Acknowledgment.—This research was supported in part by a grant (to U. R.) of the California Foundation for Biochemical Research.

Registry No.—**1**, 33867-98-0; **2**, 40959-21-5; **5**, 39013-76-8; **6**, 40959-22-6; **7**, 39062-23-2; **8**, 38759-23-8; **9**, 38759-24-9; **11**, 39013-78-0; **12**, 40848-20-2; **14**, 40848-21-3; **15**, 38759-27-2; **16**, 40848-23-5; **17**, 40848-24-6; **20**, 34617-98-6; **21**, 40848-26-8; **22**, 40848-27-9; **23**, 40848-28-0; **24**, 40848-29-1; **26**, 40959-23-7; **27**, 40848-30-4; **28**, 40848-31-5; **29**, 40848-32-6; 1-methyl-4,5-diaminouracil, 40959-24-8; 4,5-diamino-6-thiouracil, 40848-33-7; carbon disulfide, 75-15-0; acetone, 67-64-1; 1-methyl-2,8-dimethylthio-6-thiopurine, 39008-25-8.

Hydrolysis of 2,4-Dinitrophenyl Sulfate in Benzene in the Presence of Alkylammonium Carboxylate Surfactants

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Alkylammonium carboxylates markedly enhance the hydrolysis of 2,4-dinitrophenyl sulfate in benzene. The observed rate constants increase sigmoidally with increasing surfactant concentration in the region of the critical micelle concentration and linearly at higher surfactant concentrations. Rate constants are analyzed in terms of micellar and composite general-acid and general-base catalysis. The micellar catalyzed rates in benzene in the presence of alkylammonium carboxylates are factors of 21- to 70-fold greater than that obtained for the hydrolysis of 2,4-dinitrophenyl sulfate in water. The observed micellar catalysis is discussed in terms of solubilization of 2,4-dinitrophenyl sulfate in the polar micellar cavity where it is held fairly rigidly (as indicated by the remarkably large decrease in the entropy of activation with respect to that in water) and enhanced water activity and proton transfer assist the rate-determining S–O bond fission. Linear dependencies have been observed between the logarithms of rate constants for micellar and combined general-acid and -base catalysis and the number of carbon atoms in both the carboxyl and ammonium groups of the alkylammonium carboxylates. Changes in the chain length of the carboxyl and ammonium groups affect the micellar catalysis to the same extent, but general-acid catalysis depends on the chain length to a greater extent than general-base catalysis.

Rate constants for the mutarotation of 2,3,4,6-tetramethyl-α-D-glucose,[1] for the decomposition of σ complexes,[2] for the aquation of chromium(III) and cobalt(III) complexes,[3] and for the trans–cis isomerization of bis(oxalato)diaquochromate(III) anion[4] are enhanced remarkably by alkylammonium carboxylate surfactants in nonpolar solvents. These rate enhancements have been rationalized in terms of favorable substrate partitioning in the polar cavities of reversed micelles, dynamically formed from alkylammonium carboxylates,[5–8] where specific interactions, proton transfer, and enhanced water activity provide the driving force for the catalysis. Rate constants for these reactions in the reversed micellar environment in nonpolar solvents are orders of magnitude greater than those in the pure nonpolar solvents and in water.[1–5] Simple partitioning by itself is clearly an inadequate explanation for rate enhancements of this magnitude. It is likely that substrates are being held more rigidly in the polar cavities of reversed micelles than they are in aqueous "normal" micelles. This factor and the presence of a polar interior render, we believe, reversed micelles not only an inherently unique reaction media but a potentially fruitful model for biomembranes and enzymatic interactions.

