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INTRAMOLECULAR CATALYSIS IN THE HYDROLYSIS OF *p*-NITROPHENYL *o*-METHANESULFONAMIDOBENZOATE

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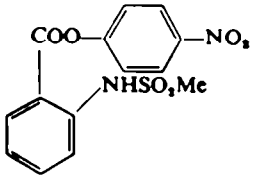
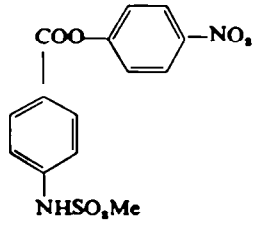
Abstract—The kinetics of hydrolysis of *p*-nitrophenyl *o*-methanesulfonamidobenzoate and *p*-nitrophenyl *p*-methanesulfonamidobenzoate were determined in 1·6% acetonitrile–water at 25° in the pH range 7–13. The ratio of observed first-order rate constants for the hydrolysis of the *ortho* and *para* compounds, k_o/k_p, is pH dependent with k_o being one-fifth k_p at pH 13 but 40-fold larger than k_p at pH 8·7. A sigmoid pH-rate profile for the *ortho* isomer is evidence for neighboring group participation and indicates that an ionizable group of pK_a 8·5 functions catalytically. This pK_a value agrees with the the spectrophotometrically determined pK_a of *p*-nitrophenyl *o*-methanesulfonamidobenzoate (8·41). Experiments with D_2O and others with azide ion as a nucleophile show that hydrolysis proceeds *via* either a general base or a general acid-specific hydroxide catalysis, and that there is no nucleophilic participation by the ionized sulfonamido substituent.

INTRODUCTION

No PREVIOUS quantitative study of neighboring group participation by the sulfonamido group has been reported. We therefore have studied the kinetics of hydrolysis of *p*-nitrophenyl *o*-methanesulfonamidobenzoate (I) at pH values above and below the pK_a of the sulfonamido group. This system is interesting since several modes of participation by the sulfonamido group in the ester hydrolysis are conceivable. The



I



II

un-ionized sulfonamido group may assist hydrolysis by donating its labile proton to the ester carbonyl as the transition state leading to the tetrahedral intermediate is forming. Such an intramolecular general acid catalysis was found, for example, in the hydrolysis of the conjugate acid of 2-N,N-dimethylaminoethyl benzoate.[1] The ionized sulfonamido group, an ambident anion, may facilitate hydrolysis in either of two ways. The nitrogen may participate in the attack of water on the ester by partially removing one of the protons of the nucleophile. Bender *et al.*[2] have demonstrated such general base catalysis in the hydrolysis of *p*-nitrophenyl salicylates. Alternatively,

[1] A. Ågren, U. Hedsten and B. Jonsson, *Acta Chem. Scand.* **15**, 1532 (1961).
[2] M. L. Bender, F. J. Kézdy and B. Zerner, *J. Amer. Chem. Soc.* **85**, 3017 (1963).

an oxygen of the anionic neighboring group, possessing considerable negative charge, may attack the ester carbonyl to close a six-membered ring. The resulting intermediate would be expected to be very unstable and to hydrolyze rapidly to the substituted benzoic acid. A similar nucleophilic participation by the amide group (with O-attack) has been shown to occur in the acid-catalyzed hydrolysis of *o*-benzamido-N,N-dicyclohexylbenzamide.[3]

It is known that sulfonamides can be acylated and sulfonylated at the nitrogen, especially in the presence of alkali. For example, benzenesulfonamide reacts with benzoyl chloride when the mixture is heated to 145°.[4] The geometry of I precludes interference from an intramolecular reaction of this type.

In order to evaluate the magnitude of a neighboring group effect it is necessary of course to estimate reactivities in the absence of such an effect.[5] This requires the study of a model compound. Sometimes conclusions are markedly dependent on the choice of the model. The difficulty lies in the impossibility of removing a neighboring group participation without changing steric and electronic factors as well. In our system, an obvious choice of the model to be used for comparison is *p*-nitrophenyl *p*-methanesulfonamidobenzoate (II). Therefore the kinetics of its hydrolysis were determined under conditions identical to those used for its *ortho* isomer.

