1:1 and 1:2 Complexes between Long-Chain Surfactant and α-Cyclodextrin Studied by NMR

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One- and two-dimensional proton NMR spectroscopy was applied to determine the equilibrium constants and the solution structures of 1:1 and 1:2 complexes between dodecyltrimethylammonium bromide (DTAB) and α-cyclodextrin (α-CD). Chemical shift data of protons of DTAB and α-CD were used to determine reliable 1:1 and 1:2 binding constants and chemical shift variations $\Delta\delta_{complex}$ at full binding. The intensity of intermolecular crosspeaks in ROESY spectra of aqueous solutions containing α-CD and DTAB allowed us to determine detailed structures of the complexes. The correlation coefficient for the relation between these ROE intensities and the effective interproton distances had a maximum at a penetration depth, where the time-average structures of the 1:1 and 1:2 complexes were determined. As the alkyl chain of a surfactant is longer, the maximum correlation coefficient decreased and the peak of the relation between these ROE intensities and the effective interproton distances became broader. Furthermore, the $\Delta\delta_{1:1complex}$ values for the DTAB protons, plotted against the position located in the α-CD cavity, had a peak near the proton H3 of α-CD. The peak became lower and broader, as the alkyl chain is longer. These relations of $\Delta\delta_{1:1complex}$ and ROE intensities with the penetration depth suggest that DTAB shuttles at a wider distance in the α-CD cavity than shorter-chain surfactants. In the 1:2 complex two α-CD molecules adopt the head-to-head structure.

Introduction

Cycloamyloses (cyclodextrins, CDs) have homogeneous toroidal structures, formed from D(+)-glucose units linked in a cycle. The toroidal structure has a hydrophilic surface, making CDs water-soluble, whereas the cavity is composed of the glucoside methin groups, giving it a hydrophobic environment. Cyclohexaamylose (α-CD) has an inner diameter and a depth of approximately 0.45 and 0.67 nm, respectively.[1,2] This CD cavity, therefore, can accommodate surfactants very well. Complex formation between surfactants and CDs has been extensively investigated by spectroscopic,[3−8] electrochemical,[9−11] surface chemical,[12,13] computational,[14,15] and crystallographic methods.[16,17]

The alkyl chains of surfactants are much longer than the depth of α-CD, so that they can bind two α-CD molecules to form 1:2 complexes.[10−13] There recently seems to be a general agreement: electromotive force measurements, fluorescence or dye method, and surface tension method provide reliable equilibrium constants of 1:1 complexes, although some of the equilibrium constants of 1:2 complexes are still in conflict with one another.[10,13] These are essentially methods for determining the concentration of a surfactant in the free state and are not very suitable for the determination of the 1:2 binding constant for the following reasons: the 1:2 binding constants are much smaller than the 1:1 binding constant for a surfactant and the observed quantities, such as electromotive forces and surface tensions, exhibit monotonic changes with increasing concentration of the surfactant and CD.

The NMR chemical shift has been utilized for binding constant determination of surfactants and CDs.[4−8] Very recently, it has been demonstrated that applications of this method require a special attention to references of chemical shifts.[6,8,18,19] This method is based on the difference in chemical shift between the free and bound states of a surfactant or CD, so that a binding constant and the chemical shift at the bound state must be estimated for a complex. This is a demerit and a merit. The chemical shift at the bound state must be treated as an adjustable parameter. This is a demerit, because an unknown parameter increases. However, observed chemical shifts of many protons of the surfactant and CD are obtained and some of them may exhibit biphasic changes with increasing concentration of the surfactant and CD. These data will allow us to detect multiple complexes and to determine multiple binding constants.[5,15] Furthermore, the observed chemical shift can provide information about the structure of a complex in solution.[5,8,15]

NMR data, such as NOE crosspeaks, vicinal spin−spin coupling constants, and chemical shifts generally provide information on rough solution structures of CD inclusion complexes.[3−8,15] Recently, on the basis of ROESY intensity data, we determined rather detailed solution structures of 1:1 complexes of 1-propanol, sodium propanesulfonate,[6] hexyltrimethylammonium (HTAB), and octyltrimethylammonium (OTAB) bromides with α-CD.[8] Because these surfactants have short chains, they form 1:1 complexes alone with α-CD. Although longer chain surfactants form 1:2 complexes with α-CD, little is known about their solution structures. Furthermore, as the chain becomes longer, it is suggested that the α-CD molecule complexed with a surfactant molecule can move more remarkably on the chain.[8]