Investigations of aquation and isomerization of chromium(III) complexes[3,4] indicated that, other factors being the same, alkylammonium carboxylate micelles enhance the rates of acid-catalyzed reactions to the greatest extent when the neutral rate is relatively small. In order to probe this contention further and to extent the range of reversed micellar interactions to hydrolyses, we have examined the hydrolysis of 2,4-dinitrophenyl sulfate in benzene in the presence of micelle-forming alkylammonium carboxylates. Our selection was somewhat governed by the availability of information on the mechanisms of 2,4-dinitrophenyl sulfate hydrolyses in water[9,10] and in aqueous micellar solutions in the absence[11] and presence[12] of nucleophilic reagents. Additionally, ^1H nmr investigations indicated that in aqueous zwitterionic 3-(dimethyldodecylammonio)propane-1-sulfonate micelles the environment of 2,4-dinitrophenyl sulfate is somewhat hydrophobic but its *in situ* hydrolysis products interact to a greater extent with the polar head groups of the micelle than the substrate.[13]

Experimental Section

The preparation and purification of 2,4-dinitrophenyl sulfate has been described.[10]

Reagent-grade benzene (<0.02% water) was distilled from

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[1] E. J. Fendler, J. H. Fendler, R. T. Medary, and V. A. Woods, *Chem. Commun.*, 1497 (1971); J. H. Fendler, E. J. Fendler, R. T. Medary, and V. A. Woods, *J. Amer. Chem. Soc.*, **94**, 7288 (1972).

[2] J. H. Fendler, *J. Chem. Soc., Chem. Commun.*, 269 (1972); J. H. Fendler, E. J. Fendler, and S. A. Chang, *J. Amer. Chem. Soc.*, **95**, 3273 (1973).

[3] C. J. O'Connor, E. J. Fendler, and J. H. Fendler, *J. Amer. Chem. Soc.*, **95**, 600 (1973); C. J. O'Connor, E. J. Fendler, and J. H. Fendler, unpublished work.

[4] C. J. O'Connor, E. J. Fendler, and J. H. Fendler, unpublished work.

[5] E. J. Fendler, S. A. Chang, J. H. Fendler, R. T. Medary, O. A. El Seoud, and V. A. Woods in "Reaction Kinetics in Micelles," E. H. Cordes, Ed., Plenum Press, New York, N. Y., 1973, p 127.

[6] J. H. Fendler, E. J. Fendler, R. T. Medary, and O. A. El Seoud, *J. Chem. Soc., Faraday Trans. 1*, **69**, 280 (1973).

[7] E. J. Fendler, J. H. Fendler, R. T. Medary, and O. A. El Seoud, *J. Phys. Chem.*, **77**, 1432 (1973).

[8] O. A. El Seoud, E. J. Fendler, J. H. Fendler, and R. T. Medary, *J. Phys. Chem.*, **77**, 1876 (1973).

[9] S. J. Benkovic and P. A. Benkovic, *J. Amer. Chem. Soc.*, **88**, 5504 (1966).

[10] E. J. Fendler and J. H. Fendler, *J. Org. Chem.*, **33**, 3852 (1968).

[11] E. J. Fendler, R. R. Liechti, and J. H. Fendler, *J. Org. Chem.*, **35**, 1658 (1970).

[12] J. H. Fendler, E. J. Fendler, and L. W. Smith, *J. Chem. Soc., Perkin Trans. 2*, 2097 (1972).

[13] E. J. Fendler, C. L. Day, and J. H. Fendler, *J. Phys. Chem.*, **76**, 1460 (1972).

