

Effects of ionic and non-ionic micelles on rate of Hydroxide ion-catalyzed hydrolysis of securinine

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ABSTRACT: The effects of micelles of cetyltrimethylammonium bromide (CTABr), tetradecyltrimethylammonium bromide (TTABr), sodium dodecyl sulfate (SDS) and polyoxyethylene 10 lauryl ether (C₁₂E₁₀) on the rates of alkaline hydrolysis of securinine were studied at a constant [OH⁻] (0.05 M). An increase in the total concentrations of CTABr, TTABr, SDS and C₁₂E₁₀ from 0.0 to 0.2 M causes a decrease in the observed pseudo-first-order rate constants (*k*_{obs}) by factors of *ca* 2.5, 3, 7 and 4, respectively. The observed data are explained in terms of pseudophase and pseudophase ion-exchange (PIE) models of micelle. The binding constants, *K*_S, of securinine with SDS, C₁₂E₁₀, CTABr and TTABr micelles are 32.4, 14.8, 22.1, and 9.1 M⁻¹, respectively. The magnitudes of the second-order rate constants, *k*_M, for the reactions in the micellar pseudophase are negligible compared with the corresponding rate constant, *k*_W, for the reaction occurring in the aqueous pseudophase for CTABr, TTABr, SDS and C₁₂E₁₀. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: securinine; cationic micelles; anionic micelle; non-ionic micelle; alkaline hydrolysis; kinetics

INTRODUCTION

Securinine (**1**), the major alkaloid from *Breynia coronata*, is a reportedly useful drug for diseases concerned with the central nervous system. It is essential for a drug molecule to be absorbed and then to diffuse through the biological membrane with essentially no activation barrier in order to repair the molecular damage that has occurred at the so-called specific diseased site of the cell.

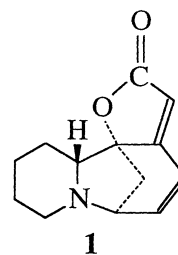
Although a normal micelle does not conform to a complete or partial model of a biological membrane, it does display certain characteristics of such membranes. Micelles of certain characteristics have been exploited as drug carriers.¹ Perhaps because of this and other related reasons, a significant amount of systematic kinetic work has been carried out during the past decades.² Micellar-mediated reactions are generally rationalized in terms of a pseudophase model for micelles^{1c,3}. Bunton⁴ has outlined both the shortcomings and usefulness of this model.

Most of the studies on the effects of micelles on the rates of organic reactions are concerned with the hydrolysis of esters, activated aromatic compounds and a few amides.^{2a,5} It appears from these studies that the rate of a bimolecular reaction involving a neutral and an anionic reactant is usually inhibited by an anionic

surfactant, i.e. a surfactant with a head group carrying a negative charge. Such an inhibition is attributed to the exclusive micellar incorporation of only one reactant. The hydrophobicity of the organic substrates used in these studies involves either an open-chain hydrocarbon of a few methylene units or an aromatic skeleton or both. We did not find any report on micellar-catalyzed organic reactions where the surfactant contained a straight-chain hydrocarbon and an organic substrate with a molecular skeleton similar to that of securinine. The present study was aimed at exploring the effects of ionic and non-ionic micelles on the rates of alkaline hydrolysis of securinine.

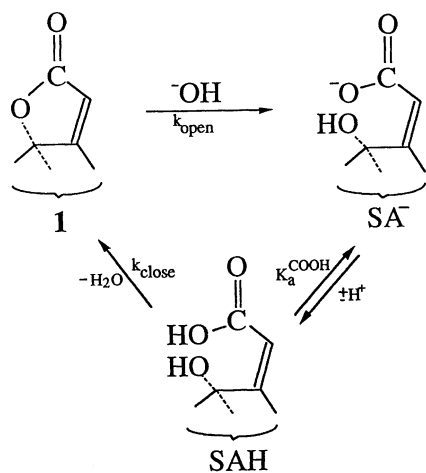
EXPERIMENTAL

Materials. Optically pure (+)-securinine (**1**) was isolated from *Breynia coronata*. Cetyltrimethylammonium bromide (CTABr) and sodium dodecyl sulfate (SDS) were



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Scheme 1

obtained from Aldrich and tetradecyltrimethylammonium bromide (TTABr) and polyoxyethylene 10 lauryl ether (C₁₂E₁₀) from Sigma. All other chemicals were of reagent grade.

Kinetic Measurements. The kinetics of the alkaline hydrolysis of securinine in the presence of ionic and non-ionic micelles were studied by monitoring the change in absorbance at 290 nm. The details of the kinetic procedure and data analysis have been described elsewhere⁶.