EXPERIMENTAL

N-*Methanesulfonylanthranilic acid.* This compound was prepared from anthranilic acid and methanesulfonyl chloride in aqNaOH according to Saunders *et al.*[6] m.p. 189–190° (lit.[6] m.p 190·5–191·5°).

p-*Nitrophenyl* o-*Methanesulfonamidobenzoate* (I). N-Methanesulfonylanthranilic acid (0·55 g, 0·0026 mole) and *p*-nitrophenyl trifluoroacetate (Aldrich, 0·70 g, 0·0030 mole) were mixed in 10 ml dry pyridine.[7] The soln was allowed to stand at room temp for 20 min, after which it was added to 40 ml ice water. The product, which separated as an oil, was dissolved in CH_2Cl_2. The organic layer was separated and dried over $CaSO_4$, and the solvent was then removed with the aid of a rotary evaporator. The crystalline residue was recrystallized 3 times from benzene to give white needles, m.p. 169–172°. (Found: C, 49·88; H, 3·59; N, 8·25. Calc for $C_{14}H_{12}N_2O_6S$: C, 49·99; H, 3·60; N, 8·33%.) Greater than 99% of the expected amount of *p*-nitrophenolate was released when a known amount of ester was added to 1N NaOH.

p-*Methanesulfonamidobenzoic acid.* This compound was prepared by the method of Saunders *et al.*[6] It was recrystallized 4 times from AcOEt–heptane, m.p. 232–235° (dec). (Found: C, 44·88; H, 4·40; N, 6·59. Calc. for $C_8H_9NO_4S$: C, 44·64; H, 4·21; N, 6·51%.)

p-*Nitrophenyl* p-*Methanesulfonamidobenzoate* (II). The ester was made from *p*-methanesulfonamidobenzoic acid by a procedure similar to that used for the prep of its *ortho* isomer (I). The material was recrystallized repeatedly from AcOEt to give pale yellow crystals, m.p. 225–227°. (Found: C, 50·46; H, 3·86; N, 8·12. Calc. for $C_{14}H_{12}N_2O_6S$: C, 49·99; H, 3·60; N, 8·33%.) The purity of the compound was checked spectrophotometrically: release of *p*-nitrophenolate in strong base was 98% of the calculated amount.

Acetonitrile (Spectro Grade) was distilled from P_2O_5. Reagent grade materials and distilled water were used to prepare buffers. Borax buffers were prepared following the procedures of Bates and Bower.[8] Buffers containing sodium azide (Fisher Purified) were filtered through sintered glass. Columbia 99·5% D_2O was used.

pK_a *Determinations.* The pK_a's of I and II were determined spectrophotometrically in 1·6% (v/v) acetonitrile–water (25·0°) at 225·0 mμ and 275·0 mμ respectively using a Cary 14 spectrophotometer.

[3] T. Cohen and J. Lipowitz, *J. Amer. Chem. Soc.* **86**, 5611 (1964).
[4] A. Mannessier-Mameli, *Rec. Trav. Chim.* **65**, 51 (1935).
[5] B. Capon, *Quart. Rev.* **18**, 45 (1964).
[6] B. C. Saunders, G. J. Stacey and I. G. E. Wilding, *Biochem. J.* 368 (1942).
[7] S. Sakakibara and N. Inukai, *Bull. Chem. Soc. Japan* **37**, 1231 (1964).
[8] R. G. Bates and V. E. Bower, *Analyt. Chem.* **28**, 1322 (1956).

Absorbance measurements were made less than 30 sec after addition of 50 μl. of a soln of the compound in acetonitrile to 3·00 ml of buffer in a cuvette. Hydrolysis at pH values near the pK_a's was so slow that extrapolation to zero time was unnecessary in most cases. The concentration of II was $5{\cdot}16 \times 10^{-6}$ M and absorbance measurements were made with a 0–0·1 slidewire. The concentration of I was about 10-fold higher. A Corning Model 12 pH meter was used for the pH measurements. The pK_a values of I and II were found to be 8·41 and 7·34 respectively and may be compared with the value of 8·31 for benzenesulfonanilide.[9]

