Ion Detection by Intramolecular Charge-transfer Absorption of Benzocrown-bipyridinium Conjugate Appending Octadecyl Chain

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Abstract
A novel chemosensor based on benzocrown-bipyridine conjugate appending an octadecyl group, 1, was prepared to investigate its ion sensing ability in acetonitrile. The addition of Li+ as the guest caused change in color of 1 from yellow to colorless. This is owing to blue shift in intramolecular charge transfer (CT) absorption at around 400 nm, which is associated with the a 1:1 host-guest complex formation. The guest-induced color change of 1 was used for alkali and alkaline metal ion sensing. It was found that 1 detected Ca2+ with highest sensitivity.

Keywords: Chemosensor, Ion sensing, Intramolecular charge transfer absorption, Host-guest chemistry, Crown ether, Bipyridinium

1. Introduction
Chemosensors that exhibit spectral variations in response to the presence of a specific analyte are of current interest because of importance for facile monitoring of biological, medical and environmental analytes1,2. Since supramolecular host-guest complexation phenomenon proceed selectively and effectively, modification of a host with an appropriate chromophore is one of effective strategies for developing such chemosensors3,4. In such system, the host and the chromophore act as the guest binding site and the transducer of the guest binding into the spectral signals, respectively. Among a various type of chemosensors developed, crown ethers have been widely used and investigated for alkali and alkaline earth metal ion detections because of easy modification with the chromophores5–9.

Recently, we have reported some benzocrown-bipyridinium conjugates as chemosensors, in which both units are connected without any spacer10–14. These conjugates were found to exhibit the donor-acceptor charge transfer (CT) absorptions in visible region and the color changes in response to the alkali and alkaline earth metal ions. In the course of our study, we designed a novel benzocrown-bipyridinium conjugate appending an octadecyl group as a long alkyl chain, 1, whose structure is similar to the previous benzocrown-bipyridinium conjugates appending butyl and dodecyl groups as a substituent14. The long alkyl chain incorporated in 1 in this study would affect the intramolecular CT absorptions as well as the guest binding properties as compared to those of previous one, although no remarkable difference was observed between the conjugates appending butyl group and dodecyl one. Herein, we describe the synthesis and guest binding behavior of 1 compared to previous compound appending butyl chain, 3, and the analogue compound, 2, which have noncrown ether structure.

2. Experimental
2.1 Materials
All chemicals were reagent grade and used without further purification unless otherwise noted. Alkali and alkaline earth metal perchlorate were used as the guest ion. Acetonitrile
used as solvent was of spectroscopic grade. Acetonitrile-d$_3$ was used for measurement of NMR spectra.

2.2 Synthesis

N-(4’-benzo-15-crown-5)-N’-octadecy-4,4’-bipyridinium hexafluorophosphate (1).

A 20 cm$^3$ solution of N-(4’-benzo-15-crown-5)-4-pyridyl-pyridinium hexafluoro-phosphate (0.2 g, 0.35 mmol) in dry acetonitrile was added over 2 h to a 100 cm$^3$ solution of 1-bromooctadecane (1.2 g, 3.6 mmol), which was heated under reflux for 4 weeks. After the solution was cooled to room temperature, the solvent was removed by rotary evaporator and the crude solid was washed with 100 cm$^3$ of diethyl ether a few times, and recrystallized from methanol and diethyl ether (1:10 v/v, 200 cm$^3$). The solid was dissolved in water (50 cm$^3$), and a saturated aqueous solution of ammonium hexafluorophosphate salt was added. The precipitate was filtered and washed with water (15 cm$^3$). The product was obtained as a yellow solid (0.07 g, 21.0%).

