72-2142

MAZZOLA, Eugene Passudette, 1942-
MICELLAR CATALYSIS IN PHOSPHONATE ESTER HYDROLYSIS.

University of Pittsburgh, Ph.D., 1971
Chemistry, organic

University Microfilms, A XEROX Company, Ann Arbor, Michigan

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

MICELLAR CATALYSIS IN PHOSPHONATE ESTER HYDROLYSIS

By

Eugene P. Mazzola

A.B., Franklin and Marshall College, 1964

Submitted to the Graduate Faculty of
Arts and Sciences in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy

University of Pittsburgh

1971

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

UNIVERSITY OF PITTSBURGH

FACULTY OF ARTS AND SCIENCES

This dissertation was presented

by

Eugene P. Mazzola

It was defended on

July 13, 1971

and approved by

Dr. T. Chapman

Dr. C. E. Griffin

Dr. J. F. Coetzee

Dr. S. Danishefsky

Dr. T. Cohen

Chairman

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

PLEASE NOTE:

Some Pages have indistinct print. Filmed as received.

UNIVERSITY MICROFILMS

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

FOREWORD

I would like to thank Drs. Eleanor J. Fendler and Claibourne E. Griffin for their interest and guidance during the course of this study.

I also wish to thank my wife, Peggy, for her understanding and technical assistance.

Finally, I would like to thank Dr. Harold Goldwhite of the California State College, Los Angeles for many helpful discussions.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE OF CONTENTS

		Page
FOREWORD		ii
I.	INTRODUCTION	1
	A. Physical Properties of Micelles and Micellar Solutions	1
	B. Solubilization in Aqueous Micellar Solutions	10
	C. Principles of Micellar Catalysis	11
	D. The Reaction Site in Micellar Catalysis	16
	E. Investigations of Micellar Effects on Phosphonate Ester Hydrolysis	18
II.	EXPERIMENTAL PROCEDURE	21
	A. Materials	21
	B. Methods	23
	1. Kinetic Procedures	23
	2. Determination of Critical Micelle Concentrations	29
III.	RESULTS	32
	A. Kinetic Results	32
	B. Evaluation of Kinetic Results	32
	C. Determination of Micelle-Substrate Binding Constants	33
	D. Calculation of Activation Parameters	35
	E. Determination of Critical Micelle Concentrations	37
IV.	DISCUSSION	86
	A. General Introduction	86
	B. Basic Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate	87

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Page

1. Introduction 87

2. Hexadecyltrimethylammonium Bromide (CTAB) Catalysis 88

3. Sodium Dodecyl Sulfate (NaLS) Anticatalysis 97

4. Polyoxyethylene(20) Nonylphenol (PENP) Anticatalysis 99

C. Basic Hydrolysis of p-Nitrophenyl Phenylphosphonate 101

1. Introduction 101

2. Hexadecyltrimethylammonium Bromide (CTAB) Catalysis 102

3. Polyoxyethylene(20) Nonylphenol (PENP) Anticatalysis 104

4. Sodium Dodecyl Sulfate (NaLS) 105

V. SUMMARY 106

VI. CONCLUSIONS 107

REFERENCES CITED 109

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

I. INTRODUCTION

A. Physical Properties of Micelles and Micellar Solutions

Questions concerning the nature of organic reactions occurring in the presence of micelle-forming surfactants have recently aroused considerable interest. This is due, in part, to the fact that such processes have long been of great importance to both the chemical and pharmaceutical industries.

The terms surfactant, detergent, and surface active agent all refer to amphiphilic substances (amphiphiles) which form high molecular weight aggregates (micelles) in dilute solution. These amphiphiles are ionic or neutral species which possess distinct regions of hydrophilic and hydrophobic character. The hydrophobic part of a surfactant usually consists of a long hydrocarbon chain, while a polar or ionic "head" group constitutes the hydrophilic moiety.

In dilute aqueous solution at concentrations less than 10^{-4} M, amphiphilic substances behave much like strong electrolytes. However, at somewhat higher concentrations, marked deviations from ideal behavior are observed. If some physical property of the solution such as conductivity, surface tension, pH, or optical absorption is measured as a function of concentration, it is seen to undergo a fairly well-defined change. A generalized representation of such variation in physical properties as a function of surfactant concentration is given in Figure 1. As indicated, this change occurs over a narrow concentration range rather than at an exact

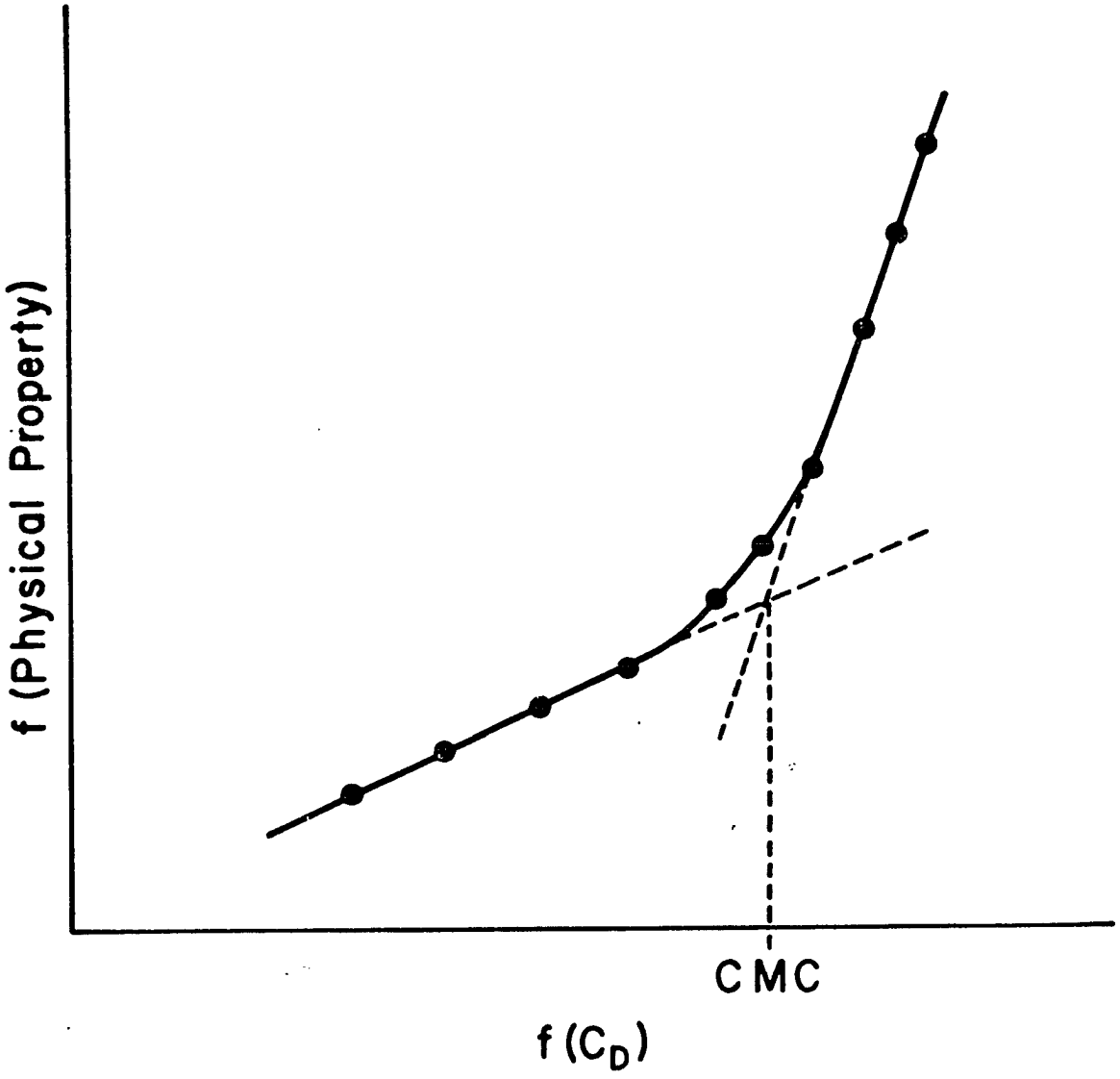
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

FIGURE 1

A Generalized Representation of the Change in a Physical Property as a Function of the Detergent Concentration, C_D.

Reproduced from Reference 1.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

point, with both the magnitude and the abruptness of this change depending somewhat on both the nature of the micelle and the physical property being measured.

The changes in these physical properties are ascribed to the association of the amphiphiles to form micelles. The amphiphilic concentration at which these micelles first appear is known as the critical micelle concentration, commonly abbreviated as CMC. Another more formal definition of the critical micelle concentration is that amphiphilic concentration at which the concentration of micelles would become zero if it were to continue to decrease as it does at a slightly higher concentration.[2]

The driving force for this micellization is the decrease in the free energy of the system which results from the self-association of the hydrophobic parts of the surfactant monomers. Submicellar aggregates such as dimers, trimers, etc. are also formed, but they result in only relatively small decreases in the overall free energy of the system.[3-5] In addition, micelles are not static entities but instead exist in a rapid dynamic equilibrium with the monomeric species.[1]

At detergent concentrations not appreciably exceeding the critical micelle concentrations, micelles are approximately spherical in shape. At much higher surfactant concentrations the micelles adopt cylindrical or rod-like forms. Typical ionic micelles contain 20 to 100 monomers and have average radii of 12 to 30 angstroms. Nonionic micelles tend to be larger in size and have greater aggregation numbers (the number of monomers per micelle) because of

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

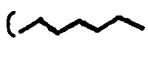
the absence of electrostatic repulsion between similarly charged "head" groups in the hydrophilic part of the amphiphiles. For detergents whose hydrophobic parts consist of long hydrocarbon chains, critical micelle concentration values generally range between 10^{-4} and 10^{-2} molar.[1,6]

A schematic two-dimensional diagram of a spherical ionic micelle is shown in Figure 2. The hydrophobic hydrocarbon chains of the surfactants are located primarily in the center of the micelle. They form the micelle's "core" which is liquid-paraffin-like in nature and averages 10 to 28 angstroms in width. In addition, these hydrocarbon chains are not believed to be extensively folded because the diameters of spherical micelles are approximately twice the length of the fully extended surfactant monomers.[7,8] The hydrophilic polar head groups are situated near the micelle-water interface in contact with, and hydrated by, a number of water molecules. These charged head groups and some of the counterions of the ionic micelle are located in a compact region, known as the "Stern layer," which is only a few angstroms wide. Most of the rest of the counterions are located in an area known as the "Gouy-Chapman electrical double layer." They are completely dissociated from the charged aggregate and are able to undergo exchange with ions in the aqueous bulk solution.[1] This outer layer can be up to several hundred angstroms in width.

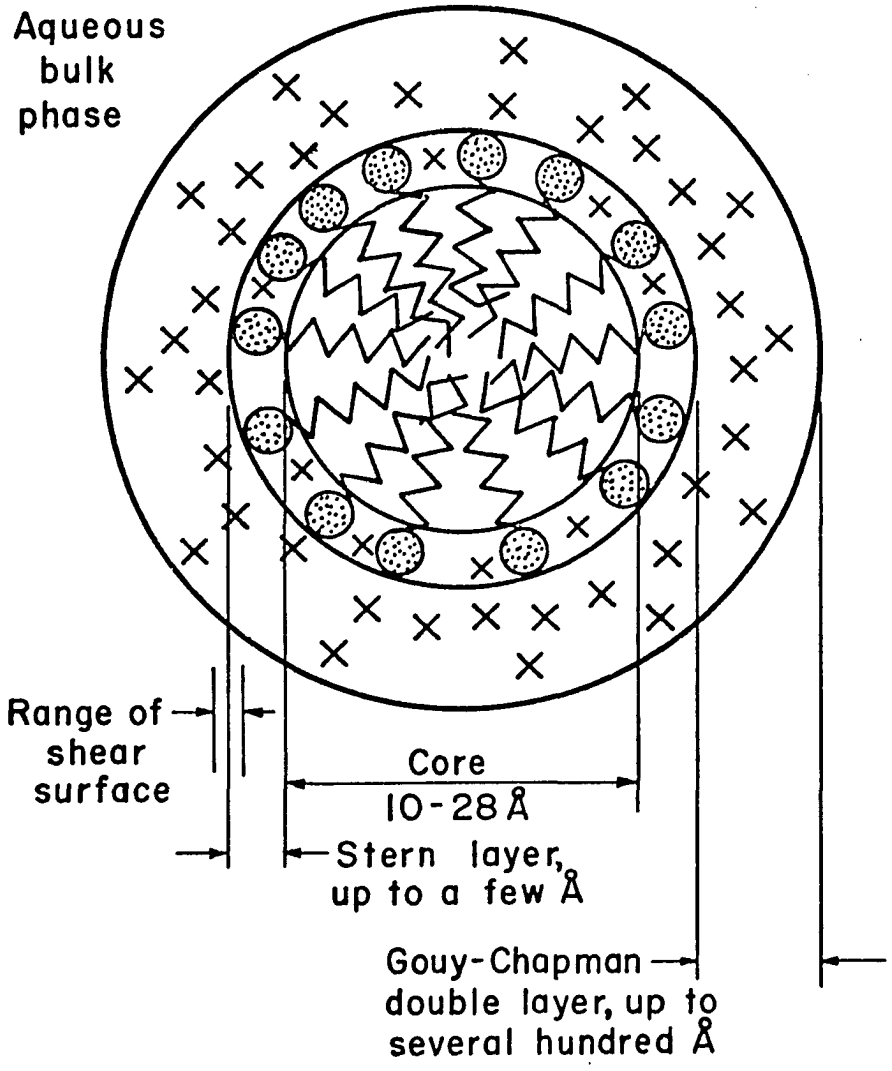
Depending on their chemical composition, detergents and the micelles which they form belong to one of the following four charge groups: cationic, anionic, nonionic, or ampholytic. The latter

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

FIGURE 2

A Two-dimensional Schematic Diagram of the Regions of a Spherical Ionic Micelle. The Counterions (X), the Head Groups ( ), and the Hydrocarbon Chains () are Schematically Indicated to Show Their Relative Locations but not Their Number, Distribution, or Configuration. Reproduced from Reference 1.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

consists of a zwitterion and, depending on the pH of the solution, can be either cationic or anionic.[9,10] The three amphiphiles employed in the present investigation are the cationic detergent hexadecyltrimethylammonium bromide (CTAB), the anionic surfactant sodium dodecyl sulfate (NaLS), and the nonionic surface active agent polyoxyethylene(20) nonylphenol (PENP). The physical parameters of these detergents are presented in Table 1.

A number of factors affect both the critical micelle concentration of a surfactant and the size and shape of the micelles formed. An increase in the hydrophobic moiety of the monomeric detergent generally results in a decrease in the critical micelle concentration and an increase in the number of monomers per micelle.[6,9] The CMC is also directly proportional to the number of polar groups and carbon-carbon double bonds, and to the extent of chain branching in the monomeric surfactant.[1] Increasing both the electrolyte and the substrate concentration leads to decreases in the critical micelle concentration and to increases in the micellar size, as does increasing both the substrate and the counterion hydrophobicity.[1,6] Non-electrolytes, such as dioxane, increase the CMC of both ionic and nonionic detergents.[11,12] However, the thermodynamics of micellization for ionic and nonionic surfactants are quite different. The aggregation number of ionic detergents decreases with increasing temperature while that of nonionic surfactants exhibits very large increases.[12] The critical micelle concentration of nonionic detergents decreases with increasing temperature. The CMC of several common ionic surfactants, however,

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 1

Micellar Physical Parameters[1]

Detergent	Charge Type	Structure	CMC, M at 25°C	Aggregation Number
Hexadecyltrimethylammonium bromide (CTAB)	cationic	$C_{16}H_{33}N(CH_3)_3Br$	9.2×10^{-4}	61
Sodium dodecyl sulfate (NaLS)	anionic	$C_{12}H_{25}SO_4Na$	8.1×10^{-3}	62
Polyoxyethylene(20) nonylphenol (PENP)	nonionic	$C_9H_{19}C_6H_4(OCH_2CH_2)_{20}OH$	$1.35\text{-}1.75 \times 10^{-4}$	62

decreases with increasing temperature at low temperatures and then displays the opposite behavior at higher temperatures. The CMC-temperature profile of sodium dodecyl sulfate, for example, exhibits a minimum at approximately 25° C.[12]

B. Solubilization in Aqueous Micellar Solutions

Solubilization is a process which is of great importance to the chemical and pharmaceutical industries. This term refers to the formation of a thermodynamically stable isotropic solution of a substrate (known as the solubilizate), normally insoluble or only slightly soluble in a given solvent, by the addition of a surface active agent (called the solubilizer).[1] Solubilization is closely related to micellization in that the solubility of a given substrate increases very little, if at all, until the critical micelle concentration of the surfactant is attained. However, once micelles are present, the increase in solubility is directly proportional to the detergent concentration over a large range.

