Acid-Catalyzed Hydrolysis of Sodium Dodecyl Sulfate

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Abstract ☐ The acid-catalyzed hydrolysis of sodium dodecyl sulfate (**1**) and the effect of 1-dodecanol (**2**) on this hydrolysis were investigated. The rate of hydrolysis was followed by measuring the rate of production of HSO_4^- using a pH-stat. The rate constant (k_{H^+}) below the critical micelle concentration (CMC) increased with increasing concentrations of **2**, up to a mole ratio of 0.5 for **2** to **1**, after which the hydrolysis rate was independent of the concentration of **2**. These results suggest the possible formation of a complex between **1** and **2**. A micellar solution of pure sodium dodecyl sulfate (20 mM) hydrolyzed 50 times faster than that of a premicellar solution at the same pH. Plots of log *k* versus pH were linear with a slope of −1 at pH <4.3. At a constant pH, the addition of NaCl resulted in a decrease in the rate of hydrolysis of a micellar solution. This is probably due to the reduction of concentration of protons at the micelle surface. Furthermore, k_{H^+} was also decreased by the addition of **2** in the region where **2** is solubilized in the micelle; again, this was probably due to the reduction of the charge density (σ) on the surface of the micelle.

Sodium dodecyl sulfate is a surfactant that is widely used for the purpose of solubilization, dispersion, and stabilization of drugs.[1] However, only a few systematic studies on the stability of sodium dodecyl sulfate and other surfactants have been reported.[2–11] Some of these studies suggest that the hydrolysis of 1 is pH independent in the pH range of 4–10 and that the rate is accelerated at pH values below 4 and is retarded at pH values above 10.[6–10]

However, many of these studies involve changes in pH with time and did not involve control of the pH with buffers or by a pH-stat. Also, the hydrolysis of sodium dodecyl sulfate was postulated to be a one-step reaction. The effect of the change in the micellar state during hydrolysis and the effect of the product on hydrolysis had not previously been studied, other than in the report by Motsavage et al.[5] who found that sodium dodecyl sulfate was readily hydrolyzed during a 3–4-d period in the presence of 1-dodecanol at pH 1.0 and 50–60°C. However, the concentration of 1-dodecanol solubilized in the micelle of sodium dodecyl sulfate was not considered in their work.

We report the acid-catalyzed hydrolysis of sodium dodecyl sulfate carried out at concentrations both above and below the critical micelle concentration (CMC). The effect of the product (1-dodecanol) on the rate has been studied as well as the molecular interaction between sodium dodecyl sulfate and 1-dodecanol below the CMC of sodium dodecyl sulfate.

Experimental Section

Materials—Sodium dodecyl sulfate (1) (Nihon Emulsion Co., Ltd., Japan) was extracted with petroleum ether in a Soxlet apparatus for at least 20 h, recrystallized twice from ethanol, and dried under reduced pressure for 24 h. The CMC value of this sample in aqueous solution was found to be 8.1 mM at 25°C by surface tension measurements using the capillary rise method. The degradation product, 1-dodecanol (2) (Nakarai Chemicals Co., Ltd., Japan) was guaranteed reagent-grade quality and was used without further purification.

Method of measurement—Since HSO_4^- is produced by the hydrolysis of 1,[12,13] the reaction was followed quantitatively by using a pH-stat (TOA Electronics Ltd., model HSM-10A, Japan) equipped with a 1-mL glass syringe which contained 0.05 M or 2.0 M NaOH as a standard. All hydrolysis studies were carried out at 25°C.

Procedure—Sodium dodecyl sulfate was dissolved in 100 mL of distilled water, with the pH adjusted (using a pH meter) to within 0.01 pH units by the addition of 0.1 M HCl. When the effect of 2 was examined, liquid 2 (mp 24°C) was added to the aqueous solution of 1 and stirred for 20 h at 25°C.

Results

Effect of 1-Dodecanol (2) on the Hydrolysis of Sodium Dodecyl Sulfate (1)—The effect of 1-dodecanol on the hydrolysis of sodium dodecyl sulfate was investigated, because the amount of 2 in the reaction increases as the hydrolysis proceeds. We used an aqueous solution of 1 at an initial concentration (0.50 mM) below the CMC, so that the effect of the micelle formation could be ignored. The CMC value of the aqueous solution of 1 in the presence of 2 is ~4 mM at 40°C, as reported by Ogino et al.[14]

Plots of the percent hydrolyzed versus time at pH 3.22 is shown in Fig. 1a, for three varying concentrations of 1-dodecanol. The rate constant (k) for the hydrolysis, shown in Fig. 1a, is defined as follows:

$$\ln (x_e - x) = \ln x_e - kt \qquad (1)$$

where x_e is the equilibrium value of hydrolysis and x is the value of 1 hydrolyzed during time t. For convenience, we used the percent of hydrolyzed 1 based on the initial concentration of 1. Plots of $\ln (x_e - x)$ versus t, calculated from the relation between the percent hydrolyzed and time, were linear as shown in Fig. 1b, where x_e is 40.