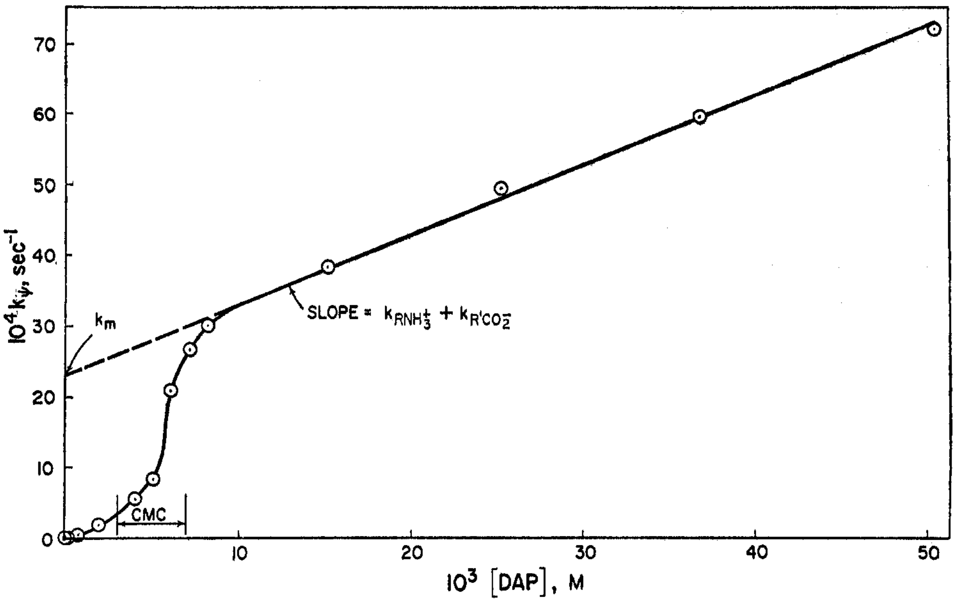

Figure 1.—Observed rate constants for the hydrolysis of 2,4-dinitrophenyl sulfate as a function of the concentration of dodecylammonium propionate in benzene at 39.8°.

sodium onto freshly activated Linde Type 5A Molecular Sieve and stored under nitrogen.

Octylammonium propionate (OAP), butyrate (OAB), nonanoate (OAN), dodecanoate (OAD), and tetradecanoate (OAT), butyl (BAP), hexyl (HAP), decyl (DeAP), and dodecyl ammonium propionate (DAP), dodecylammonium butyrate (DAB), and dodecylammonium benzoate (DABz) were prepared by the method of Kitahara[14] as described previously.[6-8] The purity of these surfactants was established by the observation of sharp melting or boiling points and by their infrared and proton magnetic resonance spectra.[6-8] Surfactants were dried on a high vacuum line for at least 12 hr immediately prior to making up the stock solutions in benzene. Some of these surfactants are very hygroscopic and appropriate care was taken to exclude atmospheric moisture in making up the stock solutions.

Rates of hydrolysis were measured spectrophotometrically by determining the absorbances of the liberated phenol at 347 nm as a function of time on a Beckman Kintrac VII recording spectrophotometer. The temperature of the thermostated bath and the cell compartment was maintained within ±0.05°, as monitored by NBS thermometers. Good first-order plots were obtained in all cases for at least 75% reaction. Pseudo-first-order rate constants, k_ψ, have been calculated by the Guggenheim method.[15] Reactions were initiated by adding *ca.* 1 mg of solid 2,4-dinitrophenyl sulfate to 5 ml of the reaction solution which had been preequilibrated at the appropriate temperature. After vigorous shaking for several seconds the mixture was filtered directly into a cell and placed in the thermostated cell compartment of the spectrophotometer. The overall concentration of 2,4-dinitrophenyl sulfate in the reaction mixture was 1-6 × 10^{-5} *M*. Spectrophotometric analysis established 2,4-dinitrophenol as the sole reaction product.[12]

Results and Discussion

2,4-Dinitrophenyl sulfate hydrolyzes in benzene in the presence of alkylammonium carboxylate surfactants. Lack of substrate solubility prevented the examination of its hydrolysis rate in pure benzene, but it is expected to be negligible. The most detailed investigation utilized dodecylammonium propionate (DAP). At the lowest DAP concentration (1.17 × 10^{-4} *M*) the hydrolysis rate is considerably lower than that in water (Table I). Increasing concentrations of the surfactants increase the hydrolysis rate. This increase is sigmoidal in the region of the critical micelle concentration, after which it continues to increase linearly (Figure 1). Markedly different types of kinetic rate profiles have been found for micellar catalysis in aqueous solution.[16-19] However, saturation type kinetics are generally observed in which a sigmoidal rate enhancement is followed by a plateau. In some cases the plateau becomes rather short and increasing surfactant concentration decreases the observed rate (*i.e.*, a rate maximum is observed). Both of these types of kinetic behavior have been observed for reactions catalyzed by reversed micelles in nonpolar solvents.[1-5] The present data (Table I) indicate that, in addition to micellar

