# Temperature Effects on CD Spectra of β-Cyclodextrin Complexes with 2-Substituted Naphthalenes

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CD spectra of β-cyclodextrin complexes with 2-naphthol, 2-naphthyloxyacetic acid, potassium 2-naphthoate, and potassium 2-naphthylacetate were measured at various concentrations of β-cyclodextrin and at temperatures ranging from 10 to 70 °C. The temperature-dependent CD spectra of the 2-naphthyloxyacetic acid complex clearly show the 1 : 1 complex formation, but the other three complexes give CD intensity changes which are inexplicable in terms of the 1 : 1 stoichiometry. The molecular ellipticity and thermodynamic parameters were determined by the least-squares method. Enthalpy and entropy are in the ranges from −22.2 to −26.8 kJ·mol$^{-1}$ and from −24 to −38 J·K$^{-1}$·mol$^{-1}$, respectively. They are strongly correlated to the volume of the substituent of the guest molecule, although the free energy is found in a quite narrow region (from −14.3 to −15.4 kJ·mol$^{-1}$). The correlation is explained on the basis of the β-cyclodextrin–guest interaction and the solvation around the guest molecule.

Cyclodextrins, which are α-1,4-linked cyclic oligosaccharides, form a number of inclusion complexes with a variety of guest molecules owing to the large cylindrical cavity in the center of the molecule.[1,2] Since cyclodextrins are asymmetric molecules, optical activity is induced when an optically inactive guest is included in the cavity.[3–7] For the cyclodextrin complexes with aromatic guests, the origin of induced optical activity was reasonably explained in terms of the Kirkwood-Tinoco coupled oscillator model.[5–7] Although CD spectra of many cyclodextrin complexes have already been reported, the molecular ellipticity of the complex has not been precisely determined. Since the induced CD is caused by cyclodextrin–guest interactions, CD spectra are expected to give information on the structure of the complex in solution. In the previous paper,[8] we reported the temperature dependence of CD spectra of α-cyclodextrin complexes with *m*- and *p*-nitrophenols. We present here the temperature effects on CD spectra of β-cyclodextrin complexes with 2-substituted naphthalenes and will discuss the structure and binding force of the complexes on the basis of the thermodynamic parameters determined by the least-squares method.

## Experimental

*Materials.* β-Cyclodextrin (G. R., Tokyo Kasei Co.) was twice recrystallized from water and dried *in vacuo* over phosphorous pentaoxide. 2-Naphthol and 2-naphthyloxyacetic acid (G. R., Tokyo Kasei Co.) were recrystallized from ethanol. Potassium 2-naphthoate and potassium 2-naphthylacetate were prepared from 2-naphthoic acid and 2-naphthylacetic acid, which were treated by KOH-saturated ethanol, and were recrystallized from water.

*CD Measurements.* Solutions were prepared with deionized and distilled water. The CD spectra were recorded on a JASCO J-40A circular dichrograph with a J-DPZ data-processor. The recording of each spectrum was repeated four times, and the averaged spectra were obtained on the data-processor. The temperature was regulated by using a Tokyo Rico TC-100 thermo-controller with an accuracy of ±0.5 °C inside the cell.

## Results

The CD spectra measured at 30 °C are shown in Fig. 1. The concentrations of β-cyclodextrin, 2-naphthol, 2-naphthyloxyacetic acid, potassium 2-naphthoate, and potassium 2-naphthylacetate are $5.0\times10^{-3}$, $1.89\times10^{-4}$, $2.12\times10^{-4}$, $1.90\times10^{-4}$, and $2.02\times10^{-4}$ M, respectively. Each complex shows negative CD bands in the wavelength region longer than 250 nm. The CD bands found in the 250—300 nm region give a peak intensity higher than the intensity of the 300—350 nm bands. A large positive-signed CD band was found in the wavelength region from 200 to 250 nm. The temperature dependence of the CD intensity was measured by increasing the temperature from 10 to 70 °C. After the measurement at 70 °C, the temperature was again lowered to 10 °C. Then, the CD intensity returned to the initial value.

