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Hydrolysis of *N*-methyl-*N*-nitroso-*p*-toluenesulphonamide in micellar media

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ABSTRACT: The acid and basic hydrolysis of *N*-methyl-*N*-nitroso-*p*-toluenesulphonamide (MNTS) was studied in different micellar aggregates (CTACl, CTABr, TTABr, LTABr, and OTACl). The effect of mixed micelles (OTAX–LTAX) was also studied. The kinetic behaviour was explained on the basis of the pseudophase model, from which the binding constants of MNTS to different micelles, the ion exchange constants and the reactivity constants in the micellar pseudophase were obtained. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: *N*-methyl-*N*-nitroso-*p*-toluenesulphonamide; hydrolysis; micellar media; pseudophase model

INTRODUCTION

A potential use of micellar media is in the control of chemical reactivity. The chemical reaction rates and equilibria observed in micellar media ca differ from those observed in conventional media, owing to solubilization of the reagents, reduction of their effective concentrations through their segregation in different 'compartments' within the bulk medium, concentration within micelles and changes in the polarity of the different regions of the system. Predictions of reaction rates in micellar media are usually based on the pseudophase model,[1] which treats aqueous, organic and/or surfactant components of the solvent medium as constituting distinct phases in which reactions occur, and between which reagents and products are distributed, in accordance with conventional laws of kinetics and mass transfer. This model has provided qualitative and quantitative correlation of a large number of experimental results,[2] often with no more than crude assumptions on the distribution of reagents between pseudophases.

N-Methyl-*N*-nitroso-*p*-toluenesulphonamide (MNTS) has proved to be a highly interesting substrate with regard to its behaviour in basic or neutral media from both biomedical[3] and chemical[4] points of view. The mechanisms of acid[5] and alkaline[6] hydrolysis of MNTS in water are well known. In an acid in medium, the slow step is the proton transfer from the medium to the substrate, whereas in an alkaline medium it is the nucleophilic attack of HO^- on the sulphur atom.

In this paper we present a study on the acid and alkaline hydrolysis of MNTS in the presence of cationic micelles: lauryltrimethylammonium bromide (LTABr), cetyltrimethylammonium bromide and chloride (CTABr and CTACl), tetradecyltrimethylammonium bromide (TTABr) and octadecyltrimethylammonium chloride (OTACl)

EXPERIMENTAL

All chemicals used were of the highest commercially available purity (Merck or Sigma) and none required further purification. The initial concentration of MNTS (1.0×10^{-4} M) was always much lower than that of the other reagents. The experimental procedure is described in detail elsewhere.[7]

RESULTS AND DISCUSSION

Micellar effects on the acid hydrolysis of MNTS

The effect of CTACl, CTABr, LTABr, TTABr and OTACl on the acid hydrolysis of MNTS was studied at $[H^+] = 0.104$ M, and the concentrations of the different surfactants were varied typically between 0 and 0.16 M. The results (Fig. 1) show the pseudo-first-order rate constant, k_0, to be markedly decreased by all the cationic surfactants. This behaviour can be rationalized in terms of the two-pseudophase model[1] in which the reaction is assumed to occur in both a micellar pseudophase and an aqueous pseudophase, with an equilibrium distribution of

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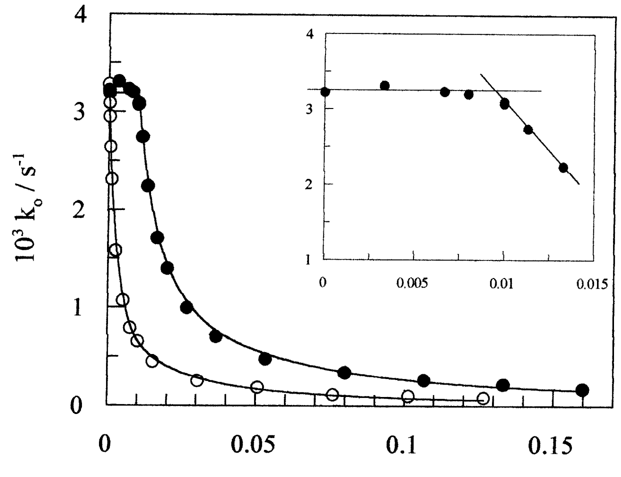
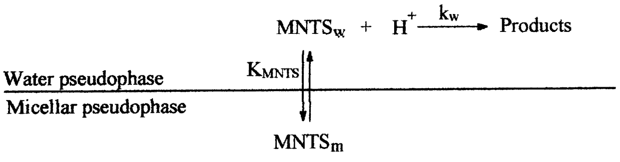


