Self-assembly of Amphiphilic Benzo-15-crown-5 Azoprobes in Response to Alkali Metal Ions in Water

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The amphiphilic benzo-15-crown-5 (B15C5) azoprobes exhibit a self-assembly in response to alkali metal ions in water based on the exciton interaction of the phenylazo groups in the probes, and the most selective response to K^+ was obtained for an azoprobe possessing a hexyl spacer unit.

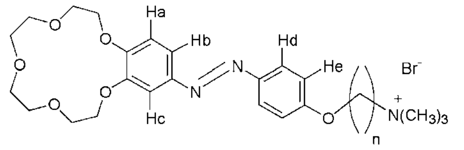
Alkali metal ion recognition in water is an emerging topic of interest due to the need to investigate profiles of ions in the cell in molecular biology and usage in clinical tests in vitro.[1] Although highly preorganized structures have been adopted as recognition sites of fluorescent probes to achieve selective sensing of alkali metal ions in water,[2] the versatile design of recognition sites exhibiting sufficiently high selectivity and efficiency remains an important objective. Recently, new approaches to alkali metal ion sensing in water, which are based on supramolecular chemistry, have attracted much attention. These supramolecular sensors utilize different types of metal-binding-induced aggregates for signal transduction, such as fluorescent bis-15-crown-5 derivatives,[3] gold nanoparticles,[4] quantum dots,[5] oligonucleotides,[6] cyclodextrin complexes,[7] and so on. It is well known that surfactants can vary the critical micelle concentration (CMC) depending on temperature, salt concentration, and alkyl chain length. The formation of self-assembled aggregates based on hydrophilicity–lipophilicity balance (HLB) is considered to be useful for the versatile design of supramolecular sensors that function in water.

Here, we report newly designed cationic azo-amphiphiles, **15C5-Azo-C*n***, possessing a B15C5 moiety as the alkali metal ion recognition site, a phenylazo group for signal transduction, and a quaternary ammonium unit with different lengths of alkyl linkers to induce the amphiphilic nature. The alkyl spacer lengths are varied from ethyl to butyl and to hexyl in order to control HLB through which proper aggregation in water can be realized.[8] As expected, these probes show high water solubility, and are found to exhibit a unique self-assembly induced spectral response to alkali metal ions in water, reflecting their alkyl spacer lengths.

We synthesized **15C5-Azo-C*n*** ($n = 2$, 4, and 6) by azo-coupling of 4′-aminobenzo-15-crown-5 with phenol, followed by introducing different lengths of alkyl spacers having a quaternary ammonium unit.[9] Their structures were fully confirmed by ^{1}H NMR, mass spectral, and elemental analyses. Figure 1a shows the UV–vis absorption spectra of **15C5-Azo-C6** (3.0 mM, $\mathrm{M} = \mathrm{mol\,dm^{-3}}$) in water containing 400 mM tetramethylammonium chloride (TMACl), KCl, or NaCl.[10] The maximum wavelength (370 nm) can be assigned to the long axis polarized π–π^* transition band of the azo group in **15C5-Azo-C6**.[11] In the presence of TMA^+ or Na^+, **15C5-Azo-C6** exhibited no significant changes in its UV–vis spectra. In contrast, the addition of 400 mM KCl caused a hypsochromic shift of the π–π^* transition band from 370 to 366 nm with a decrease in absorptivity.

Based on the exciton theory,[12] this shift implies *H*-aggregate formation of **15C5-Azo-C6** triggered by K^+ binding. It is well known that B15C5 can form a sandwich complex with K^+ in organic solvent. Although the binding ability of B15C5 with K^+ in water is very weak ($<1.0\,\mathrm{M^{-1}}$),[13] we assume that the amphiphilic nature of the probe and the π–π stacking ability of phenylazo units stabilize the *H*-aggregates formation of **15C5-Azo-C6** with K^+ in water. In Figure 1b is shown the effect of alkyl spacer length on the response selectivity. The ratios of absorbance at 370 nm to that at 420 nm (A_{370}/A_{420}) are plotted against the ionic radius of alkali metal ions (Li^+, Na^+, K^+, Rb^+, and Cs^+). The results clearly show that **15C5-Azo-C6** exhibited the highest selectivity among the probes. The ^{1}H NMR signals of the phenyl protons of **15C5-Azo-C6** are depicted in Figure 2. Compared with the proton signals in the presence of TMACl, no chemical shift was induced by the addition of 400 mM NaCl. In contrast, apparent upfield shifts of the proton signals were observed in the presence of 400 mM KCl, indicating the ring-current effect due to the formation of *H*-aggregates. The results imply the formation of a 2:1 sandwich complex of **15C5-Azo-C6** with K^+. This binding mechanism is also supported by the hypsochromic shift of the π–π^* transition band of the azo moiety in the UV–vis absorption spectrum.

