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Novel Mg^{2+}-responsive fluorescent chemosensor based on benzo-15-crown-5 possessing 1-naphthaleneacetamide moiety

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Abstract—A new fluorescent ionophore for Mg^{2+}, 4′-(1-naphthaleneacetamido)benzo-15-crown-5 (**1**), was synthesized, and its complexation behavior in acetonitrile was investigated by means of UV and fluorescence spectrometry. In the absence of a metal ion, the naphthalene moiety showed quite weak fluorescence emission (fluorescence 'Off' state). On the other hand, after the addition of Mg^{2+}, fluorescence emission from the naphthalene moiety increased (fluorescence 'On' state).

Magnesium is the eighth most abundant element on the crust of earth,[1] and is distributed widely in living bodies such as cells and bones.[2,3] Therefore, detection and determination techniques of Mg^{2+} have been attracting many scientists in the fields of biology, medical, pharmaceutical, and environmental science. There are several methods to determine the amount of Mg^{2+} such as atomic absorption, Mg^{2+}-selective electrodes,[4,5] and fluorescent chemosensors.[6–12] In the fluorescent chemosensor, the main streams are coumarin derivatives[6,7] and crown ether analogues having several fluorescent groups.[8–12] These chemosensors are based on the photo-induced electron transfer (PET) quenching process.

In our previous papers we have reported some fluorescent 'Off–On' chemosensors for Ca^{2+}, Sr^{2+}, and Ba^{2+} consisting of an oligo-ethylene oxide chain and *N*-phenylamide moiety, and fluorescent active groups, such as anthracene,[13] pyrene,[14] or naphthalene.[15] Fluorescence emission in these 'Off–On' chemosensors was quite small in the absence of a metal ion. However, after the addition of a metal ion, fluorescence emission from the fluorescent chromophore was enhanced largely. We elucidated the reason for these phenomena were due to the mechanism both of PET and twisted intramolecular charge transfer (TICT) motion at the 1-naphthaleneacetamide moiety. When the 1-naphthaleneacetamide moiety was excited, charge separation occurred through an electron transfer between the naphthalene ring and the benzene ring via the amide bond. Therefore, in the absence of a metal ion, fluorescence emission from the chemosensor was almost quenched. On the other hand, upon complexation with a metal ion, photo-induced charge transfer occurred between the naphthalene ring and the *N*-phenyl amide moiety over the methylene bond (naphthalene–CH_2–CONH–Ph), and conformational locking interfered in the TICT relaxation process, consequently the fluorescent group was strongly emitted. However, these sensors were not able to detect Mg^{2+} because of its low complexation ability. This result inspired us to make a new chemosensor capable of determining Mg^{2+}. Although these are great many reports about alkali metal ion sensors based on benzo-15-crown-5 ether (B15C5) derivatives,[16] a study on alkaline earth ionophore consisted of B15C5 is rare.[17] With these in mind, we used a B15C5 as a recognition moiety for Mg^{2+}, and 1-naphthaleneacetamide as an 'Off–On' detection moiety. We can imagine that the photo-driven TICT motion of 1-naphthaleneacetamide will be more controllable compared with that of anthracene and pyrene because the existence of a CH_2 group induced

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Keywords: 1-Naphthaleneacetamide; Benzo-15-crown-5; 'Off–On' fluorescence detection; Photo-induced electron transfer; Twisted intramolecular charge transfer.

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molecular flexibility. Moreover, Mg^{2+} preferred to coordinate onto a carboxamide group. The applications of 'Off–On' controlling both of PET and TICT through the ion complexation for chemosensors based on B15C5 are limited.

In this Letter, we wish to report the photo-chemical behavior of **1** (Fig. 1) by means of UV, fluorescence, and ^1H NMR spectrometry.

Ionophore **1** was synthesized from 1-naphthaleneacetic acid with the corresponding amine using DCC as a coupling agent in the presence of HOBT. (Yield: 60.0%).[18] This structure and purity were confirmed by the ^1H NMR spectra and elemental analysis. Fluorescence spectra were measured by a Shimadzu RF-5300PC at 25 °C. The concentration of the fluorescent reagent was 1×10^{-5} mol/dm^3 in purified acetonitrile. Alkaline earth metal cations were added into the fluorescent reagent solution as perchlorate salts.

