Table IV. Reaction Rate Constants for Pyrene Anions, P^-, with Acceptors

solute	homogeneous soln, $M^{-1}\ s^{-1}$	cationic micelle, $M^{-1}\ s^{-1}$
O_2	2.0×10^{10}	5.0×10^9
Eu^{3+}	2.7×10^9	1.3×10^7 (10^{-2} M CTAB)
MV^{2+}	2.6×10^{10}	3.3×10^7 (6×10^{-2} M CTAB) 1.8×10^7 (10^{-2} M CTAB)
cetylpyridinium chloride	2.6×10^{10}	10^7 (s^{-1}) [1st order decay]
CO_2	$\sim 10^7$	$\sim 10^7$

The data suggest that the initial electron transfer to pyrene takes place without restriction with regard to orientation of pyrene and amine. The back electron transfer however appears to be inefficient unless a significant overlap of pyrene anion and amine cation occurs, such as in an exciplex where a sandwich structure is formed. Delocalization of e^- over the pyrene ring structure hinders the back e^- transfer in other more random arrangements of the ions, such as occur in micelles, etc. Similar photo-"diode" effects are seen in systems where the donor and acceptor are joined by short methylene chains.[19]

Reactions of P^- in Micelles. Table IV shows the rate constants for reaction of P^- in CTAB micelles with CO_2, O_2, Eu^{3+}, methyl viologen, MV^{2+}, and cetylpyridinium chloride; the rate constants in homogeneous solutions of acetonitrile are also shown for comparison. In all cases the rates in homogeneous solution approach diffusion control and are $\sim 10^{10}\ M^{-1}\ s^{-1}$. The rate constant for reaction of P^- with O_2 is significantly decreased in CTAB micelles and is similar to the decreased rate of quenching of pyrene fluorescence by O_2 which is diffusion controlled in methanol but $5 \times 10^9\ M^{-1}\ s^{-1}$ in CTAB micelles.[20] This is interpreted as a decreased motion of O_2 due to the rigidity of the micellar environment.

Both Eu^{3+} and MV^{2+} show significantly decreased rates of reaction with P^- in CTAB micelles. This is not unexpected as these cations should be repelled by the positive potential of the micelle. The rates of reaction increased linearly with [cation] and are independent of [micelle] which indicates that these ions approach the micelle surface to react with P^-, rather than P^- exiting into the aqueous phase followed by an encounter with the cation.

Cetylpyridinium chloride, CP^+, is located in the micelle and the kinetic motion leading to a decreased yield of P^- is that of P^- and CP^+ on the micelle surface. The rate constant k_q is similar to that found for CP^+ quenching of excited pyrene on CTAB micelles ($k_q = 1.4 \times 10^7\ s^{-1}$)[11] and for pyrene excimer formation ($k = 5.0 \times 10^6\ s^{-1}$). These data suggest that P^- and CP^+ have to diffuse together on the micelle surface in order for the reverse e^- transfer process to occur. This process takes $\sim 10^{-7}$ s for P^- and a cation, which indicates that the DMA^+ exit rate from the CTAB micelles is much faster than 10^{-7} s. However, the rate of back reaction is not as rapid as that observed for P^- and DMA^+ in anionic NaLS micelles which occurs within 20 ns. This may be due to the higher mobility of DMA^+ on the micelle surface compared to CP^+, or to a tunneling of e^- from P^- back to DMA^+, a process which does not occur with CP^+ and P^-. There is some evidence to this effect for a rapid <1 ns back reaction of P^- and DMA^+ when linked together by a propyl chain.[19]

It is suggested that the above reactions are e^- transfer in nature. This was substantiated in the case of MV^{2+}, where the enhanced decay of P^- was matched by a concomitant rise of the reduced MV^{2+} observed at 6000 Å.

