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Ethyl Cyclohexanone-2-carboxylate in Aqueous Micellar Solutions. 1. Ester Hydrolysis in Cationic and Nonionic Micelles

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Hydrolysis rates for the ester of ethyl cyclohexanone-2-carboxylate (ECHC) were measured in aqueous dioxane mixtures and in aqueous micellar solutions of cationic, nonionic, and mixed cationic−nonionic detergents. The following cationic surfactants were used: dodecyltrimethylammonium bromide (DTABr), tetradecyltrimethylammonium bromide (TTABr), tetradecyltrimethylammonium chloride (TTACl), tetradecyltrimethylammonium acetate (TTAAc), and cetyltrimethylammonium bromide (CTABr). Poly(ethylene oxide)-9-dodecyl ether ($C_{12}E_9$) and poly(ethylene oxide)-20-cetyl ether ($C_{16}E_{20}$) were used as the nonionic surfactants. The kinetic profiles of the reactions were investigated as a function of surfactant concentration. In aqueous strong mineral acid (HCl or HBr) solutions of the cationic surfactants DTABr, TTABr, TTACl, and CTABr, the reaction was greatly inhibited at surfactant concentrations above the critical micelle concentration; the same behavior was observed for the influence of the nonionic surfactants and for the mixed surfactants DTABr + $C_{12}E_9$ analyzed in an equimolar mixture of both surfactants. Micellar effects were analyzed by means of the pseudophase model. When the hydrolysis reaction was studied in aqueous buffered solutions of acetic acid−acetate, the shape of the observed rate constant versus surfactant concentration (of TTACl and TTABr) profiles depended on surfactant concentration. At low surfactant concentration, first-order rate constants pass through maxima with increasing surfactant concentration followed by a gradual but steady decrease in the rate as the surfactant concentration increases further. By contrast, the first-order rate constant increases throughout the whole concentration range of TTAAc used. Micellar effects observed for the reaction in aqueous buffered solutions were analyzed qualitatively or quantitatively by means of the pseudophase ion exchange (PPIE) model. In every experimental situation, the reaction at the micellar interface is not negligible; however, the second-order rate constant in this region is lower than that measured in water.

Introduction

One of the most important properties of aqueous micellar solutions is their ability to solubilize a wide variety of organic solutes normally not dissolvable in water.[1,2] This phenomenon is readily noticeable through chemical reactivity studies. Aqueous micelles may increase rates of bimolecular reactions by concentrating both reactants at the interface of micellar aggregates, or they may decrease rates if both reactants are kept apart due to their differing hydrophobic/hydrophilic characters or electrostatic effects.[3−7] In these studies, a micelle is treated as a reaction medium distinct from bulk water, whose properties gradually vary, from the purely nonpolar inner core (a hydrocarbon-like solvent) out to the partially polar surface. Between these two sites, a micelle offers a gamut of solubilization environments. Reactant concentrations at micellar interfaces can be determined experimentally or estimated, and second-order rate constants can then be calculated. To do this, one must usually define the partial molar volume of the interfacial reaction region, *V*, in the micellar pseudophase where the reaction takes place to refer to concentrations in the micellar phase.[8,9]

Previous studies demonstrate that aqueous micellar solutions strongly alter the keto−enol equilibrium of β-diketones by increasing the enol tautomer concentration,[10−12] thus altering their reactivity toward electrophiles.[13,14]

In a recent study,[15] we showed that the β-keto ester, ethyl cyclohexanone-2-carboxylate (ECHC), is almost entirely enolyzed in water or that the ketonization reaction is slower than the ester hydrolysis. Therefore, the presence of micelles should have no effect on its UV−vis absorption spectrum, in contrast to what occurs with, e.g., benzoylacetone.[10] However, this compound is unstable in water, and spontaneous ester decomposition occurs at moderate rates. The reaction is catalyzed by strong mineral acids, even though the rate of the spontaneous ester hydrolysis is comparable to the acid-catalyzed pathway at moderate acid concentrations (e.g., 0.1 M). The experimentally determined first-order rate constant is $k_o = k_o^w + k_H[H^+]$, where $k_o^w = 0.987 \times 10^{-3}$ s^{-1} and $k_H = 8.98 \times 10^{-3}$ mol^{-1} dm^3 s^{-1}. The kinetic hydrogen isotope effects agree with the generally accepted mechanism for acid-catalyzed hydrolysis of esters: a rapid equilibrium step involving protonation of the ester on the carbonyl group, and subsequent hydration of the cation-like species thus formed to yield the corresponding alcohol and caboxylic acid. In aqueous buffered solutions of organic acids (acetic acid and its chloro derivatives), the reaction proves to be strongly general base catalyzed; i.e., a new reaction path through the basic form of the buffer (e.g., acetate ion) arises. A good Brønsted plot is obtained with a slope of β = 0.5, indicating that the attack of the basic form of the buffer is involved in the rate-controlling step of the reaction; that is, ester hydrolysis goes through tetrahedral intermediates (Scheme 1).

In this study we report the results of the influence of cationic, nonionic, and mixed cationic−nonionic surfactants, forming micelles, on the ester hydrolysis reaction of ECHC. The presence of either cationic or nonionic micelles with unreactive counte-

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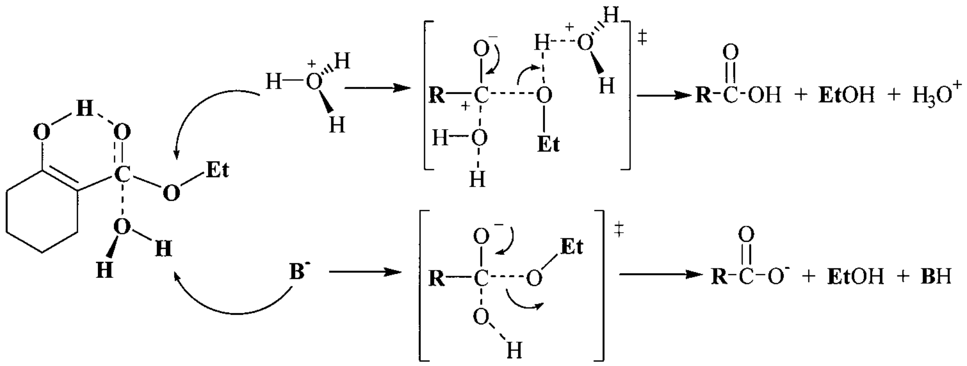
SCHEME 1: Carboxylic Esters: Mechanism of Acid- and Base-Catalyzed Hydrolysis



rions strongly inhibits the acid-catalyzed hydrolysis reaction. By contrast, small concentrations of cationic micelles catalyzed the reaction pathway promoted by the basic form of weak organic acids; however, the presence of functionalized micelles of tetradecyltrimethylammonium acetate strongly enhanced the rate of ester hydrolysis conducted in aqueous buffered solutions of acetic acid−acetate. The aim of this work is to cover the behavior of buffer solutions in the presence of surfactants,[16] a situation frequently avoided in studies with aqueous micellar solutions.

