

Solubilization of *n*-Alkylbenzenes into Octaethylene Glycol Mono-*n*-tetradecyl Ether (C₁₄E₈) Micelles

Yukiko Sato,[†] Hiromichi Nakahara,[†] Yoshikiyo Moroi,[†] and Osamu Shibata^{*,†,‡}

Division of Biointerfacial Science, Graduate School of Pharmaceutical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan, and Department of Biophysical Chemistry, Faculty of Pharmaceutical Sciences, Nagasaki International University, 2825-7 Huis Ten Bosch, Sasebo, Nagasaki 859-3298, Japan

Received March 2, 2007. In Final Form: April 20, 2007

Solubilization of benzene, toluene, ethylbenzene, *n*-propylbenzene, *n*-butylbenzene, and *n*-pentylbenzene into the micelles of octaethylene glycol monotetradecyl ether (C₁₄E₈) was studied, where equilibrium concentrations of all the solubilizates were determined spectrophotometrically at 298.2, 303.2, and 308.2 K. The concentration of the above solubilizates except benzene remained constant below the critical micelle concentration (cmc) and increased linearly with an increase in C₁₄E₈ concentration above the cmc, whereas benzene concentration was found to remain constant over the whole concentration range of C₁₄E₈. The Gibbs energy change (ΔG^0) for their solubilization was evaluated by the partitioning of the solubilizates between the aqueous phase and the micellar phase because of the large aggregation number of the C₁₄E₈ micelle. Furthermore, enthalpy and entropy changes for their solubilization were evaluated from the temperature dependence of the ΔG^0 values. From these thermodynamical parameters and the change in absorption spectra of the solubilizates due to their incorporation into the micelles, the solubilization site was found to move into the inner core of the micelle with increasing alkyl chain length of the solubilizates.

Introduction

The aqueous solubility of organic substances increases via their incorporation into micelles in surfactant solutions. The phenomenon is called solubilization.^{1,2} Indeed, solubilization has been applied to various scientific fields such as science, technology, pharmacy, medicine, and agriculture; for example, the dissolution of drugs into aqueous solution and their transport through a human body, the dissolution of aromatic compounds into cosmetics, the solution preparation of agricultural chemicals, and so on.

Nonionic surfactants have no charge, which brings about such interesting properties as low critical micelle concentration (cmc) and large molecular aggregates compared with those of ionic surfactants.^{3–5} One of the well-known groups of nonionic surfactants is polyoxyethylene alkyl ethers (C_{*n*}E_{*m*}),^{6–8} which have been extensively studied due to the advantage of their practical use.^{9,10} Nonionic surfactants of this type form micelles in dilute solution and liquid crystalline phase in the higher concentration

range,¹¹ separate into two phases upon heating,³ and can be made to have an optimal hydrophilic–lipophilic balance (HLB) value by proper combination of oxyethylene and alkyl chain parts.⁹ Fundamental studies on the physicochemical properties of C_{*n*}E_{*m*} solutions are still continuing in areas such as surface adsorption^{12,13} and thermal analysis of micellar systems.¹⁴ However, literature on studies of solubilization into C_{*n*}E_{*m*} micelles is rare,¹⁵ while that on solubilization into other nonionic micelles is common.^{15,16} In these studies, solubilization has been investigated from the viewpoint of a three-component phase diagram^{17,18} and the binding of surfactants to the third component.¹⁹

This paper aims to study the solubilization of *n*-alkylbenzenes into micelles in dilute solution in order to clarify the effect of the benzene rings and alkyl chain lengths of *n*-alkylbenzene molecules on the thermodynamic parameters of solubilization. In addition, the location of the solubilizates in the micelle is investigated by the thermodynamic parameters and the change in absorption spectra of the solubilizates.

