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Mechanism of Buffer Catalysis in the Iodine Oxidation of *N*-Acetylmethionine Methyl Ester

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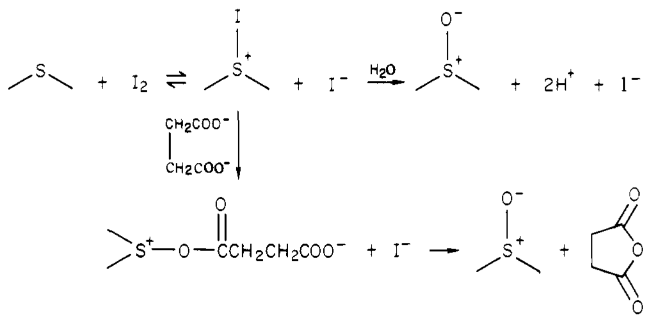
Abstract: The iodine oxidation of *N*-acetylmethionine methyl ester is catalyzed by carboxylic acid buffers. At very low concentrations, the reaction is first order with respect to buffer and follows an iodide dependence that can be described as inverse squared, changing to inverse cubed as the iodide concentration is increased. This iodide dependence is observed at all buffer concentrations examined, although the transition from inverse squared to inverse cubed occurs at higher iodide concentrations as the buffer concentration is increased. As the buffer concentration is increased, the observed rate constants become dependent upon [buffer]^2 and at "high" buffer (typically >0.3 M) the reaction again becomes first order with respect to buffer. Brøsted coefficients, based on four carboxylic acid buffers, are 1.0 and 1.5 for the first- and second-order terms, respectively. In the reaction catalyzed by acetate, acetic anhydride is produced in an amount equal to the concentration of sulfide that is oxidized. The data are rationalized in terms of a mechanism involving the rapid formation of an iodosulfonium ion which is attacked by buffer to give an intermediate *O*-acylsulfoxide. The *O*-acylsulfoxide can partition by back-reaction with iodide or by attack of buffer or water at the acyl carbon to give either anhydride or free acid. The β_{eq} for *O*-acylsulfoxide formation is estimated to be 1.5. Possible transition states for *O*-acylsulfoxide formation and the possible roles of sulfurane intermediates in these reactions are discussed.

The iodine oxidation of simple sulfides is thought to proceed through the formation of an iodosulfonium ion intermediate.[1-6] In the uncatalyzed reaction, water or hydroxide ion attacks the sulfur to give, initially, a protonated sulfoxide which rapidly loses the proton to give sulfoxide. Although the uncatalyzed oxidation reaction is very slow, the reaction is strongly catalyzed by carboxylate, phosphate, and carbonate anions.[1,2,4] The catalysis of the reaction is thought to involve nucleophilic attack of the buffer at the sulfonium sulfur to give an *O*-acylsulfoxide intermediate.[1,4] These activated esters can undergo hydrolysis by attack at either sulfur or at the acyl carbon. In the reaction catalyzed by dicarboxylate anions, attack occurs at the acyl carbon to give sulfoxide and acid anhydride.[1]

An important question in the mechanism of the catalysis of these reactions is whether the attack at sulfur is a concerted S_N2 process or if tetracoordinate sulfuranes are involved as obligatory intermediates.[3,6,7] Kinetic evidence suggesting an intermediate of this type has been presented for the iodine oxidation of the amino acid methionine to give the cyclic sulfilimine, dehydromethionine.[3] This suggestion is based on the observation of a change in rate-limiting step with increasing buffer concentration which is coupled to a change in order with respect to iodide ion inhibition. Similar studies involving the carboxylate-catalyzed oxidation of sulfides have been less revealing and often quite complicated,[1,4] displaying apparent fractional orders with respect to both buffer and iodide anion.

In order to more clearly define the nature of the carboxylate-catalyzed iodine oxidation of simple sulfides and the possible role of sulfurane intermediates in these reactions, we have investigated the catalysis of the iodine oxidation of *N*-acetylmethionine methyl ester (NAME) by a series of substituted carboxylic acid buffers.

Scheme I



Experimental Section

Material. Reagent grade inorganic salts were used without further purification. Organic acids (with the exception of reagent grade acetic acid) were recrystalized or distilled prior to use. *N*-Acetylmethionine methyl ester was prepared by esterification of *N*-acetylmethionine in methanol, saturated with HCl. After approximately 1 h at room temperature, the methanol was removed and the residue dissolved in distilled water (approximately 10 mL/g of material). The pH was adjusted to 3 with KOH solution and the ester extracted into chloroform. The recrystalized material had a melting point of 85-85.5 °C (lit.[8] 83 °C).

