and x and x' represent the number of carbon atoms in the alkylammonium and in the carboxylate group, respectively) is obeyed (Figure 3). From the slopes of these lines (a and b in eq 2 and 3), it is evident that changes in the chain length of the carboxylate and in the alkylammonium groups affect the micellar catalysis to the same extent. From the intercepts we calculate $k_m^{P^-} = 4.57 \times 10^{-4}$ sec^{-1} and $k_m^{OA^+} = 6.92 \times 10^{-4}$ sec^{-1}.

Equations analogous to eq 2 and 3 can be written for the dependency of $(k_{RNH_3^+} + k_{^-O_2CR'})$ on increasing chain length of alkylammonium propionates (eq 4)

$$\log (k_{RNH_3^+} + k_{^-O_2CR'})^{RNH_3^+P^-} = \log k_{P^-} + ax \qquad (4)$$

and octylammonium carboxylates (eq 5) (where k_{P^-}

$$\log (k_{RNH_3^+} + k_{^-O_2CR'})^{OA^+\ ^-O_2CR'} = \log k_{OA^+} + bx' \qquad (5)$$

and k_{OA^+} are the rate constants for the general base catalyzed reaction due to the propionate ion and for the general acid catalyzed reaction due to the octylammonium ion, respectively; and x and x' represent the number of carbon atoms in the alkylammonium and the carboxylate groups, respectively). Plots of the data according to eq 4 and 5 yielded good straight lines (Figure 2). It is evident that general acid catalysis is more powerful than general base catalysis. Changes in the rate per carbon atom are more than twice as great for the alkylammonium propionate series than for the octylammonium carboxylates. A qualitatively similar trend is observed for the general acid and base catalyzed hydrolyses of sulfate esters in aqueous solutions.[9,10] The values of k_{P^-} and k_{OA^+} calculated from the intercepts are 4.57×10^{-4} and 2.89×10^{-3} M^{-1} sec^{-1}.

It is difficult to compare enthalpies and entropies of activation for the reaction of DAP as a general acid and a general base (Table III) directly with those obtained for the other systems, since the values for the former were obtained from composite second-order rate constants. Nevertheless, this process appears to be energetically less favorable than hydrolysis in pure water.

Acknowledgments.—This work was supported, in part, by grants from the Robert A. Welch Foundation (to J. H. F.) and the Research Corporation (to E. J. F.). C. J. O'Connor gratefully acknowledges study leave from the University of Auckland, New Zealand, a Fulbright-Hays Travel Award, and an AAUW Fellowship. E. J. Fendler is a Career Development Awardee of the National Institutes of Health, U. S. Public Health Service.

Registry No.—2,4-Dinitrophenyl sulfate, 17396-93-9.

The Hydrolysis of 3-Methoxyphthalides in Aqueous Acid. The Effect of Substituents in the 3 Position[1,2]

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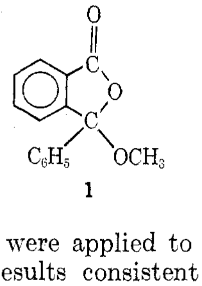
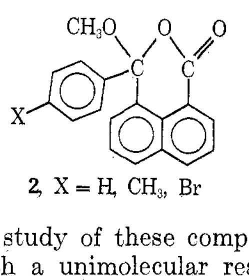
The hydrolysis of a series of 3-methoxy 3-substituted phthalides in aqueous sulfuric acid has been studied. At ~1 M acid concentration the substituents establish a relative rate order of H > CH_3 > C_6H_5 > C_2H_5 > α-naphthyl > i-C_3H_7. 3-Methoxyphthalide itself exhibits behavior consistent with a unimolecular hydrolysis mechanism when various empirical criteria such as the Zucker–Hammett hypothesis, entropy of activation, and deuterium oxide solvent isotope effect are applied. The behavior of the other compounds tends to depart from that expected from a unimolecular mechanism but can be reconciled with a unimolecular process in terms of a restriction of rotation as the molecule approaches the transition state leading to a cationic intermediate.

