Ion-responsive Intramolecular Charge-transfer Absorption Using a Pyridinium Benzocrown Ether Conjugate

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A pyridinium benzocrown ether conjugated compound, 1, and its analogue with a non-crown ether unit, 2, have been prepared. Both compounds showed similar absorption spectra with two absorption bands at around 260 and 330 nm in acetonitrile. The bands at the longer wavelength side are associated with intramolecular charge transfer (ICT) absorption, in which the dialkoxyphenyl unit in benzocrown ether and the pyridinium unit act as the donor and acceptor, respectively. The addition of a guest, such as Li⁺ or Mg²⁺, caused a blue shift in the ICT absorption band for 1, but not for 2. This is explained by the formation of a 1:1 host-guest inclusion complex of 1 with the guest. The guest-induced absorption variation of 1 can be used for alkali and alkaline metal ion sensing. Compound 1 could detect divalent cations, especially for Mg²⁺, rather than univalent ones (Li⁺, Na⁺, K⁺, Rb⁺, and Cs⁺), although Li⁺ was detected with high sensitivity among the alkali metal ions. Compound 3, which has a pyridyl unit at the para position on the pyridinium of 1, showed a similar trend to that of 1 with lower sensitivity than that of 1. The fact that the Mg²⁺/Li⁺ sensitivity ratio of 1 and 3 was estimated to be 8.63 and 5.08, respectively, suggests a higher Mg²⁺-preference of 1 rather than 3, while the Ca²⁺/Na⁺ ones were 4.98 and 4.85, respectively, when compared ions with similar ionic radii. The sensitivity values of 1 were roughly proportional to their binding constants, as shown by the binding constants with Li⁺, Na⁺, Mg²⁺, and Ca²⁺ with values of 2100, 910, 11500, and 2000 M⁻¹ for 1, respectively. The binding constants of 3 were estimated to be 1710, 650, 3000, and 1400 M⁻¹ for Li⁺, Na⁺, Mg²⁺, and Ca²⁺, respectively, but could not be obtained for alkaline metal ions. The limit concentration for the detection of 1 for Mg²⁺ was estimated to be 0.0156 mM, which was the smallest value in this system.

Keywords Chemosensor, ion sensing, intramolecular charge transfer absorption, host-guest chemistry, crown ether, pyridinium

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Introduction

Detecting specific analytes is a subject of considerable interest because of its implications in many fields: biology, medicine, environment. Although numerous analytical methods are available for the detection of the analyte, it has often been accompanied by a complicated pretreatment, large apparatuses and high cost performances. In contrast, a method based on the fluorescence and absorption spectra offers distinct advantages in sensitivity, response time, manageability as well as cost. A number of published studies attest to the level of attention devoted to chemosensors that are capable of changing in fluorescence and absorption in response to chemical species, especially metal ions.1–4 Supramolecular host-guest complexation is a key phenomenon for the development of such chemosensors. The majority of supramolecular systems are based on crown ethers and calixarens because of easy modifications with functional groups and appropriate chromophores so as to make them sophisticated.5,6 In these systems, the host and chromophore units act as the guest binding site and the transducer of the guest binding into the optical signals, respectively. Recently, we prepared bipyridinium benzocrown ether conjugates, and found that these compounds showed intramolecular charge transfer (ICT) absorptions.7–12 In spite of possessing dication in a molecule, these showed abilities to accommodate alkali and alkaline earth metal ions and to exhibit the ICT absorption variation in response to the ions. However, it still remains an issue about the effect of the charge on the guest binding ability and the ICT absorption character as well as the ion sensing ability. In the course of our study, we designed a new conjugated compound, 1, possessing a monocation of pyridinium conjugated benzocrown ether in a molecule, which has a similar structure to the previous bipyridinium conjugated benzocrown (3), with a lack of the substituent of the pyridinium at para position.10 The simple monocatonic pyridinium of 1 would affect not only the ICT absorption, but also the guest binding properties when compared to those of 3. Such a difference would cause unique guest-ion sensing abilities of 1 from that of 3. Here we wish to describe the synthesis and guest

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binding behavior of 1, which are accompanied by a remarkable guest-induced change in the ICT absorption, especially for Mg²⁺, compared with the non-crown ether analogue, 2. The ion-sensing ability of 3 was also examined for a comparison.

