Available online at www.sciencedirect.com
SCIENCE DIRECT®

Tetrahedron Letters 47 (2006) 497–500

Tetrahedron Letters

Hg^{2+}-selective fluoroionophoric behavior of pyrene appended diazatetrathia-crown ether

So Hee Kim,[a] Ki Cheol Song,[a] Sangdoo Ahn,[a] Yong Soo Kang[b] and Suk-Kyu Chang[a,*]

[a]*Department of Chemistry, Chung-Ang University, Seoul 156-756, Republic of Korea*
[b]*Department of Chemical Engineering, Hanyang University, Seoul 133-791, Republic of Korea*

Received 11 October 2005; revised 6 November 2005; accepted 11 November 2005
Available online 28 November 2005

Abstract—Bis(pyrene) derivative of diazatetrathia-crown ether has been prepared and its Hg^{2+}-selective fluoroionophoric properties were investigated. The compound showed a pronounced Hg^{2+}-selectivity and other metal ions except for Cu^{2+} showed almost no discernible responses. The Hg^{2+}-selectivity of the compound was also confirmed by the competitive experiments performed in the presence of physiologically important metal ions and the detection limit was found to be 1.6×10^{-6} M. The prominent selective and efficient fluorescence quenching behavior could be utilized as a new chemosensing system for the analysis of toxic Hg^{2+} ions in aqueous environment.

There are a number of ingeniously designed supramolecular systems for the selective chemosensing of chemically and biologically important ionic species.[1] Particularly important is the selective detection of Hg^{2+} ions due to the toxic impacts of this heavy metal ion on our environments.[2] Among many Hg^{2+}-selective chemosensors developed so far, optical detection systems attracted much research interest and are generally derived from the traditional structural skeleton of crown ethers,[3] calixarenes,[4] and other versatile molecular frameworks including proteins, oligonucleotides, and dye-based structures.[5] The molecular framework of diazatetrathia-crown ether **1** has been utilized as a platform for the construction of supramolecular systems having transition metal ion selectivity.[6] Crystal structures of Hg^{2+} complexes of a series of cage-annulated sulfur-containing cryptands, especially having diazatetrathia-crown moiety, suggest the stable complex formation of thia-crown ethers with Hg^{2+} ions.[7] Bipyridine-armed diazatetrathia-crown ether showed a specific binding ability for Cu^{2+} ions in the presence of Ni^{2+}, Co^{2+}, and Zn^{2+} ions when assisted by a vesicle forming surfactant.[8] In addition to these, an efficient Hg^{2+}-selective fluorescent sensor bearing diazatetrathia-crown moiety on the 1,8-positions of the anthracene ring has been reported.[9] Fluorescence is a particularly attractive signaling tool for the construction of chemosensors because of its sensitivity and easy of signal detection.[10] Among many fluorophores, pyrene subunits are versatile and frequently employed for the construction of important chemosensors having efficient fluorogenic behavior.[11] In this letter, we report a new fluoroionophore derived from diazatetrathia-crown ether having two pyrenylacetamide fluorophore for the sensing of transition metal ions. Designed compound exhibited a highly Hg^{2+}-selective and efficient fluorescence quenching behavior in aqueous acetonitrile solution.

The pyrene appended compound **2** was prepared by the reaction of 1,4,10,13-tetrathia-7,16-diazacyclooctadecane **1** with 2-chloro-*N*-pyren-1-yl-acetamide[4c] (K_2CO_3, KI) in acetonitrile (75% yield) (Scheme 1).[12] The complexation of targeted metal ions by the diazatetrathia-crown moiety could be further assisted by the amide carbonyl groups of the appending side chain in somewhat axial type participation as is frequently observed in lariat ethers.[13]

