Basic Hydrolysis of Substituted Nitrophenyl Acetates in -Cyclodextrin/Surfactant Mixed Systems. Evidence of Free Cyclodextrin in Equilibrium with Micellized Surfactant

ARTICLE *in* LANGMUIR · NOVEMBER 1999

Impact Factor: 4.46 · DOI: 10.1021/la981392e

6 AUTHORS, INCLUDING:

Pablo Hervés
University of Vigo
106 PUBLICATIONS **1,065** CITATIONS
SEE PROFILE

J. Ramon Leis
University of Santiago de Compostela
132 PUBLICATIONS **2,217** CITATIONS
SEE PROFILE

Juan C. Mejuto
University of Vigo
376 PUBLICATIONS **2,669** CITATIONS
SEE PROFILE

Jorge Pérez-Juste
University of Vigo
214 PUBLICATIONS **7,753** CITATIONS
SEE PROFILE

Basic Hydrolysis of Substituted Nitrophenyl Acetates in β-Cyclodextrin/Surfactant Mixed Systems. Evidence of Free Cyclodextrin in Equilibrium with Micellized Surfactant

A. R. Alvarez,† L. García-Río,*,† P. Hervés,‡ J. R. Leis,† J. C. Mejuto,‡ and J. Pérez-Juste‡

Departamento de Química Física, Facultad de Química, Universidad de Santiago, E-15706 Santiago de Compostela, Spain, and Departamento de Química Física y Química Orgánica, Facultad de Ciencias, Universidad de Vigo, Vigo, Spain

Received October 6, 1998. In Final Form: July 15, 1999

The basic hydrolysis of *o*-, *m*-, and *p*-nitrophenyl acetates (NPA) in mixed systems consisting of β-cyclodextrin (β-CD) and a surfactant—sodium dodecyl sulfate (SDS), tetradecyltrimethylammonium hydroxide (TTAOH), or tetradecyltrimethylammonium bromide (TTABr)—has been studied. β-CD was found to catalyze the basic hydrolysis of NPA via the interaction of its hydroxyl group, in deprotonated form, with the carbonyl group in the complexed substrate. In the presence of a surfactant, the rate of the reaction is initially decreased. This inhibitory effect is the result of the surfactant monomers being complexed by β-CD and the NPA being in turn displaced from the aqueous medium, which cancels the catalytic effect of the cyclodextrin. Once micellization starts, the system behaves like a typical micellar system in the hydrolysis of a hydrophobic substrate. Plots of the ratios of pseudo-first-order rate constants in micelle−CD mixed systems and in micelles—$k_{obs}^{SDS+CD}/k_{obs}^{SDS}$ and $k_{obs}^{TTAOH+CD}/k_{obs}^{TTAOH}$—versus surfactant concentration revealed the ratio to be greater than unity even at high surfactant concentrations, which is consistent with a CD-catalyzed pathway. This result is in turn consistent with the presence of a substantial concentration of free CD in equilibrium with the micellar systems. The constancy of $k_{obs}^{SDS+CD}/k_{obs}^{SDS}$ and $k_{obs}^{TTAOH+CD}/k_{obs}^{TTAOH}$ at surfactant concentrations above the critical micelle concentration suggests the absence of interactions between CD and the micellar system once the latter has been established.

Introduction

Cyclodextrins (CDs) are cyclic oligosaccharides consisting of several glucose units linked by α-1,4 glucoside bonds.[1] They possess a toroidal or hollow, truncated cone shape with a nonpolar, hydrophobic interior and two hydrophilic rims formed by the primary (narrower rim) and secondary (wider rim) HO groups. By virtue of their unusual structure, CDs can form inclusion complexes via noncovalent interactions with molecules that fit into their cavities.[2] 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. Changes in physicochemical properties, as well as reactivities, result from such host−guest interactions.[1,3] The effects of inclusion complexes on the reactivity vary widely depending on the guest, the CD, and the reaction. In some cases the reaction rate is greatly reduced, which has led to the use of CD as stabilizers; but of more interest are the situations in which CDs accelerate reactions. Moreover, the CD may even participate directly in the reaction.[1a,4]

Micellar systems and related association 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.[5] The influence of micellar systems on chemical reactivity is usually analyzed in terms of the micellar pseudophase model.[6] Adding a cyclodextrin to a micellar system alters its physicochemical properties because the oligosaccharide complexes surfactant monomers. Cyclodextrins are known to readily complex surfactant molecules; CD is believed to form 1:1 complexes with surfactants in this way.[7] Complex formation increases the concentration of surfactant required for micellization,[8] so that 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 to the CD, [$surfactant_{monomer}$·CD], and of free dissolved monomer in equilibrium with the micellized surfactant, cmc_{real}. As a result, if the stoichiometry of the complex is 1:1,[7] the

† Universidad de Santiago.

‡ Universidad de Vigo.

(1) (a) Bender, M. L.; Komiyama, M. *Cyclodextrin Chemistry*; Springer: Berlin, 1978. (b) Saenger, W. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 344.

(2) Connors, K. A. *Chem. Rev.* **1997**, *97*, 1325.

(3) (a) Iglesias, E.; Fernández, A. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1691. (b) Iglesias, E. *J. Am. Chem. Soc.* **1998**, *120*, 13057.

(4) (a) Davies, D. M.; Garner, G. A.; Savage, J. R. *J. Chem. Soc., Perkin Trans. 2* **1994**, 2531. (b) Granados, A.; de Rossi, R. H. *J. Am. Chem. Soc.* **1995**, *117*, 3690.

(5) (a) Bunton, C. A.; Savelli, G. *Adv. Phys. Org. Chem.* **1986**, *22*, 213. (b) Romsted, L. S. *Surfactants in Solution*; Lindman, B., Mittal, K. L., Eds.; Plenum Press: New York, 1984; Vol. 2, p 1015. (c) Romsted, L. S. *J. Phys. Chem.* **1985**, *89*, 5107, 5113.

(6) Fendler, J. H.; Fendler, E. J. *Catalysis in Micellar and Macromolecular Systems*; Academic Press: New York, 1975.

(7) (a) Wan Yunus, W. M. Z.; Taylor, J.; Bloor, D. M.; Hall, D. G.; Wyn-Jones, E. *J. Phys. Chem.* **1992**, *96*, 8979. (b) Junquera, E.; Aicart, E.; Tardajos, G. *J. Phys. Chem.* **1992**, *96*, 4533. (c) Smith, V. K.; Ndou, T.; Muñoz de la Peña, A.; Warner, I. M. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1991**, *10*, 471. (d) Smith, V. K.; Ndou, T.; Warner, I. M. *Appl. Spectrosc.* **1992**, *46*, 659. (e) Palepu, R.; Reinsborough, V. C. *Can. J. Chem.* **1988**, *66*, 325. (f) Junquera, E.; Tardajos, G.; Aicart, E. *Langmuir* **1993**, *9*, 1213.

(8) (a) *Comprehensive Supramolecular Chemistry. Vol. 3 Cyclodextrins*; Szejtli, J., Osa, T., Eds.; Pergamon: Exeter, 1996. (b) Saenger, W.; Muller-Fahrnow, A. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 393. (c) George, J.; Desmettre, S. *J. Colloid Sci.* **1987**, *118*, 192. (d) Saint-Aman, E.; Serve, D. *J. Colloid Interface Sci.* **1990**, *138*, 365. (e) Junquera, E.; Aicart, E.; Tardajos, G. *J. Phys. Chem.* **1992**, *96*, 4533.

10.1021/la981392e CCC: $18.00
Published on Web 09/29/1999

critical micelle concentration of a micellar system in the presence of a cyclodextrin (cmc_{app}) will be $cmc_{app} = [surfactant_{monomer}{\cdot}CD] + cmc_{real}$.

