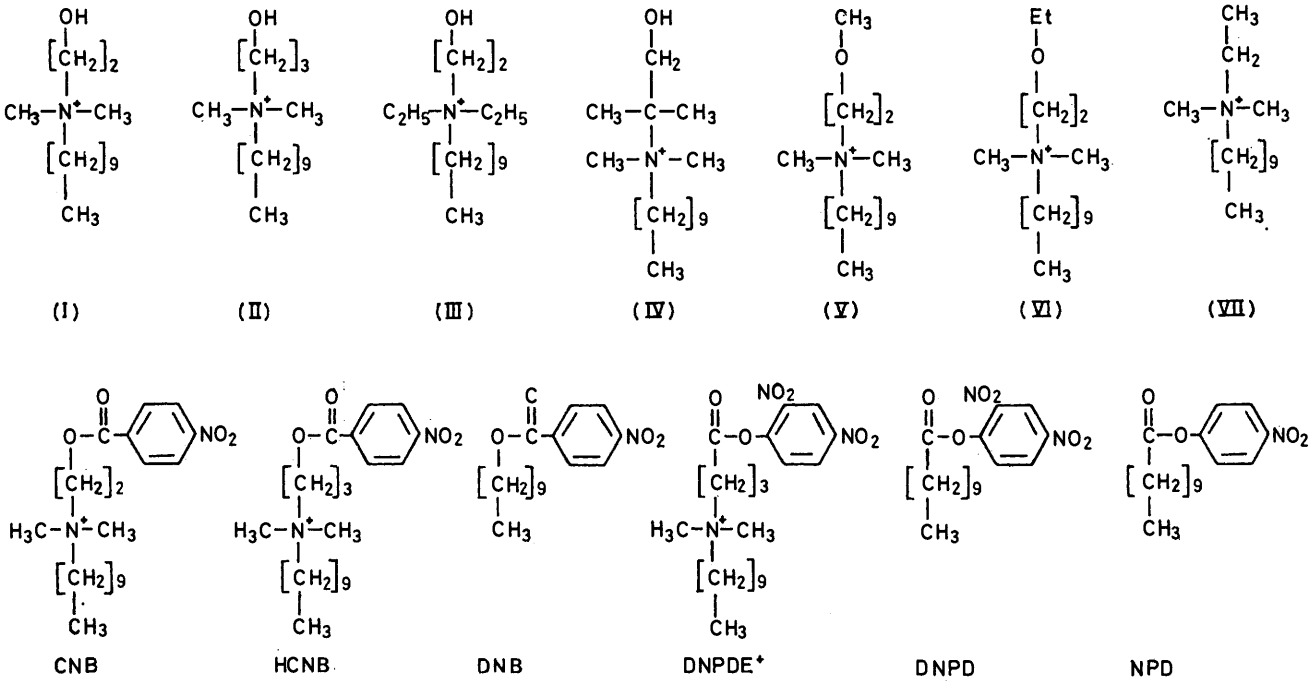
Dipolar Micelles. Part 4.[1a] Effect of Catalytic Micelles on the Hydrolysis of Neutral and Positively Charged Esters

By **Dina Wexler, Azriel Pillersdorf, Rina Shiffman, Jehoshua Katzhendler,* and Shalom Sarel,** Department of Pharmaceutical Chemistry, The Hebrew University School of Pharmacy, Jerusalem, Israel

The kinetic effects of cationic catalytic (I)—(IV) and non-catalytic (V)—(VII) micelles on micellar esters (CNB, HCNB, DNB, DNPDE$^+$, DNPD, NPD) derived from *p*-nitrobenzoic acid, *p*-nitrophenol, and 2,4-dinitrophenol were studied. Cationic esters and micelles have the following structures: n-$C_{10}H_{21}\overset{+}{N}Me_2Z\ \bar{B}r$, (I) Z = 2-hydroxyethyl; (II) Z = 3-hydroxypropyl; (III) n-$C_{10}H_{21}\overset{+}{N}Et_2CH_2CH_2OH\bar{B}r$; (IV) Z = 1,1-dimethyl-2-hydroxyethyl; (V) Z = 2-methoxyethyl; (VI) Z = 2-ethoxyethyl; (VII) Z = ethyl; CNB, Z = 2-*p*-nitrobenzoyloxyethyl; HCNB, Z = 3-*p*-nitrobenzoyloxypropyl; DNPDE$^+$, Z = n-butanoyloxy-2,4-dinitrophenyl; neutral esters; DNB, decyl *p*-nitrobenzoate; DNPD, 2,4-dinitrophenyl decanoate; NPD, *p*-nitrophenyl decanoate. The reaction of HCNB in micelle (I) and that of CNB in micelle (II), indicate that the reaction involves an esterification step *via* nucleophilic attack of the dissociated hydroxy-head group. The deuterium isotope effect is also in accord with this mechanism. The contribution of the transesterification step to the overall process was estimated for micelles (I)—(IV). A comparative study of the second-order rate constants for the cationic esters CNB, HCNB, and DNPDE$^+$ and DNB, DNPD, and NPD together with their kinetic salt effects of Br^-, suggest that proximity effects control the catalytic power of the micelles. Whereas F^- inhibits the hydrolysis of CNB, HCNB, DNB, DNPD, and NPD, in the case of DNPDE$^+$ an enhancement of the rate was noted. This phenomenon was also explained on the basis of steric and conformational factors.

THE binding of organic molecules at micellar surfaces resembles to a large extent the behaviour at the interface of proteins, biological membranes, and receptors, due to electrostatic and hydrophobic interactions. Thus, one of the advantages of using micellar systems as models is the ability to examine catalytic reactions at the hydrophilic–hydrophobic interfaces.[2] In Part 3 we showed [1a] that micelle-forming surfactants containing both charged and catalytic groups on the same molecule provide simple models that more nearly mimic enzyme-catalysed reactions. The purpose of this study is to shed more light on the nature of catalysis exhibited by hydroxylic micelles (I)—(IV). We shall focus our attention in this study on different types of substrates in which the reaction centres are located at varying distances from the micellar surface. This was achieved by establishing the kinetic effects of dipolar micelles on the hydrolyses of two classes of esters, (i) containing poor leaving-groups, such as CNB, HCNB, and DNB and (ii) with



[1] (*a*) Part 3, R. Schiffman, M. Chevion, H. Rav-Acha, J. Katzhendler, and S. Sarel, *J. Org. Chem.*, 1977, **42**, 856; (*b*) M. Bodanszky and V. du Vigneaud, *J. Amer. Chem. Soc.*, 1959, **81**, 5688.

