

Research Article

Kinetic Evidence for Near Irreversible Nonionic Micellar Entrapment of *N*-(2'-Methoxyphenyl)phthalimide (**1**) under the Typical Alkaline Reaction Conditions

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The values of pseudo-first-order rate constants (k_{obs}) for alkaline hydrolysis of **1**, obtained at 1.0 mM NaOH and within $[C_m E_n]_T$ (total concentration of $C_m E_n$) range of 3.0–5.0 mM for $C_{12}E_{23}$ and 10–20 mM for $C_{18}E_{20}$, fail to obey pseudophase micellar (PM) model. The values of the fraction of near irreversible $C_m E_n$ micellar trapped **1** molecules (F_{TI}) vary in the range ~0–0.75 for $C_{12}E_{23}$ and ~0–0.83 for $C_{18}E_{20}$ under such conditions. The values of F_{TI} become 1.0 at ≥ 10 mM $C_{12}E_{23}$ and 50 mM $C_{18}E_{20}$. Kinetic analysis of the observed data at ≥ 10 mM $C_{12}E_{23}$ shows near irreversible micellar entrapment of **1** molecules under such conditions.

1. Introduction

The 2-state Hartley model of micelle (i.e., hydrophilic head-group/palisade/Stern layer, and hydrophobic core) of 1936 is still under extensive use [1]. However, relatively recent studies involving kinetic and spectrometric probes strongly favor the multistate model of micelle [2–6]. The unusual effects of pure $C_{12}E_{23}$ and mixed CTABr- $C_{12}E_{23}$ micelles on the acid-base behavior of phenyl salicylate were observed in 1999 [7]. In order to gain a better and clear understanding of this unusual finding, we started studying such effects on the rate of alkaline hydrolysis of esters and imides under variety of reaction kinetic conditions. This includes the use of reaction kinetic probe molecules of different structural features in the presence of pure $C_m E_n$ ($m/n = 12/23, 16/20, 18/20, \text{ and } 16/10$) and mixed $C_m E_n$ -CTABr micelles [8–12]. The unusual and unexpected observations of these studies are as follows. (i) The decrease of hydroxide ions from the neighborhood of micellized reaction kinetic probe molecules with the increase of $R (= [C_m E_n]_T / [\text{NaOH}])$ at a constant value of $[\text{NaOH}]$ at a typical value of R_t which represents a typical value of $[C_m E_n]_T / [\text{NaOH}]$ above which k_{obs} versus $[C_m E_n]_T$ data fails to obey PM model. (ii) The observed data (k_{obs} versus $[C_m E_n]_T$) obey PM model at $R \leq R_t$. (iii) The rate of hydrolysis of reaction kinetic probe molecules almost ceased

when $R \gg R_t$. (iv) The unusual observation of (iii) could be detected with $C_{12}E_{23}$, $C_{16}E_{10}$, and $C_{18}E_{20}$ but not with $C_{16}E_{20}$ under approximately similar conditions.

Under the typical reaction conditions of earlier studies where $R \gg R_t$ and the rate of reaction which could not be detected within the reaction period of more than ~24 h, the possibility of whether the cessation of the rate of reaction was due to complete or near irreversible micellar binding of one of the reactants of a bimolecular reaction has not been explored. Although the meaning of “near irreversible binding” is a subjective one, we arbitrarily consider the transition of a reversible binding to near irreversible binding if the value of k_{obs} changes from $\sim 10^{-4} \text{ s}^{-1}$ (under the reversible binding condition) to $\sim 10^{-8} \text{ s}^{-1}$ (under the near irreversible binding condition). The present work was initiated with an aim to find out if the cessation of the rate of reaction at $\geq 0.01 \text{ M } C_{12}E_{23}$ was caused by the near irreversible micellar binding of **1**. The observed results and their probable explanations are described in this paper.

