 

# Supramolecular Crown Ether Probe/γ-Cyclodextrin Complex Sensors for Alkali Metal Ion Recognition in Water

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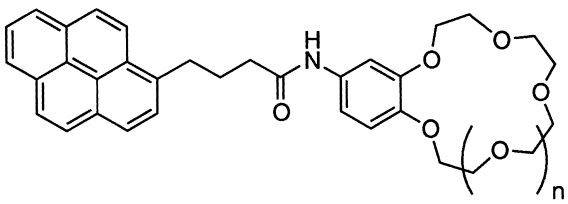
Crown ether probes **C3-12C4** and **C3-18C6**, in which the pyrenyl moieties as fluorophore and benzo-12-crown-4 or benzo-18-crown-6 acting as ion recognition sites are connected by a trimethylene spacer, have been synthesized. Their supramolecular function for alkali metal ion sensing in water is compared with that of the previously designed **C3-15C5**/γ-CyD complex sensor. The **C3-12C4**, **C3-15C5**, and **C3-18C6** are found to selectively form 2:1 complexes with $Na^+$, $K^+$, and $Cs^+$, respectively, in the presence of γ-CyD and to exhibit pyrene dimer emission in water. These results demonstrate that the selectivity of the crown ether probe/γ-CyD complexes can be tuned by simply altering their crown ether ring size. The apparent 2:1 binding constants of the probes with alkali metal ions are determined at the optimum γ-CyD concentrations for each probe. For **C3-12C4**/γ-CyD complex, the accurate binding constant could not be obtained due to the relatively large deviation for the response. However, the fitting curve reveals that the binding constant is about $10^7\ M^{-2}$. The 2:1 binding constants of the **C3-15C5**/γ-CyD complex for $K^+$ and **C3-18C6**/γ-CyD complex for $Cs^+$ are $(3.8 \pm 1.3)\times10^9\ M^{-2}$ and $(5.8 \pm 4.6)\times10^7\ M^{-2}$, respectively. These values are considerably larger than those of the corresponding benzocrown ethers in organic solvents. In the suparamolecular sensing system, the dimer formation of the probes inside the γ-CyD is selectively promoted by alkali metal ion binding in water. This is a novel sensing mechanism in which the dynamic molecular recognition events are successfully utilized for ion sensing in water.

Supramolecular chemistry concerns the novel structure and properties of a molecular assembly constructed by multiple weak non-covalent interactions such as hydrogen bonds, aromatic π-stacking, and van der Waals interactions.[1] The cooperation of individual interactions of supramolecular complexes is expected to induce a novel function which differs from that found in simple molecules. In addition to designs of various supramolecular structures,[2] unique supramolecular sensors have been extensively developed for ion and molecule recognition.[3] The advantages of supramolecular sensors are: 1) feasibility of controlling dynamic molecular recognition events, 2) enhancement of binding efficiency and selectivity by the cooperation of individual interactions, 3) better synthetic facility compared to conventional receptors in which several functional groups are covalently connected, and 4) diversity of component combinations.

Cyclodextrins (CyDs) are attractive molecules for construction of supramolecular complex structures because of the water-soluble CyDs possess nanosize hydrophobic cavities that enable them to incorporate various organic molecules in water.[4] We recently used a benzo-15-crown-5 probe (**C3-15C5**)/γ-CyD complex to selectively sense potassium ion in water (Chart 1). Dimerization of **C3-15C5** inside the γ-CyD provides a highly selective binding site for the potassium ion (Fig. 1).[5,6] In general, control of metal-crown ether interaction in water is quite difficult due to the fact that the metal ions are strongly hydrated. However our finding demonstrates that the recognition selectivity of crown ether probe/γ-CyD complexes in water can be tuned by simply altering their crown ether ring sizes. Thus the selectivity of crown ether probe/γ-CyD complex sensors can be shifted to smaller size ions by reducing the ring size from 15C5 to 12C4. Similarly, selective recognition for larger metal ions is expected by expanding the ring size to 18C6. To verify this prediction, crown ether probes **C3-12C4** and **C3-18C6** possessing benzo-12-crown-4 (B12C4) and benzo-18-crown-6 (B18C6) moieties are newly designed and their




**C3-12C4** (n = 0)
**C3-15C5** (n = 1)
**C3-18C6** (n = 2)

Chart 1. Formula.

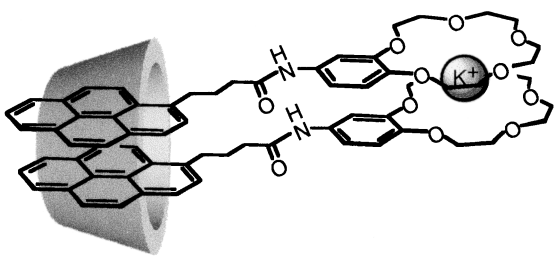



Fig. 1. Possible structure of 2:1:1 complex of **C3-15C5** with $K^+$ and γ-CyD.

supramolecular function for alkali metal ion sensing in water is compared with that of the previously designed **C3-15C5**/γ-CyD complex sensor.

