which time 75 ml of pentane was added followed by dropwise addition of water. The pentane layer was separated and dried over magnesium sulfate. The pentane was evaporated to yield an oil. Essentially one peak was present on a gas chromatogram on a 15-ft Carbowax column at 90°. A 60-mg sample was collected and submitted to nmr analysis. The spectrum was identical with that of a sample prepared earlier.[8]

Acknowledgments. We wish to acknowledge the generous financial support of the National Institutes of Health (GM 8701). We are also indebted to Mrs. Nancy Crowder Roberts who initiated some of the experiments in this project. For a generous gift of nortricyclene, we are indebted to Mr. W. Washburn.

On the Chemistry of Reactions Proceeding inside Molecular Aggregates

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Abstract: The rate constants for basic hydrolysis of *p*-nitrophenyl acetate, mono-*p*-nitrophenyl dodecanedioate, *p*-nitrophenyl octanoate, and benzoylcholine chloride (two neutral and two ionic substrates) were determined in surfactant solutions containing varying amounts of either laurate anion, *n*-dodecyltrimethylammonium cation, or *n*-dodecylpyridinium cation. Laurate inhibits hydrolysis of all four esters, *n*-dodecyltrimethylammonium cation enhances the rates, and *n*-dodecylpyridinium cation has very little effect. A kinetic scheme is proposed for the laurate system which involves partitioning of the substrates between the solution and the micellar phases. It is possible to evaluate both the substrate–micelle association constants (which are very large numbers and exceed those for many enzyme-specific substrate complexes) and the rate constants for adsorbed ester (which are within experimental error of zero). The kinetic data are discussed in terms of the complex structure of micelles.

The living cell contains a large number of particles composed of aggregates of molecules.[1] The particles associate to form subcellular bodies such as mitochondria and chloroplasts. Thus, life processes proceed mainly within complicated assemblages of molecules rather than in the free solution (where control of the reactions would be difficult). A knowledge of chemical behavior inside molecular aggregates is essential to the understanding of these highly organized biological processes. Consequently we have begun a study of the subject and present our initial results in this paper. The report concerns reactions occurring inside one particular type of biologically important aggregate,[2] the micelle. Micelles are formed in aqueous solutions by surfactants, which are compounds possessing a water-solubilizing moiety (often an ionic group) and a water-insoluble portion (a long hydrocarbon chain). Micelles are spherical aggregates, of 30 or more molecules, containing hydrocarbon interiors and ionic surfaces.[3]

Several examples have appeared recently of organic reactions whose rates are perturbed by the presence of small quantities of surfactant. The acid hydrolysis of benzylideneaniline to benzaldehyde and aniline is inhibited by cetyltrimethylammonium bromide.[4] Duynstee and Grunwald[5] showed that surfactants affect the rate of dye fading, and Kurz[6] found that acid-catalyzed hydrolysis of long-chain sodium alkyl sulfates is accelerated, and base-catalyzed hydrolysis inhibited, by micellation. Other reactions that have been studied in the presence of surfactants include the hydrolysis of Schiff bases[7] and esters,[8] the reaction of 1-fluoro-2,4-dinitrobenzene with amines,[9] and porphyrin–metal interaction.[10] Letsinger and Wagner[11] used cationic and anionic surfactants to regulate the rate of reaction of a polyuridylic acid derivative.

In this paper we elucidate the dependence of the rate constants for basic hydrolysis of four substrates A–D on the concentration of each of the three surfactants E–G. We selected ester hydrolysis for study

Substrates	Surfactants
$CH_3COOC_6H_4NO_2$ A	$^-OOC(CH_2)_{10}CH_3$ E
$^-OOC(CH_2)_{10}COOC_6H_4NO_2$ B	$(CH_3)_3N^+(CH_2)_{11}CH_3$ F
$CH_3(CH_2)_6COOC_6H_4NO_2$ C	$C_5H_5N^+(CH_2)_{11}CH_3$ G
$(CH_3)_3N^+CH_2CH_2OOCC_6H_5$ D	

because it can be followed spectrophotometrically at very low substrate concentrations where the structure of the micelles, formed by the surfactants, is not

(1) J. L. Fairley and G. L. Kilgour, "Essentials of Biological Chemistry," Reinhold Publishing Corp., New York, N. Y., 1966, p 120.
(2) P. K. Brown, I. R. Gibbons, and G. Wald, *J. Cell Biol.*, **19**, 79 (1963).
(3) (a) D. J. Shaw, "Introduction to Colloid and Surface Chemistry," Butterworth & Co. (Publishers) Ltd., London, 1966; (b) L. I. Osipow, "Surface Chemistry," Reinhold Publishing Corp., New York, N. Y., 1962.
(4) K. G. van Senden and C. Koningsberger, *Tetrahedron*, 22, 1301 (1966).
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(8) M. T. A. Behme, J. G. Fullington, R. Noel, and E. H. Cordes, *ibid.*, **87**, 266 (1965).
(9) D. G. Herries, W. Bishop, and F. M. Richards, *J. Phys. Chem.*, **68**, 1842 (1964).
(10) M. B. Lowe and J. N. Phillips, *Nature*, **190**, 262 (1962).
(11) R. L. Letsinger and T. E. Wagner, *J. Am. Chem. Soc.*, **88**, 2062 (1966).

