DOI 10.5012/bkcs.2011.32.8.2928

Rhodamine Cyclen-based Fluorescent Chemosensor for the Detection of Cd^{2+}†

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Received February 11, 2011, Accepted February 25, 2011

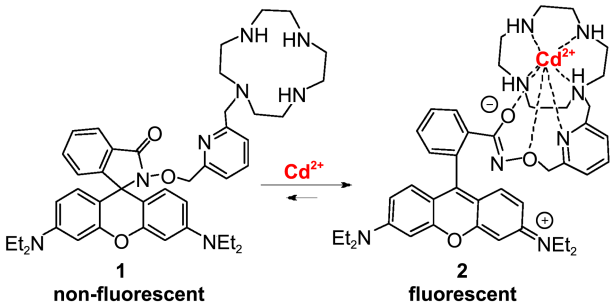
A chemosensor based on a rhodamine-hydroxamate platform containing a pyridine and a cyclen binding units has been developed for the detection of Cd^{2+} in aqueous solutions. The probe responds selectively toward Cd^{2+} over other biologically relevant metal ions. The fluorescent probe shows 1:1 binding stoichiometry and the detection limit for Cd^{2+} in water proved to be as low as 25 nM.

Key Words : Chemosensor, Cyclen, Fluorescence, Cadmium, Rhodamine

Introduction

Cadmium, one of the highly toxic heavy metal ions, is widely used in a variety of industrial products, such as Ni-Cd batteries, alloy, coloring matters, and electroplating. Cadmium is also found in fertilizer production and sewage sludge.[1] This element has detrimental effects on human health and causes serious environmental problems.[2] Chronic exposure to cadmium can cause renal dysfunction, calcium metabolism disorders, kidney diseases, and certain cancers including lung and prostate.[3] Cadmium and cadmium compounds are category I carcinogens according to the classification by the International Agency for Research on Cancer (IARC).[4] Therefore, the investigation on the method for the detection of cadmium has attracted tremendous attentions. Several methods for the detection of Cd^{2+} at trace quantity levels in various samples have been developed. They include atomic absorption spectrometry (AAS)[5] and inductively coupled plasma atomic emission spectrometry (ICP-AES).[6] Recently, the detection of heavy metal ions based on the fluorescent chemosensor method[7] has been studied extensively because it is simple and highly sensitive. Although fluorescent chemosensors for the detection of Cd^{2+} have been reported utilizing fluorophores, such as quinoline,[8] anthracene,[9] BODIPY,[10] fluorescein,[11] coumarin,[12] and others,[13] however, rhodamine-based fluorescent chemosensors for Cd^{2+} have not been studied until now. In the development of Cd^{2+}-selective chemosensors, the discrimination of Zn^{2+} from Cd^{2+} is often challenging because the two metal ions show similar coordination properties.[12,14]

Cyclen (1,4,7,10-tetraazacyclododecane) is one of the most extensively studied ligand because it coordinates strongly with transition metal ions, especially Zn^{2+},[15] Cd^{2+},[16] Pb^{2+},[13a,13b] Cu^{2+},[17] and Hg^{2+}.[18] Recently, few research groups have reported cyclen-linked fluorescent chemosensors for the detection of metal ions.[18,19] Over the past few years, we have utilized rhodamine B as a fluorophore because of its good photostability, high absorption coefficient, high fluorescent quantum yield, and excitation and emission within visible wavelengths.[20,21] In this study, we describe a rhodamine cyclen-based chemosensor, which displays highly selective and sensitive Cd^{2+}-amplified fluorescence in aqueous solutions. The mechanism is based on the ring-opening process of rhodamine amide derivatives. When Cd^{2+} is bound to the sensor, the colorless and non-fluorescent spirocyclic form of rhodamine amide is converted to the open form, which is pink and strongly fluorescent as shown in Scheme 1.



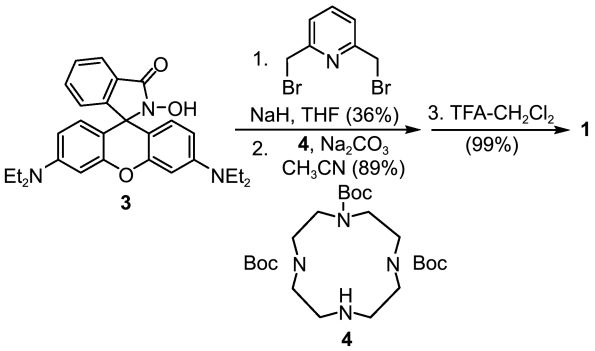
Scheme 1. Binding of Rhodamine-Cyclen Probe **1** with Cd^{2+}.