In the present work, we investigated formation of complexes between α-CD and dodecyltrimethylammonium bromide (DTAB) by ^{1}H NMR. From analysis of chemical shifts of DTAB and α-CD, rather accurate 1:1 and 1:2 binding constants and

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chemical shift variations for these complexes were determined.[10,13] From the ROESY intensity data on 1:1 and 1:2 complexes, the solution structures of these complexes were estimated. From the chemical shift variation and ROESY intensity data, it will be suggested that an α-CD molecule shuttles on the dodecyl chain.

Experimental Section

Materials. Commercial samples of α-CD (Ensuiko Research Laboratories, Yokohama), tetramethylammonium chloride (TMA, Nacalai Tesque, Kyoto), DTAB (Tokyo Kasei), and 99.9 at. % D deuterium oxide (Aldrich) were used as received.

NMR Measurements. All ^{1}H NMR experiments were carried out in deuterium oxide at 298.2 ± 0.1 K. The NMR spectra were obtained with a JEOL Lambda 500 spectrometer. The chemical shift and spin−spin coupling constant were determined by Nuts data processing software (Acorn). The chemical shifts of DTAB and α-CD proton were determined as a function of the α-CD concentration, up to 42.15 mmol dm^{-3} (mM), in the presence of 3.00 mM DTAB. These chemical shifts were referenced to the internal 0.5 mM TMA signal at 3.176 ppm, which had been determined using sodium 4,4-dimethyl-4-silapentane-1-sulfonate as the external standard.[8,18]

Two-dimensional rotating frame nuclear Overhauser effect spectroscopy (ROESY) for two solutions containing 3.00 mM DTAB and 3.30 mM α-CD as well as 3.00 mM DTAB, and 29.16 mM α-CD was performed at 500 MHz with the JEOL standard pulse sequences; the data consisted of 8 transients collected over 2048 complex points. A mixing time of 250 ms, a repetition delay of 1.2 s, and a 90° pulse width of 11.0 μs were used. The ROESY data set was processed by applying an exponential function in both dimensions and zero-filling to 2048 × 2048 real data points prior to the Fourier transformation. All ROESY spectra were made symmetrical about the diagonal. Small crosspeaks were neglected, because their magnitude was close to that of noise. The volume of a ROESY crosspeak was calculated by a summation of spectrum intensities with a certain region around the crosspeak and slightly depended on the region of integration, peak overlap, and the signal-to-noise ratio. The critical micelle concentration (cmc) of DTAB is 14 mM.[20] Therefore, all NMR measurements were carried out below the cmc. The assignment of DTAB protons was estimated from those for OTAB and HTAB.[8]

Molecular Modeling. The solution structure of the OTAB-α-CD complex was used to construct those of the DTAB-α-CD complex.[8] The α-CD molecule is almost symmetric around the *x*-axis, where the O4 plane is located at $x = 0$. The side of the primary hydroxyl groups has a negative *x* value, whereas that of the secondary hydroxyl groups has a positive *x* value. The structure of the α-CD dimer in the 1:2 complex was modeled on the basis of the crystal structures of the α-CD complexes with 4,4′-biphenyldicaboxylic acid and benzaldehyde.[21,22]

Calculations and molecular graphics were carried out simultaneously using our own software with a personal computer running Microsoft Windows 2000. The relative position of α-CD and the guest can be easily varied and be shown digitally on the display.[23]

Results

Chemical Shifts and Binding Constants. In the ^{1}H NMR spectra of the DTAB and α-CD solutions, the α- and β-methylene protons (H_α and H_β) of DTAB exhibited complicated multiplet signals around 3.3 and 1.8 ppm, respectively. The ω-methyl proton (H_ω) of DTAB exhibited a sharp triplet signal at 0.9 ppm. The intermediate nine methylene groups consist of two major signals overlapping with one another. In the absence of α-CD, the signals at the high and low field were assigned to the ς- to λ-methylene groups and the γ- to ϵ-methylene groups, respectively; these signals changed with increasing α-CD concentration (Supporting Information and Figures 1, 2, and 6 to be shown below).

