parameters it is clear that the mechanisms for the two reactions are fundamentally identical, differing only in that the spontaneous hydrolysis of the sulfinyl sulfone involves a nucleophilic substitution at sulfinyl sulfur while that of the α-disulfone involves an analogous substitution at sulfonyl sulfur.

Equation 5 postulates the reversible formation of an intermediate, XII or XIII, followed by a rate-determining step in which the scission of the S-S bond is accompanied by the transfer of one of the protons in the intermediate to the departing $ArSO_2$ group.

(5) $H_2O + Ar\text{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}\text{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}\text{-}Ar \rightleftharpoons Ar\text{-}\underset{\underset{OH_2^+}{|}}{\overset{\overset{O^{\ominus}}{|}}{S}}\text{-}SO_2Ar$ or $Ar\text{-}\underset{\underset{OH}{|}}{\overset{\overset{OH}{|}}{S}}\text{-}SO_2Ar$

XII XIII

$$\text{XII or XIII} \xrightarrow[\text{determining}]{\text{rate}} 2ArSO_2H$$

Alternatively, intermediate XIV may be formed reversibly as indicated in eq. 6a and then react according to the scheme in 6b.

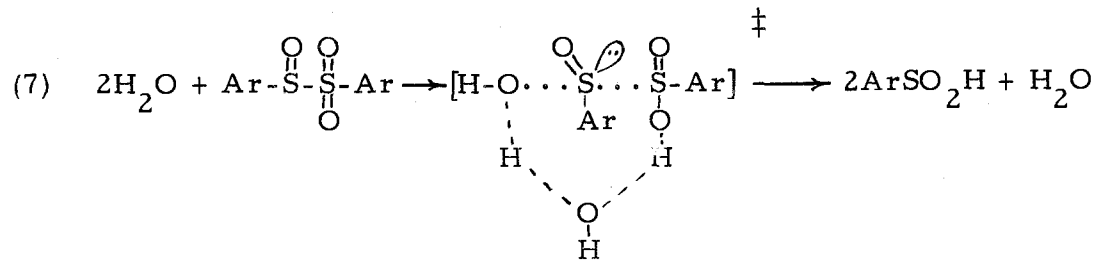
(6a) $2H_2O + ArS\text{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}\text{-}Ar \rightleftharpoons Ar\text{-}\underset{\underset{OH}{|}}{\overset{\overset{O^{\ominus}}{|}}{S}}\text{-}SO_2Ar + H_3O^+$

XIV

(6b) $\text{XIV} + H_3O^+ \xrightarrow[\text{determining}]{\text{rate}} [ArS(\overset{\delta-}{O})\text{---}\underset{\underset{Ar}{|}}{\overset{\overset{O}{\|}}{S}}\text{-}O\text{---}H\text{---}(\overset{\delta+}{O}H_2)]^{\ddagger} \longrightarrow$

$$2ArSO_2H + H_2O$$

Equation 7 is simply a variant of eq. 4 in which the same proton transfer illustrated in eq. 4 is considered to proceed through a chain of one or more intervening water molecules (eq. 7). Indeed, if the geometry of the transition state was trigonal bipyramidal with the entering water molecule and departing $ArSO_2$ occupying the apical positions, a structure such as XV would seem to be required in order to permit such a proton transfer to take place.



XV

Kice et al. (25, 28) have tended to disfavor eqs. 5 or 6 as the actual mechanism for the spontaneous hydrolysis of sulfinyl sulfones or α-disulfones primarily because there is as yet no firm evidence in the literature for intermediates akin to XII, XIII, or XIV in substitutions at sulfinyl or sulfonyl sulfur. Mechanism 7 is the one favored at present.

At this juncture one may wonder why an acid-catalyzed hydrolysis mechanism does not compete significantly with the spontaneous hydrolysis in acidic aqueous dioxane, since in the sulfide-catalyzed hydrolysis of sulfinyl sulfones concomitant acid catalysis is required. The answer which was tentatively advanced by Kice and Guaraldi was as follows. They suggested that uncharged weak nucleophiles such as R_2S or H_2O cannot directly displace a sulfinate ion, $ArSO_2^{\ominus}$, as such from sulfinyl sulfones (28). If $ArSO_2$ is to depart it must do so in its protonated form as $ArSO_2H$. Since the sulfide has no protons of its own to transfer to the departing $ArSO_2$ group, another source of protons (e. g. H_3O^+) is necessary. Water, on the other hand, has a labile proton which can be transferred to the departing

$ArSO_2$ group as depicted in either eqs. 4 or 7.

Study of the behavior of the reaction between a mercaptan, RSH, and a sulfinyl sulfone should serve as a good test as to whether the above explanation is actually correct or not. Mercaptans are sulfur nucleophiles of closely comparable strength to R_2S. If the reason for the difference with regard to acid catalysis in the behavior of H_2O and R_2S in their reactions with a sulfinyl sulfone in acidic aqueous dioxane has something to do with their difference in nucleophilicity, or the fact that one is a sulfur nucleophile while the other is not, then the RSH reaction should behave like the R_2S reaction and differently from the H_2O reaction. On the other hand, if Kice and Guaraldi are right, and the reason for the difference in behavior of R_2S and H_2O is due to the presence of a proton on H_2O that can be transferred to the departing $ArSO_2$ group, then RSH should behave like H_2O and very differently from R_2S. This was the line of reasoning that led us to undertake the study of the hydrolysis of p-toluenesulfinyl p-tolyl sulfone in the presence of n-butyl mercaptan in 60% dioxane. Our particular interest in studying the behavior of this reaction was thus to determine whether the reaction of n-BuSH itself with the sulfinyl sulfone was or was not acid catalyzed.

Results

p-Toluenesulfinyl p-tolyl sulfone (XI), currently the most

thoroughly studied aromatic sulfinyl sulfone, was selected as the substrate in this investigation. The rate of its normal hydrolysis is conveniently rapid in acidic 60% dioxane. For instance, at 21.4° C the half-life for the first order disappearance of the ultraviolet absorption maximum associated with the sulfinyl sulfone is about 160 seconds (28). M. L. Bender's technique (50) of introducing a measured drop of the substrate (or substrate solution) into the thermostatted solvolytic medium held in a spectrophotometer cell is easily adapted for studying reactions with half-lives as short as 15 seconds. With respect to the hydrolysis of XI, therefore, it is possible to study accurately the effect of catalysts that may accelerate the reaction to as much as ten times its normal rate.

The mercaptan chosen for the present work was n-butyl mercaptan. Earlier rate measurements of the n-butyl sulfide catalyzed hydrolysis of XI (28) and the discovery that n-butyl mercaptan is 10 to 100 times less reactive than n-butyl sulfide towards phenyl benzenethiolsulfinate (22) under conditions very similar to those used in this investigation prompted us to try mercaptan concentrations in the range of 0.1 to 0.2 M. At this concentration level the mercaptan was present in considerable stoichiometric excess over XI, which was 10^{-4} M in all runs.

The resulting rates were convenient. Good first order kinetics were observed, as half-lives ranged from 110 seconds for 0.095 M

n-butyl mercaptan at 0.10 M $HClO_4$ to about 60 seconds for 0.150 M mercaptan at 0.0010 M $HClO_4$. Tables 1 and 2 show the experimental first-order rate constants, k_r, for the disappearance of XI under a variety of conditions.

Listed in Table 1 are the kinetic results for the normal hydrolysis of XI at several different acid concentrations. These numbers confirm the discovery made by Kice and Guaraldi (28) that the normal hydrolysis of XI in 60% dioxane is not catalyzed by acid. Small differences in k_r are attributed to changes in the ionic strength as is demonstrated by effect of replacing $HClO_4$ with $LiClO_4$. The values of k_r observed for the five runs at 0.10 M $HClO_4$ were averaged to give $k_r^o = 4.1 \times 10^{-3} sec^{-1}$, a value used in subsequent calculations.

Table 2 is a compilation of the kinetic data obtained for the hydrolysis of XI in the presence of added n-butyl mercaptan in acidic 60% dioxane at 21.4° C. The rate constants, k_r, observed for two or more runs at given mercaptan and acid concentrations were averaged and are expressed in Table 2 as k_r^{ave}.

Each experimental rate constant, k_r, is a sum of the rate constant for the normal hydrolysis of XI, k_r^o, and the pseudo first-order rate constant, $k_M[RSH]$, for the reaction of the mercaptan with XI, i.e. $k_r = k_r^o + k_M[RSH]$. Values of k_M (see Table 3) have been calculated using the relationship

Table 1. Kinetics of the hydrolysis of p-toluenesulfinyl p-tolyl sulfone (XI)[a] in acidic 60% dioxane at 21.4° C.

[n-BuSH] M	[$HClO_4$] M	[$LiClO_4$] M	$k_r \times 10^3$ sec^{-1}
0.00	0.40	0.00	4.56
			4.63
	0.20		4.22
			4.27
	0.10		4.13
			4.19
			4.20
			3.92
			3.96
	0.010		3.63
	0.0010		4.93[b]
	0.10	0.30	4.72
			4.61

[a]Initial concentration of XI = 1×10^{-4} M.

[b]Slight curvature towards higher order was noted in first order plots for two runs which gave $k_r = 4.93 \times 10^{-3} sec^{-1}$.

Table 2. Kinetics of the reaction of p-toluenesulfinyl p-tolyl sulfone (XI)[a] with n-butyl mercaptan in acidic 60% dioxane at 21.4° C.

$[LiClO_4]$ M	[n-BuSH] M	$[HClO_4]$ M	$k_r \times 10^3$ sec^{-1}	$k_r^{ave} \times 10^3$ sec^{-1}
0.00	0.150	0.40	9.26	9.29
			9.35	
			9.25	
		0.20	8.31	8.28
			8.24	
	0.146		8.54	8.44
			8.34	
		0.10	7.40	7.43
			7.84	
			7.29	
			7.20	
	0.095		6.23	6.28
			6.07	
			6.40	
			6.43	
	0.150	0.050	7.28	7.16
			7.05	
		0.010	7.48	7.42
			7.37	
	0.149		7.52	7.37
			7.23	
	0.150	0.0050	7.87	7.80
			7.71	
	0.149	0.0040	8.36	8.30
			8.24	

Table 2. (continued)

$[LiClO_4]$ M	[n-BuSH] M	$[HClO_4]$ M	$k_r \times 10^3$ sec^{-1}	$k_r^{ave} \times 10^3$ sec^{-1}
0.00	0.150	0.0025	9.00	8.98
			8.97	
		0.0020	9.62	9.62
			9.62	
	0.149	0.0016	10.52	10.50
			10.48	
	0.150	0.0015	10.56	10.56
			10.57	
	0.149	0.0012	11.06	10.86
			10.67	
	0.150	0.0010	11.46	11.69
			11.72	
	0.149		11.47	11.28
			11.10	
0.30	0.150	0.10	16.7	16.4
			16.2	

[a]Initial concentration of XI = 1×10^{-4} M.

Table 3. Kinetics of the reaction of p-toluenesulfinyl p-tolyl sulfone (XI)[a] with n-butyl mercaptan in acidic 60% dioxane at 21.4°C including calculated values for k_M.

$[LiClO_4]$ M	[n-BuSH] M	$[HClO_4]$ M	$k_r^{ave} \times 10^3$ sec^{-1}	$k_M \times 10^3$ $M^{-1} sec^{-1}$
0.00	0.150	0.40	9.29 (9.3)	31.5[a]
		0.20	8.28 (8.3)	27
	0.146		8.44 (8.4)	28
		0.10	7.43 (7.4)	22.5
	0.095		6.28 (6.3)	23
	0.150	0.050	7.16 (7.2)	20.5
		0.010	7.42 (7.4)	22
	0.149		7.37 (7.4)	22
	0.150	0.0050	7.80 (7.8)	24.5
	0.149	0.0040	8.30 (8.3)	28
	0.150	0.0025	8.98 (9.0)	32.5
		0.0020	9.62 (9.6)	36.5
	0.149	0.0016	10.50 (10.5)	43
	0.150	0.0015	10.56 (10.6)	43.5
	0.149	0.0012	10.86 (10.9)	45.5
	0.150	0.0010	11.69 (11.7)	50.5
	0.149		11.28 (11.3)	48.5
0.30	0.150	0.10	16.4 (16.4)	82.0

[a] A value of 4.6×10^{-3} sec^{-1} was used for k_r^o when $[HClO_4] = 0.40$ M, 4.3×10^{-3} sec^{-1} when $[HClO_4] = 0.20$ M and 4.1×10^{-3} sec^{-1} for $[HClO_4] \leq 0.10$ M.

$k_M = (k_r - k_r^o)[RSH]^{-1}$, where the observed rate constant k_r is the average constant, k_r^{ave}, from Table 2. The various values of k_r^o that were used in calculating k_M are indicated in the footnote to Table 3. The values of k_M for a given acidity (e.g. 0.10 M $HClO_4$) but different mercaptan concentrations show clearly that k_M is independent of the mercaptan concentration and that the mercaptan - XI reaction is first order in RSH.

Discussion

A priori, several terms may be considered as likely contributors to the value of k_M, the first order rate constant associated with that portion of the rate of disappearance of XI in excess of the normal hydrolysis rate when n-butyl mercaptan is present in the reaction mixture (eq. 9). The terms on the right-hand side of eq. 9

(8) $$k_r = k_r^o + k_M[RSH]$$

(9) $$k_M = k_{RSH} + k'_{RSH}[H^+] + \frac{k_{RS^\ominus}K_a^{RSH}}{[H^+]} + k'_{RS^\ominus}K_a^{RSH}$$

(reading from left to right) represent (a) the direct reaction of n-BuSH with XI (eq. 10), (b) acid catalysis of the n-BuSH reaction (eq. 11), (c) direct substitution by mercaptide ion, $n\text{-}BuS^\ominus$ (eq. 12), and (d) an acid catalyzed reaction of $n\text{-}BuS^\ominus$ with XI (eq. 13).

(10) $\underline{n}\text{-BuSH} + \text{ArS}(=\text{O})_2\text{-S-Ar} \xrightarrow{k_{RSH}} \underline{n}\text{-BuS-}\underset{\underset{\text{O}}{\|}}{\text{S}}\text{-Ar} + \text{ArSO}_2\text{H}$

(11) $\underline{n}\text{-BuSH} + \text{ArS}(=\text{O})_2\text{-S-Ar} + \text{H}^+ \xrightarrow{k'_{RSH}} \underline{n}\text{-Bu}\overset{+}{\underset{\text{H}}{\text{S}}}\text{-}\underset{\underset{\text{O}}{\|}}{\text{S}}\text{-Ar} + \text{ArSO}_2\text{H}$

$\underline{n}\text{-Bu}\overset{+}{\underset{\text{H}}{\text{S}}}\text{-}\underset{\underset{\text{O}}{\|}}{\text{S}}\text{-Ar} \xrightarrow{\text{fast}} \underline{n}\text{-BuS-}\underset{\underset{\text{O}}{\|}}{\text{S}}\text{-Ar} + \text{H}^+$

(12) $\underline{n}\text{-BuS}^{\ominus} + \text{ArS}(=\text{O})_2\text{-S-Ar} \xrightarrow{k_{RS^{\ominus}}} \underline{n}\text{-BuS-}\underset{\underset{\text{O}}{\|}}{\text{S}}\text{-Ar} + \text{ArSO}_2^{\ominus}$

(13) $\underline{n}\text{-BuS}^{\ominus} + \text{ArS}(=\text{O})_2\text{-S-Ar} + \text{H}^+ \xrightarrow{k'_{RS^{\ominus}}} \underline{n}\text{-BuS-}\underset{\underset{\text{O}}{\|}}{\text{S}}\text{-Ar} + \text{ArSO}_2\text{H}$

The data in Table 3 demonstrate the effect that changes in the acid concentration have on k_M. From 0.40 to 0.10 M perchloric acid a gradual decrease in k_M is observed. This trend is believed to be due to the effect of decreasing the total ion content of the reaction mixture rather than to be a result of reducing the acid catalyzed contribution to the overall rate. The tremendous increase in rate observed when $LiClO_4$ is added (last entry in Table 3) is a strong indication that salt effects play a significant role in the determination of k_M. It is also instructive to note that in the reaction of n-butyl sulfide with XI, a reaction considered to be acid-catalyzed (28), the forty-fold increase in acid concentration from 0.01 to 0.4 M $HClO_4$ leads to a forty-fold increase in the value of the sulfide catalyzed term, k_s. By comparison, the rate of the mercaptan reaction is

less than doubled with the same forty-fold increase in acid concentration (Table 4). In view of these considerations, the acid-dependent term, $k_{RSH}[H^+]$, in eq. 9 may be effectively ignored.

Table 4. Dependence of rates of reaction of butyl mercaptan and butyl sulfide with XI on acid concentration.[a]

$[HClO_4]$ M	k_M for the n-BuSH reaction	k_s for the n-Bu_2S reaction
0.01	0.022	< 0.04
0.10	0.023	0.24
0.20	0.027	0.70
0.40	0.032	1.7

[a] All data for 60% dioxane at 21.4° C.

The value of k_M (Table 3) levels out between 0.10 - 0.01 M $HClO_4$ and then begins to climb as the acidity of the reaction medium is reduced below 0.01 M $HClO_4$. It is apparent that in the level range one or both of the pH independent reactions illustrated by eqs. 10 and 13 predominates, while the increase in rate corresponding to a reduction in the perchloric acid concentration below 0.01 M suggests that the reaction of mercaptide ion, n-$BuS^{\ominus}$, with XI is finally being detected (eq. 12).

