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Elimination in sulfobetaine micelles: effects of head group bulk

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ABSTRACT: Zwitterionic micelles of tetradecyldimethylammoniopropanesulfonate and tetradecyldibutylammoniopropanesulfonate, SB3-14 and SBBu3-14, respectively, accelerate the *E*2 reaction of OH^- with 4-nitrophenethyl bromide (**1b**), but the reaction of phenethyl bromide (**1a**) is inhibited by SB3-14 and is only slightly accelerated by SBBu3-14. Analysis of these data allows the separation of the association constants for transfer of reactants from water to micelles from the second-order rate constants in the micelles. These second-order rate constants are, as in water, larger for **1b** than **1a**, and for both substrates are higher in SBBu3-14 than in SB3-14, as found for reactions in otherwise similar cationic micelles. Rate constants in micelles, relative to those in water, are consistently higher in *E*2 than in S_N2 reactions. Copyright © 1999 John Wiley & Sons, Ltd.

KEYWORDS: Sulfobetaine micelles; elimination; head group bulk

INTRODUCTION

There are many examples of reactions of substrates with ionic reagents in solutions of association colloids, e.g., micelles, microemulsions and vesicles.[1] Ionic association colloids typically accelerate bimolecular reactions of counter-ions and inhibit those of co-ions. These observations are understandable because these colloids take up both non-ionic solutes and counter-ions and concentrating reactants in the small colloidal volume accelerates the reaction. Conversely, if one reactant is incorporated in the colloid and the other remains in water, reaction is inhibited. Bulk solvent, e.g. water, and the association colloids, e.g. micelles, act as discrete reaction regions, i.e. as pseudo-phases.[1] Provided that reactants transfer rapidly between the pseudo-phases, rate constants for the overall reaction can be written in terms of the transfer equilibria and second-order rate constants in each pseudo-phase, and it is evident that micellar rate enchancements of many reactions are governed largely by this concentration of reactants. Polar and ionic solutes are bound in the interfacial regions of aqueous association colloids and second-order rate constants in this region are usually similar to those in water,[1] but there are indications that micelles favor reactions in which there is extensive charge dispersion in the transition state, and that the discrimination increases with increasing bulk of the surfactant head group.[1,2]

The pseudo-phase model for bimolecular reactions of OH^- with moderately hydrophobic substrates, S, is described by the equation[1]

$$k_{\text{obs}} = \frac{k_{\text{W}}[\text{OH}^-_{\text{W}}] + k_{\text{M}}\text{K}_{\text{S}}[\text{OH}^-_{\text{M}}]}{1 + \text{K}_{\text{S}}[\text{D}_{\text{n}}]} \tag{1}$$

where k_{obs} is the first-order rate constant with respect to S, quantities in square brackets are concentrations in terms of total solution volume, K_S is the association constant of S with micellized surfactant (detergent) (D_n), subscripts W and M denote the aqueous and micellar pseudo-phases respectively, k_W ($\text{l mol}^{-1}\ \text{s}^{-1}$) is written with concentration as molarity and k_M (s^{-1}) is written with concentration as a mole ratio, $[\text{OH}^-{}_\text{M}]/[\text{D}_\text{n}]$. Second-order rate constants in the micellar pseudo-phase can also be written with concentration as *local* molarity, $k_2^{\text{m}}(\text{l mol}^{-1}\text{s}^{-1})$, and

$$k_2^{\text{m}} = k_\text{M}V_\text{M} \tag{2}$$

where V_M (l mol^{-1}) is the molar volume of the reaction region at the micellar surface. Surfactant exists partly as monomer whose concentration is assumed to be the critical micelle concentration (cmc), i.e.