perturbed. Moreover, basic hydrolysis of esters is a thoroughly understood reaction and one that is free from complications. Two of the substrates are neutral and two are ionic. Neutral ester C possesses a long hydrocarbon chain and is extremely water insoluble. Anionic substrate B is itself a surfactant; its labile ester moiety is distant from the ionic site. Thus, if molecule B is positioned in the micelle as are the surfactant molecules making up the micelle, then the ester group of B will be buried well within the hydrocarbon interior of the aggregate. On the other hand, the cationic benzoylcholine (D) is a short molecule. If its charged portion is forced to reside on the surface of a micelle near the water, then the reactive ester group cannot penetrate very deeply into the micelle interior. The surfactants possess important structural differences as well. Laurate anion (E) forms micelles with highly charged negative surfaces. If ester groups of a substrate are adsorbed onto a micelle surface, then nucleophilic carboxylate catalysis is a possibility. The micelles of the two cationic surfactants F and G differ in the degree of exposure of the ionic atoms, and it was of interest to determine whether this difference would manifest itself kinetically.

In summary, the purpose of this work is to determine the effect of substrate and surfactant structure on kinetic parameters in order to understand better the nature of substrate–surfactant interaction and micellar reactions in general.

Experimental Section

Materials. ***p*-Nitrophenyl Acetate (A).** This compound was prepared by the method of Chattaway[12] and recrystallized repeatedly until it was nearly colorless; mp 77–78° (lit.[13] mp 77.5–78°).

Mono-*p*-nitrophenyl Dodecanedioate (B). Dodecanedioic acid (2.0 g, 8.7×10^{-3} mole) (Matheson Coleman and Bell, recrystallized from EtOAc) and 1.0 g (4.3×10^{-3} mole) of *p*-nitrophenyl trifluoroacetate (Aldrich) were dissolved in 15 ml of dry pyridine and allowed to react at room temperature for 30 min. The solution was poured into 60 ml of ice water, and the resulting yellow precipitate was collected by filtration. The dried solid was crystallized once from benzene–hexane and several times from MeOH; mp 85.5–87°. The diacid is appreciably more soluble in MeOH, and the diester appreciably less soluble, than the monoester. *Anal.* Calcd for $C_{18}H_{25}NO_6$: C, 61.52; H, 7.17; N, 3.99. Found: C, 61.39; H, 6.99; N, 4.08.

***p*-Nitrophenyl Octanoate (C).** Substrate C, an oil, was obtained from Pierce Chemical Co. and was used without further purification.

Benzoylcholine Chloride (D). The ester was obtained commercially (Pierce), recrystallized twice from EtOH–EtOAc (1:5), and dried at 100° under reduced pressure for 12 hr; mp 206–207° (lit.[14] mp 204–205°).

Lauric Acid (E). The Eastman product was crystallized from MeOH and dried thoroughly. Its identity was checked by a mixture melting point determination.

***n*-Dodecyltrimethylammonium Bromide (F).** We thank Glovers Ltd. for a generous supply of the material marketed as Morpan D. It was recrystallized from purified acetone and dried at 100° under reduced pressure for 1 hr; mp 241.5–243.5° (lit.[15] mp 243°).

***n*-Dodecylpyridinium Chloride (G).** We were unable to obtain satisfactory material by recrystallizing commercially available surfactant and therefore prepared it ourselves from pyridine and the alkyl chloride.[16] Beautiful white crystals were obtained after many recrystallizations, but they melted at 68–72° (lit.[16] mp 86–87°). Drying them under high vacuum at 60° over P_2O_5 did not change the melting point. The melting behavior of the pyridinium salt was characteristic of a smectic mesophase and possibly the melting point disparity is related to this fact. Gravimetric analysis for chloride ion indicated that the *n*-dodecylpyridinium chloride (also called laurylpyridinium chloride) was pure.

All inorganic compounds were of reagent quality. Methanol was distilled once over magnesium.

Kinetics. The procedure is given here for one particular substrate and surfactant, and it is typical of that which was used throughout. Lauric acid (0.5402 g), NaOH (0.1 g), and KCl (1.603 g) were weighed out in a 50-ml volumetric flask. The flask was then filled to the mark with 0.02 *N* NaOH. The pH of the resulting solution (0.05 *M* laurate, $I = 0.5$) was adjusted to pH 12.14 ± 0.02 with the aid of a Corning Model 12 pH meter. The less concentrated laurate solutions were prepared from the 0.05 *M* laurate by diluting portions of it with aqueous base (pH 12.14, $I = 0.5$) containing no surfactant.