[2] (*a*) E. H. Cordes and C. Gitler, *Prog. Bio-org. Chem.*, 1973, **2**, 1; (*b*) E. H. Cordes, 'Reaction Kinetics in Micelles,' ed., E. H. Cordes, Plenum Press, New York, 1973, (*c*) C. A. Bunton, ref. 2*b*; (*d*) H. Morawetz, *Adv. Catal. Related Subjects*, 1969, **20**, 431; (*e*) E. J. Fendler and J. H. Fendler, *Adv. Phys. Org. Chem.*, 1970, **8**, 271; (*f*) E. H. Cordes and R. B. Dunlop, *Accounts Chem. Res.*, 1969, **2**, 329.

good leaving-groups such as NPD, DNPD, and $DNPDE^+$. A kinetic study of salt effects of bromides and fluorides is herein described.

EXPERIMENTAL

Micelles.—Micelle forming agents (I)—(V) and (VII) have already been described.[1a] *Decyl-2-ethoxyethyl(dimethyl)ammonium* (VI) *bromide* was prepared according to usual methods using decyl(dimethyl)amine and 2-bromoethyl ethyl ether as starting material. Recrystallization from acetone crystals, m.p. 124° (Found: C, 50.5; H, 10.5; Br, 23.4; N, 4.4. $C_{16}H_{36}BrNO$ requires C, 56.8; H, 10.65; Br, 23.65; N, 4.15%).

Esters.—The esters $DNPDE^+$, DNPD, and NPD were prepared as described in Part 3, and purified prior to use.

Decyl p-*nitrobenzoate* (DNB) was prepared by dropwise addition of *p*-nitrobenzoyl chloride (0.027 mol) to a solution of decanol (0.027 mol) in dry benzene. The mixture was heated to 60° until evolution of hydrogen chloride ceased. The solvent was evaporated and the residue recrystallized from light petroleum (b.p. 40—60°), m.p. 28° (Found: C, 66.25; H, 7.95; N, 5.6. $C_{17}H_{25}NO_4$ requires C, 66.45; H, 8.15; N, 4.55%).

Decyl (dimethyl)-2-(p-nitrobenzoyloxy)ethylammonium bromide (CNB) was prepared by the method of Bodanszky and du Vigneaud.[1b] Decyl-2-hydroxyethyl(dimethyl) ammonium bromide (0.018 mol) was added to a solution of *p*-nitrobenzoic acid (0.018 mol) and dicyclohexylcarbodiimide (0.018 mol) in acetone. The mixture was refluxed for a few days, cooled, filtered, and the solvent was evaporated. The residual oily product was recrystallized from methanol–ether at −5°. The compound is highly hygroscopic, m.p. 115° (Found: C, 54.85; H, 7.9; Br, 17.45; N, 6.0. $C_{21}H_{35}BrN_2O_4$ requires C, 54.9; H, 7.6; Br, 17.4; N, 6.1%).

Decyl(dimethyl)-3-(p-nitrobenzoyloxy)propylammonium bromide (HCNB) was prepared by reacting 3-bromopropyl *p*-nitrobenzoate (4 g, 0.013 8 mol) with decyldimethylamine at room temperature for 30 min. The product was recrystallized from ethanol–ether and is highly hygroscopic, m.p. 105—106° (Found: C, 55.7; H, 8.0; N, 5.75. $C_{22}H_{37}BrN_2O_4$ requires C, 55.7; H, 7.8; N, 5.95%).

Kinetic Measurements.—The rates of hydrolyses were determined either from measurements of the absorbance increase due to substituted phenolate and *p*-nitrobenzoate ion formation, or from the absorbance decrease due to *p*-nitrobenzoate ester. The reactions were carried out in carbonate and phosphate buffers, at 30°. pH Values were determined by Radiometer PHM26 apparatus and ranged between 9.5 and 10.8 for most esters and between 6.5 and 7.5 for $DNPDE^+$. Reactions were initiated by injecting 15 μl of a stock solution of the substrate in acetonitrile into 3 ml of micellar solution in a buffer preheated in the thermostatted cell holder of a Unicam SP 800 spectrophotometer. Substrate concentrations in the cell varied from 1×10^{-5} to 5×10^{-5}M. The formation of *p*-nitrobenzoate ion and the disappearance of *p*-nitrobenzoate ester were monitored at 300 and 250 nm, respectively. The extent of liberation of the *p*-nitrophenolate ion, and that of the 2,5-dinitrophenolate ion were computed from measurements at 400 and 410 nm, respectively. Deuterium isotope effects were examined for DNB, CNB, and HCNB in micelle (I) at four pD [3] values with 99.8% deuterium oxide. Micelle concentration used in the kinetic measurements were either 0.1 or 0.2M, amounting to at least five-fold excess over the critical micelle concentration (c.m.c.).[1a] Study has shown that at ionic strength *I* 0.4 and 0.8M the rate constants were not affected by increases in micelle concentration in the range 0.1—0.4M.

Rate Constants.—At ionic strength 0.8M, the hydrolyses of the following esters: (i) DNB, $DNPDE^+$, DNPD, and NPD in the presence of micelles (I)—(VII), (ii) CNB in micelles (I) and (III)—(VII), and (iii) HCNB in micelles (II) and (IV)—(VII) obey equation (1) in the experimental

$$V = k'\,[\text{Substrate}][OH^-];\ k' = k_{obs}/[OH^-] \quad (1)$$

pH range. For case (i) $k' = k_N' + k_{OH}'$ and for (ii) and (iii) $k' = k_{OH}'$ where k_N' and k_{OH}' refer to the second-order rate constant which is attributed to the participation of the micelle and hydroxide ion respectively. First-order rate constants were calculated either from the first-order rate equation, or by use of Guggenheim's method.