$$[\text{D}_\text{n}] = [\text{D}_\text{T}] - \text{cmc} \tag{3}$$

Ionic concentrations in the micellar pseudo-phase can

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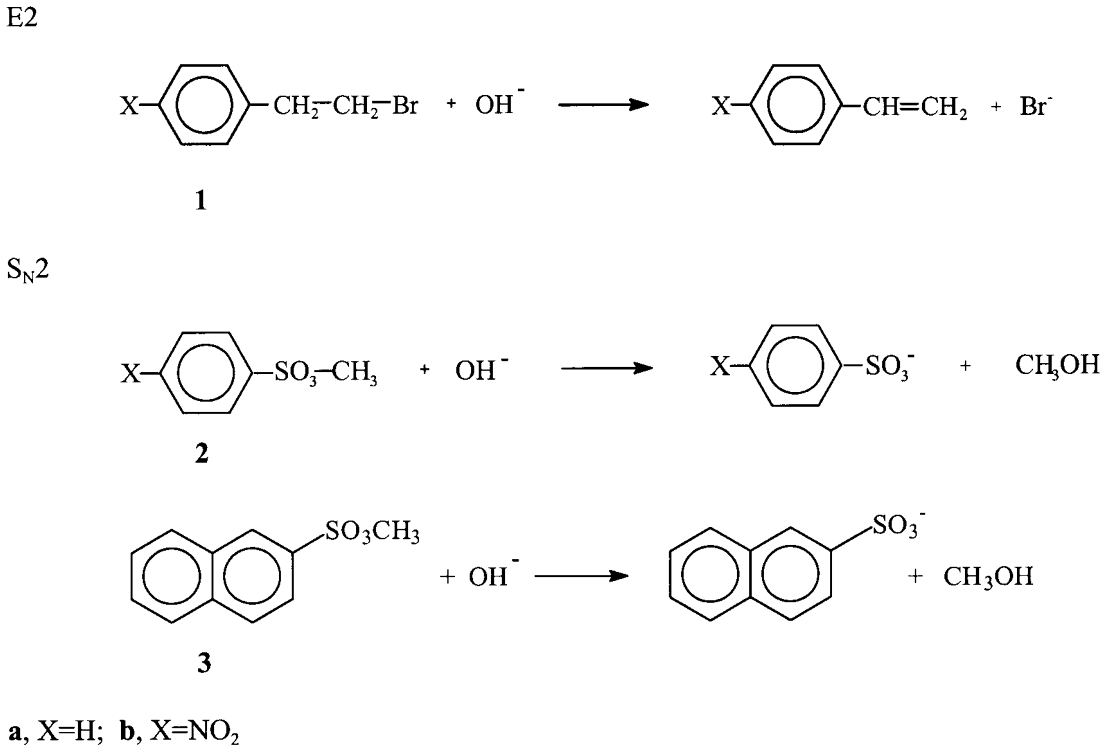

Scheme 1

sometimes be estimated experimentally,[3] but those of OH^- have to be calculated by using theoretical treatments which involve approximations, and have been discussed.[4] In this work we compared micellar effects on S_N2 and $E2$ reactions with OH^- and therefore uncertainties in the transfer equilibrium of OH^- between water and micelles factor out for a given surfactant.

We use sulfobetaine micelles with different head groups:

n-$C_{14}H_{29}N^+Me_2(CH_2)_3SO_3^-$

SB3-14

n-$C_{14}H_{29}N^+Bu_2(CH_2)_3SO_3^-$

SBBu3-14

Sulfobetaine micelles are formally neutral, but they incorporate anions, although less strongly than cationic micelles,[5] and incorporation of OH^- is described by[6]

$$K'_{OH} = [OH^-_M]/[OH^-_W]([D_n] - [OH^-_M]) \qquad (4)$$

Equations of this general form have been used to describe ion binding to counter-ionic and sulfobetaine micelles.[1b,6,7] In earlier work we compared effects of cationic micelles with different head groups on $E2$ and S_N2 reactions of OH^- (Scheme 1).[2] Equations of the form of Eqn. (4) were used to treat the binding of Br^- to sulfobetaine micelles estimated kinetically and conductimetrically with reasonable agreement between the two methods, and there was lower binding with an increase in bulk of the head group.[7]

Second-order rate constants of the S_N2 reactions in micelles are relatively insensitive to the bulk of the surfactant head groups, but an increase in head-group bulk favors $E2$ reactions, and the preference is higher with the nitro derivative, **1b**. Second-order rate constants in cationic micelles, relative to those in water, are higher for $E2$ reactions in which charge is dispersed in the transition state than for S_N2 reactions in which it is more localized.[2] We have now extended this investigation to reactions in micelles of SB3-14 and SBBu3-14. Reactions of OH^- were examined in solutions of these surfactants, values of K'_{OH} [eqn (4)] were estimated and are, as expected, much lower for sulfobetaine than for cationic micelles.[7] In addition, an increase in the bulk of a head group decreases affinities for anions in both cationic and sulfobetaine micelles.

