Hydrolysis of Di- and Trisubstituted Phosphate Esters Catalyzed by Nucleophilic Surfactants[1]

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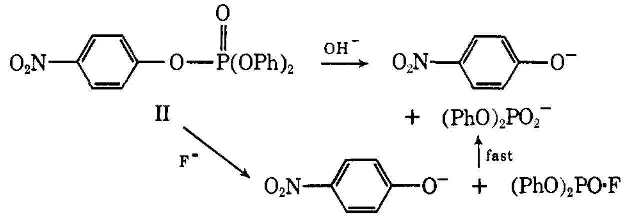
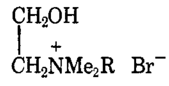
Abstract: Micelles of 1-hydroxyethyl-2-dimethylalkylammonium bromides (I, alkyl = R = n-$\mathrm{C_{12}H_{25}}$, n-$\mathrm{C_{16}H_{33}}$) are good catalysts for the hydrolysis of p-nitrophenyl diphenyl phosphate and ethyl p-nitrophenyl phosphate monoanion in the presence of hydroxide ion, with over 300-fold rate enhancement of hydrolysis of the triaryl phosphate in the presence of I (R = $\mathrm{C_{16}H_{33}}$). This catalysis, and the variation of reaction rate with hydroxide ion concentration, can be explained in terms of nucleophilic participation by the alkoxide ion of I, with p$K_a \approx 12.4$ for the ionization of the hydroxyl group of I (R = $\mathrm{C_{16}H_{33}}$) and 12.9 for that of I (R = $\mathrm{C_{12}H_{25}}$). These hydroxy substituted surfactants are no better catalysts than the corresponding alkyltrimethylammonium bromides for the reactions with fluoride ion, suggesting that electrophilic catalysis is relatively unimportant.

In most micellar catalyzed reactions, the substrate is incorporated into the micellar pseudophase and is attacked by an external reagent or decomposes spontaneously.[2] However, a number of reactions have been studied in which the surfactants (also called detergents), which make up the micelle, contain reactive groups,[7,8] or in which the reagent contains a hydrophobic residue, and is therefore taken up very strongly by the micelles,[9–11] giving greater catalysis than micellar systems which involve attack by external reagents, and these are systems of interest because they provide closer analogies with enzymic catalysts.

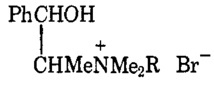
One example of such a reaction was the hydrolysis of p-nitrophenyl diphenyl phosphate (II) in the presence of hydroxide or fluoride ions and the cationic surfactant III.


II



$$\begin{array}{l}\mathrm{CH_2OH}\\ |\quad +\\ \mathrm{CH_2NMe_2R\ Br^-}\end{array}$$

I



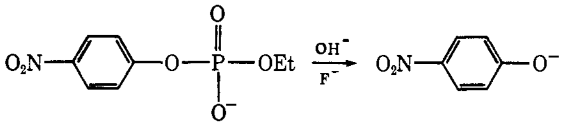
$$\begin{array}{l}\mathrm{PhCHOH}\\ |\qquad +\\ \mathrm{CHMeNMe_2R\ Br^-}\end{array}$$

III

R = alkyl

Micelles of III are better catalysts than simple cationic micelles of, for example, cetyltrimethylammonium bromide (CTABr), for reaction with hydroxide but not fluoride ion,[10–12] and it was suggested that at relatively high pH the reagent was the micellized alkoxide ion of III.

This paper describes an extension of this earlier work using micelles of the surfactant I, where R = n-$\mathrm{C_{12}H_{25}}$ and n-$\mathrm{C_{16}H_{33}}$. The substrates were p-nitrophenyl diphenyl phosphate and ethyl p-nitrophenyl phosphate monoanion (IV). We had earlier examined the reaction of bis(2,4-dinitrophenyl) phosphate with hydroxide ion in the presence of CTABr,[13] but used IV for the present investigation to avoid consecutive formation of two molecules of nitrophenoxide ion. Kirby and Younas have examined the reactions of methyl nitrophenyl phosphate monoanions with nucleophiles,[14] but we used the ethyl derivative because it should be slightly more hydrophobic and therefore taken up more readily by micelles. Tri- and diaryl phosphates which contain electron attracting groups are reactive toward "hard" nucleophiles,[15] and are convenient substrates for this type of investigation.


IV

Experimental Section

Materials. The surfactants were commercial samples (CTABr) or were prepared as the bromides by quaternizing the tertiary amine with a long-chain n-alkyl bromide in refluxing EtOH following the usual method[16] (*cf.* ref 17). They were purified by recrystallization from EtOH and had mp 198–200° (I, R = $\mathrm{C_{12}H_{25}}$) and 208–210° (I, R = $\mathrm{C_{16}H_{33}}$).

