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Dipolar Micelles. 8. Hydrolysis of Substituted Phenyl Esters in a Hydroxamic Acid Surfactant

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The reactions of hydroxamic acid catalysts of the structure $CH_3(CH_2)_nN^+(CH_3)_2(CH_2)_3CONHOH\ Br^-$ [$n = 15$ (I3C), $n = 0$ (I3M)] with substituted phenyl esters have been studied. The kinetics in I3C followed the expression: $k_{obsd} = k_0 + k_cK_a/(K_a + H^+) + k_{OH}[OH^-]$. The water catalysis rates k_0 for all the esters studied were significantly greater than the spontaneous rate constants reported in the literature for esters of identical leaving groups. The magnitude of the water rate constants, and their dependence on microenvironmental factors as displayed by mixed micellar systems, indicated that the reaction proceeds via electrophilic assistance by the onium head groups. Nucleophilic attack by the hydroxamate anion (k_c) in I3C on the esters corresponds to a β Brönsted value of -1.1. The results point out that although I3C is expected to be an α-effector catalyst, the relative enhancement of the rate constants is very small. This was explained in terms of proximity and electrostatic effects in the transition state. The basic hydrolytic rates k_{OH} and the titrimetric behavior of I3C were also discussed.

In order to gain further insight into microenvironmental parameters operating in enzymic reactions, various types of micellar catalyzed reactions have lately been investigated as model systems.[1]

It was proposed that rate acceleration by cationic micelles is generally attained for reactions characterized by a delocalized, negatively charged transition state. Recently, Kunitake[2] has suggested that the remarkable rate enhancement of some anionic nucleophiles in cationic micelles is mainly derived from the formation of hydrophobic ion pairs. The important role of ion pair formation on the reactivity of nucleophiles was also demonstrated in the case of macrocyclic paracyclophane oximes.[3]

In our previous studies[4] we have designed many surfactant models in which the following three features are all covalently bound to the same skeleton: (a) an anionic nucleophile, (b) a positively charged ammonium group, and (c) a hydrophobic long alkyl chain.

This includes a number of betaine- and choline-like derivatives. Similar investigations on the catalytic properties of nucleophilic micelles have been reported in the literature.[5-9]

Continuing the investigation on positively charged functional micelles we became interested in studying the kinetic effects displayed by a structurally related micellar system possessing an α-effector catalyst. Since the hydroxamate anion is known to be highly nucleophilic toward phenyl esters[10-13] and its catalytic reactivity is increased in cationic surfactants, a hydroxamic acid surfactant of type I3C was synthesized.

The present report describes the kinetic results obtained for the hydrolysis of substituted phenyl esters in various micellar[44] systems of I3C, II2 + I3C, I3C + III1, I3C + III2, I3C + III3 and in the analogous nonsurfactant catalyst I3M. The study also includes titrimetric data of homogenous micellar and mixed micellar systems at various ionic strengths.

Detergents:

$$CH_3(CH_2)_{15}N^+(CH_3)_2(CH_2)_3CONHOH\quad Br^-$$

I3C

$$(CH_3)_3N^+(CH_2)_3CONHOH\quad Br^-$$

I3M

$$CH_3(CH_2)_mN^+(CH_3)_2(CH_2)_nH\quad Br^-$$

II1C, II2

$$(CH_3(CH_2)_mN^+(CH_3)_2(CH_2)_nCOOH\quad Br^-$$

III1, III2, III3, III3C

II1C, $m = 15$, $n = 1$; II2, $m = 10$, $n = 2$; III1, $m = 0$, $n = 1$; III2, $m = 9$, $n = 2$; III3, $m = 9$, $n = 3$; III3C, $m = 15$, $n = 3$

Esters: Phenyl decanoate (PD), phenyl acetate (PA), tolyl decanoate (PMPD), 4-chlorophenyl decanoate (PCPD) and 3-chlorophenyl decanoate (MCPD).

Experimental Section

Materials. *N*-Cetyl-*N,N*-dimethyl-*N*-(3-hydroxylaminocarbonylpropyl)ammonium Bromide (I3C). *N*-Cetyl-*N,N*-dimethyl-*N*-(3-ethoxycarbonylpropyl)ammonium bromide (III3CE) was prepared by adding 55 g (0.21 mol) of cetyldimethylamine in 100 mL of ethanol to 40 g (0.21 mol) of ethyl 4-bromobutanoate.

The solution was kept at 40 °C for 3 days. Removal of the solvent gave an oil which was crystallized from ethanol–ether, mp 72 °C. Anal. Calcd for $C_{24}H_{50}BrNO_2$: C, 62.01; H, 10.77; N, 3.00; Br, 17.24. Found: C, 62.2; H, 10.88; N, 3.28; Br, 17.53.