Results and Discussion

The rhodamine-cyclen probe **1** was prepared in three steps (1. 2,6-bis(bromomethyl)pyridine, NaH, THF; 2. **4**,[22] Na_2CO_3, CH_3CN; 3. TFA, CH_2Cl_2) from the known rhodamine hydroxamic acid **3**[21g] (Scheme 2). Probe **1** forms a colorless solution in PBS buffer (DMF 1%, v/v) at pH 7.4, indicating that it exists in the spirocyclic form predominantly. Upon binding with Cd^{2+}, the colorless solution gradually turned to pink, clearly implying the ring-opening process of the rhodamine spirocyclic ring in **1**. Probe **1** could monitor Cd^{2+} ions in the pH 7-10 range (see Supporting Information).

Fluorescence titration experiment of **1** (5 μM) with Cd^{2+} was conducted in PBS buffer (DMF 1%, v/v) solution at 25 °C. Upon addition of Cd^{2+}, a strong fluorescence at 575 nm was observed (Figure 1) and the fluorescence intensity is saturated after addition of 1.0 equiv of Cd^{2+} (inset), which

†This paper is dedicated to Professor Eun Lee on the occasion of his honourable retirement.



Scheme 2. Synthesis of Rhodamine-Cyclen Probe **1**.

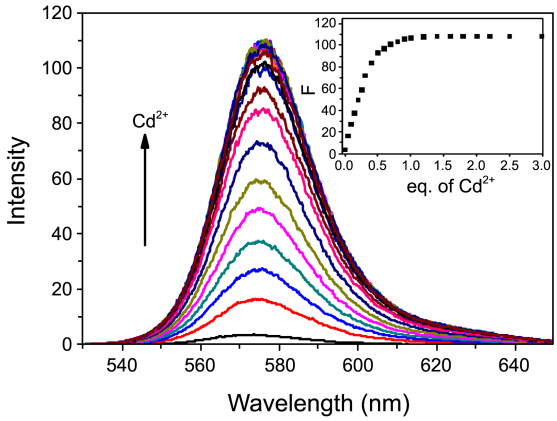


Figure 1. Fluorescence response of **1** (5 μM) upon addition of Cd^{2+} in PBS buffer (DMF 1%, v/v) at pH 7.4 (excitation at 520 nm). Inset: Plot of fluorescence intensities at 575 nm *versus* number of equivalents of Cd^{2+}.