Recently, our group developed a kinetic model that accounts for reactivity in surfactant−CD mixed systems.[9] This kinetic model is a combination of the traditional pseudophase model including ion exchange and a competitive binding model for the CD-catalyzed reaction (*i.e.*, the surfactant monomer is assumed to compete with the substrate for the binding pocket of the CD). The addition of a third component (a substrate) to a cyclodextrin−micelle mixed system further complicates the problem because it entails considering its complexation equilibria with both the CD and the micellar system. However, surfactant−CD mixed systems have been scarcely explored to date, particularly at surfactant concentrations well above the critical micelle concentration.

In this work, we carried out a comparative study of the reactivity of *o*-, *m*-, and *p*-nitrophenyl acetate in mixed systems consisting of β-CD and sodium dodecyl sulfate (SDS), β-CD and tetradecyltrimethylammonium hydroxide (TTAOH), and β-CD and tetradecyltrimethylammonium bromide (TTABr). The three substrates were chosen by virtue of the different catalytic action of β-CD on their basic hydrolysis.[10] The hydrolysis of aryl esters is probably the most widely studied reaction subject to "covalent catalysis" by CDs. The term covalent catalysis was coined by Bender and Komiyama[1a] to refer to reactions involving covalent interactions between a functional group in the CD and the substrate during the rate-determining step. The validity of the proposed kinetic model to study complexation in micellar−CD systems is supported by the comparison of the reactivity of these substrates in micellar media, both in the presence and in the absence of β-CD.

Experimental Section

The surfactants SDS and TTABr, as well as β-cyclodextrin, were supplied in the highest available purity by Sigma and used as received. The purity of the surfactants was verified by determining their critical micelle concentrations as described elsewhere.[9b] The *para* and *ortho* isomers of nitrophenyl acetate (NPA) were purchased from Aldrich, whereas the *meta* isomer was synthesized by reacting *m*-nitrophenol with acetic anhydride in pyridine.[11] The low solubility of the acetates in water required using acetonitrile as a solvent in a proportion never exceeding 1% (v/v) in the reaction mixture. Cyclodextrin solutions were made taking into account that commercial β-CD has a H_2O content of 8 mol/mol.

Cyclodextrin was fully deprotonated under the alkaline conditions used, since pK_a^{CD} was 12.2.[1a] All hydroxyl ion concentrations given were obtained by subtracting the CD concentration from that of NaOH. The reaction kinetics were monitored by measuring the absorbance of the resulting nitrophenoxide at 400 nm (*p*-NFA, $\lambda = 450$ nm), using an Applied Photophysics DX 17MV sequential stopped-flow spectrophotometer thermostated at 25 ± 0.1 °C. The substrate concentration used was always approximately 2×10^{-4} M and that of hydroxyl ion higher than 0.1 M. The procedures used to prepare the TTAOH solutions and to perform kinetic runs were described in a previous paper.[12] The reactive-ion cationic micelles (TTAOH) were prepared from solutions of TTABr by ion exchange in Amberlite IRA 400 anionic resin. The absence of bromide ions in the resulting solutions was tested with $AgNO_3$. Solutions were used shortly after preparation.

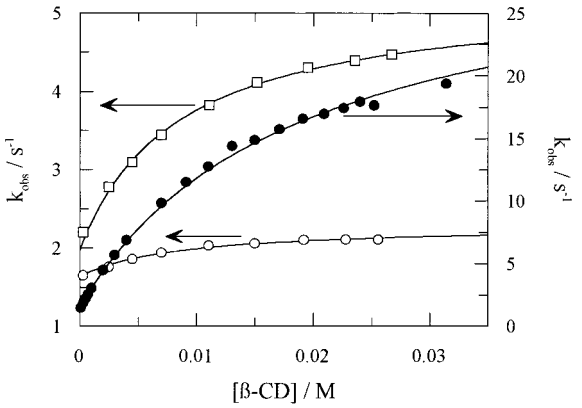


Figure 1. Influence of the β-CD concentration on k_{obs} for the basic hydrolysis of (○) *o*-, (●) *m*-, and (□) *p*-nitrophenyl acetate. [NaOH] = 0.175 M. Curves represent the fits of eq 1 to the experimental results (parameter values in Tables 1−3).

All kinetic experiments were performed with nitrophenyl acetate concentrations much smaller than that of NaOH. The absorbance−time data of all kinetic experiments were fitted by first-order integrated equations, and the values of the pseudo-first-order rate constants (k_{obs}) were reproducible to within 3%.

Results and Discussion

(A) Influence of CD on the Basic Hydrolysis of Nitrophenyl Acetates. The cleavage of aryl esters is one of the most widely studied and best known CD-catalyzed processes.[1a,13,14] However, we studied the influence of the CD concentration on these processes for better consistency with the experimental results. Figure 1 clearly reveals a catalytic effect of CD on the basic hydrolysis of the nitrophenyl acetates, consistent with the esterolysis reaction taking place via the nucleophilic attack of an ionized hydroxyl group in the CD, leading to acyl transfer.[15] For a substrate that undergoes an "uncatalyzed" reaction in a given medium and a "catalyzed" reaction via a 1:1 substrate·CD complex, the expected variation of the observed rate constant with [CD] is given by[15]

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

where K_s^{CD} is the equilibrium binding constant of the substrate to the cyclodextrin, k_{CD} the rate constant for the CD-catalyzed reaction, and k_w the rate constant for the basic hydrolysis in the aqueous medium. In Tables 1−3 the K_s^{CD} and k_{CD} values obtained by fitting the data of Figure 1 to eq 1 by a nonlinear regression method are given. Values of k_w were obtained from separate experiments in pure water.

In broad terms, VanEtten *et al.*[15] found *meta*-substituted phenyl acetate to be more readily cleaved by β-CD than were the *para* and *ortho* isomers. This type of reaction has been widely studied, and the behavior of *meta*-substituted phenyl acetates has been found to be strongly correlated with differences in transition-state binding.[13,16] The transition-state binding constants for these substrates

(9) (a) García-Río, L.; Leis, J. R.; Mejuto, J. C.; Pérez-Juste, J. *J. Phys. Chem. B* **1997**, *101*, 7383. (b) García-Río, L.; Leis, J. R.; Mejuto, J. C.; Pérez-Juste, J. *J. Phys. Chem. B* **1998**, *102*, 4581.

(10) Tee, O. S. *Adv. Phys. Org. Chem.* **1994**, *29*, 1.

(11) Spasov, A. *Ann. Univ. Sofia, II, Fac. Phys. Math., Livre 2* **1938**−**1939**, *35*, 289; *Chem. Abstr.* **1940**, *34*, 2343.

(12) Bravo, C.; Hervés, P.; Leis, J. R.; Peña, M. E. *J. Colloid Interface Sci.* **1992**, *153*, 529.

(13) Matsui, T.; Nishioka, T.; Fujita, T. *Top. Curr. Chem.* **1985**, *128*, 61.

(14) Tee, O. S.; Paventi, M.; Bennett, J. M. *J. Am. Chem. Soc.* **1989**, *111*, 2233.

(15) (a) VanEtten, R. L.; Sebastian, J. F.; Clowes, G. A.; Bender, M. L. *J. Am. Chem. Soc.* **1967**, *89*, 3242. (b) VanEtten, R. L.; Clowes, G. A.; Sebastian, J. F.; Bender, M. L. *J. Am. Chem. Soc.* **1967**, *89*, 3253.