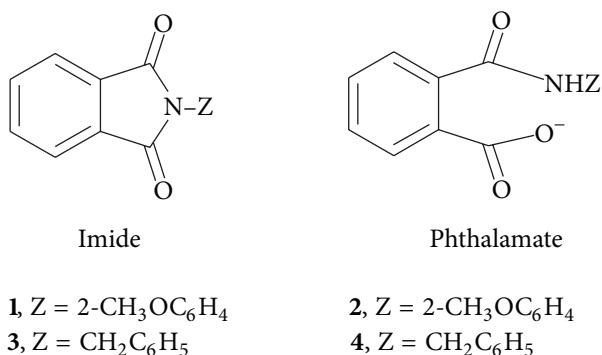
2. Materials and Methods

2.1. Materials. Synthesis of **1** (Figure 1) has been reported earlier [14], and all the other chemicals used were commercial

TABLE 1: The values of k_{obs} , δ_{ap} , and A_0 for alkaline hydrolysis of **1** in the presence of $C_{12}E_{23}$ ^a.

$[C_{12}E_{23}]_T$ M	$10^4 k_{\text{obs}}$ s^{-1}	δ_{ap} $M^{-1} \text{cm}^{-1}$	$10^2 A_0$	Y_{obs}^b	Y_{cald}^c	F_{TIT}^d
0.003	30.5 ± 1.4^e	3012 ± 53^e	24.8 ± 0.5^e	11.1	3.76	0
0.0034	19.3 ± 1.0	2691 ± 48	24.8 ± 0.5	17.6	4.13	0.13
0.0038	8.31 ± 1.89	2280 ± 158	26.3 ± 1.3	40.9	4.50	0.26
0.0042	2.21 ± 0.47	1657 ± 129	25.9 ± 0.8	154	4.87	0.46
0.005	0.273 ± 0.019	770 ± 22	23.9 ± 0.1	1245	5.61	0.75
0.01		f				
0.02		g				
0.03		h				
0.05		i				

^a $[I_0] = 0.1 \text{ mM}$, $[\text{NaOH}] = 1.0 \text{ mM}$, $\lambda = 290 \text{ nm}$, $T = 35^\circ \text{C}$, and the aqueous reaction mixture contained 2% v/v CH_3CN . ^b $Y_{\text{obs}} = k_W/k_{\text{obs}}$, where $k_W = k_{\text{obs}}$ ($= 340 \times 10^{-4} \text{ s}^{-1}$ [13]) at $[\text{micelles}] = 0$. ^cCalculated from the relationship: $Y_{\text{cald}} = \phi + \Psi [C_{12}E_{23}]$ with $\phi = 0.982$ and $\Psi = 925 \text{ M}^{-1}$ [13]. ^dThe values of F_{TIT} were calculated from (2) with $\delta_{\text{ap}}^{\text{avg}} = 3090 \text{ M}^{-1} \text{cm}^{-1}$. ^eError limits are standard deviations. ^fNo change in A_{obs} until $t = 600 \text{ h}$, where $A_{\text{obs}} = 0.246$. ^gNo change in A_{obs} until $t = 1083 \text{ h}$, where $A_{\text{obs}} = 0.261$. ^hNo change in A_{obs} until $t = 1085 \text{ h}$, where $A_{\text{obs}} = 0.271$. ⁱNo change in A_{obs} until $t = 1102 \text{ h}$, where $A_{\text{obs}} = 0.286$.

FIGURE 1: Molecular structures of compounds **1**, **2**, **3** and **4**.

products of the highest available purity. Stock solutions of **1** (5 mM and 10 mM) were prepared in acetonitrile. Throughout the text, the symbol $[X]_T$ represents the total concentration of X.

2.2. Kinetic Measurements. The rate of nonionic micellar-mediated alkaline hydrolysis of **1** was studied spectrophotometrically at 35°C by monitoring the appearance of hydrolysis product, *N*-(2'-methoxyphenyl)phthalamate (**2**) of **1** at 290 nm as a function of reaction time, t . The observed data, absorbance (A_{obs}) versus t , obeyed

$$A_{\text{obs}} = \delta_{\text{ap}} [I_0] [1 - \exp(-k_{\text{obs}}t)] + A_0, \quad (1)$$

where k_{obs} and δ_{ap} represent pseudo-first-order rate constants for alkaline hydrolysis of **1** and molar absorptivity of reaction mixture, respectively, and $[I_0]$ is the initial concentration of **1** and $A_0 = A_{\text{obs}}$ at $t = 0$. The details of the product characterization are described elsewhere [13].