The hydrolysis of 3-methoxy-3-phenylphthalide[3] (**1**) in aqueous sulfuric acid exhibits anomalous behavior with respect to the various criteria generally used to determine the mechanisms of hydrolysis reactions in moderately concentrated mineral acid.[4] The entropy of activation (ΔS^*) was −19.4 eu, which indicated a bimolecular (A2) mechanism. However, application of the Zucker–Hammett hypothesis, the Bunnett w parameter, and the deuterium oxide solvent isotope effect all gave equivocal results. Conversely, the effect on rate of substituents in the para position of the 3-phenyl ring[5] correlated very well with σ^+ which result tends to implicate a unimolecular (A1) reaction involving a cationic intermediate at the 3 position.

These puzzling results contrast strikingly with those from the acid-catalyzed hydrolysis of 3-methoxy-3-arylperinaphthalides[6] (**2**). All of the empirical criteria



1



2, X = H, CH_3, Br

which were applied to the study of these compounds gave results consistent with a unimolecular reaction mechanism.

We now report the results of a study of a series of 3-methoxy 3-substituted phthalides. We believe that these results provide greater understanding of the confusing behavior of **1** and also reveal an important in-

(1) Taken from the Ph.D. Dissertation submitted by J. P. C. to Seton Hall University, 1970.

(2) Presented, in part, at Metrochem 69 Regional Meeting of the American Chemical Society, New York, N. Y., May 1969, Abstracts, p 41.

(3) In earlier publications we have named this compound as methyl pseudo-2-benzoylbenzoate. We have found that this nomenclature is unwieldy and confusing. In this and subsequent reports we shall name these compounds as phthalides.

(4) D. P. Weeks, A. Grodski, and R. Fanucci, *J. Amer. Chem. Soc.*, **90**, 4958 (1968).

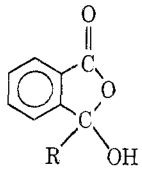
(5) D. P. Weeks and J. Cella, Abstracts, 3rd Middle Atlantic Regional Meeting of the American Chemical Society, Philadelphia, Pa., Feb 1968, No. H-58.

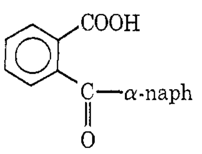
(6) D. P. Weeks and G. W. Zuorick, *J. Amer. Chem. Soc.*, **91**, 477 (1969).

sight into a limitation of several of the empirical criteria.

Results

The 3-methoxyphthalides were prepared by esterification of the appropriate *o*-ketobenzoic acids. These acids take the cyclic (lactol) form. The one compound in this work which takes the keto acid form is *o*-α-naphthoylbenzoic acid (**7**). Compounds **3** and **4** were commercially available. Compounds **5**, **6**, and **7** were prepared by allowing phthalic anhydride to react with the appropriate organocadmium. Information on the synthesis and physical properties of the *o*-ketobenzoic acids is given in Table I. Spectral data are presented in Table II.


3, R = H
4, R = CH_3
5, R = C_2H_5
6, R = *i*-C_3H_7


7

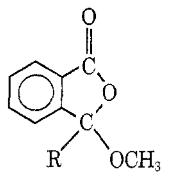

8, R = H
9, R = CH_3
10, R = C_2H_5
11, R = *i*-C_3H_7
12, R = α-naphthyl

TABLE I

SYNTHESIS AND PHYSICAL PROPERTIES OF *o*-KETOBENZOIC ACIDS

Compd (3 Substituent)	Ref	Yield,[a] %	Mp,[b] °C	Analysis,[c] % Calcd	Found
3 (H)	*d*		97.5–99 Lit.[e] 99		
4 (CH_3)	*d*		115–116 Lit.[f] 117.5		
5 (C_2H_5)	*g*	21	88–90 Lit.[g] 85–88	C 67.41 H 5.66	67.36 5.53
6 (*i*-C_3H_7)	*g*	14	118–120 Lit.[h] 120–121	C 68.74 H 6.29	68.66 6.47
7 (α-naphthyl)	*g*	45	171–173 Lit.[g] 170–171	C 78.25 H 4.38	78.27 4.54

[a] After recrystallization to constant melting point. [b] Uncorrected. [c] Microanalysis by Alfred Bernhardt (Germany) or George Robertson, Florham Park, N. J. [d] Aldrich Chemical Co., Inc. [e] E. Bernatik, *Acta Chem. Scand.*, **14**, 785 (1960). [f] E. T. Harper and M. L. Bender, *J. Amer. Chem. Soc.*, **87**, 5625 (1965). [g] P. L. deBenneville, *J. Org. Chem.*, **6**, 462 (1941). [h] R. L. Letsinger and W. J. Vullo, *ibid.*, **25**, 1844 (1960).

