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Cationic Mixed Micelles as Reaction Medium for Hydrolysis Reactions

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Abstract The influence of cationic mixed micelles composed of quartenary ammonium surfactants on hydrolysis reactions has been studied in detail. The basic hydrolysis of *N*-methyl-*N*-nitroso-*p*-toluene sulphonamide has been chosen as the reaction probe, while mixed micelles composed of lauryl trimethyl ammonium chloride and octadecyl trimethyl ammonium chloride with different molar ratios were studied as the reaction medium. The ion-exchange pseudophase model was used to fit the experimental results to obtain the kinetic and thermodynamic parameters of the reaction. The result show that the hydrophobic character of the mixed micelles drives the association of the substrate to them, leading to a local increase of reactant concentrations at the micellar interface and, therefore, to a catalytic effect. By tuning the molar ratio of the mixed micelles it is possible to control substrate binding affinity and thus the catalytic efficiency of the reaction medium.

Keywords Kinetics · Mixed micelles · Catalysis · Microheterogeneous media

1 Introduction

Micellar surfactants are amphiphilic materials which contain both apolar, hydrophobic and polar, hydrophilic groups. Micelles are highly dynamic, often polydisperse aggregates formed from surfactants above the critical micelle concentration, *cmc* [1]. Micellization is primarily driven by bulk hydrophobic interactions between the alkyl chains of the surfactant monomers and usually results from a favorable entropy change [2]. Micellar

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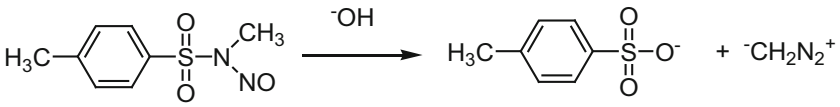
systems have the ability to alter chemical reactivity. Reaction rates and equilibrium constants in micellar media can differ from the values in bulk water. Most hydrolysis reactions provide an excellent opportunity for comparisons of micellar medium effects. Based on the mechanisms of these hydrolytic processes, one expects that the properties of the micelles, including the lower local water concentration in the micellar Stern region, the polarity of the micelles and the local charge in the micellar Stern region resulting from incomplete counterion binding, play an important role in the catalysis or inhibition of these processes [3, 4]. Kinetic studies in these systems may be interpreted on the basis of the pseudophase model [5, 6], which allowed us to explain a large number of kinetic results [7–9], with the simple assumption of reaction distribution between the two pseudophases.

The *N*-nitroso compounds are of great interest from a biological point of view, because a wide variety of structurally related compounds possessing the *N*-nitroso-*N*-alkyl functionality have demonstrated cancer chemotherapeutic potential [10, 11]. Besides, the discovery of the bioregulatory roles of nitric oxide [12–16], and its anti-carcinogen properties [17, 18], has greatly increased the interest in nitrosation reactions because nitroso compounds are able to delivery nitric oxide in a controlled manner [19]. Due to this widespread significance of nitroso compounds, knowledge of their reactions, mechanisms and kinetics is of much importance [20].

In this work, we present a study on the influence of cationic mixed micelles, composed of lauryl trimethyl ammonium chloride (LTACl) and octadecyl trimethyl ammonium chloride (OTACl) with different molar ratios, on the basic hydrolysis of *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide (MNTS). We choose these surfactants because they are similar, being the only difference the length of their hydrophobic chains. The mechanism for the basic hydrolysis of MNTS in water is well known [21], the nucleophilic attack of OH^- on the sulfur atom being the rate determining step (see Scheme 1). The purpose of the present work was to extend our studies on hydrolysis reactions to different microheterogeneous media, viz., mixed micelles of cationic surfactants.

2 Experimental

The micellar surfactants OTACl and LTACl were obtained from Sigma (purities ≥95.0 and 98.0 % respectively) and used without further purification. NaOH (Sigma, 98 %) solutions were titrated against potassium hydrogen phthalate and were prepared weekly. All aqueous solutions were prepared in doubly distilled water. The low solubility of MNTS (Sigma, 99 %) in water made it necessary to prepare its solutions in acetonitrile (from Merck, ACS grade). The percentage of acetonitrile in the reaction mixture was always 1 % by volume. The reactions were followed by recording the decrease in absorbance at 250 nm due to the disappearance of MNTS using a Hewlett Packard 8453 spectrophotometer with a cell holder thermostated at (25 ± 0.1) °C. All kinetic experiments were performed with the MNTS concentration (approximately 6×10^{-5} mol·L^{-1}) much smaller



Scheme 1 Mechanism for the basic hydrolysis of MNTS

than those of the other reagents used. The absorbance–time data of all kinetic experiments were fitted by the first-order integrated equation, and the values of the pseudo-first order rate constants, k_{obs}, were reproducible to within 3 %.