The H_1 proton of α-CD appeared near 5.1 ppm, the protons of H_3, H_5, and H_6 resonated around 3.85 ppm, and those of H_2 and H_4 were assigned to the peaks centered at 3.6 ppm.[8] Because two protons, H_{6R} and H_{6S}, of H_6 were distinguishable from each other by computer simulations of NMR spectra, we dealt with them separately (Supporting Information). The H_1, H_2, and H_4 protons are located on the outer surface of the CD cavity, whereas those of H_3 and H_5 are on the inner surface.

We presumed that the complexation and decomplexation between DTAB (AT) and α-CD (CD) are rapid on the NMR time scale and that DTAB and α-CD form 1:1 and 1:2 complexes (AT−CD and AT−CD$_2$). Under these conditions the chemical shift of DTAB can be written as

$$\delta = ([\mathrm{AT}]\delta_{AT} + [\mathrm{AT{-}CD}]\delta_{AT-CD} + [\mathrm{AT{-}CD_2}]\delta_{AT-CD2})/C_{AT}$$
$$= ([\mathrm{AT}]\delta_{AT} + K_1[\mathrm{AT}][\mathrm{CD}]\delta_{AT-CD} + K_2[\mathrm{AT}][\mathrm{CD}]^2\delta_{AT-CD2})/C_{\mathrm{AT}} \quad (1)$$

Here δ_{AT}, δ_{AT-CD}, and δ_{AT-CD_2} stand for the chemical shifts of AT in the free state, the 1:1 complex, and the 1:2 complex; K_1 and K_2 are the binding constants for 1:1 and 1:2 complexes; [AT] and [CD] are the molarities of DTAB and α-CD in the free state; and C_{AT} denotes the total molarity of DTAB. The corresponding equation holds for the chemical shift of α-CD:

$$\delta = ([\mathrm{CD}]\delta_{CD} + [\mathrm{AT{-}CD}]\delta_{AT-CD} + 2[\mathrm{AT{-}CD_2}]\delta_{AT-CD_2})/C_{CD}$$
$$= ([\mathrm{CD}]\delta_{CD} + K_1[\mathrm{AT}][\mathrm{CD}]\delta_{AT-CD} + 2K_2[\mathrm{AT}][\mathrm{CD}]^2\delta_{AT-CD_2})/C_{CD} \quad (2)$$

where C_{CD} stands for the molarity of α-CD.

Figure 1 shows the chemical shifts of protons of (a) DTAB and (b) α-CD as a function of the α-CD concentration, where the DTAB concentration was kept constant at 3 mM. Here the ordinate denotes the values of (a) $\delta - \delta_{AT}$ and (b) $\delta - \delta_{CD}$, respectively. The chemical shifts changed abruptly around 3 mM α-CD. These abrupt biphasic changes indicate that DTAB and α-CD form the 1:1 and 1:2 complexes. Roughly saying, the 1:1 complex is formed below 3 mM, whereas the 1:2 complex begins to be formed above 3 mM.

These chemical shift data were employed to determine the best-fit binding constants ($K_1 = 18200$ M^{-1} and $K_2 = 350$ M^{-1}) and chemical shift variations at full binding ($\Delta\delta_{AT-CD} = \delta_{AT-CD} - \delta_{AT}$, $\Delta\delta_{AT-CD} = \delta_{AT-CD} - \delta_{CD}$, $\Delta\delta_{AT-CD_2} = \delta_{AT-CD_2} - \delta_{AT}$, and $\Delta\delta_{AT-CD_2} = \delta_{AT-CD_2} - \delta_{CD}$) using eqs 1 and 2. Table 1 summarizes the binding constants and chemical shift variations for the DTAB−α-CD systems. Our chemical shift variations at full binding are consistent with the literature values for shorter-chain surfactants.[8,24]

For DTAB the binding constants $K_1 = 17000$ M^{-1} and $K_2 = 1000$ M^{-1} were determined by electromotive force measurements[10] and $K_1 = 17000$ M^{-1} was determined by surface tension measurements.[13] The binding constant $K_1 = 2480$ M^{-1}, deter-

