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_\text{obs}) for alkaline hydrolysis of 1, obtained at 1.0 mM NaOH and within [C_mE_n]_T (total concentration of C_mE_n) range of 3.0–5.0 mM for C_{12}E_{23} and 10–20 mM for C_{16}E_{20}, fail to obey pseudophase micellar (PM) model. The values of the fraction of near irreversible C_mE_n micellar trapped 1 molecules (F_{\text{IT}}) vary in the range ~0–0.75 for C_{12}E_{23} and ~0–0.83 for C_{16}E_{20} under such conditions. The values of F_{\text{IT}} become 1.0 at \geq 10 mM C_{12}E_{23} and 50 mM C_{16}E_{20}. Kinetic analysis of the observed data at \geq 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 headgroup/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_mE_n (m/n = 12/23, 16/20, 18/20, and 16/10) and mixed C_mE_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_mE_n]_T/[NaOH] at a constant value of [NaOH]) at a typical value of R, which represents a typical value of [C_mE_n]_T/[NaOH] above which k_{\text{obs}} versus [C_mE_n]_T data fails to obey PM model. (ii) The observed data (k_{\text{obs}} versus [C_mE_n]_T) obey PM model at R \leq R_i. (iii) The rate of hydrolysis of reaction kinetic probe molecules almost ceased when R \gg R_i. (iv) The unusual observation of (iii) could be detected with C_{12}E_{23}, C_{16}E_{20}, 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, and the rate of reaction which could not be detected within the reaction period of more than \sim 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_{\text{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 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
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, 4. The least-squares calculated values of $F_{T_{11}}$ were calculated from (2) with $\delta_{ap}^{obs}$ = 3090 M$^{-1}$ cm$^{-1}$. Errors limits are standard deviations. No change in $A_{obs}$ until $t$ = 600 h, where $A_{obs} = 0.246$. No change in $A_{obs}$ until $t$ = 1083 h, where $A_{obs} = 0.261$. No change in $A_{obs}$ until $t$ = 1085 h, where $A_{obs} = 0.271$. No change in $A_{obs}$ until $t$ = 1102 h, where $A_{obs} = 0.286$.

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 M 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 $k_{obs}$, $\delta_{ap}$, 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 $k_{obs}$, $\delta_{ap}$, 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 $\delta_{ap} = \delta_2 - \delta_1$, where $\delta_2$ represents molar absorptivity of 2 (Figure 1). The values of $\delta_1$ and $\delta_2$, at 290 nm, are 2480 and 5570 M$^{-1}$ cm$^{-1}$ [15], respectively, in aqueous alkaline solvent containing 2% v/v CH$_3$CN. The values of $\delta_1$ are independent of $[C_{12}E_{23}]_T$ [13]. The values of $\delta_2$ [13] reveal that the values of $\delta_2$ are also independent of $[C_{12}E_{23}]_T$ within its range of 0.0–3.0 mM for $C_{18}E_{20}$ and $C_{12}E_{23}$ as well as 0.0–5.0 mM for $C_{18}E_{20}$. However, the values of $\delta_2$ show a nonlinear increase from 5570 to 8450 M$^{-1}$ cm$^{-1}$ at 290 nm with the increase in the content of CH$_3$CN from 2 to 80% v/v in mixed H$_2$O-CH$_3$CN solvent [15]. Thus, the decrease in $\delta_{ap}$ with increase in $[C_{12}E_{23}]_T$ is the initial concentration of 1 and $A_0 = A_{obs}$ at $t = 0$. The details of the product characterization are described elsewhere [13].

### Table 1: The values of $k_{obs}$, $\delta_{ap}$, and $A_0$ for alkaline hydrolysis of 1 in the presence of $C_{12}E_{23}$.

| $[C_{12}E_{23}]_T$ M | $10^4 k_{obs}$ s$^{-1}$ | $\delta_{ap}$ M$^{-1}$ cm$^{-1}$ | $10^8 A_0$ | $Y_{obs}$ | $Y_{cald}$ | $F_{T_{11}}$ |
|------------------|-------------------|-------------------|---------|--------|--------|--------|
| 0.003            | 30.5 ± 1.4         | 3012 ± 53         | 24.8 ± 0.5 | 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   |