RESULTS AND DISCUSSION

The rate-surfactant profiles for $E2$ reactions of phenethyl- and 4-nitrophenethyl bromide (**1a**, **b**) are shown in Figs 1 and 2. Rate constants of reaction of **1a** are only slightly affected by the surfactant, which is often taken to indicate that micelles do not affect local reactivity, but analysis of the rate data by using Eqns (1)–(4) shows that this

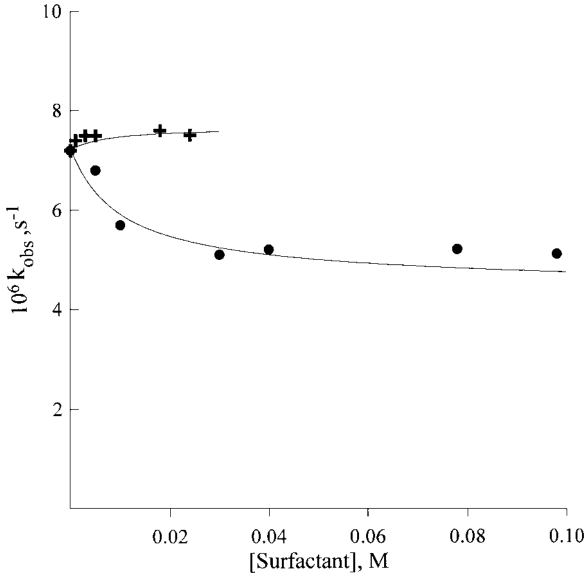

Figure 1. Values of k_{obs} for reaction of phenethyl bromide (**1a**) in SB3-14 (●) and SBBu3-14 (✚) in 0.2 M NaOH. Lines here and in Fig. 2 calculated with Eqns (1), (3) and (4) and the parameters in Table 1

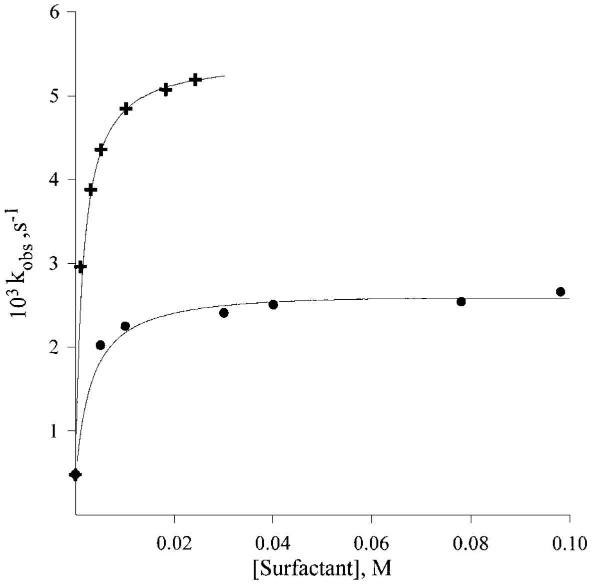

Figure 2. Values of k_{obs} for reaction of 4-nitrophenethyl bromide (**1b**) in SB3-14 (●) and SBBu3-14 (✚) in 0.2 M NaOH

conclusion is incorrect. However, reaction of the nitro derivative, **1b**, is clearly micellar accelerated (Fig. 2).

The association constant for **1b** to micellized SBBu3-14 is 500 l mol^{-1}, based on the saturation-solubility method.[8] This value is similar to that of 540 l mol^{-1} in micellized cetyltrimethylammonium bromide (CTABr),[2] indicating that changes in the head-group charge do not have large effects on K$_s$, although typically binding constants are larger in zwitterionic than in cationic micelles.[9]

The fitting parameters for the data in Figs 1 and 2 are given in Table 1. The values of K$_s$ are similar to those used earlier in fitting kinetic data for reactions in cationic micelles and 'kinetic' values (Table 1) are similar to those measured in cationic micelles, or estimated kinetically.[2] As in other systems, acceptable fits can be obtained with minor variations in the fitting parameters.[1] Consistently k_M for a given substrate increases with increasing bulk of the surfactant head group, and with introduction of a nitro group (Table 1). Our values of k_M for the $E2$ reactions are slightly lower than those estimated by Wilk in cationic micelles,[10] but she used a mixed-ion system and data fitting had to allow for interionic competition.

