

of subtler considerations since at high enough surfactant concentrations presumably all of the substrate will be associated with the micellar phase regardless of chain length. Thus increasing chain length must either cause a more favorable geometrical disposition of the substrate with respect to the Stern layer, or result from increased surface charge on the micelle itself,¹⁴ or both. At any event, these observations are consistent with the arguments developed above. In agreement with our findings, Kurz has observed that the acid-catalyzed hydrolysis of micellar sodium alkyl sulfates becomes more rapid with increasing size of the alkyl chain.¹⁴ Finally, we have observed that the maximal rate accelerations obtained for the sodium alkyl sulfate catalyzed hydrolysis of methyl orthobenzoate decrease with

increasing temperature. Put another way, the enthalpy of activation for the surfactant-catalyzed reaction is less than that for the uncatalyzed reaction. Similarly, Kurz has observed that the catalysis of hydrolysis of sodium alkyl sulfates which accompanies micellation of these substrates is due to changes in the enthalpy of activation and not in the entropy of activation.¹⁴ Preliminary considerations indicate that the situation in our case is more complicated: a large favorable enthalpy decrease (which may approach 10 kcal/mol in some cases) is substantially offset by a large decrease in the entropy of activation. The result is the observed modest rate increases. Why the activation parameters should change in this fashion for these reactions is not clear at this time.

Secondary Valence Force Catalysis. VII. Catalysis of Hydrolysis of *p*-Nitrophenyl Hexanoate by Micelle-Forming Cationic Detergents¹

L. R. Romsted and E. H. Cordes²

Contribution No. 1594 from the Department of Chemistry, Indiana University, Bloomington, Indiana 47401. Received February 5, 1968

Abstract: The hydroxide ion dependent hydrolysis of *p*-nitrophenyl hexanoate and *p*-nitrophenyl laurate is subject to marked catalysis by alkyltrimethylammonium detergent salts. In contrast, the rate of the corresponding reaction of *p*-nitrophenyl acetate is rather insensitive to the concentration of these species. Evaluation of the pertinent equilibrium constants for association of the acetate and hexanoate with micelles formed from tetradecyltrimethylammonium chloride through molecular sieve chromatography on Sephadex G-10 reveals that the distinct behavior exhibited by these esters is principally a reflection of the greater tendency of the latter to associate with the catalyst in solution. Catalysis of the basic hydrolysis of *p*-nitrophenyl hexanoate by alkyltrimethylammonium salts is accentuated as the length of the alkyl chain is increased from 8 to 18. Monovalent anions are potent inhibitors of the tetradecyltrimethylammonium chloride catalysis for the basic hydrolysis of *p*-nitrophenyl hexanoate; an increase in bromide ion concentration from zero to 0.20 *M* inhibits the detergent-dependent reaction by more than an order of magnitude. The increasing order of effectiveness of anions as inhibitors of this reaction is: $F^- < Cl^- < Br^- < NO_3^-$. These facts suggest that the inhibition is largely a consequence of displacement of hydroxide from the surface of the micelle as a consequence of binding of other anions.

Particular points of interest for the development of an understanding of the mechanism of catalysis of organic reactions occurring on the surface of micelles have been discussed in the accompanying report.³ In this paper, we describe, in some detail, catalysis by alkyltrimethylammonium ions for the hydrolysis of *p*-nitrophenyl esters. This work is an extension and elaboration of our previous efforts with these systems.⁴ A preliminary account of some of this work has been published.⁵

(1) Supported by Grant AM-08232-04 from the National Institutes of Health.

(2) Career Development Awardee of the National Institutes of Health.

(3) R. B. Dunlap and E. H. Cordes, *J. Am. Chem. Soc.*, **90**, 4395 (1968).

(4) M. T. A. Behme, J. G. Fullington, R. Noel, and E. H. Cordes, *ibid.*, **87**, 266 (1965).

(5) L. R. Romsted, R. B. Dunlap, and E. H. Cordes, *J. Phys. Chem.*, **71**, 4581 (1967).

Experimental Section

Materials. *p*-Nitrophenyl acetate was synthesized from *p*-nitrophenol and acetic anhydride according to the general method of Bender and Nakamura.⁶ *p*-Nitrophenyl laurate⁷ was prepared by a slight modification of this procedure: 0.125 mol of *p*-nitrophenol, 0.10 mol of lauroyl chloride, and 0.10 mol of pyridine were dissolved in 100 ml of dry toluene and refluxed for 1 hr. The solution was neutralized with saturated NaHCO₃ and washed with water, 5% NaOH, 0.1 *N* HCl, and finally with water. The toluene solution was dried over anhydrous MgSO₄ and evaporated to dryness. The ester obtained was a light yellow waxy solid, mp 40–41° (lit.⁷ 46°), carbonyl stretching frequency (liquid film) at 1755 cm⁻¹, and was not purified further. *p*-Nitrophenyl hexanoate was prepared through the dropwise addition of 12.8 g of hexanoic acid in 100 ml of benzene to a refluxing solution prepared by mixing 13.9 g of *p*-nitrophenol in 150 ml of tetrahydrofuran and 25 g of dicyclohexyl-

(6) M. L. Bender and K. Nakamura, *J. Am. Chem. Soc.*, **84**, 2577 (1962).