The first-order rate constants for HCNB in the presence of (I), (III), and (IV) were determined from equation (2). The reaction of CNB in micelle (II) followed equation (3). In all cases, the first-order rate constants (k) are linearly dependent on the hydroxide ion concentration in the pH range 9.5—10.8. The second-order rate constants (k') were calculated from the slopes of the plot of k_{obs} against $[OH^-]$.

Kinetic Salt Effects.—The effects of bromide and fluoride ions was examined at various concentrations of external salts (KBr or KF) and 0.05M-carbonate buffer. Whereas in the case of DNB, CNB, and HCNB the salts were added to the reacting systems containing 0.2M-micelle, in the cases of $DNPDE^+$ and NPD the micelle concentration was 0.1M.

RESULTS AND DISCUSSION

Mechanism.—In Part 3 [1a] we have shown that hydroxy micelles of type (I)—(IV) do participate in the hydrolyses of phenyl esters *via* nucleophilic attack of the dissociated head groups of the micelles. The reaction mechanism was characterized kinetically from a study of deuterium isotope effects, the Brönsted correlation, and the effect of external nucleophiles. However, in the hydrolysis of *p*-nitrobenzoate esters CNB and HCNB, direct kinetic evidence for a nucleophilic mechanism has been established. This is due to the involvement of a transesterification step which contributes significantly to the rate of product formation.

From the experimental time-course of product formation (Figures 1a and b), it can be seen that the hydrolytic reaction of both CNB and HCNB in micelles (II) and (I), respectively, is a consecutive process. Thus the accumulation of an intermediate specimen along the hydrolytic pathway is deduced either by the induction time as observed during the reaction of HCNB in (I), or by the biphase reaction observed in the hydrolysis of CNB in micelle (II).

The above mentioned kinetic behaviour can be explained in terms of an intramolecular benzoyl-transfer reaction, resulting from the nucleophilic participation of a neighbouring micellized alkoxide ion (k_1) which then, in turn, is debenzoylated (k_2) to yield the products. A

[3] T. H. Fife and T. C. Bruice, *J. Phys. Chem.*, 1961, **65**, 1079.

simultaneous competitive hydrolytic route (k_3) is also involved during the kinetic process. The various modes

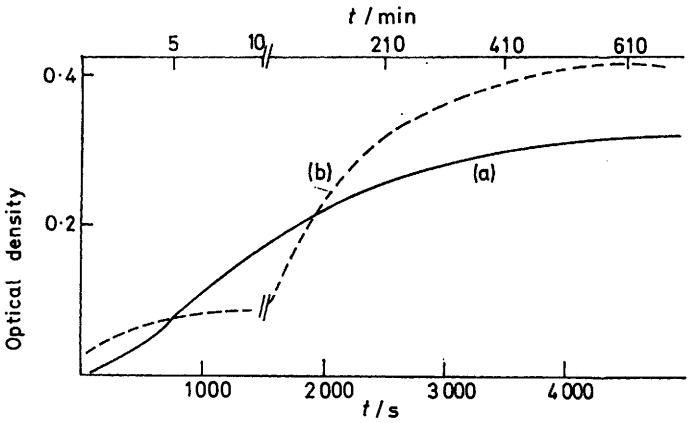
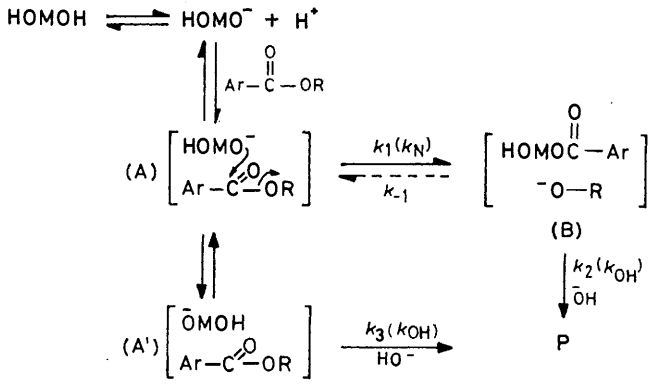


FIGURE 1 Time course of *p*-nitrobenzoate liberation at 30°: (*a*) 0.1M-HCNB in micelle (I) (lower time scale); (*b*) 0.1M-CNB in micelle (II) (upper time scale).

of reaction are delineated in Scheme 1. HOMOH and $HOMO^-$ represent the hydroxy micelle and its conjugated base, respectively; (A') and (A) represent the substrate–micelle complex formed in the vicinity of an undissociated hydroxy-head group and alkoxide ion,



SCHEME 1

respectively; (B) is the ester formed *via* benzoyl migration to a neighbouring oxyanion.

The shapes of the curves in Figures 1a and b are markedly dependent on the relative rate constants of k_1—k_3. In cases where $k_2 \gg k_1 > k_3$, the time-course of *p*-nitrobenzoate formation is expected to follow a sigmoid type curve. However, in the cases where $k_2 < k_3 \sim k_1$, the release of *p*-nitrobenzoate ion should exhibit a biphase reaction. The initial rapid stage of hydrolysis in the latter case is attributed to the competition between the fast catalytic transbenzoylation step (k_1) and the hydrolytic route (k_3), whereas the second slower stage of hydrolysis, is due to the debenzoylation step (k_2) of intermediate (B). Indeed, inspection of Table 1 reveals that the relationships between the rate constants of the transbenzoylation reaction in Scheme 2 are in accord with the preceeding predictions for the kinetic curves (Figures 1a and b).

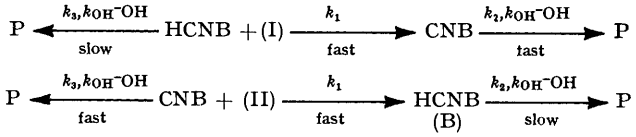
TABLE 1

Second-order rate constants (l mol^{-1} s^{-1}) in the hydrolysis of long-chain esters derived from substituted benzoic acid and phenol at 30° and *I* 0.8M

	Ester					
Micelle	DNB [d]	CNB [d]	HCNB [d]	DNPD [b,c]	DNPDE+ [b,c]	NPD [b,c]
None		13	1.7		1 689	
(I)	0.16	18	11 [a]	505	6 000	78
(I) (D_2O)	(0.13)	(31.2)	(20)			
(II)	0.10	82 [e]	1.3	63	1 500	8.3
		(1.2) [f]				
(III)	0.19	17.6	10 [a]	700	12 000	86
(IV)	0.13	20	6.3 [a]	405	3 200	39
(V)		12	2.0	30	1 553	2.9
(VI)	0.022	14	2.0	11.2	1 280	1.4
(VII)	0.025	12	1.7	11.7	2 200	1.6

[a] Second-order rate constants ($k'_1 + k'_3$) were derived from equation (2). [b] Data taken from ref. 1(*a*). [c] Micelle concentration 0.1M. [d] Micelle concentration 0.2M. [e] Second-order rate constant ($k' + k'_3$) derived from equation (4), for the initial first stage of hydrolysis. [f] Second-order rate constant derived from the second stage of hydrolysis. All other rate constants (k') were determined from equation (1).