The Rate Constant and pH—Next, the pH dependency was examined. The relationship between the percent hydrolyzed and time and the plots of $\ln (x_e - x)$ versus time at the

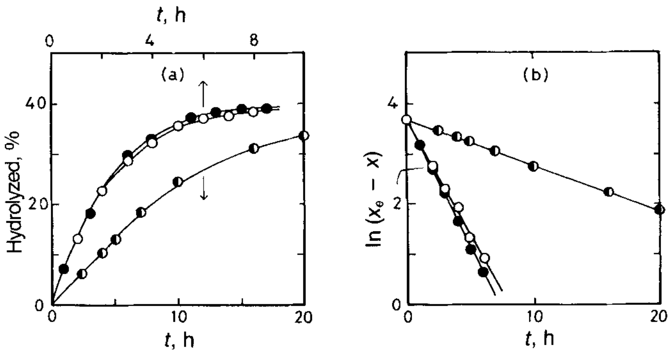

Figure 1—*Effect of 1-dodecanol (2) on the hydrolysis of sodium dodecyl sulfate (1) below the CMC: (a) percent hydrolyzed versus time; (b) ln (x_e − x) versus time. Key: C_2/C_1: (◐) 0.297, (○) 0.446, and (●) 0.892; concentration of 1 (C_1): 0.50 mM; pH: 3.22.*

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mole ratio of 0.594 of 2 to 1 are shown in Fig. 2. The values of x_e are 100, 100, 40, and 20 for the samples at pH 2.61, 2.91, 3.22, and 3.45, respectively. The value of x_e was 100 at pH values below 3, and the value of x_e decreased with increasing pH values above 3, as shown in Fig. 2b.

The relationship between pH and the rate constants obtained from Fig. 2 is shown as line a in Fig. 3. As can be seen in Fig. 3, the plot of log k versus pH is linear with a slope of -1, indicating that the hydrolysis reaction is apparent first order in hydrogen ion concentrations, and can be described by:

$$k = k_{H^+}[H^+] \tag{2}$$

where k_{H^+} is the second-order rate constant for the proton-catalyzed hydrolysis. The relationship between the rate constant obtained from the slopes of the plots in Fig. 1, and the concentration of 2, C_2, or the mole ratio of 2 to 1, C_2/C_1, added before the beginning of the reaction, is shown in Fig. 4. When the initial concentration of 1 is below the CMC, as in Fig. 4, the solution contains only premicellar 1; the rate constants for hydrolysis are low, but the rate constant increases by the addition of 2. Above a mole ratio of 0.5 of 2 to 1, the rate constant is independent of the 1-dodecanol concentration.

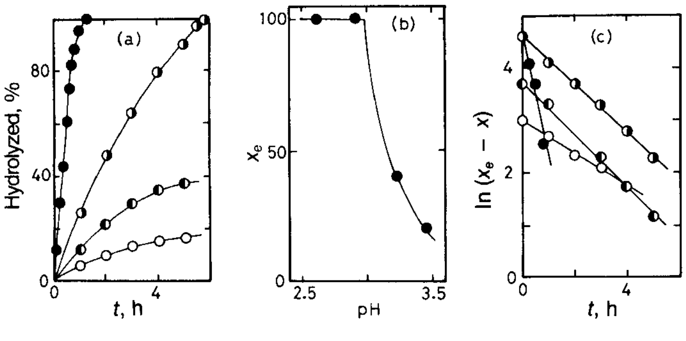

Figure 2—*Effect of pH on the hydrolysis of sodium dodecyl sulfate (1) when a complex has been formed: (a) the percent hydrolyzed versus time, (b) x_e versus pH, and (c) ln ($x_e - x$) versus time. Key: pH values—(●) 2.61, (◑) 2.91, (◐) 3.22, and (○) 3.45; C_2/C_1 = 0.594; C_1 = 0.50 mM.*