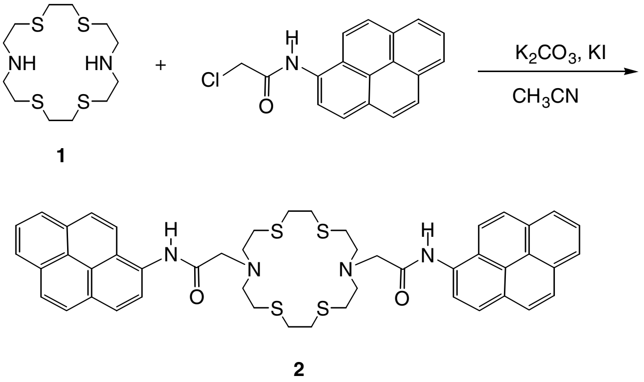
First, the fluoroionophoric properties of **2** toward representative alkali, alkaline earth, and transition metal ions were investigated in aqueous organic solutions. Among the surveyed systems of common water miscible organic

---

Keywords: Diazatetrathia-crown ether; Fluoroionophore; Pyrene; Hg^{2+}-selectivity; Chemosensor.

* Corresponding author. Tel.: +82 2 820 5199; fax: +82 2 825 4736; e-mail: skchang@cau.ac.kr

0040-4039/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2005.11.060



Scheme 1. Synthesis of pyrene appended diazatetrathia-crown ether.

solvents, aqueous acetonitrile was found to be relatively well suited for the selective responses of a specific transition metal ion. To have a more optimized condition for a specific metal ion, the effects of water composition on fluorescence behavior were investigated (Fig. 1). As the composition of water increases, the fluorescence intensity of pyrene monomer emission at 387 nm decreases progressively. Similar decreases, but with much larger changes in lower water composition region, were also observed for **2** in the presence of 100 equiv of Hg^{2+} or Cu^{2+} ions. The maximum selectivity toward target metal ions seems to be obtained in relatively lower water composition region between 0% and 20%. Based on this profile the fluorescence measurements were carried out in 90% aqueous acetonitrile solution (CH_3CN–H_2O = 90:10, v/v) where both requirements for the use of aqueous solution in the analysis of real samples and the high selectivity toward Hg^{2+} and Cu^{2+} ions are fulfilled.

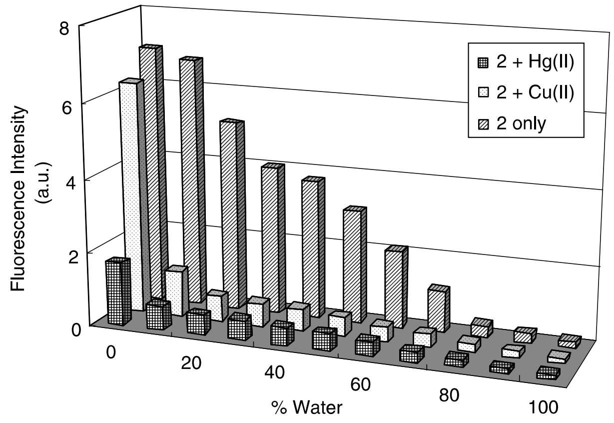


Figure 1. Changes in fluorescence intensity of **2**, **2**-Hg^{2+}, and **2**-Cu^{2+} systems as a function of water composition in aqueous acetonitrile. [**2**] = 5.0×10^{-6} M. [Hg^{2+} or Cu^{2+}] = 5.0×10^{-4} M as perchlorate salt. λ_{ex} = 340 nm and fluorescence intensities were measured at 387 nm. Buffered at pH 4.8 with acetate buffer (10^{-2} M).