A solution of 2.9 g (0.054 mol) of sodium methoxide in 25 mL of methanol was added to 3.8 g (0.054 mol) of hydroxylamine hydrochloride in 25 mL of methanol. After filtration the solution was cooled to 0 °C and 10 g (0.021 mol) of III3CE in 40 mL of methanol was added dropwise over 1.5 h. The solution was kept at 0 °C for 3 weeks. The methanol was removed in vacuo and the remaining viscous oil was dissolved in water, washed with ether, and lyophilized to dryness. The residue was recrystallized from ethanol–ether, mp 180 °C. Anal. Calcd

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Table I. Titrimetric Behavior of Micellar Hydroxamic and Carboxylic Acids[d] at Various Ionic Strengths (μ)

	pK_a	pK_{int}	μ	n	S
I3C[b]	9.10	8.62	0.15	1.51	0.96
I3C[b]	9.14	9.03	1	1.12	0.22
I3C + II2[a]	9.04	8.80	0.15	1.25	0.48
I3C + II2[a]	9.08	9.02	1	1.06	0.12
I3C + III1[a]	9.20	8.60	0.15	1.63	1.20
I3C + III3[a]	9.20	8.60	0.15	1.63	1.20
IV + II1C[c]	9.04	8.55	0.01	1.50	0.970
IV + II1C[c]	9.75	9.72	0.5	1.03	0.05
V + II1C[c]	9.38	8.95	0.01	1.45	0.85
V + II1C[c]	10.7	10.33	0.5	1.39	0.74
VI + II1C[c]	8.41	8.20	0.01	1.21	0.40
VI + II1C[c]	9.72		0.5	0.93	
III3[b]	4.10	3.87	0.1	1.24	0.46
III3[b]	4.35	4.15	0.8	1.21	0.40
III3[b]	4.55	4.30	2.5	1.26	0.50
III3C[b]	4.30	3.60	0.1	1.73	1.4
III3C[b]	4.70	4.15	0.8	1.57	1.1
III3C[b]	4.86	4.36	2.5	1.52	1.0

[a] Total concentration of I3C + II2 = 0.1 M, the ratio I3C:II2 = 0.1 M, t = 30 °C, ionic strength maintained by KBr. [b] Detergent concentration = 0.1 M, t = 30 °C, ionic strength maintained by KBr. [c] See ref 13c. [d] IV, *N*-hydroxy-*N*-lauryl-4-imidazolecarboxamide (LImHA1); V, *N*-hydroxy-*N*-lauryl-3-(4-imidazolyl)-propionamide (PrHA4); VI, *N*-laurylbenzohydroxamic acid (LBHA6).

for $C_{22}H_{47}BrN_2O_2$: C, 58.55; H, 10.42; N, 6.20; Br, 17.73. Found: C, 58.40; H, 10.16; N, 5.95; Br, 18.

***N*-(3-Hydroxylaminocarbonylpropyl)-*N,N,N*-trimethylammonium Bromide (I3M).** *N*-(3-Ethoxycarbonylpropyl)-*N,N,N*-trimethylammonium bromide (III3ME) was prepared by the above method from 39 g (0.2 mol) of ethyl 4-bromobutanoate and 35.5 g (0.6 mol) of trimethylamine in methanol, mp 150 °C. Anal. Calcd for $C_9H_{20}BrO_2N$: C, 42.52; H, 7.87; N, 5.51; Br, 31.49. Found: C, 42.74; H, 8.05; N, 5.55; Br, 31.87. Compound I3M was prepared from III3ME by a procedure similar to that described for I3C, mp 160 °C. Anal. Calcd for $C_7H_{17}BrN_2O_2$: C, 34.85; H, 7.05; N, 11.61; Br, 33.19. Found: C, 35.05; H, 7.19; N, 11.67; Br, 34.00.

The Esters: PD, PA, PMPD, PCPD, and MCPD were prepared as previously described.[4a]

The Detergents: II2, III1, III2, III3, and III3C were available from a previous study.[4d]

Kinetics. Kinetic measurements were made with a unicam SP800 spectrophotometer, equipped with jacketed cell holder. Water was circulated through the cuvette holder at 30 °C. The reaction of long-chain esters was carried out with (i) 0.1 M of catalyst (I3C) at ionic strength of μ = 0.15 M (KBr), (ii) 0.1 M of mixed micelles (I3C + II2) at a ratio of 1(I3C):4(II2) and at ionic strength of μ = 1 M (KBr), and (iii) 0.1 M of mixed micelles: I3C + II2, I3C + III1, I3C + III2, and I3C + III3 at a ratio of 1(I3C):4(II2,III1,III2,III3) and at ionic strength of μ = 0.15 M (KBr).

At a pH range of 8.2–9.8 the kinetic runs were conducted without the addition of an external buffer. To maintain constant pH's below pH 8.0 and above pH 10.0, phosphate and carbonate buffers were employed, respectively. The concentration of the buffers in each kinetic experiment was 0.05 M. From the extrapolation of the rate constants to zero buffer concentration it was found that the buffers effect (at 0.05 M) on the rate constants was negligible.