3. Results

3.1. Effects of $[C_{12}E_{23}]_T$ and $[C_{18}E_{20}]_T$ on Pseudo-First-Order Rate Constants (k_{obs}) for Hydrolysis of **1 at 1.0 mM NaOH and 35°C .** The rate of alkaline hydrolysis of **1** was studied within $[C_{12}E_{23}]_T$ range of 3–50 mM, but the absorbance of the reaction mixtures within $[C_{12}E_{23}]_T$ range of 10–50 mM remained unchanged in the reaction time (t) range of ~15 s–623 h. However, the observed data (A_{obs} versus t), obtained within $[C_{12}E_{23}]_T$ range of 3–5 mM, were found to fit to (1). The least-squares calculated values of k_{obs} , δ_{ap} , and A_0 , obtained under such conditions, are shown in Table 1. Similarly, the kinetic runs for the rate of alkaline hydrolysis of **1** were carried out within $[C_{18}E_{20}]_T$ range of 10–50 mM. But the absorbance of the reaction mixture at 50 mM $C_{18}E_{20}$ remained unchanged within the t range of ~15 s–~260 h. The calculated values of k_{obs} , δ_{ap} , and A_0 for the kinetic runs carried out within $[C_{18}E_{20}]_T$ range of 10–20 mM are shown in Table 2.

4. Discussion

4.1. Evidence for the Near Irreversible $C_{12}E_{23}$ Micellar Binding of **1 under the Typical Reaction Conditions.** It can be easily shown from the derivation of (1) that $\delta_{\text{ap}} = \delta_2 - \delta_1$, where δ_2 represents molar absorptivity of **2** (Figure 1). The values of δ_1 and δ_2 , at 290 nm, are 2480 and $5570 \text{ M}^{-1} \text{cm}^{-1}$ [15], respectively, in aqueous alkaline solvent containing 2% v/v CH_3CN . The values of δ_1 are independent of $[C_m E_n]_T$ [13]. The values of δ_{ap} [13] reveal that the values of δ_2 are also independent of $[C_m E_n]_T$ within its range of 0.0–3.0 mM for $C_{16}E_{20}$ and $C_{12}E_{23}$ as well as 0.0–5.0 mM for $C_{18}E_{20}$. However, the values of δ_2 show a nonlinear increase from 5570 to $8450 \text{ M}^{-1} \text{cm}^{-1}$ at 290 nm with the increase in the content of CH_3CN from 2 to 80% v/v in mixed $\text{H}_2\text{O}-\text{CH}_3\text{CN}$ solvent [15]. Thus, the decrease in δ_{ap} with increase

TABLE 2: The values of k_{obs} , δ_{ap} , and A_0 for alkaline hydrolysis of **1** in the presence of $C_{18}E_{20}$ ^a.

$[C_{18}E_{20}]_T$ M	$10^4 k_{\text{obs}}$ s^{-1}	δ_{ap} $M^{-1} s^{-1}$	$10^2 A_0$	Y_{obs}^b	Y_{cald}^c	F_{ITI}^d
0.01	41.9 ± 0.3^e	3233 ± 9^e	27.2 ± 0.0^e	7.92	7.89	0
0.012	15.7 ± 0.5	2637 ± 30	28.0 ± 0.1	21.1	9.27	0.17
0.014	11.6 ± 0.4	2459 ± 31	28.6 ± 0.2	28.6	10.6	0.23
0.016	7.11 ± 0.24	1239 ± 15	29.1 ± 0.1	46.7	12.0	0.61
0.018	5.89 ± 0.38	898 ± 19	29.5 ± 0.1	56.4	13.4	0.72
0.02	2.17 ± 0.22	546 ± 26	29.9 ± 0.1	153	14.8	0.83
0.05	f					