3 Results and Discussion

The influence of cationic mixed micelles on the basic hydrolysis of MNTS was studied at seven different LTACl:OTACl molar ratios (1:0, 1:0.25, 1:0.5, 1:1, 0.5:1, 0.25:1 and 0:1). Although the hydrolysis of MNTS in the presence of pure cationic micelles has been previously studied by our group [22], here we examined the influence of LTACl and OTACl concentration on the hydrolysis reaction to ensure good consistency in the evaluations of the experimental results. All the experiments were carried out at [NaOH] = 0.085 mol·L^{-1} and the surfactant concentrations were varied between 0 and 0.18 mol·L^{-1}. Figure 1 shows the results for three molar ratios (1:0.25, 1:1 and 0.25:1; Fig. S1 in the Supporting Information shows the other molar ratios and the pure surfactants for comparison). It can be observed that initially, at surfactant concentrations below the *cmc*, the ratio between the observed reaction rate and the rate in absence of micelles (k_{obs}/$k_{obs,w}$) remains unchanged. A further increase in the surfactant concentration above the *cmc* lead to an increase in (k_{obs}/$k_{obs,w}$) up to a maximum, followed by a decrease (see Fig. 1). The kinetic data were quantitatively explained by using the ion-exchange pseudophase model, assuming that the cationic nature of the surfactants favored the presence of OH^- at the micellar pseudophase. The overall reaction rate will be, therefore, equal to the sum of the rates at the micellar and aqueous pseudophases (see Scheme 2, where subscripts w and m denote the aqueous and micellar pseudophases, and k_w and k_m are the rate constants in the respective pseudophases).

This model lead to the following equation for the observed rate constant:

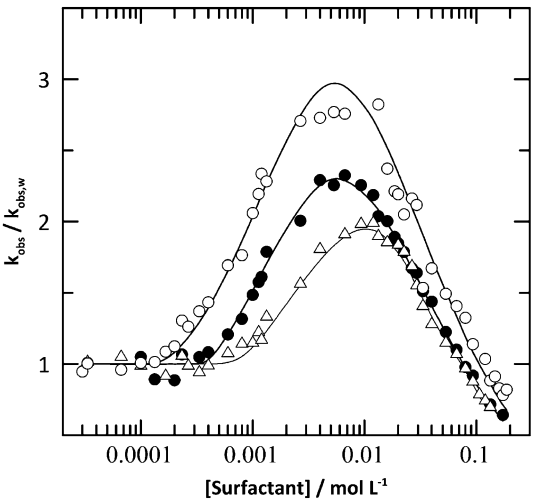
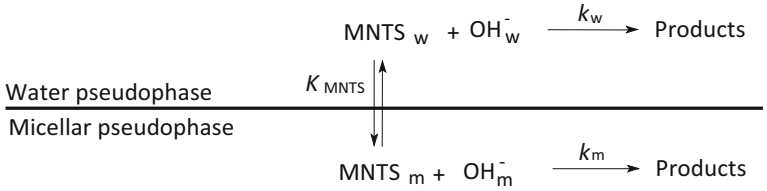


Fig. 1 Influence of LTACl:OTACl mixed surfactant concentration on the basic hydrolysis of MNTS. [OH^-] = 0.085 mol·L^{-1} at different molar ratios (*open circle*) 0.25:1 (*filled circle*) 1:1 and (*open triangle*) 1:0.25. The lines represent the best fit of Eq. 3 to the experimental data (see text for details)



Scheme 2 Ion-exchange pseudophase model

$$k_{obs} = \frac{k_w[OH^-]_w + k_m K_{MNTS}[OH^-]_m}{1 + K_{MNTS}[D_n]} \quad (1)$$

where $k_w[OH^-]_w$ is the observed rate constant in pure water ($k_{obs,w}$) and K_{MNTS} is the association constant or constant of substrate distribution between the two pseudophases and D_n is the concentration of micellized surfactant ([surfactant]-cmc):

$$K_{MNTS} = \frac{[MNTS]_m}{[MNTS][D_n]} \quad (2)$$

The *cmc* values were obtained from the kinetic data and calculated as the minimum concentration of surfactant necessary to produce a change in the reaction rate. These values, in the presence of OH^- (see Table 1), are satisfactorily correlated with the expected behavior of *cmc* values when the length of the surfactant chain increases, which is a linear decrease of the logarithm of *cmc* with the number of carbons in the chain and then with its hydrophobicity [23]. In our case, the *cmc*s increase with the percentage of the surfactant with longer chain in the mixed micelles.