Solubilization, like micellar properties, is dependent on a number of factors such as the nature of the surfactant, substrate, and solvent, the presence of additional polar and nonpolar solutes, and the temperature. The interpretation of solubilization phenomena is thus complicated because several of the parameters which affect the solubility of the substrate also affect the properties of the micelles. The critical micelle concentration, micellar shape, and aggregation number, for example, are known to be altered both by the addition of electrolytes or organic solvents and by changes in the

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

temperature or detergent counterion. However, the parameters mentioned above also affect the solubility of substrates in both the aqueous and micellar phases.[13-16] In addition, specific interactions between the substrate and the surface active agent can be of considerable importance. Because of the number and complexity of the factors governing solubilization, quantitative description of this very important process is, at present, unavailable. Solubilization patterns for a given system, too, are often quite difficult to predict even qualitatively.

C. Principles of Micellar Catalysis

The rate accelerations or inhibitions which micelles exhibit on organic reactions can be ascribed, basically, to the different rates of reaction of the substrate in the micellar phase and in the bulk solution and the distribution of the substrate between these two phases.[1,7] These often substantial effects result predominantly from the interactions between the substrate and the specifically oriented hydrophobic and hydrophilic parts of the micelle. To a certain extent these rate effects can be understood by considering both the electrostatic and the hydrophobic interactions which occur between the substrate, the micelle, and other solutes such as salts or nucleophiles.[1,6] Large organic species, for instance, may be incorporated into the micelles and thereby act as inhibitors by preventing the incorporation of some of the substrate.[1,6,17-28] On the basis of electrostatic considerations, cationic micelles would be expected to accelerate anion-molecule reactions, ie. those

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

involving an uncharged organic substrate and an anionic nucleophile, anionic micelles to be rate-retarding, and nonionic micelles to have a small effect, if any, on the rate. Such effects have, in fact, been observed in many cases.[7,18-22,25,27,29-34]

However, in some instances electrostatic factors are insufficient to account for the strikingly different behavior of structurally similar substances. As in the case of enzymatic catalysis, such substrate specificity can, in many cases, be attributed to hydrophobic interactions, ie. to subtle differences in the nature and extent of substrate-micelle binding which result in differences in the reactivity of the substrate in the micellar phase and in the bulk solution.[6,7,27,28,30,35,36]

The incorporation of a substrate into a micellized surfactant and the differing reactivities in the micellar and bulk phases can be treated quantitatively in a manner analogous to that used for enzymatic catalysis:

$$\begin{array}{ccccc} M & + & S & \overset{K}{\rightleftharpoons} & MS \\ & & \downarrow{\scriptstyle k_o} & & \downarrow{\scriptstyle k_m} \\ & & \multicolumn{3}{c}{\text{products}} \end{array} \qquad (1)$$

where M is the micelle, S is the substrate, MS is the micelle-substrate complex, and k_o and k_m are the rate constants for product formation in the bulk solution and in the micellar phase, respectively. The rate equation for the equilibrium expression 1 is:

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$$-\frac{d[S]_t}{dt} = \frac{-d([S] + [MS])}{dt} = \frac{d[P]}{dt} \tag{2}$$

and

$$\frac{d[P]}{dt} = k_o[S] + k_m[MS] \tag{3}$$

where $[S]_t$ is the stoichiometric concentration of the substrate at time t and is given by equation 4:

$$[S]_t = [S] + [MS] \tag{4}$$

The observed rate constant for the formation of product, k_ψ, is given by the following expression:

$$k_\psi = \frac{-\frac{d[S]_t}{dt}}{[S]_t} = \frac{k_o[S]}{[S]_t} + \frac{k_m[MS]}{[S]_t} \tag{5}$$

or

$$k_\psi = k_o F_o + k_m F_m \tag{6}$$

where F_o and F_m are the fractions of substrate in the bulk solvent and in the micellar phase, respectively, and are given by the following relationships:

$$F_o = \frac{[S]}{[S]_t} \tag{7}$$

$$F_m = \frac{[MS]}{[S]_t} \tag{8}$$

The equilibrium expression for equation 1 is the following:

$$K = \frac{[MS]}{[M][S]} \tag{9}$$

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Rearrangement of equation 4 and substitution into equation 9 yields the following relationship:

$$K = \frac{[MS]}{[M]([S]_t - [MS])} \tag{10}$$

or

$$K = \frac{\frac{[MS]}{[S]_t}}{[M]\left[\frac{[S]_t - [MS]}{[S]_t}\right]} = \frac{\frac{[MS]}{[S]_t}}{[M]\left[1 - \frac{[MS]}{[S]_t}\right]} \tag{11}$$

Substitution of equation 8 into equation 11 produces the following expression:

$$K = \frac{F_m}{[M](1 - F_m)} \tag{12}$$

Solving equation 6 for the fraction of substrate in the micellar phase one obtains the following:

$$F_m = \frac{k_\psi - k_o}{k_m - k_o} \tag{13}$$

Substitution of equation 13 into equation 12 and subsequent rearrangement gives the following expression:

$$\frac{k_\psi - k_o}{k_m - k_\psi} = [M]K \tag{14}$$

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Now the concentration of micelles, [M], can be expressed as:

$$[M] = \frac{C_D - CMC}{N} \tag{15}$$

where C_D is the total concentration of the detergent, CMC is the critical micelle concentration, and N is the aggregation number. Finally, substitution of equation 15 into equation 14 yields the following relationship:

$$\frac{k_\psi - k_o}{k_m - k_\psi} = \frac{K(C_D - CMC)}{N} \tag{16}$$

The equilibrium constant for formation of the micelle-substrate complex, K, (commonly called the binding constant), can be calculated from a plot of the left side of equation 16 against the detergent concentration, C_D. The slope of this plot, m, is given by equation 17:

$$m = \frac{K}{N} \tag{17}$$

The binding constant, K, can then be readily determined from a knowledge of this slope and the aggregation number.[17,18,20-22,24] Employment of equation 16 is necessarily restricted to those rate constants whose values are not too similar to k_o or k_m because of the very large uncertainties introduced into the calculation of the ordinate when $k \simeq k_o$ or $k \simeq k_m$.

The derivation of equation 16 is based on the following critical assumptions:[1,7] (a) the substrate does not complex with the surfactant monomer; (b) the substrate associates with the micelles in a 1:1 stoichiometry; (c) the substrate does not

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

appreciably alter the process of micellization; and (d) equation 15 satisfactorily gives the number of micelles. Even with these limitations, binding constants from good linear plots have, none the less, been obtained from this type of treatment.[7,17,18,20-22,24,37] Moreover, these binding constants have been found to agree with those values derived from solubility measurements.[1,18] Exact agreement between these two independent methods is not to be expected because of the effect of hydroxide ion on both the micellar aggregation number, and the equilibrium constant for incorporation of the substrate into the micelle.[18]

D. The Reaction Site in Micellar Catalysis

Several lines of evidence strongly suggest that most reactions of polar organic substrates occur at the surface of the micelle, in the charged Stern layer which surrounds the core of the micelle and not within the hydrocarbon core itself.[6,25-29] However, it should be remembered that a distinct line cannot be drawn between the micellar surface and the micelle interior due to the rough nature of the former.[6,38,39] In addition, nmr evidence indicates that there is appreciable penetration of water into the micellar interior.[1,6,40-45] The micellar surface can therefore be considered to encompass the first 2 or 3 methylene groups of the hydrocarbon chain of the surfactant molecules as well as the charged, or polar, head groups.[6,26] The important point, however, is that reaction takes place in a region of considerable aqueous character and not in

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

one having essentially hydrocarbon-like properties. These arguments are supported by substantial nmr evidence which strongly suggests that organic molecules possessing appreciable polar character are localized predominantly at the micellar surface.[46,47]

Based on the above consideration the principal features of the chemistry of the Stern layer include the following:[26,39] (a) the hydration of charged groups within the Stern layer is similar to that of charged groups alone;[48,49] (b) the micellar surface is rough and thus allows strong hydrophobic interactions between the substrate and the micelle;[38] (c) the thickness of the Stern layer is approximately equal to that of the hydrated ionic head groups;[49] (d) a very substantial fraction of the ionic groups (about 70-90 percent) are neutralized through the inclusion of counterions. Several of these characteristics will be discussed later when micellar effects on the hydrolysis of phosphonate esters are evaluated.

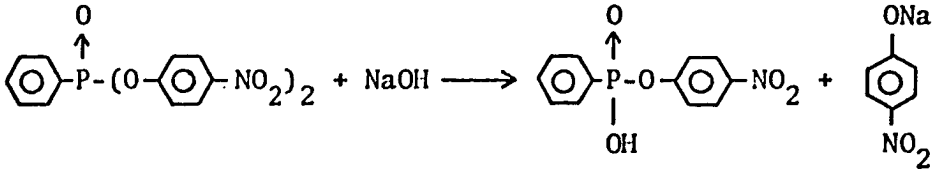
While most bond-changing processes are believed to occur in the Stern layer, there are many examples of reactions in which incorporation of reactants into the micellar phase has little, or no, kinetic consequence.[7,18,21,37] In many of these cases the substrate is probably located in the outer, water-rich region of the micelle, where it is exposed to the external reagent.[24,46,47,50-52] Conversely, in some special cases the substrate is solubilized in an inner region of an uncharged micelle where it is shielded from external reagents. Alternatively the substrate may be located in the outer region of the micelle but oriented in such a way that the functional group undergoing reaction is directed away from an

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

external reagent.[24] Therefore, the location and the orientation of the substrate in the micelle are as critical to micellar catalysis as the degree of substrate incorporation into the micellar phase. Some of the spectroscopic techniques which have been employed to investigate the micellar environment of solubilizates include (a) ultraviolet and visible spectral shifts;[51] (b) proton and fluorine magnetic resonance;[41-47] and (c) electron paramagnetic resonance.[52]

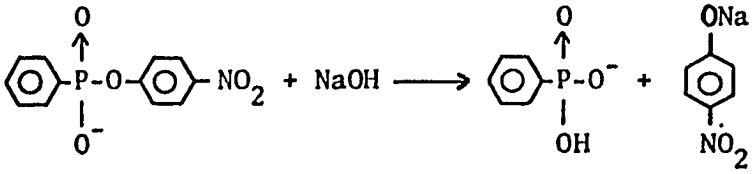
E. Investigations of Micellar Effects on Phosphonate Ester Hydrolyses

Although phosphate and phosphonate (having a general formula of $RP(O)(OR)_2$) esters are biologically important, relatively little is known of the effects of micelles upon their hydrolyses. The present investigation examines micellar effects on the basic hydrolysis of bis p-nitrophenyl phenylphosphonate to the monoester monoanion:



(18)

and p-nitrophenyl phenylphosphonate to ultimately the dianion of phenylphosphonic acid:



(19)

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Bunton and coworkers have investigated the effects of micelles on the hydrolysis of phosphate monoesters,[17] diesters,[24] and triesters.[19,20,22] Especially pertinent to the present work are Bunton's studies of micellar effects on the basic hydrolysis of the phosphate triester, p-nitrophenyl diphenyl phosphate,[20] and the phosphate diester monoanion, bis 2,4-dinitrophenyl phosphate.[24] The former is clearly analogous to the bis p-nitrophenyl phenylphosphonate currently being examined, while the latter is similar, but less so, to the p-nitrophenyl phenylphosphonate.

Bunton has reported that the basic hydrolysis of p-nitrophenyl diphenyl phosphate is accelerated by the cationic surfactant, hexadecyltrimethylammonium bromide (CTAB), and inhibited by both the anionic detergent, sodium dodecyl sulfate (NaLS), and a nonionic amphiphile, polyoxyethylene(24) dinonylphenol (DNPE).[20] The cationic CTAB micelles increase the second-order rate constant approximately 11-fold, and Bunton has found that this catalysis is due to a substantial increase in the entropy of activation of the hydrolysis reaction. Conversely, anionic NaLS and nonionic DNPE micelles decrease the second-order rate constants by approximately 25- and 11-fold, respectively. In both cases the inhibition is apparently due to increase in the energy of activation of the hydrolysis reactions.

The addition of sodium hydroxide and dioxane to the aqueous detergent solutions slightly decreased the critical micelle concentrations of the ionic surfactants. On the other hand, that of the nonionic detergent DNPE was not noticeably affected.[11,12]

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

In addition, binding constant data was determined for the sodium dodecyl sulfate and DNPE retarded reactions. The binding constant was calculated to be approximately 10^6 M^{-1} for NaLS, while for DNPE the $\frac{K}{N}$ quotient was found to be approximately 10^4 M^{-1}. The binding constant itself could not be determined because the aggregation number of DNPE is not known. These large values suggest that the p-nitrophenyl diphenyl phosphate substrate is strongly solubilized by both surface active agents.

The basic hydrolysis of bis 2,4-dinitrophenyl phosphate is considerably slower than that of the triester.[24] Like the latter anion-molecule reaction, this anion-anion reaction is also catalyzed by cationic hexadecyltrimethylammonium bromide micelles. CTAB micelles increase the second-order rate constant by approximately 30-fold. Inhibition is also observed in the presence of nonionic DNPE micelles which decrease the second-order rate constant by approximately 10-fold. However, anionic sodium dodecyl sulfate has no significant effect on this reaction.

The objective of this research was to examine the nature and the magnitude of the effects of certain micelles on the two stages of the basic hydrolysis of bis p-nitrophenyl phenylphosphonate. When practicable, activation parameters and binding constants were determined to aid in elucidating the manner in which the three representative surfactants (ie. cationic, anionic, and nonionic) effect their rather striking rate accelerations or retardations.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

II. EXPERIMENTAL PROCEDURE

A. Materials

1. Phosphonate Esters

Bis p-nitrophenyl phenylphosphonate and p-nitrophenyl phenylphosphonate, cyclohexylammonium salt, were prepared by Dr. Eleanor J. Fendler.

2. Dioxane

Reagent grade dioxane was refluxed over sodium, fractionally distilled from molten sodium, and stored over Linde Type 4A molecular sieve.

3. Buffer Solutions

Sodium tetraborate buffer, 0.01 M, was used in the range pH 8.0-10.8. Disodium hydrogen phosphate buffer, 0.01 M, was used for pH 11.0-12.0.

Sodium hydroxide and sodium deuteroxide were used for solutions which were 0.01 molar or greater.

The pH of the buffer solutions was adjusted to the desired value by the addition of 0.10 M sodium hydroxide or hydrochloric acid and was measured with a Radiometer PHM 26 expanded scale pH-meter at the same temperature at which the hydrolyses were carried out.

4. Strong Bases

Sodium hydroxide solutions, 0.08, 0.09, 0.10, 0.20, 0.30, 0.40, 0.50, 0.70, 0.75, 1.00, 2.00, 3.00, 4.00, and 5.00 M, were

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

prepared by dilution of British Drug House (B.D.H.) concentration volumetric solution ampoules, or dilution of 0.10 and 1.00 M solutions prepared therefrom, with filtered, deionized water to the appropriate volume.

Sodium deuteroxide solutions, 0.25, 0.50, 0.75, 1.00, 2.00, 3.00, and 4.00 M, were prepared by dilution to the appropriate volume of standardized 0.975 and 4.88 M solutions with 99.5% deuterium oxide (provided by Dr. E. M. Arnett) and were stored in Teflon bottles under dry nitrogen. The 4.88 M solution was prepared by dilution of carbonate-free 40% sodium deuteroxide in D_2O (Stohler) and standardized by titration with 1.00 M hydrochloric acid (B.D.H.) using lacmoid as the indicator.

5. Surfactants

Hexadecyltrimethylammonium bromide (Eastman) and sodium dodecyl sulfate (City Chemical Corp.) were further purified according to the procedures of Mysels[2] and Grunwald[31] by Dr. Eleanor J. Fendler.

Polyoxyethylene(20) nonylphenol (General Aniline and Film Corp., Ipegal CO-850), which has been designated as PENP, was used without further purification.