(16) (a) Tee, O. S.; Takasaki, B. K. *Can. J. Chem.* **1985**, *63*, 3540. (b) Tee, O. S.; Mazza, C.; Du, X. X. *J. Org. Chem.* **1990**, *55*, 3603.

Table 1. Results Obtained by Fitting Eqs 2−4, 6, 12, and 14 to the Experimental Data for the Basic Hydrolysis of *o*-Nitrophenyl Acetate in *β*-CD/Surfactant Mixtures[a]

system	cmc_{app}/M	$[CD_f]$/M	cmc_{real}/M	K_s^m/M^{-1}	$k_w/M^{-1}\ s^{-1}$	k_m/s^{-1}	$k_2^m/M^{-1}\ s^{-1}$
SDS			1.00×10^{-3}	47 ± 1	9.3 ± 0.1		
TTAOH			1.40×10^{-3}	86 ± 2	9.3 ± 0.1	6.30 ± 0.02	0.882
TTABr			1.20×10^{-3}	63 ± 2	9.3 ± 0.1	7.74 ± 0.08	1.084
SDS + *β*-CD	3.92×10^{-3}	1.42×10^{-3}	3.36×10^{-4}	47 ± 1	8.47 ± 0.04		
TTAOH + *β*-CD	5.85×10^{-3}	1.54×10^{-4}	1.00×10^{-3}	86 ± 2	9.3 ± 0.1	6.88 ± 0.05	0.963
TTABr + *β*-CD	5.42×10^{-3}	2.35×10^{-4}	6.55×10^{-4}	63 ± 2	9.3 ± 0.1	9.10 ± 0.01	1.274

[a] $k_{CD} = 2.30 \pm 0.03\ s^{-1}$, $K_s^{CD} = 117 \pm 15\ M^{-1}$, $k_{50\%dioxane} = 4.54 \pm 0.05\ M^{-1}\ s^{-1}$, $K_{monomer}^{SDS} = 8000 \pm 500\ M^{-1}$, $K_{monomer}^{TTAX} = 30\,000 \pm 1000\ M^{-1}$.

Table 2. Results Obtained by Fitting Eqs 2−4, 6, 12, and 14 to the Experimental Data for the Basic Hydrolysis of *m*-Nitrophenyl Acetate in *β*-CD/Surfactant Mixtures[a]

system	cmc_{app}/M	$[CD_f]$/M	cmc_{real}/M	K_s^m/M^{-1}	$k_w/M^{-1}\ s^{-1}$	k_m/s^{-1}	$k_2^m/M^{-1}\ s^{-1}$
SDS			1.00×10^{-3}	51 ± 1	9.0 ± 0.1		
TTAOH			1.50×10^{-3}	77 ± 3	9.0 ± 0.1	7.3 ± 0.1	1.022
TTABr			1.20×10^{-3}	63 ± 4	9.0 ± 0.1	10.0 ± 0.2	1.400
SDS + *β*-CD	3.92×10^{-3}	1.42×10^{-3}	3.36×10^{-4}	51 ± 1	9.1 ± 0.5		
TTAOH + *β*-CD	5.85×10^{-3}	1.54×10^{-4}	1.00×10^{-3}	77 ± 3	9.0 ± 0.1	7.8 ± 0.1	1.092
TTABr + *β*-CD	5.42×10^{-3}	2.35×10^{-4}	6.55×10^{-4}	63 ± 4	9.0 ± 0.1	12.9 ± 0.3	1.806

[a] $k_{CD} = 31 \pm 2\ s^{-1}$, $K_s^{CD} = 54 \pm 5\ M^{-1}$, $k_{50\%dioxane} = 6.84 \pm 0.07\ M^{-1}\ s^{-1}$, $K_{monomer}^{SDS} = 8000 \pm 500\ M^{-1}$, $K_{monomer}^{TTAX} = 30\,000 \pm 1000\ M^{-1}$.

Table 3. Results Obtained by Fitting Eqs 2−4, 6, 12, and 14 to the Experimental Data for the Basic Hydrolysis of *p*-Nitrophenyl Acetate in *β*-CD/Surfactant Mixtures[a]

system	cmc_{app}/M	$[CD_f]$/M	cmc_{real}/M	K_s^m/M^{-1}	$k_w/M^{-1}\ s^{-1}$	k_m/s^{-1}	$k_2^m/M^{-1}\ s^{-1}$
SDS			1.00×10^{-3}	40 ± 1	11.3 ± 0.1		
TTAOH			1.40×10^{-3}	65 ± 4	11.3 ± 0.1	16.4 ± 0.2	2.296
TTABr			1.30×10^{-3}	75 ± 4	11.3 ± 0.1	17.5 ± 0.3	2.450
SDS + *β*-CD	3.92×10^{-3}	1.42×10^{-3}	3.36×10^{-4}	40 ± 1	9.8 ± 0.1		
TTAOH + *β*-CD	5.85×10^{-3}	1.54×10^{-4}	1.00×10^{-3}	65 ± 4	11.3 ± 0.1	19.5 ± 0.1	2.730
TTABr + *β*-CD	5.42×10^{-3}	2.35×10^{-4}	6.55×10^{-4}	75 ± 4	11.3 ± 0.1	21.7 ± 0.5	3.038

[a] $k_{CD} = 5.26 \pm 0.09\ s^{-1}$, $K_s^{CD} = 119 \pm 9\ M^{-1}$, $k_{50\%dioxane} = 14.4 \pm 0.1\ M^{-1}\ s^{-1}$, $K_{monomer}^{SDS} = 8000 \pm 500\ M^{-1}$, $K_{monomer}^{TTAX} = 30\,000 \pm 1000\ M^{-1}$.

are consistent with the view that *meta* substituents, regardless of their nature, position the phenyl group of the ester in the CD cavity in a geometry that facilitates the attack of an ionized hydroxyl group and the formation of the transition state for acyl transfer. In contrast, *para* substituents position the ester in the CD cavity in such a way that a nucleophilic attack is more difficult; also, they tend to interfere with transition-state binding.

(B) Basic Hydrolysis of Nitrophenyl Acetates in SDS, TTAOH, and TTABr Micellar Systems. We examined the influence of the concentration of anionic (SDS), functionalized cationic (TTAOH), and unfunctionalized cationic micelles (TTABr) on the basic hydrolysis of nitrophenyl acetates (see Figures 2, 4, and 6). The results can be accurately accounted for in terms of the pseudophase formalism[6] as expanded to include potential exchange of reactant counterions.[5]

The rate of the process is always decreased by the presence of SDS micelles as a result of the nitrophenyl acetate being incorporated into the micelles and HO^- ion being excluded by the effect of electrostatic repulsions.[5,6] Using the pseudophase model, eq 2 can be obtained. Fitting

$$k_{obs} = \frac{k_w[HO^-]}{1 + K_s^m[D_n]} \qquad (2)$$

the experimental results to eq 2 by a nonlinear regression method (curve in Figure 2), the binding constants of substrate to the micelles (K_s^m) were obtained, namely, $(K_s^{SDS})_{ortho} = 47 \pm 1\ M^{-1}$, $(K_s^{SDS})_{meta} = 51 \pm 1\ M^{-1}$, and $(K_s^{SDS})_{para} = 40 \pm 1\ M^{-1}$ for the *ortho*, *meta*, and *para* isomers, respectively. In the fitting, the rate constant in aqueous medium, k_w, was assumed to be constant and equal to the previous value obtained in pure water (data in Tables 1−3).

