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Detection of Organic Compounds by Dual Fluorescence of Bis(1-pyrenecarbonyl)-γ-cyclodextrins

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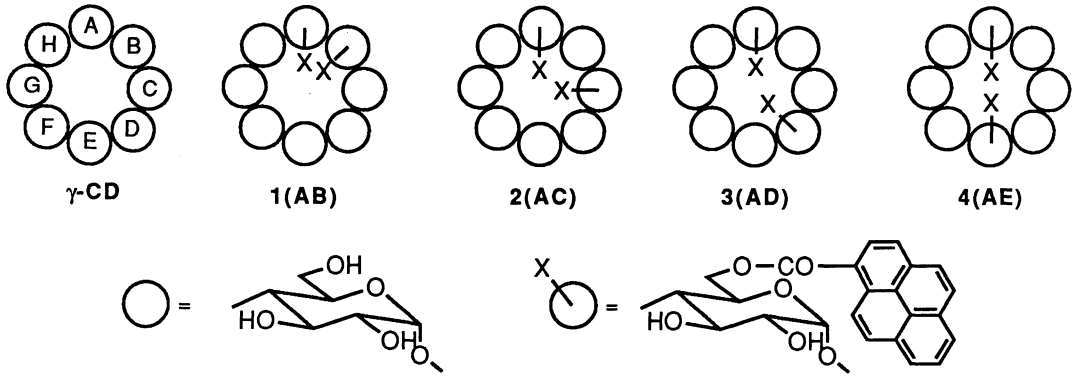
The regioisomers of $6^A,6^X$-bis(1-pyrenecarbonyl)-γ-cyclodextrins (**1-4**) showed dual fluorescence composed of normal and excimer emissions in 30% aqueous DMSO solution. The fluorescence spectra of **1-4** were different from one another and varied upon guest addition in different manners depending on both host and guest. The guest-induced increases or decreases in the excimer emission intensity were used for detecting various organic compounds.

Detection of organic species, especially neutral ones, without damage is an attractive area in analytical chemistry. In this context, we have shown that some modified β- and γ-cyclodextrins (CDs) with an appropriate fluorophore or chromophore are useful to detect spectroscopically inactive monoterpenes and steroidal compounds with favorable selectivity and sensitivity.[1] The modified CDs form complexes with guest compounds and exhibit changes in fluorescence or circular dichroism spectra associated with guest induced conformational changes of the hosts. In the case of γ-CD derivatives bearing a pyrene moiety, [1a] they form association dimers that exhibit a strong excimer emission arising from the face-to-face interaction between two pyrene moieties in the dimers and the guest-induced reduction in the excimer emission intensity was used for detecting organic compounds. Although the systems worked as sensory systems, they have a disadvantage that the host concentration must be set at a constant value to obtain comparable response values for various guests. Furthermore, the selectivity and the sensitivity of the systems were still limited. Therefore, we have prepared bichromophoric γ-CDs,[2] $6^A,6^X$-bis(1-pyrenecarbonyl)-γ-CDs (**1**, **2**, **3**, and **4** for X=B, C, D, and E, respectively), as systems which are capable of forming intramolecular excimers whose emission may change depending on guest, reflecting various conformations of the complexes. In addition, since they are a series of