C₁₄E₈ micelles have a large aggregation number and take on various shapes such as spherical micelles, wormlike micelles, and disklike micelles, depending on the concentration.²⁰ Furthermore, the cmc and aggregation number of C₁₄E₈ change with temperature as well.^{3,21,22} Therefore, the solubilization of

* Corresponding author. Address: Department of Biophysical Chemistry, Faculty of Pharmaceutical Sciences, Nagasaki International University, 2825-7 Huis Ten Bosch, Sasebo, Nagasaki 859-3298, Japan. E-mail: wosamu@niu.ac.jp.

[†] Kyushu University.

[‡] Nagasaki International University.

(1) McBain, M. L. E.; Hutchinson, E. *Solubilization and Related Phenomena*; Academic Press: New York, 1955.

(2) Elworthy, P. H.; Florence, A. T.; Macfarlane, C. B. *Solubilization by Surface-Active Agents and Its Application in Chemistry and Biological Sciences*; Chapman & Hall: London, 1968.

(3) Muhammad, R.; Moroi, Y.; Hlaing, T.; Matsuoka, K. *Bull. Chem. Soc. Jpn.* **2005**, *78*, 604.

(4) Matsuoka, K.; Moroi, Y.; Saito, M. *J. Phys. Chem.* **1993**, *97*, 13006.

(5) Yoshida, N.; Matsuoka, K.; Moroi, Y. *J. Colloid Interface Sci.* **1997**, *187*, 388.

(6) Kahlweit, M.; Busse, G. *J. Chem. Phys.* **1993**, *99*, 5605.

(7) Yeh, M. C.; Chen, L. J. *J. Chem. Phys.* **2001**, *115*, 8575.

(8) Tamura, T.; Takeuchi, Y.; Kaneko, Y. *J. Colloid Interface Sci.* **1998**, *206*, 112.

(9) Berthod, A.; Tomer, S.; Dorsey, J. G. *Talanta* **2001**, *55*, 69.

(10) Bruillete, D.; Perron, G.; Desnoyers, J. E. *J. Solution Chem.* **1998**, *27*, 151.

(11) Richtering, W. H.; Burchard, W.; Jahns, E.; Finkelmann, H. *J. Phys. Chem.* **1988**, *92*, 6032.

(12) Lee, Y.-C.; Stebe, K. J.; Liu, H.-S.; Lin, S.-Y. *Colloids Surf., A* **2003**, *220*, 139.

(13) Islam, M. N.; Kato, T. *Langmuir* **2003**, *19*, 7201.

(14) Grell, E.; Lewitzki, E.; von Raumer, M.; Hormann, A. *J. Therm. Anal. Calorim.* **1999**, *57*, 371.

(15) Xiarchos, I.; Doulia, D. *J. Hazard. Mater.* **2006**, *136*, 882.

(16) Mitra, S.; Dungan, S. R. *J. Agric. Food Chem.* **2001**, *49*, 384.

(17) Sottmann, T.; Strey, R. *J. Phys.: Condens. Matter* **1996**, *8*, A39.

(18) Aboofazeli, R.; Lawrence, C. B.; Wicks, S. R. *Int. J. Pharm.* **1994**, *111*, 63.

(19) Knaapila, M.; Almasy, L.; Garamus, V. M.; Pearson, C.; Pradhan, S.; Petty, M. C.; Scherf, U.; Burrows, H. D.; Monkman, A. P. *J. Phys. Chem. B* **2006**, *110*, 10248.

(20) Hamada, N.; Einaga, Y. *J. Phys. Chem. B* **2005**, *109*, 6990.

(21) Bakshi, M. S.; Kaura, A.; Mahajan, R. K. *Colloids Surf., A* **2005**, *262*, 168.

