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Photoswitchable Multi-response Sensor of Azobenzene-modified γ-Cyclodextrin for Detecting Organic Compounds

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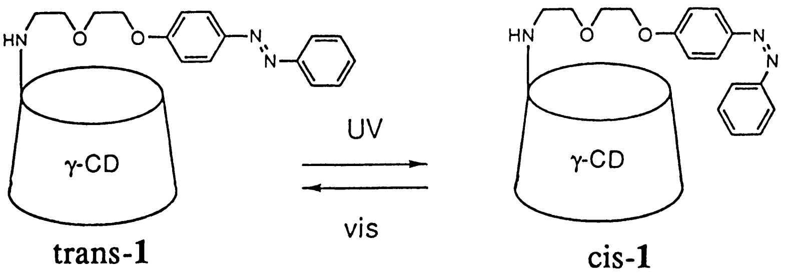
Azobenzene-modified γ-cyclodextrin (**1**) can be used as a multi-response type of host-guest sensory system, which works on the basis of guest-induced circular dichroism variations of trans and cis forms of **1**.

Cyclodextrins (CDs), which are cyclic oligomers of D-glucose named as α, β, and γ for hexa-, hepta-, and octamers, form inclusion complexes with a variety of organic compounds in aqueous solution.[1)] Although native CDs are spectroscopically inactive, they may be converted into spectroscopically active hosts by modification with chromophores. Recently, such modified CDs have been shown to change absorption, fluorescence and circular dichroism spectra upon complexation with guest species, and used as host-guest sensors.[2-5)] If a host gives several responses to a guest, the sensory host may be more useful to identify the compound. In the present study, we have undertaken the attempt to get several responses from a host on the basis of the different absorption bands (π-π* and n-π*) and the different structures (trans and cis) of azobenzene-modified CD (**1**), and we wish to report here the first example of the hosts that give several responses.

Compound **1** was prepared by reaction of 6-(2-naphthylsulfonyl)-γ-CD with 5-(4-phenylazophenoxy)-3-oxapentylamine in N,N-dimethylformamide at 80 °C for 24 h. Repeated recrystallization from water afforded **1** as orange crystals, yield 17%.[6)]



trans-1 **cis-1**

The photoisomerization of the azobenzene moiety of **1** has been performed by UV irradiation (310 <λ<390 nm) in aqueous solution, the cis content at the photostationary state being 79 %. The cis form was returned back to the original trans form with the half life of 35 h at 25 °C or immediately by visible light irradiation.

Figure 1 shows circular dichroism spectra of **1** (5.55 x 10^{-5} mol dm^{-3}), alone or in the presence of lithocholic acid (**9**) or *l*-menthol (**4**) before and after UV irradiation. The trans form of **1** exhibits a strong dichroism band at 335 nm associated with the π-π^* transition of the azobenzene moiety while a weak broad band above 400 nm associated with the n-π^* transition.

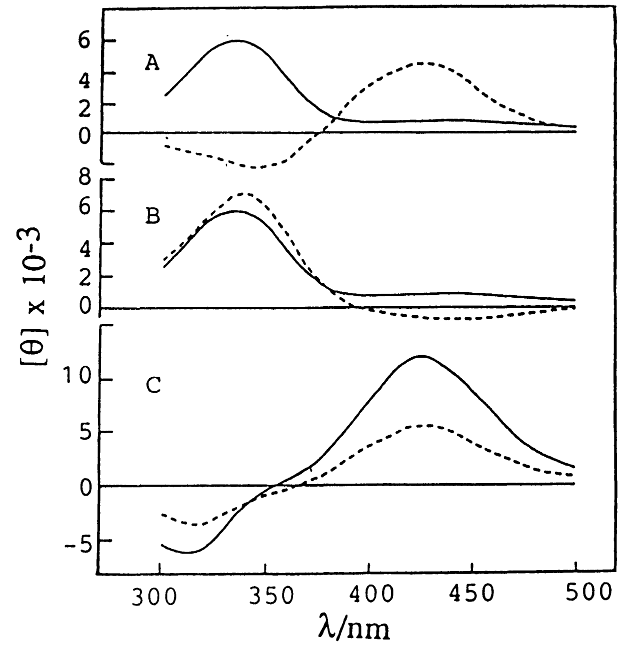


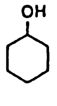
Fig. 1. Circular dichroism spectra of **1**, alone (—) or in the presence of guest (--- : **9** (A,C), 0.1; **4** (B), 2.0 mmol dm^{-3}) before (A, B) and after (C) UV irradiation.