On the assumption that the change in absorbance is induced



15C5-Azo-Cn

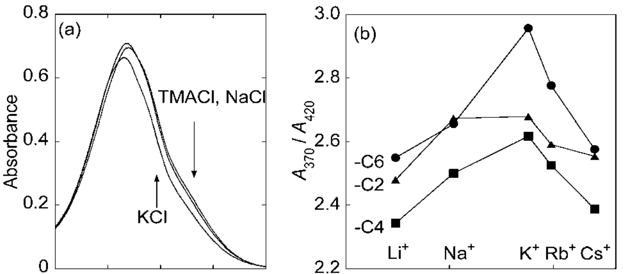


Figure 1. (a) UV–vis absorption changes of **15C5-Azo-C6** on addition of TMACl, NaCl, and KCl. Optical path length is 0.01 cm. (b) Dependence of A_{370}/A_{420} on the ionic radius of alkali metal ions. $[\mathrm{MCl}] = 400$ mM ($M^+ = Li^+$, Na^+, K^+, Rb^+, and Cs^+), [**15C5-Azo-C*n***] = 3 mM ($n = 2$, 4, and 6).

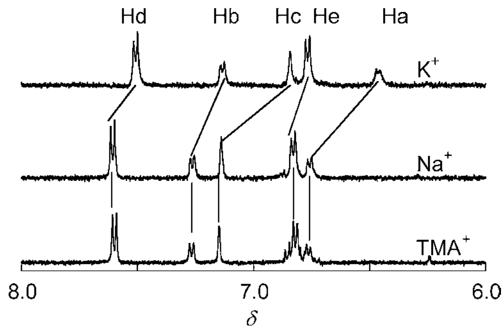


Figure 2. ^{1}H NMR chemical shifts of phenyl protons of **15C5-Azo-C6** (3 mM) on addition of 400 mM MCl (M = K^+, Na^+, and TMA^+) in D_2O at 298 K.

by the 2:1 complex formation between the azoprobe (L) and the metal ion (M^+) as shown by eq 1, the relationship between absorbance (Abs.) and concentration of alkali metal ion ($[M^+]$; $[M^+] \gg [L]_t$) is expressed by eq 3:

$$M^+ + 2L \rightleftharpoons ML_2 \tag{1}$$

$$K_{21} = \frac{[ML_2]}{[M^+][L]^2} \tag{2}$$

$$\text{Abs.} = \frac{l}{4K_{21}[M^+]}\left(B\varepsilon_L + \frac{B^2\varepsilon_{ML2}}{4}\right)$$
$$B = -1 + \sqrt{1 + 8K_{21}[M^+][L]_t} \tag{3}$$

where $[L]_t$ is the total concentration of **15C5-Azo-C*n***, l is the optical path length (0.01 cm), and ε_L, ε_{ML2} represent the molar absorptivities of L and ML_2, respectively. The absorbance changes at 420 nm as a function of $[M^+]$ for **15C5-Azo-C*n*** are shown in Figure 3, where the ionic strength is kept constant (400 mM) with TMACl. For K^+, the observed results were well fitted with eq 3 (solid lines in Figure 3) using a nonlinear least-squares program, and the 2:1 binding constants (K_{21}) were determined to be $(2.5 \pm 0.4) \times 10^3\,M^{-2}$ for **15C5-Azo-C6**, $(0.5 \pm 0.1) \times 10^3\,M^{-2}$ for **15C5-Azo-C4**, and $(0.2 \pm 0.2) \times 10^3\,M^{-2}$ for **15C5-Azo-C2**. For Na^+, the absorbance changes were small with relatively large deviations, and thus the K_{21} values could not be determined from eq 3. It is evident that **15C5-Azo-C6** has the highest K^+/Na^+ selectivity.

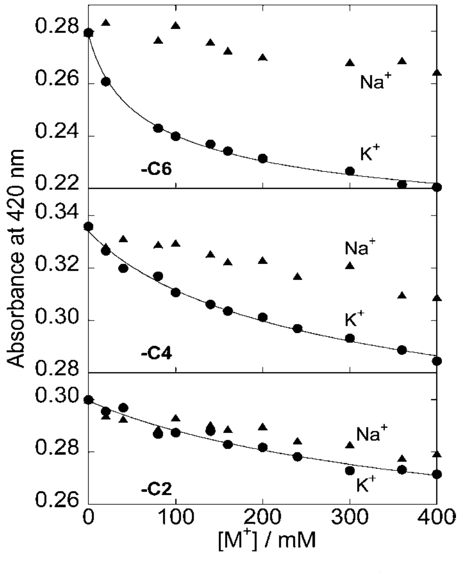


Figure 3. UV–vis changes at 420 nm of **15C5-Azo-C6**, **-C4**, **-C2** (3 mM) as a function of alkali metal concentration. KCl (●) or NaCl (▲). Ionic strength is adjusted to 400 mM by the addition of TMACl.

In conclusion, we have designed novel crown ether azo-amphiphiles that exhibit the K^+-selective spectral responses in water based on selective H-aggregates formation induced by the K^+ binding. The alkyl spacer length of **15C5-Azo-C*n*** is found to strongly affect response efficiency and selectivity. Consequently, the highest response to K^+ is obtained for **15C5-Azo-C6** possessing the hexyl spacer unit. To control sensitivity and selectivity, further molecular tunings of crown ether azo-amphiphiles by lengthening the alkyl spacer and changing the crown ether ring size are underway in our laboratory.

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9 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

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