Photochromic molecular recognition of β-cyclodextrin bearing spiropyran moiety for organic guests

Fumio Hamada,*[a] Koutarou Hoshi,[a] Yutaka Higuchi,[a] Kouichi Murai,[a] Youichi Akagami[b] and Akihiko Ueno*[c]

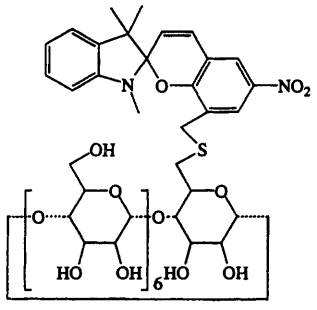
[a] *Department of Materials Engineering and Applied Chemistry, Mining College, Akita University, Tegata, Akita 010, Japan*
[b] *Akita Prefectural Industrial Center, 4–11 Sanuki, Araya, Akita 010, Japan*
[c] *Department of Bioengineering, Faculty of Bioscience and Biotechnology, Tokyo Institute of Technology, 4259 Nagatsuta, Yokohama 227, Japan*

The photochromic behaviour and guest binding properties of β-cyclodextrin modified with 1′,3′,3′-trimethyl-6-nitro-8-methylspiro[2*H*-1-benzopyran-2,2′-indoline] (1) has been investigated. Compound 1 exhibits a unique photochromic response in comparison to those of the 1′-(3-oxopropyl)-3′,3′-dimethyl-6-nitrospiro[2*H*-1-benzopyran-2,2′-indoline] modified β- and γ-cyclodextrins (2 and 3, respectively). Compound 1 shows reverse photochromism in aqueous or ethylene glycol solutions, however, in less polar solvent such as dimethyl sulfoxide, 1 exhibits a mixed type of normal and reverse photochromism. The closed form of 1 in aqueous solution is converted to the opened form by keeping it in the dark. The half-lives of the closed form in the dark are affected by the presence of a guest. The highest value is obtained when 1-borneol was used. The magnitude of the half-lives and the binding constant for a guest examined are comparable, and is dependent on the guest molecular size.

Introduction

Cyclodextrins are torus-shaped cyclic oligomers of D-glucopyranose which can form host–guest complexes with a variety of guests in their cavity and have attracted much interest as model compounds for the study of enzymes.[1] When we study host–guest complexation behaviour of native cyclodextrins by spectroscopic methods such as fluorescence, induced circular dichroism (ICD) or absorption intensity changes, spectroscopically active guests should be used because cyclodextrins themselves are spectroscopically inert. Cyclodextrins can, however, become spectroscopically active compounds by modification with chromophores and spectroscopically inert guests can be recognized by the spectral change of modified cyclodextrins upon addition of a guest. During the last decade we have reported several cyclodextrins modified with chromophores such as naphthalene, anthracene and dancylglycine, which show a spectroscopic change in the fluorescence, ICD or absorption intensity upon accommodation of a guest, even though we used a spectroscopically inert guest. In these systems the chromophores act as a probe of the host–guest complexation behaviour, and act as a cap to increase the hydrophobic interaction with a guest or as a spacer to regulate the cyclodextrin cavity size.[2] On the other hand, we have used a photochromic compound such as spiropyran or azobenzene as a chromophore; the structures of these compounds are changed by photoirradiation resulting in a change in the affinity of the binding site for the guest molecules.

Recently we reported the photochromic molecular recognition system using spiropyran-modified γ-cyclodextrin **3**.[3] In this system, the spiropyran moiety is included in the cyclodextrin cavity and a small guest such as cyclohexanol is accommodated and the isomerization of the closed form to the opened form is depressed. On the other hand, when a larger guest such as *l*-borneol was used, the isomerization was accelerated because the spiropyran moiety is displaced from the cyclodextrin cavity by a guest molecule. Although the β-cyclodextrin analogue **2**[4] shows photochromic behaviour which is independent of the nature of the guest species because of the small cavity size of β-cyclodextrin. Here, the spiropyran moiety simply comes close to the cyclodextrin cavity, not inside, and acts as a hydrophobic cap, finally both the closed and opened forms of **2** exhibit almost the same binding abilities for a couple of guests examined. It is reported that some of the spiropyran derivative, which is a 6-SO_3^-–spiropyran, can be included by the β-cyclodextrin and the inclusion complex between the closed form and the cyclodextrin is more stable than that



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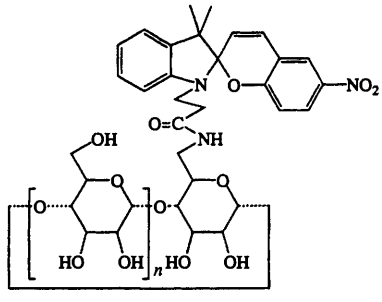


n=6; **2**

n=7; **3**

between the opened form and the cyclodextrin.[5] Based on this result, if the spiropyran-modified β-cyclodextrin can be made which can form an intramolecular complex between the appended spiropyran moiety and the cyclodextrin, different photochromic behaviour should be observed compared with those of **2** or **3**. In this study, we would like to report the photochromic molecular recognition system using **1**, which exhibits the new type of molecular recognition system based on the photochromic change in the presence or absence of a guest molecule.