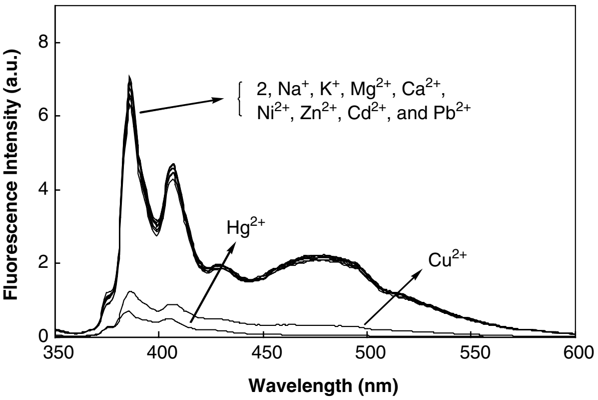


Figure 2. Fluorescence spectra of **2** in the presence of varying metal ions in aqueous acetonitrile. [**2**] = 5.0×10^{-6} M. [M^{n+}] = 5.0×10^{-4} M as perchlorate salts. λ_{ex} = 340 nm in CH_3CN–H_2O (90:10, v/v) buffered at pH 4.8 with acetate buffer (10^{-2} M).

Fluorescence spectra of **2** in aqueous acetonitrile solution comprised of two prominent emissions due to the pyrene moiety: that is characteristic monomer emissions around 370–440 nm and a broad excimer emission centered around 480 nm (Fig. 2). Upon interaction with varying alkali (Na^+, K^+), alkaline earth (Mg^{2+}, Ca^{2+}), and transition metal (Ni^{2+}, Cu^{2+}, Zn^{2+}, Pb^{2+}, Cd^{2+}, Hg^{2+}) ions, the fluorescence of **2** was selectively quenched only with Hg^{2+} and Cu^{2+} ions. The pronounced Hg^{2+}- and Cu^{2+}-selectivities are not unexpected with reference to the other systems based on the azathia-crown ethers.[7–9,14] Generally, the azamacrocycles having appended pyrene moiety signal the complexation event by the mechanism of PET (photoinduced electron transfer) type fluorescence enhancements.[15] In the present case, the fluorescence quenching effect induced by the complexed Hg^{2+} and Cu^{2+} ions having intrinsic quenching nature was operative more pronouncedly than the PET type complexation-induced fluorescence enhancements.

The quenching efficiency expressed by I_0/I (I_0 and I denote the fluorescence intensity of **2** in the absence and the presence of metal ions, respectively) was larger than 9.7 for Hg^{2+} ions and 5.1 for Cu^{2+} ions in monomer emission region at 387 nm. The degree of fluorescence quenching in excimer emission region (measured at 480 nm) was more dramatic for Hg^{2+} ions ($I_0/I = 38$ for Hg^{2+} and 6.4 for Cu^{2+} ions). All the other metal ions surveyed revealed relatively constant I_0/I values of 0.93–1.02. The effective fluorescence quenching of **2** might be due to the intrinsic quenching nature of the selectively complexed Hg^{2+} ions as described earlier.[16] In this case, the excimer emissions are also completely disappeared, which might be originated from the conformational changes of the ionophore upon complex formation leading to the separation of the two nearby situated pyrene moieties for the excimer emission.[17] That is the metal ions are nested at the center of the macrocycle with further ligations with amide carbonyl groups of the appended pyrene moiety in somewhat axial type mode, which resulted in the extended conformation of **2** with two divergent pyrene fluorophores. Under this situation, the fluorescences of pyrene excimer as well as monomer region would be effectively quenched with complexed Hg^{2+} ions. Fluorescence quenching was also observed with another intrinsic quenching Cu^{2+} ions,[16] however, in this case the quenching behavior was less effective in monomer region as well as in excimer emissions than Hg^{2+} ions even with 100 equiv metal ions.

