Micellar Effects upon the Hydrolysis of Activated Amides. Mechanistic Aspects

Antonio Cipiciani, Paolo Linda,¹ Gianfranco Savelli,*

Dipartimento di Chimica, Universitá di Perugia, 06100, Perugia, Italy

and Clifford A. Bunton*

Department of Chemistry, University of California, Santa Barbara, California 93106 (Received: February 18, 1983; In Final Form: May 3, 1983)

Reactions of OH^- in water with N-acylpyrrole, -indole, and -carbazole (acyl = acetyl or benzoyl) are second order in OH^- in 10^{-3} M NaOH and first order in more concentrated OH^- , but reaction in micelles of cetyltrimethylammonium bromide (CTABr) is first order in micellar-bound OH^- for both 10^{-3} and 0.05 M NaOH. Reactions are inhibited by anionic micelles of sodium lauryl sulfate (NaLS). The rate–surfactant profiles for rate enhancements in CTABr, and inhibition in NaLS, are analyzed in terms of the distribution of OH^- and amide between aqueous and micellar pseudophases: second-order rate constants for attack of OH^- upon amide are lower in the micellar pseudophase than in water. Micellar effects upon reaction of OH^- with anilides have been analyzed, giving second-order rate constants in the micellar pseudophase which are very similar to those in water.

The base hydrolysis of acetylpyrrole (1), and related amides, involves initial attack of OH^- followed by base-catalyzed decomposition of the tetrahedral intermediate (2)^{2,3} (Scheme I).

The first-order rate constant, k_{Ψ} , is given by

$$k_{\Psi} = k_1 k_2 [\text{OH}^-]^2 / (k_{-1} + k_2 [\text{OH}^-])$$
(1)

and the order with respect to $[OH^-]$ changes from second to first with increasing $[OH^-]$.²⁻⁴

Acylpyrroles, -indoles, and related compounds are much more reactive toward OH^- than simple amides, because the lower C–N bond order increases the electrophilicity of the acyl group.^{2,3,5}

The aim of the present work was to examine micellar effects upon the reaction of OH^- with a variety of acylpyrroles, -indoles, and -carbazoles. Cationic micelles effectively speed attack by OH^- and other nucleophiles or bases.⁶ The distribution of counteranions between water and ionic micelles has been treated quantitatively,^{6b-d-10} and it appears that the micellar Stern layer is similar to a concentrated ionic solution.¹⁰ If this conclusion is correct, the concentration of OH^- in the Stern layer of a cationic

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micelle could be such that a tetrahedral intermediate such as 2 will always go forward to products, even though the overall concentration of OH⁻ in the solution may be low.

The substrates were N-acetyl- or N-benzoylpyrrole, N-acetyl- or N-benzoylindole, and N-acetylcarbazole (1, 3-6). In water reaction is close to second order with



respect to $[OH^-]$ in 10^{-3} M OH⁻, and close to first order in 0.05 M OH⁻,^{2,3} so we used these concentrations of OH⁻ for reactions in aqueous cetyltrimethylammonium bromide (CTABr, C₁₆H₃₃NMe₃Br). Some experiments were also made in solutions of anionic micelles of sodium lauryl sulfate (NaLS, C₁₂H₂₅SO₄Na) which should inhibit reaction with OH^{-,6-10}

Micellar enhancements of bimolecular reactions are due largely to increased reactant concentration in the micellar pseudophase, and the variation of rate constant with [surfactant] can be treated quantitatively in terms of a pseudophase ion-exchange model. Overall rate enhancements are larger for third-order than for second-order reactions, as shown, for example, by third- and secondorder benzidine rearrangements, in accord with this model.¹¹ We were interested in the possibility that we would see corresponding differences in micellar effects

⁽¹⁾ Present address: Istituto Chimico, Universitá di Trieste, Piazzale Europa 1, 34100 Trieste, Italy.

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Figure 1. Reaction of N-acetylpyrrole (

) and N-benzoylpyrrole (

) in anionic micelles of NaLS and 0.05 M NaOH. The curves are predicted.

upon second- and third-order amide hydrolyses.