From Eq. 1 and taking into account that $[OH^-]_m$ is the concentration of hydroxyl ions on the micellar pseudophase we can derived the following equation:

$$k_{obs} = \frac{k_w[OH^-]_{total} + (k_m K_{MNTS} - k_w) m_{OH}[D_n]}{1 + K_{MNTS}[D_n]} \quad (3)$$

where m_{OH}, which denotes the $[HO^-]_m/[D_n]$ ratio, satisfies the equation:

Table 1 Kinetic and thermodynamic parameters obtained for the basic hydrolysis of MNTS in the presence of mixed micelles of LTACl:OTACl

LTACl:OTACl	*cmc*/mol·L^{-1}	K_{MNTS}/mol·L^{-1}	k_m/s^{-1}	k_m^2/L·mol^{-1}·s^{-1}
1:0	0.011 ± 0.001	97 ± 14	(6.3 ± 0.3) × 10^{-2}	8.8 × 10^{-3}
1:0.25	(7.5 ± 0.3) × 10^{-4}	119 ± 16	(5.3 ± 0.3) × 10^{-2}	7.4 × 10^{-3}
1:0.5	(4.0 ± 0.3) × 10^{-4}	173 ± 12	(5.2 ± 0.2) × 10^{-2}	7.3 × 10^{-3}
1:1	(2.5 ± 0.4) × 10^{-4}	207 ± 15	(6.0 ± 0.2) × 10^{-2}	8.4 × 10^{-3}
0.5:1	(2.0 ± 0.5) × 10^{-4}	307 ± 43	(5.2 ± 0.3) × 10^{-2}	7.3 × 10^{-3}
0.25:1	(1.5 ± 0.4) × 10^{-4}	362 ± 33	(5.7 ± 0.3) × 10^{-2}	8.0 × 10^{-3}
0:1	(6.5 ± 1.0) × 10^{-5}	424 ± 26	(7.0 ± 0.2) × 10^{-2}	9.8 × 10^{-3}

$k_w = 0.083$ L·mol^{-1}·s^{-1}, $K_{Cl}^{OH} = 10$

$$m_{OH}^2 + m_{OH}\left[\frac{[OH^-]_{total}+K_{Cl}^{OH}[X^-]_{total}}{(K_{Cl}^{OH}-1)[D_n]} - \beta\right] - \left[\frac{\beta[OH^-]_{total}}{(K_{Cl}^{OH}-1)[D_n]}\right] = 0 \quad (4)$$

where β is the fraction of charge neutralized by the counterion. This value has been set constant an equal to 0.8, which is the value obtained by Chaimovich et al. [24], and it seems to be the most frequently used value. K_{Cl}^{OH} is the ion-exchange constant for the equilibrium:

$$OH_m^- + Cl_W^- \rightleftharpoons OH_W^- + Cl_m^- \quad (5)$$

The value of K_{Cl}^{OH} can be obtained from the influence of salts on the observed rate constant (vide infra).

As mentioned above, upon increasing the surfactant concentration the ratio $k_{obs}/k_{obs,w}$ reaches a maximum followed by a decrease (see Fig. 1). Such a decrease can be initially ascribed to an increase in the concentration of the chloride ion, which competes with hydroxyl ions for the micellar surface sites. To check this possibility, we have performed series of kinetic runs with increasing amounts of NaCl at a fixed amount of surfactant where the reaction rate reaches the maximum. Figure 2 shows the influence of sodium chloride concentration on the observed rate constant for the basic hydrolysis of MNTS at a constant concentration of OTACl (5.3×10^{-3} mol·L^{-1}). It can be observed that as the chloride concentration increases k_{obs} decreases exponentially, confirming the assumption of competition between hydroxyl and chloride ions at the micellar interface. This effect is in quantitative agreement with the pseudophase ion exchange model (Eqs. 3, 4). The fitting procedure was performed by means of a non-linear fitting program based on Marquardt's algorithm. The solid line in Fig. 2 represents the best fit of the experimental data to Eqs. 3 and 4. The fit was carried out using *cmc* values calculated from the kinetic data, and k_w was the experimental value in bulk water (0.083 L·mol^{-1}·s^{-1}) [25], to find the values of K_{MNTS}, k_m and K_{Cl}^{OH} that best reproduce the kinetic data. A value of $K_{Cl}^{OH} = 10$ was determined. It should be mentioned that the pseudophase ion-exchange model predicts (Eqs. 4, 5 and