To have more insights into the analytical possibility of the chemosensing behavior of **2**, the fluorescence titrations with two most responding metal ions of Hg^{2+} and Cu^{2+} were performed. With Hg^{2+} ions, the quenching was very efficient and addition of 1 equiv metal ion resulted in the quenching of more than 95% of the total fluorescence intensity changes, which implies that the **2**-Hg^{2+} complex is quite stable (Fig. 3). As shown in the inset of Figure 3, a well-defined titration break around 1 equiv of Hg^{2+} ions suggests a 1:1 stoichiometry of the **2**-Hg^{2+} complex system.[18] The association constant (K_{assoc}) calculated by the nonlinear curve fitting procedure of the concentration dependent fluorescence changes[19] was very large and only provides lower limit of $10^7\ M^{-1}$. Titration with Cu^{2+} ions also yielded progressive fluorescence quenching, however, the K_{assoc} ($7.6 \times 10^3\ M^{-1}$) was found to be much smaller than **2**-Hg^{2+} system. The complexation of compound **2** with Hg^{2+} ions was further evidenced by the IR and MALDI mass measurements. Compound **2** exhibited a shift in the absorption band of amide carbonyl group from 1668 to 1638 cm^{-1} upon interaction with Hg^{2+} ions,[20] which manifests participation of the carbonyl functions in complex formation. In MALDI measurements, a diagnostic peak at $m/z = 1041.2$ for **2**-Hg^{2+} complex was also observed. However, ^1H NMR titration of compound **2** with $Hg(OAc)_2$ in CD_3CN or $CDCl_3$ resulted in much broadened resonances and did not provide any useful informations.

Finally, to have a practical applicability of the compound as a chemosensor for the analysis of physiological samples, Hg^{2+}-selective responses under competitive condition were investigated. The fluorescence titration was carried out in the presence of physiologically important background metal ions ($[Na^+] = 138$ mM, $[K^+] = 4$ mM, $[Mg^{2+}] = 1$ mM, $[Ca^{2+}] = 3$ mM, $[Zn^{2+}] = 0.02$ mM, and $[Cu^{2+}] = 0.015$ mM)[21] including most interfering Cu^{2+} ions in 90% buffered aqueous acetonitrile solution ($CH_3CN–H_2O = 90:10$, v/v). The Hg^{2+}-selectivity of the compound was retained and a nice profile of concentration dependent fluorescence changes was observed. From the fluorescence titrations, detection limit[22] for the analysis of Hg^{2+} ions in this physiologically relevant condition was calculated to be 1.6×10^{-6} M.

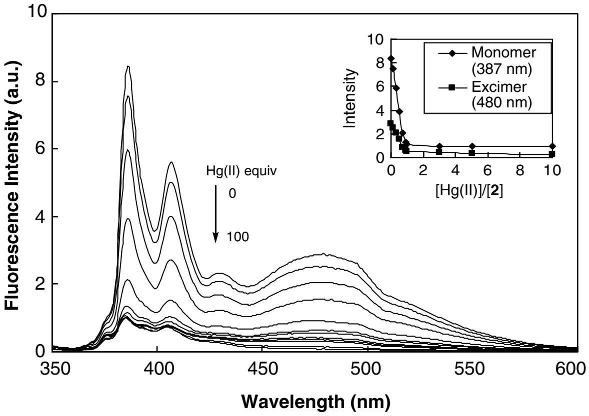


Figure 3. Fluorescence titration of **2** with $Hg(ClO_4)_2$ in aqueous acetonitrile. $[\mathbf{2}] = 5.0 \times 10^{-6}$ M. $\lambda_{ex} = 340$ nm in $CH_3CN–H_2O$ (90:10, v/v) buffered at pH 4.8 with acetate buffer (10^{-2} M). The inset shows the changes in fluorescence intensities of pyrene monomer and excimer emissions measured at 387 and 480 nm, respectively.

In summary, the diazatetrathia-crown ether derivative having two appended pyrenylacetamide subunits exhibited a prominent Hg^{2+}-selectivity over other representative alkali, alkaline earth, and transition metal ions. The Hg^{2+}-selectivity of the compound was retained and not affected significantly under competitive condition having physiologically important metal ions. The compound could be utilized as a new fluorescent chemosensor for the analysis of micromolar concentration range of Hg^{2+} ions in aqueous environment.