The pH of the kinetic solutions was determined prior to and at the completion of reactions using a Radiometer Model 26 pH meter. To determine pD the glass electrode correction equation was employed.[14]

The kinetic measurements of the phenyl acetate ester were performed at: (i) serial concentrations of detergent (I3C) in the range of 5×10^{14}–0.2 M, pH 8.97, and at ionic strength of μ = 0.25 M (KBr); (ii) four concentrations of catalyst I3M (0.01–0.05) at each of four pH values. Stock solutions of the esters were prepared in acetonitrile and kept cold when not used. The reactions were initiated by addition of 5–10 μL of the ester to a cuvette containing the catalyst solution equilibrated at 30 °C. The rate of phenoxide ion liberation was determined at the following wavelengths: *p*-H, 277 nm; *p*-CH$_3$, 288 nm; *p*-Cl, 287 nm; *m*-Cl, 280 nm.

The pseudo-first-order rate constants were calculated either by the method of Guggenheim[15] or by the first-order rate plots log [$(OD_\infty - OD_0)/(OD_\infty - OD_t)$] vs. time ($t$).

pK_a Determinations. The pK_a of I3M, I3C + II2, I3C + III1, I3C + III2, and I3C + III3 were titrimetrically determined. Solutions of 0.1 M of surfactants at appropriate ionic strength (see Table I) were titrated with concentrated potassium hydroxide using a microburet. The solutions were thermostated at 30 °C and the pH was measured.

Cmc Determinations. The surface tension of I3C was measured with a Fisher automatic surface "Tensiomat" on aqueous solutions in a jacketed cell thermostated at 30 °C, μ = 0.15 (KBr). The cmc was determined as 5×10^{-4} M from a graph of the observed surface tension vs. log (concentration) of the surfactant.

Results and Discussion

Titrimetric Results. It is well known that functional micelles behave as polyelectrolytes and their apparent dissociation constant (K_{app}) varies with the degree of dissociation α. In many cases the dependency found between pK_{app} and α is linear within a wide range, thus the titration data are in accord either with the modified Henderson–Hasselbach[16] eq 1 or with the Linderstrom-Lang eq 2 accepted in polymer chemistry[17]

$$pK_a = pH + n \log (1 - \alpha)/\alpha \qquad (1)$$

where the pK_a value is the pK_{app} at α = 0.5

$$pK_{app} = pH + \log (1 - \alpha)/\alpha = pK_0 - 0.434e\psi/kT = pK_{int} + S\alpha \qquad (2)$$

where S is the slope of the plot pK_{app} vs. α, ψ is the electric surface potential, pK_0 is the pK_{app} value at ψ = 0, pK_{int} is the pK_{app} at α = 0, and e is the elementary charge. Equation 2 can also be expressed by

$$\psi = S(1 - \alpha)kT/0.434e \qquad (3)$$

From eq 3 it is evident that there is a decrease in the electric surface potential ψ with the increased degree of dissociation of long chain cationic micelles. Table I summarizes the pK_a, pK_{int}, n, and S values of several hydroxamic and betaine-like micelles.

Several factors which were assumed to affect the surface electric potential and consequently S and n values have been reported in the literature: (i) the ionic strength of the solution;[18] (ii) the dielectric constant, the solvent structure and property at the interface;[19] and (iii) conformational and steric arrangement of the polyelectrolyte units.[20]

From Table I it is observed that regarding the homogeneous micelles I3C and III3C the shifts of the pK_a's and the S values due to variation of ionic strength are in the expected direction. As the S value decreases the pK_a value increases accordingly. On the other hand, this is not the case with III3. Takiwa and Ohki[20] have suggested that the reduced electric charge of dodecyldihydroxyethylamine oxide, compared to dodecylamine oxide, might originate from the looser packing of aggregates in the former micelle. This conclusion explained the considerably higher S values of micelle III3C than that observed in III3; however, it is not consistent with the unaffected S values of III3 as a function of the ionic strength. This suggests that in addition to the effect of the surface charge density on the S and the pK_a values, other microenvironmental factors derived from changes in the micelle aggregation number,[18,21] micelle shape,[22] micelle cmc,[18,21,23] micelle hydration,[24] counterion penetration,[25] and the location of the dissociable head groups[4a,d] play a major role as the ionic strength is varied. The microenvironmental factors might lead to parallel lines on the plot of pK_{app} vs. α and consequently result in a shift in the pK_a value while the slope remains constant. This titrimetric behavior was actually found in the case of dodecyldimethylamine oxide.[20]

Table II. Rate Constants k_0 (s^{-1}), k_c (s^{-1}), and k_{OH} (M^{-1} s^{-1}) for the Hydrolyses of PMD, PD, PCPD, and MCPD in Micelles II2 and I3C + II2 at 30 °C (μ = 1 M (KBr))

		PMD			PD			PCPD			MCPD		
surfactants	pK_a	10^3k_0	10^3k_c	k_{OH}	10^3k_0	10^3k_c	k_{OH}	10^3k_0	10^3k_c	k_{OH}	10^3k_0	10^3k_c	k_{OH}
I3C + II2[a]	9.08	0.03	0.92	0.18	0.09	1.3	0.3	0.2	8.2	1.2	0.3	17.6	2.3
II3[b]				0.018			0.023			0.062			0.094

[a] Ratio of 1(I3C):4(II2); total concentration of mixed detergents is 0.1 M. [b] Detergent concentration is 0.1 M.