^a $[I_0] = 0.1$ mM, $[\text{NaOH}] = 1.0$ mM, $\lambda = 290$ nm, $T = 35^\circ\text{C}$, and the aqueous reaction mixture contained 2% v/v CH_3CN . Footnotes ^b and ^c represent respective footnotes ^b and ^c of Table 1 with replacement of $[C_{12}E_{23}]$ by $[C_{18}E_{20}]$ as well as $k_W = 338 \times 10^{-4} s^{-1}$, $\phi = 0.998$, and $\Psi = 689 M^{-1}$ [13]. ^dThe values of F_{ITI} were calculated from (2) with $\delta_{\text{ap}}^{\text{avg}} = 3190 M^{-1} \text{cm}^{-1}$. ^eError limits are standard deviations. ^fSpectrophotometrically undetectable reaction within the reaction period of ~ 260 h, where $A_{\text{obs}} = 0.392$.

in $[C_m E_n]_T$ (Tables 1 and 2) rules out the possibility of $C_m E_n$ ($m/n = 16/20, 12/23,$ and $18/20$) micellar binding of **2** in a micellar environment of lower concentration of water compared with water concentration of bulk aqueous phase. These observations show that the effects of $[C_m E_n]_T$ on δ_1 and δ_2 cannot explain the observed decrease in δ_{ap} with increase in $[C_m E_n]_T$ at the typical values of $[C_m E_n]_T$ (Tables 1 and 2). Thus, the most plausible reason for such decrease in δ_{ap} is due to near irreversible micellar trapping of unreacted **1**. Under such circumstances, the observed data (k_{obs} versus $[C_m E_n]_T$) listed in Tables 1 and 2 cannot be expected to obey pseudophase micellar model (PM).

It can be shown that the fraction of near irreversibly $C_m E_n$ micellar trapped **1** at $t = \infty$ (F_{ITI}) may be given as

$$F_{\text{ITI}} = 1 - \left(\frac{\delta_{\text{ap}}}{\delta_{\text{ap}}^{\text{avg}}} \right), \quad (2)$$

where δ_{ap} and $\delta_{\text{ap}}^{\text{avg}}$ represent apparent molar absorptivity of the reaction mixture at $F_{\text{ITI}} \neq 0$ and $F_{\text{ITI}} = 0$, respectively. The derivation of (2) involves the assumption that the absorbance due to medium microturbidity remains unchanged within the reaction period of $t = 0$ to $t = \infty$. The values of F_{ITI} were calculated from (2) at different $[C_m E_n]_T$ and these values are summarized in Table 1 for $C_{12}E_{23}$ and Table 2 for $C_{18}E_{20}$. It is evident from the calculated values of F_{ITI} that the value of $[C_m E_n]_T/[\text{NaOH}] (=R)$ is nearly 3.6-fold larger for $C_{18}E_{20}$ than that for $C_{12}E_{23}$ to result in nearly same value of F_{ITI} , while the value of F_{ITI} remains zero even at $R = 170$ for $C_{16}E_{20}$ [13]. The typical value of $R (=R_t)$, at which $F_{\text{ITI}} = 0.13$, is 3.4 for $C_{12}E_{23}$. Similarly, the value of R_t , at which $F_{\text{ITI}} = 0.17$, is 12.0 for $C_{18}E_{20}$. The values of F_{ITI} and F_{IT3} are ~ 0 [13] and 0.60 [11], respectively, at $R = 170$ for $C_{16}E_{20}$ micelles which reveal that the structural features of imide substrates (**1** and **3**) (Figure 1) affect the values of F_{ITI} at a fixed value of R . It is interesting and amazing to note that the difference of only 2 methylene (CH_2) groups between $C_{18}E_{20}$ and $C_{16}E_{20}$ has so much different effects on F_{ITI} .

If micellar entrapment of unreacted **1**, as shown by F_{ITI} values in Tables 1 and 2, is indeed an irreversible or near

irreversible process, then the values of A_{obs} at $t \geq 10$ half-lives (Reaction time t at ~ 10 half-lives is equivalent to t_{∞} because more than 99.9% reaction is progressed during the reaction period of 10 half-lives and therefore, at t_{∞} , $A_{\text{obs}} = A_{\infty}$) should remain essentially unchanged with the increase in t at $t = t_{\infty}$ or at t , where $A_{\text{obs}} = A_{\infty}$. In order to test this conclusion, the kinetic reaction mixtures at 0.01, 0.02, 0.03, and 0.05 M $C_{12}E_{23}$ were left at 35°C for the reaction period of $\sim 1.10 \times 10^3$ h and the values of A_{obs} , during these reaction periods, remained essentially unchanged (Table 1).

