region 0.01–0.40 M $HClO_4$ with the variation in k_S for the butyl sulfide catalyzed hydrolysis of **1a** over the same range of acid concentrations.

We conclude from this that the explanation previously offered[3] for why the sulfide-catalyzed hydrolysis of **1a** requires acid catalysis while the ordinary hydrolysis does not is apparently the correct one.

Experimental Section

Preparation and Purification of Materials.—p-Toluenesulfinyl p-tolyl sulfone (**1a**) and dioxane were prepared and/or purified in the manner described in an earlier paper.[3] n-Butyl mercaptan was freshly fractionally distilled under nitrogen, bp 97–98°.

Procedure for Kinetic Runs.—The general procedure for following the kinetics of the disappearance of **1a** was the same as that outlined previously.[3] To initiate a run the proper amount of a stock solution of **1a** in *anhydrous* dioxane was added to an aqueous dioxane solution containing the appropriate amounts of perchloric acid, n-butyl mercaptan, etc., both solutions having been brought to 21.4° before mixing. The disappearance of **1a** was then followed by monitoring the decrease in the optical density, A, of the solution at 300 mμ in the manner described in an earlier paper.[3] Plots of log $(A - A_\infty)$ *vs.* time were nicely linear. One should note that in those runs in which the reaction of mercaptan with **1a** accounts for most of the rate A_∞ is significantly larger than when one is following only the hydrolysis of **1a**, because of the fact that the thiolsulfinate product of the mercaptan–**1a** reaction, n-BuSS(O)Ar, has a significant extinction coefficient at 300 mμ, unlike the sulfinic acid, $ArSO_2H$, which is effectively transparent at this same wavelength. The spectra obtained at the end of the experiments in the presence of mercaptan corresponded to those expected for the formation of a mixture of thiolsulfinate (from the mercaptan–**1a** reaction) and sulfinic acid (from the normal hydrolysis) in the proportions predicted by comparison of k_1 in the presence of mercaptan and in its absence.

Registry No.—**1a**, 788-86-3; n-BuSH, 109-79-5; n-Bu_2S, 544-40-1.

Mechanisms of Substitution Reactions at Sulfinyl Sulfur. VII. General Base Catalysis by a Tertiary Amine of the Hydrolysis of an Aryl Sulfinyl Sulfone[1]

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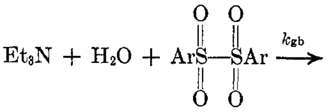
The hydrolysis of p-anisyl p-methoxybenzenesulfinyl sulfone (**2a**, eq 2) in aqueous dioxane or glyme can be catalyzed by various tertiary amines. The results for N-benzyldiethylamine, $(k_{R_3N}^{H_2O}/k_{R_3N}^{D_2O}) = 2.4$, clearly indicate that the amine is acting in that case as a general base catalyst and represent the first reported example of general base catalysis of a simple substitution at sulfinyl sulfur. On the other hand, the data for catalysis of the hydrolysis by pyridine point toward that amine acting as a nucleophilic rather than a general base catalyst. This, and the behavior of N-benzylpyrrolidine, both suggest that fairly modest changes in amine structure which merely reduce the steric hindrance around nitrogen can be sufficient to switch one from a situation where the tertiary amine acts as a general base catalyst to one where nucleophilic catalysis is observed to predominate instead. This, of course, means that each future example of tertiary amine catalysis of a substitution at sulfinyl sulfur will have to be examined carefully on an individual basis before decision can be reached as to whether nucleophilic or general base catalysis is involved.

It was shown[3] recently that catalysis of the hydrolysis of aryl α-disulfones (**1**) by triethylamine in aqueous glyme or dioxane involves general base catalysis (eq 1),

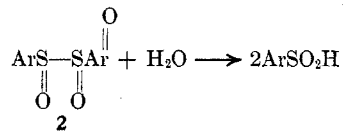


1

$$Et_3N + H_2O + ArS(O_2)\text{—}S(O_2)Ar \xrightarrow{k_{gb}} Et_3NH^+ + ArSO_3H + ArSO_2^- \quad (1)$$

even though n-alkyl primary and secondary amines react with **1** as nucleophiles. This reaction represented the first reported case of general base catalysis of a substitution at sulfonyl sulfur, although another example has subsequently been reported.[4]