It is instructive to note that MV^{2+} quenches excited pyrene P^* with $k_q = 10^{10}\ M^{-1}\ s^{-1}$ in methanol and $5.0 \times 10^7\ M^{-1}\ s^{-1}$ in CTAB micelles. The decreased rate constant observed in CTAB compared to acetonitrile, 1/200, is close to that observed in similar experiments for the reaction of P^- and MV^{2+}. This also suggests that for reaction to occur, MV^{2+} approaches either P^- or P^* in the micelle surface. There is no evidence of e^- tunneling to MV^{2+}.

Conclusion

The present data show that photoinduced electron transfer occurs more efficiently in micellar systems where the more water soluble product is repelled from the micellar surface due to electrostatic repulsion of product and micelle. Location of the reactants away from the water-colloid interface leads to lower ion yields; lower yields also result from a decreased mobility of the ion fragments in the medium. Time-resolved studies indicate that the e^- transfer process with the original photoexcited pair and with subsequent ionic reactions is diffusion controlled. No evidence of transfer of e^- over large distances (>5 Å) is observed.

These data are helpful in constructing assemblies that may be used for efficient photoinduced e^- transfer reactions and photo-"diode" effects, leading to ionic products.

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(19) Eisenthal, K. *Acc. Chem. Res.* **1975**, *8*, 118.
(20) Thomas, J. K. *Acc. Chem. Res.* **1977**, *10*, 133.

Hydrolysis of 3-(*m*-Nitrophenyl)-3-methoxyphthalide

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South Orange, New Jersey 07079. *Received January 5, 1981*

Abstract: The hydrolysis of 3-(*m*-nitrophenyl)-3-methoxyphthalide to *o*-(*m*-nitrobenzoyl)benzoic acid is general-base catalyzed in acetate buffers at pH 4–6. The rate expression is: $k_{obsd} = 1.60 \times 10^{-6} + 6.38 \times 10^{-4}[H^+] + 2.08 \times 10^{-5}[^-OAc] + 49[^-OH]$. Entropies of activation are −26.6, −39.0, and −6.59 eu at pH 1.26, 5.08, and 7.70, respectively. The solvent isotope effect on the catalytic rate constant is 2.65. In acidic solution the reaction proceeds by an A1 mechanism, in basic solution, a $B_{AC}2$. The buffer catalysis is interpreted as general-base catalysis of nucleophilic attack by water on the carbonyl carbon.

Reactions of acyl compounds in aqueous solution provide many examples of how the reaction mechanism can change with subtle changes in structure or reaction conditions. In partial acylals, **1**, an "ester" carbonyl is combined with an "acetal" carbon atom. These compounds provide the interesting union of two functional groups each of which reacts readily in aqueous solution.

Salomaa[1] has shown that simple partial acylals react in aqueous acid as acetals do. That is, the mechanism is an acid-catalyzed unimolecular (A1) process. If the ester carbonyl is used as a point of reference this is an $A_{AL}1$ mechanism. Newman and Hishida[2]

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(1) Salomaa, P. *Acta Chem. Scand.* **1957**, *11*, 132, 141, 235.

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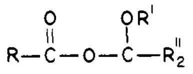
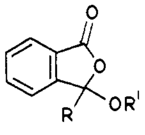
and Bhatt et al.[3] have studied the hydrolysis of the cyclic partial acylals, **2**, in aqueous base. The reaction occurs via a bimolecular attack of hydroxide ion on the ester carbonyl ($B_{AC}2$).



$$R-\overset{\overset{O}{\|}}{C}-O-\overset{\overset{OR'}{|}}{C}-R''_2$$

1



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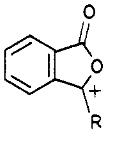
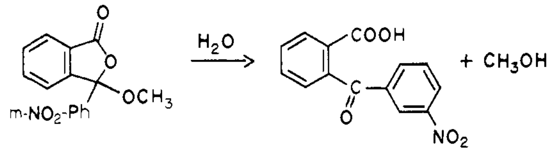


3

In acidic solutions compounds of the general structure **2** suffer hydrolysis via an A1 pathway involving rate-determining formation of the cyclic cation, **3**.[4] Compounds where R = H, alkyl, phenyl, and substituted phenyl fit this pattern. We report here an investigation of the hydrolysis of 3-(*m*-nitrophenyl)-3-methoxyphthalide (**4**) to *o*-(*m*-nitrobenzoyl)benzoic acid (**5**) in dilute aqueous solutions from pH 1.3–7.9.