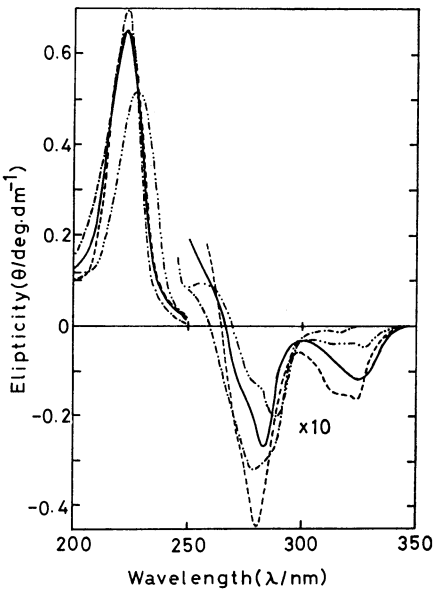


Fig. 1. CD spectra of β-cyclodextrin complexes with 2-naphthol (——), 2-naphthyloxyacetic acid (– – –), potassium 2-naphthylacetate (–·–·), and potassium 2-naphthoate (–··–) at 30 °C. The concentrations of β-cyclodextrin, 2-naphthol, 2-naphthyloxyacetic acid, potassium 2-naphthylacetate, and potassium 2-naphthoate are $5.0\times10^{-3}$, $1.89\times10^{-4}$, $2.12\times10^{-4}$, $2.02\times10^{-4}$, and $1.90\times10^{-4}$ M, respectively.

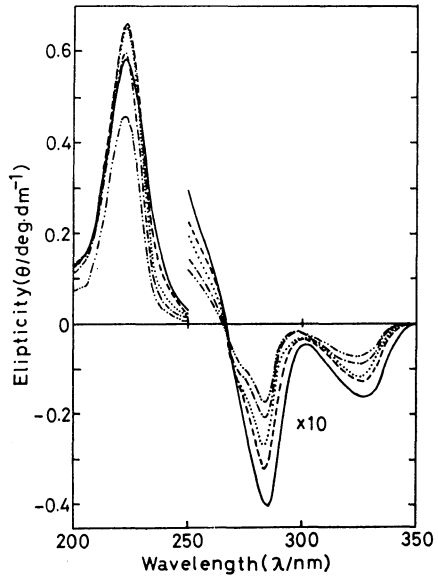


Fig. 2. CD spectra of β-cyclodextrin–2-naphthol complex measured at 10 °C (——), 20 °C (– – –), 30 °C (·····), 50 °C (–·–·), and 70 °C (– ·· –). The concentrations of β-cyclodextrin and 2-naphthol are $5.0\times10^{-3}$ and $1.89\times10^{-4}$ M, respectively.

*β-Cyclodextrin–2-Naphthol Complex.* The CD spectra measured at 10, 20, 30, 50, and 70 °C are shown in Fig. 2. With the increase of temperature, the negative CD bands lower their intensity. The intensity change in these bands is more rapid at lower temperature conditions. When the temperature is raised from 10 to 30 °C, the CD intensity of the 285 nm band decreases by 0.14 deg·dm$^{-1}$, which corresponds to 33% of the intensity measured at 10 °C. On the other hand, the intensity change is only 0.035 deg·dm$^{-1}$ between the temperatures of 50 and 70 °C. The 285 nm band is slightly sharpened by increasing the temperature, and a shoulder appears at 274 nm. A similar sharpening is observed in the positive CD band centered at 222 nm. The intensity change in the 222 nm band is different from that of the negative-signed bands measured in the longer wavelength region. The CD intensity enhances when the temperature is raised up to 20 °C; after that, however, the intensity lowers with increasing temperature. Figure 4a gives the more detailed intensity change measured at 222 nm. In this case, the concentration of 2-naphthol is adjusted to $1.83\times10^{-4}$ M, and the intensity was measured at β-cyclodextrin concentrations of $1.0\times10^{-3}$, $2.0\times10^{-3}$, and $9.0\times10^{-3}$ M. At each β-cyclodextrin concentration, the highest CD intensity was not observed at 10 °C. The temperature which gives the maximum CD intensity becomes lower with the decrease of the β-cyclodextrin concentration. At $9.0\times10^{-3}$ M β-cyclodextrin concentration, the CD intensity increases with the temperature up to 40 °C, and after that decreases gradually. The intensity maxima were also observed at 20 and 15 °C at the β-cyclodextrin concentrations of $2.0\times10^{-3}$ and $1.0\times10^{-3}$ M, respectively. The molecular ellipticity of the complex and thermodynamic parameters were determined by the least-squares method (see Appendix) on the basis of the assumption of the 1 : 1 stoichiometry. The intensity data measured at temperatures lower than 40 °C ($9.0\times10^{-3}$ M), 30 °C ($2.0\times10^{-3}$ M), and 25 °C ($1.0\times10^{-3}$ M) were not included in the calculation, since these values systematically deviated from the expected ones and can not be explained on the basis of the 1 : 1 stoichiometry. The calculated intensity is shown by the solid line in Fig. 4a. The 1 : 1 stoichiometry predicts the monotonous decrease of the CD intensity with the increase of the temperature. The molecular ellipticity of the complex is $5.7(1)\times10^{4}$ deg·cm$^{2}$·dmol$^{-1}$, and the dissociation constant at 25 °C is $2.0(2)\times10^{-3}$ mol. The free energy at 25 °C, enthalpy, and entropy for the complex formation are −15.4(3), −26.8(9) kJ·mol$^{-1}$, and −38(3) J·K$^{-1}$·mol$^{-1}$, respectively.