The kinetic expression for the product formation in the hydrolysis of HCNB in micelles (I), (III), and (IV) at



SCHEME 2

time *t* is given by equation (3) where $[(A) + (A')]_0$ and [P] denote the initial concentration of substrate and

$$[P] = [(A) + (A')]_0\left[1 + \frac{k_1}{k_2 - k_1 - k_3}e^{-k_2t} - \frac{k_2 - k_3}{k_2 - k_1 - k_3}e^{-(k_1+k_3)t}\right] \quad (2)$$

product concentration respectively, and k_2 and k_3 are first-order rate constants which were determined independently.

The first-order rate constant k_1 was calculated by fitting the kinetic plot to equation (2) on a CDC computer according to a non-linear least squares program. It was noted that the time-course for the liberation of *p*-nitrobenzoate ion when measured after the inflection point demonstrated first-order kinetics. The rate constant thus obtained fits the value of $(k_1 + k_3)$ which is derived from equation (2).

In the case of CNB in micelle (II), where $k_2 \ll k_3, k_1$, the first exponential term in equation (2) during the initial time period is approximately unity and the kinetic expression then becomes (3). Since the kinetic term

$$[P] = \frac{k_3}{k_1 + k_2}[(A) + (A')]_0[1 - e^{-(k_1+k_3)t}] \quad (3)$$

$k_3[(A) + (A')]_0/(k_1 + k_3)$ denotes the maximum release of *p*-nitrobenzoate ion in the first stage of hydrolysis, equation (3) reduces to (4) where $[P]_\infty$ is related to the first plateau region of the kinetic curve (Figure 1b).

$$[P]_\infty - [P] = [P]_\infty e^{-(k_1+k_3)t} \quad (4)$$

The first-order rate constants ($k_1 + k_3$) are obtained from the slope of the linear plot of log ($[P]_\infty - [P]$) against t. Subsequently, the second stage of the hydrolysis as represented in Figure 1b, corresponds to the deacylation catalysis (k_2) of the intermediate (B). This reaction is in accord with equation (1), and the rate constant k_{obs} was determined either by the first-order rate equation, or by Guggenheim procedure. The fact that the rate constants of the second hydrolytic stage are in very good agreement with those determined independently from the reaction of HCNB in micelle (II) confirms the hydrolytic pathways which are shown in Scheme 1.

In view of the following reasons, it seems likely that steps k_2 and k_3 comprise specific based catalysed processes. The data in Table 1 reveal that the values of the second-order rate constant of CNB in micelle (I) and that of HCNB in micelle (II) resemble those produced by same esters in presence of the noncatalytic micelles (V)—(VII). Since the reaction in the latter proceeds only by specific base catalysis it is most likely that same route is also followed by CNB and HCNB in micelles (I) and (II), respectively. The observed slight variation in rates can be attributed to microscopic environmental factors. Furthermore, the value of the kinetic deuterium solvent isotope effect, $k'(H_2O)/k'(D_2O)$ 0.58 for the case of CNB in micelle (I), is in accord with the previously reported value of 0.5—0.7 for specific-base catalysis of phenyl esters in micellar system.[1a] In view of this, a general base-specific mechanism should be ruled out because the deuterium isotope effect of such a route is expected to fall within the range 1.1—2.1.

From Table 1, it can be seen that the catalytic effect induced by hydroxy micelles on esters bearing good leaving groups (DNPD, DNPDE$^+$, and NPD) is not the same. In comparison to non-catalytic micelles (V) and (VII) the increases of the second order rate constants (k'_N) of NPD and DNPD in micelle (I) are 26—47 and 24—42 respectively. But, in the case of DNPDE$^+$, the relative enhancement is only 1.7—2.8 fold. A similar kinetic view to the above is also observed when comparing the latter ester in other hydrolytic micelles such as (II)—(IV). In all these micelles the magnitude of the relative rate value of DNPDE$^+$ is the smallest. Therefore it seems likely that the catalytic efficiency is dependent on the site of the reaction. When the reaction centre resides on the micelle surface, in the vicinity of the 'onium group, the catalytic efficiency is increased, but if the reaction site is closer to the outer region of the micelle, as is assumed for DNPDE$^+$, then the catalytic efficiency is reduced. In the cases of the less activated esters (DNB, CNB, and HCNB) the catalytic effect of the micelles is not parallel. First, the extent of catalysis in the latter esters is less pronounced then in the substituted phenyl esters. Secondly, the relative enhancements for all three esters in each micelle are similar. The corresponding values for DNB and HCNB in micelle (I), and for DNB and CNB in micelle (II) are 6.2—5.4, 7.4—4.5, 3.5—3.0, and 5.8—3.5.

The involvement of alkoxide ions in acyl-transfer reactions is well documented.[4] Capon [4a] and Kirby [4c] have demonstrated the very high effectiveness of lactonization reactions (k_N', k_c) compared with specific base hydrolysis (k_{OH}) of analogous esters.

$$V = k_N'[ROH]\,[\bar{O}H][E] = k_cK_a/K_w[RO^-][E] \quad (5)$$

The relative ratios k_c/k_{OH} for 2-hydroxyphenyl acetate and phenyl 4-hydroxybutyrate were found to be 5.5×10^3 and 4.3×10^5 respectively. In order to compare the catalytic efficiency of an alkoxide ion in an intramolecular system with that of micelle (I), we estimated the lactonization rate constant for a model, derived from phenyl 4-hydroxybutyrate, where the pK_a value of the hydroxy-group is the same as that of micelle (I). [The pK_a of the micellized alkoxide (I) is assumed to fall in the range 13.1—13.5.[5]] Using the data of Capon [4a] and considering a Brönsted β coefficient of 0.76 [4g] for the attacking nucleophile, it was found that the first-order rate constant k_c of phenyl 4-hydroxybutyrate which possessed a catalytic group of pK_a 13.1—13.5 is 4.0—8.2 $\times 10^3$ s^{-1}. The respective k_c/k_{OH} ratio is 3.2—3.5 $\times 10^3$ mol l^{-1}.