4 **5**

Experimental Section

Melting points were taken on a Thomas Hoover apparatus and are uncorrected. Infrared spectra were taken on a Perkin-Elmer Model 567 and NMR spectra were recorded on a Varian T-60. Ultraviolet spectra and kinetics measurements were run by using a Beckman Acta, DU, or DB-GT Spectrophotometer. Acetonitrile was spectral grade and used without further purification. Measurements of pH were taken on a Fisher Model 610. Doubly distilled water was used throughout.

3-(*m*-Nitrophenyl)-3-methoxyphthalide (4) was prepared from *o*-(*m*-nitrobenzoyl)benzoic acid[5] by the method described for 3-phenyl-3-methoxyphthalide[6] and recrystallized from methanol: mp 127–128.5 °C; IR (Nujol) 1775 cm^{-1}; NMR (acetone-d_6) δ 7.5 (m, 8), 2.82 (s, 3).

Anal. Calcd for $C_{15}H_{11}O_5N$: C, 63.16; H, 3.89; N, 4.91. Found: C, 63.12; H, 3.93; N, 4.80.

Kinetics Methods. Reactions were followed by measuring the increase in absorbance due to the product at 235 or 250 nm. Ionic strength (μ) was maintained at 0.300 with KCl for all runs. In a typical run 48.5 mL of buffer was equilibrated at 70.0 ± 0.1 °C for at least 1 h. A stock solution (1.5 mL) of **4** in acetonitrile was added and mixed. The concentration of **4** was about 3×10^{-5} M and solutions contained 5% acetonitrile. Aliquots of about 2 mL were removed at appropriate times, immediately cooled in ice, and analyzed. Rate constants were obtained by plotting log ($A_\infty - A_t$) vs. time. The reactions were followed for at least 2 half-lives in most cases. Correlation coefficients (r) were always better than 0.994. The values of A_∞ were determined after 10 half-lives and were stable. For very slow reactions rate constants were determined by using a modified Guggenheim method.[7] The validity of this method was checked periodically by following the reaction to 5 half-lives and adding 3.1% of the total absorbance change to obtain A_∞. Measurements of pH were taken at room temperature and adjusted to 70 °C when necessary.[8a] Hydroxide ion concentrations were obtained by using the adjusted pH and K_w values of 13.03, 12.82, and 12.63 for 60, 70, and 80 °C, respectively.[8b]

Table I. Hydrolysis of 3-(*m*-Nitrophenyl)-3-methoxyphthalide. The Effect of Buffer Concentration

pH	[A$^-$], M	$10^6 k_{obsd}$,[a] s^{-1}	$10^5 k_{cat.}$,[b] M^{-1} s^{-1}	$10^6 k_0$,[c] s^{-1}
		[HOAc]/[$^-$OAc] = 1.00		
4.61	0.300	8.54 ± 0.36	1.02	2.42
	0.150	5.37 ± 0.16		
	0.075	4.00 ± 0.01		
		[HOAc]/[$^-$OAc] = 0.333		
5.08	0.300	8.80 ± 0.10	1.54	2.81
	0.200	6.97 ± 0.25		
	0.100	4.76 ± 0.04		
		[HOAc]/[$^-$OAc] = 0.282		
5.15	0.300	9.28 ± 0.07	1.66	2.91
	0.200	7.33 ± 0.04		
	0.150	5.86 ± 0.20		
	0.075	4.59 ± 0.04		
		[HOAc]/[$^-$OAc] = 0.143		
5.45	0.300	9.83 ± 0.27	1.82	3.78
	0.150	7.20 ± 0.01		
	0.075	5.14 ± 0.07		
		[$H_2PO_4^-$]/[HPO_4^{2-}] = 0.235		
7.35	0.100	148 ± 3		
	0.050	127 ± 1		
	0.025	124 ± 5		