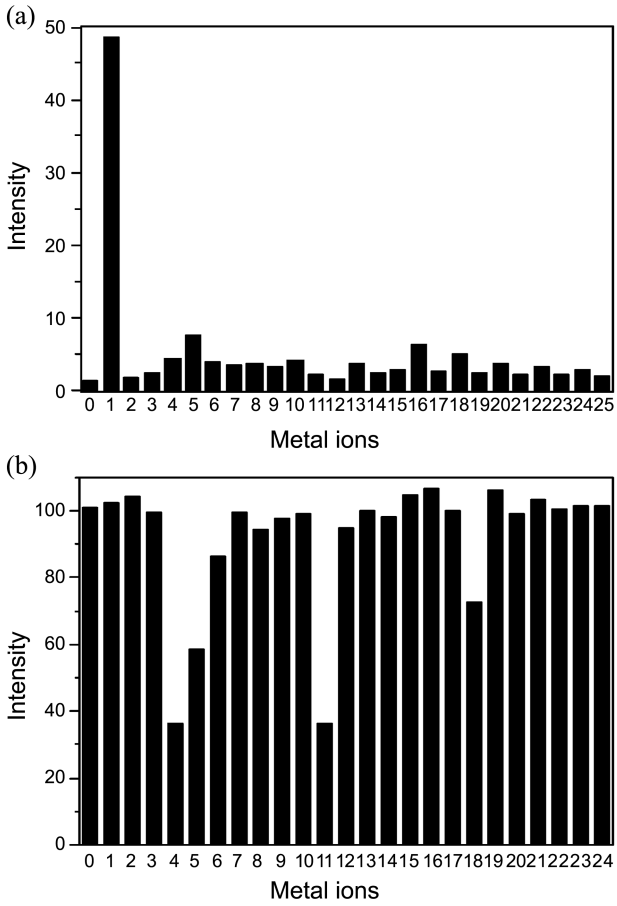


Figure 2. Fluorescence intensities of **1** (5 μM) in PBS buffer (DMF 1%, v/v) at 575 nm (excitation at 520 nm): (a) In the presence of 1.0 equiv of the following metal ions: 0, only; 1, Cd^{2+}; 2, Fe^{2+}; 3, Au^{3+}; 4, Hg^{2+}; 5, Zn^{2+}; 6, Pb^{2+}; 7, Ca^{2+}; 8, Co^{2+}; 9, Mn^{2+}; 10, Mg^{2+}; 11, Cu^{2+}; 12, Fe^{3+}; 13, Al^{3+}; 14, Cr^{3+}; 15, Au^{+}; 16, Ag^{+}; 17, Na^{+}; 18, Li^{+}; 19, Pd^{2+}; 20, Pt^{2+}; 21, Ru^{3+}; 22, Rh^{2+}; 23, Ni^{2+}; 24, K^{+}; 25, Ba^{2+}. (b) In the presence of 1.0 equiv of Cd^{2+} and 1.0 equiv the following metal ions: 0, none; 1, Fe^{3+}; 2, Fe^{2+}; 3, Au^{3+}; 4, Hg^{2+}; 5, Zn^{2+}; 6, Pb^{2+}; 7, Ca^{2+}; 8, Co^{2+}; 9, Mn^{2+}; 10, Mg^{2+}; 11, Cu^{2+}; 12, Al^{3+}; 13, Cr^{3+}; 14, Au^{+}; 15, Ag^{+}; 16, Na^{+}; 17, Li^{+}; 18, Pd^{2+}; 19, Pt^{2+}; 20, Ru^{3+}; 21, Rh^{2+}; 22, Ni^{2+}; 23, K^{+}; 24, Ba^{2+}.

implies a 1:1 stoichiometry for the coordination between **1** and Cd^{2+}. The Job's plot[23] confirms the 1:1 complex and the binding constant (K_a = 7.0 × 10^5 M^{-1})[24] calculated in PBS buffer (DMF 1%, v/v) solution from the fluorescence titration experiments based on the 1:1 binding model shows strong binding ability of **1** with Cd^{2+}. Addition of 1.0 equiv of Na_2S to a mixture of **1** and Cd^{2+} decreases fluorescence intensities of the solution and leads disappearance of the pink color (see Supporting Information). This implies the reversible binding properties of **1** with Cd^{2+} in aqueous solutions. However, other anions (5.0 equiv SH^-, CN^-, F^-) and amine ligands (5.0 equiv ethylenediamine, *N,N*-dimethyl-ethylenediamine, and EDTA disodium salt) do not cause fluorescence intensity changes, which indicates strong binding between **1** and Cd^{2+} (see Supporting Information).

Next, we tested fluorescence responses of **1** (5 μM) to other biologically and environmentally relevant metal ions in PBS buffer (DMF 1%, v/v). Upon additions of 1.0 equiv of metal ions (Cd^{2+}, Fe^{2+}, Au^{3+}, Hg^{2+}, Zn^{2+}, Pb^{2+}, Ca^{2+}, Co^{2+}, Mn^{2+}, Mg^{2+}, Cu^{2+}, Fe^{3+}, Al^{3+}, Cr^{3+}, Au^{+}, Ag^{+}, Na^{+}, Li^{+}, Pd^{2+}, Pt^{2+}, Ru^{3+}, Rh^{2+}, Ni^{2+}, K^{+}, Ba^{2+}), only Cd^{2+} leads to a dramatic enhancement in fluorescence intensity in aqueous solution. Other metal ions develop no significant fluorescence intensity changes (Figure 2(a)). The competition experiments carried out in the presence of 1.0 equiv of Cd^{2+} and 1.0 equiv of other metal ions show no interference by the presence of other metal ions except few metal ions, such as Hg^{2+}, Zn^{2+}, and Cu^{2+}, which are known to coordinate strongly with the cyclen ligand.[16c] Although these metal ions bind with the cyclen ring, they do not induce the ring opening reaction of **1**. Therefore, only Cd^{2+} leads fluorescence enhancements of **1** under the titration conditions.

