

11-5; 9,10-phenanthrenequinone, 84-11-7; cyclohexanone, 108-94-1; 4-thiacyclohexanone, 1072-72-6; fluorenone, 486-25-9; cyclohexane-1,4-dione, 637-88-7.

### References and Notes

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## Catalytic Dipolar Micelles. 7.

### Catalytic Effects of Positively Charged Hydroxylic Micelles on the Hydrolysis of Phenyl and Benzoate Esters

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The catalytic effects of 13 hydroxylic micelles on the hydrolysis of positively charged benzoate esters and on long-chain phenyl esters were measured. The micelles are of the general structure:  $\text{CH}_3(\text{CH}_2)_n\text{N}^+(\text{R}_1)_2\text{C}(\text{R}_2)_2\text{CHR}_3(\text{CH}_2)_m\text{OH Br}^-$ , where  $\text{R}_3 = \text{R}_2 = \text{H}$ ,  $\text{R}_1 = \text{CH}_3$ ,  $m = 0$ ,  $n = 9$  (I);  $m = 0$ ,  $n = 11$  (IA);  $m = 0$ ,  $n = 13$  (IB);  $m = 0$ ,  $n = 15$  (IC);  $m = 1$ ,  $n = 13$  (IIB);  $m = 1$ ,  $n = 15$  (IIC);  $\text{R}_3 = \text{R}_2 = \text{H}$ ,  $m = 0$ ,  $\text{R}_1 = \text{Et}$ ,  $n = 9$  (II);  $\text{R}_1 = \text{Et}$ ,  $n = 15$  (IIIC);  $\text{R}_3 = \text{H}$ ,  $\text{R}_1 = \text{R}_2 = \text{CH}_3$ ,  $m = 0$ ,  $n = 9$  (IV);  $\text{R}_1 = \text{R}_3 = \text{CH}_3$ ,  $\text{R}_2 = \text{H}$ ,  $m = 0$ ,  $n = 9$  (V);  $n = 13$  (VB);  $n = 15$  (VC). Noncatalytic micelles were employed for comparison purposes where the functional group OH was replaced by hydrogen and  $\text{R}_1 = \text{CH}_3$ ,  $\text{R}_2 = \text{R}_3 = \text{H}$ ,  $m = 0$ ,  $n = 9$  (VI) or  $n = 15$  (VIC). The benzoate esters studied possessed the above alkoxide catalysts as leaving groups. The corresponding *p*-nitrobenzoate esters were IE, IIE, IIIE, IVE, IVE, VE, ICE, IIICE, IIICE, and VCE, and the corresponding *p*-methylbenzoate esters were IEM and IEM. *p*-Nitrophenyl decanoate (NPD) and 2,4-dinitrophenyl decanoate (DNPD) were also included in the study. The cmc values of micelles I-IIIC and those of V-VC were determined. In each of these micelles it was found that the contribution of the head groups to the cmc is negligible. The free energy of micellization per methylene group in hydroxylic micelles was found to be 590 cal. The *trans*-benzoylation stage in the hydrolysis of benzoate esters was established. From the rate-pH profile of the least reactive esters IEM and IEM in highly basic solutions and in the presence of micelle I, the apparent  $\text{p}K_a$  value of the micellized alkoxide I was estimated to be 13.4-13.5. All other  $\text{p}K_a$  values of micelles I-VC were also estimated either from the catalytic rates of NPD and DNPD or from the substituent effect on the dissociation constants of analogous compounds. The results from the first-order rate constants of the nucleophilic attack by the micellized alkoxide ions (I-VC) in the substrate-micelle complex ( $k_c$ ) on benzoate esters indicated that relative to the basicity, the catalytic efficiency of micelle I was low. However, micelle II exhibited a high catalytic reactivity. These phenomena were explained by proximity factors. The second-order rate constants ( $k_{\text{MH}}$ ) of the specific base catalysis in the hydrolysis of IE, IIE, IIIE, IVE, VE, ICE, IIICE, IIICE, and VCE at moderate basic pH values were measured. The  $\beta$  Brønsted coefficient (0.55) found for these esters was higher than that (0.3) previously observed for the substituted phenyl esters and is consistent with the higher basicity of the leaving groups.

Surfactants containing imidazole,<sup>1</sup> amine,<sup>2</sup> thiol,<sup>3</sup> hydroxamate,<sup>4</sup> hydroxyl,<sup>5</sup> and carboxy<sup>6</sup> head groups catalyzed effectively ester hydrolyses. This phenomenon has focused general attention on micellar systems as probable models for the enzymatic processes.

In order to provide a closer analogy with the mechanistic features of the enzyme-catalyzed hydrolysis of esters, bifunctional micelles<sup>7</sup> have also been used in several studies.

One of the models for the acylation reaction of the serine oxygen in esteratic enzymes is the hydroxylic micelle. Bunton et al.<sup>5b,c</sup> have demonstrated that zwitterionic cholinium micelle exhibited phosphoryl transfer in the hydrolysis of phosphate esters. This finding is in accordance with our previously reported results,<sup>5b</sup> in which we established the involvement of the benzoyl transfer stage in the hydrolysis of benzoate esters within an identical micellar system.

In our continued investigations on micellar systems, it has become important to elucidate some microenvironmental and conformational parameters which affect the benzoyl transfer reaction at the interfaces of various types of cholinium mi-

celles. Therefore, in this present study, 13 hydroxylic surfactants possessing substituted head groups of variable chain lengths were employed as catalysts.

### Experimental Section

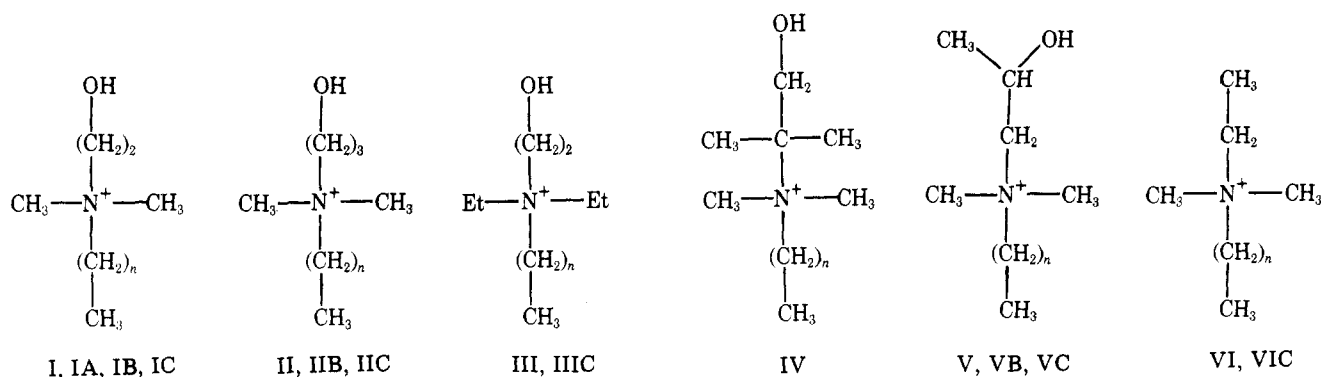
**Materials.** Phenyl esters, benzoate esters, and detergents (Chart I) were prepared by standard methods as previously described.<sup>5j,h,6</sup> Melting point data of the various detergents are given in Table I.

**Kinetics.** Hydrolytic reactions were followed spectrophotometrically at  $30 \pm 0.1$  °C using a Unicam SP-800 spectrophotometer with a water-jacketed cell compartment. The release of *p*-nitrophenolate, *p*-nitrobenzoate, and *p*-methylbenzoate anions was detected at 350, 300, and 262 nm, respectively. The surfactant concentration in the reaction cells was 0.1 M, and the substrate concentration in most cases was  $1-5 \times 10^{-5}$  M. The kinetic measurements were carried out at several pH values (9.3-10.5) with 0.05 M potassium carbonate buffer. The pH of the medium was measured on a Radiometer pH meter 26, with a combined glass electrode, before and after each run.