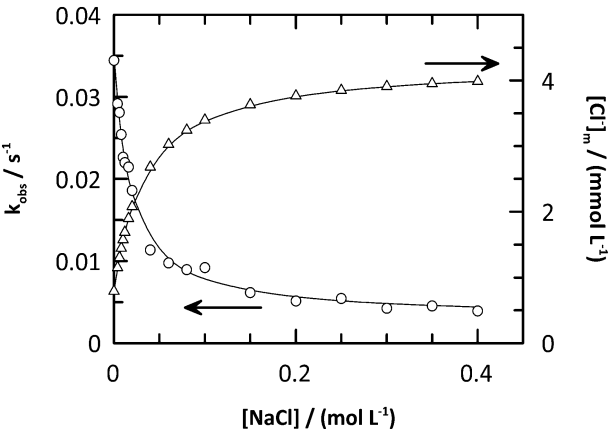


Fig. 2 *Left* influence of NaCl concentration upon the basic hydrolysis of MNTS, [NaOH] = 0.12 mol·L^{-1} and [OTACl] = 5.4×10^{-3} mol·L^{-1}; *right* influence of the NaCl concentration on the chloride ion concentration in the micellar pseudophase according to Eq. 4 and assuming $K_{Cl}^{OH} = 10$ (see text for details)

assuming $K_{Cl}^{OH} = 10$) an exponential increase of the chloride ion concentration in the micellar pseudophase with the addition of extra unreactive chloride ions (see Fig. 2 right).

Now the biphasic pattern observed in Fig. 1 can be easily explained. On the one hand, surfactant concentrations above the *cmc* lead to an increase in the relative concentrations of MNTS and OH^- in the Stern layer, which increase the observed rate constant, and the ascending branch of the curve is observed. On the other hand, a further increase in the surfactant concentration leads to an increased concentration of unreactive chloride ions and a displacement of reactive ions (OH^-) from the micellar surface, as predicted by Eq. 5. Such competition leads to a decrease in the observed rate constant, as we have confirmed by studying the effect of NaCl on the observed rate constant (see Fig. 2). The relative contribution of both competing factors results in the experimental maximum observed.

Analogously, the solid lines in Fig. 1 represent the best fit of Eqs. 3 and 4 to the experimental data, but now using the value of K_{Cl}^{OH} obtained from the influence of NaCl ($K_{Cl}^{OH} = 10$). We can see in Figs. 1 and S1 that the model fits to the experimental data at the seven molar ratios studied within the experimental error. This allows us to obtain again values of K_{MNTS} and k_m in good agreement with those found in the study of the influence of NaCl. The obtained values for these constants for the different LTACl:OTACl mixed systems are listed in Table 1.

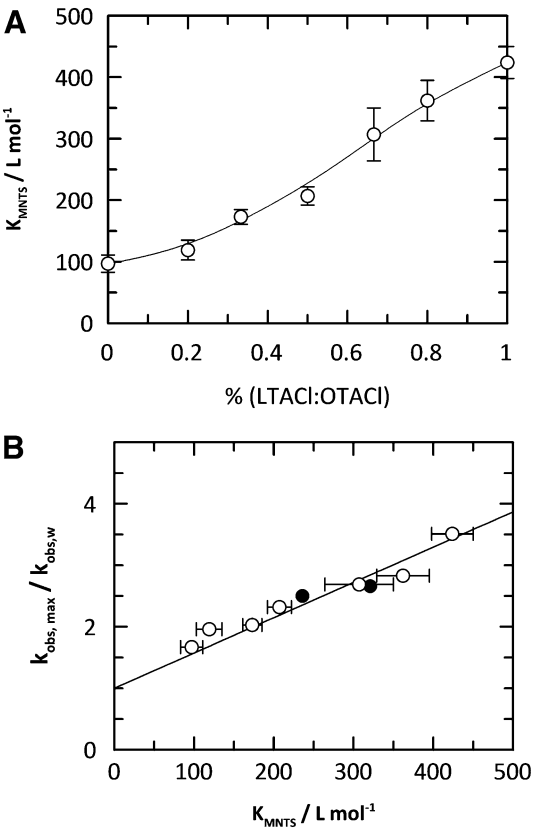


Fig. 3 **a** Influence of the percentage of OTACl in the mixed micelles on the values of K_{MNTS}. **b** (*open circle*) Influence of K_{MNTS} on the catalytic efficiency of the LTACl:OTACl mixed micelles (*filled circle*). Literature values for TTACl and CTACl