Product Analysis. The hydroxide ion-catalyzed hydrolysis of the lactone moiety of **1** is shown in Scheme 1, where k_{open} represents the rate constant for the hydroxide ion-catalyzed opening of the lactone ring. When the alkaline hydrolysed product(s) mixture was acidified, the lactonization of SAH was affirmed by the similarity of the UV spectra of the acidic reaction mixture (obtained at the end of the experiment when no further change in the UV spectrum was noticed) and authentic securinine. A reaction mechanism similar to Scheme 1 has been shown to occur in the hydrolytic cleavage of champtothecin.⁷ It should be noted that at alkaline pH, i.e. at pH > 7, the cyclization of SA⁻ via SAH does not occur⁶. Similarly, the k_{open} step is kinetically undetectable at acidic pH.⁶ Thus, under the experimental conditions of this study, pseudo-first-order rate constants, k_{obs} , represent the k_{open} step only (i.e. k_{obs} is not a composite of k_{open} and k_{close}).

RESULTS AND DISCUSSION

Effects of anionic micelles on reaction rates

The rates of hydroxide ion-catalyzed cleavage of securinine were studied using 0.05 M NaOH at 35 °C

and with total sodium dodecyl sulfate concentration, [SDS]_T, in the range $9.00 \times 10^{-4} - 0.20$ M. The pseudo-first-order rate constants, k_{obs} , decreased slightly more than seven fold with increase in [SDS]_T from 0.00 to 0.20 M. Such an inhibitory effect caused by the increase in micelle concentration might be attributed to the following reasons: (i) one of the two reactants, (either securinine or ⁻OH) is excluded from binding with micelles; (ii) the two micelle-bound reactants are not located in the same micellar environment; and (iii) the securinine molecules are located in an environment of apparent low dielectric constant where the nucleophile (⁻OH) loses its intrinsic nucleophilicity owing to possible formation of a loose ion pair with its counterion (Na⁺). It is known from literature that ⁻OH ions do not bind effectively with SDS micelles.⁸ Hence only the first possibility applies, where only securinine seems to have a binding affinity with SDS micelles.

The observed rate constants, k_{obs} , were found to obey the following empirical relationship:

$$k_{\text{W}}/k_{\text{obs}} = A + B[\text{SDS}]_{\text{T}} \quad (1)$$

where k_{W} is k_{obs} at [SDS]_T = 0. The empirical parameters *A* and *B* were calculated from equation (1) using the linear least-squares method and the calculated values of *A* and *B* are 1.01 ± 0.03 and $32.4 \pm 0.4 \text{ M}^{-1}$, respectively. The fitting of the observed data to equation (1) is evident from the standard deviations associated with the values of *A* and *B* and from the plot in Fig. 1 where a straight line is drawn through the least-squares calculated points.

Reaction in the presence of cationic micelles

A series of kinetic runs were carried out to study the effects of [CTABr] and [TTABr] on the pseudo-first-order rate constants, k_{obs} , for the alkaline hydrolysis of securinine. The results are summarized in Tables 1 and 2, respectively. These results showed a decrease in the rate of hydrolysis with increase in [CTABr] and [TTABr]. The decrease in k_{obs} with increase in concentration of cationic micelles cannot be ascribed to the exclusive micellar incorporation of only one of the reactants. It is known that hydroxide ions bind effectively with cationic micelles.⁹ The observed rate constants, k_{obs} , were treated with the empirical equation (1) with [SDS]_T replaced by [CTABr]_T or [TTABr]_T. The least-squares calculated empirical parameters are $A = 0.868 \pm 0.031$ and $B = 7.2 \pm 0.3 \text{ M}^{-1}$ for CTABr and $A = 1.11 \pm 0.09$ and $B = 9.6 \pm 1.0 \text{ M}^{-1}$ for TTABr. The fitting of the observed data to equation (1) may be seen from the standard deviations associated with the calculated empirical parameters and from the plots in Fig. 1 where straight lines are drawn through the least-squares calculated points.