Table III. Rate Constants k_0 (s^{-1}), k_c (s^{-1}), and k_{OH} (M^{-1} s^{-1}) for the Hydrolysis of Phenyl Decanoate in Micelle I3C and Mixed Micelles of I3C at 30 °C (μ = 0.15 M (KBr))

	I3C[e]	I3C + II2[a]	I3C + III1[a]	I3C + III2[a]	I3C + III3[a]	I3M
pK_a	9.1	9.04	9.20	9.20	9.20	8.95
10^3k_0	2.5 (1.5)[b]	0.08	0.25	0.16	0.4	
10^3k_c	16 (14)[b]	5.4	3	8.1	5.5	1900[c,d]
k_{OH}						1.42[c]

[a] Ratio of 1(I3C):4(II2,III1,III2,III3), total concentration of mixed detergents is 0.1 M. [b] In D_2O. [c] For PA. [d] Second-order rate constants (M^{-1} s^{-1}). [e] For the ester PCPD the rate constants are 10^3k_0 = 15 s^{-1}; 10^3k_c = 97 s^{-1}.

The electric surface potential of the mixed micelles composed of I3C + II2 and I3C + III(1,3) is not directly related to the slope S expressed by eq 3, since ψ does not approach zero as $\alpha \to 1$. However, the slope S might serve as a qualitative indication for the changes of Ψ associated with the increasing degree of α. From Table I it is inferred that as compared to I3C, the slope S of the mixed micelle composed of I3C(C_{16}) and II2(C_{10}) is smaller and shows higher sensitivity to changes of ionic strength. On the other hand in the case of the mixed micelles I3C + III1 and I3C + III3 the slope S is significantly greater than that of I3C + II2 and III3. These phenomena should be related to differences in the HLB (hydrophilic–lipophilic balance) of the various systems.

The effect of ionic strength on the titrimetric behavior of the mixed micelles reported by Kunitake,[13c] IV + III1C, V + III1C, and VI + III1C, is more pronounced as observed by the shift of the corresponding pK_a values. Although the slope S decreases with an increase in ionic strength the magnitude of the variation does not show a proportional correlation.

Catalysis by Hydroxamate Ion. The observed first-order rate constants for the reaction of substituted phenyl esters with I3C and with mixed micelles of I3C + II2 and I3C + III(1,2,3) are well correlated by

$$k_{obsd} = k_0 + k_cK_a/(K_a + [H^+]) + k_{OH}[\overline{O}H] \qquad (4)$$

where k_c represents the first-order nucleophile rate constant of hydroxamate ion attack upon ester, k_0 the water hydrolysis, and k_{OH} the basic hydrolysis of the esters.

The first-order rate constants k_0 and k_c were obtained from the respective intercept and slope of the plot of k_{obsd} vs. the degree of hydroxamic acid ionization α. The second-order rate constant k_{OH} was determined from the slope of k_{obsd} against hydroxide ion concentration of pH values above α = 1. The intercept of the latter plot was in good agreement with the value $k_0 + k_c$ obtained from the former plot. A theoretical fit for the experimental points of the pH–rate profiles of esters PD, PMD, PCPD, and MCPD in the mixed micelle I3C + II2 at μ = 1 are given in Figure 1. Similar pH–rate profiles were obtained for other mixed micelles employed in this study. The derived rate constants are given in Tables II and III. The reaction with the nonmicellar catalyst I3M is dependent on the total catalyst concentration C_T and fits eq 4 well where $k_c = k_c'C_T$. To derive k_0, k_c, and k_{OH}, k_{obsd} vs. C_T is plotted at constant pH to give slope $k_cK_a/(k_a + [H^+])$ and intercept $k_0 + k_{OH}[OH]$. From secondary plots of slopes vs. $K_a/(K_a + [H^+])$ and intercepts vs. [OH] the various rate constants can be determined.

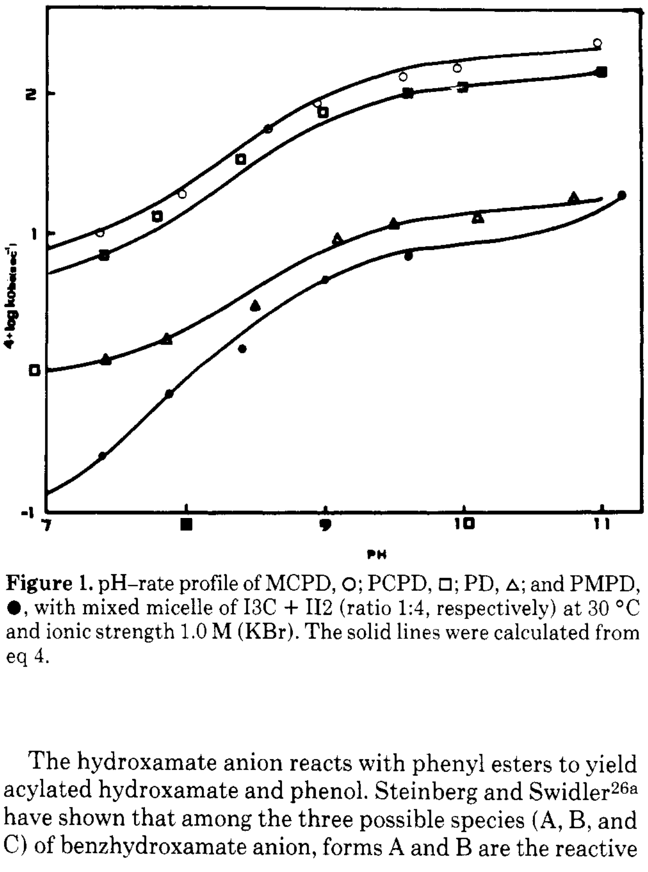
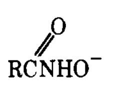
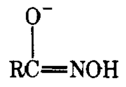
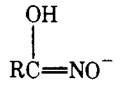