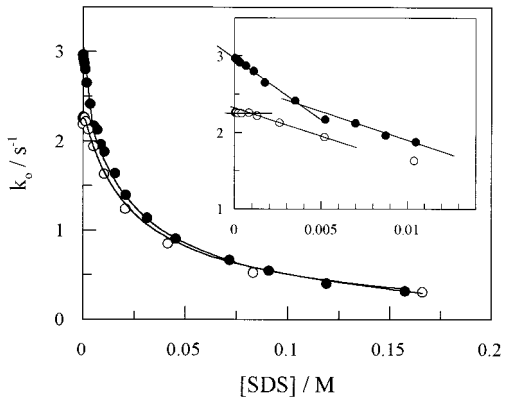


Figure 2. Influence of the SDS concentration on k_{obs} for the basic hydrolysis of *p*-nitrophenyl acetate in the presence and in the absence of *β*-CD: (○) [CD] = 0 and (●) [CD] = 5.00×10^{-3} M. [NaOH] = 0.175 M. Curves represent the fits of eqs 2 and 6 to the experimental results (parameter values in Table 3).

The critical micelle concentration was obtained kinetically as the minimum surfactant concentration required to induce a substantial change in the observed rate constant. The obtained value, cmc = 1.00×10^{-3} M, is much smaller than the reported cmc for SDS, 8.00×10^{-3} M,[6] which is ascribed to the known effect of the presence of salts on the critical micelle concentration of surfactants.[17]

(17) Stinger, D. *Electrostatic Interactions in Aqueous Enviroments*; IUPAC Comission: La Joya, NY, 1975.

In the presence of functionalized micelles of TTAOH, the rate constant increased with increasing surfactant concentration up to a peak value (see Figure 4 for hydrolysis of *o*-nitrophenyl acetate). This catalytic effect was a result of the reactants concentrating in the micellar pseudophase.[5,6] This behavior can be analyzed in quantitative terms on the basis of the micellar pseudophase model, eq 3. The experimental results were fitted by means of a nonlinear regression method. We used the fraction of neutralized micellar charge $\beta = 0.8$ as it was seemingly the most frequently employed value for this purpose.[18] The value of k_w was, again, kept constant and equal to the value previously obtained in pure water. From the fit the binding constant of the substrate to the micelles, K_s^{TTAOH}, and the rate constant in the micellar pseudophase, k_m, are obtained.

$$k_{obs} = \frac{k_w([HO^-]_{add} + [TTAOH]_{monomer} + (1-\beta)[D_n]) + k_m K_s^{TTAOH}\beta[D_n]}{1 + K_s^{TTAOH}[D_n]} \quad (3)$$

The goodness of the fit to the experimental data confirms that the assumption of a constant β value is correct, consistent with the results for the acid hydrolysis of *p*-nitrobenzaldehyde acetals in micelles of alkanesulfonic acids[19] and notwithstanding the failure of the model with CTAOH or CTAF micelles. In these latter cases, the reaction rate does not reach a limiting value when the substrate has been completely incorporated into the micelles, but rather increases steadily as the likely result not of an intrinsic failure in the kinetic model but of the fact that the assumption of constancy in β does not hold under these conditions.[20] The accuracy of the underlying hypothesis in the micellar pseudophase model for micelles possessing a reacting counterion for anionic and cationic micellar systems was recently confirmed by our group.[12,21]

Fitting the experimental data to eq 3 provided the corresponding K_s^{TTAOH} and k_m values. The K_s^{TTAOH} values for the *ortho*, *meta*, and *para* isomers (86 ± 2, 77 ± 3, and 65 ± 3 M^{-1}, respectively) are consistent with those obtained in SDS micelles and with the variation of the binding constant of the substrate to micellar systems as a function of the number of carbon atoms in the surfactant. As with SDS micelles, the cmc value is much smaller than the cmc in the absence of NaOH, which is attributed to the known effect of added salts on the cmc. On the other hand, the k_m values obtained, s^{-1}, are not strictly comparable with those pertaining to an aqueous medium, k_w (M^{-1} s^{-1}). However, on the assumption that the volume element of the reaction in the micellar phase is equal to the volume of the Stern layer, which is estimated to be $\bar{V} = 0.14$ dm^3 mol^{-1},[22] we can obtain a bimolecular reaction rate constant in the micellar phase as, $k_2^m = k_m \bar{V}$ (k_2^m with units M^{-1} s^{-1}). The obtained values, $(k_2^m)_{ortho}^{TTAOH} = 0.882$ M^{-1} s^{-1}, $(k_2^m)_{meta}^{TTAOH} = 1.022$ M^{-1} s^{-1}, and $(k_2^m)_{para}^{TTAOH} = 2.296$ M^{-1} s^{-1}, differ from those in the aqueous medium, $k_w^{ortho} = 9.3$ M^{-1} s^{-1}, $k_w^{meta} = 9.0$ M^{-1} s^{-1}, and $k_w^{para} = 11.3$ M^{-1} s^{-1}. This differential reactivity sequence is consistent with a decreased polarity of the micellar interface relative to the aqueous medium. Thus, the bimolecular rate constants in a 50:50 (v/v) dioxane/water mixture, $k_{50\%dioxane}^{ortho} = 4.54 \pm 0.05$ M^{-1} s^{-1}, $k_{50\%dioxane}^{meta} = 6.84 \pm 0.07$ M^{-1} s^{-1}, and $k_{50\%dioxane}^{para} = 14.4 \pm 0.1$ M^{-1} s^{-1}, exhibit a substituent dependence similar to that observed on the micellar surface. This altered reactivity must be the result of a structural change in the transition state with the composition of the medium.

In the presence of TTABr micelles, the pseudo-first-order rate constant, k_{obs}, increases with increasing surfactant concentration up to a maximum value, beyond which it starts to decrease (see Figure 6 for hydrolysis of *p*-nitrophenyl acetate). The maximum can be ascribed to two opposing effects in the micellar pseudophase model as modified to include ion exchange. The addition of TTABr increases the relative concentrations of the substrate and HO^- ions in the Stern layer, thereby also increasing the reaction rate. As the surfactant concentration is raised, so is the concentration of Br^- ions added to the medium. Bromide ions (unreactive) compete with HO^- ions in the Stern layer and inhibit the reaction. The relative contributions of these two processes result in the maximum in the experimental k_{obs} *vs* [TTABr] plot. Application of the micellar pseudophase formalism on the assumption of ion exchange yields the following expression for k_{obs}:

$$k_{obs} = \frac{k_w[HO^-]_w + (k_m K_s^{TTABr} - k_w)m_{OH}[D_n]}{1 + K_s^{TTABr}[D_n]} \quad (4)$$

where m_{OH} was obtained by applying the ion exchange formalism.[5]

$$m_{OH}^2 - m_{OH}\left[\frac{[HO^-]_T + K_{HO}^{Br}[Br^-]_T}{(K_{HO}^{Br} - 1)[D_n]} - \beta\right] - \left[\frac{\beta[HO^-]_T}{(K_{HO}^{Br} - 1)[D_n]}\right] = 0 \quad (5)$$

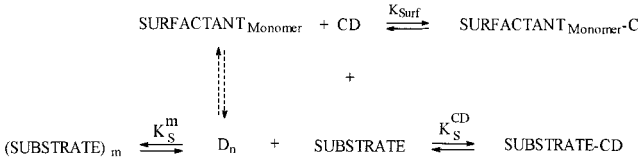
Solving eq 5 entails the prior knowledge of the ion exchange constant, K_{HO}^{Br}, and the fraction of neutralized micellar charge, β. We used reported values of $K_{HO}^{Br} = 14$[21ac,23] and $\beta = 0.8$.[18]

Fitting the experimental results to eq 4, by a nonlinear regression method, provided the following values for the binding constants of the substrates to TTABr micelles: $(K_s^{TTABr})_{ortho} = 63 \pm 2$ M^{-1}, $(K_s^{TTABr})_{meta} = 63 \pm 4$ M^{-1}, and $(K_s^{TTABr})_{para} = 75 \pm 4$ M^{-1}. These values are consistent with those for the reaction in TTAOH micelles. The corresponding k_2^m values, $(k_2^m)_{ortho}^{TTABr} = 1.08$ M^{-1} s^{-1}, $(k_2^m)_{meta}^{TTABr} = 1.40$ M^{-1} s^{-1}, and $(k_2^m)_{para}^{TTABr} = 2.45$ M^{-1} s^{-1}, are also consistent with those obtained in the presence of functionalized cationic micelles.

