Basic Hydrolysis of *m*-Nitrophenyl Acetate in Micellar Media Containing *β*-Cyclodextrins

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The alkaline hydrolysis of *m*-nitrophenyl acetate (*m*-NPA) was studied in sodium dodecyl sulfate (SDS) and tetradecyltrimethylammonium (TTAX; X = Br^- or HO^-) micellar systems containing *β*-cyclodextrin, CD. CD catalyzes the alkaline hydrolysis of *m*-NPA through reaction of the complexed substrate with the hydroxyl group of the cyclodextrin. The presence of aggregates at concentrations below the cmc exert an inhibitory effect. Above their cmc's, SDS or TTAX micelles exhibit the typical inhibitory and catalytic effects, respectively, on the alkaline hydrolysis of hydrophobic substrates. This behavior is explained in terms of two competing equilibria involving complexation of the substrate and the surfactant monomers by CD. The kinetic model combines the pseudophase model, including ion exchange, with a competitive binding model for the CD-catalyzed hydrolysis of *m*-NPA. In this model, counterions do not bind to the surfactant ion in the surfactant·CD complex and neither CD nor the surfactant·CD complex bind to micelles. Competitive complexation by CD and self-association (micellization) of the surfactant monomers results in the presence of a substantial amount of free (uncomplexed) CD. Once micelles are formed, no effect of cyclodextrin addition is observed on their properties.

Introduction

Cyclodextrins (CDs) are cyclic oligosaccharides composed of glucose units.[1] The best characterized forms are α-, *β*- and *γ*-cyclodextrins consisting of six, seven, and eight D-glucose units, respectively. Cyclodextrins are regulators of chemical[2] and photochemical reactivity.[3] Their ability to modulate reactivity depends on their capacity to complex organic substances; i.e., molecules with an appropriate size and shape form inclusion complexes with cyclodextrins. A number of thermodynamic studies on the complexation of various types of substances by cyclodextrins have been carried out.[4] As a rule, the interaction is not covalent, but a combination of the hydrophobic effect and van der Waals forces, and in some cases, hydrogen bonding between the ligand and cyclodextrin.[5] There is much interest in manipulating the complex-forming ability of cyclodextrins with a view to developing crucial pharmacological,[6] analytical,[7] organic synthesis,[6] and photophysical applications.[3,8]

Recently, special attention has been given to the impact of a third component on the formation of host−guest complexes of cyclodextrins.[9] Studies of third-party effects have examined inter- and intramolecular excimer formation within CD cavities,[10] alteration of the quenching of a guest fluorescence probe by use of a quencher that may also be complexed by CDs,[11] and the effect of a surfactant as a third component on the chemical behavior of the system.[11d,12]

Micellar systems and related associations colloids also have the ability to alter chemical reactivity. Reaction rates and equilibria in micellar media are affected by solubilization of reactants, changes in local concentrations due to compartmentalization of reaction media, and changes in physicochemical properties of the medium.[13] The influence of micellar systems on chemical reactivity is usually analyzed in terms of the micellar pseudo-phase model.[14]

Recently, we developed a kinetic model based on the micellar pseudo-phase formalism to study the effect of CDs in micellar systems.[15] The model was successfully applied to the alkaline hydrolysis of *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide, which involves a nucleophilic attack of OH^- on the sulfonamide SO_2 group and is not catalyzed by CDs. In this work, we present a formalism based on the micellar pseudo-phase model that is applicable to a CD acting as a catalyst. The formalism was applied to the alkaline hydrolysis of *m*-nitrophenyl acetate (*m*-NPA) in micelle + *β*-cyclodextrin systems (viz. SDS + CD, TTAOH + CD, and TTABr + CD).

Experimental Section

The surfactants SDS and TTABr, and *β*-cyclodextrin, were supplied by Sigma in the highest available purity and used without further purification. To check the purity of the surfactants we performed both conductometric and surface tension measurements of cmc, obtaining results consistent with literature values. Conductometric cmc values of $(7.9 \pm 0.5) \times 10^{-3}$ and $(3.5 \pm 0.3) \times 10^{-3}$ M and surface tension cmc values of $(7.5 \pm 0.5) \times 10^{-3}$ and $(3.1 \pm 0.5) \times 10^{-3}$ M were obtained for SDS and TTABr, respectively. *m*-Nitrophenyl acetate was synthesized by reacting *m*-nitrophenol with acetic anhydride in pyridine.[16] Owing to the low solubility of *m*-NPA in water, its stock solutions were prepared in acetonitrile. The percentage of acetonitrile in the reaction mixtures was always lower than 1% v/v.