Kinetic measurements. The rate of liberation of *p*-nitrophenol was measured spectrophotometrically at 400·0 mμ on a Cary 14 recording spectrophotometer with a cell compartment thermostated at 25·0 ± 0·1°. Reactions were initiated by adding 50 μl. of substrate dissolved in acetonitrile to a thermostated cuvette containing 3·00 ml buffer of ionic strength 0·1, and stirring with a glass rod flattened at one end. The hydrolysis of I at pH 13·04 was followed to greater than 8 half-lives and the logarithmic plot for first-order kinetics was linear to greater than 90% reaction. This was true also for the hydrolysis of II at pH 12·97. For the slow reactions at lower pH values, use was made of the fact that absorbance *vs.* time curves of first-order processes are very nearly linear for the first 5% of reaction. For these runs (0–0·1 slidewire) the concentration of substrate was such that the Cary pen would traverse the entire width of the chart paper after less than 10% of the reaction was over. In this way accurate measurements of initial rates could be made. Determination of rate constants by this method requires the knowledge of the pH-dependent ε's of the product. These were calculated from the known ε's at 400 mμ of *p*-nitrophenol and *p*-nitrophenolate (84·7 and 18,320), the pK_a of *p*-nitrophenol (7·04), and the pH of the buffer. It is estimated that the rate constants are accurate to within ±5% except those for the hydrolysis of II at the two lowest pH values (Table 2) for which the experimental error approaches 15%.

KOH buffers were used for pH values above 12, phosphate buffers for the range 11–12, Borax buffers for the range 8–10·5, and phosphate buffers for the range 6–8. Hydrolysis catalyzed by buffer species was insignificant. For example, at 0·025 M total phosphate (pH = 11·12, I = 0·1), k_{obs} for the hydrolysis of I is $2{\cdot}65 \times 10^{-4}$ sec^{-1}. At 0·005 M phosphate (pH = 11·12, I = 0·1), $k_{obs} = 2{\cdot}55 \times 10^{-4}$ sec^{-1}. Even smaller changes were observed upon decreasing Borax and phosphate concentrations 5-fold at lower pH's. KCl was used throughout to maintain ionic strength.

Product analysis. The nearly quantitative formation of *p*-nitrophenol from hydrolysis of I and II was mentioned above. The second hydrolysis product of the ester I was identified by stirring 0·035 g ($1{\cdot}04 \times 10^{-4}$ mole) of the compound in 1·5 ml of 0·33N NaOH until soln was complete. The clear yellow liquid was cooled in ice water and slowly acidified with 1N HCl, resulting in separation of white crystals. This material was removed by filtration, washed with a little cold water and dried with the aid of a vacuum pump. The crystals weighed 0·017 g (76%), and had a m.p and IR identical to those of N-methanesulfonylanthranilic acid.

RESULTS

The observed first-order constants for hydrolysis of *p*-nitrophenyl *o*-methanesulfonamidobenzoate (I) and *p*-nitrophenyl *p*-methanesulfonamidobenzoate (II) at various pH values are given in Tables 1 and 2. The data are presented graphically in Figs. 1 and 2. The extraordinary pH-rate profile for the *ortho* isomer, shown in Fig. 1-A, resembles the profile found by Bender *et al.*[2] for hydrolysis of *p*-nitrophenyl 5-nitrosalicylate. The log k *vs.* pH profile for the *para* isomer indicates a simple hydroxide ion-catalyzed hydrolysis in the pH range 9–13.

The rate expression for the hydrolysis of I is theoretically composed of six terms[1] corresponding to hydrolysis *via* hydronium ion catalysis, hydroxide ion catalysis, and a "water reaction" of both the un-ionized (AH) and the ionized (A^-) form of the substrate (pK_a = 8·31). Only three of the terms could be detected in the pH range of this study (7–13).

$$v = [AH][k_1[H^+] + k_2[H_2O] + k_3[OH^-] + [A^-][k_1'[H^+] + k_2'[H_2O] + k_3'[OH^-]].$$

[9] A. V. Willi, *Helv. Chim. Acta* **39**, 46 (1956).

