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Mini Review

Design of Supramolecular Cyclodextrin Complex Sensors for Ion and Molecule Recognition in Water

TAKASHI HAYASHITA[1]*, AKIYO YAMAUCHI[1], AI-JUN TONG[2], JONG CHAN LEE[3], BRADLEY D. SMITH[4] and NORIO TERAMAE[1]

[1]*Department of Chemistry, Graduate School of Science, Tohoku University, Aoba-ku, Sendai 980-8578, Japan;* [2]*Department of Chemistry, Tsinghua University, Beijing 100084, PR China;* [3]*Department of Chemistry, Chung-Ang University, Seoul 156-756, Korea;* [4]*Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556, USA*

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Abstract

The design and function of novel supramolecular fluoroionophore/cyclodextrin (CyD) complex sensors for ion and molecule recognition in water are reviewed. For the crown ether fluoroionophore/γ-CyD complex, the dimerization of the fluoroionophore inside the γ-CyD is found to be selectively promoted by alkali metal ion binding, thereby resulting in metal-ion-selective pyrene dimer emission in water. This supramolecular function is successfully utilized in the design of a podand fluoroionophore/γ-CyD complex for sensing toxic lead ion in water. The boronic acid fluoroionophore/β-CyD complex binds sugars and produces increased fluorescence emission in water. The response mechanism appears to be due to the suppression of the photoinduced electron transfer (PET) from pyrene donor to trigonal phenylboronic acid acceptor. This is a novel emission function provided by the boronic acid fluoroionophore/β-CyD complex sensors in water.

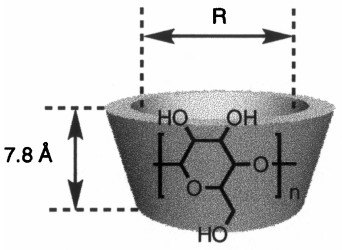
Introduction

Host–guest chemistry has recently been elegantly extended into supramolecular chemistry based on self-assembly and self-organization systems that mimic biological functions [1, 2]. The cooperation among individual interactions of supramolecular complexes has the potential to induce novel functions that differ from those found in simple molecules. In addition to the design of various supramolecular structures [3], unique supramolecular sensors have been extensively developed for ion and molecule recognition [4]. The advantages of supramolecular sensors are as follows: (1) the feasibility of controlling dynamic molecular recognition events; (2) the enhancement of binding efficiency and selectivity through the cooperation among individual interactions, resulting in signal amplification; (3) better synthetic facility than conventional receptors in which several functional groups are covalently bonded; and (4) the diversity of component combinations corresponding to target ions and molecules.

Cyclodextrins (CyDs) are cyclic oligomers of α-D-glucose connected *via* α-1,4 bonds and have a doughnut-shaped structure bearing one rim lined with primary hydroxyl groups and the other rim lined with secondary hydroxyl groups [5]. Three CyDs are widely known: α-CyD containing six glucose units; β-CyD, seven units; and γ-CyD, eight units. As shown in Figure 1, the inner cavity diameter of CyDs increases with increasing number of glucose units from 5.7 Å (α-CyD) to 7.8 Å (β-CyD), and to 9.5 Å (γ-CyD). The water-soluble CyDs have chiral hydrophobic cavities that enable them to incorporate various organic molecules in water. In addition, optically inert CyDs can be efficiently combined with various types of chromo- and fluoroionophores. Thus, CyDs are attractive components for the construction of supramolecular sensors.

The complexation behaviors of CyDs have been studied extensively [6] and covalently modified CyDs have been synthesized to create artificial enzymes [7], drug delivery systems [8], molecular devices [9], as well as molecular sensors [10]. However, to our knowledge, there have been no attempts at using lipophilic chromo- and fluoroionophores incorporated inside the CyD cavities for ion and molecule recognition. We are interested in how the nanosize cavities of CyDs affect the sensing function of the chromo- and fluoroionophores in water. Our recent approaches to the design of supramolecular

* Author for correspondence. E-mail: haya@anal.chem.tohoku.ac. jp



Cyclodextrin	n	Cavity diameter R / Å
α-CyD	6	5.7
β-CyD	7	7.8
γ-CyD	8	9.5

Figure 1. Structure of cyclodextrins (CyDs).

fluoroionophore/CyD complex sensors for the selective recognition of alkali metal ions, heavy metal ions, and sugars in water are reviewed herein [11–16].

Alkali metal ion recognition by crown ether fluoroionophore/γ-CyD complex sensors

Alkali metal ion recognition by crown ether fluoroionophore/γ-CyD complex sensors is examined first [11]. In order to insert a fluoroionophore inside the γ-CyD cavity, a benzocrown ether binding site is simply connected with a pyrene fluorophore *via* an alkyl amide spacer of appropriate length.

The response function of benzo-15-crown-5 (B15C5) fluoroionophore **1a** in organic solution has been reported [17]. **1a** is classified as a photoinduced electron transfer (PET) sensor [18], and exhibits dual fluorescence originating from monomer and intramolecular exciplex formation between the B15C5 amide donor and the pyrene acceptor (Figure 2). However, the observed response selectivity for alkali metal ions is insufficient due to the 1:1 complex formation ability of the B15C5 moiety [19], and hence moderate Na^+ selectivity is obtained.