We also applied the pseudophase ion-exchange model to the second-order reaction of anilides (7-9) with OH⁻ in



aqueous CTABr and we estimated rate constants for reaction in the micellar pseudophase. The overall effects of CTABr upon these reactions were examined by Broxton and Duddy¹² (cf ref 13).

Experimental Section

Materials. N-Acetyl-14 and N-benzoylpyrrole,³ Nacetyl-15 and N-benzoylindole,16 and N-acetylcarbazole15 were prepared by methods already described. The purification of CTABr and NaLS has been described.^{9,11} There were no minima in plots of surface tension against [surfactant]. Solutions were made up by using CO₂-free, redistilled, deionized water.

Kinetics. Reactions were followed spectrophotometrically, in water or aqueous surfactant, at 25.0 °C by using the following wavelengths: ^{2,3} N-acetylpyrrole, 238 nm; N-benzovlpvrrole, 255 nm; N-acetvlindole, 236 nm; Nbenzovlindole, 248 nm; N-acetvlcarbazole, 270 nm. Substrate concentrations were in the range 10^{-5} – 10^{-4} M. The first-order rate constants, k_{Ψ} , are in reciprocal seconds.

Substrate Binding to Micelles. Binding constants for inert solutes were estimated from solubilities following general methods.6a

Results

Reactions in Anionic Micelles. The inhibition by micelles of NaLS is illustrated in Figures 1 and 2. The variation of rate constant with [surfactant] is generally treated on the assumption that substrate, S, is distributed between the aqueous and micellar pseudophases, designated by subscripts W and M, respectively (Scheme II), and can react in each pseudophase, with the first-order rate



Figure 2. Reaction of N-acetylindole (O), N-benzoylindole (◊), and N-acetylcarbazole (D). Conditions as in Figure 1. The curves are predicted.

Scheme II



constants being k'_{W} and k'_{M} . The micellized surfactant (detergent) is designated D_n , and its concentration is that of the total surfactant concentration, less that of monomeric surfactant, and $K_{\rm S}$ is the equilibrium constant for substrate binding (eq 2 and 3).

$$K_{\rm S} = [S_{\rm M}] / ([S_{\rm W}][D_{\rm n}])$$
⁽²⁾

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

Provided that equilibrium is maintained between reactants in the pseudophases, the first-order rate constant is given by¹⁷

$$k_{\Psi} = \frac{k'_{\rm W} + k'_{\rm M} K_{\rm S}[{\rm D}_{\rm n}]}{1 + K_{\rm S}[{\rm D}_{\rm n}]} \tag{4}$$

Equation 4 can be solved readily for spontaneous, unimolecular reactions, and for micellar-inhibited reactions. The approach is to rearrange it to eq $5.^{17}$

$$\frac{1}{k_{\Psi} - k'_{M}} = \frac{1}{k'_{W} - k'_{M}} + \frac{1}{(k'_{W} - k'_{M})K_{\rm S}[D_{\rm n}]}$$
(5)

However, the use of eq 5 requires estimation of the concentration of monomeric surfactant, which is often assumed to be given by the critical micelle concentration, cmc. This assumption is strictly correct only at the cmc, and in addition, solutes, especially hydrophobic substrates, may affect the cmc. Therefore, the "kinetic" cmc is often taken as an adjustable parameter,⁶ with the proviso that it must be lower than that in water. Unfortunately the form of eq 5 makes it very sensitive to the value of the cmc, especially for reactions of hydrophobic substrates. A way around this problem is to use the generalization that for many micellar-inhibited reactions $k'_{\rm W} \gg k'_{\rm M}$, 6,17,18 so that eq 5 gives 6d

$$k_{\Psi} = k'_{W} / (1 + K_{\rm S}[{\rm D_n}])$$
 (6)

and eq 6 can be readily fitted to the data. We did the fitting using computer simulation, and directly measured