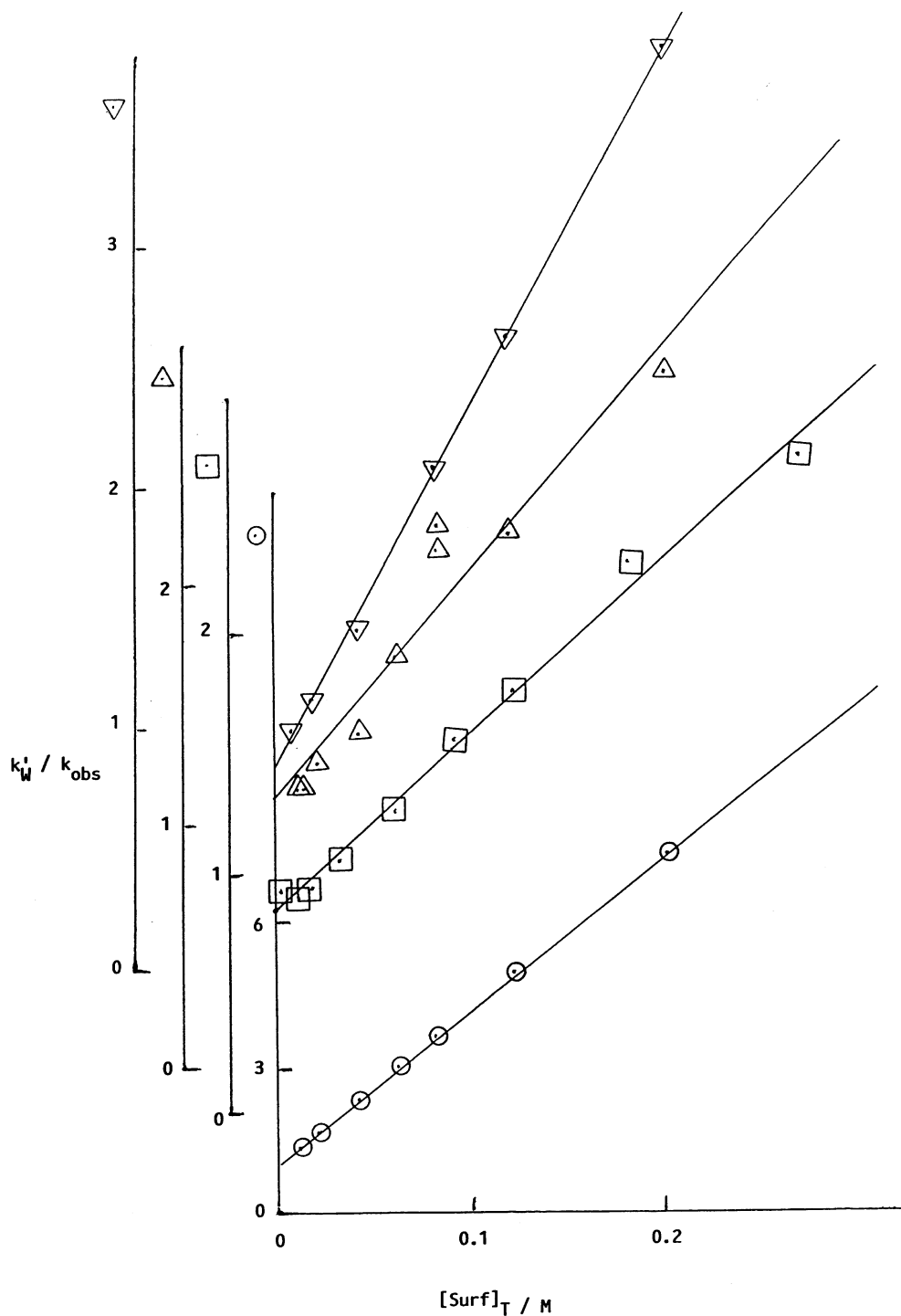


Figure 1. Plots showing the dependence of k'_W/k_{obs} upon total concentration of surfactant, $[Surf]_T$, for (○) SDS, (□) CTABr, (△) TTABr and (▽) $C_{12}E_{10}$. Solid lines are drawn through the least-squares calculated points using equation (1) as described in the text

Reaction in the presence of non-ionic micelles

The rates of alkaline hydrolysis of securinine were studied in 0.05 M NaOH at different concentrations of $C_{12}E_{10}$. An increase in $[C_{12}E_{10}]$ causes a significant decrease in the values of the pseudo-first-order rate constants, k_{obs} . The observed rate constants showed a

satisfactory fit to equation (1) (with $[SDS]_T$ replaced by $[C_{12}E_{10}]$) with least-squares calculated values of $A = 0.878 \pm 0.035$ and $B = 14.8 \pm 0.3 \text{ M}^{-1}$. The decrease in k_{obs} with increase in $[C_{12}E_{10}]$ may be attributed either to extremely weak micellar binding of highly hydrophilic hydroxide ions or to different preferential locations of the two reactants, OH^- and securinine, in the micelles.