Compound 1: mp: 268–271°C. ¹H NMR (500 MHz; CD$_3$CN): δ 9.11 (d, 2H), 8.91 (d, 2H), 8.51 (d, 2H), 8.45 (d, 2H), 7.31 (m, 2H), 7.18 (d, 1H), 4.62 (t, 2H), 4.21–4.18 (m, 4H), 3.86–3.83 (m, 4H), 3.68–3.66 (m, 4H), 3.63–3.61 (m, 4H), 1.42–1.23 (m, 22H), 0.87 (t, 3H) ppm. ¹³C NMR (125 MHz; CD$_3$CN): δ = 152.45, 150.49, 150.45, 150.20, 146.20, 146.01, 135.91, 127.85, 127.58, 113.98, 110.11, 71.22, 71.17, 70.35, 70.32, 69.86, 69.61, 69.23, 69.21, 62.76, 32.23, 31.58, 29.98, 29.94, 29.82, 29.66, 29.22, 26.18, 22.98, 13.97 ppm. Anal. Calcd for C$_{42}$H$_{64}$N$_2$O$_5$P$_2$F$_{12}$: C 52.17, H 6.68, N 2.90%. Found: C 52.84, H 6.87, N 2.99%.

N-(3,4-dimethoxyphenyl)-N’-octadecy-4,4’-bipyridinium hexafluorophosphate (2).

A 15 cm$^3$ solution of N-(3,4-dimethoxyphenyl)-4-pyridyl-pyridinium hexafluoro-phosphate (0.2 g, 0.46 mmol) in dry acetonitrile was added over 2 h to the 200 cm$^3$ solution of 1-bromooctadecane (3.8 g, 11.4 mmol), which was heated under reflux for 4 weeks. The product was purified in the same manner as in the case of compound 1 and was obtained as a pale yellow solid (0.23 g, 61.1%).

Compound 2: mp: 267–271°C. ¹H NMR (500 MHz; CD$_3$CN): δ 9.14 (d, 2H), 8.92 (d, 2H), 8.53 (d, 2H), 8.47 (d, 2H), 7.34 (m, 2H), 7.22 (d, 1H), 4.62 (t, 2H), 3.95 (s, 3H), 3.94 (s, 3H), 1.42–1.23 (m, 22H), 0.88 (t, 3H) ppm. ¹³C NMR (125 MHz; CD$_3$CN): δ = 152.70, 150.89, 150.52, 150.22, 146.18, 146.04, 135.86, 127.85, 127.55, 112.57, 108.49, 78.75, 62.78, 56.74, 56.60, 32.23, 31.58, 30.48, 29.98, 29.94, 29.82, 29.66, 29.22, 26.18, 22.98, 13.97 ppm. Anal. Calcd for C$_{36}$H$_{54}$N$_2$O$_2$P$_2$F$_{12}$: C 51.67, H 6.51, N 3.35%. Found: C 51.89, H 6.44, N 3.22%.

2.3 Apparatus and measurements

¹H-NMR and ¹³C-NMR spectra were recorded in acetonitrile-d$_3$ on a Bruker AVANCE 500 III HD. Melting point was recorded on AS ONE ATM-02. Absorption spectra were measured in acetonitrile by using Shimadzu UV 3150 spectrophotometer equipped with Taitech ZL100 thermometer with a 1 cm quartz cuvette at 25°C. The concentration of 1 and 2 was 1 mM for ¹H-NMR measurements and 0.02 mM for absorption measurements. The concentration dependencies of 1 and 2 were checked in absorption measurements from 5×10⁻⁶ to 1×10⁻⁴ M by using 2 cm and 2 mm cells when the solution concentration was lower and higher, respectively.

2.4 Evaluation of binding constants

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

$$ H + G \rightleftharpoons H-G $$

where H, G and H-G represent free host, guest and the host-guest complex, respectively. The binding constants of hosts for alkali and alkaline earth metal ions with 1:1 host-guest stoichiometry, $K_s$, were evaluated using the following equation (1):

$$ \Delta I = \frac{\Delta I_{\text{max}}}{2 \cdot H_0} \left[ (G_0 + H_0 + 1/K_s) - \left( (G_0 + H_0 + 1/K_s)^2 - 4 \cdot G_0 \cdot H_0 \right)^{1/2} \right] $$

where $H_0$ and $G_0$ represent the initial concentration of host, and the guest, and $\Delta I$ represents the guest-induced absorption variation. When all hosts exist as the complex, $\Delta I$ is equal to $\Delta I_{\text{max}}$. The analysis was performed by 430 nm for host.