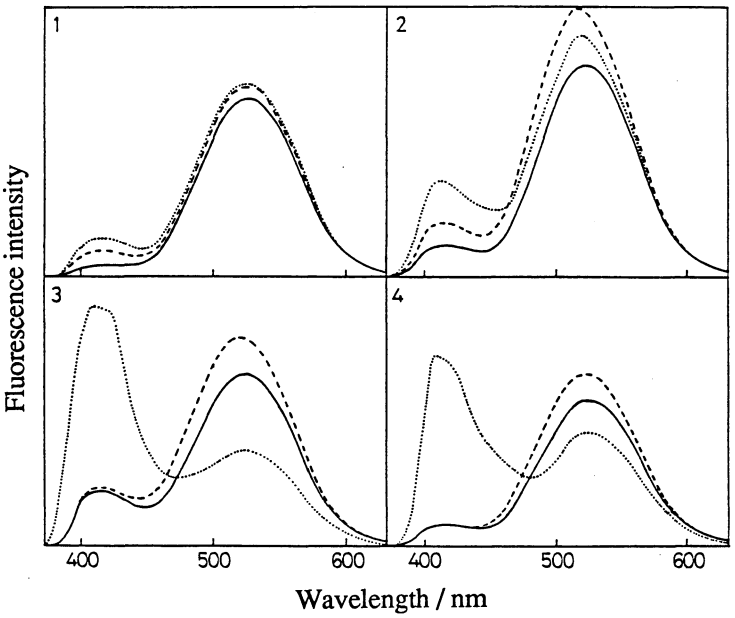


Fig. 1. Fluorescence spectra of **1-4**, alone (ca. 7.5 x 10^{-6} M; ——) or in the presence of *l*-borneol (1.0 mM; - - -) or in the presence of lithocholic acid (0.1 mM;·····) in 30% aqueous DMSO solution.

regioisomers, it is interesting how these hosts are different in fluorescence and binding properties.

Compounds **1-4** were synthesized by the reactions of 6^{A},6^{X}-bis(2-naphthylsulfonyl)-γ-CD[3] and sodium 1-pyrenecarboxylate in dimethylsulfoxide (DMSO) at 80 °C for 24 h, and purified with preparative HPLC. The yields of **1**, **2**, **3**, and **4** are 19, 22, 31, and 23% , respectively.[4]

Figure 1 shows uncorrected fluorescence spectra of **1-4**, alone (solid lines) or in the presence of guests (dashed lines for *l*-borneol (**9**) and dotted lines for lithocholic acid (**12**)) in 30% aqueous DMSO solution. When **1-4** are in the solution alone, their spectral patterns are similar, each exhibiting a strong excimer emission around 520 nm and a weak normal emission around 420 nm. The possibility of association dimer or oligomer formation as the origin of the excimer emission was ruled out because of the fact that the negligible spectral changes were found in the concentration range of 10^{-5} - 10^{-9} M (mol dm^{-3}). The pyrene excimer is therefore formed between the pyrene moieties connected to the same γ-CD framework. The fluorescence spectra of **1-4** changed upon guest addition; **9** caused an increase in the intensity of both normal and excimer emissions, but **12** decreased the intensity of the excimer emission and increased the intensity of the normal fluorescence of **3** and **4** and increased the intensity of both normal and excimer emissions of **1** and **2**. The guest-induced intensity variation (ΔI) measured at the peak of the excimer emission for each of **1-4** was used as a sensitivity parameter for guest detection of **1-4**. The ΔI values were normalized by initial fluorescence intensities (I_0). The responses of **1-4** to various guests are shown in Fig. 2. Compounds **5-11** (*d*-fenchone, **5**; *l*-fenchone, **6**; nerol, **7**; geraniol, **8**; *l*-borneol, **9**; *d*-menthol, **10**; *l*-menthol, **11**) are monoterpenes and increased the excimer emission intensities of **1-4**. Among them, relatively large $\Delta I/I_0$ values of **1-4** were found for bicyclic compounds (**5**, **6**, **9**), as is the case of other CD derivatives.[1] Monocyclic compounds (**10**, **11**) induced less variations than acyclic compounds (**7**, **8**). These results suggest that the molecular shape of the guests is a crucial factor for them to be detected with high sensitivities. The important aspect of the results is that **3** exhibits a marked discrimination between **7** and **8** as shown by a high sensitivity for **7** in contrast to no response for **8**. On the other hand, the discrimination between enantiomers was difficult with these systems as shown by small differences between **5** and **6** and between **10** and **11**. For five cholic acid derivatives (lithocholic acid, **12**;