The fluorescence selectivity of **1** for Cd^{2+} is well matched when **1** is employed as a colorimetric detector. While treatment of **1** (5 μM) with 1.0 equiv Cd^{2+} in PBS buffer (DMF 1%, v/v) results in clear colorless to pink-red color changes, no significant color changes are promoted by other metal ions (Figure 3). The cyclen-binding metal ions, such as Hg^{2+}, Zn^{2+}, and Cu^{2+}, do not induce color changes of **1**. This further confirms that these metal ions do not induce the ring opening reaction of **1**.

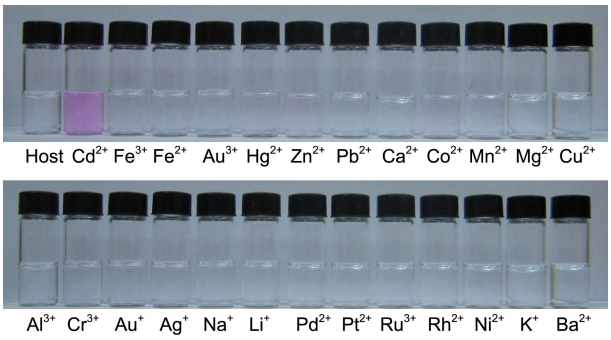


Figure 3. Color changes of **1** (5 μM) upon addition of metal ions (1.0 equiv) in PBS buffer (DMF 1%, v/v) at pH 7.4 (25 °C).

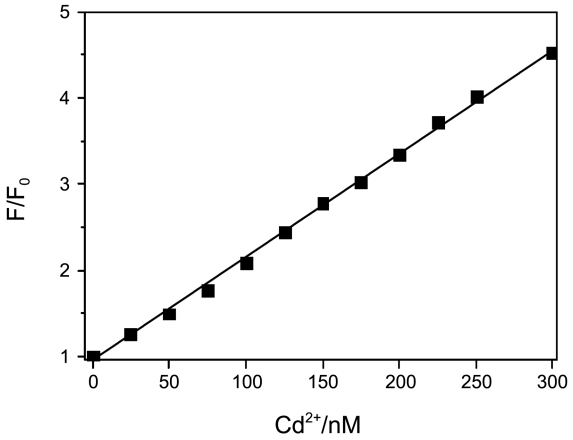


Figure 4. Fluorescence intensity changes of **1** (5 μM) upon additions of Cd^{2+} (by 25 nM) in PBS buffer (DMF 1%, v/v) at 574 nm (excitation at 520 nm).

To demonstrate the potential application of this probe, we tested the fluorescence detection limit of **1**. The fluorescence titration of probe **1** (5 μM) with Cd^{2+} in PBS buffer (DMF 1%, v/v) indicates that the detection limit of Cd^{2+} is possible at the 25 nM (about 8 ppb) level. Under these conditions, the fluorescence intensity (F/F_0) of **1** is nearly proportional to the amount of Cd^{2+} (0-300 nM), indicating that probe **1** is capable of distinguishing the toxic level of Cd^{2+} in a bottled water (~4-40 nM of Cd^{2+} is allowed according to the U.S. EPA standard).[25]

We have tested the corresponding rhodamine hydroxamates with only either a pyridine or a cyclen moiety to see the cooperative effects of the pyridine and the cyclen moiety of **1** for the selective binding with Cd^{2+} (see Supporting Information). These model compounds exert poor metal-ion selectivities and very weak binding properties with Cd^{2+}, which implies that the two binding sites (the pyridyl and the cyclen groups) of **1** bind cooperatively with Cd^{2+} to display the observed selectivity. The structure **2** in Scheme 1 shows a proposed binding complex, where all three binding groups are participating in the complexation with Cd^{2+}.

In summary, we have developed a novel fluorescent and colorimetric sensor based on a cyclen-linked rhodamine hydroxamate for the detection of Cd^{2+} in aqueous solutions. The three binding units (hydroxamate, pyridine, and cyclen sites) work cooperatively to give the observed high selectivity for Cd^{2+} in aqueous solutions. The probe could detect ~nM level of Cd^{2+} in aqueous solutions which suggests the possibility of practical applications in cadmium ion detections.