[a] All rate constants are the average of at least two runs; $T = 70$ °C, $\mu = 0.300$ (KCl), pH was ±0.02. [b] Obtained from a plot of k_{obsd} vs. [buffer]. [c] Obtained by extrapolation of k_{obsd} to zero buffer concentration.

Table II. Hydrolysis of 3-(*m*-Nitrophenyl)-3-methoxyphthalide. The Effect of Temperature

pH	T, °C	$10^6 k_{obsd}$,[a] s^{-1}
1.26	60.0	17.5 ± 0.1
	70.0	36.8 ± 0.9
	80.0	86.9 ± 1.5
$\Delta H^\ddagger$ = 18.0 kcal/mol		$\Delta S^\ddagger$ = −26.6 eu
5.08	60.0	4.17 ± 0.12
	70.0	8.80 ± 0.10
	80.0	15.9 ± 0.1
$\Delta H^\ddagger$ = 14.8 kcal/mol		$\Delta S^\ddagger$ = −39.0 eu
7.70	60.0	113 ± 3
	70.0	332 ± 19
	80.0	889 ± 16
$\Delta H^\ddagger$ = 23.4 kcal/mol		$\Delta S^\ddagger$ = −6.59 eu

[a] All rate constants are the average of at least two runs.

Product Analysis. The product of hydrolysis was identified as **5** in two ways. First, the substrate, **4** (0.45 g), was dissolved in 70 mL of 6 M HCl and refluxed for 4 h. Crude product was obtained in 94% yield and was completely soluble in aqueous base. The IR spectrum of the crude material matched that of genuine **5**. After one recrystallization from 80% acetic acid the mp was 184.5–186 °C [lit.[5] 184–186 °C]. Second, a solution of **4** (3.00×10^{-5} M) was hydrolyzed in a pH 10 (5% acetonitrile) solution for several hours at 70 °C. The UV spectrum of the resulting solution was identical with that of a 3.00×10^{-5} M solution of genuine **5**.

Results

Pseudo-first-order rate constants, k_{obsd}, for the hydrolysis of 3-(*m*-nitrophenyl)-3-methoxyphthalide in various buffer solutions are plotted vs. pH in Figure 1. We surmised from the discontinuity in the pH–rate profile that a component of the buffer was catalyzing the hydrolysis. Data in Table I are from a study of the effect on rate of varying the concentration of the buffer at constant pH, temperature, and ionic strength. These data show that between pH 4.61 and 5.45 the reaction is buffer catalyzed. At pH 7.35 and higher no buffer catalysis is evident. Previous work[6] has shown no detectable buffer catalysis of the hydrolysis of 3-phenyl-3-methoxyphthalide at pH 2.00.

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(2) Newman, M.; Hishida, S. *J. Am. Chem. Soc.* **1962**, *84*, 3582.

(3) Bhatt, M. V.; Rao, K. S.; Rao, G. V. *J. Org. Chem.* **1977**, *42*, 2687.

(4) (a) Weeks, D.; Crane, J. *J. Org. Chem.* **1973**, *38*, 3375. (b) Weeks, D.; Cella, J.; Chen, L. T. *J. Org. Chem.* **1973**, *38*, 3383.

(5) Rainer, M. *Ber.* *29*, 180.

(6) Weeks, D.; Grodski, A.; Fanucci, R. *J. Am. Chem. Soc.* **1968**, *90*, 4958.

(7) Swinbourne, E. S. *J. Chem. Soc.* **1960**, 2371.