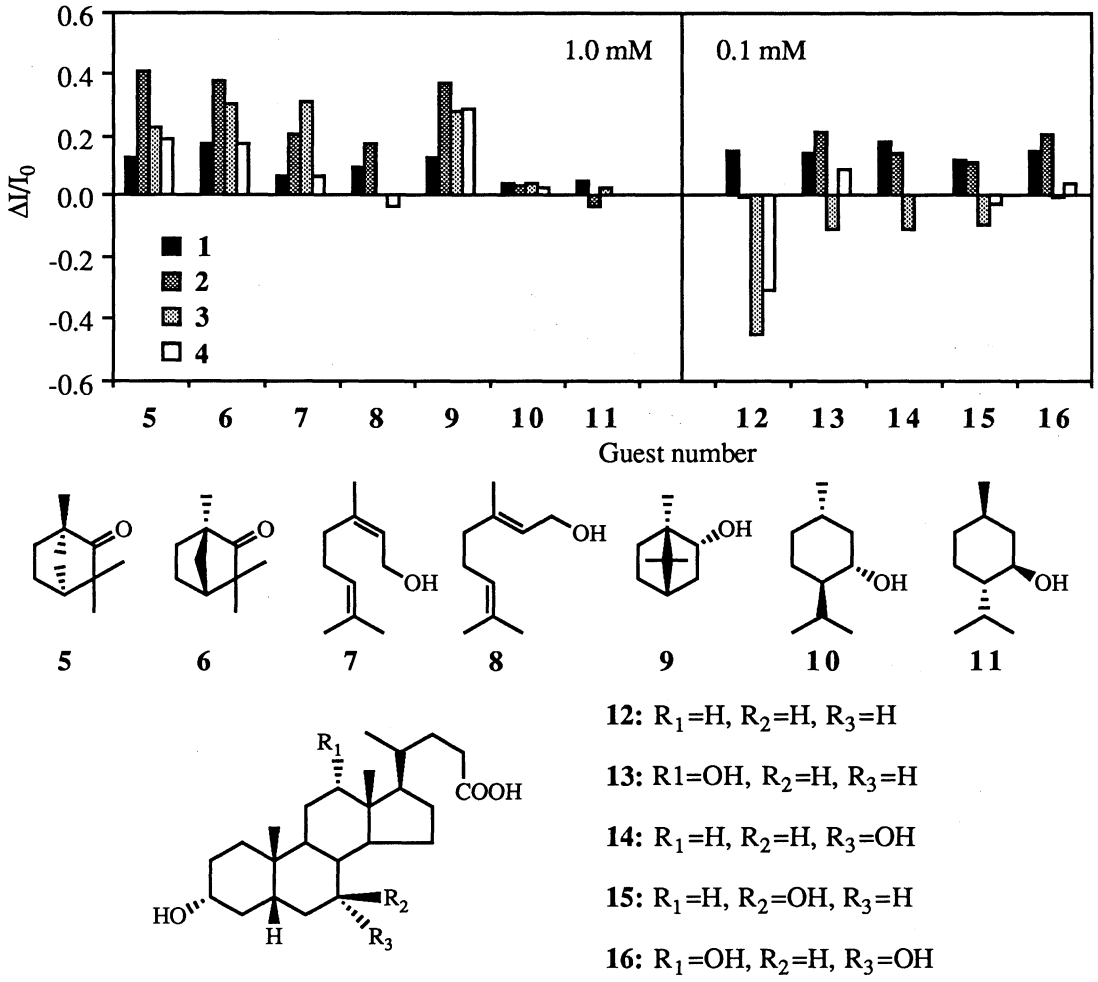


Fig. 2. The sensitivity factors $\Delta I/I_0$ of **1-4** for various guests.

deoxycholic acid, **13**; chenodeoxycholic acid, **14**; ursodeoxycholic acid, **15**, cholic acid, **16**) measured at their concentration of 0.1 mM, **1** showed positive values of $\Delta I/I_0$ with moderate recognition ability. On the other hand, **3** showed negative values of $\Delta I/I_0$ to all cholic acid derivatives with different sensitivities in the order of **12** > **13** ≅ **14** ≅ **15** > **16**. This order was completely proportional to the number of the hydroxyl groups of the steroids, indicating that **3** can recognize the hydrophobicity of the cholic acid derivatives. The other hosts, **2** and **4**, showed complicated responses to the steroids. Although the response patterns of monochromophoric CDs reported earlier[1] were all similar even in the cases where parent CDs were different (β- and γ-CD), those of **1-4**, were different from one another. All these results may be related to the structural features of the complexes.