In contrast to the sensing ability of **1a** in organic media, **1a** exhibits a novel supramolecular function by forming an inclusion complex with γ-CyD in water. Figure 3a shows the typical fluorescence spectra of **1a** in 5.0 mM γ-CyD aqueous solution containing 0.10 M tetramethylammonium chloride (TMAC1) or alkali metal chloride [11, 12]. Although no fluorescence is noted for **1a** in the absence of γ-CyD, significant

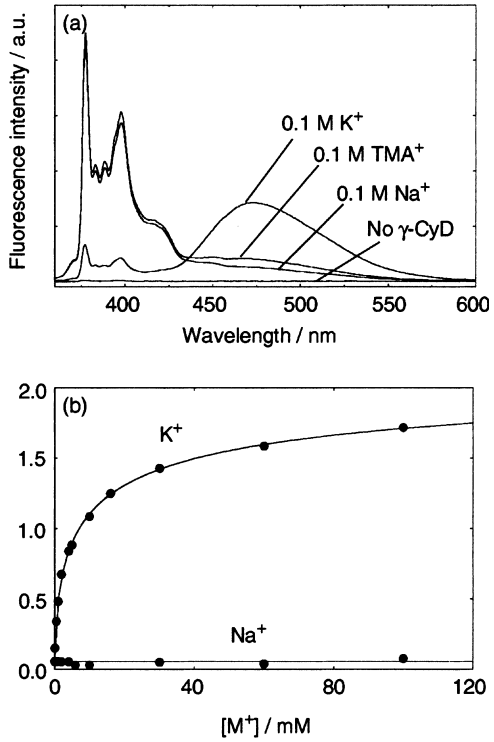


Figure 3. (a) Fluorescence spectra of **1a**: [**1a**] = 0.5 μM in 99% water/1% MeCN (v/v), λ_{ex} = 330.5 nm, (i) [γ-CyD] = 0.0 mM, (ii) [γ-CyD] = 5.0 mM and [MCI] = 0.10 M ($M^+ = Na^+$, K^+, TMA^+). (b) Dependence of fluorescence intensity ratio (I_{470}/I_{378}) on the concentrations of K^+ and Na^+. Reprinted with permission from [12]. Copyright (2000) American Chemical Society.

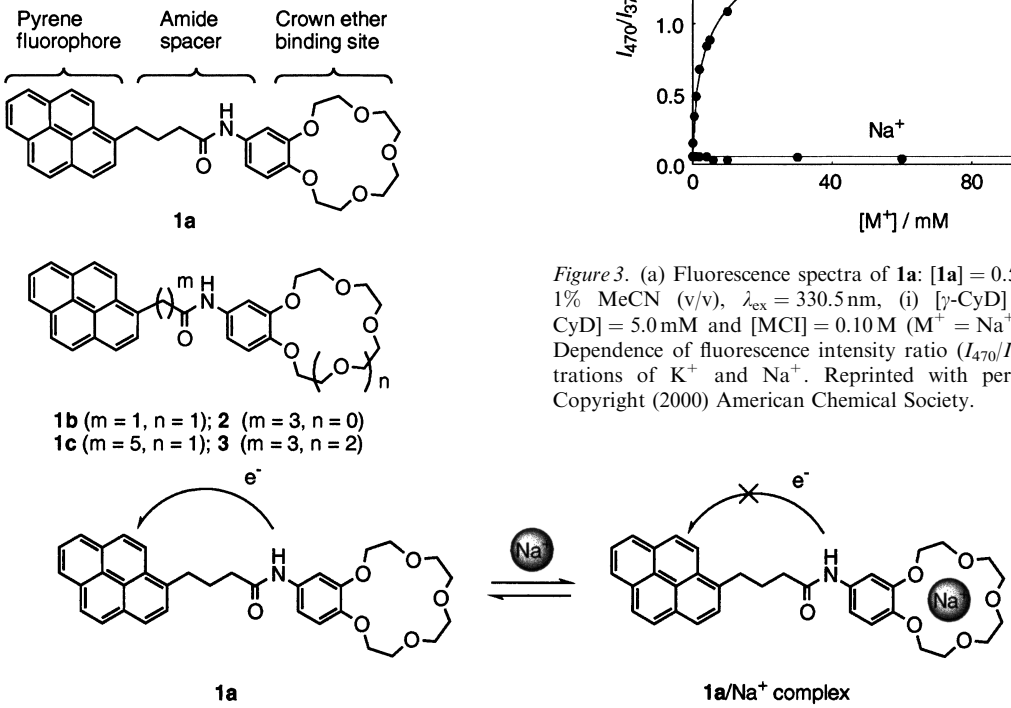


Figure 2. PET mechanism of **1a** in organic media.