Structural effects on micellar reactivity

Regardless of the estimated fitting parameters, the differences in values of k_{obs} (Figs 1 and 2) show that micellar rate enhancements are more significant for a nitro-substituted than for an unsubstituted derivative, as with reactions in cationic micelles.[2] This substituent effect is much stronger in $E2$ than in S_N2 reactions, and we note that in non-micellar conditions a decrease in solvent polarity favors $E2$ over S_N2 reactions.[11,12]

Water is not excluded from the interfacial region of ionic micelles but, based on spectrometric probes, the polarities appear to be lower than that of water,[13] consistent with kinetic data on spontaneous reactions.[1b–e,14] Therefore, micellar medium effects upon relative rates of $E2$ and S_N2 reactions are analogous to those of organic solvents as compared with water. There is extensive evidence that electronic substituent effects are typically larger for $E2$ than for S_N2 reactions[10] when based on structurally similar substrates and we see this pattern for reactions in micelles. We compare the behaviors of $E2$ reactions of **1a** and **b** with those of S_N2 reactions of **2a** and **b**. The rate increases induced by a

Table 1. Fitting parameters for reactions of **1a** and **b**[a]

Substrate	Surfactant	K$_s$ (l mol^{-1})	10^3 k_M (s^{-1})
1a	SB3-14	260	0.045
	SBBu3-14	260	0.163
	CTAOH	340	0.110
	CTPAOH	260	0.200
1b	SB3-14	450	42.0
	SBBu3-14	500	116
	CTAOH	450	46.0
	CTPAOH	420	120

[a] At 25.0 °C, with 0.2 M NaOH in sulfobetaines and 0.1 M NaOH for the other surfactants.[2]

[b] Fitting parameters for reactions in the sulfobetaines are k_W = 3.61×10^{-5} and 2.40×10^{-3} l mol^{-1}s^{-1} for **1a** and **b**, respectively,[2] K'_{OH} = 0.35 and 0.25 l mol^{-1} for SB3-14 and SBBu3-14, respectively, and cmc = 1×10^{-4}M.

Table 2. Micellar effects on S_N2 and $E2$ reactions[a]

	Reaction medium				
	H_2O[b]	CTAOH[b]	CTPAOH[b]	SB3-14	SBBu3-14
S_N2 reactions of **2a**, **b**	4	7.5	13		
$E2$ reactions of **1a**, **b**	67	400	650	520	700

[a] Values of $k_M(NO_2)/k_M(H)$.
[b] From data in Ref. 2.

4-nitro group are compared for S_N2 and $E2$ reactions in water and in micelles of SB3-14 and SBBu3-14 and of cetyltrimethyl- and tripropylammonium hydroxide (CTAOH and CTPAOH, respectively) (Table 2). These rate comparisons indicate how micelles favor reactions in which charge is delocalized in the transition state, as in $E2$ compared with S_N2 reactions, and the extent to which the effects are increased by increasing the bulk of the surfactant head group.

The relation between rate constants in the micellar interfacial region, relative to those in water, and the 'softness' of the transition state applies to spontaneous unimolecular and also bimolecular micellar-mediated reactions, and examples in decarboxylation and dephosphorylation are given elsewhere.[14–16] Head-group effects upon reactivities in the micellar pseudo-phase are largest for reactions in which charge is delocalized in a 'soft' transition state. Substrate hydrophobicity, of itself, does not seem to be of major importance in controlling reactivity in the micellar interfacial region. For example, micellar head-group effects are similar for reactions of **2a** and methyl naphthalene-2-sulfonate, **3**, in both cationic[2,17] and sulfobetaine[7] micelles, despite differences in hydrophobicities and values of K_s. This behaviour is understandable if a hydrophobic moiety is relatively isolated from the reaction center and its interactions with the association colloid do not change on going from the initial to the transition state and provided that the hydrophobic moiety does not change the location of the reaction center in the interfacial region.[18]