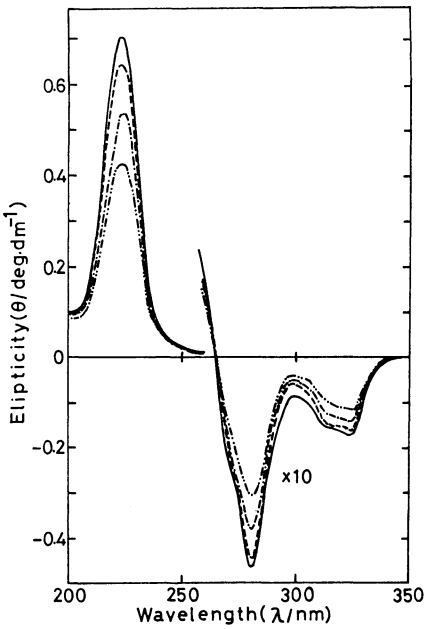


Fig. 3. CD spectra of β-cyclodextrin–2-naphthyloxyacetic acid complex measured at 10 °C (——), 30 °C (– – –), 50 °C (–·–·), and 70 °C (– ·· –). The concentrations of β-cyclodextrin and 2-naphthyloxyacetic acid are 5.0 $\times10^{-3}$ and $2.13\times10^{-4}$ M, respectively.

*β-Cyclodextrin–2-Naphthyloxyacetic Acid Complex.* The CD spectra of the 2-naphthyloxyacetic acid complex measured at 10, 30, 50, and 70 °C are shown in Fig. 3. Unlike the 2-naphthol complex, the intensity change is slow in the temperature range from 10 to 30 °C. Two weak CD bands are centered at 313 and 326 nm, while the larger negative band found at 280 nm has a weak shoulder at 273 nm. The intensity of these CD bands becomes lower with the increase of the temperature, and the intensity change is more rapid at higher temperature. The intensity of the 280 nm peak reduces to *ca.* 65% of the intensity measured at 10 °C when the temperature is raised to 70 °C. The intensity of the positive CD band, which is centered at 224 nm, also decreases with increasing temperature. The intensity at 70 °C is about 60% of that measured at 10 °C. Figure 4b shows plots of the intensity change measured at 224 nm against the temperature. The concentration of