The 3-methoxyphthalides where R = methyl and α-naphthyl (**9** and **12**) were prepared by treatment of the *o*-ketobenzoic acid with thionyl chloride followed by reaction with dry methanol containing 1 equiv of urea.[7] The others (**8**, **10**, and **11**) were prepared by allowing the keto acid to reflux in methanol which had been saturated with dry hydrogen chloride. The phthalides were separated from their isomers, the methyl *o*-ketobenzoates, by fractional crystallization. Data on the synthesis and physical properties of the phthalides are contained in Table III, and spectral data in Table IV. Two 3-methoxyphthalides and their corresponding acids, in addition to those described here, *viz.*, R = CH_2Br and R = CH_2Ph, were prepared. However, the hydrolysis of these compounds could not be followed, since there was no detectable change in the ultraviolet region as the hydrolysis reaction proceeded.

TABLE II

SPECTRAL PROPERTIES OF *o*-KETOBENZOIC ACIDS

Compd (3 Substituent)	Infrared,[a] cm^{-1} OH	C=O	Ultraviolet,[b] nm (ε)	Chemical shift,[c] ppm (mult, no.)
5 (C_2H_5)	3310	1740	281 (1200)	0.92 (t, 3, *J* = 7.5 Hz)
			287 (1100)	2.26 (m, 2, *J* = 7.5 Hz)
				4.92 (s, 1)
				7.36–8.00 (m, 4)
6 (*i*-C_3H_7)	3310	1740	233 (9500)	0.92 (d, 3, *J* = 7 Hz)
			276 (1250)	1.07 (d, 3, *J* = 7 Hz)
			283 (1200)	2.44 (m, 1)
				4.34 (s, 1)
				7.50–8.05 (m, 4)
7 (α-naphthyl)	3050	1680	323 (74,000)	7.28–8.00 (m, 11)
		1662		9.65 (s, 1)

[a] Nujol mulls. [b] In 1 *M* aqueous sulfuric acid. [c] 10% in $CDCl_3$.

TABLE III

SYNTHESIS AND PHYSICAL PROPERTIES OF 3-METHOXYPHTHALIDES

Compd (3 Substituent)	Ref	Yield,[a] %	Mp,[b] °C	Analysis,[c] % Calcd	Found
8 (H)	*d*	50	44–45 Lit.[d] 42–44	C 65.85 H 4.91	65.86 5.04
9 (CH_3)	*e, f*	18	44–45.5	C 67.41 H 5.66	67.54 5.59
10 (C_2H_5)	*g*	19	49–51 Lit.[h] 51–52	C 68.74 H 6.29	68.99 6.20
11 (*i*-C_3H_7)	*g*	22	47–49	C 69.89 H 6.84	70.04 6.99
12 (α-naphthyl)	*e, f*	48	131–134	C 78.61 H 4.86	78.44 4.94

[a] After recrystallization to constant melting point. [b] Uncorrected. [c] Microanalysis by Alfred Bernhardt (Germany) or George Robertson, Florham Park, N. J. [d] M. L. Bender, J. A. Reinstein, M. S. Silver, and R. Mikulak, *J. Amer. Chem. Soc.*, **87**, 4545 (1965). [e] M. S. Newman and L. K. Lala, *Tetrahedron Lett.*, 3767 (1967). [f] M. S. Newman and C. D. McCleary, *J. Amer. Chem. Soc.*, **63**, 1537 (1941). [g] K. W. Kohlransch and R. Seka, *Chem. Ber.*, **77**, 469 (1944). [h] L. K. Cresmer, A. Fischer, and J. Vaughan, *J. Chem. Soc.*, 2141 (1962).