CD is fully deprotonated under the alkaline conditions used since $pK_a^{CD} = 12.2$.[1a] All [OH^-] values given below were

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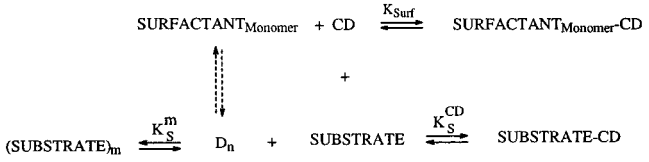
SCHEME 1



obtained by subtracting the CD concentration from that of NaOH. The reaction kinetics were monitored by measuring the absorbance of *m*-NPA at 400 nm, using an Applied Photophysics DX. 17MV sequential stopped-flow spectrofluorimeter thermostated at (25.0 ± 0.1) °C. The substrate concentration was always $\cong 2 \times 10^{-4}$ M and $[OH^-] > 0.1$ M. Methods for preparation of TTAOH solutions and to perform kinetic runs were described previously.[17]

Results and Discussion

Methodology. Adding a cyclodextrin to a micellar system alters its physicochemical properties because the oligosaccharide complexes surfactant monomers. Complex formation increases the surfactant concentration required for micellization, and the critical micelle concentration of a micellar system in the presence of a cyclodextrin (cmc_{app}) is equivalent to the combined concentrations of surfactant monomers complexed by the CD, [$surf_{monomer}$·CD], and that of free dissolved monomer in equilibrium with the micellized surfactant, cmc_{real}, i.e., $cmc_{app} = [surf_{monomer}·CD] + cmc_{real}$.

Simultaneously with complexation of its monomers by the CD, surfactant also self-associates (micellizes); as a result, the micellar system always contains an appreciable concentration of free (uncomplexed) CD, [CD_f] (see Scheme 1).

In the absence of a cyclodextrin, the concentration of surfactant monomers in equilibrium with micellized surfactant once micellization has started is assumed to be constant and equal to cmc_{real}. In micelle + CD mixed systems, both the free CD and the free monomer concentrations are assumed to remain constant after micellization and are the same as those present when the total surfactant concentration is equal to cmc_{app}. This assumption is reasonable because the surfactant monomer concentration above the cmc is essentially constant and therefore the concentration of surfactant·CD complex is constant. The addition of a third component (substrate) to the cyclodextrin + micelle mixed system requires accounting for its complexation equilibria with CD and micelles.

Surfactant·CD complexes are predominantly 1:1 stoichiometry.[12c] Only in the presence of high cyclodextrin concentrations and long hydrocarbon chains is the 1:2 complex formed to an appreciable extent.[18]

An expression for the free CD concentration, [CD_f], is derived for use in kinetic equations (see below) based on Scheme 1. We assume both the surfactant·CD and substrate·CD complexes to be of 1:1 stoichiometry. The substrates, MNTS[15] and *m*-NPA, are small enough to fit within the CD cavity without needing two CD molecules to complex them. We also assume that counterions do not bind to the surfactant ion in the surfactant·CD complex and that neither the CD nor the surfactant·CD complex binds to micelles.

The complexation constants for binding of the substrate by CD, by micelles, and for surfactant monomers by CD are expressed as

$$K_s^{CD} = \frac{[\text{substrate} - \text{CD}]}{[\text{substrate}]_w[CD_f]}$$

$$K_s^m = \frac{[\text{substrate}]_m}{[\text{substrate}]_w[D_n]}$$

$$K_{monomer}^{surf} = \frac{[surf_{monomer} - \text{CD}]}{[surf_{monomer}[CD_f]} \quad (1)$$

The mass balances for the total concentrations of cyclodextrin, surfactant, and substrate

$$[CD]_T = [CD_f] + [surf_{monomer}·CD] + [substrate·CD] \quad (2)$$

$$[surf]_T = [surf_{monomer}] + [surf_{monomer}·CD] + [D_n] \quad (3)$$

$$[substrate]_T = [substrate]_w + [substrate·CD] + [substrate]_m \quad (4)$$

are combined with the binding constants to give a third-order equation for [CD_f].

$$\alpha[CD_f]^3 + \beta[CD_f]^2 + \gamma[CD_f] - [CD]_T = 0 \quad (5)$$

where

$$\alpha = K_{monomer}^{surf}K_s^{CD} \quad (6)$$

$$\beta = \{K_{monomer}^{surf} + K_s^{CD} + K_s^{CD}K_{monomer}^{surf}([surf]_T - [CD]_T + [substrate]_T)\} \quad (7)$$

$$\gamma = \{1 + K_{monomer}^{surf}([surf]_T - [CD]_T) + K_s^{CD}([substrate]_T - [CD]_T)\} \quad (8)$$

Solving eqs 5−8 requires values for $K_{monomer}^{surf}$ and K_s^{CD}. The latter are estimated from experiments in the absence of surfactant; the former, however, is difficult to obtain. There are many reported equilibrium constants for surfactant−cyclodextrin complexes.[19,20] However, $K_{monomer}^{surf}$ values are highly disparate and those obtained by using some experimental techniques such as conductimetry have been questioned.[21] This led us to use simulated values for the complexation constants of surfactant monomers with CD in this work.[15]

Hydrolysis of *m*-NPA in an Aqueous Medium Containing CD. Although the hydrolysis of aryl esters (particularly phenyl acetates) in the presence of CDs has been thoroughly studied[1,2a,22] we examined the influence of the CD concentration on the alkaline hydrolysis of *m*-nitrophenyl acetate to ensure good consistency in the evaluations of the experimental results. Cyclodextrins catalyze the alkaline hydrolysis of phenyl acetates by acyl transfer from the ester to the ionized hydroxyl group of CD.