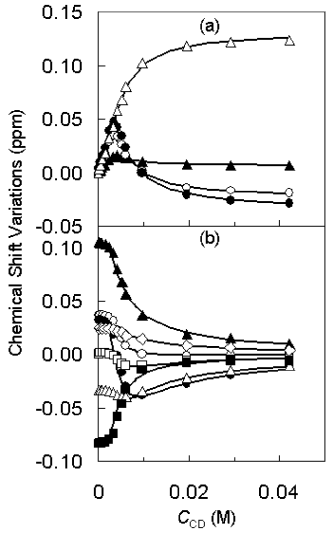

Figure 1. Chemical shift variations of protons of (a) DTAB and (b) α-CD for solutions of 2.998 mM DTAB and α-CD as a function of α-CD concentrations. (a) H_α; ○, H_β; ●, H_ω; △, H_N; ▲, and (b) H_1; ○, H_2; ●, H_3; △, H_4; ▲,H_5; □, H_{6S}; ■, H_{6R}; ▽. The solid lines are calculated using the values of K_1, K_2, and $\Delta\delta_{AT-CD}$ given in Table 1.

TABLE 1: Binding Constants and Chemical Shift Variations (ppm)[a] for the 1:1 and 1:2 Complexes of DTAB and α-CD

	1:1	1:2
K (mM^{-1})	18.2	0.35
$\Delta\delta_{H_\omega}$	0.042	0.133
$\Delta\delta_{H_\gamma}$	0.076[b]	-0.091[b]
$\Delta\delta_{H_\beta}$	0.063	-0.036
$\Delta\delta_{H_\alpha}$	0.047	-0.025
$\Delta\delta_{HN}$	0.018	0.006
$\Delta\delta_{H1}$	0.037	-0.009
$\Delta\delta_{H2}$	0.040	-0.087
$\Delta\delta_{H3}$	-0.030	-0.068
$\Delta\delta_{H4}$	0.102	0.052
$\Delta\delta_{H5}$	0.002	-0.024
$\Delta\delta_{H6S}$	-0.083	-0.013
$\Delta\delta_{H6R}$	0.023	0.023

[a] $\Delta\delta = \delta_{complex} - \delta_{AT}$ for DTAB and $\Delta\delta = \delta_{complex} - \delta_{CD}$ for α-CD. [b] These values were not used to determine the binding constants, because of the low accuracy of observed chemical shifts.

mined by electric conductance measurements for dodecyltrimethylammonium chloride, is rather small.[9] In comparison with these literature values, the present 1:1 and 1:2 binding constants for DTAB and α-CD are reasonable.

ROESY Spectra and Structures of Complexes. A partial ROESY spectrum of a solution containing 3.00 mM DTAB and 3.30 mM α-CD is shown in Figure 2. Under this condition the concentration of the 1:1 complex DTAB−CD is 2.34 mM. A crosspeak between the *N*-methyls (H_N) and the β-methylenes (H_β) is observed. This peak is due to the proximity of these protons in a DTAB molecule. Such intramolecular crosspeaks for each of DTAB and α-CD are useful to establish the assignments of signals. The intermolecular ROE crosspeaks between DTAB and α-CD can provide information about the structures of complexes.

The volume (ROE intensity) of the crosspeak was determined by integration. The ROE intensity, *ROE*, of the crosspeak is proportional to the number of equivalent protons. When the numbers of equivalent protons of α-CD and DTAB in the crosspeak are denoted by n_{CD} and n_{AT}, respectively, $ROE/n_{CD}n_{AT}$ becomes larger with decreasing distance between these protons. In Table 2, the $ROE/n_{CD}n_{AT}$ values are given for intermolecular

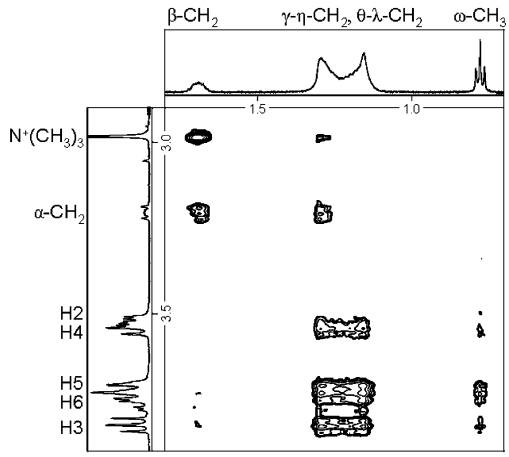

Figure 2. ROESY spectrum of a solution containing 3.00 mM DTAB and 3.30 mM α-CD.