6. Salts

Solutions (1.00 M) of sodium chloride, sodium bromide, potassium chloride, and sodium perchlorate were prepared in the following way. The reagent grade salts (Baker) were first dried *in vacuo* over P_2O_5 for at least 12 hours. Filtered, deionized

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

water was added to the weighed, powdered, dried salts, and the solutions were made up to the appropriate volumes.

7. Dyes

Pinacyanol chloride (Eastman) and bromphenol blue (Eastman) were used without further purification.

B. Methods

1. Kinetic Procedures

The hydrolyses of bis p-nitrophenyl phenylphosphonate and p-nitrophenyl phenylphosphonate were followed by measuring the increase in absorbance of the p-nitrophenoxide ion at 403 nm in the thermostated cell compartments of either a Beckman DU or Beckman DU-2 recording spectrophotometer. The temperature was measured inside the cells and was maintained within ±0.05° as monitored by NBS thermometers. Since the rates of these hydrolyses varied considerably, three experimental procedures were employed depending on whether the rate of the reaction in question was very fast ($t_{1/2}$ < 1 minute), very slow ($t_{1/2}$ > several hours), or intermediate.

The basic hydrolyses of bis p-nitrophenyl phenylphosphonate with hexadecyltrimethylammonium bromide micelles were the most rapid of all and comprise the first group mentioned above. Kinetic runs were carried out by adding a solution consisting of the buffer, surfactant, and part of the required dioxane to the cell and then allowing 30 minutes for temperature equilibration in the cell compartment. Prior to mixing, the solutions were allowed to attain

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

the water bath temperature, which was usually within one degree of the desired cell compartment temperature, while the cells were thermally equilibrated in the cell compartment. After the temperature equilibration period, a ca. 10^{-5} M solution of the phosphonate diester in dioxane was injected into the cell through a small bore in the Teflon stopper, and the change in absorbance recorded.

The basic hydrolyses of bis p-nitrophenyl phenylphosphonate in water and in the presence of sodium dodecyl sulfate and the nonionic detergent polyoxyethylene(20) nonylphenol were less rapid and constitute the intermediate rate group cited above. Kinetic runs were conducted in a manner similar to those previously described. In this case, however, the dioxane-phosphonate diester solution could be pipetted into the buffer, dioxane, and detergent (if required) solution since speed in mixing was not critical. Part of the resulting solution was then added to the cell and the change in absorbance recorded. As before, both the solutions and the cells were thermally equilibrated prior to mixing.

The basic hydrolyses of p-nitrophenyl phenylphosphonate, as previously noted, are very much slower than those of the diester. This greatly simplified the kinetic treatment since, for all practical purposes, two separate hydrolyses are occurring rather than two partially simultaneous reactions. These reactions in water and in the presence of all three surfactants form the last group. In this case a sodium hydroxide or sodium deuteroxide and detergent (if required) solution was added to a very small amount of the solid phosphonate monoester salt in a volumetric flask. The resulting

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

solution was then shaken vigorously and equilibrated to the bath temperature, after which aliquots were removed from the volumetric flasks at appropriate time intervals and analyzed spectrophotometrically for p-nitrophenoxide ion. For this series of hydrolyses the bath, rather than the cell compartment, was adjusted to the desired reaction temperature.

The spectroscopic data obtained by these different methods were treated in the same manner. The basic hydrolyses of both phosphonate esters obey overall second-order kinetics, being first-order in both ester and hydroxide ion. However, the kinetic treatment was simplified considerably by carrying out these hydrolyses under pseudo-first-order conditions. This was done by keeping the ester concentration at least 100-fold lower than that of the hydroxide ion.

The concentration of the phosphonate ester at time t is equal to the initial concentration of the phosphonate ester less that of the p-nitrophenoxide ion which has been formed. Since the Beer-Lambert Law has been shown to be obeyed for p-nitrophenoxide ion solutions over the concentration range employed in the present study,[53] then the concentration of the phosphonate ester at time t is the infinity value less the amount of p-nitrophenoxide ion formed. Data for a typical run are given in Table 2. The pseudo-first-order rate constants were determined by plotting the logarithm of the phosphonate ester concentrations, ie. $\log(OD_\infty - OD_t)$, against time. A typical plot is shown in Figure 3. The observed rate constants are equal to the value of the slope of

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 2

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate at pH 10.11 in 6.00×10^{-3} M Sodium Dodecyl Sulfate (NaLS) Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C., 0.01 M $Na_2B_4O_7$ buffer

Time (min.)	OD_t	$2 + \log(OD_\infty - OD_t)$
0	0.178	2.026
1.11	0.208	2.014
2.00	0.236	2.002
4.00	0.295	1.975
6.00	0.352	1.948
8.00	0.409	1.920
9.00	0.432	1.908
11.00	0.481	1.880
14.00	0.550	1.839
17.50	0.618	1.794
20.50	0.671	1.755
23.50	0.721	1.715
26.50	0.770	1.673
30.00	0.814	1.629
38.00	0.905	1.525
44.50	0.970	1.431
49.50	1.010	1.362

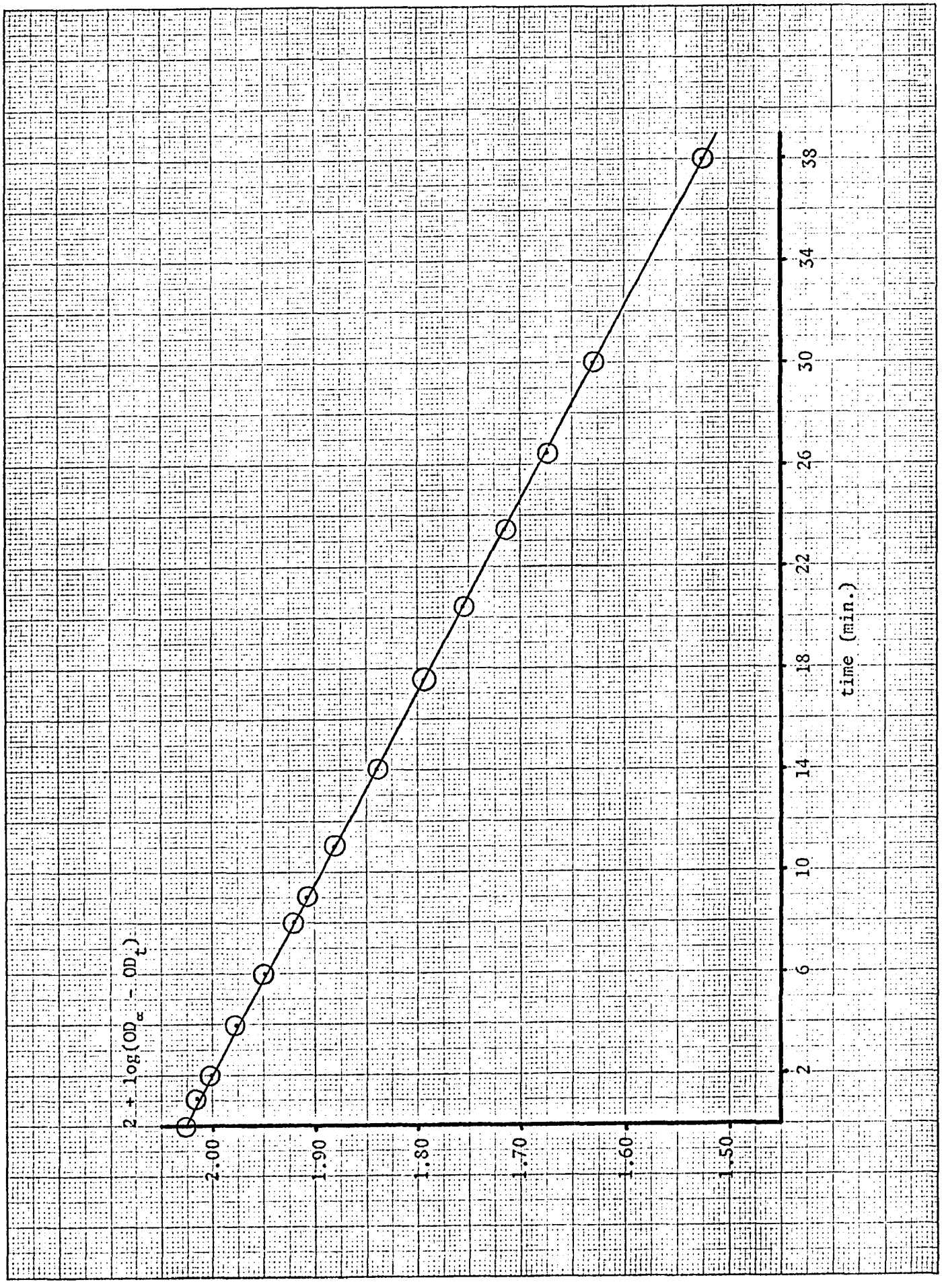
∞ 1.239, 1.240, 1.239, 1.239, 1.240, 1.241, 1.240

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

FIGURE 3

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate at pH 10.11 in 6.00×10^{-3} M Sodium Dodecyl Sulfate Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C., 0.01 M $Na_2B_4O_7$ buffer.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



KEUFFEL & ESSER CO.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

the straight lines so obtained multiplied by -2.303 and are calculated from the following expression:

$$k_{\psi} = \frac{-2.303[\log(OD_{\infty} - OD_{t_2}) - \log(OD_{\infty} - OD_{t_1})]}{t_2 - t_1} \qquad (20)$$

Substrate concentrations were generally in the range of 10^{-5} - 10^{-4} molar. Good pseudo-first-order rate plots, over at least one to two half-lives, were obtained in all cases.

2. Determination of Critical Micelle Concentrations

The hydrolyses of the phosphonate diesters were, in most cases, conducted not only in the presence of detergents but also in solutions containing strong electrolytes, viz. 0.01 M buffers, and 5% dioxane. As stated previously, the critical micelle concentrations of ionic surfactants and, to a much lesser extent, nonionic amphiphiles are dependent on a number of parameters such as the presence of organic solvents and strong electrolytes.[11,12] The critical micelle concentrations of hexadecyltrimethylammonium bromide and sodium dodecyl sulfate, and perhaps polyoxyethylene(20) nonylphenol, were therefore expected to be smaller than those values obtained in the absence of electrolytes or other additives.

One of the most common techniques for determining critical micelle concentrations is the spectral change method.[54] Dyes such as pinacyanol chloride and bromphenol blue form highly insoluble salts with oppositely charged surfactants in aqueous solution. As in

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

the case of detergents, the terms cationic and anionic refer to the charge on the bulky organic moiety of the dye rather than that on the considerably smaller counterion. The dye-detergent salts of certain dyes absorb at one characteristic frequency in aqueous detergent solutions and at still another when incorporated into micelles.[54]

In the spectral change method, the changes in absorption at one or more frequencies of a series of solutions containing a constant dye and varying detergent concentrations were measured using a Cary 14 recording spectrophotometer. A plot of absorption against detergent concentration exhibits one or more "breaks" depending on the dye being employed. These discontinuities in absorption are indicative of a significant change in the environment of the dye-detergent salt, namely the incorporation of the salt into micelles, and hence the point at which the micelles begin to appear.

Bromphenol blue was used to determine the critical micelle concentration of hexadecyltrimethylammonium bromide, sodium tetraborate buffer, and dioxane solutions while pinacyanol chloride was employed for similar sodium dodecyl sulfate, sodium tetraborate, and dioxane solutions. These solutions were prepared so as to include a range of surfactant concentrations extending from the literature values of the critical micelle concentration to concentrations below which any detergent effects had been observed. In addition, these solutions contained the same sodium tetraborate buffer and dioxane concentrations used in the kinetic runs. An

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

arbitrary intermediate pH value of 9.20, ie. unadjusted $Na_2B_4O_7$ buffer, was selected for the sodium tetraborate solution. Into these surfactant, buffer, and dioxane solutions were pipetted 0.10 ml. portions of ca. 10^{-5} M stock solutions of the dyes. The resulting dye-detergent solutions were then shaken vigorously. Because of fading on exposure to light soon after mixing, the dye-detergent solutions were kept in the dark for three hours before the changes in optical density were recorded.

The resulting absorbances were plotted against the surfactant concentrations. The plots for both detergents display the typical breaks which serve to identify the critical micelle concentration. In both cases these apparent critical micelle concentrations agreed well with those estimated from the detergent concentration-rate profiles.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

III. RESULTS

A. Kinetic Results

The pseudo-first-order rate constants for the hydrolysis of bis p-nitrophenyl phenylphosphonate in dioxane-water are given in Table 3. Those for the hydrolysis in the presence of hexadecyltrimethylammonium bromide, polyoxyethylene(20) nonylphenol, and sodium dodecyl sulfate are listed in Tables 4, 7, 8, 11, 12, and 15.

The pseudo-first-order rate constants for the hydrolysis of p-nitrophenyl phenylphosphonate in these three detergents are presented in Tables 20, 21, and 22.

Tables 23 and 24 give the pseudo-first-order rate constants for the hydrolysis of p-nitrophenyl phenylphosphonate in certain sodium and potassium hydroxide solutions. Those for the hydrolysis in various salt solutions are listed in Table 25. The rate constants for the hydrolysis of some sodium deuteroxide solutions are given in Table 26.

The pH of the buffered solutions was measured, in all cases, at the same temperature at which the hydrolyses were conducted.

B. Evaluation of Kinetic Results

The hydrolyses were carried out under pseudo-first-order conditions, and the kinetic results fitted the first-order rate equation mentioned above. The observed rate constants were calculated from the slopes of graphs in which the logarithm of the

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

phosphonate ester concentration is plotted against time. The former is expressed by physical properties to which it is linearly related, in this case, the absorbance of the p-nitrophenoxide ion. The units of the observed rate constants, k_ψ, are $sec.^{-1}$ and those of the second-order rate constants, k_2, are liter $mole^{-1}sec.^{-1}$

C. Determination of Micelle-Substrate Binding Constants

The basic hydrolysis of bis p-nitrophenyl phenylphosphonate was carried out initially in aqueous dioxane (90/10, v/v) at 25.00°C. (Table 3). The second-order rate constant for this reaction in the absence of surfactant was taken as that for the reaction in the aqueous bulk phase (k_o). Low solubility of the phosphonate diester in water necessitated the use of dioxane as a cosolvent for all kinetic studies. Detergent concentration-rate profiles were then determined for this hydrolysis reaction over a wide range of surfactant concentrations in aqueous dioxane solutions of CTAB, NaLS, and PENP. These plots are given in Figures 6, 7, and 8 and the data is summarized in Tables 5, 9, and 13. The profile for CTAB goes through a maximum at approximately 2×10^{-3} M detergent. Those for PENP and NaLS, however, are seen to initially decrease rapidly and then remain essentially constant over a considerably large range of surfactant concentrations.

Binding constants were calculated from the slopes of plots of detergent concentration against the left side of equation 16:

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$$\frac{k_\psi - k_o}{k_m - k_\psi}$$

and equation 17:

$$\text{slope} = \frac{K}{N}$$

The data for these plots are given in Tables 6, 10, and 14. The rate constants in the micellar phase, k_m in the above expression, are obtained from the previously described detergent concentration-rate profiles. For CTAB, k_m is taken as the maximum rate constant in the detergent concentration-rate profile. For the inhibiting surfactants there are no corresponding minimum numbers. Here k_m is taken as the average value of those rate constants located in the region of the detergent concentration-rate profiles where the slope is very close to zero.

Straight lines were obtained in these binding constant plots for those second-order rate constants whose values are not too similar to k_o or k_m. Since the rate acceleration and retardations were appreciable for all three surfactants, it was possible to select "intermediate" detergent concentrations which would give rise to rate constants meeting these requirements. The binding constants thus calculated for these surfactants are listed in Table 16. They are the product of the slope values multiplied by the appropriate aggregation numbers, which are also given in Table 16. The three binding constants are quite large and indicate that the bis p-nitrophenyl phenylphosphonate substrate is extensively solubilized by each of the detergents.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

D. Calculation of Activation Parameters

Because of the sensitivity of micellar properties, such as shape, critical micelle concentration, and aggregation number to variation in temperature,[11,12] the temperature range over which activation parameters could be determined was restricted. Second-order rate constants were determined, therefore, only at 15.00°, 25.00°, and 35.00°C. Several factors which preclude the use of a wider temperature range are the following. First, changes in the above micellar properties affect the rates of reaction in the micellar phase.[1,6,24,29] In order to obtain meaningful activation parameters, it is obvious that such changes should be kept as small as possible. Second, temperature effects have also been observed for the incorporation of substrates into micelles.[1,13-16,20,23,26,28] However, since the three micelle-substrate binding constants for bis p-nitrophenyl phenylphosphonate are so large (Table 16), it is felt that small variations in temperature should not affect solubilization significantly.