## Experimental

**Apparatus.** UV-vis absorption spectra were recorded on a Hitachi U-3000 spectrophotometer with 5-cm quartz cells. The absorption spectra of each sample were obtained by subtraction of the spectra of γ-CyD solution containing 1% acetonitrile (MeCN) in the absence of probe. Fluorescence spectra were obtained on a JASCO FP-770 spectrofluorometer using excitation and emission bandwidths of 5 and 1.5 nm, respectively. These spectra were collected at 298 ± 0.5 K under an aerated condition. $^1$H NMR spectra were obtained using a JEOL-GSX270 (270 MHz; JEOL DATUM).

**Reagents.** Water was doubly distilled and deionized by a Milli-Q Labo system (Millipore) before use. Acetonitrile (fluorescence reagent, Nakalai Tesque) was used as-received. All other chemicals were commercially available and were used without further purification unless otherwise stated.

**Synthesis of *N*-(2,3,5,6,8,9-Hexahydro-1,4,7,10-benzotetraoxacyclododecin-12-yl)-4-(1-pyrenyl)butyramide (C3-12C4).** 3.46 g (0.015 mol) of benzo-12-crown-4 were dissolved in chloroform (110 cm$^3$) containing acetic acid (110 cm$^3$). Then 70% nitric acid (32 cm$^3$, 0.50 mol) was carefully added dropwise. After stirring for 6 h at room temperature, the chloroform layer was removed using a separatory funnel, and then it was washed with water and 5% aqueous $Na_2CO_3$. The chloroform layer was dried ($MgSO_4$) and the solvent was removed in vacuo. The resulting residue was purified by recrystallization from ethanol to give 4′-nitrobenzo-12-crown-4 (3.77 g, 93%). $^1$H NMR ($CDCl_3$, 270 MHz) $\delta$ 7.91 (dd, $J$ = 8.9 Hz, 3.2 Hz, 1H, ArH), 7.86 (d, $J$ = 3.2 Hz, 1H, ArH), 6.96 (d, $J$ = 8.9 Hz, 1H, ArH), 4.21–4.30 (m, 4H, $CH_2$), 3.80–3.92 (m, 4H, $CH_2$), 3.73–3.79 (m, 4H, $CH_2$). 4′-Nitrobenzo-12-crown-4 (1.0 g, 0.0037 mol) was dissolved in 100 cm$^3$ THF containing 10% Pd/C (0.3 g) and hydrazine monohydrate (16 cm$^3$, 1.0 mol). The mixture was stirred under reflux condition for 1 h. The reaction mixture was filtrated through a glass filter, and the filtrate was evaporated to give 4′-aminobenzo-12-crown-4 as yellow gelatinous solid. $^1$H NMR ($CDCl_3$, 270 MHz) $\delta$ 6.82 (d, $J$ = 9.9 Hz, 1H, ArH), 6.30 (d, $J$ = 2.4 Hz, 1H, ArH), 6.23 (dd, $J$ = 9.9 Hz, 2.4 Hz, 1H, ArH), 4.09–4.16 (m, 4H, $CH_2$), 3.75–3.91 (m, 8H, $CH_2$), 3.33–3.58 (s, Br, 2H, $NH_2$). 4′-Aminobenzo-12-crown-4 (0.66 g, 0.0028 mol) and 1-pyrenebutyric acid (0.66 g, 0.0023 mol) were dissolved in $CH_2Cl_2$ (340 cm$^3$). Then, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.50 g, 0.0026 mol) dissolved in $CH_2Cl_2$ (50 cm$^3$) was added. The mixture was kept in an ice-water bath for 2 h while being stirred. This was followed by stirring for 46 h at room temperature. The residue obtained after removal of the solvent was purified by chromatography on silica gel with $CH_2Cl_2$–MeOH (9/1) and $CH_2Cl_2$–MeOH–EtOAc (10/0.5/0.5) as eluent, and by recrystallization from $CH_2Cl_2$–MeOH to give the product as white solid (0.17 g, 14%). $^1$H NMR (DMSO-$d_6$, 270 MHz) $\delta$ 9.81 (s, 1H, NH), 7.94–8.44 (m, 9H, pyrenyl), 7.34 (d, $J$ = 2.4 Hz, 1H, ArH), 7.10 (dd, $J$ = 8.6 Hz, 2.4 Hz, 1H, ArH), 6.94 (d, $J$ = 8.6 Hz, 1H, ArH), 3.94–4.07 (m, 4H, $CH_2$), 3.56–3.74 (m, 8H, $CH_2$), 2.00–2.15 (m, 2H, $CH_2$). Anal. Calcd for $C_{32}H_{31}NO_5$: C, 75.42; H, 6.13; N, 2.75%. Found: C, 75.15; H, 5.81; N, 2.70%.