TABLE 2: Intensities, $ROE/n_{AT}n_{CD}$, of ROESY Crosspeaks for the 1:1 Complex of DTAB and α-CD Obtained from an Aqueous Solution Containing 3.00 mM DTAB and 3.30 mM α-CD

	DTAB−α-CD			
	H_3	$H_{2,4}$	H_5	H_6
H_N	0	0	0	0
H_α	0	0	0	0
H_β	0.18	0	0.14	0
$H_{\gamma-\eta}$	1.51	0.42	1.63	0.29
$H_{\theta-\lambda}$	1.63	0.46	2.28	0.43
H_ω	0.31	0.25	0.83	0.22

crosspeaks. Because there is no crosspeak between H_1 and the protons of DTAB, the H_1 region was omitted from Figure 2 and Table 2. The signals of H_2 and H_4 were overlapped with each other, and they were regarded as being equivalent protons ($n_{CD} = 12$). Similarly, the intermediate methylene protons of DTAB except for H_α and H_β were regarded as two groups of equivalent protons; $H_{\gamma-\eta}$ ($n_{AT} = 10$) and $H_{\theta-\lambda}$ ($n_{AT} = 8$). The methyl group (H_ω) exhibits larger crosspeaks with H_5 than those with H_3 and the α-methylene group (H_α) has no crosspeak with any of the α-CD protons. These findings indicate that the dodecyl group of DTAB is incorporated in the cavity of α-CD from the secondary alcohol side.

When internal rotations of a molecule are slower than the overall tumbling, we can expect eq 3:[25,26]

$$ROE = k \sum_{i=1}^{n_{CD}} \sum_{j=1}^{n_{AT}} d_{CDiATj}^{-6} \quad (3)$$

Here d_{CDiATj} denotes the distance between a CD proton (CD*i*) and an AT proton (AT*j*). For simplicity the effective distance, d_{eff}, is defined as:

$$(d_{eff})^{-6} = (1/n_{CD}n_{AT}) \sum_{i=1}^{n_{CD}} \sum_{j=1}^{n_{AT}} d_{CDiATj}^{-6} \quad (4)$$

From eqs 3 and 4 we can expect that $ROE/n_{CD}n_{AT}$ increases, as the two protons become closer.

We constructed a starting structure of the 1:1 α-CD complex of DTAB by substituting the dodecyl chain on the basis of the solution structure of the α-CD complex of OTAB.[8] Then, the DTAB molecule was moved along the symmetry axis of α-CD so that better structures could be found. We assumed that the

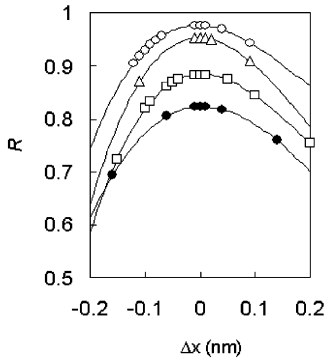

Figure 3. Dependence of the correlation coefficient on the penetration depth, *x*, of the guest in a fixed α-CD cavity for PrOH (open circles), HTAB (triangles), and OTAB (squares), and DTAB (closed circles). The displacement of the guest from the most probable position is denoted by Δ*x*, where the primary hydroxyl side has a positive Δ*x* value. The original data on PrOH, HTAB, and OTAB were taken from Funasaki et al,[6] and Funasaki et al.[8].

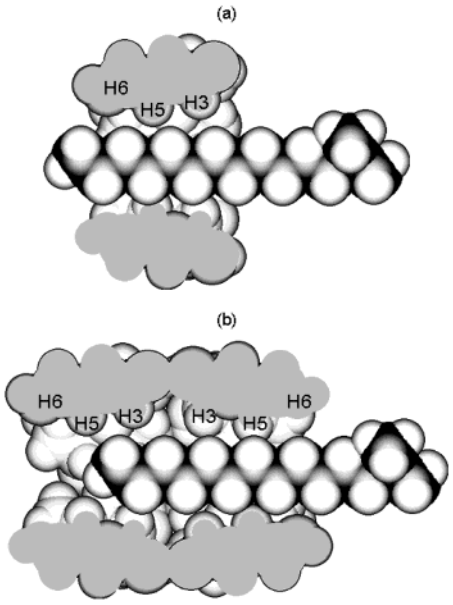

Figure 4. Time-average structures of (a) the 1:1 DTAB−α-CD complex and (b) the 1:2 DTAB−α-CD_2 complex.