The rate constant for the basic hydrolysis of *m*-NPA in an aqueous medium is $k_w = (9.0 \pm 0.1)\ M^{-1}\ s^{-1}$. In the presence of CD, saturation kinetics are observed, eq 9. Analysis of the dependence of k_{obs} on the stoichiometric CD concentration (not shown) gives $k_{CD} = (31 \pm 2)\ s^{-1}$ and $K_s^{CD} = (54 \pm 5)\ M^{-1}$.

$$k_{obs} = \frac{k_w[HO^-] + k_{CD}K_s^{CD}[CD]}{1 + K_s^{CD}[CD]} \quad (9)$$

Hydrolysis of *m*-NPA in SDS + CD Mixed Systems. Added SDS decreases the rate of alkaline hydrolysis of *m*-NPA. This behavior, typical of the alkaline hydrolysis of hydrophobic substrates in the presence of anionic micelles, is explained by

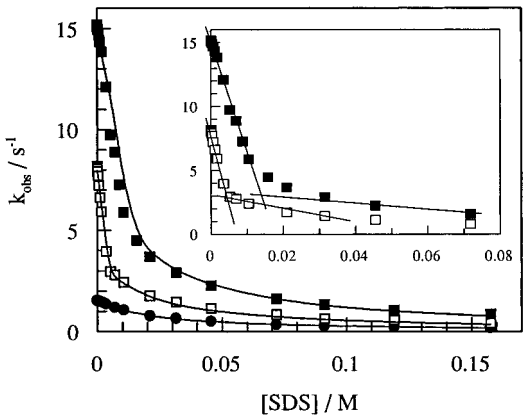


Figure 1. Influence of [SDS] on k_{obs} for the alkaline hydrolysis of *m*-NPA in 0.175 M NaOH in the presence of (●) 0.00 M, (□) 5.00×10^{-3} M, and (■) 1.50×10^{-2} M CD, at 25 °C. The curves were obtained by fitting eq 11 to the experimental results (see Table 1). The inset illustrates the kinetic determination of cmc_{app} (for details, see text).

using the micellar pseudo-phase model.[13,14] Equation 10 relates the observed rate constant for the alkaline hydrolysis of *m*-NPA with surfactant concentration where $[D_n]$ denotes the concentration of micellized surfactant and $[surfactant]_{tot} = [D_n] + cmc$. The critical micelle concentration was obtained kinetically as the minimum surfactant concentration required to induce a substantial change in the observed rate constant.

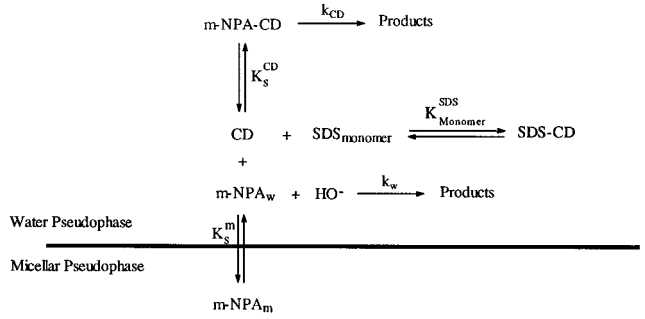
$$k_{obs} = \frac{k_w[HO^-]}{1 + K_s^m[D_n]} \qquad (10)$$

By fitting eq 10 to the experimental results (the solid line in Figure 1), the association constant of *m*-NPA to SDS micelles and the critical micelle concentration were calculated: $K_S^m = (51 \pm 1)\ M^{-1}$ and $cmc = 1.00 \times 10^{-3}$ M. The latter is much smaller than the reported cmc for SDS, 8.00×10^{-3} M,[14] which is ascribed to the known effect of the presence of salts on the critical micelle concentrations of surfactants.[23,24]

To study the effect of SDS micelles on the hydrolysis of *m*-NPA containing CD, we conducted experiments at constant CD concentration (5.00×10^{-3} or 1.5×10^{-2} M) and variable SDS concentrations, Figure 1. In all cases, the reaction rate decreased with increasing SDS concentration. The k_{obs} values obtained by extrapolating to a zero SDS concentration at each CD concentration are quantitatively consistent with the k_{obs} values obtained in the presence of the CD and in the absence of SDS. The increase in k_{obs} with increasing [CD] is ascribed to the catalytic effect of the cyclodextrin on the transfer of the acyl group from *m*-NPA. The inhibitory effect of added SDS below the concentration where SDS micellization starts is attributed to complexation of the surfactant monomers by CD and release of *m*-NPA into the bulk aqueous medium. This decreases k_{obs} by reducing the concentration of CD·*m*-NPA complexes.