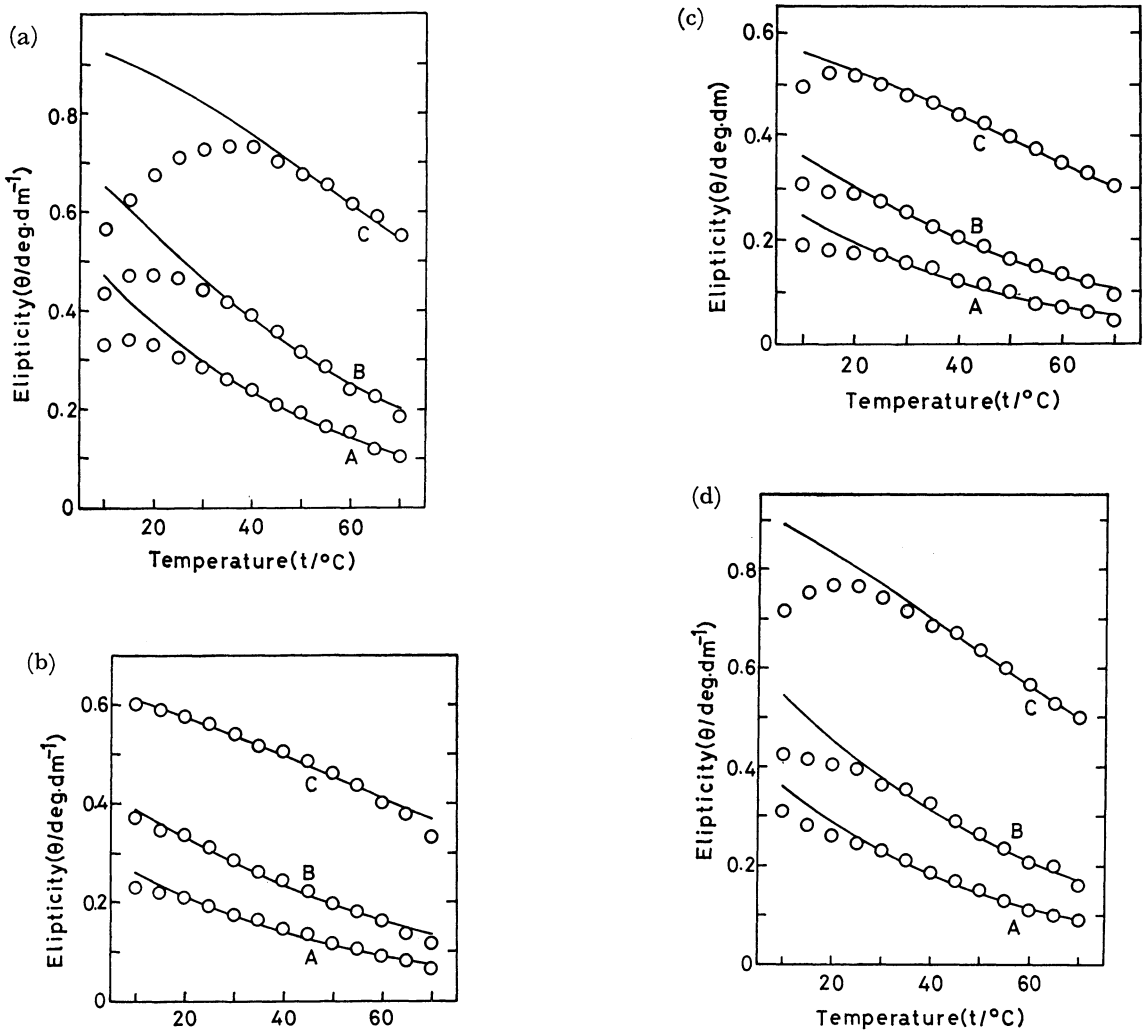


Fig. 4. Plots of CD intensity against the temperature; the intensity is measured at 222 nm for the 2-naphthol complex (a), 224 nm for the 2-naphthyloxyacetic acid complex (b), 230 nm for the potassium 2-naphthoate complex (c), and 224 nm for the potassium 2-naphthylacetate complex (d) with the concentrations of $1.83\times10^{-4}$, $1.73\times10^{-4}$, $1.71\times10^{-4}$, and $1.96\times10^{-4}$ M, respectively. The concentration of β-cyclodextrin is $1.0\times10^{-3}$ (A), $2.0\times10^{-3}$ (B), and $9.0\times10^{-3}$ M (C). Solid lines are calculated intensity by using molecular ellipticity and thermodynamic parameters which are determined by the least-squares method on the basis of a 1:1 complex.

2-naphthyloxyacetic acid is $1.73\times10^{-4}$ M, and the measurement was carried out at the β-cyclodextrin concentrations of $1.0\times10^{-3}$, $2.0\times10^{-3}$, and $9.0\times10^{-3}$ M. The least-squares calculation was done by using all the intensity data measured. The CD intensity decreases monotonously with the temperature increase, and the calculated values (shown by solid lines) fitted well with the observed ones. In this case, the molecular ellipticity is $4.20(4)\times10^{4}$ deg·cm²·dmol⁻¹, and the dissociation constant at 25 °C is $2.7(1)\times10^{-3}$ mol. The free energy at 25 °C, enthalpy, and entropy are −14.6(1), −22.5(5) kJ·mol⁻¹, and −24(2) J·K⁻¹·mol⁻¹, respectively.

*β-Cyclodextrin–Potassium 2-Naphthoate Complex.* This complex shows two weak peaks at 328 and 312 nm in the longer wavelength region, while in the 250—300 nm region there is found a negative CD peak at 289 nm and a shoulder at 281 nm. The positive CD band is observed at 230 nm. The intensity change measured at 230 nm is shown in Fig. 4c. The concentration of the guest is $1.71\times10^{-4}$ M. At the β-cyclodextrin concentration of $9.0\times10^{-4}$ M, an enhancement of the CD intensity is observed when the temperature is raised from 10 to 15 °C, but after that, the intensity decreases with the increase of the temperature. At the β-cyclodextrin concentrations of $2.0\times10^{-3}$ and $1.0\times10^{-3}$ M, an intensity decrease was observed during the temperature increase up to 70 °C. In the least-squares calculation, the intensity data measured at temperatures less than 20 °C were not included because of the reasons mentioned above. The molecular ellipticity of the complex is $3.88(7)\times10^{4}$ deg·cm²·dmol⁻¹, and the dissociation constant at 25 °C was determined to be $2.7(2)\times10^{-3}$ mol. The free energy at 25 °C, enthalpy, and entropy are −14.6(2), −25.5(8) kJ·mol⁻¹, and −37(2) J·K⁻¹·mol⁻¹, respectively.

