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# Conductometric Determination of the Association Constants of *β*-Cyclodextrin with Amphiphilic Ions

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**Synopsis.** The association constants ($K$) of $\beta$-cyclodextrin with 13 amphiphilic ions were determined. For a homologous series 1-alkanesulfonate ions, the saturation phenomenon of $K$ occurred at the number of carbon atoms of 10. The values of $K$ for amphiphilic ions with dodecyl chain were similar to one another.

It is well-known that the hydrophobic interaction between hydrophobic moieties of host and guest molecules plays an important role in the complexation of cyclodextrins.[1] In this connection, studies have been made for the associations of cyclodextrins with fatty acids[2] and amphiphilic ions[3–6] which have a long hydrocarbon chain of varying hydrophobicity. With a homologous series 1-alkanesulfonate ions, we found that the association constant of $\alpha$-cyclodextrin ($\alpha$CD) increases monotonously with increasing carbon atom ($n$) and become abruptly constant at $n=10$.[4] A similar saturation phenomenon of the association constant has also been observed for the complexation of fatty acid salts with $\alpha$- and $\beta$-cyclodextrins.[7] We also found that the association constants of $\alpha$CD for ionic surfactants with the same alkyl chain length are similar to one another regardless of the sign of ionic head group.[4]

In order to elucidate the effect of cavity size on the cyclodextrin-amphiphilic ion interactions, the conductometric investigation was made in this paper for the association constants ($K$) of $\beta$-cyclodextrin ($\beta$CD) with ionic surfactants and their homologs.

## Experimental

**Materials.** Sodium 1-alkanesulfonates with $n$ from 8 to 12 were synthesized from the corresponding alkyl bromides purified by vacuum distillation.[8] Dodecylammonium chloride (DAC) was prepared from dodecylamine (purity>99%, Nakarai Chemicals Ltd.).[9] Sodium dodecyl sulfate (SDS, Nakarai Chemicals Ltd.) and 1-dodecylpyridinium chloride (DPC, Tokyo Kasei Kogyo Co. Ltd.) were purified further by the procedures described elsewhere.[4] Sodium 1-alkanesulfonates with $n$ from 5 to 7 (Tokyo Kasei Kogyo Co. Ltd., guaranteed grade), sodium *p*-dodecylbenzenesulfonate (SDBS, purity>99%, Wako Pure Chemical Industry Co. Ltd.), dodecyltrimethylammonium bromide (DTAB, purity>99%, Tokyo Kasei Kogyo Co. Ltd.), and $\beta$-cyclodextrin ($[\alpha]_D^{25}=+162°$, Seikagaku Kogyo Co. Ltd.) were used without further purifications. Deionized water was obtained by passing twice distilled water through the mixed ion bed (Bio-Rad AG501-X8).

**Measurements.** The conductivity was measured to a precision of 0.1 μS by using a TOA Electronics Ltd. Conductivity Meter model CM-50AT and the conductivity cell with cell constant of 1.000 $\text{cm}^{-1}$ at 25 °C. The concentration of $\beta$CD was determined by drying aliquots of the stock solution over phosphorus pentaoxide in vacuo at 110 °C. The conductivity was followed as a function of $\beta$CD concentration, $C_h$, under the conditions of a constant amphiphile concentration, $C$.

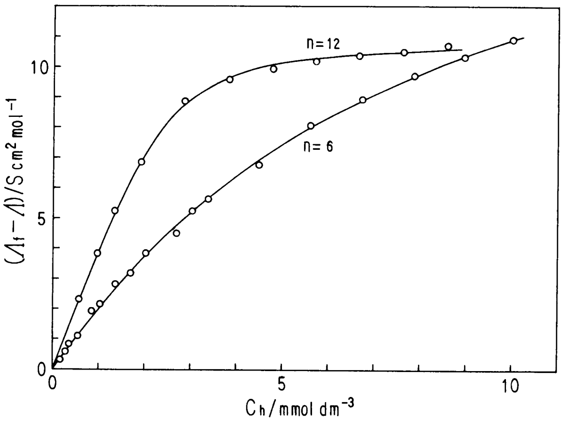

Fig. 1. Plots of $\Lambda_f-\Lambda$ vs. $\beta$CD concentration ($C_h$) for sodium 1-alkanesulfonates with $n=6$ and 12 at 25°C. $C=2.584$ mmol $\text{dm}^{-3}$ ($n=6$), 2.434 mmol $\text{dm}^{-3}$ ($n=12$) O, observed; solid line: calculated curve from Eq. 1 with parameters shown in Table 1.

The solution viscosities of $\alpha$- and $\beta$CD were measured by a Ubbelohde's viscometer at 25 °C.