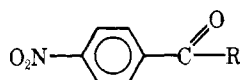
**Rate Constants.** At a moderate pH range of 9.3-10.5 the reaction rates of (i) phenyl esters in micelles I-VIC, (ii) the ester IE in micelles I-IC and III-VIC, (iii) the ester IIE in micelles II-IIC, VI, and VIC, and (iv) the esters IIIE, IVE, and VE in micelles III, IV, and V fol-

Chart I<sup>a</sup>

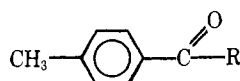
## Detergents



I, II, III, V, VI,  $n = 9$ ; IA,  $n = 11$ ; IB, IIB, VB,  $n = 13$ ; IC, IIC, IIC, VC, VIC,  $n = 15$ ; ID,  $n = 17$

Benzoate Esters<sup>a</sup>

ChE: IE, R = I'; ICE, R = IC'; HChE: IIE, R = II'; IIICE, R = IIC'; DEChE: IIIE, R = III'; IIIICE, R = IIIC'; DMChE; IVE, R = IV'; MChE; VE, R = V'; VCE, R = VC'



ChEM: IEM, R = I'; HChEM: IIEM, R = II'

## Phenyl Esters

*p*-nitrophenyl decanoate (NPD)    2,4-dinitrophenyl decanoate (DNPD)

<sup>a</sup> Key to abbreviations: ChE, esters derived from cholinium-type detergents; HChE, esters derived from the homocholesterol-type detergents; DEChE, diethyl cholinium esters; DMChE, dimethyl cholinium esters; MChE, methyl cholinium esters; ChEM, methyl cholinium benzoate esters. I'-VC' are the alkoxy groups derived from the above given hydroxylic detergents (I-VC).

lowed a first-order rate equation. First-order rate constants were determined in the usual manner from the semilogarithmic plots of absorbance change ( $OD_{\infty} - OD_t$ ) against time ( $t$ ), where  $OD_{\infty}$  and  $OD_t$  are the optical densities at  $t_{\infty}$  and  $t$ , respectively.

All of the first-order rate constants at the above pH range were linearly dependent on hydroxide ion concentration according to eq 1. The second-order rate constants were calculated from the plots of  $k_{mH}$  vs.  $[\text{OH}^-]$ . The hydrolytic rate of the ester IE in micelles II, IIB, and IIC and of the ester IIE in micelles I-IC and III-VC followed Scheme I, in which the first-order rate constants were determined.

$$k_{\text{obsd}} = k_{mH} = k_{mH}'[\text{OH}^-] \quad (1)$$

In all of the latter cases, it was found that at the experimentally employed pH range (i.e., pH 9.3–10.5), the first-order rate of the *trans*-benzoylation stage ( $k_1$ ) obeyed eq 1.

Table I. Surfactants and Esters Prepared<sup>a</sup>

micelle	mp, °C	micelle	mp, °C
IB	207	IIIE	130
IIB	86	IVE	135
IIC	85	VE	129
IIIC	130	ICE	85
V		IIICE	87
VB	72	IIICE	138
VC	82	VCE	45
VIC	195	IEM	92
		IIEM	163

<sup>a</sup> Satisfactory combustion analytical data for C, H, N, and Br ( $\pm 0.4\%$ ) were provided for these compounds.

**Determination of Cmc.** The cmc values<sup>8a</sup> of the detergents I-VC were determined with a Fisher automatic surface "Tensiomate" in aqueous solutions at 30 °C without an external salt.

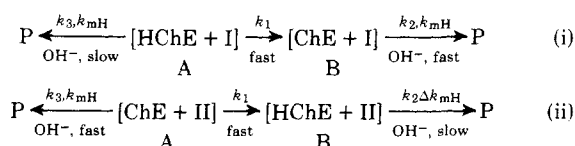
## Results

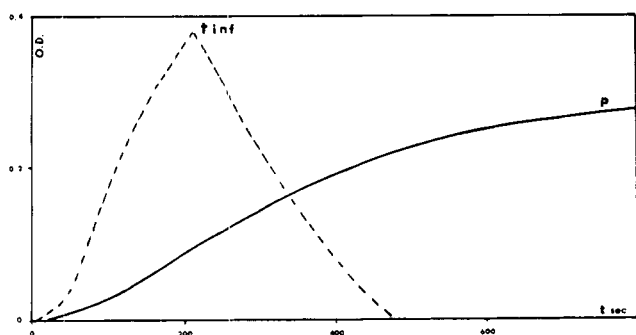
**Hydrolyses of Benzoate Esters.** In Part 4<sup>5h</sup> it was shown that the catalytic hydrolyses of the benzoate esters IE and IIE in micelles II and I, respectively, followed the general outline of Scheme I, where A denotes the corresponding substrate-micelle intracomplex, B is the intracomplex of the *trans*-benzoylated intermediate, and P represents the hydrolytic product (benzoate anion + alcohol).

In separate experiments, the UV absorbance spectra of each ester and the respective benzoate anion product were recorded. The monitored absorbance curves for all of the benzoate esters which possessed the same polar substituents (nitro or methyl) coincided. Thus, the change in absorbance measured during the kinetic run at a fixed wavelength is not attributed to the *trans*-benzoylation stage, but either to the benzoate anion formation or to the ester disappearance.

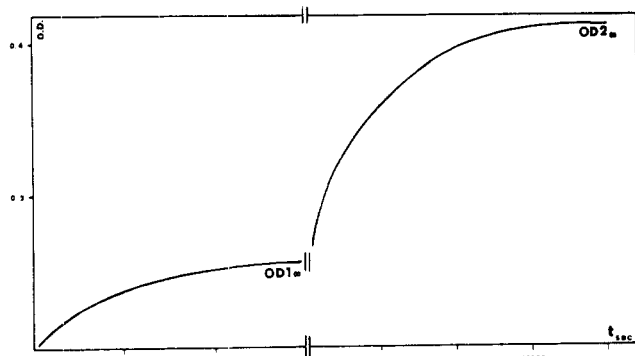
The rate constants  $k_2$  and  $k_3$  depicted in Scheme I were

## Scheme I





**Figure 1.** The time course of *p*-nitrobenzoate liberation (solid line) and the first derivative  $d(\text{OD})/dt$  (dashed line) in the hydrolysis of IIE in micelle I at 30 °C, pH 9.66,  $t_{\text{inf}} = 225$  s.