Experimental Section

Ethyl cyclohexanone-2-carboxylate (ECHC), a Merck product of maximum purity, was used as supplied. Surfactants of the highest purity available, dodecyltrimethylammonium bromide (DTABr), tetradecyltrimethylammonium bromide (TTABr), cetyltrimethylammonium bromide (CTABr), poly(ethylene oxide)-9-dodecyl ether ($C_{12}E_9$), and poly(ethylene oxide)-20-cetyl ether ($C_{16}E_{20}$) were purchased from Sigma and were used without further purification. Both tetradecyltrimethylammonium chloride (TTACl) and tetradecyltrimethylammonium acetate (TTAAc) were prepared through ion exchange of a solution of TTABr, using an Amberlite IRA-400 (Cl) anionic exchange resin that, in the case of TTAAc, was previously saturated with acetate ions. The same kinetic results are obtained when working with commercial samples of TTACl; the purity of TTAAc has been probed by titration with HCl. All other reagents were supplied by Merck and were used as received. Solutions were prepared with doubly distilled water (first distilled over potassium permanganate solution and then redistilled).

Pure ECHC was dissolved in dry dioxane (spectrophotometric grade). The hydrolysis reaction of ECHC was initiated with the addition of 10 or 15 μL of a solution of ECHC in dioxane into a thermostated cell containing the acid and the surfactant solutions, to reach a final reaction volume of 3.0 mL. The ECHC concentration in the reaction medium was 6.0×10^{-5} M.

The kinetic measurements were recorded with a Kontron-Uvikon (Model 942) double-beam spectrophotometer, provided with multiple cell carriers thermostated by circulating water. The pH was measured with a Crison pH meter equipped with a GK2401B combined glass electrode and calibrated using commercial buffers at pH 4.01 and 7.01. All experiments were performed at 25 °C.

The kinetic runs were performed under pseudo-first-order conditions, with the acid concentration greatly exceeding the ethyl cyclohexanone-2-carboxylate concentration. In each kinetic experiment the integrated method was applied. The decreasing absorbance due to the reactant ECHC was monitored at 256 nm[15] during the course of the reaction. Pseudo-first-order rate constants (k_o) were obtained by a nonlinear least-squares fit of the experimental data (absorbance−time, $A-t$) by the first-order rate equation expressed in eq 1

$$A_t = A_\infty + (A_0 - A_\infty)e^{-k_o t} \tag{1}$$

with A_0, A_t, and A_∞ being the absorbance readings at zero, t, and infinite times, respectively. Values of A_∞ were consistent with the experimental ones. Absorbance changes ($\Delta A = A_0 - A_\infty$) higher than 0.7 unit were monitored in each kinetic experiment to ensure accurate values of k_o. In the fitting process of $A-t$ data to eq 1, correlation coefficients higher than 0.9999 were obtained.

Results

The influences of several variables were investigated to elucidate the mechanism of the ECHC hydrolysis reaction in micelles.

Influence of the Solvent. The ester hydrolysis of ECHC was studied in aqueous dioxane mixtures at $[H^+] = 0.083$ M (HCl). The experimental data of $A-t$ perfectly fit the first-order integrated equation, and k_o decreases as the percentage of dioxane in the reaction mixture increases; e.g. at approximately 10 M dioxane the observed rate constant is nearly 34 times less than the value determined in water. However, the k_o versus [dioxane] profile does not indicate any change in the reaction mechanism. Typical results are shown in Figure 1. The reaction was also studied in several solvents. The observed rate constants measured in 83% v/v organic solvent at $[H^+] = 0.083$ M are displayed in Table 1.

Influence of Cationic Surfactants. The influence of cationic surfactants on the ester hydrolysis reaction of ECHC was investigated by using strong mineral acids: HBr with TTABr and DTABr surfactants, and HCl with TTACl and CTABr surfactants. (Aqueous solutions of CTABr precipitate in the presence of HBr at 25 °C). Whatever the cationic surfactant, the observed rate constant decreased as the surfactant concentration increased and reached a saturation limit at high [surfactant]. Figure 2 shows typical results obtained from working with TTACl and TTABr surfactants.

Influence of Nonionic and Mixed Cationic−Nonionic Surfactants. The acid-catalyzed hydrolysis of the ester function of ECHC was studied in aqueous micellar solutions of the nonionic surfactants $C_{12}E_9$ and $C_{16}E_{20}$ and of the mixed cationic−nonionic surfactants DTABr−$C_{12}E_9$ at equal molar ratio (i.e., $r = [C_{12}E_9]/[DTABr] = 1$). We used HCl as the strong mineral acid. The presence of micelles reduced k_o values, with the inhibition effect depending on the nature of the micelles and on their concentration. Figure 3 shows representative results.

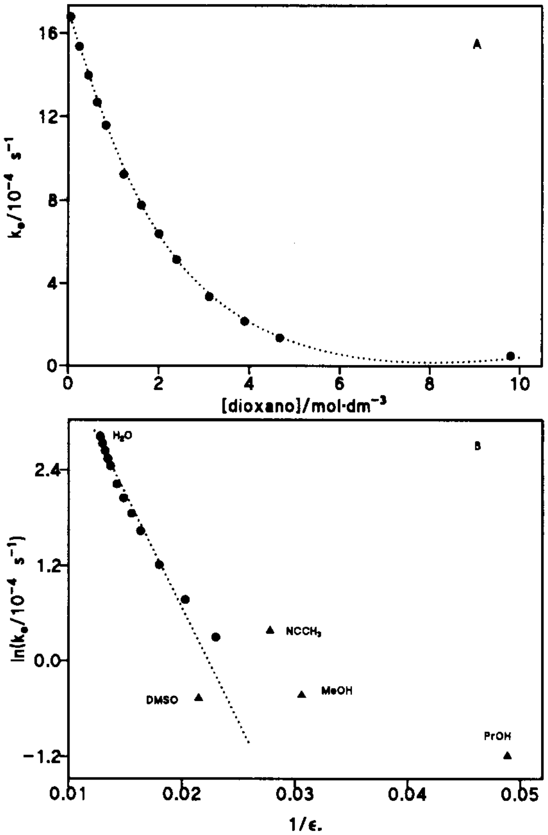


Figure 1. (A) Variation of the observed rate constant, k_o, obtained in the acid-catalyzed hydrolysis of ethyl cyclohexanone-2-carboxylate ([ECHC] = 6.0×10^{-5} M) at [HCl] = 0.083 M as a function of [dioxane]. (B) Plot of ln(k_o) versus $1/\epsilon$ (ϵ, relative permittivity of the solvent); (▲) values obtained in 83% indicated solvent−water mixture (DMSO, dimethyl sulfoxide; MeOH, methanol; PrOH, propanol).