(8) (a) Perrin, D. D.; Dempsey, B. "Buffers for pH and Metal Ion Control"; Chapman and Hall: London, 1974; Chapter 2. (b) "International Critical Tables"; McGraw-Hill: New York, 1929; Vol. 6, p 152.

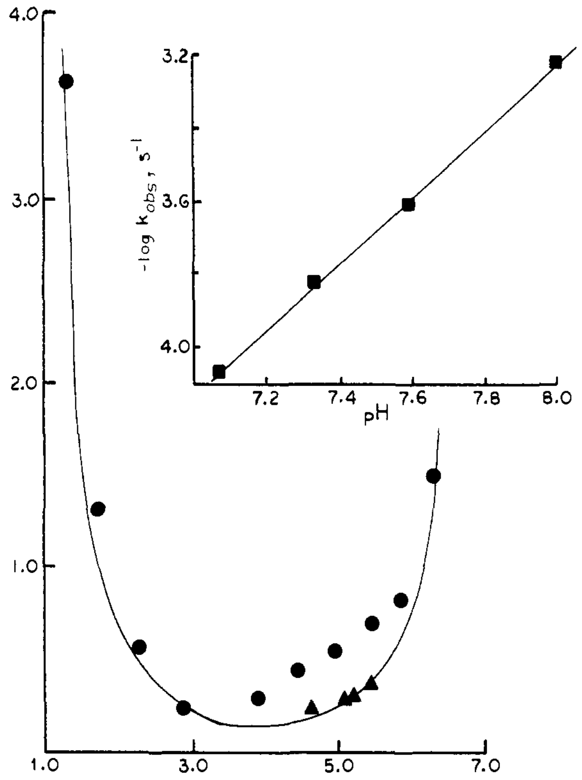


Figure 1. Hydrolysis of 3-(*m*-nitrophenyl)-3-methoxyphthalide; plot of k_{obsd} (●) and k_0 (▲) against pH. The calculation of the line is described in the text. The insert shows a continuation of the plot above pH 7; plot of log k_{obsd} against pH. The buffers were HCl/KCl below pH 2.25, HOAc/NaOAc from pH 2.8–6.0, and NaH_2PO_4/Na_2HPO_4 above pH 6.2. The temperature was 70 °C. All rate constants are the average of at least two runs. $\mu = 0.30$ (KCl).

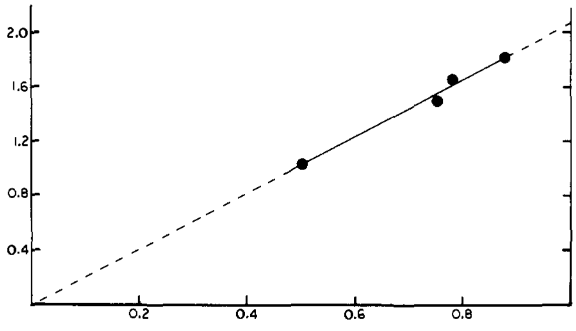


Figure 2. Hydrolysis of 3-(*m*-nitrophenyl)-3-methoxyphthalide; plot of the apparent catalytic rate constant, k_{cat}, against the fraction of free base in the buffer solutions.

A plot of k_{obsd} vs. [$^-$OH] at pH 7.07–7.91 is linear giving $k_{^-OH} = 49$ M^{-1} s^{-1}. A plot of k_{obsd} vs. [H^+] at pH 1.26–2.24 is linear giving $k_{H^+} = 6.38 \times 10^{-4}$ M^{-1} s^{-1}. A value for the rate constant of the uncatalyzed reaction was calculated from data on the acid and on the base side of the pH–rate profile giving $k_{H_2O} = (1.6 \pm 0.2) \times 10^{-6}$ s^{-1}.

