Fluorescence Chemosensor with Specific Response for Mg^{2+}

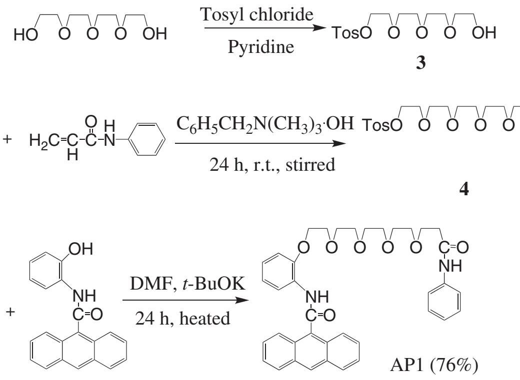
Jeongsik Kim,[1] Tatsuya Morozumi,[2] and Hiroshi Nakamura*[2]
[1]*Graduate School of Environmental Science, Hokkaido University, Sapporo, Hokkaido 060-0810*
[2]*Research Faculty of Environmental Earth Science, Hokkaido University, Sapporo, Hokkaido 060-0810*

(Received July 22, 2009; CL-090683; E-mail: nakamura@ees.hokudai.ac.jp)

A fluorescent chemosensor AP1 showed specific selectivity for Mg^{2+}. Fluorescence characteristics of AP1 for Mg^{2+} are distinguished in comparison to those of Ca^{2+}, Sr^{2+}, and Ba^{2+} by three components: a high fluorescence intensity ratio (nine times), peak wavelength shift (30 nm), and monomer emission shape.

Fluorescent chemosensors play an important role in detection of alkali and alkaline earth metal cations in biological systems. During the last few decades, extensive study has been devoted to development of fluorescent chemosensors for alkali and alkaline earth metal cations.[1] Crown ethers[2] and polyethers[3] with fluorescent detecting moieties as a fluorescent chemosensor are useful photochemical sensors for detection and characterization of alkali or alkaline earth metal cations. Fluorescence spectroscopy has become a powerful tool for detection of alkali and alkaline earth metal cations. Most studies using fluorescence spectroscopy have specifically examined fluorescence intensity ratios or fluorescence "Off–On" to detect metal ions. To obtain detailed characteristic information of metal cations, a variety of components are also required, e.g., spectral shape and the maximum emission position.[4]

Recently, we have studied fluorescence behaviors of twisted intramolecular charge transfer (TICT) on linear polyether compounds with anthracene, naphthalene, or pyrene moieties.[5] Fluorescence emission of symmetric compounds bearing *N*-phenyl-9-anthracenecarboxamide units (9-AC) was largely quenched in solution.[5a] TICT quenching occurred in the absence of metal ions (nonfluorescent: "off" state). Upon complex formation, photoinduced rotation of the 9-AC moiety was interrupted by a strong cooperative binding between the carbonyl and ethylenoxy moieties for metal ions. Hence, the TICT relaxation pathway should be controlled by the complexation with metal ions, and a fluorescence emission of 9-AC moiety was observed (fluorescent: "on" state). TICT quenching was also controlled by alkaline earth metal ions in asymmetric compounds with compact stoppers (e.g., *n*-propyl, benzene, or naphthalene). Chemosensors bearing *n*-propyl and benzene moieties as stoppers showed different spectral structure in Mg^{2+} complex compared to Ca^{2+}, Sr^{2+}, and Ba^{2+} complexes, with similar fluorescent intensity ratio.[5b] On the other hand, chemosensors bearing naphthalene moiety as a stopper exhibited larger fluorescent intensity in Ca^{2+} complex compared to other cations.[5c] These chemosensors were distinguished from other cations by only one factor: fluorescent intensity, or spectral structure, or maximum emission position. In these studies, we found that chemosensors based on a tetra-polyether chain with various stoppers have difficulty in detecting alkaline earth metal ions by multiple responses. In this work, we report the synthesis and photochemical behavior of fluorescent chemosensor AP1 based on penta-polyether showing a high selectivity with multiple responses for Mg^{2+}.