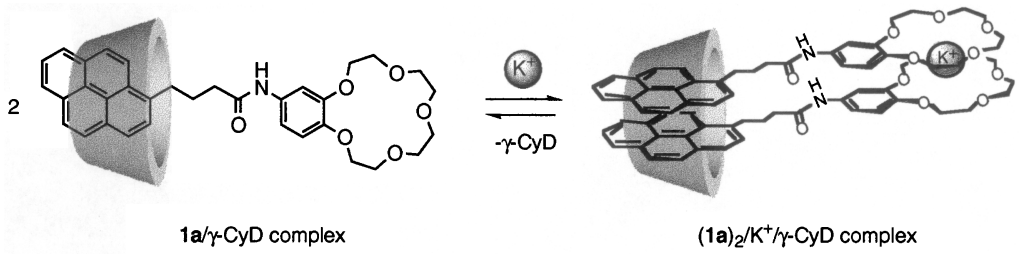


Figure 4. Response mechanism of **1a**/γ-CyD complex for K^+ in water.

fluorescence emission appears in the presence of 5.0 mM γ-CyD, indicating that **1a** is solubilized in water by forming an inclusion complex with γ-CyD. The **1a**/γ-CyD complex exhibits no obvious change upon the addition of 0.10 M Na^+. By contrast, the broad featureless band with an emission maximum at 470 nm is strongly intensified by the addition of 0.10 M K^+, with quenching of the monomer fluorescence emission at 370–410 nm. Figure 3b shows the dependence of the fluorescence intensity ratio at 470 nm to that at 378 nm on the concentration of Na^+ and K^+. It is evident that a high selectivity for K^+ rather than for Na^+ is obtained by the **1a**/γ-CyD complex in water. B15C5 is known to form a 2:1 complex (ligand:metal) with K^+. Thus, the observed selectivity suggests the 2:1 complex formation of **1a** with K^+ inside the γ-CyD (Figure 4). In fact, an equilibrium analysis of the fluorescence behavior of **1a** by varying γ-CyD concentration reveals that the major component for the broad emission at 470 nm is a 2:1:1 complex of **1a** with K^+ and γ-CyD [12]. Thus, the fluorescence emission detected at 470 nm in the presence of K^+ can be assigned to pyrene dimer emission.

Based on the response mechanism in which the change in fluorescence is induced only by the 2:1 complex formation between a fluoroionophore (L) and a metal ion (M^+), the fluorescence intensity ratio (I_D/I_M) is expressed as follows [20]:

$$\frac{I_D}{I_M} = \frac{4\frac{\phi_{fD}}{\phi_{fM}} + \frac{\phi_{cD}}{\phi_{fM}}\left(-1 + \sqrt{1 + 8K[M^+][L]_0}\right)}{4 + \frac{\phi_{cM}}{\phi_{fM}}\left(-1 + \sqrt{1 + 8K[M^+][L]_0}\right)}, \quad (1)$$

$$K = \frac{[ML_2^+]}{[M^+][L]^2}, \quad (2)$$

where $[L]_0$ is the initial concentration of the fluoroionophore, and ϕ_{fD} and ϕ_{fM} are the fluorescence quantum yields for the fluoroionophore at the dimer emission wavelength and the monomer emission wavelength, respectively. Similarly, ϕ_{cD} and ϕ_{cM} are those for the 2:1 complex at the dimer and monomer emission wavelengths, respectively. The value of ϕ_{fD}/ϕ_{fM} can be determined from the fluorescence intensity ratio (I_D/I_M) in the absence of metal ions. The points are fitted well with Equation (1) in the presence of K^+ (Figure 3b). The 2:1 binding constant of the **1a**/γ-CyD complex for K^+ calculated by the non-linear program is (3.8 ± 1.3)× $10^9\ M^{-2}$. The selectivity for K^+/Na^+ exceeds 2600 in water.

The response function of the CyD complex sensor is strongly affected by the structure of crown ether fluoroionophores. Figure 5a presents the effect of alkyl spacer length in the fluoroionophores on the response selectivity of the CyD complexes for alkali metal ions [12]. In contrast to the response function of the **1a**/γ-CyD complex, **1b** possessing the shortest methylene spacer exhibits no emission response in the presence of γ-CyD. It appears that the —CH_2— bond in **1b** is too rigid to form the 2:1 complex inside the γ-CyD. In the case of **1c**, the fluorescence intensity ratio (I_{470}/I_{378}) in the presence of Li^+ or Na^+ is larger than that for **1a**, revealing that **1c** having a pentamethylene spacer easily forms a dimer inside the γ-CyD cavity. However, due to the flexibility of the binding site inside the γ-CyD, **1c** can form a dimer with metal ions of different sizes, thereby

