The Circular Dichroism Spectra of the β-Cyclodextrin Complex with Naphthalene Derivatives

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The circular dichroism spectra of β-cyclodextrin complexes with naphthalene derivatives were investigated. A remarkable difference in the spectra was observed between the 1-substituted naphthalene complex and the 2-substituted naphthalene complex, indicating that the steric effect of substituents on the formation of the complex is so strong that the structures may be different for these complexes. The calculation of the rotational strength by the method of Kirkwood-Tinoco revealed that the structure of the 2-substituted naphthalene complex is an axial inclusion.

Cyclodextrins, which are produced by the action of *Bacillus macerans* amylase on starch, are cyclic α-1,4-linked D-glucose oligomers. The rings with six, seven, and eight glucose residues in the molecule have different internal diameters ranging from 6 Å to 10 Å.

Cyclodextrins form a number of crystalline adducts with aromatic compounds, paraffins, alkyl halides, *etc.* Of those crystalline adducts, the α-cyclodextrin-iodine complex[1] and the α-cyclodextrin-potassium acetate complex[2] were found by X-ray structure analysis to be inclusion compounds, and the other crystalline adducts have been also regarded as inclusion compounds.

The evidence for the formation of inclusion compounds in a solution have been derived from the kinetic data[3] and the NMR spectra.[4] The interior cavity of the cyclodextrin ring is hydrophobic in nature and binds a hydrophobic portion of the guest molecule, usually forming a 1 : 1 complex. Moreover, cyclodextrins catalyze a number of chemical reactions, such as hydrolysis,[5] oxidation,[6] and decarboxylation,[7] and have been shown to be a good model for enzyme-catalyzed reactions. Tutt and Schwartz[8] showed, in their work on the β-cyclodextrin-catalyzed hydrolysis of penicillin derivatives, that the reaction rate of 2-naphthylpenicilin is four times as fast as that of 1-naphthylpenicillin, although the dissociation constant of the 2-naphthylpenicillin complex is five times as large as that of 1-naphthylpenicillin complex.

Our aim of the present paper is to reveal the structure of the β-cyclodextrin complex with naphthalene derivatives in an aqueous solution by means of the circular dichroism (CD) spectra. When optically-inactive compounds form complexes with cyclodextrins, these compounds exhibit optical activity.[9,10] The circular dichroism spectra of these complexes will give information about their structures, since the optical activity will be induced by the interaction between the cyclodextrin and the guest molecule.

Experimental

The β-cyclodextrin(β-CDx) and naphthalene derivatives were commercial products. β-CDx was recrystallized three times from an aqueous solution. Potassium salts of 1-naphthylacetic acid(1-NAT), 2-naphthylacetic acid(2-NAT), 1-naphthoic acid(1-NA) and 2-naphthoic acid(2-NA) were prepared because these acids are insoluble in water, and were recrystallized from ethanol. 1-Naphthylamine (1-NAM), 2-naphthylamine(2-NAM), 1,8-diaminonaphthalene(1,8-DAN) and 2,3-diaminonaphthalene (2,3-DAN) were recrystallized from a dilute HCl solution as hydrochlorides.

The circular dichroism and absorption spectra were measured using a JASCO J-10 Spectropolarimeter at room temperature. The concentration of β-CDx was adjusted to 0.01 M throughout the measurements. The CD spectra of the 1-substituted naphthalene derivatives were not measurable in the wavelength region longer than 250 nm because of the low intensity. In the region of high absorbancy, the intensity of the CD spectra has a large experimental error, about $\pm 1\times 10^{-5}$ in $\Delta\varepsilon/\varepsilon$.

In the solution, the following equilibrium is established:

β-CDx + naphthalene derivatives ⇌ complex.