A cuvette was filled with 3.00 ml of one of the laurate solutions, stoppered, and placed in the thermostated chamber (25.0 ± 0.1°) of a Cary 14 PM recording spectrophotometer. After about 15 min, 25 μl of an aqueous solution of benzoylchloline chloride (prepared immediately before the spectrophotometry) was added to the cuvette with the aid of a small stirring rod flattened at one end. The decrease in absorbance at 274 mμ was then traced as a function of time. The hydrolysis of the ester (initial concentration: 8.65×10^{-4} *M*) was usually followed to completion. A final pH reading was taken to ensure that no pH change had occurred during the reaction.

The runs with the *p*-nitrophenyl esters were performed in sodium borate buffers of lower pH values at which the laurate was insoluble. Hence, it was necessary to carry out the kinetics at 50°. The pH measurements of the buffers were also made at 50° after standardizing the meter at this temperature using 0.01 *M* sodium borate (pH (at 50°) 9.01[17]). There is no such solubility problem with the cationic surfactants, and all the runs using these were performed at 25°. The hydrolyses of the *p*-nitrophenyl esters were studied in the same manner as described above except that the substrates were dissolved in methanol and an increase in absorbance at 400 mμ, due to *p*-nitrophenolate liberation, was utilized to follow the reactions.

First-order plots were linear to greater than 80% of the reactions. Duplicate runs agreed to better than 4%.

Critical Micelle Concentration. The concentration at which a surfactant abruptly associates into micelles is called its critical micelle concentration (CMC). The CMC of laurate at 50°, pH 9.59, was determined by the spectral-change technique[18] (which is not as accurate as other methods but which is very convenient particularly when the temperature must be elevated). Each of the laurate solutions used in the kinetic runs was equilibrated in a cuvette at 50° inside a Cary 14 compartment and the absorbance at 610 mμ was adjusted to zero. A methanolic solution of pinacyanol chloride (25 μl) was added to obtain a dye concentration of 1.05×10^{-5} *M*. An absorbance reading was then taken. A plot of absorbance *vs.* laurate concentration shows a striking change at 0.009 *M*. The CMC of laurate at the specified conditions is assigned this value. A spectrophotometer is in fact unnecessary for the CMC determination: above the CMC the solutions are a bright blue, while below it they are a light shade of pink.

Results

The rate constants for hydrolysis of *p*-nitrophenyl acetate (A), mono-*p*-nitrophenyl dodecanedioate (B), and *p*-nitrophenyl octanoate (C) at pH 9.59, 50°, in the presence of varying amounts of laurate (E) are plotted in Figure 1. The curves were constructed from rate data such as those given in Table I. The hydrolysis rates of the three esters in the absence of laurate differ from each other by only a small factor, indicating that neither B nor C is in any way an unusual substrate due to intramolecular carboxylate catalysis or to "burying" of the ester group in a folded hydrocarbon chain. The

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(13) M. L. Bender and B. W. Turnquest, *J. Am. Chem. Soc.*, **79**, 1652 (1957).
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(15) M. J. McDowell and C. A. Kraus, *J. Am. Chem. Soc.*, **73**, 2170 (1951).
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(17) R. G. Bates, *J. Res. Natl. Bur. Std.*, **66A**, 179 (1962).
(18) M. L. Corrin, H. B. Klevens, and W. D. Harkins, *J. Chem. Phys.*, **14**, 480 (1946).

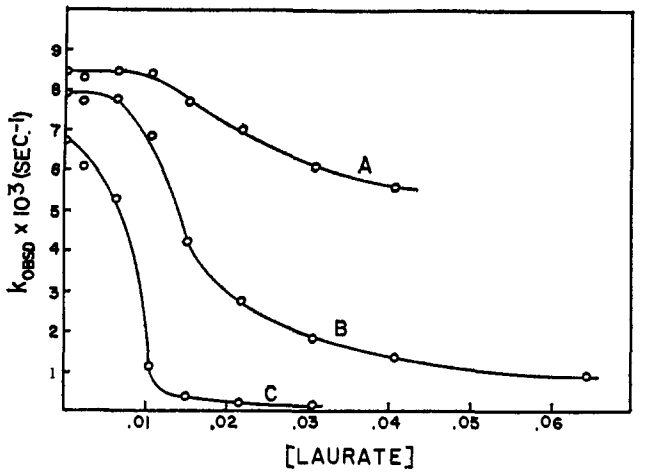

Figure 1. Plots of observed rate constants for the hydrolysis of *p*-nitrophenyl acetate (A), a mono-*p*-nitrophenyl dodecanedioate (B), and *p*-nitrophenyl octanoate (C) at pH 9.59, I = 0.1, 50.0°, *vs.* concentration of laurate. The rate constants of A have been divided by 2.00 to bring the curve on scale.