Scheme 1. Synthesis of compound AP1.

The AP1 chemosensor was synthesized according to Scheme 1. Tetraethylene glycol (3.88 g, 0.02 mol) in pyridine (50 mL) was stirred at under 10 °C with the addition of *p*-toluenesulfonyl chloride (3.80 g, 0.02 mol) for 1 h and was stored in a refrigerator for one day. The solution was treated with HCl and water and then extracted with benzene and $CHCl_3$. The $CHCl_3$ phase was dried using $MgSO_4$ and evaporated to obtain **3**. The crude **3** was dissolved in benzyltrimethylammonium hydroxide and stirred for 24 h with addition of *N*-phenyl acrylamide. The crude product (3.29 g, 0.014 mol) of **4** in 20 mL of DMF was added dropwise to the DMF solution (20 mL) of *t*-BuOK (1.12 g, 0.0014 mol) and *N*-(2-hydroxyphenyl)-9-anthrylamide (3.14 g, 0.0014 mol). The reaction mixture was heated for one day at 110 °C. The reaction mixture was evaporated under reduced pressure and then dissolved in $CHCl_3$. The solution was washed with distilled water, dried over $MgSO_4$, and evaporated. Compound AP1 was purified using silica gel column chromatography (Wakogel C-200, eluent; chloroform/ethyl acetate (9:1); Wako Pure Chemical Industries, Ltd.). Its structure and purity were confirmed using ^1H NMR spectra and elemental analysis.[6] Fluorescence and UV–vis spectra were recorded at 25 °C using appropriate devices (RF-5300PC and UV-2400PC; Shimadzu Corp.).

Figure 1 portrays fluorescence spectra of AP1 as a function of the Mg^{2+} (a) and Ca^{2+} (b) concentrations in acetonitrile. In the absence of cation, AP1 showed weak emission at around 455 nm, which was attributed to the exciplex emission of 9-AC. The fluorescence response of AP1–Mg^{2+} complex is prominent compared to those of Ca^{2+}, Sr^{2+}, and Ba^{2+} complexes. Upon increasing Mg^{2+}, the emission intensity is noticeably enhanced with the vibrational shape; the peak position resembled that of anthracene monomer emission at around 410 nm. These structured peaks result from the absence of charge-transfer interaction between the anthracene and the amide group. In contrast to AP1, a symmetric compound based on penta-polyether similar to AP1 showed quite weak emission and a poor vibrational shape

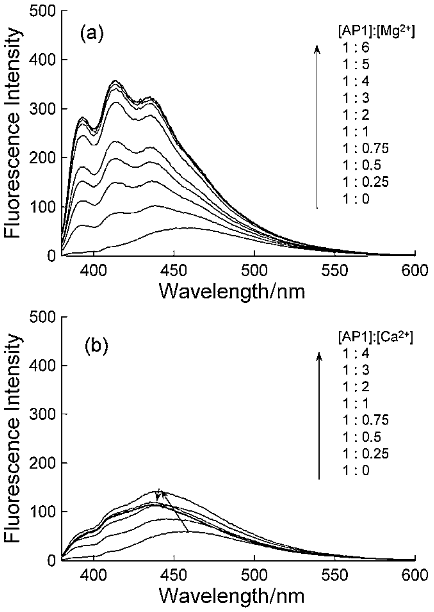


Figure 1. Fluorescence spectra of AP1 and its Mg^{2+} (a) and Ca^{2+} (b) complexes. Excitation wavelength: 363 nm. [AP1] = 1×10^{-5} mol dm^{-3}.