Experimental

Materials
All chemicals were of reagent grade, and were used without further purification. Alkali and alkaline earth metal perchlorate were used as the guest ion. Compound 3 was prepared according to our previous report.¹⁰

Synthesis
N-(4'-Beno-15-crown-5)-4-phenyl-pyridinium hexafluorophosphate (1). A 10-mL ethanol solution of N-(2,4-dinitrophenyl)-pyridinium chloride (0.54 g, 1.93 mmol) was added over 10-min to a 10 mL ethanol solution of 4'-aminobenzo-15-crown-5 (0.51 g, 1.80 mmol) at 80°C. The reaction mixture was stirred at 80°C for 20 h. After removing the solvent, the crude solid was dissolved in diethyl ether several times, and recrystallized from methanol and diethyl ether several times. The solid was dissolved in 5 mL of water, and 2 mL of a saturated aqueous solution containing ammonium hexafluorophosphate salt was added. The precipitate was collected, and was dissolved in 5 mL of water. The precipitate was dissolved in 2 mL of acetone and poured into cold water. The precipitate was filtered and washed with cold water.

Compound 1: ¹H NMR (400 MHz; CD₃CN): δ 8.90 (d, 2H), 8.65 (t, 1H), 8.15 (t, 2H), 7.26 (d, 1H), 7.25 (d, 1H), 7.18 (d, 1H), 4.23 - 4.15 (m, 4H), 3.85 (m, 4H), 3.71 - 3.61 (m, 8H). Anal. Calcd for C₁₆H₁₄NO₂PF₆: C 43.23, H 3.91, N 3.88%. Found: C 43.37, H 3.75, N 3.89%.

Compound 2: ¹H NMR (400 MHz; DMSO-d₆): δ 9.43 (d, 2H), 8.85 (t, 1H), 8.40 (t, 2H), 7.68 (d, 1H), 7.55 (dd, 1H), 7.38 (d, 1H), 4.00 (s, 3H), 3.98 (s, 3H). Anal. Calcd for C₁₆H₁₄NO₂PF₆: C 43.23, H 3.91, N 3.88%. Found: C 43.37, H 3.75, N 3.89%.

Apparatus
¹H-NMR was measured in acetonitrile-δ₂ and DMSO-d₆ with a Bruker AVANCE 400. Absorption spectra were measured at 25°C in acetonitrile by using a Shimadzu UV 3150 spectrophotometer equipped with a Taiotech ZL100 thermocoupler with a 1-cm quartz cuvette.

Determination of binding constants
The host-guest binding constants for 1:1 association, K, were evaluated based on the following equation:

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\Delta I = \frac{\Delta I_{\text{max}}[(G₀ + H₀ + 1/K) - ([G₀ + H₀ + 1/K]² - 4G₀H₀)]^{1/2}}{2H₀}
\]

where \(H₀\) and \(G₀\) represent the initial concentration of the host, 1 or 3, and the guest; \(\Delta I\) represents the guest-induced absorption variation. When all hosts exist as the inclusion complex, \(\Delta I\) is equal to \(\Delta I_{\text{max}}\). The analysis was performed by 340 nm for hosts 1, and by 390 nm for 3.