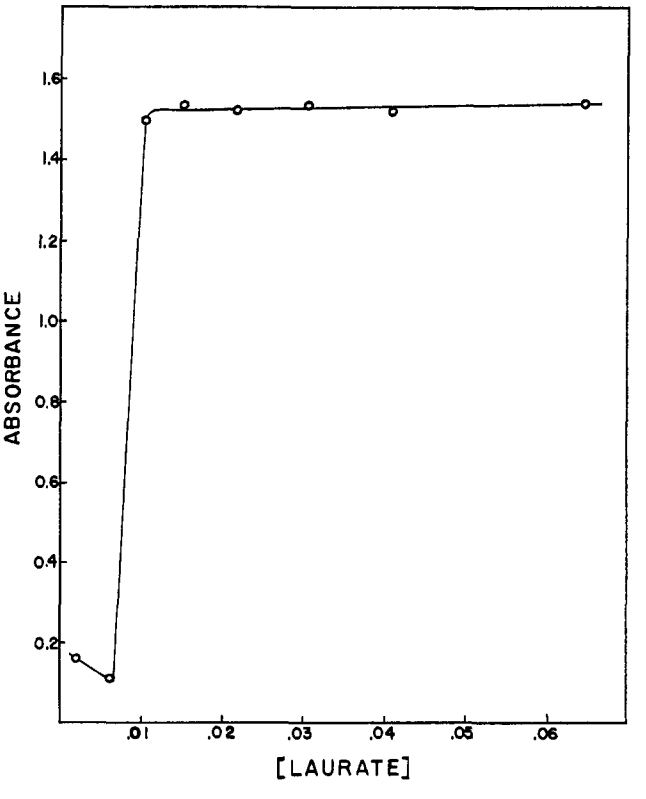

Figure 2. The absorbance of 1.05 × 10^{-5} M pinacyanol chloride at 610.0 mμ in pH 9.59 sodium borate buffer (I = 0.1) at 50.0° *vs.* laurate concentration.

plots show that laurate significantly inhibits hydrolysis of the esters, but that the effect is large only above 0.01 M laurate. This is the concentration (the critical micelle concentration) at which laurate abruptly associates into micelles, a fact demonstrated in Figure 2. In this graph the absorbance at 610 mμ of 1.05 × 10^{-5} M pinacyanol chloride (under conditions identical with those used for the kinetic runs) is plotted *vs.* [laurate]. The sudden increase in absorbance is caused by absorption of the dye onto or into the soap micelles.[18] The shapes of the curves of Figure 1 prove that simple

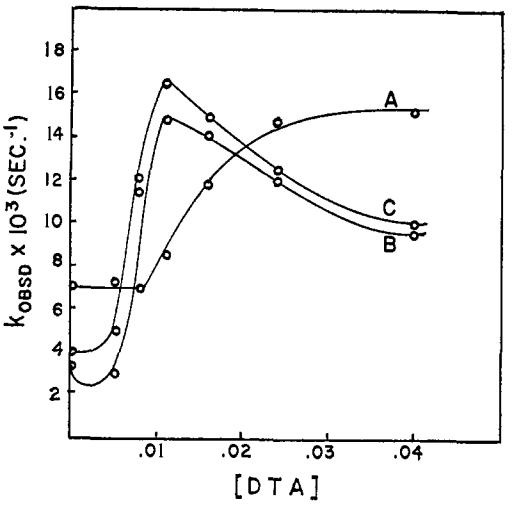

Figure 3. Plots of observed rate constants for the hydrolysis of *p*-nitrophenyl acetate (A), mono-*p*-nitrophenyl dodecanedioate (B), and *p*-nitrophenyl octanoate (C) at pH 10.49, I = 0.2, 25.0°, *vs.* concentration of *n*-dodecyltrimethylammonium bromide (DTA).

1:1 complexation between substrate and surfactant cannot be the cause of the rate inhibitions.[19] Clearly, interaction between the esters and *micellar* surfactant is the source of the rate perturbations.

Table I. The Observed Rate Constants for Hydrolysis of Mono-*p*-nitrophenyl Dodecanedioate in Laurate Solutions[a]

(Laurate) × 10^2, M	k_{obsd} × 10^3, sec^{-1}
0.00	7.90
0.216	7.69
0.634	7.78
1.05	6.89
1.52	4.22
2.17	2.78
3.06	1.84
4.08	1.40
6.48	0.94

[a] In 0.8% methanol-water (v/v) at 50.0°; pH 9.59; I = 0.1; ester concentration = 5.79 × 10^{-5} M.