Figure 2 shows the fluorescence spectra of compound **1** and its Mg^{2+} complex in acetonitrile. Fluorescence emissions from the naphthalene moiety were quite weak in the absence of Mg^{2+} ion. On the other hand, when Mg^{2+} was added, **1** and Mg^{2+} formed a complex, and a strong emission was observed. The shapes of fluorescence spectra clearly indicated a naphthalene monomer emission, which showed a maximum intensity around 338 nm. Similar 'Off–On' behavior was also observed in the presence of other alkaline earth metal ions. The 'Off–On' response abilities were expressed as I_{max}/I_0 values for the guest ions, and are listed in Table 1. The largest value for Mg^{2+} (40.6) was the strongest and showed usefulness for an Mg^{2+} responsive sensor. In contrast, negligible spectral changes were observed in the presence of Na^+, Li^+ and K^+.

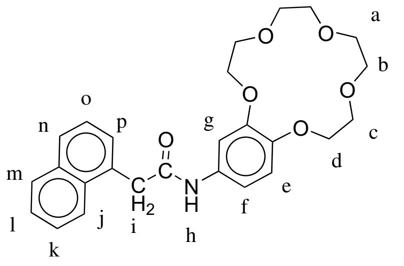

Figure 1. The structure of **1**.

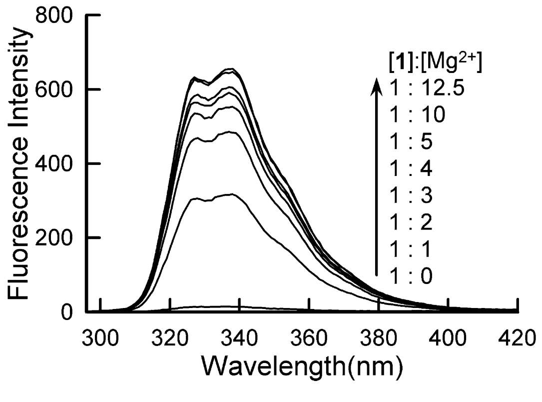

Figure 2. Fluorescence spectra of **1** and its Mg^{2+} complex in acetonitrile at 25 °C. Excitation wavelength: 283 nm. $[\mathbf{1}] = 1 \times 10^{-5}$ mol/dm^3.

Figure 3 shows the UV absorption spectra of **1** and its Mg^{2+} complex. When Mg^{2+} was added, the absorbance derived from the naphthalene moiety was slightly decreased, whereas its shape (~280 nm) changed a little. This result suggested that a large conformational change did not occur around the naphthalene. On the other hand, the absorption spectrum around 250 nm, attributed to the benzo-crown moiety, showed a large blue-shift and an increase of intensity. This result can be explained by the disruption of the π-conjugated system between benzene and the amide bond at the binding event.

The increase of monomer emission clearly depended on the concentration of the metal ion. The complex formation constants (*K*) were determined from the titration curves by means of a nonlinear least-square curve-fitting method (Marquardt's method),[19] and are listed in Table 1. These results indicated that the association of **1** for Mg^{2+} is not always larger than that of other metal ions. Presumably an ionic radius of Mg^{2+} provided a complex structure, which showed an effective cut off the quenching process of **1**.

As above, spectral data evidently showed the structural changes of **1** upon complexation with metal ions. To

Table 1. Complex formation constants (*K*)[a] and fluorescent response (I_{max}/I_0) of **1** for various metal ions in acetonitrile at 25 °C

log *K* (I_{max}/I_0)			
Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}
5.53 (40.6)	5.90 (26.5)	5.97 (14.0)	5.89 (8.64)

[a] $K = [\mathbf{1}\cdot M^{2+}]/[\mathbf{1}][M^{2+}]$.

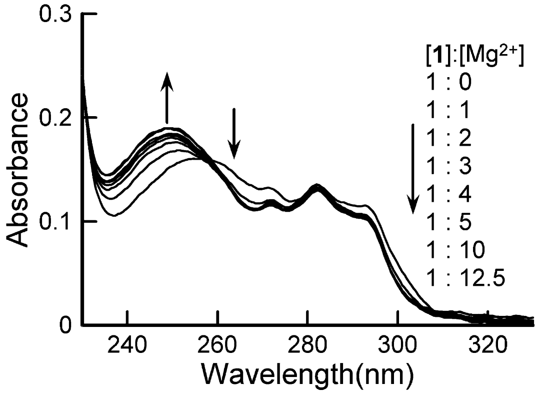

Figure 3. UV spectra of **1** and its Mg^{2+} complex in acetonitrile at 25 °C.