At pH = 13·04 (Table 1), $k_{obs} = 4{\cdot}53 \times 10^{-3}\ sec^{-1} = k_3'[OH^-]$ because $[H^+]$ and [AH] are very small and the k_2' term contributes less than 5%. The hydroxide ion-catalyzed hydrolysis of *p*-nitrophenyl *o*-methanesulfonamidobenzoate anion, described by k_3', is mechanistically uninteresting, and the contribution from this reaction to the k_{obs} at the lower pH values may be subtracted in order to simplify analysis. For example, $k_{obs} = 6{\cdot}55 \times 10^{-4}\ sec^{-1}$ for the hydrolysis of I at pH = 12·04. The observed rate constant excluding the contribution from the k_3' step (indicated by k'_{obs}) would be $2{\cdot}02 \times 10^{-4}\ sec^{-1}$, that is $6{\cdot}55 \times 10^{-4} - 0{\cdot}1 \times 4{\cdot}53 \times 10^{-3}\ sec^{-1}$. At pH values below 10·22 the contribution of the k_3' term becomes negligible and $k_{obs} = k'_{obs}$. A plot of k'_{obs} *vs.* pH is shown in Fig. 1-B. This is a typical sigmoid relationship and indicates that an ionizable group is functioning catalytically.

TABLE 1. THE OBSERVED RATE CONSTANTS FOR HYDROLYSIS OF *p*-NITROPHENYL *o*-METHANESULFONAMIDOBENZOATE (I)[a]

pH	k_{obs}
13·04	$4{\cdot}53 \times 10^{-3}\ sec^{-1}$
12·04	$6{\cdot}55 \times 10^{-4}$
11·76	$4{\cdot}53 \times 10^{-4}$
11·12	$2{\cdot}65 \times 10^{-4}$
10·22	$2{\cdot}22 \times 10^{-4}$
9·34	$1{\cdot}92 \times 10^{-4}$
8·62	$1{\cdot}44 \times 10^{-4}$
8·14	$8{\cdot}38 \times 10^{-5}$
7·78	$3{\cdot}26 \times 10^{-5}$
7·57	$2{\cdot}46 \times 10^{-5}$
7·39	$1{\cdot}58 \times 10^{-5}$
7·18	$9{\cdot}90 \times 10^{-6}$

[a] 25·0°, in 1·6% acetonitrile-water (v/v) of ionic strength 0·1. Ester concn = $6{\cdot}24 \times 10^{-4}$ M.

TABLE 2. THE OBSERVED RATE CONSTANTS FOR HYDROLYSIS OF *p*-NITROPHENYL *p*-METHANESULFONAMIDOBENZOATE (II)[a]

pH	k_{obs}
12·97	$2{\cdot}14 \times 10^{-3}\ sec^{-1}$
11·65	$1{\cdot}31 \times 10^{-4}$
10·99	$3{\cdot}40 \times 10^{-4}$
10·11	$5{\cdot}34 \times 10^{-5}$
9·23	$9{\cdot}17 \times 10^{-6}$
8·65	$3{\cdot}4 \times 10^{-6}$
8·17	$2{\cdot}0 \times 10^{-6}$

[a] 25·0°, in 1·6% acetonitrile-water (v/v) of ionic strength 0·1. Ester concn = $5{\cdot}16 \times 10^{-4}$ M.

TABLE 3. THE DEPENDENCY OF THE RATIO OF OBSERVED RATE CONSTANTS FOR HYDROLYSIS OF I AND II ON pH[a]

pH	k_{ortho}/k_{para}[b]
13·04	0·19
12·04	0·22
11·76	0·27
11·12	0·62
10·22	3·5
9·34	19·0
8·65	42·0

[a] Based on data taken from Table 1 and Fig. II.
[b] k_{ortho} and k_{para} refer to the observed rate constants for hydrolysis of *p*-nitrophenyl *o*-methanesulfonamidobenzoate (I) and *p*-nitrophenyl *p*-methanesulfonamidobenzoate (II) respectively.