On the other hand, the corresponding intermolecular reaction ratio k_c/k_{OH} for prop-2-yn-1-ol [4h] (pK_a 13.55) and for *N*-acetylserinamide [4g] (pK_a 13.6) as catalysts, during the hydrolysis of phenyl and *p*-nitrophenyl acetate, respectively, are only 18.9 and 18. The above mentioned calculated rate ratio for the esters NPD, DNPD, HCNB, and DNB in micelle (I), showed values of 9—22, 8—20, 14—3.5, and 1.1—2.7 respectively. Therefore, it can be concluded, that the effectiveness of an alkoxide ion in the micelle (I) is much lower than that of a non-micellar intramolecular model, and resembles that of an intermolecular process.

The intramolecular catalytic efficiency of micelle (II) compared with (I), and the dissociation ratio K_a(II)/K_a(I), could also be estimated on the basis of the kinetic data.

In our previous report [1a] it was found that the Brönsted β coefficient of substituted-phenyl esters in micelle (I) and (VII) was −0.36 and −0.31, respectively. These values of the Brönsted relationship are also demonstrated by the data in Table 1. From the second-order rate constants k_N' of DNPD and NPD it was deduced that the ratio [log k_N' (DNPD)/k_N'(NPD)]/ΔpK_a in micelles (I)—(VII) was in the range 0.3—0.4. Consequently, the reaction of NPD or DNPD with various

[4] (*a*) B. Capon, S. T. McDowell, and W. V. Raftery, *J.C.S.* 1973, 1118; (*b*) T. H. Fife and B. Benjamin, *J. Amer. Chem. Soc.*, 1973, **95**, 2060; (*c*) A. J. Kirby and G. J. Lloyd, *J.C.S. Perkin II*, 1974, 637; (*d*) C. J. Belke, S. C. K. Su, and J. A. Shafer, *J. Amer. Chem. Soc.*, 1971, **93**, 4552; (*e*) B. A. Cunningham and G. L. Schmir, *ibid.*, 1967, **89**, 917; (*f*) T. C. Bruice and F. H. Marquardt, *ibid.*, 1962, **84**, 365; (*g*) T. C. Bruice, T. H. Fife, J. J. Bruno, and N. F. Brandon *Biochemistry* 1962, **7**; (*h*) W. P. Jencks and M. Gilchrist, *J. Amer. Chem. Soc.*, 1968, **90**, 2622.

[5] The extrapolated data of (*a*) C. A. Bunton and L. G. Ionescu, *J. Amer. Chem. Soc.*, 1973, **95**, 2912; (*b*) C. A. Bunton and S. Diaz, *ibid.*, 1976, **98**, 5663 gave a value of *ca.* 13.1. We have estimated the higher value of 13.4—13.5 (unpublished results).

strong nucleophiles such as micelles (I) and (II) should manifest the same Brönsted slope. Therefore, the differences between the pK_a values of micelles (I) and (II) can be determined according to equations (6) and (7). Since the average experimental ratio k_N'(I)/

$$\log [k_c(I)/k_c(II)] = \log [k_N'(I)k_a(II)/k_N'(II)K_a(I)] = 0.3 - 0.36[pK_a(I) - pK_a(II)] \quad (6)$$

$$\log [k_N'(I)/k_N'(II)] = 0.7 - 0.64[pK_a(II) - pK_a(I)] \quad (7)$$

k_N'(II), for DNPD and NPD, is *ca.* 10, the resulting ΔpK_a value is in the range 1.4—1.6.

From the betaine series $C_{10}H_{21}N^+(CH_3)_2[CH_2]_nCO_2H$ Br^- where the corresponding pK_a values are 2.66, 3.76, and 4.56, when n 1, 2, and 3 respectively at 30° and I 2.5M (KCl), it seems likely that a lower limit of 1.4 is the appropriate value for the difference in the pK_a between micelles (I) and (II). Thus, the calculated relative rate constants, k_c[(II)–CNB]/k_{OH}[(II)–CNB] 27—68, show that micelle (II) is 19 times as efficient a catalyst as (I).

The estimated ΔpK_a value for the pair (I) and (II) allows the evaluation of the Brönsted coefficient for the specific base hydrolysis of CNB and HCNB. The ΔpK_a value of the leaving groups in the latter ester is identical with those found for micelles (I) and (II). Therefore, on using a ΔpK_a value (of 1.4) it was found that in the presence of micelles (V)—(VII) the β value is *ca.* 0.59. While for the hydroxy micelles (I) and (II) the estimated value is *ca.* 0.8.

These values are in accord with general views on bond making and breaking in the transition state, which is reflected by the β coefficients. As the difference in basicity between the attacking nucleophile and the leaving group becomes smaller the β coefficient increases proportionally. The larger β value for hydroxy micelles compared with those for micelles (V)—(VII) can be attributed to microenvironmental factors which affect the transition states to a different extent in both systems.

The low catalytic effect of micelle (IV) might be attributed to the shielding effect of the head groups. Similar arguments have been put forward to explain the decrease in catalytic efficiency produced by highly branched surfactants.[6] The kinetic data suggested that the steric shielding of the head groups could not be the dominant factor. From Table 1 it could be seen that the surfactants (V) and (VI) exhibited the same effect on the reaction rate, while (VI) was expected to be more efficient in screening of the hydroxide ion.