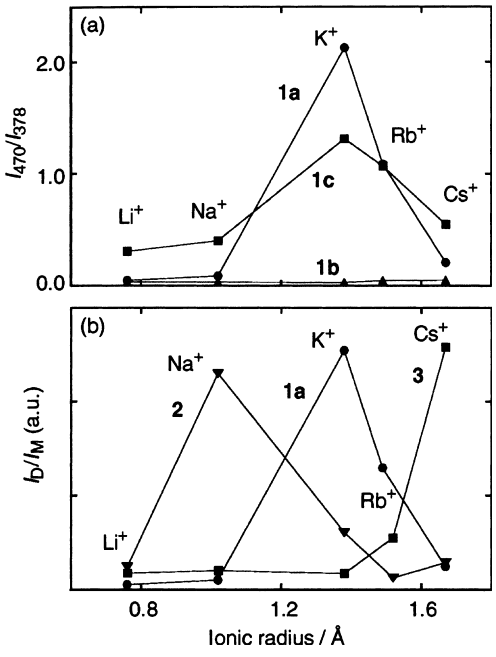


Figure 5. (a) Effect of alkyl spacer length on response selectivity: [**1**] = 0.5 μM in 99% water/1% MeCN (v/v), [γ-CyD] = 5.0 mM, [MCl] = 0.10 M, λ_{ex} = 330.5 nm for **1a** and **1c**, and 328.0 nm for **Ib**. Reprinted with permission from [12]. Copyright (2000) American Chemical Society, (b) Effect of crown ether ring size on response selectivity: [**1a**], [**2**], [**3**] = 0.5 μM in 99% water/1% MeCN (v/v), [γ-CyD] = 5.0 mM, [MCl] = 0.10 M, λ_{ex} = 330.5 nm for **1a**, 331.0 nm for **2**, and 329.0 nm for **3**. The emission wavelengths for dimer/monomer fluorescence are 470/378 for **1a**, 480/377 for **2**, and 470/377 for **3** [15].

diminishing its response selectivity. Consequently, the highest K^+ selectivity in water is obtained for the **1a**/γ-CyD complex.

In general, the control of metal–crown ether interaction in water is quite difficult because the metal ions are strongly hydrated. However, our findings lead us to hypothesize that the recognition selectivity of crown ether fluoroionophore/γ-CyD complexes in water can be tuned by simply altering their crown ether ring sizes. To verify this hypothesis, crown ether fluoroionophores **2** and **3** possessing benzo-12-crown-4 (B12C4) and benzo-18-crown-6 (B18C6) binding sites, respectively, are additionally designed [15]. The results are depicted in Figure 5b. As expected, fluoroionophores **2**, **1a**, and **3** selectively form 2:1 complexes with Na^+, K^+, and Cs^+, respectively, in the presence of γ-CyD and exhibit pyrene dimer emission in water. The apparent 2:1 binding constants of the fluoroionophore/γ-CyD complexes with alkali metal ions are determined for each fluoroionophore with Equation (1). The binding constants of the **2**/γ-CyD complex for Na^+, the **1a**/γ-CyD complex for K^+, and the **3**/γ-CyD complex for Cs^+ are summarized in Table 1, together with those of the corresponding benzocrown ethers in organic media [15]. It is interesting to note that the observed binding constants are considerably larger in water than in organic solvents. This is evidence of the unique supramolecular function of the crown ether fluoroionophore/γ-CyD complex sensors in water.

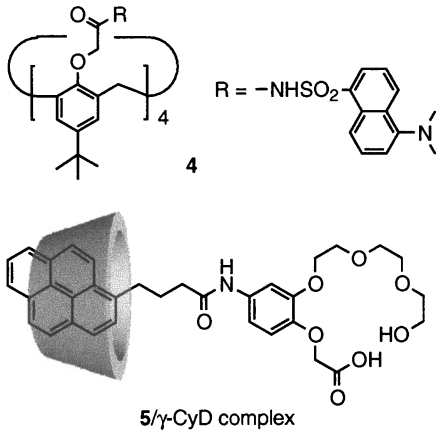
Lead ion recognition by podand fluoroionophore/γ-CyD complex sensor

The real time and *in situ* monitoring of toxic Pb^{2+} in the environment as well as in biological systems remains an important issue [21]. Although many efficient fluoroionophores have been developed for heavy metal ion sensing, the number of Pb^{2+}-selective fluoroionophores is still limited [22]. The calix[4]arene fluoroionophore **4** recently developed by Métivier exhibits high sensitivity to and selectivity for Pb^{2+}, but it requires 60% CH_3CN/40% water (v/v) medium for analysis [23]. The difficulty in designing Pb^{2+}-selective fluoroionophores lies mainly in the lack of a design concept and problems in fluorescence quenching by heavy metal ions based on

Table 1. 2:1 binding constants of the fluoroionophore/γ-CyD complex with alkali metal ions [15]

Fluoroionophore (binding site)	Ion	K/M^{-2}	
		In γ-CyD aqueous soln.	Benzocrown ether in organic soln. [19]
2 (B12C4)	Na^+	~10^7	3.2×10^{4}[a]
1a (B15C5)	K^+	$(3.8 \pm 1.3)\times10^{9}$	1.4×10^{6}[b]
3 (B18C6)	Cs^+	$(5.8 \pm 4.6)\times10^{7}$	1.9×10^{6}[c]

[a] B12C4 for Na^+ in MeCN; [b] B15C5 for K^+ in MeOH; [c] B18C6 for Cs^+ in MeOH.



enhanced spin-orbital coupling [24] and electron or energy transfer [25].