Stock solutions of *N*-acetylmethionine methyl ester were prepared at about 0.1 M in glass-distilled water. Iodine stock solutions were 0.1 M in 1 M KI. Reactions were initiated by the addition of a small amount of the iodine solution to preequilibrated cuvettes containing buffer, *N*-acetylmethionine methyl ester, KI solution, and the required amount of KCl to give an ionic strength of 1.0. Chloride ion did not inhibit the oxidation reaction. Glass-distilled water was used throughout; the pH of each cell was measured at the completion of the experiment with a Corning 130 pH meter equipped with a combined glass electrode.

Kinetic Measurements. The rates of disappearance of I_3^- were followed at 353 nm with a Hitachi 100-60 spectrophotometer equipped with an automatic cell changer and a thermostated cell compartment. First-order rate constants were determined from semilogarithmic plots of $A_\infty - A_t$ against time and were typically linear for 3-4 half-times. Constants for buffer catalysis were obtained from second-order replots of $k_{obsd}/[B]$ vs. [B], second-order catalytic constants from the initial linear region, and first-order catalytic constants from the limiting values at high buffer.

Evidence for the formation of acetic anhydride was obtained by using aniline to trap the anhydride formed in the oxidation reaction, as described by Gensch and co-workers.[1] Acetanilide was identified, along with sulfoxide, by retention time on high performance liquid chromatography with use of a reverse-phase column and a 0-60% water/acetonitrile linear gradient. Aniline does not react significantly with I_2

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(1) Gensch, K.-H.; Pitman, I. H.; Higuchi, T. *J. Am. Chem. Soc.* **1968**, *90*, 2096.

(2) Higuchi, T.; Gensch, K.-H. *J. Am. Chem. Soc.* **1966**, *88*, 5486.

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Table I. Carboxylate Catalysis of the Iodine Oxidation of *N*-Acetylmethionine Methyl Ester[a]

buffer	pK_a[b]	$[K_1k_Bk_b/k_{-2}]$,[c] M^{-1} s^{-1}	K_1k_B,[d] M^{-1} s^{-1}	$[k_{-2}/k_b]$[e]	$[k_b/k_0]$,[f] M^{-1}
propionic acid	4.87	3.2×10^2	7.89×10^1	15 (25)	33
acetic acid	4.75	1.63×10^2	5.03×10^1	18 (31)	33
benzoic acid	4.17	$>3.4 \times 10^1$[g]	1.38×10^1	36 (>41)	11
glycolic acid	3.83	6.3	>9.2[g]	51 (<146)	8

[a] Aqueous solution, 25 °C, ionic strength 1.0 with KCl. [b] Thermodynamic pK_a; ref 17. [c] Catalytic constant based on the linear region of second-order replots; see text. [d] Catalytic constant based on limiting values of second-order replots; see text. [e] Calculated partitioning ratios for *O*-acylsulfoxides; see Scheme II. Values are based on the position of the break from second- to first-order buffer dependence at high buffer concentrations. Values in parentheses are estimated from the ratios of catalytic constants. [f] Partitioning ratio for *O*-acylsulfoxide for reaction with buffer and solvent. [g] Limiting value.

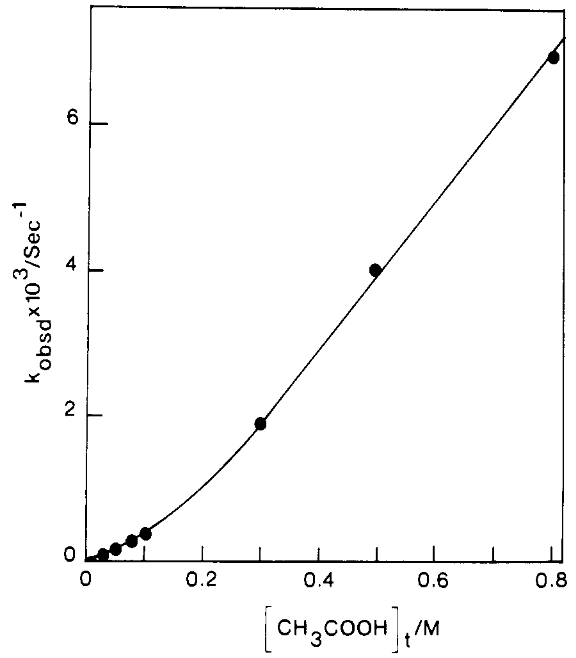

Figure 1. Plot of observed first-order rate constant for the iodine oxidation of *N*-acetylmethionine methyl ester against the concentration of acetic acid buffer; pH 5.48, 90% base, 25 °C. Initial concentrations: [NAME] = 1.67×10^{-3} M; $[I_2] = 1.67 \times 10^{-5}$ M; $[I^-] = 0.01$ M. The ionic strength was 1.0 with KCl.

under these conditions, nor with the substrates or products of the oxidation reaction. The aniline concentration in the cuvette was 5×10^{-4} M, and the decreae in the absorbance at 280 nm was used to estimate the amount of anilide formed; the initial absorbance of aniline at this wavelength was about 0.7.