(7) H. Zahn and F. Schade, *Chem. Ber.*, **96**, 1747 (1963).

carbodiimide in 100 ml of benzene. The reaction mixture was refluxed for 24 hr, filtered, then washed six times with 5% NaHCO_3 , once with 0.1 N HCl , and once with water followed by drying over anhydrous MgSO_4 . Removal of solvent yielded 24.2 g of impure ester. The material was placed on a column containing 600 g of silica gel and eluted with hexane containing increasing quantities of ether. *p*-Nitrophenyl hexanoate was eluted when the ether content reached 10% by volume. The solvent was removed by evaporation and the residue was distilled *in vacuo*; 11.3 g of *p*-nitrophenyl hexanoate was collected (bp 145° (1 mm)).

A series of *n*-alkyltrimethylammonium bromides were prepared from commercially obtained *n*-alkyl bromides and trimethylamine according to the method of Scott and Tartar.⁸ The salts were recrystallized from anhydrous ethanol-ether mixtures a minimum of three times prior to use in kinetic studies. The purity of the tetradecyltrimethylammonium bromide, which was employed extensively in kinetic studies, was checked by the following two methods. First, 10 g of this detergent was converted to the quaternary ammonium hydroxide, through reaction with Ag_2O , which was then subjected to a Hofmann degradation. Analysis of the resulting olefin by vapor phase chromatography revealed it to be at least 97% pure. Second, the surface tensions of aqueous solutions of this detergent containing 0.03 M added bromide ion were measured as a function of detergent concentration: the results are shown in Figure 1. Surface tensions were measured at room temperature with a simple Cenco-DuNouy tensiometer. The shape of the surface tension concentration plot is satisfactory and the derived critical micelle concentration (cmc), $7.25 \times 10^{-4} M$, is in reasonable agreement with published values.^{9,10} Tetradecyltrimethylammonium chloride was prepared from the corresponding bromide through two successive passages of aqueous solutions of the latter through columns of Bio-Rad AG-1-X4, 50-100 mesh, anion-exchange resin in the chloride form. The resulting solution was lyophilized to dryness and the detergent salt residue recrystallized three times from ethanol-ether mixtures.

Other reagents were obtained commercially. Inorganic salts were employed without further purification. Glass-distilled water was employed throughout.

Kinetic measurements were performed spectrophotometrically with the aid of a Zeiss PMQ II spectrophotometer equipped with a heatable cell holder through which water from a thermostated bath was continuously circulated. All measurements were performed at 25° . All reactions were monitored at 400 $m\mu$, the absorption maximum of the *p*-nitrophenolate ion. Each reaction mixture initially contained $3 \times 10^{-5} M$ ester. First-order rate constants were calculated from the slopes of plots of $\log(\text{OD}_\infty - \text{OD}_t)$ against time in the usual manner. Values of pH were obtained with the aid of a Radiometer PHM4c pH meter equipped with a glass electrode.

Equilibrium constants for association of *p*-nitrophenyl acetate and hexanoate with micelles formed from tetradecyltrimethylammonium chloride were evaluated from molecular sieve chromatography on Sephadex G-10 as described by Herries, *et al.*¹¹

Results

The initial phase of this work involved the determination of the effect of chain length of *n*-alkyltrimethylammonium bromides on the rate of basic hydrolysis of *p*-nitrophenyl acetate (PNPA), *p*-nitrophenyl hexanoate (PNPH), and *p*-nitrophenyl laurate (PNPL). In Figure 2, first-order rate constants for the reaction of each of these esters with hydroxide ion at 25° and pH 10.07 ± 0.05 are plotted as a function of the detergent concentration. Each reaction mixture contained, in addition to ester and detergent, 0.01 M potassium chloride and 0.01 M carbonate buffer, 50% base. The data for PNPA and PNPH in the presence of tetradecyltrimethylammonium bromide is in satisfactory agreement with that previously published.⁴ It proved impossible to measure the rate constants for PNPL in the absence

(8) A. B. Scott and H. V. Tartar, *J. Am. Chem. Soc.*, **65**, 692 (1943).

(9) K. J. Mysels, *J. Colloid Sci.*, **10**, 507 (1955).