Salt Effects.—Added salts to cationic micelles are known to reduce the extent of micellar catalysis. From the iceberg [7] model it is clear that counter ions with structure-breaking ability could reach the micellar surface and modify its charge. On the other hand, counter-ions of structure-promoting characteristics are due to interaction with the surfaces of the micelle to a small extent only. The degree of binding was found to be in the order iodide > bromide > chloride > fluoride.[8] The size of ion hydration [9] and ion-pair formation with tetra-alkylammonium compounds [10,11] have the same order of counter-ion binding. Several explanations have been put forward to account for the inhibiting capacity of added anions relating to electrostatic,[12-14] proximate,[15] and medium [16] effects. These are interpreted as follows. (a) Added anions decrease the charge density on cationic micelles,[12,13] and accordingly, electrostatic interactions of the surface with a negatively charged transition-state are also decreased. (b) Added anions compete with the reactants for binding space at the micellar surface and as a result, the proximity of the reactants to the micellar surface decreases, (c) A change in solvent structure,[17] a decrease in c.m.c.,[8,18] an increase in aggregation number,[18] and a change in micellar shape [9,19] might also be a result of added anions.[18]

Since in the present study the nucleophile is part of the cationic surfactant and the reaction site of the esters may be located at varying regions close to the micellar surface, the inhibiting capacity of the added anions is also expected to vary with the ester structure. Inspection of Table 2 reveals that in the presence of micelle (I), the salt effect produced by the bromide ion is large and similar to that for most of the esters. An exception was obtained for $DNPDE^+$ which exhibited a very small salt effect in micelle (I) and none in micelle (VII). On the basis of the assumption that the source of the salt effect is in the interference of counter-ions of the electrostatic interactions at the surface as indicated by Romsted and Cordes [12a] in analogous compounds, it seems likely

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that when the reaction site is located closer to the micellar surface then the inhibiting effect of the bromide ion is increased. Indeed, this is the case in the course of the specific base-catalysis reaction of NPD in (VII) and of DNB in (I), where the aliphatic chain which inserts itself into the interior region of the micelle compels the carbonyl ester to be at the surface. The maximal salt effects observed for the latter esters in specific-base catalysis are 32.1 and 18, respectively (see Table 2).

A lower salt effect is observed in the case of nucleophilic catalysis produced by the dissociated hydroxy-head group [NPD in micelle (I)]. This may indicate that hydroxide ion and the bound alkoxy nucleophile are affected to a different degree by the added salts. However, the relatively large salt effect on NPD in (I) indicates that both the nucleophile and the anionic transition states are located on the micelle surface as illustrated in Figure 2A. This view is consistent with the proposed structure of betaine surfactants [20] and the large surface area of 2-dodecylaminoethanol.[9]

The similarity in the bromide ion salt effect of the micellar esters DNB, HCNB, and CNB in specific base hydrolysis could not be anticipated since the reaction centres of the latter two esters are supposed to be closer to the cationic surface. This turned out to be the case. The alkyl chain of the ester function in HCNB and CNB most probably assume a folded conformation allowing the phenyl group to penetrate the Stern layer, thus forcing the carbonyl group to reside on the boundary area. This entails that the microscopic environment of the reaction site in HCNB and in CNB resemble that in DNB and as a consequence, the salt effects in the three esters are likely to by the same. The conformational preference is illustrated in Figure 2B. Similar associations between quaternary ions and aromatic compounds are well documented.[21,22] Figure 2B is constructed on the basis of similar solubilization arguments which suppose that (a) the polar groups in aromatic acids orient themselves mainly to the water layer and (b) the interactions of aliphatic acids with water are rather similar to those with micelles.[23] Thus, it follows that the aliphatic chain bearing the head group in cationic esters lie on rather than within the micelle surface.

The salt effect in the catalytic hydrolyses (k_1') of HCNB and CNB in micelles (I) and (II), respectively, is not similar. With micelle (I) as a catalyst, the extent of salt effects is large and close to the values observed for CNB and DNB. On the other hand, with micelle (II) as catalyst the extent of the salt effect is very small and the decrease in rate of CNB was only 6.5-fold at 3M-KBr. It is assumed that two main factors govern the extent of salt effect in the above models: (*a*) the conformation of the esters and the hydroxy-head groups, and (b) the charge distribution in the anionic transition state. It is conceivable that the hydroxy-head group in both micelles (I) and (II) is folded. However, the degree of

TABLE 2

Effect of bromide ion to the hydrolytic rate constants k'/l mol^{-1} s^{-1} of NPD, DNPDE$^+$, DNB, CNB, and HCNB in micelles (I)—(III) and (VII) at 30° [a,b]

Micelle	(I)	(III)	(VII)	(I)	(VII)	(I)	(I)
				Ester			
[Br$^-$]/M	NPD	NPD	NPD	DNPDE$^+$	DNPDE$^+$	DNB	CNB
0.1	375 (1)	446 (1)	13.5 (1)	28,800 (1)	2,200 (1)	0.72	81.5
0.2	142 (2.64)	160 (2.78)	9.2 (1.46)	22,200 (1.29)		0.45 (1)	65.0 (1)
0.3	130 (2.88)	135 (3.30)	7.0 (1.92)	17,000 (1.69)		0.40 (1.12)	48.7 (1.33)
0.4	118 (3.20)	120 (3.70)	5.0 (2.70)	12,000 (2.40)	2,200 (1)	0.32 (1.40)	39. (1.66)
0.75	78 (4.80)	86 (5.18)	1.6 (8.43)	6,000 (4.36)	2,200	0.16 (2.81)	18. (3.61)
1.0	58 (6.46)	76 (5.86)	1.2 (11.2)	5,800 (4.36)	2,200	0.11 (4.09)	15.8 (4.11)
1.5	32 (11.72)	52 (8.57)	0.9 (15.0)	5,800 (4.96)	2,200 (1)	0.055 (8.18)	7.8 (8.33)
2.0	20 (18.75)	42 (10.67)	0.6 (22.5)	5,800 (4.96)		0.035 (12.8)	4.0 (16.25)
2.5	16 (23.4)	36 (12.38)	0.48 (28.1)			0.035 (12.8)	4.0 (16.25)
3.0	16 (23.4)	36 (12.38)	0.42 (32.1)	5,800 (4.96)	2,180	0.025 (18.0)	4.0 (16.25)