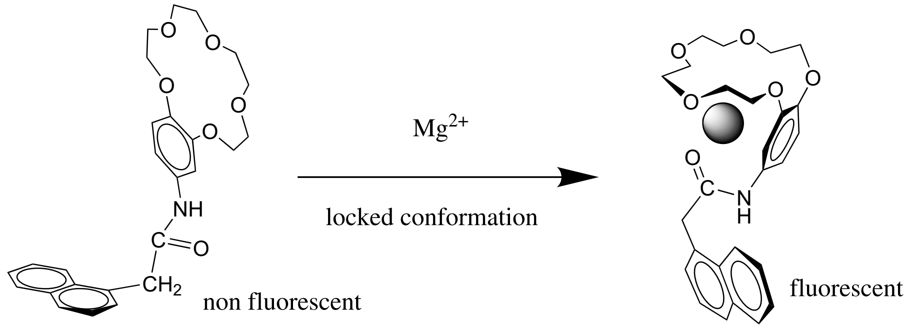

Figure 4. Schematic presentation of the structural change of **1** before and after addition of Mg^{2+}.

clarify these changes, a ^{1}H NMR study of **1** was carried out in the absence and presence of Mg^{2+} in acetonitrile-d_3 at 30 °C. Peak assignments were made by ^{1}H–^{1}H COSY and NOESY spectra. In the **1**·Mg^{2+} complex (refer to the scheme for peak assignments), crown ether moiety peaks (a–d) were shifted to a lower magnetic field (0.34, 0.34, 0.37, and 0.40 ppm, respectively). The peak of amide protons (h) showed large lower magnetic field shift changes (0.77 ppm). Benzene protons (e–g) were shifted to a lower magnetic field (0.29, 0.26, and 0.11 ppm, respectively) and proton (i) shifted to lower magnetic field (0.13 ppm). These results were showed that Mg^{2+} was bound cooperatively with the crown ether moiety and a carbonyl group, resulting that a molecular motion around the amide group and benzene was freezed. The chemical shift changes of naphthalene protons (j–p) were not to be observed. This observation indicated that these protons did not receive an electron or ring-current effect upon complexation.

On the bases of fluorescence and ^{1}H NMR studies, an expected structural change of **1** before and after the addition of Mg^{2+} on the ground state is illustrated in Figure 4. Before complexation, the excited state of **1** was induced a charge separation state via a photoinduced electron transfer (PET) accompanied with a twisted motion between CONH bond and the benzene ring. However, the coordination of Mg^{2+} on crown ether moiety and amide bond restrained the twisted motion. Since the ICT process included the twisted motion should be shut off. Thus, the fluorescence emission from naphthalene can be observed.

In summary, a novel fluorescent chemosensor **1** based on B15C5 having a naphthaleneacetamide moiety showed 'Off–On' fluorescent response upon the addition of Mg^{2+}. Chemosensor **1** bound Mg^{2+} with crown ether and the carbonyl group cooperatively showing the fluorescent emission. The coordination of Mg^{2+} in **1** induced a freezing molecular rotation around the amide bond. This 1·Mg^{2+} structure provided an effective control both of PET and TICT relaxation process. We believe that **1** will be available as a photo-detecting system for Mg^{2+}.

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18. 4′-(1-Naphthaleneacetamido)benzo-15-crown-5 (**1**): Yield 60.0%. White solid. Mp: 190 °C (from EtOH). ^{1}H NMR (CD_3CN) $\delta = 3.61$ (C–CH_2–O, m, 8H), 3.75 (–C–CH_2–O, m, 4H), 4.00 (–C–CH_2–O, t, 4H), 4.10 (CO–CH_2-naph, s, 2H), 6.81 (aromatic, d, 1H), 6.96 (aromatic, d, 1H), 7.24 (aromatic, t, 1H), 7.43 (aromatic, t, 2H), 7.47–7.58 (aromatic, m, 4H), 7.84 (aromatic, t, 1H), 7.91 (aromatic, d, 1H), 8.09 (aromatic, d, 1H), 8.30 (NH, s, 1H). Calcd for $C_{26}H_{29}NO_6{\cdot}1/5H_2O$: C, 68.64; H, 6.48; N, 3.08. Found: C, 68.63; H, 6.44; N, 3.09.
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