(10) P. Debye, *J. Phys. Chem.*, **53**, 1 (1949).

(11) D. G. Herries, W. Bishop, and F. M. Richards, *ibid.*, **68**, 1842 (1964).

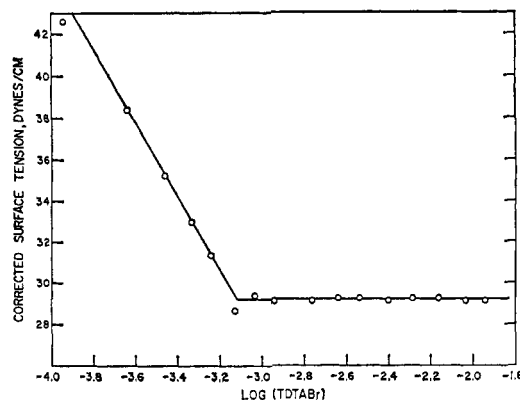


Figure 1. Plot of surface tension as a function of the logarithm of the concentration of tetradecyltrimethylammonium bromide in aqueous solution containing 0.03 M additional bromide ion.

of detergent or in the presence of very low detergent concentrations due to the insolubility of this species. There are two principal conclusions to be drawn from the data of Figure 2. First, the catalysis of the basic hydrolysis is most marked for PNPL and least marked for PNPA. Second, the catalytic effectiveness of the detergents increases with increasing length of the alkyl chain.

For detailed study of catalysis by cationic detergents of the reaction between esters and hydroxide ion, *p*-nitrophenyl hexanoate was chosen as substrate and tetradecyltrimethylammonium chloride as catalyst. The chloride form of the detergent was chosen since preliminary observations suggested that bromide ion was a potent inhibitor of the detergent-dependent reaction. Attention was focused on two aspects of this reaction: the partitioning of ester between aqueous and micellar phases and the effect of inorganic anions on the detergent-dependent reaction.

Equilibrium constants for association of PNPA and PNPH with micelles formed from tetradecyltrimethylammonium chloride in aqueous solution containing 0.20 M NaCl were approximated through measurement of the extent to which various detergent concentrations accelerated the passage of the esters through a column of Sephadex G-10.¹¹ The rather high salt concentration proved necessary in order to avoid hydrolysis of the esters during the chromatographic runs. Esters were placed on the column at an initial concentration of 0.01 M . Chromatography was carried out at room temperature (*ca.* 23°). Runs were monitored spectrophotometrically. Results of these experiments may be qualitatively appreciated through inspection of Figure 3 in which the effluent volumes for the esters are shown at a variety of detergent concentrations (see figure legend). Clearly, increasing detergent concentration decreases the effluent volume and the effect is more marked for PNPH than for PNPA. Quantitatively, the quantity $\bar{v}(K - 1)$ may be evaluated from the slope and intercept of plots of the ratio of imbibed volume (V_i) to the difference between effluent volume (V_e) and void volume (V_0) against detergent concentration.¹¹ In this expression K is the association constant for absorption of ester onto or into the micellar phase, $K = (\text{ester})_{\text{micelle}}/(\text{ester})(\text{detergent})$, and \bar{v} is the partial specific volume of the detergent. Such plots, constructed from the data in Figure 3 and the appropriate ancillary