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⁽¹⁷⁾ Menger, F. M.; Portnoy, C. E. J. Am. Chem. Soc. 1967, 89, 4968. (18) There may be a minor contribution from reactions of anions in anionic micelles, especially in solutions containing added electrolytes. This contribution is understandable in terms of the ion-exchange model of counterion binding.19

TABLE I: Inhibition by Micelles of NaLS^a

substrate	10 ³ × (cmc), M	$k'_{\mathrm{W}}, \mathrm{s}^{-1}$	$K_{\mathrm{S}}, \mathrm{M}^{-1}$	
N-acetylpyrrole N-benzoylpyrrole N-acetylindole N-benzoylindole N-acetylcarbazole	$6 \\ 3 \\ 3 \\ 1.5 \\ 1.7$	$\begin{array}{c} 0.19 \\ 0.014 \\ 0.043 \\ 0.054 \\ 0.032 \end{array}$	$\begin{array}{r} 22 \\ 250 \\ 210 \\ 1700 \\ 2500 \end{array}$	

 a In 5 × 10⁻² M NaOH at 25.0 °C.

TABLE II: Effect of $\mathbf{OH}^{\scriptscriptstyle -}$ on Overall Micellar Rate $\mathsf{Effects}^a$

substrate	10 ⁻³ M NaOH	0.05 M NaOH	
N-acetylpyrrole	6	1.5	
N-benzoylpyrrole	37	31	
N-acetylindole	9.5	3	
N-benzoylindole	13.5	5.4	
N-acetylcarbazole	21.6	7.2	

 a Values of rate enhancements at optimum [CTABr] at 25.0 $^\circ\mathrm{C}.$



Figure 3. Reaction of *N*-acetylpyrrole (\blacklozenge), *N*-benzoylpyrrole (\diamondsuit), *N*-acetylindole (O), *N*-benzoylindole (\diamondsuit), and *N*-acetylcarbazole (\Box) in CTABr and 10⁻³ M NaOH. The curves are predicted.

values of k'_{W} . The fits are illustrated in Figures 1 and 2 and values of K_S and cmc are in Table I.

The values of $K_{\rm S}$ increase with increasing hydrophobicity of the substrate.

Reactions in Cationic Micelles. Cationic micelles of CTABr speed reactions of all the substrates in 10^{-3} and 5×10^{-2} M NaOH (Figures 3–5). The rate enhancements are larger in 10^{-3} M NaOH than in 5×10^{-2} M NaOH, where reaction in water is second order (Table II). However, the differences do not depend in any obvious way upon the hydrophobicities of the substrates or upon the overall micellar rate enhancements. In order to understand the source of these differences we have to estimate the rate constants in the micellar pseudophase.

Equation 4 has to be modified to take into account that the first-order rate constants, k'_W and k'_M , depend upon the concentration of OH⁻ in the micellar and aqueous pseudophases. In relatively concentrated NaOH (e.g., 0.05 M) the rate equation in water is close to first order in OH⁻,^{2,3} and

$$k'_{\rm W} = k_{\rm W} [\rm OH_{\rm W}^{-}] \tag{7}$$

It is reasonable to assume that in 0.05 M OH^- reaction in the micellar pseudophase will also be first order with



Figure 4. Reaction of *N*-acetylpyrrole (\bullet), *N*-benzoylpyrrole (\bullet), and *N*-acetylindole (O) in CTABr and 0.05 M NaOH. The curves are predicted.



Figure 5. Reaction of *N*-benzoylindole (\Diamond) and *N*-acetylcarbazole (\Box). Conditions as in Figure 4. The curves are predicted.

respect to $[OH^-]$. However, in 10^{-3} M NaOH reaction in water is approximately second order with respect to $[OH_W^-]^{2,3}$ and therefore may also be second order in the micellar pseudophase. This possibility was considered, and the variation of k_{Ψ} with [CTABr] in 10^{-3} M OH⁻ could be fitted on the assumption that reaction is second order in OH⁻ in both the aqueous and micellar pseudophases. But, although the rate-surfactant profiles could be fitted to the model, the derived kinetic parameters were inconsistent with the reaction mechanism. The actual fits are not shown here, but the inconsistency of the derived parameters with mechanism is discussed later in this paper. Therefore, we assume that reaction is first order in micellar-bound OH⁻ in 10^{-3} and 0.05 M NaOH.