The latter point is substantiated by reviewing the appropriate kinetic expression for k_M (eq. 14) where K_a^{RSH} is the acid

dissociation constant of the mercaptan and plotting k_M *vs* $1/[H^+]$. The plot is satisfactorily linear (Figure 1).

$$(14) \qquad k_M = k_{RSH} + k_{RS^\ominus}\frac{K_a^{RSH}}{[H^+]} + k'_{RS^\ominus}K_a^{RSH}$$

The question yet remains concerning the relative importance of the pH independent reactions 10 and 13 as contributors to the rate of disappearance of XI. As Figure 1 shows, the intercept ($k'_{RS^\ominus}K_a^{RSH} + k_{RSH} = 0.02$) is nearly 700 times as large as the slope ($k_{RS^\ominus}K_a^{RSH} = 3 \times 10^{-5}$). This means that one or both of the rate constants ($k'_{RS^\ominus}$ and k_{RSH}) included in the intercept is considerably larger than $k_{RS^\ominus}$. Kice and Guaraldi (28) learned that for all other anionic nucleophiles studied, such as $Cl^\ominus$, $Br^\ominus$ or $I^\ominus$, the magnitude of the rate constant for the acid-catalyzed reaction of Nu with XI (k'_{Nu}) is no greater than five times the rate constant (k_{Nu}) for the uncatalyzed reaction of Nu with the same substrate. Assuming that this feature is also characteristic of $RS^\ominus$, i.e. that $k'_{RS^\ominus}/k_{RS^\ominus} \leqq 5$, then it is evident that k_{RSH} (eq. 10) is far more important than $k'_{RS^\ominus}K_a^{RSH}$ (eq. 13) in establishing the value of k_M.

The original goal that inspired this series of studies on the reaction of n-butyl mercaptan with XI was to determine whether the reaction of RSH with an aromatic sulfinyl sulfone is or is not subject to acid catalysis. If this question could be resolved, then one could

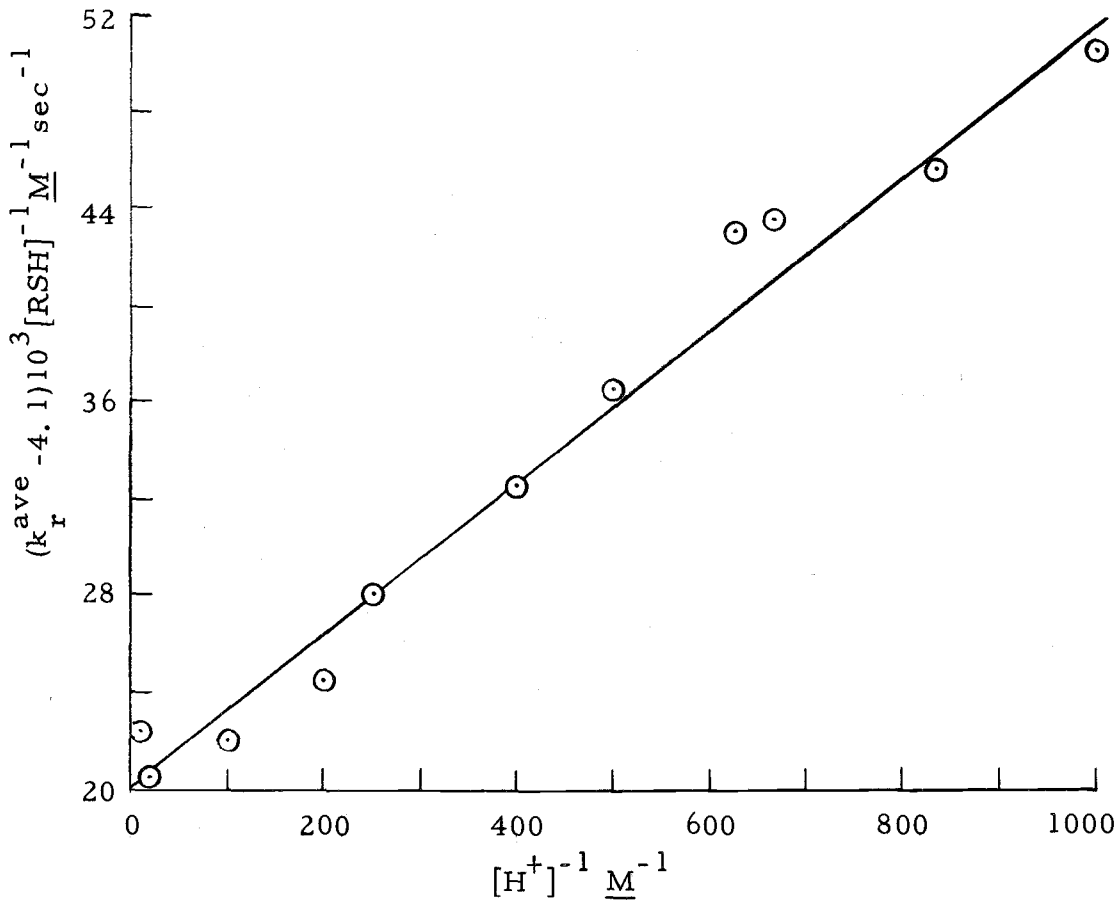


Figure 1. Reaction of p-toluenesulfinyl p-tolyl sulfone (XI) with n-butyl mercaptan in acidic 60% dioxane at 21.4° C. Plot of $k_M = (k_r^{ave} - k_r^o)10^3[RSH]^{-1}$ *vs* $[H^+]^{-1}$ where $k_r^o = 4.1 \times 10^{-3}\ sec^{-1}$.

be more precise in his conclusions regarding the mechanisms for the interaction of water and alkyl sulfides with sulfinyl sulfones.

We have learned that in the kinetics of its reaction with XI n-butyl mercaptan behaves much more like water than like n-butyl sulfide in terms of the dependence of reaction rate on acidity of the medium. Like the water reaction the reaction between n-BuSH and XI is not subject to significant acid catalysis. The two reactions are also similar in their sensitivity towards changes in the ionic strength of the reaction mixture.

It is apparent, then, that the hypothesis described in the introduction is correct--namely that an uncharged weak nucleophile such as water or RSH does not require concomitant acid catalysis in its reaction with a sulfinyl sulfone in acidic aqueous dioxane because it has a labile proton that can be transferred to the departing $ArSO_2$ group. On the other hand, an alkyl sulfide R_2S, lacking an active proton of its own, is incapable of displacing the $ArSO_2$ group without the aid of another proton source. In other words, it is not because of a difference in nucleophilicity or because one is a sulfur nucleophile while the other is not that the R_2S-reaction is catalyzed by acid in acidic aqueous dioxane while normal hydrolysis is not. The mechanistic difference is totally and intriguingly a result of the nucleophile's (water) self-contained source of protons.

Experimental

Purification of Materials

Dioxane was purified by the method of Wiberg (51, p. 245). The perchloric acid used (Baker Analyzed Reagent) contained less than 5×10^{-4}% chloride ion as an impurity. All stock solutions of the perchloric acid were standardized (acid-base). n-Butyl mercaptan was fractionally distilled under nitrogen directly before using, b. p. 97-98°.

p-Toluenesulfinyl p-Tolyl Sulfone

The procedure outlined by F. Kurzer (15, p. 93) was used as a guide in the preparation of p-toluenesulfinyl chloride. A 42.8 g (0.20 mole) sample of powdered sodium p-toluenesulfinate dihydrate (Aldrich Chemical Company) was added in small portions with stirring to 179 g (108 ml, 1.5 mole) freshly distilled thionyl chloride at room temperature. Ultimately a reduced pressure distillation afforded 18.4 g (53%) of the sulfinyl chloride, b. p. 73-79°/0.5-0.4 torr (lit. 99-102/0.5 torr).

A 23.3 g (0.109 mole) sample of sodium p-toluenesulfinate dihydrate was heated at 180°C and 0.25 torr for seven hours. The residue was cooled to room temperature and 100 ml anhydrous ether

was added under dry-prepurified nitrogen. Then in dropwise fashion, following the technique of H. Brederick et al. (5), 18.4 g (0.105 mole) p-toluenesulfinyl chloride was added. The mixture was stirred for one hour and was then poured into ice water. The precipitate was filtered off and triturated several times with ice water and then with ether. The yield was 27.4 g (88% based on the sulfinyl chloride), m.p. 87° sharp (lit. 87°). The material was stored at -15° in a desiccator.

Preparation of Solutions for Kinetic Runs

Acidified 60% Dioxane Solutions (Mercaptan Excluded). Concentrated perchloric acid (7.05×10^{-3} moles $HClO_4$/g. of standardized solution) was weighed into a volumetric flask and carefully measured quantities of water and dry dioxane were added to make the solution exactly 60.0% dioxane-40.0% water by volume.

The acid content was decreased by taking aliquots of the stock solution and diluting with 60% dioxane in a volumetric flask.

Sixty Percent Dioxane Solutions Containing n-Butyl Mercaptan. A weighed amount of freshly distilled n-butyl mercaptan was placed in a volumetric flask and diluted with acidified or neutral (as the case required) 60% dioxane. The mercaptan was found to be soluble in acidic 60% dioxane at room temperature up to concentrations of about 0.15 M mercaptan.

The mercaptan concentration was decreased while the acid concentration was maintained at a constant value by taking aliquots of the acidic 60% dioxane-mercaptan solution and diluting with appropriately acidified 60% dioxane.

The acid concentration was decreased while the concentration of the mercaptan was held constant by taking aliquots and diluting with a neutral 60% dioxane-mercaptan diluent.

Procedure for Kinetic Runs

In general, the spectrophotometric method used by Kice and Guaraldi (28) was employed to follow the reaction kinetics of p-toluenesulfinyl p-tolyl sulfone (XI). In particular, between 0.1450 and 0.1490 g of XI was dissolved in 10 ml dry dioxane (0.05 M). Usually this solution was used when it was fresh; it was not used if it was more than six hours old. A six microliter drop of the 0.05 M XI-dioxane solution was transferred to the flattened end of a glass stirring rod and introduced rapidly and with thorough mixing into 3.0 ml of the appropriate aqueous dioxane mixture contained in a silica cell thermostatted at 21.4° in a Cary 15 ultraviolet spectrophotometer. The disappearance of XI was then followed by monitoring the decrease in the optical density, A, of the solution at 300 nm. Plots of log $(A - A_\infty)$ vs time were satisfactorily linear.

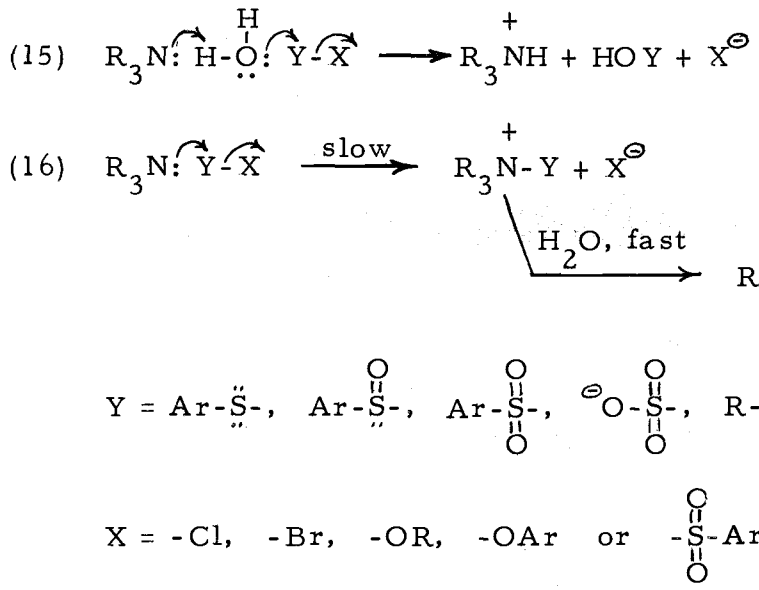
It was observed that A_∞ for the runs in which n-butyl

mercaptan was primarily responsible for the disappearance of XI was consistently a few percent higher than the A_∞ for reactions of XI in which the mercaptan was excluded. The thiolsulfinate product of the mercaptan-XI reaction, n-BuSS(O)Ar, has a significant extinction coefficient at 300 nm, whereas the sulfinic acid, $ArSO_2H$, is effectively transparent at this same wavelength.

II. THE REACTIONS OF p-METHOXYBENZENESULFINYL p-ANISYL SULFONE WITH TERTIARY AMINES

Introduction

In principle a tertiary amine can catalyze the hydrolysis of a carboxylic acid derivative or a sulfur substrate either by acting as a general base catalyst (eq. 15) or as a nucleophilic catalyst (eq. 16). Known examples of either type of catalysis by tertiary amines with sulfur substrates are somewhat rare.



One case reported recently by O. Rogne involved benzenesulfonyl chloride as the substrate and pyridine as the catalyst (49). The study showed that in the hydrolysis of benzenesulfonyl chloride in aqueous media, pyridine catalyzes the reaction via nucleophilic attack on the sulfonyl sulfur (eq. 17).

(17) $\phi\text{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}\text{-Cl} + C_5H_5N \xrightarrow[\text{determining}]{\text{rate}} \phi\text{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}\text{-}\overset{+}{N}C_5H_5 + Cl^{\ominus}$

$\phi\text{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}\text{-}\overset{+}{N}C_5H_5 \xrightarrow[\text{fast}]{H_2O,} \phi SO_2OH + C_5H_5NH^{+}$

Kice and Kasperek investigated the catalysis of the hydrolysis of α-disulfones by various nucleophiles including the tertiary amine, triethylamine (24). Nearly all the nucleophiles that were tested reacted with the α-disulfone by direct substitution at the sulfur center (eq. 18). Azide ion, and primary and secondary amines gave isolable

(18) $Nu^{\ominus} + Ar\text{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}\text{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}\text{-Ar} \xrightarrow[\text{rate determining}]{k_{Nu}} Ar\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}\text{-Nu} + ArSO_2^{\ominus}$

$Ar\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}\text{-Nu} \xrightarrow[\text{fast}]{H_2O,} ArSO_3H + H^{+} + Nu^{\ominus}$

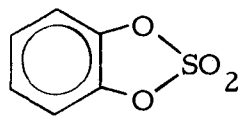
substitution products. On the other hand, triethylamine acted as a general base catalyst (eq. 19). The steric bulk of the highly branched

(19) $Et_3N + H_2O + Ar\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}\text{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}Ar \xrightarrow{k_{gb}} \overset{+}{Et_3}NH + Ar\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}\text{-OH} + ArSO_2^{\ominus}$

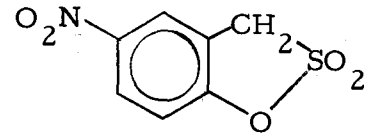
triethylamine apparently instigated the change in the mode of the reaction.

E. T. Kaiser and coworkers (16) have studied the catalytic effect of imidazole and N-methylimidazole on the hydrolysis of catechol cyclic sulfate (XVI) and 2-hydroxy-5-nitro-α-toluenesulfonic

acid sultone (XVII). Imidazoles are widely recognized as nucleophilic catalysts in the hydrolysis of the phenyl esters of carboxylic acids (6, p. 46-66). Their effectiveness as nucleophiles is directly related



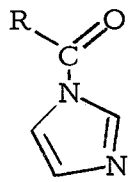
XVI



XVII

to the nature of the leaving group. Since both substrates XVI and XVII have excellent leaving groups, one would be inclined to predict that nucleophilic catalysis by the imidazoles would occur in this case as well. The Kaiser group, however, detected none. They found that the imidazoles serve as catalysts for the hydrolysis of XVI and XVII only in the general base sense.

Whether a given case is one of general base or nucleophilic catalysis may be determined experimentally in one of two ways (6, p. 57). Detection or isolation of a reaction intermediate is one method which points to the nucleophile-catalyzed mechanism (eq. 16). In the case of the hydrolysis of carboxylic esters, for instance, acylimidazole intermediates (e.g. XVIII and XIX) have been identified (6, p. 54).



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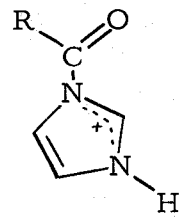
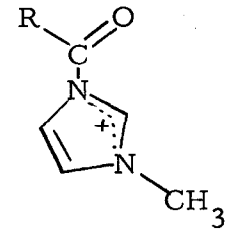


XVIII



XIX

Another technique for distinguishing between the two mechanisms is to determine the magnitude of the deuterium solvent isotope effect. One would expect the solvent isotope effect (k_{H_2O}/k_{D_2O}) to be close to a value of one for the nucleophile catalyzed mechanism, but much larger, around two or more, for the general base mechanism (17, p. 90; 24). Table 5 gives the solvent isotope effects reported for the examples of sulfonyl substrates mentioned above.

While some data are now available describing the action of tertiary amines in the hydrolysis of sulfonyl substrates, nothing has yet been reported concerning tertiary amine catalysis of hydrolysis at sulfinyl sulfur. It was of interest to determine if tertiary amines would in fact catalyze the hydrolysis of sulfinyl substrates and, if they did, to learn which amines acted as nucleophilic catalysts and which as general base catalysts.

Potentially, the aforementioned mechanistic test could be used to help explain why sulfinyl sulfones react 10^4 to 10^7 times more rapidly than α-disulfones do with the same nucleophiles (25). As reported by Kice and Kasperek (25) the only important difference in

Table 5. The solvent isotope effects and proposed mechanisms for several amine catalyzed hydrolysis reactions of various sulfur substrates.

Substrate	Base	$k_A^{H_2O}/k_A^{D_2O}$	Mechanism	Reference
$C_6H_5SO_2Cl$	pyridine	1.10	Nucleophilic	49
$C_6H_5SO_2SO_2C_6H_5$	triethylamine	1.9	General Base	24
XVI	imidazole	3.6		16
	N-methylimidazole	4.2		
XVII	imidazole	3.5		
	N-methylimidazole	3.5		

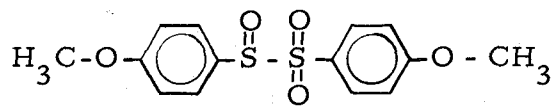
reaction parameters between α-disulfones and sulfinyl sulfones in their reactions with nucleophiles other than the rate is in the activation energies. The activation energy for the spontaneous hydrolysis of phenyl α-disulfone in 60% dioxane, for example, is about 6 kcal larger than that for the analogous sulfinyl sulfone. It is of interest to learn the extent to which steric factors, as contrasted with electrostatic factors due to the partial negative charge on the extra oxygen attached to the sulfur of a sulfonyl group, contribute to such a difference in activation energies. To accomplish this one could compare the catalytic mechanisms of a series of amines interacting with a given sulfinyl sulfone to a similar series of amines reacting with the analogous α-disulfone. If one were to find that a switch in mechanism from nucleophilic to general base catalysis in the sulfinyl system were to occur only when one went to structurally more hindered amines than those required to cause a switch from nucleophilic to general base catalysis in the hydrolysis of the analogous sulfonyl substrate, then one could conclude that steric hindrance is truly a significant factor in the retardation of the rate (relative) of nucleophilic substitution at sulfonyl sulfur.