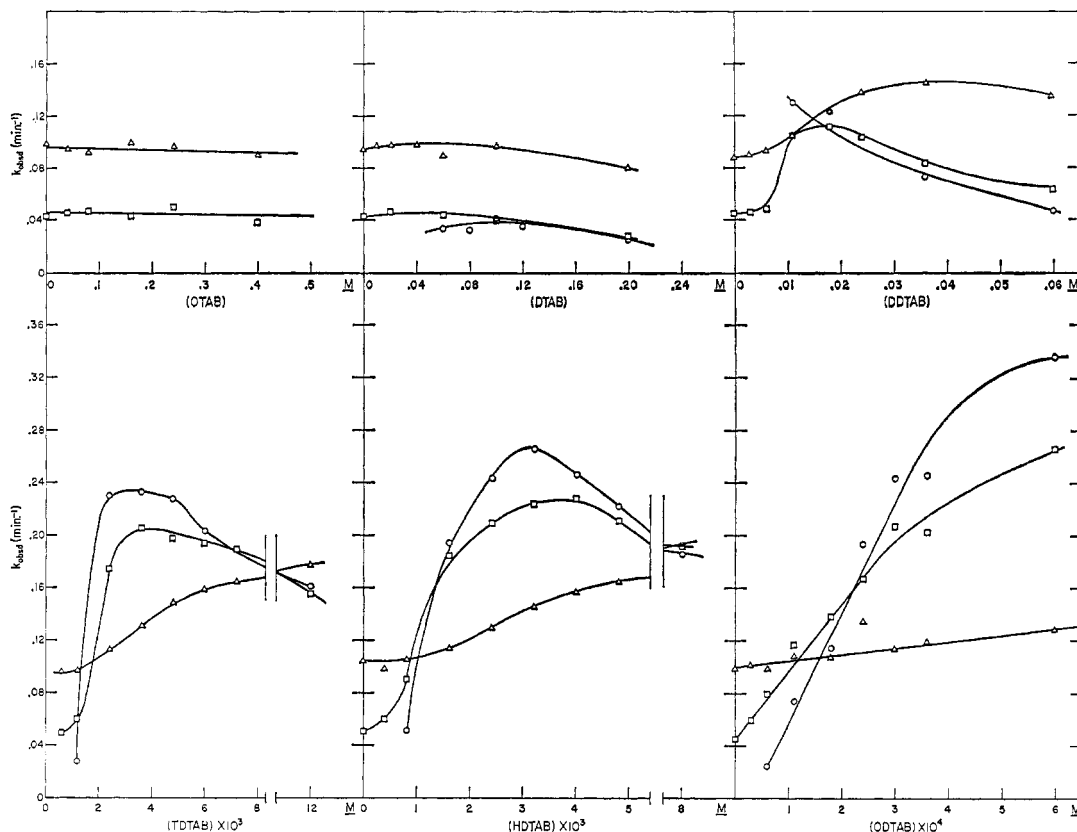


Figure 2. First-order rate constants for the basic hydrolysis of *p*-nitrophenyl acetate (Δ), *p*-nitrophenyl hexanoate (\square), and *p*-nitrophenyl laurate (\circ) at 25° and pH 10.07 plotted as a function of the concentration of a series of *n*-alkyltrimethylammonium bromides: from left to right starting at the top, the *n*-alkyl groups are octyl, decyl, dodecyl, tetradecyl, hexadecyl, and octadecyl.

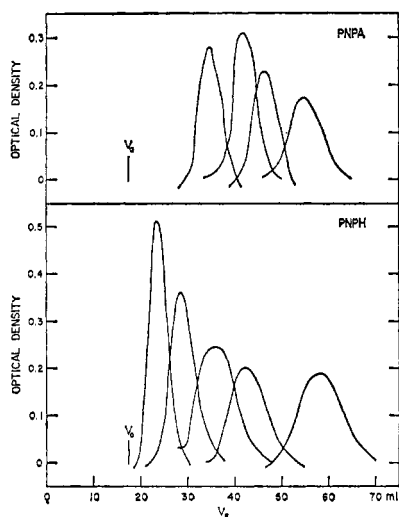


Figure 3. Optical density at 325 $m\mu$ plotted as a function of effluent volume for chromatography of *p*-nitrophenyl acetate (above) and *p*-nitrophenyl hexanoate (below) in 0.20 *M* NaCl on Sephadex G-10 for various concentrations of tetradecyltrimethylammonium chloride. Detergent concentrations for runs involving PNPA are (for peaks from left to right) 0.15, 0.10, 0.075, and 0.05 *M*. Those for runs involving PNPH are (for peaks from left to right) 0.05, 0.025, 0.015, 0.010, and 0.008 *M*.

quantities, for the systems of interest here are shown in Figure 4. Satisfactory straight lines were obtained in both cases from which a value of $\bar{v}(K-1)$ of 1.3×10^4 for PNPH and 27 for PNPA were calculated. Assuming the partial specific volume of tetradecyltrimethylammonium chloride to be near 0.8, we obtain the following

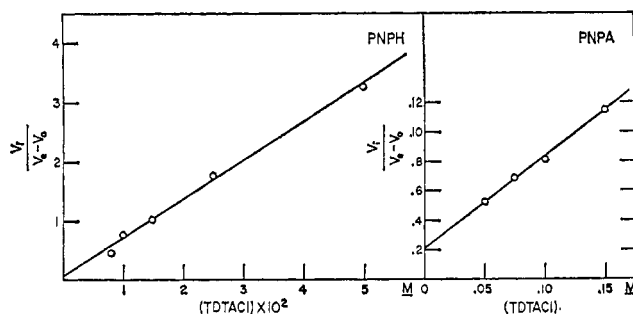


Figure 4. Plots of $V_i/(V_e - V_0)$ against detergent concentration for chromatography of *p*-nitrophenyl hexanoate (left) and *p*-nitrophenyl acetate (right) on Sephadex G-10 in 0.20 *M* NaCl in the presence of tetradecyltrimethylammonium chloride.

approximate values: $K_{\text{PNPH}} = 1.6 \times 10^4 M^{-1}$ and $K_{\text{PNPA}} = 33 M^{-1}$.