Results and Discussion

Absorption spectra of 1, 2, and 3
Figure 1 shows the absorption spectra of 1, 2, and 3 in acetonitrile. Compound 1 exhibited two absorption bands at 259 (ε = 7370) and 333 nm (ε = 3890) in acetonitrile, although the latter bands were broader. Because of no observation of the absorption band above at 300 nm for pyridinium substituted by the alkyl group, the latter band observed around 330 nm can be associated with the conjugated structure of the benzocrown ether and pyridinium unit. The direct bonding of the π-electron rich dialkoxyphenyl unit in benzocrown ether and π-electron deficient pyridinium unit should generate the charge-transfer (CT) absorption, where each act as a donor and an acceptor, respectively. To clarify the origin of the CT absorption, the concentration dependency of 1 was checked because of
possessing a positive charge in pyridinium and the crown ether attractive to the positive charge in a molecule of 1 simultaneously. It was no observation of the concentration dependency in the spectral shape and the molecular extinction coefficient at 260 and 330 nm for 1 in the range from $5 \times 10^{-6}$ to $1 \times 10^{-4}$ M. This suggests that the CT absorption of 1 generates intramolecularly, but not intermolecularly. Compound 2 revealed that the absorption spectrum is similar to 1 with the peaks at 258 and 330 nm, which were slightly shifted to the blue side by 1 - 3 nm as compared to those of 1. This may be due to the non-crown ether structure. The similar absorption spectrum of 1 and 2 indicates a similar $\pi$-electron distribution character. No intermolecular interaction of 2 was also confirmed by an experiment concerning the concentration dependency. On the other hand, compound 3 exhibited pale yellow with two absorption bands at 270 and 362 nm in acetonitrile; the latter band was ascribed to the ICT absorption. The ICT absorption was observed at the longer wavelength side by ca. 30 nm, as compared to 1 and 2. This may result from the acceptor character of the pyridinium unit substituted by the pyridyl group at the para position for 3. The pyridyl group unit would enhance the acceptor character of the pyridinium unit relative to non-substituted pyridinium of 1 and 2.

**Guest-induced absorption spectra of 1, 2, and 3**

Upon the addition of Li$^+$ as the alkali metal ion guest into the solution containing 1, the ICT absorption band observed at 333 nm for 1 was shifted to the blue side, which became remarkable upon increasing the concentration of Li$^+$ (Fig. 2a). In the presence of 4 mM of Li$^+$, the ICT absorption peak of 1 was observed at 316 nm (Table 1). Such a Li$^+$-induced shift of the ICT absorption can be interpreted in terms of the complex formation of 1 with Li$^+$. Upon the accommodation of Li$^+$ in the crown ether cavity of 1, the unshared pair of electrons on the oxygen atoms in the crown ether unit would have an electrostatic interaction with Li$^+$, resulting in a decrease in the donor character of the benzocrown ether unit. Such a guest-induced variation in the donor-acceptor property in the molecule of 1 would lead the spectral variation. The isosbestic point observed at 329 nm indicates that 1 forms an inclusion complex with Li$^+$ with a 1:1 host-guest stoichiometry, which was also confirmed by good fitting of a curve-fitting analysis for estimating the binding constant, discussed below. A similar guest-induced spectral variation of 1 was observed upon the addition of other alkali metal ions, although the magnitude in the spectral variation became small as the ionic radius increased, as shown in Table 1. In the case of Rb$^+$ and Cs$^+$, a negligible change in the guest-induced absorption variations of 1 was observed, suggesting that 1 could not form inclusion complexes or weak interactions with these ions.

On the other hand, the absorption spectrum of 2 was hardly affected by the presence of the ion. Figure 3 shows the absorption spectra of 2, alone and in the presence of Li$^+$ in acetonitrile. The $\lambda_{\text{max}}$ observed at 330 nm for 2 was not shifted even in the presence of a large excess of Li$^+$ (20 mM), suggesting that 2 have no guest binding ability. This is due to the non-crown ether structure of 2.

When alkaline earth metal ions were used as the guest, remarkable changes in the absorption spectra of 1 were observed, as compared to those in the case of alkali metal ions. Figure 2b

![Figure 2](image1.png)

**Figure 2** Absorption spectra of 1 (0.02 mM), alone and in the presence of metal ion in acetonitrile. (a) [Li$^+$]: (1) 0 mM, (2) 0.28 mM, (3) 0.63 mM, (4) 1.43 mM. (b) [Mg$^{2+}$]: (1) 0 mM, (2) 0.07 mM, (3) 0.14 mM, (4) 0.71 mM.