The circular dichroism spectrum of trans-**1** in the presence of **9** exhibits a negative band around 345 nm whereas it exhibits a positive band around 425 nm. Many other guests also exhibit similar guest-induced circular dichroism changes. However, when we examined the effect of **4** on the circular dichroism of trans-**1**, we found that the changes induced by this guest are different from those of others, exhibiting enhanced and depressed dichroism intensities for the π-π^* and the n-π^* transition bands, respectively (Fig. 1, B).

Since an arene moiety included in the CD cavity with an orientation parallel to the CD axis (axial inclusion) shows a positive dichroism band while that with the orientation perpendicular to the CD axis (equatorial inclusion) shows a negative band,7,8) the positive band observed for trans-**1**, alone, indicates that the moiety is included with the axial orientation and on the contrary the negative band observed for trans-**1** in the presence of each guest except for **4** indicates that the moiety is included with the equatorial orientation. The exceptional enhancement in the dichroism band of the azobenzene π-π^* band induced by **4** suggests that the azobenzene moiety in this complex is oriented more parallel to the CD axis than that of trans-**1**, alone. These results suggest that the trans-azobenzene moiety of trans-**1** acts as a cap in the complexes with ordinary guests whereas acts as a spacer in the complex with **4**.2)

The circular dichroism spectra of **1** after UV irradiation exhibit a negative band around 312 nm and a positive band around 425 nm. The absolute dichroism intensities of the bands diminishes upon addition of guest compounds. Although the orientation of the cis azobenzene moiety in the CD cavity is not clear due to its nonplanar structure, the decreased dichroism intensities suggest that the azobenzenen moiety is excluded from the cavity associated with accommodation of the guest species.

Figure 2 shows the variations of the dichroism intensities of **1** induced by guest species. The measurements were undertaken at 335 and 425 nm for trans-**1** and 425 nm for cis-**1**, here the values for cis-**1** being those for **1** after UV irradiation. The $(\theta_0-\theta_x)/\theta_0$ value was used as the sensitivity parameter, where θ_0 and θ_x are the molecular ellipticities of the host, alone and in the presence of guest, respectively. The order of sensitivity obtained at the guest concentration of 2 mmol dm^{-3} for the 335-nm band of trans-**1** and for the 425-nm band of cis-**1** is cyclohexanol (**2**) <*l*-borneol (**3**) <cholic acid (**5**), and the sensitivities for the 425-nm band of trans-**1** are negligible with these guests. Compound **4** is exceptional with the sensitivity values negative at 335 nm and remarkably positive at 425 nm for trans-**1**. The sensitivity parameters of the 335-nm band of trans-**1** obtained at 0.2 mmol dm^{-3} for the steroidal compounds including **5**, deoxycholic acid (**6**), chenodeoxycholic acid (**7**), and ursodeoxycholic acid (**8**) are different in spite of the fact that they have the same steroidal framework. The order of sensitivity of the three steroids **5**, **6**, and **7** is **5**<**6**<**7**, suggesting that the number and the position of hydroxyl group are important. Compounds **6**, **7**, and **8** are stereochemical isomers, one hydroxyl group is located at C-12 for **6** and at C-7 for **7** and **8** and the orientation of the C-7 hydroxyl group is opposite between **7** and **8**. Therefore the remarkable differences in the sensitivity observed for **6** and **7** and for **7** and **8** indicate that trans-**1** has an appreciable ability of molecular recognition. The fact that **5** was detected with much smaller sensitivity may be explained by the presence of one more hydroxyl group in this compound than **6**, **7**, and **8**, which makes **5** less hydrophobic. The sensitivity parameters of trans and cis forms of **1** for **9**, which were obtained on the solution of 0.1 mmol dm^{-3} owing to its poor solubility, are the largest among the steroids examined here. This result is consistent with the fact that **9** is most hydrophobic as indicated by one or two