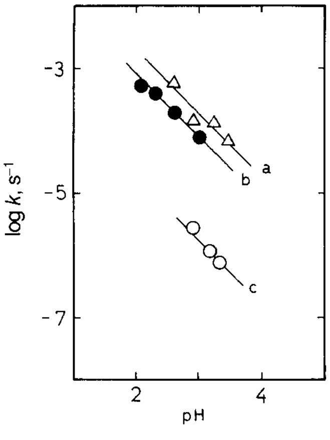

Figure 3—*Plot of log k versus pH: (a) complex state—C_2/C_1 = 0.594, C_1 = 0.50 mM, (b) micellar state—C_1 = 20 mM, and (c) free state—C_1 = 0.50 mM.*

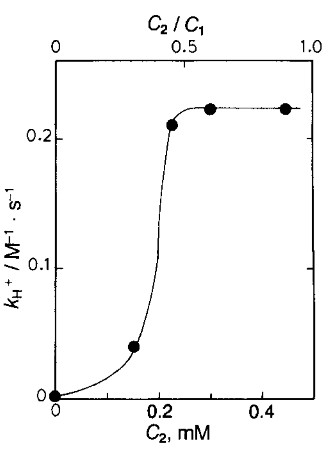

Figure 4—*Effect of 2 on the rate constant for hydrolysis, k_{H^+}, of 1 below the CMC: C_1 = 0.50 mM, pH = 3.22.*

Hydrolysis of Sodium Dodecyl Sulfate Above the Critical Micelle Concentration—To investigate the effect of micelle formation on hydrolysis, a solution of 1 with a initial concentration of 20 mM, as a concentration above the CMC, was investigated. The relationship between the percent hydrolyzed and time is shown in Fig. 5a, and the value of x_e is plotted against pH in Fig. 5b. Next, the plots of ln ($x_e - x$) versus time at pH 2.09 and 2.30, calculated from the values of x_e and shown by a solid line in Fig. 5b, are shown in Fig. 5c. As can be seen in Fig. 5c, the plot is not a single line. This is probably due to the alteration in the micellar state with time.

It has been reported that 4.20 mM of 2 is solubilized by a 17.4 mM aqueous solution of 1 at 40°C.[15] This corresponds to a mole ratio of 0.24 2 to 1. In our experimental conditions, the solubilization limit of 2 was found to be C_2/C_1 = 0.20 from the observation of turbidity of the mixed solution.

In Fig. 5c, the values of C_2/C_1 are ~0.20 at the first break points, indicating the limit point of 2 solubilized in the micelle. The second break is considered to be caused by the complete breakdown of the micellar structure to that of a complex formation.

Therefore, the plots of ln ($x_e - x$) against t for hydrolysis in the solubilization region, which correspond to the first linear part in Fig. 5c, are shown in Fig. 5d. The values of x_e, shown by a dotted line in Fig. 5b, are used for the calculation of ln ($x_e - x$). The micellar samples at pH values above 2.6 indicated a smaller value of x_e than 20. The rate constants for the initial hydrolysis in the solubilization region were compared, and a plot of log k against pH is shown as line b in Fig. 3.

Line c in Fig. 3 indicates the relation between log k and pH for the solution containing only premicellar 1 (0.50 mM), in the absence of added 2. In this case, it was difficult to follow the hydrolysis at pH both above 3.2 and below 2.9, because of the low concentration of 1.

It is evident from Fig. 3 that the plots of log k against pH are linear with a slope of -1 as defined by eq. 2 in all cases. It is apparent that the micellar 1 (line b) undergoes hydrolysis 50 times faster than that of free 1 (line c).

Effect of Electrolyte on Hydrolysis—To ascertain that the enhanced rate for hydrolysis of micellar 1 is due to the surface potential of the micelle, NaCl was added to the reaction, and the expected decrease in the rate was observed. When the concentration of 1 was 20 mM, the relationship between the percent hydrolyzed and time, and the plots of ln ($x_e - x$) against t for x_e = 13 at pH 2.61, are shown in Fig. 6. The rate constants obtained from Fig. 6b are plotted against the ionic strength, $\sqrt{J}$, in Fig. 7. The ionic strength is calculated and includes the concentration of hydronium ions. As can be seen, the rate constant is smaller as the ionic strength is increased.

Effect of 1-Dodecanol Hydrolysis—The effect of 2 on the rate of hydrolysis at pH 2.09 is shown in Fig. 8. The curve indicated by the closed circles represents the hydrolysis behavior of the micellar solution to which no 2 was added at time zero for the reaction. The other four curves indicate where the mole ratio of 2 to 1 was 0.115, 0.167, 0.335, and 0.669, respectively.