$^a$ Calculated from the relationship; $\lambda_{max} = \phi + \Psi [C_{12}E_{23}]_T$ with $\phi = 0.027$ and $\Psi = 925$ M$^{-1}$ [13]. $^b$ The values of $F_{T_{11}}$ were calculated from (2) with $\delta_{ap}^{obs}$ = 3900 M$^{-1}$ cm$^{-1}$. $^c$ Errors limits are standard deviations.
These observations show that the effects of \([C_{18}E_{20}]\) on \(\delta_2\) and \(\delta_3\) cannot explain the observed decrease in \(\delta_{ap}\) with increase in \([C_{18}E_{20}]\) at the typical values of \([C_{18}E_{20}]\) (Tables 1 and 2). Thus, the most plausible reason for such decrease in \(\delta_{ap}\) is due to near irreversible micellar trapping of unreacted 1. Under such circumstances, the observed data (\(k_{obs}\) versus \([C_{18}E_{20}]\)) 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 \(C_{18}E_n\) micellar trapped 1 at \(t = \infty\) (\(F_{IT1}\)) may be given as

\[
F_{IT1} = 1 - \left( \frac{\delta_{ap}}{\delta_{ap}^{avg}} \right),
\]

where \(\delta_{ap}\) and \(\delta_{ap}^{avg}\) represent apparent molar absorptivity of the reaction mixture at \(F_{IT1} \neq 0\) and \(F_{IT1} = 0\), 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 \(F_{IT1}\) were calculated from (2) at different \([C_{18}E_{20}]\) and these values are summarized in Table 2 for \(C_{12}E_{23}\) and Table 2 for \(C_{18}E_{20}\). It is evident from the calculated values of \(F_{IT1}\) that the value of \([C_{18}E_{20}]/[NaOH] (= R)\) 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 \(F_{IT1}\), while the value of \(F_{IT1}\) remains zero even at \(R = 170\) for \(C_{16}E_{20}\) [13]. The typical value of \(R (= R)\), at which \(F_{IT1} = 0.13\), is 3.4 for \(C_{12}E_{23}\). Similarly, the value of \(R\), at which \(F_{IT1} = 0.17\), is 12.0 for \(C_{18}E_{20}\). The values of \(F_{IT1}\) and \(F_{IT2}\) are \(\sim 0\) [13] and 0.60 [11], respectively, at \(R = 170\) for \(C_{18}E_{20}\) micelles which reveal that the structural features of imide substrates (1 and 3) (Figure 1) affect the values of \(F_{IT1}\) at a fixed value of \(R\). It is interesting and amazing to note that the difference of only 2 methylene (CH2) groups between \(C_{18}E_{20}\) and \(C_{16}E_{20}\) has so much different effects on \(F_{IT1}\).

If micellar entrapment of unreacted 1, as shown by \(F_{IT1}\) 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 \(\sim 10\) half-lives is equivalent to \(t_{obs}\)) because more than 99.9% reaction is progressed during the reaction period of 10 half-lives and therefore, at \(t_{obs}, A_{obs} = A_{cal}\) should remain essentially unchanged with the increase in \(t\) at \(t = t_{obs}\) or at \(t\), where \(A_{obs} = A_{cal}\). In order to test this conclusion, the kinetic reaction mixtures at 0.01, 0.02, 0.03, and 0.05M \(C_{12}E_{23}\) were left at 35°C for the reaction period of \(-1.10 \times 10^3\) 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 \(F_{IT1}\) increase non-linearly with the increase of \(R\) at a typical value of \(R (= R)\) and the values of \(F_{IT1}\) 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 \(R > R\) to \(R < R\), by sudden external addition of known amount of NaOH to the reaction mixture at \(t > t_{obs}\), must cause near irreversible bound \(1M\) molecules to become reversible bound \(1M\) 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\(^2\) 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\(^2\) 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 \(k_{obs}, \delta_{ap}\), and \(A_0\) are summarized in Table 3. Similar kinetic runs were carried out at different \(t\) (600 h) and \([C_{12}E_{23}]_\theta = (0.02, 0.03, and 0.05M)\) and the values of \(k_{obs}, \delta_{ap}\), 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 \([C_{12}E_{23}]_\theta\) (ranging from 10 to 50 mM) and [NaOH] (ranging from 4.2 to 30.0 mM). The spectrophotometrically observed

### Table 2: The values of \(k_{obs}, \delta_{ap}\), and \(A_0\) for alkaline hydrolysis of 1 in the presence of \(C_{18}E_{20}\).