TABLE I
RATE CONSTANTS FOR HYDROLYSIS OF 2,4-DINITROPHENYL SULFATE IN BENZENE IN THE PRESENCE OF DAP

Temp 24.5°		Temp 39.8°	
10^3 [DAP], *M*	10^4 k_ψ, sec^{-1}	10^3 [DAP], *M*	10^4 k_ψ, sec^{-1}
	0.27[a]		1.45[a]
5.06	3.99	0.117	0.045
10.1	8.82	0.468	0.166
11.7	9.94	0.701	0.237
25.3	12.9	0.935	0.402
50.6	18.5	1.01	0.427
75.9	22.4	2.02	1.83
101	28.5	4.05	5.48
142	40.5	5.06	8.28
189	45.7	6.06	21.1
202	48.2	7.08	26.7
208	49.2	8.09	30.2
237	55.0	15.2	38.3
293	66.7	25.3	49.4
402	86.9	50.6	71.4
501	104		
610	125		

[a] In water at pH 8.0 in the presence of 2.5 × 10^{-3} *M* $Na_2B_4O_7$ buffer, taken from ref 11.

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[14] A. Kitahara, *Bull. Chem. Soc. Jap.*, **28**, 234 (1955); **30**, 586 (1957).

[15] E. A. Guggenheim, *Phil. Mag.*, **2**, 538 (1926).

[16] E. H. Cordes and R. B. Dunlap, *Accounts Chem. Res.*, **2**, 329 (1969).

[17] E. J. Fendler and J. H. Fendler, *Advan. Phys. Org. Chem.*, **8**, 271 (1970).

[18] T. C. Bruice in "The Enzymes," 3rd ed, Vol. 2, Academic Press, New York, N. Y., 1970, p 217.

[19] E. H. Cordes and C. Gitler, *Progr. Bioorg. Chem.*, **2**, 1 (1973).

catalysis, components of dodecylammonium propionate also enhance the hydrolysis rate. The observed rate constant for the hydrolysis of 2,4-dinitrophenyl sulfate at a given DAP concentration, or more generally at a given alkylammonium carboxylate concentration, k_ψ, can be described by eq 1, where k_m is the rate constant

$$k_\psi = k_\mathrm{m} + (k_{\mathrm{RNH_3^+}} + k_{\mathrm{^-O_2CR'}})[\mathrm{RNH_3^+\ ^-O_2CR'}] \qquad (1)$$

for the micellar catalysis, and $k_{\mathrm{RNH_3^+}}$ and $k_{\mathrm{^-O_2CR'}}$ represent rate constants due to the alkylammonium and carboxylate groups of the surfactant, respectively. Below the critical micelle concentration, the hydrolysis is entirely due to $k_{\mathrm{RNH_3^+}} + k_{\mathrm{^-O_2CR'}}$. The uncertainty in the precise onset of micellar catalysis as well as the possibility of catalysis by dimers, trimers, etc., do not allow meaningful calculation of the rate constants in this region. Above the critical micelle concentration, however, eq 1 is obeyed over a sufficiently large concentration range (see Table I, for example) such that k_m values can be calculated from the intercept of the extrapolated straight lines obtained on plotting k_ψ *vs.* [surfactant], and $k_{\mathrm{RNH_3^+}} + k_{\mathrm{^-O_2CR'}}$ values can be obtained from the slopes (see Figure 1). The true values of k_m, of course, are likely to be higher than those obtained from the extrapolation.

In order to assess the relative importance of k_m, $k_{\mathrm{RNH_3^+}}$, and $k_{\mathrm{^-O_2CR'}}$, the hydrolysis of 2,4-dinitrophenyl sulfate has been investigated in a series of alkylammonium propionates and of octylammonium carboxylates. Information on the effects of chain length in the alkylammonium and in the carboxylate group on the rate constants have been obtained from these data. For most of these surfactants, k_ψ values have only been obtained above the critical micelle concentration where they were found to be linear functions of the surfactant concentration. From the slopes and intercepts of these lines, values for $k_{\mathrm{RNH_3^+}} + k_{\mathrm{^-O_2CR'}}$ and k_m were calculated, in a manner analogous to that indicated in Figure 1, and are given in Table II.