The goals of the work discussed in this chapter were: (1) to determine if catalysis of the hydrolysis of aryl sulfinyl sulfones by tertiary amines could be observed; (2) to study such catalysis for various amines of differing steric requirements and to determine in

each case whether the catalysis involved was nucleophilic or general base; (3) to see what conclusions could be drawn about the relationship between the type of catalysis observed and the structure of the amine. The approach used was to measure the rate of hydrolysis of the sulfinyl sulfone in amine/amine$\cdot H^+$ buffers containing varying amounts of amine in aqueous dioxane or aqueous glyme as the solvent.

Results

The relatively "hard" base character of an alkyl amine as classified by HSAB theory (47) and the medium hardness of the sulfinyl sulfur center (25) would lead one to predict that the interaction between the amine and an aromatic sulfinyl sulfone could proceed quite rapidly--too rapidly, perhaps, to be measured conveniently. Also, depending on the magnitude of the pK_b of the amine and the reaction conditions, a large contribution to the overall rate could result from nucleophilic attack on sulfinyl sulfur by the hard base hydroxide ion. These likelihoods were considered in making the selection of the substrate for this study, p-methoxybenzenesulfinyl p-anisyl sulfone XX.



XX

The methoxy groups at the para positions have a net

rate-retarding influence on nucleophilic substitution at the sulfinyl center causing XX to be one of the least reactive aromatic sulfinyl sulfones in this respect (27). Reaction kinetics for XX can be followed readily by observing the disappearance of the strong ultraviolet absorption maximum associated with the substrate at 306 nm (ϵ = 13,000).

n-Butylamine, pK_b = 3.39 at 25° (13), was the first base to be tested. A buffer solution containing 0.001 M n-$BuNH_2$ and 0.001 M n-$BuNH_3^+ClO_4^\ominus$ in 60% dioxane was prepared and the sulfinyl sulfone was added to it. The reaction was complete in less than 10 seconds, however, which was much too fast to allow for any kinetic measurement whatsoever by our technique. To go to smaller initial concentrations of the buffer was to invite complications in the sense that the kinetics would no longer be pseudo first order. One would no longer be able to assume that the concentration of the amine remained effectively constant throughout the reaction.

Since n-butylamine proved to be too reactive with XX, the more hindered base triethylamine, pK_b = 3.33 at 25° (10), was tested. A few trial runs at a 1 to 1 buffer ratio, $[Et_3N] = [Et_3NH^+ClO_4^\ominus]$ = 0.001 M, showed that the reaction between the sulfinyl sulfone and triethylamine (TEA) was indeed slower than with the primary amine, but still inconveniently fast. The estimated half life for the reaction with 0.001 M TEA was about 1 second; i.e. at least six half lives had

passed before the cell compartment of the uv spectrophotometer could be closed and the recorder switched on.

Several runs were recorded for the TEA-aqueous dioxane solvolysis of XX by adding the measured drop of the substrate solution to the spent amine solution of the preceding run. Runs 1, 2, and 3 of the first series (including runs 4-8) are not listed in Table 6 because they were too fast to measure, but by the time the fourth drop of substrate solution was added the effective buffer ratio $[TEA]/[TEAH^+]$ had dropped from 1 to about 0.42 and the rate was slow enough to record the last 10 to 20% of the reaction. Most of the first order kinetic plots were linear.

Duplicate runs using a fresh amine-aqueous dioxane solution for each run were recorded for a series at effective buffer ratios, $[TEA]/[TEAH^+]$, varying from 0.41 to 0.0865 (Table 7). The last three runs listed in Table 7 are the results of a test to determine if a common ion effect due to $p\text{-}CH_3OC_6H_4SO_2^{\ominus}$ was involved in the TEA-aqueous dioxane solvolysis of XX.

In an attempt to reduce the rate of the TEA reaction to allow greater latitutde for studying the reaction kinetics, the solvent system was changed to 60% glyme (vol/vol) (Table 8). When this was done the rates were reduced, but not as much as had been anticipated. At amine concentrations of approximately 1×10^{-3} M and buffer ratios varying from 0.177 to 0.813 (Table 8) the observed half-life

Table 6. TEA catalyzed hydrolysis of XX in 60% dioxane at 21.4°.[a]

Run	init[TEA] $\times 10^4$ M	init[$TEAH^+$] $\times 10^4$ M	eff[TEA] $\times 10^4$ M	eff[$TEAH^+$] $\times 10^4$ M	$\frac{\text{eff[TEA]}}{\text{eff[TEAH}^+\text{]}}$	$k_{obs} \times 10^3$ sec^{-1}
4[b]	6.7	12.7	5.7	13.7	0.42	186
5	5.7	13.7	4.7	14.7	0.32	161
6	4.7	14.7	3.7	15.7	0.24	126
7	3.7	15.7	2.7	16.7	0.16	86
8	2.7	16.7	1.7	17.7	0.096	55
1	4.8	4.8	3.8	5.8	0.655	290[c]
2	3.8	5.8	2.8	6.8	0.41	133
3	2.8	6.8	1.8	7.8	0.23	81

[a]All runs contained 0.01 M $LiClO_4$ and an initial concentration of 5×10^{-5} M XX.

[b]The first three runs of this series (runs 4-8) were too fast to measure.

[c]The value for $k_{obs} = 0.290\ sec^{-1}$ is based on only two points on the kinetic plot.

Table 7. TEA catalyzed hydrolysis of XX in 60% dioxane at 21.4°.[a]

$[CH_3OC_6H_4SO_2Na]$ x 10^4 M	init[TEA] x 10^4 M	init[$TEAH^+$] x 10^4 M	eff[TEA] x 10^4 M	eff[$TEAH^+$] x 10^4 M	$\frac{\text{eff[TEA]}}{\text{eff[TEAH}^+\text{]}}$	k x 10^3 sec^{-1}
0.00	2.4	2.4	1.4	3.4	0.41	160 152
	4.0	14.9	3.0	15.9	0.189	105 110
	3.2	11.9	2.2	12.9	0.171	84.5 86.1
	2.4	8.95	1.4	9.95	0.141	55.1 49.5
	1.6	5.95	0.6	6.95	0.0865	40.5 40.5
1.03 5.57 10.3	2.4	2.4	1.4	3.4	0.41	128 106 119

[a]All runs contained 0.01 M $LiClO_4$ and 5 x 10^{-5} M XX (initial concentration).

Table 8. TEA catalyzed hydrolysis of XX in 60% glyme at 21.4°.[a]

init[TEA] $\times 10^4$ M	init[$TEAH^+$] $\times 10^4$ M	eff[TEA] $\times 10^4$ M	eff[$TEAH^+$] $\times 10^4$ M	$\frac{\text{eff[TEA]}}{\text{eff[TEAH}^+\text{]}}$	k $\times 10^3$ sec^{-1}
9.7	9.7	8.7	10.7	0.813	243
10	50	9.0	51	0.177	191
10	20	9.0	21	0.429	221

[a]No $LiClO_4$ was used. All runs contained 5×10^{-5} M XX (initial concentration).

was about three seconds.

Aniline and its derivatives such as m-nitro, N-methyl or N, N-dimethylaniline could not be used as nucleophiles because the ultraviolet spectra of these bases interferes with that of the sulfinyl sulfone, XX. For example, when the concentration of aniline in isooctane is 0.102 grams per liter (approximately 0.001 M) in a 1.0 cm uv cell the transmission at 306 nm is about 90%; at 1.02 grams per liter the solution is opaque (1). Solutions of N-methyl or N, N-dimethylaniline absorb to a greater extent than aniline does at 306 nm.

In contrast to triethylamine, tribenzylamine (TBA), pK_b = 6.4 ca (11), did not enhance the rate of hydrolysis of XX in 60% dioxane at 21.4°. A pair of runs were measured at a constant buffer ratio ($[TBA]/[TBAH^+]$) of 1.0 but different amine concentrations. The k_{obs} for 0.01 M TBA/0.01 M $TBAH^+$ was 2.93×10^{-3} sec^{-1}. The other, at 0.001 M TBA/0.001 M $TBAH^+$, gave $k_{obs} = 2.96 \times 10^{-3}$ sec^{-1} and 2.90×10^{-3} sec^{-1} (duplicate runs). A slight curvature was noted in the first order plots.

The observed rate for the TBA-XX hydrolysis (k_{obs} = 2.9×10^{-3} sec^{-1}) was about 1.7 times faster than the rate for spontaneous hydrolysis of XX ($k_{obs}^{spont} = 1.7 \times 10^{-3}$ sec^{-1}, 60% dioxane, 0.1 M $HClO_4$, 21.4°). At first glance one might think that the difference was due to hydroxide ion catalysis. But a pair of runs at constant amine concentration (0.01 M) and different buffer ratios

([TBA]/[$TBAH^+$] = 5/1 and 5/3) gave k_{obs} = 2.97 and 2.95 x 10^{-3} sec^{-1} respectively. The slight curvature in the first order plots and the small rate enhancement associated with the TBA-XX hydrolysis are believed to be due to an impurity in the dioxane that is converted to its active form in alkaline dioxane solutions (17, 24).

N-Benzylpyrrolidine (NBP), pK_b = 4.49 (7), was prepared and tested for its catalytic effect on the hydrolysis of XX in 60% glyme. As the data listed in Table 9 indicate, the reaction was quite rapid and consistent kinetic measurements were difficult to obtain. Thus NBP was abandoned as a catalyst.

A compromise between the inconveniently fast N-benzylpyrrolidine and the inactive tribenzylamine was sought and found in diethylbenzylamine (DEBA), pK_b = 4.44 (4). The kinetics were measured for the reaction of DEBA with XX in buffered 60% glyme at 21.4° C. The rates were very convenient, e.g. at a constant buffer ratio ([DEBA]/[$DEBAH^+$]) of 1.00 and an amine concentration ranging from 5.1 x 10^{-3} to 1.0 x 10^{-3} M the first order half-lives varied from 11 to 31 seconds (see Table 10). A series of runs using buffered 40/60 D_2O-glyme (vol/vol) as the solvent was also measured (Table 10) to determine the solvent-isotope effect.

The data from Table 10 are displayed in Figures 2 and 3 with the observed rate constant plotted against the amine concentration. The slopes of the plots for the hydrolysis at the two different buffer ratios

Table 9. NBP catalyzed hydrolysis of XX in 60% glyme at 21.4°.[a]

init[NBP] $\times 10^3$ M	init[$NBPH^+$] $\times 10^3$ M	eff[NBP] $\times 10^3$ M	eff[$NBPH^+$] $\times 10^3$ M	$\frac{\text{eff[NBP]}}{\text{eff[NBPH}^+\text{]}}$	$k_{obs} \times 10^3$ sec^{-1}
1.18	1.00	1.08	1.10	0.98	251 216
1.00	0.96	0.90	1.06	0.85	177 176
0.90	0.84	0.80	0.94	0.85	173 159
0.82	0.72	0.72	0.82	0.88	141 131

[a]All runs contained 0.01 M $LiClO_4$ and 5×10^{-5} M XX (initial concentration).

Table 10. DEBA catalyzed hydrolysis of XX in 60% glyme at 21.4°.[a]

Solvent	[DEBA] x 10^3 M	[$DEBAH^+$] x 10^3 M	$\frac{[DEBA]}{[DEBAH^+]}$	k_{obs} x 10^3 sec^{-1}
H_2O-glyme	5.10	5.10	1.00	62.7
	4.08	4.08		52.2
	3.06	3.06		44.0[b]
	2.04	2.04		32.8
	1.02	1.02		22.3
	1.01	1.01		21.4
	3.91	1.57	2.49	64.7
	2.93	1.18		55.0
	1.96	0.784	2.50	44.2
	0.978	0.392		34.8
D_2O-glyme	5.07	5.20	0.975	38.3
	4.05	4.16		34.8
	3.04	3.12		30.0
	2.03	2.08		25.9

[a]All runs contained 0.01 M $LiClO_4$ and 5 x 10^{-5} M XX (initial concentration).

[b]The temperature of this run alone was somewhat higher (< 1°) than 21.4°.

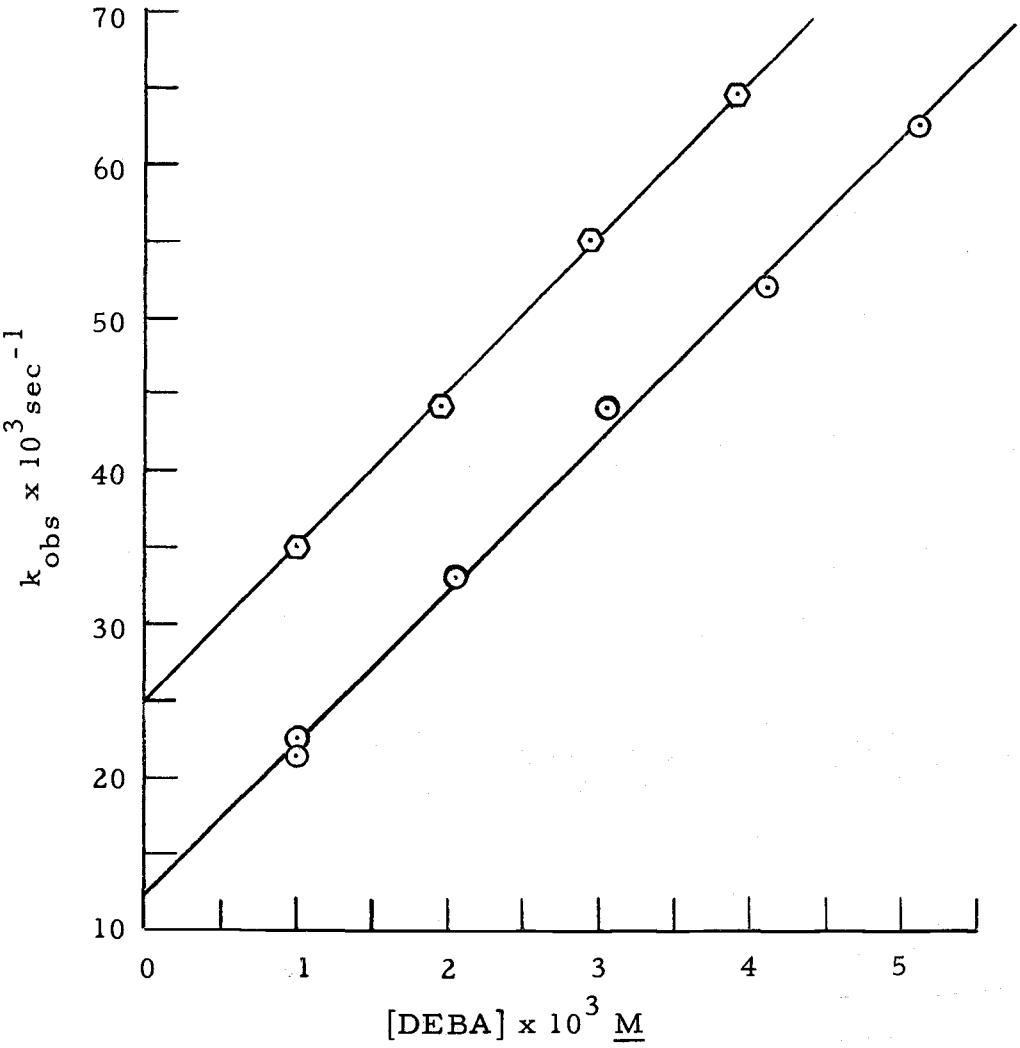


Figure 2. Diethylbenzylamine (DEBA) catalyzed hydrolysis of p-methoxybenzenesulfinyl p-anisyl sulfone in buffered 60% glyme at 21.4° C.

⊙ 1 to 1 [DEBA]/[$DEBAH^+$]
⊙ 2.5 to 1 [DEBA]/[$DEBAH^+$]

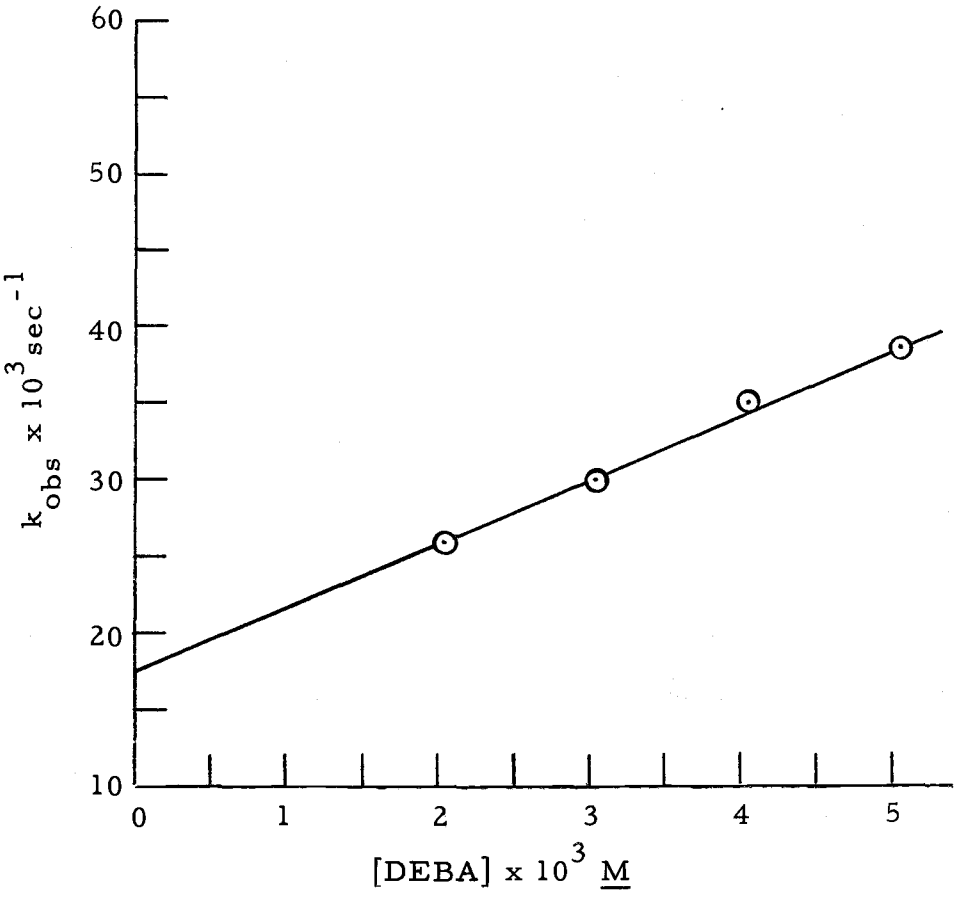


Figure 3. Diethylbenzylamine (DEBA) catalyzed hydrolysis of p-methoxybenzenesulfinyl p-anisyl sulfone in 1/1 [DEBA]/[$DEBAD^+$], 40% D_2O - 60% glyme at 21.4° C.

are very nearly identical (slope = k_A = 10.2 $\underline{M}^{-1}sec^{-1}$ for a buffer ratio of 2.5 and 9.9 $\underline{M}^{-1}sec^{-1}$ for a buffer ratio of 1.00). The deuterium solvent isotope effect ($k_A^{H_2O}/k_A^{D_2O}$) at a buffer ratio of 1.0 is 2.4.