Figure 1. Influence of surfactant concentration on the acid hydrolysis of MNTS. [MNTS] = 1 × 10^{-4} M, [HCl] = 0.104 M. (○) OTACl; (●) LTABr. The inset shows the kinetic determination of the cmc for LTABr.

MNTS between the two pseudophases. Based on electrostatic considerations,[8] the proton concentration at the micellar pseudophase must be very low owing to the cationic character of the micelles. This virtually complete exclusion of H^+ means that the reaction is taking place only in the aqueous pseudophase (see Scheme 1). This model yields the following equation:

$$k_0 = \frac{k_w[H^+]}{1 + K_{MNTS}[D_n]} \qquad (1)$$



Scheme 1

where k_w is the bimolecular rate constant in bulk water, K_{MNTS} is the binding constant of the substrate to the micellar pseudophase, and $[D_n]$ is the concentration of micellized surfactant ([surfactant]−cmc). The critical micellar concentration (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 (Fig. 1). These values in the presence of H^+ are satisfactorily correlated with the expected behaviour of cmc values when the length of the surfactant chain increases, which is a linear decrease in the logarithm of cmc with increase in the number of carbons in the chain.[9] The solid line in Fig. 1 represents the best fit of Eqn. (1) to the experimental data. The fitting results for different surfactants are shown in Table 1.

As can be observed in Table 1, the association constant increased with increase in the number of carbon atoms in the surfactant chain. The value for LTABr is close to that obtained for SDS[7] since both surfactants have the same number of carbons in their chains. These results indicate that the association of the substrate is controlled mainly by hydrophobic forces and not by the electrostatic properties of the head group.[10]

Effects of LTAX and OTAX mixed micelles on the acid hydrolysis of MNTS

The dependence of the pseudo-first-order rate constant, k_0, for the acid denitrosation of MNTS on the total surfactant concentration (LTA and OTA) was studied in a series of experiments at fixed LTAX:OTAX molar ratios (1:0, 1:0.25, 1:0.5, 1:1, 0.5:1, 0.25:1 and 0:1). As shown in Table 2, the cmc values for these mixtures decrease with increasing percentage of OTAX.

The observed rate constant, k_0, decreases as the total surfactant concentration increases (see Supplementary material). This behaviour is analogous to that found for pure surfactant micelles (see above). The best fits of

Table 1. Kinetic parameters obtained from applying Eqns (1), (3) and (4) to the hydrolysis of MNTS in the presence of different cationic surfactants

Surfactant	cmc (M)	k_w (l mol^{-1} s^{-1})	K_{MNTS} (l mol^{-1})	K_X^{OH}	k_m (s^{-1})	k^2_m (l mol^{-1} s^{-1})
Acid hydrolysis:						
LTABr	0.010 ± 0.0005	0.031[a]	132			
TTABr	(1.00 ± 0.05) × 10^{-3}	0.031[a]	270			
CTABr	(4.0 ± 0.5) × 10^{-4}	0.031[a]	310			
CTACl	(4.0 ± 0.5) × 10^{-4}	0.031[a]	310			
OTACl	(5.0 ± 1.0) × 10^{-5}	0.031[a]	410			
Basic hydrolysis:						
LTABr	0.012 ± 0.002	0.083[a]	132[b]	17	(7.10 ± 0.02) × 10^{-2}	0.00994
TTABr	(1.4 ± 0.1) × 10^{-3}	0.083[a]	270[b]	17	(6.10 ± 0.01) × 10^{-2}	0.00854
CTABr	(2.0 ± 0.5) × 10^{-4}	0.083[a]	310[b]	17	(6.99 ± 0.02) × 10^{-2}	0.00978
CTACl	(2.0 ± 0.5) × 10^{-4}	0.083[a]	310[b]	10	(9.10 ± 0.02) × 10^{-2}	0.01274
OTACl	(5.0 ± 1.7) × 10^{-5}	0.083[a]	410[b]	10	(8.60 ± 0.03) × 10^{-2}	0.01204