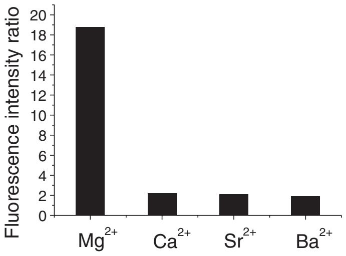


Figure 2. Fluorescence intensity ratio (I_{max}/I_0) at the 413 nm for Mg^{2+} and 440 nm for Ca^{2+}, Sr^{2+}, and Ba^{2+}, where fluorescence maximum peaks were observed. $[Mg^{2+}] = [Ca^{2+}] = [Sr^{2+}] = [Ba^{2+}] = 1 \times 10^{-4}$ mol dm^{-3}. [AP1] = 1×10^{-5} mol dm^{-3}.

for Mg^{2+} under the same conditions.[5a] In the case of AP1–Ca^{2+} complex as presented in Figure 1b, fluorescence spectra were observed in structureless exciplex emission at around 440 nm, which are attributed to emission from anthracene aromatic amide moieties. The shape and wavelength of the Mg^{2+} complex at the peak maximum are distinct from those of the Ca^{2+}, Sr^{2+}, and Ba^{2+} complexes.

The analytical usefulness of the free reagent and the complexes was assessed respectively using low and high emission intensities. The fluorescence "Off–On" responses were evaluated as I_{max}/I_0 values (Figure 2). The I_{max}/I_0 values were measured at 413 nm for Mg^{2+} and 440 nm for Ca^{2+}, Sr^{2+}, and Ba^{2+} which were respective fluorescence emission maxima. The I_{max}/I_0 values of AP1 were of the order of Mg^{2+} (18.8) > Ca^{2+} (2.2) > Sr^{2+} (2.1) > Ba^{2+} (1.9). Obviously, AP1 showed high selectivity for Mg^{2+}, while weak fluorescence emission of Ca^{2+}, Sr^{2+}, and Ba^{2+} complexes was observed. These results (I_{max}/I_0 values, spectral shape and emission maximum wavelength) reveal that AP1 can readily discriminate Mg^{2+} and other metal cations using fluorescence spectroscopy. The complex formation constants ($\log K$) were determined from the curve by means of a nonlinear least-squares curve fitting method (Marquardt's method).[7] The $\log K$ was 4.79 for Mg^{2+} but could not be calculated for Ca^{2+}, Sr^{2+}, and Ba^{2+}. No response for alkali metal ions (Na^+ and K^+) was observed.

In summary, the new reagent AP1 is found to be sensitive and selective to Mg^{2+} compared with other cations as follows: (1) fluorescence intensity response (19 for Mg^{2+} and 2 for Ca^{2+}, Sr^{2+}, and Ba^{2+}), (2) spectral shape (monomer for Mg^{2+} and exciplex for Ca^{2+}, Sr^{2+}, and Ba^{2+}), and (3) emission maximum wavelength (410 nm for Mg^{2+} and 440 nm for Ca^{2+}, Sr^{2+}, and Ba^{2+}). The present chemosensor AP1 will be useful to discriminate Mg^{2+} using fluorescence spectra. Regarding the origin of specific observations between Mg^{2+} and Ca^{2+}, Sr^{2+}, Ba^{2+}, we intend to continue our work.

References and Notes

1 a) Y. Suzuki, H. Komatsu, T. Ikeda, N. Saito, S. Araki, D. Citterio, H. Hisamoto, Y. Kitamura, T. Kubota, J. Nakagawa, K. Oka, K. Suzuki, *Anal. Chem.* **2002**, *74*, 1423. b) G. Grynkiewicz, M. Poenie, R. Y. Tsien, *J. Biol. Chem.* **1985**, *260*, 3440. c) A. Minta, J. P. Kao, R. Y. Tsien, *J. Biol. Chem.* **1989**, *264*, 8171. d) T. Nagano, T. Yoshimura, *Chem. Rev.* **2002**, *102*, 1235. e) H. Komatsu, N. Iwasawa, D. Citterio, Y. Suzuki, T. Kubota, K. Tokuno, Y. Kitamura, K. Oka, K. Suzuki, *J. Am. Chem. Soc.* **2004**, *126*, 16353.