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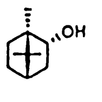

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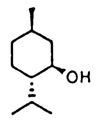

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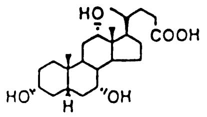

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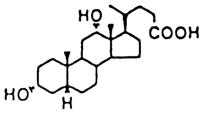

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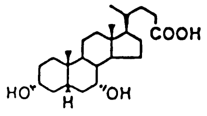

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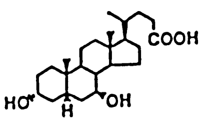

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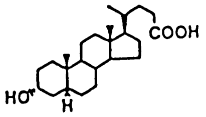

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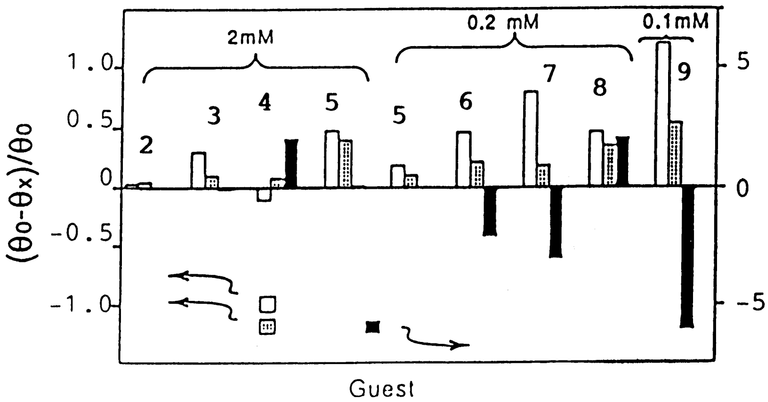

Fig. 2. Guest-induced circular dichroism variations at 335 nm (trans-**1**, □) and 425 nm (trans-**1**, ■ ; cis-**1**, ▤). The guest concentrations are 2.0, 0.2, and 0.1 mM (mM=mol dm^{-3}).

less number of hydroxyl group than **5**, **6**, **7**, and **8**. The sensitivity parameter of the 425-nm band of trans-**1** is nearly zero for **5**, whereas negative for **6**, **7**, and **9** and positive for **8**. The result indicates again that the molecular recognition ability of trans-**1** is remarkable. Particularly, it is interesting that the stereoisomers of **7** and **8** were detected with the sensitivity parameters opposite in the sign. The features of the sensitivity parameters of cis-**1** (425 nm) are also different from those of trans-**1** (335, 425 nm) , and all these parameters form a set of response pattern for each guest. Since the pattern depends on the size and the kind of guest species, it might be used to identify each compound by comparison with the response patterns of the standard samples.

Table 1. Binding constants of trans and cis forms of **1** for steroidal compounds in aqueous solution (pH 6.95) at 25 °C[a)]

Guest	K/mol-1 dm3 trans-**1**	 cis-**1**
5	1330	800
6	5770	3790
7	13100	5290
8	27400	11400
9	>200000	17000

a) Determined by the guest-induced circular dichroism variations.

Table 1 shows binding constants of trans and cis forms of **1** for the steroidal compounds. Both forms of **1** exhibit the same tendency in the binding constants, **5**<**6**<**7**<**8**<**9**. This order is roughly parallel to that of the sensitivity parameters, but it is important that the sensitivity parameter is not completely determined by the binding strength; both binding and structural features of the complexes are reflected in the sensitivity parameters. It is noted that the binding ability of trans-**1** is larger than that of cis-**1**, and consequently photocontrol of guest binding is possible with this host.

In conclusion, we have shown that a multi-response pattern for each guest can be constructed even with a single host by using plural transition bands and photoswitchable nature of the host.

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