**Figure 2.** The time dependence of *p*-nitrobenzoate formation in the hydrolysis of IE in micelle II at 30 °C, pH 9.4.

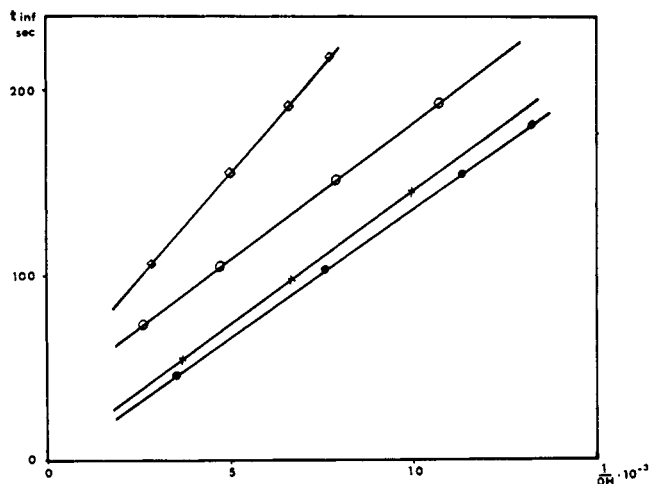
independently determined. This was attained by measuring the rate constants ( $k_2$ ,  $k_3$ ) of the appropriate esters under experimental conditions in which no *trans*-benzoylation stage was involved in the hydrolytic pathway (i.e., IIE in micelle II or IE in micelle I). The time course of *p*-nitrobenzoate released indicated that the system was comprised of a consecutive reaction. In the cases where  $k_3 \ll k_1 < k_2$  (route i, Scheme I; HChE in micelles I–IC, III–VC), the product formation followed a sigmoid-type curve as is shown in Figure 1. The accurate time period for the appearance of the inflexion point ( $t_{\text{inf}}$ ) was experimentally determined by monitoring simultaneously the optical density of the reaction mixture and the first derivative of the kinetic curve.

In cases where  $k_1 > k_3 \gg k_2$  (route ii, Scheme I; ChE in micelles II–IIC), the time course of the reaction is biphasic (Figure 2). The liberation of the product was rapid during the initial stage and became slower as the reaction proceeded.

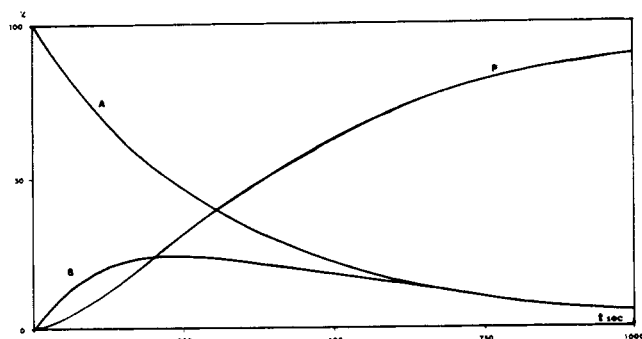
The rate expression for the benzoate ion formation ( $P$ ) was derived (eq 2) according to the general treatment as shown in the literature,<sup>8b</sup> where  $A_0$  is the initial concentration of the substrate and  $k_{1,2,3}$  are the first-order rate constants.

$$P = A_0 \left[ 1 + \frac{k_1}{k_2 - k_1 - k_3} e^{-k_2 t} - \frac{k_2 - k_3}{k_2 - k_1 - k_3} e^{-(k_1 + k_3)t} \right] \quad (2)$$

The *trans*-benzoylation rate constants  $k_1$  for route i (Scheme I) were evaluated from the kinetic data by several methods. (a) The shape of the time-absorbance curves was fitted to eq 2 by a nonlinear least-square procedure of one variable, using a computer program ( $k_2$  and  $k_3$  were known values). (b) Under the constraints that  $k_3 \ll k_1 < k_2$  and  $k_1 + k_3 < k_2$ , the first exponential term in eq 2 decreased with time ( $t$ ) faster than the second term. For the case shown in Figures 1 and 4, the ratio between the first and the second



**Figure 3.** The linear dependency of  $t_{\text{inf}}$  vs.  $1/[\text{OH}^-]$  in the hydrolysis of IIE in micelles III (—●—), IV (—○—), I (—\*—), and VC (—□—) at 30 °C.



**Figure 4.** The time course of substrate (A), the *trans*-benzoylated intermediate (B), and the product (P) during the hydrolysis of IIE in micelle I at 30 °C, with pH 9.66,  $t_{\text{inf}} = 225$  s, and  $t_{\text{max}} = 241$  s.

exponential terms equalled 0.1 at 590 s. Therefore, after a long time period, the slope of the linear part of the plot of  $\ln(\text{OD}_\infty - \text{OD}_t)$  vs. time ( $t$ ) should be  $k_1 + k_3$ . (c) By the differentiation of eq 2, the dependency of  $t_{\text{inf}}$  on the rate constants  $k_1$ ,  $k_2$ , and  $k_3$  could be derived (eq 3).

$$t_{\text{inf}} = \ln \frac{(k_1 k_2^2)'}{(k_2 - k_3)'(k_1' + k_3')^2} \times \frac{1}{(k_2 - k_1 - k_3)'[\text{OH}^-]} \quad (3)$$

All of the rate constants in eq 3 are of a second order. Thus, the known experimental values of  $t_{\text{inf}}$ ,  $k_2'$ , and  $k_3'$  allowed the determination of the *trans*-benzoylation rate constant  $k_1'$ .

According to eq 3, the experimentally determined  $t_{\text{inf}}$  values are linearly dependent on  $1/[\text{OH}^-]$  (Figure 3).

Furthermore, it should be noted that the  $t_{\text{max}}$  value attributed to the maximal accumulation of the intermediate B<sup>8e</sup> is unequal to that of the  $t_{\text{inf}}$  since

$$t_{\text{max}} = \ln \frac{k_2'}{(k_1 + k_3)'} \times \frac{1}{(k_2 - k_1 - k_3)'[\text{OH}^-]} \quad (4)$$

Figure 4 illustrates the time course of the species A, B, and P in the hydrolysis of IIE with micelle I as a catalyst.

The *trans*-benzoylation rate constant  $k_1$  for route ii (Scheme I) was determined as follows. (a) Under the kinetic conditions where  $k_1, k_3 \gg k_2$  and during the initial period, the rate expression 2 can be reduced to eq 5. The value  $k_3(A_0)/(k_1 + k_3)$  is the infinite value of absorbance ( $\text{OD}_{1_\infty}$ ) at the first stage of the reaction, and thus eq 5 can be expressed by eq 6. The value of  $\text{OD}_{1_\infty}$  was measured from the plot of  $\ln(\text{OD}_{2_\infty} - \text{OD}_t)$  against time. This plot became linear as the initial burst (Figure 2) was completed. Extrapolation of the plot to zero time gave an absorbance value which, when subtracted

from the total absorbance at  $t_\infty$  (i.e., OD $_{2\infty}$ ), resulted in the value of OD $_{1\infty}$ . The first-order rate constants  $k_1 + k_3$  were then determined (eq 6) from the slope of the linear plot of  $\ln(\text{OD}_{1\infty} - \text{OD}_t)$  vs. time during the initial stage of hydrolysis. In each case it was found that the rate constants of the second stage of hydrolysis coincided with the independently measured rate constants of the intermediate B. (b) The ratio of OD $_{1\infty}$  and OD $_{2\infty}$  equaled  $k_3/(k_1 + k_3)$ . Thus, by knowing the rate constant  $k_3$ , the value of  $k_1$  could be determined.

$$P = \frac{k_3}{k_1 + k_3} A_0(1 - e^{-(k_1+k_3)t}) \quad (5)$$

$$\text{OD}_{1\infty} - \text{OD}_t = \text{OD}_{1\infty} e^{-(k_1+k_3)t} \quad (6)$$

All of the rate constants which were determined by the above mentioned alternative methods showed very good correlation.