*β-Cyclodextrin–Potassium 2-Naphthylacetate Complex.*

TABLE 1. MOLECULAR ELLIPTICITY AND THERMODYNAMIC PARAMETERS OF β-CYCLODEXTRIN COMPLEXES WITH 2-SUBSTITUTED NAPHTHALENES

| | $\lambda_{max}$ | $[\theta]$ | $K_d$(298 K) | $\Delta G$(298 K) | $\Delta H$ | $\Delta S$ |
|---|---|---|---|---|---|---|
| | nm | $10^4$ deg·cm²·dmol$^{-1}$ | $10^{-3}$·mol | kJ·mol$^{-1}$ | kJ·mol$^{-1}$ | J·K$^{-1}$·mol$^{-1}$ |
| 2-Naphthol | 222 | 5.7(1) | 2.0(2) | −15.4(3) | −26.8(9) | −38(3) |
| 2-Naphthyloxyacetic acid | 224 | 4.20(4) | 2.7(1) | −14.6(1) | −22.2(5) | −24(2) |
| Potassium 2-naphthoate | 230 | 3.88(7) | 2.7(2) | −14.6(2) | −25.5(8) | −37(2) |
| Potassium 2-naphthylacetate | 224 | 5.5(1) | 3.1(2) | −14.3(2) | −23.0(6) | −29(2) |

In the longer wavelength region, a very weak CD band is centered at 318 nm. The larger negative peak is observed at 279 nm, while a shoulder is observed at 288 nm. In the shorter wavelength region, a positive CD band is found at 224 nm. The temperature dependence of the 224 nm band was measured at the guest concentration of $1.96\times10^{-4}$ M, as shown in Fig. 4d. At the β-cyclodextrin concentration of $9.0\times10^{-3}$ M, the CD intensity increased with the temperature up to 20 °C, then decreases with increasing temperature. Only an intensity decrease was observed at the β-cyclodextrin concentrations of $2.0\times10^{-3}$ and $1.0\times10^{-3}$ M. The least-squares calculation was done by using the intensity data measured at the temperatures higher than 30 °C for the β-cyclodextrin concentration of $9.0\times10^{-3}$ M and 20 °C for the concentrations of $2.0\times10^{-3}$ and $1.0\times10^{-3}$ M. The molecular ellipticity of the complex is $5.5(1)\times10^4$ deg·cm²·dmol$^{-1}$, and the dissociation constant at 25 °C is $3.1(2)\times10^{-3}$ mol. The free energy at 25 °C, enthalpy, and entropy are −14.3(2), −23.0(6) kJ·mol$^{-1}$, and −29(2) J·K$^{-1}$·mol$^{-1}$, respectively.

## Discussion

*Structure and Stoichiometry of the Complex.* β-Cyclodextrin complexes with four 2-substituted naphthalenes give similar CD spectra: two negative CD bands in the 250—350 nm region and a positive CD band in the 200—250 nm region. The origin of induced CD by cyclodextrins is reasonably interpreted in terms of the Kirkwood-Tinoco coupled oscillator model.[5-7] The rotational strength with an electric transition-dipole-moment of $\mu_{oa}$ is given by

$$R_{oa} \approx (A_{oa}+B_{oa}\cos 2\theta)\mu_{oa}^2 \qquad (1)$$

where $A_{oa}$ and $B_{oa}$ are constants dependent only on the wavelength, and $\theta$ is the angle made by the dipole moment and the molecular axis of β-cyclodextrin. Since $A_{oa}$ and $B_{oa}$ are positive values and $A_{oa}$ is about one-third of $B_{oa}$, the sign of the induced CD is determined only by the relative orientation of the dipole moment in the β-cyclodextrin cavity. The dipole moment parallel to the molecular axis of β-cyclodextrin gives a positive CD and the perpendicularly polarized dipole moment produces a negative CD. The CD bands observed in the 200—250 and 250—300 nm regions indicate that the guest molecule is included with the naphthyl group parallel to the molecular axis of β-cyclodextrin. The CD band found in the 300—350 nm region may be ruled out since the Kirkwood-Tinoco model should be applied to the transition with a strong electric dipole moment.