In fitting the variation of k_{Ψ} with [CTABr] we use the following kinetic equations:

(i) In 0.05 M NaOH, reaction is first order in $[OH^-]$ in both pseudophases. In water k'_W is given by eq 7, and in the micellar pseudophase k'_M by eq 8

$$k'_{\rm M} = k_{\rm M} m_{\rm OH}^{\rm s} \tag{8}$$

where m_{OH}^{s} is a mole ratio,^{6d,9} i.e.

$$m_{\rm OH^s} = [\rm OH_M^-]/([\rm CTABr] - cmc)$$
 (9)

(square brackets here and elsewhere denote molarities in

TABLE III: Kinetic Parameters for Reaction in CTABr^a

	10 ⁻³ M NaOH			$5 imes 10^{-2}$ M NaOH		
substrate	10 ⁴ (cmc)	$K_{\rm S},{\rm M}^{-1}$	$k_{\rm M}, {\rm s}^{-1}$	10^4 (cmc)	$K_{\rm S}, {\rm M}^{-1}$	$k_{\rm M}, {\rm s}^{-1}$
N-acetylpyrrole	8.0	45	0.38 (377)	6.0	65	1.55 (3.74)
N-benzoylpyrrole	7.0	350	0.98(470)	5.5	450	1.45(2.76)
N-acetylindole	7.5	300	0.24(388)	5.0	450	0.47(0.86)
N-benzoylindole	6.5	1400	0.30 (608)	2.5	2400	0.60(1.08)
N-acetylcarbazole	6.5	2900	0.31(416)	1.0	4400	0.44(0.65)

^a At 25 °C. Values in parentheses are the third- and second-order rate constants in 10^{-3} and 5×10^{-2} M NaOH, respectively, in the absence of surfactant. Values of $K_{\rm S}$ and $k_{\rm M}$ calculated with $\beta = 0.78$ and $K_{\rm Br}^{\rm OH} = 15$.

terms of total solution volume).

(ii) In 10^{-3} M NaOH $k'_{\rm M}$ is given by eq 8 and 9, and $k'_{\rm W}$ by eq 10

$$k'_{\rm W} = k''_{\rm W} [\rm OH_{\rm W}^{-}]^2$$
 (10)

where $k''_{\rm W}$ is a third-order rate constant. Equations 4, 8, and 9 give

$$k_{\Psi} = \frac{k'_{W} + k_{M}K_{S}m_{OH}{}^{s}[D_{n}]}{1 + K_{S}[D_{n}]}$$
(11)

with k'_{W} given by eq 7 or 10 depending upon [NaOH].

The problem then becomes that of estimating the concentration of OH⁻ in the micellar pseudophase. The distribution of counterions, e.g., OH⁻ and Br⁻, between aqueous and micellar pseudophases is often assumed to follow eq 12.6c,d,7-10

$$K_{\rm Br}^{\rm OH} = [OH_{\rm W}^{-}][Br_{\rm M}^{-}]/([OH_{\rm M}^{-}][Br_{\rm W}^{-}])$$
 (12)

Equation 12 and mass-balance relations for OH⁻ and Br⁻ can be used to estimate $[OH_M]$ based on the assumption that the fractional ionization, α , of the micelle is independent of the nature and concentrations of the counterions,^{6c,d,8-10} so that

$$[OH_{W}^{-}] + [Br_{W}^{-}] = \alpha([CTABr] - cmc) + cmc \qquad (13)$$

$$[OH_{M}] + [Br_{M}] = \beta([CTABr] - cmc)$$
(14)

where

$$\beta = 1 - \alpha \tag{15}$$

Evidence for the (approximate) constancy of α is discussed in ref 10. Most of the values of $K_{\rm Br}^{\rm OH}$ are derived from rate or equilibrium studies and range from approximately 10 to $40.^{7,8,19-22}$ However, the higher values were calculated on different assumptions from the others, and most values are in the range 10-20, and we will use these limits. It is more difficult to decide whether ion-exchange constants, e.g., $K_{\rm Br}^{\rm OH}$, are independent of concentrations of the counterions, because in most kinetic experiments [surfactant] has been varied and the concentration of the reactive ion has been constant, or not varied widely.