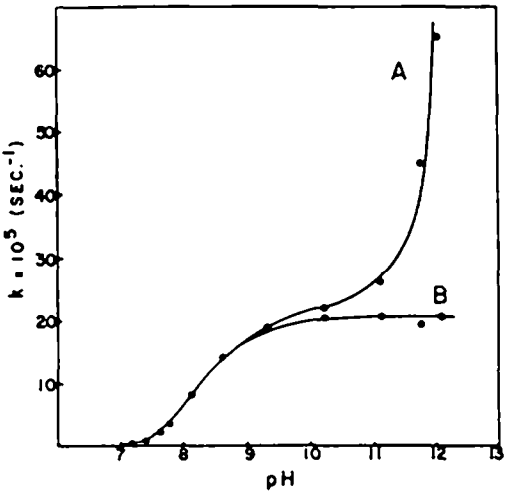


FIG. 1. Curve A: The pH dependency of observed first-order rate constants (k_{obs} in text) for hydrolysis of *p*-nitrophenyl *o*-methanesulfonamidobenzoate (I) in 1·6% acetonitrile–water at 25°. Curve B: The pH dependency of the rate constants of Curve A minus the contribution from the reaction of hydroxide ion with ionized substrate (k'_{obs} in text).

It is possible to evaluate the pK_a of the catalytic group by means of the equation below, in which k_{lim} refers to the rate constant in the pH-independent region (above pH 10) of the pH-rate profile of Fig. 1-B. The pK_a is derived from the

$$\frac{1}{k'_{obs}} = \frac{1}{k_{lim}} + \frac{[H^+]}{k_{lim} K_a}$$

slope of a plot of $1/k'_{obs}$ *vs.* $[H^+]$, and is found to be 8·5 ± 0·1, in good agreement with the spectrophotometrically determined value of 8·41 for the ionization of the sulfonamido group of I.

The pH dependency of the ratio of observed rate constants for hydrolysis of I and II (Table 3) is a striking indication of neighboring group participation by the *ortho* sulfonamido group of I. At pH = 13·04 the *ortho* isomer hydrolyzes less than one-fifth as fast as the *para* compound. At pH = 8·65 the *ortho* compound hydrolyzes over 40-fold faster than its isomer. As was mentioned above, the rate constants at

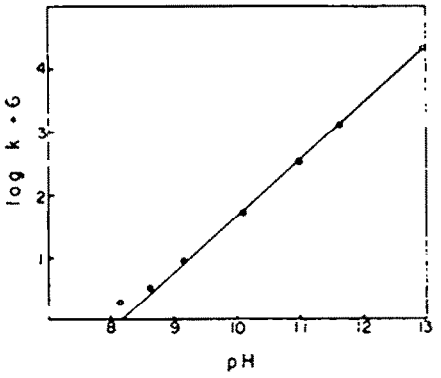


FIG. 2. The logarithm of the observed first-order rate constants for hydrolysis of *p*-nitrophenyl *p*-methanesulfonamidobenzoate (II) in 1·6% acetonitrile–water at 25° as a function of pH.

pH 13·04 are a measure of the reactivity of the ionized substrates with hydroxide ion. While it is impossible to evaluate quantitatively the various factors which determine the *ortho*:*para* ratios, it is clear that electrostatic repulsion of the hydroxide ion at the reactive site by the negative charge on the ionized sulfonamido group is less in the *para* compound II than in the *ortho* substituted ester I. The greater reactivity of the *para* compound at pH = 13·04 must be due, at least in part, to this effect. As the pH is lowered from 13 to 9 the observed first-order constants for hydrolysis of the *para* compound decrease in direct proportion to the decrease in hydroxide ion concentration (Fig. 2). This is not true for the *ortho* ester. Another reaction involving neighboring group participation becomes important as the hydroxide ion-substrate anion reaction diminishes. The result is the inversion in the magnitude of the $k_{ortho}:k_{para}$ ratio evident in Table 3. Experiments which establish the mechanism of the anchimeric assistance are described in the next section.

The rate expression for the hydrolysis of ester II in basic media may be assumed to be the sum of two terms. In the

$$v = k_{AH}[AH][OH^-] + k_A[A^-][OH^-]$$

pH range 9–13 the observed rate constant is directly proportional to $[OH^-]$. Since the pK_a of II is 7·34 (determined spectrophotometrically), the first term must be negligible in this pH range. At pH = 8·17 the rate is faster than would be expected on this basis (Fig. 2). Contribution from the reaction of hydroxide with un-ionized substrate (or its kinetic equivalent, $H_2O + A^-$) is thus beginning to manifest itself.

Unfortunately, the extremely slow reaction rates prevented accurate measurement of the rate constants at pH values closer to the pK_a of the substrate, where the contribution from the first term would be larger.