We were interested in determining whether general base catalysis by a tertiary amine could also be observed in an analogous substitution at sulfinyl sulfur. We have accordingly investigated the catalysis of the hydrolysis (eq 2) of an aryl sulfinyl sulfone (**2**) by several tertiary amines under the same conditions. While the rapidity of the catalyzed reaction limited the range of tertiary amines that could be examined, we have still been able to demonstrate that, although certain tertiary amines like pyridine catalyze the hydrolysis by acting as nucleophilic catalysts, the more sterically hindered tertiary alkyl amine, N-benzyldiethylamine, catalyzes the hydrolysis by general base catalysis. To our knowledge this is the first example of general base catalysis of the hydrolysis of a sulfinyl compound, and it shows that this type of catalysis, which has been widely encountered in substitutions of carboxylic acid derivatives[5] and recently observed[3,4] in substitutions at sulfonyl sulfur, can also be important in appropriate substitutions at sulfinyl sulfur.



2

$$ArS(O)\text{—}S(O_2)Ar + H_2O \longrightarrow 2ArSO_2H \quad (2)$$

Results

Catalysis of the hydrolysis of p-anisyl p-methoxybenzenesulfinyl sulfone (**2a**, Ar = p-$CH_3OC_6H_4$) by various tertiary amines was investigated in either 60% glyme–40% water (v/v) or 60% dioxane–40% water (v/v) as

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(1) (a) This research was supported by the National Science Foundation, Grant GP-10732X. (b) Preceding paper in this series: J. L. Kice and J. D. Campbell, *J. Org. Chem.*, **36**, 2288 (1971).

(2) Department of Chemistry, University of Vermont, Burlington, Vt. 05401.

(3) J. L. Kice and G. J. Kasperek, *J. Amer. Chem. Soc.*, **92**, 3393 (1970).

(4) E. T. Kaiser, *Accounts Chem. Res.*, **3**, 145 (1970).

(5) T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms," Vol. 1, W. A. Benjamin, New York, N. Y., 1966, pp 27–118.

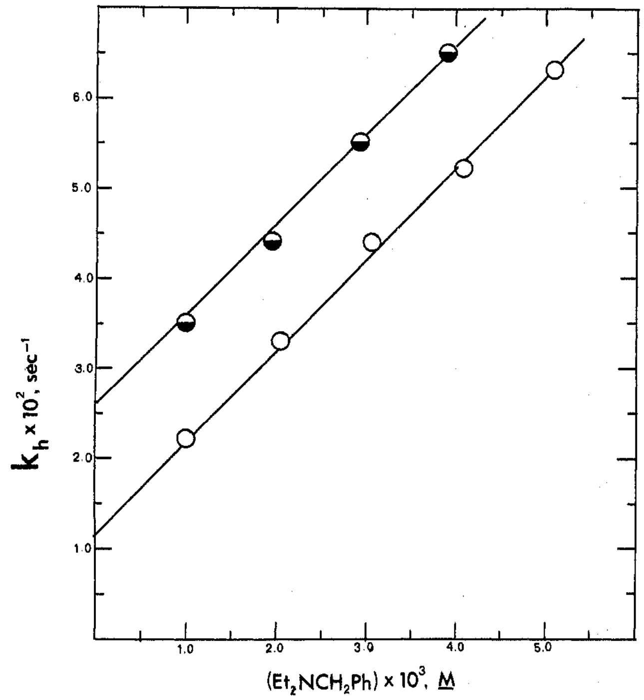

Figure 1.—Rate of hydrolysis of **2a** in 60% glyme in *N*-benzyldiethylamine buffers at 21.4°: ◒, runs in 2.5:1 Et_2NCH_2Ph-$Et_2\overset{+}{N}HCH_2Ph$ buffer; ○, runs in 1:1 Et_2NCH_2Ph-$Et_2\overset{+}{N}HCH_2Ph$ buffer.

solvents at 21.4°. Rates were followed spectrophotometrically using previously described procedures.[6] All runs were carried out at constant ionic strength in amine–ammonium ion buffers with both buffer components present in large stoichiometric excess over the sulfinyl sulfone. The disappearance of **2a** followed good first-order kinetics under all conditions investigated.