Temperature effects on the shape, CMC, and aggregation number of the two ionic detergents are not believed to be large for the limited temperature range employed in these activation parameter determinations. In addition, relatively small changes in the CMC were compensated for in the following way. Those surfactant concentrations corresponding to the k_m values (whose selection is described above) were employed in the basic hydrolyses conducted at 15.00° and 35.00°C. If the critical micelle concentrations were not substantially altered (and hence the detergent concentration-rate

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

profiles commensurately displaced), these surfactant concentrations would still approximate the desired maximum or minimum values.

Activation parameters for the hydrolysis of bis p-nitrophenyl phenylphosphonate in hexadecyltrimethylammonium bromide and sodium dodecyl sulfate are given in Table 17.

In the case of PENP, however, even the small variations in temperature described above changed the micellar properties sufficiently (especially the aggregation number) to preclude the calculation of activation parameters. On the other hand, micellar effects on the hydrolyses of p-nitrophenyl phenylphosphonate are very small or negligible for all three detergents. Therefore, neither binding constants nor activation parameters were determined for this substrate because of the relatively large errors attendant in measurements involving small differences.

The energies of activation were calculated from the slopes of plots of the logarithm of the second-order rate constants against the reciprocal of the temperature by means of the following relationship:

$$E_a = -2.303\ R\ (\text{slope}) \qquad (21)$$

The entropies of activation at 25.00°C. were obtained by substituting into the following expression:

$$\Delta S^* = 2.303R\ [\log k_2 - \frac{\log ek_BT}{h} + \frac{E_a}{2.303RT}] \qquad (22)$$

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

where k_B is the Boltzmann constant and h is Planck's constant. The enthalpies of activation at 25.00°C. are also included and are related to the energies of activation in the following way:

$$\Delta H^* = E_a - RT \qquad (23)$$

The units of E_a and ΔH^* are kcal. $mole^{-1}$, and ΔS^* is expressed in entropy units, e.u.

E. Determination of Critical Micelle Concentrations

In the case of CTAB and NaLS, but not PENP, the appearance of micellar effects occurred at detergent concentrations below the critical micelle concentration values given in Table 1. However, dioxane, buffers, and solubilized material are known to affect the CMC. "Apparent critical micelle concentrations" can be estimated from detergent concentration-rate profiles as those surfactant concentrations at which micellar effects are first observed. For purposes of comparison the CMC values of the two ionic detergents were determined independently by the spectral change method. Bromphenol blue was used for hexadecyltrimethylammonium bromide and pinacyanol chloride for sodium dodecyl sulfate. The bromphenol blue plot exhibits the characteristic discontinuity, or "break," which serves to identify the critical micelle concentration. The pinacyanol chloride plot, however, is rather spectacular in that three absorbances can be monitored, and they undergo considerable change at almost precisely the same sodium dodecyl sulfate

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

concentration. The changes in optical density at various wavelengths with changing detergent concentrations are given in Tables 18 and 19 and Figures 4 and 5.

The critical micelle concentrations of the ionic surfactants are much more sensitive to added electrolytes and organic solvents than that of the nonionic detergent.[11,12] As anticipated, the critical micelle concentrations of the former were found to be smaller than their literature values, ie. those determined in aqueous surfactant systems. The CMC of hexadecyltrimethylammonium bromide decreased from a value of 9.2×10^{-4} M in aqueous solution[1] to approximately 1.3×10^{-4} M in the dioxane-buffer solutions employed in the present work. Similarly, the CMC of sodium dodecyl sulfate decreased from 8.1×10^{-3} M[1] to approximately 2.5×10^{-3} M. In both cases these experimentally determined critical micelle concentrations, given in Figures 4 and 5, agree well with those estimated from the detergent concentration-rate profiles, shown in Figures 6 and 7.

Conversely, the concentrations of dioxane and buffer (5% and 0.01 M, respectively) employed in the present study were not considered large enough to affect the relatively insensitive critical micelle concentration of the nonionic surfactant.[11,12] The CMC of polyoxyethylene(20) nonylphenol determined in an aqueous surfactant solution is approximately $1.35 - 1.75 \times 10^{-4}$ M.[1] Indeed, the detergent concentration-rate profile, shown in Figure 8, indicates that micellar inhibition commences within this surfactant

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

concentration range. It therefore appears that the critical micelle concentration of PENP is not decreased significantly.

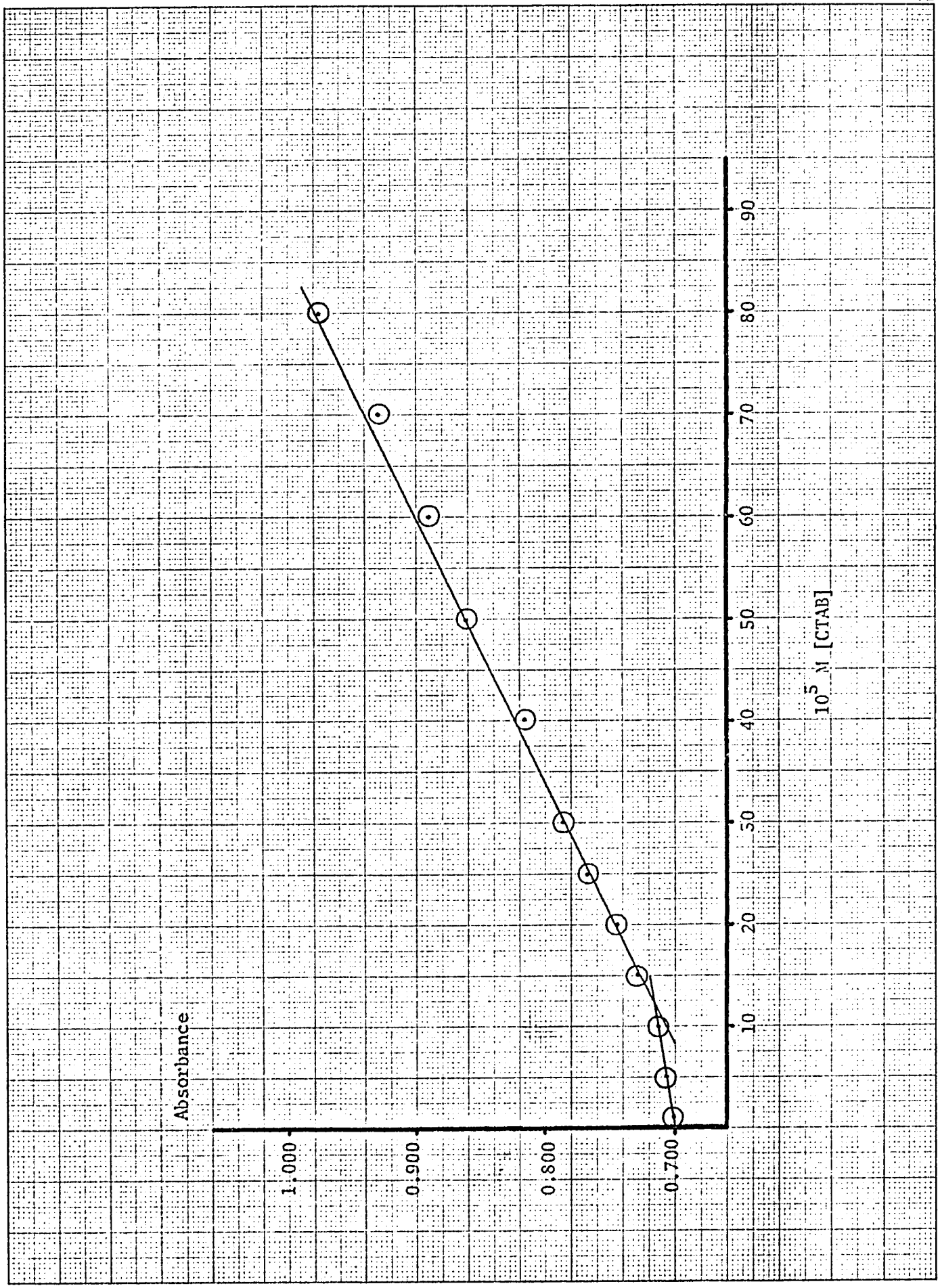
The spectral changes and micellar effects described above can also be attributed to the formation of submicellar aggregates. Such n'mers (ie. dimers, trimers, tetramers, etc.) are, in fact, probably partially responsible for the observed apparent decreases in critical micelle concentration. However, precise particle size-determining experiments are needed to elucidate the nature of the catalysts and inhibitors at detergent concentrations at which incipient micellar effects are observed.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

FIGURE 4

The Detergent Concentration-Absorbance Profile for 0.01 M $Na_2B_4O_7$ and 5.00/95.00 Dioxane-water (v/v) Hexadecyltrimethylammonium Bromide and 4.50×10^{-4} M Bromphenol Blue Solutions.

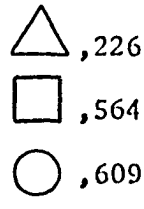
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



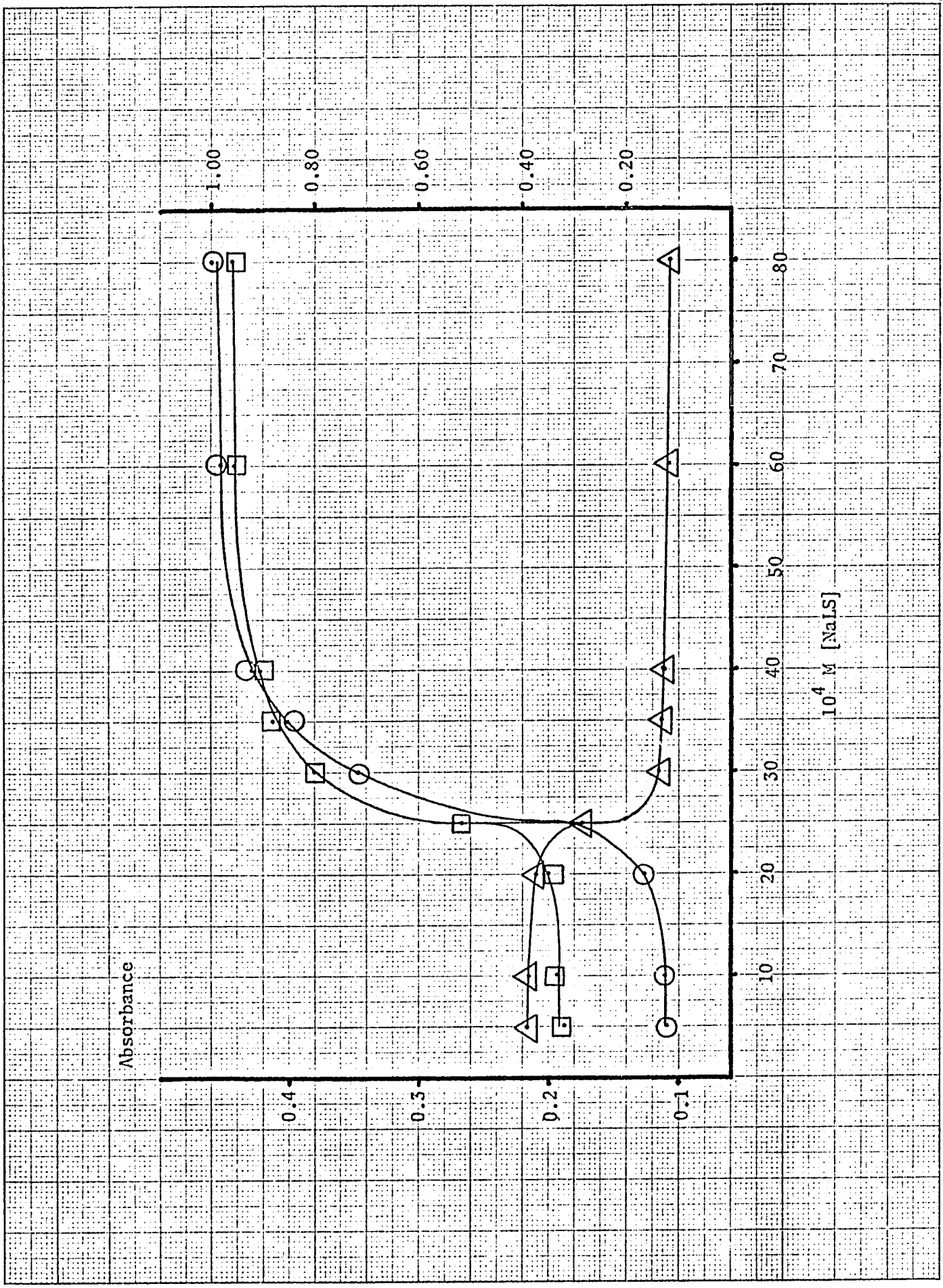
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

FIGURE 5

The Detergent Concentration-Absorbance Profile for 0.01 M $Na_2B_4O_7$ and 5.00/95.00 Dioxane-water (v/v) Sodium Dodecyl Sulfate and 6.43 x 10^{-4} M Pinacyanol Chloride Solutions. The Left-hand Scale Relates to the Absorptions at 226 and 564 nm, the Right to that at 609 nm:



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

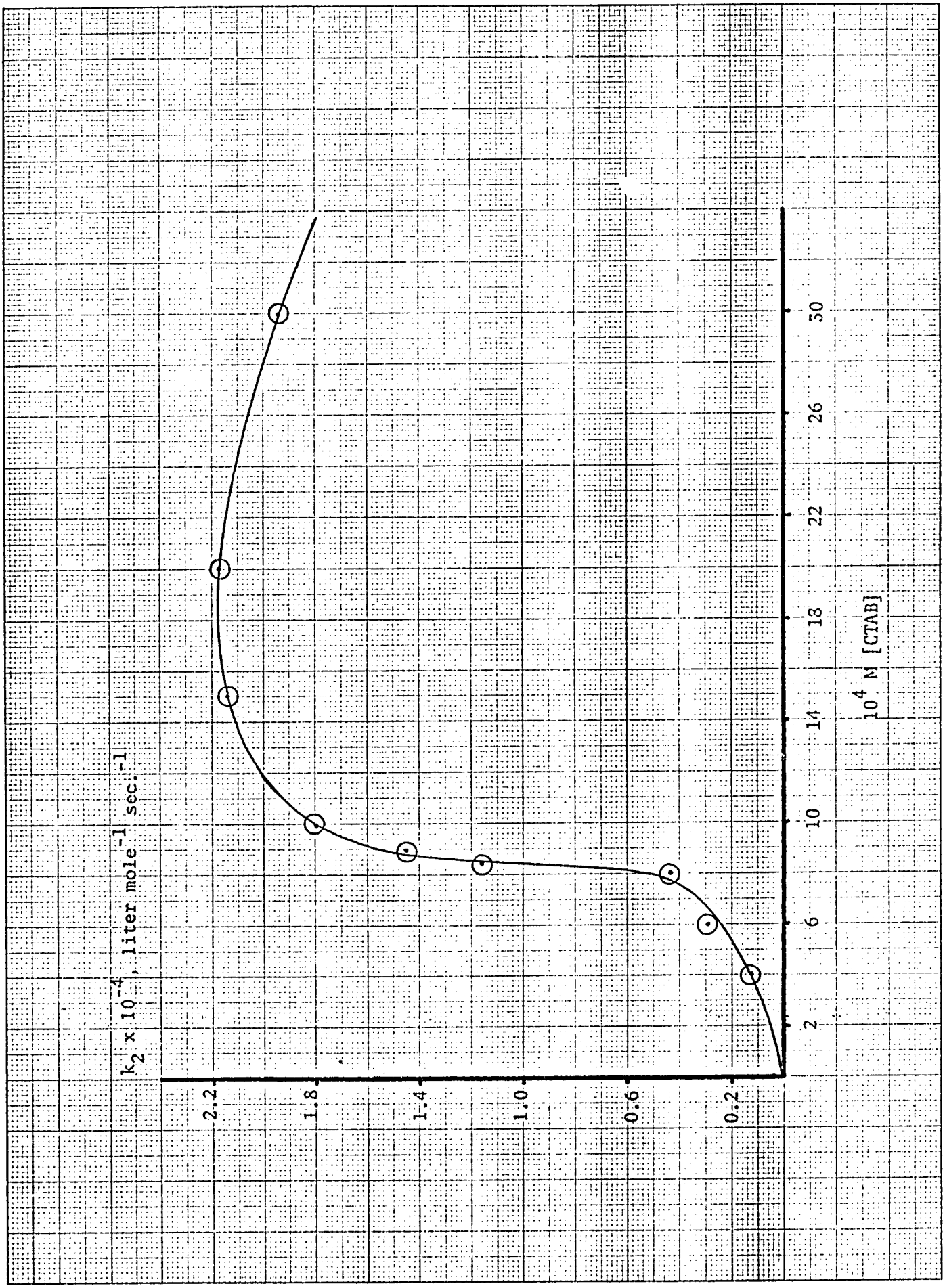


Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

FIGURE 6

The Detergent Concentration-Rate Profile for the Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Hexadecyltrimethylammonium Bromide Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