![Figure 3](image2.png)

**Figure 3** Absorption spectra of 2 (0.02 mM), alone and in the presence of 20 mM of Li$^+$ and 2 mM Mg$^{2+}$ in acetonitrile.

| Guest (ionic radius/pm) | None | Li$^+$ (90) | Na$^+$ (116) | K$^+$ (152) | Rb$^+$ (166) | Cs$^+$ (181) | Mg$^{2+}$ (86) | Ca$^{2+}$ (114) | Ba$^{2+}$ (149) |
|------------------------|------|------------|--------------|-------------|-------------|-------------|-------------|-------------|---------------|
| $\lambda_{\text{ICT}}$ | 333  | 316$^a$    | 313$^b$      | 324$^b$     | 328$^b$     | 331$^c$     | 294$^d$     | 292$^b$     | 307$^c$       |
| $\lambda_{\text{c}}$  | —    | 329        | 324          | 331         | —           | —           | 313         | 314         | 319           |

Concentration metal of ions are set to be at a. 20 mM, b. 4 mM, and c. 2 mM.
shows the Mg$^{2+}$-induced absorption variation of 1. The ICT absorption peak of 1 was observed at 294 nm in the presence of 2 mM of Mg$^{2+}$ (Table 1). When we used other alkaline earth metal ions, such as Ca$^{2+}$ and Ba$^{2+}$, the $\lambda_{\text{max}}$ of CT peak of 1 was observed at an extremely shorter wavelength side as compared to those in the presence of alkali metal ones. These results indicate that 1 form inclusion complexes with alkaline earth metal ions with larger affinity as compared to those with alkali metal ions. The magnitude in the guest-induced spectral variation became small with increasing the ionic radii of the alkaline earth metal ion, which is a similar trend to that in the case of alkalai metal ions. These results may be associated with the positively charged host, which would lead to the guest-induced absorption peak of 1 was observed at 330 nm in the presence of 2 mM of Mg$^{2+}$.

**Guest sensing ability of 1 and 3**

We examined the ion sensing ability of 1 by using the guest-induced spectral variation, as compared with that of 3, which have a pyridyl group at the para position in the pyridinium ring, as the substituent. The value of the guest-induced absorption change normalized by the original absorbance at 340 nm was used as sensitivity parameters to evaluate the ion sensing ability for 1, while that at 390 nm was used for 3.

Figure 4 shows the result concerning the sensing abilities for 1 and 3. Among the guests used in this study, 1 detected Mg$^{2+}$ with the highest sensitivity. The sensitivity values of 1 decreased with increasing the ionic radii of alkaline earth metal ions, as shown by the fact that Ca$^{2+}$ and Ba$^{2+}$ were detected by 1 with a roughly one-half and a quarter values of that for Mg$^{2+}$, respectively. Among alkalai metal ions, 1 could detect Li$^+$ with the highest sensitivity, although the value was much smaller than that of Mg$^{2+}$ in spite of similar ionic radius of Li$^+$ and Mg$^{2+}$ (Table 1). This indicates that 1 showed different recognition patterns between alkali metal ions and alkaline earth metal ions. With increasing the ionic radii of alkalai metal ions, the sensing abilities of 1 decreased, which is a similar trend in the case of alkaline earth metal ions. Rb$^+$ and Cs$^+$, whose ionic radius are larger than K$^+$, were hardly detected by 1. These results suggest that 1 prefer the divalent ions, rather than univalent ones, and the ion with smaller ion radii. The order of the sensitivities of 1 for guests was Mg$^{2+}$ > Ca$^{2+}$ > Ba$^{2+}$ > Li$^+$ > Na$^+$ > K$^+$ > Rb$^+$ > Cs$^+$. These results are good agreements with those obtained in absorption measurements. On the other hand, 3 also detected Mg$^{2+}$ with the highest sensitivity, although the value of 3 was one-half as compared to that of 1. The ion-recognition pattern of 3 for alkali metal ions and alkaline earth metal ions is similar to that of 1 with small sensitivity values as compared to that of 1. However, it was found that the Mg$^{2+}$-preference of 1 is more remarkable than that of 3. The Mg$^{2+}$/Li$^+$ sensitivity ratios of 1 and 3 were estimated to be 8.63 and 5.08, respectively, while the Mg$^{2+}$/Ca$^{2+}$ ones of 1 and 3 were 2.42 and 1.59, respectively. Taking account of the similar Ca$^{2+}$/Na$^+$ sensitivity ratio of 1 and 3 with the value of 4.98 and 4.85, respectively, 1 seems to have ca. a 1.5-times higher sensitivity for Mg$^{2+}$, rather than 3 in addition to ca. 5-times the divalent cation-preference for both hosts. Such higher Mg$^{2+}$ selectivity of 1 is an interesting phenomenon, because both 1 and 3 possess the crown ether unit with the same size. The reason for this is not clear, but the π-electron character on the pyridinium benzocrown conjugate rather than the structural factor may affect such a selectivity, where the pyridyl group in 3 act as a π-electron withdrawing unit. The preference to the divalent cation of 1 and 3 may be associated with the positively charged host, which would lead to enhance the selectivity to divalent cationic guests rather than univalent ones.