At a higher SDS concentration above cmc_{app}, micelles form and the typical inhibitory effect of anionic micelles on alkaline hydrolysis of hydrophobic substrates is observed. Our treatment results in an appreciable amount of free CD in the aqueous phase because the cmc of SDS (and the free monomer concentration) is small. All surfactant in micellar form is in a separate phase, and this surfactant does not participate in the equilibria in the aqueous pseudophase. This, and the associated catalytic effect on the alkaline hydrolysis of *m*-NPA, is why the k_{obs} vs [SDS] curves lead to limiting k_{obs} values that are dependent on the CD concentration at high SDS concentrations.[25]

SCHEME 2



This experimentally observed behavior can be explained quantitatively by assuming simultaneous alkaline hydrolysis of *m*-NPA in the aqueous pseudophase (with k_w) and transfer of the acyl group from CD-complexed *m*-NPA to the secondary hydroxyl group of CD (with k_{CD}), Scheme 2 and eq 11. Again, the hydrolysis rate in SDS micelles is asumed to be negligible.

$$k_{obs} = \frac{k_w[HO^-] + k_{CD}K_s^{CD}[CD_f]}{1 + K_s^{CD}[CD_f] + K_s^m[D_n]} \qquad (11)$$

Solving eq 11 requires knowing cmc_{app}, which was kinetically evaluated as the surfactant concentration where an abrupt change in the k_{obs} vs [SDS] inhibition curve is observed, Figure 1. This change is caused by a change in the inhibition process, i.e., from a decrease in k_{obs} caused by displacement of NPA by dodecyl sulfate anion to the typical inhibitory effect of anionic micelles on the alkaline hydrolysis of hydrophobic substrates. The cmc_{app} values obtained are given in Table 1.

The free CD concentration below cmc_{app} was calculated by solving eqs 5−8. In previous work,[15] we estimated $K_{monomer}^{SDS}$ for the binding of the dodecyl sulfate anion to CD to be $(8000 \pm 500)\ M^{-1}$, and setting $K_s^{CD} = (54 \pm 5)\ M^{-1}$ allowed $[CD_f]$ to be calculated at each SDS concentration. Above cmc_{app} $[CD_f]$ is assumed to be constant and equal to the value obtained at cmc_{app}. Calculated values are in Table 1. To simplify the fitting of eq 11 to the experimental results in Figure 1, K_s^{CD} and k_{CD} were taken to have the same values as in the absence of surfactant and k_w and K_s^m were treated as disposable parameters.

The k_w and K_s^m values obtained in the absence and presence of CD are very similar, indicating that CD does not interact with SDS micelles.

Hydrolysis of *m*-NPA in TTAOH + CD Mixed Systems. Figure 2 shows the effect of increasing TTAOH concentration on k_{obs} for the alkaline hydrolysis of *m*-NPA in the absence and presence of CD. The value of k_{obs} in the absence of CD increases with increasing [TTAOH] to a plateau consistent with other reactions in reactive counterions surfactants. The plateau occurs because once all *m*-NPA is micellar-bound reaction occurs in pseudo-phase containing an approximately constant concentration of HO^-. This behavior was analyzed quantitatively by using the micellar pseudo-phase model (see Scheme 3).

In the absence of CD, k_{obs} is composed of reactions in the aqueous, k_w, and micellar, k_m, pseudophases

$$k_{obs} = \frac{k_w[HO^-]_w + (k_mK_s^m - k_w)m_{OH}[D_n]}{1 + K_s^m[D_n]} \qquad (12)$$

TABLE 1: Results of Fitting Eq 11 to the Experimental Data for the Basic Hydrolysis of *m*-NPA in CD/SDS Mixtures

[CD]/M	cmc_{app}/M	$[CD_f]$/M	cmc_{real}/M	K_s^m/M^{-1}	$k_w/M^{-1}\ s^{-1}$
0			1.00×10^{-3}	51 ± 1	9.0 ± 0.1
5.00×10^{-3}	5.00×10^{-3}	7.26×10^{-4}	7.26×10^{-4}	51 ± 1	11 ± 3
1.50×10^{-2}	1.30×10^{-2}	2.57×10^{-3}	5.70×10^{-4}	46 ± 2	9.0 ± 0.1

$K_{monomer}^{SDS} = (8000 \pm 500)\ M^{-1}$

$K_s^{CD} = (54 \pm 5)\ M^{-1}$; $k_{CD} = (31 \pm 2)\ s^{-1}$

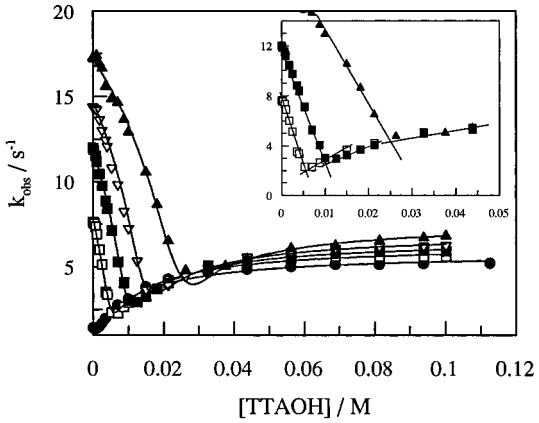
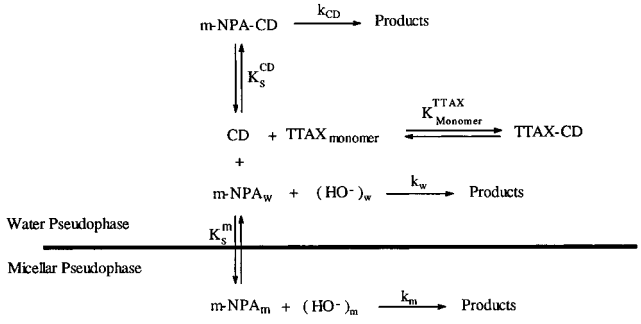