The supramolecular function of crown ether fluoroionophore/γ-CyD complexes discussed in the former section can be used in the design of Pb^{2+}-selective fluoroionophores because the recognition site is efficiently separated from the photosignal transduction site by an alkyl chain spacer to avoid fluorescence quenching. For selective Pb^{2+} recognition, we have proposed a design concept based on a hard binding site constructed from O-donor atoms to reduce the interaction with other relatively soft heavy metal ions, and a podand structure possessing a flexible pseudo-crown ether cavity to stabilize chelate complexes with large metal ions such as Pb^{2+} while reducing the interaction with alkali metal cations [26].

Based upon the above concept, a podand fluoroionophore **5**/γ-CyD complex sensor has been designed [16]. Figure 6a shows the fluorescence spectra of **5** in 98% water/2% methanol (v/v) at pH 4.3. Similar to the crown ether fluoroionophores **1–3**, significant fluorescence emission appears in the presence of 12.0 mM γ-CyD, indicating that **5** is solubilized in water by forming an inclusion complex with γ-CyD. Upon addition of 1.0 mM Pb^{2+}, the broad dimer emission observed at 471 nm is intensified with quenching of the pyrene monomer emission at 370–410 nm. The results strongly demonstrate that the dimer formation of **5** inside γ-CyD is induced by Pb^{2+} binding in accordance to our design concept. Figure 6b shows plots of the fluorescence intensity ratio as a function of Pb^{2+} concentration. The observed points are fitted well with Equation (1), and the 2:1 binding constant is calculated to be $(1.17 \pm 0.75)\times10^{9}\,M^{-2}$. The fluorescence responses of the **5**/γ-CyD complex in the presence of Zn^{2+} and Cu^{2+} are also shown in Figure 6b. The **5**/γ-CyD complex does not show any obvious spectral changes upon the addition of Zn^{2+} and Cu^{2+}, indicating that fluorescence quenching by heavy metal ions is negligible. The lack of fluorescence response upon the addition of 1.0 mM K^+, Mg^{2+}, Ca^{2+}, Ni^{2+}, Co^{2+}, and Cd^{2+} is also confirmed [16]. Thus, the **5**/γ-CyD complex is proved to have a selective sensing ability for Pb^{2+} in water.

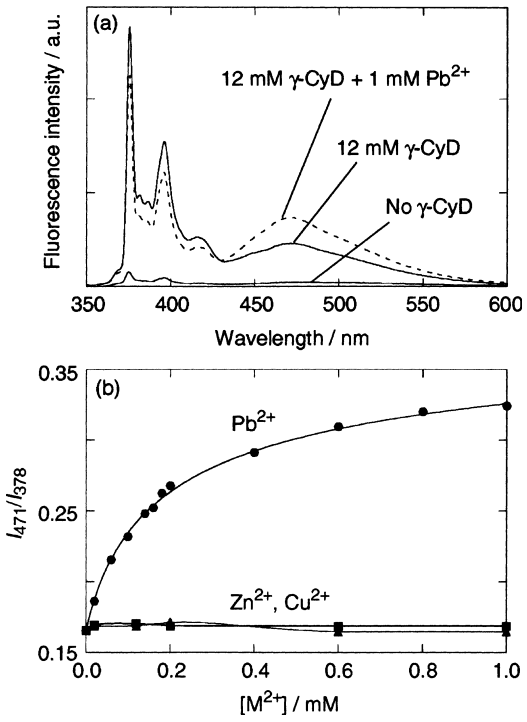
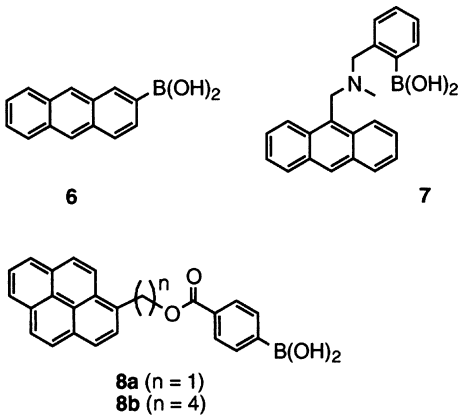


Figure 6. (a) Fluorescence spectra of **5**: [**5**] = 2.0 μM in 98% water/2% MeOH (v/v), λ_{ex} = 328.0 nm, pH = 4.3 adjusted with 0.010 M acetate buffer, (i) [γ-CyD] = 0.0 mM, (ii) [γ-CyD] = 12.0 mM, (iii) [γ-CyD] = 12.0 mM and [$Pb(NO_3)_2$] = 1.0 mM [16]. (b) Dependence of I_{417}/I_{378} on the concentration of Pb^{2+}, Cu^{2+}, and Zn^{2+}; pH = 4.3 adjusted with 0.010 M acetate buffer (I = 0.10 with $NaNO_3$) [16]. Reproduced by permission of The Royal Society of Chemistry.