3. Results and Discussion

3.1 Absorption spectra of 1 and 2

Figure 1 shows the absorption spectra of 1 and 2, alone and in the presence of Li$^+$ and Ca$^{2+}$ as the guest in acetonitrile. Both compounds exhibited yellow and similar...
absorption spectra with two absorption bands around at 260 and 400 nm. The latter bands were approximately a quarter in intensity and broader in shape as compared with former bands for 1 and 2, whose molecular extinction coefficients were approximately 24700 and 6600 \text{dm}^3/\text{mol}\cdot\text{cm} at 260 and 400 nm, respectively. Since usual bipyridinium derivatives which is obvious because of the noncrown ether structure.

The concentration coefficients at 260 and 400 nm for 2 indicates that the CT absorptions of 1 occur intramolecularly but not intermolecularly. Similarly, no observation in concentration dependencies in the spectral shape and the molecular extinction coefficients at 260 and 400 nm for 2 indicates that the visible band is ascribed to the intramolecular CT absorption, which is obvious because of the noncrown ether structure.

Fig. 1 Absorption spectra of compounds 1 and 2 (0.02 mM), alone and in the presence of Li⁺ or Ca²⁺ in acetonitrile. The concentrations of Li⁺ and Ca²⁺ are 20 mM.

Table 1 The wavelength of the intramolecular CT absorption for compounds 1 and 2, alone and in the presence of guests. The concentration of guest is (a) 20 mM, (b) 4 mM and (c) 2 mM.

<table>
<thead>
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<th>Guest (ionic radius / pm)</th>
<th>(a) 20 mM</th>
<th>(b) 4 mM</th>
<th>(c) 2 mM</th>
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<tbody>
<tr>
<td>none</td>
<td>396</td>
<td>394</td>
<td>393</td>
</tr>
<tr>
<td>Li⁺</td>
<td>397</td>
<td>394</td>
<td>393</td>
</tr>
<tr>
<td>Na⁺</td>
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<td>K⁺</td>
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<td>Ba²⁺</td>
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Concentration of metal ions are set to be at (a) 20 mM, b. 4 mM, and c. 2 mM.

3.2 Guest-induced absorption spectra of 1 and 2

Upon the addition of Li⁺ as the guest, 1 changed color from yellow to colorless in acetonitrile, as shown in Fig. 1. This color change is associated with the blue shift in the intramolecular CT absorption band of 1, which became remarkably with increasing the concentration of Li⁺. The intramolecular CT absorption peak was observed at 371 nm in the presence of 20 mM of Li⁺ (Table 1). Such guest-induced blue shift in the intramolecular CT absorption can be explained by the complex formation of 1 with Li⁺. The Li⁺ included in the crown ether cavity would have electrostatically interaction with the unshared pair of electrons on the oxygen atoms in the crown ether unit, which would cause the decrease in the donor character of the benzocrown ether unit (16). The change in the donor-acceptor property in the molecule of 1 resulted in the color change. The observation of an isosbestic point at 386 nm in the guest-induced spectral variation suggests a 1:1 host-guest stoichiometry of the complex. When Na⁺ was added to the solutions of 1, a similar absorption variation to that in the case of Li⁺ was observed, while the guest-induced absorption variation was small in the case of K⁺, Rb⁺, and Cs⁺. These results indicate that 1 could not form inclusion complexes or weak interactions with the alkali metal ions with an ionic radius larger than K⁺.