Figure 1. pH–rate profile of MCPD, ○; PCPD, □; PD, △; and PMPD, ●, with mixed micelle of I3C + II2 (ratio 1:4, respectively) at 30 °C and ionic strength 1.0 M (KBr). The solid lines were calculated from eq 4.

The hydroxamate anion reacts with phenyl esters to yield acylated hydroxamate and phenol. Steinberg and Swidler[26a] have shown that among the three possible species (A, B, and C) of benzhydroxamate anion, forms A and B are the reactive


$$\overset{\displaystyle O}{\overset{\displaystyle /\!\!/}{RCNHO^-}}$$
A


$$\overset{\displaystyle O^-}{\overset{|}{RC{=}NOH}}$$
B


$$\overset{\displaystyle OH}{\overset{|}{RC{=}NO^-}}$$
C

species which exist in approximately equal concentrations. Exner,[26b] however, considered form B to be predominant in all stronger and mediately strong hydroxamic acids.

Hudson proposed that in analogy to oximate anions[11a] the ionized hydroxamic acid probably reacts by its oximino form B via concerted intramolecular base catalysis. In the case of micelle I3C as catalyst the deuterium solvent kinetic isotope effect ($k(H_2O)/k(D_2O)$ = 1.14 for PD) indicates that the reaction proceeds via a nucleophilic pathway.

The Brönsted plot for the reaction of the mixed micelles I3C + II2 with PMD, PD, PCPD, and MCPD is shown in Figure

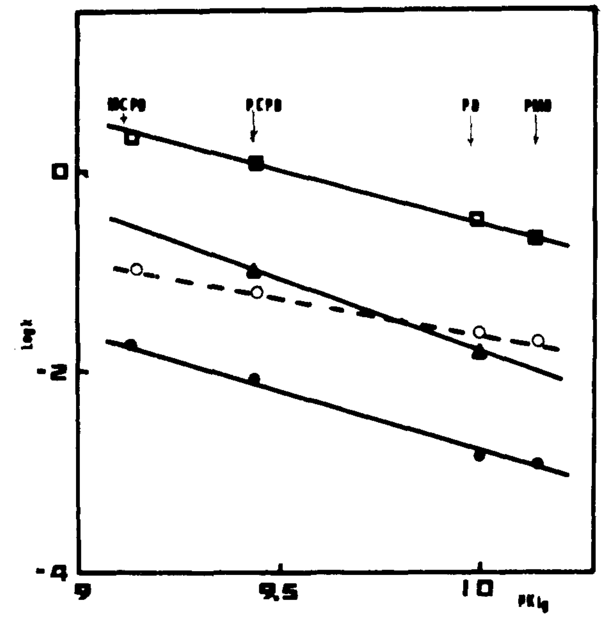


Figure 2. The dependence of the rate constants (k_0, k_c, and k_{OH}) for the reaction of substituted phenyl esters on the pK of the leaving aryloxide ion at 30 °C. k_{OH} in mixed micelles I3C + II2, μ = 1.0 M (KBr), □; k_c in micelle I3C, μ = 0.15 M (KBr), ▲; k_{OH} in micelle II2, μ = 1.0 M (KBr), ○; k_c in mixed micelles I3C + II2, μ = 1.0 M, ●.

2. The dependence of log k_c on the basicity of the leaving groups (pK_{lg}) correlates with

$$\log k_c = -1.1(\mathrm{p}K_{lg}) + 8.17 \qquad (5)$$

It has been noted previously that reaction of α-effector catalysts is associated with a large degree of sensitivity to the attacking nucleophile.[11b,27] Indeed, many nucleophilic reactions of hydroxamate anions showed a β_{nuc} Brönsted relation of 0.68,[13a] 0.72[10b,c] toward p-nitrophenyl acetate (PNPA). Brönsted β_{lg} values of −0.69–0.97 were reported for reactions of substituted phenyl esters with a series of substituted benzhydroxamic acids.[10c]