Experimental

Materials

The commercially available guaranteed reagents were used without further purification. *N*,*N*-Dimethylformamide (DMF), ethylene glycol (EG) and dimethyl sulfoxide (DMSO) were Dotite-spectrosol grade.

Spectroscopy

The UV and induced circular dichroism (ICD) spectra were measured at 25 °C with a Hitachi U-2000 spectrophotometer and a JASCO J-700 spectropolarimeter, respectively. The ICD intensities were expressed as molar ellipticity ([Θ]) (in degrees cm^2 $dmol^{-1}$). Photoirradiation was performed with a 500 W xenon lamp (Ushio Electric Inc. UI-502Q) using cut-off filters Corning 7-37 and 3-73 for isolating UV (320–380 nm) and visible (425–500 nm) light, respectively.

Preparation of spiropyran-modified β-cyclodextrin (1)

6-Deoxy-6-sulfanyl-β-cyclodextrin[6] (1.0 g, 0.87 mmol) was added to a solution of 1′,3′,3′-trimethyl-6-nitro-8-(chloromethyl)-spiro[2*H*-1-benzopyran-2,2′-indoline][7] (0.48 mg, 1.31 mmol) in 50 ml of DMF. The reaction mixture was heated at 50 °C for 24 h under a nitrogen atmosphere. After cooling, the reaction mixture was poured into 500 ml of acetone. The resultant precipitate was resolved in a small amount of water. The insoluble fraction was filtered and the filtrate was purified by chromatography (CM-Sephadex C-50 column; 7 × 25 cm) using water as eluting solvent to yield pure **1** (252 mg; 20%) as a violet powder. R_f: 0.59 (vol. ratio of butan-1-ol–ethanol–water 5:4:3). δ_H([$^2H_6$]DMSO) 1.12–1.32 (6 H, m, CH_3), 2.09 (3 H, s, NCH_3), 3.10–3.78 (m, 42 H, CyD protons), 4.47 (6 H, br s, O-6-H), 4.83 (7 H, m, C-1-H), 5.60–5.95 (14 H, br s, O-2-H and O-3-H), 6.0 (1 H, d, J = 11 Hz, CH=C*H*-nitrobenzene), 6.62 (1 H, t, J = 8 Hz, aromatic-H), 6.82 (1 H, t, J = 8 Hz, aromatic-H), 7.04–7.26 (3 H, m, aromatic-H), 8.0 (1 H, br s, aromatic-H of nitrobenzene), 8.18 (1 H, br s, aromatic-H of nitrobenzene) (Found: C, 43.99; H, 6.37; N, 1.27; S, 1.84. Calc. for $C_{62}H_{88}O_{37}N_2S$·12H_2O: C, 43.76; H, 6.63; N, 1.64; S, 1.88%.) MS (FAB) *m*/*z* 1486 ([M+H]$^+$).

Results and discussion

Photochromism

Fig. 1 shows the absorption spectra of **1** in aqueous solution. When the aqueous solution of **1** was placed in the dark or irradiated by UV, **1** shows an absorption band at 513 nm, which is characteristic of the opened form, while after visible light irradiation the absorption band disappeared as the closed form was produced. This photochromic behaviour, named reverse photochromism, is the same as observed for the spiropyran-modified β- and γ-analogues (**2** and **3**, respectively). The photochromic behaviour of **1** in different solvent systems is summarized in Table 1. In EG solution, **1** shows reverse photochromism in which the closed form is produced by visible light irradiation or the opened one is obtained by UV irradiation or leaving in the dark. On the other hand, **1** in DMSO exhibits a mixed type of normal and reverse photochromism. The closed form of **1** obtained by visible light irradiation is converted to the opened form when the closed one is kept in the dark. Although the opened form produced by UV irradiation is converted to the closed one in the dark, which is assigned as normal photochromism. This photochromic behaviour is different to that of **2** and **3**. This result indicates that the polarity of solvents affects the photochromism of **1**. In different solvents the absorption band attributed to the opened form of **1** was shifted to a shorter wavelength with increasing solvent polarity as shown by the shift from 560 nm in dimethyl sulfoxide to 513 nm in aqueous solution. Fig. 2 shows the increase in the absorbance intensity at 513 nm of **1** in aqueous solution in the presence or absence of a guest. The conversion of **1** alone from the closed form to the opened one has been achieved completely by keeping it in the dark for 9 h. On the other hand, it takes a longer time for the complete isomerization when *l*-borneol or adamantanol was used as a guest. This fact suggests that the photochromic change of **1** should be affected by the presence or absence of a guest.