It is apparent from Tables 1 and 2 that the values of F_{ITI} increase nonlinearly with the increase of R at a typical value of $R (=R_t)$ and the values of F_{ITI} appear to become 1 at $R \geq 10$ for $C_{12}E_{23}$ (Table 1) and at $R = 50$ for $C_{18}E_{20}$ (Table 2). If the reversible and near irreversible nonionic micellar binding of **1** is a function of R , then the change of inequality from $R > R_t$ to $R < R_t$, by sudden external addition of known amount of NaOH to the reaction mixture at $t > t_{\infty}$, must cause near irreversible bound I_M molecules to become reversible bound I_M molecules. Consequently, the rate of appearance of product (2) of this reaction mixture would follow (1) and the value of k_{obs} may then be compared with k_{obs} obtained by carrying out another kinetic run by the use of authentic sample of **1** under essentially similar experimental conditions. Such an attempt is described as follows.

To 3.0 cm^3 of the reaction mixture containing 0.1 mM **1**, 1.0 mM NaOH, and 10 mM $C_{12}E_{23}$ (i.e., $R = 10$), 0.02 cm^3 of 1.0 M NaOH was added at $t = 432$ h. The absorbance change of the resulting reaction mixture was quickly monitored spectrophotometrically at 290 nm as a function of reaction time (t). The observed data (A_{obs} versus t) were found to fit to (1) and the least-squares calculated values of kinetic parameters k_{obs} , δ_{ap} , and A_0 are summarized in Table 3. Similar kinetic runs were carried out at different t (≥ 600 h) and $[C_{12}E_{23}]_T$ ($=0.02, 0.03,$ and 0.05 M) and the values of k_{obs} , δ_{ap} , and A_0 , obtained under these conditions, are also shown in Table 3.

A few kinetic runs were carried out using authentic sample of **1** freshly prepared at 35°C , 0.1 mM **1**, different values of $[C_{12}E_{23}]_T$ (ranging from 10 to 50 mM) and $[\text{NaOH}]$ (ranging from 4.2 to 30.0 mM). The spectrophotometrically observed

TABLE 3: Values of k_{obs} , δ_{ap} , and A_0 calculated from (1) for alkaline hydrolysis of **1** in the presence of $C_{12}E_{23}$ micelles^a.

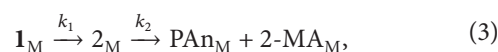
$10^3 [C_{12}E_{23}]_T$ M	$10^3 [\text{NaOH}]$ M	$10^3 k_{\text{obs}}$ s^{-1}	δ_{ap} $\text{M}^{-1} \text{cm}^{-1}$	$10^3 A_0$	k_{OH}^b $\text{M}^{-1} \text{s}^{-1}$	F_{IT1}^c	R^d	t^e h	$10^8 k_1^f$ s^{-1}
9.9 ^g	7.6	64.2 ± 0.8^h	2088 ± 25^h	256 ± 3^h	8.45	0.68	1.30	432	25
9.9	7.6	66.1 ± 1.1	1691 ± 32	267 ± 3	8.70	0.55	1.30	600	27
10.0 ⁱ	7.6	67.8 ± 0.5	3293 ± 25	260 ± 3	8.92		1.32		
19.8	11.0	44.4 ± 0.5	2127 ± 19	303 ± 2	4.04	0.70	1.82	623	16
19.8	11.0	35.0 ± 0.2	1564 ± 7	314 ± 1	3.18	0.51	1.82	1083	18
20.0 ⁱ	11.0	51.2 ± 0.2	3344 ± 13	282 ± 1	4.65		1.82		
29.5	17.4	69.9 ± 0.9	2714 ± 45	297 ± 5	4.02	0.89	1.70	600	5.5
29.5	17.4	70.3 ± 0.3	2271 ± 92	310 ± 9	4.04	0.74	1.70	1085	7.6
30.0 ⁱ	17.0	64.8 ± 0.3	3325 ± 16	331 ± 2	3.81		1.76		
48.5	30.0	86.3 ± 1.5	3302 ± 93	291 ± 9	2.88	1.08	1.62	622	—
48.5	30.0	88.1 ± 1.8	2789 ± 89	324 ± 9	2.94	0.91	1.62	1102	2.3
48.5 ⁱ	30.0	78.6 ± 2.5	3365 ± 129	406 ± 13	2.62		1.62		