(C) Basic Hydrolysis of Nitrophenyl Acetates in β-CD/SDS Mixtures. *1. Experimental Approach.* Figure 2 shows the influence of SDS concentration on k_{obs} for the basic hydrolysis of *p*-nitrophenyl acetate both in the presence and in the absence of β-CD. The inhibitory effect

(18) *Micellization, Solubilization and Microemulsions*; Mittal, K. L., Ed.; Plenum Press: New York, 1977.
(19) Bunton, C. A.; Romsted, L. S.; Savelli, G. *J. Am. Chem. Soc.* **1979**, *101*, 1253.
(20) (a) Vera, S.; Rodenas, E. *Tetrahedron* **1986**, *42*, 143. (b) Al-Lohedan, H. A. *J. Chem. Soc., Perkin Trans. 2* **1989**, 1181. (c) Santana Neves, M. de F.; Zanette, D.; Quina, F.; Tadeu Moretti, M.; Nome, F. *J. Phys. Chem.* **1989**, *93*, 1502. (d) Vera, S.; Rodenas, E. *J. Phys. Chem.* **1986**, *90*, 3414. (e) Rodenas, E.; Vera, S. *J. Phys. Chem.* **1985**, *89*, 513.
(21) (a) Bravo, C.; Hervés, P.; Leis, J. R.; Peña, M. E. *J. Phys. Chem.* **1991**, *94*, 8816. (b) García-Río, L.; Hervés, P.; Leis, J. R.; Mejuto, J. C. *Langmuir* **1997**, *13*, 6088. (c) García-Río, L.; Hervés, P.; Leis, J. R.; Mejuto, J. C.; Pérez-Juste, J. *J. Phys. Org. Chem.* **1998**, *11*, 577.
(22) (a) Bunton, C. A.; Romsted, L. S.; Savelli, G. *J. Am. Chem. Soc.* **1979**, *101*, 1253. (b) Bunton, C. A. *Catal. Rev. Sci. Eng.* **1979**, *20*, 1.
(23) (a) Castro, A.; Leis, J. R.; Peña, M. E. *J. Chem. Soc., Perkin Trans. 2* **1990**, 1221. (b) Cuccovia, I. M.; Feitosa, E.; Chamimovich, H.; Sepulveda, L.; Reed, W. *J. Phys. Chem.* **1990**, *94*, 3722.

Scheme 1



observed as the surfactant concentration is raised before micellization is attributed to the complexation of surfactant monomers by CD and the resulting release of *p*-nitrophenyl acetate into the aqueous medium. This decreases the reaction rate by virtue of the catalytic effect of CD on the substrate being lost upon complexation. As the surfactant concentration is further increased, micellization eventually takes place and the typical inhibitory effect of anionic micelles on the basic hydrolysis of hydrophobic substrates is observed.

This experimentally observed behavior can be explained by assuming simultaneous alkaline hydrolysis of the nitrophenyl acetate in the aqueous pseudophase (with k_w) and transfer of the acyl group from CD-complexed substrate to the secondary hydroxyl group of CD (with k_{CD}) (Scheme 1).

$$k_{obs} = \frac{k_w[HO^-] + k_{CD}K_s^{CD}[CD_f]}{1 + K_s^{CD}[CD_f] + K_s^{SDS}[D_n]} \qquad (6)$$

On the basis of the proposed model, the competition of SDS monomers for binding to CD or self-associating (micellizing) will give rise to a substantial concentration of free CD in the reaction medium. Figure 3 shows the variation of the ratio of k_{obs} values in the presence and in the absence of CD, $k_{obs}^{SDS+CD}/k_{obs}^{SDS}$, as a function of the surfactant concentration. The total SDS concentration was used below the micellization point and that of micellized surfactant, $[D_n]$, above it. The results reveal that the $k_{obs}^{SDS+CD}/k_{obs}^{SDS}$ ratio decreases with increasing [SDS] through complexation of surfactant monomers with CD and then remains constant with $[D_n]$ (with a different limiting value for each nitrophenyl acetate).

It should be noted that the $k_{obs}^{SDS+CD}/k_{obs}^{SDS}$ ratio was greater than unity for the three substrates studied. This suggests that, regardless of the surfactant concentration, there is a catalytic effect that can be tentatively ascribed solely to the presence of CD. Also, the upper limit for the ratio is directly related to the catalytic action of β-cyclodextrins on the basic hydrolysis of the nitrophenyl acetates studied. This allows one to conclude that the medium contains a substantial amount of free CD in equilibrium with the micellized system.

The constancy in the $k_{obs}^{SDS+CD}/k_{obs}^{SDS}$ ratio with $[D_n]$ also allows one to state that the free CD concentration does not change once micellization has started. In simple micellar systems (in the absence of CD), the concentration of surfactant monomers in equilibrium with micellized surfactant is assumed to remain constant and equal to cmc_{real} after micellization begins. Therefore, we may assume that, after micellization, both the concentration of free CD and that of free surfactant monomers in micelle−CD systems remain constant at the values they have when the total surfactant concentration equals cmc_{app}.

From eqs 2 and 6, eq 7 for the ratio $k_{obs}^{SDS+CD}/k_{obs}^{SDS}$ can be obtained. From the $k_{obs}^{SDS+CD}/k_{obs}^{SDS}$ ratio, eq 7, the concentration of free CD in equilibrium with the micellar system can be calculated by using k_w, k_{CD}, and K_s^{CD} values

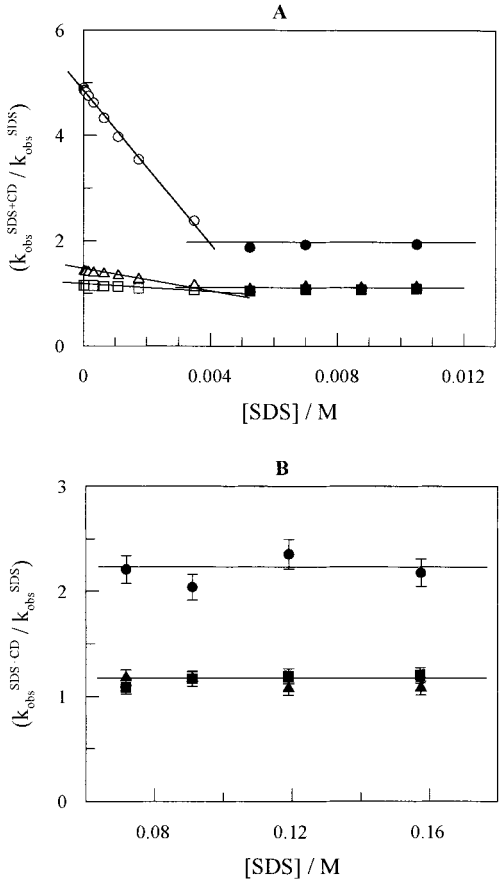


Figure 3. Influence of the surfactant concentration on the $k_{obs}^{SDS+CD}/k_{obs}^{SDS}$ ratio for the basic hydrolysis of (□, ■) *o*-, (○, ●) *m*-, and (△, ▲) *p*-nitrophenyl acetate. Open symbols represent total surfactant concentrations below cmc_{app} and solid symbols $[D_n]$ values (see the text). $[CD] = 5.00 \times 10^{-3}$ M.