The intensity of the CD spectra depends on the concentration of the complex. In the present work, $\Delta\varepsilon$ was estimated by assuming that all the molecules of the naphthalene derivatives in the solution form the complex.*

Calculation

The coupled oscillator model of Kirkwood[11] may account for most of the rotational strength of a strong electric-dipole transition interacting with far-ultraviolet transitions of the vicinal groups. In the Kirkwood model as developed by Tinoco[12] the contributions of individual groups of perturbers were emphasized. According to the Kirkwood-Tinoco expression, the rotational strength is given as follows:

$$R_{0aj} = \frac{\pi \nu_a \nu_0^2 \mu_{0a}^2 (\alpha_{33}-\alpha_{11})_j (\mathrm{GF})_j}{c(\nu_0^2-\nu_a^2)} \qquad (1)$$

$$(\mathrm{GF})_j = \frac{1}{r_j^3}\left[\vec{e}_{0a}\cdot\vec{e}_j - \frac{3(\vec{e}_{0a}\cdot\vec{r}_j)(\vec{e}_j\cdot\vec{r}_j)}{r_j^2}\right]\vec{e}_{0a}\times\vec{e}_j\cdot\vec{r}_j$$

where $\vec{e}_{0a}$ is the unit vector in the direction of the electric dipole moment; $\vec{\mu}_{0a}$, that of the transition from 0 to a, and ν_a, its frequency; $\vec{e}_j$ is the unit vector in the direction of the symmetry axis of the j group, and $\vec{r}_j$ is the distance from the chromophor to the j group with the frequency ν_0 of the exited state; α_{33} and α_{11} are the electric polarizabilities parallel and perpendicular respectively to the symmetry axis of the j group. The values of α_{33}, α_{11},[13] and ν_0 are listed in Table 1. The ν_0 value of the C–C bonds

* Our discussion is not affected by this assumption.

TABLE 1. THE VALUES OF α_{33}, α_{11} AND ν_0.

Bond	$\nu_0 \times 10^{-15}$(1/s)	α_{33}(Å^3)	α_{11}(Å^3)
C-O	1.67	0.089	0.046
C-C	2.00	0.098	0.027

was estimated from the absorption spectra of cyclohexane.[14] The midway value of the first absorption bands of ethylether and ethanol[15] was used as the ν_0 value of the C–O bonds. The transition frequency, ν_a, and the dipole strength, μ_{0a}^2, were estimated from the absorption spectra. The coordinates of β-CDx, which was assumed to have a seven-fold symmetry axis, were estimated on the basis of the coordinates of a glucose residue taken from the X-ray data of the α-cyclodextrin-potassium acetate complex. The origin of the coordinate was fixed on the plane determined by the seven O_4 atoms as is shown in Fig. 6. In the calculation, the effects of all the C_6–O_5 and O–H bonds were neglected because of the flexibility; the effects of all the C–H bonds were also neglected since these bonds may be isotropic and may contribute little to the rotational strength.

Results and Discussion

Figures 1—4 show the absorption and CD spectra of β-CDx complexes with naphthalene derivatives. The CD curves of 1- and 2-substituted naphthalene complexes are remarkably different from each other. For example, in the 2-NAT complex, the ^1L_b and ^1L_a transitions both give negative CD curves, while the ^1B_b transition gives a positive CD curve. On the other hand, the 1-NAT complex shows two weak CD bands with positive and negative signs in the 200—250 nm region. The difference in spectral shape between the 1- and 2-substituted naphthalene com-

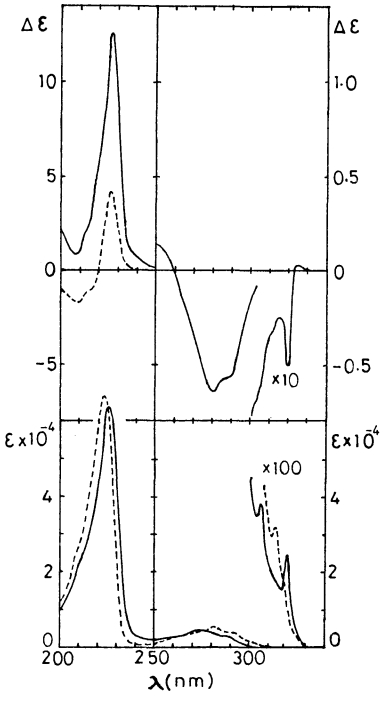

Fig. 1. Absorption and CD spectra of potassium 1-naphthylacetate (----) and potassium 2-naphthylacetate (——) at 0.002 M (250—350 nm) and 0.0002 M (200—250 nm), in 0.01 M β-cyclodextrin solution.