References and notes

1. (a) Desvergne, J. P.; Czarnik, A. W. *Chemosensors of Ion and Molecule Recognition*; Kluwer: Dordrecht, 1997; (b) *Fluorescent Chemosensors for Ion and Molecule Recognition*; Czarnik, A. W., Ed.; American Chemical Society: Washington, DC, 1992.
2. Boening, D. W. *Chemosphere* **2000**, *40*, 1335.
3. (a) Prodi, L.; Bargossi, C.; Montalti, M.; Zaccheroni, N.; Su, N.; Bradshaw, J. S.; Izatt, R. M.; Savage, P. B. *J. Am. Chem. Soc.* **2000**, *122*, 6769; (b) Rurack, K.; Kollmannsberger, M.; Resch-Genger, U.; Daub, J. *J. Am. Chem. Soc.* **2000**, *122*, 968.
4. (a) Gutsche, C. D. *Calixarenes Revisited*; The Royal Society of Chemistry: Cambridge, 1998; (b) Talanova, G. G.; Talanov, V. S.; Bartsch, R. A. *Chem. Commun.* **1998**, 1329; (c) Kim, J. H.; Hwang, A.-R.; Chang, S.-K. *Tetrahedron Lett.* **2004**, *45*, 7557.
5. (a) Nolan, E. M.; Lippard, S. J. *J. Am. Chem. Soc.* **2003**, *125*, 14270, and references cited therein; (b) Guo, X.; Qian, X.; Jia, L. *J. Am. Chem. Soc.* **2004**, *126*, 2272; (c) Moon, S. Y.; Cha, N. R.; Kim, Y. H.; Chang, S.-K. *J. Org. Chem.* **2004**, *69*, 181; (d) Chen, P.; He, C. *J. Am. Chem. Soc.* **2004**, *126*, 728; (e) Thomas, J. M.; Ting, R.; Perrin, D. M. *Org. Biomol. Chem.* **2004**, *2*, 307; (f) Ono, A.; Togashi, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 4300; (g) Nolan, E. M.; Lippard, S. J. *J. Mater. Chem.* **2005**, *15*, 2778; (h) Ros-Lis, J. V.; Marcos, M. D.; Martínez-Máñez, R.; Rurack, K.; Soto, J. *Angew. Chem., Int. Ed.* **2005**, *44*, 4405.
6. (a) Beer, P. D.; Nation, J. E.; McWhinnie, S. L. W.; Harman, M. E.; Hursthouse, M. B.; Ogden, M. I.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1991**, 2485; (b) Beer, P. D.; Wheeler, J. W.; Moore, C. P. *J. Chem. Soc., Dalton Trans.* **1992**, 2667; (c) Tsukube, H.; Uenishi, J.; Higaki, H.; Kikkawa, K.; Tanaka, T.; Wakabayashi, S.; Oae, S. *J. Org. Chem.* **1993**, *58*, 4389; (d) Bordunov, A. V.; Bradshaw, J. S.; Zhang, X. X.; Dalley, N. K.; Kou, X.; Izatt, R. M. *Inorg. Chem.* **1996**, *35*, 7229; (e) Blake, A. J.; Gould, R. O.; Li, W.-S.; Lippolis, V.; Parsons, S.; Radek, C.; Schröder, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 293; (f) Love, J. B.; Vere, J. M.; Glenny, M. W.; Blake, A. J.; Schröder, M. *Chem. Commun.* **2001**, 2678.
7. Marchand, A. P.; Cal, D.; Mlinarić-Majerski, K.; Ejsmont, K.; Watson, W. H. *J. Chem. Crystallogr.* **2002**, *32*, 447.
8. Tsukube, H.; Hamada, T.; Tanaka, T.; Uenishi, J. *Inorg. Chim. Acta* **1993**, *214*, 1.