Table 1. Effect of [CTABr] on the alkaline hydrolysis of securinine (**1**)^a

[CTABr] (M)	$10^3 k_{\text{obs}}$ (s ⁻¹)	$10^3 k_{\text{calcd}}^{\text{b}}$ (s ⁻¹)	$10^3 k_{\text{calcd}}^{\text{c}}$ (s ⁻¹)	$10^3 k_{\text{calcd}}^{\text{d}}$ (s ⁻¹)
0.0	1.83	—	—	—
0.002	1.97 ± 0.03 ^e	1.92	1.94	2.06
0.010	2.05 ± 0.03	1.99	1.99	1.98
0.015	1.93 ± 0.04	1.96	1.95	1.91
0.030	1.72 ± 0.03	1.78	1.77	1.72
0.060	1.45 ± 0.04	1.44	1.44	1.42
0.090	1.18 ± 0.03	1.20	1.21	1.21
0.120	1.04 ± 0.02	1.03	1.03	1.05
0.180	0.800 ± 0.009	0.798	0.803	0.837
0.270	0.670 ± 0.012	0.597	0.600	0.640
$10^9 \Sigma d_i^2$		16.61	12.83	17.18

^a $[1]_0 = 1.38 \times 10^{-4}$ M, [NaOH] = 0.05 M, $\lambda = 290$ nm, temperature = 35 °C and the reaction mixture contained 4%, (v/v) MeCN.

^b Calculated from equation (7) with $k'_M = (7.57 \pm 0.20) \times 10^{-3}$ s⁻¹, $K_S = 22.1 \pm 2.6$ M⁻¹, $K_{\text{Br}}^{\text{OH}} = 5$ and CMC = 1×10^{-4} M.

^c Calculated from equation (7) with $k'_m = (13.8 \pm 0.4) \times 10^{-3}$ s⁻¹, $K_S = 15.6 \pm 1.3$ M⁻¹, $K_{\text{Br}}^{\text{OH}} = 20$ and CMC = 1×10^{-4} M.

^d Calculated from equation (7) with $k'_m = 1.968 \pm 0.150$ s⁻¹, $K_S = 8.9 \pm 0.6$ M⁻¹, $K_{\text{Br}}^{\text{OH}} = 10^4$ and CMC = 1×10^{-4} M.

^e Error limits are standard deviations.

Table 2. Effect of [TTABr] on the alkaline hydrolysis of securinine (**1**)^a

[CTABr] (M)	$10^3 k_{\text{obs}}$ (s ⁻¹)	$10^3 k_{\text{calcd}}^{\text{b}}$ (s ⁻¹)	$10^3 k_{\text{calcd}}^{\text{c}}$ (s ⁻¹)
0.0	2.26	—	—
0.010	1.97 ± 10.03 ^d	2.05	2.02
0.015	1.94 ± 0.05	1.92	1.92
0.020	1.79 ± 0.02	1.82	1.83
0.040	1.64 ± 0.03	1.53	1.54
0.40	1.65 ± 0.03	1.53	1.54
0.060	1.32 ± 0.02	1.33	1.33
0.060	1.35 ± 0.02	1.33	1.33
0.08	1.06 ± 0.02	1.18	1.18
0.080	0.992 ± 0.009	1.18	1.18
0.120	1.03 ± 0.02	0.967	0.957
0.200	0.788 ± 0.012	0.714	0.695
$10^9 \Sigma d_i^2 =$		93.54	90.20

^a $[1]_0 = 1.424 \times 10^{-4}$ M, [NaOH] = 0.05 M, $\lambda = 290$ nm, temperature = 36 °C and the reaction mixture contained 4% (v/v) MeCN.

^b Calculated from equation (7) with $k'_M = (-0.7 \pm 7.2) \times 10^{-3}$ s⁻¹, $K_S = 4.8 \pm 4.8$ M⁻¹, $K_{\text{Br}}^{\text{OH}} = 4$ and CMC = 0.0035 M.

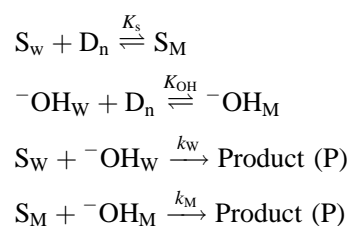
^c Calculated from equation (7) with $k'_M = (3.14 \pm 1.76) \times 10^{-3}$ s⁻¹, $K_S = 9.1 \pm 5.2$ M⁻¹, $K_{\text{Br}}^{\text{OH}} = 4$ and CMC = 0.0010 M.

^d Error limits are standard deviations.