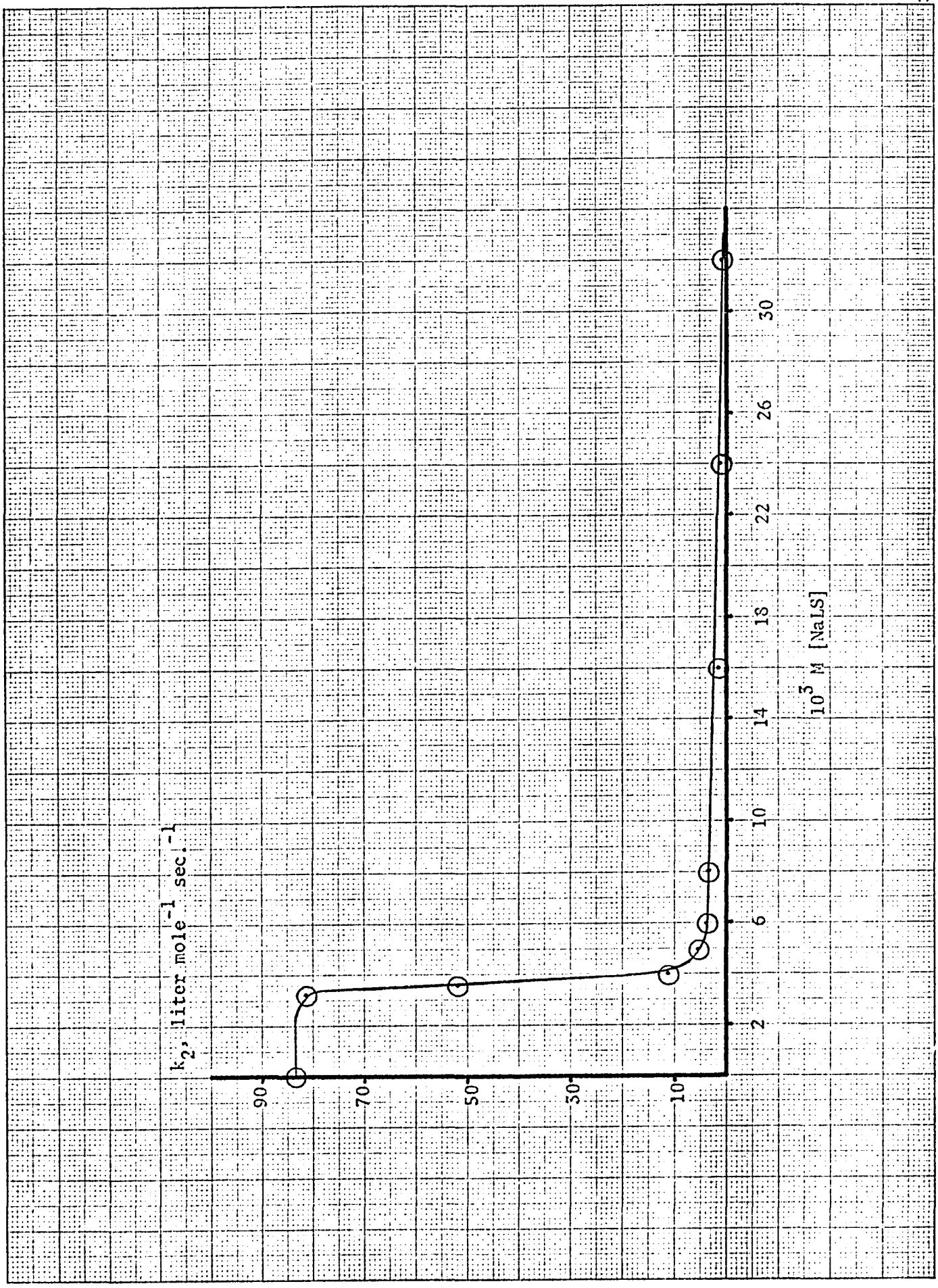


Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

FIGURE 7

The Detergent Concentration-Rate Profile for the Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Sodium Dodecyl Sulfate Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

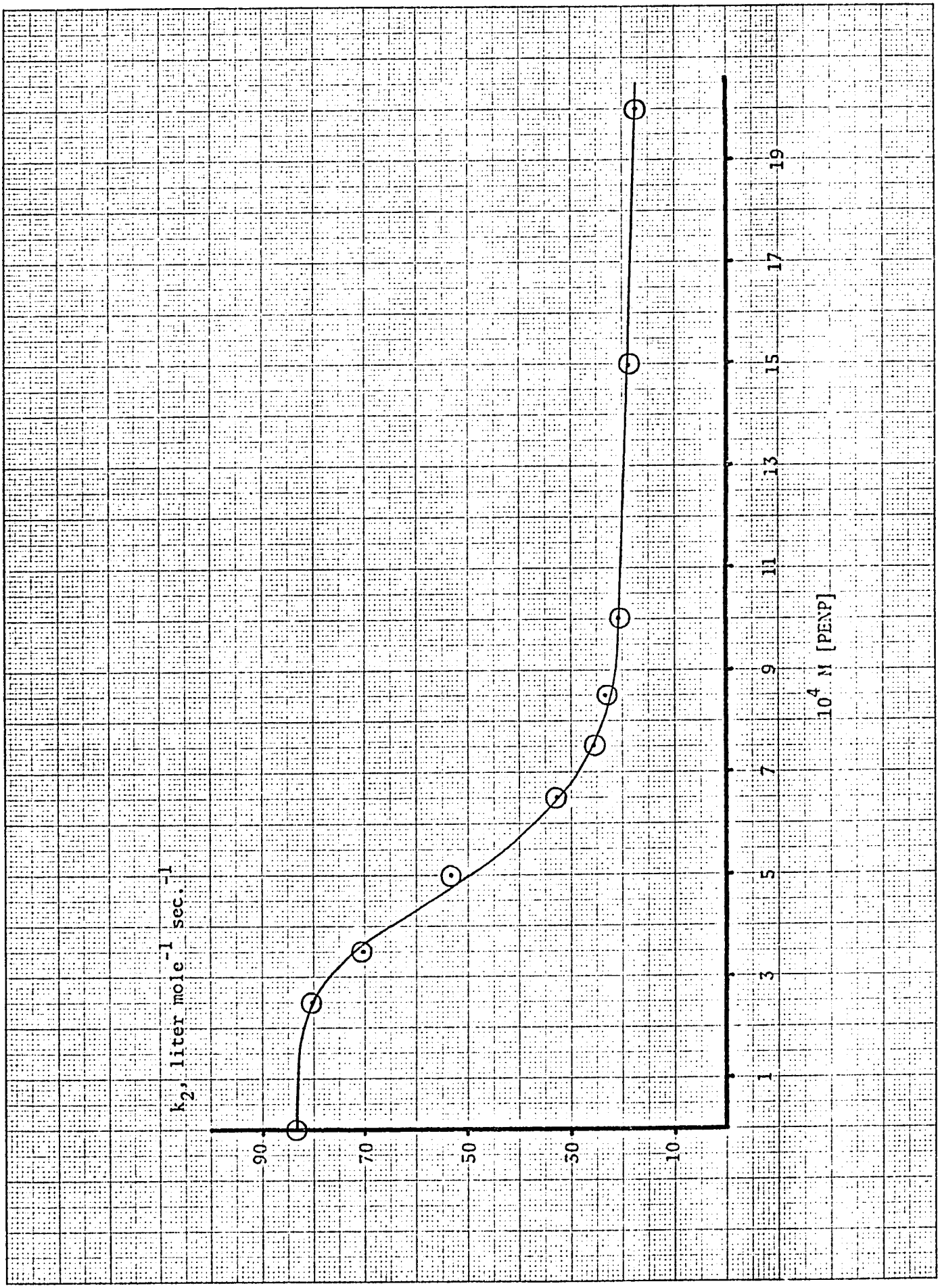


Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

FIGURE 8

The Detergent Concentration-Rate Profile for the Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Polyoxyethylene(20) Nonylphenol Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 3

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in 10.00/90.00 Dioxane-water (v/v) at 15.00°, 25.00°, and 35.00°C.

	15.00°C.	25.00°C.	35.00°C.
pH*		$10^4 k_\psi$, sec.$^{-1}$	
8.59		3.22	
8.62			5.91
8.71	2.48		
8.72			7.54
8.73		4.44	
8.88	3.68	6.43	
8.90			11.2
9.05		9.40	16.0
9.06	5.55		
9.15		12.1	
9.18		12.7	
9.20	7.64		
9.23			24.3
9.30	9.90		
9.40	11.8		
9.42		22.2	
		k_2, liter mole^{-1} sec.$^{-1}$	
	48.1	83.5	141

*0.01M $Na_2B_4O_7$ buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 4

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Hexadecyltrimethylammonium Bromide (CTAB) Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

	10^4 M [CTAB]	
	4.00	6.00
pH*	$10^3 k_\psi$, sec.$^{-1}$	
8.34		6.34
8.45		8.15
8.51		9.40
8.61	4.56	
8.70	5.70	
8.75		16.3
8.79	6.97	
8.88		21.9
8.90	9.07	
9.10	14.6	
9.13	15.1	
	$10^{-3} k_2$, liter mole^{-1} sec.$^{-1}$	
	1.12	2.89

*0.01 M $Na_2B_4O_7$ buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 4 (Continued)

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Hexadecyltrimethylammonium Bromide (CTAB) Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

	10^4 M [CTAB]	
	8.00	8.50
pH*	$10^3 k_\psi$, sec.$^{-1}$	$10^2 k_\psi$, sec.$^{-1}$
8.18	6.77	
8.20		1.86
8.30	9.47	
8.34		2.55
8.35	9.58	
8.47		3.42
8.48	13.2	
8.39		4.49
8.79		7.14
8.97		10.6
9.03		12.5
	$10^{-3} k_2$, liter mole^{-1} sec.$^{-1}$	
	4.38	11.6

*0.01 M $Na_2B_4O_7$ buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 4 (Continued)

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Hexadecyltrimethylammonium Bromide (CTAB) Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

	10^4 M [CTAB]	
	9.00	10.00
pH*	10^2k_ψ, sec.$^{-1}$	
8.08	1.70	2.12
8.24	2.49	
8.28		3.27
8.35	3.28	
8.52		6.12
8.56	5.33	
8.68		8.68
8.72	7.65	
8.90		14.3
8.93	12.4	
8.97	13.4	
9.10		22.6
9.12		23.1
	$10^{-4}k_2$, liter mole^{-1} sec.$^{-1}$	
	1.45	1.80

*0.01 M $Na_2B_4O_7$ Buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 4 (Continued)

Hydrolysis of Bis p-Nitropheny1 Phenylphosphonate in Hexadecyltrimethylammonium Bromide (CTAB) Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

	10^3 M [CTAB]	
	1.50	2.00
pH*	$10^2 k_\psi$, sec.$^{-1}$	
8.03	2.34	2.50
8.23		3.54
8.27	4.03	
8.48	6.43	6.50
8.69	10.7	10.9
8.81	13.3	
8.89		16.6
9.00	21.0	
9.03	22.3	
9.11		28.8
9.13		29.1
	$10^{-4} k_2$, liter mole^{-1} sec.$^{-1}$	
	2.14	2.17

*0.01 M $Na_2B_4O_7$ buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 4 (Continued)

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Hexadecyltrimethylammonium Bromide (CTAB) Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

	3.00×10^3 M [CTAB]
pH*	$10^2 k_\psi$, $sec.^{-1}$
8.03	1.85
8.12	2.50
8.27	3.31
8.34	4.10
8.43	5.18
8.51	6.10
8.72	10.1
8.80	12.2
8.92	16.1
8.96	18.4
8.98	18.6
	$10^{-4} k_2$, liter $mole^{-1}$ $sec.^{-1}$
	1.94

*0.01 M $Na_2B_4O_7$ buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 5

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Hexadecyltrimethylammonium Bromide (CTAB) Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

10^4 M (CTAB)	10^{-3} k_2, liter $mole^{-1}$ $sec.^{-1}$
	0.084
4.00	1.12
6.00	2.89
8.00	4.38
8.50	11.6
9.00	14.5
10.00	18.0
15.00	21.4
20.00	21.7
30.00	19.4

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 6

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Hexadecyltrimethylammonium Bromide (CTAB) Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

10^4 M [CTAB]	$\frac{k_\psi - k_o}{k_m - k_\psi}$
6.00	0.15
8.00	0.25
8.50	1.15
9.00	2.06
10.00	3.91

slope = 1.81×10^4

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 7

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in 2.00 x 10^{-3} M Hexadecyltrimethylammonium Bromide (CTAB) Solution in 5.00/95.00 Dioxane-water (v/v) at 15.00° and 35.00°C.

pH*	15.00°C $10^2 k_\psi$, sec.$^{-1}$	35.00°C $10^2 k_\psi$, sec.$^{-1}$
8.03		3.73
8.09	1.10	
8.17		5.10
8.18	1.24	
8.33	1.80	
8.36		8.02
8.46	2.42	
8.55		12.1
8.68	4.10	
8.70		17.0
8.94	7.45	
9.00	8.70	
	$10^{-3} k_2$, liter mole^{-1} sec.$^{-1}$	
	8.75	33.9

*0.01 M $Na_2B_4O_7$ buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 8

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Polyoxyethylene(20) Nonylphenol Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

	10^4 M [PENP]	
	2.50	3.50
pH*	$10^4 k_\psi$, sec.$^{-1}$	
8.76	4.63	
8.91	6.50	
9.07	9.51	
9.14		9.74
9.20	12.9	
9.24	13.6	
9.26		12.8
9.43		18.8
9.44	22.2	
9.49		21.4
9.50	25.5	
9.57	29.7	
9.61		28.3
9.78	47.8	
	k_2, liter mole^{-1} sec.$^{-1}$	
	80.1	70.2

*0.01 M $Na_2B_4O_7$ buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 8 (Continued)

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Polyoxyethylene(20) Nonylphenol Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

	10^4 M [PENP]	
	5.00	6.50
pH*	$10^4 k_\psi$, sec.$^{-1}$	
9.28	10.3	
9.32	10.9	
9.44	14.5	
9.45		9.06
9.55	18.8	
9.63		13.8
9.65	23.8	
9.68		15.2
9.81		20.8
9.84	36.3	
9.96		30.2
10.08		37.7
	k_2, liter mole^{-1} sec.$^{-1}$	
	53.1	32.3

*0.01 M $Na_2B_4O_7$ buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 8 (Continued)

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Polyoxyethylene(20) Nonylphenol Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

	10^4 M [PENP]	
	7.50	8.50
pH*	$10^3 k_\psi$, sec.$^{-1}$	
9.71	1.31	1.22
9.76	1.48	1.34
9.88	1.95	1.79
10.05		2.61
10.07	2.99	
10.14		3.20
10.17	3.80	
10.26		4.19
10.27	4.73	
	k_2, liter mole^{-1} sec.$^{-1}$	
	25.6	23.4

*0.01 M $Na_2B_4O_7$ buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 8 (Continued)

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Polyoxyethylene(20) Nonylphenol Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

	10^3 M [PENP]	
	1.00	1.50
pH*	$10^3 k_\psi$, sec.$^{-1}$	
9.78		1.14
9.80	1.32	
9.93	1.79	1.62
10.09	2.56	2.32
10.17	3.05	2.77
10.30		3.74
10.38	4.93	
10.40		4.74
10.50	6.54	
	k_2, liter mole^{-1} sec.$^{-1}$	
	20.8	18.9

*0.01 M $Na_2B_4O_7$ buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 8 (Continued)

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Polyoxyethylene(20) Nonylphenol Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

	2.00×10^3 M [PENP]
pH*	$10^4 k_\psi$, sec.$^{-1}$
9.70	9.05
9.79	10.6
9.92	14.6
10.07	20.7
10.16	26.0
10.21	28.2
10.27	32.2
10.38	42.3
10.52	58.2

k_2, liter mole^{-1} sec.$^{-1}$
17.5

*0.01 M $Na_2B_4O_7$ buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 9

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Polyoxyethylene(20) Nonylphenol Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

10^4 M (PENP)	k_2, liter $mole^{-1}$ $sec.^{-1}$
	83.5
2.50	80.1
3.50	70.2
5.00	53.1
6.50	32.3
7.50	25.6
8.50	23.4
10.00	20.8
15.00	18.9
20.00	17.5

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 10

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Polyoxyethylene(20) Nonylphenol Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

10^4 M [PENP]	$\frac{k_\psi - k_o}{k_m - k_\psi}$
5.00	0.895
6.50	3.88
7.50	8.91
8.50	14.0
10.0	36.9

Slope = 5×10^4

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 11

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in 1.50×10^{-3} M Polyoxyethylene(20) Nonylphenol Solution in 5.00/95.00 Dioxane-water (v/v) at 15.00° and 35.00°C.