Micelle	(I)	(II)	(II)	(III)	(III)	(III)
			Ester			
[Br$^-$]/M	HCNB	CNB	HCNB	DNB	CNB	HCNB
0.1	41.8	350	6.3	0.9	101	51
0.2	33.6 (1)	208 (1)	5.06 (1)	0.6 (1)	69 (1)	38 (1)
0.3	22. (1.52)	185 (1.12)	4.06 (1.4)	0.43 (1.4)	42 (1.54)	19.5 (1.94)
0.4	20. (1.68)			0.3 (2.0)	30 (2.3)	17.6 (2.18)
0.75	11. (3.0)	82 (2.53)	1.3 (3.8)	0.19 (3.9)	17.6 (3.9)	10. (2.8)
1.0	9.2 (3.65)					
1.5	4.8 (7.0)			0.095 (6.3)	8.3 (8.31)	8.3 (8.31)
2.0	3.2 (10.5)					
2.5	2.5 (13.4)					
3.0	2.0 (16.3)	32 (6.5)	0.22 (23)		5.7 (12.1)	5.7 (12.1)

[a] Measurements were carried out with added 0.05M-potassium carbonate buffer. [b] Concentration of micelles is that given in Table 4.

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population of the folded conformation in (I) seems to be higher than that of (II). This conformational view may account for the differences in the salt effect of the latter micelles in their catalytic reactions.

The importance of ester conformation on the kinetic salt effect is inferred from (a) the small effect of the bromide ion in the case of micelle (III), and (b) the very small effect in the case of $DNPDE^+$ in the presence of micelles (I) and (VII).

The case of micelle (III) could be explained in terms of availability of a more ' open ' surface [24] compared with micelles (I) and (II). In this case the charge density on

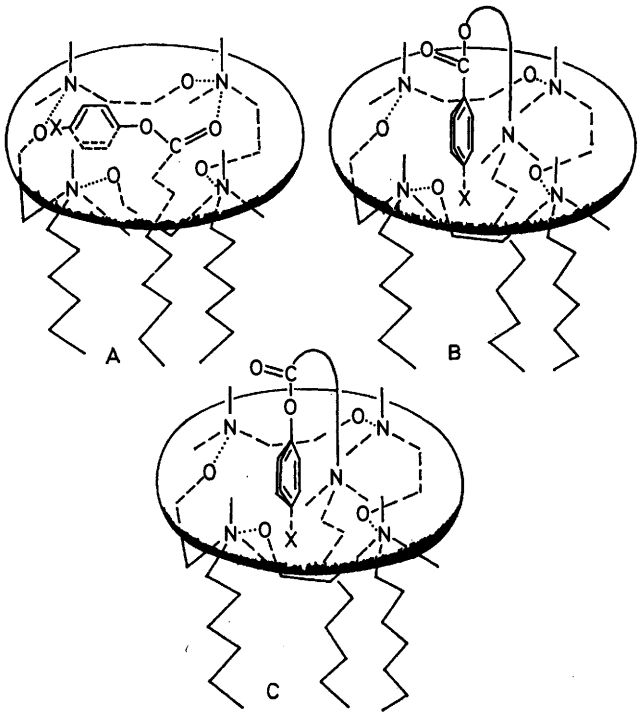

FIGURE 2 Possible conformations of long chain esters on the surface of micelle (I): A, NPD; B, CNB and HCNB; C, $DNPDE^+$

the micelle surface is decreased, and as a result, the population of conformation in Figure 2B is also decreased because of the reduced interaction between the cationic surface and the ester aromatic ring. It is also plausible to assume that an open surface is more hydrated and of higher effective dielectric constant in comparison with a 'closed ' surface and consequently of lower potential energy.

In the case of factor (b) governing the salt effect it seems likely that the π interaction between the phenyl group of $DNPDE^+$ and the positively charged surface is relatively small due to the strong electron-withdrawing dinitro-groups. Thus the population of the folded conformation in the latter ester compared with CNB and HCNB, is expected to be significantly lower. An additional factor which might be the cause of the low salt effect in $DNPDE^+$ is the increased distance between the reaction site of the ester in a folded conformation, and the surface. This is illustrated in Figure 2C.

Supporting evidence for the conformationals depicted in Figure 2 is adduced from calculating the contribution of internal nucleophilic catalysis, due to the dissociated hydroxy-head group in micelle (I), to the overall rate at various concentrations of bromide ions. Inspection of Tables 2 and 3 reveals that although an increase in bromide ion concentration significantly lowers the reaction rates of HCNB and NPD, the contribution of the internal nucleophilic rate (k_N',k_1) to the total hydrolysis varies only slightly. This could be interpreted on the basis of Figures 2A and B supposing that both the reaction site of the esters and the nucleophiles reside close to the cationic surface and in a similar microenvironment. The addition of a salt in such a case should affect to the same extent both internal nucleophilic attack and the competitive specific-base reaction (k_{OH}).

TABLE 3

Calculated percentage of transesterification and internal catalysis in the hydrolysis of HCNB, $DNPDE^+$, and NPD at 30° in micelle (I) at various bromide ion concentrations

	Contributions (%)		
[Br]/M	HCNB	$DNPDE^+$	NPD
0.1	84.9	92	96
0.2	84.4	90	94
0.3	81.5	87	95
0.75	82—88	66	96
3	89	62	98

The situation with $DNPDE^+$ is quite different. From Table 3 it is clear that in the case of $DNPDE^+$ the contribution of k_N' increases in inverse proportion to the concentration of the added bromide. This again is in accord with our view expressed above on the decisive role of ester conformation on the reaction pathway. The population of the folded conformation (Figure 2c) most likely increases and the reaction centre becomes more susceptible to internal nucleophilic attack. The high sensitivity of the ratio $k_N'/(k_N' + k_{OH}')$ to a change in the ionic strength is probably due to the weak binding of the aromatic ring in $DNPDE^+$ to the positively charged surface.

Fluoride Ion.—The effects of fluoride ion on micellar esters can be inferred from the data in Table 4. The inhibiting power of the fluoride ion is indeed small, and the rate constants of all the esters are decreased by a factor of 1.6—4.0 fold only, as the salt concentration reaches 2M. The diminished salt effect of the fluoride ion is attributed to the decrease in binding of the counter-ion to the surface. This is in accord with previously reported cationic systems.