The phosphate esters were prepared by standard methods.[10,14] Ethyl p-nitrophenyl phosphate was prepared as the lithium salt from the diethyl phosphate[18] using LiCl in acetone followed by

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[1] Support of this work by the Arthritis and Metabolic Diseases Institute of the USPHS is gratefully acknowledged.

[2] For reviews of micellar catalysis and inhibition, see ref 3–6.

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

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[12] C. A. Bunton, L. Robinson, and M. Stam, *J. Amer. Chem. Soc.*, **92**, 7393 (1970).

[13] G. T. Buist, C. A. Bunton, L. Robinson, L. Sepulveda, and M. Stam, *ibid.*, **92**, 4072 (1970).

[14] A. J. Kirby and M. Younas, *J. Chem. Soc. B*, 1165 (1970).

[15] R. G. Pearson and J. Songstad, *J. Amer. Chem. Soc.*, **89**, 1827 (1967).

[16] A. B. Scott and H. V. Tartar, *ibid.*, **65**, 692 (1943).

[17] E. Zissmann, *C. R. Acad. Sci.*, **245**, 237 (1957).

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precipitation with Et_2O. The molecular weight calculated from complete hydrolysis was 251 by analysis of inorganic phosphate,[19] and 250 by spectrophotometric determination of *p*-nitrophenol (the theoretical value is 253).

Kinetics. The slower reactions were followed spectrophotometrically using a Gilford spectrometer with a water-jacketed cell compartment.[10-12] The triaryl phosphate was added to a cell as a solution in dioxane so that the final solution contained 0.5 mol % dioxane. Lithium ethyl *p*-nitrophenyl phosphate was added as an aqueous solution.

The faster reactions, for example, of *p*-nitrophenyl diphenyl phosphate with hydroxide ion in the presence of the nucleophilic surfactants, were followed using a Durrum-Gibson stopped flow spectrophotometer. An aqueous solution of the substrate was in one syringe and an aqueous solution of the surfactant and hydroxide ion was in the other. The final concentrations of substrate were approximately 10^{-5} *M*, and all experiments were at 25.0°

The units of the first-order rate constants, k_ψ, are in $\sec^{-1}$, and the second-order rate constants, k_2, were calculated from k_ψ and the reagent concentration. The surfactant concentration is typically expressed as C_D. In all our reactions, *p*-nitrophenoxide ion was formed, and there was no attack by fluoride or alkoxide ion upon the aryl group.

Results and Discussion

Reactions in the Presence of CTABr. The reactions of ethyl *p*-nitrophenyl phosphate monoanion with hydroxide or fluoride ion in the presence of CTABr have kinetic forms similar to those found earlier for reactions of bis(2,4-dinitrophenyl) phosphate and *p*-nitrophenyl diphenyl phosphate.[10-13] The rate enhancements are not large, being *ca.* sixfold for reaction with hydroxide ion and fivefold for reaction with fluoride ion (Tables I and II). The micellar catalyzed reaction is approximately first order with respect to hydroxide ion, and in both the presence and absence of cationic micelles, the reactivity of hydroxide is greater than that of fluoride ion. The reaction of hydroxide ion and ethyl *p*-nitrophenyl phosphate monoanion in micellized CTABr is inhibited by added salts (Table III). The salt effects increase with decreasing charge density of the anion and are relatively independent of the nature of the cation, as is typical of attack by nucleophilic anions catalyzed by cationic micelles.[3,5,11]

Table I. Reaction of Ethyl *p*-Nitrophenyl Phosphate with Hydroxide Ion in CTABr[a]

10^2C_{CTABr}, *M*	C_{NaOH}, *M*	
	0.02	0.10
	0.75	0.75
0.25	1.25	0.85
0.29		1.83
0.50	2.94	2.81
0.59		3.57
0.88		4.08
1.00	4.36	4.00
1.50	3.86	3.36
2.00	3.50	2.84

[a] Values 10^2k_2, l. mol^{-1} sec^{-1} at 25.0°.

Table II. Reaction of Ethyl *p*-Nitrophenyl Phosphate with Fluoride Ion in CTABr[a]

10^2C_{CTABr}, *M*	10^4k_ψ, sec^{-1}	10^2C_{CTABr}, *M*	10^4k_ψ, sec^{-1}
	1.56	1.50	7.28
0.25	4.38	2.00	6.67
0.50	6.54	3.00	4.83
1.00	6.90		

[a] At 25.0° with 0.1 *M* NaF at pH 9 (10^{-2} *M* borate buffer).

Table III. Salt Effects upon the Reaction of Ethyl *p*-Nitrophenyl Phosphate with Hydroxide Ion in CTABr[a]

	Salt				
C_{salt}, *M*	NaCl	KCl	KBr	KNO_3	NaOTos
0.0050	2.83			2.44	1.42
0.010		2.64	2.17	1.63	1.00
0.015	2.25				
0.020	1.94	2.19	1.60	1.24	0.62
0.025			1.39		
0.030	1.36	1.73	1.21	0.89	0.15

[a] Values of 10^3k_ψ, sec^{-1} at 25.0° in 0.1 *M* NaOH and 0.88×10^{-2} *M* CTABr. In the absence of added salt $10^3k_\psi = 4.08$ sec^{-1}.