Values of second-order rate constants, k_M, are estimated unambiguously from the transfer equilibrium of a reagent between water and micelles, but we have to estimate local molarity at the micellar surface, if they are to be compared with second-order rate constants in water, k_W ($l\,mol^{-1}\,s^{-1}$). Local molarities for some ions can be estimated by dediazonization trapping,[3d,e] but this method fails for basic anions. Local molarities can be estimated theoretically,[1,4] but these methods involve assumptions and approximations and some of them have not been tested with micelles that have bulky head groups. The usual approach is to apply Eqn. (2), although the value of V_M and the implied assumption of a uniform micellar reaction region are uncertain.[18,19] This problem of the definition of 'concentration' complicates the comparison of second-order rate constants in cationic and sulfobetaine micelles, although we note the similarities of values of k_M under these conditions. Similar questions regarding the meaning of concentration expressed as molarity also apply to comparisons between second-order rate constants in homogeneous solutions of mixed solvents and different compositions.

Table 3. Comparison of second-order rate constants in micelles and in water with increasing head-group bulk[a]

Substrate	Surfactant	k_2^m/k_W
1a	SB3-14	0.27
	SBBu3-14	0.63
1b	SB3-14	2.5
	SBBu3-14	6.8

[a] $k_w = 3.61 \times 10^{-5}$ and 2.40×10^{-3} $l\,mol^{-1}\,s^{-1}$ for **1a** and **b** [2], respectively.

With these reservations we show k_2^m/k_w, calculated with $V_M = 0.14\ l\,mol^{-1}$ (Table 3), as elsewhere.[1b]

On the basis of the above value of V_M, second-order rate constants of $E2$ reactions in micellar pseudo-phases follow similar patterns. Reactions of **1a** are slightly slower in micelles than in water, but those of **1b** are faster (Table 3), because delocalization of charge into the nitro group in the anionic transition state increases k_2^m/k_w. These micellar effects are larger in SBBu3-14 than in SB3-14 because the bulky butyl group decrease the polarity in the interfacial region. There are compilations of values of k_2^m/k_w for reactions of OH^- with a variety of organic substrates,[1] generally in cationic micelles, and it appears that $k_2^m < k_w$ for biomolecular reactions at saturated carbon and at acyl and phosphoryl centers, where charge is localized, but $k_2^m \geq k_w$ for aromatic nucleophilic substitution and $E2$ reactions[10] where there is extensive charge delocalization in the transition state. The factors that control relative rate constants in water and in cationic micelles also apply to sulfobetaine micelles. There is uncertainty in the estimation of local ionic concentrations, e.g. of OH^-, in micellar pseudo-phases, but the problem is reduced by comparing micellar effects upon reactions with different mechanisms, which involve a common ionic reagent. The effects of substrate and surfactant structures on k_2^m/k_w for reactions of **1a** and **b** (Table 3) are quantitatively similar to those observed for $E2$ reactions of the hydrophobic 1,2-dihalo-1,2-

diphenylethanes in cationic micelles.[20] Hence uncertainties in the values of V_M and K'_{OH} [Eqns (2) and (4)] do not cloud the overall conclusions.

EXPERIMENTAL

Materials. Substrates and surfactants were materials described earlier.[2,20,21] Reaction solutions were prepared in distilled, deionized, CO_2-free water.

Kinetics. Reactions were followed spectrophotometrically at 264 and 350 nm for reactions of **1a** and **b**, respectively, as described,[2] with 10^{-4} M substrate introduced in MeCN, so that the reaction solution contained 1 vol.% MeCN. Values of k_{obs} were calculated by using the integrated first-order rate equation with correlation coefficients of 0.999 or better. Fitting of the k_{obs} vs [surfactant] profiles, by using Eqn. (1),[1] was insensitive to values of K_s in the range 260 ± 50 l mol^{-1} for **1a**, and 450 ± 100 l mol^{-1} for **1b**, based on visual fitting.

Substrate binding. The value of K_s for **1b** in SBBu3-14 was determined by the saturation-solubility method,[8] as described.[2]

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