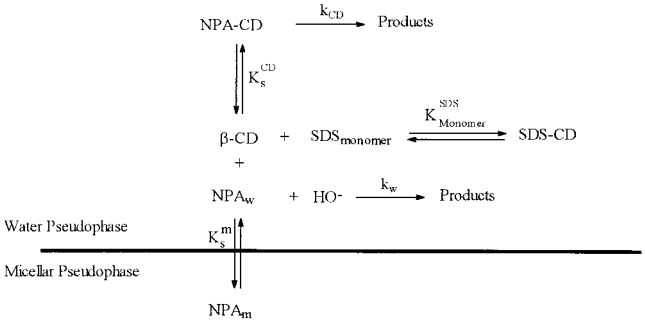
previously obtained for the reaction in water and in the presence of β-CD (Tables 1−3). The values of $[CD_f]$

$$\frac{k_{obs}^{SDS+CD}}{k_{obs}^{SDS}} = \frac{k_w[HO^-] + k_{CD}K_s^{CD}[CD_f]}{k_w[HO^-] + k_{obs}^{SDS}K_s^{CD}[CD_f]} \qquad (7)$$

calculated using the experimental data for the basic hydrolysis of *o*-, *m*-, and *p*-nitrophenyl acetate were 3.40×10^{-3}, 1.42×10^{-3}, and 1.37×10^{-3} M, respectively. These calculated values for the *meta* and *para* isomers are consistent. The divergence of the *ortho* isomer in this respect can be ascribed to the weak catalytic effect of β-CD on its hydrolysis. We shall henceforth use the $[CD_f]$ value obtained using the experimental data for the basic hydrolysis of *m*-nitrophenyl acetate. This choice is due to the high catalytic effect of β-CD upon the basic hydrolysis of the *meta* isomer that results in an increase of accuracy in the determination of $[CD_f]$.

The $[CD_f]$ value obtained for the basic hydrolysis of *m*-nitrophenyl acetate exceeded that previously found at the same CD concentration, $[CD_f] = 7.26 \times 10^{-4}$ M.[9b] The difference can be ascribed to the uncertainty in the determination of the critical micelle concentration of SDS in the presence of β-CD. In fact, determining cmc_{app} for this type of system is not as easy as in the absence of CD. This parameter was determined kinetically as the surfactant concentration where an abrupt change in the k_{obs} *vs* [SDS] curve was observed (see Figure 2). Such a change was due to a different nature of the inhibitory effect; the

Scheme 2



decreased catalytic effect of CD was combined with the typical inhibitory effect of anionic micelles on the basic hydrolysis of hydrophobic substrates.

2. Quantitative Approach. The experimental behavior can be explained quantitatively by assuming simultaneous alkaline hydrolysis of the substrate in the aqueous pseudophase (with k_w) and transfer of the acyl group from CD-complexed substrate to the secondary hydroxyl group of CD (with k_{CD}), Scheme 1 and eq 6. Solving eq 6 requires knowing cmc_{app}, which was kinetically evaluated (values in Tables 1−3), and $[CD_f]$.

An expression for the free CD concentration, $[CD_f]$ is derived on the basis of Scheme 2. We assume both the surfactant·CD and substrate·CD complexes to be of 1:1 stoichiometry. The substrates 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 and by micelles and for surfactant monomers by CD are expressed as

$$K_s^{CD} = \frac{[\text{substrate}\cdot\text{CD}]}{[\text{substrate}]_w[CD_f]} \qquad K_s^m = \frac{[\text{substrate}]}{[\text{substrate}]_w[D_n]}$$

$$K^{surf}_{monomer} = \frac{[\text{surf}_{monomer}\cdot\text{CD}]}{[\text{surf}_{monomer}][CD_f]}$$

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

$$[CD]_T = [CD_f] + [\text{surf}_{monomer}\cdot\text{CD}] + [\text{substrate}\cdot\text{CD}]$$

$$[\text{surfactant}]_T = [\text{surf}_{monomer}] + [\text{surf}_{monomer}\cdot\text{CD}]$$

$$[\text{substrate}]_T = [\text{substrate}]_w + [\text{substrate}\cdot\text{CD}]$$

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

$$A[CD_f]^3 + B[CD_f]^2 + C[CD_f] - [CD]_T = 0 \qquad (8)$$

where

$$A = K^{surf}_{monomer}K_s^{CD} \qquad (9)$$

$$B = \{K^{surf}_{monomer} + K_s^{CD} + K_s^{CD}K^{surf}_{monomer}([\text{surf}]_T - [CD]_T + [\text{substrate}]_T) \qquad (10)$$

$$C = \{1 + K^{surf}_{monomer}([\text{surf}]_T - [CD]_T) + K_s^{CD}([\text{substrate}]_T - [CD]_T) \qquad (11)$$

Solving eqs 8−11 entails the prior knowledge of the binding constants of the surfactant monomer and the substrate to the CD ($K^{surf}_{monomer}$ and K_s^{CD}, respectively). The latter can be readily obtained from experiments performed in the absence of surfactant. On the other hand, the marked differences between reported $K^{surf}_{monomer}$ values[24] led us to use simulated values for the complexation constant of the surfactant monomer to CD.[9] In a previous work[9a] we estimated $K^{surf}_{monomer}$ for the binding of the dodecyl sulfate anion to CD to be $K^{surf}_{monomer} = 8000 \pm 500\ M^{-1}$.

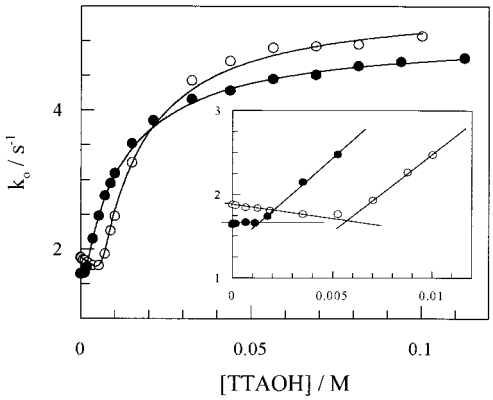


Figure 4. Influence of the TTAOH concentration on k_{obs} for the basic hydrolysis of *o*-nitrophenyl acetate in the presence and in the absence of *β*-CD: (●) [CD] = 0 and (○) [CD] = 5.00×10^{-3} M. [NaOH] = 0.175 M. Curves represent the fits of eqs 3 and 12 to the experimental results (parameter values in Table 1).

Solving eq 6 the free CD concentration below cmc_{app} was calculated by solving eqs 8−11. Above the cmc_{app}, $[CD_f]$ is assumed to be constant and equal to the value obtained at cmc_{app}. In this way, the experimental data of Figure 2, and similar ones obtained for the *ortho* and *meta* isomers of nitrophenyl acetate, were fitted by a nonlinear regression method to eq 6 (solid curve in Figure 2). To simplify the fitting of eq 6 to the experimental results in Figure 2, K_s^{CD} and k_{CD} were taken to have the same values as in the absence of surfactant and K_s^{SDS} the same values as in the absence of CD. The k_w values corresponding to the reaction rate in aqueous medium were optimized. As can be seen from Tables 1−3, the k_w values obtained in the presence and in the absence of CD were very similar, indicating that CD does not interact with SDS micelles.