The second-order rate constant  $k_1'$  is kinetically attributed to a specific base catalysis of the undissociated micelle-substrate intracomplex. The first-order rate constant  $k_c$  of the internal nucleophilic attack by the micellized alkoxide head group is related to  $k_1'$  by eq 7, where  $K_a$  and  $K_w$  are the dissociation constants of the hydroxylic group and water, respectively. When  $[\text{H}^+] \gg K_a$ , eq 7 is reduced to eq 8.

$$k_c = k_1' K_w / (K_a + [\text{H}^+]) \quad (7)$$

$$k_1 = k_c K_a / K_w \times [\text{OH}^-] = k_1' \times [\text{OH}^-] \quad (8)$$

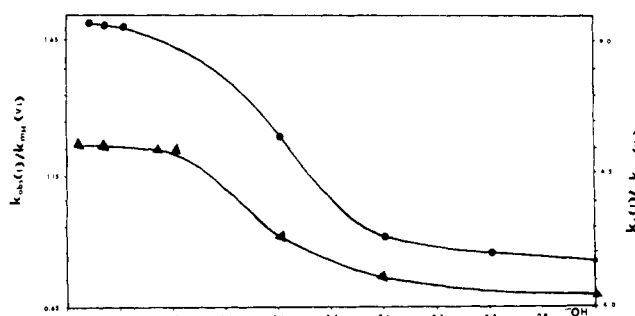
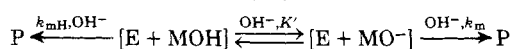
The hydrolysis of phenyl esters in micelles I-VC obeyed eq 8, and their first-order rate constants  $k_c$  were calculated from the second-order rates  $k_{mH}'$ . In each case the corresponding rate constant in the noncatalytic micelle VI, VIC was subtracted.

**Reactions in Solutions of High Basicity.** At a moderate pH range of 9.3-10.5, where most of the hydroxylic detergents exist in an undissociated form, the first-order rate constants ( $k_{\text{obsd}}$ ) were linearly dependent on hydroxide ion concentration. However, in more basic solutions (0.1-1 M KOH) it was anticipated that the increased amount of the dissociated head groups would affect the kinetic behavior of all reaction modes. For reactions where the *trans*-benzoylation step was not involved in the hydrolytic route ( $k_{mH}$ ,  $k_2$ ,  $k_3$ ), it seems likely that electrostatic repulsion between the micellized alkoxide groups and the attacking hydroxide ion should retard the kinetic rates of the basic hydrolysis.

This is explained in Scheme II, where  $[\text{E} + \text{MO}^-]$  and  $[\text{E} + \text{MOH}]$  are the substrate-micelle intracomplexes of the ester E with the dissociated ( $\text{MO}^-$ ) and undissociated ( $\text{MOH}$ ) hydroxylic head groups of the micelle, respectively.

Based on Scheme II, the apparent rate constant ( $k_{\text{obsd}}$ ) is expressed by eq 9, where  $F_{mH}$  and  $F_m$  are the corresponding molar fractions of the undissociated and dissociated forms of the hydroxylic detergent. Since  $F_{mH} = 1/(K'[\text{OH}^-] + 1)$  and  $F_m = K'[\text{OH}^-]/(K'[\text{OH}^-] + 1)$ , then eq 9 can be expressed as eq 9a. From eq 9a it can be seen that the curve of  $k_{\text{obsd}}$  vs.  $[\text{OH}^-]$  is nonlinear and does not level off with a high concentration of base. However, in contrast to the above system, the dependence of reaction rates [ $k_{mH}$  (VI)] on  $[\text{OH}^-]$  for esters in the nonhydroxylic micelle VI should be linear and obey eq 1, even at concentrated basic solutions. Moreover, if  $k_{mH}'$  is of a similar order of magnitude to that of  $k_m'K'$ , then the ratio  $k_{\text{obsd}}(\text{I-VC})/k_{mH}(\text{VI})$  is expected to give a descending sigmoidal-type curve with the increased concentration of hydroxide ion. In order to examine this suggestion about the kinetic behavior of hydroxylic and nonhydroxylic micelles, we have measured the rate constants of the least reactive ester

#### Scheme II



**Figure 5.** Relative first-order rate constants  $k_{\text{obsd}}(\text{I})/k_{mH}(\text{VI})$  for the hydrolysis of IEM (left ordinate,  $\bullet$ ) and  $k_1(\text{I})/k_{mH}(\text{VI})$  for the hydrolysis of IIEM (right ordinate,  $\blacktriangle$ ) in high basic solutions at 30 °C,  $\mu = 2.5$  M (KBr), detergent concentration = 0.1 M.

IEM in micelle I and VI [0.1 M of detergent,  $T = 30$  °C,  $\mu = 2$  M (KBr)] at various hydroxide ion concentrations.

$$k_{\text{obsd}}(\text{I-VC}) = k_{mH}'[\text{OH}^-]F_{mH} + k_m'[\text{OH}^-]F_m \quad (9)$$

$$k_{\text{obsd}}(\text{I-VC}) = \frac{k_{mH}'[\text{OH}^-] + k_m'K'[\text{OH}^-]^2}{K'[\text{OH}^-] + 1} \quad (9a)$$

From Figure 5 it is apparent that the rate ratio  $k_{\text{obsd}}(\text{I})/k_{mH}(\text{VI})$  is represented by a descending sigmoidal curve. This is consistent with the conclusion that different factors affect hydrolytic reactions in micelle I as compared to micelle VI. Since the site of the descending curve is reflected by the magnitude of  $K'$ , it is expected that a similar type of curve will also be produced for the *trans*-benzoylation step  $k_1$ . Indeed, when plotting  $k_1(\text{I})/k_{mH}(\text{VI})$  vs.  $[\text{OH}^-]$  for the reaction of IIEM in micelle I, this was found to be the case.

On the basis of these experiments, the value of  $K' = K_a/K_w$  was found to be 2.85-3.34. The activity coefficient factor  $\gamma_{\text{OR}^-}\gamma_{\text{H}_2\text{O}}/\gamma_{\text{ROH}}\gamma_{\text{OH}^-}$  can be approximated as unity. This is assumed from data on the activity coefficient ratio obtained in the hydrolysis of the acetate anion<sup>8c</sup> at  $\mu = 2$  M. On using a value<sup>8d</sup> of 0.75 for  $\gamma_{\text{H}^+}\gamma_{\text{OH}^-}/a_{\text{H}_2\text{O}}$  and a value of 13.833 for  $\text{p}K_w$ , we calculated  $\text{p}K_a \sim 13.4-13.5$  ( $T = 30$  °C,  $\mu = 2$  M) for micelle I. As expected, this value is smaller than that found for choline (i.e.,  $\text{p}K_a = 13.9$ ) but larger than the  $\text{p}K_a$  value of 12.9 found by Bunton<sup>5c</sup> for compound IA.

In Table II we have summarized the second-order rate constants ( $k_1' + k_3'$ ),  $k_{mH}'$  of the phenyl and benzoate esters, and the cmc values of micelles I-VC.

In order to estimate the contribution of the nucleophilic route produced by the micellized alkoxide in benzoate and phenyl esters to the overall hydrolytic process, the ratios  $100k_1'/(k_1' + k_3')$  and  $100[k_{mH}'(\text{I-VC}) - k_{mH}'(\text{VI, VIC})]/k_{mH}'(\text{I-VC})$  were calculated. The results, which are based on the second-order rate constants, exhibit the apparent partition between the various modes of reaction in the above mentioned esters (Table III).