From the significance generally associated with the β Brönsted coefficients[28] it is assumed that β_{lg} of −1.1 determined in the present study reflects much bond formation between the hydroxamate nucleophile and the reaction center in the transition state. Although the large β_{lg} predicts a large α effect, it was not experimentally observed. In our previous study[4e] it was shown that the rate constants for nucleophilic attack by hexadecylcholinium bromide VII2C (pK_a = 12.8) and by hexadecylhomocholinium bromide VII3C (pK_a = 13.4) on p-nitrophenyl acetate in the micelle substrate intracomplex at μ = 0.15 M are 90 and 285 s^{-1}, respectively. By dividing these values by a factor of 7.5[29,30] and applying a β Brönsted coefficient of 0.76[31] attributed to oxy ions, the rate of PD hydrolysis in hydroxylic micelles of similar basicity to that of I3C could be estimated. The predicted rate constants of PD in the hydroxylic micelles VII2C and VII3C of reduced pK_a values (pK_a = 9.08) should be 18 × 10^{-3} and 19.8 × 10^{-3} s^{-1}, respectively.[32]

By similar calculations, the rate constant of nucleophilic attack by micellized carboxylate anion of identical basicity with I3C (pK_a = 9.08) on PD ester was estimated to be in the range of 23 × 10^{-3}–12 × 10^{-3} s^{-1}.[33]

These results surprisingly point out that the α effect displayed by surfactant I3C is either markedly small or does not exist at all. The rate enhancement associated with anionic nucleophiles such as hydroximate and oximate ions in cationic surfactants had been attributed[13c] to the activation of the nucleophile due to hydrophobic ion pairs.

Comparison between the catalytic reactivities of N-methylmyristoylhydroxamic acid + II1C, IV + II1C, and VI + II1C with that of I3C reveals that the former systems are ~10–20-fold more effective. The kinetic data reported by Bender and Hershfield[12] on the hydrolysis of p-nitrophenyl esters with macrocyclic hydroxamic acid, although conducted under different experimental conditions, also showed catalytic effectiveness which is superior to that of I3C. The highly increased reactivity of the macrocyclic system with the increased acyl chain length of the substrate suggested the formation of stereospecific productive binding between the reactive species. It has been recognized recently that in analogy to intramolecular processes, the catalytic effect produced in the substrate–micelle complex is very sensitive to the spatial orientation of both the catalyst and the substrate. It seems to us that although surfactant I3C bears important potential catalytic functions such as a hydrophobic binding site, and a nucleophilic group and positively charged center on the same skeleton, the relatively reduced catalytic effect might stem in part from steric and microenvironmental factors.

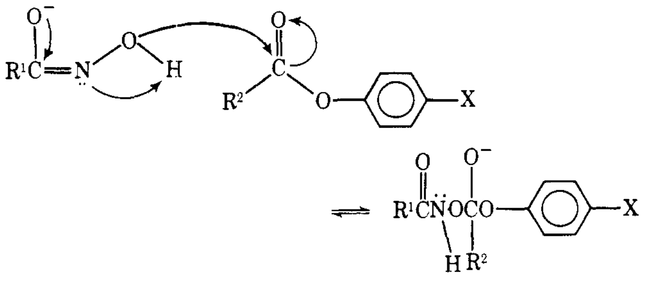
An indication for the role of the microenvironmental factors in controlling the effectiveness of the reaction can be found in the kinetic results of the mixed micelle experiments. Table III implies that the reactivities of mixed micelles composed of surfactant I3C with the betaine type surfactants III1, III2, and III3 varied in spite of their identical dissociation constant. In comparison with I3C + II2, the catalytic rate constant of I3C + III1 decreases by a factor of 1.8 and that of I3C + III2 increases 1.5-fold, whereas the rate constant of I3C + III3 is not affected. Catalysis and inhibition by cationic or anionic micelles was generally rationalized on the assumption that charged micelles interact most effectively with ions of highly dispersed charge.[5e] Thus, the carboxylate anion is expected to destabilize the anionic transition state and consequently tends to reduce the reaction rate.

Indeed, this is the case with I3C + III1. However, in the case of the mixed micelles I3C + III2 the kinetic effect cannot be ascribed to similar arguments. Therefore, it is assumed that the carboxylate group in each of the mixed micelles is placed at a different area on the Stern layer and the moderately increased rate constant in I3C + III2 is attributed to a nonuniform microenvironmental region formed around the transition state. This can be viewed by considering the carboxylate anion of the zwitterionic micelle as serving mainly to induce a favorable proton shift, while the onium group functions to stabilize the negatively charged transition state.

The capability of carboxylate ion to enhance (i) the reactivity of N-methylphthalhydroxamic acid monoanion[13a] toward PNPA; (ii) the transformation of the enol form of acetylacetone to the keto form in alkylammonium propionate micelle,[34] and (iii) the hydrolysis of arylsulfonylmethyl perchlorate[35] in the presence of II1C is consistent with the above mentioned view on the role of the betaine surfactant III2.

Complexation of PA with I3C. The dependence of the first-order rate constant (k_{obsd}) of PA ester on the concentration of surfactant I3C is demonstrated in Figure 3. The

Scheme I



experimental data agree with the kinetic model proposed by Bruice et al.[36] and viewed by Piszkiewicz[37] as analogous to the Hill model

$$\text{product} \xleftarrow{k_w} \text{S} + n\text{D} \underset{k_\text{D}}{\rightleftharpoons} \text{D}_n\text{S} \xrightarrow{k_m} \text{product}$$

where S is the substrate, D is the surfactant monomer, and D_n denotes the micelle.