	15.00°C.	35.00°C.
pH*	$10^4 k_\psi$, sec.$^{-1}$	$10^4 k_\psi$, sec.$^{-1}$
8.58		5.86
8.74		8.57
8.90		12.3
9.02		17.0
9.07		17.6
9.22		26.0
9.50	4.94	
9.55	5.40	
9.63	6.60	
10.13	21.0	
10.20	24.7	
10.24	26.2	
10.46	44.5	
10.56	56.5	
10.65	68.1	
	k_2, liter mole^{-1} sec.$^{-1}$	
	15.4	155

*0.01 M $Na_2B_4O_7$ buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 12

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Sodium Dodecyl Sulfate (NaLS) Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

3.20×10^{3} M [NaLS]

pH*	$10^{4}k_{\psi}$, sec.$^{-1}$
8.28	1.55
8.39	2.02
8.57	3.04
8.74	4.47
8.82	5.35
8.98	7.78
9.08	9.77
9.15	11.5
9.25	14.4
9.43	21.8

k_2, liter mole^{-1} sec.$^{-1}$

81.3

*0.01 M $Na_2B_4O_7$ buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 12 (Continued)

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Sodium Dodecyl Sulfate (NaLS) Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

3.60×10^{3} M [NaLS]

pH*	$10^{4}k_{\psi}$, sec.$^{-1}$
8.48	1.56
8.62	2.17
8.80	3.30
8.90	4.17
9.05	5.95
9.10	6.48
9.21	8.41
9.40	12.9
9.53	17.7
9.63	22.0
10.09	63.4
10.59	150.

k_2, liter mole^{-1} sec.$^{-1}$
52.0

*0.01 M $Na_2B_4O_7$ buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 12 (Continued)

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Sodium Dodecyl Sulfate (NaLS) Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

	10^3 M [NaLS]	
	4.00	5.00
pH*	$10^4 k_\psi$, sec.$^{-1}$	
9.68	5.47	
9.81	7.46	
9.84	7.85	
9.95		4.82
9.96	10.2	
10.08		6.43
10.10	14.2	
10.23	19.2	
10.24		9.39
10.34		11.8
10.43		14.7
10.58		20.6
	k_2, liter mole^{-1} sec.$^{-1}$	
	11.3	5.37

*0.01 M $Na_2B_4O_7$ buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 12 (Continued)

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Sodium Dodecyl Sulfate (NaLS) Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

	10^3 M [NaLS]	
	6.00	8.00
pH*	$10^4 k_\psi$, sec.$^{-1}$	
9.61		1.44
9.98	3.90	3.34
10.11	5.10	
10.29	7.76	
10.32		7.30
10.40	9.89	
10.51	12.8	
10.59		13.7
10.65	17.7	
10.85		26.2
11.26		64.5
	k_2, liter mole^{-1} sec.$^{-1}$	
	3.95	3.50

*pH 9.61 - 10.85, 0.01 M $Na_2B_4O_7$ buffer

pH 11.26, 0.01 M Na_2HPO_4 buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 12 (Continued)

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Sodium Dodecyl Sulfate (NaLS) Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

	10^2 M [NaLS]		
	1.60	2.40	3.20
pH*	$10^4 k_\psi$, sec.$^{-1}$		
10.16	1.74		
10.44	3.40		
10.52	4.02		
10.70	5.82		
10.90		7.53	
11.14	17.0	14.2	
11.16			11.1
11.34	31.2		17.1
11.40		42.6	
11.66	58.1		35.8
11.70	60.6		
	k_2, liter mole^{-1} sec.$^{-1}$		
	1.25	1.02	0.78

*pH 10.16 - 10.70, 0.01 M $Na_2B_4O_7$ buffer

pH 10.90 - 11.70, 0.01 M Na_2HPO_4 buffer

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 13

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Sodium Dodecyl Sulfate (NaLS) Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

10^3 M (NaLS)	k_2, liter $mole^{-1}$ $sec.^{-1}$
	83.5
3.20	81.3
3.60	52.0
4.00	11.3
5.00	5.37
6.00	3.95
8.00	3.50
16.00	1.25
24.00	1.02
32.00	0.78

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 14

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in Sodium Dodecyl Sulfate (NaLS) Solution in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

10^3 M [NaLS]	$\frac{k_\psi - k_o}{k_m - k_\psi}$
3.60	0.63
4.00	7.0
5.00	18.0
6.00	26.9
8.00	32.1

slope = 1.10×10^4

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 15

Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate in 2.40×10^{-2} M Sodium Dodecyl Sulfate (NaLS) Solution in 5.00/95.00 Dioxane-water (v/v) at 15.00° and 35.00°C.

	15.00°C.	35.00°C	
pH	$10^4 k_\psi$, sec.$^{-1}$	$10^4 k_\psi$, sec.$^{-1}$	Buffer
9.76		3.52	0.01 M $Na_2B_4O_7$
9.95		5.36	"
10.05		6.77	"
10.22		10.1	"
10.33		12.7	"
10.41		15.3	
11.13	4.80		0.01 M Na_2HPO_4
11.18	5.31		"
11.23	5.87		"
11.44	9.55		"
11.64	15.3		"
11.83	23.4		"
	k_2, liter mole^{-1} sec.$^{-1}$		
	0.35	6.0	

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 16

Binding Constants of Bis p-Nitrophenyl Phenylphosphonate in 5.00/95.00 Dioxane-water (v/v) at 25.00°C.

Detergent	N	10^4 [slope]	$10^{-5}K$, M^{-1}
NaLS	62	1.10	6.8
CTAB	61	1.81	11.1
PENP	62	5.4	31

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 17

Activation Parameters for the Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate

Detergent	10^3 M $[C_D]$	E_a (kcal. $mole^{-1}$)	ΔH^*	ΔS^* (e.u.)†
		10.0	9.4	-18
CTAB	2.00	12.0	11.4	-1
NaLS	24.0	18.3	17.7	+1
PENP	1.50	----	----	---

†25.00°C.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 18

Absorbance (O.D.) of Bromophenol Blue in 0.01 M $Na_2B_4O_7$ and 5.00/95.00 Dioxane-water (v/v) Hexadecyltrimethylammonium Bromide (CTAB) Solutions

10^5 M [CTAB]	O.D. (602nm)
1.00	0.701
5.00	0.706
10.0	0.713
15.0	0.728
20.0	0.744
25.0	0.768
30.0	0.786
40.0	0.816
50.0	0.862
60.0	0.890
70.0	0.929
80.0	0.976

[Bromophenol Blue] = 4.50×10^{-5} M

Apparent CTAB Critical Micelle Concentration = 1.24×10^{-4} M

Literature CTAB Critical Micelle Concentration = 9.1×10^{-4} M[1]

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 19

Absorbance (O.D.) of Pinacyanol Chloride in 0.01 M $Na_2B_4O_7$ and 5.00/95.00 Dioxane-water (v/v) Sodium Dodecyl Sulfate (NaLS) Solutions

10^4 M [NaLS]	O.D. (226nm)	O.D. (564nm)	O.D. (609nm)
5.00	0.217	0.188	0.122
10.0	0.215	0.194	0.126
20.0	0.210	0.200	0.164
25.0	0.174	0.267	0.533
30.0	0.115	0.380	0.712
35.0	0.113	0.412	0.850
40.0	0.111	0.422	0.920
60.0	0.108	0.442	0.980
80.0	0.107	0.444	1.00

[Pinacyanol Chloride] = 6.43×10^{-4} M

Apparent NaLS Critical Micelle Concentration = 2.5×10^{-3} M

Literature NaLS Critical Micelle Concentration = 8.1×10^{-3} M [1]

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 20

Hydrolysis of p-Nitrophenyl Phenylphosphonate in 0.003 M Hexadecyltrimethylammonium (CTAB) Bromide Solution at 45.00° C.

pH	$10^5 k_\psi$, sec.$^{-1}$	M [NaOH]
12.90	3.44	0.08
12.95	3.87	0.09
13.00	4.30	0.10
13.30	8.61	0.20
13.48	12.9	0.30

$k_2 = 4.30 \times 10^{-4}$ liter mole $^{-1}$ sec.$^{-1}$

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 21

Hydrolysis of p-Nitrophenyl Phenylphosphonate in 0.024 M Sodium Dodecyl Sulfate (NaLS) Solution at 45.00°C.

pH	$10^5 k_\psi$, sec.$^{-1}$	M [NaOH]
12.90	2.50	0.08
12.95	2.87	0.09
13.00	3.18	0.10
13.30	6.36	0.20
13.48	9.60	0.30

$10^4 k_2$, liter mole^{-1} sec.$^{-1}$	
No Detergent*	0.024 M NaLS
3.42	3.20

*Unpublished results of E. J. Fendler.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 22

Hydrolysis of p-Nitrophenyl Phenylphosphonate in 0.002 M Polyoxyethylene(20) Nonylphenol Solution at 45.00°C.

pH	$10^5 k_\psi$, sec.$^{-1}$	M [NaOH]
12.95	2.32	0.09
13.00	2.60	0.10
13.30	5.21	0.20
13.48	7.85	0.30
13.60	10.5	0.40

$k_2 = 2.62 \times 10^{-4}$ liter mole^{-1} sec.$^{-1}$

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 23

Hydrolysis of p-Nitrophenyl Phenylphosphonate in Sodium Hydroxide Solution at 25.00°C.

M (NaOH)	$10^4 k_\psi$, sec.$^{-1}$
0.25	0.137
0.50	0.290
1.00	0.673
2.00	2.38
3.00	4.66
4.00	9.56
5.00	17.9

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 24

Hydrolysis of p-Nitrophenyl Phenylphosphonate in Potassium Hydroxide Solution at 25.00°C.

M [KOH]	$10^5 k_\psi$, sec.$^{-1}$
0.75	0.558
1.00	0.807
2.00	2.25
3.00	5.18
4.00	10.6
5.00	18.9

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 25

Basic Hydrolysis of p-Nitrophenyl Phenylphosphonate in the Presence of Electrolytes at 25.00°C.

M [Salt]	M [NaOH]	$10^5 k_\psi$, sec.$^{-1}$
	1.00	6.73*
1.00 M $NaClO_4$	1.00	8.58
1.00 M KCl	1.00	9.57
1.00 M NaBr	1.00	9.94
1.00 M NaCl	1.00	10.4

*Unpublished results of E.J. Fendler.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE 26

Hydrolysis of p-Nitrophenyl Phenylphosphonate in Sodium Deuteroxide Solution at 25.00° and 45.00°C.

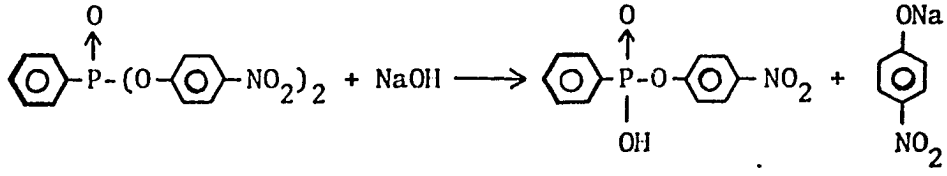
	25.00°C.	45.00°C.
M [NaOD]	$10^5 k_\psi$, sec.$^{-1}$	$10^5 k_\psi$, sec.$^{-1}$
0.10		2.37
0.25	1.32	6.97
0.35		10.3
0.50	3.00	16.3
0.75	5.26	28.2
1.00	7.74	
2.00	24.9	
3.00	46.1	
4.00	78.5	

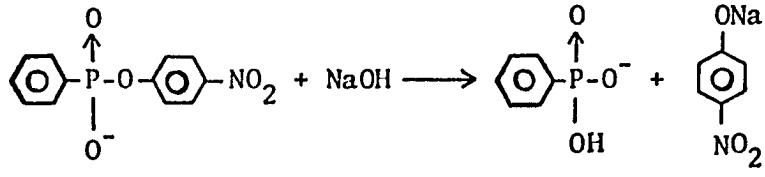
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

IV. DISCUSSION

A. General Introduction

The basic hydrolysis of bis p-nitrophenyl phenylphosphonate takes place in two distinct stages (equations 18 and 19):





The first step involves nucleophilic attack of hydroxide ion on the uncharged phosphonate diester (an anion-molecule reaction). The second step occurs slowly even at very high base concentration and entails nucleophilic attack of hydroxide ion on the resulting p-nitrophenyl phenylphosphonate monoester (an anion-anion reaction). Because of the fundamental differences between these two classes of reactions, they are discussed separately.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

B. Basic Hydrolysis of Bis p-Nitrophenyl Phenylphosphonate

1. Introduction

The second-order rate constant for the basic hydrolysis of bis p-nitrophenyl phenylphosphonate is increased approximately 250-fold by cationic hexadecyltrimethylammonium bromide (CTAB) micelles, decreased nearly 80-fold by anionic sodium dodecyl sulfate (NaLS) micelles, and reduced about 4-fold by nonionic micelles of polyoxyethylene(20) nonylphenol (PENP). These rate effects can be understood superficially by considering (a) the different rates of reaction of the phosphonate diester in the micellar and bulk phases and (b) the distribution of the diester substrate between these two phases.[1,7]

The binding, or association, constants (equation 1) of bis p-nitrophenyl phenylphosphonate with these detergents are both very large and of approximately the same magnitude (Table 16). Two conclusions can be drawn from these facts. First, the magnitude of these binding constants indicates that the phosphonate diester is extensively solubilized by all three detergents. Second, their similarity in magnitude suggests that differences in the micellar effects of these three surfactants can be ascribed essentially to differing rates of reaction in the micellar phase relative to that in the bulk solution. The latter inference allows direct comparison of micellar effects on the basis of reaction rates in the micellar phase since the phosphonate diester is solubilized to approximately the same extent in all three detergents.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Differences in rates of reaction in the micellar phase relative to the bulk solution can be attributed basically to electrostatic and hydrophobic interactions between the micelles and the reactants and transition states.[1,6] Discussion of these interactions requires the definition of the micellar system and the initial and transition states of the reaction under consideration.

Micellar systems consisting of a solubilized substrate and an external reactant are, by definition, heterogenous. Because of the equilibrium which exists between the solubilized and nonsolubilized substrate, reaction can take place, in principle, in both the micellar and bulk phases. However, analysis is greatly simplified if reaction occurs almost exclusively in the micellar phase. This condition is achieved when (a) the substrate is located almost entirely in the micellar phase, ie. the micelle-substrate binding constant is very large, and (b) the rate of reaction in the micellar phase is considerably greater than that in the bulk solution.