Figure 2. Influence of [TTAOH] on k_{obs} for the alkaline hydrolysis of *m*-NPA in 0.175 M NaOH at (●) [CD] = 0.00 M, (□) [CD] = 5.05×10^{-3} M, (■) [CD] = 1.00×10^{-2} M, (▽) [CD] = 1.50×10^{-2} M, (▲) [CD] = 2.50×10^{-2} M, at 25 °C. The curves were obtained by fitting eq 14 to the experimental results (see Table 2). The inset illustrates the kinetic determination of the cmc_{app} (for details, see text).

SCHEME 3



where m_{OH} is the concentration of OH^- ions in the micellar pseudophase, defined as the mole ratio ($m_{OH} = [OH^-]_m/[D_n]$). Because the only counterions present in the reaction medium are OH^- ions, their concentration in the micellar pseudophase, $m_{OH} = \beta$, the fraction of bound counterions which is often assumed to be approximately constant.[28] The fraction of bound counterions is often assumed to be constant although this is only an approximation and is basically wrong, especially for HO^- counterions and at high concentrations of added counterions in general.[27] However, in our case this assumption is pretty good because of the high concentration of added HO^-. Addition of TTAOH does not appreciably change the total OH^- concentration in the aqueous phase, and therefore the concentration of HO^- at the micellar surface also remains approximately constant. The concentration of $[OH^-]$ ions in the aqueous pseudo-phase will be sum of that added to the medium, $[OH^-]_{add}$, that supplied by the surfactant monomers—equal to the cmc once micellization has started—and that contributed by the dissociation of the micellized surfactant ($\alpha[D_n]$) where $\alpha = 1 - \beta$. Thus, one to obtains the following equation:

$$k_{obs} = \frac{k_w([HO^-]_{add} + [TTAOH]_{monomer} + \alpha[D_n]) + k_m K_s^m \beta [D_n]}{1 + K_s^m [D_n]} \quad (13)$$

As with SDS micelles, the cmc was determined kinetically from the minimum surfactant concentration needed to alter the rate constant. The value thus obtained, 1.5×10^{-3} M, is much smaller than the cmc in the absence of NaOH, which is attributed to the known effect of added salts on cmc. Fitting eq 13 to the experimental results (solid line in Figure 2) gave K_s^m and k_m values of $(77 \pm 3)\ M^{-1}$ and $(7.3 \pm 0.1)\ s^{-1}$, respectively (see Table 2). The rate constant for the micellar pseudophase, k_m, has atypical dimensions for a bimolecular rate constant because the concentration of OH^- ions in the micellar pseudophase is defined as a mole ratio.[13a] To compare k_m values to those of ordinary rate constants (in $M^{-1}\ s^{-1}$ units), k_m must be corrected for the molar volume of the micellar pseudo-phase, $K_2^m = \bar{V} k_m$, $\bar{V} = 0.14\ M^{-1}$.[28a] The rate constant for the micellar pseudophase, $K_2^m = 1.02\ M^{-1}\ s^{-1}$, is smaller than that for the aqueous medium, $k_w = 9.0\ M^{-1}\ s^{-1}$. The difference between the K_2^m and k_w values is consistent with that found in other alkaline hydrolysis processes in cationic micelles and can ascribed to the decreased polarity of the micellar pseudo-phase relative to the aqueous medium.[13a]

The influence of CD + TTAOH mixtures on the alkaline hydrolysis of *m*-NPA was studied by changing the TTAOH concentration at various CD concentrations (5.00×10^{-3}, 1.00×10^{-2}, 1.50×10^{-2}, and 2.50×10^{-2} M), Figure 2. Values of k_{obs} initially decrease with increasing surfactant concentration and then increase to a maximum value. The TTAOH concentration at which k_{obs} starts to increase increases with cyclodextrin concentration. The behavior observed at low [TTAOH] (below the cmc_{app}) is similar to that in SDS. If the surfactant concentration is raised further, micellization eventually starts. The increase k_{obs} with increase in [TTAOH] at medium to high surfactant concentrations is typical of micellar catalyzed reactions.