Table 1 Photochromism and absorption of **1** at 25 °C

Solvent[a]	Photochromism	λ_{max}/nm
H_2O	Reverse	513
EG	Reverse	529
DMSO	Normal and reverse mixed type	560

[a] EG: ethylene glycol; DMSO: dimethyl sulfoxide.

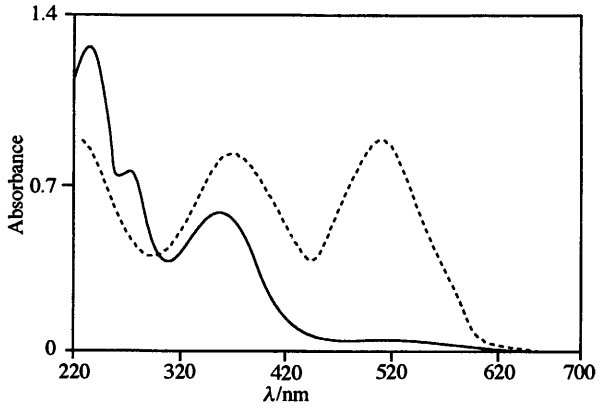


Fig. 1 Absorption spectra of the closed (——) and the opened form (- - - - - -) of **1** in aqueous solution (1 × 10^{-4} mol l^{-1})

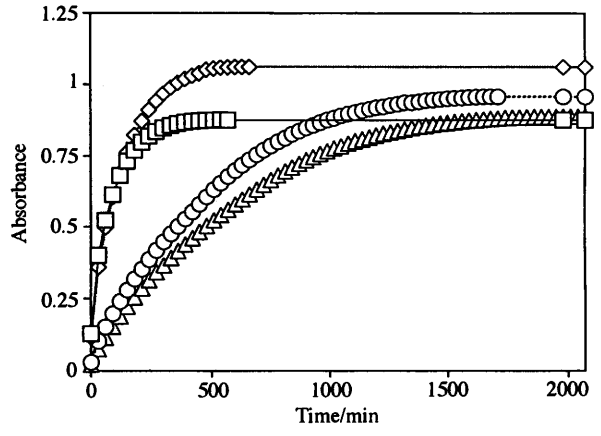


Fig. 2 Time-courses of increase in the absorbance at 513 nm of **1** (1 × 10^{-4} mol l^{-1}) in the absence of a guest (—□—) and in the presence of nerol (1 × 10^{-3} mol l^{-1}) (···◇···), *l*-borneol (1 × 10^{-3} mol l^{-1}) (···○···) and adamantanol (1 × 10^{-3} mol l^{-1}) (···△···)

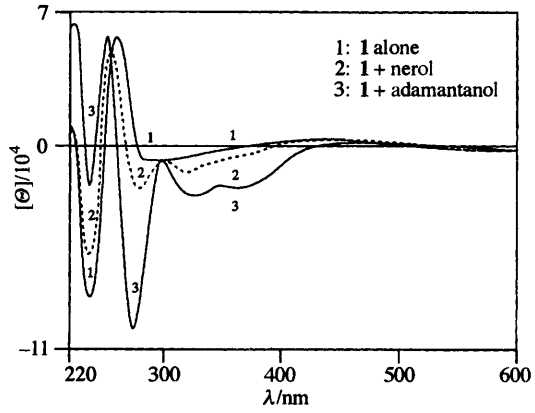


Fig. 3 ICD spectra of closed form of **1** (1×10^{-4} mol l^{-1}) in aqueous solution in the absence of a guest or in the presence of nerol (1×10^{-3} mol l^{-1}) and adamantanol (1×10^{-3} mol l^{-1})