The equilibrium constant for the formation of I_3^- from I_2 and I^- is 723 M^{-1}.[9] In experiments in which very low concentrations of iodide were used in order to determine iodide dependence, the concentration of iodide was corrected for I_3^- formation with use of this constant.

Results

Observed first-order rate constants for the iodine oxidation of *N*-acetylmethionine methyl ester increase rapidly as the concentration of carboxylate buffer is increased. Significant upward curvature is evident in these plots of k_{obsd} against total buffer concentration, suggesting the reaction is higher order with respect to buffer (Figure 1). However, attempted linearization of the data by replots of $k_{obsd}/[B]$ vs. [B] (a standard "second-order" replot) gives a series of curves having a short linear region at low buffer concentration, and becoming *independent* of buffer at higher concentrations (Figure 2). This behavior is consistent with a mechanism in which both first- and second-order buffer terms contribute to k_{obsd} *and* in which a kinetically significant intermediate participates. At high buffer concentrations, the formation of this intermediate becomes rate limiting and the reaction again becomes first order with respect to buffer. For a mechanism such as this, rate constants for the first-order process can be obtained from the limiting values of replots such as Figure 2, and second-order catalytic constants can be obtained from the initial slopes of these replots. The apparent first-order catalytic constants are a linear function of the fraction of the buffer in the base form; catalytic constants, extrapolated to 100% base, are given in Table I (K_1k_B). Similar replots of the second-order catalytic constants are nonlinear, becoming linear when plotted as k_{cat}/(fraction base) vs. (fraction base). Values for these second-order constants are also given in Table I ($(K_1k_Bk_b)/k_{-2}$).

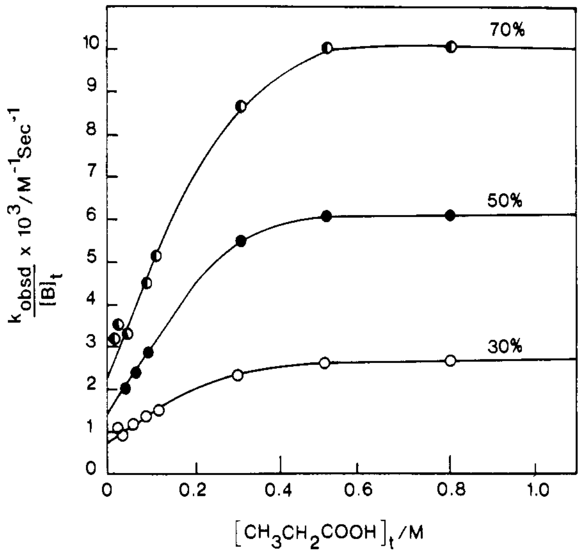

Figure 2. Second-order replot of the observed rate constants for the iodine oxidation of *N*-acetylmethionine methyl ester, divided by the concentration of propionic acid buffer, against the concentration of propionic acid buffer. Initial concentrations: [NAME] = 1.67×10^{-3} M; $[I_2] = 1.67 \times 10^{-5}$ M; $[I^-] = 0.01$ M. The ionic strength was 1.0 with KCl, 25 °C. The fraction of the buffer in the basic form is indicated in the figure.

The rate constants for the oxidation reaction are strongly inhibited by iodide anion. At high concentrations of iodide, the inhibition approaches an inverse-cubed relationship. Part of this inhibition is due to the depletion of I_2 by reaction with iodide to give I_3^-. The equilibrium between I_2 and I^- is rapid on the time scale of the oxidation reaction and rate constants were routinely corrected for this inverse iodide dependence. A double logarithmic plot showing a typical iodide dependence is given in Figure 3. The observed rate constants are corrected for I_3^- formation and the theoretical line is drawn for slopes of −1 changing to −2 at about 0.04 and 0.01 M iodide.