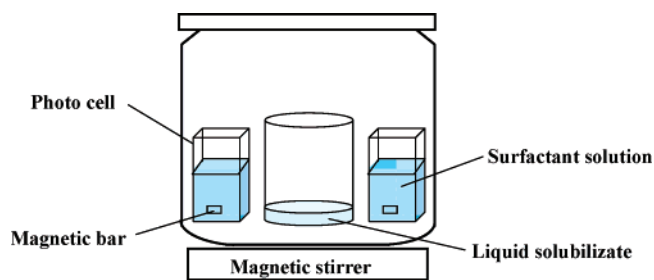


Figure 1. Solubilization apparatus for volatile solubilizes.

n-alkylbenzenes was studied by the partitioning of the solubilize molecules between the micellar aggregate phase and the aqueous phase in order to exclude changes in the size and shape of the micelles with $C_{14}E_8$ concentration and with temperature. Partitioning was also used because the resulting micelles incorporated with the solubilizates do not keep the physicochemical properties of the parent micelles.²³

Experimental

Materials. Octaethylene glycol monotetradecyl ether ($C_{14}E_8$, >99%) was purchased from Nikko Chemicals Co., Ltd., and was used as received, because the gas chromatograph attached for purity certification had only one sharp peak. The purity was further checked by an elemental analysis: C, 63.60 (63.42); H, 10.95% (11.01), where the values in parentheses are the calculated ones. Benzene (Nacalai Tesque; thiophene-free and 99.5%) was used as received. Toluene (>99.0%), ethylbenzene (>99.0%), *n*-propylbenzene (>99%), *n*-butylbenzene (>99%), and *n*-pentylbenzene (>98%) from Tokyo Chemical Industry Co., Ltd. were purified by extraction five times with concentrated sulfuric acid, followed by washing five times with a large volume of thrice-distilled water.

Solubilization. A stock solution of $C_{14}E_8$ was filtrated through a membrane filter of 0.1 μm pore size (Millipore MILLEX VV) to remove dust, and was diluted to prepare surfactant solutions of nine different concentrations. Nine surfactant solutions were poured separately into nine photocells, which were then set into a solubilization apparatus (Figure 1). About 30 μL of benzene and toluene was placed on the bottom of a small vessel in the middle of the glass apparatus in order for absorbance to be less than 0.7. As for the other alkylbenzenes, 1 mL of liquid solubilizates was dropped inside the middle vessel. The whole glass apparatus with its cover was kept in a thermostat controlled within ± 0.1 K at 298.2, 303.2, and 308.2 K for 24 and 48 h to reach complete solubilization equilibrium, where the surfactant solutions were agitated with a rotor in each photocell. After the equilibration, each photocell was capped immediately. The solubilize concentrations in the surfactant solutions were determined spectrophotometrically by the optical density of the solutions and the molar extinction coefficient. The molar extinction coefficients (ϵ) of the previous study were employed to determine the concentration of the solubilizates; the ϵ values at 260 nm were 232, 216, 201, 211, and 222 $\text{mol}^{-1} \text{dm}^3 \text{cm}^{-1}$ for toluene, ethylbenzene, *n*-propylbenzene, *n*-butylbenzene, and *n*-pentylbenzene, respectively, and the value at 254 nm was 188 $\text{mol}^{-1} \text{dm}^3 \text{cm}^{-1}$ for benzene.²⁴

Results and Discussion

The values of the cmc and micellar aggregation number of $C_{14}E_8$ determined previously by surface tension measurement and the light-scattering method, respectively, are given in Table 1,³ where the aggregation number at 303.2 K was evaluated by

(22) Meguro, K.; Takasawa, Y.; Kawasaki, N.; Tabata, Y.; Ueno, M. *J. Colloid Interface Sci.* **1981**, *83*, 50.

(23) Moroi, Y. *Micelles: Theoretical and Applied Aspects*; Plenum Press: New York, 1992.

(24) Take'uchi, M.; Moroi, Y. *Langmuir* **1995**, *11*, 4719.