TABLE II

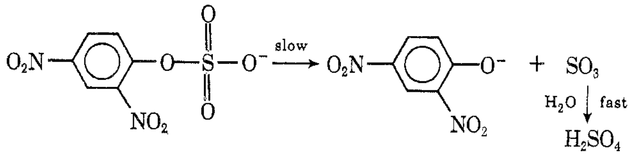
k_m AND ($k_{\mathrm{RNH_3^+}} + k_{\mathrm{^-O_2CR'}}$) VALUES IN BENZENE IN THE PRESENCE OF ALKYLAMMONIUM CARBOXYLATE SURFACTANTS AT 24.5°

Registry no.	Surfactant	$10^4\ k_\mathrm{m}$, sec^{-1}	$10^3\ (k_{\mathrm{RNH_3^+}} + k_{\mathrm{^-O_2CR'}})$, M^{-1} sec^{-1}
17081-35-5	BAP	5.76	1.50
39107-99-8	HAP	7.37	3.32
39108-00-4	OAP	6.56	4.90
39108-01-5	DeAP	13.4	12.0
17448-65-6	DAP	9.20	18.7
	DAP[a]	23.2	99.1
41029-73-6	OAB	11.5	4.00
41029-74-7	OAN	14.3	11.6
41029-75-8	OAD	19.0	11.4
17463-35-3	OAT	16.5	9.77

[a] At 39.8°.

Rate constants for the reversed micellar catalyzed hydrolysis of 2,4-dinitrophenyl sulfate in benzene, k_m values, at 24.5° are in the range of $5.7\text{–}19 \times 10^{-4}$ sec^{-1} (Table II). These values are 21- to 70-fold greater than that obtained for the neutral hydrolysis of 2,4-dinitrophenyl sulfate in water.[11] Although no data are available for the rate enhancement with respect to benzene, it is likely to be considerably greater than that with respect to water. Once again, therefore, catalysis of the hydrolysis of 2,4-dinitrophenyl sulfate by reversed micelles is not the sole consequence of favorable partitioning. Furthermore, the magnitude of the catalysis markedly exceeds that generally observed in "normal" micellar systems in aqueous solution. Cationic hexadecyltrimethylammonium bromide and uncharged poly(oxyethylene)(24)nonylphenol enhance the rate of neutral hydrolysis of 2,4-dinitrophenyl sulfate by factors of 3.2 and 2.6, respectively.[11]

The proposed mechanism for the hydrolysis of 2,4-dinitrophenyl sulfate in water and in aqueous micellar systems involves rate-determining sulfur–oxygen bond fission with the elimination of 2,4-dinitrophenoxide ion.[9,10] The transition state was suggested to involve



appreciable charge separation and to resemble, therefore, the hydrolysis product to a greater extent than the reactants. An essentially analogous mechanism is proposed for the hydrolysis of 2,4-dinitrophenyl sulfate in benzene in the presence of alkylammonium carboxylates. Lack of substrate solubility in pure benzene implies that the reaction site is the reversed micellar pseudophase. Based on ^{1}H nmr investigations of other solubilizates in alkylammonium carboxylate–nonpolar solvent systems,[20] it is probable that 2,4-dinitrophenyl sulfate is solubilized in the reversed micellar cavity with the anionic sulfate group and the dipolar nitro groups oriented toward the ammonium ions of the surfactants (Figure 2A). However, it is possible, but less likely, that the aromatic nucleus interacts with the hydrophobic hydrocarbon chains of the surfactant not far from the polar micellar cavity and that only the sulfate group interacts with the ammonium ions surrounding the cavity (Figure 2B). In either case, of course, the ionized sulfate group binds electrostatically to the ammonium ion. S–O bond fission is the overall result of several complex processes. Throughout the concentration range, the alkylammonium and carboxylate ions act as a general acid and a general base. Superimposed on these, above the critical micelle concentration, enhanced activity of the substrate in the micellar microenvironment relative to that in water as well as proton transfer contribute to the observed micellar catalysis. If the environment(s) of the reaction products are different from that of the reactant, as in the case of the *in situ* reactions of 2,4-dinitrophenyl sulfate in aqueous micelles,[12] then some energy is utilized for this reorganization which would otherwise be available for promoting the reaction.