Evidence for carboxylic acid anhydride formation during the oxidation reaction was obtained by trapping the anhydride by reaction with aniline, as described by Gensch and co-workers.[1] The decrease in the aniline absorption at 280 nm is a direct measure of the anhydride that is present. For both concentrations of iodine that wee examined (Table II), the decrease in the aniline maximum was essentially identical with the decrease observed under the same conditions when iodine was omitted and comparable concentrations of acetic anhydride were added. Although it is possible that the acetanilide arises from direct acyl transfer

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[9] Daniele, G. *Gazz. Chim. Ital.* **1960**, *90*, 1096.

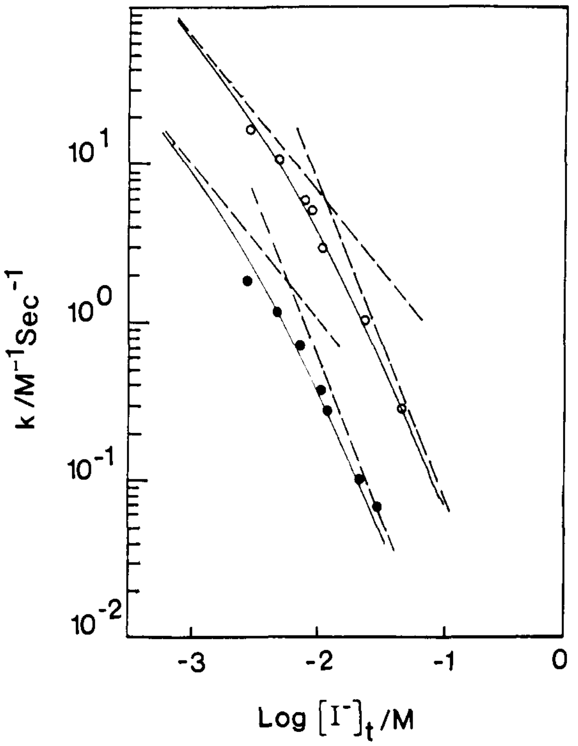


Figure 3. Double logarithmic plot of $k' = k_{obsd}[I^-]$ against iodide concentration. The dashed lines have slopes of −1 and −2; the solid line is calculated for the change in order occurring at 0.042 and 0.01 M. Concentrations: [NAME] = 1.67 × 10^{-3} M; $[I_2]$ = 1.67 × 10^{-5} M; acetic acid buffer, 90% base, 0.08 M (○) and 0.02 M (●). μ = 1.0; 25 °C.

Table II. Evidence for Anhydride Formation in the Carboxylate-Catalyzed Iodine Oxidation of *N*-Acetylmethionine Methyl Ester[a]

$[I_2]$ × 10^4, M	[NAME] × 10^3, M	[aniline] × 10^4, M	[acetic anhydride] × 10^4, M	ΔA_{280}
1.67	3.3	5.0		−0.051
3.3	3.3	5.0		−0.10
		5.0	1.67	−0.05
		5.0	3.3	−0.11

[a] Aqueous solution, 25 °C, ionic strength 1.0 with KCl, pH 5.28, 1.0 M acetate buffer. [b] Absorbance change at 280 nm as aniline is converted to acetanilide.

to aniline from the intermediate *O*-acylsulfoxide, the rate constant for the attck of aniline would have to be about 10^4 larger than the rate constant for attack of a carboxylate anion of roughly comparable pK_a. For acyl transfer from the 1-acetoxy-4-methoxypyridinium ion, a fair analogy for an *O*-acylsulfoxide, the second-order rate constants for acetate and aniline differ by only about 50-fold.[10]

Discussion

The upward curvature evident in plots of observed rate constants against total buffer concentration (Figure 1) requires a mechanism that is greater than first order with respect to buffer. The fact that second-order replots of the data curve downward, and eventually become buffer independent (Figure 2), requires a change in rate-limiting step in the buffer-catalyzed reaction. In Figure 4, observed rate constants for the acetate-catalyzed reaction are plotted on a double logarithmic scale (90% base, open symbols; 70% base, closed symbols). The data for acetate, 90% base, are readily described by the theoretical line with breaks from slopes of 1 to 2 and back to 1 as the concentration of buffer is increased. It should also be noted that the data are also quite nearly linear with an apparent slope of about 1.5, perhaps explaining earlier reports in which fractional orders were assigned to these reactions.[1,4] The data for acetate, 70% base (Figure 4), more clearly define the slope of unity at low buffer concentrations.