Sugar recognition by boronic acid fluoroionophore/β-CyD complex sensors

Sugars are biological molecules that are essential in nutrition, metabolism, and cell structure [27]. Boronic acid binding sites have been extensively utilized in the design of fluorescent sugar sensors, because boronic acids can readily form stable cyclic esters with the diol moiety of sugars in water [28]. For example, Czarnik reported the properties of anthrylboronic acid **6**, which senses sugars in neutral aqueous solution *via* a fluorescence quenching process [29]. Shinkai and coworkers have also developed notable fluorescent sugar sensors such as **7**, in which the phenylboronic acid is connected to the fluorophore *via* a tertiary amine unit [30]. Sugar binding with **7** results in fluorescence enhancement due to strengthening of the boron–nitrogen Lewis acid–base interaction that suppresses electron transfer quenching in neutral aqueous methanol solution.

To develop a novel boronic acid fluoroionophore/CyD complex sensor for sugar recognition in water, we have designed boronic acid fluoroionophores **8a** and **8b** bearing alkyl spacers of different lengths ([13]; the results for **8a** are unpublished). In Figure 7a are shown the UV–Vis spectra of **8a** in water containing different amounts of dimethyl sulfoxide (DMSO) and β-CyD. The absorption peaks of **8a** in 2% DMSO are quite broad compared to those in 25% DMSO solution, indicating that **8a**



aggregates in water. However, the absorption spectrum of **8a** in 2% DMSO solution containing 5.0 mM β-CyD is similar to that in 25% DMSO solution. This indicates the presence of monomeric **8a** in 2% DMSO solution that forms an inclusion complex with β-CyD. The effect of D-fructose addition on the intensity of pyrene monomer emission (376.5 nm) of **8a** is examined at pH 7.5 in 2% DMSO solution, 25% DMSO solution, and 2% DMSO solution containing 5.0 mM β-CyD (Figure 7b). The fluorescence intensity of the **8a**/β-CyD complex in 2% DMSO solution increases as the D-fructose concentration is increased from 0 to 30 mM. In contrast, no fluorescence response is noted for **8a** in 2% DMSO solution and in 25% DMSO solution. Thus, only the supramolecular **8a**/β-CyD complex exhibits an efficient fluorescence emission response for D-fructose in water. A similar response function has been obtained for the **8b**/β-CyD complex [13].

In order to clarify the response mechanism, the fluorescence behavior of the **8**/β-CyD complex is examined under different pH conditions. The pH-dependent changes in the fluorescence intensity of the **8**/β-CyD complex in the absence and presence of 30 mM D-fructose are shown in Figure 8. The solid lines show the theoretical curves calculated using Equation (3):

$$I = \frac{\beta[L]_t\left(\phi_{HL} + \phi_L \dfrac{K_a}{[H^+]}\right)}{1 + \dfrac{K_a}{[H^+]}}, \qquad (3)$$

where ϕ_{HL} and ϕ_L are the fluorescence quantum yields for HL and L^- species of **8**, respectively, and β is a constant that is proportional to the intensity of the excitation light and the molar extinction coefficient of **8**. K_a represents the boronic acid dissociation constant of **8**. The results reveal that the addition of 30 mM D-fructose decreases the apparent pK_a value from 8.26 ± 0.02 to 6.30 ± 0.01 for **8a** and from 7.95 ± 0.03 to 6.06 ± 0.03 for **8b**. This pK_a shift enables **8** to recognize D-fructose at neutral pH. In this recognition process, four main equilibria must be considered (Figure 9). As shown in Figure 9, the fluorescence quantum yield for **8** apparently increases when **8** is converted into its tetrahedral boronate form. Thus, the

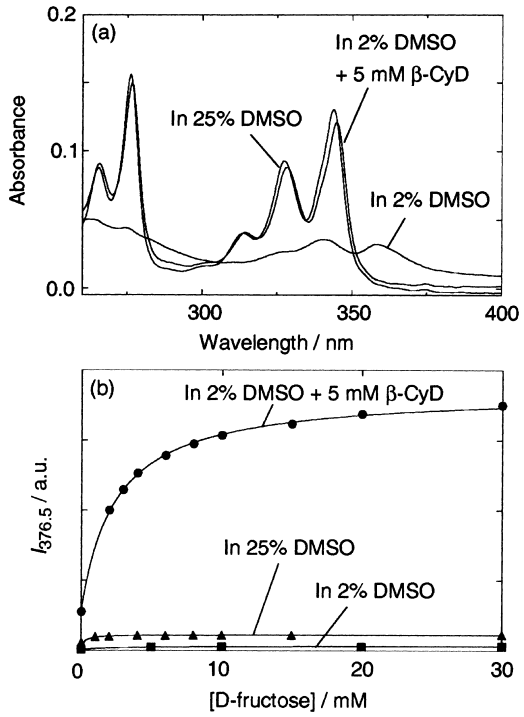


Figure 7. (a) UV–Vis spectra of **8a**: [**8a**] = 1.05 μM in (i) 2% DMSO–98% water (v/v), (ii) 25% DMSO–75% water (v/v), and (ii) 2% DMSO–98% water (v/v) containing 5.0 mM β-CyD. pH = 7.5 adjusted with 0.015 M phosphate buffer (I = 0.08 with NaCl). (b) Dependence of fluorescence intensity ratio at 376.5 nm on the concentration of D-fructose: λ_{ex} = 328.0 nm.