The binding constants of 1 for the guest could be estimated by a nonlinear least-square curve fitting analysis from their guest-induced absorption variation at 340 nm. Figure 5 shows a typical example of saturation curves of 1 for Li$^+$ and Mg$^{2+}$. A similar fitting could be obtained for other guests, such as Na$^+$, K$^+$, Ca$^{2+}$ and Ba$^{2+}$ with good fitting, suggesting that 1 binds these ions with 1:1 host-guest stoichiometry, which was also confirmed by observations of the isosbestic points in the guest-induced absorption variations, as shown in Table 1. The binding constants of 1 and 3 estimated for Li$^+$, Na$^+$, K$^+$, Mg$^{2+}$,
Ca<sup>2+</sup> and Ba<sup>2+</sup> are listed in Table 2. The values of 1 for the guests are slightly larger than those of 3, except for that for Mg<sup>2+</sup>, which is much large value as compared to that of 3. This result is well coincident with the data obtained in ion sensing experiments. The binding constants for alkali metal ions with a larger ionic radius than K<sup>+</sup> could not be obtained for 1 and 3 because of small guest-induced spectral variations. In conclusion, the binding constants of 1 and 3 for the guest are roughly parallel to their sensitivity values, although the binding constants are relatively small as compared to other crown ether systems. This may be due to the electrostatic repulsions between the positively charged hosts, 1 and 3, and cationic guest ions for association.

Finally, the limit concentrations, which are the guest concentrations detectable by the absorption variations of 1 and 3, are estimated from three-times standard deviation values. Table 3 summarizes the limit concentrations of the detection of 1 and 3 for Li<sup>+</sup>, Na<sup>+</sup>, Mg<sup>2+</sup>, and Ca<sup>2+</sup>. Both hosts showed lower limit concentration for the detection for Mg<sup>2+</sup>; the values of 3 not only for Mg<sup>2+</sup>, but also other ions were smaller than those of 1. These results suggest that the lower limit concentrations of detection might be given by the guest showing the larger binding constant with the host. When compared between hosts, however, this is inconsistent with the fact that the binding constants of 1 for the guests were larger than those of 3 for all guests. The reason of this may be due to the larger standard deviation of 1 as compared to that of 3, as shown by the values of 2.8 × 10<sup>–3</sup> and 5.5 × 10<sup>–4</sup> at the average of the absorption intensity of 0.077 and 0.099 for 1 and 3, respectively. Compound 1 may be unstable in acetonitrile, as compared to 3. The substituent on the pyridinium ring might cause increase in the stability of the compound in the solution.

### Conclusions

A monocationic pyridinium benzocrown conjugate, 1, and its analogue with non-crown ether unit, 2, have been synthesized for developing a new chemosensor. These compounds showed the ICT absorption at around 330 nm, in which the dialkoxyphenyl and bipyridinium units act as the donor and acceptor, respectively. The addition of the guest ions caused the blue shift in the ICT absorption band for 1, but not for 2. The guest-induced absorption change of 1 is associated with 1:1 host-guest complex formation, and can be used for alkali and alkaline metal ion sensing. It was found that 1 could detect the divalent cation, especially, Mg<sup>2+</sup>, remarkably, even in compared with 3, which has a pyridyl group on the pyridinium ring as the substituent. The sensitivity values of 1 were roughly proportional to its binding constants. The pyridinium benzocrown conjugates capable of guest-induced ICT variation is interesting from the viewpoint not only of ion sensing, but also of host-guest chemistry. All of these data demonstrate that this system and more sophisticated systems designed on this basis may be applicable for the detection of metal ions.

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