best structure has the largest correlation coefficient *R* in the following empirical equation:

$$ROE/n_{CD}n_{AT} = kd_{eff}^{-a} \quad (5)$$

According to eqs 3 and 4, the exponent *a* in eq 5 should be 6. The value for d_{eff} was calculated as a function of the penetration depth (*x*) of the decyl chain, and then the correlation coefficient (*R*) was evaluated. The primary hydroxyl side has a positive *x* value and the O_4 plane of α-CD is located at $x = 0$. As shown in Figure 3, the largest *R* value ($R^2 = 0.678$) was obtained at an *x* value, when the values for *k* and *a* were 0.1312 nm^6 and 2.20. The ordinate is expressed as the displacement from the best penetration depth. For this best structure (Figure 4, part a), the observed $ROE/n_{CD}n_{AT}$ values are plotted against the d_{eff} values in Figure 5. The *R* values for the α-CD complex with propanol (PrOH), hexyltrimethylammonium bromide (HTAB), and octyltrimethylammonium bromide (OTAB) are also shown in Figure 3. Here it is noted that the *R* value decreases with increasing chain length of surfactants.

A partial ROESY spectrum of a solution containing 3.00 mM DTAB and 29.16 mM α-CD is shown in Figure 6. Because

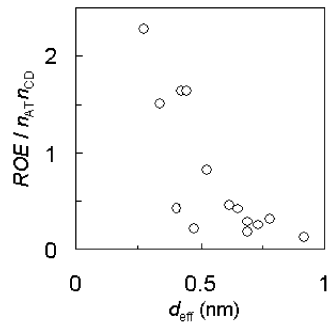

Figure 5. Plots of ROE intensities against the effective interproton distances calculated for the time-average structure of the 1:1 DTAB−α-CD complex (Figure 4).

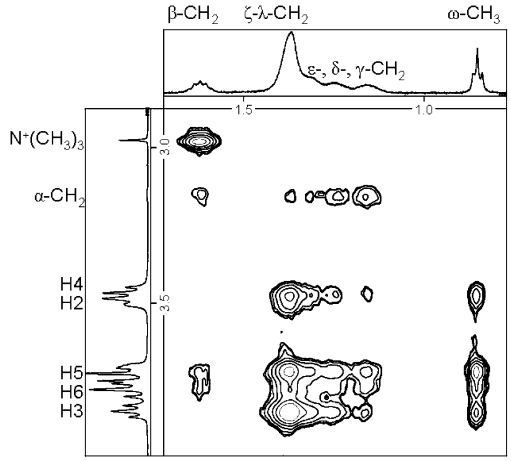

Figure 6. ROESY spectrum of a solution containing 3.00 mM DTAB and 29.16 mM α-CD.

TABLE 3: Intensities, $ROE/n_{AT}n_{CD}$, of ROESY Crosspeaks for the 1:2 Complex of DTAB and α-CD Obtained from an Aqueous Solution Containing 3.00 mM DTAB and 29.16 mM α-CD

	DTAB−α-CD_2		
	H_3	$H_{2,4}$	$H_{5,6}$
H_N	0	0	0
H_α	0	0	0
H_β	0	0	0.10
H_γ	0.11	0.01	0.29
H_δ	0.84	0.06	0.44
$H_{\epsilon-\lambda}$	2.27	0.29	0.53
H_ω	1.20	0.38	1.18

under this condition the mole percent $[AT-CD_2]/C_{AT}$ is 89, most of these intensities will be due to the 1:2 complex AT−CD_2. Here it is noted that the intermediate methylenes are better resolved than those for the 1:1 complex (Figure 2). The ROE intensity for these methylenes and the α-methylene generally decreased with increasing distance. However, this rule does not hold for β-methylene. Because α- and β-methylenes have a spin−spin coupling, the ROE intensity is decreased.[26] The γ-methylene exhibited a large low-field shift on 1:1 complex formation, whereas it exhibited a large high-field shift on 1:2 complex formation (Table 1 and Figures 2 and 6). Because the signals of H_5 and H_6 were overlapped with each other, they were regarded as being equivalent protons. The ROE intensities for intermolecular crosspeaks alone were given in Table 3. In comparison with the 1:1 complex (Table 2), the ROE intensities for H_ω are large. This indicates that the terminal methyl group is incorporated in an α-CD cavity.

