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GREATER GUEST BINDING ABILITY
OF β -CYCLODEXTRIN HAVING BOTH A CAP AND FLOOR

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β -Cyclodextrin having both 2-naphthalenesulfonyl and tosyl moieties as the cap and floor has a greater ability to bind guests than β -cyclodextrin which has a cap only.

KEYWORDS — β -cyclodextrin; inclusion complex; circular dichroism; naphthalene; binding constant; host-guest

Cyclodextrins can bind a variety of guests in their molecular cavities.¹⁾ The host-guest complexation occurs usually in aqueous solution mainly due to hydrophobic interaction between ether-like cyclodextrin walls and lipophilic guests. Consequently, the binding is stronger when the environment around the included guest is made more hydrophobic by modifying the native cyclodextrins with hydrophobic moieties (cap or floor).^{2,3)} Heretofore, such modification has been performed at one side of the cyclodextrins, that is, at either side of the primary or secondary hydroxyls. In this study, based on the recent establishment⁴⁾ of a secondary site-modification method for β -cyclodextrin, we have prepared a β -cyclodextrin (cycloheptaamylose) derivative **1**, which bears two different aromatic moieties as the cap and floor at opposite sides of the cavity. This system enables guest molecules to be totally encapsulated in the hydrophobic cavity of **1** by co-operation of the cyclodextrin wall, cap, and floor.

Compound **1** was prepared by treating 2-naphthalenesulfonyl chloride with one equiv. of β -cyclodextrin-2-O-tosylate⁴⁾ in pyridine at room temperature for 1 h. Evaporation of the reaction solution followed by column chromatography on Sephadex LH-20 with N,N-dimethylformamide/water (1:1) as the eluting solvent afforded the product in 10% yield. Compound **2**, which bears a 2-naphthalenesulfonyl moiety at the primary side of β -cyclodextrin, was also prepared by treating 2-naphthalenesulfonyl chloride with β -cyclodextrin in pyridine as the reference compound of **1**. Both compounds were identified by ¹H-NMR, UV, IR, and elemental analyses.⁵⁾

The circular dichroism (CD) spectrum of **2** reveals positive peaks around 227 nm ([θ]=+26700) and 275 nm ([θ]=+3700) associated with the naphthalene ¹B_b (ϵ_{229} =112000) and ¹L_a (ϵ_{277} =8140) transitions, respectively. The intensities of the

Table I. Binding Constants of **1** and **2** for Various Guests in water at 25 °C^{a)}

Guest	Host	K / mol ⁻¹ l
(-)-Borneol	1	4070 ± 90
	2	1020 ± 60
Cyclohexanol	1	138 ± 9
	2	67 ± 4
t-BuOH	1	7.8 ± 0.8
	2	3.3 ± 0.2
n-BuOH	1	5.0 ± 0.3
	2	3.7 ± 0.7

a) The values were obtained by the analysis of the CD intensities at 237 and 275 nm for **1** and **2**, respectively.