Reactions with Hydroxide Ion in the Presence of the Hydroxy Substituted Surfactant III ($R = C_{12}H_{25}$). The reaction of ethyl *p*-nitrophenyl phosphate monoanion (IV) and hydroxide ion was followed in the presence of micelles of III ($R = C_{12}H_{25}$). Despite the shorter length of the alkyl groups, these micelles are almost as good catalysts as those of CTABr (Tables I and IV) suggesting that there is some effect due to the hydroxyl group as was found earlier for reaction of *p*-nitrophenyl diphenyl phosphate,[12] but because the rate enhancement was relatively small, we did no further work on this system.

Table IV. Reaction of Ethyl *p*-Nitrophenyl Phosphate with NaOH in the Presence of III, $R = C_{12}H_{25}$[a]

10^2C_D, *M*	10^3k_ψ, sec^{-1}	10^2C_D, *M*	10^3k_ψ, sec^{-1}
	0.75	1.00	3.05
0.25	1.67	1.50	3.48
0.25	0.23[b]	2.00	3.47
0.50	2.09	2.50	3.40
0.50	0.34[b]	3.00	2.86

[a] At 25.0° with 0.10 *M* NaOH unless specified. [b] With 0.01 *M* NaOH.

Reactions in the Presence of the Hydroxy-Substituted Surfactants (I). Micelles of the hydroxy-substituted surfactants (I, $R = C_{12}H_{25}$ and $C_{16}H_{33}$) are good catalysts for the reactions of *p*-nitrophenyl diphenyl phosphate and ethyl *p*-nitrophenyl phosphate monoanion with hydroxide ion. The rate enhancements (up to 300-fold) of the reaction with hydroxide ion (Figures 1-4) contrast sharply with the relatively small rate enhancements of the reaction with fluoride ion (Table V).

Table V. Reaction of *p*-Nitrophenyl Diphenyl Phosphate with Fluoride Ion in the Presence of I, $R = C_{12}H_{25}$; $C_{16}H_{33}$[a]

C_D, *M*	$R = C_{12}H_{25}$	$R = C_{16}H_{33}$
	0.11	0.11
0.00125		3.81
0.0025		5.52
0.0050		4.12
0.010	1.00	3.44
0.015	1.34	2.82
0.020	1.30	2.29
0.030	1.12	1.74
0.040	0.96	1.46
0.050	0.85	
0.070	0.65	

[a] Values of 10^2k_ψ, sec^{-1}, at 25.0° at pH 9.0 (10^{-2} *M* borate buffer) with 0.01 *M* NaF.

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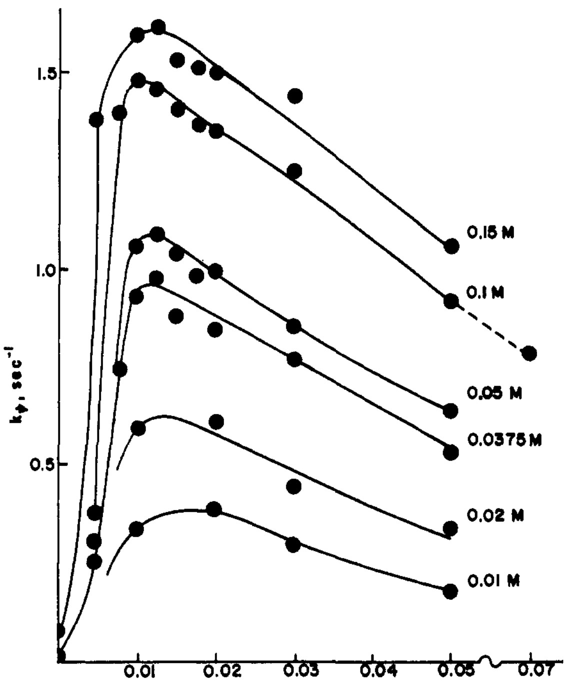


Figure 1. Hydrolysis of *p*-nitrophenyl diphenyl phosphate in I ($R = C_{12}H_{25}$), with the indicated concentrations of hydroxide ion at 25.0°.