Rate enhancement of 2,4-dinitrophenyl sulfate hydrolysis by DAP micelles in benzene is the combined result of substantial decreases in both the enthalpy and entropy of activation with respect to those in water (Table III). It is also apparent from Table III that the decreases in the activation enthalpy and entropy relative to water are far greater in the reversed micellar

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(20) O. A. El Seoud, E. J. Fendler, and J. H. Fendler, *J. Chem. Soc., Faraday Trans. 1*, in press.

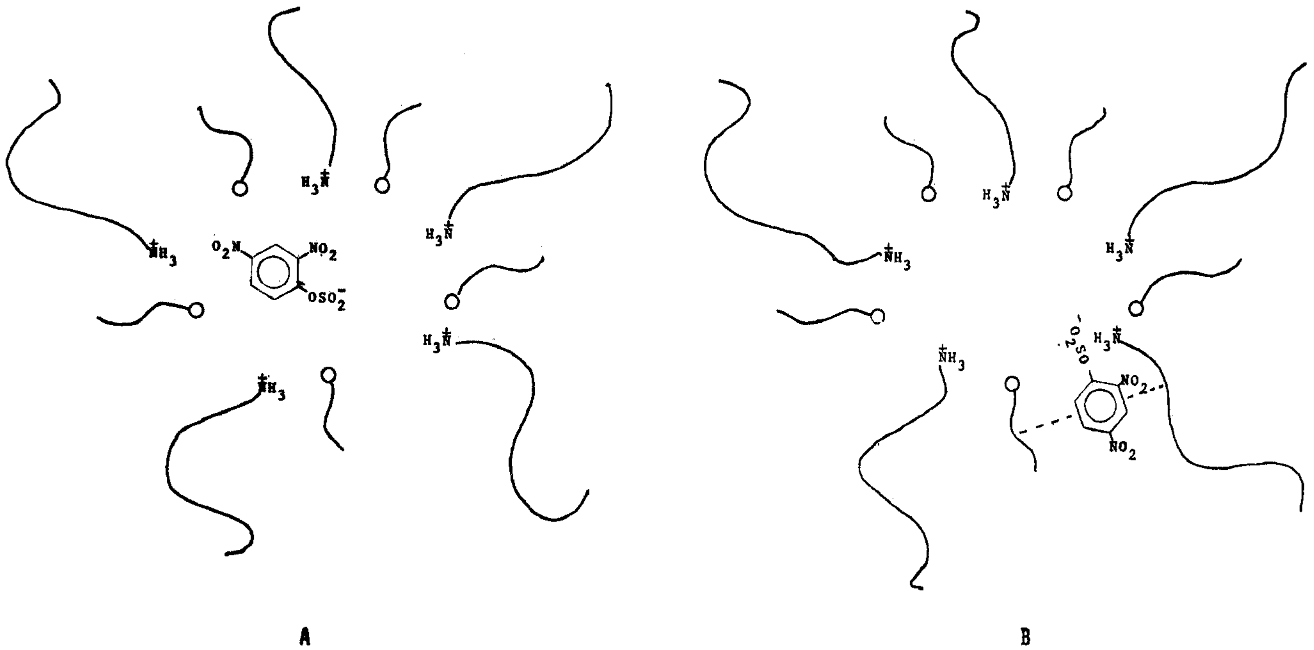

Figure 2.—Generalized schematic representation of the solubilization sites of 2,4-dinitrophenyl sulfate in reversed alkyl-ammonium carboxylate micelles.