In Figure 2 the apparent catalytic rate constants, k_{cat}, determined at various pH values are plotted against the fraction of free base in the buffers. The intercept at the fraction of free base equal to 1.0 is $k_{^-OAc}$ and the fact that the extrapolated line goes through the origin at the fraction of free base equal to 0 indicates no catalysis by the acidic component of the buffer, viz., acetic acid. The rate expression for the hydrolysis of 4 is:

$$k_{obsd} = 1.6 \times 10^{-6} + 6.38 \times 10^{-4}[H^+] + 2.08 \times 10^{-5}[^-OAc] + 49[^-OH] \quad (1)$$

The line in Figure 1 is calculated from eq 1 omitting the term for catalysis by acetate ion. Note that the points for k_0 (the observed rate constant extrapolated to zero buffer concentration) fall on this line.

Table III. Hydrolysis of 3-(*m*-Nitrophenyl)-3-methoxyphthalide in Deuterium Oxide. The Deuterium Oxide Solvent Isotope Effect on Acetate Catalysis[a]

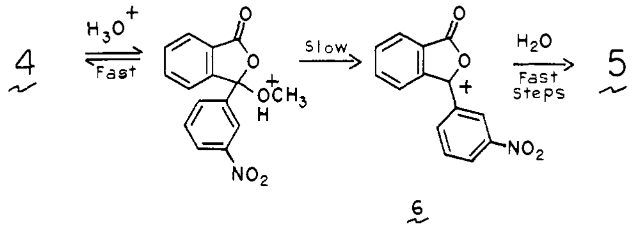
[$^-$OAc], M	$10^6 k_{obsd}$, s^{-1}
[DOAc]/[$^-$OAc] = 0.143	
0.300	4.80
0.150	3.75
0.075	3.00

$k_{cat.}(D_2O) = 6.87 \times 10^{-6}$ M^{-1} s^{-1}

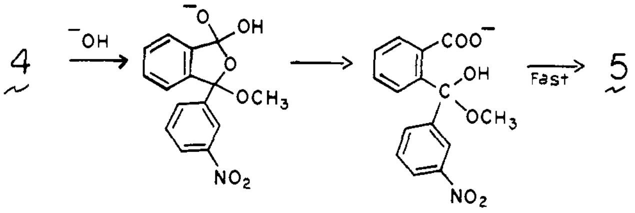
$k_{cat.}(H_2O)^b/k_{cat.}(D_2O) = 1.82 \times 10^{-5}/6.87 \times 10^{-6} = 2.65$

[a] $T = 70$ °C, $\mu = 0.300$ (KCl). [b] This is $k_{cat.}$ at [HOAc]/[$^-$OAc] = 0.143 (see Table II).

Scheme I



Scheme II



The rate of hydrolysis of 4 was studied as a function of temperature at pH 1.26, 5.08, and 7.70. Rate constants are listed in Table II along with the activation parameters calculated from these data. Since the entropy of activation of the buffer-catalyzed reaction is important to this work we subtracted k_{OH} from k_{obsd} at pH 5.08 and found the entropy of activation to be −41.7 eu. The contribution from k_{H_2O} to k_{obsd} at this pH is less than 20%. Thus, the entropy of activation calculated from k_{obsd} at pH 5.08 is representative of that for the buffer-catalyzed reaction. The deuterium oxide solvent isotope effect on the catalytic rate constant was determined. The results appear in Table III.

Discussion

In aqueous solutions more acidic than pH 2.5 the hydrolysis of 4 occurs by an A1 process (Scheme I) analogous to that described for other 3-methoxyphthalides.[4] Results in this work which support an A1 mechanism are log k_{obsd} is linear with [H^+] and activation parameters at pH 1.26 (Table II) are very similar to those determined for comparable compounds in earlier studies. For example, 6-nitro-3-phenyl-3-methoxyphthalide hydrolysis has $\Delta H^{\ddagger} = 15.3$ kcal/mol and $\Delta S^{\ddagger} = -27.8$ eu[4b] compared with 18.0 kcal/mol and −26.6 eu in this work. It is unlikely that the hydrolysis of 4 would be general-acid catalyzed at low pH since 3-phenyl-3-methoxyphthalide hydrolysis is not subject to buffer catalysis.[6,9] That is, the presence of the *m*-nitro group in 4 will make the cyclic cation, 6, *less* stable than the same cation from the unsubstituted compound but observation of general-acid catalysts occurs only for acetals which form especially stable cations.[10]