Anions are potent inhibitors of tetradecyltrimethylammonium chloride catalyzed hydrolysis of *p*-nitrophenyl hexanoate. In Table I, first-order rate constants for this reaction with $3 \times 10^{-5} M$ ester in aqueous solution, pH 10.15, in the presence of 0.009 *M* detergent are collected as a function of several anions. pH was maintained by use of a 0.02 *M* triethylamine-ammonium chloride buffer. These results are presented graphically in Figure 5. Clearly, each of the anions is an inhibitor and inhibitory power increases in the order $F^- < Cl^- < Br^- < NO_3^-$. It is difficult to place sulfate ion in this sequence since it seems to be a potent inhibitor at low concentrations but relatively ineffective at high concentrations. Note that the abscissa in Figure 5 is the total

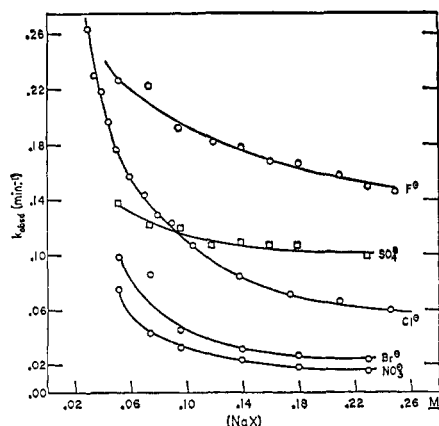


Figure 5. First-order rate constants for hydrolysis of *p*-nitrophenyl hexanoate in the presence of 0.009 *M* tetradecyltrimethylammonium chloride, pH 10.15, as a function of the concentration of several anions.

anion concentration which includes contributions from the detergent itself as well as from the buffer systems. Hence the value for the hydrolysis rate in the absence of any further additions is given by the point at the lowest concentration of chloride ion (*ca.* 0.03 *M*), *i.e.*, 0.26

Table I. First-Order Rate Constants for Hydrolysis of *p*-Nitrophenyl Hexanoate in Aqueous Solution, pH 10.15, Containing 0.009 *M* Tetradecyltrimethylammonium Chloride as a Function of the Concentration of Several Anions^a

Anion	Concn, ^b <i>M</i>	<i>k</i> _{obsd} , min ⁻¹	Anion	Concn, ^b <i>M</i>	<i>k</i> _{obsd} , min ⁻¹
Fluoride	...	0.262	Chloride	0.029	0.262
	0.022	0.226		0.034	0.230
	0.044	0.222		0.039	0.218
	0.065	0.192		0.044	0.196
	0.090	0.182		0.049	0.177
	0.110	0.178		0.059	0.158
	0.130	0.168		0.069	0.144
	0.150	0.162		0.079	0.129
	0.180	0.158		0.089	0.124
	0.200	0.150		0.104	0.107
	0.220	0.146		0.137	0.085
Nitrate	0.022	0.075	0.173	0.072	
	0.044	0.044	0.209	0.066	
	0.066	0.033	0.245	0.059	
	0.110	0.024			
	0.150	0.019			
Bromide	0.200	0.016			
	0.022	0.099	Sulfate	0.022	0.138
	0.044	0.086		0.044	0.122
	0.066	0.046		0.066	0.119
	0.110	0.032		0.088	0.107
	0.150	0.027		0.110	0.109
	0.200	0.024		0.130	0.107
		0.150		0.107	
		0.200	0.099		

^a All reactions carried out at 25° in the presence of 0.02 *M* triethylamine-ammonium chloride buffer. Reaction mixtures contained 3% acetonitrile by volume. ^b The concentrations indicated are those for the ion indicated only. Thus for chloride ion the concentrations are the total ions present while for the others a total of 0.029 *M* chloride ion is present as well (contributed from the buffer and from the detergent). In Figure 5, the total anion concentrations are plotted on the abscissa.

min⁻¹. Several additional anions, including perchlorate, fluoroborate, and iodide, could not be examined as inhibitors since they yielded insoluble material in the

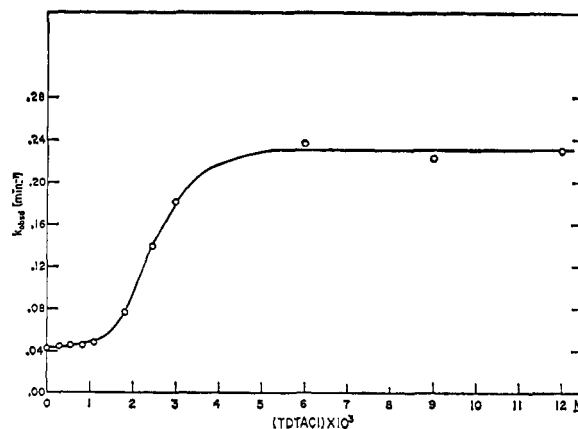


Figure 6. First-order rate constants for hydrolysis of *p*-nitrophenyl hexanoate at pH 10.15 plotted as a function of the concentration of tetradecyltrimethylammonium chloride at a constant total chloride ion concentration of 0.02 *M*.