The inhibitory effect of laurate is strongly dependent on the structure of the substrate. While 0.02 M laurate reduces the rate of hydrolysis of C to 4% of that in the absence of surfactant, the reactivity of A is lowered to only 83% of normal. In all the kinetic runs the initial substrate concentration was well below 10^{-4} M, making it very unlikely that the difference in behavior between the substrates is caused by one of them inducing micellation or else seriously perturbing the structure of the micelles. In this connection it is important to note that the reactions were first order in substrate at the high dilutions. The causes for the rate differences will be discussed in the following section.

In Figure 3 the dependence of the rate constants for hydrolysis of A, B, and C at pH 10.49, 25°, on the concentration of *n*-dodecyltrimethylammonium cation (F) is presented. The bell-shaped curves are similar to that found for basic hydrolysis of benzylideneacetophenone in cetyltrimethylammonium ion solutions.[4] *n*-Dodecylpyridinium ion (G), on the other hand, has hardly

(19) F. M. Menger and M. L. Bender, *J. Am. Chem. Soc.*, **88**, 131 (1966).

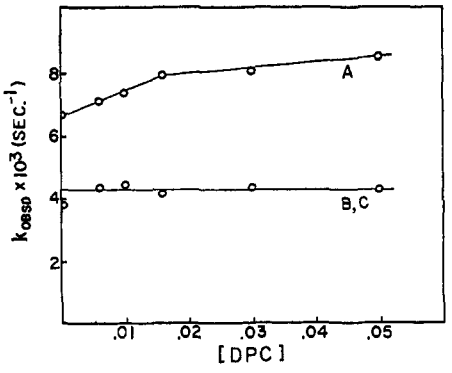

Figure 4. Plots of observed rate constants for the hydrolysis of *p*-nitrophenyl acetate (A), mono-*p*-nitrophenyl dodecanedioate (B), and *p*-nitrophenyl octanoate (C) at pH 10.48, I = 0.5, 25.0°, *vs.* concentration of *n*-dodecylpyridinium chloride (DPC). Points for B and C are virtually superimposable.

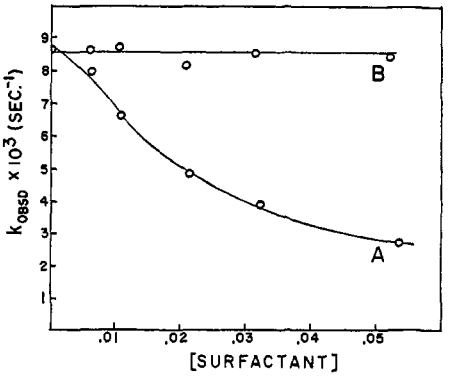

Figure 5. Plots of observed rate constants for hydrolysis o benzoylcholine at pH 12.14, I = 0.5, 25.0°, *vs.* concentration o laurate (A) and *n*-dodecyltrimethylammonium bromide (B).

any effect on the hydrolysis of the three *p*-nitrophenyl esters (Figure 4). The rate constants for hydrolysis of our only cationic substrate, benzoylcholine (D), in laurate and *n*-dodecyltrimethylammonium ion solutions are given in Figures 5A and 5B, respectively.

Discussion

In a homogeneous surfactant solution (above the critical micelle concentration) the reactive site of a substrate may exist in one or more of the following environments: the micelle interior, the micelle–water interface, and the bulk solvent. A few comments about these regions are necessary for the understanding of our interpretation of the kinetic data.

The nature of the micelle interior, formed by the lyophobic portion of the surfactant, is not fully understood. From high-resolution nmr experiments it appears that (a) the center of the micelle is similar to liquid hydrocarbon[20] and that (b) water can penetrate the micelle[21] so that part of the alkyl chain, perhaps the first five carbons from the ionic group,[22] is exposed to the solvent. (In addition it is believed that folding of the chains in the interior is not extensive because the diameter of the Hartley spherical micelle is roughly twice that of the fully extended surfactant molecule.[23]) An ester substrate adsorbed into the very inner part of a micelle would be inert to hydroxide ion catalyzed hydrolysis because the anionic nucleophile is certainly absent in the hydrocarbon. Unfortunately, it is less clear what the effect would be of adsorption of an ester into the outer aqueous portion of the interior. If the micelle is a very compact unit, then most of the interior water will be highly structured; all available evidence[19,24] indicates that basic hydrolysis would be markedly impeded in such a situation. However, it is more likely that the micelle is a loose aggregation[25] and that the water within the micelle resembles bulk water containing some organic solvent. In this case the kinetic perturbation of adsorption would not be expected to be large. Long-range electrostatic effects originating from the charged micelle interface could well be the major factor affecting hydrolysis rates inside the interior aqueous shell.