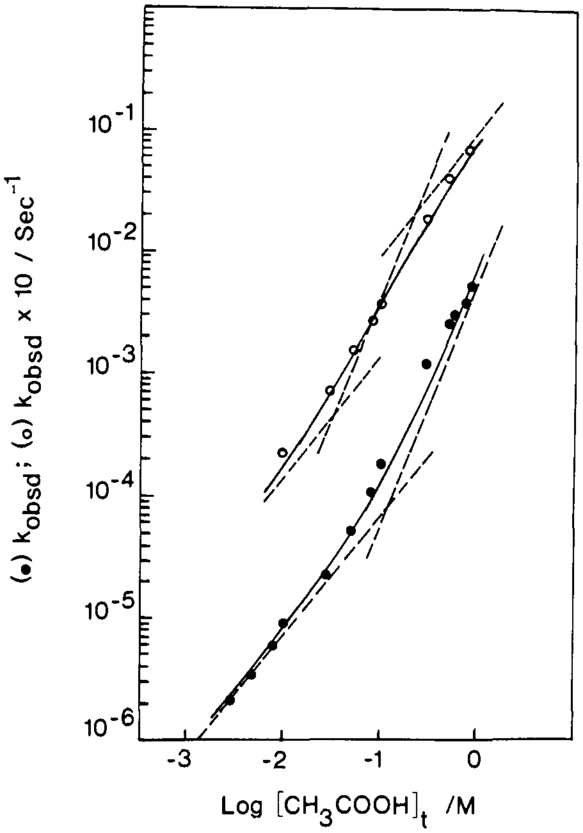
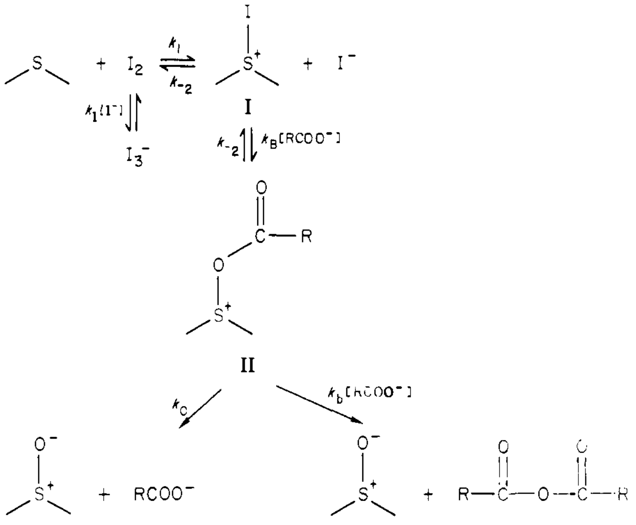


Figure 4. Double logarithmic plot of observed rate constants for the iodine oxidation of *N*-acetylmethionine methyl ester against the concentration of acetic acid buffers, (○) 90% base and (●) 70% base. Initial concentrations: [NAME] = 1.67 × 10^{-3} M; $[I_2]$ = 1.67 × 10^{-5} M; $[I^-]$ = 0.01 M. The ionic strength was 1.0 with KCl, 25°C. The dashed lines have slopes of 1 and 2, the solid lines are calculated for transitions of 1 to 2 to 1 (90% base) and 1 to 2 (70% base).

Scheme II



A mechanistic scheme that is consistent with the observed kinetic and analytical data is shown in Scheme II. Free iodine, in rapid equilibrium with I^-, reacts with the sulfide to form an intermediate iodosulfonium ion. The fact that the reaction order with respect to iodide ion inhibition approaches an inverse cubed dependence at $[I^-] \simeq 0.01$ M means that the initially formed iodosulfonium–iodide encounter pair must be sufficiently stable so that diffusion apart is both rapid and reversible. This is contrary

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(10) Jencks, W. P.; Gilchrist, M. *J. Am. Chem. Soc.* **1968**, *90*, 2622.

to the observed iodide dependence in the oxidation of both methionine[3] and *N*-acetylmethionine[11] where intramolecular cyclization reactions occur.

The observed first-order rate constant for the mechanism in Scheme II is given in eq 1.[12] Inspection of this equation verifys

$$k_{\mathrm{obsd}}/[\mathrm{NAME}] = \{k_1 k_{\mathrm{B}}[\mathrm{B}](k_{\mathrm{b}}[\mathrm{B}] + k_0)\}/\{K_{\mathrm{I}} k_{\mathrm{B}}[\mathrm{B}][\mathrm{I}^-] \times (k_{\mathrm{b}}[\mathrm{B}] + k_0) + K_{\mathrm{I}} k_{-1}[\mathrm{I}^-]^2(k_{\mathrm{b}}[\mathrm{B}] + k_0) + K_{\mathrm{I}} k_{-1} k_{-2}[\mathrm{I}^-]^3\} \quad (1)$$