presence of the detergent. The first-order rate constant for hydrolysis of *p*-nitrophenyl hexanoate at pH 10.15 in the absence of detergent is near 0.045 min⁻¹ (Figure 2). Thus, above about 0.10 *M*, both bromide and nitrate ions actually convert the detergent-catalyzed reaction into a detergent-inhibited one (Table I and Figure 5).

The data presented in Figure 2 indicate that the first-order rate constants for basic hydrolysis of PNPH and PNPL in the presence of cationic detergents first increase with increasing detergent concentration, level off, and finally begin to decrease with increase in this parameter. Since these experiments were performed in the presence of constant amounts of added salt and buffer (see above), the actual anion concentration increases with increasing detergent concentration due to the contribution of the counterion (bromide) of the detergent itself. Since anions have proved to be potent inhibitors of the detergent-dependent processes, it is possible that the inhibition at high detergent concentrations is, in fact, a salt effect. To examine this possibility, the first-order rate constants for hydrolysis of PNPH in the presence of increasing concentrations of tetradecyltrimethylammonium chloride at pH 10.15 maintained with 0.02 *M* triethylamine buffer and at a constant total chloride concentration of 0.02 *M*, maintained with sodium chloride, were measured. The results, shown graphically in Figure 6, indicate that the inhibition has, in fact, disappeared.

Discussion

Data obtained in this study of the surfactant-dependent hydrolysis of *p*-nitrophenyl esters are pertinent to the following two points: what factors are responsible for the specificity of these reactions for substrate and what factors are responsible for the observed catalysis by the cationic detergents? We discuss each of these questions in turn.

As observed in this study and previously,⁴ *p*-nitrophenyl esters derived from long-chain aliphatic acids are rather more susceptible to surfactant-dependent hydrolysis than are those derived from acetate. We have previously suggested that this fact probably reflects the greater tendency of the former substrates to associate with the micelles rather than any inherent difference in

reactivity once the esters are incorporated into the micellar phase.⁴ Estimates obtained in this study of the equilibrium constants for association of *p*-nitrophenyl esters of hexanoic and acetic acids with micelles formed from tetradecyltrimethylammonium chloride strongly support this conclusion; thus the pertinent equilibrium constants are near 16,000 and 33 M^{-1} , respectively. Thus, the free energy of transfer of the hexanoate from the aqueous to the micellar phase is about 3.7 kcal/mol more favorable than that for the acetate. This value is well within the maximum that one might have expected on the basis of a favorable free energy change of 1.4 kcal for transfer of a single methylene group from an aqueous to a hydrocarbon medium.¹² These equilibrium constants account well for the observed kinetic behavior. Thus, the rate of hydrolysis of *p*-nitrophenyl hexanoate in the presence of tetradecyltrimethylammonium bromide is maximal (about five times the catalyzed rate) near $4 \times 10^{-3} M$ detergent, a condition under which more than 95% of the ester ought to be incorporated into the micellar phase. Under the same conditions, the rate of *p*-nitrophenyl acetate hydrolysis has increased by about 30% (*i.e.*, only about 7% of the expected total catalysis) and one predicts that about 12% of the ester is incorporated into the micellar phase. One cannot place great reliance on exact quantitative agreement in calculations of this kind since the equilibrium constants, which are estimates in any event, were measured in the presence of a great deal more salt than were the rate constants. The change in salt concentration certainly affects the critical micelle concentration and probably the equilibrium constants for association with the substrate. The important point is that the equilibrium constants provide a good qualitative and semiquantitative explanation for the dependence of the rates of hydrolysis of the two esters on the surfactant concentration. It seems likely that a similar explanation will serve to rationalize the observation that the hydrolysis of ortho esters by anionic surfactants becomes more pronounced as the substrates become increasingly hydrophobic.⁴

The initiation of catalysis of hydrolysis of *p*-nitrophenyl hexanoate by tetradecyltrimethylammonium bromide is well correlated with the critical micelle concentration for this surfactant measured under similar conditions (see Figures 1 and 2). Our earlier conclusion that catalysis was initiated at concentrations of surfactant below the cmc⁴ is the consequence of the use of an insufficiently pure sample of the surfactant.