The micelle surface is another possible site of substrate adsorption. The ionic portions of the surfactant molecules form highly charged surfaces which attract small counterions from the solution in order to relieve electrostatic repulsion. Thermal motion, which tends to produce uniform distribution of the ions, disturbs the ionic array resulting in the well-known diffuse electrical double layer. Basic ester hydrolysis is not very sensitive to ionic strength changes, so that the high concentration of ions at the double layer would not in itself greatly affect the reaction. However, adsorption of an ester at the surface of a cationic micelle could result in considerable rate enhancement because hydroxide ion (along with other anions) collect in this region. Several rate enhancements have been attributed to this phenomenon.[5,8]

A third possibility is that a substrate is not adsorbed by the micelles and exists in the free solution. The less water soluble a substrate, the more extensively it will be partitioned into the micellar phase.[26]

Little evidence exists at this time concerning where adsorption occurs within the micelle, but a particularly interesting article on this point has recently appeared. Eriksson and Gillberg[27] showed by resonance line shifts and line-width changes in the nmr that cetyltrimethylammonium bromide adsorbs cyclohexane and cumene into the inner hydrocarbon portion of the micelles, whereas N,N-dimethylaniline and nitrobenzene reside in the aqueous section of the interior not far from the surface.

We now direct attention to Figure 1 which shows that laurate micelles inhibit hydrolysis of *p*-nitrophenyl acetate (A), mono-*p*-nitrophenyl dodecanedioate (B), and *p*-nitrophenyl octanoate (C) with an increasing order of effectiveness.[28] The solubilities of the substrates in water decrease in the same order, suggesting that the differences in behavior between the substrates may be due, at least in part, to varying degrees of non-

(20) J. Clifford and B. A. Pethica, *Trans. Faraday Soc.*, **60**, 1483 (1964).
(21) J. Clifford, *ibid.*, **61**, 1276 (1965).
(22) M. J. Vold and R. D. Vold, "Colloid Chemistry," Reinhold Publishing Corp., New York, N. Y., 1964, p 63.
(23) H. B. Klevens, *Chem. Rev.*, **47**, 1 (1950).
(24) E. F. J. Duynstee and E. Grunwald, *Tetrahedron*, 21, 2401 (1965).
(25) Reference 3b, Chapter 9.
(26) M. E. L. McBain and E. Hutchinson, "Solubilization and Related Phenomena," Academic Press Inc., New York, N. Y., 1955.
(27) J. C. Eriksson and G. Gillberg, *Acta Chem. Scand.*, 20, 2019 (1966).
(28) The fact that surfactants have a larger effect on the hydrolysis of long-chain, as opposed to short-chain, esters has already been established.[8]

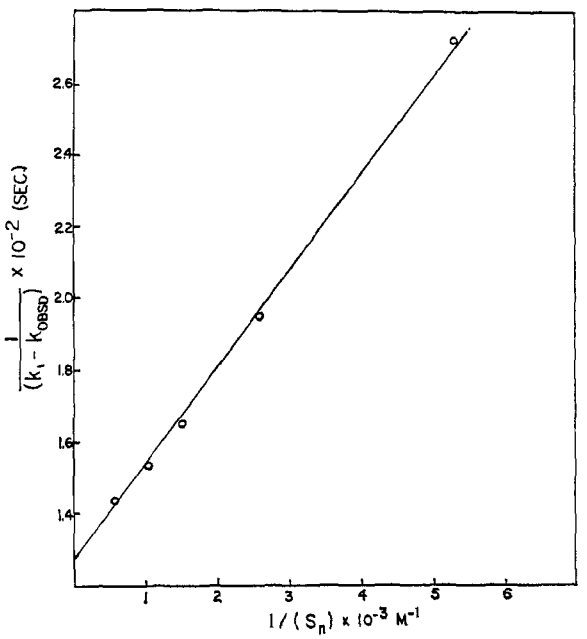

Figure 6. The determination of the rate constant for hydrolysis of adsorbed mono-*p*-nitrophenyl dodecanedioate. See eq 3 and accompanying text.

micellar material. Thus, the scheme shown in eq 1 is proposed in which S_n, E, and S_nE represent micellar surfactant, free ester, and adsorbed ester, respectively.[29] In order to evaluate the micelle concentration we make use of the "phase-separation" concept which assumes that the unassociated surfactant concentration remains

$$\begin{array}{ccc} S_n + E & \overset{K}{\rightleftharpoons} & S_nE \\ & \downarrow k_1 \quad \downarrow k_2 & \\ & P \quad P & \end{array} \qquad (1)$$

constant above the CMC. (This assumption has experimental support[30] and greatly simplifies matters here, but it also has limitations.)[31] If the average number of molecules per laurate micelle is 33,[32] then the micelle concentration is approximated by eq 2 where

$$(S_n) = \frac{(\text{laurate})_t - \text{CMC}}{33} \qquad (2)$$

$(\text{laurate})_t$ signifies the total concentration of laurate. The rate constant for hydrolysis of adsorbed substrate, k_2, can now be determined from eq 3[33] by plotting

$$\frac{1}{(k_1 - k_{obsd})} = \frac{1}{(k_1 - k_2)} + \frac{1}{(k_1 - k_2)K(S_n)} \qquad (3)$$