The kinetic results for *N*-benzyldiethylamine as catalyst in 60% glyme are shown in Table I. Those for pyridine as catalyst in 60% dioxane are given in Table II.

We also investigated catalysis by several other tertiary amines, namely, tribenzylamine, triethylamine, and *N*-benzylpyrrolidine. Tribenzylamine was without any catalytic effect at a concentration of 0.01 *M* in a 1:1 $(PhCH_2)_3N$-$(PhCH_2)_3NH^+$ buffer. In either 1:1 or 1:5 Et_3N-Et_3NH^+ buffers rates of hydrolysis of **2a** were too fast to measure accurately in either 60% glyme or 60% dioxane, even at the lowest amine concentrations (1×10^{-3} *M*) that could be used if one was to maintain an effectively constant Et_3N-Et_3NH^+ ratio throughout the course of the reaction.[7]

N-Benzylpyrrolidine was also too reactive to permit an accurate determination of its catalytic rate constant and is therefore a significantly better catalyst than *N*-benzyldiethylamine, even though they are presumably of closely comparable base strength.

TABLE I

HYDROLYSIS OF *p*-ANISYL *p*-METHOXYBENZENESULFINYL SULFONE IN THE PRESENCE OF *N*-BENZYLDIETHYLAMINE IN 60% GLYME[a]

Et_2NCH_2Ph-$Et_2\overset{+}{N}HCH_2Ph$ buffer ratio	$(Et_2NCH_2Ph) \times 10^3$, *M*	$k_h \times 10^2$, sec^{-1}	$k_{Et_2NCH_2Ph}$, M^{-1} sec^{-1} [b]	$k_{OH}(OH^-) \times 10^2$, sec^{-1} [c]
1:1	1.01	2.2		
	2.04	3.3		
	3.06	4.4	10.2	0.97
	4.08	5.2		
	5.10	6.3		
2.5:1	0.98	3.5		
	1.96	4.4	10.0	2.4
	2.93	5.5		
	3.91	6.5		
1:1	2.0	2.6 (D_2O)		
	3.0	3.0 (D_2O)	4.2 (D_2O)	1.7 (D_2O)
	4.0	3.5 (D_2O)		
	5.0	3.8 (D_2O)		

[a] All runs at 21.4° with ionic strength held constant at 0.01 by addition of $LiClO_4$; initial concentration of **2a**, 5×10^{-5} *M*. [b] Calculated from slope of plot of k_h *vs.* (Et_2NCH_2Ph). [c] Intercept at (Et_2NCH_2Ph) of 0.00 *M* equals 0.19×10^{-2} sec^{-1} + $k_{OH}(OH^-)$.

TABLE II

HYDROLYSIS OF *p*-ANISYL *p*-METHOXYBENZENESULFINYL SULFONE IN THE PRESENCE OF PYRIDINE IN 60% DIOXANE[a]

C_5H_5N-$C_5H_5NH^+$ buffer ratio	$(C_5H_5N) \times 10^3$, *M*	$k_h \times 10^2$, sec^{-1}	$k_{C_5H_5N}$, M^{-1} sec^{-1} [b]
1:1	9.7	4.0	
	4.9	2.1	
	2.9	1.3	3.9
	1.95	0.99	
	0.97	0.64	
1:1	10.0	2.8 (D_2O)	
	8.0	2.1 (D_2O)	2.7
	6.0	1.7 (D_2O)	
	4.0	1.1 (D_2O)	
1:1	10.0[c]	3.9	
	10.0[d]	3.5	

[a] All runs at 21.4° with ionic strength held constant at 0.01 by addition of $LiClO_4$; initial concentration of **2a**, 5×10^{-5} *M*. [b] Calculated from slope of plot of k_h *vs.* (C_5H_5N). [c] *p*-$MeOC_6H_4SO_2Na$, 5×10^{-4} *M*, added initially. [d] *p*-$MeOC_6H_4SO_2Na$, 1×10^{-3} *M*, added initially.