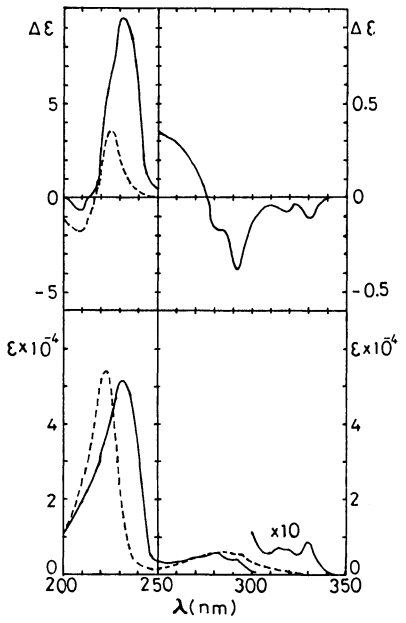

Fig. 2. Absorption and CD spectra of potassium 1-naphthoate (----) and potassium 2-naphthoate (——) at 0.002 M (250—350 nm) and 0.0002 M (200—250 nm), in 0.01 M β-cyclodextrin solution.

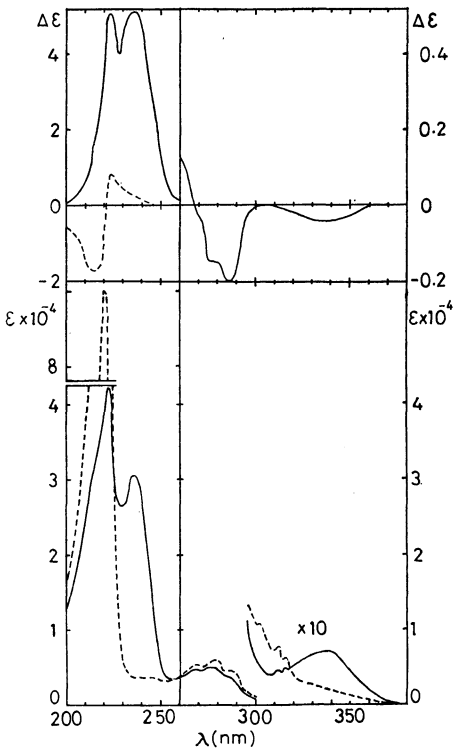

Fig. 3. Absorption and CD spectra of 1-naphthylamine (----) and 2-naphthylamine (——) at 0.002 M (260—380 nm) and 0.0002 M (200—260 nm), in 0.01 M β-cyclodextrin solution.

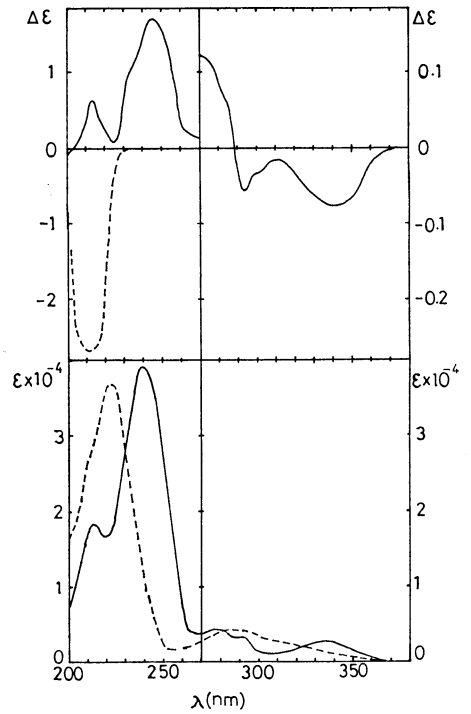

Fig. 4. Absorption and CD spectra of 1,8-diaminonaphthalene (----) and 2,3-diaminonaphthalene (——) at 0.002 M (270—380 nm) and 0.0002 M (200—270 nm), in 0.01 M β-cyclodextrin solution.