the kinetic complexity of the oxidation reaction. Multiple changes in rate-limiting step are possible and can be induced by changing either iodide or buffer concentration. Thus, following the buffer dependence, at very low concentrations $k_{\mathrm{b}}[\mathrm{B}]$ will be less than the rate constant for the uncatalyzed hydrolysis of the intermediate *O*-acylsulfoxide (k_0) and the equation will simplify to eq 2. At

$$\frac{k_{\mathrm{obsd}}}{[\mathrm{NAME}]} = \frac{k_1 k_{\mathrm{B}}[\mathrm{B}] k_0}{K_{\mathrm{I}} k_{-1} k_0 [\mathrm{I}^-]^2 + K_{\mathrm{I}} k_{-1} k_{-2} [\mathrm{I}^-]^3} \quad (2)$$

$[\mathrm{I}^-] = 0.01$ M and [acetate buffer] < 0.05 M (pH 5.47; 90% base), the experimental buffer dependence approaches first order (Figure 4, open symbols). This is more evident in the data for 70% ionized acetate buffer, shown as the dark circles in this same figure.

The iodide dependence in this region of low buffer is also nonlinear, breaking from an inverse-squared to an inverse-cubed dependence as the iodide concentration is raised above about 0.01 M. According to eq 1, the observed first-order rate constants in this region can be described according to

$$\frac{k_{\mathrm{obsd}}}{[\mathrm{NAME}]} = \frac{k_1 k_{\mathrm{B}}[\mathrm{B}]}{K_{\mathrm{I}} k_{-1}[\mathrm{I}^-]^2} \quad (3)$$

at low iodide and changing to

$$\frac{k_{\mathrm{obsd}}}{[\mathrm{NAME}]} = \frac{k_1 k_{\mathrm{B}}[\mathrm{B}] k_0}{K_{\mathrm{I}} k_{-1} k_{-2}[\mathrm{I}^-]^3} \quad (4)$$

at higher concentrations of iodide anion.

As the buffer concentration is increased further, the upward curvature seen in the linear k_{obsd} vs. [buffer] plots (Figure 1) manifests itself as a region in which the buffer dependence approaches second order. This is clearly seen in the data for acetate, 70% base (Figure 4, closed symbols), and in the positive slopes of the second-order replots of data for propionate buffers at concentrations below 0.3 M in Figure 2. The experimental iodide dependence in this region is also nonlinear, being described by a transition from inverse squared at low concentrations (eq 3) to inverse cubed at high concentrations (>0.01 M, following eq 5).

$$\frac{k_{\mathrm{obsd}}}{[\mathrm{NAME}]} = \frac{k_1 k_{\mathrm{B}} k_{\mathrm{b}}[\mathrm{B}]^2}{K_{\mathrm{I}} k_{-1} k_{-2}[\mathrm{I}^-]^3} \quad (5)$$

As the buffer concentration is increased still further, eq 1 predicts a return to a first-order dependence. Experimentally, this is clearly demonstrated by the leveling observed in the second-order plots in Figure 2. The change in rate-limiting step is less evident, but nevertheless present, in the double logarithmic plots in Figure 4. Mechanistically, this changeover occurs when the buffer concentration becomes sufficiently large so that the partitioning of the *O*-acylsulfoxide (II) to give anhydride becomes significantly faster than the iodide reduction of this species (k_{-2}). When this occurs, the rate-limiting step becomes the formation of the *O*-acylsulfoxide and the observed rate constant becomes equal to eq 3 at low iodide and changes to eq 4 at higher iodide anion concentration.

The predicted changes in iodide dependence are consistent with the data in Figure 3, which is a double-logarithmic plot of $k_{\mathrm{obsd}}[\mathrm{I}^-]$ in the region of low buffer concentration. The solid lines are drawn for slopes of −1 changing to −2 at about 0.04 and 0.01 M potassium iodide.

Buffer plots such as those in Figure 2 can be analyzed in terms of the catalytic constants for the two buffer-mediated steps. The limiting value in Figure 2, when formation of *O*-acylsulfoxide is rate limiting, gives the term $K_1 k_{\mathrm{B}}$ for the given fraction base. Extrapolation of data such as these to 100% base gives the catalytic constants listed in Table I for propionic, acetic, benzoic, and glycolic acids. Since K_1, the equilibrium constant for iodosulfonium ion formation, should be a constant within the series, the pK_{a} dependence of these values describes the change in effective charge in the carboxylate anion upon reaching the transition state for the formation of the *O*-acylsulfoxide. This plot, shown in Figure 5, gives a value of $\beta_{\mathrm{nuc}} = 1.0$.