Discussion

Catalysis by *N*-Benzyldiethylamine.—Figure 1 shows plots of the rate of hydrolysis of **2a**, k_h, *vs.* (amine) for runs with added *N*-benzyldiethylamine in 60% glyme at two different Et_2NCH_2Ph-$Et_2N^+HCH_2Ph$ buffer ratios (1:1 and 2.5:1). The slope of the plots is independent of the buffer ratio while the intercepts of the plots, when corrected for the small contribution to k_h from the spontaneous rate of hydrolysis of **2a** under these conditions[6] (0.19×10^{-2} sec^{-1}), show that the intercept for the runs at the 2.5:1 buffer ratio is exactly 2.5 times larger than the intercept for the plot for the 1:1 buffer ratio runs. This behavior shows that under these conditions k_h is given as shown in eq 3 where

$$k_h - k_{spont} = k_{OH}(OH^-) + k_{Et_2NCH_2Ph}(Et_2NCH_2Ph) \qquad (3)$$

$k_{Et_2NCH_2Ph}(Et_2NCH_2Ph)$ is the contribution from the amine-catalyzed reaction and $k_{OH}(OH^-)$ is the contribu-

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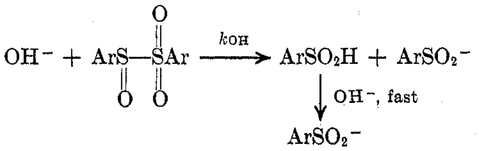
[6] J. L. Kice and G. Guaraldi, *J. Amer. Chem. Soc.*, **89**, 4113 (1967).

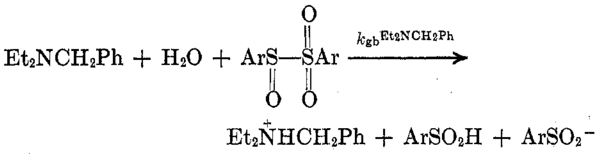
[7] Since an initial **2a** concentration of 5×10^{-5} *M* is about as low as one can conveniently go, and since hydrolysis of **2a** yields 2 mol of sulfinic acid (eq 2), one is restricted to amine concentrations above 9×10^{-4} *M* if one wants to maintain a constant pH during the course of the reaction. The latter is necessary since with relatively basic tertiary amines, like *N*-benzyldiethylamine and triethylamine, the direct reaction of hydroxide with **2a** is a significant contributor to the total rate in 1:1 amine–ammonium ion buffers (see discussion of results with $PhCH_2NEt_2$).

tion from a direct reaction of hydroxide ion with **2a** (eq 4).



$$OH^- + Ar\underset{O}{\underset{\|}{S}}-\overset{O}{\overset{\|}{\underset{\underset{O}{\|}}{S}}}Ar \xrightarrow{k_{OH}} ArSO_2H + ArSO_2^- \quad (4)$$
$$\big\downarrow OH^-,\ \text{fast}$$
$$ArSO_2^-$$

Measurements of the rate of the amine-catalyzed reaction in 60% glyme–40% D_2O (Table I) reveal that $k_{Et_2NCH_2Ph}$ is 2.4 times smaller in this solvent than it is in 60% glyme–40% H_2O. Such a solvent isotope effect of $(k^{H_2O}{}_{Et_2NCH_2Ph}/k^{D_2O}{}_{Et_2NCH_2Ph}) = 2.4$ provides clear evidence that the catalysis of the hydrolysis of **2a** by Et_2NCH_2Ph must involve general base catalysis (eq 5) and not nucleophilic catalysis. Thus, hydrolyses in



$$Et_2NCH_2Ph + H_2O + Ar\underset{O}{\underset{\|}{S}}-\overset{O}{\overset{\|}{\underset{\underset{O}{\|}}{S}}}Ar \xrightarrow{k_{gb}{}^{Et_2NCH_2Ph}}$$
$$Et_2\overset{+}{N}HCH_2Ph + ArSO_2H + ArSO_2^- \quad (5)$$

which amines act as nucleophilic catalysts normally exhibit rather small solvent isotope effects (k_{H_2O}/k_{D_2O} = 0.9–1.4) while those where general base catalysis is involved show much larger values of k_{H_2O}/k_{D_2O}, 1.9–4.4.[8]

As far as we can tell this represents the first example of general base catalysis of a hydrolysis of a sulfinyl derivative and shows that this phenomenon can also be observed in substitutions at this oxidation state of sulfur.