(D) Basic Hydrolysis of Nitrophenyl Acetates in *β*-CD/TTAOH Mixtures. *1. Experimental Approach.* Figure 4 shows the effect of the TTAOH concentration on the basic hydrolysis of *o*-nitrophenyl acetate in the presence and absence of *β*-CD. As can be seen, in the presence of *β*-CD, k_{obs} initially decreases with increasing surfactant concentration and then increases to a maximum value. The behavior observed at low concentrations of surfactant (below its cmc) is a result of its monomers being complexed by the cyclodextrin. As the surfactant concentration is further increased, micellization eventually starts. The subsequent increase in k_{obs} with an increase in [TTAOH] at medium to high surfactant concentrations is typical of a process catalyzed by functionalized micelles.

(24) (a) Okubo, T; Kitano, H.; Ise, N. *J. Phys. Chem.* **1976**, *80*, 2661. (b) Satake, I.; Yoshida, S.; Hayakawa, K.; Maeda, T.; Kusumoto, Y. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 3991. (c) Park, J. W.; Song, H. J. *J. Phys. Chem.* **1989**, *93*, 6454. (d) Dharmawardana, U. R.; Christian, S. D.; Tucker, E. E.; Taylor, R. W.; Scamehorn, J. F. *Langmuir* **1993**, *9*, 2258. (e) Wan Yunus W. M. Z.; Taylor, J.; Bloor, D. M.; Hall, D. G.; Wyn-Jones, E. *J. Phys. Chem.* **1992**, *96*, 8979. (f) Sasaki, K. J.; Christian, S. D.; Tucker, E. E. *J. Colloid Interface Sci.* **1990**, *134*, 412. (g) Funasaki, N.; Yodo, H.; Hada, S.; Neya, S. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1323 (and references therein).

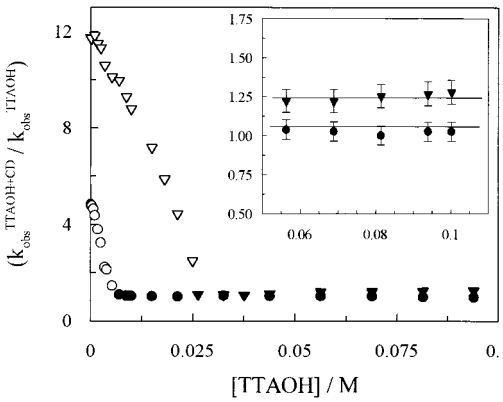


Figure 5. Influence of the surfactant concentration on the $k_{obs}^{TTAOH+CD}/k_{obs}^{TTAOH}$ ratio for the basic hydrolysis of *m*-nitrophenyl acetate in the presence of β-CD: (○, ●) [CD] = 5.00×10^{-3} M and (▽, ▼) [CD] = 2.50×10^{-2} M. Open symbols represent total surfactant concentrations below cmc_{app} and solid symbols [D_n] values (see the text).

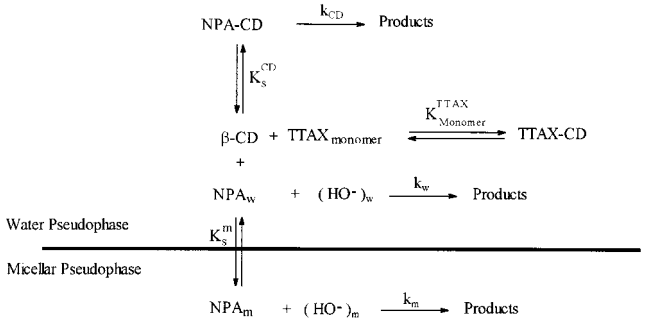
As shown above, in the presence of SDS micelles, the anionic form of β-CD does not interact with the micellar system once this has been formed, probably because of the high hydrophobicity of the cyclodextrin. By extrapolation of these results, one would expect CD not to bind to cationic micelles. However, the anionic character of CD under the working conditions does not exclude the potential binding of CD, as a counterion, to the micelles. The results of Figure 4 suggest that such an interaction either does not exist or is negligible under the prevailing working conditions. The potential binding of β-CD as a counterion would entail the establishment of an ion exchange equilibrium between HO^- ions and the anionic form of CD. As a result, the observed rate constant would never have peaked as the TTAOH concentration was increased.

Additional confirmation for the absence of interaction can be obtained from Figure 5. As with SDS, the $k_{obs}^{TTAOH+CD}/k_{obs}^{TTAOH}$ ratio was plotted against the concentration of micellized surfactant at levels above its critical micelle concentration and against the total surfactant concentrations at levels below that where the micelle system was formed. Figure 5 shows the data for the basic hydrolysis of *m*-nitrophenyl acetate at two different CD concentrations (5.00×10^{-3} and 2.50×10^{-2} M). As can be seen, the $k_{obs}^{TTAOH+CD}/k_{obs}^{TTAOH}$ ratio initially decreased with increasing surfactant concentration through complexation of TTAOH monomers by cyclodextrin and then reached a limiting value that remained constant whatever the value of [D_n]. Such a limiting value increased with increasing overall CD concentration in the medium through an increase in [CD_f]. The fact that the limiting value is independent of [D_n] indicates that CD does not interact with the micellar system.

The above experimental results can be interpreted in terms of the pseudophase formalism (Scheme 3). In the pseudophase model, reaction in the aqueous phase occurs via free OH^- ions with unbound substrate or in the substrate·CD complex and in micellar pseudophase between micellar bound substrate and associated counterions. The rate expression for k_{obs} is

$$k_{obs} = \frac{k_w([HO^-]_{add} + [TTAOH]_{monomer} + (1-\beta)[D_n]) + k_m K_s^m \beta [D_n] + k_{CD} K_s^{CD} [CD_f]}{1 + K_s^m [D_n] + K_s^{CD} [CD_f]} \quad (12)$$

Scheme 3



The ratio $k_{obs}^{TTAOH+CD}/k_{obs}^{TTAOH}$ can be obtained from eqs 3 and 12

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

From the $k_{obs}^{TTAOH+CD}/k_{obs}^{TTAOH}$ ratio, eq 13, the concentration of free CD in equilibrium with the micellar system can be calculated by using k_w, k_{CD}, and K_s^{CD} values previously obtained for the reaction in water and in the presence of β-CD (Tables 1−3). Equation 13 yields [CD_f] (data in Figure 5) values of 1.54×10^{-4} and 2.51×10^{-4} M for total cyclodextrin concentrations of 5.00×10^{-3} and 2.50×10^{-2} M, respectively.

2. Quantitative Approach. Interpreting the experimental results in quantitative terms entails solving eq 12, which in turn requires the prior knowledge of the free CD concentration at each TTAOH concentration. Again, we calculated the concentration of free CD by using eqs 8−11. To this end, we assumed the binding constant of TTAOH monomer to CD to be identical to that for TTABr. This assumption is supported by the fact that only the alkyl chain of the surfactant lies within the CD cavity.[25] Again, the marked dispersion of reported $K_{monomer}^{TTABr}$ values[7e,24b−g,26,27] led us to use a simulated value. We shall thus henceforth use a $K_{monomer}^{TTAOH}$ value identical to that for TTABr, *viz.*, 30 000 ± 1000 M^{-1}.[9] Once micellization starts, the variation of the rate constant with the surfactant concentration is attributed to incorporation of the substrate into the micellar pseudophase. 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}.

For simplicity, we assumed the parameter values for the reaction in the presence of CD (K_s^{CD} and k_{CD}) to be constant. Also, the binding constant of NPA to the micellar pseudophase, K_s^{TTAOH}, was fixed, and the rate constant for the reaction in the pseudophase, k_m, was optimized. The invariability of the binding constant of the substrate to the micellar pseudophase was demonstrated in a previous paper.[9] The parameter values obtained by fitting eq 12 to the experimental results are given in Tables 1−3. As can be seen, the k_m values (or the corresponding k_2^m values), *viz.*, 0.97, 1.10, and 2.70 M^{-1} s^{-1} for the *ortho*, *meta*, and

(25) This similarity is consistent with the CD cavity holding only the alkyl chain of the surfactant.