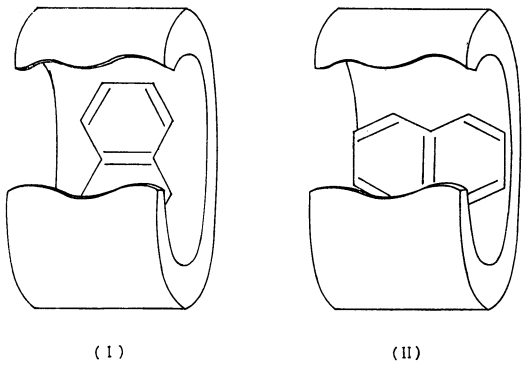

Fig. 5. The two models of the complex; equatorial inclusion (I) and axial inclusion (II).

plexes is considered to be due to the fact that the structure of the 1-substituted naphthalene complex is different from that of the 2-substituted naphthalene complex. As may be seen in Fig. 5, it is impossible for 2-substituted naphthalene, especially 2,3-DAN, to form an equatorial inclusion complex. Therefore, the CD spectra of the 2-substituted naphthalene complex will be atributed to the structure of the axial inclusion. In the case of the 1-substituted naphthalene complex, both types of inclusion are possible, and from a study of the molecular models it is not found which structure is more reasonable.

The two models of the inclusion compounds of β-CDx with naphthalene derivatives, shown in Fig. 5, were examined by comparing the calculated rotational strength with the observed one. The calculation of the rotational strength of the 2-NAT complex was

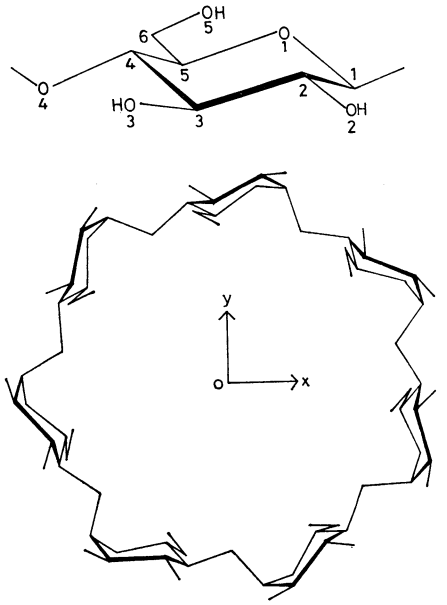

Fig. 6. The assumed structure of β-cyclodextrin.

Table 2. Calculated and observed rotational strength of β-cyclodextrin complex with potassium 2-naphthylacetate.

	$R\times10^{40}$(cgs)	
	^1L_a	^1B_b
Calculation		
(I) Equatorial	1.52	−30.4
(II) Axial	−0.76	60.7
Experimental	−2.65	22.9

carried out by putting the center of the electric dipole moment on the point of origin and by assuming its direction to be the same as that of naphthalene.[16] In the cases of the ^1L_a and ^1B_b transitions, the results are listed in Table 2, along with the observed values. The signs of the calculated rotational strengths based on the axial inclusion complex are in agreement with the observed ones, whereas the signs based on the equatorial inclusion complex are opposite to those observed; thus, the structure of the 2-NAT complex is estimated to be an axial inclusion and the other 2-substituted naphthalene complexes are thought to have similar structures.

The naphthalene ring which is included in the cavity of β-CDx has two degrees of freedom along the symmetry axis of β-CDx, the translation and the rotation. If an electric dipole moment makes the θ angle with the z-axis, as is shown in Fig. 7, its position and direction are determined by θ, φ, and z. In the cases of the ^1L_a and ^1B_b transitions, the rotational strength was shown to be independent of φ. The z-dependence of the rotational strength is shown in Fig. 8. It is found that the complex gives a large CD value when the naphthalene group is situated in the cavity; the rotational strength of the ^1B_b transition takes its maximum value when the electric dipole moment is almost at the center of the cavity, while that

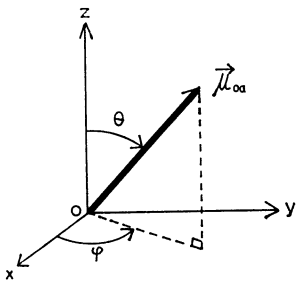

Fig. 7. The coordinate system of the electric dipole moment.