TABLE 1: Observed Rate Constants Obtained in 83% v/v Organic Solvent/Water at [HCl] = 0.083 M in the Acid Hydrolysis of ECHC (6.3×10^{-5} M)

solvent	ϵ	$k_o/10^{-5}$ s^{-1}
dioxane	2.2	4.95
propanol	20.5	3.05
methanol	32.7	6.50
acetonitrile	36.0	14.7
dimethyl sulfoxide	46.5	6.25

[a] From ref 20.

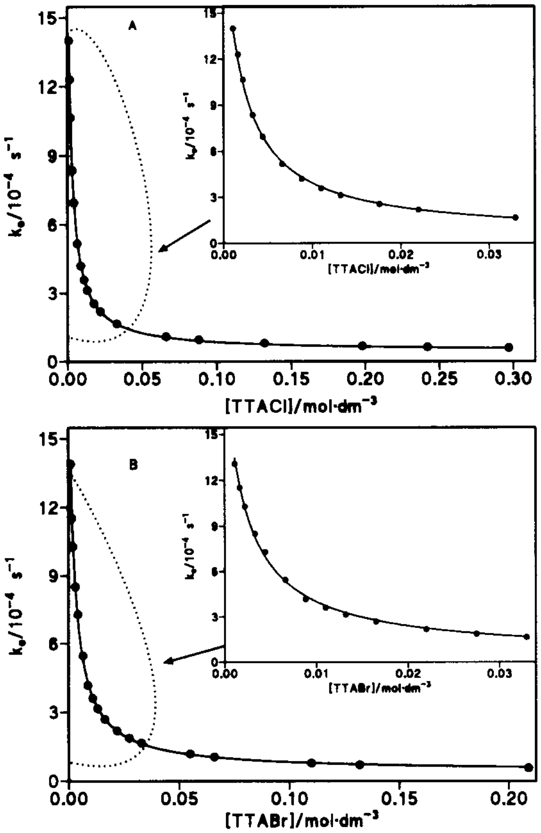


Figure 2. Influence of cationic surfactants TTACl (A) and TTABr (B) on the pseudo-first-order rate constant obtained in the kinetic study of the acid-catalyzed hydrolysis of ECHC (6.0×10^{-5} M) at [H$^+$] = 0.050 M by using HCl (A) or HBr (B).

Reaction in Acetic Acid−Acetate Buffers. Figure 4 shows typical results of the influence of cationic surfactants on the ester hydrolysis reaction carried out in buffer solutions of acetic acid−acetate at pH 4.1 and 4.6 at total [buffer] = 0.067 and 0.15 M. At low [TTAX] catalysis was observed, and k_o goes through maxima and decreases at high [TTAX]. The maximum catalytic effect, measured as the ratio k_o^{max}/k_o, is higher with TTACl than with TTABr; it decreased as the [buffer] increased, and the [TTAX] required to reach the k_o^{max} was somewhat higher with TTACl than with TTABr. The results reported in Table 2 summarize these observations. In $C_{12}E_9$ micelles, k_o decreases for the increasing nonionic surfactant concentration, Figure 5.

All these observations suggest an ionic exchange between acetate ions and Br$^-$ or Cl$^-$ ions.

Hydrolysis in Functionalized Micelles. The study of the reaction in functionalized micelles of TTAAc should provide valuable information on ion exchange between acetate ions and surfactant counterions.

This unusual surfactant was prepared through an ion-exchange resin saturated with sodium acetate (NaAcO). To test the micellization process, the electrical conductivity of aqueous solutions of TTAAc was measured at surfactant concentrations below and above the critical micelle concentration (cmc). The results are shown in Figure 6. The micellization process was investigated in pure water as well as in an aqueous buffer solution of acetic acid−acetate at pH 4.40, with the aim of reproducing the kinetic conditions.

Data in Figure 6A are representative of a micellization process: two linear regions of κ vs [surfactant] were obtained. The least-squares fitting of both linear portions afforded the following results: (i) above the cmc, κ/mS·cm^{-1} = (0.216 ± 0.002) + (26.64 ± 0.08)[TTAAc], $r = 0.9999_5$; (ii) below the cmc, κ/mS·cm^{-1} = (0.0024 ± 0.0004) + (63.3 ± 0.2)[TTAAc], $r = 0.9999_6$. The intersection point was used to obtain the cmc, and the ratio of slopes above (m_2) and below (m_1) the cmc provides the micelle ionization degree, α ($=m_2/m_1$).[17] The obtained results were cmc = 5.8×10^{-3} M and $\alpha = 0.42$.

The electrical conductivity measurements performed in a buffer of acetic acid−acetate at pH 4.40 and [buffer]$_t$ = 0.10 M are typical of a normal micellization process, Figure 6B. The break point corresponding to the cmc is not well-defined due to the higher conductivity of the solvent. However, from the straight line above the cmc, κ/mS·cm^{-1} = (2.787 ± 0.005) + (25.58 ± 0.02)[TTAAc] ($r = 0.999_8$), one may note that the slope value is quite close to that determined in water. This allows us to conclude that the presence of the buffer does not modify the characteristics of TTAAc micelles.