Pseudophase model of micelle

The rate of alkaline hydrolysis of securinine was found to be first order with respect to each of the two reactants, securinine and hydroxide ion.⁶ The contribution of uncatalyzed (i.e. solvent-assisted) hydrolysis to the rate turned out to be negligible compared with that of hydroxide ion-catalyzed hydrolysis even at $[\text{OH}^-] = 0.02$ M. The observed pseudo-first-order rate constants, k_{obs} , at different micelle concentrations (D_n) can be explained quantitatively in terms of the pseudophase model of micelles. Both reactants, securinine (S)

and OH^- , may be assumed to be distributed between the aqueous (W) and micellar (M) pseudophases as shown in Scheme 2, where D_n represents the micellized surfactant.



Scheme 2

The concentration of micelles ($[D_n]$) is given by the total surfactant concentration $[D]_T$ less that of the monomer remaining in the aqueous pseudophase, taking this as the corresponding critical micellar concentration (CMC). There are several assumptions involved in the data treatment in terms of Scheme 2 which are best explained by Bunton.^{2c} In Scheme 2, K_S and K_{OH} represent the micelle–securinine and micelle–hydroxide ion association constants, respectively. The OH^- -catalyzed rate constants for the reaction taking place in the aqueous pseudophase (W) is represented by k_w and that in the micellar pseudophase (M) by k_M . Since it is not possible to know the exact volume of the specific micellar region where micellar-bound hydroxide ions exist, the rate of micellar mediated reaction is defined as rate = $k_M [S_M][\text{OH}_M^-]/[D_n]$.

The observed rate law (rate = $k_{\text{obs}} [S]_T$, where $[S]_T = [S_w] + [S_M]$) and the derived rate law based on Scheme 2 may give the equation

$$k_{\text{obs}} = \frac{k'_w + k'_M K_{\text{OH}} K_S [D_n]}{(1 + K_{\text{OH}} [D_n])(1 + K_S [D_n])} \quad (2)$$

where $[D_n] = [D]_T - \text{CMC}$, $k'_w = k_w [\text{OH}]_T$, $k'_M = k_M [\text{OH}]_T / V_M$ (where V_M is the partial molar

volume of the reactive region in the micellar pseudo-phase) and $[\text{OH}^-]_{\text{T}} = [\text{OH}^-]_{\text{W}} + [\text{OH}^-]_{\text{M}}$. All concentrations used refer to the total volume of the solutions and the dimensions of k'_{W} , k'_{M} , k_{M} and V_{M} are s^{-1} , M s^{-1} , $\text{M}^{-1} \text{s}^{-1}$ and M^{-1} , respectively.

The highly hydrophilic hydroxide ion is known to exhibit an extremely weak binding affinity towards anionic SDS micelles. It is therefore conceivable to assume that $1 \gg K_{\text{OH}}[\text{D}_n]$ under the experimental conditions imposed and this assumption reduces equation (2) to

$$k_{\text{obs}} = \frac{k'_{\text{W}} + k'_{\text{M}} K_{\text{OH}} K_{\text{S}} [\text{D}_n]}{1 + K_{\text{S}} [\text{D}_n]} \quad (3)$$

The reported value of CMC for SDS is 0.008 M.^{2b} The decrease of nearly 30% in k_{obs} with increase in $[\text{SDS}]_{\text{T}}$ from 0.0 to 0.01 M, however, indicates the probable reduction in the CMC under the presence of 1.38×10^{-4} M securinine. An attempt to fit the observed data to equation (3) with CMC = 0.008 M was unsuccessful. The comicellization of a micelle-forming substance in the presence of a hydrophobic solute is well known.¹⁰ It is interesting that comicellization of SDS could not be detected¹¹ in the presence of PS^- (where PS^- represents anionic phenyl salicylate), whereas a nearly 10-fold decrease in the CMC of CTABr was observed in the presence of 2×10^{-4} M PS^- .¹²

The kinetic CMC of SDS was determined as follows. The unknown parameters, $k_{\text{M}} K_{\text{OH}}$ and K_{S} and the least-squares, Σd_i^2 (where $d_i = k_{\text{obs}i} - k_{\text{calc}i}$), values were calculated from equation (3) at a given value of the CMC using the non-linear least-squares method. The magnitudes of the least squares (Σd_i^2) were determined at different values of the CMC and the specific CMC at which the Σd_i^2 value turned out to be minimum was considered to be the kinetic CMC. The value of the kinetic CMC for SDS was found to be 9×10^{-4} M under the experimental conditions of the present study. The calculated values of $k'_{\text{M}} K_{\text{OH}}$ and K_{S} are $(1.9 \pm 6.2) \times 10^{-5} \text{ s}^{-1}$ and $35.1 \pm 3.8 \text{ M}^{-1}$ respectively, with CMC = 9×10^{-4} M and $k'_{\text{W}} = 0.00183 \text{ s}^{-1}$ (the value of k'_{W} was obtained by carrying out the kinetic run in the absence of micelles). The calculated value of $k'_{\text{M}} K_{\text{OH}}$ is associated with a relative standard deviation of > 300% and hence it is not statistically different from zero. The maximum contribution of $k'_{\text{M}} K_{\text{OH}} K_{\text{S}} [\text{D}_n]$ to $k'_{\text{W}} + k'_{\text{M}} + K_{\text{OH}} K_{\text{S}} [\text{D}_n]$ turned out to be < 8% under the experimental conditions of the study. This showed that $k'_{\text{M}} K_{\text{OH}} K_{\text{S}} [\text{D}_n]$ may be neglected in comparison with k'_{W} in equation (3). Under such conditions, equation (3) is reduced to