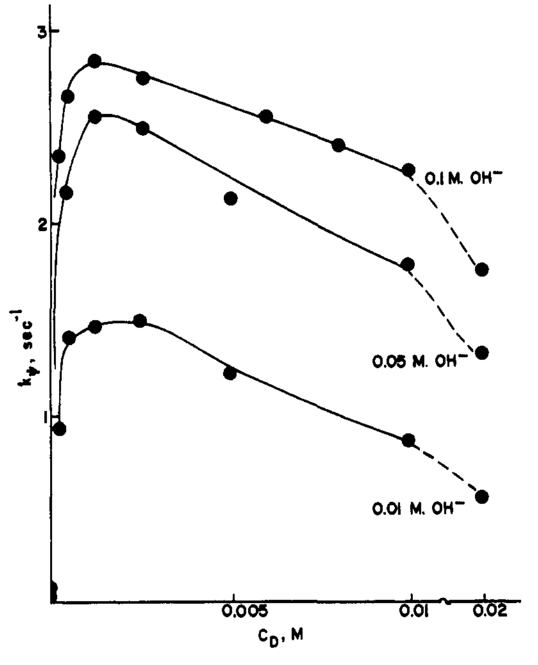


Figure 2. Hydrolysis of *p*-nitrophenyl diphenyl phosphate in I ($R = C_{16}H_{33}$), with the indicated concentrations of hydroxide ion at 25.0°.

Table VI. Second-Order Rate Constants for the Reaction of Ethyl *p*-Nitrophenyl Phosphate with Fluoride Ion Catalyzed by I, $R = C_{12}H_{25}$[a]

C_{NaF}, *M*	10^3k_2, l. mol^{-1} sec^{-1}
	1.56
0.05	5.6
0.10	6.0
0.15	5.3
0.50	4.6

[a] Maximum values of k_2 at 25.0° in 10^{-2} *M* borate buffer pH 9.

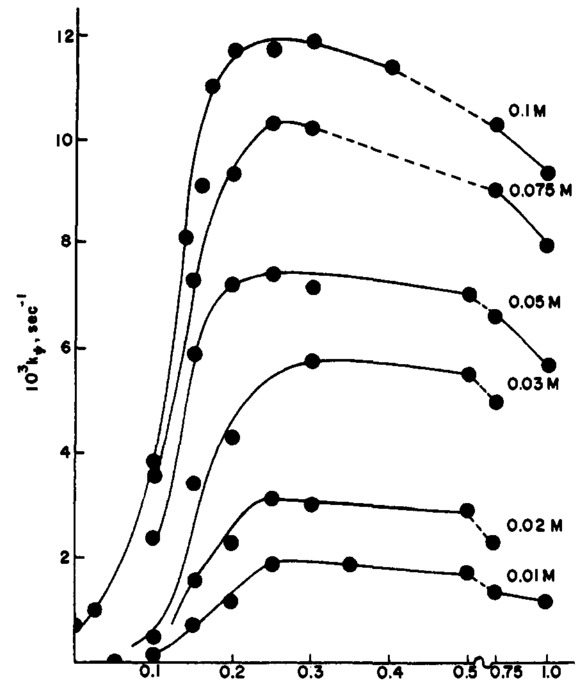


Figure 3. Hydrolysis of ethyl *p*-nitrophenyl phosphate in I ($R = C_{12}H_{25}$), with the indicated concentrations of hydroxide ion at 25.0°.

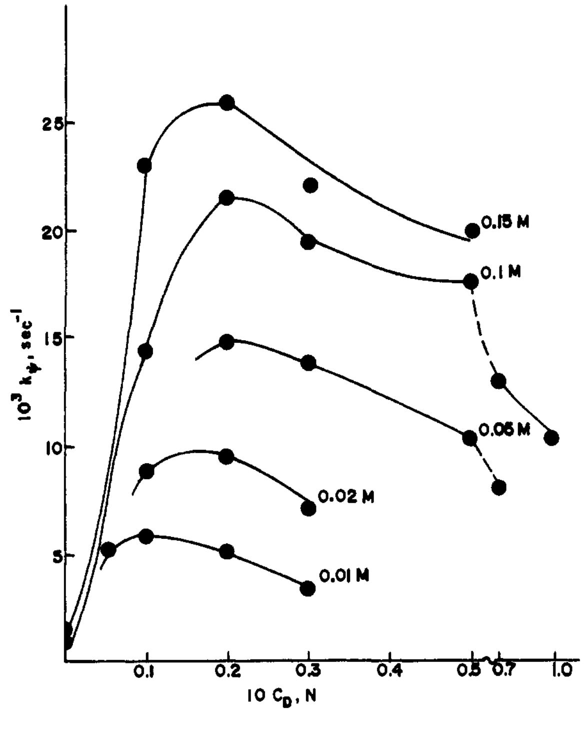


Figure 4. Hydrolysis of ethyl *p*-nitrophenyl phosphate in I ($R = C_{16}H_{33}$), with the indicated concentrations of hydroxide ion at 25.0°.