The results in Figure 2 are treated quantitatively on the basis of Scheme 3. In the pseudophase model, reaction in the aqueous occurs via free OH^- ions with unbound *m*-NPA or in the *m*-NPA·CD complex and in micellar pseudophase between micellar bound *m*-NPA and associated counterions. The rate expression for k_{obs} is

$$k_{obs} = \{k_w([HO^-]_{add} + [TTAOH]_{monomer} + \alpha[D_n]) + k_m K_s^m \beta [D_n] + k_{CD} K_s^{CD} [CD_f]\}/\{1 + K^m{}_s [D_n] K_s^{CD} [CD_f]\} \quad (14)$$

As before, the concentration of free CD was calculated by solving eqs 5−8. We used an equilibrium constant for the complexation of TTAOH monomers by CD identical with that for the complexation of TTABr monomers, i.e., $K_{monomer}^{TTAOH} = (30\,000 \pm 1000)\ M^{-1}$,[15] based on our assumptions that the CD

TABLE 2: Results of Fitting Eq 14 to Experimental Data for the Basic Hydrolysis of *m*-NPA in CD/TTAOH Mixtures

[CD]/M	cmc_{app}/M	$[CD_f]$/M	cmc_{real}/M	K_s^m/M^{-1}	k_m/s^{-1}	$k_2^m/M^{-1}\ s^{-1}$
0			1.50×10^{-3}	77 ± 3	7.3 ± 0.1	1.02
5.00×10^{-3}	5.50×10^{-3}	2.20×10^{-4}	7.20×10^{-4}	77 ± 3	7.8 ± 0.8	1.09
1.00×10^{-2}	1.05×10^{-2}	3.67×10^{-4}	8.67×10^{-4}	77 ± 3	8.2 ± 0.1	1.15
1.50×10^{-2}	1.55×10^{-2}	4.87×10^{-4}	9.87×10^{-4}	77 ± 3	8.6 ± 0.2	1.20
2.50×10^{-2}	2.50×10^{-2}	8.91×10^{-4}	8.91×10^{-4}	77 ± 3	9.3 ± 0.7	1.30

$K_{monomer}^{TTAOH} = (30000 \pm 1000)\ M^{-1}$
$K_s^{CD} = (54 \pm 5)\ M^{-1}$; $k_{CD} = (31 \pm 2)\ s^{-1}$

cavity only hosts the alkyl chain of the surfactant and not its counterion. Once micellization starts, the variation of the rate constant with the surfactant concentration is attributed to incorporation of *m*-NPA into the micellar pseudo-phase. Consequently, the surfactant concentration at the minimum in the k_{obs} vs [TTAOH] curves is taken as the onset of micellization and equal to cmc_{app}, see Figure 2. The $[CD_f]$ and cmc_{app} values were used to fit eq 14 to the curves in Figure 2. The values of the parameters obtained in the presence of CD alone, viz., $K_s^m = (54 \pm 5)\ M^{-1}$ and $k_{CD} = (31 \pm 2)\ s^{-1}$, were used in the simulations. The association constant for *m*-NPA to TTAOH micelles was assumed to be the same as that in TTAOH micelles alone, $K_s^m = (77 \pm 3)\ M^{-1}$, and the rate constant in the micellar pseudophase, k_m, was optimized. The assumed invariability of the association constant for *m*-NPA to TTAOH micelles in the presence of CD is supported by invariability of *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide association constants in micelle + CD mixed systems.[15] The results for *m*-NPA in SDS + CD systems (see above) also confirm that K_s^m is independent of the presence of CD. Table 2 gives the parameter values obtained by fitting eq 14 to the experimental data. Values of k_m and K_2^m (in $M^{-1}\ s^{-1}$ units) are virtually constant and independent of the CD concentration in the medium. This confirms that the properties of the micellar system are not significantly altered by the presence of cyclodextrins.

As an additional test, we fitted eq 14 to the experimental data with various pairs of optimized K_s^m and k_m values. Values for the [K_s^m (M^{-1}), k_m (s^{-1})] pairs are: (77 ± 3, 7.3 ± 0.1), (70 ± 8, 7.9 ± 0.2), (73 ± 14, 8.3 ± 0.3), (93 ± 31, 8.4 ± 0.4) and (160 ± 160, 8 ± 1) at CD concentrations of 0, 5.00×10^{-3}, 1.00×10^{-2}, 1.50×10^{-2}, and 2.50×10^{-2} M, respectively. The clearest trend is that the imprecision in the values of K_s^m increases with increasing cyclodextrin concentration in the reaction medium.

The rate constant at the minimum in the k_{obs} vs [TTAOH] curves, cmc_{app} (Table 2), and also the limiting k_{obs} values at high surfactant concentrations increase with increasing [CD]. The dependence of the minimum k_{obs} values on [CD] is attributed to two combined factors. First, as cmc_{app} increases so does the concentration of OH^- ions in the medium because the surfactant monomers are assumed to be fully dissociated in water as are the TTAOH·CD complexes. Second, as the total CD concentration in the medium increases, so does that of free CD and hence its catalytic effect on the reaction rate. The observed increase in the limiting value of the k_{obs} vs [TTAOH] curves with increase in [CD] is then attributed to an increase in the concentration of free CD present at high TTAOH concentrations as [CD] is increased.[29] Increasing the total CD concentration in the system also increases the fraction of *m*-NPA that is complexed by CD at higher TTAOH concentration. To confirm this hypothesis, we plotted the limiting value of k_{obs} at high TTAOH concentrations as a function of the free CD concentration. As can be seen from Figure 3, the k_{obs} increases in proportion to [CD] in the presence and absence of TTAOH.