| \([C_{18}E_{20}]_\theta\) M | \(10^3 k_{obs}\) s\(^{-1}\) | \(\delta_{ap}\) M\(^{-1}\) s\(^{-1}\) | \(10^3 A_0\) | \(Y_{obs}\) | \(Y_{calc}\) | \(F_{IT1}\) |
|------------------------|-----------------|-----------------|-----------------|---------|---------|---------|
| 0.01                   | 41.9 ± 0.3°     | 3233 ± 9°      | 27.2 ± 0.0°     | 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    | 0.72    |
| 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               |                 |                 |         |         |         |

\(^a\)[\(\delta\)] = 0.1 mM, [NaOH] = 1.0 mM, \(\lambda = 290\) nm, \(T = 35^\circ\) C, and the aqueous reaction mixture contained 2% v/v CH\(_3\)CN. Footnotes \(^b\) and \(^c\) represent respective errors limits are standard deviations. \(^d\) Spectrophotometrically undetectable reaction within the reaction period of \(-260\) h, where \(A_{obs} = 0.392\).
data for these kinetic runs followed strictly (1) as evident from the standard deviations associated with the calculated kinetic parameters $k_{\text{obs}}$, $\delta_{ap}$, and $A_0$ (Table 3). The values of $k_{\text{OH}}$ ($=k_{\text{obs}}/[\text{NaOH}]$) are 4-fold smaller than $k_{\text{OH}}$ ($=36\text{ M}^{-1}\text{s}^{-1}$) [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 I, i.e., $I_{103}$, under such conditions, is >90%, where $K_S = 925\text{ M}^{-1}$ [13]).

The values of $k_{\text{obs}}$, 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 [NaOH] was increased from 1.0 mM to ≥7.6 mM and ≤30.0 mM, are comparable with the corresponding values of $k_{\text{obs}}$ 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 $R \gg R_i$. The observed values of $A_{\text{obs}}$ at $t \geq 600$ h as well as ≤1102 h and [C$_{12}$E$_{23}$]$_T$ range of 10–50 mM (Table 1) reveal that the values of $F_{\text{ITT}}$ must be nearly 1. But the calculated values of $F_{\text{ITT}}$ at $t \approx 600$ 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 $F_{\text{ITT}}$ at $t$ range of 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 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 no 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:

$$I_M + k_1 \overset{k_1}{\rightarrow} I_M \overset{k_3}{\rightarrow} PAn_M + 2 - M_{A-M}$$  \hspace{1cm} (3)

where PAn and 2-MA represent phthalic anhydride and 2-methoxyaniline, respectively, and subscript M represents micellar pseudophase. The values of $k_2$ (35°C) are almost zero and $12 \times 10^{-4}$ s$^{-1}$ at 1.0 mM NaOH and 49 mM HCl, respectively [15]. The efficient reactivity of nonionized 2 (i.e., 2H) towards the formation of PAn is primarily due to intramolecular carboxylic group—assisted cleavage of 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$_{10}$]$_T \leq 30$ mM, and at [C$_{16}$E$_{10}$]$_T \geq 50$ 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 $R \gg R_i$ with a constant value of [NaOH] caused decrease in pH of micellar environment of micellized ionized phenyl salicylate [7, 9]. In view of this study, at [C$_{12}$E$_{23}$]$_T \geq 10$ mM, the pH of the micellar environment of 2M dropped to a level where there was significant amount of 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 $\delta_1$, $\delta_2$, $\delta_{2H}$, and $\delta_{\text{PAn}}$ (with $\delta_X$ representing molar absorptivity of X) at 290 nm are ~2420 [13], 5570–8450, 4545–7490, and 2300–2000 M$^{-1}$ cm$^{-1}$ [11] within CH$_3$CN content range of 2–80% v/v in mixed aqueous solvent. Close similarity of the values of $\delta_1$ and $\delta_{\text{PAn}}$ coupled