2 a) A. P. de Silva, H. Q. N. Gunaratne, T. Gunnlaugsson, A. J. M. Huxley, C. P. McCoy, J. T. Rademacher, T. E. Rice, *Chem. Rev.* **1997**, *97*, 1515. b) L. Fabbrizzi, A. Poggi, *Chem. Soc. Rev.* **1995**, *24*, 197. c) B. Valeur, I. Leray, *Coord. Chem. Rev.* **2000**, *205*, 3. d) D. T. McQuade, A. E. Pullen, T. M. Swager, *Chem. Rev.* **2000**, *100*, 2537. e) J. Kim, T. Morozumi, H. Nakamura, *Tetrahedron* **2008**, *64*, 10735.

3 a) G. McSkimming, J. H. R. Tucker, H. Bouas-Laurent, J.-P. Desvergne, *Angew. Chem., Int. Ed.* **2000**, *39*, 2167. b) T. Nabeshima, A. Hashiguchi, T. Saiki, S. Akine, *Angew. Chem., Int. Ed.* **2002**, *41*, 481. c) T. Nabeshima, Y. Yoshihira, T. Saiki, S. Akine, E. Horn, *J. Am. Chem. Soc.* **2003**, *125*, 28. d) J. B. Ames, K. B. Hendricks, T. Strahl, I. G. Huttner, N. Hamasaki, J. Thorner, *Biochemistry* **2000**, *39*, 12149. e) N. R. Cha, S. Y. Moon, S.-K. Chang, *Tetrahedron Lett.* **2003**, *44*, 8265. f) A. Momotake, T. Arai, *Tetrahedron Lett.* **2003**, *44*, 7277.

4 a) T. Morozumi, H. Hiraga, H. Nakamura, *Chem. Lett.* **2003**, *32*, 146. b) E. Arunkumar, P. Chithra, A. Ajayaghosh, *J. Am. Chem. Soc.* **2004**, *126*, 6590. c) W. J. Youngblood, D. T. Gryko, R. K. Lammi, D. F. Bocian, D. Holten, J. S. Lindsey, *J. Org. Chem.* **2002**, *67*, 2111. d) E. Arunkumar, A. Ajayaghosh, J. Daub, *J. Am. Chem. Soc.* **2005**, *127*, 3156. e) A. Ajayaghosh, *Acc. Chem. Res.* **2005**, *38*, 449. f) A. Ajayaghosh, E. Arunkumar, J. Daub, *Angew. Chem., Int. Ed.* **2002**, *41*, 1766.

5 a) T. Morozumi, T. Anada, H. Nakamura, *J. Phys. Chem. B* **2001**, *105*, 2923. b) J. Kim, T. Morozumi, H. Nakamura, *Org. Lett.* **2007**, *9*, 4419. c) J. Kim, T. Morozumi, N. Kurumatani, H. Nakamura, *Tetrahedron Lett.* **2008**, *49*, 1984. d) T. Morozumi, H. Hama, H. Nakamura, *Anal. Sci.* **2006**, *22*, 659.

6 Reagent AP1, ^{1}H NMR (acetonitrile-d_3) δ 2.45 (CO–CH_2–C, t, 2H), 2.85 (C–CH_2–O, t, 2H), 3.07 (C–CH_2–O, m, 4H), 3.24 (–C–CH_2–O, t, 2H), 3.39 (–C–CH_2–O, t, 2H), 3.45 (–C–CH_2–O, d, 2H), 3.54 (–C–CH_2–O, t, 2H), 3.66 (–C–CH_2–O, t, 2H), 4.05 (–C–CH_2–O, t, 2H), 7.02 (aromatic, m, 1H), 7.08 (aromatic, m, 2H), 7.18 (aromatic, m, 1H), 7.22 (aromatic, m, 1H), 7.50–7.54 (aromatic, m, 5H), 8.11 (aromatic, m, 4H), 8.41 (C–CO–NH, s, 1H), 8.46 (aromatic, d, 1H), 8.61 (aromatic, s, 1H), 8.80 (C–NH–CO, s, 1H). Found: C, 71.49; H, 6.39; N, 4.41%. Calcd for $C_{38}H_{40}O_7N_2$: C, 71.68; H, 6.33; N, 4.40%.

7 D. W. Marquardt, *J. Soc. Ind. Appl. Math.* **1963**, *11*, 431.