In the complexes with 2-naphthol, the temperature dependent CD intensity change can not be fully explained on the basis of a 1:1 complex model. The 1:1 stoichiometry predicts the monotonous decrease of the CD intensity with the increase of the temperature. But, an intensive enhancement of the CD intensity is observed in the lower temperature region. The discrepancy in these results may be interpreted in terms of the structural change of the complex with the temperature increase and/or the formation of the complexes with higher stoichiometry than a 1:1 molar ratio. But the structural change seems to be less likely in this case if we consider only a 1:1 complex. The guest molecule must rotate around the axis perpendicular to the naphthyl plane to reduce the CD intensity of the 222 nm band. But such a rotation also decreases the intensity of the 285 nm band, although the observed intensity change clearly shows the opposite tendency. The displacement of the naphthyl group either to the primary hydroxyl side or to the secondary hydroxyl side also decreases the intensity of both 222 and 285 nm bands. Moreover, according to the inspection of molecular models, the naphthyl group is expected to be tightly packed in the β-cyclodextrin cavity. The tight packing may impose a strong restriction upon the translational and rotational freedom of the naphthyl group because of the repulsive interaction between hydrogen atoms of β-cyclodextrin and the naphthyl group.

The formation of a complex with higher stoichiometry than a 1:1 molar ratio is more plausible. The temperature which gives the intensity maxima of positive CD bands becomes lower with the increase of β-cyclodextrin concentration. The discrepancy found between observed and calculated intensities is more remarkable at higher β-cyclodextrin concentrations. These facts suggest that the association at lower temperature produces a complex in which two or more β-cyclodextrin molecules are bound to one guest molecule. It seems unlikely that β-cyclodextrin binds two or more guest molecules since the concentration of the guest is lower than one-fifth of the β-cyclodextrin concentration. In the crystalline complexes,[9-11] two β-cyclodextrin molecules are linked by many hydrogen bonds between secondary hydroxyl groups to form a dimer structure with a head-to-head arrangement. Therefore, the β-cyclodextrin dimer with the same structure may be formed in aqueous solutions.[11] The rotational strengths of a 2:1 complex were estimated by assuming that the transition-dipole-moment is located at the center of the dimer; the structure of β-cyclodextrin and the parameters used in the calculation were those used in the earlier work.[5] For the transition-dipole-moments parallel and perpendicular to the β-cyclodex-

trin axis, the rotational strengths are $1.25\times10^{-4}\,\mu_{\parallel}^2$ (at 222 nm) and $-0.26\times10^{-4}\,\mu_{\perp}^2$ (at 285 nm), respectively. On the other hand, the corresponding rotational strengths in the 1:1 complex are $1.53\times10^{-4}\,\mu_{\parallel}^2$ and $-0.15\times10^{-4}\,\mu_{\perp}^2$. Therefore, the formation of the 2:1 complex may decrease the intensity of positive CD and enhance the negative CD, giving an explanation for the observed intensity change.

In the 2-naphthyloxyacetic acid complex, the calculated CD intensity based on the thermodynamic parameters determined by the least-squares method is in good agreement with the observed intensity (Fig. 4d). This indicates that the association of two or more β-cyclodextrin molecules does not occur in this case. The guest molecule has a relatively large substituent, so that the substituent group may hinder the formation of complexes with higher stoichiometry.

*Thermodynamic Parameters and Binding Force in the Complex.* Free energies at 298 K are in the range from −14.3 to −15.4 kJ·mol$^{-1}$, a remarkably narrow region in spite of the different guest molecules. Enthalpy and entropy are in the range from −22.2 to −26.8 kJ·mol$^{-1}$ and −24 to −38 J·K$^{-1}$·mol$^{-1}$, respectively. A plot of $\Delta H$ against $\Delta S$ is given in Fig. 5. $\Delta H$ is linearly correlated to $\Delta S$. A similar correlation has been also observed in the α-cyclodextrin complexes.[12] Changes in $\Delta H$ are almost compensated by changes in $\Delta S$. Therefore, the free energy is restricted in a quite narrow region. Such compensation phenomena are widely observed in water solutions.[13]

The thermodynamic parameters indicate that $\Delta H$ and $\Delta S$ are strongly correlated to the molecular volume of the guest. Figure 6 shows plots of $\Delta H$ and $\Delta S$ against the van der Waals volume of the substituent in the guest molecule. The volumes were estimated according to Bondi.[14] $\Delta H$ and $\Delta S$ decrease in magnitude with an increase of the substituent volume. Changes in $\Delta H$ and $\Delta S$ can be explained on the basis of the β-cyclodextrin–guest interaction and solute–solvent interaction. Owing to the cylindrical cavity of β-cyclodextrin, a guest molecule with a smaller substituent may fit better into the cavity. A bulky substituent seems to inhibit the close packing of the guest molecule, and to impose an unfavorable conformational change on β-cyclodextrin. The tight inclusion of the guest molecule also imposes restrictions on the conformational flexibility of β-cyclodextrin as well as on translational and rotational freedom of the guest molecule.[15] Therefore, a guest molecule with a small substituent may give large values of enthalpy and entropy of complex formation compared with the guest molecule having a bulky substituent.