| $10^3$ [C$_{12}$E$_{23}$]$_T$ | $10^3$ [NaOH] | $10^3 k_{\text{obs}}$ | $\delta_{ap}$ | $10^4 A_0$ | $k_{\text{OH}}$ | $F_{\text{ITT}}$ | $R$ | $t$ | $10^8 k_i$ |
|-------------------------|---------------|------------------|-------------|-------------|-------------|---------------|-----|-----|-------------|
| M                      | M             | M$^{-1}$ cm$^{-1}$ | s$^{-1}$ | M$^{-1}$ s$^{-1}$ | s$^{-1}$ | h          |     |     | s$^{-1}$ |
| 9.9                     | 7.6           | 65.2 ± 0.8       | 2088 ± 25  | 256 ± 3     | 8.45       | 0.68        | 1.30 | 432 | 25         |
| 9.9                     | 7.6           | 68.1 ± 1.1       | 1691 ± 32  | 267 ± 3     | 8.70       | 0.55        | 1.30 | 600 | 27         |
| 10.0                    | 7.6           | 67.2 ± 0.5       | 3293 ± 25  | 260 ± 3     | 8.92       | 1.32        |      |     |             |
| 19.8                    | 11.0          | 44.1 ± 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                    | 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 ± 9   | 310 ± 9     | 4.04       | 0.74        | 1.70 | 1085 | 7.6         |
| 30.0                    | 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                    | 30.0          | 78.6 ± 2.5       | 3365 ± 129 | 406 ± 13    | 2.62       | 1.62        |      |     |             |

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Table 3: Values of $k_{\text{obs}}$, $\delta_{ap}$, and $A_0$ calculated from (1) for alkaline hydrolysis of 1 in the presence of C$_{12}$E$_{23}$ micelles$^a$.  

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$^a$[1]= 0.1 mM, λ = 290 nm, $T=35°C$, and the aqueous reaction mixture contained 2% v/v CH$_3$CN. $^b$k$_{\text{OH}}$ = $k_{\text{obs}}$ [NaOH]. $^c$F$_{\text{ITT}}$ = $\delta_{ap}/\delta_{ap}$ with $\delta_{ap}$ = 3058 M$^{-1}$ cm$^{-1}$. $^d$R = [C$_{12}$E$_{23}$]$_T$/[NaOH]. $^e$t = reaction time ($t \geq t_o$) where the kinetic reaction mixture was used for micellar entrapment experiment. $^f$Calculated from the relationship: $k_f = (1/t) \ln(1/F_{\text{ITT}})$. $^g$Value of [C$_{12}$E$_{23}$]$_T$ after external addition of [NaOH]. $^h$Error limits are standard deviations. $^i$Reaction mixture for kinetic run was freshly prepared, where $\delta_{ap}$ = $\delta_{ap}$.
with significantly higher values of \( \delta_2 \) or \( \delta_{2H} \) compared with those of \( \delta_1 \) and \( \delta_{PAH} \), reveal that \( k_2 \geq k_1 \). These observations explain the observed constancy of \( A_{obs} \) within reaction time (\( t \)) ranging from \( \sim 15 \) s to \( \leq 1102 \) h at 10–50 mM \( C_{12}E_{23} \) (Table 1). The rough and approximate values of \( k_1 \) were obtained from the relationship: 
\[
 k_1 = \frac{1}{t} \ln\left(\frac{1}{1 - f_T}\right)
\]
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 \( I \) to 2 could occur at \( t = 1102 \) h (Table 3). The values of \( k_1 \) decreased from \( \sim 26 \times 10^{-8} \) to \( 2.3 \times 10^{-8} \) 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 \( \sim 3\)-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 \( \sim 3.5 \), in mixed aqueous solvent containing 2% v/v CH\(_3\)CN, is \( 67 \times 10^{-8} \) s\(^{-1} \) [16]. Under such typical conditions, the value of \( k_2 \) is \( 120 \times 10^{-8} \) s\(^{-1} \) and it decreases from \( 120 \times 10^{-5} \) to \( 6.6 \times 10^{-5} \) s\(^{-1} \) with increase in \( \text{CH}_3\text{CN} \) 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 \( \times 10^{-8} \)–0.05 M (Tables 1 and 3). The value of \( k_M \) (= rate constant for hydrolysis of \( I \) 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 \( I \) \( (K_S) \) increase significantly \( (\sim 10^2\)-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 \( n_1I_M \) 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, \( n_3I_M, n_2I_M, n_1I_M, \) and \( n_5I_M \) 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 \( I \) within the \( R \) range of 10–50, where \( R = [C_{12}E_{23}]/[\text{NaOH}] \), with a constant value of [NaOH] (= 1.0 mM). These values of \( k_1 \) are \( >10^2\)-fold smaller than \( k_{obs} \) at \( R \leq 1.4, \)

\[
 R = [C_{12}E_{23}]/[\text{NaOH}]
\]

where pseudophase micellar (PM) reveals that \( k_M \approx 0 \) and \( K_S = 925 \) M\(^{-1} \) [13]. The kinetic data of this paper show that the half-lives of alkaline hydrolysis of \( I \) 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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