In crystals CDs form several packing structures.[27] The dimer of α-CD in the 1:2 complex AT−CD_2 is most likely to form

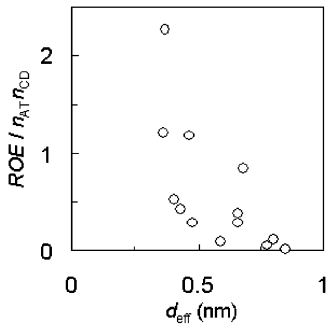

Figure 7. Plots of ROE intensities against the effective distances calculated for the most probable structure of the 1:2 DTAB−α-CD_2 complex.

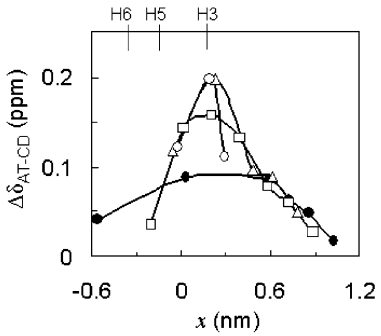

Figure 8. The $\Delta\delta_{AT-CD}$ values of methyl and methylene protons plotted against the distance, x, from the O_4 plane of α-CD for PrOH (open circles), HTAB (triangles), OTAB (squares), and DTAB (closed circles). The primary hydroxyl side has a positive x value and the O_4 plane of α-CD is located at $x = 0$. The original data on PrOH, HTAB, and OTAB were taken from Funasaki et al.[6] and Funasaki et al.[8]

the channel structure. This structure can be subdivided into three structures called head-to-head, head-to-tail, and tail-to-tail. As the head-to-head and tail-to-tail structures, the crystal structure of the 4,4′-biphenyldicaboxylic acid complex was employed.[21] As the head-to-tail structure, the crystal structure of benzaldehyde complex was used.[22] For each of these structures the dodecyl chain was moved along the α-CD cavity to seek the best structure satisfying eq 5. The values for n_{CD} and d_{eff} were calculated for two CD molecules in the 1:2 complex.

The correlation coefficient was calculated for each penetration depth and was used as the criterion of best fitting. The correlation coefficient at the best penetration depth for the head-to-head structure was 0.800, whereas those for the head-to-tail structure and the tail-to-tail structure were 0.726 and 0.740, respectively. In the last two structures, the DTAB molecule is rather distant from the second α-CD molecule. In the ROESY spectrum for the 1:2 complex, no crosspeak of H_1 with H_5 and H_6 was observed. This finding is inconsistent with the head-to-tail structure. Therefore, the head-to-head structure was the best of the three structures. Finally, the best structure of the 1:2 complex AT−CD_2 is shown in part b, Figure 4. The ROE intensities are plotted against the effective distances calculated for this best structure in Figure 7: the best fit parameters of $k = 0.0363$ nm^6 and $a = 3.639$ in eq 5 were obtained.

Correlation between Chemical Shifts and Structures. Chemical shift variations $\Delta\delta_{complex}$ provide some information about the structure of the complex. Although those values, quantitatively analyzed on the basis of ring current effects of benzene, were used to determine the solution structures of CD complexes of aromatic guests,[28,29] this was not the cases for aliphatic guests.[30] Very recently, however, we have found empirical relationships between the chemical shift variation and the solution structure for the α-CD complexes with PrOH, HTAB, and OTAB.[8] These relationships were applied to the 1:1 α-CD complexes with DTAB.

In Figure 8 the $\Delta\delta_{AT-CD}$ values for DTAB protons are plotted against the distances of protons from the O_4 plane of α-CD that is located at $x = 0$. The x values for equivalent protons were averaged over these protons. The $\Delta\delta_{AT-CD}$ values for the α-CD complexes with PrOH, HTAB, and OTAB are also shown in Figure 8. The $\Delta\delta_{AT-CD}$ values for protons near H_3 have a maximum of about 0.2 ppm. Here it is noted that the $\Delta\delta_{AT-CD}$ values for DTAB have a small and broad peak. This finding suggests that α-CD shuttles on the dodecyl chain, if the $\Delta\delta_{AT-CD}$ value is a function of x alone in an α-CD cavity.