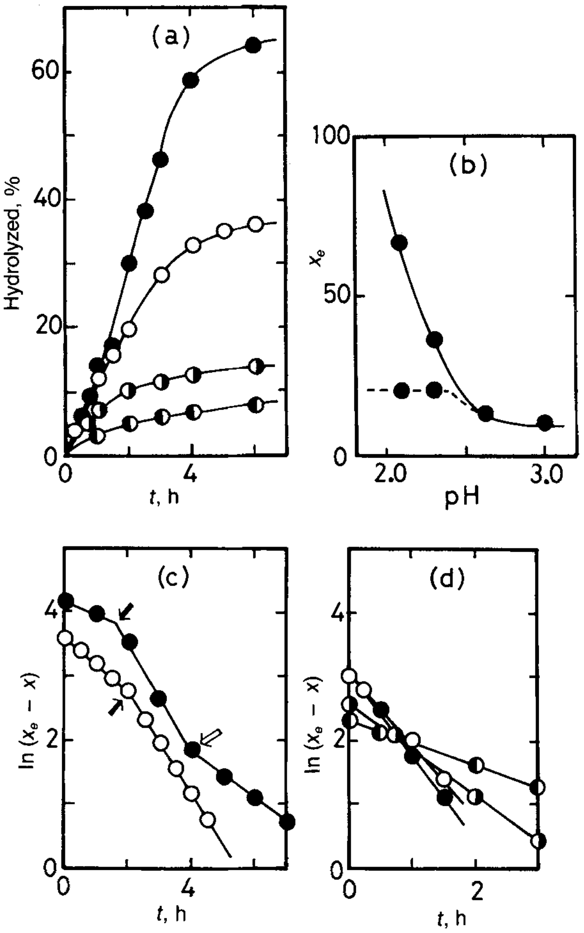

Figure 5—*Relationship between the hydrolysis of micellar 1 and pH: (a) percent hydrolyzed versus time; (b) x_e versus pH. Key: (——) x_e as the final equilibrium value for the hydrolysis; (------) x_e for the hydrolysis in the solubilization region of 2 in the micelles. (c) The ln (x_e − x) versus time for x_e shown by (——) in Fig. 5b. (d) The ln (x_e − x) versus time for x_e shown by (------) in Fig. 5b, the hydrolysis in the solubilization region of 2 in the micelles. Key: pH values—(●) 2.09, (○) 2.30, (◑) 2.61, and (◐) 2.99; C_1 = 20 mM.*

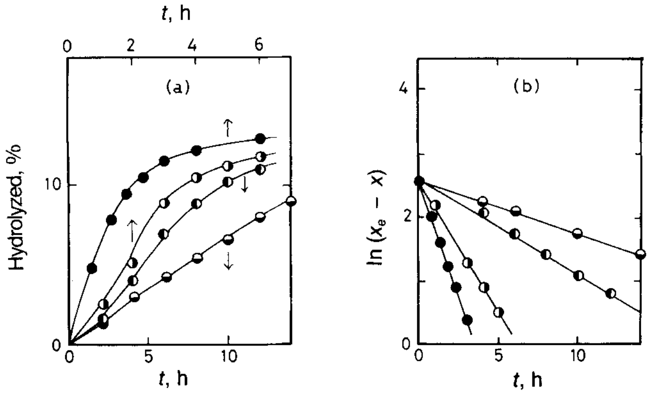

Figure 6—*Effect of electrolyte (NaCl) on the hydrolysis of micellar 1: (a) percent hydrolyzed versus time and (b) ln (x_e − x) versus time; C_1 = 20 mM; pH = 2.61; C_{NaCl}: (●) 0, (◑) 5, (◐) 20, and (◒) 50 mM.*

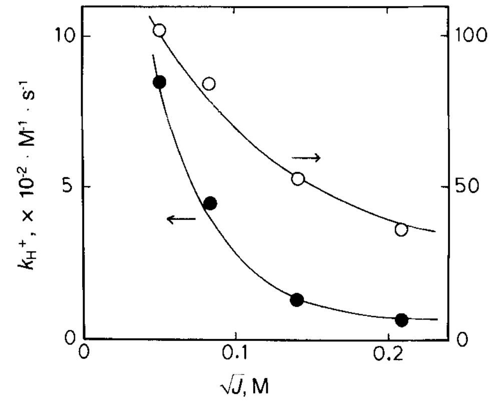

Figure 7—*Effect of ionic strength on k_{H^+} of micellar 1: C_1 = 20 mM; pH = 2.61; (——) theoretical curves by the Gouy–Chapman equation for σ = −2.01 × 10^{-6} C · cm^{-2}; (●) k_{H^+} versus $\sqrt{J}$; (○) ψ versus $\sqrt{J}$.*