The dependence of the extent of surfactant-dependent catalysis of ester hydrolysis on the chain length of the surfactant may also reflect the importance of hydrophobic bonding in formation of the substrate-micelle complex. Thus, catalysis tends to become somewhat more marked as the chain length increases (Figure 2). However, other factors are likely to be important as well, including the positioning of the substrate in or on the micelle. No data are, at present, available to probe this factor although studies are in progress concerning this point.

The inhibition of surfactant-dependent hydrolysis of *p*-nitrophenyl hexanoate at quite high concentrations of the surfactants (Figure 2) disappears if the total anion concentration is maintained constant as the concentra-

tion of the surfactant is increased (Figure 6). Hence, this inhibition is almost certainly the result of inhibition due to increasing concentration of the counterion of the surfactant. A similar explanation for the related behavior of *p*-nitrophenyl laurate seems warranted although hydrolysis of this substrate has not been specifically examined under conditions of constant total anion concentration.

The foregoing conclusions account qualitatively for the shape of the plots of rate constant against surfactant concentration. At surfactant concentrations below the cmc, the rate constants are substantially independent of this parameter. At higher concentrations, the rate constants increase with increasing surfactant concentration in a manner dictated by the nature of the surfactant and substrate and, at still higher surfactant concentrations at which substantially all of the substrate has been incorporated into the micellar phase, the rate constants decrease with increasing surfactant concentration as a result of counterion inhibition of the reaction.

The results provided herein concerning the effect of substrate and surfactant structure on the kinetics of the micellar phase reactions are in substantial agreement with previous findings. Menger and Portnoy have reported dodecyltrimethylammonium ion catalysis for the basic hydrolysis of PNPA and *p*-nitrophenyl octanoate and that catalysis is more marked with the latter substrate.¹³ These findings corroborate our earlier report.⁴ These workers also report marked inhibition of hydrolysis of these substrates by sodium lauryl sulfate,¹³ a finding fully consonant with our earlier report of inhibition of the reactions of hydroxide ion and leucine with similar substrates.⁴

The question of the site of reaction of basic ester hydrolysis within the micellar phase cannot be resolved with certainty at this time. For the reasons detailed in the accompanying communication³ and particularly in view of the results of Eriksson and Gillberg revealing that molecules of appreciably polar character are adsorbed onto the surface of cationic micelles and not into their interior,¹⁴ we are not inclined to accept the conclusion of Menger and Portnoy that *p*-nitrophenyl esters are incorporated into the micellar interiors.¹³ It seems quite likely that the basic hydrolysis of *p*-nitrophenyl esters, whether in the presence of cationic or anionic surfactants, occurs at the Stern layer of the micelles.³ We adopt this conclusion in the discussion below. Certain of the pertinent features relating to the chemistry of the Stern layer and their relationship to kinetics of organic reactions have been pointed out³ and will not be repeated here.

The observation of Mukerjee and Ray that the dielectric constant at the surface of micelles derived from *N*-alkylpyridinium ions is near 36¹⁵ coupled with the observations on the basic hydrolysis of methyl 1-naphthoate in water and aqueous dioxane solutions suggest that the change in dielectric constant in going from water to the micellar surface should have a mild retarding effect on the reaction rate.¹⁶ At any event, such

(13) F. M. Menger and C. E. Portnoy, *J. Am. Chem. Soc.*, **89**, 4698 (1967).

(14) J. C. Eriksson and G. Gillberg, *Acta Chem. Scand.*, **20**, 2019 (1966).

(15) P. Mukerjee and A. Ray, *J. Phys. Chem.*, **70**, 2144 (1966).

(16) E. F. J. Duynstee and E. Grunwald, *Tetrahedron*, **21**, 2401 (1965).

(12) P. Mukerjee, *Advan. Colloid Interface Sci.*, **1**, 241 (1967).

effects alone seem inadequate to account for all the relevant observations including the dramatic salt effects observed in this study; for these, one must be concerned with electrostatic effects as well. The ground state for *p*-nitrophenyl hexanoate hydrolysis in the presence of any substantial concentration of tetradecyltrimethylammonium ion must be regarded as composed of the ester in the micellar phase and the hydroxide ion free in solution. The transition state for this reaction within the micellar phase possesses a full negative charge localized in part on the attacking hydroxide ion and in part on the incipient tetrahedral intermediate derived from the substrate (or on the incipient carboxylate ion derived from the ester if a tetrahedral intermediate is not formed¹⁷). Thus, the observed catalysis may result, in part at least, from electrostatic stabilization of the negatively charged transition state by the positively charged micellar surface. These conclusions suffice to account for the following observations. First, the reaction of esters with anionic reagents such as hydroxide ion and leucine, but not the reactions with the uncharged species morpholine, are subject to catalysis by cationic detergents.^{5,13} Second, anions which might reasonably be expected to compete with, for example, hydroxide ion for available binding sites within the Stern layer or diffuse double layer surrounding the micelles are potent inhibitors of the surfactant-dependent reactions (Figure 5). Indeed, at sufficiently high concentrations, nitrate and bromide actually convert the catalysis into inhibition. Finally, this explanation also suffices to account for related observations relevant to rates of organic reactions in the presences of cationic surfactants including the hydroxide ion dependent fading of cationic dyes,¹⁸ the reaction of methyl bromide with cyanide ion,¹⁹ the alkaline decomposition of indoaniline dyes,²⁰ and the alkaline hydrolysis of methyl 1-naphthoate¹⁶ and several other esters in addition to these investigated here,¹³ and for the catalysis of the basis hydrolysis of monolayers of octadecyl acetate upon incorporation of cationic surfactants into such monolayers.²¹