Discussion

Rather reliable binding constants for surfactant−CD systems forming multiple complexes were obtained by potentiometry,[10,11] surface tension,[12] NMR chemical shift,[5] and fluorescence probe methods.[31] These methods used quantitative analyses of monotonic changes in observed quantities with increasing concentration of surfactant or CD. The present NMR data provide qualitative, as well as quantitative, evidence for multiple complexations: as shown in Figure 1, the chemical shifts for H_α, H_β, H_1, H_2, and H_5 change the direction of variation at the 1:1 molar ratio of DTAB and α-CD (3 mM). These variations allowed us to determine more reliable 1:2 binding constants than other methods. The present 1:1 binding constant determined by NMR in deuterium oxide is larger than those determined by electromotive force and surface tension measurements in hydrogen oxide by 6%.[10,13] This enhancement in deuterium oxide has been found for many systems of cyclodextrins.[32]

The widely used internal standard for NMR studies in aqueous solution is sodium 4,4-dimethylsilyl-4-silapentane-1-sulfonate (DSS), but it can interact with CDs and cationic peptides, diminishing its value for such studies.[18,33] TMA is a good internal standard for CD and cationic surfactants.[18] New internal standards have been proposed for such systems.[33,34]

The chemical shift variation $\Delta\delta_{complex}$ with complex formation has not been fully used to estimate the structure of the CD complex with various guest molecules, except for aromatic molecules.[28−30] In Figure 8 it is notable that $\Delta\delta_{AT-CD}$ has a small and broad peak. Propanol binds rather firmly to α-CD by hydrophobic and hydrophilic interactions; minor displacements from the stable structure cause major unfavorable interactions.[6] On the other hand, a large displacement of DTAB would have only a small effect on the stability of the 1:1 complex, as expected from the structure of part a in Figure 4. As expected from Figure 8, an intermediate proton of DTAB has a chemical shift variation of ca. 0.2 ppm near H_3 and a smaller value associated with being distant from there. Then, the time-average value will be observed. Therefore, even if the time-averaged position is close to H_3, the observed chemical shift variation for the DTAB proton is smaller than those for shorter surfactants.

For CD complexes, ROE intensity data are usually categorized in a qualitative grade, such as strong (++) and weak (+) peaks.[30] The merit of a quantitative treatment of these data is to account for the number of protons. A guest molecule and CD have several equivalent protons, respectively, and some crosspeaks can consist of nonequivalent protons having similar chemical shifts. The ROE intensity of the crosspeak divided by the number of these protons can be connected with the interproton distance by eqs 4 and 5 and allows us to determine a rather detailed solution structure of the CD complex. Equation 5 is an empirical relation, which would take account of

translational and other motions of DTAB relative to α-CD. For a rigid molecule, such as sodium taurocholate, the exponent *a* in eq 5 is 6, as expected from eqs 3 and 4.[35]

The effect of the translational motion of DTAB also appears in Figure 3. The best correlation coefficient for DTAB is smaller than those for the shorter surfactants. The structures of the complexes shown in Figure 4 will be time-averaged and should not be regarded as rigid bodies. The observed ROE intensity will be proportional to the population of a complex, apart from the interproton distance. The dodecyl protons of DTAB are present at various positions in the α-CD cavity as the result of a rapid shuttle motion. This leads to a worse correlation with a single structure of the complex. For instance, a small ROE crosspeak between protons H_β and H_5 is observed, despite a large effective distance of 0.9 nm (Figures 4 and 5). This distance is much larger than the upper limit of about 0.4 nm for crosspeaks.[30] Protons H_β and H_5 can approach each other below this limit for a shallower penetration of DTAB, though this is a less probable structure.

Very recently, cyclodextrin-based interlocked molecules have attracted strong research interests.[36] The DTAB−α-CD complex is an interlocked molecule called a pseudorotaxane. It has been demonstrated that α-CD molecules shuttle on a poly(ethylene oxide) chain,[37−39] where the head-to-head/head-to-tail ratio is estimated to be 2:1.[38] The present NMR study suggests that an α-CD molecule shuttles on a dodecyl chain in aqueous solution, and indicates that the head-to-head structure of the α-CD dimer is found in the 1:2 complex (Figure 4). The present result and approach will be applicable to other supramolecular systems.[35]

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Supporting Information Available: One-dimensional 500 MHz NMR spectra of 3 mM DTAB and α-CD (up to 42.15 mM) are available. This material is available free of charge via the Internet at http://pubs.acs.org.

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