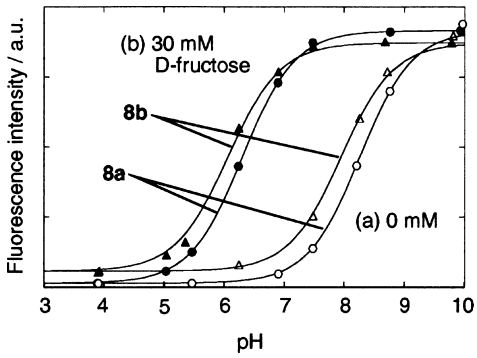


Figure 8. Dependence of fluorescence intensity at 376.5 nm for **8a** and 377.5 nm for **8b** on pH: [**8**] = 1.05 μM in 2% DMSO–98% water (v/v) containing 50 mM β-CyD, (a) [D-fructose] = 0.0 mM, (b) [D-fructose] = 30.0 mM. λ_{ex} = 328.0 nm [13].

increased amount of tetrahedral boronate induced by sugar binding causes an enhancement in the emission intensity. This pH-dependent fluorescence profile is opposite to that observed with previously reported fluorescence quenching probes [29] as well as Shinkai's fluorescence emission probes [30], in which the fluorescence intensities are reduced with increasing pH. This demonstrates a clear difference in the response mechanism of the **8**/β-CyD complexes.

The low fluorescence intensity of **8** when its boronic acid group is trigonal suggests that the phenylboronic acid can act as an acceptor of electron from the excited-state pyrene donor [31]. To verify this mechanism, we have examined 1-methylpyrene and 4-methoxycarbonylphenylboronic acid as donor and acceptor models of the intramolecular pyrene/phenylboronic acid system in **8** [13]. A fluorescence quenching study in 95% methanol/5% water (v/v) reveals that the fluorescence of 1-methylpyrene is significantly quenched by the addition of the acid form of the phenylboronic acid without changing its UV–Vis spectra. However, when 40 mM benzyltrimethylammonium hydroxide is added, which converts the phenylboronic acid into its tetrahedral boronate form, no quenching behavior is observed. Thus, it is evident that electron transfer takes place from the excited 1-methylpyrene to the acid form of the phenylboronic acid that acts as an electron acceptor. These results strongly support the intramolecular PET from the pyrene donor in **8** to the trigonal form of its phenylboronic acid acceptor. As shown in Figure 10, sugar binding converts the boronic acid into tetrahedral boronate, which decreases the amount of PET quenching and increases monomer fluorescence intensity. In this PET mechanism, the fluorescence response efficiency is strongly affected by the alkyl spacer length in **8**. In fact, it is notable that the quantum yield ratio

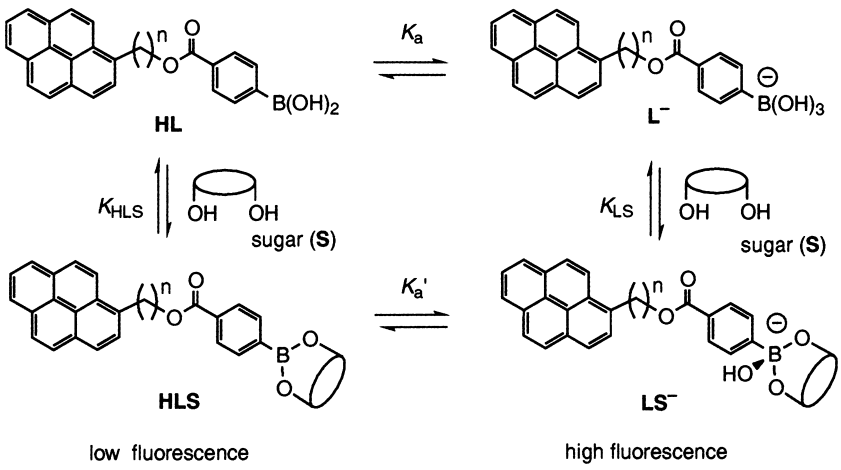


Figure 9. Proton dissociation and sugar binding equilibria of **8** in aqueous solution [13].

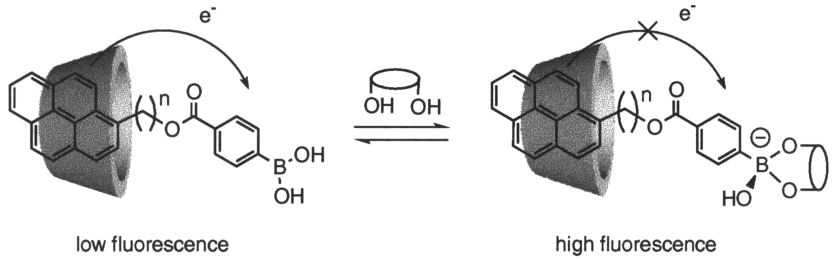


Figure 10. Response mechanism of the **8**/β-CyD complex for sugar binding [13].

between the acidic and basic forms of **8** (ϕ_L/ϕ_{HL}) increases from 15.2 for **8b** to 57.4 for **8a**.