The catalytic nature of pyridine, pK_b = 8.75 (39), in the hydrolysis of XX in 60% dioxane was investigated. Several kinetic runs were recorded using a 1/1 [pyr]/[$pyrH^+$] buffer system. The amine concentration was varied from about 10 x 10^{-3} $\underline{M}$ to 1 x 10^{-3} $\underline{M}$ while $LiClO_4$ was added to maintain a constant ionic strength for the series (see Table 11). A plot of $k_{obs} - k_{un}$, where k_{un} is the rate constant for the spontaneous hydrolysis of XX in 60% dioxane, versus the pyridine concentration exhibits a slope of 3.86 $\underline{M}^{-1}sec^{-1}$ and an intercept very close to a value of zero (Figure 4). A switch from H_2O to D_2O for a similar series of runs resulted in a small deuterium solvent isotope effect of 1.4 (Table 11, Figure 4).

A test was made to determine whether or not the pyridine catalyzed hydrolysis of XX is subject to a common ion effect. The sodium salt of p-methoxybenzenesulfinic acid was added to the reaction mixture up to a concentration of 1.0 x 10^{-3} $\underline{M}$ which is nearly seven times the final concentration of the sulfinate anion produced in the hydrolysis of 7.5 x 10^{-5} $\underline{M}$ XX. As demonstrated by the results listed in Table 12, there appears to be a small reduction in the rate; the effect is larger the greater the concentration of added sulfinate.

Table 11. Pyridine catalyzed hydrolysis of XX in 60% dioxane at 21.4° C.[a]

Solvent	[pyr] x 10^3 M	[pyr·H^+] x 10^3 M	[$LiClO_4$] x 10^3 M	k_{obs} x 10^3 sec^{-1}	(k_{obs}-k_{un}) x 10^3 sec^{-1}
H_2O-dioxane	9.74	9.78	0.00	39.2	37.5
	4.87	4.89	5.09	20.5	18.8
	2.93	2.94	6.84	13.4	11.7
	1.95	1.96	8.12	9.91	8.21
	0.97	0.98	9.29	6.35	4.65
D_2O-dioxane	10.0	10.0	0.00	27.9	27.2
				27.5	
	8.0	8.0		20.6	20.7
				22.6	
			2.0	20.6	
	6.0	6.0	4.0	17.0	16.5
	4.0	4.0	6.0	11.5	11.0

[a]Initial concentration of XX in all runs was 7.5 x 10^{-5} M.

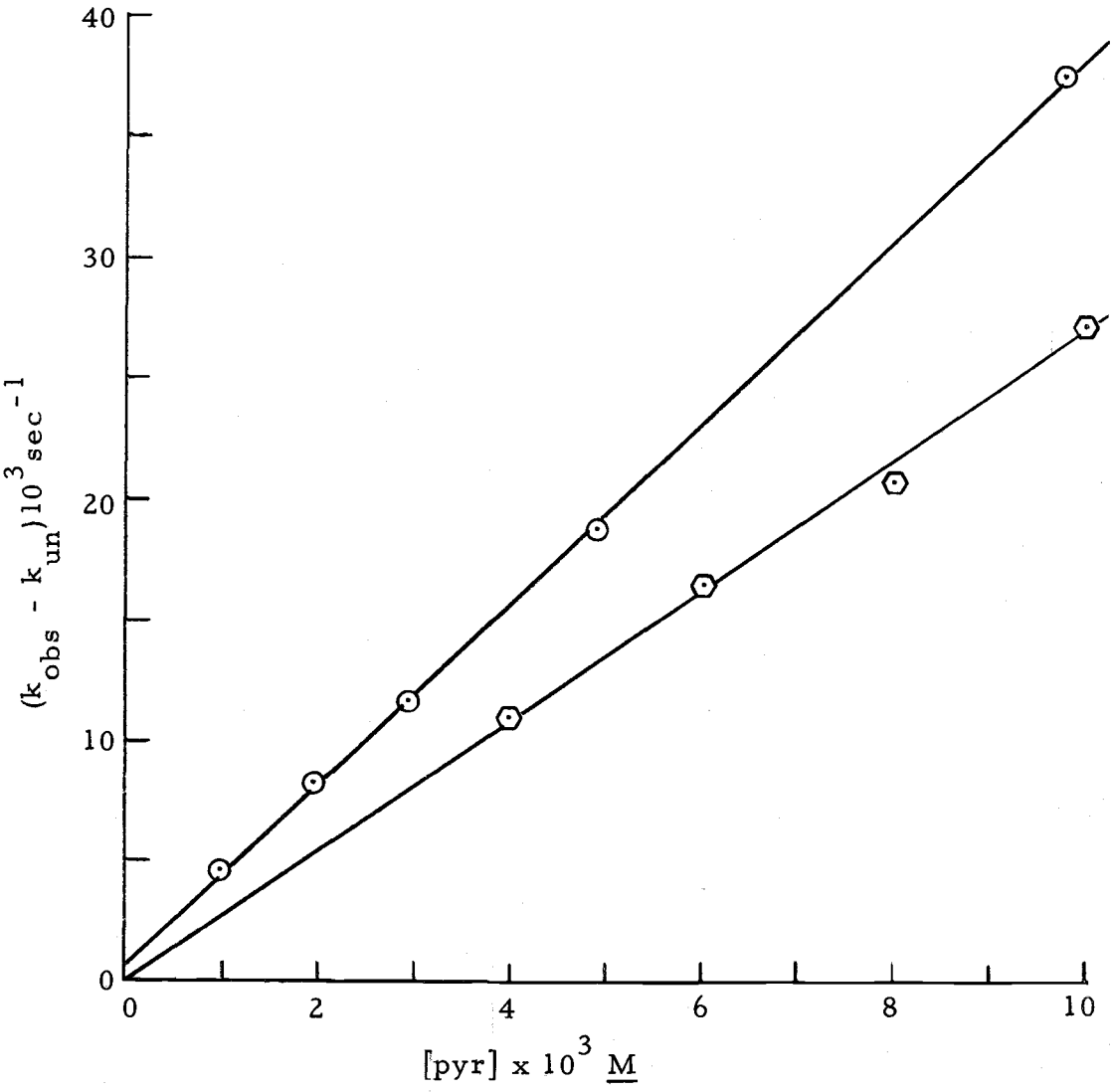


Figure 4. Pyridine catalyzed hydrolysis of p-methoxybenzenesulfinyl p-anisyl sulfone in 1/1 [pyr]/[pyr·H^+], 60% dioxane at 21.4° C.

⊙ 40% H_2O-60% dioxane; $k_{un} = 1.7 \times 10^{-3} sec^{-1}$

⊙ 40% D_2O-60% dioxane; $k_{un} = 0.53 \times 10^{-3} sec^{-1}$

Table 12. Test for rate retardation by $ArSO_2^{\ominus}$ in 60% dioxane at 21.4°C.[a]

$[NaSO_2Ar]$ x 10^3 M	$[LiClO_4]$ x 10^3 M	k_{obs} x 10^3 sec^{-1}
0.00	10.0	42.7
0.10	9.9	40.8
0.50	9.5	39.0
1.0	9.0	35.0

[a]All runs contained 0.01 M pyridine and 0.01 M pyridine·H^+, and the initial concentration of XX was 7.5 x 10^{-5} M.

Discussion

That tertiary amines can exert a rate accelerating influence on the hydrolysis of aromatic sulfinyl sulfones in aqueous dioxane or diglyme is amply demonstrated by the kinetic results recorded in the preceding section of this Chapter. Of course, one must be aware that hydroxide ion also can play a role in the disappearance of the sulfinyl sulfone since this important nucleophile is present in concentrations that vary with the pK_b and concentration of the amine. The extent to which one nucleophile (or base) competes with the other in the reaction is readily differentiated by controlling the concentrations of each nucleophile in buffered solutions. For instance, the specific catalytic effect of the amine is found by studying the change in rate caused by altering the concentration of the amine while maintaining a constant buffer ratio. Conversely, the kinetics of the reaction measured at different buffer ratios while holding the concentration of the amine constant may be used to determine the effect of the hydroxide ion on the rate.

As the data in Table 11 (Results) indicate, pyridine exhibited a conveniently measurable catalytic effect on the hydrolysis of the chosen substrate, p-methoxybenzenesulfinyl p-anisyl sulfone (XX), in 60% dioxane; half lives ranged from 18 to 110 seconds. The catalytic effect, when monitored for a 1/1 pyridine-pyridinium ion buffer,

appeared to be entirely due to the amine (k_A = 3.86 $M^{-1}sec^{-1}$). That there was no contribution to the observed rate from reaction of the sulfinyl sulfone with hydroxide ion is evident in Figure 4 which shows that as the pyridine concentration nears zero, the rate approaches that for spontaneous hydrolysis, k_{un} (i.e. $k_{obs}-k_{un}$ = zero at zero [pyr]).

Three features of the pyridine-catalyzed hydrolysis of XX in 60% dioxane suggest that pyridine is acting as a nucleophilic catalyst rather than a general base catalyst. To begin with, pyridine is a weak base having a relatively large pK_b of 8.75. One would not expect a base as weak as pyridine to function effectively as a general base catalyst in a hydrolysis reaction such as this one. In order to account for the high reactivity of pyridine towards XX, one would be more inclined to think that the amine must be reacting at the sulfur center in the rate determining step as a nucleophile.

Table 12 shows that there is a small (but measurable) reduction in the rate of hydrolysis of XX when sulfinate ion, $ArSO_2^{\ominus}$, is added initially to the reaction mixture. The effect is somewhat smaller than that found by Kice and Guaraldi for the hydrolysis of XX in 60% dioxane in acetate-acetic acid buffers (29). As the initial concentration of $ArSO_2^{\ominus}$ is increased, the decline in the rate of hydrolysis is larger with each added increment of sulfinate. This behavior dictates against the possibility that pyridine is acting as a general base

catalyst (eq. 20). If the latter is true, it would be difficult to

(20) $C_5H_5N + HOH + ArS(=O)(=O)-S(=O)-Ar \longrightarrow [C_5H_5\overset{\delta+}{N}\cdots H\cdots O\cdots \underset{\displaystyle O}{\overset{\displaystyle Ar}{S}}\cdots \overset{\delta-}{SO_2}Ar]^{\ddagger}$

$$\longrightarrow \quad C_5H_5NH^{+} + ArSO_2H + ArSO_2^{\ominus}$$

understand why added sulfinate retards the reaction. Instead, the common ion effect is readily accounted for by the nucleophile-catalyzed mechanism shown in eq. 21.

(21) $C_5H_5N + ArS(=O)(=O)-S(=O)-Ar \underset{k_{-1}}{\overset{k_A}{\rightleftharpoons}} ArS(=O)^{+}NC_5H_5 + ArSO_2^{\ominus}$

$$ArS(=O)^{+}NC_5H_5 \xrightarrow[H_2O]{k_2} ArSO_2H + HNC_5H_5^{+}$$

The third aspect of the hydrolysis reaction that supports the contention that pyridine is acting as a nucleophilic catalyst is the relatively small solvent isotope effect ($k_A^{H_2O}/k_A^{D_2O} = 1.4$) that was observed for the hydrolysis of XX in 1/1 buffered 60% dioxane. Solvent isotope effects are generally quite small ($k^{H_2O}/k^{D_2O} =$ 0.9 to 1.3) for hydrolyses in which the amines act as nucleophilic catalysts (24). The small magnitude of the effect is believed to be due to the lack of proton transfer in the rate determining step. For hydrolyses in which the amines serve as general base catalysts on the other hand, the observed solvent isotope effect should be substantially larger because a proton (deuteron) is being transferred from H_2O

(D_2O) to the general base in the rate determining step. Values of k^{H_2O}/k^{D_2O} ranging from 1.9 to 4.4 have been recorded for several amine catalyzed hydrolyses for which additional evidence strongly suggests that the general base mechanism is operative (14). The value of 1.4 observed for the pyridine-catalyzed hydrolysis of XX is significantly closer to the established range for a nucleophile-catalyzed mechanism.

Diethylbenzylamine (DEBA) also proved to be a catalyst for the hydrolysis of XX (Table 10). Its effectiveness as a catalyst was such that 60% glyme was selected as the solvent. In 60% glyme the reaction proceeds more slowly than it would in 60% dioxane thus allowing one greater latitude in his choice of amine and buffer concentrations.

Another reason for switching from the more common 60% dioxane to 60% glyme as the solvent in the DEBA catalyzed hydrolysis of XX was to avoid the problem encountered by Kice and Kasperek (17, 24) with catalysis by an unidentified peroxidic impurity in the dioxane that is converted to its active form under basic conditions. As a base, DEBA ($pK_b = 4.44$) is probably strong enough to activate the impurity in the dioxane and thereby stimulate the unwanted extra catalysis. The prevention of any additional catalysis due to impurities is particularly important if one wishes to determine the contribution of the reaction of hydroxide ion with XX to the rate of disappearance of XX.

Figure 2 (Results) shows a plot of k_{obs} versus [DEBA] at a 1/1 and 2.5/1 $[DEBA]/[DEBAH^+]$ ratio. The slopes for the two plots are very nearly identical; slope = k_A = 9.9 and 10.2 $\underline{M}^{-1}sec^{-1}$, respectively. The intercepts at zero amine concentration include the rate constant for spontaneous hydrolysis, $k_{un} = 1.80 \times 10^{-3} sec^{-1}$ in 60% glyme at 21.4°. When k_{un} is subtracted from the values for the intercepts for the 1/1 and 2.5/1 buffers, one obtains 1.06×10^{-2} and $2.29 \times 10^{-2} sec^{-1}$ respectively. One then sees that while the buffer ratios differ by a factor of 2.5, the corrected intercepts change by a factor of 2.2. This is a good indication that the rate at the intercept (uncorrected) is due to a combination of uncatalyzed hydrolysis, k_{un}, and the reaction of hydroxide ion with the sulfinyl sulfone, $k_{OH}[OH^{\ominus}]$.

The data for the DEBA catalyzed hydrolysis of XX may be used to make a reasonable estimate of k_{OH}. Two major steps are involved in estimating k_{OH} and they are as follows: (a) to determine as accurately as possible the hydroxide ion concentration for a given amine buffer solution, and (b) to calculate k_{OH} using the $[OH^{\ominus}]$ and the intercept at zero amine concentration, $k_{OH}[OH^{\ominus}]$, for the plot of $k_{obs}-k_{un}$ $\underline{vs.}$ the amine concentration for the same buffer solution.

For DEBA-$DEBAH^+$ buffered solutions $[OH^{\ominus}]$ is found from eq. 22 where K_w is the autoprotolysis constant of water and

$$(22) \qquad [OH^{\ominus}] = \frac{K_w[DEBA]}{K_a^{DEBAH^+}[DEBAH^+]}$$

$K_a^{DEBAH^+}$ is the acid dissociation constant of $DEBAH^+$. Unfortunately, neither K_w nor $K_a^{DEBAH^+}$ is known for 60% glyme solutions, but by making certain assumptions one can come up with very reasonable approximations for these two quantities. For K_w one should be justified in using the value for the constant measured in 60% dioxane ($K_w = 64 \times 10^{-19}$) (12), because of the structural similarity of dioxane and glyme. The acid dissociation constant, $K_a^{DEBAH^+}$, may be closely approximated by comparing it to the acid dissociation constant of triethylamine (TEA) which is known for 60% dioxane solutions ($K_a^{TEAH^+} = 3.16 \times 10^{-10}$) (46). For the same reason as stated above, $K_a^{TEAH^+}$ in 60% glyme should be essentially equal to the 60% dioxane value. If one makes the further assumption that the K_a of $DEBAH^+$ differs from that of $TEAH^+$ by the same amount in 60% glyme as it does in water ($K_a^{DEBAH^+} = 12.8 \times K_a^{TEAH^+}$), then $K_a^{DEBAH^+}$ in 60% glyme should be close to $12.8 \times 3.16 \times 10^{-10}$ or 4.04×10^{-9}. When these values for K_w and $K_a^{DEBAH^+}$ are substituted into eq. 22, the $[OH^{\ominus}]$ for a 1/1 $[DEBA]/[DEBAH^+]$ buffer in 60% glyme comes out to be 1.58×10^{-9} M.

