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Marked Differences in Molecular Association Behavior between Two Regioisomers of γ-Cyclodextrin Derivatives Bearing a Pyrenecarbonyl Moiety at C-2 and C-3

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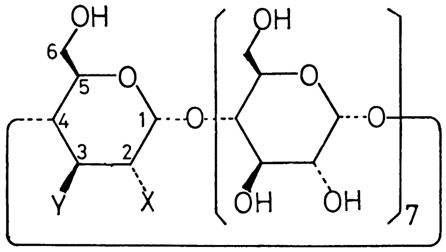
γ-Cyclodextrin derivatives bearing a pyrenecarbonyl moiety at C-2 and at C-3 (1 and 2, respectively) showed marked differences in the fluorescence spectra; 1 exhibits remarkable excimer emission whereas 2 exhibits almost pure monomer emission, suggesting that 1 forms a stable association dimer while 2 exists as a monomer species. Upon addition of l-borneol, the association dimer of 1 was converted into a 1:1 host-guest complex with the binding constant, 5.1-fold larger than that of 2.

Cyclodextrins (CD's), which are cyclic oligosaccharides composed of six, seven, eight, and more D-glucopyranose units (α, β, γ, etc.), are typical hosts and bind a variety of compounds in their central cavities.[1)] The binding abilities of the native CD's have been shown to be changed by modification with various groups.[2)] Recently we have prepared γ-CD derivatives bearing a pyrenebutanoyl moiety at C-2 and C-3 as well as those bearing the moiety at C-6,[3)] and found that the formers exist as monomer species whereas the latters easily form association dimers in aqueous solution. We considered that the absence of any significant difference between the C-2 and C-3 derivatives was mainly due to the presence of the flexible alkyl chain between the pyrene moiety and the γ-CD unit. To clarify this point, we have prepared new γ-CD derivatives bearing a pyrenecarbonyl moiety at C-2 (1) and at C-3 (2), in which a pyrene ring is more closely connected to the γ-CD framework. We report here marked differences in molecular association behavior existing between 1 and 2.

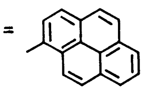
Compounds 1 and 2 were prepared by a reaction of γ-CD and 4-nitrophenyl 1-pyrenecarboxylate, which was prepared by DCC coupling reaction of 4-nitrophenol and 1-pyrenecarboxylic acid, in an alkaline aqueous DMF solution (pH ca. 10).[4)]



1: X=OCOPy ,Y=OH

2: X=OH , Y=OCOPy

Py =



Both 1 and 2 were generated together with a ratio of ca. 1:1 in the reaction. Purification on a preparative HPLC equipped with a reversed phase column (ODS, 20 x 250 mm, water-MeOH as eluent), followed by lyophilization afforded 1 and 2 as pale yellow powders. Satisfactory spectral data (^{13}C-NMR, ^{1}H-NMR, IR, MS (FAB)), and elementary analyses were obtained.$^{5,6)}$

Fluorescence spectra of 1 and 2 in aqueous solution are shown in Fig.1. Compound 1 exhibits prominent excimer emission with a maximum intensity around 500 nm in addition to monomer emission, which exists as a shoulder around 420 nm. The ratio of excimer to monomer emission intensity decreased markedly with decreasing concentration of 1. Similar fluorescence variations were observed by raising temperature and by increasing the content of organic solvent (DMSO) in the solution. These results suggest that 1 forms an association dimer in which two pyrene moieties are faced each other. We attempted to obtain the association constant (K) from concentration dependency of absorption spectra of 1 provided that the monomer and the association dimer are in an equilibrium (Eq. 1). However, the concentration range of 1 suitable for such analysis was too low to enable the K value evaluated accurately. To overcome this limitation, we used the excitation spectra of 1, which gave information of the concentration dependency of 1 even below 10^{-8} M (=mol dm^{-3}). The analysis gave 2.7 x 10^{6} M^{-1} as K of 1 (Fig.2). This extremely large K value indicates that the association dimer of 1 is very stable in aqueous solution. In marked contrast to 1, compound 2 exhibits strong monomer fluorescence at 420 nm and negligible excimer emission in longer wavelength region.