The influence of TTAAc micelles on the hydrolysis reaction was studied in 0.10 M acetic acid−acetate buffer at pH 4.40. Figure 7 shows the variation of k_o as a function of [TTAAc], and no maxima is found. Under these experimental conditions

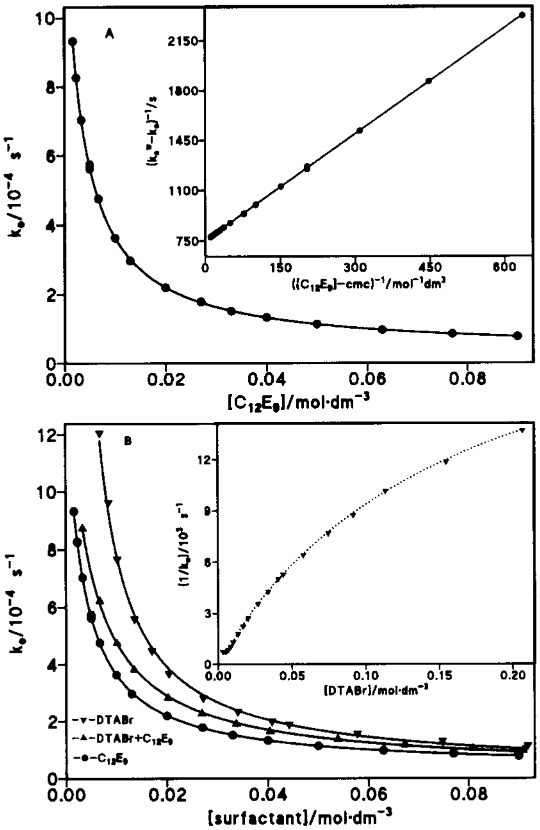


Figure 3. (A) Influence of the nonionic surfactant, $C_{12}E_9$, on k_o at $[H^+] = 0.050$ M (HCl). The curve fits eq 2; the inset shows the linearization of the data according to eq 3; for parameters, see Table 3. (B) Variation of k_o as a function of (▼) [DTABr] at [HBr] = 0.050 M; (▲) [DTABr] + $[C_{12}E_9]$, equimolar mixture of both surfactants at [HCl] = 0.050 M; and (●) the same as in (A).

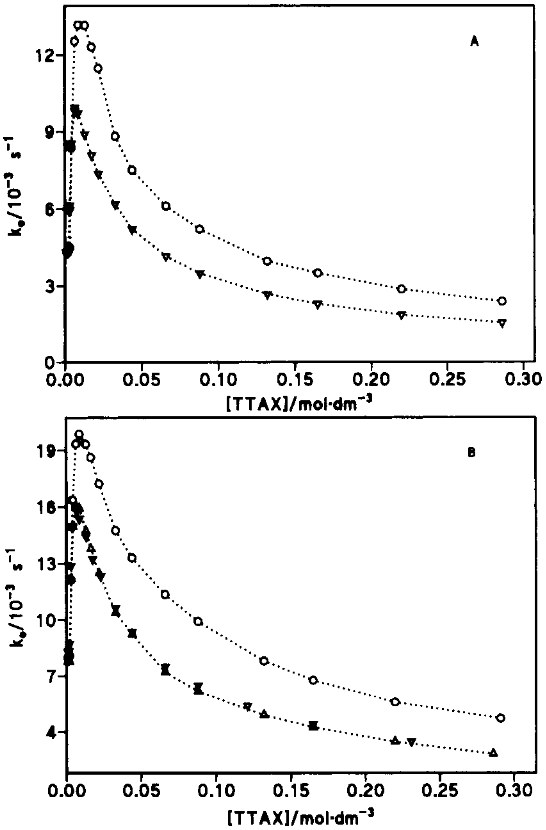


Figure 4. (A) Influence of (○) [TTACl] and of (▽) [TTABr]on the pseudo-first-order rate constant of the base-catalyzed hydrolysis of ECHC in aqueous buffered solutions of 0.067 M acetic acid–acetate at pH 4.60. (B) Variation of k_o as a function of (○) [TTACl] at [buffer] = 0.067 M and pH 4.57; (△) [TTABr] at [buffer] = 0.07 M, pH 4.57; and (▽) [TTABr] at [buffer] = 0.15 M, pH 4.11. Dotted line to guide the eye.

there is no possibility of ion exchange between acetate ions and micellar counterions; thus, k_o increases with [surfactant] throughout the range concentration. The typical observed behavior of functionalized micelles, or micelles with reactive counterions, is an increase of k_o along with the increasing surfactant concentration, leveling off at high [surfactant].

Discussion

The ester hydrolysis reaction is both acid and base catalyzed. In acid medium the reaction mechanism involves protonation of the carbonyl group in a rapid and reversible reaction step followed by attack of water. This mechanism is consistent with the decrease in k_o as both water concentration and solvent polarity decrease. The transition state is a cation-like intermediate; consequently a reduction of the relative permittivity of the solvent causes destabilization of the transition state due to the reduction of solvating power. The data in Figure 1B show the typical $\ln(k_o)$ versus $1/\epsilon$ profile expected for a bimolecular reaction between an ion and a polar molecule[18] yielding a transition state more polar than the reactants, so that the rate constant increases with the increase in the dielectric constant of the solvent. Values of ϵ for aqueous dioxane mixtures were determined following the work of Anderson.[19] With the purpose of including also in Figure 1B the k_o values determined in 83% solvent–water, the ϵ values corresponding to these mixtures were taken as for pure solvents.[20]

Reaction rates in the presence of cationic micelles were analyzed quantitatively in terms of the pseudophase model (Scheme 2), where the substrate ECHC in water associates with micellized surfactant, Dn, forming ECHC complexed to a micelle, $ECHC_m$, with an association constant K_s. Reaction may occur in the aqueous or micellar pseudophases, with first-order rate constants k_w and k_o^m, respectively. The rate constant in water is the sum of rate constants via the uncatalyzed ($k_o^w = k_{H_2O}[H_2O]$) or acid-catalyzed (k_H) reaction; i.e. $k_w = k_o^w + k_H[H^+]$. Still, as the $[H^+]$ at the surface of a cationic micelle must be negligible, the rate constant for the reaction in the micellar phase only accounts for the reaction through the attack of water molecules, that is, spontaneous hydrolysis.