CD bands are reduced in the presence of guests, indicating that the naphthalenesulfonyl moiety, which is inserted into the cyclodextrin cavity, is extruded when a guest molecule enters the cavity. Figure 1 (left) shows the absorption and CD spectra of **1** in water. The CD patterns of **1** in the 210–250 nm region are quite different from the simple positive band of **2**: a sinusoidal CD curve with a change in sign from minus to plus from the longer wavelength side appears in the absence of a guest, while the CD curve with an opposite change in sign occurs in the presence of an excess guest. These sinusoidal CD curves, which were observed for **1** and not for **2**, are likely to result from the exciton coupling⁶⁾ between the two aromatic rings of the cap and floor. The guest-induced CD variations therefore indicate that the positional relationship between the cap and floor changes by guest accommodation. It is reasonably thought that **1** is a mixture of several isomers which are different in the mutual positions of the tosyl and naphthalenesulfonyl moieties. However, attempts to identify the mixtures of **1** have not been successful. Furthermore, we observed an isoellipticity point at 233 nm in the CD spectra of the solutions with different guest concentrations (Fig. 1 (right)). Such an isoellipticity point usually appears in the system of 1:1 host-guest complexation of modified cyclodextrins.⁷⁾ The present CD variations of **1** can also be analyzed based on a simple 1:1 stoichiometry of complexation⁷⁾ using the CD intensities at 237 nm. Table I shows the binding constants of **1** and **2** for various guests. The values are in the order of n-BuOH < t-BuOH < cyclohexanol < (-)-borneol for both **1** and **2**. For any of the guests, the binding ability of **1** is larger than that of **2** with 4.0, 2.1, 2.4, and 1.4-fold stronger binding for (-)-borneol, cyclohexanol, t-BuOH, and n-BuOH, respectively. The strongest binding of **1** observed for (-)-borneol may be attributed to the largest contact area of the guest to both cap and floor. From these data, it has been shown that both the cap and floor of **1** co-operate in producing the improved hydrophobic environment around the guest molecule in **1** by adjusting their locations.

Another aspect of compound **1**, which has two reactive sulfonyl units, is that it can be used as a starting material to construct unique hosts or enzyme models with two appropriate functional moieties at the opposite sides of β -cyclodextrin. A study along this line is now under way.

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REFERENCES AND NOTES

- 1) M. L. Bender and M. Komiyama, "Cyclodextrin Chemistry", Springer-Verlag (1978).
- 2) J. Emert and R. Breslow, J. Am. Chem. Soc., 97, 670 (1975).
- 3) I. Tabushi, K. Shimokawa, N. Shimizu, H. Shirakata, and K. Fujita, J. Am. Chem. Soc., 98, 7855 (1976).
- 4) A. Ueno and R. Breslow, Tetrahedron Lett., 1982, 3451.
- 5) Data of **1**: Rf 0.58 (n-BuOH:EtOH:water 5:4:3 by volume); IR (KBr) cm^{-1} : 1355, 1180; $^1\text{H-NMR}$ (DMSO- d_6 , 60 $^\circ\text{C}$) δ : 1.20 (3H, s, CH_3), 3.0-4.0 (br, m, cyclodextrin protons other than C_1H and OH), 4.2 (6H, br, m, O_6H), 4.8 (7H, br, m, C_1H), 5.55 (13H, br, s, O_2H , O_3H), 7.6-8.3 (11H, m, Ar-H); Anal. Calcd for $\text{C}_{59}\text{H}_{82}\text{O}_{39}\text{S}_2 \cdot 5\text{H}_2\text{O}$: C, 45.15; H, 5.91; S, 4.09. Found: C, 45.28; H, 5.89; S, 4.42.
Data of **2**: Rf 0.55 (n-BuOH:EtOH:water 5:4:3 by volume); IR (KBr) cm^{-1} : 1355, 1180; $^1\text{H-NMR}$ (DMSO- d_6 , 60 $^\circ\text{C}$) δ : 3.0-4.0 (br, m, cyclodextrin-H other than C_1H and OH), 4.2 (6H, br, m, O_6H), 4.8 (7H, br, m, C_1H), 5.55 (14H, br, m, O_2H , O_3H), 7.6-8.3 (7H, m, Ar-H); Anal. Calcd for $\text{C}_{52}\text{H}_{76}\text{O}_{37}\text{S} \cdot \text{H}_2\text{O}$: C, 46.50; H, 5.85; S, 2.39. Found: C, 46.76; H, 6.43; S, 2.53.
- 6) N. Harada and K. Nakanishi, "Circular Dichroic Spectroscopy, Exciton Coupling in Organic Stereochemistry", Tokyo-Kagaku-Dojin, Tokyo (1982).
- 7) A. Ueno, F. Moriwaki, T. Osa, F. Hamada, and K. Murai, Bull. Chem. Soc. Jpn., 59, 465 (1986).

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