In addition, CTABr and I ($R = C_{16}H_{33}$) catalyze the reaction to similar extents (for reaction in CTABr $k_\psi \sim 3.4 \times 10^{-2}$ sec^{-1} with 0.01 *M* sodium fluoride[11]), but I is always a much better catalyst than CTABr for reactions with hydroxide ion. Similar observations were made on the reaction of fluoride ion with ethyl *p*-nitrophenyl phosphate monoanion catalyzed by I ($R = C_{12}H_{25}$) (Figure 5 and Table VI). The differences be-

Table VII. Rate Enhancements for Reactions with Hydroxide and Fluoride Ions[a]

Reaction	Surfactant			
	$C_{12}H_{25}NMe_3Br$	CTABr	I (R = $C_{12}H_{25}$)	I (R = $C_{16}H_{33}$)
$O_2NC_6H_4OPO(OPh)_2 + OH^-$	4.8[b] (0.015)	12[c] (0.003)	83 (0.012)	310 (0.002)
$O_2NC_6H_4OPO_3Et^- + OH^-$		6.3 (0.01)	29 (0.025)	86 (0.015)
$O_2NC_6H_4OPO(OPh)_2 + F^-$	10.5[b] (0.015)	35[c] (0.002)	13 (0.015)	52 (0.003)
$O_2NC_6H_4OPO_3Et^- + F^-$		4.6 (0.015)	4.2 (0.02)	

[a] Rate enhancements calculated from values of k_ψ at the optimum surfactant concentration relative to reaction in the absence of surfactant at 25.0° and calculated for 0.01–0.02 *M* NaOH or NaF; the values in parentheses are the approximate surfactant molarities for maximum rate enhancement. [b] Reference 12. [c] Reference 11.

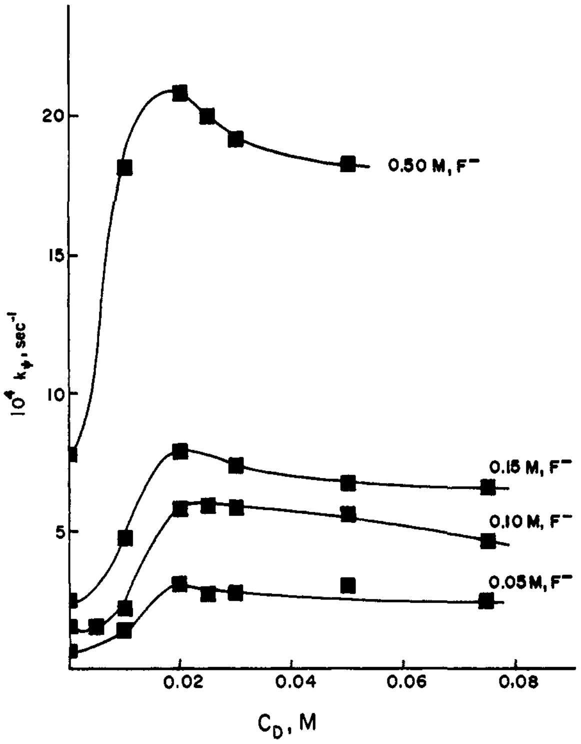


Figure 5. Reaction of ethyl *p*-nitrophenyl phosphate in I (R = $C_{12}H_{25}$) and fluoride ion at 25.0°.

tween the catalytic effectiveness of these nucleophilic and nonnucleophilic surfactants for reactions of hydroxide and fluoride ions are illustrated by the maximum rate enhancements relative to reaction in the absence of surfactant (Table VII). (These rate enhancements depend upon reagent concentration, but small changes in the concentration of hydroxide or fluoride ion affect them only slightly. The surfactant concentrations for maximum catalysis are given in parentheses in Table VII.)

In all our experiments, the micellar catalysis increased as expected with increasing length of the long alkyl group of the surfactant. However, for reactions of fluoride ion, changes in the head groups of the surfactant had little effect on the overall rate enhancements; *cf.* ref 11.

In our earlier work we noted that because micelles of the hydroxy substituted surfactants (III) were no better catalysts than simple cationic micelles for the reaction of fluoride ion with *p*-nitrophenyl diphenyl phosphate, the catalysis did not involve nucleophilic attack by an external anion, concerted with electrophilic assistance to P–O bond breaking, as in the hypothetical transition state (V).[12] The present results strengthen this conclusion.

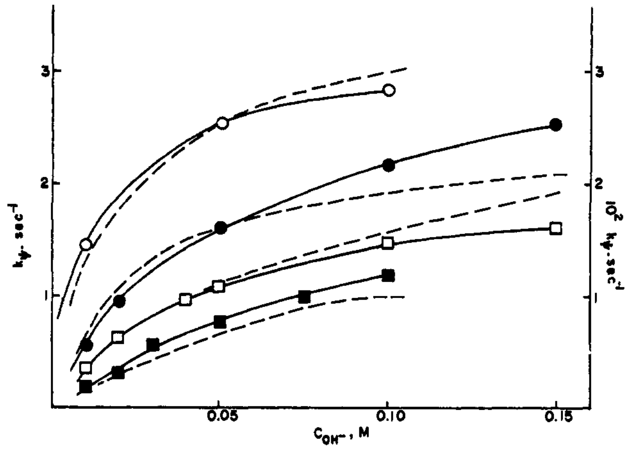
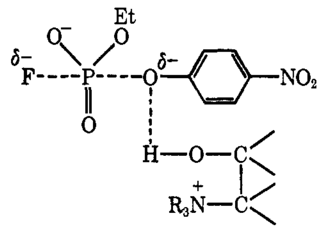


Figure 6. Variation of the maximum rate constants for reaction in the micellar phase with hydroxide ion concentration. Open points, *p*-nitrophenyl diphenyl phosphate (left-hand scale); solid points, ethyl-*p*-nitrophenyl phosphate (right-hand scale). Squares, I (R = $C_{12}H_{25}$); circles, I (R = $C_{16}H_{33}$). The broken lines are calculated using eq 1 and the data given in Tables IX and X.