In comparison with the bromide ion, the kinetic effects of the fluoride ion should be more pronounced in cases where the reaction site of the ester molecule is in proximity to the charge surface, but should be diminished as the reaction site is forced to the outer region of the micelle. It is anticipated therefore, that the rates of

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the esters NPD, DNPD, CNB, and HCNB will be reduced to a larger extent than that of DNPDE$^+$. Surprisingly, it was found that the fluoride ion markedly accelerated also indicates that the origin of the rate acceleration is in the fluoride ion assistance to the specific base catalysis. Reasonable explanations to this effect may be as

TABLE 4

Kinetic salt effect of fluoride ion on the hydrolysis (k'/l mol^{-1} s^{-1}) of DNB, CNB, HCNB and NPD in micelles (I) and (III) at 30 °C, [a, b]

[Br$^-$] + [F$^-$]/M	[F$^-$]/[Br$^-$]	(I) DNB	(I) CNB	(I) HCNB	(III) DNB	(III) CNB	(III) HCNB	[F$^-$]/[Br]	(I) NPD	(VII) NPD
0.1		0.72	81.5	41.8	0.90	101	51	0	375(1)	13.5(1)
0.2	0	0.45(1)	65(1)	33.6(1)	0.60(1)	69(1)	38(1)			
0.3	0.5		61(1.06)	23(1.46)		62.2(1.10)		2.0	338(1.05)	
0.4	1				0.60(1)		30(1.26)	3.0	328(1.08)	
0.75	2.75		52(1.25)	24(1.40)	0.40(1.50)	52(1.32)		6.5	300(1.19)	10.0(1.35)
1.0	4.05	0.40(1.12)	46(1.41)	24(1.40)	0.28(2.14)	45(1.53)	25(1.52)	8.0	283(1.26)	8.4(1.60)
1.5	6.50	0.32(1.40)	40(1.62)		0.18(3.33)	36.8(1.87)	21(1.80)	14.0	252(1.41)	5.2(2.50)
2.0	2.00	0.27(1.66)	36(1.80)	20(1.68)	0.16(3.75)	32(2.15)	18.8(2.02)	19.0	222(1.60)	4.4(3.07)
3.0	14.40							19.0	172.(207)	4.2(3.21)

[a] All measurements were carried out with 0.05M-potassium carbonate buffer. [b] The concentration of micelles in the hydrolyses of DNB, CNB, and HCNB was 0.2M In the hydrolyses of NPD the concentration of micelles was 0.1M. [c] The concentration of bromide ion was identical to that of micelle concentration. [d] The numbers in parentheses are the relative rates k'(0.2 or 0.1M)/k'.

the hydrolytic rate of DNPDE$^+$ in micelles (I) and (VII) obeying equation (8).

$$k_{obs} = k_F[F^-] + k_{FB}[F-][OH] \qquad (8)$$

Equation (8) was derived from the curves in Figure 3 exhibiting a linear relationship between k_{obs} and the hydroxide ion concentration in the presence of various salt concentrations. The inhibiting effect of the fluoride ion on the reaction of DNPD suggests that the acceleration effect in DNPDE$^+$ springs from the location of the reaction site, and not from the characteristic of the leaving

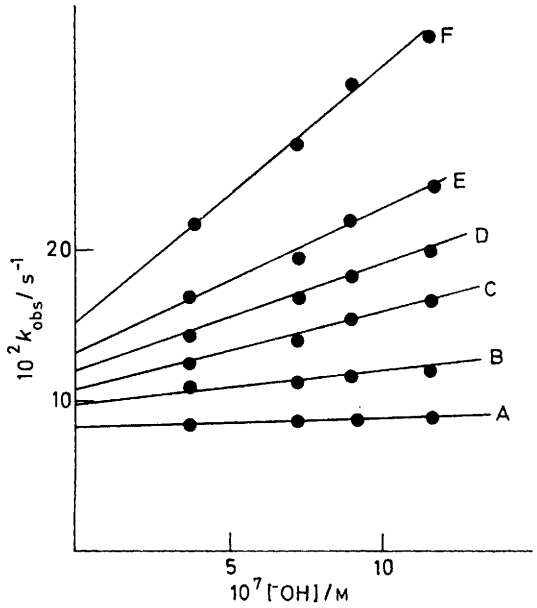

FIGURE 3 Dependence of the first-order rate constant k_{obs} on hydroxide ion concentration in the hydrolysis of DNPDE$^+$ with micelle (I) at 30° and various concentrations of KF: A, 0.4; B, 0.8; C, 1.2; D, 1.6; E, 2.0; F. 3.0M

group. Moreover, the non-specificity of this effect to the hydroxy micelle, and its occurrence with micelle (VII) follows. (a) The fluoride hydration shell could interact with the surface micelle as shown by Figure 4. From this

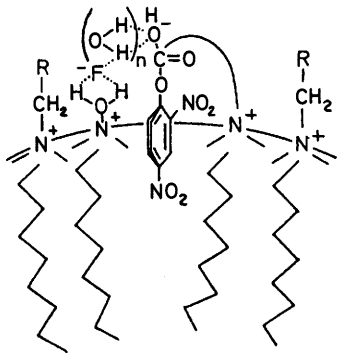

FIGURE 4 Assumed binding of F$^-$ to the micelle surface

microscopic viewpoint an augmentation of the reaction rate could be due to a better orientation of the nucleophile towards the reaction centre. (b) Stabilization of the reaction site may occur by increased hydration in the transition state. More kinetic work supports the view expressed in Figure 4 indicating that nucleophilic attack by F$^-$ in cationic micelles is considerably hampered compared with other nucleophiles. Jencks [4h] has noted that the rates of nucleophilic attack of the azide (k_A) and the fluoride (k_F) ions on 2,4-dinitrophenyl acetate (DNPA) at 25° are 0.95 and 3.1 × 10^{-3} l mol^{-1} s^{-1}, respectively. In previous work,[1a] the rate of azide attack on DNPDE$^+$ was found to be 2.62.

This demonstrates the acute reduction of the relative ratio k_F(DNPDE$^+$)/k_A(DNPA) = 3.05 × 10^{-4}[the second-order rate constant k_F of DNPDE$^+$ in micelle (VII) is 0.8 × 10^{-3} l mol^{-1} s^{-1}] and is in accord with our view of the binding region illustrated in Figure 4.

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