## Discussion

**Cmc of Hydroxylic Micelles.** Inspection of Table II reveals that the cmc values of the hydroxylic micelles I-VC are mainly dependent on the hydrocarbon chain length of micelles. The data, however, do not show any significant effect from variation in substitution of the head groups on the cmc. This observation seems to be reasonable since it has been shown<sup>12</sup> that the change in the electrostatic self free energy of charged head groups, between water and the aggregate state, is only  $\sim 1.7kT$  as compared to the hydrophobic contribution of an alkyl long chain, which amounts to  $(\sim 10-16)kT$  ( $k$  denotes the Boltzman constant). On the other hand, head groups with the ability to change (a) charge distribution,<sup>9</sup> (b) bound water,<sup>10</sup> and (c) hydrophobicity of the system<sup>11</sup> are

**Table II. Second-Order Rate Constants ( $s^{-1} M^{-1}$ ) ( $k_1' + k_3'$ ) and  $k_{mH'}$  in the Hydrolysis of Phenyl and Benzoate Esters in 0.1 M Hydroxylic Surfactants at 30 °C**

micelles	esters				cmc $\times 10^3$ , M
	IE	IIE	NPD	DNPD	
I	81.5	42	375	3466	30
IA	80	50.6	505	5248	10.3
IB	87	54	812	7547	3.1
IC	94	62	977	9036	0.85
IC	(123, ICE) <sup>b</sup>				(ID) 0.28 <sup>a</sup>
II	350	6.3	57	526	30
IIB	430	7.1	79	761	3.1
IIC	530	7.7	91	846	0.97
III	101	51	446	5250	29
III	(114, IIIE) <sup>b</sup>				
IIC	115	60	1070	7333	0.67
IIC	(125, IIICE) <sup>b</sup>				
IV	85	27	208	2666	
IV	(65, IVE) <sup>b</sup>				
V	80	6.8	59	545	30
V	(16.6, VE) <sup>b</sup>				
VB	80	9.1	72	615	3.21
VC	75	19	147	1388	0.97
VC	(40, VCE) <sup>b</sup>				
VI	52	6.1	13.5	142	
VIC	78	7.5	18.5	189	

<sup>a</sup> Cmc for ID. <sup>b</sup> Second-order rate constant of the ester in parentheses instead of ester IE.

**Table III. Contribution (%) of Nucleophilic Mode of Reaction by Alkoxide Ions (I-VC) in the Hydrolysis of IE, IIE, NPD, and DNPD**

esters	I	IC	II	IIC	III	IIC	IV	V	VC
IIE	85	88			87	88	76	4	96
IE			77	85					
NPD	96	98	76	80	97	98	94	77	87
DNPD	96	98	73	78	97	97	95	74	86

known to affect the hydrophilic-lipophilic balance (HLB) of micelles. Thus, only strong electron-donating or -withdrawing substituents might significantly affect the micellar cmc values, which is not the case in our systems. The hydrophobic contribution of the alkyl head groups becomes important apparently only with long-chain head groups, rather than those of micelles I-VC. This has been adduced from the results of Evans<sup>13</sup> and Lin<sup>11</sup> for the isomers of sodium *n*-tetradecyl sulfate, in which the position of the sulfate group changed from position 1 to 7. It must be pointed out that the cmc values of micelles I-VC cannot be used as criteria for the relationship between the head group structure and the catalytic efficiency since the catalytic process is produced in the Stern layer of the micelle and consequently it is sensitive to the microscopic environment induced by the head groups.

The cmc values determined for the hydroxylic micelles depicted in Table II are related to the number of carbon atoms (*n*) on the alkyl chain of the micelle monomer by eq 10. In the series of alkyltrimethylammonium bromides<sup>14</sup> and alkyl-dimethylbenzylammonium bromides,<sup>15</sup> the corresponding relationships between the cmc and *n* are  $\log \text{cmc} = 1.77 - 0.292n$  and  $\log \text{cmc} = 2.251 - 0.369n$ . Thus, it is apparent that as compared to the latter cationic surfactants, the micellization of hydroxylic amphiphiles is less sensitive to chain lengthening. This behavior of HLB in hydroxylic micelles is consistent with the results which emerged from potentiometric studies on amine oxide surfactants,<sup>16</sup> where it was concluded that dihydroxyethylenealkylamine micelles have a looser micellar structure than those of dimethylalkylamine oxides.

$$\log \text{cmc} = 1.003 - 0.250n \quad (10)$$

To estimate the free energy change per CH<sub>2</sub> group between the micellar and singly dispersed state in hydroxylic micelles one can use the relationship between the cmc and the number of carbon atoms (*n*) on the alkyl chain as expressed by eq 11, where *K<sub>g</sub>* is the effective coefficient of the electrical energy and *W* is the free-energy change of an aliphatic methylene group between its micellar and monomer states. For alkyltrimethylammonium bromide<sup>17</sup> and chloride<sup>14</sup> at 25 °C the values of *K<sub>g</sub>* were found to be 0.65 and 0.64, respectively.

$$\log \text{cmc} = \frac{-Wn}{2.303(l + K_g)kT} + C \quad (11)$$

In the lyotropic series, Larsen and Magid<sup>18</sup> found that 77% of the total bromide ions were bound to a CTAB micelle (*K<sub>g</sub>* = 0.77). Conductivity measurements of hydroxylic micelles<sup>19</sup> at various concentrations allowed us to estimate the effective micellar charge by using Evans' <sup>13</sup> equation. The effective micellar charge of I was found to be 0.33, and therefore a value of 0.67 was introduced for the parameter *K<sub>g</sub>*. Hence, the corresponding free energy of micellization (*W*) per methylene group is  $-0.96kT$  (591 cal at 37 °C). This value is slightly lower than the value of  $1.08kT$  found in micellization of other hydrocarbon chains, which might indicate that in hydroxylic micelles the methylene groups closest to the surface are partially exposed to an aqueous environment.

**Hydrolyses of Phenyl Esters.** From the data in Tables II and III it is inferred that the rate of hydrolyses of both NPD and DNPD increases with an increase in the chain length of the surfactant. This augmentation of rates is also observed in the homologous series of the noncatalytic micelle VI, but as compared to the hydroxylic micelles the relative enhancement is lower.

**Table IV. First-Order Rate Constants  $k_c$  ( $s^{-1}$ ) and Estimated  $pK_a$  Values for the Hydrolyses of Phenyl Esters NPD and DNPD in Hydroxylic Micelles I-VC at 30 °C ( $\mu = 0.1$  M)**

	I	IC	II	IIC	III	IIIC	IV	V	VC
$pK_a$ (NPD)	13.4	12.8	14.7	14.4	13.3	12.7	13.8	14.7	14.1
$pK_a$ (DNPD)	13.4	12.8	14.7	14.4	13.2	12.9	13.6	14.7	14
$pK_a$			14.5–14.9 <sup>a</sup>				13.53 <sup>a</sup>	14.4–14.9 <sup>a</sup>	
$k_c$ ( $s^{-1}$ , NPD)	133 (9.8)	90 (4.7)	320 (23.7)	285 (15.4)	126 (9.3)	77 (4.2)	96 <sup>a</sup> (7.1)	334 (24.7)	237 (12.8)
$k_c$ ( $s^{-1}$ , DNPD)	1226 (8.9)	819 (4.3)	2827 (19.9)	2597 (13.7)	1497 (10.5)	833 (4.4)	1256 <sup>b</sup> (8.8)	2966 (20.8)	1761 (9.3)

<sup>a</sup> Estimated from dissociation constants of alcohols and acids; see text. <sup>b</sup> Calculated by  $pK_a = 13.53$ . Numbers in parentheses are the effective molarities:  $k_c(I-VC)/k_{mH}(VI, VIC)$ .

Much of the data on rate acceleration or retardation in micellar systems can be attributed to hydrophobic binding,<sup>20,21</sup> electrostatic interactions,<sup>5a,20</sup> hydrophobic desolvation of the surface,<sup>4,22,23</sup> and proximity factors.<sup>5h,6</sup> However, it seems likely that the rate constants in this present study are mainly reflected by the change in the  $pK_a$  value of the hydroxylic catalysts. Current reports have shown that cationic micelles increase the ionization of many functional groups, such as carboxy,<sup>24</sup> imidazolyl,<sup>1a</sup> iminium ion,<sup>25</sup> thiol,<sup>3a</sup> and phenol.<sup>26</sup>

In the case of cholinium micelles, Bunton<sup>5c</sup> estimated  $pK_a$  values of 12.9 and 12.4 for Ia and IC, respectively (the  $pK_a$  of choline is 13.9). Hence, the increase of the hydrocarbon chain by four carbon atoms causes a decrease of the  $pK_a$  by 0.5 units, and the second-order rate constants as determined by eq 1 are increased accordingly.