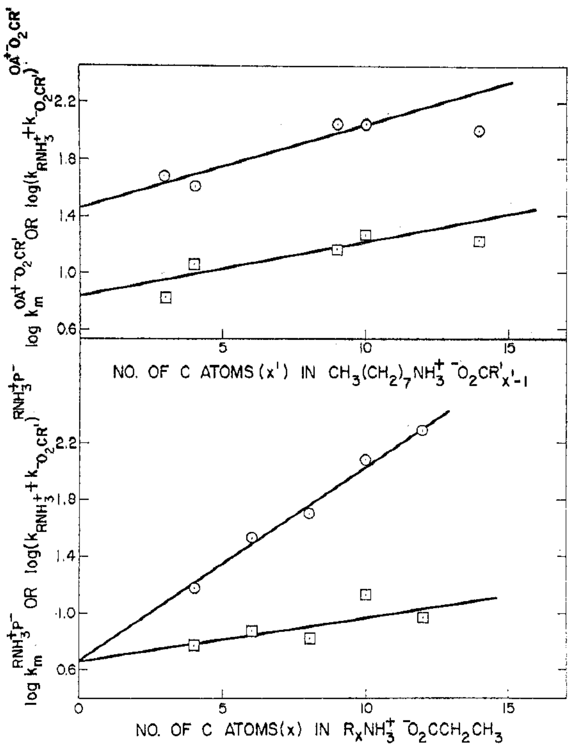

Figure 3.—The dependence of log $k_m^{RNH_3^+P^-}$ and log $k_m^{OA^+\ -O_2CR'}$ on the alkyl chain length x and x' (□) and of log ($k_{RNH_3^+} + k_{-O_2CR'}$) on x and x' (○) at 24.5°.

TABLE III

ARRHENIUS PARAMETERS FOR THE HYDROLYSIS OF 2,4-DINITROPHENYL SULFATE

Condition	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu[a]
Water[b]	18.2	−18.0
6.0 × 10^{-3} M CTAB-water[b]	16.0	−23.3
DAP-benzene, k_m	11.8	−37
DAP-benzene, ($k_{RNH_3^+} + k_{-O_2CR'}$)[c]	20.6	−1

[a] Calculated at 25.0°. [b] Taken from ref 11. [c] Second-order rate constant for the catalysis due to the general acid and base catalysis of DAP.

system than for the "normal" hexadecyltrimethylammonium bromide (CTAB) micelles in aqueous solution. These results are compatible with the entropic argument for enzymatic catalysis proposed by Jencks[21] wherein the protein-induced concentration effect at the active site and restriction of rotational movement overcome the necessity for conformational changes in the catalyst. It is quite probable from ^1H nmr chemical shifts and line broadening studies of solubilizates in reversed micellar systems[20] that substrates are held fairly rigidly, *i.e.*, freedom of motion is restricted, and are specifically oriented in the interior of reversed alkylammonium carboxylate micelles. Consequently, it is plausible that the remarkably large decrease in the entropy of activation (−18.0 to −37 eu, Table III) obviates or overshadows any energy requirement for structural reorganization of the micelle. These activation parameters for catalysis in reversed micellar systems as compared to those in aqueous micellar ones also suggest that the former are far superior to the latter as simple models for enzymatic catalysis.

Rate constants for the micellar catalysis, k_m, increase with increasing hydrocarbon chain length of both the alkylammonium and carboxylate groups (Table II). For the alkylammonium propionate series the relationship of eq 2 and for the octylammonium carboxylate

$$\log k_m^{RNH_3^+P^-} = \log k_m^{P^-} + ax \qquad (2)$$

series the relationship of eq 3 (where $k_m^{RNH_3^+P^-}$ and

$$\log k_m^{OA^+\ -O_2CR'} = \log k_m^{OA^+} + bx' \qquad (3)$$

$k_m^{OA^+\ -O_2CR'}$ are the rate constants for the alkylammonium propionate and octylammonium carboxylate micellar catalyzed reactions, respectively; $k_m^{P^-}$ and $k_m^{OA^+}$ are those due to the micellar catalysis by the propionate and the octylammonium ion, respectively;

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[21] M. J. Page and W. P. Jencks, *Proc. Nat. Acad. Sci.*, **68**, 1678 (1971).

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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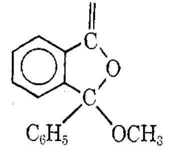
Received September 19, 1972

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



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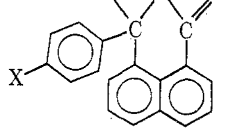

2, X = H, CH_3, Br

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-

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[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).