The k_{OH}, therefore, for the 1/1 DEBA buffer solutions is

calculated to be 1.06×10^{-2} $sec^{-1}/1.58 \times 10^{-9}$ $\underline{M}$ or about 7×10^{6} $\underline{M}^{-1}sec^{-1}$; for the 2.5/1 buffer, $k_{OH} = 6 \times 10^{6}$ $\underline{M}^{-1}sec^{-1}$.[2]

Figure 3 (Results) shows a plot of k_{obs} $\underline{vs}$ amine concentration for the DEBA catalyzed reaction in 40% D_2O-60% glyme at a 1/1 buffer ratio. The slope, $k_A^{D_2O}$, is 4.16 $\underline{M}^{-1}sec^{-1}$. The solvent isotope effect, $k_A^{H_2O}/k_A^{D_2O} = 9.9/4.16 = 2.4$, indicates that DEBA catalyzes the hydrolysis of XX as a general base. This represents the first experimental demonstration of general base catalysis of the hydrolysis of a sulfinyl sulfur derivative to have been reported.

At this juncture a few comments should be made regarding the three other amines that were tested for their catalytic effect on the hydrolysis of XX in either 60% dioxane or 60% glyme. One of the three amines, tribenzylamine (TBA), was totally ineffective as a catalyst. Presumably its fairly large pK_b (6.4) and its bulky electron withdrawing alkyl groups are collectively responsible for its inactivity. The other two amines, triethylamine (TEA) and N-benzylpyrrolidine (NBP), accelerated the hydrolysis to the point that it was impossible to obtain anything other than rough kinetic data (Tables 6, 7, 8 and 9). These data are based at the very best on only the last

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[2] When this figure is compared to the k_{OH} for the hydrolysis of p-anisyl α-disulfone (24) one can see that hydroxide ion is approximately 10^5 times more reactive with sulfinyl sulfones than it is with α-disulfones.

20-25% of the reaction. Consequently, any conclusions drawn at this time concerning the details of the catalytic activity of TEA or NBP are necessarily tentative.

The fact that NBP catalyzes the hydrolysis much more effectively than DEBA has some possible important conotations. First, one should remember that NBP has a pK_b that is essentially identical to that for DEBA. If NBP catalysis of the hydrolysis of XX were due to hydroxide ion interaction coupled with general base catalysis by NBP, then the kinetic results should presumably be effectively the same as those for the DEBA catalyzed reaction. Instead, the NBP catalyzed reaction was observed to proceed at a rate that was at least ten times faster than that catalyzed by DEBA under identical conditions. Since their pK_b's are the same, the difference in the catalytic effectiveness of this pair of amines must certainly be due to steric considerations. One is led by these data to believe that because NBP is not as bulky as DEBA it catalyzes the reaction as a nucleophile rather than a general base. If this is the case, then what we have witnessed is a striking demonstration of the very delicate balance between the two mechanisms for catalysis of the hydrolysis of sulfinyl sulfones.

If the foregoing hypothesis concerning NBP is ultimately proven by the solvent isotope effect and other yet untapped evidence to be correct, then a useful method has been revealed which can be

employed in probing the steric nature of a given nucleophilic center. An abrupt shift from the predominance of one catalytic mechanism to the other caused solely by a relatively minor change in the structure such as that illustrated by NBP vs DEBA would aid in making a quantitative measurement of the steric hindrance to the incoming nucleophile at the site of substitution.

The same steric test is potentially capable of helping to determine if steric hindrance is the main factor in the origin of the 6 kcal/mole difference in the energy of activation for nucleophilic substitution at sulfinyl sulfur in sulfinyl sulfones vs sulfonyl sulfur in α-disulfones. Kice and Kasperek have pointed out the tremendous difference in the rates of nucleophilic substitution for the two systems, sulfinyl sulfones being 10^4 to 10^7 times more reactive than α-disulfones with the same nucleophile (hydroxide ion being no exception as noted earlier in this thesis); they have also shown that these rate differences are apparently due almost solely to differences in the energy of activation for substitutions at the two centers (25). The question has been raised whether non-bonded interactions are the primary deterrent slowing the attack at sulfonyl sulfur, or alternatively whether electron inductive factors play the key role. The dipolar character of an $\overset{\delta+}{\text{S}} = \overset{\delta-}{\text{O}}$ bond means that an oxygen attached to sulfur could exert a purely electronic repulsion toward an attacking electron-rich nucleophile. If one were to find that the

crossover point from nucleophilic to general base catalysis for hydrolysis of α-disulfones occurred when changing from NBP to DEBA as appears to be the case for sulfinyl sulfones, then one would be forced to conclude that steric hindrance is not the principal factor responsible for the difference in reactivity of the sulfonyl and sulfinyl sulfur. On the other hand, if NBP was found to catalyze the hydrolysis of α-disulfones as a general base, the indication would be that at least part of the 6 kcal difference is definitely due to steric factors. It would be instructive to continue testing with other tertiary amines of successively diminished bulk to find the crossover point.

Experimental

Purification of Materials

Dioxane was purified by the method of Wiberg (51, p. 245). Glyme was refluxed over sodium, distilled, refluxed over lithium aluminum hydride and distilled just prior to use. Commercial tribenzylamine was recrystallized from absolute ethanol and dried *in vaccuo* over Drierite, m. p. 93-95° (lit. 92-93° C). Pyridine and triethylamine (Eastman Kodak) were purified by the method of Wiberg (51, p. 247).

N-Benzylpyrrolidine

N-Benzylpyrrolidine was prepared by the method of Fery and

van Hove (9). A 41 ml portion of freshly distilled α-chlorotoluene was added over a two hour period to a rapidly stirred, ice-cooled mixture of 33 g pyrrolidine, 100 ml diethyl ether and 50 g potassium carbonate. The mixture was stirred an additional two hours, then left to stand overnight. The mixture was acidified with 200 ml 6 N HCl and extracted with ether. The aqueous phase was neutralized with concentrated KOH and extracted with ether. The ether extract was dried overnight with anhydrous $MgSO_4$. Removal of the ether and distillation gave 52 g (70%) of the desired product, b.p. 45°/0.7 torr, n_D^{20} = 1.527 [lit. n_D^{20} = 1.5265 (9)].

Diethylbenzylamine

Diethylbenzylamine was prepared in essentially the same manner as N-benzylpyrrolidine using 63.3 g α-chlorotoluene, 36.5 g diethylamine, 55 g potassium carbonate and 100 ml diethyl ether. The reaction mixture was stirred at room temperature for 12 hours. The yield was 30 g (37%) b.p. 79-80°/7 torr, n_D^{25} = 1.4957 [lit. 84-85°/12 torr, (41), n_D^{25} = 1.5014 (3)].

p-Methoxybenzenesulfinyl p-Anisyl Sulfone

Anisole (40 g, 0.37 mole) in 150 ml chloroform was treated with chlorosulfonic acid (86.2 g, 49 ml, 2 equiv, 0.74 mole) according to the procedure outlined by Morgan and Cretcher (42). The product,

p-methoxybenzenesulfonyl chloride, was purified by vacuum distillation (lit. b. p. 103-105°/0. 25 torr). The yield was 33. 2 g (43. 3%); m. p. 38-41° C (lit. 41-42° C).

Following the method of Overberger and Godfrey (45) the 33. 2 g (0. 16 mole) portion of sulfonyl chloride was added with stirring to 40. 5 g (0. 32 mole) sodium sulfite in 350 ml dilute sodium hydroxide. The total reaction time at 70° C was three hours. The yield of sodium p-methoxybenzenesulfinate was 17. 2 g (55%).

From this point on the procedure of Kice and Guaraldi was employed (26). A slight excess of thionyl chloride in hexane was added slowly with stirring to a 3. 3 g (0. 017 mole) portion of the dry sodium p-methoxybenzenesulfinate suspended in hexane. After one hour the mixture was filtered and the hexane and excess thionyl chloride were pumped off. A 3. 3 g sample of sodium p-methoxybenzenesulfinate was added to a dry ether solution of the sulfinyl chloride and stirred for 30 minutes at 0° C to give the crude sulfinyl sulfone which was filtered from the reaction mixture. After numerous triturations with ice water, followed by several with ice-cold ether and drying at -20° C, 3. 0 g (54%) of the sulfinyl sulfone was obtained, m. p. 97-98° [lit. 100-101° C (26)]. The material was stored in a desiccator at -20° C.

Preparation of Buffered Solutions for Kinetic Studies

Pyridine, 1/1 Buffer in H_2O. Pure, dry pyridine was weighed

into a volumetric flask, dissolved in water and standardized with standard perchloric acid to give a 0.192 M pyridine stock solution. A 50.0 ml portion of 0.192 M pyridine was combined with 48.32 ml of standard 0.0996 M perchloric acid to form 0.0487 M pyr and 0.0489 M pyr·H^+. The 1×10^{-2} M pyr/1×10^{-2} M pyr·H^+ solution for kinetics was prepared by adding 20.60 ml water and 60.90 ml dry dioxane to 20.0 ml of the 0.0487 M pyr/0.0489 M pyr·H^+. Portions of the 1×10^{-2} M solution were diluted to 50.0 ml with 60% dioxane and an appropriate amount of anhydrous $LiClO_4$ was added to maintain constant ionic strength.

Four buffered pyridine solutions were made up from the 0.0487 M buffer for the purpose of examining the effect of added $NaSO_2Ar$ (Ar = p-$MeOC_6H_4$-) on the kinetics. A 10.0 ml portion of the buffer was combined with 30.45 ml dry dioxane, a weighed amount of the salt ($NaSO_2Ar$), a measured volume of water and enough lithium perchlorate to balance the ionic strength.

Pyridine, 1/1 Buffer in D_2O. A 0.1776 g sample of standard 7.05×10^{-3} mole/g $HClO_4$ was diluted to 25 ml with D_2O. In like manner 0.1988 g pyridine was dissolved in 25 ml D_2O. A 15 ml aliquot of each solution was combined to form 0.025 M pyr/0.025 M pyr·D^+. From this stock solution a series of solutions at constant ionic strength and constant buffer ratio (1/1) but different buffer concentrations (0.010, 0.0080, 0.0060 and 0.0040 M) in 60% dioxane

were then prepared for the kinetic runs.

Tribenzylamine (TBA). A commercial sample of tribenzylamine was recrystallized from 95% ethyl alcohol (m.p. 93-95°, lit. 92-93°). A pair of solutions (0.01 M TBA/0.01 M TBA·H^+ and 0.001 M TBA/0.001 M TBA·H^+) were prepared by dissolving a weighed amount of the base in the necessary volume of standard 0.0996 M $HClO_4$ and adding water and dioxane.

In a similar fashion a series of tribenzylamine solutions having a range of buffer ratios (1.25, 1.67, 2.5 and 5.0) at a fixed concentration (0.010 M) was also prepared.

N-Benzylpyrrolidine (NBP). A 0.0119 M stock solution of N-benzylpyrrolidine in dry glyme was prepared by dissolving 0.0963 g NBP in 50.0 ml dry glyme. Aliquots of the stock solution were then transferred via pipet into a 25 ml volumetric flask and combined with measured amounts of water, standard 0.00995 M $HClO_4$, lithium perchlorate and additional dry glyme sufficient to make four solutions at constant ionic strength, initial NBP concentrations of 1.18, 1.00, 0.90 and 0.82 x 10^{-3} M, and initial NBP·H^+ concentrations of 1.00, 0.96, 0.84 and 0.72 x 10^{-3} M respectively.

N, N-Diethylbenzylamine (DEBA). The buffered H_2O-glyme solutions of N, N-diethylbenzylamine (DEBA) have a fixed buffer ratio of 1/1, a constant ionic strength and different buffer concentrations were made up as follows: 0.1665 g of freshly prepared DEBA was

weighed into a volumetric flask and dissolved in 62.10 ml dry glyme. To this solution was added 5.12 ± 0.01 ml standard 0.0996 N $HClO_4$, 20.0 ml 0.05 M $LiClO_4$ and 16.3 ml H_2O (final concentration: [DEBA] = [DEBA·H^+] = 5.1×10^{-3} M). A diluent was prepared by combining 15 ml 0.05 M $LiClO_4$, 16.05 ml H_2O and 46.58 ml glyme. Then 20.0, 15.0, 10.0 and 5.0 mls (respectively) of the 5.1×10^{-3} M buffer was diluted to 25 mls with the diluent.

In a similar manner a series of buffered H_2O-glyme solutions of DEBA at a fixed buffer ratio of 2.5/1 were prepared. The initial DEBA solution consisted of 0.1118 g DEBA dissolved in 62.1 ml glyme, 19.7 ml standard 0.00995 M $HClO_4$, 20.0 ml 0.05 M $LiClO_4$ and 1.70 ml H_2O (final concentration: 4.89×10^{-3} M buffer).

The preparation of the buffered D_2O-glyme solutions of DEBA for the kinetic studies involved a slightly different scheme. A 0.1007 g sample (6.16×10^{-4} moles) of DEBA was dissolved in 36.9 ml glyme. To this solution 0.0448 g of 7.05×10^{-3} mole/g standard solution of $HClO_4$ (3.12×10^{-4} moles $HClO_4$), 0.0640 g anhydrous $LiClO_4$ and 24.6 ml D_2O were added (final concentration: [DEBA] = 5.07×10^{-3} M, [DEBA·D^+] = 5.20×10^{-3} M). A diluent was prepared by dissolving 0.0426 g anhydrous $LiClO_4$ in 16.6 ml D_2O and adding 24.9 ml dry glyme. Then 20.0, 15.0 and 10.0 ml of the initial DEBA-DEBA·D^+ solution was diluted, respectively, to 25 mls total.

Procedure for Kinetic Runs

The procedure for setting up and following the kinetics for the amine catalyzed hydrolysis of p-methoxybenzenesulfinyl p-anisyl sulfone (XX) was identical except for the chemicals used and their quantities to the kinetic procedure recorded in Chapter I of this thesis. A 0.0710 to 0.0720 g portion of XX was dissolved in 10 ml of dry glyme or dry dioxane and a 7 to 8 microliter drop of this solution was transferred to 3.0 ml of appropriate buffer solution contained in the thermostatted uv cell. The disappearance of XX was monitored at 306 nm. The first order plots were satisfactorily linear.

III. STUDIES ON THE ANHYDRIDE OF 2-METHYL-2-PROPANESULFINIC ACID

Introduction

Reference was made in Chapter I of this thesis to the lengthy period of time that transpired between the date of the original discovery of sulfinyl sulfones and the more recent recognition by Bredereck (5) that the structure of these derivatives of sulfinic acids was not that of a true anhydride, RS(O)OS(O)R, which prior to 1960 was the popularly accepted version for their structure. At the present time, numerous examples of sulfinyl sulfones are known (26, 31, 33).

Kice and Ikura prepared a series of alkyl sulfinyl sulfones (XXII, R = Me, n-Bu, and $C_6H_5CH_2$) by reaction of the appropriate alkanesulfinyl chloride with the sodium salt of the corresponding sulfinic acid (eq. 23) (31). When they attempted to extend this reaction

(23) $$RSO_2^{\ominus}Na^{+} + R\underset{\underset{O}{\|}}{S}\text{-}Cl \longrightarrow R\text{-}\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{S}}\text{-}R + Na^{+}Cl^{\ominus}$$

XXII

to the preparation of the t-butyl compound (XXII, R = t-Bu) they found that the reaction was so slow, presumably due to the hindrance exerted by the t-butyl group to nucleophilic attack at the sulfur of the sulfinyl chloride, that only starting material was recovered when the

reaction was worked up at the end of a reaction time which had been more than adequate to lead to complete reaction of the other sulfinyl chlorides.

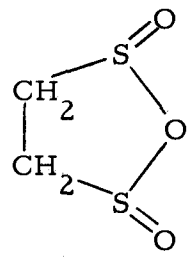
In an effort to drive the t-butyl reaction to completion in a reasonable period of time they decided to employ the silver salt of the sulfinic acid rather than the sodium salt. When this was done t-BuS(O)Cl did indeed react quite rapidly with the sulfinate, but after removal of the silver chloride which had been formed by filtration, work-up of the reaction mixture gave a product which could be shown to have the sulfinic anhydride (XXIII) rather than the sulfinyl sulfone structure.

$$t\text{-}BuSO_2^{\ominus}Ag^{+} + t\text{-}Bu\underset{\underset{O}{\|}}{S}\text{-}Cl \longrightarrow t\text{-}Bu\underset{\underset{O}{\|}}{S}\text{-}O\text{-}\underset{\underset{O}{\|}}{S}Bu\text{-}t + AgCl\downarrow$$

XXIII

That the compound had the sulfinic anhydride structure rather than the sulfinyl sulfone one was clear from a variety of pieces of spectral evidence. First, there was the fact that in the 7.5-9.2μ region in the infrared the compound exhibited only a single strong bond at 8.8μ, the usual strong sulfone absorption at about 7.6μ in the spectra of XXII being completely absent, as was also the band at 9.2μ found in the spectra of XXII and due to the $R\text{-}\underset{\underset{O}{\|}}{S}\text{-}SO_2$ sulfinyl group. Second, there was the fact that the nmr showed all of the methyl groups in the two t-butyl groups to be magnetically equivalent. That the sulfinic

anhydride XXIII was indeed isomeric with a sulfinyl sulfone was shown by the fact that upon hydrolysis the compound yielded two molecules of t-$BuSO_2H$, identified as its benzenediazosulfone derivative, t-$BuSO_2N{=}NC_6H_5$. Shortly after the report by Kice and Ikura of the preparation of this first authentic sulfinic anhydride, another research group reported the preparation of a second example of this class of compound, ethanedisulfinic anhydride (XXIV) (43).



XXIV

Two explanations suggest themselves for why the reaction of t-BuS(O)Cl with t-$BuSO_2Ag$ gives the sulfinic anhydride XXIII when the reaction of all the less hindered alkanesulfinyl chlorides RS(O)Cl with RSO_2Na give the isomeric sulfinyl sulfones XXII.

First, in the reaction of t-$BuSO_2Ag$ with t-BuS(O)Cl, the reaction probably involves the reaction of t-$BuSO_2^{\ominus}$ with t-$BuSO^+$, while in the other reactions involving the sodium salts the reaction presumably involves a nucleophilic displacement by $RSO_2^{\ominus}$ on the sulfinyl chloride RS(O)Cl. The sulfinate ion is, of course, an ambident anion, and it is well known in the reactions of $RSO_2^{\ominus}$ with R-X and R^+ (35) that while the reaction with the halide gives the sulfone, that with the carbonium ion gives the sulfinate ester. If the

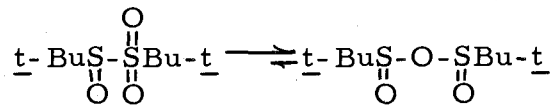
same sort of effect should be operative in the reaction of $RSO_2^{\ominus}$ with RS(O)Cl *vs* RSO^+, then the formation of the sulfinic anhydride in the case of the *t*-butyl system would be merely the result of the fact that the silver salt was used in that reaction rather than the sodium salt.