Experimental Section

General Method. THF was distilled from sodium under nitrogen immediately prior to use and CH_3CN was distilled from calcium hydride under nitrogen immediately prior to use. HPLC grade of DMF without further purification and de-ionized distilled water were used for the fluorescence experiments. All the reagents used for the fluorescence experiments were used as received. Chromatographic purifications were performed on silica gel (230-400 mesh) with the solvent systems indicated. Recorded melting points are uncorrected. NMR spectra were recorded with reference to tetramethylsilane as an internal standard. Organic extracts were dried over anhydrous $MgSO_4$.

Synthesis. The rhodamine-hydroxamic acid **3** was prepared according to the known procedure.[21g] The Boc_3-cyclen **4** was prepared according to the known procedure.[22]

Compound 1. To a solution of rhodamine-hydroxamic acid **3** (195 mg, 0.43 mmol) in THF (3 mL) was added a suspension of sodium hydride (51 mg, 1.28 mmol) in THF (1 mL) at 0 °C. After stirring for 30 min, 2,6-bis(bromomethyl) pyridine (226 mg, 0.85 mmol) in THF (1 mL) was added dropwise. The solution was warmed to room temperature and stirred for 1 hr, quenched with water (10 mL), extracted with ethyl acetate (3 × 10 mL). The collected organic layers were dried over anhydrous $MgSO_4$, concentrated *in vacuo* and the crude product was purified by column chromatography (hexanes/EtOAc = 9:1 to 1:1) to give 99 mg (0.15 mmol, 36%) of a white solid.

This white solid (80 mg, 0.12 mmol) and sodium carbonate (26 mg, 0.25 mmol) were mixed in dry acetonitrile (3 mL). Compound **4** (59 mg, 0.12 mmol) in 2 mL acetonitrile was added dropwise and the solution was refluxed for 48 hr. The reaction mixture was filtered, concentrated *in vacuo* and the crude product was purified by column chromatography (CH_2Cl_2/MeOH = 99:1 to 90:10) to give 110 mg (0.11 mmol, 89%) of the Boc-protected cyclen-rhodamine conjugate. This solid was dissolved in dichloromethane (2 mL) and TFA (2 mL) and the solution was stirred for 6 hr at room temperature. Volatiles were removed *in vacuo* and the residue was dissolved in aqueous 5% NaOH solution and extracted with CH_2Cl_2 (5 mL × 3). The collected organic layers were dried over anhydrous $MgSO_4$ and concentrated to give **1** (72 mg, 99%) as a light yellow solid: R_f = 0.1 (silica gel, CH_2Cl_2/MeOH = 9:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, J = 6.8 Hz, 1 H), 7.56−7.45 (m, 3 H), 7.22 (d, J = 6.6 Hz, 1 H), 7.10 (d, J = 7.2 Hz, 2 H), 6.55 (d, J = 8.8 Hz, 2 H), 6.39 (s, 2 H), 6.30-6.37 (m, 2 H), 4.83 (s, 2 H), 3.70 (s, 2 H), 3.33 (q, J = 7.2 Hz, 8 H), 2.78-2.72 (m, 12 H), 2.62 (s, 4 H), 1.16 (t, J = 7.0 Hz, 12 H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 164.6, 158.5, 155.4, 153.9, 150.3, 149.1, 137.3, 133.3, 129.0, 128.8, 128.6, 124.0, 123.2, 122.0, 108.2, 105.0, 97.9, 80.3,

65.6, 60.3, 52.1, 47.0, 45.9, 45.5, 44.5, 12.8; HRMS (FAB) *m/z* calcd for $C_{43}H_{56}N_8O_3$ ($M + H^+$) 733.4554; found 733.4559.

Acknowledgments. This work was supported by CBMH (Yonsei University) through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (MEST) (No. 2011-0001126).