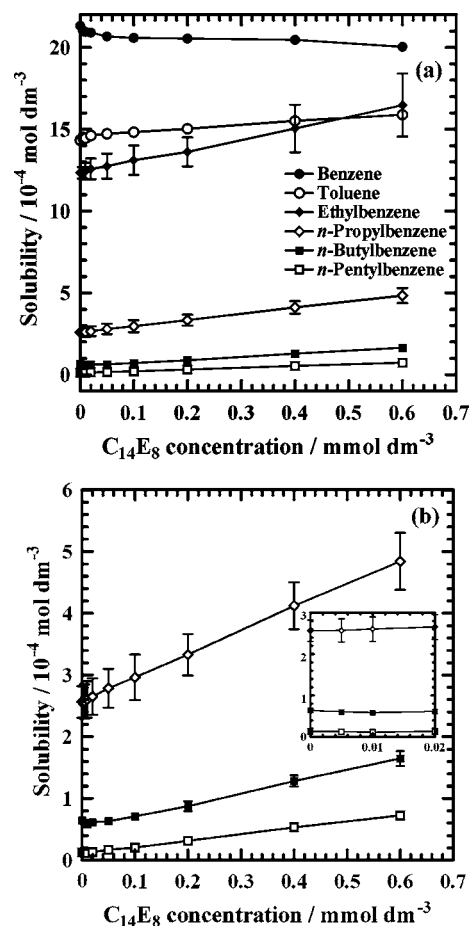


Figure 2. (a) Concentration changes of *n*-alkylbenzene with $C_{14}E_8$ concentration at 298.2 K after standing for 24 h. (b) The changes by exaggerated ordinate for longer alkylbenzenes.

Table 1. The cmc and the Aggregation Number of $C_{14}E_8$ at Different Temperatures

temperature (K)	cmc $\times 10^5$ (mol dm^{-3})	aggregation number ($\times 1000$)
298.2	1.81	1.34
303.2	1.72	1.36
308.2	1.67	1.74

interpolation of the aggregation numbers at different temperatures fitted by a quadratic equation.

Inside the apparatus, the volatile solubilizates (*n*-alkylbenzenes) easily evaporate because of their high volatility, thus the chemical potential of the gaseous solubilize molecule should become the same throughout the phases under equilibrium, or the concentration of monomeric solubilize can be set identical in the nine solutions.

The changes in concentration for *n*-alkylbenzenes with $C_{14}E_8$ concentration are illustrated in Figure 2a,b. Solubilize concentrations below the cmc remain almost constant for all the solubilizates, which indicates the constancy of the chemical potential of solubilize molecules throughout the phases inside the glass apparatus as mentioned above. In addition, for ethylbenzene, *n*-propylbenzene, *n*-butylbenzene, and *n*-pentylbenzene, their aqueous solubilities (at 0 mM $C_{14}E_8$ concentration in Figure 2a,b) are consistent with the reference values.^{25–27} The

(25) Sanemasa, I. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 1054.

(26) Tewari, Y. B.; Miller, M. M.; Wasik, S. P.; Martire, D. E. *J. Chem. Eng. Data* **1982**, *27*, 451.

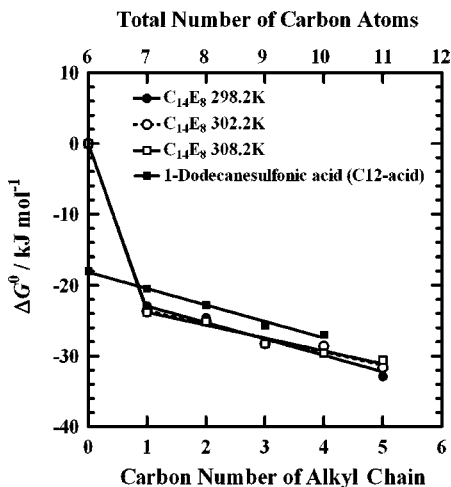


Figure 3. The Gibbs energy change (ΔG^0) for solubilization against the carbon number of the alkyl chain of solubilizates at different temperatures. The change in ΔG^0 for other systems is also shown.²⁴