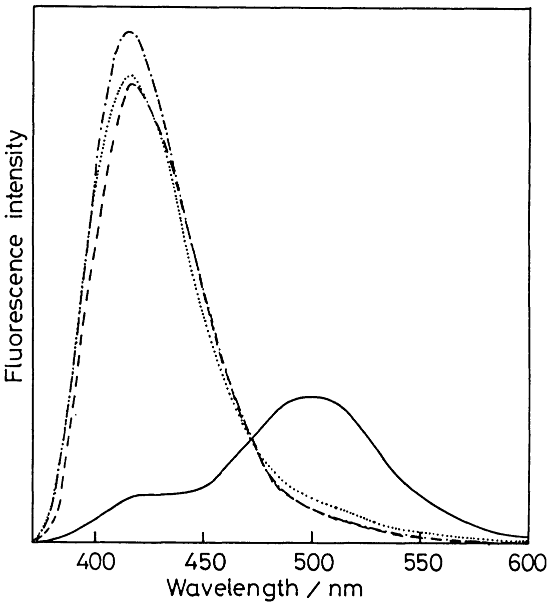


Fig.1. Fluorescence spectra of 1 alone (———) or in the presence of l-borneol (2.00 x 10^{-4} M; - -) and 2 alone (·····) or in the presence of l-borneol (3.33 x 10^{-3} M; —·—·). Concentrations of 1 and 2 were 2.89 x 10^{-5} M and 2.91 x 10^{-5} M, respectively.

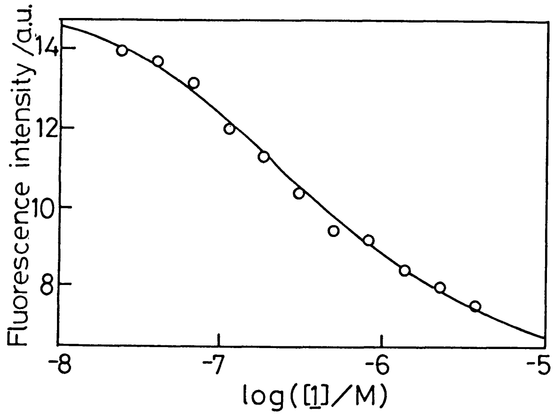


Fig.2. Digital simulation data for the fluorescence intensities of the excitation spectra of 1. Solid line is the calculated curve for K_D = 2.70 x 10^{6} M^{-1}.

Figure 3 shows the induced circular dichroism (ICD) spectra of 1 and 2 in aqueous solution at 25 °C. The compound 1 exhibits a complicated pattern with large ellipticities, which may arise from the interaction between the two pyrene moieties in the association dimer. In contrast, 2 exhibits ICD bands closely related with the absorption bands. The directions of the transition moments, which caused the ICD bands, were determined by measuring the circular dichroism spectra of methyl 1-pyrenecarboxylate in a cholesteryl liquid-crystalline medium.[7)] The spectra indicated that the 286 nm transition occurs along the short axis of the pyrenecarbonyl moiety while others (271, 358, 386 nm) along the long axis. It was theorized that the ICD sign is positive when long axis of a chromophore is parallel to the CD axis.[8)] The pyrenecarbonyl moiety of 2 is therefore suggested to be inserted into the γ-CD cavity with an orientation almost parallel to the CD axis (axial inclusion).

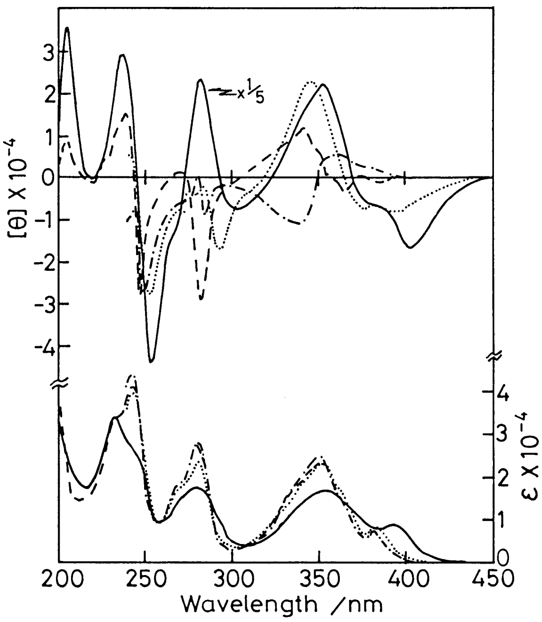


Fig.3. Circular dichroism(top) and absorption(bottom) spectra of 1 alone (———) or in the presence of l-borneol (2.00 x 10^{-4} M; - -) and 2 alone (·····) or in the presence of l-borneol (3.33 x 10^{-3} M; -·-·). Concentrations of 1 and 2 were 2.89 x 10^{-5} M and 2.91 x 10^{-5} M, respectively.