**Synthesis of *N*-(2,3,5,6,8,9,11,12,14,15-Decahydro-1,4,7,10,13,16-benzohexaoxacyclooctadecin-18-yl)-4-(1-pyrenyl)butyramide (C3-18C6).** This compound was synthesized from the corresponding benzocrown ether in a similar manner to that described for **C3-12C4**. 4′-Nitrobenzo-18-crown-6 was purified by recrystallization from ethanol-hexane to give the product as pale yellow crystals (3.3 g, 74%). $^1$H NMR ($CDCl_3$, 270 MHz) $\delta$ 7.87 (dd, $J$ = 8.0 Hz, 2.6 Hz, 1H, ArH), 7.72 (d, $J$ = 2.6 Hz, 1H, ArH), 6.86 (d, $J$ = 8.0 Hz, 1H, ArH), 4.14–4.30 (m, 4H, $CH_2$), 3.91–4.01 (m, 4H, $CH_2$), 3.62–3.91 (m, 12H, $CH_2$). 4′-Aminobenzo-18-crown-6: brown viscous liquid. $^1$H NMR ($CDCl_3$, 270 MHz) $\delta$ 6.68 (d, $J$ = 8.2 Hz, 1H, ArH), 6.26 (d, $J$ = 2.6 Hz, 1H, ArH), 6.19 (dd, $J$ = 8.2 Hz, 2.6 Hz, 1H, ArH), 4.01–4.12 (m, 4H, $CH_2$), 3.78–3.93 (m, 4H, $CH_2$), 3.60–3.76 (m, 12H, $CH_2$). **C3-18C6** was purified by chromatography on silica gel with $CH_2Cl_2$–MeOH–EtOAc (10/0.2/0.5) and $CH_2Cl_2$–MeOH (9/1) as eluent, and by recrystallization from $CH_2Cl_2$–MeOH to give the product as white solid (50 mg, 6%) . $^1$H NMR (DMSO-$d_6$, 270 MHz) $\delta$ 9.75 (s, 1H, NH), 7.95–8.42 (m, 9H, pyrenyl), 7.27 (d, $J$ = 2.4 Hz, 1H, ArH), 7.07 (dd, $J$ = 8.4 Hz, 2.4 Hz, 1H, ArH), 6.86 (d, $J$ = 8.4 Hz, 1H, ArH), 3.95–4.06 (m, 4H, $CH_2$), 3.67–3.79 (m, 4H, $CH_2$), 3.47–3.66 (m, 12H, $CH_2$), 2.02–2.19 (m, 2H, $CH_2$). Anal. Calcd for $C_{36}H_{39}NO_7 \cdot 0.2H_2O$: C, 71.91; H, 6.60; N, 2.33%. Found: C, 71.91; H, 6.58; N, 2.44%.

## Results and Discussion

**Synthesis of C3-12C4 and C3-18C6 Probes.** The **C3-12C4** and **C3-18C6** probes were prepared in three steps from the commercially available benzocrown ethers. The benzocrown ethers were first nitrated in chloroform/acetic acid solution containing nitric acid, followed by reduction to 4′-aminobenzocrown ethers in THF of hydrazine monohydrate with 10% Pd/C. The **C3-12C4** and **C3-18C6** probes were obtained by condensing the 4′-aminobenzocrown ethers with 1-pyrene butylic acid in $CH_2Cl_2$ containing 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride. The products were purified by chromatography on silica gel followed by recrystallization from $CH_2Cl_2$/methanol. The structures of **C3-12C4** and **C3-18C6** probes were fully confirmed by $^1$H NMR and combustion analysis.

**Sensing Properties of Crown Ether Probe/γ-CyD Complexes.** Since the solubility of crown ether probes in water was very low, the probes were first dissolved in acetonitrile as stock solution. The sample solutions of probe/γ-CyD complexes in water containing 1% acetonitrile were prepared by diluting the stock solution with water containing γ-CyD and the corresponding chloride salts. In this procedure, a consistent concentration of probe solutions was obtained. In our preliminary study, an increase of acetonitrile content in the sample solution was found to diminish the response function of **C3-15C5**/γ-CyD complex. Thus fluorescence measurements were carried out for the probe/γ-CyD complexes in water containing 1% acetonitrile. The concentration of probe was fixed to 0.50 μM (1 M = 1 mol dm$^{-3}$). Figure 2 shows the fluorescence spectra of crown ether probe/γ-CyD complex sensors in water containing 0.10 M TMACl or alkali metal chlorides. Without γ-CyD, only weak fluorescences are noted when the solution contains 0.10 M TMACl (condition 1). In contrast, significant fluorescence emissions appear in the presence of 5.0 mM γ-CyD (condition 2). This appearance of fluorescence indicates that crown ether probes form inclusion complexes with γ-CyD.[7] For **C3-12C4**/γ-CyD complex, the broad emis-