On the other hand, another entirely different explanation for the preference for the formation of XXIII in the *t*-butyl case is also a possibility. In the sulfinic anhydride structure, RS(O)OS(O)R, the two R groups are separated from each other by one more atom than in the sulfinyl sulfone structure $RS(O)SO_2R$. If the sulfinyl sulfone and sulfinic anhydride structures do not differ by a great deal in energy then it could well be possible that while for less bulky alkyl groups like methyl or *n*-butyl the sulfinyl sulfone structure will be favored thermodynamically at equilibrium

$$R\text{-}\overset{\overset{O}{\|}}{\underset{O}{S}}\text{-}O\text{-}\overset{\overset{O}{\|}}{\underset{O}{S}}\text{-}R \rightleftharpoons R\text{-}\overset{\overset{O}{\|}}{\underset{O}{S}}\text{-}\overset{\overset{O}{\|}}{\underset{O}{S}}\text{-}R$$

R = Me, *n*-Bu, $C_6H_5CH_2$

with the bulky *t*-butyl groups there is enough hindrance between the two R groups in the sulfinyl sulfone structure, hindrance which is decreased significantly in the sulfinic anhydride structure where the two R groups are further apart, that the isomeric sulfinic anhydride structure now becomes the thermodynamically favored one at equilibrium.

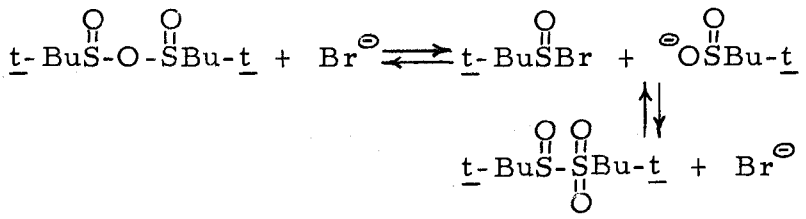


Two obvious approaches suggest themselves as ways to test out which, if either, of these two possible explanations is the correct one. The first approach is to determine whether the reaction of the silver salt of a sulfinic acid like CH_3SO_2H with $CH_3S(O)Cl$ will lead to $CH_3S(O)SO_2CH_3$, the same product isolated from the reaction of $CH_3SO_2^{\ominus}$ and $CH_3S(O)Cl$, or whether because of the use of the silver salt one will also get here, as one did in the t-butyl case, the sulfinic anhydride, $CH_3S(O)OS(O)CH_3$. If the sulfinic anhydride could be isolated as the major product from the metathesis of $CH_3S(O)Cl$ and CH_3SO_2Ag, then it would be very likely that it is the use of t-$BuSO_2Ag$ rather than t-$BuSO_2Na$ that leads to the different behavior of the t-butyl system. Alternatively, if the methanesulfinyl sulfone is isolated as the major product, support will have been given to the contention that the influence of the cation on the outcome of the reaction is negligible and that one or more other factors, such as the steric hindrance between R groups in the sulfinyl sulfone, are responsible for the different product formed in the reaction of the t-butyl compounds.

In seeking an experimental answer to the question of the relative thermodynamic stability of t-BuS(O)OS(O)Bu-t vs t-$BuS(O)SO_2$Bu-t one can attempt to see if XXIII can be caused to isomerize to the

sulfinyl sulfone. From other work (32) it is known that XXIII reacts rapidly with bromide ion to give $\underline{t}\text{-BuSO}_2^{\ominus}$ and $\underline{t}\text{-BuS(O)Br}$. In a solvent such as dry acetonitrile where $\underline{t}\text{-BuS(O)Br}$ cannot undergo hydrolysis, $\underline{t}\text{-BuSO}_2^{\ominus}$ and $\underline{t}\text{-BuS(O)Br}$ once formed can revert back to either XXIII or the isomeric sulfinyl sulfones (eq. 24). The

(24)



system should therefore provide a simple route for the equilibration of XXIII and the isomeric sulfinyl sulfone. If a significant amount of the sulfinyl sulfone, $\underline{t}\text{-BuS(O)SO}_2\text{Bu-}\underline{t}$, is present once equilibrium is reached it should reveal its presence by the appearance of a significant absorption in the infrared in the 7.6μ region due to the sulfone function present in $\underline{t}\text{-BuS(O)SO}_2\text{Bu-}\underline{t}$. Such an observation would afford a concrete conclusion to the question of the relative thermodynamic stability of these closely related isomers.

We have accordingly carried out studies of both of the types just described and the results are presented and discussed in this section of the thesis.

Results

Reaction of $CH_3S(O)Cl$ with CH_3SO_2Ag

The silver salt of methanesulfinic acid, CH_3SO_2Ag, was combined with methanesulfinyl chloride, $CH_3S(O)Cl$, in dry acetonitrile under pre-purified nitrogen in semidarkness at ice-salt bath temperatures. The product that was ultimately isolated was identical in all respects to the material produced by the same procedure when the sodium salt of methanesulfinic acid was used. The infrared spectra of the purified products matched up perfectly and the melting points were the same. The yields were low due to the considerable number of recrystallizations and washings required to bring the moisture and temperature sensitive compound up to its best quality, but the percentage yields from either combination were essentially the same. The reaction and its product(s) were handled in such a way that the temperature of the system containing it never exceeded 0° C. The infrared and ultraviolet spectra and the melting points of the products prepared from both salts matched those of the methanesulfinyl sulfone, XXII (R = Me), prepared via the sodium salt CH_3SO_2Na by Kice and Ikura (31). The characteristic ir peaks at 7.6, 8.4 and 9.6μ appeared for these samples with the same relative intensities as on the Kice-Ikura ir spectra for

$CH_3S(O)SO_2CH_3$. Similarly a broad absorption maximum in the ultraviolet was observed at the same wavelength (250 nm) as it was with the Kice-Ikura compound and the molar extinction coefficient was 1370 as compared to the Kice-Ikura value of ϵ = 1650 at 250 nm.

Attempts to Isomerize 2-Methyl-2-Propanesulfinic Anhydride to the Sulfinyl Sulfone

Several attempts were made to see if in dry acetonitrile t-BuS(O)OS(O)Bu-t could be isomerized in whole or in part to the sulfinyl sulfone t-BuS(O)SO_2Bu-t by the catalytic action of bromide ion, which is known from the work of Kice and Ikura (32) to be a nucleophile that reacts readily with t-BuS(O)OS(O)Bu-t to give t-BuS(O)Br and t-$BuSO_2^{\ominus}$. Once t-BuS(O)Br and t-$BuSO_2^{\ominus}$ are present in the solution they can react with each other either to regenerate the sulfinic anhydride or to give the isomeric sulfinyl sulfone, since the sulfinate ion is an ambident anion.

In general the procedure involved first dissolving a measured amount of the freshly prepared anhydride (XXIII) and a small amount of LiBr in dry acetonitrile and then withdrawing a portion of the acetonitrile solution periodically to analyze for any changes that may have occurred in the infrared spectrum. The acetonitrile solutions of XXIII were variously stored at room temperature or at temperatures as low as -15°, and in the light or dark. In all instances bromide ion

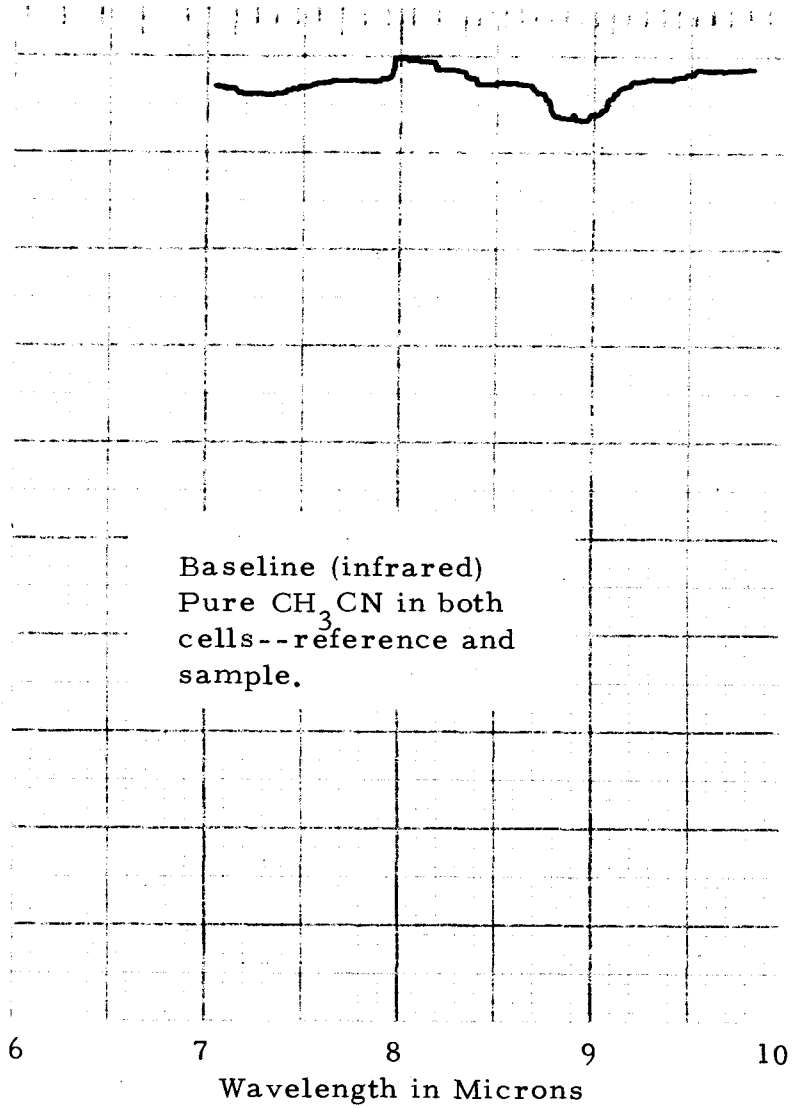
failed to show that it had any influence whatsoever on the spectral changes that were observed. Similar changes in the spectra for all the CH_3CN solutions proceeded at about the same slow rate whether LiBr had been added to the solution or not.

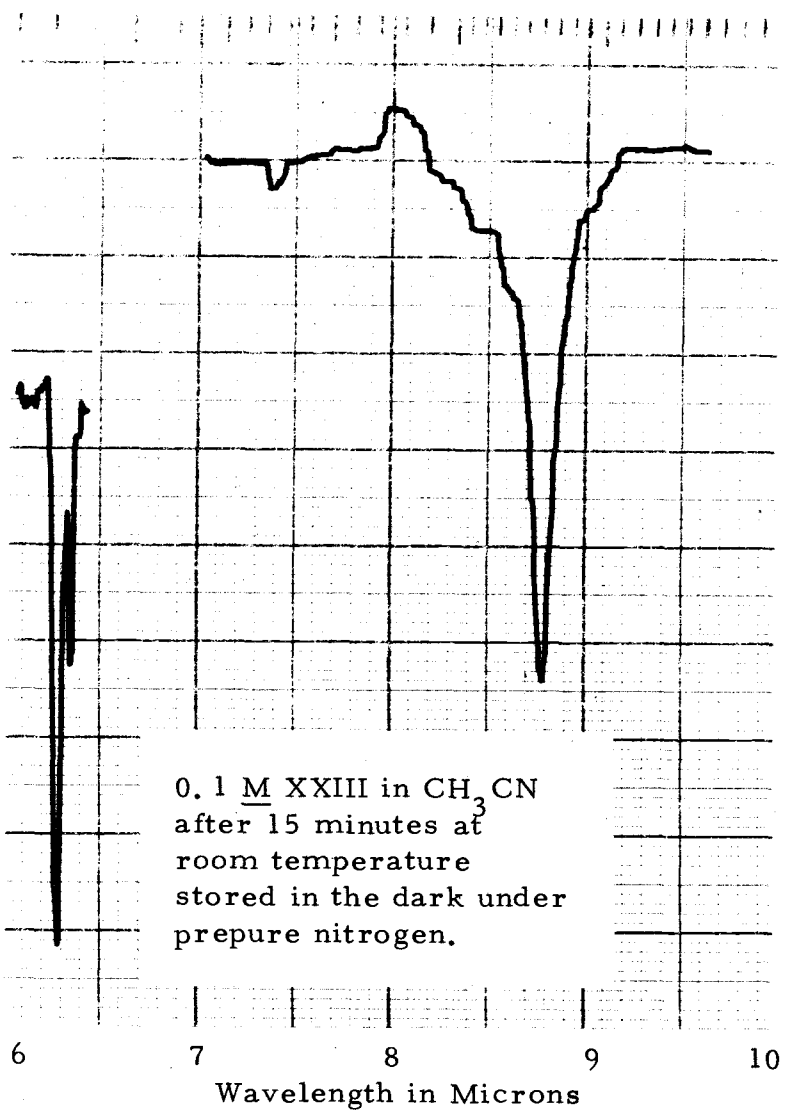
The nature of these spectral changes was as follows: First the prominent peak observed initially at 8.8μ would slowly give way to an absorption that developed at 9.0μ. After several hours the peak at 9.0μ would begin to shrink while the disappearing peak at 8.8μ gradually grew again but changed shape and position slightly to become a very sharp peak at 8.7μ. Simultaneously with the latter process a new peak of medium intensity gradually developed at 7.5μ. When several days had passed the spectrum displayed a peak of medium intensity at 7.5μ, a strong sharp peak at 8.7μ and no absorption at 9.0μ (see Figure 5). The process associated with the spectral changes could be halted at any stage by immersing the reaction mixture in a -78° bath.

Removal of the solvent from an acetonitrile solution of XXIII that had stood for several hours at room temperature under a nitrogen atmosphere by reduced-pressure rotary evaporation left an oily residue which was only partially soluble in carbon tetrachloride. Thin layer chromatograms of the residue revealed the presence of at least four different materials.

The ir experiments with XXIII just described were carried

Figure 5. A set of infrared spectra showing the spectral changes with time for a 0.1 M solution of t-BuS(O)OS(O)Bu-t in dry CH_3CN at room temperature protected from light and air.


Baseline (infrared)
Pure CH_3CN in both cells--reference and sample.
6
7
8
9
10
Wavelength in Microns


0.1 M XXIII in CH_3CN after 15 minutes at room temperature stored in the dark under prepure nitrogen.
6
7
8
9
10
Wavelength in Microns

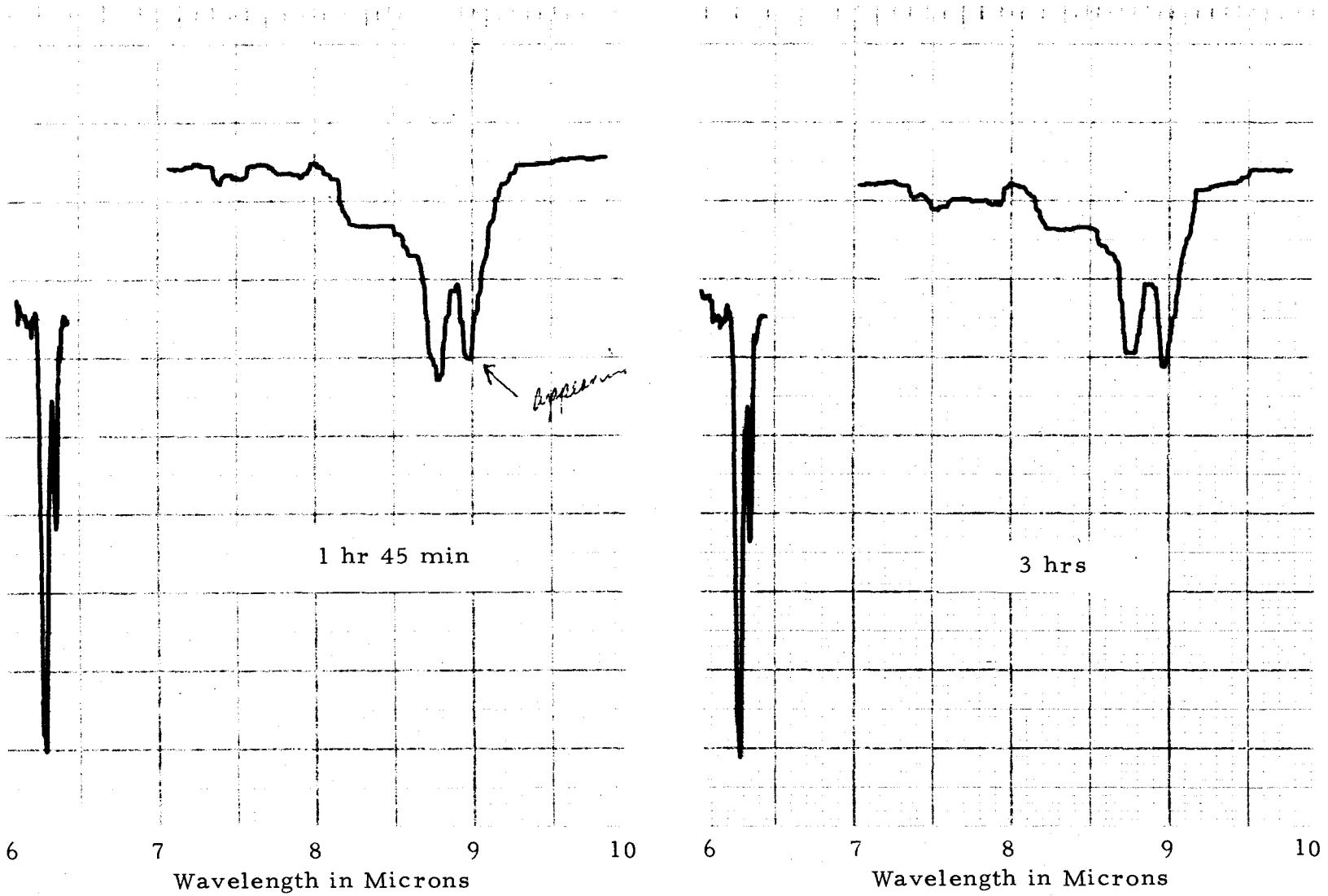


Figure 5 (continued)