References

1. (a) Murray, C. B.; Norris, D. J.; Bawendi, M. G. *J. Am. Chem. Soc.* **1993**, *115*, 8706. (b) Beck, F.; Rüetchi, P. *Electrochim. Acta* **2000**, *45*, 2467. (c) Satarug, S.; Baker, J. R.; Urbenjapol, S.; Haswell-Elkins, M.; Reilly, P. E. B.; Williams, D. J.; Moore, M. R. *Toxicol. Lett.* **2003**, *137*, 65. (d) Mendes, A. M. S.; Duda, G. P.; do Nascimento, C. W. A.; Silva, M. O. *Sci. Agric.* **2006**, *63*, 328.
2. Dobson, S. *Cadmium-Environmental Aspects*; World Health Organization: Geneva, 1992.
3. (a) *Cadmium in the Human Environment*: *Toxicity and Carcinogenicity*; Nordberg, G. F.; Herber, R. F. M.; Alessio, L.; Eds; Oxford University Press: Oxford, 1992. (b) Friberg, L.; Elinger, C. G.; Kjelström, T. *Cadmium*; World Health Organization: Geneva, 1992. (c) Benjamin, M. W.; Honeyman, B. D. In: Butcher, S. S.; Chalrson, R. J.; Orians, G. H.; Wolfe, G. V. Eds.; Editors *Global Biogeochemical Cycles*; Academic, London, 1992, 317. (d) Goyer, R. A.; Liu, J.; Waalkes, M. P. *Biometals* **2004**, *17*, 555. (e) Waisberg, M.; Joseph, P.; Hale, B.; Beyersmann, D. *Toxicology* **2003**, *192*, 95.
4. *Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*; Beryllium, Cadmium, Mercury, and Exposures in the Glass Manufacturing Industry; Vol. 58, International Agency for Research on Cancer: Lyon, France, 1993.
5. (a) Anthemidis, A. N.; Karapatouchas, C. P. *Microchim. Acta* **2008**, *160*, 455. (b) Kaya, G.; Yaman, M. *Talanta* **2008**, *75*, 1127.
6. Davis, A. C.; Calloway, C. P.; Jr, Jones, B. T. *Talanta* **2007**, *71*, 1144.
7. For reviews and books, see: (a) Bryan, A. J.; de Silva, A. P.; de Silva, S. A.; Rupasinghe, R. A. D. D.; Sandanayake, K. R. A. S. *Biosensors* **1989**, *4*, 169. (b) Bissell, R. A.; de Silva, A. P.; Gunaratne, H. Q. N.; Lynch, P. L. M.; Maguire, G. E. M.; Sandanayake, K. R. A. S. *Chem. Soc. Rev.* **1992**, *21*, 187. (c) Tsien, R. Y. *Am. J. Physiol.* **1992**, *263*, C723. (d) Czarnik, A. W. *Acc. Chem. Res.* **1994**, *27*, 302. (e) Fabbizzi, L.; Poggi, A. *Chem. Soc. Rev.* **1995**, *24*, 197. (f) 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. (g) Valeur, B.; Laray, I. *Coord. Chem. Rev.* **2000**, *205*, 3. (h) Rurack, K. *Spectrochim. Acta Part A* **2001**, *57*, 2161. (i) de Silva, A. P.; Fox, D. B.; Moody, T. S.; Weir, S. M. *Pure Appl. Chem.* **2001**, *73*, 503. (j) James, T. D.; Shinkai, S. *Top. Curr. Chem.* **2002**, *218*, 159. (k) Martinez-Manez, R.; Sancenon, F. *Chem. Rev.* **2003**, *103*, 4419. (l) Jiang, P.; Guo, Z. *Coord. Chem. Rev.* **2004**, *248*, 205. (m) Domaille, D. W.; Que, E. L.; Chang, C. J. *Nat. Chem. Biol.* **2008**, *3*, 168. (n) *Fluorescent Probes*; ed. Beddard, G. S.; West, M. A.; Eds.; Academic. London, 1981. (o) Haugland, R. P.; *The Handbook–A Guide to Fluorescent Probes and Labeling Technologies*, 10th ed.; Invitrogen. Eugene, OR, 2005.