(26) (a) Satake, I.; Ikenoue, T.; Takeshita, T.; Hayakawa, K.; Maeda, T. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2746. (b) Palepu, R.; Reinsborough, V. *Can. J. Chem.* **1989**, *67*, 1550.

(27) Mwakibete, H.; Cristantino, R.; Bloor, D. M.; Wyn-Jones, W.; Holzwarth, J. F. *Langmuir* **1995**, *11*, 57 and references therein.

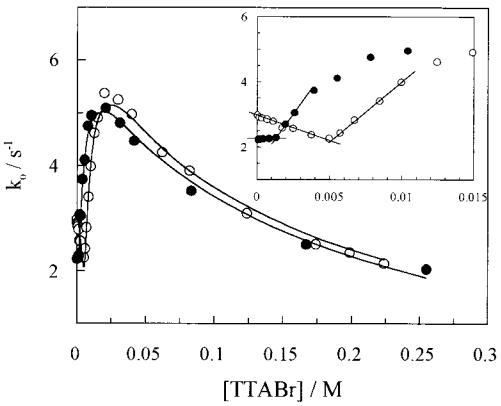


Figure 6. Influence of the TTABr concentration on k_{obs} for the basic hydrolysis of *p*-nitrophenyl acetate in the presence and absence of *β*-CD: (●) [CD] = 0 and (○) [CD] = 5.00×10^{-3} M. [NaOH] = 0.175 M. Curves represent the fits of eqs 4 and 14 to the experimental results (parameter values in Table 3).

para isomers, respectively, are not significantly different from those obtained in the absence of CD (0.88, 1.02, and 2.30 M^{-1} s^{-1}, respectively). This result confirms that the properties of the micellar system are not altered by the presence of cyclodextrins.

(E) Basic Hydrolysis of Nitrophenyl Acetates in *β*-CD/TTABr Mixtures. Figure 6 shows the variation of the rate constant for the basic hydrolysis of *p*-nitrophenyl acetate, k_{obs}, in the presence and in the absence of *β*-CD. The dependence of the rate constant on the CD concentration is a result of the catalytic effect of cyclodextrins on the basic hydrolysis of NPA. Thus, the k_{obs} value obtained by extrapolation to zero surfactant concentration is consistent with the values found in the absence of surfactant (Figure 1). The initial decrease in k_{obs} down to a minimum value with increasing the surfactant concentration is due to the complexation of TTABr monomers by CD, which displaces the substrate from the substrate·CD complex, thus suppressing the CD-catalyzed route for its basic hydrolysis. Subsequently, k_{obs} increases until an inhibitory effect occurs, consistent with the behavior of cationic micelles in the basic hydrolysis of hydrophobic substrates.

The experimental behavior observed can be quantitatively interpreted in terms of the micellar pseudophase formalism with provisions for ion exchange. We must consider three different, simultaneous reaction pathways, namely, the reaction of free substrate in the aqueous medium, that of CD-complexed substrate, and that of micelle-bound substrate with HO^- ions present on the micellar surface (see Scheme 3 with inclusion of ion exchange). This mechanistic scheme allows one to derive the following expression for the rate constant:

$$k_{obs} = \frac{k_w[HO^-] + (k_m K_s^m - k_w) m_{OH}[D_n] + k_{CD} K_s^{CD}[CD_f]}{1 + K_s^m[D_n] + K_s^{CD}[CD_f]} \quad (14)$$

Equation 14 was fitted to the experimental results by using a procedure similar to that previously employed with the TTAOH−CD mixed system. The free CD concentration was determined from eqs 8−11, and the concentration of HO^- ions in the micellar pseudophase, m_{OH}, was obtained similarly to that in the absence of CD. The critical micelle concentration was kinetically determined by a procedure similar to that for TTAOH on the assumption that the minimum in the k_{obs} *vs* [TTABr] plot would correspond to the start of the micellization process and hence that the TTABr concentration at that point would be cmc_{app}.

For simplicity, the parameters for the CD-catalyzed pathway, K_s^{CD} and k_{CD}, were assumed to be constant and equal to those obtained in the absence of surfactant. Also, the binding constant of NPA to the micellar pseudophase, K_s^{TTAOH}, was fixed, and the rate constant for the reaction in the pseudophase, k_m, was optimized. The optimized values for the rate constant in the micellar pseudophase, k_m, or those for k_2^m (M^{-1} s^{-1}) are shown in Tables 1−3. As can be seen, the k_m values (or the corresponding k_2^m values 1.274, 1.806, and 3.038 M^{-1} s^{-1} for the *ortho*, *meta*, and *para* isomers, respectively) are not significantly different from those obtained in the absence of CD (0.88, 1.02, and 2.30 M^{-1} s^{-1}, respectively). This result confirms that the properties of the micellar system are not altered by the presence of cyclodextrins.

Conclusions

A comparison of the observed rate constant values in the presence and in the absence of CD, $k_{obs}^{SDS+CD}/k_{obs}^{SDS}$ and $k_{obs}^{TTAOH+CD}/k_{obs}^{TTAOH}$, reveals the absence of interaction between the micellar system and cyclodextrin. The sole effect of CD on the system is the complexation of surfactant monomers, which delays the formation of the micellar system (by increasing cmc_{app}). The competition of the surfactant monomers for binding to the cyclodextrin and self-association (micellization) gives rise to the presence of a substantial concentration of free CD in the reaction medium, as shown by the fact that the $k_{obs}^{SDS+CD}/k_{obs}^{SDS}$ and $k_{obs}^{TTAOH+CD}/k_{obs}^{TTAOH}$ ratios are both greater than unity. The results obtained in this work provide direct evidence of the presence of an appreciable amount of free CD after micellization starts. This behavior had never previously been documented, and the authors assume it is one of the reasons for the disparity among reported binding constants for surfactant complexation by CD.

The proposed kinetic model, an extension of the pseudophase formalism, has been satisfactorily applied to a CD-catalyzed reaction in this work. The model considers two simultaneous pathways in the aqueous medium that involve free hydroxyl ions and the substrate−CD complex, respectively. In those cases where hydroxyl ions may be present in the micellar pseudophase, one must consider their potential reaction with micelle-bound substrate. From the data in Tables 1−3, it follows that the presence of CD favors micellization by lowering cmc_{real}. This effect is well documented in the literature[28] but not fully explained; it is believed to be related to the influence of additives on micellization.[29] It was especially marked in anionic SDS micelles, which suggests that it is related to the effect of added salts on cmc.[17] The absence of interaction between the anionic form of CD and the micellar system in the presence of cationic micelles is consistent with the less marked decrease in cmc_{real}.

Acknowledgment. Financial support from Xunta de Galicia (Project XUGA 30105A97) and from the Dirección General de Investigación Científica y Técnica of Spain (Project PB96-0954) is gratefully acknowledged. J.P.-J. also thanks the Ministerio de Educación y Cultura for a FPU research-training grant.

LA981392E

(28) Jiang, Y. B.; Wang, X. *J. Appl. Spectrosc.* **1994**, *48*, 1428.
(29) (a) Hunter, R. J. *Foundations of Colloid Science*; Clarendon Press: Oxford, 1987; Vol. 1. (b) Schwuger, M. *Ber. Bunsen-Ges. Phys. Chem.* **1971**, *75*, 167.