magnitude of the error bars attached for the points indicates twice the standard deviation of the concentrations determined at least five times. As for benzene and toluene, the standard deviation was not determined, because the liquid volume placed inside changed for each experiment. On the other hand, the concentrations, except for the two mentioned above, were the maximum additive concentrations (MACs), because the solubilize phase coexisted in the system. The mean value of the solubilize concentrations below the cmc can be used for the monomer concentration in aqueous bulk [R] of the solubilize molecules. An increase in the solubilize concentration above the cmc is brought about by the incorporation of solubilize into micellar aggregates. Especially for benzene, the solubilize concentrations appear to decrease with C₁₄E₈ concentration, but they remain almost constant within the experimental error, which indicates that benzene molecules are not concentrated or incorporated into C₁₄E₈ micelles. The concentration of *n*-alkylbenzenes decreased in the order of (benzene > toluene >) ethylbenzene > *n*-propylbenzene > *n*-butylbenzene > *n*-pentylbenzene, which is the same order as the decrease in aqueous solubility, where (benzene > toluene >) represents the concentration dependence of the liquid volume placed inside. In other words, the results indicate that the solubilized amount in the aggregates becomes larger for more soluble solubilize in an aqueous bulk.

Once the size of micellar aggregates was found to be quite large (Table 1), the partition equilibrium was adopted to evaluate the Gibbs energy change for the transfer of solubilize molecules from the aqueous bulk to the large aggregate. In other words, the large molecular aggregate was regarded as a separate phase to examine whether reasonable values for the Gibbs energy change could be obtained by the partition equilibrium. The mole fractions of the solubilizates in an aqueous phase and the aggregate phase are given by eqs 1 and 2, respectively:

$$X_R^W = [R]/(55.5 + [R] + \text{cmc}) \quad (1)$$

$$X_R^A = ([R_t] - [R])/([C - \text{cmc}] + ([R_t] - [R])) \quad (2)$$

where [R_t] is the total equivalent concentration of the solubilize, C is the total concentration of the surfactant, and cmc is the critical micelle concentration at which solubility starts to increase

with surfactant concentration. The mole fractions can easily be determined from Figure 2a,b. The subscript R refers to the solubilize, and the superscripts W and A refer to the aqueous phase and the aggregate phase, respectively. The chemical potential in each phase is expressed as follows at temperature T and pressure P:

$$\mu_R^W = \mu_R^{\theta,W}(T,P) + RT \ln X_R^W \quad (3)$$

$$\mu_R^A = \mu_R^{\theta,A}(T,P + \Delta P) + RT \ln X_R^A \quad (4)$$

where ΔP is the difference in pressure between the aqueous phase and the aggregate phase, μ^θ is the standard chemical potential at infinite dilution for the aqueous phase, and μ^0 is the standard chemical potential for the micellar phase based upon a symmetrically standardized state. The assumption of ideality in eqs 3 and 4 can be reasoned by a small interaction parameter value (β value) for the mixed micellization of nonionic surfactants.²⁸ The following relationship results for the solubilize molecule under equilibrium:

$$RT \ln(X_R^A/X_R^W) = -\{\mu_R^{\theta,A}(T,P + \Delta P) - \mu_R^{\theta,W}(T,P)\} = -\Delta G^0 \quad (5)$$

From this equation, we can determine the Gibbs energy change for transfer (ΔG^0) of solubilize molecules from the aqueous phase to the aggregate phase. The ΔG^0 values thus obtained were plotted against the number of carbon atoms in the alkyl chain of the solubilizates at different temperatures (Figure 3). The ΔG^0 values after standing for 24 and 48 h did not show any significant difference, which suggests that the C₁₄E₈ solutions reached complete solubilization equilibrium within 24 h. The ΔG^0 value of 0 kJ mol⁻¹ for benzene indicates the fact that benzene molecules are not concentrated into C₁₄E₈ micelles. That is, its mole fraction in a micelle is assumed to be practically equal to that in an aqueous bulk phase, because ΔG^0 cannot be positively infinite. On the other hand, for other *n*-alkylbenzenes, the Gibbs energy change decreased with increasing alkyl chain length, or the solubilizates became more stabilized by solubilization with increasing the alkyl chain length of the solubilizates. The contribution per ethylene group of an *n*-alkyl chain of carbon number 1–5 to the Gibbs energy change ($\Delta G_{\text{CH}_2}^0$) is evaluated to be -2.3 kJ mol⁻¹ at 298.2 K, -1.9 kJ mol⁻¹ at 303.2 K, and -1.8 kJ mol⁻¹ at 308.2 K from the slope in the figure. The value at 298.2 K is smaller in magnitude compared with the values of -2.35 to -2.81 kJ mol⁻¹ for ionic surfactant systems.^{24,29,30} Therefore, it is more difficult for *n*-alkylbenzenes to be solubilized into the inner core of C₁₄E₈ micelles than into that of ionic surfactant micelles. Although the aggregation number of C₁₄E₈ is larger than that of ionic surfactant systems,³ the smaller Gibbs energy decrease for the transfer results from the larger hydrophilic part of the oxyethylene groups outside the micellar core.