Rate constants for the hydrolysis of the 3-methoxyphthalides to the keto acids were determined in various aqueous sulfuric acid solutions and are shown in Table V. Rate constants at 0.97 *M* sulfuric acid have been determined for all phthalides studied. A relative rate order of H > CH_3 > C_6H_5 > C_2H_5 > α-naphthyl > *i*-C_3H_7 has been established. Plots of the logarithms of the pseudo-first-order rate constants against the acidity function, H_0 (Zucker–Hammett hypothesis)[8] appear in Figure 1. One can see that each compound gives an excellent linear correlation. The slopes of these lines are given in Table VI. When one treats these data according to the Bunnett *w* parameter[9] the lines are severely curved, as was the line established by **1**.[4]

Activation parameters for these hydrolysis reactions and the data from which they were determined are

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[7] M. S. Newman and L. K. Lala, *Tetrahedron Lett.*, 3267 (1967).

[8] L. Zucker and L. P. Hammett, *J. Amer. Chem. Soc.*, **61**, 2791 (1939).

[9] J. F. Bunnett, *J. Amer. Chem. Soc.*, **83**, 4956, 4968, 4973, 4978 (1961).

TABLE IV

SPECTRAL PROPERTIES OF 2-METHOXYPHTHALIDES

Compd (3 Substituent)	Infrared,[a] cm^{-1}	Ultraviolet,[b] nm (ϵ)	Chemical shift,[c] ppm (mult, no.)
8 (H)	1765	228 (9600)	3.63 (s, 3)
		272 (850)	6.34 (s, 1)
		280 (820)	7.40–8.05 (m, 4)
9 (CH_3)	1760	230 (9300)	1.84 (s, 3, CCH_3)
		272 (930)	3.07 (s, 3, OCH_3)
		281 (880)	7.35–7.98 (m, 4)
10 (C_2H_5)	1760	227 (10,500)	0.89 (t, 3, J = 7 Hz)
		273 (1050)	2.13 (m, 2, J = 7 Hz)
		280 (980)	3.05 (s, 3)
			7.35–7.98 (m, 4)
11 (i-C_3H_7)	1765	229 (9400)	0.87 (d, 3, J = 7 Hz)
		274 (1200)	1.01 (d, 3, J = 7 Hz)
		281 (1100)	2.39 (m, 1)
			3.04 (s, 3)
			7.40–8.04 (m, 4)
12 (α-naphthyl)	1760	282 (64,000)	3.37 (s, 3)
			7.15–7.26 (m, 10)
			9.05–9.80 (m, 1)

[a] Nujol mulls. [b] In methanol. [c] 10% in $CDCl_3$.

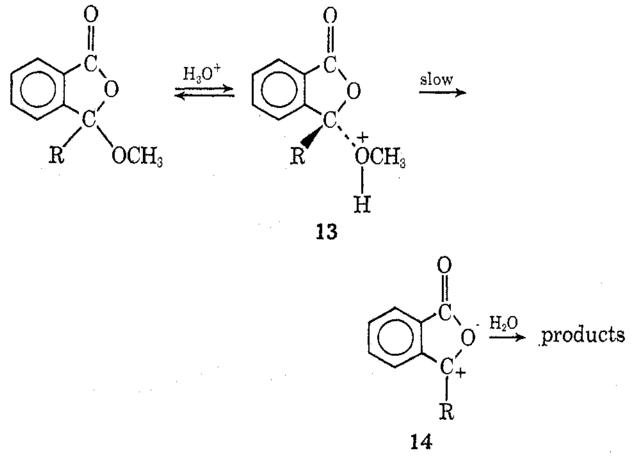
provided in Table VII. In the case of each compound a plot of the logarithm of the rate constant against the reciprocal of the absolute temperature gave a straight line.

The rate constants for the hydrolysis of these compounds were determined in solutions of sulfuric acid-d_2 and deuterium oxide in order to calculate the deuterium oxide solvent isotope effect (k_{H_2O}/k_{D_2O}). These data appear in Table VIII.