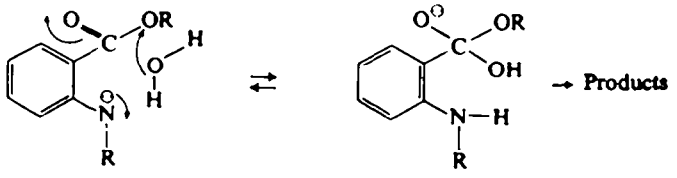
Nevertheless we can calculate, from the deviation (D) of the rate constant from linearity at pH = 8·17, that k_{HA} is approximately 9-fold larger than k_A.

$$a \log D = \frac{k_{AH}[OH^-]}{\frac{K_a}{[H^+]} + 1}$$

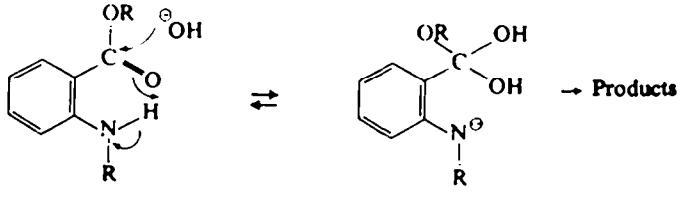
DISCUSSION

The kinetics of hydrolysis of *p*-nitrophenyl *o*-methanesulfonamidobenzoate (I) demonstrate the presence of neighboring group participation by the *ortho* sulfonamido group. Three mechanisms are consistent with the data.

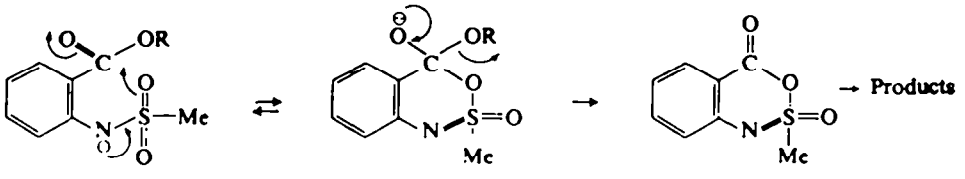
(A) *General base catalysis*



(B) *General acid-specific hydroxide catalysis*



(C) *Nucleophilic catalysis*



While it is clear that mechanisms A and C are consistent with the sigmoid pH rate profile, it is perhaps somewhat less obvious that mechanism B is likewise in agreement with this result. It may simply be pointed out that mechanisms A and B involve transition states which are identical except for the positions of the atoms, and therefore the kinetics cannot distinguish between the mechanisms. Nor can mechanisms A and B be distinguished from C by the pH-rate data because it is impossible to detect the presence or absence of a solvent molecule in the transition state from such data. Other experiments are necessary to prove which mechanism is applicable.

A method for distinguishing general base catalysis from the kinetically equivalent general acid-specific hydroxide catalysis has recently been devised by Bender *et al.*[8] If general acid-specific hydroxide catalysis (mechanism B) is occurring, then anchimeric assistance should be observed with the un-ionized ester whether the nucleophile is water, hydroxide ion, azide ion or any other species, since catalysis is the result of carbonyl activation and does not directly involve the nucleophile. For example, it was shown that azide ion reacts with un-ionized *p*-nitrophenyl 5-nitrosalicylate only 5·8-fold faster than it does with the ester without the ortho hydroxyl group (*p*-nitrophenyl 3-nitrobenzoate). On the other hand, assuming that catalysis occurs *via* a general acid-specific hydroxide route, it can be calculated that hydroxide ion reacts with un-ionized salicylate with a rate constant of about $1{\cdot}0 \times 10^4$ M^{-1} sec^{-1}, which is 458 times larger than the second-order rate constant for the reaction of hydroxide ion with the model benzoate ester. Thus azide ion and hydroxide ion show appreciably different relative reactivities. The assumption of a general acid-specific hydroxide catalysis must be discarded in favor of a general base mechanism because one would have expected the un-ionized *ortho* hydroxyl group to accelerate nucleophilic attack of azide ion and hydroxide ion by roughly the same factor.