In fact, the same explanation may also account for the low second-order rate constants as displayed by the homocholinium catalysts II–IIC. The  $pK_a$  values assigned to these catalysts are higher than those of the cholinium catalysts, and consequently at a moderate pH range the effective concentration of the dissociated oxy ion in the homocholinium series should decrease. Yet, the question asked is whether the surface area and the surface potential are sensitive to change in alkyl chain length. Israelachvili and Ninham<sup>12</sup> have investigated the properties of the allowed shapes of micelles with respect to packing constraints. One of the constraints assumed was that the surface area per amphiphile is equal or close to an optimal constant area at which the free energy per amphiphile is at a minimum. Indeed, based on the aggregation values<sup>27</sup> that were found for the betaine-type micelles ( $C_8$ – $C_{15}$ ), it was shown that the surface of the hydrophobic core is practically invariant. Applying a similar type of calculation for the spherical models of I, IA, IB, and IC, the surface area per amphiphile at the hydrocarbon–water interface was found to be 61–63 Å. The corresponding maximal aggregation numbers are 43, 55, 73, and 93.<sup>28</sup> These calculations show that the surface area is fairly constant. On the other hand, Tanford<sup>29</sup> calculated the surface area per amphiphile at positions where the charged ionic groups are presumed to be located (~1.5 Å outside the core) and found that this area is significantly decreased with an increase of the chain length. This approach led to the conclusion that the charge density on the surface increased also in the same order.

Since the charge density on the micellar surface affects the dissociation constant of the hydroxylic head groups, the suggestion that the second-order rate constants are mainly reflected by the  $pK_a$  values of these catalysts seems reasonable. It is therefore possible to estimate the  $pK_a$  values of the various catalytic micelles from the kinetic data (eq 12). This was carried out using a Brønsted correlation with a  $\beta$  coefficient of 0.3 for the nucleophilic attack of the micellized alkoxide ions on NPD and DNPD. The  $\beta$  value of 0.3 is consistent with our previous results,<sup>5g</sup> where a  $\beta$  value of  $-0.36$  was determined for the leaving groups in the reaction of substituted

phenyl decanoate esters in micelle I. The value of 0.3 is also in accord with the reported  $\beta$  coefficient of 0.2–0.3 for the rate-determining attack of oxy anions on oxygen esters in nonmicellar systems:

$$\log k_c = \log [k_{mH}''(I-VC)K_w/K_a] = 0.3pK_a + C \quad (12)$$

where  $k_{mH}''$  are the corrected second-order rate constants attained by subtraction of the corresponding rate constants measured in the noncatalytic micelles VI or VIC [ $k_{mH}'(VI, VIC)$ ] from those displayed by the hydroxylic micelles [ $k_{mH}'(I-VC)$ ] [i.e.,  $k_{mH}'' = k_{mH}'(I-VC) - k_{mH}'(VI, VIC)$ ].

The Brønsted equation for the second-order rate constants is given by eq 12a.

$$\log k_{mH}''(I-VC) = 0.7pK_a + C' \quad (12a)$$

It is well known that the apparent dissociation constant of micelles varied with the degree of dissociation, and consequently affected the cmc.<sup>30</sup> However, the kinetic  $pK_a$  values as calculated by eq 12a are related to a lower degree of ionization and to minor changes in the micellar structure. The significance of these results lies more in their relative values.

Since the  $pK_a$  values of the hydroxylic micelles were determined by using the value of I as a reference, it becomes necessary to find the best approximation for the basicity of I in the kinetic runs. The reported  $pK_a$  value of 12.9 for micelle IA seems to be underestimated. The  $\Delta pK_a$  values as measured in our laboratory for (a) micellar and nonmicellar betaines, (b) the pair of amines  $RN^+(CH_3)_2(CH_2)_3NH_2$ , where  $R = CH_3$  and  $C_{10}H_{21}$ , and (c) the pair of hydroxamic acids (analogous to b)  $RN^+(CH_3)_2(CH_2)_3CONHOH$  were 0.2, 0.35, and 0.15, respectively.

Although the betaine and hydroxamic micelles displayed higher  $pK_a$  values than those of the corresponding nonmicellar compounds, the opposite was true for the analogous amines, and the  $\Delta pK_a$  values for all three preceding pairs are quite small. Thus, since it was experimentally found that the micellization of alkoxide ion increased its dissociation constant, the anticipated  $pK_a$  value of I should be 13.6–13.7. The  $pK_a$  value of 13.4–13.5 as determined in the present study is in satisfactory agreement with the above prediction.

From Table IV it is apparent that the estimated  $pK_a$  values from the kinetic data of NPD and DNPD are fairly consistent. The maximal deviation is 0.2  $pK_a$  units (IIIC and IV). Lengthening the hydrocarbon chain by six carbon atoms decreases the  $pK_a$  of the cholinium micelle I as expected by 0.65 units.<sup>5c</sup> However, the decrease of  $pK_a$  in the homocholinium micelle is only 0.3 units. The substituent effect on the ionization constants of the hydroxylic micelles seems also to operate in the expected order and magnitude (except for IV). The calculated  $\Delta pK_a$  of 1.3 for the pair I and II agrees well with that found for the difference between glycine and  $\beta$ -alanine ( $pK_a = 1.2$ ).<sup>31</sup> Alternatively, by applying the Hammett correlation<sup>32</sup> ( $pK_a(RCH_2OH) = 1.42\sigma^*$ ) and using a fall-off factor of 2.2 for the substituent inductive effect in the

**Table V. First-Order Rate Constants  $k_c$  ( $s^{-1}$ ) in the Hydrolysis of Benzoate Esters IE and IIE in 0.1 M Hydroxylic Micelles I-VC at 30 °C<sup>a</sup>**

	I	IC	II	IIC	III	IIIC	IV	V	VC
IIE	13.1 (2.0)	5.0 (0.8)			11.6 (1.8)	4.8 (0.6)	10.2 (1.6)	2.2 (0.3)	21.2 (2.8)
IE			1903 (23.3)	1654 (20.2)					

<sup>a</sup> The numbers in parentheses are the concentrations of hydroxide ion which gave rise to identical rates in a bimolecular reaction ( $k_{mH'}$ ).

homocholinium monomer II relative to I, a  $\Delta pK_a$  of 1.5 was determined.

For comparison of the  $\Delta pK_a$  value found for the difference between micelles V and I, we have considered the dissociation constants of ethanol and 2-propanol. The reported  $\Delta pK_a$  between these alcohols is 1.5 units;<sup>33</sup> however, measurements in the gas phase<sup>34</sup> give a value of 1. The experimental value as calculated from the kinetic rates ( $\Delta pK_a = 1.3$ ) falls in between these values.

The difference in the ionization constant between the pair I and IV could be estimated by comparing propionic and trimethylacetic acid ( $\Delta pK_a = 0.16$ ) and using the relationship<sup>35</sup>  $pK_a(\text{RCOOH}) = -14.42 + 1.21pK_a(\text{RCH}_2\text{OH})$ . The calculated  $\Delta pK_a$  is 0.13.

This  $\Delta pK_a$  can also be calculated from the above mentioned Hammett equation ( $\Delta\sigma^* = 0.065$ ), which yielded a value of 0.092. The preceding estimations are lower than those obtained from the kinetic data. This may suggest that steric factors are involved in the hydrolytic route of IV.