In the uncomplexed state, the guest molecule is surrounded by solvent molecules, while some water molecules are included in the β-cyclodextrin cavity.[16] These water molecules may be removed by the complex formation and become bulk water. The enthalpy change for the process is expressed as

$$\Delta H^{s} = H^{s}(\beta\text{-cyclodextrin–guest}) + H^{s}(n\mathrm{H_2O}) - H^{s}(\beta\text{-cyclodextrin–}n\mathrm{H_2O}) - H^{s}(\text{guest}) \quad (2)$$

$$= \Delta H_{c}^{s} + \Delta H_{e}^{s} + \Delta H_{v}^{s}. \quad (3)$$

$H_{c}^{s}$ is the energy required to create a cavity to accomodate the solute molecule in solution, and is calculated according to Pierotti.[17] $H_{e}^{s}$ and $H_{v}^{s}$ are the electrostatic interaction energy and the van der Waals interaction energy, respectively, between solute and solvent molecules. The detailed descriptions of $H_{e}^{s}$ and $H_{v}^{s}$ are given in the earlier paper.[18] In the crystalline state, the uncomplexed β-cyclodextrin contains 2.5 water molecules in the center of the cavity.[16] Therefore, $n=2.5$ was assumed in this calculation. The calculated enthalpy, which is in the range from −21.9 to −24.3 kJ·mol$^{-1}$ (Table 2), suggests that the bulky substituent group decreases the enthalpy of complex formation.

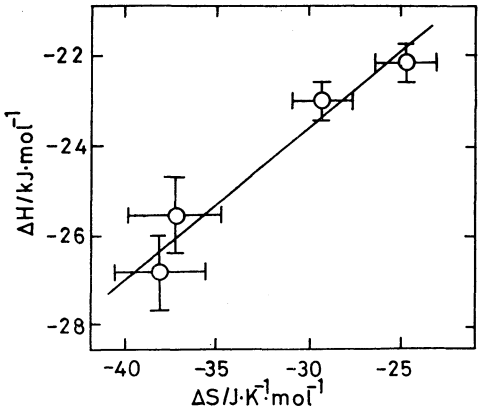


Fig. 5. Plot of $\Delta H$ against $\Delta S$. Vertical and horizontal bars indicate error limits.

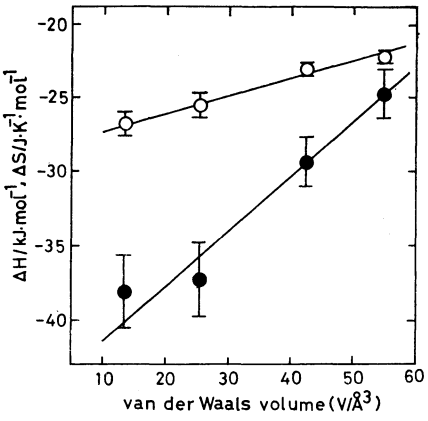


Fig. 6. Plots of $\Delta H$ (○) and $\Delta S$ (●) against van der Waals volumes of substituent in naphthalene derivatives. Vertical bars indicate error limits.

Table 2. Calculated solvation effects on $\Delta H$ for the complex formation of β-cyclodextrin with 2-substituted naphthalenes

| | $V$[a] / Å$^3$ | $\Delta H$ / kJ·mol$^{-1}$ |
|---|---|---|
| 2-Naphthol | 13.4 | −24.3 |
| 2-Naphthoate ion | 25.6 | −21.9 |
| 2-Naphthylacetate ion | 42.5 | −24.1 |
| 2-Naphthyloxyacetic acid | 55.1 | −22.1 |

a) The van der Waals volume of the substituent.

The calculated results also indicate that the naphthyl group is highly hydrophobic, so that it may be more favorable for the group to be located in the hydrophobic cavity of β-cyclodextrin than in the aqueous environment.