9. Kwon, J. Y.; Soh, J. H.; Yoon, Y. J.; Yoon, J. *Supramol. Chem.* **2004**, *16*, 621.
10. de Silva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515.
11. (a) Winnik, F. M. *Chem. Rev.* **1993**, *93*, 587; (b) Kim, J. S.; Noh, K. H.; Lee, S. H.; Kim, S. K.; Kim, S. K.; Yoon, J. *J. Org. Chem.* **2003**, *68*, 597; (c) Yuasa, H.; Miyagawa, N.; Izumi, T.; Nakatani, M.; Izumi, M.; Hashimoto, H. *Org. Lett.* **2004**, *6*, 1489.
12. Preparation of **2**. To a mixture of 1,4,10,13-tetrathia-7,16-diazacyclooctadecane **1** (0.5 mmol, 164 mg), K_2CO_3(1 mmol, 138 mg), and KI (0.1 mmol, 17 mg) in acetonitrile was added 2-chloro-*N*-pyren-1-yl-acetamide (1.1 mmol, 323 mg). The reaction mixture was refluxed for 10 h and the progress of the reaction was followed by TLC. After cooling the mixture was filtered and the filtrate was evaporated under reduced pressure. The residue was partitioned between CH_2Cl_2 and water. The organic layer was separated and evaporated, and the crude product was purified by column chromatography (silica gel, CH_2Cl_2–MeOH, 10:1, v/v) to yield slightly amber colored product **2**. Yield: 75%. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 10.25 (s, 2H), 8.59 (d, $J = 8.4$ Hz, 2H), 8.44 (d, $J = 9.3$ Hz, 2H), 8.19–7.86 (m, 14H), 3.39 (s, 4H), 2.82–2.76 (m, 24H). ^{13}C NMR (DMSO-d_6, 373 K, 150 MHz) δ 166.0, 130.5, 130.0, 127.8, 126.6, 126.55, 125.9, 125.7, 124.6, 124.4, 124.2, 124.1, 123.6, 122.7, 121.4, 121.1, 58.1, 54.2, 31.9, 29.7. HR-MS (FAB, *m*-NBA), calcd for $C_{48}H_{49}N_4O_2S_4$ $m/z = 841.2738$. Found 841.2746.
13. Gokel, G. W.; Schall, O. F. Lariat Ethers. In *Comprehensive Supramolecular Chemistry*; Elsevier: Oxford, 1996; pp 97–152.
14. Descalzo, A. B.; Martínez-Máñez, R.; Radeglia, R.; Rurack, K.; Soto, J. *J. Am. Chem. Soc.* **2003**, *125*, 3418.
15. (a) de Silva, A. P.; de Silva, S. A. *J. Chem. Soc., Chem. Commun.* **1986**, 1709; (b) Kubo, K.; Kato, N.; Sakurai, T. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 3041; (c) Valeur, B.; Leray, I. *Coord. Chem. Rev.* **2000**, *205*, 3; (d) de Silva, A. P.; Fox, D. B.; Huxley, A. J. M.; Moody, T. S. *Coord. Chem. Rev.* **2000**, *205*, 41.
16. Rurack, K. *Spectrochim. Acta Part A* **2001**, *57*, 2161.
17. Moon, S.-Y.; Youn, N. J.; Park, S. M.; Chang, S.-K. *J. Org. Chem.* **2005**, *70*, 2394.
18. Schneider, H.-J.; Yatsimirsky, A. K. *Principles and Methods in Supramolecular Chemistry*; John Wiley & Sons: Chichester, 2000; p 149.
19. Kuzmič, P. *Anal. Biochem.* **1996**, *237*, 260, The software DynaFit can be obtained from BioKin, Ltd at http://www.biokin.com.
20. The IR spectra were measured on Teflon film to minimize the possible interaction with other metal ions such as KBr. The compound **2** was treated with 2 equiv of $Hg(ClO_4)_2$ in CH_3CN–MeOH and the mixture was applied on the Teflon IR film and dried under vacuum before measurements.
21. Hay, R. W. *Bio-inorganic Chemistry*; Ellis Horwood: Chichester, 1984; p 10.
22. Shortreed, M.; Kopelman, R.; Kuhn, M.; Hoyland, B. *Anal. Chem.* **1996**, *68*, 1414.