$1/(k_1 - k_{obsd})$ *vs.* $1/(S_n)$ using measured values of k_1 and k_{obsd} (the rate constants for ester hydrolysis in the absence and presence of surfactant such as given in Table I). Such a plot for substrate B (mono-*p*-nitrophenyl dodecanedioate) is presented in Figure 6. Its linearity is remarkable in view of the assumptions made in this analysis: (a) substrate does not complex with surfactant monomer; (b) substrate does not perturb micellation; (c) substrate associates with the micelles in a 1:1 stoichiometry; (d) micellation occurs exactly at the CMC rather than over a small concentration range; (e) eq 2 is valid.

Since the intercepts of the reciprocal plots for substrates A and B are within the experimental error of $1/k_1$, the rate of hydrolysis of these substrates when adsorbed into the micelles must be zero![34] Application of eq 3 to substrate C fails because K is too large for an accurate plot, but clearly micellar C is also unreactive since 0.03 M laurate reduces the hydrolysis rate to less than 3% of that in the absence of surfactant. The only reason that surfactant affects the rate of hydrolysis of *p*-nitrophenyl acetate (A) less than the other substrates (Figure 1) is that partitioning of A into the micellar phase from the solvent is less favorable.

The remarkable rate inhibitions may be explained by ester adsorption into the hydrocarbon center of the micelles where presumably there is no anionic nucleophile. Alternatively, adsorption could occur within the outer aqueous areas of the micelles where the hydroxide ion concentration might be greatly reduced because of electrostatic factors originating at the micelle surface. We favor the former rationale for two reasons. First of all, substrate B is ionic; this means that one end of the adsorbed molecule is in the aqueous region of the micelle. The ester moiety, many carbons away from the ionic end, must then be directed toward the center of the micelle (unless B forms a loop within the aggregate). Indeed, substrate B was selected for study because it was considered a useful compound for examining the properties of the inner regions of micelles. Second, while it is conceivable that there is a lowered hydroxide ion concentration in the aqueous portion of the micelles, there still remains a very high concentration of another nucleophile, carboxylate anion. Intramolecular carboxylate catalysis of ester hydrolyses can lead to enormous rate increases,[35] suggesting that the ester sites are not very near the micelle surface. This seems to be true even for a cationic substrate, benzoylcholine (D; Figure 5A).

It is possible to evaluate the association constant for micelle–substrate interaction (K) from eq 3. The value of K, defined as $(S_nE)/(S_n)(E)$, for substrate B is 4.5×10^3 M^{-1}. Laurate micelles thus bind B better than α-chymotrypsin binds many of its specific substrates. The truly sizeable association constant is further evidence of internal adsorption as it is difficult to imagine why surface adsorption would be so efficient.

The effect of *n*-dodecyltrimethylammonium ion (F) on the hydrolyses of the four substrates can be seen in Figures 3 and 5B. The hydrolysis rates of the long-chain substrates B and C decrease with increasing surfactant in the region above the CMC. Partitioning of the esters into the hydrocarbon interior of the micelles seems to be occurring much like it does in the laurate system. The substrate–micelle association constants for anionic B and neutral C are similar in the cationic soap solutions, whereas laurate micelles bind B less ef-

(29) See A. K. Colter, S. S. Wang, G. H. Megerle, and P. S. Ossip, *J. Am. Chem. Soc.*, **86**, 3106 (1964), for a similar scheme describing a nonmicellar system.

(30) (a) K. Shinoda and E. Hutchinson, *J. Phys. Chem.*, **66**, 557 (1962); (b) J. T. Yang and J. F. Foster, *ibid.*, **57**, 628 (1953).

(31) M. Abu-Hamdiyyah and K. J. Mysels, *ibid.*, 71, 418 (1967).

(32) Reference 3a, p 67.

(33) Equation 3 holds only for those runs in which $(S_n) >$ (substrate), that is, where $(\text{laurate})_t >$ CMC.

(34) It is interesting that surfactants can significantly inhibit *unimolecular* light-induced reactions as well: F. M. Menger, S. P. Pappas, and R. Gresham, unpublished observations.