In fitting the variation of k_{Ψ} with [CTABr] to eq 11-14 we initially assume constancy of both $K_{\rm Br}^{\rm OH}$ and α . The equations can then be combined to predict the variation of k_{Ψ} with [CTABr] for a given concentration of OH⁻. In practice we use computer simulation to predict this variation for the various parameters in eq 11–14 as described elsewhere.^{9,21} We initially assumed that $K_{\rm Br}^{\rm OH}$ is in the range 10–15, and independent of [CTABr] and the nature TABLE IV: Calculated Rate and Binding Constants for Micellar Hydrolysis of Anilides^a

acyl group	$K_{\rm S},{\rm M}^{_{-1}}$	$k_{\rm M}, {\rm s}^{-1}$	${{k_{\rm W}},{}^b}{{\rm M}^{{\scriptscriptstyle -1}}{ m s}^{{\scriptscriptstyle -1}}}$
$CH_2C_6H_4NO_2(4)$	420	0.044 (0.006)	0.0041
CH ₂ SPh	1800	0.062(0.009)	0.015
CH ₂ OPh	700	0.16 (0.023)	0.049

^a At 30.0 °C and 5.8×10^{-3} M OH⁻, calculated with cmc = 8×10^{-4} M, $\beta = 0.78$, and $K_{\rm Br} {}^{\rm OH} = 15$. Values of $k_2^{\rm m}$ are in parentheses. ^b Reference 12.

TABLE V: Predicted Rate Constants for Anilide Hydrolysis in CTABr^a

10 ³ × [OH ⁻].	104	$10^4 k_{\Psi}$		104/	$^{2}\Psi$
M	$exptl^b$	caled	M	$exptl^b$	calcd
1.16 3.49 5.82	$38.0 \\ 94.6 \\ 140$	38.0 96.0 141	8.14 11.6	172 208	178 204

^{*a*} For reaction of 9 in 3×10^{-3} M CTABr at 30.0 °C. ^b Reference 12.

of the substrate, and $\alpha = 0.78^{23,24}$ The value of the cmc under kinetic conditions is taken as ca. $8 \times 10^{-4} \text{ M}^{25}$ for reactions of the less hydrophobic substrates in 10^{-3} M NaOH, but lower values are taken for reactions of the hydrophobic substrates and in 0.05 M NaOH.

The predicted plots of k_{Ψ} against [CTABr] (Figures 3–5) were calculated by taking the parameters in Table III. A value of $K_{\rm Br}^{\rm OH} = 15$ was used in simulating all the

data, although small variations in this parameter did not markedly affect the fit. This value is in reasonable agreement with values estimated by a variety of methods.^{7,8,20,21} Values of $K_{\rm S}$ follow the hydrophobicities of the substrates and are similar to those in NaLS (Tables I and III). The fitting of the rate data is insensitive to the value of $K_{\rm S}$ for the more hydrophobic substrates. The value of $K_{\rm S}$ for the more hydrophobic solutes is not very different from that of 7×10^3 M⁻¹ for N-methylcarbazole in NaLS estimated by solubility. The apparent increase of $K_{\rm S}$ with [NaOH] is consistent with other evidence.^{21,27}

Discussion

The variation of k_{Ψ} with [CTABr] follows the generally accepted treatment of rate enhancements of bimolecular reactions by micelles. However, in water the order with respect to OH⁻ changes from 2 toward 1 with increasing

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agrees reasonably well with values estimated electrochemically. (25) This value is close to that of the cmc in water, which is reduced

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⁽²⁷⁾ The predicted variation of k_{Ψ} with [CTABr] is not very sensitive to the value of $K_{\rm S}$ for the more hydrophobic, and more strongly bound, substrates.