2. Hexadecyltrimethylammonium Bromide (CTAB) Catalysis

The CTAB catalyzed basic hydrolysis of bis p-nitrophenyl phenylphosphonate meets both of the above requirements. The initial state of this reaction consists of the phosphonate diester located in the micellar phase and the hydroxide ion nucleophile situated in the bulk phase. Typically, in such anion-molecule reaction systems, the uncharged substrate interacts with the micellar phase by virtue of its hydrophobic properties while the charged species interacts electrostatically with this phase.[6] The transition state is a

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

large, low charge density, monoanionic entity. It can be regarded as a composite species, possessing the character of both an S_N2-type transition state and an anionic pentacovalent adduct similar to that postulated for the basic hydrolysis of carboxylic esters.[55,56] Activation parameters determined for the basic hydrolysis of bis p-nitrophenyl phenylphosphonate in the absence of detergent (Table 17) agree with those generally found for nucleophilic attack on the phosphorus atom of trisubstituted phosphonate and phosphate esters and thus support the above transition state description.[20,55-59]

The general features of micellar catalyzed ion-molecule reactions are the following: (a) solubilization of an uncharged reactant by the micelle, (b) favorable location and orientation of this substrate in the micelle so that it is both accessible to an external reactant and can form an activated complex without losing its binding to the micelle.[19,23,24] (c) electrostatic attraction of a charged reactant by an oppositely charged micelle, and (d) electrostatic stabilization of an ionic transition state by an oppositely charged micelle. Each of these characteristics is now discussed in turn.

Solubilization is crucial to micellar catalysis because, obviously, its absence precludes micellar effects. However, solubilization of a substrate stabilizes the initial state. Any decrease in the free energy of the initial state must, of itself, reduce the rate of reaction in the micellar phase.[20] Bis p-nitrophenyl phenylphosphonate possesses three highly hydrophobic aryl groups and, as previously mentioned, is extensively solubilized

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

by CTAB micelles. This initial state stabilization is manifested by a 2 kcal/mole increase in the enthalpy of activation of the reaction in the micellar phase relative to that in the bulk solution (Table 17). Similar results have been reported by Bunton and Robinson for the CTAB catalyzed basic hydrolysis of p-nitrophenyl diphenyl phosphate.[20]

Decreases in the enthalpy of activation have been observed for several micellar catalyzed reactions.[17,18,21] However, the substrates in these cases are either monoaryl phosphate dianions or dinitrohalobenzenes, and none of these should be as extensively solubilized as bis p-nitrophenyl phenylphosphonate. Their smaller binding constants support this conclusion of decreased hydrophobicity.

Conversely, it should be remembered that micellar effects are not predicated by the occurrence of substrate solubilization, but rather depend critically on both the location and orientation of the substrate in the micellar phase.[1,24,32] Substantial nmr evidence indicates that polar molecules like bis p-nitrophenyl phenylphosphonate are solubilized near the micellar surface where they are exposed to external reactants.[46,47] The reactivity of the phosphonate diester in the CTAB micellar phase supports this conclusion.

The importance of micellar electrostatic effects on organic equilibria has been recognized for many years.[60] Simple electrostatic considerations predict that (a) cationic micelles should accelerate anion-molecule reactions, (b) anionic micelles should retard them, and (c) nonionic micelles should have little or no effect on these reactions.[1] Several types of interactions which provide the basis for the above predictions are the following: (a) electrostatic attraction and repulsion of reactants, and

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

(b) electrostatic stabilization of the transition state relative to the initial state of the reactants.

The initial state of the reaction presently under consideration has been defined as consisting of the phosphonate diester in the micellar phase and the hydroxide ion nucleophile in the bulk phase. However, these hydroxide ions are not thought to be evenly distributed in the bulk solution. At least ten percent, and perhaps as high as thirty percent, of the total micellar charge is unneutralized;[1] hydroxide ions congregate in the vicinity of the cationic micelles and compete with the detergent counterions for available binding sites in the Stern layer.[7,25-27,29,30,32,35] This type of electrostatic attraction in which an external reactant is concentrated in close proximity to a solubilized one is known as "reactant approximation."

Concentration of hydroxide ions in the vicinity of a solubilized phosphonate diester should require considerably less organization of this reactant when undergoing reaction in the micellar phase than when reacting in the bulk solution. Such reactant approximation should therefore be manifested by a more positive entropy of activation for the micellar reaction, since this parameter is a measure of the difference in the various degrees of freedom between the transition state and the reactants.[61] Moreover, this reactant juxtaposition should greatly facilitate reaction when a substantial net charge exists on the micelles.[7,25-27,29,30,32]

The entropy of activation of the CTAB catalyzed basic hydrolysis of bis p-nitrophenyl phenylphosphonate is 17 e.u. more positive than that for the reaction carried out in the absence of

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

detergent (Table 17). The observed rate enhancement of this process thus arises from the very favorable entropy of activation which more than offsets the previously mentioned increase in enthalpy of activation. Similar results have been reported for the CTAB catalyzed basic hydrolysis of p-nitrophenyl diphenyl phosphate[20] and for the acidic hydrolysis of sodium dodecyl sulfate.[62]

A second type of electrostatic interaction involves stabilization and destabilization of charged transition states. In a study of the reaction of dinitrohalobenzenes with hydroxide ion, Bunton and coworkers found that large, low charge density cations, like tetraalkylammonium ions, stabilize low charge density, anionic transition states relative to small, high charge density anions.[21,63] They examined the effect of high and low charge density cations and anions on (a) the solubility of the dinitrohalobenzenes and on (b) the activity coefficient ratio f_{OH^-}/f^*_{TS}, which comes from the following expression:

$$k_2^s = k_2^o \frac{f_{ArX}\, f_{OH^-}}{f^*_{TS}} \qquad (24)$$

where k_2^s and k_2^o are the second-order rate constants in the presence and absence of salt, respectively, and f_{ArX}, f_{OH^-}, and f^*_{TS} are the activity coefficients of the dinitrohalobenzene, hydroxide ion, and transition state, respectively. Activity coefficients of the dinitrohalobenzenes are obtained from the relative solubilities of these compounds by means of the Setschenov equation:

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

$$\log \frac{S_o}{S} = \log \frac{f}{f_o} \qquad (25)$$

where the standard state for all species is taken as that used for the determination of k_2^o.[21,63]

Both low charge density anions and cations (as their sodium and chloride salts, respectively) decrease the activity coefficients of, ie. "salt-in," the dinitrohalobenzenes. It has been observed that such substrate stabilization must, of itself, reduce the reaction rate.[20] However, low charge density cations greatly increase the f_{OH^-}/f^*_{TS} ratio, and this increase more than offsets the above rate-retarding effect. On the other hand, low charge density anions slightly decrease this activity coefficient ratio.[21,63]

The mean ion activity coefficients of the alkali metal hydroxides increase with decreasing charge density of the cation, but the overall effects are small.[64] Moreover, these effects may well arise from changes in the activity coefficient of the cation, rather than the anion, particularly because hydration of the cation depends very markedly on its charge density. In addition, the empirical parameters which are used in the calculation of individual ion activity coefficients by the extended Debye-Hückel equation are very similar for Na^+, K^+, Rb^+, Cs^+, and $(CH_3)_4N^+$.[65,66] These two pieces of evidence strongly suggest that the individual ion activity coefficient of hydroxide ion is little dependent on the nature of the univalent cation.[63] Variations in the f_{OH^-}/f^*_{TS} ratio are therefore felt to reflect primarily changes in the activity coefficient (and therefore stability) of the anionic transition state, rather than the nucleophilic anion.[21,63]

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Bunton believes that simple analogies can be drawn between the stabilization of anionic transition states by large, low charge density cations and cationic micelles and the destabilization of these transition states by low charge density anions and anionic micelles.[18,21] Grunwald has noted similar behavior, with the effects of micelles being much larger than those of simple salts.[34] Since changes in f_{OH^-}/f^{*}_{TS} ratio should be manifested in the enthalpy of activation, transition state stabilization has been invoked for those micellar catalyzed reactions, mentioned previously, whose acceleration arises from a decrease in this activation parameter.[17,18,21] In the present case it appears that transition state stabilization by CTAB micelles partially offsets the extensive solubilization of bis p-nitrophenyl phenylphosphonate.

Low solubility of the phosphonate diester in water necessitated the use of dioxane as a cosolvent in kinetic studies of both the micellar and nonmicellar hydrolyses. Recently Bunton and coworkers have reported effects due to dioxane on the CTAB catalyzed basic hydrolysis of bis 2,4-dinitrophenyl phosphate. They observed that addition of 1.5 volume percent dioxane approximately doubled both the first- and second-order rate constants of the micellar catalyzed reaction. They concluded that this dioxane effect was primarily due to a reduction in the polarity of the CTAB micelles.[24] Kostenbauder and Shotton have reported rate accelerations of micellar catalyzed reactions upon addition of alcohols and have similarly attributed these effects to decreases in the polarity of the medium along the surface of the micelles.[62,67]

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Decreases in the polarity of the medium in the Stern layer should increase electrostatic interactions in this region.[62,67] It has been noted that electrostatic interactions, which result in (a) congregation of hydroxide ions in the vicinity of the micelles and (b) transition state stabilization, are responsible for the catalytic effect of CTAB micelles on the basic hydrolysis of bis p-nitrophenyl phenylphosphonate. The rate-enhancing effect of dioxane on micellar catalyzed anion-molecule reactions can therefore be ascribed to increased electrostatic interaction between the micelles and the reactants and transition states.

Another feature of the CTAB catalyzed basic hydrolysis of bis p-nitrophenyl phenylphosphonate which merits attention is the multiphasic behavior of its detergent concentration-rate profile. This profile does not exhibit a plateau region as predicted by the following relationship:

$$k_{\psi} = \frac{k_o + k_m K[M]}{1 + K[M]} \qquad (26)$$

but instead displays a maximum. Equation 26 (which is a rearranged form of equation 14) predicts that the observed rate constant, k_{ψ}, should remain at a maximum value (k_m) when all of the substrate is incorporated into the micelles. However, rate maxima have been observed for this and many other micellar catalyzed anion-molecule reactions.[6,7,18-22,26-28,30,68]

Cordes has attributed these rate maxima to detergent counterion, negative salt effects. He argues that at

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

sufficiently high detergent concentrations, surfactant counterions effectively exclude similarly charged reactants, such as hydroxide ions, from the neighborhood of the cationic micelles.[6,26-28,30,68]

An alternative explanation has been proposed by Bunton. He ascribes these rate maxima to deactivation of the anionic nucleophiles by excess cationic micelles.[18-22] He suggests that the optimum number of micelles in this system which involves an oppositely charged external reactant (hydroxide ion) is reached when the bulk of the substrate is incorporated into the existing micelles. Any additional micelles, formed by addition of more detergent, will take up this oppositely charged reactant. Surplus micelles result in a decrease in the reaction rate because a substrate in one micelle should not react with a nucleophile in another.[18,20] Bunton offered the latter explanation when he observed an absence of rate maxima in the CTAB catalyzed hydrolyses of dinitrophenyl phosphates, which otherwise are subject to large rate-retarding effects by added anions.[17] Hydrolyses of 2,4-dinitrophenyl phosphate were later carried out at very high cationic detergent concentrations (up to 0.4 M) with no obvious kinetic effects.[24] These results suggest that the critical factor in cationic detergent catalyzed anion-molecule reactions is not the actual counteranion concentration, but that relative to the concentration of detergent cations.[24]

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

3. Sodium Dodecyl Sulfate (NaLS) Anticatalysis

The basic hydrolysis of bis p-nitrophenyl phenylphosphonate in the presence of NaLS micelles cannot be treated in the simplified manner employed for the CTAB catalyzed reaction. While the micelle-substrate binding constant is also very large (Table 16), the rate of reaction in the micellar phase is much slower than that in the bulk solution. Reaction can now occur in both the micellar phase, where virtually all of the phosphonate diester is located, and in the bulk phase, since the nonmicellar reaction is much faster than the micellar one. The magnitudes of both the micelle-substrate binding constant and the 80-fold rate retardation suggest that reaction in the micellar phase makes a substantial contribution to the overall process.

In order for hydroxide ions in the bulk phase to react with bis p-nitrophenyl phenylphosphonate in the micellar phase, they must overcome electrostatic repulsive forces which impede their approach into the neighborhood of the NaLS micelles.[20] Electrostatic repulsions between the anionic NaLS micelles and the hydroxide ion nucleophiles, moreover, should give rise to an increase in the enthalpy of activation. Activation parameters have been determined for the NaLS inhibited hydrolysis reaction, but caution must be taken in their interpretation since reaction can take place in both the micellar and bulk phases. Complications arise because, in addition to the reaction under investigation in the micellar phase, changes in temperature can also affect (a) the rate of that part of

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

the reaction which occurs in the bulk phase, (b) the equilibrium binding constant for incorporation of the substrate into the micelles, and (c) the physical properties of the micelles, such as shape and aggregation number.[1,6,11-16,20,23,24,26,28,29]

The enthalpy of activation for the basic hydrolysis of bis p-nitrophenyl phenylphosphonate carried out in the presence of NaLS detergent is over 8 kcal/mole larger than that for the reaction conducted in the absence of surfactant (Table 17). The magnitude of the increase in this term supports the conclusion that reaction in the micellar phase contributes significantly to the overall hydrolysis reaction. A large increase in the enthalpy of activation has also been found by Bunton and Robinson for the NaLS inhibited basic hydrolysis of p-nitrophenyl diphenyl phosphate.[20]

A second factor which contributes to the rate-inhibiting effect of NaLS detergent on the basic hydrolysis of bis p-nitrophenyl phenylphosphonate, has been discussed for the CTAB catalyzed reaction: solubilization of the phosphonate diester by surfactant micelles. Extensive substrate solubilization gives rise to considerable stabilization of this reactant. This initial state stabilization, in turn, results in an increase in the enthalpy of activation of the reaction taking place in the micellar phase.

A third factor contributing to the anticatalytic effect of NaLS on the reaction under consideration is the previously mentioned tendency of large, low charge density anions to slightly destabilize anionic transition states relative to high charge density anions, ie. to increase the activity coefficient ratio

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

f_{OH^-}/f^*_{TS}.[21,63] These effects are smaller than, and opposite to, those of low charge density cations and should be associated with an increase in the enthalpy of activation of the micellar phase reaction. It is thus seen that (a) micelle-reactant electrostatic repulsion, (b) substrate solubilization, and (c) transition state destabilization should all contribute to the large increase in the enthalpy of activation observed for this hydrolysis reaction.

4. Polyoxyethylene(20) Nonylphenol (PENP) Anticatalysis

The basic hydrolysis of bis p-nitrophenyl phenylphosphonate is retarded approximately 4-fold by nonionic micelles of polyoxyethylene(20) nonylphenol (PENP). Reaction can thus take place in both the micellar and bulk phases, and the kinetic consequences are not very different for these two reaction sites. As mentioned previously, activation parameters could not be determined over even a 20° C. temperature range because of marked temperature effects on the physical properties (especially the aggregation number) of the PENP micelles.

Nonionic detergents generally have very little, if any, kinetic effect on anion-molecule reactions.[17,18,21,29] The modest 4-fold rate inhibition observed in this case is a relatively large micellar effect. The reason for this atypical rate reduction lies in the fact that the substrates, cited in the above references, possess less hydrophobic character, and should consequently be less extensively solubilized, than bis p-nitrophenyl phenylphosphonate. The situation is thus similar to that

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

encountered with the ionic detergents, viz. initial state stabilization due to solubilization of the phosphonate diester is retarding the hydrolysis reaction occurring in the micellar phase. In addition, electrostatic repulsion of the hydroxide ion nucleophile by lone pair electrons on the oxygen atoms of the head groups can also make a small contribution to the rate-inhibiting effect of PENP. However, such ion-lone pair repulsive forces would obviously be expected to be much smaller than the corresponding ion-ion repulsive forces postulated for the NaLS inhibited hydrolysis reaction.

Bunton and coworkers were able to determine the activation parameters for the basic hydrolysis of p-nitrophenyl diphenyl phosphate in the presence of a nonionic detergent which is structurally similar to PENP.[20] The micelle-substrate binding constant could not be determined, but it was estimated to be of the same order of magnitude as those given in Table 16. The similarities between the substrates, detergents, and binding constants suggest that these two nonionic micellar systems may behave in essentially the same manner. Bunton found that the enthalpy of activation increased by approximately 3 kcal/mole while the entropy of activation became somewhat more positive.[20] This observed increase in enthalpy of activation is consistent with the above explanation which attributes inhibition to initial state stabilization.

Electrostatic interactions are precluded in nonionic micellar systems, and ion-lone pair interactions should usually be of only minor importance. These systems clearly demonstrate that,

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

in the case of ionic micellar systems, hydrophobic effects can reinforce or offset electrostatic interactions to an appreciable extent and should not be overlooked when overall micellar effects are evaluated.