The observed first-order rate constant for this mechanism is given by

$$k_\text{obsd} = \frac{k_w k_\text{D} + k_\text{m}[\text{D}]^n}{K_\text{D} + [\text{D}]^n} \qquad (6)$$

The data were fitted to the linear plot of log $[k_\text{obsd} - k_0]/[k_m - k_\text{obsd}]$ vs. log [D] where k_m was chosen by a process of trial and error. The slope n of the linear plot describes the index of cooperativity and the intercept equals log K_D. By employing this procedure the rate constant k_m (at pH 8.97), the index n, and K_D were determined to be 210×10^{-3} s^{-1}, 0.96, and 0.144 M, respectively (correlation coefficient 0.9983). These results show that the dissociation constant K_D of the intracomplex substrate–micelle is relatively high, as compared to other hexadecyl ammonium bromide micelles.[38a] Moreover, the K_D value determined above is surprisingly greater than the K_D values reported in the literature for the hydrolyses of PNPA in the presence of functional and nonfunctional onium micelles of shorter alkyl chain length.[38c] The low cooperativity index value of $n = 1$ is also in accord with the view of inhibited intracomplex formation. Furthermore, the effective molarity of k_m(I3C,PA)/$k_\text{cat}\alpha$(I3M,PA) = 0.22 M clearly indicates that the micellar catalysis is of low efficiency. Since the effective molarity of decylcholinium bromide micelle (VII2) toward PNPA was found to be 0.95[4e] it seems likely that the differences in the effectiveness between the above systems can be attributed to proximity factors. This could be verified by the observation that the relative rate constant k(PNPA)/k(PNPD)[4a] for decylcholinium bromide (VII2) is unlike the ratio k_c(PA)/k_c(PD) determined in micelle I3C. The corresponding ratios are 5.1 and 30. Thus, it is suggested that either the substrates or the nucleophiles in the compared systems reside at different locations on the micellar surfaces, and consequently the spatial orientations of the reactants in these systems are not similar.

In analogy to the binding of dyes to DNA,[39] two binding sites have been suggested with micelles: (i) a weak binding site on the exterior of the micelle due to electrostatic interactions (adsorbed state) and (ii) a strong binding site at the interior region due to hydrophobic interaction (adsorbed state).

Since the structure of the micellar surface affects the mode of binding, K_D, n, and k_m, it is likely that the magnitude of all these parameters accentuates the properties of the micellar surface.

Water Hydrolysis (k_0). From Tables II and III it is inferred that the water rate constants k_0 are strongly dependent on the composition and the ionic strength of the mixed micelles studied. In previous reports[25a,b] it was demonstrated that the micellar environment can control the stereochemical pathways of many reactions. The dependency between the binding properties of counterions and micelle-induced partitioning of reactive intermediate was rationalized by solvent interaction with micellar surface. Furthermore, the absence of catalysis in salicylate ester by hexadecyltrimethyl ammonium bromide (II1C) was attributed to lack of water availability near the micelle surface.[40] The behavior of mixed cationic–anionic micellar catalyst toward ester hydrolysis[13c] also strongly suggests the formation of hydrophobic ion pairs and the reduced solvation of the nucleophiles.

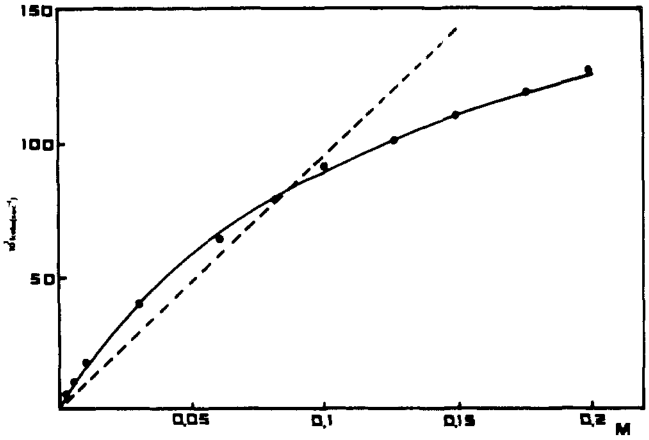


Figure 3. The dependence of the first-order rate constant (k_obsd) for the reaction of PA with surfactant I3C on I3C concentration at 30 °C, μ = 0.25 M, pH 8.97. The solid line was calculated from eq 6. The dashed line was calculated for the reaction (k_c) of PNPA with I3M as a function of the catalyst concentration at 30 °C, μ = 0.15 M and pH 8.97.

In a study on the reaction of substituted benzhydroxamic acids with p-nitrophenyl acetate Kunitake et al.[13a] suggested that in the case of the monoanion of the N-methylphthalhydroxamic acid the reaction proceeds via nucleophilic attack by the undissociated hydroxamic acid assisted by general base catalysis of the carboxylate group. Such a kinetic pathway might also operate in the case of the mixed micelles I3C + III3.