$$k_{\text{obs}} = k'_{\text{W}} / (1 + K_{\text{S}} [\text{D}_n]) \quad (4)$$

which is similar to the empirical equation (1) with $A = 1 - K_{\text{S}} \text{CMC}$ and $B = K_{\text{S}}$. It is interesting that the calculated value of A (= 1.01) revealed a negative value

of CMC (= -0.0002 M), which is physically meaningless, and the value of B (= 32.4 M^{-1}) is not significantly different from K_{S} (= 35.1 M^{-1}).

The observed data obtained in the presence of $\text{C}_{12}\text{E}_{10}$ micelles showed a reasonably good fit to equation (1) [which is equivalent to equation (4)]. This may be attributed to the extremely weak binding of hydroxide ion to $\text{C}_{12}\text{E}_{10}$ micelles, i.e. $1 \gg K_{\text{OH}}[\text{D}_n]$ and hence $k'_{\text{W}} \gg k'_{\text{M}} K_{\text{OH}} K_{\text{S}} [\text{D}_n]$. It seems that the high hydrophilicity of the hydroxide ion makes its binding affinity extremely weak towards even neutral $\text{C}_{12}\text{E}_{10}$ micelles. The value of K_{S} for $\text{C}_{12}\text{E}_{10}$ was found to be 14.8 M^{-1} , which is nearly half of the value of K_{S} for SDS.

Pseudophase ion-exchange model of micelle. For ionic micellar mediated reactions where a reactive ion (such as OH^-) and an inert counterion (such as Br^-) carry a similar charge, the pseudophase ion-exchange (PIE) model is generally used to discuss the observed data. The assumptions involved and the usefulness and weaknesses of this model were critically discussed by Bunton *et al.*^{13,14} In terms of the PIE model, the nucleophile (OH^-) and inert counterion (Br^-) of a cationic micelle compete at the micellar surface according to the ion-exchange equilibrium described by the equation



The relationships $[\text{OH}^-]_{\text{T}} = [\text{OH}^-]_{\text{W}} = [\text{OH}^-]_{\text{M}}$, $[\text{Br}^-]_{\text{T}} = [\text{Br}^-]_{\text{W}} + [\text{Br}^-]_{\text{M}}$, $m_{\text{OH}} + m_{\text{Br}} = \beta$, where $m_{\text{OH}} = [\text{OH}^-]_{\text{M}} / [\text{D}_n]$ and $m_{\text{Br}} = [\text{Br}^-]_{\text{M}} / [\text{D}_n]$ and equation (5) yield the equation

$$m^2_{\text{OH}} + m_{\text{OH}} \left\{ \frac{[\text{OH}^-]_{\text{T}} + [\text{Br}^-]_{\text{T}} K_{\text{Br}}^{\text{OH}}}{(K_{\text{Br}}^{\text{OH}} - 1) [\text{D}_n]} - \beta \right\} - \frac{\beta [\text{OH}^-]_{\text{T}}}{(K_{\text{Br}}^{\text{OH}} - 1) [\text{D}_n]} = 0 \quad (6)$$

The PIE model was initially developed to account for the observed biphasic plots of k_{obs} versus $[\text{D}_n]$ where the first-order rate constants, k_{obs} , increased sharply with increase in $[\text{D}_n]$ at low $[\text{D}_n]$ followed by a slow, non-linear decrease with increase in $[\text{D}_n]$ at high $[\text{D}_n]$. The PIE model has been also applied to micellar mediated reactions where the usual biphasic plots of k_{obs} versus $[\text{D}_n]$ were not obtained.¹⁵ The pseudo-first-order rate constants, k_{obs} , reveal a slight increase (ca 12%) with increase in $[\text{CTABr}]_{\text{T}}$ from 0.0 to 0.010 M followed by a significant decrease (ca 67%) with increase in $[\text{CTABr}]_{\text{T}}$ from 0.010 to 0.27 M. However, an increase in k_{obs} with increase in $[\text{TTABr}]_{\text{T}}$ could not be detected within the $[\text{TTABr}]_{\text{T}}$ range 0.010 – 0.200 M.