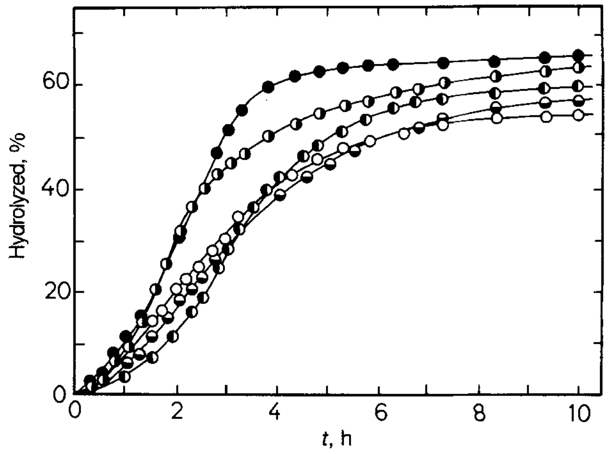

Figure 8—*Effect on 2 on the hydrolysis behavior of 1: percent hydrolyzed versus time. Key: C_2/C_1—(●) 0, (◑) 0.115, (◐) 0.167, (◒) 0.335, and (○) 0.669; C_1 = 20 mM; pH = 2.09.*

In those cases where exogenous 2 had not been added, or was added at a ratio of <0.5 of C_2/C_1, the transition from the micellar structure to the complex structure, through the breakdown of the micelle, is considered to take place as the result of an increase in the amount of 2 in the micelle during hydrolysis. Therefore, hydrolysis in the solubilization region of 2 in the micelles was investigated first. In those cases where exogenous 2 had been added, eq. 1 for the hydrolysis of 1 is rewritten as follows:

$$\ln (x_e - x - a) = \ln (x_e - a) - kt \qquad (3)$$

where a is the percent of added 2 based on the initial concentration of 1. The plots of ln ($x_e - x - a$) against t for the hydrolysis in the solubilization region are shown in Fig. 9a, where the values of ($x_e - a$) are 20, 8.5 (20 − 11.5 = 8.5), and 3.3 (20 − 16.7 = 3.3) when the values of (C_2/C_1) are 0, 0.115, and 0.167, respectively.

The rate constants in the solubilization region are shown in Fig. 9b. The abscissa of Fig. 9b indicates the concentration of added 2 and the mole ratio of 2 to 1. The value of k_{H^+} decreases with increasing concentrations of 2.

The values of x_e which are observed in Fig. 8 are shown in Fig. 10a. The values of ln ($x_e - x$) are calculated from the values shown in Fig. 8 and plotted against t in Fig. 10b. In Fig. 10b, the black arrows indicate the limit point of 2 solubilized in the micelle, and the white arrows indicate the

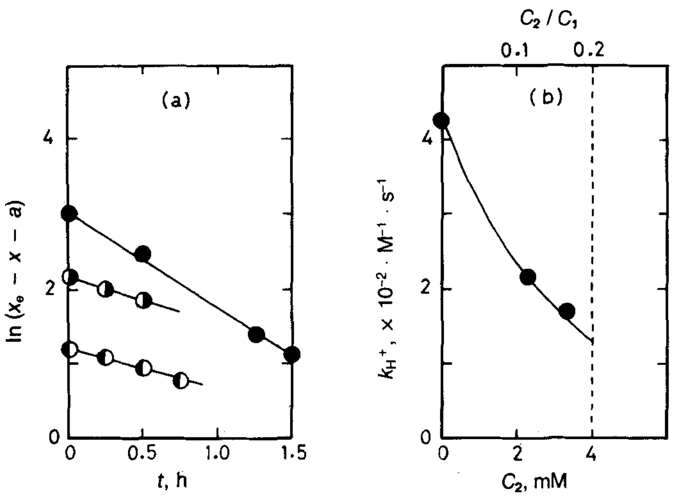

Figure 9—*Effect of 2 on the hydrolysis of 1 in the solubilization region of 2 in the micelles: (a)* $\ln (x_e - x - a)$ *versus time and (b)* k_{H^+} *versus* C_2/C_1. *Key:* C_2/C_1*—(●) 0, (◑) 0.115, and (◐) 0.167;* C_1 *= 20 mM; pH = 2.09.*