The first-order rate constant for the overall reaction, k_o, is given by

$$k_o = \frac{k_w + k_o^m K_s[Dn]}{1 + K_s[Dn]} \qquad (2)$$

If k_o^m were negligible, then plots of $1/k_o$ against [Dn] would be straight lines. Nevertheless, curves such as those shown in the inset of Figure 3B for the case of DTABr are observed in every case. This means that the reaction in the micellar phase is not negligible. Therefore, the observed rate constants measured as a function of surfactant concentration can be fitted by using either eq 2 or its linear form given in eq 3.

$$\frac{1}{k_w - k_o} = \frac{1}{k_w - k_o^m}\left(1 + \frac{1}{K_s}\cdot\frac{1}{[Dn]}\right) \qquad (3)$$

Equation 3 is a type of Lineweaver–Burk representation, and this data analysis method has the slight disadvantage of leading

TABLE 2: Experimental Conditions and Values of k_o and k_o^{max} Obtained in the Study of the Influence of TTABr and TTACl Surfactant Concentration in the Ester Hydrolysis Reaction of ECHC Performed in Acetic Acid–Acetate Buffers

surfactant	$[buffer]_t$/ M	pH	$k_o/10^{-3}$ s^{-1}	$k_o^{max}/10^{-3}$ s^{-1}	k_o^{max}/k_o	$[Dn]_{max}$[a]
TTABr	0.067	4.11	4.33	9.81	2.3	4.6×10^{-3}
TTABr	0.15	4.11	8.32	15.86	1.9	4.6×10^{-3}
TTABr	0.067	4.60	8.10	16.03	2.0	4.6×10^{-3}
TTACl	0.067	4.11	4.35	13.19	3.0	5.8×10^{-3}
TTACl	0.067	4.60	7.80	20.92	2.7	5.8×10^{-3}
TTACl	0.070	4.57	8.00	19.90	2.5	5.8×10^{-3}

[a] Micelle concentration (=$[surfactant]_t$ − cmc) at which k_o^{max} is observed.

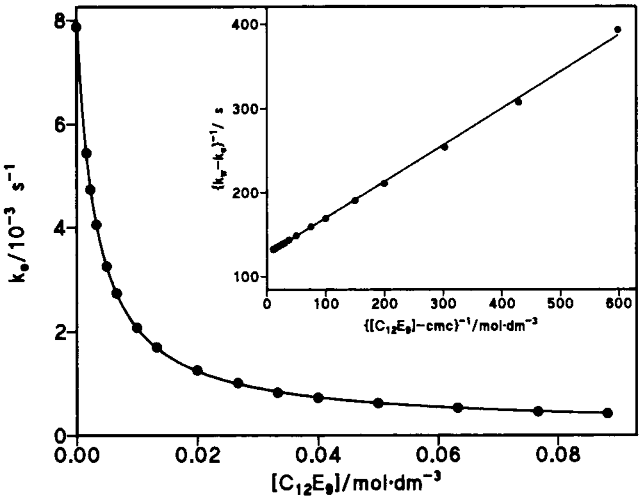


Figure 5. Influence of nonionic surfactant ($C_{12}E_9$) concentration on the overall rate constant, k_o, measured in the base-catalyzed hydrolysis of ECHC (6.0×10^{-5} M) in aqueous buffered solutions of 0.067 M acetic acid–acetate at pH 4.57. The curve fits eq 2; for parameters, see Table 3. The inset shows the linearization according to eq 3.

to a plot in which most of the points tend toward one end of the line. Hence, we used the nonlinear regression analysis of the experimental data, k_o − $[surfactant]_m$ according to eq 2. Curves in Figures 2 and 3 show the corresponding fits; the Figure 3A inset shows an example of the linear representation according to eq 3. In each case, satisfactory agreement between the experimental data and the theoretical treatment was attained.

Aqueous micellar solutions of pure nonionic surfactants or mixed cationic and nonionic surfactants behave as pure cationic micellar solutions. Because of the high hydrophilic character of H^+, together with the low polarity of the micellar interface, the rate of the acid-catalyzed reaction in this region is negligible. Therefore, the quantitative analysis undertaken with cationic micelles works here also.

The parameters determined, along with the experimental conditions, are listed in Table 3.The fact that the reaction in the micellar phase is not zero indicates that ECHC is dissolved not in the micellar core but in the micellar interface, where the presence of water molecules is very important.[21,22] This notion applies to either cationic or nonionic micelles, which indicates that the higher solubilization of ECHC in the micellar phase is due to hydrophobic effects. The cyclic structure of the enol of a β-keto ester (like ECHC), stabilized by intramolecular H-bonding, strongly favors the intermolecular forces between solute and micellar interface as compared with solute and water, thus resulting in a modification of the interfacial partition coefficient with respect to the hypothetic noncyclic structure.[23] The main factor that could control the value of the association constant of ECHC enol to micelles is the phase hydrophobicity, which increases along with the hydrocarbon chain length of the surfactant. In line with this, Figure 8 shows the correlation between $\ln(K_s)$ and No, the number of carbon atoms in the hydrocarbon chain of the surfactant. Association to the nonionic surfactants turns out to be higher than that to the homologous cationic surfactant. This effect can be explained by considering the solute hydrogen-bond acidity, which favors incorporation into the micelles and seems to be more important in nonionic micelles.

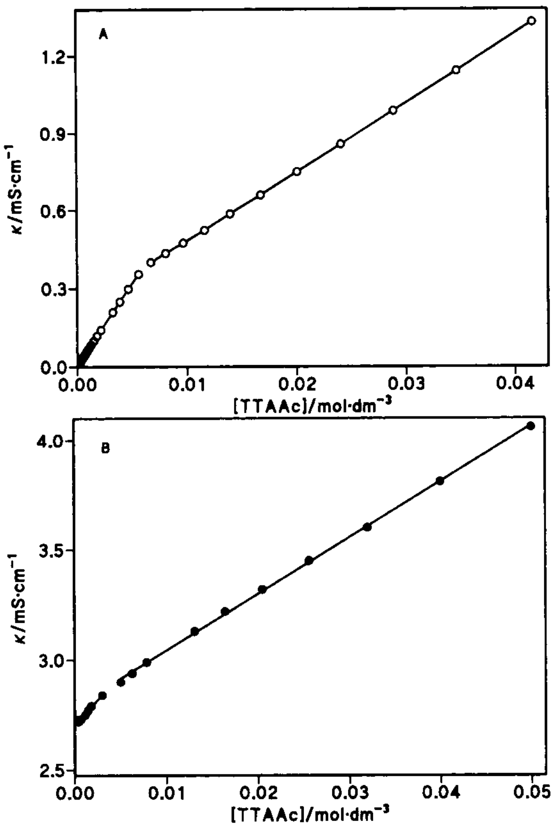


Figure 6. Electrical conductivity measurements of aqueous solutions of tetradecyltrimethylammonium acetate, TTAAC, as a function of [TTAAc] measured (A) in water and (B) in a buffer solution of 0.10 M acetic acid–acetate at pH 4.40.