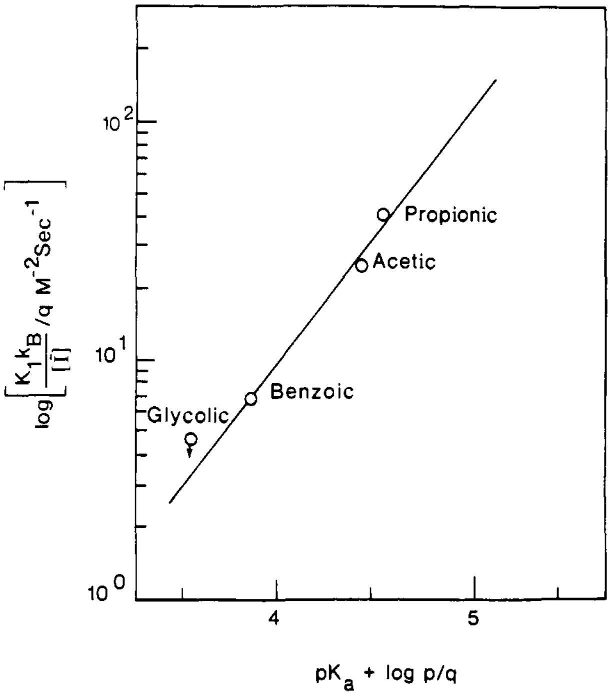

Figure 5. Brønsted plot of the catalytic constants obtained from the limiting rate constants in plots such as Figure 2; see eq 3. The point for glycolic acid is an upper limit.

The regions of positive slopes in Figure 2 give catalytic constants for the combined first- and second-order processes: slope = $(k_1 k_{\mathrm{B}} k_{\mathrm{b}}/k_{-1} k_{-2}[\mathrm{I}^-]^2)$. These slopes are second-order functions of the fraction of the buffer in the basic form. Thus, replots of slope/fraction of base vs. fraction of base are linear and give the values of $K_1 k_{\mathrm{B}} k_{\mathrm{b}}/k_{-2}$ listed in Table I. The pK_{a} dependence of these combined constants is shown in Figure 6; the slope, β_{nuc}, is equal to 1.5. Since the β_{nuc} for $K_1 k_{\mathrm{B}}$ is 1.0, the Brønsted coefficient for the (k_{b}/k_{-2}) term is 1.5 − 1.0 = 0.5.

The presence of the multiple changes in rate-limiting step that are observed in this reaction allow independent determinations of the partitioning coefficients for the various intermediates. The partitioning of the *O*-acylsulfoxide between deacylation by buffer and reduction by iodide anion can be most readily obtained from the position of the break in the iodide inhibition plot (Figure 3). At this break, $k_{\mathrm{b}}[\mathrm{B}] = k_{-2}[\mathrm{I}^-]$; the ratio k_{-2}/k_{b} is therefore about 20. Similar values can be obtained from buffer plots; when the buffer dependence changes from second to first order, $k_{\mathrm{b}}[\mathrm{B}]$ and $k_{-2}[\mathrm{I}^-]$ are again equal. Based on the data in Figure 4, the partitioning ratio is about 16. For all of the acetate data, the best value of this ratio seems to be about 18 ± 4. Values for this partition ratio for the remainder of the buffers used in these studies are collected in Table I. In a similar manner, the ratio k_{b}/k_0 can be estimated from buffer plots in regions where the buffer concentrations are small. These estimated values are also collected in Table I.

In order to fully evaluate the meaning of the Brønsted coefficients for the two steps in the reaction, it is necessary to know the equilibrium β for the formation of the *O*-acylsulfoxide intermediate. This value can be estimated from the data in Figures 5 and 6 by assuming that the β for the deacylation step is small. This seems likely since the substituent effect on the nucleophilicity

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(11) Young, P. R.; Hsieh, L.-S. *J. Org. Chem.*, in press.
(12) Gilbert, H. F. *J. Chem. Educ.* **1977**, *54*, 492.