V

The reactions in the presence of I are reasonably close to first order with respect to fluoride ion (Table VI), but for those with hydroxide ion plots of k_ψ against C_{OH^-} are nonlinear (Figure 6) in agreement with earlier results on hydroxide ion reactions in the presence of III.[12]

These micellar catalyzed reactions are inhibited by added salts (Figure 7 and Table VIII) as is typical of bimolecular micellar catalyzed reactions. The salt effects as measured by k_s/k_0 (where k_s and k_0 are respectively the rate constants in the presence and absence of added salt) are generally larger in 0.01 *M* than in 0.15 *M* hydroxide ion (Table VIII), possibly because of mechanistic differences depending on the concentration of hydroxide ion. However, salt effects upon micellar catalysis depend upon both exclusion of reagents from the micelle and changes in its structure,[20] and it is there-

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(20) C. A. Bunton, M. J. Minch, and L. Sepulveda, *J. Phys. Chem.*, 75, 2707 (1971); C. A. Bunton, A. Kamego, and M. J. Minch, *J. Org. Chem.*, 37, 1388 (1972); C. A. Bunton in "Reaction Kinetics in Micelles and Membranes," E. H. Cordes, Ed., Plenum Press, New York, N. Y., 1972.

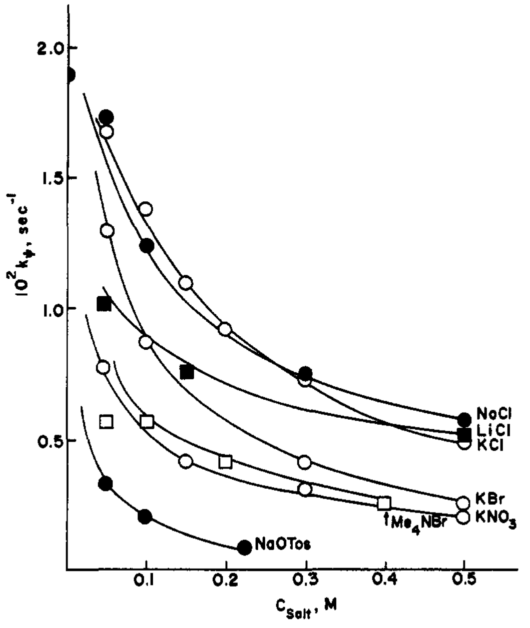


Figure 7. Salt inhibition of the reaction between ethyl *p*-nitrophenyl phosphate and 0.01 *M* NaOH in the presence of 0.025 *M* I (R = $C_{12}H_{25}$).

Table VIII. Effect of Hydroxide Ion upon the Salt Effects upon the Hydrolysis of Ethyl *p*-Nitrophenyl Phosphate in the Presence of I, R = $C_{12}H_{25}$

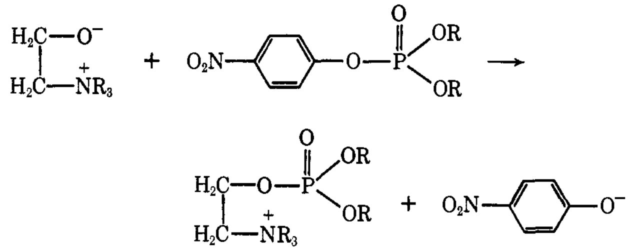
Salt	C_S, *M*	C_{OH^-}, *M*	
		0.01	0.15
NaCl	0.10	0.65	0.71
	0.20		0.63
	0.30	0.40	0.55
	0.40		0.52
	0.50	0.30	0.43
KCl	0.05	0.88	0.72
	0.10	0.73	0.65
	0.30	0.39	0.52
	0.50	0.27	0.43
KNO$_3$	0.05	0.41	0.57
	0.10		0.48
	0.30	0.15	0.33
	0.50	0.11	0.25
KBr	0.10	0.46	0.51
	0.30	0.22	0.34
	0.50	0.17	0.26
NaOTos	0.05	0.18	0.27
	0.10	0.11	0.14
	0.225	0.05	0.08

[a] Values of k_s/k_0 in 0.025 *M* surfactant at 25.0°; in the absence of added salt $10^2 k_0 = 0.18$ in 0.01 *M* and 1.6 sec^{-1} in 0.15 *M* NaOH.

fore difficult to make mechanistic assignments from these effects.