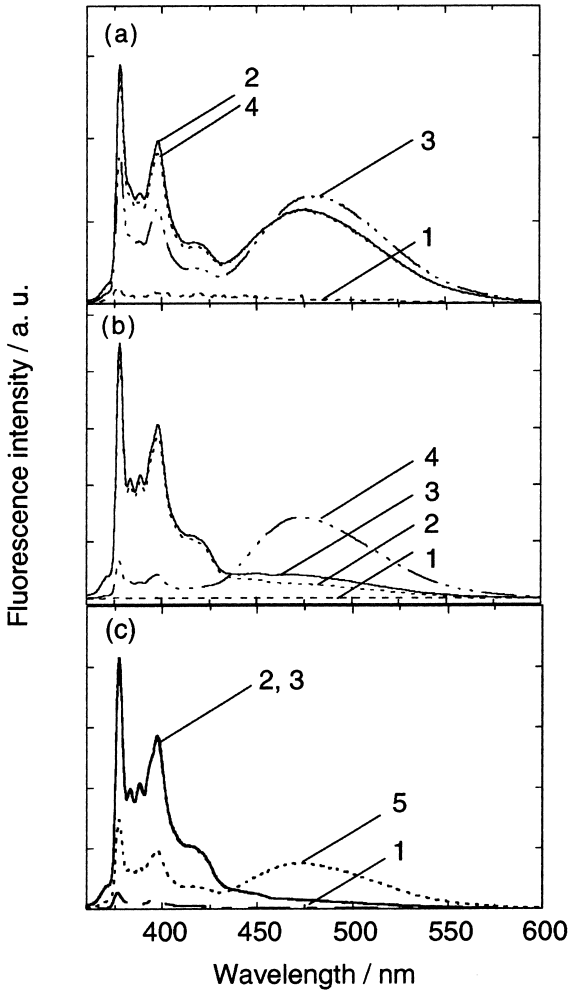



Fig. 2. Fluorescence spectra of probes ([probe] = 0.50 μM in 99% water/1% MeCN (v/v)) with added species. (a) **C3-12C4** excited at 331.0 nm, (b) **C3-15C5** excited at 330.5 nm and (c) **C3-18C6** excited at 329.0 nm. (1) [γ-CyD] = 0 mM and 0.10 M TMACl. (2) [γ-CyD] = 5.0 mM and 0.10 M TMACl. (3) [γ-CyD] = 5.0 mM and 0.10 M NaCl. (4) [γ-CyD] = 5.0 mM and 0.10 M KCl. (5) [γ-CyD] = 5.0 mM and 0.10 M CsCl.

sion band at around 470 nm is clearly seen even in the absence of metal ions (Fig. 2a). The excitation spectrum monitored at 470 nm does not fit with that recorded at 377 nm. Thus the broad emission band is assigned to the pyrene dimer emission formed in the ground state.[8] The **C3-12C4**/γ-CyD complex shows no obvious spectral change upon addition of 0.10 M KCl instead of 0.10 M TMACl. However, in the presence of 0.10 M NaCl, the dimer emission is intensified with quenching of the monomer emission (condition 3 in Fig. 2a). The UV-vis spectrum of the **C3-12C4**/γ-CyD complex in the presence of $Na^+$ shows a reduction in the resolution and intensity of absorption, which indicates the ground state interaction between two pyrenyl moieties.[9,10] These absorption and excitation spectral changes demonstrate that the dimer formation of **C3-12C4** is promoted inside the γ-CyD cavity in the presence of $Na^+$. Figure 2b shows the fluorescence spectra of **C3-15C5** probe reported in previous papers.[5,6] The **C3-15C5**/γ-CyD complex exhibits no spectral change in the presence of 0.10 M TMACl or NaCl. However, upon addition of 0.10 M KCl, the broad featureless band with an emission maximum at 470 nm (dimer emission) is strongly intensified and there is quenching of the monomer emission. The fluorescence spectra of **C3-18C6** probe are also shown in Fig. 2c. For **C3-18C6**/γ-CyD complex, the broad emission band at around 470 nm intensifies with concomitant decrease in the intensity of the monomer fluorescence only in the presence of 0.10 M CsCl. Similar to the **C3-15C5**/γ-CyD and the **C3-12C4**/γ-CyD complexes, the absorption spectrum of **C3-18C6**/γ-CyD complex exhibits a reduction in the resolution and intensity of absorption in the presence of $Cs^+$, which indicates that the dimer formation is promoted inside the γ-CyD cavity.