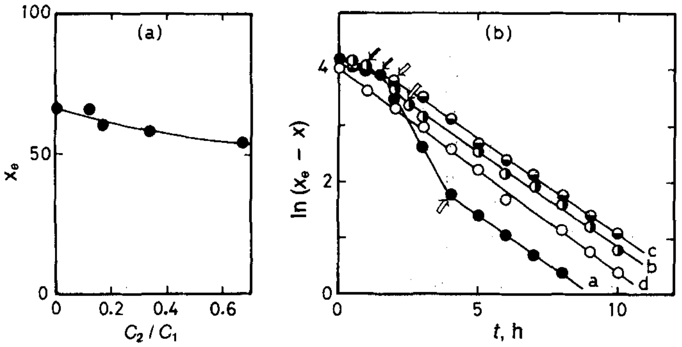

Figure 10—*Effect of 2 on the hydrolysis of 1: (a)* x_e *versus* C_2/C_1 *and (b)* $\ln (x_e - x)$ *versus time for the hydrolysis of 1. Key:* C_2/C_1*—(a) 0, (b) 0.115, (c) 0.335, and (d) 0.669;* C_1 *= 20 mM; pH = 2.09.*

complete breakdown of the micellar structure to that of a complex, as shown in Fig. 5c. The slopes for the final linear parts of those four lines were approximately the same.

Discussion

Formation of a Complex—When 2 was added, the rate constant was found to give a constant value when the mole ratio of 2 to 1 was >0.5, as shown in Fig. 4. This is probably due to the formation of a complex[14–19] whose composition is expressed stoichiometrically by the formula $[1]_2[2]$. By differential thermal analysis,[16] the heat of complex formation was 7–8 kcal/mol. This suggested that the complex was formed by a force similar to hydrogen bonding between alcohol and sulfate molecules. This conclusion was also supported by IR spectroscopy[16–18] and X-ray diffraction.[17,18]

The hydrolysis of 1 in the complex state proceeds faster than that of the premicellar and noncomplexed state. This may be because a proton is supplied by the hydrogen bonding from 2 to 1 in competition with a proton from the aqueous solution in the first step of the hydrolysis mechanism.[12,13] In the cases of lines a and c in Fig. 3, where a 0.5 mM concentration of 1 is used and only premicellar 1 exists, the rate constant becomes ~120 times larger on the addition of 2 to form a complex with 1.

Effect of Micellization—The rate constant was ~50 times larger (after micellization) than the rate constant of the solution containing only premicellar 1, as shown by comparing lines b and c in Fig. 3. However, Motsavage and Kostenbauder[5] have reported that the rate constant is 36 times larger after micellization. Their value is smaller than ours, probably because they used 10 mM 1 for their micellar concentration. In this case, only a small amount of the 1 is in the micelle form, since 10 mM is a concentration only slightly above the CMC (8.1 mM).

The enhanced rate of hydrolysis in the micelle state may be caused by the enhanced proton concentration near the surface of the micelle which results from the negative, electrostatic charge at the surface. The electrostatic effect is well-known in the various reactions involving micellar catalysis of various surfactants.[20–22]

The surface potential of the micelle can be estimated from the rate constants observed for micellar and premicellar solutions, k_m and k_f, respectively, of pure 1 by assuming that k_{H^+} of eq. 2 is the same for micellar and premicellar solutions. The effective proton concentration $[H^+]$, however, depends on the change of the surface potential by micellization, $\Delta\psi$, as follows:

$$\frac{k_m}{k_f} = \frac{[H^+]_m}{[H^+]_f} = \exp\left(-zF_A\Delta\psi/RT\right) \qquad (4)$$

where z is the valency of the proton, F_A is the Faraday constant, and R is the gas constant. By substituting $z = +1$, $F_A = e \cdot N_A = 9.648 \times 10^4$ $(C \cdot M^{-1})$, $R = k_B N_A = 8.314$ $(J \cdot M^{-1} \cdot K^{-1})$, and $T = 298.15$ K at 25°C:

$$\frac{\Delta\psi}{\text{mV}} = -59.16 \log \frac{k_m}{k_f} \qquad (5)$$

where N_A is defined as Avogadro's number, C as the coulombs, and mV is millivolts. Thus, the surface potential of the micelle, $\Delta\psi$, was determined from the measured rate constants, k_m and k_f. The value of $\Delta\psi$ is calculated as −100.3 mV from lines b and c in Fig. 3.

We obtained a value of −73 mV at an ionic strength of 0.02 M for the surface potential of the micelle by measuring the fluorescence intensity of ammonium 8-anilino-1-naphthalenesulfonate as a fluorescent probe.[23] In the literature, values of: −129 mV at an ionic strength of 0.01 M using methyl orange,[24] −108 mV at an ionic strength of 0.1 M, using bromophenol blue,[25] and from −68 to −134 mV at an ionic strength of 0.01–0.1 M using hydroxycoumarin, aminocoumarin, orange OT, and oil red N-1700 have been reported.[26–28] Therefore, the value obtained from the rate constants for hydrolysis of −100.3 mV seem to be quite reasonable.