From the variation of ΔG^0 with temperature, the enthalpy and entropy changes (ΔH^0 and ΔS^0) of solubilization can be evaluated by the following relations:

$$\Delta H^0 = \left[\frac{\partial(\Delta G^0/T)}{\partial(1/T)} \right]_P \quad (6)$$

$$\Delta S^0 = -(\Delta G^0 - \Delta H^0)/T \quad (7)$$

The enthalpy change can be estimated from the slope of the plots of $\Delta G^0/T$ versus $1/T$ (Figure 4). The ΔH^0 and $-T\Delta S^0$ values are illustrated in Figure 5, where the former value is a mean value

(27) Myrdal, P.; Ward, G. H.; Dannenfelser, R. M.; Mishra, D.; Yalkowsky, S. H. *Chemosphere* **1992**, *24*, 1047.

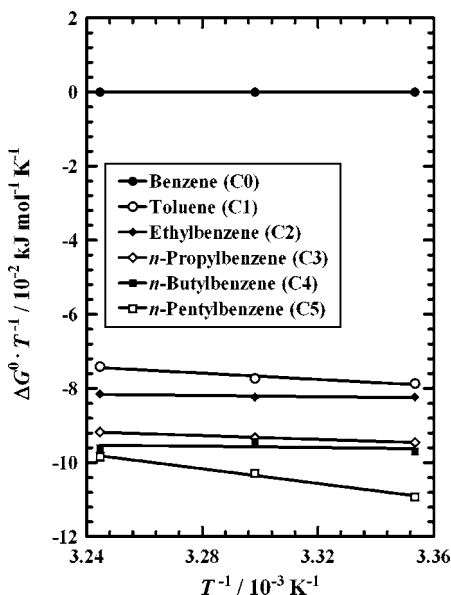


Figure 4. Plots of $\Delta G^0/T$ against T^{-1} to evaluate the enthalpy change (ΔH^0) for solubilization.

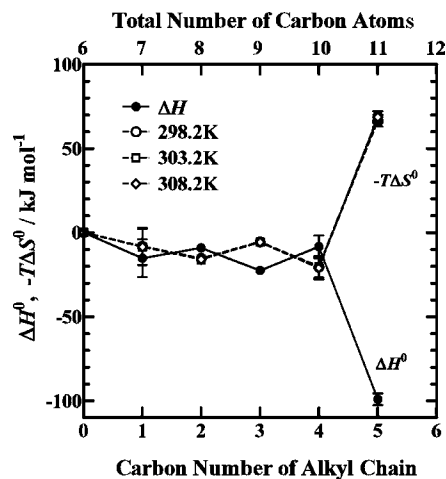


Figure 5. The enthalpy and the entropy changes for solubilization against the carbon number of the alkyl chain of solubilizates.

for different temperatures, whereas the latter values are obtained from ΔG^0 values at different temperatures.