In contrast, the absorption spectrum of 2 was hardly affected by the presence of Li⁺ in acetonitrile, as shown in Fig. 1. The intramolecular CT absorption peaks of 2 were observed at 398 and 393 nm in the absence and the presence of Li⁺ (20 mM), respectively. Such negligible shift in intramolecular CT absorption peak for 2 suggests no guest binding ability of 2. This is owing to the noncrown ether structure. Other guest such as Na⁺, K⁺, Rb⁺, and Cs⁺ also did not cause the shift in intramolecular CT absorption peak, suggesting that 2 could not form inclusion complexes with the alkali metal ions.

On the other hand, the addition of alkaline earth metal ions such as Mg²⁺, Ca²⁺, and Ba²⁺ also caused spectral variations
of 1 similar to those in the case of Li⁺ and Na⁺. However, their variations were remarkable, as shown in Fig. 1 and Table 1. The λmax of CT peaks of 1 in the presence of alkaline earth metal ions in acetonitrile were observed at extremely shorter wavelength side as compared to those in the presence of alkali metal ones. These results indicate that 1 forms the inclusion complexes with alkaline earth metal ions with larger interaction as compared to those with alkali metal ions in spite of similar ionic radii of Li⁺, Na⁺, K⁺ with Mg²⁺, Ca²⁺, and Ba²⁺, respectively. The fact that 2 showed the intramolecular CT absorption peak at 392 nm in the presence of 20 mM of Ca²⁺ suggests the negligible interaction of 2 with the alkaline earth metal ions as like alkali ones.

3.3 Guest-induced 1H-NMR spectra of 1 and 2
The complex formation of 1 was confirmed by 1H-NMR spectroscopy. Figure 2 shows the 1H-NMR spectra of 1 and 2 in the absence and presence of Li⁺ in CD₃CN. As shown in Fig. 2a, four signals ascribed to crown ether protons around 3.6–4.2 ppm for 1 were shifted to downfield with a value of approximately 0.1 ppm upon addition of Li⁺, although octadecyl protons including α-methylene protons, terminal methyl ones, and other alkyl ones were not shifted, which were observed around at 4.62, 0.87, 1.2–1.45 ppm, respectively. Two singlet signals ascribed to methoxy protons at 3.95 and 3.94 ppm for 2 as well as the signals of octadecyl group were hardly affected by the presence of Li⁺. The aromatic protons of 1 were also affected in the presence of Li⁺ (Fig. 2b). The protons of the dialkoxyphenyl unit in benzocrown ether unit observed around 7.2–7.4 ppm for 1 were shifted to downfield with a value of approximately 0.1 ppm in the presence of Li⁺. Four doublet signals of the bipyridinium unit were also shifted to downfield slightly by the presence of Li⁺. In contrast, the protons of the dialkoxyphenyl unit in benzocrown ether unit and the bipyridinium ones observed around 7.2–9.2 ppm for 2 were hardly affected in the presence of Li⁺. All these results indicate the interaction with Li⁺ for 1, but not for 2, which are in good agreement with the data obtained in the absorption spectra.