It is reasonably expected that the stronger is the affinity between host and guest, the larger is the variation in the fluorescence intensity induced. In this context, we obtained host-guest binding constants of **1-4** for **9** and **12** from the guest-induced variations in fluorescence or circular dichroism intensity. The results are summarized in Table 1. For **9**, host **3** has the largest binding constant among the four hosts, the value being 19000 M^{-1}. The largest sensitivity, however, was obtained by **2** whose binding constant was 10000 M^{-1}. The host whose sensitivity is secondary for **9** was **4**, but its binding constant is 7500 M^{-1} which is the smallest among the values

Table 1. 1:1 Host-Guest Binding Constants of **1-4** in 30% Aqueous DMSO Solution at 25 °C

	K/M^{-1}			
Guest	**1**	**2**	**3**	**4**
9	9300[a]	10000[a]	19000[a]	7500[a]
12	420000[a]	b[a]	5000000[a]	400000[a]
	b[c]	1100000[c]	3700000[c]	370000[c]

a) Determined from guest-induced fluorescence intensity variations. b) The values could not be determined accurately due to the small spectral variations. c) Determined from guest-induced circular dichroism intensity variations.

of **1-4**. Although **2** has a relatively large value as the binding constant for **12** (1100000 M^{-1}), it was ineffective to detect the guest. These results strongly indicate that the sensitivities of **1-4** are governed by the conformations of the host-guest complexes rather than by the binding affinities. This feature is very different from that of monochromophoric CDs which exhibit good correlations between the binding affinities and the sensitivities.

In conclusion, host molecules **1-4** show remarkable molecular recognition abilities in guest binding. They show different fluorescence changes from which various response patterns are formed. Size, shape, and polarity of the guests may be reflected in the patterns.

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References

1) a) A. Ueno, I. Suzuki, and T. Osa, *Anal. Chem.*, **62**, 2461 (1990); b) A. Ueno, S. Minato, I. Suzuki, M. Fukushima, M. Ohkubo, T. Osa, F. Hamada, and K. Murai, *Chem. Lett.*, **1990**, 605; c) Q. Chen, I. Suzuki, T. Osa, and A. Ueno, *Makromol. Chem., Rapid. Commun.*, **12**, 113 (1991); d) M. Fukushima, T, Osa, and A. Ueno, *Chem. Lett.*, **1991**, 709.

2) S. Minato, T. Osa, and A. Ueno, *J. Chem. Soc., Chem. Commun.*, **1991**, 107.

3) A. Ueno, F. Moriwaki, A. Azuma, and T. Osa, *J. Org. Chem.*, **54**, 295 (1989).

4) All spectral data will be shown later. **1:** Anal. Found: C, 50.93; H, 5.56%. Calcd for $C_{82}H_{96}O_{42}\cdot 10H_2O$: C, 50.93; H, 6.05%. MS (FAB) M/Z 1753 ([M+H]$^+$). **2**: Anal. Found: C, 51.09; H, 5.63%. Calcd for $C_{82}H_{96}O_{42}\cdot 10H_2O$: C, 50.93; H, 6.05%. MS (FAB) M/Z 1753 ([M+H]$^+$). **3**: Anal. Found: C, 52.42; H, 5.68%. Calcd for $C_{82}H_{96}O_{42}\cdot 7H_2O$: C, 52.29; H, 5.90%. MS (FAB) M/Z 1753 ([M+H]$^+$). **4**: Anal. Found: C, 52.79; H, 5.54%. Calcd for $C_{82}H_{96}O_{42}\cdot 6H_2O$: C, 52.90; H, 5.85%. MS (FAB) M/Z 1753 ([M+H]$^+$).

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