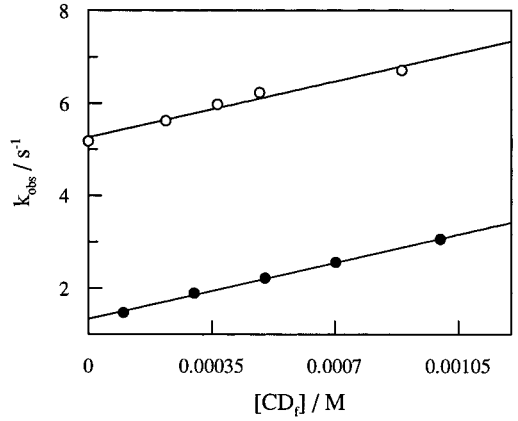


Figure 3. Variation of the limiting value of k_{obs} obtained in the presence of TTAOH micelles (○) with $[CD_f]$ relative to the absence of surfactant (●).

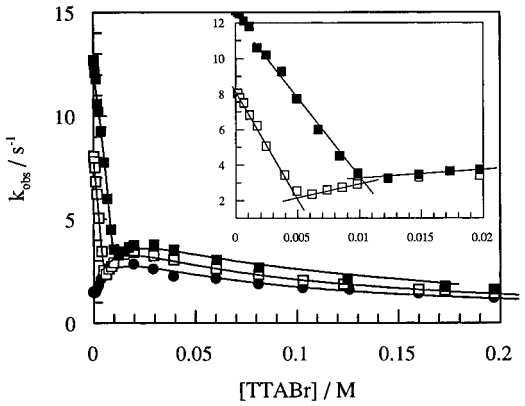


Figure 4. Influence of [TTABr] on k_{obs} for the alkaline hydrolysis of *m*-NPA in the presence of (●) [CD] = 0.00 M and [NaOH] = 0.164 M, (□) [CD] = 5.05×10^{-3} M and [NaOH] = 0.175, (■) [CD] = 1.03×10^{-2} M and [NaOH] = 0.175, at 25 °C. The curves were obtained by fitting eq 16 to the experimental results (see Table 3). The inset illustrates the kinetic determination of the cmc (for details, see text).

Hydrolysis of *m*-NPA in TTABr + CD Mixed Systems. Figure 4 shows the variation of k_{obs} with [TTABr] in the alkaline hydrolysis of *m*-NPA in the presence and absence of CD. The behavior in the absence of CD is typical of the alkaline hydrolysis of organic substrates by cationic micelles. The observed rate is the sum of the rates in the aqueous and micellar pseudophases. The rate constant, k_{obs}, increases with increasing [TTABr] to a maximum and then decreases steadily. The origin of the maximum is ascribed to two opposing effects in pseudophase models involving ion exchange. The addition of TTABr increases the relative concentrations of *m*-NPA and OH^- in the Stern layer, which speeds the reaction. As the [TTABr] is increased, Br^- concentration is added to the solution.

TABLE 3: Results Obtained by Fitting Eq 16 to Experimental Data for the Alkaline Hydrolysis of *m*-NPA in CD/TTABr Mixtures

[CD]/M	cmc_{app}/M	$[CD_f]$/M	cmc_{real}/M	K_s^m/M^{-1}	k_m/s^{-1}	$k_2^m/M^{-1}\ s^{-1}$
0			1.20×10^{-3}	63 ± 4	10.0 ± 0.2	1.4
2.50×10^{-3}	3.00×10^{-3}	1.26×10^{-4}	6.26×10^{-4}	68 ± 11	11.6 ± 0.6	1.6
5.05×10^{-3}	5.20×10^{-3}	3.27×10^{-4}	4.77×10^{-4}	69 ± 8	12.3 ± 0.4	1.7
1.03×10^{-2}	1.00×10^{-2}	7.67×10^{-4}	4.07×10^{-4}	81 ± 32	14 ± 1	1.9

$K_{monomer}^{TTAOH} = (30000 \pm 1000)\ M^{-1}$
$K_s^{CD} = (54 \pm 5)\ M^{-1}$; $k_{CD} = (31 \pm 2)\ s^{-1}$

Bromide ions (nonreactive) compete with OH^- ions in the Stern layer, thereby inhibiting the reaction. These two factors give rise to the maximum in the k_{obs} vs [TTABr] curve.

The pseudophase ion exchange model combines eq 12 for k_{obs} with eq 15 for the interfacial concentration of OH^-:[30]

$$m_{OH}^2 - m_{OH}\left[\frac{[HO^-]_T + K_{OH}^{Br}[Br^-]_T}{(K_{OH}^{Br} - 1)[D_n]} - \beta\right] - \left[\frac{\beta[HO^-]_T}{(K^{Br}_{OH} - 1)[D_n]}\right] = 0 \quad (15)$$

Solving eq 15 requires the knowledge of the ion-exchange constant K_{OH}^{Br}. Reported values for this constant are rather disparate, so we chose to determine it experimentally.[17] We studied the effect of added NaBr on k_{obs} for *m*-NPA hydrolysis at the catalytic maximum of the k_{obs} vs [TTABr] curve (not shown). A value of $K_{OH}^{Br} = 14$ was obtained using eqs 12 and 15, which is consistent with previously reported values.[13a] Equation 15 was solved using this value and m_{OH} values thus obtained were used in eq 12 to fit the experimental results, Figure 4, which provided $K_s^m = (63 \pm 4)\ M^{-1}$ and $k_m = (10.0 \pm 0.2)\ s^{-1}$, Table 3.