Effect of Electrolyte—As shown in Fig. 7, the rate constant becomes smaller as the ionic strength is increased by adding NaCl. This can be explained by the decrease of the hydronium ion concentration at the micelle surface, which is due to a decrease of the surface potential of the micelle, $|-\psi|$, caused by the increase in the ionic strength.

The change of the surface potential of the micelle by the addition of NaCl, $\Delta\psi_S$, can be expressed as:

$$\frac{\Delta\psi_S}{\text{mV}} = -59.16 \log \frac{k}{k_0} \qquad (6)$$

where k_0 and k are the rate constants in the absence and presence of NaCl, respectively. The surface potential of the micelle in the presence of NaCl, ψ, is, therefore:

$$\psi = -100.3 + \left(-59.16 \cdot \log \frac{k}{k_0}\right) \qquad (7)$$

where −100.3 mV is the ψ value at an ionic strength of 2.5 mM (pH 2.61) in the absence of NaCl as determined above, and k_0 is $8.430 \times 10^{-2} \cdot \mathrm{M}^{-1} \cdot \mathrm{s}^{-1}$, the latter being merely k_m of eq. 5. The surface potential of the micelle thus obtained is shown at the right side of the ordinate in Fig. 7.

According to the Gouy–Chapman theory, the relation between the surface potential, ψ, and the surface charge density, σ, is expressed as:

$$\frac{\sigma}{\mathrm{C} \cdot \mathrm{cm}^{-2}} = -5.8673 \times 10^{-6} \sqrt{\sum_i \left[\left(\frac{C_i}{\mathrm{M}} C_i \mathrm{M} C_i \mathrm{M} \right) \left\{ \exp \left(-0.03892\, z_i \frac{\psi}{\mathrm{mV}} \right) - 1 \right\} \right]} \tag{8}$$

where 78.54[29] is used as the value of the relative dielectric constant of water at 25°C. The value of σ thus calculated was found to be independent of ionic strength and was equal to about $-2.01 \times 10^{-6}\ \mathrm{C} \cdot \mathrm{cm}^{-2}$, where $\mathrm{C} \cdot \mathrm{cm}^{-2}$ is the coulombs per unit area. By using this σ value, the theoretical values of the micellar surface potential and of the rate constant were calculated by using eqs. 7 and 8, respectively, and represented by the solid lines in Fig. 7. Thus, the relationship between the ionic strength, the micellar surface potential and the rate constant was found to be represented well by the Gouy–Chapman theory.

Effect of 1-Dodecanol—The effect of **2** on the hydrolysis of **1** at pH 2.09, in the region where **2** is solubilized in the micelles, is shown in Fig. 9. As shown in Fig. 9b, the initial rate constant decreased with increasing concentrations of **2**. Motsavage and Kostenbauder[5] have reported that the addition of 27 mM **2** to the 10 mM **1** results in a doubling of the rate of hydrolysis. However, our results indicate that the rate constant is decreased by the addition of **2**. This discrepancy probably exists because they postulated the hydrolysis to be a one-step reaction and that the amount of micelle formed from **1** at a concentration of 10 mM was too small to have any effect.

Hydrolysis at a concentration of **2** below the limit of solubilization is thought to be that of micellar **1**. The retardation in the rate is thought to be caused by the reduction of the hydrogen ion concentration at the micelle surface as a result of the reduction of the negative charge density at the surface by adding **2** to the micelle. By using equations similar to eqs. 7 and 8, the value of σ is calculated as -2.01×10^{-6}, -1.63×10^{-6}, and $-1.28 \times 10^{-6}\ \mathrm{C} \cdot \mathrm{cm}^{-2}$, when (C_2/C_1) is 0, 0.115, and 0.167, respectively.

The relationship between surface charge density, $|\sigma|$, and area occupied, A, is expressed as:

$$\frac{\mathrm{A}}{\mathrm{cm}^2 \cdot \mathrm{molecule}^{-1}} = \frac{F_{\mathrm{A}}}{|\sigma| N_{\mathrm{A}}} = \frac{\mathrm{A}_2^0 C_2 + \mathrm{A}_1^0 \mathrm{C}_1}{C_1} \tag{9}$$

The area A is, therefore, calculated from the value of $|\sigma|$ shown above. From the plot of A versus (C_2/C_1), it was confirmed that $|\sigma|$ decreases with increasing the ratio of **2** and with increasing the area occupied by **2**. The area occupied by a 1-dodecanol molecule was estimated as 25 Å^2 from the slope of the plot of eq. 9. Furthermore, the dissociation degree, α, of the micelle was calculated[31] as 0.073 from the intercept of the plot of eq. 9 and the value of the area occupied by a sodium dodecyl sulfate molecule, 58 Å^2; $\alpha = 58/\mathrm{A}_1^0$. This value ($\alpha = 0.073$) is nearly the same as the value ($\alpha = 0.102$) obtained in our previous report,[23] so the values obtained in this paper seem to be quite reasonable.