Equation (2) can be rearranged to give

$$k_{\text{obs}} = \frac{k_{\text{w}}[\text{OH}^-]_{\text{T}} + (k''_{\text{M}}K_{\text{S}} - k_{\text{w}})m_{\text{OH}}[\text{D}_{\text{n}}]}{1 + K_{\text{S}}[\text{D}_{\text{n}}]} \quad (7)$$

where $k_{\text{M}}'' = k'_{\text{M}}/[\text{OH}^-]_{\text{T}} = k_{\text{M}}/V_{\text{M}}$. In order to calculate unknown parameters, k'_{M} and K_{S} from equation (7), the values of m_{OH} at different $[\text{D}_{\text{n}}]$ were calculated from equation (6) at a given value of $K_{\text{Br}}^{\text{OH}}$ with known values of $[\text{OH}^-]_{\text{T}}$, $[\text{Br}^-]_{\text{T}}$ and $\beta = 0.8$. These values of m_{OH} were subsequently used in equation (7) to calculate k'_{M} , K_{S} and least-squares ($\sum d_i^2$, where $d_i = k_{\text{obs}i} - k_{\text{calcd}i}$) values using the non-linear least-squares method. The reported values of CMC for CTABr range from 1×10^{-4} to 9×10^{-4} M,¹² depending on the presence or absence of a solute in the micellar solution. The CMC for CTABr was considered to be 1×10^{-4} M.¹⁶ Such calculations were carried out at different presumed values of $K_{\text{Br}}^{\text{OH}}$ (range $5 - 10^4$). The $\sum d_i^2$ values differ only slightly with increase in the magnitude of $K_{\text{Br}}^{\text{OH}}$ from 5 to 10^4 . The calculated values of the rate constants, k_{calcd} , at $K_{\text{Br}}^{\text{OH}} = 5, 20$ and 10^4 are given in Table 1. In terms of these values of k_{calcd} , it is not easy to ascertain which value of $K_{\text{Br}}^{\text{OH}}$ is the most appropriate. This is a general weakness of PIE model, as mentioned by Germani *et al.*¹⁷ It is interesting that a change in $K_{\text{Br}}^{\text{OH}}$ from 5 to 10^4 increases k_{M}'' from 7.57×10^{-3} to $1968 \times 10^{-3} \text{ s}^{-1}$ and decreases K_{S} from 22.1 to 8.9 M^{-1} . Most of the reported values of $K_{\text{Br}}^{\text{OH}}$ lie between 2 and 20.¹⁵⁻¹⁸ The calculated values of k''_{M} and K_{S} are $(7.57 \pm 0.20) \times 10^{-3} \text{ s}^{-1}$ and $22.1 \pm 2.6 \text{ M}^{-1}$, respectively, with $K_{\text{Br}}^{\text{OH}} = 5$, $\beta = 0.8$ and $\text{CMC} = 1 \times 10^{-4}$ M. It is interesting that the values of k''_{M} [$(7.60 \pm 0.24) \times 10^{-3} \text{ s}^{-1}$] and K_{S} ($= 22.8 \pm 3.3 \text{ M}^{-1}$) at $\text{CMC} = 9 \times 10^{-4}$ M are not appreciably different from the corresponding values at $\text{CMC} = 1 \times 10^{-4}$ M.

Although the exact value of V_{M} is difficult to obtain, the estimated values of V_{M} vary in the range $0.14 - 0.37 \text{ M}^{-1}$.¹³ If we consider $V_{\text{M}} = 0.25 \text{ M}^{-1}$, the value of k_{M} turns out to be $18.9 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$, which is nearly 19-fold smaller than k_{w} . Although the value of $k_{\text{w}}/k_{\text{M}} = 19$ is a crude estimate, it certainly indicates that the hydroxide ion-catalyzed reaction is much slower in the micellar pseudophase than in the aqueous pseudophase. The maximum contribution of the $(k''_{\text{M}}K_{\text{S}} - k_{\text{w}})m_{\text{OH}}[\text{D}_{\text{n}}]$ term in equation (7) obtained at 0.27 M CTABr is 56% with $K_{\text{Br}}^{\text{OH}} = 5$ and $\text{CMC} = 1 \times 10^{-4}$ M. Although the calculated value of k''_{M} is associated with a reasonably good standard deviation, it cannot be considered very reliable because of its relatively small contribution to k_{obs} ($\leq 56\%$) and uncertainty in the values of $K_{\text{Br}}^{\text{OH}}$ and β .