^a $[I_0] = 0.1 \text{ mM}$, $\lambda = 290 \text{ nm}$, $T = 35^\circ\text{C}$, and the aqueous reaction mixture contained 2% v/v CH_3CN . ^b $k_{\text{OH}} = k_{\text{obs}} [\text{NaOH}]$. ^c $F_{\text{IT1}} = \delta_{\text{ap}}/\delta_{\text{ap}}^{\text{avg}}$ with $\delta_{\text{ap}}^{\text{avg}} = 3058 \text{ M}^{-1} \text{ cm}^{-1}$. ^d $R = [C_{12}E_{23}]_T/[\text{NaOH}]$. ^e t is reaction time ($t \geq t_{\infty}$) where the kinetic reaction mixture was used for micellar entrapment experiment. ^fCalculated from the relationship: $k_1 = (1/t) \ln(1/F_{\text{IT1}})$. ^gValue of $[C_{12}E_{23}]_T$ after external addition of $[\text{NaOH}]$. ^hError limits are standard deviations. ⁱReaction mixture for kinetic run was freshly prepared, where $\delta_{\text{ap}} = \delta_{\text{ap}}^{\text{avg}}$.

data for these kinetic runs followed strictly (1) as evident from the standard deviations associated with the calculated kinetic parameters k_{obs} , δ_{ap} , and A_0 (Table 3). The values of k_{OH} ($=k_{\text{obs}}/[\text{NaOH}]$) are >4-fold smaller than k_{OH} ($=36 \text{ M}^{-1} \text{ s}^{-1}$) [15] obtained under similar kinetic conditions in the absence of micelles. These results may be attributed to merely nonionic micellar inhibitory effect (the fraction of micellized **1**, i.e., $\mathbf{1}_M$, under such conditions, is >90%, where $K_S = 925 \text{ M}^{-1}$ [13]).

The values of k_{obs} , obtained from the reaction mixtures at different $[C_{12}E_{23}]_T$ and the reaction time t (ranging from 432 to 1102 h) at which the value of $[\text{NaOH}]$ was increased from 1.0 mM to $\geq 7.6 \text{ mM}$ and $\leq 30.0 \text{ mM}$, are comparable with the corresponding values of k_{obs} , obtained from authentic sample of **1** (Table 3). These observations support the proposal of near irreversible entrapment of **1** molecules by $C_{12}E_{23}$ micelles at $R \gg R_t$. The observed values of A_{obs} at $t \geq 600 \text{ h}$ as well as $\leq 1102 \text{ h}$ and $[C_{12}E_{23}]_T$ range of 10–50 mM (Table 1) reveal that the values of F_{IT1} must be nearly 1. But the calculated values of F_{IT1} at $t \approx 600 \text{ h}$, as summarized in Table 3, increase from ~ 0.55 to ~ 1.0 with the respective increase in $[C_{12}E_{23}]_T$ from 10 to 50 mM. Similarly, the values of F_{IT1} at t range of ≈ 1083 –1102 h, shown in Table 3, increase from 0.51 to 0.91 with the respective increase in $[C_{12}E_{23}]_T$ from 20 to 50 mM. These results show that, even at the highest value of $[C_{12}E_{23}]_T$ ($=50 \text{ mM}$) of the present study, nearly 9% hydrolysis of **1** occurred within the reaction time (t) of 1102 h. Thus, it is apparent that there is not any absolute/complete irreversible micellar entrapment of **1** molecules—a situation encountered with usual shielding effect of the micelles. A qualitative explanation of these observations may be described as below.