In aqueous solutions more basic than pH 7 the hydrolysis of 4 occurs via a $B_{AC}2$ process (Scheme II) like that described for

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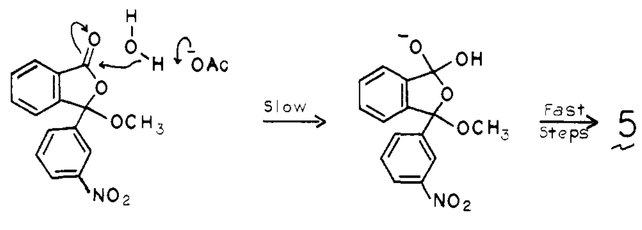
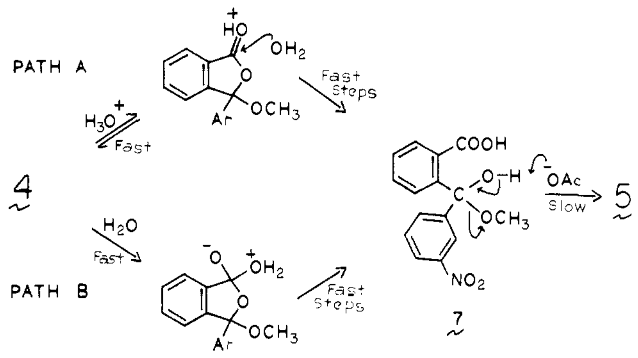
[9] We have determined that 3-phenyl-3-methoxyphthalide hydrolysis does not show buffer catalysis at pH 4.61.

[10] Fife, T. H. *Acc. Chem. Res.* **1972**, *5*, 264.

Scheme III



Scheme IV



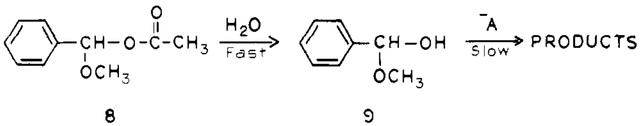
other 3-methoxyphthalides.[2,3] Support for this is that log k_{obsd} is linear with [^-OH] and no buffer catalysis is observed. The anomalously high value of the entropy of activation (−6 eu) is puzzling. Bimolecular reactions usually have entropies of activation in the range of −15 to −25 eu.[11] Bhatt[3] has determined a value of −19 eu for this reaction but his studies were carried out in 70% dioxane. The high value of $\Delta S^{\ddagger}$ may result from a rate-determining ring opening. We plan further study in this area.

The hydrolysis of **4** in solutions of pH 3–6 is the main point of interest in this study. We assert that the experimental evidence supports the mechanism in Scheme III and that the other possible mechanisms are unlikely (vide infra).

The mechanism in Scheme III is general-base catalysis of nucleophilic attack by water on the ester carbonyl. It is consistent with the observation of catalysis by only the basic component (^-OAc) of the buffer solutions. The very low value of the entropy of activation (−39 eu) is accounted for by the large degree of organization required in the transition state of the slow step. Bruice and Benkovic[11] found entropies of activation of about −40 eu for several ester hydrolysis reactions involving general-base catalysis of nucleophilic attack. A deuterium oxide solvent isotope effect of 2.65 is indicative of proton transfer in the transition state. Indeed, the experimental evidence is in complete agreement with that presented for this mechanism by Jencks.[12]