Figure 3 shows plots of the ratio of the dimer emission to that of the monomer emission ($I_D/I_M$) vs the ionic radius of alkali metal cations. The selectivity of the crown ether probe/γ-CyD complexes is consistent with the extraction selectivity of bis-crown ethers.[11] Thus **C3-12C4**, **C3-15C5**, and **C3-18C6** probes form 2:1 complexes with $Na^+$, $K^+$, and $Cs^+$, respectively, inside the γ-CyD cavity and exhibit selective dimer emission in water. These results clearly demonstrate that the selectivity of the crown ether probe/γ-CyD complex sensor is tunable by regulating the crown ether ring size of the probes.

**Binding Constants of Crown Ether Probe/γ-CyD Complexes.** When one wants to determine the binding constants of probe/γ-CyD complexes, the increase in dimer emission with the alkali metal ion binding must be recorded under proper experimental conditions. As shown in Fig. 4, the fluorescence intensity ratio ($I_D/I_M$) is strongly dependent on γ-CyD concentration. Thus the concentration of γ-CyD should be optimized for each probe. The binding constant of the **C3-15C5**/γ-CyD complex for $K^+$ is determined in the presence of 5 mM γ-CyD, [5,6] because the increase in the intensity ratio, $I_D/I_M$, shows the maximum at 5 mM of γ-CyD concentration (Fig. 4b). The **C3-12C4** probe exhibits the response maximum for $Na^+$ binding when the γ-CyD concentration is ca. 15 mM (Fig. 4a). On the other hand, the increase in $I_D/I_M$ of **C3-18C6** for $Cs^+$ binding is maximized when the concentration of γ-CyD is 5-10 mM (Fig. 4c). Thus, the binding constant for alkali metal ions is determined in the presence of 15 mM γ-CyD for **C3-12C4**, and 5 mM γ-CyD for **C3-18C6**, respectively.

Figure 5a shows the fluorescence spectra of **C3-12C4**/γ-CyD complex upon addition of $Na^+$. With increasing $Na^+$ concentration, the intensity of monomer emission decreases, while that of the dimer emission increases. Figure 5b plots the intensity ratio ($I_D/I_M$) as a function of $Na^+$ concentration. On the assumption that the change in fluorescence is induced only by 2:1 complex formation between the probe (**L**) and the metal ion ($M^+$), the fluorescence ratio ($I_D/I_M$) can be expressed by the following equations:[12]

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

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

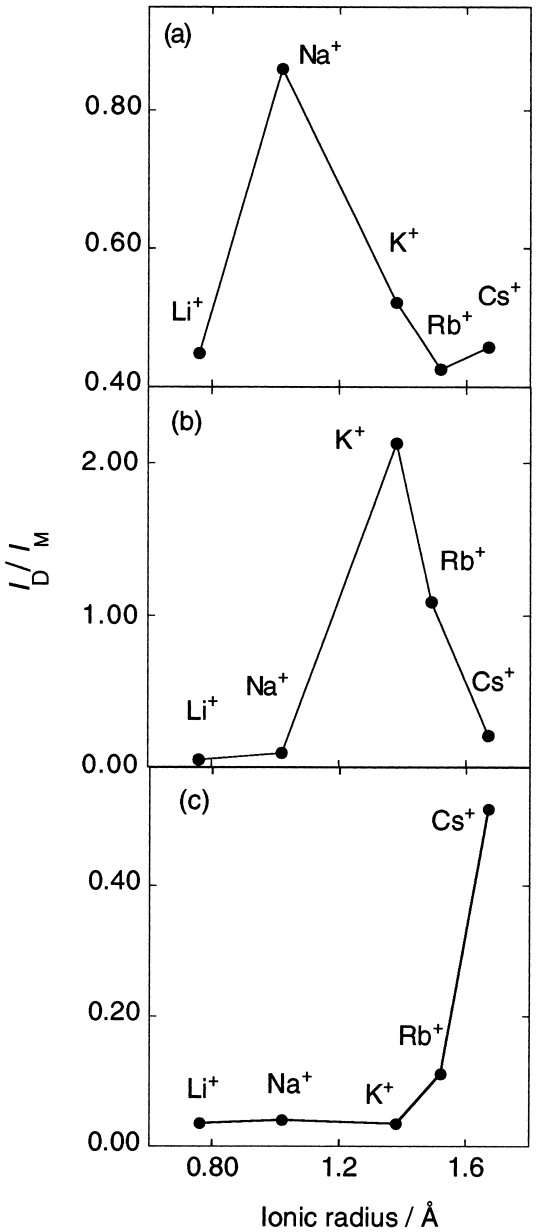



Fig. 3. Dependence of fluorescence intensity ratio, $I_D/I_M$, of (a) **C3-12C4**, (b) **C3-15C5**, and (c) **C3-18C6** on the ionic radius of alkali metal ions. [probe] = 0.50 μM in 99% water/1% MeCN (v/v). [γ-CyD] = 5.0 mM. [MCl] = 0.10 M ($M^+$ = $Li^+$, $Na^+$, $K^+$, $Rb^+$, $Cs^+$). The emission wavelengths for the dimer/monomer fluorescence are (a) 480/377 nm, (b) 470/378 nm, and (c) 470/377 nm, respectively.