Induced circular dichroism

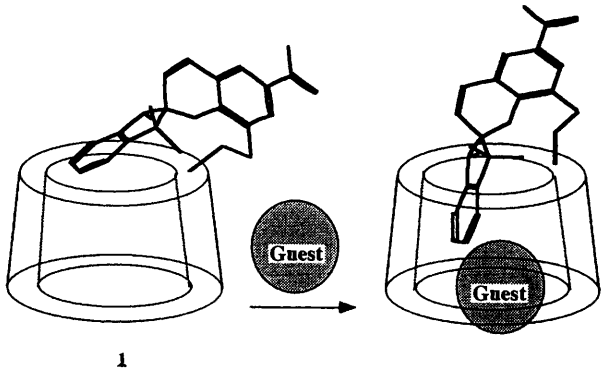
Fig. 3 shows the ICD spectra changes of the closed form of **1** alone or in the presence of a guest. When adamantanol was used as a guest, the [Θ] value of the positive band at around 238 nm decreases and the new negative band at 274 nm appears with high intensity, together with an increase in the negative bands at around 325 and 370 nm. On the other hand, the change in the [Θ] values in the presence of nerol is smaller than with adamantanol. These results suggest that **1** recognizes adamantanol much more than nerol as the ICD spectra change indicates the magnitude of the host–guest complexation. It is well known that the increase in ICD intensity means the appended moiety is included in the chiral environment of the cyclodextrin cavity, while the decrease means the appended moiety is distant from it. However, the ICD spectra of **1** in the presence of a guest shows that there is large decrease in the negative band at 238 nm, or large increase at 274 nm. This phenomena suggests the movement of the appended spiropyran moiety on accommodation of a guest in the cavity is not simple because of the twisted structure of the spiropyran. One possibility is illustrated in Scheme 1. It is expected that some part of the spiropyran moiety is excluded and the other part is included in the cavity with accommodation of a guest inside. The guest-induced variations in ICD intensities at 238 nm were used to obtain the binding constants (K) of **1** by using eqn. (1), which can be used in the presence of a large excess of a guest.[8]

$$\frac{\Theta_h - \Theta_x}{C_g} = k\Theta_x - k\Theta_c \qquad (1)$$

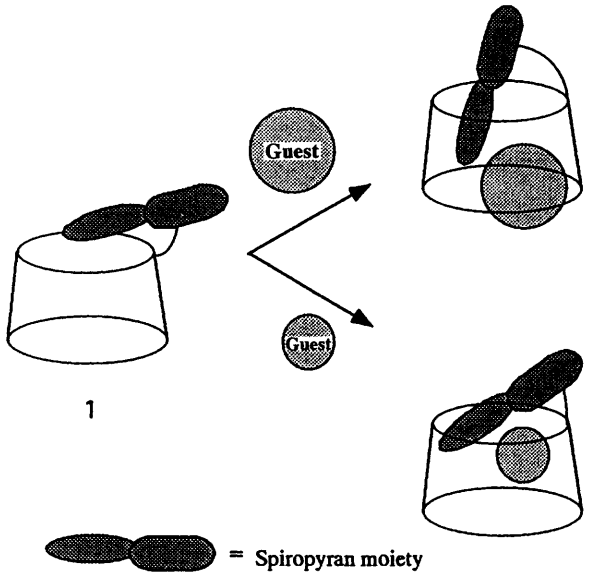
In eqn. (1), Θ is the molar ellipticity (the molar ellipticity at 238 nm in this study), Θ_x for the complex, Θ_h for the host alone, Θ_c for the complex and C_g the total guest concentration. Table 2 shows the half-life and binding constants of **1** for nerol, *l*-borneol and adamantanol. The binding constants are roughly in the order of guest sizes, ranging from 2 300 l mol^{-1} for nerol to 18 800 l mol^{-1} for adamantanol, the results indicate that **1** recognizes the larger guest, as shown by the greater intensity, than that of the smaller guest. It is also interesting that the magnitude of the binding constants and half-lives of **1** for these guests are comparable. The mechanism of the host–guest complexation behaviour of **1** is probably illustrated as shown in Scheme 2. When a larger guest *e.g.* adamantanol, is used, the spiropyran moiety is included deep into the cyclodextrin cavity to come in contact with a guest because the larger guest is included to a limited extent. However, nerol is included more deeply into the cavity, so the appended moiety does not need to come so deep into the cavity. The behaviour of the appended moiety in the cyclodextrin cavity should affect the photochromic response of

Table 2 Binding constants and half-life of **1** at 25 °C

Guest	K/l mol^{-1}	$t_{1/2}$/min
No guest	—	70
Nerol	2 300 ± 230	80
l-Borneol	12 600 ± 170	340
Adamantanol	18 800 ± 400	400



Scheme 1 Schematic diagram of the host–guest binding mechanism of **1**



Scheme 2 Complexation behaviour depended on molecular size of **1**

1. There is no doubt that the closed form of the spiropyran in the cyclodextrin cavity is more stable than that of the opened form, which results in a longer half-life of the closed form of **1** for *l*-borneol than that of nerol or for no guest.

Conclusions

The photochromic response observed in the system of **1** in the presence of a guest should be used as a photochromic indicator, and this result is the first example demonstrating that a photochromic change in the modified β-cyclodextrin can describe the host–guest binding ability and mechanism of the complexation between cyclodextrin and a guest molecule.

Acknowledgements

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