According to the equilibria shown in Figure 9, the fluorescence intensity of the **8**/β-CyD complex is expressed as follows:

$$I = \frac{\beta[L]_t\left(\phi'_{HL} + \phi'_L \dfrac{K_a(1+K_{LS}[S])}{[H^+](1+K_{HLS}[S])}\right)}{1+\dfrac{K_a(1+K_{LS}[S])}{[H^+](1+K_{HLS}[S])}}, \quad (4)$$

$$\phi'_{HL} = \frac{\phi_{HL} + \phi_{HLS}K_{HLS}[S]}{1+K_{HLS}[S]}, \quad (5)$$

$$\phi'_L = \frac{\phi_L + \phi_{LS}K_{LS}[S]}{1+K_{LS}[S]}, \quad (6)$$

where ϕ_{HLS} and ϕ_{LS} are the fluorescence quantum yields for HLS and LS^- species of the **8**/β-CyD complex, respectively. It is known that the trigonal boronate esters (HLS) are very unstable, and only anionic boronate complexes (LS^-) are formed in water [32]. Thus, the formation of the HLS complex is negligible ($1 \gg K_{HLS}[S]$). In addition, as the fluorescence intensity of the **8**/β-CyD complex in the presence of D-fructose reaches the same level as that of the sugar-free **8**/β-CyD complex at pH 10, we can assume that ϕ_L is almost equal to ϕ_{LS}. Thus, Equation (4) is more simply expressed as

$$I = \frac{\beta[L]_t\left(\phi_{HL} + \phi_L \dfrac{K_a}{[H^+]}(1+K_{LS}[S])\right)}{1+\dfrac{K_a}{[H^+]}(1+K_{LS}[S])}. \quad (7)$$

Equation (7) indicates that the binding constant (K_{LS}) can be determined by non-linear curve fitting analysis of the fluorescence intensity (I) as a function of sugar concentration ([S]) at a fixed pH.

The fluorescence intensity changes of the **8**/β-CyD complex as a function of D-fructose concentration at pH 7.5 in water are fitted well with Equation (7), and the 1:1 binding constants are calculated to be $(2.80 \pm 0.07)\times 10^3\,M^{-1}$ for **8a** and $(2.50 \pm 0.13)\times 10^3\,M^{-1}$ for **8b**. The monosaccharide binding selectivity of the **8**/β-CyD complex is essentially the same as that of phenylboronic acid. Thus, the binding selectivity decreases in the following order: D-fructose ≫ L-arabinose > D-galactose > D-glucose [13].

It should be noted that Shinkai and coworkers [30], and other groups [33–35] have already developed efficient glucose sensors as well as probes for chiral sugar recognition, by incorporating two or more boronic acid units as sugar recognition sites. In comparison, the advantages of the supramolecular **8**/β-CyD complex sensors lie in the high fluoroionophore solubility in water and the high fluorescence quantum yield due to inclusion complex formation. In addition, the combination of boronic acid fluoroionophores with the CyD derivatives bearing various functional groups [36] may provide multipoint sugar recognition with chiral recognition ability. The **8**/γ-CyD complex exhibits fluorescence response in both monomer and dimer emission regions in the presence of sugars, which makes evaluation of the binding mechanism difficult [14]. However, the dimer formation inside γ-CyD is expected to induce more sophisticated binding selectivity compared with a simple 1:1 interaction. These are the interesting features of the supramolecular CyD complex sensors for ion and molecule recognition in water.

Conclusions

In this review, we have shown that cooperation among individual interactions of supramolecular CyD complex sensors provides novel functions that differ from originally intended ones. The crown ether fluoroionophore/γ-CyD complex sensors are primarily designed to selectively sense alkali metal ions in water. Dimerization of the fluoroionophore inside the γ-CyD provides a highly selective binding site for target alkali metal ions. The observed 2:1 binding constants of the fluoroionophore for alkali metal ions are considerably larger in water than in organic solvents. By utilizing this design concept, we have also developed a podand fluoroionophore/γ-CyD complex sensor for toxic Pb^{2+} recognition. In this system, the recognition site is efficiently separated from the photosignal transduction site by an alkyl chain spacer to avoid fluorescence quenching. For selective Pb^{2+} recognition, a podand structure possessing the pseudo-18-crown-6 struc-

ture that can stabilize Pb^{2+} chelate complexes while reducing interaction with alkali metal cations is successfully used. The boronic acid fluoroionophore/β-CyD complex binds sugars and produces increased fluorescence emission in water. Upon the addition of D-fructose, the apparent pK_a decreases to lower pH, resulting in an increased fluorescence at neutral pH. The fluorescence emission mechanism appears to be due to the suppression of PET from pyrene donor to trigonal phenylboronic acid acceptor. This is a novel sugar-sensing mechanism for the supramolecular boronic acid fluoroionophore/β-CyD complex sensors in water.

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