Upon addition of l-borneol to the solution of 1, the excimer intensity ratio decreased and the strength of ICD became smaller. The results may arise from the conversion of the association dimer of 1 into a 1:1 host-guest complex, in which the pyrenecarbonyl moiety is inserted in part into the cavity. The ICD data of 1 suggests that the pyrenecarbonyl moiety is oriented axially in the complex. On the other hand, the complex of 2 exhibits the ICD bands with inverted signs in the wavelength region above 300 nm. This may indicate that 2 changed the orientation of its pyrenecarbonyl moiety upon guest binding from axial to equatorial-like inclusion.

The association constant (K_g) between 1 and l-borneol was determined by the analysis of guest-induced ICD variation at 402 nm based on the following equations.

$$2\,\underline{1} \overset{K}{\rightleftharpoons} (\underline{1})_2 \qquad (1)$$

$$\underline{1} + \text{l-borneol} \overset{K_g}{\rightleftharpoons} (\underline{1}\text{:l-borneol}) \qquad (2)$$

In the case of 2, the guest-induced ICD variation at 345 nm was analyzed based on a simple Benesi-Hildebrand type equation.[9)] The association constants were 35000 M^{-1} and 6900 M^{-1} for 1 and 2, respectively. It is of significant interest that 1 has a strong binding ability in spite of its remarkable tendency to form the association dimer.

Since the only structural difference between 1 and 2 is whether the pyrenecarbonyl moiety is attached to C-2 or C-3, the marked differences in spectroscopic and molecular association properties between them are surprising.

The examination of molecular models (CPK) indicates that the pyrenecarbonyl moiety attached to C-2 of γ-CD is oriented toward the interior of the cavity whereas that attached to C-3 oriented toward the exterior of the cavity, and the present results demonstrate that this orientation difference is an important factor which governs the properties of 1 and 2.

In conclusion, we have shown that 1 and 2 have markedly different properties. The association dimer was formed only for 1, suggesting that the interaction between two pyrenecarbonyl moieties is facilitated only when the moiety is oriented toward the interior of the cavity. The stronger binding of 1 in comparison with 2 may be understood in terms of the in-out orientation difference of the appended moiety with regard to the γ-CD cavity. The results may guide us to effective sensory systems,[10] with which guest molecules can be detected as absorption or fluorescence variations with high sensitivities.

References

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4) Experimental conditions similar to those reported in the following report were used: A.Ueno and R. Breslow, Tetrahedron Lett., 1982, 3451.

5) Spectral data of 1: ^{13}C-NMR (DMSO-d_6, DMSO=39.50) δ=59.61-60.43 (C-6), 69.44 (C-3'), 71.68-73.71 (C-2, C-3, and C-5), 78.15 (C-4'), 79.97-81.16 (C-4), 97.34 (C-1'), 100.58-101.66 (C-1), 123.19-130.34 (pyrene's C-2 - C-16), 133.43 (pyrene's C-1), 166.78 (carbonyl); ^{1}H-NMR (DMSO-d_6, TMS) δ=3.15-3.90 (others), 4.36-4.78 (m, 8H, O_6H), 4.80-5.10 (m, 8H, C_1H), 5.25-5.92 (m, 15H, O_2H and O_3H), 8.13-9.25 (m, 9H, aromatics); IR (KBr) 1720 cm^{-1} (C=O); MS (FAB) M/Z 1525 ($[M+H]^+$), 1547 ($[M+Na]^+$), 1563 ($[M+K]^+$); Anal. Found: C, 45.75; H, 5.92%. Calcd for $C_{65}H_{88}O_{41}$ $10H_2O$: C, 45.78; H, 6.38%.

6) Spectral data of 2: ^{13}C-NMR (DMSO-d_6, DMSO=39.50) δ=59.85-60.00 (C-6), 71.68-73.71 (C-2, C-3, and C-5), 75.24 and 76.74 (C-3' and C-4'), 80.39-81.12 (C-4), 101.02-101.78 (C-1), 123.41-130.54 (pyrene's C-2 - C-16), 133.16 (pyrene's C-1),166.78 (carbonyl); ^{1}H-NMR (DMSO-d_6, TMS) δ=3.00-3.97 (others), 4.20-4.78 (m, 8H, O_6H), 4.80-5.16 (m, 8H, C_1H), 5.44-5.96 (m, 15H, O_2H and O_3H), 8.12-9.22 (m, 9H, aromatics); IR (KBr) 1720 cm^{-1} (C=O); MS (FAB) M/Z 1525 ($[M+H]^+$), 1547 ($[M+Na]^+$), 1563 ($[M+K]^+$); Anal. Found: C, 47.07; H, 6.00%. Calcd for $C_{65}H_{88}O_{41}$ $7H_2O$: C, 47.27; H, 6.23%.

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