C. Basic Hydrolysis of p-Nitrophenyl Phenylphosphonate

1. Introduction

As noted previously, p-nitrophenyl phenylphosphonate monoanion, formed in the basic hydrolysis of bis p-nitrophenyl phenylphosphonate, is itself subject to slow alkaline hydrolysis at high base concentration. The basic hydrolysis of p-nitrophenyl phenylphosphonate is accelerated by cationic CTAB micelles, retarded by nonionic PENP micelles, and essentially unaffected by anionic NaLS micelles. The same criteria used to evaluate micellar effects on anion-molecule reactions can be applied to anion-anion reactions. Since the detergent concentration-rate profiles exhibit very little change, micelle-substrate binding constants were not calculated because they could not be determined with reasonable accuracy under these conditions.[1] In addition, since the magnitude of the micellar effects is so small, activation parameters were not determined because the effects of necessarily small changes in temperature would have been indiscernible.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

2. Hexadecyltrimethylammonium Bromide (CTAB) Catalysis

The effects of cationic CTAB micelles on the basic hydrolysis of p-nitrophenyl phenylphosphonate are similar in character (although much smaller in magnitude) to those described previously for the parent phosphonate diester. Since only a 2-fold rate enhancement is observed, reaction can occur in both the micellar and bulk phases.

Reactant approximation due to the attraction of hydroxide ions by cationic micelles should accelerate that part of the overall reaction which takes place in the micellar phase. Electrostatic stabilization of the dianionic transition state by CTAB micelles is also expected to enhance the micellar phase reaction.

Conversely, incorporation of p-nitrophenyl phenylphosphonate into the micelles ought to retard the reaction. However, this rate-retarding effect should be smaller than that observed for bis p-nitrophenyl phenylphosphonate because solubilization of the phosphonate monoester is expected to be less extensive than that of the parent phosphonate diester due to the fact that the former possesses one less hydrophobic p-nitrophenyl group than the latter.

An additional effect was observed for the CTAB catalyzed basic hydrolysis of p-nitrophenyl phenylphosphonate. Plots of first-order rate constants versus nucleophile concentration were found to be non-linear at high nucleophile concentrations. Similar effects have also been noted for several other micellar catalyzed reactions.[18,23,24]

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Salt anions are known to retard a large number of anion-molecule and anion-anion reactions which are catalyzed by cationic micelles by (a) impeding the approach of an anionic nucleophile into the neighborhood of the micelle and/or by (b) preventing the incorporation of an anionic substrate into the micelle.[6,17-28] The inhibiting effectiveness of these anions increases with decreasing charge density. High charge density anions, like hydroxide and chloride ions, do not exhibit significant rate-decelerating effects until their concentration reaches approximately 0.1 M.[17,24] Thus, at the high base concentrations used in the hydrolysis of the phosphonate monoester, hydroxide ion acts both as an inhibitor, by hindering the incorporation of the monoanionic phosphonate monoester into the cationic micelles, and as the reagent. However, because of its high charge density, it should not be a very effective inhibitor.[24]

In addition, at high base concentrations cationic micelles can become "saturated" with hydroxide ions.[18,23,24] This phenomenon occurs when hydroxide ions are present in sufficiently high quantity that some of them become incorporated into the cationic micelles. It was argued previously that such incorporation (due then to excess micelles) should deactivate the solubilized hydroxide ions.[18,20] This hydroxide ion deactivation inhibits both the micellar and nonmicellar reactions. Similar results have been reported by Bunton and coworkers for the CTAB catalyzed basic hydrolysis of bis 2,4-dinitrophenyl phosphate.[24]

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

3. Polyoxyethylene(20) Nonylphenol (PENP) Anticatalysis

The effects of nonionic PENP micelles on the basic hydrolysis of p-nitrophenyl phenylphosphonate should be the same as that previously described for the parent bis p-nitrophenyl phenylphosphonate. In the latter case, initial state stabilization due to solubilization of the phosphonate diester is believed to retard that part of the overall reaction occurring in the micellar phase.

In the CTAB catalyzed hydrolysis it was suggested, moreover, that the phosphonate monoester should be less extensively solubilized than the parent phosphonate diester due to the absence of a third aryl group. Furthermore, in the case of PENP solubilization of the former should also be less than that of the latter due to the previously described ion-lone pair repulsions operating, in this instance, between the nonionic micelles and the anionic substrate. In addition, it was also felt that this decreased solubilization would result in a smaller rate-retarding effect on that part of the overall hydrolysis reaction taking place in the micellar phase. This reasoning would predict a smaller rate-decelerating effect for the phosphonate monoester than for the parent phosphonate diester because of the same decrease in initial state stabilization.

The 2-fold rate decrease found for the hydrolysis of p-nitrophenyl phenylphosphonate in the presence of PENP micelles compared to the 4-fold decrease observed for the parent bis p-nitrophenyl phenylphosphonate supports the above conclusions. Analogous results have been found for the effects of a

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

structurally similar nonionic detergent on the basic hydrolyses of bis 2,4-dinitrophenyl phosphate[24] and 2,4-dinitrophenyl sulfate.[37]

4. Sodium Dodecyl Sulfate (NaLS)

The basic hydrolysis of p-nitrophenyl phenylphosphate is very slightly retarded by anionic micelles of NaLS. As a rule, anionic micelles are expected to have virtually no effect on anion-anion reactions on the basis of simple electrostatic considerations.[1,7,18,21,24,26,32,34] Both hydroxide and p-nitrophenyl phenylphosphonate ions should be repelled by anionic NaLS micelles, and reaction should then occur only in the bulk solution.[24]

However, the rate of the hydrolysis reaction conducted in the presence of NaLS detergent differs slightly from that carried out in the absence of surfactant (Table 21). This difference in reaction rates may be due to a small change in the nature of the bulk solvent caused by the presence of non-micellized NaLS detergent.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

V. SUMMARY

Micellar effects on the basic hydrolysis of bis p-nitrophenyl phenylphosphonate to give p-nitrophenyl phenylphosphonate have been examined. The reaction is catalyzed up to 250-fold by cationic micelles of hexadecyltrimethylammonium bromide (CTAB), with the rate reaching a maximum at ca. 2×10^{-3} M detergent. The surfactant increases the activation enthalpy; the rate enhancement arises from a marked decrease in the activation entropy. Anionic micelles of sodium dodecyl sulfate (NaLS) strongly inhibit the reaction, while nonionic micelles of polyoxyethylene(20) nonylphenol (PENP) retard it to a much lesser degree. The kinetic data can be interpreted quantitatively in terms of incorporation of bis p-nitrophenyl phenylphosphonate and hydroxide ion into the micelles. Each of the micelle-substrate binding constants is calculated to be approximately 10^6 M^{-1} at 25.00° C.

The effects of micelles on the second stage of the reaction, the basic hydrolysis of p-nitrophenyl phenylphosphonate, have also been investigated. The cationic detergent slightly accelerates the reaction while the nonionic surfactant slightly decelerates it. The anionic detergent has essentially no effect on the rate of hydrolysis.

Micellar effects on the basic hydrolysis of bis p-nitrophenyl phenylphosphonate and p-nitrophenyl phenylphosphonate are discussed in terms of electrostatic and hydrophobic interactions.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

VI. CONCLUSIONS

The interest which has developed in the study of organic reactions in the presence of micelle-forming detergents has grown concomitantly with the belief that reactions occurring in association colloidal systems might serve as models for reactions taking place in complex biological systems, eg. enzyme-catalyzed transformations. Ideally, model reactions for enzymatic processes should include an association, through weak bonding forces, of the substrate and the catalyst or other reactant leading to facilitation of bond-changing reactions and conferring some degree of specificity on the reaction.[29] Points of similarity between enzyme-catalyzed and micelle-catalyzed reactions include the following.[26] First, the catalysts are structurally related in terms of their molecular weights and the relative dispositions of their hydrophobic and hydrophilic portions with respect to the aqueous solvent. Second, micelle-catalyzed reactions, like their enzymatic counterparts, exhibit substrate specificity.[6,7,27,28,30,35,36] Third, both enzymatic and micellar reactions display kinetic behavior characterized by saturation of the catalyst with substrate.[6,29,30,35] Fourth, substrate-induced micellization has parallels in substrate-induced conformation changes in enzymes.[30]

Comparisons of enzymatic and micellar processes are only really useful if the reaction pathways and the modes of catalysis for the enzymatic reaction and the corresponding nonenzymatic one are closely related. When these conditions are satisfied, then some

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

understanding can perhaps be gained on the extent to which the following types of interactions contribute to reaction velocity and specificity for particular reaction types. First, micellar systems permit the examination of proximity effects in systems in which weak interactions are employed to approximate the reactants. Second, micellar systems accentuate the effects of electrostatic interactions on reaction rates. Cordes has observed that the rate-inhibiting effects exhibited by low charge density anions on certain micellar catalyzed reactions, for example, have parallels in protein and enzyme chemistry.[27] Third, micellar systems provide an indication of the extent to which hydrophobic interactions between the substrate and catalyst contribute to enzymatic specificity.[6] This last point, however, merits further comment. While stereoselective catalysis has been observed for the basic hydrolysis of an optically active carboxylic ester in the presence of micelles derived from an optically active detergent,[36] the generally low specificity of micellar catalysts, observed to date, contrasts rather sharply with the high specificity of most enzymatic reactions. One must be careful, therefore, not to overdraw the analogies described above. In this respect Bunton has suggested that micelles are best regarded as "models for the binding between enzyme and substrate."[22]

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

REFERENCES CITED

1. E. J. Fendler and J. H. Fendler, Advan. Phys. Org. Chem., 8, 271 (1970).

2. R. J. Williams, J. N. Phillips, and K. J. Mysels, Trans. Faraday Soc., 51, 728 (1955).

3. J. L. Kavanau, "Structure and Function in Biological Membranes," Vol. 1, Holden-Day, Inc., San Francisco, Ca., 1965.

4. D. Eagland and F. Franks, In "Chemistry, Physics and Application of Surface Active Substances. Proceedings of the IVth International Congress on Surface Active Substances, Brussels, 7-12 September, 1964." J. T. G. Overbeek, ed., Vol. 2, Gordon and Breach Publishers, New York, N.Y., 1967.

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

6. E. H. Cordes and R. B. Dunlap, Accounts Chem. Res., 2, 329 (1969).

7. F. M. Menger and C. E. Portnoy, J. Amer. Chem. Soc., 89, 4698 (1967).

8. A. B. Klevens, Chem. Rev., 47, 1 (1950).

9. P. Molyneux, C. T. Rhodes, and J. Swarbrick, Trans. Faraday Soc., 61, 1043 (1964).

10. J. Swarbrick and J. Daruwala, J. Phys. Chem., 73, 2627 (1969).

11. K. Shinoda, T. Nakagawa, B-U. Tamamushi, and T. Isemura, "Colloidal Surfactants, Some Physicochemical Properties," Academic Press, New York, N.Y., 1963, Chapters 1 and 2.

12. P. H. Elworthy, A. T. Florence, and C. B. McFarlane, "Solubilization by Surface Active Agents and its Application in Chemistry and the Biological Sciences," Chapman and Hall, Ltd., London, 1968, Chapter 1.

13. A. Ray and P. Mukerjee, J. Phys. Chem., 70, 2138 (1966).

14. P. Mukerjee and A. Ray, ibid., 70, 2144 (1966).

15. P. Mukerjee and A. Ray, ibid., 70, 2150 (1966).

16. P. Mukerjee, K. J. Mysels, and P. Kapavan, ibid., 71, 4166 (1967).

17. C. A. Bunton, E. J. Fendler, L. Sepulveda, and K-U. Yang, J. Amer. Chem. Soc., 90, 5512 (1968).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

18. C. A. Bunton and L. Robinson, ibid., 90, 5972 (1968).

19. C. A. Bunton, L. Robinson, and L. Sepulveda, ibid., 91, 4813 (1969).

20. C. A. Bunton and L. Robinson, J. Org. Chem., 34, 773 (1969).

21. C. A. Bunton and L. Robinson, ibid., 34, 780 (1969).

22. C. A. Bunton, L. Robinson, and L. Sepulveda, ibid., 35, 108 (1970).

23. C. A. Bunton and L. Robinson, J. Amer. Chem. Soc., 92, 356 (1970).

24. G. J. Buist, C. A. Bunton, L. Robinson, L. Sepulveda, and M. Stam, ibid., 92, 4072, (1970).

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

26. R. B. Dunlap and E. H. Cordes, J. Amer. Chem. Soc., 90, 4395 (1968).

27. L. R. Romsted and E. H. Cordes, ibid., 90, 4404 (1968).

28. R. B. Dunlap and E. H. Cordes, J. Phys. Chem., 73, 361 (1969).

29. M. T. Behme and E. H. Cordes, J. Amer. Chem. Soc., 87, 260 (1965).

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

31. E. F. Duynstee and E. Grunwald, ibid., 81, 4540 (1959).

32. E. F. Duynstee and E. Grunwald, ibid., 81, 4542 (1959).

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

34. E. F. Duynstee and E. Grunwald, Tetrahedron, 21, 2401 (1965).

35. E. H. Cordes, Progr. Phys. Org. Chem., 4, 1 (1967).

36. C. A. Bunton, L. Robinson, and M. F. Stam, Tetrahedron Lett., 121 (1971).

37. E. J. Fendler, R. R. Liechti, and J. H. Fendler, J. Org. Chem., 35, 1658 (1970).

38. D. Stigter and K. J. Mysels, J. Phys. Chem., 59, 45 (1955).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

39. D. Stigter, J. Colloid Interface Sci., 23, 379 (1967).

40. J. Clifford, Trans. Faraday Soc., 61, 1276 (1965).

41. N. Muller and R. H. Birkhahn, J. Phys. Chem., 71, 957 (1967).

42. N. Muller and R. H. Birkhahn, ibid., 72, 583 (1968).

43. N. Muller and T. W. Johnson, ibid., 73, 2042 (1969).

44. N. Muller and E. F. Platko, ibid., 75, 547 (1971).

45. N. Muller and H. Simsohn, ibid., 75, 942 (1971).

46. P. A. Arrington, A. Clouse, D. Doddrell, R. B. Dunlap, and E. H. Cordes, ibid., 74, 665 (1970).

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

48. P. Mukerjee, J. Colloid Sci., 19, 722 (1964).

49. D. Stigter, J. Phys. Chem., 68, 3603 (1964).

50. M. Donbrow and C. T. Rhodes, J. Chem. Soc., 6166 (1964).

51. M. Donbrow and C. T. Rhodes, J. Pharm. Pharmacol., 18, 424 (1966).

52. A. S. Waggoner, O. H. Griffith, and C. R. Christensen, Proc. Natl. Acad. Sci., 57, 1198 (1967).

53. E. J. Fendler, Ph.D. Thesis, University of California, Santa Barbara, 1966.

54. P. Mukerjee and K. J. Mysels, J. Amer. Chem. Soc., 77, 2937 (1955).

55. J. R. Cox and O. B. Ramsay, Chem. Rev., 64, 317 (1964).

56. R. F. Hudson, "Structure and Mechanism in Organo-Phosphorus Chemistry," Academic Press, New York, N.Y., 1965, Chapter 8.

57. R. F. Hudson and L. Keay, J. Chem. Soc., 2463 (1956).

58. T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms," Vol. II, W. A. Benjamin, Inc., New York, N.Y., 1966, Chapter 6.

59. A. J. Kirby and S. G. Warren, "The Organic Chemistry of Phosphorus," Elsevier Publishing Co., New York, N.Y., 1967, Chapter 10.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

60. G. S. Hartley, Trans. Faraday Soc., 30, 444 (1934).

61. L. L. Schaleger and F. A. Long, Advan. Phys. Org. Chem., 1, 1 (1963).

62. V. A. Motsavage and H. B. Kostenbauder, J. Colloid Sci., 18, 603 (1963).

63. C. A. Bunton and L. Robinson, J. Amer. Chem. Soc., 90, 5965 (1968).

64. R. A. Robinson and R. H. Stokes, "Electrolyte Solutions," Butterworth and Co., Ltd., London, 1959, Appendix 8.10.

65. J. Kielland, J. Amer. Chem. Soc., 59, 1675 (1937).

66. J. N. Butler, "Ionic Equilibrium," Addison Wesley Publishing Co., Inc., Reading, Mass., 1964, p. 435.

67. B. W. Barry and E. Shotton, J. Pharm. Pharmacol., 19, 785 (1967).

68. R. B. Dunlap, G. A. Ghanin, and E. H. Cordes, J. Phys. Chem., 73, 1898 (1969).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.