## Appendix

When β-cyclodextrin forms a 1 : 1 complex with a guest in an aqueous solution,

$$\beta\text{-cyclodextrin} + \text{guest} \rightleftarrows \beta\text{-cyclodextrin–guest}, \quad \text{(A1)}$$

the dissociation constant at the temperature of $T_i$ K is given by

$$K_{di} = (a-x_{ij})(b_j-x_{ij})/x_{ij} \quad \text{(A2)}$$

where $a$, $b_j$, and $x_{ij}$ are the concentrations of the guest, β-cyclodextrin, and the complex, respectively. The observed CD intensity is expressed by using the molecular ellipticity of $\theta_m$: as

$$\theta_{ij} = \theta_m x_{ij}. \quad \text{(A3)}$$

Then, by substituting Eq. A3 to Eq. A2,

$$K_{di} = \frac{ab_j\theta_m}{\theta_{ij}} - a - b_j + \frac{\theta_{ij}}{\theta_m} \quad \text{(A4)}$$

If we assume that the enthalpy ($\Delta H$) and entropy ($\Delta S$) for the complex formation are independent of temperature under the experimental conditions, the free energy for the complex formation is given by

$$\Delta G_i = \Delta H - T_i\Delta S \quad \text{(A5)}$$

$$= RT_i \ln K_{di}. \quad \text{(A6)}$$

By substituting Eq. A4 to Eq. A6, we obtain

$$\ln\left(\frac{ab_j\theta_m}{\theta_{ij}} - a - b_j + \frac{\theta_{ij}}{\theta_m}\right) - \frac{\Delta H}{RT_i} + \frac{\Delta S}{R} = 0 \quad \text{(A7)}$$

$\theta_m$, $\Delta H$, and $\Delta S$ can be determined by the least-squares technique if we know the rough values of $\theta_m^\circ$, $\Delta H^\circ$, and $\Delta S^\circ$:

$$\theta_m = \theta_m^\circ + \Delta\theta_m \quad \text{(A8)}$$

$$\Delta H = \Delta H^\circ + \Delta(\Delta H) \quad \text{(A9)}$$

$$\Delta S = \Delta S^\circ + \Delta(\Delta S). \quad \text{(A10)}$$

Then, by expanding $\ln K_{di}$, we obtain

$$\ln K_{di} = \ln K_{di}^\circ + \Delta\theta_m\left(\frac{ab_j}{\theta_{ij}} - \frac{\theta_{ij}}{\theta_m^{\circ 2}}\right)\Big/ K_{di}^\circ \quad \text{(A11)}$$

where

$$K_{di}^\circ = \frac{ab_j\theta_m^\circ}{\theta_{ij}} - a - b_j + \frac{\theta_{ij}}{\theta_m^\circ} \quad \text{(A12)}$$

Therefore, the quantity to be minimized is given by

$$M = \sum_{ij}\left[\left(\frac{ab_j}{\theta_{ij}} - \frac{\theta_{ij}}{\theta_m^{\circ 2}}\right)\Delta\theta_m/K_{di}^\circ - \frac{\Delta(\Delta H)}{RT_i} + \frac{\Delta(\Delta S)}{R} + \Delta_{ij}\right]^2 \quad \text{(A13)}$$

with

$$\Delta_{ij} = \ln K_{di}^\circ - \frac{\Delta H^\circ}{RT_i} + \frac{\Delta S^\circ}{R} \quad \text{(A14)}$$

If $\theta_{ij}$ is measured at more than two β-cyclodextrin concentrations, $\theta_m^\circ$, $\Delta H^\circ$, and $\Delta S^\circ$ are determined by Eqs. 4, 5, and 6. But if the measurement is carried out without changing the concentration, $\theta_m^\circ$ may be estimated on the basis of the observed $\theta_{ij}$. By solving the simultaneous equation of

$$\partial M/\partial\Delta\theta_m = 0, \quad \partial M/\partial\Delta(\Delta H) = 0,$$

and

$$\partial M/\partial\Delta(\Delta S) = 0 \quad \text{(A15)}$$

$\Delta\theta_m$, $\Delta(\Delta H)$, and $\Delta(\Delta S)$ are obtained. This procedure should be repeated until the magnitudes of $\Delta\theta_m$, $\Delta(\Delta H)$, and $\Delta(\Delta S)$ are sufficiently smaller than the corresponding standard deviation, which is given by

$$\sigma_p = [m_{pp}^{-1}(\sum_{ij}\Delta_{ij}^2)/(N-3)]^{1/2} \quad \text{(A16)}$$

where $m_{pp}^{-1}$, $\Delta_{ij}$, and $N$ are the $p$-th diagonal element of the inverse matrix, the residual for $\theta_{ij}$, and the number of data, respectively. Usually, the convergence is achieved within ten cycles.

## References


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