Figure 6. Reaction of anilides in CTABr and 0.005 M OH⁻: ¹² 7 (●), 8 (III), 9 (). The curves are predicted.

[OH⁻],^{2,3} so that it is useful to apply the model to micellar effects upon anilide hydrolyses which are first order with respect to OH⁻ over a range of [OH⁻] in water.¹²

Anilide Hydrolyses in Micelles. Broxton and co-workers have examined hydrolyses of anilides (7-9) in aqueous CTABr, with 0.0058 M NaOH at 30 °C.¹² In water these hydrolyses are first order with respect to OH^- , so that formation of anionic tetrahedral intermediate should be rate limiting in both aqueous and micellar pseudophase. We fitted the variation of k_{Ψ} with [CTABr] in NaOH using eq 7, 11, 12, and 14 (Figure 6), and the parameters are in Table IV. We then used these parameters to predict the variation of k_{Ψ} with [NaOH] at a given [CTABr], and the agreement between observed and predicted values of k_{Ψ} is satisfactory (Table V). In making these calculations we assumed that a temperature change from 25 to 30 °C will have little effect on β and the ion-exchange parameter $K_{\rm Br}^{\rm OH}$. The agreement between the observed and predicted values of k_{Ψ} (Tables IV and V and Figure 6) supports the values of $K_{\rm Br}^{\rm OH}$ and β used in the calculation, and $K_{\rm S}$ values parallel the hydrophobicities of the substrates.

Kinetic Parameters for Reaction in Micelles. For reactions of the acylazoles the variations of k_{Ψ} with [CTABr] can be fitted to the pseudophase ion-exchange model, eq 7–11, assuming that β and $K_{\rm Br}^{\rm OH}$ do not change with an increase of [NaOH] from 10⁻³ to 0.05 M, but with a small increase in K_S which could be caused by NaOH "salting-out"^{21,27} the substrate and driving it into the micelle.^{21,27} However, the calculated values of $k_{\rm M}$ are higher in 0.05 than in 10⁻³ M NaOH by factors of 1.5-4 (Table III).

There have been a number of estimations of secondorder rate constants for reactions of OH⁻ in the micellar pseudophase, but generally the concentration of OH⁻ has not been varied as widely as in the present investigation^{7,9,22,28-30} (cf. Tables II-IV).

TABLE VI: Second-Order Rate Constants for Reactions of Acylazoles in Water and Micelles^a

substrate	$k_2^{\text{m}}, \mathrm{M}^{-1} \mathrm{s}^{-1}$	$k_2^{\rm m}/k_{\rm W}$	_
N-acetylpyrrole	0.22	0.06	
N-benzoylpyrrole	0.21	0.08	
N-acetylindole	0.07	0.08	
N-benzoylindole	0.09	0.08	
N-acetylcarbazole	0.06	0.10	

^a For reactions in 0.05 M NaOH.

The most probable explanation for the difference in the values of $k_{\rm M}$ with changing [OH⁻] is that reaction in the molecular pseudophase at 10⁻³ M NaOH is not strictly first order with respect to micellar-bound OH⁻, as assumed in our treatment; in other words, in the micelle the tetrahedral intermediate (2) does not go forward wholly to products, but sometimes returns to staring material (Scheme I). We see no simple way of treating a mixedorder reaction in a micellar pseudophase, especially if the order changes with increasing [surfactant].

An experimental point is that the largest dependence of $k_{\rm M}$ upon total [OH⁻] is for reaction of N-acetylpyrrole (1) (Table III). This may be an experimental artifact because overall micellar effects upon this reaction are relatively small (Figure 3), and our fitting procedure is therefore insensitive to variations in $k_{\rm M}$, whose value is least certain for this substrate.