The effect of **2** on the hydrolysis of **1** at pH 2.09 is shown in Fig. 10b, where the values of x_e shown in Fig. 10a were used for the calculation of $\ln (x_e - x)$. The second break is considered to be caused by the complete breakdown of the micellar structure to that of a complex formation. A multicomponent self-diffusion study demonstrated that solubilized alcohols do cause a breakdown of the micelle.[30] In the case of no added **2** (case a in Fig. 10b) the mole ratio of unhydrolyzed **1** to produced **2** becomes 2:1 when the hydrolysis has proceeded to 33.3% of completion, which corresponds to $\ln (x_e - x) = 3.49$. However, the time of appearance of the second break is about 2 h later than expected, which suggests that the transition from a mixed micelle to a complex structure requires extra time.

In case b, when **2** was added at the mole ratio of 0.115 of **2** to **1**, which is in the region of 1-dodecanol solubilization in the micelle, the second break appears at a smaller value of percent hydrolyzed than that of case a. In case b, the time of complete formation of the complex is later than that of the theoretical estimation [$\ln (x_e - x) = 3.68$] where the hydrolysis has proceeded to 25.7% of completion, [1(1 − 0.257), 2(0.115 + 0.257) = 2:1]. In case c, when **2** was added at the mole ratio of 0.335 of **2** to **1**, the time of complete formation of the complex, based on when the break occurs, is about the same as that of the theoretical estimation [$\ln (x_e - x) = 3.85$] where the hydrolysis has proceeded to 11.0% of completion, [1(1 − 0.110), 2(0.335 + 0.110) = 2:1]. In this case, the first break as shown in cases a and b cannot be seen, because the amount of **2** added was in excess of the amount of the limit of solubilization of **2** in the micelle. In case d, **2** was added at 0.5 above the mole ratio of **2** to **1**; only one straight line is seen, indicating that the hydrolysis of **1** is from the complex structure. It is possible to conclude that the final linear parts shown in Fig. 10b (the third linear part of cases a and b, the second linear part of case c and the first linear part of case d) indicate the hydrolysis of **1** in the complex state. Therefore, the rate constant of these four cases shown here had approximately the same value: $k_{\mathrm{H}^+} = 1.2 \times 10^{-2}\ \mathrm{M}^{-1} \cdot \mathrm{s}^{-1}$.

If the rate constant for the first linear part shown in Fig. 10b is estimated, the values of k_{H^+} are 7.85×10^{-3}, 4.43×10^{-3}, 1.86×10^{-3}, 4.25×10^{-3}, and $1.22 \times 10^{-2}\ \mathrm{M}^{-1} \cdot \mathrm{s}^{-1}$ for the samples at the mole ratio of 0, 0.115, 0.167, 0.335 and 0.669 of **2** to **1**. This indicates that the initial rate constant decreases with increasing concentration of **2** and the rate constant becomes minimum at the solubilization limit of **2** in the micelle ($C_2/C_1 = 0.20$), and that the rate constant increases at above the limit of solubilization. Therefore, this is thought to be caused by the mixed micelle being broken down to form a complex.

Conclusions

It has been found that the addition of **2**, which is also produced by the hydrolysis of **1**, exerts influence on the rate for hydrolysis of **1** as follows: (*a*) at concentrations of **1** below the CMC, the hydrolysis is accelerated by the formation of a 2:1, 1:2 complex; (*b*) at above the CMC, the hydrolysis is initially suppressed in the presence of **2**; (*c*) at concentrations below the limit of solubilization in the micelle, the charge density is reduced on the surface of the micelle. Furthermore, the hydrolysis of **1** above the CMC is enhanced markedly, probably by the electrostatic effect resulting in an increased concentration of protons at the micelle surface.

These results lead to the suggestion that attention must be paid to the conditions used to formulate **1**, namely: (*a*) the pH of the solution, and (*b*) the drugs which are used with **1** when the latter is used particularly as a solubilizer, a stabilizer, and a dispersing agent at concentrations above and/or below the CMC. This is because the following results can be anticipated: (*a*) the effect of **1** as a dispersing agent, solubilizer, or stabilizer may be deteriorated by the significant hydrolysis of **1**, and (*b*) the effect of the drug may be deteriorated by the acidification of the solvent as a result of the hydrolysis of 1, when 1 is added to an acidic drug or to a drug which is capable of hydrogen bonding to 1.

References and Notes

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