In view of the earlier reports [8, 11] on the related reaction systems, the rate of hydrolysis of **1** at 1.0 mM NaOH, 35°C , and within $[C_{12}E_{23}]_T$ range of 0.01–0.05 M may be expected to follow an irreversible consecutive reaction path:



where PAN and 2-MA represent phthalic anhydride and 2-methoxyaniline, respectively, and subscript M represents micellar pseudophase. The values of k_2 (at 35°C) are almost zero and $12 \times 10^{-4} \text{ s}^{-1}$ at 1.0 mM NaOH and 49 mM HCl, respectively [15]. The efficient reactivity of nonionized **2** (i.e., $\mathbf{2H}$) towards the formation of PAN is primarily due to intramolecular carboxylic group—assisted cleavage of $\mathbf{2H}$ [15]. The respective absence and presence of the formation of PAN in the aqueous cleavage of **3** at 1.0 mM NaOH, $[C_{16}E_{10}]_T \leq 30 \text{ mM}$, and at $[C_{16}E_{10}]_T \geq 50 \text{ mM}$ have been ascribed to the consequence of the effects of $[C_{16}E_{10}]_T$ on the pH of micellar environment of nonionized **4** (Figure 1) [11]. Spectrophotometric evidence revealed the fact that the increase in $[C_{12}E_{23}]_T$ at $R \gg R_t$ with a constant value of $[\text{NaOH}]$ caused decrease in pH of micellar environment of micellized ionized phenyl salicylate [7, 9]. In view of this study, at $[C_{12}E_{23}]_T \geq 10 \text{ mM}$, the pH of the micellar environment of $\mathbf{2}_M$ dropped to a level where there was significant amount of $\mathbf{2H}$ which caused kinetically detectable occurrence of k_2 —step (see (3)) within $[C_{12}E_{23}]_T$ range of 10–30 mM.

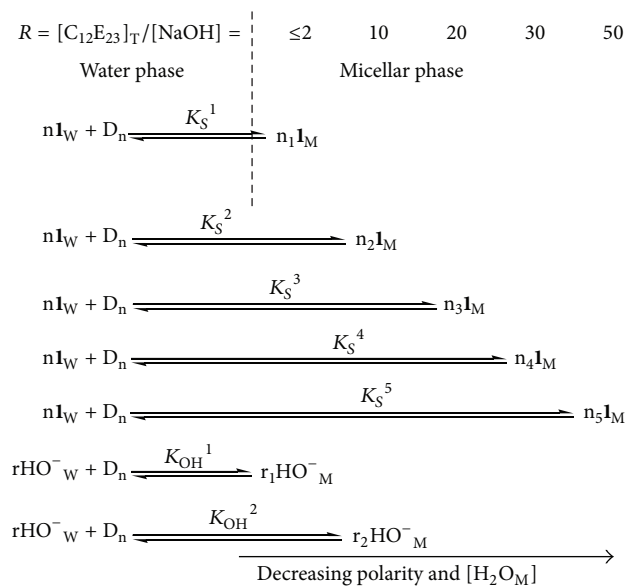
The respective values of δ_1 , δ_2 , $\delta_{\mathbf{2H}}$, and δ_{PAN} (with δ_X representing molar absorptivity of X) at 290 nm are ~ 2420 [13], 5570–8450, 4545–7490, and 2300–2000 $\text{M}^{-1} \text{ cm}^{-1}$ [11] within CH_3CN content range of 2–80% v/v in mixed aqueous solvent. Close similarity of the values of δ_1 and δ_{PAN} coupled