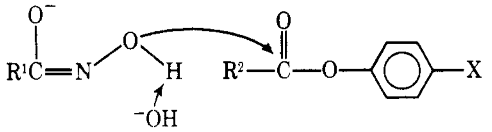
The possibility can be excluded that the water rate k_0 in the latter micellar system includes a general base catalytic term resulting from the participation of the carboxylate anion in the water nucleophilic reaction or a nucleophilic catalytic term subject to the nucleophilic attack by the carboxylate anion. In our previous study[4d] on the kinetic effects associated with the betaine series it was found that in the presence of micelle III3 the hydrolytic rate constant of m-nitrophenyl decanoate (MNPD) at 60 °C (μ = 0.8 M) is only 7.5×10^{-4} min^{-1}. This finding shows that although MNPD consists of a better leaving group than that in PD, and its hydrolytic rate was conducted at higher temperature, the k_0 value determined for the PD ester in I3C + III3 is 32-fold greater than that of MNPD in micelle III3. Furthermore, the intramolecular catalytic rate constant observed in monophenyl glutarate ester[41] at 25 °C is also 1/40 as fast as the k_0 value determined for the PD ester in the mixed micelle I3C + III3.

The water rates k_0 presented in Tables II and III are significantly greater than spontaneous rate constants reported in the literature for phenyl acetate and even greater than other substituted phenyl acetate esters consisting of better leaving groups. The corresponding spontaneous rates of phenyl acetate, 4-nitrophenyl acetate and 2,4-dinitrophenyl acetate are 1.83×10^{-8}, 4.31×10^{-7}, and 1.1×10^{-5} s^{-1}, respectively. In a study of a large series of o-nitrophenyl esters, Holmquist and Bruice[42] have shown that the HO$^-$ rate and the H_2O rate are related by log k_OH = 0.84 log $k_{\text{H}_2\text{O}}$ + 8.0. Applying this relationship to the known k_OH (0.3 M^{-1} s^{-1}) value of PD in I3C + II2 at μ = 1 M, a k_0 value of 1.3×10^{-7} s^{-1} is derived, which is 1/700 as fast as the value experimentally observed.

In view of the high water rates in micelle I3C and in the mixed micelles studied, it seems likely that the positively charged surface plays an important role in stabilizing the transition state of the water attack by electrophilic assistance.

Basic Hydrolysis k_OH. From the data presented in Tables II and III it appears that the first-order rate constants k_c and the values of the second-order rate constants k_OH determined in the mixed micelle I3C + II2 can be correlated by: log k_c(I3C + II2) = 1.17 log k_OH(I3C + II2) − 2.2. The coefficient value

Scheme II



of 1.17 might suggest that the basic hydrolysis k_{OH} and the catalytic reaction k_c are of almost equal sensitivity to steric and electronic effects. On the other hand the k_{OH} values determined in I3C + II2 and those determined in micelle II are related by: $\log k_{OH}(\mathrm{I3C + II2}) = 1.49 \log k_{OH}(\mathrm{II2}) + 2.22$. This relationship indicates a different influence of the two micellar systems on the transition state of the basic hydrolysis.

In addition it should be noted that the k_{OH} value determined for PD ester is similar to the values reported in the literature.[27a] This can be rationalized by the following points: (a) In our previous work[4b] on the hydrolysis of benzoates and betaine-like esters in cationic micelles it has been argued that the hydrated shell of fluoride ion might assist nucleophilic attack of OH^- via spatial orientation of the nucleophile. A similar situation might also occur in the case of the mixed I3C + II2 where in comparison to the mixed micelles IV + II1C and VI + II1C the hydroxamate anion in the former mixed micelle is assumed to be highly solvated. This leads also to (b) the transition state in the mixed micelle I3C + II2 being more solvated than in II2. (c) The hydroxamate anion increases the activity of the ground state in I3C + II2 due to the perturbation of its negatively charged group to the electrostatic interactions between HO^- and the positively charged surface, and (d) the basic hydrolysis k_{OH} in the mixed micelle I3C + II2 might proceed through an entirely different transition state than that considered for the specific base catalysis reaction. A conceivable concerted mechanism for nucleophilic attack by hydroximate anion assisted by HO^- is presented in Scheme II. These proposed routes associated with the basic hydrolysis in I3C + II2 have to be considered as a qualitative rationale to the experimental results since the existing data do not allow conclusions concerning the operative paths.

Registry No.—PD, 14353-75-4; PA, 122-79-2; PMPD, 68367-32-8; PCPD, 68367-33-9; MCPD, 68367-34-0; I3C, 68367-35-1; I3M, 68367-36-2; III1, 5938-06-7; III2, 26543-24-8; III3, 62851-20-1; III3C, 64252-74-0; II2, 68367-37-3; III3CE, 68367-38-4; III3ME, 68367-39-5; ethyl 4-bromobutanoate, 2969-81-5; cetyldimethylamine, 112-69-6; trimethylamine, 75-50-3.

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