The enols of both benzoylacetone (BZA) and ECHC have quite similar structures, and both substrates form complexes with cationic or nonionic micelles yielding quite similar values for the association constants, K_s.[10] A reason for this may emerge if it is the cyclic structure of the enol that controls the higher solubility of this tautomer in a less polar medium, such as the micellar interface. However, greater differences are found in the complexes of both compounds with β-cyclodextrin (β-CD): the enol of ECHC forms inclusion complexes[15] with β-CD that are nearly 3 times more stable than those formed by the enol of BZA.[24] Interactions between the secondary −OH groups in β-CD and the −OEt moiety in the ECHC enol could account for these differences.

Values of k_o^m listed in Table 3 account for the rates of ester hydrolysis in the micellar phase under the attack of H_2O, but with the water concentration referring to the total solution volume. A comparison between k_o^m and k_o^w (=0.987×10^{-3} s^{-1}) indicates that the former rate constant is more than 20 times lower than the value of the latter. It should also be noted that the k_o^m values reported in Table 3 compare quite well with the k_o values in Table 1; i.e. the rate constants observed in the micellar interface are similar to rates measured in solvents with

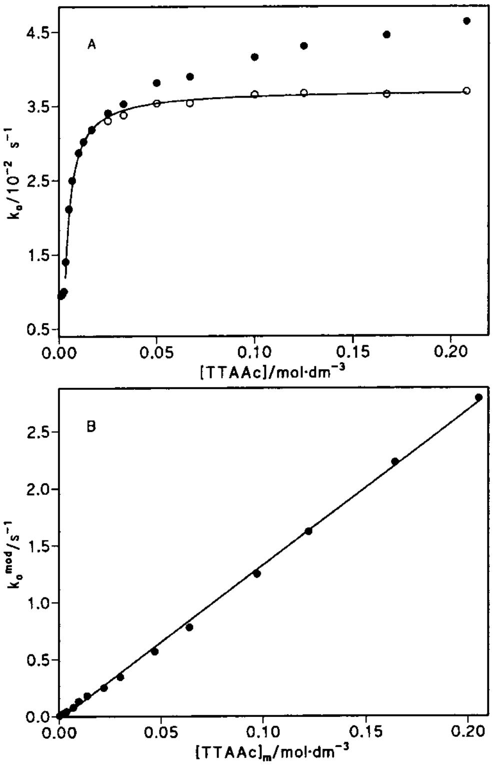
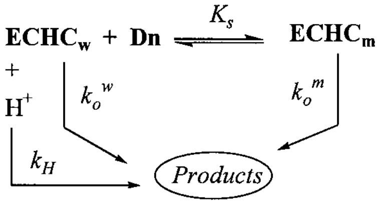


Figure 7. (A) Experimental values (●) of k_o measured as a function of [TTAAc] in the base-catalyzed hydrolysis of ECHC studied in aqueous buffered solutions of 0.10 M acetic acid−acetate at pH 4.40; (○) corrected k_o values to refer them at pH 4.40. The curve fits eq 5; for parameters and data, see Tables 3 and 4, respectively. (B) Plot of k^{mod} $\{=k_o(1 + K_s[TTAAc]_m) - k_w^{cor}\}$ against the micellized TTAAc concentration.

SCHEME 2: Mechanism of Acid-Catalyzed Hydrolysis of ECHC in Cationic Micelles



a water content of approximately 10 M. To compare reactivities in micelles with those in water, we have to assume a volume for the micellar phase. With this volume fraction estimated as $V = 0.15$ dm^3 mol^{-1},[8] then $Vk_o^m = k_{H_2O}^m$ represents the bimolecular rate constant between ECHC and H_2O at the micellar interface. This rate constant is 4 times lower than the bimolecular rate constant measured in water ($k_{H_2O} = 1.78 \times 10^{-5}$ mol^{-1} dm^3 s^{-1}). The difference probably comes from the lower hydration power in the micellar interface, which makes the transition state more unstable, even though the water nucleophilicity could increase, making the H_2O attack on the ester more effective.

When the reaction is performed in aqueous buffered solutions of acetic acid−acetate, the observed rate constant is given by $k_o = k_o^w + k_H[H^+] + k_B[AcO^-]$, where k_B represents the catalytic rate constant by acetate ions, AcO$^-$. At the same time, by considering the values of these rate constants obtained in water,[15] namely, $k_o^w = 0.987 \times 10^{-3}$ s^{-1}; $k_H = 8.97 \times 10^{-3}$ mol^{-1} dm^3 s^{-1}, and $k_B = 0.269$ mol^{-1} dm^3 s^{-1} (for acetate ions), one can easily see that, e.g., at pH >3, the second term in the previous sum is negligible. Then, under the experimental conditions of acetic acid−acetate buffer solutions of total buffer concentration equal to 0.067 or 0.15 M and at pH values of 4.11 or 4.57, the expression of k_o is that which is reported in eq 4, where $[AcO^-] = [buffer]_t K_a/(K_a + [H^+])$, with K_a being the acidity constant of acetic acid, pK_a = 4.77.[25]

$$k_o = k_o^w + k_B[AcO^-] \qquad (4)$$

In the presence of cationic micelles of TTACl or TTABr, k_o goes through maxima as the surfactant concentration increases; i.e., k_o increases at low [surfactant] and then decreases at high [surfactant] (see Figure 4). These k_o–[surfactant] profiles may be understood in terms of the pseudophase ion exchange model (PPIE),[26] according to which the surfaces of ionic micelles are viewed as ion exchangers and competition between reactive and inert counterions is characterized by an empirical exchange constant, K_I. Here, acetate ions are reactive counterions that exchange with Cl$^-$ or Br$^-$ ions when the reaction is carried out in the presence of TTACl or TTABr, respectively. The exchange constant between Cl$^-$ ions (or Br$^-$ ions) at the micellar surface and acetate ions in water ($X^-_m + AcO^-_w \rightleftharpoons X^-_w + AcO^-_m$, X = Cl or Br) has been determined as $K_{Cl}^{AcO} = 0.5$ (or $K_{Br}^{AcO} = 0.098$).[27] Hence, low [TTAX] means low [Cl$^-$] (or [Br$^-$]) and competition for the micellar surface is favorable to acetate ions. This fact, together with the high concentration of ECHC enol in the micellar pseudophase, causes a catalysis of the reaction; however, a further increase in [surfactant] also increases the Cl$^-$ (or Br$^-$) ions, with the concomitant reduction of acetate ions at the micellar interface. Furthermore, the increase of micelles reduces the ECHC enol concentration at the micellar pseudophase. On the other hand, since the exchange constant for Cl$^-$ at the micellar surface by Br$^-$ in the aqueous phase is $K_{Cl}^{Br} = 5.1$, the catalysis is higher with TTACl micelles than with TTABr micelles.