That not all tertiary amines, however, catalyze the hydrolysis of **2a** by acting as general base catalysts is indicated by results with several other amines. Let us first consider the results with pyridine.

Catalysis by Pyridine.—Figure 2 shows a plot of k_h *vs.* (amine) for the pyridine-catalyzed runs of Table II (1:1 C_5H_5N-$C_5H_5NH^+$ buffer). Since the line through the data points for each set of runs intercepts the k_h axis at a value equal to the spontaneous rate of hydrolysis of **2a**, this means that there is no contribution to the rate from the $k_{OH}(OH^-)$ term (eq 4) under these conditions. This is not surprising because, pyridine being a substantially weaker base than Et_2NCH_2Ph, the hydroxide concentration in a 1:1 C_5H_5N-$C_5H_5NH^+$ buffer should be much smaller than in a 1:1 buffer of the other amine.

Figure 2 shows that the slope of the k_h *vs.* (C_5H_5N) plot is somewhat lower in 60% dioxane–40% D_2O than it is in 60% dioxane–40% H_2O, corresponding to a solvent isotope effect of $(k^{H_2O}{}_{C_5H_5N}/k^{D_2O}{}_{C_5H_5N})$ of 1.4. Note that this is significantly smaller than the solvent-isotope effect of 2.4 found in the Et_2NCH_2Ph-catalyzed reaction. Although at the upper end of the range of values normally observed when nucleophilic catalysis by an amine is involved, it is significantly lower than those (1.9–4.4) usually associated with general base catalysis by the same species. We therefore conclude that the solvent isotope effect associated with the pyridine-catalyzed reaction is indicative of its involving nucleophilic catalysis by pyridine.

Two other aspects of the results also point toward the same conclusion. First, one sees that, although pyridine is over four powers of ten weaker base than Et_2NCH_2Ph,[9] $k_{C_5H_5N}$ in 60% dioxane is only 2.5 times smaller than $k_{Et_2NCH_2Ph}$ in 60% glyme. Although earlier work[3] has shown some increase in the rate constant for the Et_3N-catalyzed hydrolysis of **1** on going from 60% glyme to 60% dioxane, the magnitude of the effect is at most about a factor of ten. Thus, unless the Brønsted β associated with the general base catalyzed hydrolysis of **2a** were quite small, one could not have $k_{C_5H_5N}$ as large as it is and still have pyridine acting as a general base catalyst. It seems more reasonable to assume that $k_{C_5H_5N}$ is as large as it is because pyridine is functioning as a nucleophilic catalyst and is, because the nitrogen atom is much less sterically hindered than the one in an amine like Et_2NCH_2Ph, much more reactive as a nucleophile in relation to its basicity than is Et_2NCH_2Ph.[10] Second, there is the fact that the initial addition of 10^{-3} *M* sodium *p*-methoxybenzenesulfinate leads to a small but definite decrease in $k_{C_5H_5N}$ (see last two runs in Table II). This effect of added sulfinate is understandable if the pyridine-catalyzed reaction involves nucleophilic catalysis by C_5H_5N and the mechanism shown in eq 6, since in the presence of sufficient added $ArSO_2^-$ the k_{-1} step becomes competitive with the k_2 step, and $k_{C_5H_5N}$, which is equal to $k_1k_2(H_2O)/[k_2(H_2O) + k_{-1}(ArSO_2^-)]$, decreases. Were the pyridine-catalyzed reaction to involve general base catalysis by the amine no such effect of added sulfinate would be observed.