Viewing electrostatic stabilization of the transition state with respect to the ground state as the primary driving force for catalysis by cationic surfactants for the basic hydrolysis of *p*-nitrophenyl esters, one must conclude that the large salt effects observed for the micellar reactions are a consequence of weakening this electrostatic interaction. The trivial explanation that the salt effects are a consequence of exclusion of the substrate from the micellar phase cannot be true since (i) the equi-

librium constant for association of *p*-nitrophenyl hexanoate with the micellar phase was measured in the presence of high concentrations of salt and is sufficiently large to ensure that substantially all of the substrate is so associated under the conditions in which the salt effects were measured; and (ii) such a mechanism cannot account for decreases in the rate constant below that observed in the absence of surfactant. Through binding of the inhibitory anions to the micellar surface and thus decreasing the extent of ionization of the quaternary ammonium functions, the electrical field at the surface would be considerably reduced. Such a reduction would tend to reduce the rate of reaction at the micellar surface through lessened stabilization of the anionic transition state. Additional understanding of the nature of the salt effects may be obtained by considering salt effects on the preequilibrium binding of hydroxide ion to the micellar surface. Clearly a reduction of the electrical potential of the micellar surface will weaken its affinity for this nucleophilic reagent. Furthermore, there will exist direct competition between hydroxide ion and the inhibitory anions for available binding sites at the micellar surface. These conclusions are strongly supported by parallels between the inhibitory capacity of the anions, $\text{NO}_3^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$, and their capacity to lower the cmc and increase the polymerization number for cationic surfactants,²²⁻²⁴ to cause phase separation in solutions of cationic surfactants,²⁵ and their ability to ion pair with tetraalkylammonium ions in water²⁶⁻²⁸ and to associate with strong base anion exchange resins.²⁹

The anion inhibition data described above have many parallels in protein and enzyme chemistry. A particularly good example is provided by the recent work of Coleman with the enzyme carbonic anhydrase.³⁰ The relative efficiencies of anions in binding to this protein and in inhibiting the enzymatic reaction and the suggested mechanism for the inhibition are almost exactly parallel to the related considerations for the micellar reaction observed here.

Acknowledgment. We are indebted to Dr. W. P. Jencks of Brandeis University and to Dr. Lawrie Benjamin of Proctor & Gamble, Inc. and to their associates for helpful discussions regarding matters pertaining to both this work and that presented in the accompanying report.³

(17) W. P. Jencks and M. Gilchrist, *J. Am. Chem. Soc.*, **90**, 2622 (1968).

(18) E. F. J. Duynstee and E. Grunwald, *ibid.*, **81**, 4540, 4542 (1959).

(19) L. J. Winters and E. Grunwald, *ibid.*, **87**, 4608 (1965).

(20) L. K. J. Tong, R. L. Reeves, and R. W. Andrus, *J. Phys. Chem.*, **69**, 2357 (1965).

(21) J. T. Davies, *Advan. Catalysis*, **6**, 1 (1954).

(22) E. W. Anacker and H. M. Ghose, *J. Phys. Chem.*, **67**, 1713 (1963); *J. Am. Chem. Soc.*, **90**, 3161 (1968).

(23) R. L. Venable and R. V. Nauman, *ibid.*, **68**, 3499 (1964).

(24) M. F. Emerson and A. Holtzer, *ibid.*, **71**, 1898 (1967).

(25) I. Cohen and T. Vassiliades, *ibid.*, **65**, 1774 (1961).

(26) S. Lindenbaum and G. E. Boyd, *ibid.*, **68**, 911 (1964).

(27) R. M. Diamond, *ibid.*, **67**, 2513 (1963).

(28) K. Tamaki, *Bull. Chem. Soc. Japan*, **40**, 38 (1967).

(29) G. E. Boyd, S. Lindenbaum, and G. E. Myers, *J. Phys. Chem.*, **65**, 577 (1961).

(30) J. E. Coleman, *J. Biol. Chem.*, **242**, 5212 (1967).