The Gibbs energy change includes two terms, the enthalpy change (ΔH^0) and the entropy change ($-T\Delta S$). For toluene, ethylbenzene, *n*-propylbenzene, and *n*-butylbenzene, the negative values of both the enthalpy and the entropy terms positively contribute to the negative Gibbs energy changes in the present solubilizations. The results indicate that the solubilization was brought about equally both (1) by the negative enthalpy change that results mainly from London dispersion force between the solubilizate and the surfactant molecules in the micellar phase and (2) by the positive entropy change due to the destruction of the ordered structure of water molecules around the alkyl chain. On the other hand, the solubilization of *n*-pentylbenzene turns out to be enthalpy driven. This suggests that the fixation of *n*-pentylbenzene molecules in the micelle is driven more by a stronger interaction between the micelle and the solubilizate relative to that of the other *n*-alkylbenzenes. Consequently, the

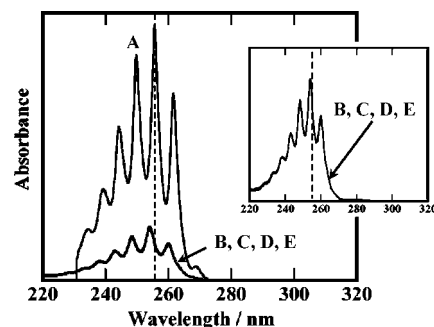


Figure 6. Absorption spectra of benzene (A) in *n*-dodecane, (B) in $C_{14}E_8$ aqueous solution above the cmc, (C) in $C_{14}E_8$ aqueous solution at the cmc, (D) in $C_{14}E_8$ aqueous solution below the cmc, and (E) in water, and the highest peak of the spectrum in *n*-dodecane (- - -). (Inset) Enlarged absorbance ordinate.

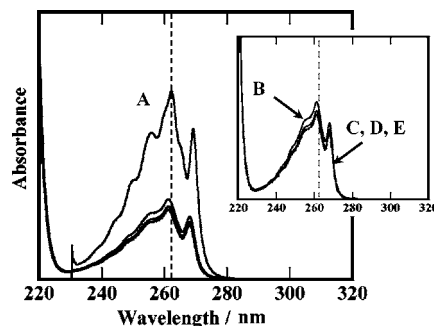


Figure 7. Absorption spectra of toluene (A) in *n*-dodecane, (B) in $C_{14}E_8$ aqueous solution above the cmc, (C) in $C_{14}E_8$ aqueous solution at the cmc, (D) in $C_{14}E_8$ aqueous solution below the cmc, and (E) in water, and the highest peak of the spectrum in *n*-dodecane (- - -). (Inset) Enlarged absorbance ordinate.

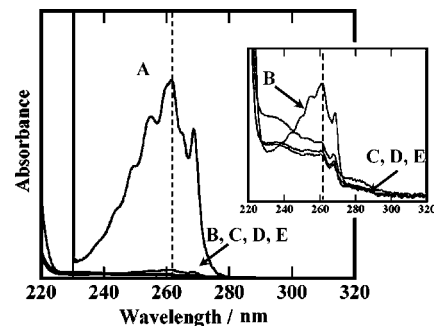


Figure 8. Absorption spectra of *n*-butylbenzene (A) in *n*-dodecane, (B) in $C_{14}E_8$ aqueous solution above the cmc, (C) in $C_{14}E_8$ aqueous solution at the cmc, (D) in $C_{14}E_8$ aqueous solution below the cmc, and (E) in water, and the highest peak of the spectrum in *n*-dodecane (- - -). (Inset) Enlarged absorbance ordinate.

ΔH^0 value contributes more to the negative Gibbs energy change than does the $-T\Delta S^0$ value, the effect of a less movable fixation of the solubilizate molecules in the micelles upon solubilization.

Finally, the spectrum changes were investigated in order to get more detailed information about the location of the solubilizates in the micelle. As shown in Figures 6 and 7, the absorption spectra below, above, and at the cmc for benzene and toluene can be traced together, and the highest peak of the spectrum shifted to a higher wavelength in *n*-dodecane, where the dotted lines in the figures indicate the wavelength at the highest peak in *n*-dodecane. The absorption spectrum of a molecule depends on the dielectric constant of the environment where the molecules locate, and the dielectric constants of water, *n*-dodecane, and ethylene glycol (EG_n ; $n = 1-6$) are 79, 2, and 15-40,

(28) Rubingh, D. N. In *Solution Chemistry of Surfactants*; Mittal, K. L., Ed.; Plenum Press: New York, 1979; Vol. 1, p 337.