The effects of CD on the alkaline hydrolysis of *m*-NPA in TTABr micelles were determined in a series of experiments at variable surfactant concentrations and three different CD concentrations, Figure 4. The rate constant, k_{obs}, varied with CD concentration.

Following a similar approach as in the case of TTAOHm three simultaneous pathways were included in the treatment sumarized in Scheme 3, viz., reaction of the free substrate with HO^- in the aqueous medium catalyzed reaction of CD-complexed substrate and reaction of *m*-NPA with HO^- in TTABr micelles. The following rate expression was derived for k_{obs} based on Scheme 3:

$$k_{obs} = \frac{k_w[HO^-] + (k_m K_s^m - k_w)m_{OH}[D_n] + k_{CD}K_s^{CD}[CD_f]}{1 + K_s^m[D_n] + K_s^{CD}[CD_f]} \quad (16)$$

Equation 16 was fitted to the experimental data by using a procedure similar to that employed with the TTAOH + CD mixed system. The concentration of free CD was obtained from eqs 5−8, and that of OH^- in the micellar pseudo-phase was calculated from eq 15 in the absence of CD. The cmc was determined kinetically by assuming that the minimum in the k_{obs} vs [TTABr] curve marked the start of micellization, so the TTABr monomer concentration at that point should be identical with cmc_{app}. All parameters for the reaction via CD were kept constant, viz., $K_s^{CD} = (54 \pm 5)\ M^{-1}$ and $k_{CD} = (31 \pm 2)\ s^{-1}$. Table 3 gives the optimized values for the rate constant in the micellar pseudo-phase (k_m), or the corresponding K_2^m values (in $M^{-1}\ s^{-1}$), and those for the association constant of *m*-NPA to the micellar system (K_s^m). The rate and association constants are virtually independent of the CD concentration, which is consistent with the absence of a significant interaction between TTABr micelles and cyclodextrin.

The k_{obs} values increase with increasing [CD], both at the minimum of the curve and at higher [TTABr]. The increase in k_{obs} at the minimum is attributed to an increase in the $[CD_f]$ with added CD. The relative increase in $(k_{obs})_{min}$ with added CD relative to [CD] = 0 is 1.27, 1.50, and 2.08 at a CD concentration of 2.5×10^{-3}, 5.05×10^{-3}, and 1.03×10^{-2} M, respectively, consistent with CD^- speeding the cleavage of *m*-NPA. The ratio of the minimum in k_{obs} vs [TTABr] curve and the maximum micellar catalysis should be constant if the effect were exclusively due to the presence of free CD. However, the effect changed with the CD concentration; in fact, the $(k_{obs})_{max}/(k_{obs})_{min}$ ratio was 1.80, 1.62, 1.45, and 1.16 at a CD concentration of 0, 2.5×10^{-3}, 5.05×10^{-3}, and 1.03×10^{-2} M, respectively. This decrease in the catalytic activity of the micellar system is probably caused by an increase in the overall bromide concentration relative to that of micellized surfactant as the CD concentration is raised. The surfactant·CD complex is formed without the counterion, so the effect of increasing the CD concentration is similar to that of adding bromide to the reaction medium (viz., competition with reactive OH^- ions for association to the Stern layer).

From the results of Tables 1, 2, and 3 it follows that adding CD favors micellization by decreasing cmc_{real}. This phenomenon is well-documented[15,31] but not fully explained; it is believed to be related to the influence of additives on micellization.[32]

Conclusions

We recently applied the pseudophase formalism to micelle + CD systems. In the alkaline hydrolysis of *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide (MNTS)[15] this reaction is not catalyzed by CD but decreases the hydrolysis rate by complexing MNTS and removing it from the aqueous medium. Here we developed a formalism that includes reaction between CD and the complexed substrate. The model includes two simultaneous reaction pathways in the aqueous medium, reaction via HO^- ions and that via the substrate·CD complex. In cationic micelles hydrolysis in the micelles is included.

Values of the formation constants for surfactant·CD complexes, $K_{monomer}^{SDS} = (8000 \pm 500)\ M^{-1}$ and $K_{monomer}^{TTABr} = (30000 \pm 1000)\ M^{-1}$, are estimated from the results and are in good agreement with those obtained for the alkaline hydrolysis of MNTS.[15] The agreement between these values for two different types of reactions, one not catalyzed by CD (the alkaline hydrolysis of MNTS) and the other catalyzed by CD (the alkaline hydrolysis of *m*-NPA), indicates the robustness of the proposed model. The complex-formation equilibrium constants for the surfactants lie within the reported ranges, namely 210−25600 M^{-1} for $K_{monomer}^{SDS}$ and 9610−44000 M^{-1} for

$K_{monomer}^{TTABr}$;[19,20] however, these ranges are so wide that they provide little support for the values obtained here.

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