Discussion

We believe that the experimental observations on the hydrolysis of 3-methoxyphthalides can be reconciled best with an A1 mechanism (Scheme I) proceeding through a cation at the 3 position of the erstwhile phthalide. We shall set out to explain how our observations fit the mechanism in Scheme I and, in the process, attempt to eliminate alternative pathways.

SCHEME I



13

14

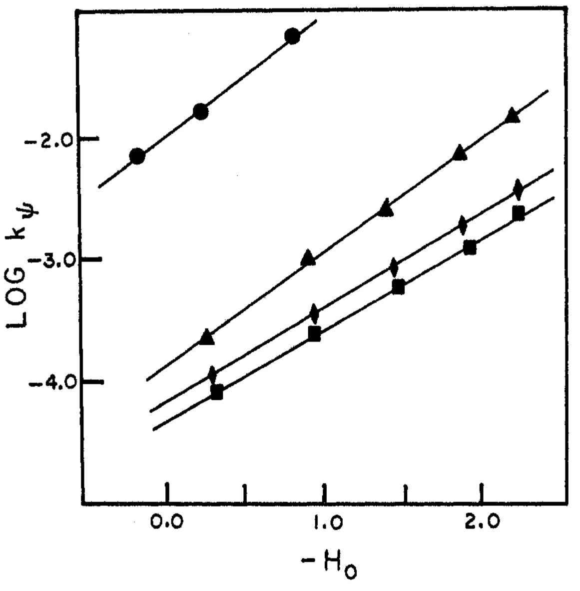


Figure 1.—Hydrolysis of 3-methoxy 3-substituted phthalides (8, ●; 9, ▲; 10, ■; 12, ◆) in sulfuric acid solutions at 25°; plot of log k_ψ against $-H_0$. The slopes are given in Table VI.

Data presented in the two papers which follow[10,11] strengthen our arguments.

In terms of the empirical criteria used in this work, 3-methoxyphthalide (**8**) itself is an example of reasonably well-behaved A1 hydrolysis. The slope of the straight line resulting from a plot of log k_ψ against $-H_0$ is 0.96. This value is close enough to unity to satisfy Hammett's[8] requirements for an A1 process. The value of -3.1 eu for ΔS^* is about what one would expect[12] for a mechanism involving rapid protonation followed by rate-determining unimolecular cleavage. The k_{H_2O}/k_{D_2O} of 0.51 is within the generally accepted range[13] for an A1 hydrolysis of a weakly basic substrate, albeit just on the upper border. While no one of these criteria can be depended upon to give an accurate assignment of mechanism, agreement between all three gives us confidence that the hydrolysis is a unimolecular process.

If the mechanism in Scheme I is at play it is clear that the order of relative rate of hydrolysis of 3-methoxy 3-substituted phthalides cannot be due to the inductive stabilization of the transition state leading to the cation **14**. One would certainly expect that 3-methoxy-3-phenylphthalide (**1**) would react more rapidly than 3-methoxy-3-methylphthalide (**9**), which would, in turn, be faster than **8**. The general trend here seems to be established by the steric bulk of the 3 substituents.

The observed decrease in reaction rate with increasing steric bulk could be due to a bimolecular mechanism in which a molecule of water attacks at C-3 as a molecule of methanol departs. Of all the alternate mechanisms, this is the most difficult to refute. We rely on the following points. First, there is a more satisfying explanation for the relative rate order and other data based on the unimolecular process in Scheme I. This is presented in the next paragraph. Second,

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[10] D. P. Weeks and F. H. Field, *J. Org. Chem.*, **38**, 3380 (1973).

[11] D. P. Weeks, J. Cella, and L. T. Chen, *J. Org. Chem.*, **38**, 3383 (1973).

[12] R. W. Taft, Jr., *J. Amer. Chem. Soc.*, **74**, 5374 (1952); R. W. Taft, Jr., E. L. Purlee, P. Riesz, and G. A. DeFazio, *ibid.*, **77**, 1584 (1955).

[13] E. H. Cordes, *Progr. Phys. Org. Chem.*, **4**, 1 (1966).