There are several other mechanisms which must be considered for the hydrolysis of **4** between pH 3 and 6. For example, a direct nucleophilic attack by acetate ion on the ester carbonyl might lead to an intermediate more susceptible to hydrolysis than the starting material. This type of nucleophilic catalysis is observed for *p*-nitrophenyl acetate hydrolysis catalyzed by imidazole.[13] This mechanism is not suitable for the hydrolysis of **4** since nucleophilic catalysis seems to require the presence of a good leaving group to activate the acyl compound,[14] a feature which is absent in **4**. The observation of a sizable deuterium oxide solvent isotope effect in this work rules out nucleophilic catalysis since no proton transfer occurs in the transition state of such a process. In addition, an entropy of activation of −39 eu seems too highly negative for a simple bimolecular mechanism.[11]

In Scheme IV are shown two mechanisms which involve slow decomposition of the hemiacetal, **7**, formed from **4** in a series of rapid steps. These are considered in view of recent findings of Capon[15] and of Jensen[16] that such mechanisms do occur. Capon studied the hydrolysis of α-methoxybenzyl acetate (**8**) at pH 3.7–6.3. He found catalysis by the basic component of the buffer and a surprisingly rapid rate of hydrolysis. He proposed a rapid, uncatalyzed reaction to the hemiacetal, **9**, followed by slow decomposition of **9** to product. Jensen, studying benzaldehyde acetals, proposed that the initial portion of the hydrolysis occurred via rate-determining decomposition of the hemiacetal. His conclusions were supported by the observation of a reproducible induction time and a pH–jump experiment in which he observed a continuation of product formation for a short time after the acetal hydrolysis had been quenched with base.[17] Both of these observations indicate the accumulation of an intermediate.



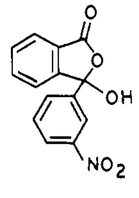
$$C_6H_5-\underset{OCH_3}{\underset{|}{CH}}-O-\overset{O}{\overset{\|}{C}}-CH_3 \xrightarrow[\text{Fast}]{H_2O} C_6H_5-\underset{OCH_3}{\underset{|}{CH}}-OH \xrightarrow[\text{Slow}]{^-A} \text{PRODUCTS}$$

8 **9**

Several considerations make the mechanisms in Scheme IV unlikely in this case. Each would require rapid ring opening of a neutral or positively charged intermediate but evidence from the study of the hydrolysis of these compounds in aqueous acid strongly suggests that the ring is a stable entity.[4a] The most reasonable route from **4** to **7** would involve initial (rapid) protonation followed several steps later by rate-determining proton abstraction from **7** by acetate ion (path A). This would be specific hydronium ion–general base catalysis and, while it would account for buffer catalysis, it would require a catalytic term for the acidic component of the buffer. We observe no catalysis of this sort.

Uncatalyzed ring opening to **7** followed by general-base catalysis (path B) would obey the kinetics observed. We reject this possibility on the grounds that the reactions cited by Capon[15] proceed at a convenient rate at 15 °C with $k_{cat.} = 0.18\ M^{-1}\ s^{-1}$. Compound **4**, in this work, undergoes reaction very slowly even at 70 °C with $k_{cat.} = 1.66 \times 10^{-5}\ M^{-1}\ s^{-1}$. Capon saw no evidence for a change in mechanism from pH 3.7 to 6.3 while we do. These differences indicate that the two reactions are not mechanistically similar. Capon predicts that methoxyphenylphthalides like **4** *will not* build up significant amounts of hemiacetal. Jensen[18] also feels that hemiacetal buildup will not occur for systems like **4**. He concludes that above pH 4 the base-catalyzed rate of decomposition of hemiacetal is very large.[16]

Brief consideration must be given to a mechanism in which the slow step is the general-base-catalyzed decomposition of the pseudoacid, **10**, which is the ring tautomer of the product. We rule out this mechanism because cases in which it has been observed always involve rapid formation of the cation, in this case **6**, made possible by the combination of a good leaving group and a stable cation neither of which is found here.[19]



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[17] A pH–jump experiment would not work in this case because **4** suffers very rapid hydrolysis via a different mechanism at higher pH.

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[19] A referee has noted that an absence of a lag time in the first-order kinetic plot is evidence against this possibility.