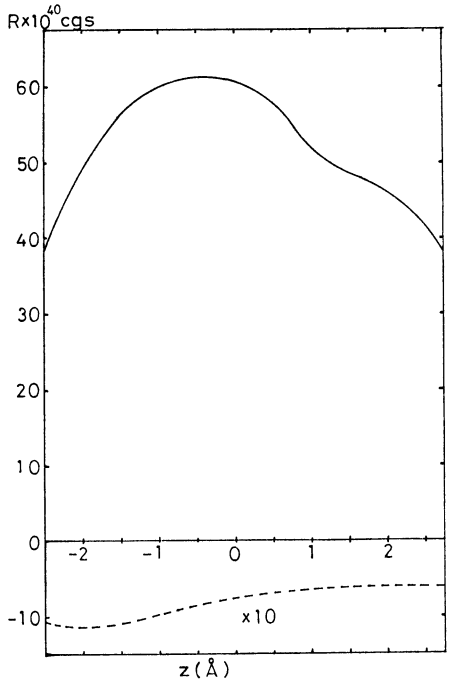

Fig. 8. The z-dependence of rotational strengths of ^1L_a (----) and ^1B_b (——) transition.

of the ^1L_a transition takes its minimum value at −2.0 Å.

It is interesting to calculate the dependence of the rotational strength of θ. If $\vec{e}_{0a}=(\sin\theta, 0, \cos\theta)$, Eq. (1) is expressed as follows:

$$R_{0a} = [A_{0a} + B_{0a}\cos 2\theta + C_{0a}\sin 2\theta]\mu_{0a}^2$$

where A_{0a}, B_{0a}, and C_{0a} are shown in Fig. 9. R_{0a} takes its maximum value at $\theta=0°$ and its minimum value at $\theta=90°$, since C_{0a} is negligible, so the transition with an electric dipole moment parallel to the z-axis gives a positive CD value and the transition with an electric dipole moment perpendicular to the z-axis gives a negative CD value. Thus, it is possible to estimate the orientation of the chromophor in the cavity of β-CDx if the direction of the electric dipole moment in the chromophor is known.

Conclusion

Both experiments and calculations proved that the structure of β-CDx complexes with 2-substituted naphthalene is an axial inclusion and that the assumed

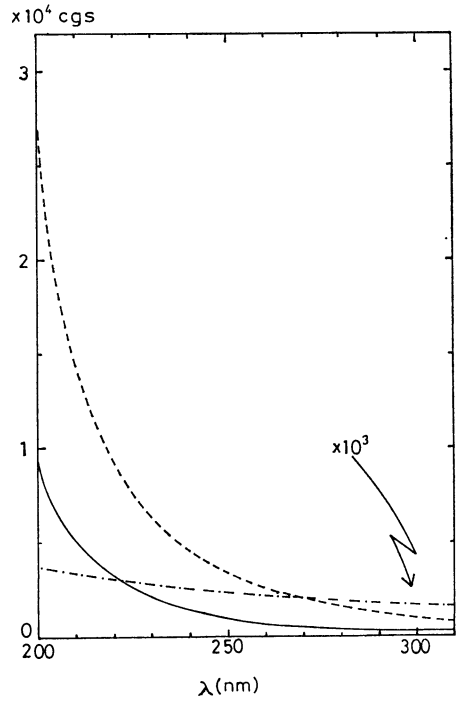

Fig. 9. The wavelength-dependence of A_{0a} (——), B_{0a} (----) and C_{0a} (-·-·-).

conformation of β-CDx is reasonable. The calculated rotational strength is in fairly good agreement with the observed value in spite of the use of a crude approximation. The calculated rotational strengths do not explain the CD spectra of the 1-substituted naphthalene complexes; the positive CD band in the 200—250 nm region suggests an axial inclusion, while the nagative CD band suggests the equatorial inclusion. It is possible that the two species exist in equilibrium.

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