TABLE V

3-METHOXYPHTHALIDE HYDROLYSIS IN AQUEOUS SULFURIC ACID AT 25.0°

Compd (3 Substituent)	$10^4 k_\psi$,[a] $\sec^{-1}$ at $[H_2SO_4]$ 0.49 *M*	0.97 *M*	2.04 *M*	3.06 *M*	3.99 *M*	4.89 *M*
8 (H)	70.7	153.0	599.0			
9 (CH_3)		2.88	9.19	22.8	50.1	137.0
10 (C_2H_5)		0.651	1.73	4.86	8.82	18.3
11 (i-C_3H_7)		0.0116				
12 (α-naphthyl)		0.446	1.44	3.23	7.62	18.0
1 (Ph)		0.68[b]				

[a] Average of at least two runs. [b] Extrapolated from data in ref 4.

TABLE VI

3-METHOXYPHTHALIDE HYDROLYSIS.
SLOPES RESULTING FROM A PLOT OF LOG k_ψ AGAINST $-H_0$

Compd (3 Substituent)	Slope	Correlation coefficient
8 (H)	0.96	0.999
9 (CH_3)	0.80	0.998
10 (C_2H_5)	0.71	0.998
12 (α-naphthyl)	0.77	0.999
1 (Ph)	0.67[a]	

[a] Taken from ref 4.

we return to the notion that the correlation of rate with h_0 *and* a solvent isotope effect of 0.50 are not consistent with a bimolecular process and, taken together, support a unimolecular one.

Ignoring, for the moment, 3-methoxy-3-α-naphthylphthalide (**12**), one can see in Table VII that ΔS^* steadily becomes more negative as the steric bulk of the 3 substituent increases. Indeed, the enthalpies of activation (ΔH^*) for all these reactions are nearly equal and so the order of relative rate is due to the entropies. We assert that the increasingly negative ΔS^* is due to a *restriction of rotation as the molecule proceeds from the protonated form*, **13**, *to the transition state* leading to **14**. The 3 carbon in **13** is tetrahedral and the phenyl ring bisects the angle formed by the substituents R and CH_3OH^+. When CH_3OH^+ departs the 3 carbon becomes trigonal and R is required to be coplanar with the phenyl ring. Only when R = H is there no interference between R and the hydrogen atom on C-4. When R = CH_3 the van der Waals radii of R and the C-4 hydrogen overlap. Thus, free rotation of R is lost and ΔS^* becomes more negative. Compounds **10**, **1**, and **11** fit nicely into this picture. There are a number of published examples of unusually low entropies of activation allegedly caused by hindered rotation.[14-16]

3-Methoxy-3-α-naphthylphthalide (**12**) was not included in our original program of study. We prepared and investigated this compound in order to test the hypothesis in the preceding paragraph. The α-naphthyl group is so large that even in **13**, R = α-naphthyl, there is hindered rotation of R. We reasoned that this compound would have less to lose in going to **14** and would have a ΔS^* more positive than compounds such as **1** and **11**. In fact ΔS^* for **12** is -9.2 eu, that is, more positive than all the other compounds except **8**.

The simple loss of a rotational degree of freedom in the transition state for these reactions is not sufficient to account for the magnitude of ΔS^*. Humphreys and Hammett[17] have estimated that 4–6 eu may be lost owing to a restriction of rotation of a methyl group. The remaining decrease in entropy (5–7 eu) is probably caused by an increase in solvent electrostriction around the transition state. A number of authors have suggested such an effect.[15,18-23]

An unusual increase in solvation upon reaching the transition state may provide a reason why the Zucker–Hammett slopes in Table VI deviate from the expected value of 1.0. The assumption on which the Zucker–Hammett hypothesis is based is that the ratio of the activity coefficients of the substrate and the transition state must be about equal to that of a Hammett base and its conjugate acid. Unusual solvation has been shown to negate that assumption.[24-26]