We have determined the rate constants for the reaction of azide ion with un-ionized esters I and II. The runs were performed at an azide concentration of 0·40 M and a pH = 6·72, so that hydrolysis and the reaction of azide ion with ionized material would be both negligible. It was found that azide ion reacts with un-ionized *p*-nitrophenyl *o*-methanesulfonamidobenzoate (I) 4·2 times faster than it does with its un-ionized *para* isomer. The rate constant k_g for reaction of hydroxide ion with un-ionized ester I may be calculated from the equation below if it is assumed that general acid-specific hydroxide

$$k'_{obs} = \frac{k_g[OH^-]}{1 + \dfrac{K_a}{[H^+]}}$$

catalysis properly describes this system. The k'_{obs} refers to the observed first-order rate constants plotted in Fig. 1-B. The second-order rate constant k_g is found to be 82·9 M^{-1} sec^{-1}, which is 14 times larger than the rate constant for reaction of hydroxide ion with un-ionized *p*-nitrophenyl *p*-methanesulfonamidobenzoate (II). Clearly the difference in the rate ratios (4·2 and 14) of the azide and hydroxide reactions is not of such a magnitude that the general acid-specific hydroxide assumption can be regarded as incorrect.

If it is assumed that the catalysis is by a general base mechanism, then it is possible to calculate the efficiency of the process by comparing the two pH-independent regions of the pH profile of Fig. 1-B. It is found that the reaction of ionized *p*-nitrophenyl *o*-methanesulfonamidobenzoate (I) with water is at least 21 times faster than the reaction of the un-ionized ester with water. This can be compared with the accelerating effect of 30 found in the salicylate case.[8] In both the salicylate and the sulfonamidobenzoate systems the catalytic effects are relatively small. In the former, the facile reaction is best described as an intramolecular general base catalysis. In the latter it is not possible to distinguish between general base and general acid-specific hydroxide catalysis.

General acid-specific hydroxide catalysis and general base catalysis, differing only in the pre-equilibrium step which occurs in the latter, would both be expected to lead to the same deuterium oxide solvent isotope effect (usually found to be a rate ratio in water and deuterium oxide of 2-3).[9] The solvent isotope effect may be used only to distinguish nucleophilic catalysis (mechanism C) from the other two types (mechanism A and B). The rate constant for hydrolysis of *p*-nitrophenyl *o*-methanesulfonamidobenzoate (I) was determined in deuterium oxide at a pD = 10·13 and compared with the rate constant in water at pH = 9·73 (pD = meter pH + 0·4).[10] The pH and pD values were selected because they lie on the flat portion of the pH-rate profile of Fig. 1-B and because there is very little interference from the reaction of hydroxide ion with ionized substrate. The deuterium oxide solvent isotope effect, k_w/k_D, was calculated to be 2·02. Neighboring group participation cannot be ascribed to nucleophilic attack by the *ortho* sulfonamido group since such a mechanism would have resulted in a ratio close to unity.

The ester group is extremely labile to intramolecular nucleophilic attack. For example, the hydroxide ion-catalyzed hydrolysis of methyl 2-formylbenzoate, which proceeds 10^5 faster than expected, is believed to involve intramolecular nucleophilic attack on the ester carbonyl by the monoanion of the hydrate of the aldehyde group.[11] The *p*-nitrophenyl ester of 4-4'-imidazolylbutyric acid is hydrolyzed with a rate enhancement of 3×10^4 due to nucleophilic catalysis by the imidazole group.[12] Even a poor nucleophile and very weak base, the amide oxygen, can react intramolecularly and cause an appreciable increase in the rate of hydrolysis of carboxylic acid derivatives.[3] Hydrolysis rates are sensitive indeed to intramolecular nucleophilic participation. Therefore the lack of anchimeric assistance by an oxygen of the ionized sulfonamido group of I vividly demonstrates the unreactivity of this atom.

Acknowledgement—The authors are grateful to the McCandless Fund of Emory University for assistance.

[10] P. K. Glasoe and F. A. Long, *J. Phys. Chem.* **64**, 188 (1960).
[11] M. L. Bender and M. S. Silver, *J. Amer. Chem. Soc.* **84**, 4589 (1962).
[12] T. C. Bruice and J. M. Sturtevant, *J. Amer. Chem. Soc.* **81**, 2860 (1959).