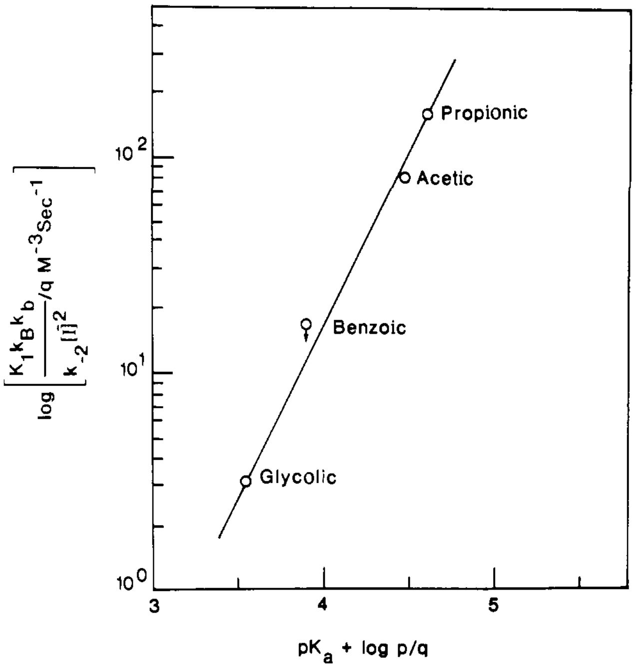
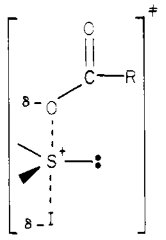


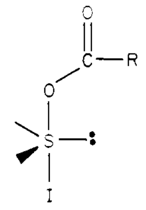
Figure 6. Brønsted plot of the catalytic constants obtained from the linear portion of curves such as those in Figure 2; see eq 5. The point for benzoic acid is an upper limit.

of the attacking carboxylate will roughly parallel the substituent effect on the reactivity of the *O*-acylsulfoxide, regardless of the exact nature of the transition state, as long as no serious charge imbalance is present.[14] If β_{nuc} for the k_b step is indeed small, then β_S for k_{-2} is about 1.0 − 1.5 = −0.5 and the equilibrium β for *O*-acylsulfoxide formation is 1.5. It should be pointed out that the k_{-2} step is the attack of iodide anion on the sulfur of an *O*-acylsulfoxide. Since *O*-acylsulfoxides are typically unstable compounds at room temperature, usually undergoing Pummerer-type rearrangements,[13] the reactivity of these compounds toward substitution at sulfur can only be studied under conditions such as these they are present only as short-lived reaction intermediates. The present data suggest that it will be possible to systematically study the reactivity of these compounds through the continued study of the catalyzed iodine oxidation reaction.

If β_{eq} for the formation of the *O*-acylsulfoxide intermediate is about 1.5, then it appears "as if" the carboxylate anion has had a change in effective charge from −1 to 0 in the rate-limiting transition state.[14] A possible transition state that is consistent with the experimental Brønsted coefficient is shown below (III).



III



IV

This transition state represents a simple S_N2 reaction in which bond formation to the sulfur is about 66% complete and the iodide anion has about 0.66 negative charge. Since complete formation of the oxygen-sulfur bond results in a change in effective charge of about 1.5, the carboxylate would appear as if it were neutral, consistent with the observed β_{nuc} of 1.0.

A second transition state that is consistent with the data is one involving, or closely resembling, a tetracoordinate sulfurane such as IV. Since the central sulfur in IV is neutral, the β_{eq} for sulfurane formation would be expected to be about 1. Since the observed value of β_{nuc} is 1.0, a transition state involving essentially complete sulfurane formation is consistent with the experimental data. It is also interesting to speculate that the rate-limiting step may involve a conformational change, perhaps pseudorotation[15,16] of a fully formed sulfurane intermediate. In order for pseudorotation to be a necesary process, the initially formed sulfurane must have entering and leaving groups positioned axial–equatorial. Such a geometry is certainly possible in these types of compounds since the electronegativities of carbon and iodine are approximately the same.

Acknowledgment. This work was supported by a grant from the National Science Foundation, CHE 80-00054.

Registry No. *N*-Acetylmethionine methyl ester, 35671-83-1; propionic acid, 79-09-4; acetic acid, 64-19-7; benzoic acid, 65-85-0; glycolic acid, 79-14-1; I_2, 7553-56-2.

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On the Rotation–Inversion Controversy on Photoisomerization of Azobenzenes. Experimental Proof of Inversion

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Abstract: We report on the direct cis–trans photoisomerization reaction of two azobenzenophanes for which inversion is the only possible isomerization pathway. Thermal cis–trans relaxation is also observed. For one of the azobenzenophanes we can determine trans–cis isomerization quantum yields which are wavelength independent in contrast to those of the parent azobenzene. On the basis of our results we suggest different isomerization mechanisms in different excited states for normal azobenzenes.

Ethylenes and diazenes (azo compounds) are textbook representatives for the phenomenon of cis–trans isomerism demonstrating the rotoresistant property of the π double bond. Cis and trans compounds are normally well-defined molecules which, however, can be interconverted either by heat or by light. There is no doubt that the weakening of the double bond by excitation

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