We cannot at present exclude the possibility that rate and ion-exchange constants in the micellar pseudophase are affected by *large* changes in [NaOH] (cf. ref 29). In addition, the fractional ionization, α , of a CTABr micelle could be sensitive to added NaOH because Br⁻ appears to bind much more strongly than OH⁻ to the micelle. Nevertheless, these parameters apparently do not change with a 10-fold variation of [OH⁻], as shown by the agreement between experimental and predicted values of k_{Ψ} for hydrolysis of anilide 9 (Table V).

Rate Constants in Aqueous and Micellar Pseudophases. The second-order rate constants, $k_{\rm M}$, of reactions in the micellar pseudophase have the dimensions of reciprocal time, because concentration of OH⁻ is written as a mole ratio. This choice of units allows an unambiguous definition of concentration in the micellar pseudophase, but $k_{\rm M}$ cannot be compared directly with the second-order rate constants in water, $k_{\rm W}$, whose units are generally M⁻¹ s⁻¹. But comparison can be made provided that we specify the volume element of reaction in the micellar pseudophase, which could be that of the micelle or of its Stern layer. Elsewhere the molar volume of the Stern layer of CTABr has been assumed to be 0.14 L,^{6d,9} so that

$$k_2^{\rm m} = 0.14k_{\rm M} \tag{16}$$

where k_2^{m} , M^{-1} s⁻¹, can be compared directly with k_W . For anilide hydrolysis k_2^{m} and k_W are within factors of 2 (Table IV), but for hydrolysis of acyl azoles k_W is con-

sistently larger than k_2^{m} , based on experiments in 0.05 M OH⁻ (Tables III and VI).

There are many examples of reactions for which second-order rate constants in micelles are similar to those

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1982, 64, 1981

^{1982, 86, 1881.}

⁽³⁰⁾ In one study a wide range of [OH-] was used and the results could not be fitted to the ion-exchange model. It was suggested that reaction across the micelle-water interface was occurring at high [OH-] (>1 M).28 For reported breakdowns of the model and discussions of this question, see ref 31 and 32.

TABLE VII:Hypothetical Third-Order Rate Constantsof Reaction in the Micellar Pseudophase^a

substrate	10 ⁴ × (emc), M	$\substack{K_{S},\\M^{-1}}$	$k^{\prime\prime}{}_{ m M}^{}$, s ⁻¹
N-acetylpyrrole	5.0	80	2000 (1300)
N-benzoylpyrrole	4.0	350	7200 (5000)
N-acetyl indole	5.0	500	1600 (3400)
N-benzoylindole	4.0	3500	2000 (3300)
N-acetylcarbazole	3.0	5000	2000 (4500)

^a At 25.0 °C and 10⁻³ M NaOH. Values in parentheses are third-order rate constants, $k''_{\rm M}$, divided by $k_{\rm M}$, which gives $k_{2,\rm m}/k_{-1,\rm m}$; see text.

in water,^{6c,d,22,28,31} and this generalization can be used to predict overall rate enhancements. The rate constants for anilide hydrolysis follow the expected pattern, but they apparently do not for hydrolysis of the acylazoles (Table VI). However, the differences in rate constants in aqueous and micellar pseudophases are probably smaller than indicated by the values of $k_2^{\rm m}/k_{\rm W}$ in Table VI, because $k_{\rm W}$ is estimated on the assumption that reaction is strictly second order in aqueous 0.05 M NaOH, i.e., that in eq 1 $k_2[OH^-] \gg k_{-1}$. As noted earlier this requirement is probably not fully met, so that our values of $k_{\rm W}$, as given by $k_{\Psi}/[OH^-]$, are probably too high. Nonetheless, there does seem to be a marked difference in the behavior of anilides and acylazoles, which is not related in any obvious way to substrate hydrophobicity (Tables IV and VI). It is reasonable to associate this difference with the lower carbon-nitrogen bond order in the transition state for attack of OH^- upon acylazoles.^{2,3} This difference would lead to more localization of charge on oxygen in reactions of acylazoles as compared with anilides. The micellar surface has a lower polarity than water,³³ so a transition state with localized charges would be disfavored in the micellar pseudophase.