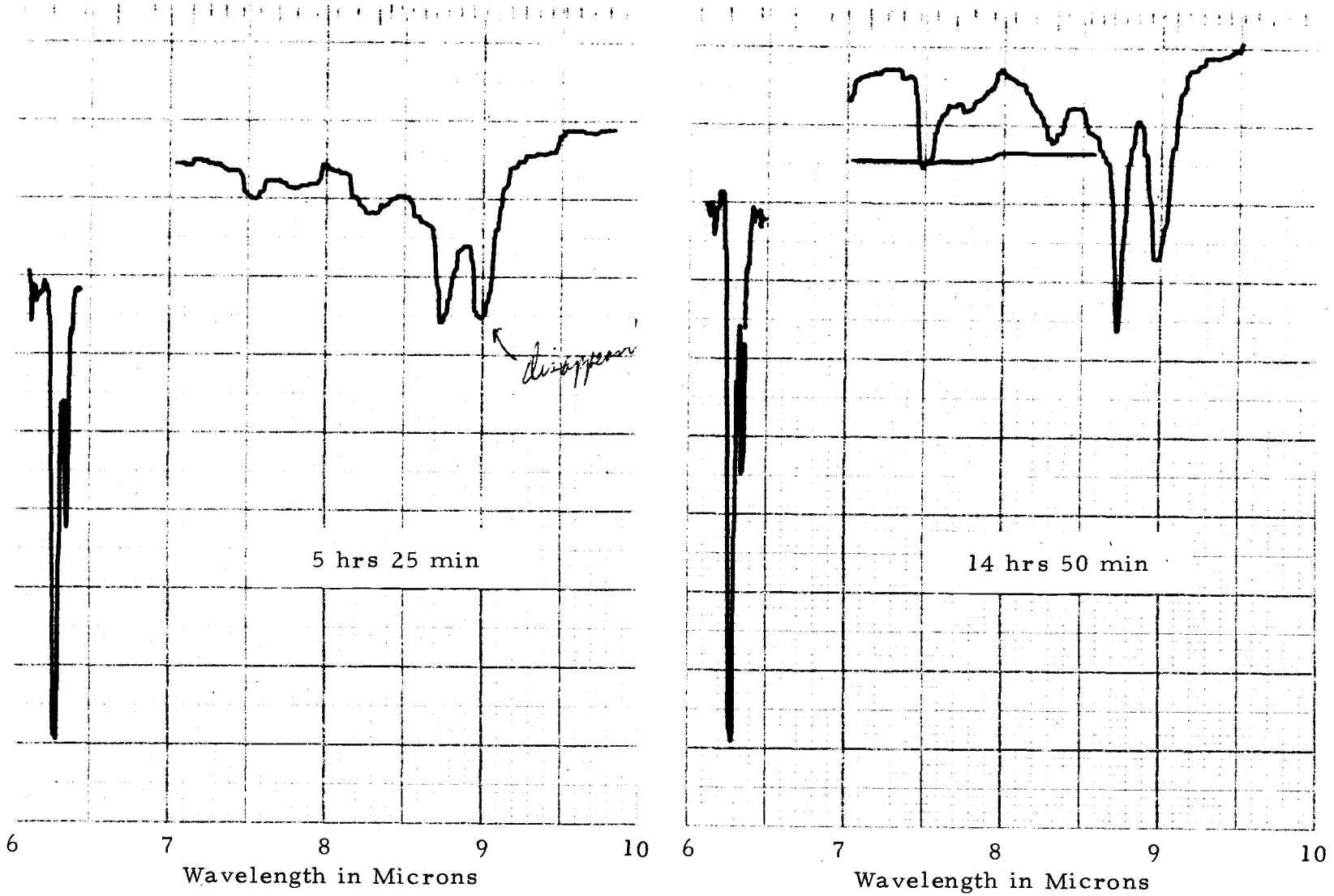


Figure 5 (continued)

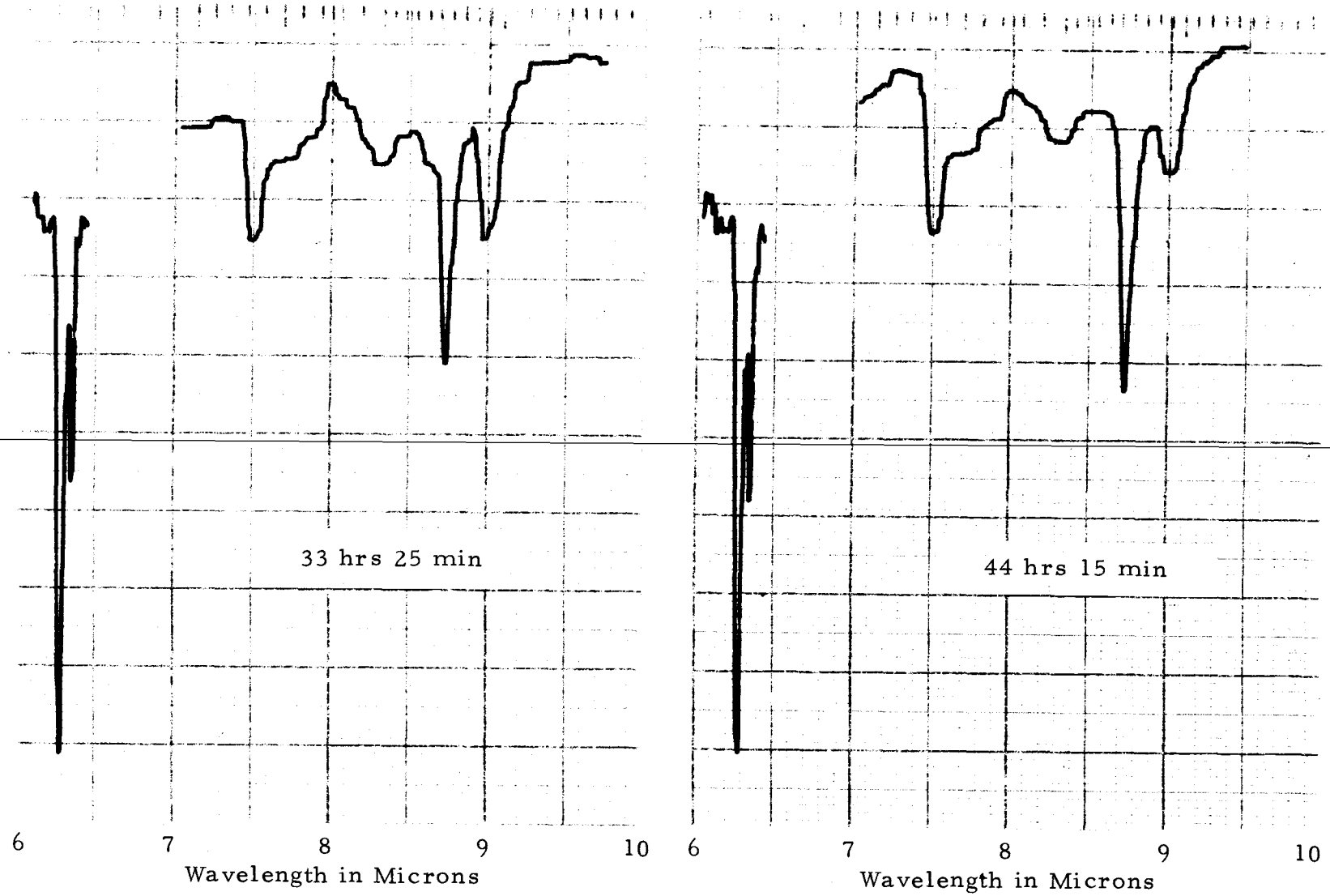


Figure 5 (continued)

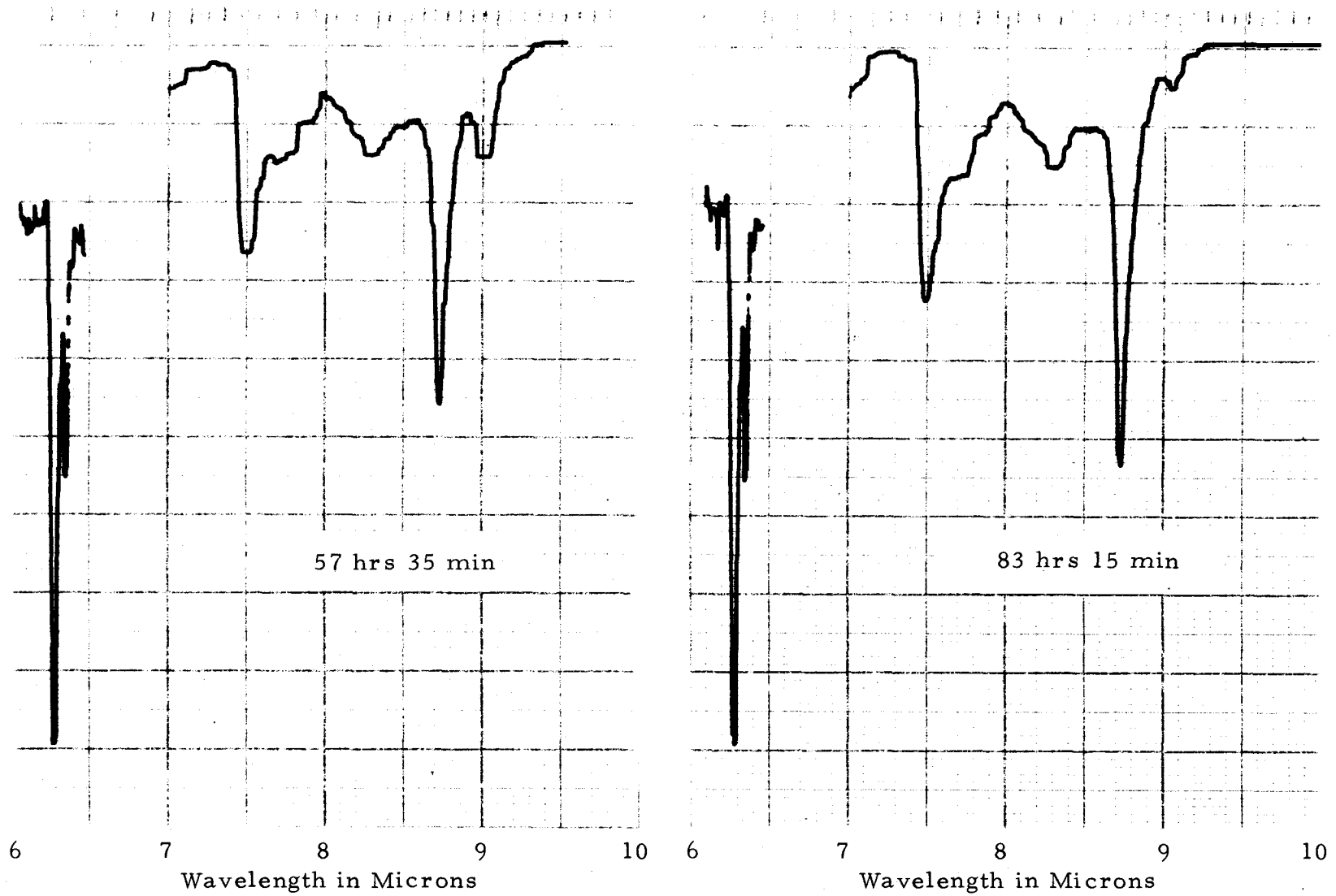


Figure 5 (continued)

out using XXIII concentrations of about 0.1 M, the minimum concentration allowing for a reasonably good ir spectrum, while the LiBr concentration varied from 9.0×10^{-3} to 2.0×10^{-3} M.

In a later ir experiment, when the concentration of the catalyst was boosted to 0.046 M while that of the anhydride was 0.090 M, a new problem arose--the formation of a white precipitate. The experiment at the higher concentration of LiBr was approached in two different ways. In one procedure, the dry LiBr was dissolved completely in a small amount of dry acetonitrile. When the solid anhydride was added to this solution, a heavy precipitate of finely divided white particles formed immediately. Most (but not all) of the precipitate dissolved as a much larger quantity (~10 times as much) of the solvent was added. Only when a few drops of water were added did the solution clear up completely. The second approach taken was to dissolve the catalyst and anhydride individually in equal volumes of the dry acetonitrile and then combine them. But when the two solutions were combined the fine white precipitate again appeared immediately upon mixing. The precipitate was too finely divided to be filtered out using a filter finger of fine porosity.[3] Consequently it

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[3] In one experiment when the precipitate just described had formed, the solution was filtered by ordinary (open air) suction filtration to isolate the white material. The material did not melt below 230°, it dissolved readily in water and a test ($AgNO_3$) for the presence of bromide ion in the precipitate was negative.

was impossible to proceed any further with this phase of the ir analyses using solutions of XXIII containing the higher concentration of the catalyst, LiBr.

Rate of Reaction of Bromide Ion with XXIII in Acetonitrile Solvent

An experiment was devised in an attempt to measure specifically the rate at which bromide ion attacks the sulfinic acid anhydride, XXIII, under essentially the same conditions as those used in the ir studies. The approach taken was to observe the disappearance of the anhydride by monitoring the decrease in the absorbance of the solution at 238 nm as a function of time for solutions of XXIII in acidified 95% acetonitrile containing small amounts of bromide ion. The purpose in having just a little water ($[H_2O] \cong 2$ M) in the system was to prevent the reversal of the bromide substitution on the anhydride while at the same time not significantly altering the character of the solvent from what it was in the ir experiments. The perchloric acid, at 0.1 M, was included with partly the same intention, that it help prevent the reversal of the initial bromide substitution by protonating the leaving sulfinate group (eq. 25). In addition, the 0.1 M

(25) $$Br^{\ominus} + t\text{-BuS(=O)-O-S(=O)Bu-}t \xrightarrow[95\%\ CH_3CN]{0.1\ M\ HClO_4} t\text{-BuS(=O)Br} + HOS(=O)Bu\text{-}t$$

$$t\text{-BuS(=O)Br} \xrightarrow{H_2O} t\text{-BuS(=O)OH} + HBr$$

acid would neutralize any basic impurities that might be present thereby reducing the likelihood that part of the disappearance of XXIII was due to these extraneous nucleophiles. The results of the kinetic runs with and without bromide ion in the reaction mixture are summarized in Table 13.

Table 13. Kinetics of the disappearance of XXIII in 95% acetonitrile-0.1 M $HClO_4$ solutions at 21.4°.

init[XXIII] x 10^3 M	[LiBr] x 10^3 M	k_{obs} x 10^3 sec^{-1}
0.54	---	---[a]
0.43	2.3	3.87[b]
0.41	4.5	3.84[b]

[a]Calculation of the rate constant for the disappearance of XXIII in acidified 95% acetonitrile in the absence of bromide ion was impossible due to the complicated changes in the uv spectrum at 238 nm observed with passing time; i.e. during the first two hours at 21.4° the absorbance at 238 nm gradually decreased from 1.1 to 0.62, then it slowly began to rise again to 0.75 in the next two hours.

[b]The runs containing LiBr followed perfect first order kinetics.

Discussion

As noted in the Introduction to this section, Kice and Ikura (31) found that reaction of t-BuS(O)Cl with t-$BuSO_2Ag$ gave the sulfinic anhydride XXIII rather than the isomeric sulfinyl sulfone. They did not know whether this was because of the fact that a silver

salt was used in the synthesis rather than the sodium sulfinates used in the syntheses leading to sulfinyl sulfones, or whether it was simply a reflection of the fact that when the R groups in the sulfinyl sulfone or sulfinic anhydride were bulky ones like t-butyl the sulfinic anhydride became thermodynamically somewhat more stable than the sulfinyl sulfone. The reason that the anhydride could be thermodynamically the more stable when R = t-Bu and yet be the less stable when R = Me or n-Bu is because the two R groups are further apart in the anhydride structure and should R be large and bulky so that there is steric crowding between the R groups in the sulfinyl sulfone this could be relieved on isomerization to the anhydride structure.

In the present work the results of the reaction between methanesulfinyl chloride and the silver salt of methanesulfinic acid suggest that the type of cation in the salt has no influence over which product will be favored. Methanesulfinyl methyl sulfone was the only organic product isolated. But before fully accepting this conclusion, one may wish to consider the possibility that the sulfinic anhydride, $CH_3S(O)OS(O)CH_3$, is formed initially as the reaction product and then isomerizes to the sulfinyl sulfone, $CH_3S(O)SO_2CH_3$, during the workup of the reaction mixture.

It was with the aforementioned possibility in mind that we selected reaction conditions which should minimize isomerization

during work-up: (1) the temperature was maintained near -10° throughout the reaction and in subsequent operations it did not exceed 0°; (2) the reaction and first filtration (but not the subsequent recrystallizations) were carried out in semidarkness. Dry acetonitrile was selected instead of ether as the reaction solvent because of the former solvent's inertness and proven ability to dissolve sulfinyl sulfones more easily than does ether. The expectation was that if the anhydride was formed instead of, or along with, the sulfinyl sulfone, it too would be soluble in the acetonitrile.

If any methanesulfinic acid anhydride was formed initially and was still present in the untreated residue which was isolated from the original reaction mixture by filtration from the silver chloride precipitate followed by low temperature evaporation of the acetonitrile, it was not evident in the ir spectrum ($CHCl_3$) of the crude material.

The ir spectrum of the crude product obtained from the methanesulfinic acid silver salt reaction was very similar to the spectrum of the crude product formed in the sodium salt reaction. Both spectra showed that the majority of the material in each product was the sulfinyl sulfone. Furthermore, the percentage yields of pure methanesulfinyl sulfone obtained from either starting salt were roughly the same. One would not expect to observe such similarities in the results of the two reactions if the silver salt reaction, but not the sodium salt reaction, produced the anhydride initially. Therefore,

considering the lack of evidence for the presence of methanesulfinic acid anhydride in the crude product together with the parallel results for the reaction of either the sodium or silver salt of methanesulfinic acid with $CH_3S(O)Cl$, one would seem to have grounds enough to conclude that the type of cation in the salt has no effect on the structural outcome of the reaction between alkanesulfinic acids and their chlorides.