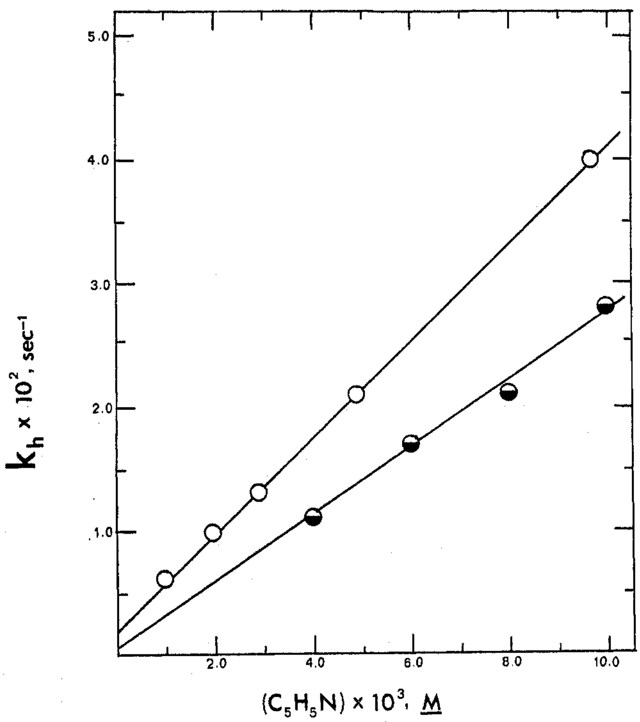


Figure 2.—Rate of hydrolysis of **2a** in pyridine buffers at 21.4°: ○, runs in 1:1 C_5H_5N-$C_5H_5NH^+$ buffer in 60% dioxane–40% H_2O; ◒, runs in 1:1 C_5H_5N-$C_5H_5ND^+$ buffer in 60% dioxane–40% D_2O.

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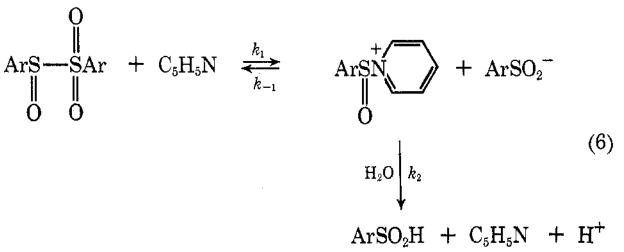
[8] For a tabulation of most of the pertinent data, see S. J. Johnson, *Advan. Phys. Org. Chem.*, **5**, 281 (1967).

[9] M. Bouregeaud and A. Dondelinger, *C. R. Acad. Sci.*, **179**, 1159 (1924).

[10] A referee has suggested that pyridine may exhibit nucleophilic catalysis and *N*-benzyldiethylamine general base catalysis not for the reasons just cited but because the reversal of the first step in the nucleophilic catalysis mechanism for $PhCH_2NEt_2$ (analogous to step k_{-1} in eq 6) is unusually fast relative to k_2 for this amine as compared to the situation with pyridine, so that any potential nucleophilic catalysis by $PhCH_2NEt_2$ is effectively suppressed and the general base catalyzed mechanism becomes dominant. Although we think it unlikely that a change from pyridine to $PhCH_2NEt_2$ would lead to a change in k_{-1}/k_2 large enough to have an effect of this magnitude, we cannot completely rule out this possibility.

We thus feel that the weight of the evidence points toward the pyridine-catalyzed hydrolysis involving nucleophilic catalysis by pyridine according to the mechanism shown in eq 6.



(6)

Catalysis by Other Tertiary Amines.—As mentioned earlier, *N*-benzylpyrrolidine is significantly more reactive as a catalyst for the hydrolysis of **2a** than is *N*-benzyldiethylamine, being in fact too reactive to permit an accurate determination of its catalytic rate constant. Since the two amines are of almost exactly equal base strength (pK_b of Et_2NCH_2Ph = 4.4;[9] pK_b of *N*-benzylpyrrolidine = 4.5[11]), they should be of essentially equal reactivity as general base catalysts for the hydrolysis of **2a**. The fact that *N*-benzylpyrrolidine is a significantly better catalyst than Et_2NCH_2Ph suggests that the pyrrolidine is probably catalyzing the hydrolysis by acting not as a general base but rather as a nucleophilic catalyst. Due to two of the substituents on the nitrogen being tied back in a ring, the nitrogen in the pyrrolidine is presumably much less sterically hindered than the one in Et_2NCH_2Ph, and the pyrrolidine should be considerably more reactive than Et_2NCH_2Ph as a nucleophile toward **2a**, even though the two amines are of equal basicity toward a proton.

The results in the present paper thus suggest that tertiary amines can catalyze the hydrolysis of sulfinyl derivatives either by nucleophilic or general base catalysis and that the particular type of catalysis actually observed with a given substrate may change with only a fairly modest change in amine structure. Regrettably this means that in further studies of such catalysis each individual sulfinyl compound–tertiary amine system will have to be examined in detail independently before one can be sure which type of catalysis is involved in that particular system.