## Results and Discussion

On the basis of the assumption of a 1 : 1 reaction scheme, the change in the equivalent conductivity, $\Lambda$, with $\beta$CD concentration can be described as follows.[4]

$$\Lambda_f - \Lambda = \frac{\lambda_f-\lambda_a}{2KC}[K(C+C_h) + 1 - \sqrt{\{K(C+C_h) + 1\}^2 - 4K^2CC_h}] \qquad (1)$$

Here, $\Lambda_f$ refers to the equivalent conductivity in the absence of $\beta$CD, and $\lambda_f$ and $\lambda_a$ to the ionic equivalent conductivities of unassociated and associated amphiphilic ion, respectively. Thus the nonlinear least squares treatment of $\Lambda_f$—$\Lambda$ vs. $C_h$ plots permits the simultaneous determinations of $K$ and $\lambda_f$—$\lambda_a$.[4]

In FIg. 1 is shown the typical plots of $\Lambda_f$—$\Lambda$ vs. $C_h$ for sodium 1-hexane- and 1-dodecanesulfonates at 25 °C, together with the calculated curves which give the best fit of the experimental data. An excellent agreement between observed and calculated conductivity curves supports the foregoing assumption of a 1 : 1 reaction scheme for $\beta$CD- amphiphilic ion interaction. This is also the case for whole systems studied. The association constants and the conductometric parameters thus determined are summarized in Table

Table 1. The Conductometric and Thermodynamic Parameters of βCD-Amphiphile Systems

| Amphiphile | $C$ | Temp | $\Lambda_f$ | $\lambda_f-\lambda_a$ | $K$ | $-\Delta G^\circ$ |
|---|---|---|---|---|---|---|
| | mmol dm$^{-3}$ | °C | S cm$^2$ mol$^{-1}$ | S cm$^2$ mol$^{-1}$ | dm$^3$ mol$^{-1}$ | kJ mol$^{-1}$ |
| $C_nH_{2n+1}SO_3Na$ | | | | | | |
| $n=5$ | 2.947 | 10 | 52.5 | 12.2 | 66 | 19.3 |
| | 2.365 | 25 | 77.0 | 18.9 | 60 | 20.1 |
| | 1.539 | 40 | 104.7 | 26.9 | 52 | 20.7 |
| $n=6$ | 2.886 | 10 | 50.8 | 11.8 | 191 | 21.8 |
| | 2.584 | 25 | 74.0 | 18.1 | 177 | 22.8 |
| | 1.936 | 40 | 100.4 | 24.7 | 150 | 23.5 |
| $n=7$ | 2.665 | 25 | 73.6 | 16.7 | 436 | 25.0 |
| $n=8$ | 2.838 | 10 | 49.8 | 9.8 | 1090 | 25.9 |
| | 2.409 | 25 | 73.1 | 15.0 | 1030 | 27.2 |
| | 1.841 | 40 | 99.2 | 20.2 | 914 | 28.2 |
| $n=9$ | 2.512 | 10 | 49.0 | 8.9 | 2210 | 27.6 |
| | 2.501 | 25 | 71.2 | 13.5 | 2170 | 29.0 |
| | 1.761 | 40 | 96.5 | 17.0 | 2150 | 30.4 |
| $n=10$ | 2.502 | 25 | 70.2 | 12.2 | 4090 | 30.6 |
| $n=11$ | 2.567 | 25 | 69.4 | 11.8 | 4130 | 30.6 |
| $n=12$ | 2.434 | 25 | 68.6 | 11.0 | 4340 | 30.7 |
| SDS | 2.597 | 25 | 68.8 | 12.0 | 3630 | 30.3 |
| SDBS | 0.740 | 25 | 69.1 | 8.7 | 7040 | 31.9 |
| DAC | 2.025 | 25 | 96.7 | 13.2 | 4760 | 30.9 |
| DTAB | 2.024 | 25 | 97.4 | 12.5 | 4880 | 31.0 |
| DPC | 1.991 | 25 | 89.7 | 10.8 | 4980 | 31.0 |

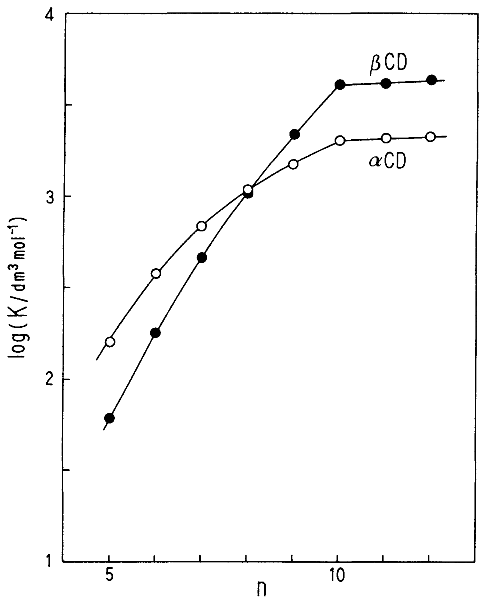

Fig. 2. The chain length dependence of $K$ for sodium 1-alkanesulfonate at 25°C. ●, βCD; ○, αCD.[4)]

1. In this table is also given the standard free energy change of complex formation, $\Delta G^\circ$ $(=-RT \ln K_X=-RT \ln 55.5K)$. Figure 2 shows the chain length dependence of $K$ for 1-alkanesulfonate ion. For the sake of comparison, the previous data for αCD[4)] are also shown in this figure.