The large change in ΔS^* for this series of compounds might indicate a change in mechanism from A1 to A2 as one proceeds from R = H to R = i-C_3H_7. Several observations make this unlikely. The substitution of an alkyl group for hydrogen at C-3 would tend to encourage the development of a cation at that position. A proposal of a change from A1 to A2 would require that **8** form a cation more readily than **9**. Additionally, one would expect the k_{H_2O}/k_{D_2O} value to change as the mechanism changed. Further evidence against a change in mechanism is presented in a subsequent paper.[11]

Recently a number of examples of hydrolytic reactions proceeding *via* an A-SE2 mechanism have been described.[27] Such a pathway for the 3-methoxyphthalides may be rejected on the basis of the low value of k_{H_2O}/k_{D_2O} and the absence of any detectable buffer catalysis.[4]

Note that protonation followed by unimolecular ring opening could form cation **15**. This process is also an A1 mechanism but it is less satisfying since it cannot explain the observed relative rate order. On the basis of electronic considerations one would predict a greater stability for **15**, since an $-OCH_3$ group would be better

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(14) T. C. Jones and E. R. Thornton, *J. Amer. Chem. Soc.*, **89**, 4863 (1967).

(15) F. P. Price, Jr., and L. P. Hammett, *J. Amer. Chem. Soc.*, **63**, 2387 (1941).

(16) R. W. Taft, Jr., *J. Amer. Chem. Soc.*, **75**, 4534 (1953).

(17) H. H. Humphreys and L. P. Hammett, *J. Amer. Chem. Soc.*, **78**, 521 (1956).

(18) J. E. Leffler and E. Grunwald, "Rates and Equilibrium of Organic Reactions," Wiley, New York, N. Y., 1963, p 118.

(19) L. L. Schlager and F. A. Long, *Advan. Phys. Org. Chem.*, **1**, 1 (1963).

(20) F. A. Long, J. G. Pritchard, and F. E. Stafford, *J. Amer. Chem. Soc.*, **79**, 2362 (1957).

(21) T. H. Fife, *J. Amer. Chem. Soc.*, **87**, 271 (1965).

(22) D. Watts, *J. Chem. Soc. B*, 543 (1968).

(23) G. Kohnstam, Transition State Symposium, Chemical Society, Special Publication No. 16, 1962, p 182.

(24) E. M. Arnett, *Progr. Phys. Org. Chem.*, **1**, 237 (1963).

(25) W. M. Schubert and R. H. Quacchia, *J. Amer. Chem. Soc.*, **85**, 1278 (1963).

(26) W. M. Schubert, H. Burkett, and A. L. Schy, *J. Amer. Chem. Soc.*, **86**, 2520 (1964).

(27) T. H. Fife and L. K. Jao, *J. Amer. Chem. Soc.*, **90**, 4081 (1968); E. Anderson and T. H. Fife, *ibid.*, **91**, 7163 (1969).

TABLE VII
3-METHOXYPHTHALIDE HYDROLYSIS IN 0.97 M SULFURIC ACID AT VARIOUS TEMPERATURES. ACTIVATION PARAMETERS

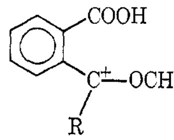
Compd (3 Substituent)	Temp, °C	$10^4 k_\psi$, sec^{-1}	ΔH^*, kcal mol^{-1}	ΔS^*, eu
8 (H)	9.7	25.5		
	15.0	47.5		
	25.0	153.0	19.0 ± 0.2	−3.1 ± 1.0
	34.5	421.0		
9 (CH_3)	25.0	2.88	18.0 ± 0.3	−14.4 ± 1.3
	35.0	7.69		
	45.1	21.6		
	55.4	52.0		
10 (C_2H_5)	25.0	0.651	18.6 ± 0.2	−15.2 ± 1.0
	35.0	1.89		
	45.1	4.93		
	55.5	13.5		
11 (i-C_3H_7)	25.0	0.0116	19.8 ± 0.5	−19.2 ± 2.0
	35.0	0.0348		
	45.0	0.103		
12 (α-naphthyl)	25.0	0.446	20.6 ± 0.5	−9.2 ± 2.0
	35.0	1.47		
	44.0	3.77		
1 (Ph)			17.0 ± 0.3	−20.6 ± 1.3[a]

[a] Taken from ref 4. Calculated at 30.0°.