Since triethylamine (pK_b = 3.25) is a significantly stronger base than Et_2NCH_2Ph, one cannot tell from the fact that this amine is also too reactive as a catalyst to permit measurement of k_{Et_3N} whether this is due to its acting as a nucleophilic rather than a general base catalyst. It could equally well be due to the fact that the greater basicity of Et_3N makes k_{gb} for this amine significantly larger than k_{gb} for Et_2NCH_2Ph. (With the Et_2NCH_2Ph runs we are already close enough to the upper limit of the rates that we can measure accurately that k_{gb} for Et_3N would only need to be about four times larger than k_{gb} for Et_2NCH_2Ph in order for k_{Et_3N} to be too large for us to be able to measure it accurately.)

Experimental Section

Preparation and Purification of Materials. ***N*-Benzylpyrrolidine** was prepared by the method of Fery and van Hove.[12] Benzyl chloride (41 ml) was added over a 2-hr period to a rapidly stirred, ice-cooled mixture of 33 g of pyrrolidine, 100 ml of ether, and 50 g of potassium carbonate. The final mixture was stirred for 2 hr more and then allowed to stand overnight. It was then acidified with 200 ml of 6 *N* HCl and extracted with ether. The aqueous phase was neutralized with concentrated potassium hydroxide solution and extracted with ether. The ether extract was dried over anhydrous magnesium sulfate. Subsequent removal of the ether and distillation gave 52 g (70%) of *N*-benzylpyrrolidine, bp 45° (0.7 mm), $n^{20}D$ 1.5271. ***N*-Benzyldiethylamine** was prepared in essentially the same manner as *N*-benzylpyrrolidine using 63.3 g of benzyl chloride and 36.5 g of diethylamine. The final distillation gave 30 g (37%) of *N*-benzyldiethylamine, bp 79–80° (7 mm), $n^{25}D$ 1.4957 [lit.[13] 84–85° (12 mm), $n^{25}D$ 1.5014]. ***p*-Anisyl *p*-methoxybenzenesulfinyl sulfone** was prepared as described by Kice and Guaraldi.[14] Pyridine was purified by refluxing analytical reagent grade material over barium oxide and then fractionally distilling. Dioxane, glyme, and triethylamine were purified by previously published procedures.[3,6] Tribenzylamine (Eastman) was recrystallized from ethanol before use, mp 93–95°.

Procedure for Kinetic Runs.—The various amine–ammonium ion buffers were prepared by adding the calculated amount of standard perchloric acid to a standard solution of the amine. The ionic strength was maintained constant by the addition of lithium perchlorate. To carry out a run 3.0 ml of the appropriate amine buffer in either 60% glyme or 60% dioxane was placed in a 1-cm spectrophotometer cell and brought to 21.4° in a thermostated cell compartment of a Cary Model 15 spectrophotometer. Then 7–8 μl of a freshly prepared 0.02 *M* solution of sulfinyl sulfone **2a** in either anhydrous glyme or dioxane was introduced into the buffer solution on the flattened end of a glass stirring rod and rapidly and thoroughly mixed with the solution in the cell. The rate of disappearance of **2a** was then followed spectrophotometrically in the manner described by Kice and Guaraldi.[6] The spectra at the conclusion of the hydrolysis corresponded to those that have been obtained in those hydrolyses of **2a** to sulfinic acid studied earlier.[6]

Registry No.—**2a,** 13737-19-4; *N*-benzyldiethylamine, 772-54-3; pyridine, 110-86-1; *N*-benzylpyrrolidine, 29897-82-3.

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(11) L. C. Craig and R. M. Hixon, *J. Amer. Chem. Soc.*, **53**, 4367 (1931).

(12) L. P. A. Fery and L. van Hove, *Bull. Soc. Chim. Belg.*, **69**, 63 (1960).

(13) R. F. Borch, *Tetrahedron Lett.*, 61 (1968); V. M. Micovic and M. L. Mihailovic, *J. Org. Chem.*, **18**, 1190 (1953).

(14) J. L. Kice and G. Guaraldi, *ibid.*, **31**, 3568 (1966).