Kinetic Order of Reaction in the Micellar Pseudophase. In the Results section we noted the possibility that, with 10^{-3} M NaOH, reaction in the micellar pseudophase was second order with respect to micellar-bound OH⁻. Indeed the rate-surfactant profiles can be fitted reasonably well on this assumption, applying eq 17. The parameters $K_{\rm S}$

$$k'_{\rm M} = k''_{\rm M} (m_{\rm OH}^{\rm s})^2 \tag{17}$$

and $k''_{\rm M}$ used in this fitting are in Table VII, and the binding constants, $K_{\rm S}$, are not very different from those given in Table III. The values of $K_{\rm Br}^{\rm OH} = 15$ and $\beta = 0.78$ were used. However, this treatment is almost certainly incorrect. For reaction to be second order in OH⁻ the intermediate 2 has to be in equilibrium with the reactants; in other words, it has to return to starting material much faster than it goes forward to products. Therefore, in Scheme III $k_{-1,m} \gg k_{2,m} m_{\rm OH}^{\rm s}$. In Scheme III S is substrate and $k_{1,m}$ and $k_{2,m}$ are second-order rate constants written in terms of the concentration of OH⁻ in the micelle written as a mole ratio, $m_{\rm OH}^{\rm s}$ (eq 9). Therefore, if reaction in 10^{-3}



Figure 7. Variation of m_{OH}^{s} with [CTABr]: solid line, 0.05 M NaOH, n = 2; broken line, 10^{-3} M NaOH, n = 3. The left-hand *y*-axis ordinate gives the concentration of OH⁻ as a mole ratio, and the right-hand as a molarity in the micellar Stern layer.

Scheme III

$$S_M + OH_M^- \xrightarrow[k_{-1,m}]{k_{-1,m}} SOH_M^- \xrightarrow[OH^-]{k_{2,m}} products$$

M NaOH is second order with respect to micellar-bound OH⁻, the rate constant k''_{M} (eq 17) is given by

$$k''_{\rm M} = k_{1,\rm m} k_{2,\rm m} / k_{-1,\rm m} \tag{18}$$

The value of $k_{1,m}$ in 10^{-3} M NaOH (Scheme III) should not be very different from the value of $k_{\rm M}$ for reaction in CTABr and 0.05 M NaOH (Table III) and, if reaction in 10^{-3} M NaOH in the micellar pseudophase is second order in OH⁻, $k_{2,m}/k_{-1,m}$ should be given by $k''_{\rm M}/k_{\rm M}$, and these values are in parentheses in Table VII. Equilibrium between S and SOH⁻ (Scheme III) requires that $m_{\rm OH}{}^{\rm s}k_{2,m}/k_{-1,m}$ be much less than unity, but inspection of the values in parentheses in Table VII and the estimated values of $m_{\rm OH}{}^{\rm s}$ in CTABr and 10^{-3} M OH⁻ (Figure 7) shows that this requirement is far from fulfilled under any conditions. For example, even in 0.05 M CTABr where $m_{\rm OH}{}^{\rm s} \approx 4 \times 10^{-3}$, and is at its lowest value, SOH⁻ will go forward to products much faster than it returns to reactants (Scheme III), and the partitioning to products will be even more favorable in the more dilute CTABr.

These observations show that the successful fitting of rate-surfactant profiles can lead to incorrect mechanistic conclusions and that the mechanism followed in a micellar pseudophase may be very different from that in the aqueous pseudophase, because of high reagent concentrations at the micellar surface.

It is also important to note that the concentration of OH⁻ in the micellar pseudophase, m_{OH}^{s} , can be almost as large in 10⁻³ M NaOH and dilute CTABr (n = 3) as in 0.05 M NaOH and more concentrated CTABr (n = 2) (Figure 7). This figure also gives the concentration of OH⁻ expressed as a molarity in the Stern layer, i.e., as $7m_{OH}^{s}$ (eq 16 and ref 6d and 9).

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