Further evidence of the exchange process is shown by the data in Table 4. We can see that increasing the [TTACl] causes a decrease in the pH of the bulk aqueous solution because the ionization equilibrium of acetic acid is enhanced as more acetate ions are taken up by the micellar surface, according to the Le Châtelier principle. In fact, the presence of $C_{12}E_9$ micelles inhibits the reaction throughout the surfactant concentration range; see Figure 5 (no ionic exchange is possible). The enol of ECHC binds strongly to $C_{12}E_9$ micelles, but acetate anions are not concentrated at the micellar surface; therefore, the separation of both reactants results in a reduction of the reaction rate. By fitting the experimental data by eq 2, the following results are obtained: $k_w = (8.0 \pm 0.2) \times 10^{-3}$ s^{-1}; $K_s = 312 \pm 3$ mol^{-1} dm^3, and $k_o^m = (1.5 \pm 0.1) \times 10^{-4}$ s^{-1}; see Table 3. Notice that k_o^m obtained here is approximately 5 times the k_o^m value obtained for the effect of the same surfactant in the presence of HCl (acid-catalyzed hydrolysis). It is unlikely that acetate ions would reside at the interface of $C_{12}E_9$ micelles. The effect could be due to a different stabilization of the transitition state because, in 83% v/v acetonitrile−water, e.g., the observed k_o has a value quite similar to that of the k_o^m obtained here and also to the k_o^m value obtained in anionic micelles (see part 2[28]).

The previous results call for more work with functionalized micelles of TTAAc. One might expect the reaction to occur in both aqueous and micellar pseudophases, but with different rate constants in each medium (see Scheme 3). The spontaneous decomposition in water represents around 10% of the k_o value under the experimental conditions used in this work. However, the acetate ion concentration at the interface of TTAAc micelles

TABLE 3: Experimental Conditions and Parameters Obtained in the Study of the Influence of Cationic and Nonionic Micelles on the Acid-Catalyzed ([Acid] = 0.050 M) and Base-Catalyzed (Acetic Acid−Acetate) Hydrolysis of ECHC

surfactant	acid	cmc/10^{-3} M	$k_w/10^{-3}$ s^{-1}	K_s/mol^{-1} dm^{-3}	$k_o^m/10^{-4}$ s^{-1}	cc
DTABr	HBr	11.4	1.45 ± 0.01	219 ± 6	0.395 ± 0.04	0.999_7
TTABr	HBr	0.85	1.445 ± 0.01	312 ± 7	0.34 ± 0.06	0.999_5
TTACl	HCl	1.0	1.44 ± 0.01	331 ± 6	0.43 ± 0.05	0.999_8
CTABr	HCl	0.065	1.415 ± 0.013	446 ± 4	0.49 ± 0.03	0.999_8
$C_{12}E_9$	HCl	0.23	1.395 ± 0.01	310 ± 5	0.305 ± 0.016	0.9999_5
$C_{16}E_{20}$	HCl	0.008	1.395 ± 0.002	480 ± 3.5	0.324 ± 0.015	0.999_8
$C_{12}E_9$ + DTABr	HCl	0.6	1.405 ± 0.015	222 ± 2	0.285 ± 0.03	0.999_8
$C_{12}E_9$	buffer[a]	0.18	8.05 ± 0.02	312 ± 3	1.53 ± 0.11	0.9999_5
TTAAc	buffer[b]	2.6 ± 0.7	9.5 ± 0.6	305 ± 9	376 ± 14	0.999_5

[a] 0.067 M acetic acid−acetate at pH 4.57. [b] 0.10 M acetic acid−acetate at pH 4.40.

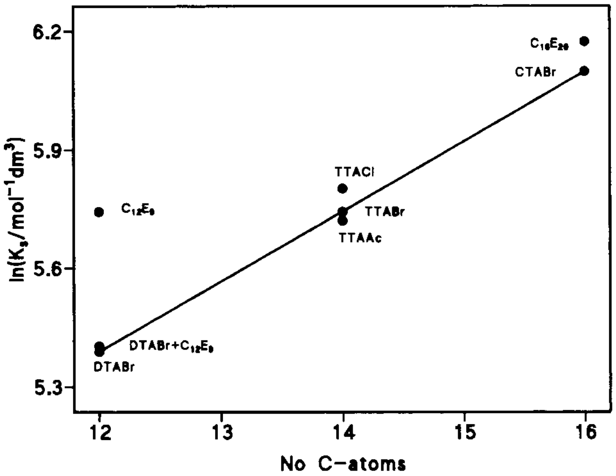


Figure 8. Correlation of values for the association equilibrium constant, K_s, of ECHC and the number of carbon atoms in the hydrocarbon chain of the surfactant.

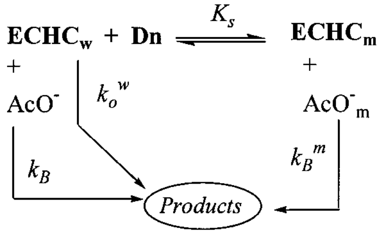
TABLE 4: Pseudo-First-Order Rate Constant Obtained as a Function of Surfactant Concentration in the Study of the Hydrolysis Reaction of ECHC in Aqueous Buffered Solutions of Acetic Acid−Acetate

TTACl; [buffer]$_t$ = 0.070 M			TTAAc; [buffer]$_t$ = 0.10 M		
[TTACl]/M	$k_o/10^{-3}$ s^{-1}	pH	[TTAAc]/M	$k_o/10^{-3}$ s^{-1}	pH
1.1×10^{-3}	7.98	4.57	0.833×10^{-3}	9.42	4.40
2.2×10^{-3}	8.10	4.57	1.25×10^{-3}	9.53	4.41
3.3×10^{-3}	12.13	4.56	1.67×10^{-3}	9.61	4.42
4.4×10^{-3}	16.36	4.55	2.50×10^{-3}	10.0	4.41
6.6×10^{-3}	19.36	4.54	3.33×10^{-3}	14.0	4.42
8.8×10^{-3}	19.88	4.53	5.00×10^{-3}	21.1	4.42
0.0132	19.34	4.51	6.67×10^{-3}	25.0	4.43
0.0165	18.64	4.49	0.010	28.7	4.43
0.022	17.23	4.48	0.0125	30.2	4.44
0.033	14.75	4.47	0.0167	31.8	4.45
0.044	13.20	4.46	0.025	34.1	4.48
0.066	11.36	4.46	0.033	35.3	4.51
0.088	9.92	4.45	0.050	38.1	4.59
0.132	7.81	4.45	0.067	38.9	4.64
0.165	6.77	4.45	0.100	41.5	4.73
0.220	5.60	4.44	0.125	43.0	4.81
0.291	4.73	4.44	0.167	44.5	4.91
			0.208	46.3	5.00

is much higher than that in the aqueous phase. This fact, together with a much faster reaction hydrolysis via the general base catalysis than via the water attack, makes it more reasonable to neglect spontaneous decomposition at the micellar phase of the TTAAc micelles. Thus, the observed first-order rate constant is written as in eq 5.