(29) Doi, Y.; Kawashima, Y.; Matsuoka, K.; Moroi, Y. *J. Phys. Chem. B* **2004**, *108*, 2594.

(30) Lee, J. N.; Moroi, Y. *J. Colloid Interface Sci.* **2004**, *273*, 645.

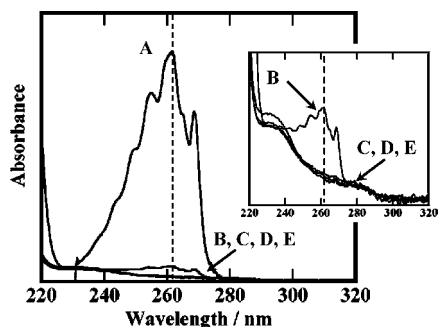


Figure 9. Absorption spectra of *n*-pentylbenzene (A) in *n*-dodecane, (B) in C₁₄E₈ aqueous solution above the cmc, (C) in C₁₄E₈ aqueous solution at the cmc, (D) in C₁₄E₈ aqueous solution below the cmc, and (E) in water, and the highest peak of the spectrum in *n*-dodecane (---). (Inset) Enlarged absorbance ordinate.

respectively.^{31–33} Hence, it can be said that benzene and toluene do not locate in the core of micelle. In addition, the fact that the spectra of benzene and toluene remain the same both above and below the cmc must result from their location in the medium of relatively high dielectric constant made of oxyethylene parts and water molecules, because there are many water molecules around the E₈ groups in the micelles. As far as the spectra are concerned, they are quite the same for benzene and toluene, which means that the location of their benzene rings is very similar (an outer micelle). However, the methyl group of toluene plays a very important role in solubilization. On the other hand, for *n*-butylbenzene and *n*-pentylbenzene, their spectra above the cmc shifted to a higher wavelength and were quite similar to those

(31) *Handbook of Chemistry and Physics*, 50th ed.; The Chemical Rubber Co.: Cleveland, OH, 1969.

(32) Schrödle, S.; Buchner, R.; Kunz, W. *J. Phys. Chem. B* **2004**, *108*, 6281.

(33) Rivas, M. A.; Iglesias, T. P.; Pereira, S. M.; Banerji, N. *J. Chem. Thermodyn.* **2006**, *38*, 245.

in *n*-dodecane (Figures 8 and 9). These changes in spectrum were also observed for *n*-alkylbenzenes solubilized into micelles of other ionic surfactant systems,³⁰ which supported the fact that the solubilized longer *n*-alkylbenzenes moved into the inner core of the micelles.

Conclusions

The concentration of toluene, ethylbenzene, *n*-propylbenzene, *n*-butylbenzene, and *n*-pentylbenzene increased with the C₁₄E₈ concentration above the cmc. However, the concentration of benzene remained constant over the C₁₄E₈ concentration range examined, which indicated that benzene molecules were not concentrated into C₁₄E₈ micelles. The Gibbs energy change of solubilization evaluated by using the phase separation model decreased with increasing alkyl chain length of the solubilizates. Therefore, it was easier for more hydrophobic substance to be solubilized into C₁₄E₈ micelles. The ΔH^0 and $-T\Delta S^0$ values for solubilization and the spectral change of *n*-alkylbenzenes indicated that shorter *n*-alkylbenzenes were located in the outer micelle, while the solubilization site moved into the inner core of the micelle with increasing alkyl chain length of the solubilizates.

Acknowledgment. This work was supported by Grant-in-Aid for Scientific Research 17310075 from the Japan Society for the Promotion of Science and by Grant 17650139 from the Ministry of Education, Science and Culture, Japan, and by the Japan–Taiwan Joint Research Program, which are gratefully acknowledged. This work (H.N.) was also supported by Research Fellowships of the Japan Society for the Promotion of Science for Young Scientists (18.9587).

LA700612X