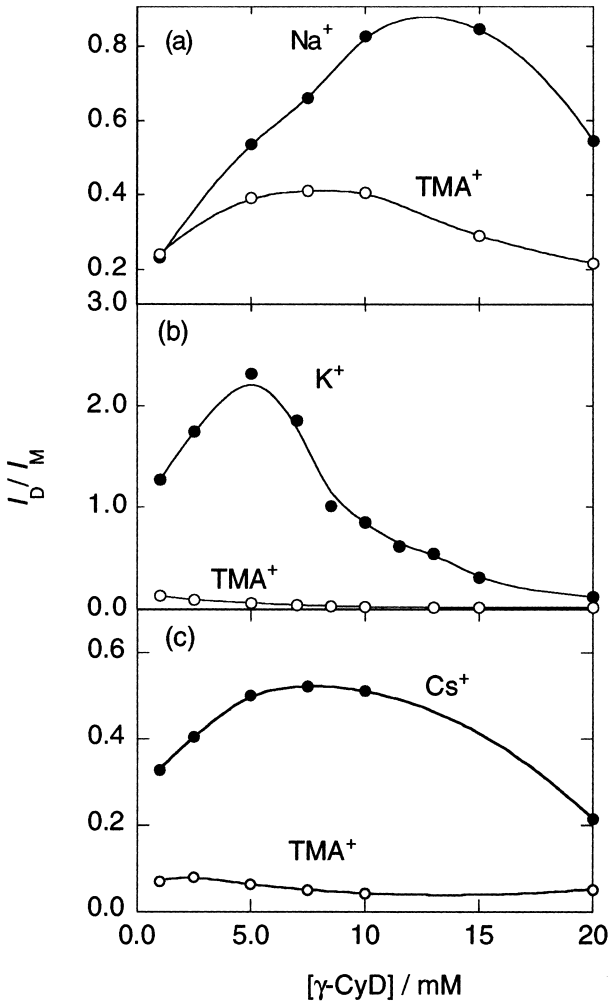



Fig. 4. Fluorescence intensity ratio, $I_D/I_M$, of (a) **C3-12C4**, (b) **C3-15C5**, and (c) **C3-18C6** with 0.10 M (○) TMACl and 0.10 M (●) MCl as a function of γ-CyD concentration. [probe] = 0.50 μM in 99% water/1% MeCN (v/v). The guest cation and emission wavelengths for the dimer/monomer fluorescence are (a) $Na^+$, 480/377 nm, (b) $K^+$, 470/378 nm, and (c) $Cs^+$, 470/377 nm, respectively.

where $[\mathbf{L}]_0$ is the initial concentration of the probe, and $\phi_{fD}$ and $\phi_{fM}$ are the fluorescence quantum yields for the probe at the emission wavelength for the dimer fluorescence and that for the monomer fluorescence, respectively. Similarly, $\phi_{cD}$ and $\phi_{cM}$ are those for the 2:1 complex at dimer and monomer emission wavelengths, respectively. The value of $\phi_{fD}/\phi_{fM}$ can be determined from the intensity ratio ($I_D/I_M$) when $[M^+] = 0$ M.

Although the experiments were repeated three times, the deviations of points in Fig. 5b were relatively large, and an accurate $K$ value could not be determined from the nonlinear least-square fitting with Eq. 1. However, the fitting curve reveals that the $K$ value is about $10^7$ $M^{-2}$. In this system, the response for $K^+$ is very small. Thus, high $Na^+$ selectivity is obtained.