It was noted that in contrast to the cholinium micelles, an increase of the chain length in the analogous betaine series  $\text{CH}_3(\text{CH}_2)_n\text{N}^+(\text{CH}_3)_2(\text{CH}_2)_m\text{COOH Br}^-$  caused an increase in the  $pK_a$  value of the betaine micelle. However, the magnitude of the changes in  $\Delta pK_a$  in betaine micelles is very similar to that observed in the cholinium micelles. The  $\Delta pK_a$  value of 1.1 between the pairs  $n = 9, m = 1$  and  $n = 9, m = 2$  is as expected from the cholinium pair.

Moreover, the difference between the  $pK_a$ 's of the betaine micelles ( $n = 9, m = 1$  and  $n = 15, m = 1$ ) is 0.5 units, which is again in very close agreement with the magnitude found in the corresponding cholinium micelles.

The small difference in the  $\Delta pK_a = 0.3$  between the homocholinium micelles II and IIC is also consistent with the measured difference in the corresponding betaine series. In fact, the lengthening of the hydrocarbon chain of the betaine micelle from  $n = 9, m = 3$  to  $n = 15, m = 3$  resulted in a change in the  $pK_a$  value of 0.2 units. These results suggest that there is less interaction between the cationic surface and the hydroxylic head group in the homocholinium series as compared to cholinium surfactant. It is possible that in the homocholinium series the extended conformation of the alkoxide hydrocarbon chain is preferred due to the increased solvation of the catalyst by the bulk.

In Table III the contribution of the nucleophilic reaction produced by the alkoxide head groups to the overall hydrolytic process was determined. Since the calculated values in Table II were based on the second-order rate constants  $k_{mH'}$ , the resulting data reflects both the catalytic efficiency and the effective concentration of the reactive species. However, the first-order rate constants  $k_c$  represented in Table IV are directly related to the catalyst effectiveness.

The kinetic data given in Table IV revealed that the most efficient catalysts are the homocholinium micelles II and IIC and those of the cholinium micelles V and VC. Comparison of the first-order rate constants  $k_c$  of the phenyl ester hydrolyses with the second-order rate constants  $k_{mH'}$  of the same esters in the noncatalytic micelles VI and VIC showed that the micellized alkoxide catalyst is more effective than hydroxide

ion. The hydroxide ion concentration which gives an equivalent rate to that found with hydroxylic micelle fell in the range of 4.3 to 24.7 M (the effective molarity of each micelle is listed in parentheses in Table IV).

It should be noted that due to solvation of the hydroxide ion, an alkoxide ion with a comparable basicity is a better catalyst. Therefore, the apparent effective molarities of the present systems indicate that the catalysis displayed by the micellar system is low. Indeed, additional results have shown that the effectiveness of the cholinium micelle I as a catalyst is similar to that of its nonmicellar counterpart. Based on the data previously reported,<sup>5g</sup> the first-order rate constant  $k_c$  and the second-order rate constant for the hydrolysis of *p*-nitrophenyl acetate with micelle I ( $pK_a = 13.4$ ) and with choline ( $pK_a = 13.9$ ) as catalysts [at 30 °C,  $\mu = 0.8$  M (KBr)] were found to be  $146 s^{-1}$  and  $215 s^{-1} M^{-1}$ , respectively. With a  $\beta$  Brønsted coefficient of 0.3, a  $k_c$  value of  $204 s^{-1}$  was calculated for the hydrolysis of *p*-nitrophenyl acetate ion with a cholinium micelle which possessed an alkoxide head group of identical basicity to that of the choline ( $pK_a = 13.9$ ). Thus, the effective molarity of I is only 0.95 M. Similar observations with other types of functional micelles are documented in the literature,<sup>3c,6a,14</sup> indicating that a premicelle catalyst exhibits a higher reactivity than that of the micelle aggregate.

These results are ascribed to a more restricted orientation of both the catalytic group and the substrate in the micelle compared to the monomeric state.

**Hydrolyses of Benzoate Esters.** From Table V it is apparent that cholinium micelles are not a highly reactive catalyst with the homocholinium ester IIE. Their effective molarities fell in the range of only 0.3 to 2.8. On the other hand, the catalytic efficiency of the homocholinium micelles II and IIC toward the ester IE is high. One can see that whereas the effective molarity of the alkoxide catalyst of II in the case of the ester IE is similar to that observed with the ester NPD, micelle IIC is more effective toward IE than toward NPD. Furthermore, the reactivities of the homocholinium catalysts are greater than those of the cholinium analogues with the same basicities. Micelle V ( $pK_a = 14.7$ ), for example, shows a comparable effectiveness to that of micelle II ( $pK_a = 14.7$ ) in the hydrolysis of phenyl esters, but in the case of the benzoate ester IIE the effectiveness of V was significantly lower. These results can be interpreted on the basis of the changes in the rate-determining step as the basicity of the nucleophiles and the leaving groups is varied. In the reaction of alkoxide ion with oxygen esters it is known that the alkoxide attack is rate determining when the  $pK_a$  of the nucleophile ( $pK_{nuc}$ ) is greater than that of the leaving group ( $pK_{lg}$ ), while when  $pK_{lg} > pK_{nuc}$  the departure of the leaving group is rate determining.

Since it is expected that the reaction of micellized alkoxides with esters followed the same pattern, the rate-determining step for the reactions of micelles II and IIC with the esters IE, NPD, and DNP and for micelles I-VC with the esters NPD and DNP is the attack by the nucleophile. On the other hand, the expulsion of the leaving group is rate determining for the reactions of micelles I-VC with the ester IIE. Thus, as compared to the former reactions, the latter reactions should

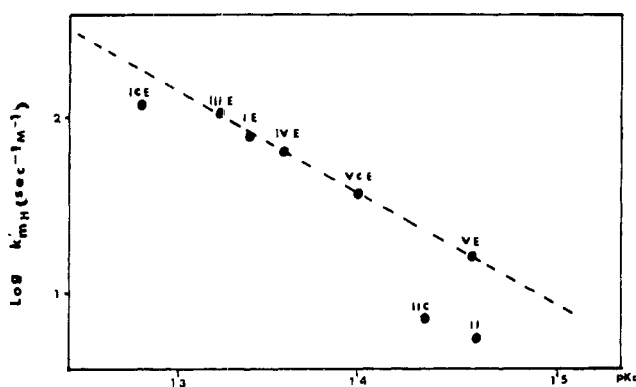


Figure 6. The Brønsted correlation for the basic hydrolysis ( $k_{mH'}$ ) of cationic esters at 30 °C.

be less sensitive to nucleophilic attack by the micellized alkoxides and consequently their effective molarities are lower.

In general, the catalysis of hydroxylic micelles is in inverse proportion to the hydrocarbon chain length of the surfactant. This is not the case with micelles V and VC. The most effective catalyst in the cholinium series is micelle VC; however, relative to its basicity, micelle V appears to be a poor catalyst. The low reactivity of V might be ascribed to an unfavorable orientation of the reaction center with respect to the nucleophile at its juxtaposition. The slightly reduced reactivity of IV can also be explained in the same terms.

In Figure 6 a Brønsted plot of the  $k_{mH'}$  rate constants for the hydroxide ion attack on the benzoate esters (ChE and HChE) vs. the values of  $pK_{1g}$  is shown. It is apparent that the cholinium esters fit well into a linear plot, with a  $\beta$  coefficient of 0.55, while the homocholinium esters exhibited a negative deviation.