3.4 Guest sensing ability of 1
Such guest-induced color change of 1 could be used to evaluate the ion sensing ability. The value of the guest-induced absorption variation normalized by the original absorbance at 430 nm (ΔI/I₀) was used as the sensitivity parameters. Compound 3, which is similar structure to 1 but different in butyl group instead of the octadecyl group of 1, were also used for comparison. The results are shown in Fig. 3. In this study, 1 detected Ca²⁺ with highest sensitivity, and the value was roughly two times larger than those of Mg²⁺ and Ba²⁺. Although a similar ion-sensing pattern was observed for 3, it was found that Ca²⁺ preference of 1 was higher than that of 3. This was supported by the Ca²⁺/Mg²⁺ selectivity with the value of 1.70 and 1.06 for 1 and 3, respectively. Ba²⁺ was detected by 1 with the similar value of Li⁺, which was detected with highest sensitivity in the alkali metal ions. Among alkali metal ions, Na⁺ was detected by 1 with roughly one-half value compared to the value of Li⁺. K⁺, having similar ionic radius of Ba²⁺, was hardly detected by 1.
Such ion sensing behavior of 1 for alkali metal ions is similar to that of 314. Therefore, both 1 and 3 could not detect the alkali metal ions with larger ionic radius than K+, such as Rb+ and Cs+, which is similar to 3. The order of the sensitivity of 1 for guests was Ca2+ > Mg2+ > Ba2+ > Li+ > Na+ > K+ > Rb+ > Cs+. This ion-recognition pattern of 1 was similar to that of 3. These results suggest 1 and 3 show the remarkable ion-recognition for divalent ions, especially, 1 shows that for Ca2+. As discussed previous paper, the preference of 3 for divalent ions is associated with the positive charge of the host14. Compound 1 also showed similar trend to 3 because of the similar structure to 3. The remarkable Ca2+ preference of 1 may be due to the long alkyl chain, which is different from 3. Form consideration with molecular models (Corey-Pauling-Koltun model), it is possible for 1 to adopt the conformation that the long alkyl chain come close the crown ether unit because of a long and flexible alkyl chain of the octadecyl group, but not for 3. This may enhance the hydrophobic environment around the crown ether for 1. Since it is known that 15-crown-5 fits Na+ well, which is similar ionic radius to Ca2+, Ca2+ may accommodate into the cavity of 15-crown-5 in 1 rather than Mg2+ under the hydrophobic environment. Therefore, it can be considered that both the charge effect and the hydrophobic environment one for 1 would result in Ca2+ preference.

The binding constants of 1 for the guest could be estimated by a nonlinear least-square curve fitting analysis by using an equation (1) for 1:1 host-guest complex formation but not for 2:1 ones, from which their guest-induced absorption variation at 430 nm were used. Good fitting of the data and the theoretical curves could be obtained for Li+, Na+, Mg2+ and Ca2+ with R2 values with 0.998, 0.998, 0.997 and 0.996, respectively, indicating a 1:1 host-guest complex formation, and giving the binding constants of 1 with the values of $8.70 \times 10^2$, $3.10 \times 10^3$, $2.90 \times 10^5$, and $1.40 \times 10^7$ M$^{-1}$, respectively. The binding constants could not be obtained for other guests because of small spectral variations except for Ba2+. These values of binding constants of 1 are similar to those of 3, which are $9.10 \times 10^2$, $2.60 \times 10^5$, $8.20 \times 10^5$, and $2.30 \times 10^5$ M$^{-1}$ for Li+, Na+, Mg2+ and Ca2+, respectively, but are relatively small when compared to other crown ether system. This can be interpreted in terms of the electrostatic repulsions between the positively charged hosts of 1 and 3, and cationic guest for association. However it is clear that the binding constants estimated for 1 are roughly parallel to their sensitivity values. Therefore, the sensing ability of 1 seems to be governed by the binding constants.

Finally, the limit concentrations that can be detected by the absorption variation of 1 have been estimated from three times the standard deviations values. The limit concentrations of detection of 1 are estimated to be 0.23, 0.51, 0.17 0.083 mM for Li+, Na+, Mg2+ and Ca2+, which are similar values to those of 3 (0.25, 0.59, 0.072, and 0.057 mM for Li+, Na+, Mg2+ and Ca2+, respectively). However, it was found that the detection limits for Mg2+ and Ca2+ were slightly improved by using 1, which may be the result of the effect of the long alkyl chain.

4. Conclusions

A new chemosensor, 1, benzocrown-bipyridinium conjugate incorporating a long alkyl chain, showed the guest-induced color change from yellow to colorless based on the blue shift in the intramolecular CT absorptions, which are associated with 1:1 host-guest complex formation. Such guest-induced color change of 1 can be used for alkali and alkaline metal ion sensing, especially for Ca2+. All these results demonstrate that the benzocrown-bipyridinium conjugate is interesting not only from the perspective of guest sensing accompanied with color change but also from host-guest chemistry. More sophisticated systems can be designed for detecting these ions on this basis.

References