In these experiments we did not study the variation of k_ψ with low surfactant concentration in great detail, but as is generally found, small amounts of surfactants have little effect on the rates of reactions, which increase sharply as micelles are formed from the monomeric surfactant.[3-6]

Scheme I



Reactions with Hydroxide Ion. In our earlier work on the reaction of *p*-nitrophenyl diphenyl phosphate with hydroxide ion in the presence of cationic micelles of surfactants which contained a hydroxyl group, we assumed that reaction followed Scheme I, where the substrate was incorporated in the micelle. Provided that all the substrate is incorporated into the micelle, the variation of rate constant, k_ψ, with hydroxide ion can be explained in terms of the following equations[12]

$$(\text{DOH})_{n+1} + \text{OH}^- \overset{K'}{\rightleftharpoons} (\text{DOH})_n\text{DO}^-$$

$$(\text{DOH})_n\text{DO}^- + \text{S}_m \xrightarrow{k'} \text{products}$$

where D = $\text{R}\overset{+}{\text{N}}\text{Me}_2\text{CH}_2\text{CH}_2\text{–}$ and S_m is the substrate in the micellar phase and $K' = K_a/K_w$. The first-order rate constant k' refers to the decomposition of the micellized surfactant in a micelle having one ionized hydroxyl group. (In this treatment we assume that only one substrate is taken up per micelle, but we could instead assume that the micelle has reactive sites each of which can take up only one surfactant molecule.) The two treatments lead to the same conclusions. Provided that $C_{OH^-} \gg C_{DOH}$ and the maximum values of k_ψ at the optimum surfactant concentration (Figures 1-4) give k^m, the first-order rate constant for reaction in the micelle, we obtain eq 1,[12] where K_a is the acid dissociation constant of the micellized surfactant.

$$k^m = \frac{k' C_{OH^-}(K_a/K_w)}{1 + C_{OH^-}(K_a/K_w)} \tag{1}$$

The values of $k'K_a/K_w$ (Table IX) are given by the initial slopes of plots of k_ψ against C_{OH^-}, provided that reaction in the absence of hydroxide ion and of surfactant can be neglected. Equation 1 can be rearranged to eq 1a, and a plot of the left-hand side term of

$$\frac{k'K_a C_{OH^-}}{k^m K_w} = 1 + \frac{K_a}{K_w} C_{OH^-} \tag{1a}$$

eq 1a against C_{OH^-} gives K_a/K_w. These plots are shown in Figure 8.

Table IX. Kinetic and Equilibrium Parameters for Reactions in the Presence of Nucleophilic Surfactants

Surfactant	$k'K_a/K_w$ II	$k'K_a/K_w$ IV	K_a/K_w
I, R = $C_{12}H_{25}$	36	0.21	12
I, R = $C_{16}H_{33}$	150	0.96	40

The slopes of these lines should depend upon the nature of the surfactant, and be independent of the substrate, but this condition is only partially satisfied (Figure 8). However, the slopes of the broken lines drawn in Figure 8 give approximate values of K_a/K_w for micelles of I (R = $C_{12}H_{25}$, $C_{16}H_{33}$) which give the values of the first-order rate constant k' (Table X). (This table also contains data for nonnucleophilic surfactants for comparison purposes.) These parameters

Table X. Comparison of Rate Constants for Reactions of Alkoxide Ion of I and Hydroxide Ion in Cationic Micelles[a]

	k', sec^{-1}		k_2, l. mol^{-1} sec^{-1}	
Substrate	I, R = $C_{12}H_{25}$	I, R = $C_{16}H_{33}$	$C_{12}H_{25}$-NMe_3Br	CTABr
$NO_2C_6H_4OPO(OPh)_2$	3 (1.8)	3.8 (0.7)	1.65	5.5
$NO_2C_6H_4OPO_2Et^-$	0.017	0.024 (0.5)		0.044

[a] The values in parentheses are the concentrations of hydroxide ion calculated to give the same rates of reaction in the presence of nonnucleophilic cationic micelles as those found for chemical decomposition of the substrate–micelle complexes formed from the corresponding nucleophilic surfactants (I, R = $C_{12}H_{25}$; $C_{16}H_{33}$).

used in eq 1a give a reasonably satisfactory fit for the variation of k_ψ with C_{OH^-} as shown in Figure 6, where the broken lines are calculated using the rate and equilibrium parameters given in Tables IX and X. The fit with experiment is as good as can be expected because our treatment neglects the effects of substrates and electrolytes upon the properties of the micelles[20,21] and upon the rate and equilibrium constants. Salt effects upon the overall reaction rates (Figure 7 and Table III) are small for low concentrations of salts, except for salts having anions of relatively low charge density, *e.g.*, tosylate, and should therefore be small for the hydroxide ion, except at the higher concentrations where the deviations are largest. These deviations (Figures 6 and 8) are similar to those observed earlier using the nucleophilic surfactant (III).[12]