(35) T. C. Bruice and U. K. Pandit, *J. Am. Chem. Soc.*, **82**, 3386 (1960).

fectively than C (Figure 1). This is not surprising; the anionic end of B can be readily included within the electrical double layer of surfactant F micelles. Since B is more water soluble than C, it is clear that the affinity of *n*-dodecyltrimethylammonium ion micelles for B is in reality larger than for C. The small substrate A shows a modest rate increase above the CMC, which is consistent with inclusion of the ester within the outer aqueous portion of the micelle interior or else directly on the micelle surface. An interesting feature of Figure 3 is that the hydrolysis rates of the long-chain esters are enhanced *below* the CMC, while *p*-nitrophenyl acetate is not affected in this concentration range. The rate of basic hydrolysis of benzylideneacetophenone also increases in a cationic surfactant solution below the CMC.[4] This was explained by association of the Schiff base with one or more surfactant molecules to form a positively charged complex which reacts readily with hydroxide ion. Our findings are in agreement with this rationale since the only substrates which display pre-CMC rate perturbations are ones which possess large hydrocarbon moieties that can hydrophobically bind to surfactant. Perhaps the small rate drop below the CMC in Figure 1C is also caused by nonmicellar complexation.

n-Dodecylpyridinium ion (G) has either a small effect (Figure 4A) or no effect at all (Figures 4B and 4C) on the esters. Therefore, k_1 is nearly equal to k_2 (eq 1) or else there is little substrate adsorption (K is a small number). Some complexation is taking place because the solubilities of esters B and C are increased in the presence of *n*-dodecylpyridinium ion micelles. We conjecture that, because of the bulk and flatness of the surfactant "heads," the micelles are unusually loose structures containing considerable amounts of water. Association constants and rate perturbations are consequently not large. In any event the properties of solutions of *n*-dodecylpyridinium ion and *n*-dodecyltrimethylammonium ion are appreciably different despite the structural similarity of the surfactants.

A great deal remains to be learned about the effect of micellation upon reaction rates. In addition, virtually nothing is known about how surfactants affect the stereochemistry and product distribution of thermal and photochemical reactions. These important aspects of molecular aggregate chemistry are also currently under investigation in these laboratories.

Acknowledgment. The authors are grateful to the McCandless Fund of Emory University and to the Petroleum Research Fund for assistance. National Defense Education Act predoctoral support for Carolyn E. Portnoy is also appreciated.

Aggregation of Metallochlorophylls[1]

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Abstract: The self-aggregation of divalent nickel, copper, and zinc methyl pheophorbides a and b has been examined by infrared spectroscopy. Of these, only the zinc compounds show significant coordination aggregation. Nmr measurements on zinc pheophytin a and zinc methyl pheophorbide a and b show that both coordination aggregation and $\pi-\pi$ aggregation occur in nonpolar solvents. Nmr and infrared measurements indicate that under comparable conditions in nonpolar solvents the zinc chlorophylls are aggregated to a considerably lesser extent than are the magnesium chlorophylls. Visible and infrared spectra of nickel, copper, and zinc methyl pheophorbides a and b are reported, and tentative band assignments are made. Considerations of absorption position and relative intensities suggest that the extent of metal–ligand interaction follows the order: Ni > Cu > Zn > Mg.

Metal ions play a decisive but little understood role in the photosynthetic unit. For example, the most important compound of photosynthesis, chlorophyll, is a magnesium(II) complex of a dihydroporphyrin (chlorin) ligand. Examination of chlorophyll derivatives in which magnesium is replaced by other metal ions (metallochlorophylls) are valuable in that they provide information about the contribution of the metal to the various properties and functions of chlorophyll. The state of aggregation of chlorophyll is one property in particular that is a subject of keen interest today.[3] Association of chlorophyll molecules in solution can occur in a number of ways. One mechanism, designated coordination aggregation, involves the intermolecular coordination of the ketone oxygen of one chlorophyll molecule to a magnesium atom in another molecule.[4] An important question then is: is coordination aggregation a unique property of magnesium-containing chlorophylls, or do other metallochlorophylls show similar behavior? The aggregation properties of metallochlorophylls in solution appear not to have been previously studied.

This paper presents some new information derived from infrared and nmr measurements on the aggregation behavior of divalent nickel, copper, and zinc chlorophylls. The structural formulas, nomenclature, and proton numbering of the materials studied are given

(1) Based on work performed under the auspices of the U. S. Atomic Energy Commission.

(2) Resident Research Associate, 1964–1966.

(3) See, for example, J. J. Katz, R. C. Dougherty, and L. J. Boucher in "The Chlorophylls," L. P. Vernon and G. R. Seely, Ed., Academic Press Inc., New York, N. Y., 1966, p 186.

(4) J. J. Katz, G. L. Closs, F. C. Pennington, M. R. Thomas, and H. H. Strain, *J. Am. Chem. Soc.*, **85**, 3801 (1963).