with significantly higher values of δ_2 or δ_{2H} compared with those of δ_1 and δ_{pAn} reveal that $k_2 > k_1$. These observations explain the observed constancy of A_{obs} within reaction time (t) ranging from ~ 15 s to ≤ 1102 h at 10–50 mM $C_{12}E_{23}$ (Table 1). The rough and approximate values of k_1 were obtained from the relationship: $k_1 = (1/t) \ln(1/F_{TT1})$ and such calculated values of k_1 at two different t and three $[C_{12}E_{23}]_T$ (10, 20, and 30 mM) are shown in Table 3. It is evident from these results that the values of k_1 at two different t and at a constant $[C_{12}E_{23}]_T$ are comparable within the limits of experimental uncertainties. But the values of k_1 decrease almost nonlinearly with the increasing values of $[C_{12}E_{23}]_T$. Thus, the values of k_1 became almost zero at 50 mM $C_{12}E_{23}$ and as a consequence only $\sim 9\%$ conversion of **1** to **2** could occur at $t = 1102$ h (Table 3). The values of k_1 decreased from $\sim 26 \times 10^{-8}$ to $2.3 \times 10^{-8} \text{ s}^{-1}$ with the increase in $[C_{12}E_{23}]_T$ from 10 to 50 mM. The values of k_1 were found to decrease by ~ 3 -fold, while the values of k_2 remained unchanged with the increase of $[C_{16}E_{10}]_T$ from 50 to 88 mM in the aqueous cleavage of **3** [11]. Although the calculated values of k_1 are not very reliable because they are derived from only either two or one data point(s), these values of k_1 appear to be plausible for the reason that the value of k_1 at pH ~ 3.5 , in mixed aqueous solvent containing 2% v/v CH_3CN , is $67 \times 10^{-8} \text{ s}^{-1}$ [16]. Under such typical conditions, the value of k_2 is $120 \times 10^{-5} \text{ s}^{-1}$ and it decreases from 120×10^{-5} to $6.6 \times 10^{-5} \text{ s}^{-1}$ with increase in CH_3CN content from 2 to 82% v/v [15].

The values of k_{obs} and k_1 show a nonlinear decrease with the increase of $[C_{12}E_{23}]_T$ within its range of 1.0×10^{-6} – 0.05 M (Tables 1 and 3). The value of k_M (=rate constant for hydrolysis of **1** in the micellar pseudophase) remained kinetically undetectable under such conditions. The observed data failed to obey the pseudophase micellar (PM) model at >1.4 mM $C_{12}E_{23}$ because the values of micellar binding constant of **1** (K_S) increase significantly ($\sim 10^3$ -fold) with the increase in $[C_{12}E_{23}]_T$ from 1.4 to 50 mM at 1.0 mM NaOH (Tables 1 and 3). Similar but not identical observations have been obtained in CTABr-(cetyltrimethylammonium bromide-) mediated pH-independent hydrolysis of *N*-(2-hydroxyphenyl)phthalimide [17]. The scenario exhibited by these observations supports the multicompartamental model of micelle [2, 18, 19] and it may best be represented by Scheme 1, where $n_1 I_M$ molecules are in equilibrium with $n I_W$ molecules and equilibrium or micellar binding constant K_S^1 at $R \leq 2$ and $[NaOH] = 1.0$ mM. Similarly, $n_2 I_M$, $n_3 I_M$, $n_4 I_M$, and $n_5 I_M$ molecules are in equilibrium with $n I_W$ molecules and equilibrium constants K_S^2 , K_S^3 , K_S^4 , and K_S^5 at respective $R = 10, 20, 30,$ and 50 and a constant 1.0 mM NaOH.

5. Conclusions

The new and notable aspects of the present paper are the experimentally determined pseudo-first-order rate constants ($k_1 \equiv k_{obs}$) of the order of 10^{-7} – 10^{-8} s^{-1} for the hydrolysis of **1** within the R range of 10–50, where $R = [C_{12}E_{23}]_T/[NaOH]$, with a constant value of $[NaOH]$ (= 1.0 mM). These values of k_1 are $>10^5$ -fold smaller than k_{obs} at $R \leq 1.4$,



SCHEME 1

where pseudophase micellar (PM) reveals that $k_M \approx 0$ and $K_S = 925 \text{ M}^{-1}$ [13]. The kinetic data of this paper show that the half-lives of alkaline hydrolysis of **1** at 1.0 mM NaOH and 35°C vary in the order 24 s, 6 min, 7 h, 31, 47, 122, and 349 days at $R = 0.2, 3.4, 5.0, 10, 20, 30,$ and 50 , respectively. Such quantitative information may be useful for designing nonionic micelles as the carrier of drug molecules containing imide functionality. These kinetic data also provide quantitative but indirect evidence for the multistate model of micelle suggested, to the best of our knowledge, in only a few reports [2–6, 18, 19].

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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