$$k_o = \frac{(k_o^{\,w} + k_B[\mathrm{AcO^-}]_w) + k_B^{\,m} K_s m_{Ac}[\mathrm{TTAAc}]_m}{1 + K_s[\mathrm{TTAAC}]_m} \qquad (5)$$

SCHEME 3: Mechanism of Base-Catalyzed Hydrolysis of ECHC in Cationic Micelles



According to the pseudophase model, micelle formation begins at the cmc, and it is assumed that all additional surfactant forms micelles, with the monomer concentration remaining constant and equal to the cmc. Meanwhile, the simple pseudophase model assumes that the micellar neutralized degree of ionic micelles, β (=1 − α), remains constant upon increasing surfactant concentration. In this study, the surfactant counterions are AcO$^-$ ions, and the bulk water phase is an aqueous buffered solution of acetic acid−acetate: [buffer]$_t$ = 0.104 M, pH 4.40. Table 4 reports values of k_o measured at each TTAAc concentration, along with the measured pH value of the sample mixture. Evidently, the [H$^+$] decreases from 4.0×10^{-5} M to 1.0×10^{-5} M as the [TTAAc] increases from 0.83×10^{-3} M to 0.208 M; nevertheless, the ionized acetate ions (that come from the surfactant) increase from 0.83×10^{-3} M to 0.086 M (=cmc + α[TTAAc]$_m$; α = 0.42). These results suggest that only a small fraction of the ionized acetate ions is responsible for the pH variation. This assumption is quite reasonable if we assume that β is constant. On that basis, a correction of k_o values referred to the same initial pH (=4.40) yields the open points in Figure 7. A quantitative analysis of these data indicates that the term denoted by k_w^{cor} (=k_o^w + k_B[AcO$^-$]$_w$) in eq 5 is now constant. On the other hand, [AcO$^-$]$_m$ = β[TTAAc]$_m$, and $k_B^m m_{Ac} = \beta k_{2B}^m/V$, where k_{2B}^m is the second-order rate constant for the reaction referred to the volume fraction, V, of the micellar phase where the reaction takes place. The values of the parameters that best fit the experimental results for the reaction hydrolysis of the ester of ECHC in TTAAc micelles are k_w^{cor} = (9.5 ± 0.6) × 10^{-3} s^{-1}, $\beta k_{2B}^m/V$ = (3.76 ± 0.02) × 10^{-2} s^{-1}, and K_s = 305 ± 9 mol^{-1} dm^3; the last two parameters were treated as adjustable parameters. The solid line in Figure 7 represents the values of k_o calculated with these parameters in eq 5.

The fit of theory and experiment is entirely favorable; in addition, K_s takes a value comparable to that obtained for ECHC association to TTACl or TTABr micelles because the nature of the counterion should not strongly affect micelle hydrophobicity. From the value calculated for $\beta k_{2B}^m/V$, and assuming V = 0.15 dm^3 mol^{-1}, one determines k_{2B}^m = (9.72 ± 0.05) × 10^{-3} mol^{-1} dm^3 s^{-1} for the bimolecular reaction between acetate ions and ECHC at the micellar interface. This rate constant is lower than the corresponding one for water (k_B = 0.269 mol^{-1} dm^3 s^{-1}) as a consequence of the lower polarity of the micellar interface and of the lower water content, which decreases the hydration degree of the leaving group in the transition state, resulting in a less stable activation complex. Therefore, the lower water content, together with the low polarity of the micellar interface, accounts for the estimated reduction in k_{2B}^{m}, even though the observed effect is a catalysis due to concentration effects.

Further evidence of the validity of the quantitative treatment is obtained by plotting a modification of k_o, k_o^{mod}, defined as $k_o^{mod} = k_o(1 + K_s[\mathrm{TTAAc}]_m) - k_w^{cor}$, against $[\mathrm{TTAAc}]_m$. To calculate values of k_o^{mod}, we assume that $K_s = 320$ mol^{-1} dm^3, i.e., the average value obtained with TTACl and TTABr micelles, and cmc $= 3.0 \times 10^{-3}$ M, i.e., the lowest [TTAAc] at which micellar effects have been observed. This graph can be shown in Figure 7B and features a straight line with a zero intercept at the origin, as eq 5 predicts. The slope of the corresponding straight line ($=k_B^m m_{Ac} K_s$) has been determined as 12.7 ± 0.1 mol^{-1} dm^3 s^{-1} ($r = 0.999_3$), in good agreement with the results obtained by nonlinear regression analysis.

Conclusions

Both cationic and nonionic micelles decrease the rate of the acid-catalyzed hydrolysis of the ester function of ethyl cyclohexanone-2-carboxylate. This β-keto ester associates strongly to cationic or nonionic micelles by hydrophobic interactions due to the greater stability of the enol tautomer in a less polar solvent, such as the micellar interface. The micelle-solubilized substrate self-decomposes while the substrate in the bulk water phase also hydrolyzes via the acid-catalyzed pathway. The bimolecular rate constant for the H_2O attack to the ester residing on the micellar surface is more than 5 times the value found in water. The base-catalyzed hydrolysis goes through maxima as the TTACl (or TTABr) concentration increases. However, the addition of TTAAc enhances k_o values throughout the concentration range. The behavior observed is the consequence of the ion exchange between acetate ions and Cl^- or Br^- ions at the micellar surface. However, the second-order rate constant of hydrolysis catalyzed by acetate ions at the micellar interface is lower than the rate constant in water. The lower polarity or lower water content of the micellar interface explains the difference in the rate constants, even though the observed effect is a catalysis as a consequence of concentration effects in the small volume of the micelle.

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