The k_m values obtained are almost constant (0.070–0.052 s^{-1}) and without any tendency within the different cationinc mixed micelles. These values cannot be directly compared to k_w (the bimolecular rate constant in water), because both constants are defined in different terms (k_m in terms of mole per mole concentration in surfactant; k_w in terms of mole per volume concentration). However, assuming the molar volume of the Stern layer of (ca 0.14 $L \cdot mol^{-1}$) [5, 6], we have calculated the bimolecular reactivity constant in the micellar interphase, k_m^2, to be (0.0098–0.0073 $L \cdot mol^{-1} \cdot s^{-1}$). It is about one-tenth that in pure water ($k_w = 0.083$ $L \cdot mol^{-1} \cdot s^{-1}$) [25]. This suggests that the hydrolysis rate in the Stern layer is intrinsically one-tenth that in the aqueous pseudophase, which confirms that the origin of the catalytic effect observed in the presence of micelles (Fig. 1) does not correspond to an increase in reactivity but, rather, to a local increase in the reagent concentration in the Stern layer. This intrinsically decreased reactivity may be attributed to the polarity at the micellar interphase, which is lower than that in water. In fact, the Stern layer has a dielectric constant of ca. 35 [26], markedly lower than that of water. The influence of the lowering of the dielectric constant upon the reaction rate was investigated by our group in dioxane–water [27] mixtures and acetonitrile–water mixture [28]. The results obtained showed that, in fact, the effect of decreasing polarity of the solvent is a decrease in the reaction rate.

We can see in Table 1 that the association constant of MNTS to the pure cationic micelles is higher for OTACl (424 $L \cdot mol^{-1}$) than for LTACl (97 $L \cdot mol^{-1}$), while it increases as the percentage of OTACl in the mixed micelles increases; in fact a sigmoidal dependence is observed when we plot the values of K_{MNTS} versus the percentage of LTACl:OTACl (see Fig. 3a). This result indicates that the association constant of the organic substrate to the micelles is driven mainly by hydrophobic forces.

The catalytic efficiency (viz., the ratio between the maximum observed rate constant at a given OH^- concentration and the rate constant in pure water, $k_{obs,max}/k_{obs,w}$), increases with increasing the percentage of OTACl in the LTACl:OTACl mixed micelles. In pure OTACl micelles it is more than two times higher than that for LTACl and the efficiency of the mixed micelles LTACl:OTACl with a molar ratio of 0.25:1 is almost 1.7 times higher than that with molar ratio 1:0.25. A linear relationship between the catalytic efficiency, $k_{obs,max}/k_{obs,w}$, and the values of K_{MNTS} is also observed (see Fig. 3b). The observed tendency can be understood considering that OTACl micelles are more hydrophobic than LTACl. The increase of the percentage of OTACl in the mixed micelles leads to more hydrophobic micelles with higher values of the association constant (see Fig. 3a) with higher capacity to dissolve organic substrates. Then, the increase of the values of K_{MNTS} due to the increase of the percentage of OTACl leads finally to a higher catalytic efficiency of the mixed micelles. We have also included in Fig. 3b the bibliographic values of the catalytic efficiency of TTACl and CTACl micelles whose chain length are between OTACl and TTACl [22]. We can see in Fig. 3b that their catalytic efficiencies match perfectly with those of the mixed micelles. Interestingly, the catalytic efficiency of OTACl micelles is about 20 times lower than that for the same reaction in the presence of DODAC vesicles [29]. The higher catalytic efficiency of vesicles is a consequence of the high substrate dissolving capacity of the vesicles.

In conclusion, we found that cationic mixed micelles of LTACl:OTACl catalyze the basic hydrolysis of MNTS. The kinetic behavior was satisfactorily explained using the pseudophase ion-exchange model, which let us to obtain the thermodynamic and kinetic parameters of the reaction. We found that the hydrophobic character of the mixed micelles drives the association of the substrate to the micellar pseudophase and the catalytic

efficiency of the micelles. It can also be addressed that the catalysis observed in these systems is due to the increase of local reagents concentrations at the micellar interface rather than to the decrease in the energy of activation required for the OH^- attack to take place.

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