TABLE VIII
3-METHOXYPHTHALIDE HYDROLYSIS IN SOLUTIONS OF SULFURIC ACID-d_2 AND DEUTERIUM OXIDE AT 25.0°. THE DEUTERIUM OXIDE SOLVENT ISOTOPE EFFECTS

Compd (3 Substituent)	[D_2SO_4], M	$10^4 k_\psi$,[a] sec^{-1}	k_{H_2O}/k_{D_2O}[b] ~1 M	~5 M
8 (H)	0.97	299.0	0.51	
9 (CH_3)	0.97	5.25	0.55	
	4.89	143.0		0.96
10 (C_2H_5)	0.97	1.33	0.49	
	4.89	26.3		0.70
12 (α-Naphthyl)	0.97	0.895	0.50	
	4.89	30.8		0.58
1 (C_6H_5)			0.50[c]	0.56[c]

[a] Average of at least two runs. [b] Values for k_{H_2O} may be found in Table V. [c] Taken from ref 4.



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able to stabilize a cation than an -OCO- would. However, the constraint of the ring will add stability to **14** by locking the cation into virtually perfect overlap with the neighboring phenyl ring. The cation is benzylic and already quite stable. This may make the difference in stabilizing effect of the two oxygen-containing groups trivial. Experimental evidence indicates that the cyclic system tends to be more stable than the ring-opened system. Thus, studies of the behavior of o-benzoylbenzoic acids in concentrated sulfuric acid[28] and in polyphosphoric acid[29] have indicated the cyclic cation as the preferred structure. Also, studies of the relative stabilities of pseudo (cyclic) esters and normal (ring-opened) esters of o-ketobenzoic acids have shown the cyclic systems to predominate at equilibrium[30] or to be kinetically favored.[31]

In Table VIII we have reported values of k_{H_2O}/k_{D_2O} at about 5 M acid concentration for **1**, **12**, **10**, and **9**. These are accurate and reproducible values for which we have no explanation at this time.

Finally, it is necessary to comment briefly on the fact that the hydrolysis of 3-methoxy-3-phenylperinaphthalide (**2**), which suffers hydrolysis by a pathway identical with that in Scheme I, yields an entropy of activation of 0.7 eu.[6] This molecule, with bulk around C-3 the same as that in 3-methoxy-3-phenylphthalide, does not show an effect of hindered rotation. An inspection of models shows that because of the ring geometry of the cyclic cation formed from **2** the R group is not required to lie coplanar with the naphthalene ring and there is no hindrance of rotation. We have attempted to prepare compounds of this type where R is much more bulky without success so far.

Experimental Section

Materials.—The preparation of the compounds used in this study has been summarized in the Results section and Tables I–IV. The details of these preparations were not substantially different from those in the literature and will not be repeated here.

Deuteriosulfuric acid solutions were prepared by diluting sulfuric acid-d_2 (Merck Sharp and Dohme) with deuterium oxide (Stohler Isotope Chemicals). Doubly distilled water was used for all aqueous solutions.

Rate Determinations.—The hydrolyses of the 3-methoxyphthalides were followed in the ultraviolet at 260 nm, the one exception being 3-methoxy-3-α-naphthylphthalide, which was studied at 320 nm. It was determined that all the compounds followed Beer's law in the region of concentration used (10^{-4}–10^{-5} M). A full spectrum of the hydrolysis run after 10 half-lives was superimposable on a spectrum of the appropriate keto acid at the same concentration. A larger sample of each 3-methoxyphthalide was allowed to hydrolyze in aqueous acid containing a suitable cosolvent. In each case the corresponding keto acid was isolated in yields of 90% or greater. The details of the kinetics method have been described previously.[4,6]

Registry No.—**1**, 7335-63-9; **3**, 16859-59-9; **4**, 1828-76-8; **5**, 40893-22-9; **6**, 6962-79-4; **7**, 5018-87-1; **8**, 4122-57-0; **9**, 1077-59-4; **10**, 40893-27-4; **11**, 40893-28-5; **12**, 40893-29-6.

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