It can immediately be seen that the association constant of βCD increases more rapidly than that of αCD with increasing chain length but become also constant at $n=10$. In the complexation of homologous series amphiphilic ions, therefore, the hydrophobic cavity of βCD is supposed to accomodate the hydrocarbon tail in a similar manner to αCD, even though the degree of interaction is different from each other. However, it seems difficult to interpret the observed saturation phenomena at $n=10$ in terms of the hydrophobic interaction alone, since the hydrophobic cavities of α- and βCD molecules are of the order of 0.67—0.7 nm[1a)] in depth and can accomodate at most 6 methylene groups of a fully extended chain. A tentative application of Einstein equation to the viscosity data for cyclodextrin solutions leads immediately to the hydrodynamic volumes of α- and βCD molecules of 1.40 and 1.90 nm$^3$, which correspond to the diameters of 1.40 and 1.54 nm respectively. On the other hand, the head-to-tail distance of 1-decanesulfonate ion with a fully extended chain can be estimated to be 1.55 nm on the basis of an assumption that the radius of hydrated sulfonate group is comparable to that of $HSO_3^-$ ion (0.23 nm[10)]). In connection with the saturation phenomena of $K$ at $n=10$, it is interesting to note that the estimated size of 1-decanesulfonate ion is slightly larger than the diameter of hydrated αCD but almost identical with that of hydrated βCD. Moreover, the methylene group adjacent to head group has been recognized to make little or no contribution to the hydrophobic interaction.[11)] With these observations in mind, α- and βCD molecules seem to include the successive 10 methylene groups of 1-alkanesulfonate ion with $n$ larger than 10 in such a manner as the head group and first methylene group in hydration shell on one side of the cavity, succeeding 6 methylene groups in the hydrophobic cavity, and the residual 3 methylene groups in hydration shell on another side of the cavity. If this is really the case, the thermodynamic parameters such as the enthalpy and entropy of complexing will probably reflect the difference in the microscopic environment around hydrocarbon chain.

Table 2. The Thermodynamic Parameters of Complexing for Sodium 1-Alkanesulfonates with $n$=5, 6, 8, and 9 at 25 °C

| $n$ | $\Delta H^\circ$ | $\Delta S^\circ$ | $\Delta(\Delta H^\circ)$ | $\Delta(\Delta S^\circ)$ |
|---|---|---|---|---|
| | kJ mol$^{-1}$ | J K$^{-1}$mol$^{-1}$ | kJ mol$^{-1}$ | J K$^{-1}$mol$^{-1}$ |
| 5 | −5.87 | 47.7 | ≈0 | 9.1 |
| 6 | −5.86 | 56.8 | | |
| 8 | −4.39 | 76.5 | 3.7 | 18.3 |
| 9 | −0.74 | 94.8 | | |

Table 2 shows the standard enthalpy and entropy changes estimated for 1-alkanesulfonate ions with $n$=5, 6, 8, and 9 from temperature dependence of $K_X$. In last two columns are given the increments of $\Delta H^\circ$ and $\Delta S^\circ$ per methylene group which correspond to the enthalpy and entropy changes for transferring one methylene group from an aqueous medium to the complex state respectively. It should be noted that the observed increment of $\Delta H^\circ$ accompanying the increase in $n$ from 5 to 6 is comparable to the enthalpy changes per methylene group characteristic of hydrophobic interaction. For example with heptane-βCD system, Wishnia and Lappi[12] obtained $\Delta H^\circ$ of 0.84 kJ mol$^{-1}$ at 20 °C, which corresponds roughly to 0.12 kJ mol$^{-1}$ per methylene group. In the case of micellization process, the enthalpy change per methylene group has been found to be of the order of 0.2 kJ mol$^{-1}$.[13] On the contrary, the increments of $\Delta H^\circ$ and $\Delta S^\circ$ accompanying the change in $n$ from 8 to 9 are quite different from those from 5 to 6. In a previous paper,[4] we assumed the partial breakdown of the hydration shell around lateral hydrophilic surface through which hydrocarbon tail penetrates. Apart from the plausible explanation of the effect of hydrocarbon tail on hydration shell, the thermodynamic data seem to support the foregoing geometric consideration on the inclusion mechanism of long-chain 1-alkanesulfonate ions. In their study of the complexation of homologous series fatty acid salts, Ono et al.[7] found that the saturation phenomenon of $K$ occurs at $n$=8 for αCD and $n$=12 for βCD respectively. They assumed a trans to gauche conformational change of hydrocarbon chain in cavity of βCD.

The qualitative features of the association constants of βCD for surfactant ions with dodecyl chain are identical with those of αCD.[4] As was pointed out previously,[4] a marked resembrance in the values of $K$ for sodium 1-dodecanesulfonate, DAC, DTAB, and DPC suggests that the interaction between βCD and surfactant ion does not depend appreciably on the chemical and electrical properties of ionic head group. A striking increase in $K$ for SDBS can also be attributed to the presence of the aromatic ring which interacts strongly with βCD.[1]

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