Figure 6a shows the fluorescence spectra of **C3-18C6**/γ-CyD complex upon addition of $Cs^+$. With an increase in $Cs^+$ concentration, the dimer emission intensity of the **C3-18C6**/γ-CyD complex increases and that of monomer emission decreases. Figure 6b represents the dependence of the intensity ratio ($I_D/I_M$) upon the concentrations of alkali metal cations. The points in Fig. 6b are fitted well with Eq. 1 (solid line) in the presence of $Cs^+$. The binding constant calculated by the non-linear program is $(5.8 \pm 4.6) \times 10^7$ $M^{-2}$. For $Cs^+$ ion sensing with **C3-18C6**/γ-CyD complex, the detection limit estimated from $3\sigma$ of the deviation of blank fluorescence ratio ($I_D/I_M$) is $1.4 \times 10^{-4}$ M. In this system, the response for $Na^+$ is negligible. Although there are a few examples of $Cs^+$ selective indicators, they have been utilized only in organic media.[13]

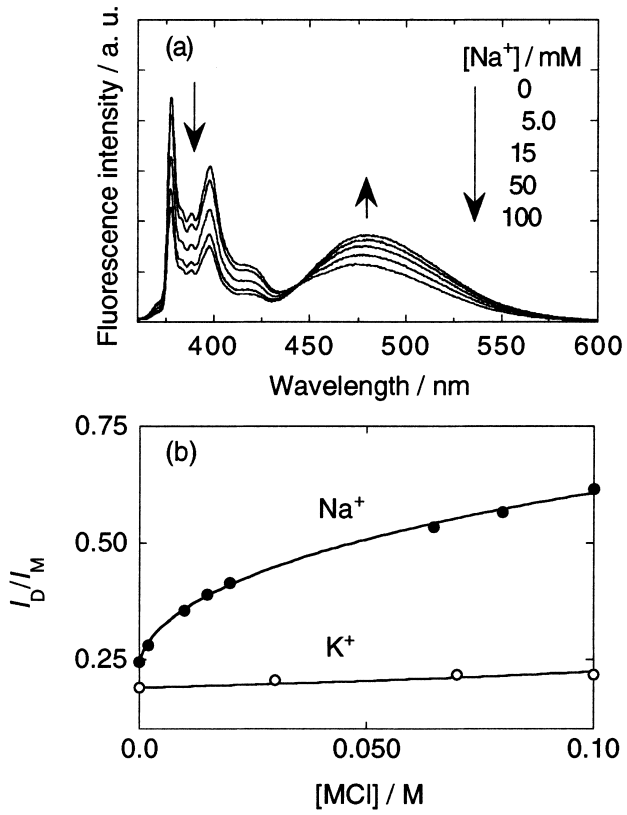



Fig. 5. (a) Fluorescence spectra of **C3-12C4**. [**C3-12C4**] = 0.50 μM in 99% water/1% MeCN (v/v); [γ-CyD] = 15 mM. Excitation wavelength: 331.0 nm. (b) Dependence of $I_D/I_M$ on the concentration of (●) $Na^+$ and (○) $K^+$. The emission wavelengths for the dimer/monomer fluorescence are 480/377 nm.

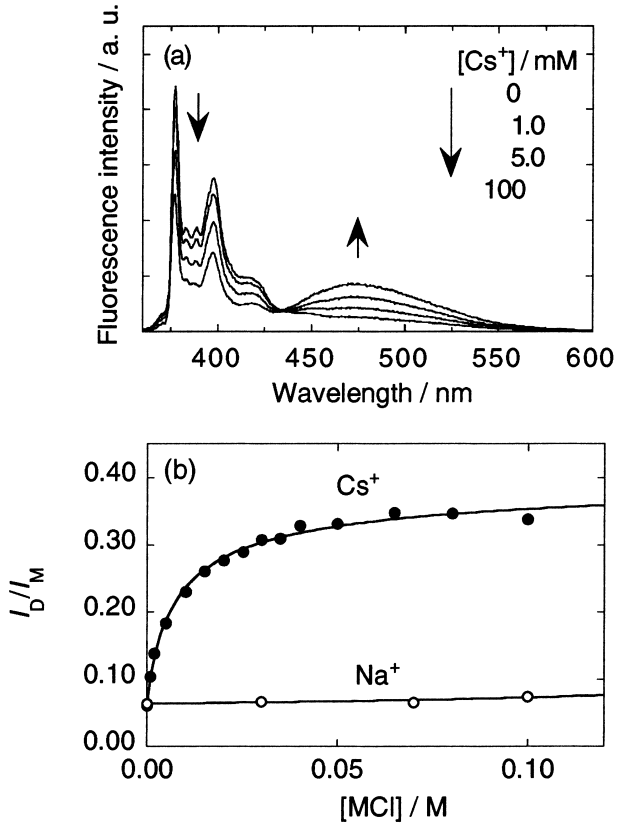



Fig. 6. (a) Fluorescence spectra of **C3-18C6**. [**C3-18C6**] = 0.50 μM in 99% water/1% MeCN (v/v). [γ-CyD] = 5.0 mM. Excitation wavelength: 329.0 nm. (b) Dependence of $I_D/I_M$ on the concentration of (●) $Cs^+$ and (○) $Na^+$. The emission wavelengths for the dimer/monomer fluorescence are 470/377 nm.