[a] Value taken from the bulk water.
[b] Values taken from the acid hydrolysis.

Table 2. Association constant values between MNTS and different mixtures of OTACl and LTABr obtained[a] by applying Eqn (1).

OTACl:LTABr	cmc (M)	K_{MNTS} (l mol^{-1})
1:0	$(5.0 \pm 1.0) \times 10^{-5}$	410
1:0.25	$(2.5 \pm 0.4) \times 10^{-4}$	406
1:0.5	$(3.0 \pm 1.0) \times 10^{-4}$	359
1:1	$(4.0 \pm 0.8) \times 10^{-4}$	295
0.5:1	$(6.0 \pm 1.0) \times 10^{-4}$	217
0.25:1	$(7.0 \pm 1.2) \times 10^{-4}$	160
0:1	0.010 ± 0.0005	132

[a] With $k_w = 0.1$ lmol^{-1} s^{-1} measured in bulk water.

Eqn(1) to the experimental data yield the values of K_{MNTS} shown in Table 2. The association constant increases with increasing percentage of OTACl. These results indicate that mainly hydrophobic forces control the association of the substrate.

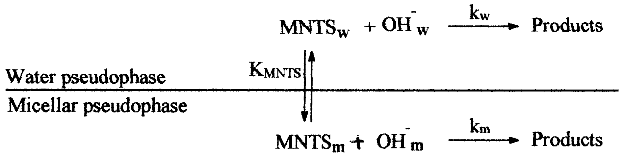
Micellar effects on the basic hydrolysis of MNTS

We studied the influence of the five cationic micelles (CTACl, CTABr, TTABr, LTABr and OTACl) on the basic hydrolysis of MNTS. All the experiments were carried out at [NaOH] = 0.117 M and the surfactant concentrations were varied between 0 and 0.2 M. The results (Figure 2) follow the typical biphasic pattern. The reaction rate passes through a maximum as the surfactant concentration increases. The existence of a maximum can be explained in terms of two competing effects in the ion-exchange model. Added surfactant increases the relative concentrations of MNTS and HO$^-$ in the Stern layer, which increases the reaction rate, and the ascending branch of the curve is observed. As the concentration of surfactant increases, the concentration of the reagents in the micellar pseudophase decreases, and further the excess of unreactive counterions, X$^-$, compete with HO$^-$ for available sites in the Stern layer, so that the reaction rate decreases. The relative contribution of these competing factors results in the experimental maximum. This experimental behaviour can be explained quantitatively again on the basis of the pseudophase model. Unlike the acid hydrolysis, where H$^+$ ions are virtually completely excluded from the micellar pseudophase, the cationic nature of the surfactant favours the presence of OH$^-$ at the micellar pseudophase. The overall reaction rate was, therefore, equal to the sum of the rates at the micellar and aqueous pseudophases (see Scheme 2). Scheme 2 allows us to obtain the following equation:

$$k_o = \frac{k_w[\mathrm{OH^-}]_w + k_m K_{MNTS}[\mathrm{OH^-}]_m}{1 + K_{MNTS}[\mathrm{D_n}]} \qquad (2)$$