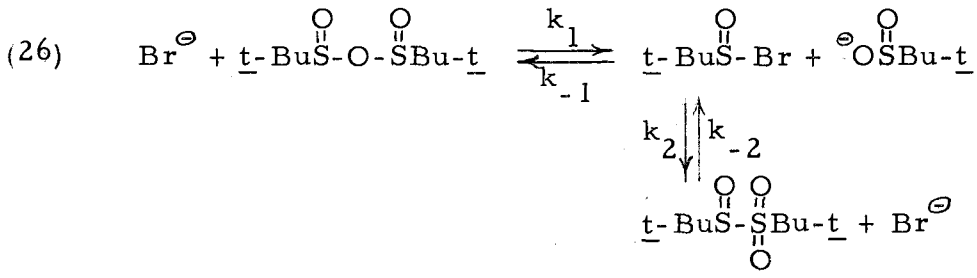
The answer to the question raised earlier concerning the t-butyl reaction then would seem to be that the formation of the anhydride XXIII is favored not as a result of the change from the sodium to the silver salt, but rather as the result of steric interactions between the bulky t-butyl groups. Apparently such steric hindrance is not important in the methyl case, nor, for that matter, in the case of the n-butyl, or benzyl reactions as well--each of which leads to the formation of the corresponding sulfinyl sulfone via the sodium salt.

We thus conclude that the formation of XXIII is the result of the fact that for R = t-Bu the sulfinic anhydride structure is favored thermodynamically over the sulfinyl sulfone.

As described in the Results section, several attempts were made to see if one could find the conditions under which XXIII would be isomerized in whole or in part to the corresponding sulfinyl sulfone. A priori the scheme involving bromide ion as the catalyst for

the isomerization looked very promising. Bromide ion is a good nucleophile and sulfinate anions, $^{\ominus}O\text{-}\overset{O}{\overset{\|}{S}}\text{-}Ar$ are reasonably good leaving groups. Once $\underline{t}\text{-}BuSO_2^{\ominus}$, an ambident anion, is liberated by bromide ion attack on the anhydride XXIII in dry acetonitrile, it should be able to react with the $\underline{t}\text{-}BuS(O)Br$ also formed in the first step either to regenerate the anhydride (step k_{-1}) or to form the sulfinyl sulfone XXIV (step k_2, eq. 26).

(26)



XXIV

When solutions of XXIII in acetonitrile were treated with small amounts of LiBr no changes other than those already observed in the absence of added $Br^{\ominus}$ took place.

The observed lack of bromide ion catalysis of the process responsible for the gradual changes in the ir spectrum of XXIII in dry acetonitrile shows that if the anhydride is isomerizing to XXIV at all, it is not doing so <u>via</u> the sulfinyl bromide (steps k_1 and k_2, eq. 26). If the sulfinyl bromide is formed, it either reverts back to

the anhydride, slowly decomposes, or remains unchanged in solution.[4] The fact that the ir spectrum changes in a like manner whether a catalytic amount of bromide ion is present or not is a reasonable indication that thermal decomposition of the unreacted anhydride is the process being observed.

The results of the ultraviolet experiments (Table 12) which were designed to test the speed with which bromide ion attacked the sulfinic acid anhydride in 95% acetonitrile were quite revealing. First of all, the ultraviolet runs in which no LiBr catalyst had been added were slow and exhibited complicated behavior in the change of the absorbance at 238 nm with time. The gradual decrease in the absorbance during the first two hours that the solution was monitored followed by a slower rise in the absorbance is very likely related to the process observed with the infrared spectrophotometer, namely the thermal decomposition of XXIII.

When lithium bromide was added to the reaction mixture at a concentration five times higher than the concentration of XXIII, the rate of disappearance of absorbance at 238 nm increased dramatically over the rate for the uncatalyzed reaction. The first order plots

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[4] In these experiments the concentration of the bromide ion was too small ($\sim 5 \times 10^{-3}$ M) to provide for the formation of enough sulfinyl bromide to be detected in the ir. Experiments involving significantly higher concentrations of bromide ion were frustrated by solubility difficulties as described in the Results section.

of the kinetic data were perfectly linear (three minute half-life). It is also significant to note that although a lower concentration (about 20% less) of the anhydride was present in the bromide ion catalyzed runs than in the uncatalyzed reaction, the initial absorbance was noticeably higher. But most important of all, when the concentration of the bromide ion was doubled, the first order rate of decrease in the absorbance was identical to the previous bromide ion catalyzed run, i. e. doubling the bromide ion concentration from five to ten times that of the concentration of XXIII had no further effect on the rate of the observed process.

The most probable explanation for the fact that changes in the concentration of bromide ion had no effect on the rate of the uv-monitored bromide ion-catalyzed process is that the excess of bromide ion reacted very rapidly and irreversibly with the anhydride to form the sulfinyl bromide, t-BuS(O)Br, and that the process being followed in the uv kinetically was then the hydrolysis of the sulfinyl bromide (eq. 27). This, of course, will be present initially in a concentration equal to the amount of XXIII taken and independent of the concentration of LiBr since a large excess of the latter over XXIII was used in both runs.

(27) $Br^{\ominus} + \underline{t}\text{-Bu-}\overset{\overset{O}{\|}}{S}\text{-O-}\overset{\overset{O}{\|}}{S}\text{Bu-}\underline{t} + H^{+} \longrightarrow \underline{t}\text{-Bu}\overset{\overset{O}{\|}}{S}\text{-Br} + HO\overset{\overset{O}{\|}}{S}\text{Bu-}\underline{t}$

$\downarrow H_2O$ rate determining

$\underline{t}\text{-BuSO}_2\text{H} + \text{HBr}$

The unexpected increase in the initial absorbance at 238 nm that was observed with the use of a lower initial concentration of the anhydride in the bromide ion catalyzed runs than was used in the uncatalyzed run is also indicative that sulfinyl bromide had formed completely by the time the uv cell was in position for analysis (6-10 sec). The increase in absorbance is most likely due to a larger molar extinction coefficient at 238 nm for $\underline{t}$-BuS(O)Br than for $\underline{t}$-BuS(O)OS(O)Bu-$\underline{t}$.

The discovery that the sulfinyl bromide is formed rapidly and irreversibly by the attack of $Br^{\ominus}$ on XXIII in 95% acetonitrile solutions would seem to account for the difficulties encountered in the infrared experiments discussed earlier where a large concentration of LiBr was used. In those instances where the concentration of lithium bromide in dry acetonitrile was considerably lower than the concentration of XXIII, bromide ion was probably used up instantaneously and the observed changes in the ir spectrum would have been merely those associated with the thermal breakdown of the more highly concentrated anhydride. In the ir experiments involving higher concentrations of LiBr the precipitate that formed

immediately when dry acetonitrile solutions of LiBr and XXIII were combined is probably also the result of the rapid bromide ion interaction with XXIII forming the sulfinyl bromide and the lithium sulfinate salt. The latter is probably not as soluble in MeCN as is LiBr.

In summary we have shown that the nature of the cation in the sulfinic acid salt is not responsible for the switch from the formation of the sulfinyl sulfone $RS(O)SO_2R$, where R = Ar, n-Bu, $C_6H_5CH_2$- or Me, to anhydride formation were R = t-Bu. The evidence is provided by the fact that methanesulfinyl methyl sulfone is the sole organic product isolated whether the starting sulfinic acid salt was the sodium or the silver salt. Secondly, we have shown that t-BuS(O)Br is much more stable in dry or 95% acetonitrile than either the sulfinic acid anhydride XXIII or the sulfinyl sulfone (XXII, R = t-Bu). There was no definite evidence that t-$BuS(O)SO_2Bu$-t was ever formed in our work. The results suggest that, in fact, t-$BuS(O)SO_2Bu$-t was never formed even though the conditions for its formation should have been ideal. Apparently the steric interaction of the bulky t-butyl groups is great enough so that the sulfinic anhydride is significantly preferred over the sulfinyl sulfone at equilibrium. The synthesis in the t-butyl case therefore follows the lower energy pathway to the sulfinic acid anhydride.

Experimental

2-Methyl-2-Propanesulfinic Acid Anhydride (XXIII)

2-Methyl-2-propanesulfinic acid was prepared by careful acidification of a chilled (0° C) solution of the magnesium salt of the sulfinic acid (48) with 60% sulfuric acid. The cold acidified solution was extracted several times with ether, the extract was dried over anhydrous magnesium sulfate and the ether was pumped off at 0° C to give the sulfinic acid. The crude sulfinic acid was purified by several low temperature recrystallizations from anhydrous ether.

A 7.0 g (0.057 mole) portion of 2-methyl-2-propanesulfinic acid (m.p. 84-86°) was dissolved in dry methanol and stirred for 1.5 hours with 10 g (0.12 moles) anhydrous sodium bicarbonate. The solution was filtered and the methanol was removed from the filtrate at reduced pressure. The white residue was washed with acetone and ether. The yield of $\underline{t}$-$BuSO_2Na$ was 7.05 g (85%). The 7.05 g (0.049 moles) of $\underline{t}$-$BuSO_2Na$ was dissolved in 10 moles of water and combined in a darkened room with an equimolar amount of silver nitrate dissolved in 10 ml of water. The silver salt of the sulfinic acid was filtered out, washed with ether and dried at ambient temperature and reduced pressure in a vacuum oven. Phosphorus pentoxide was the desiccant. The yield of the silver salt, $\underline{t}$-$BuSO_2Ag$, was

9.9 g (88%).

A 3.7 g (0.030 mole) sample of the sulfinic acid, t-$BuSO_2H$, was dissolved in ether and added dropwise to an ethereal solution of thionyl chloride (3.61 g, 0.030 moles). After two hours stirring at room temperature the ether was pumped off leaving 4.06 g (95%) of the sulfinyl chloride, a yellowish green liquid, t-BuS(O)Cl. The material was used directly in the succeeding reaction without distillation.

The dry silver salt (7.1 g, 0.031 moles), t-$BuSO_2Ag$, was placed in a carefully dried three necked flask under a prepurified nitrogen atmosphere. The flask was fitted with a gas inlet tube, a magnetic stirrer and a dropping funnel. While a positive pressure (nitrogen) was maintained in the system, the flask was placed in an ice-salt bath. Anhydrous ether (50 ml) was added *via* the dropping funnel. Then an ethereal solution of 4.06 g (0.029 moles) t-BuSOCl was added dropwise over a 30 minute period. Stirring of the reaction mixture at -5 to -10° was continued for four more hours. A filter finger glass-welded to the end of a long bent glass tube passing through a rubber stopper was fitted into the reaction flask while nitrogen was flowing through the flask to prevent external air from entering. Then the ether solution was filtered off with suction from the silver chloride precipitate into a second three necked flask immersed in an ice-salt bath. In this manner the filtration was accomplished while

maintaining the temperature at or below 0° C and while protecting the contents of the reaction vessel from the moist laboratory air. Excess solvent was pumped off leaving the crude sulfinic acid anhydride.

Three low temperature recrystallizations from anhydrous ether under a prepurified nitrogen atmosphere followed by an ether washing produced 2.5 g (38%) of 2-methyl-2-propanesulfinic acid anhydride [m.p. 43-45°, lit. 45-56° (31)]. One neck of the flask containing the anhydride was inserted into a prepurified nitrogen-filled plastic dry-bag so that one could withdraw small samples of the anhydride without exposing the main supply to the air or to room temperatures. The dry-bag sampling operation was carried out while prepurified nitrogen was flowing into the flask (and into the bag) through another neck of the three necked flask. The anhydride being stored in the flask under prepurified nitrogen at -78° showed no sign of decomposition or other contamination over a period of four weeks.

Methanesulfinyl Methyl Sulfone (XXII, R = Me)

Via the Sodium Salt of Methanesulfinic Acid. Methanesulfinyl chloride was prepared by the Douglass-Norton procedure (8). The sodium salt of methanesulfinic acid was prepared as follows: A 22.8 g (0.2 mole) portion of methanesulfonyl chloride was stirred at ice-bath temperature with 50.4 g (0.4 mole) sodium sulfite. The basicity of the solution was maintained during the reaction by periodic addition of

small quantities of 50% sodium hydroxide. When further additions of base were no longer necessary to keep the solution basic, the water was removed by reduced pressure distillation and the salt completely dried. The dried salt was dissolved in methanol (absolute), filtered to remove insoluble material, the methanol was pumped off from the filtrate and the salt was dried in vaccuo at 60°. The yield of $MeSO_2Na$ was 15.6 g (70%).

Using the same apparatus and technique as described for the preparation of 2-methyl-2-propanesulfinic acid anhydride, sodium methanesulfinate (2.0 g, 0.02 mole) was placed in dry acetonitrile (25 ml) and methanesulfinyl chloride (1.8 g, 0.018 mole) in dry acetonitrile was slowly added with stirring at -5 to -10° C. After one hour's stirring at ice-salt bath temperatures, the mixture was filtered via a filter finger into the second three necked flask which was immersed in salted ice. The acetonitrile was pumped off and the residue was recrystallized once from anhydrous ether and then washed once with the same solvent. The yield was 1.0 g (35%) of fairly pure sulfinyl sulfone (m.p. 52-56°; lit. 62-64°). The ir spectrum for this material compared very closely to that for an authentic sample prepared by Kice and Ikura (31).

Via the Silver Salt of Methanesulfinic Acid. At 10.5 g (0.103 mole) quantity of sodium methanesulfinate was dissolved in 40 ml water. To this solution a 25 ml aqueous solution of 17.5 g (0.103

mole) silver nitrate was added. The heavy white precipitate that formed was filtered with suction and washed with a few milliliters of dry ether. All the preceding operations with the silver salts were carried out in semidarkness. The residue was dried in vaccuo at 60° with phosphorus pentoxide used as the desiccant. The yield of dry silver salt, $MeSO_2Ag$, was 8.20 g (43%).

Using the same apparatus and procedure as described in the preparation of the sulfinic anhydride, silver methanesulfinate (8.20 g, 0.044 mole) was placed in 25 ml dry acetonitrile under prepurified nitrogen and 3.94 g (0.040 mole) methanesulfinyl chloride was added dropwise over a 20 minute period. The suspension was stirred at ice-salt bath temperatures for an additional 2.5 hours before filtering through a filter finger into another ice-cooled three necked flask. The acetonitrile was pumped off from the filtrate and the crystalline residue remaining after removal of the solvent was treated with 75-100 ml of dry ether at room temperature (20-30 minutes). Since all the crystals did not dissolve the mixture was filtered into another three necked flask via the filter finger. The ether filtrate was then cooled in a dry ice-acetone bath to produce a small batch of white crystals. After three further recrystallizations of the product from dry ether the melting point was 60-62° C. The ir spectrum of the material corresponded closely to that for an authentic sample of methanesulfinyl methyl sulfone. An absorption maximum was

observed at 250 nm, ϵ = 1370 [lit. λ_{max}^{250}, ϵ = 1650 (31)]. The yield was 1 to 1.5 g (20-30%).

Rate Measurements in 95% Acetonitrile-0.1 M Perchloric Acid

Reagent grade acetonitrile (Matheson, Coleman and Bell) was refluxed over phosphorus pentoxide for 24 hours, distilled, refluxed for 12-24 hours over calcium hydride and distilled. Distilled water (10.53 g) and 71% $HClO_4$ (3.09 g) were added to 169.92 g of the dry acetonitrile to form a solution that was 95% CH_3CN-0.1 M $HClO_4$ (stock solution A). Portions of stock solution A were combined with weighed amounts of anhydrous lithium bromide to give solutions of 2.3×10^{-3} and 4.5×10^{-3} M LiBr in 95% CH_3CN-0.1 M $HClO_4$ (Solutions B and C, respectively). Three milliliter aliquot samples of solutions A, B or C were transferred to 1 cm silica cells (sample and reference cells) which were then equilibrated at 21.4° in the thermostatted cell compartment of a Cary-15 uv-visible recording spectrophotometer. After the cells had equilibrated (~15 minutes) a 7 µl drop of XXIII (1.71 M) in dry CH_3CN was transferred carefully to a small glass rod which was then immediately inserted into the sample cell with stirring. (The resultant initial concentration of XXIII in 95% CH_3CN at the beginning of each kinetic run was, therefore, 4.0×10^{-4} M). The cell compartment was closed, the instrument was switched on and the decrease in absorbance of the solution

at 238 nm as a function of time was recorded.

Infrared Studies on XXIII in Dry Acetonitrile Solutions

Several acetonitrile-XXIII solutions containing a catalytic amount of LiBr were prepared and analyzed as follows: A few tenths of a milligram of anhydrous LiBr was weighed on a microgram balance in a tared, prepurified nitrogen-filled container. In a dry-bag under prepure nitrogen a measured amount of dry acetonitrile (2-5 mls) was added to the LiBr and a weighed sample of the anhydride (XXIII) was dissolved in this solution. The initial concentration of the anhydride was about 0.1 M (2-3% by weight) in all runs, while the LiBr concentration varied from 2×10^{-3} to 9×10^{-3} M. The solutions were then stored under a variety of conditions listed as follows: (a) at ~-15° C in a freezer, (b) at room temperature and exposed to laboratory lighting, and (c) at room temperature protected from light. Sampling of the solutions for infrared analysis was performed in a dry-bag. A portion of the reaction mixture was transferred via syringe to a 0.05 mm ir cell (NaCl windows) and pure, dry acetonitrile was injected into a matching reference cell. Spectra were recorded on a Beckmann IR-8 double beam spectrophotometer scanning each sample from 7 to 9.5 microns. The time that elapsed between the preparation of the original reaction mixture containing XXIII and the beginning of the ir scan was recorded to the nearest

minute.

Dry acetonitrile solutions of XXIII (0.1 M) containing LiBr at concentrations greater than 3×10^{-2} M could not be analyzed by ir due to the formation of a white precipitate that was too finely divided to be conveniently filtered out with a filter finger.

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