Pseudo-first-order rate constants, k_{obs} , for the cleavage of securinine obtained at different $[\text{TTABr}]_{\text{T}}$ in the presence of 0.05 M NaOH were treated with equation (7) considering $\text{CMC} = 3.5 \times 10^{-3} \text{ M}^8$ and $1 \times 10^{-3} \text{ M}$.¹⁶ The non-linear least-squares calculated best values of k''_{M} and K_{S} at $K_{\text{Br}}^{\text{OH}} = 4$ turned out to be

$(-0.7 \pm 7.2) \times 10^{-3} \text{ s}^{-1}$ and $4.8 \pm 4.8 \text{ M}^{-1}$, respectively, at $\text{CMC} = 3.5 \times 10^{-3} \text{ M}^8$ and $(3.14 \pm 1.76) \times 10^{-3} \text{ s}^{-1}$ and $9.1 \pm 5.2 \text{ M}^{-1}$ at $\text{CMC} = 1 \times 10^{-3} \text{ M}$.¹⁶ The fitting of the observed data to equation (7) may be realized from the calculated values of the rate constants, k_{calcd} , listed in Table 2. Although the fitting of the observed data to equation (7) appears to be slightly better at $\text{CMC} = 1 \times 10^{-3} \text{ M}$, the value of k''_{M} is not very reliable because of its extremely small contribution (nearly 0%) to k_{obs} in equation (7).

The lower value of K_{S} ($= 9.1 \text{ M}^{-1}$) in TTABr micelles compared with K_{S} ($= 22.1 \text{ M}^{-1}$) in CTABr micelles is conceivable in view of the reported data on a related system.¹⁶

The significantly lower rate of alkaline hydrolysis of S_{M} compared with that of S_{W} in cationic micelles cannot be attributed to the ionic strength effect (the ionic strength of the ionic micellar surface is roughly estimated to be $3 - 5 \text{ M}^3$) because the rate of alkaline hydrolysis of securinine was found to be almost independent of ionic strength within the range $0.2 - 1.2 \text{ M}$.⁶ Pseudo-first-order rate constants for the alkaline hydrolysis of securinine revealed a decrease of approximately four fold due to the increase in the MeCN content from 4 to 50% (v/v) in mixed aqueous solvents.⁶ The dielectric constant of the micellar surface is concluded to be $34 - 46$.¹⁹ Hence part of the non-ionic and cationic micellar inhibition of the alkaline hydrolysis of S_{M} may be attributed to the medium polarity effect. The lower reactivity of S_{M} compared with S_{W} may be partly attributed to the different sites of average location of both reactants (S_{M} and $^-\text{OH}_{\text{M}}$) at the micellar surface.²⁰ The anionic micellar inhibition of the alkaline hydrolysis of securinine may be attributed to the micellar incorporation and exclusion of securinine and ^-OH , respectively.

CONCLUSIONS

The values of the kinetically determined binding constants, K_{S} , of securinine with anionic (SDS), neutral ($\text{C}_{12}\text{E}_{10}$) and cationic (CTABr and TTABr) micelles have been found to lie within the range $35 - 9 \text{ M}^{-1}$. These values are significantly smaller than K_{S} ($= 2 \times 10^3 \text{ M}^{-1}$)²¹ for phenyl saicylate (PSH) with SDS micelles. Both securinine and PSH contain 12 carbons and could be considered as moderately hydrophobic. Hence the nearly 100-fold larger value of K_{S} with SDS micelles for PSH than for securinine cannot be attributed to the intrinsic hydrophobicity (based upon the number of carbon atoms present in the molecule) of these molecules. The most plausible reason we could speculate at the moment is that significant steric interaction might result if the highly hindered securinine molecule is incorporated with a micelle of a surfactant with straight-chain methylene units. The nearly 100-fold larger value of K_{S} with SDS micelles for PSH than for securinine may be partly

attributed to probable hydrogen bonding between the phenolic hydrogen of PSH and anionic headgroups of SDS micelles.

The rate constants, k_M , for hydroxide ion-catalyzed cleavage of securinine in the micelles of SDS, C₁₂E₁₀, CTABr and TTABr turned out to be considerably lower than the corresponding rate constant, k_W , in the aqueous pseudophase. This may be attributed to one or both of the following reasons: (i) different average locations of reactant molecules, ${}^{-}\text{OH}_M$ and S_M , in the non-ionic and cationic micellar pseudophase or $[{}^{-}\text{OH}_M] \approx 0$ in the SDS micellar pseudophase; (ii) the micellized securinine molecules, S_M , are located in the micellar region of very low dielectric constant.

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