from which we can obtain the equation

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



Scheme 2

where k_w is the bimolecular rate constant in bulk water, k_m is the rate constant in the micellar pseudophase, K_{MNTS} ($K_{MNTS} = [\mathrm{MNTS}]_m/[\mathrm{MNTS}]_w\,[\mathrm{D_n}]$) is the binding constant of the substrate to the micellar pseudophase and [D$_n$] is the concentration of micellized surfactant ([surfactant]−cmc). m_{OH}, which denotes the $[\mathrm{HO^-}]_m/[\mathrm{D_n}]$ ratio, satisfies the following equation:

$$m^2_{OH} + m_{OH}\left[\frac{[\mathrm{OH^-}]_{total} + K_X{}^{OH}[\mathrm{X^-}]_{total}}{(K_X{}^{OH} - 1)[\mathrm{D_n}]} - \beta\right] - \left[\frac{\beta[\mathrm{OH^-}]_{total}}{(K_X{}^{OH} - 1)[\mathrm{D_n}]}\right] = 0 \qquad (4)$$

where $K_X{}^{OH}$ ($K_X{}^{OH} = [\mathrm{OH^-}]_w\,[\mathrm{X^-}]_m/[\mathrm{OH^-}]_m\,[\mathrm{X^-}]_w$) is the ion-exchange constant, obtained from the influence of salts upon k_0 (see below). The cmc values were obtained from the kinetic data and calculated as the minimum concentration of surfactant necessary to induce a change in the reaction rate (see inset in Fig. 2) and are listed in Table 1. ß is the fraction of surfactant ions neutralized by counterions, which the ion-exchange pseudophase model assumes to be constant and independent of the concentration of surfactant.[1a,c] The usual value of ß is in the

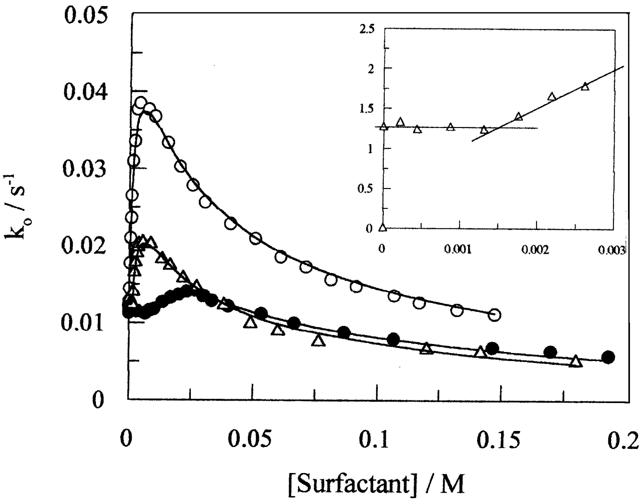


Figure 2. Influence of surfactant concentration on the basic hydrolysis of MNTS. [MNTS] = 1×10^{-4} M, [NaOH] = 0.117 M. (○) OTACl; (Δ) TTABr; (●) LTABr. The inset shows the kinetic determination of the cmc for TTABr.

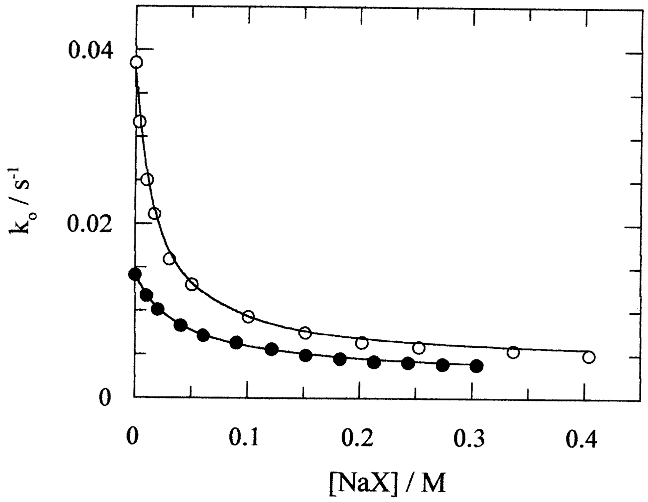


Figure 3. Influence of inert salts on the basic hydrolysis of MNTS. [MNTS] = 1×10^{-4} M, [NaOH] = 0.117 M. (○) [OTACl] = 4.07×10^{-3} M, X = Cl; (●) [LTABr] = 0.0233 M, X = Br.