Comparison of the values of the first-order rate constant, k', and the second-order rate constants, k_2, for reactions of the substrates with hydroxide ion in the absence of added surfactant show that the alkoxide ion in the micelle is a very effective catalyst. The rate enhancements are similar to those found for reactions involving effective intramolecular nucleophiles.[22] For example, for the reactions of *p*-nitrophenyl diphenyl phosphate with the hexadecyl surfactant (I, R = $C_{16}H_{33}$), k' = 3.8 sec^{-1}, whereas for reaction with hydroxide ion in the absence of surfactant[23] k_2 = 0.48 l. mol^{-1} sec^{-1}; *i.e.*, the rate constant in the micellar phase is that calculated for aqueous 8 *M* sodium hydroxide and for the corresponding reaction of ethyl *p*-nitrophenyl phosphate monoanion k' = 0.024 sec^{-1} and $k_2 \approx 0.007$ l. mol^{-1} sec^{-1}, so that the rate constant in the micellar phase is that calculated for aqueous 3.5 *M* sodium hydroxide. As noted earlier these comparisons underestimate the effectiveness of the alkoxide ion in the micelle as a nucleophile because the negative charge should be able to migrate rapidly about the micelle, and therefore be close to the substrate for only a fraction of the time.[12]

The nucleophilicity toward *p*-nitrophenyl diphenyl phosphate of the micellized alkoxide ion of I (R = $C_{12}H_{25}$), as given by the value of k' = 3 sec^{-1}, is considerably greater than that of the alkoxide ion of III (R = $C_{12}H_{25}$) which is used in our earlier investigation,[12] and for which k' = 0.6 sec^{-1}, probably because III is a secondary alcohol, and the nucleophilicity of its alkoxide ion will be reduced sterically and electronically by the phenyl group. The choline anion is a good nucleophile toward *p*-nitrophenyl diphenyl phosphate, being approximately 35 times as reactive as the hydroxide ion,[12] and this high reactivity is also shown by its micellized derivatives (I). This high nucleophilicity, relative to basicity, can be ascribed, at least in part, to favorable electrostatic interactions between the quaternary cationic center in choline and its derivatives, and the dispersed negative charge in the transition state.[12]

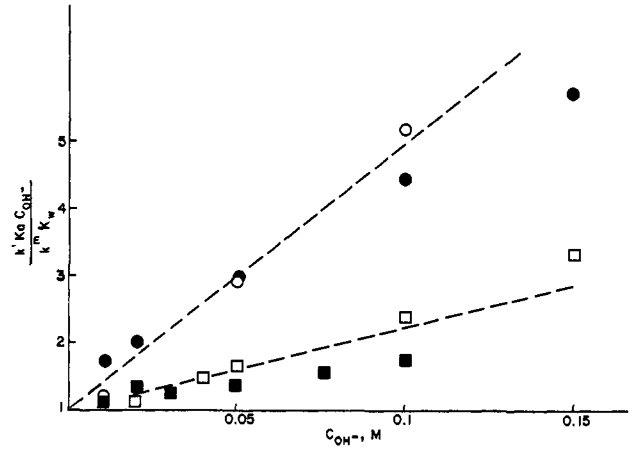


Figure 8. Kinetic analysis of the reaction of *p*-nitrophenyl diphenyl phosphate (open points) and ethyl *p*-nitrophenyl phosphate (solid points) with hydroxide ion in the presence of optimum concentration of surfactant (squares I (R = $C_{12}H_{25}$); circles, I (*R* = $C_{16}H_{33}$).

The values of the first-order rate constant, k', for reactions of these nucleophilic surfactants are compared with those of the second-order rate constants, k_2, for reaction with hydroxide ion in the presence of the optimum amounts of nonnucleophilic cationic micelles (Table X). The values in parentheses are the hydroxide ion concentrations which would give equivalent rates to those found with the alkoxide ions, assuming that reaction with hydroxide ion is second order.

The values of k' for the micellized alkoxide ion–substrate complex (Table X) increase only slightly with increasing length of the alkyl group of the micelle, and the greater catalytic effectiveness of I (R = $C_{16}H_{33}$) over I (R = $C_{12}H_{25}$) is related to more effective substrate incorporation and greater ionization of the hydroxyl group (*i.e.*, larger K_a) than to the reactivities of the alkoxide ions.

Assuming that the micellized surfactant does not affect the autoprotolysis constant of water, we calculate p$K_a \approx 12.9$ for the dodecyl and 12.4 for the hexadecyl surfactants (I). These values are very similar to p$K_a \approx 12.7$ for the dodecyl surfactant (III) and are, as expected, slightly smaller than p$K_a \approx 13.9$ for choline.[24] They depend, however, upon the questionable assumption that the autoprotolysis constant of water in close proximity to the micelle is the same as that in bulk water, and the micelles might cause major changes in the structure of water which is solvating the micelle.

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