From the solubility properties of phenyl groups<sup>24,36</sup> in cationic micelles as well as from the kinetic salt effect of the benzoate esters, we assumed in Part 4<sup>5b</sup> that the hydrocarbon chain possessing the benzoate moiety in both the cholinium ester IE and the homocholinium ester IIE is in a folded conformation. Therefore, it was expected that the esters of HChE would correlate with the Brønsted plot. However, since the kinetic measurements of the esters were conducted in various hydroxylic micelles, where for each ester the micelle monomer was identical with that of the leaving group (i.e., IE in I, IIE in II, etc.), it seems that the homocholinium micelles displayed different microenvironmental effects on the reaction centers than those of the cholinium micelles. Actually, it was noticed earlier that various substituted polar head groups on micelles affect the hydrolytic rates of the phenyl and benzoate esters by  $\sim 2$ -fold. Thus, the lower rate observed for the homocholinium esters can be attributed to this phenomenon.

From Figure 6 it can also be seen that the rate constants of the esters IVE and VE are in accordance with the basicities of their leaving groups. This indicates that steric factors ascribed for IV and V as catalysts are diminished when monomers IV and V are the leaving groups.

In our earlier study we reported<sup>5b</sup> that the assumed  $\beta$  coefficient (based on a two-point Brønsted plot of I and II) was  $\sim 0.8$ . In view of the present data, it seems that this prediction was too high.

Regarding the reaction of IE in the cholinium micelles (Table II), it seems that the rate increase due to the lengthening of the hydrocarbon chain cannot be attributed to the *trans*-benzoylation route since a similar increase of the rate is also observed with the noncatalytic micelles (VIC compared to V). However, the rate increase in the case of micelle III might stem from the *trans*-benzoylation process. For reactions of micelles IV, V, and VC with IE, it is clear that the *trans*-

benzoylation stage is not involved in the hydrolytic route.

In conclusion, it has been shown that the hydrolytic route of esters in hydroxylic micelles, I-VC ( $k_c$ ), proceeds via nucleophilic attack of the dissociated head groups. The  $pK_a$  value of micelle I was experimentally determined, and  $pK_a$  values of all of the other micelles were estimated from the kinetic data of the long-chained phenyl esters (NPD and DNPD). The differences in the ionization constants ( $\Delta pK_a$ ) between the various micelles studied well with the known  $\Delta pK_a$  values of related compounds with a similar structure. The Brønsted plot for the hydroxide ion attack on benzoate esters, derived from the cholinium-type surfactants (ChE, DEChE, and DMChE), also correlated with the estimated  $pK_a$  values.

It seems to us that the reactivity of the cationic hydroxylic micelles toward ester hydrolysis can be attributed to electrostatic parameters (i.e., charge density of the surface) which affect the basicity of the head groups. This view is in accord with the decreased reactivity of the micellized catalyst with the increase of the hydrocarbon chain length of the surfactant.

When the rate-determining step is the nucleophilic attack on the ester, micellized alkoxide catalysts are significantly more effective than the hydroxide ion. However, the relative effectiveness of the micellized alkoxide strongly decreased when the expulsion of the leaving group is rate determining. With respect to the bimolecular reaction of alkoxide ions, the effective molarity of the micellized alkoxides approaches unity. In some cases, the present results indicated that proximity factors might also be involved in the reaction pathway. Although the discussion in this paper was based on the estimated  $pK_a$  values of the micellized alkoxide ions whose possible variation is  $\pm 0.3$  units, the relative effect of the micelles investigated remained the same.

**Registry No.**—I, 39995-55-6; IE, 68796-84-9; IEM, 68796-92-9; IA, 7009-61-2; IB, 68796-78-1; IC, 20317-32-2; ICE, 68796-85-0; II, 61063-29-4; IIE, 68796-91-8; IIE, 68796-93-0; IIB, 68796-79-2; IIC, 63989-29-7; III, 60535-37-7; IIIE, 68796-86-1; IIIC, 68796-80-5; IIIIE, 68796-87-2; IV, 61063-31-8; IVE, 68796-88-3; V, 68796-81-6; VE, 68796-89-4; VB, 68796-82-7; VC, 68796-83-8; VCE, 68796-90-7; VI, 39995-56-7; VIC, 124-03-8; NPD, 1956-09-8; DNPD, 61063-34-1.

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## Kinetics and Mechanisms for the Acid-Catalyzed Oxidative Decarboxylation of Benzoylformic Acid

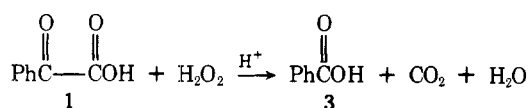
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The pH-rate profile for hydrogen peroxide promoted oxidative decarboxylation of benzoylformic acid to benzoic acid and carbon dioxide has been determined from  $H_0 - 9$  to pH +8. In aqueous solutions more acidic than pH 2, a combination of acid- and water-catalyzed reaction mechanisms accounts for the observed data. Similar kinetic results are obtained from perchloric, nitric, and sulfuric acid solutions. Saturation kinetics are observed for the reversible addition of hydrogen peroxide to the  $\alpha$ -keto carbonyl group with a pH-dependent  $K_d$  value of 0.25 M at  $H_0 - 2$ ; the pH-independent value for  $K_d$  is 2.0 M. The  $pK_a$  of the proposed protonated (monocation) tetrahedral intermediate is  $-1.3$ . A linear free-energy relationship correlates the observed rate constant and the  $pK_a$  of the leaving group produced by oxygen-oxygen bond cleavage for hydrogen peroxide, *tert*-butyl hydroperoxide, and peracetic acid promoted reactions.

The study of enzymatic oxidations in which molecular oxygen is used to convert olefinic, aromatic, or aliphatic substrates into the corresponding hydroxylated derivatives has lead to current interest in the class of enzymes known as mixed function oxidases.<sup>2</sup> These metalloenzymes, which effect a wide variety of biochemical oxidations, require, in addition to the substrate of interest, a stoichiometric equivalent of a coreductant. One class of mixed function oxidases, responsible for several of the biosynthetic aliphatic hydroxylations, utilizes 2-ketoglutaric acid as the cofactor for reactivity.<sup>3</sup> Inasmuch as the chemical role of the 2-ketoglutarate is not well understood, we have initiated an investigation of the mechanisms for the hydrogen peroxide promoted oxidative decarboxylation of the 2-keto acid, benzoylformic acid (1), in aqueous



media.<sup>4a,b</sup> Results from this partial model study may likely provide insight into the chemistry of the enzyme-catalyzed process. Although basic hydrogen peroxide is a well-known and synthetically useful reagent for the decarboxylation of 2-keto acids,<sup>4c</sup> we herein report the finding of an acid-cata-

lyzed reaction which is as kinetically facile as the base-promoted oxidation. Furthermore, on the basis of kinetic data we propose mechanisms which account for our observations over a wide pH range.

### Results

Over 30 min at ambient temperatures a 7.5 M aqueous perchloric acid solution ( $H_0 - 4$ ) containing 0.16 M benzoylformic acid (1) and 2 M hydrogen peroxide evolves carbon dioxide and produces benzoic acid (3) as the only isolatable organic product in yields greater than 90%. The reaction rates of dilute solutions ( $5 \times 10^{-3}$  M) of 1 may be conveniently followed at 32.0 °C by monitoring the time-dependent change in the ultraviolet absorption spectrum. The oxidative decarboxylation exhibits good first-order kinetics with respect to 1 through greater than 90% completion. If hydrogen peroxide is omitted from the reaction mixture, no significant loss of starting material occurs over several hours. However, after several days in the acidic medium benzoylformic acid (1) does undergo decarbonylation to produce benzoic acid (3) at rates comparable to those previously reported for this reaction.<sup>6</sup>

As illustrated in Figure 1, the rate constant exhibits three major variations with pH. First, between pH ( $H_0$ )  $-5$  and  $+3$ , a bell-shaped pH-rate profile is produced with a maximum