range 0.6–0.9.[11] We used ß = 0.8, as it seems to be the most frequently used value. Changes in ß (in the range 0.6–0.9) do not affect the fitting results. The good fit to the experimental data shows that the assumption of constant ß is satisfactory, and in our case independent of the nature of the counterion. The subscripts *m* and *w* denote micellar and aqueous pseudophases, respectively

Since we believe that the observed inhibition (Fig. 2) is caused by X^- ions competing for surface sites, we performed series of kinetic runs with increasing amounts of NaX ([NaX] = 0–0.4 M) and a fixed amount of each surfactant ([OTAX] = 4.7×10^{-3} M, [LTAX] = 2.3×10^{-3} M, [CTAX] = 4.5×10^{-3} M and [TTAX] = 5.5×10^{-3} M). Inhibition was indeed observed (see Fig. 3), in quantitative agreement with the pseudophase ion-exchange model [Eqns (3) and (4)]. The solid lines in Fig. 3 represent the best fit of Eqns (3) and (4) to the experimental data. The calculations were performed by means of a non-linear fitting program based on Marquardt's algorithm. The fit was carried out using cmc values calculated from the kinetic data, k_{w} was the experimental value in bulk water and K_{MNTS} was obtained from fitting of kinetic data for the acid hydrolysis in order to find the values of k_{m} and $K_{\mathrm{X}}^{\mathrm{OH}}$ that best reproduce the kinetic data. The solid line in Fig. 2 represents the best fit of Eqns (3) and (4) to the experimental data, using the value of $K_{\mathrm{X}}^{\mathrm{OH}}$ obtained from the influence of salts upon the basic hydrolysis of MNTS in the presence of cationic surfactants. This allows us to obtain again values of k_{m} in good agreement with those found in the study of the influence of salts. The values of $K_{\mathrm{X}}^{\mathrm{OH}}$ are in accordance with the values reported in the literature.[2b,c,g] The fitting results for different surfactants are shown in Table 1.

For comparing the reactivities in the micellar pseudophase with the corresponding reactivities in bulk water, k_{m} (defined in terms of mole per mole concentrations and expressed in s^{-1}) are converted into k^2_{m} expressed in $\mathrm{l\,mol^{-1}}\ s^{-1}$. Using the well known molar volume of the Stern layer (*ca* 0.14 $\mathrm{l\,mol^{-1}}$),[12] the k^2_{m} values are 10 times lower than the corresponding k_{w} values in bulk water. This can be attributed, at least partly, to a medium effect. In fact, the Stern layer has a dielectric constant of *ca* 35,[13] markedly lower than that of water. The influence of lowering the dielectric constant upon the reaction rate was investigated by studying the hydrolysis of MNTS in dioxane–water mixtures.[2b] The results obtained show that, in fact, the effect of decreasing polarity of the solvent is a decrease in the reaction rate. The catalytic effects observed are due only to the increase in the local reagent concentration at the Stern layer.

The catalytic efficiency of the different micelles (viz. $k_{\mathrm{max}}/k_{\mathrm{w}}$, see Table 1) increases with increasing chain length (1.25:1.67:1.74 for LTABr:TTABr:CTABr and 2.39:3.11 for CTACl:OTACl). The trend is due to the higher value of K_{MNTS}.

In conclusion, the pseudophase ion-exchange model is highly successful in explaining the results obtained for the acid and alkaline hydrolysis of MNTS in cationic micelles. It can also be addressed that hydrophobic forces drive the association of substrate with the micellar pseudophase and that the catalysis observed in these systems is not due to an intrinsically larger kinetic constant in the micellar pseudophase but to a local concentration effect.

SUPPLEMENTARY MATERIAL

Kinetic determination of cmc in all cases and kinetic results for the surfactant mixtures are available as supplementary material.

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