Table 1. 2:1 Binding Constants of the Probes with Alkali Metal Ions

| Probe | Ion | $K/M^{-2}$ | |
|---|---|---|---|
| | | In γ-CyD aqueous soln. | Benzocrown ether in organic soln.[11] |
| **C3-12C4** | $Na^+$ | $\sim 10^7$ | $3.2 \times 10^{4(a)}$ |
| **C3-15C5** | $K^+$ | $(3.8 \pm 1.3) \times 10^9$ | $1.4 \times 10^{6(b)}$ |
| **C3-18C6** | $Cs^+$ | $(5.8 \pm 4.6) \times 10^7$ | $1.9 \times 10^{6(c)}$ |

(a) B12C4 for $Na^+$ in MeCN, (b) B15C5 for $K^+$ in MeOH, (c) B18C6 for $Cs^+$ in MeOH.

Thus the **C3-18C6**/γ-CyD complex would be a promising candidate to be used for the in situ monitoring of $Cs^+$ in water.

The apparent binding constants of the probe/γ-CyD complexes with alkali metal ions are summarized in Table 1. For all probe/γ-CyD complexes, the binding constants are considerably larger than those of the benzocrown ethers in organic solvent.[11] These abnormally high binding constants in water reveal the characteristic supramolecular function of the probe/γ-CyD complex sensors. It is evident that the dimer formation of the probe inside γ-CyD is selectively promoted by alkali metal ion binding in water. This is a novel sensing mechanism in which the dynamic molecular recognition events are successfully utilized for ion sensing in water. The apparent binding constant of the **C3-12C4**/γ-CyD complex for $Na^+$ is much smaller than that of the **C3-15C5**/γ-CyD complex for $K^+$. This may be attributed to a weak binding ability of B12C4 with $Na^+$ in water. The sensitivity of **C3-18C6**/γ-CyD complex for $Cs^+$ is also lower than that of the **C3-15C5**/γ-CyD complex for $K^+$. For β-CyD complex, the **C3-15C5** exhibits no response by the addition of $K^+$, indicating that the cavity size of β-CyD is too small to incorporate the probe dimer. Similarly the inclusion behavior of probes into γ-CyD strongly depends on the probe structure.[6,14] Since the apparent binding constant includes the equilibrium constants of the inclusion complexes with γ-CyD, the binding constant of the probe/γ-CyD complex with an alkali metal cation can not be directly compared among different ring sizes of crown ether probes. However, the present results clearly demonstrate that the supramolecular crown ether probe/γ-CyD complexes provide a selective alkali metal ion recognition system in water.

## Conslusions

This study demonstrated that the selectivity of crown ether probe/γ-CyD complex sensors for alkali metal ions was tunable by simply varying the crown ether ring size of probes. Thus **C3-12C4**, **C3-15C5**, and **C3-18C6** selctively responded to $Na^+$, $K^+$, and $Cs^+$, respectively, by forming 2:1 complexes with target alkali metal ions inside the γ-CyD in water. For the

**C3-12C4**/γ-CyD complex, the accurate binding constant could not be determined because of the relatively large deviation for the response. However, the fitting curve revealed that the *K* value was about $10^7$ $M^{-2}$. The 2:1 binding constant of B12C4 with $Na^+$ in acetonitrile was $3.2 \times 10^4$ $M^{-2}$. The high *K* value of the **C3-12C4**/γ-CyD complex suggested that the formation of 2:1 complex between **C3-12C4** and $Na^+$ was facilitated by γ-CyD. The apparent binding constants of the **C3-15C5**/γ-CyD complex for $K^+$ and **C3-18C6**/γ-CyD complex for $Cs^+$ were $(3.8 \pm 1.3) \times 10^9$ $M^{-2}$ and $(5.8 \pm 4.6) \times 10^7$ $M^{-2}$. These values were also higher than the 2:1 binding constants of B15C5 for $K^+$ ($1.4 \times 10^6$ $M^{-2}$) and B18C6 for $Cs^+$ ($1.9 \times 10^6$ $M^{-2}$) in methanol. In both systems, response for $Na^+$ was negligible. Thus, selective sensing of $K^+$ by **C3-15C5**/γ-CyD complex and $Cs^+$ by **C3-18C6**/γ-CyD complex in water was feasible. Although an optimum structure of crown ether probes has not been clarified, the novel supramolecular function of these crown ether probe/γ-CyD complexes would be useful for the monitoring of alkali metal ions in clinical and environmental aqueous samples in combination with autoanalyzer systems.[15]

The present results showed that the function of the probe/CyD complexes could be tuned by proper design of the ionophores and applied to various lipophilic chromo- and fluoroionophores. We have recently reported that the supramolecular boronic acid fluorophore/β-CyD complex can selectively sense sugars in water.[16,17] We expect that these supramolecular complex systems will create a novel analytical methodology for the development of more sophisticated sensing systems for ion and molecule recognitions in water.

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