8. (a) Prodi, L.; Montalti, M.; Zaccheroni, N.; Bradshaw, J. S.; Izatt, R. M.; Savage, P. B. *Tetrahedron Lett.* **2001**, *42*, 2941. (b) Tang, X.; Peng, X.-H.; Dou, W.; Mao, J.; Zheng, J.-R.; Qin, W.-W.; Liu, W.-S.; Chang, J.; Yao, X.-J. *Org. Lett.* **2008**, *10*, 3653. (c) Xue, L.; Liu, C.; Jiang, H. *Org. Lett.* **2009**, *11*, 1655. (d) Xue, L.; Liu, Q.; Jiang, H. *Org. Lett.* **2009**, *11*, 3454.
9. (a) Choi, M.; Kim, M.; Lee, K. D.; Han, K.-N.; Yoon, I.-A.; Chung, H.-J.; Yoon, J. *Org. Lett.* **2001**, *3*, 3455. (b) Gunnlaugsson, T.; Lee, T. C.; Parkesh, R. *Org. Lett.* **2003**, *5*, 4065. (c) Gunnlaugsson, T.; Lee, T. C.; Parkesh, R. *Tetrahedron* **2004**, *60*, 11239.
10. (a) Peng, X.; Du, J.; Fan, J.; Wang, J.; Wu, Y.; Zhao, J.; Sun, S.; Xu, T. *J. Am. Chem. Soc.* **2007**, *129*, 1500. (b) Cheng, T.; Xu, Y.; Zhang, S.; Zhu, W.; Qian, X.; Duan, L. *J. Am. Chem. Soc.* **2008**, *130*, 16160.
11. Liu, W.; Xu, L.; Sheng, R.; Wang, P.; Li, H.; Wu, S. *Org. Lett.* **2007**, *9*, 3829.
12. Taki, M.; Desaki, M.; Ojida, A.; Iyoshi, S.; Hirayama, T.; Hamachi, I.; Yamamoto, Y. *J. Am. Chem. Soc.* **2008**, *130*, 12564.
13. (a) Lu, C.; Xu, Z.; Cui, J.; Zhang, R.; Qian, X. *J. Org. Chem.* **2007**, *72*, 3554. (b) Saleh, N.; Rawashdeh, A.-M. M.; Yousef, Y. A.; Al-Soud, Y. A. *Spectrochim. Acta Part A* **2007**, *68*, 728. (c) Luo, H.-Y.; Jiang, J.-H.; Zhang, X.-B.; Li, C.-Y.; Shen, G.-L.; Yu. R.-Q. *Talanta* **2007**, *72*, 575. (d) Zhou, Y.; Xiao, Y.; Qian, X. *Tetrahedron Lett.* **2008**, *49*, 3380. (e) Lee, H. N.; Kim, H. N.; Swamy, K. M. K.; Park, M. S.; Kim, J.; Lee, H.; Lee, K.-H.; Park, S.; Yoon, J. *Tetrahedron Lett.* **2008**, *49*, 1261.
14. (a) Akkaya, E. U.; Huston, M. E.; Czarnik, A. W. *J. Am. Chem. Soc.* **1990**, *112*, 3590. (b) Huston, M. E.; Engleman, C.; Czarnik, A. W. *J. Am. Chem. Soc.* **1990**, *112*, 7054. (c) Dakternieks, D. *Coord. Chem. Rev.* **1990**, *98*, 279. (d) Lim, N. C.; Yao, L.; Freake, H. C.; Brückner, C. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 2251. (e) Hanaoka, K.; Kikuchi, K.; Kojima, H.; Urano, Y.; Nagano, T. *J. Am. Chem. Soc.* **2004**, *126*, 12470. (f) Nolan, E. M.; Ryu, J. W.; Jaworski, J.; Feazell, R. P.; Sheng, M.; Lippard, S. J. *J. Am. Chem. Soc.* **2006**, *128*, 15517. (g) Zhang, L.; Clark, R. J.; Zhu, L. *Chem. Eur. J.* **2008**, *14*, 2894. (h) Yunus, S.; Charles, S.; Dubois, F.; Vander Donckt, E. *J. Fluoresc.* **2008**, *18*, 499.
15. (a) Koike, T.; Watanabe, T.; Aoki, S.; Kimura, E.; Shiro, M. *J. Am. Chem. Soc.* **1998**, *118*, 12696. (b) Kimura, E.; Koike, T. *Chem. Commun.* **1998**, 1495. (c) Aoki, S.; Kawatani, H.; Goto, T.; Kimura, E.; Shiro, M. *J. Am. Chem. Soc.* **2001**, *123*, 1123. (d) Aoki, S.; Kaido, S.; Fujioka, H.; Kimura, E. *Inorg. Chem.* **2003**, *42*, 1023. (e) Aoki, S.; Kagata, D.; Shiro, M.; Takeda, K.; Kimura, E. *J. Am. Chem. Soc.* **2004**, *126*, 13377. (f) Aoki, S.; Kimura, E. *Chem. Rev.* **2004**, *104*, 769. (g) Shiraishi, Y.; Kohno, Y.; Hirai, T. *Ind. Eng. Chem. Res.* **2005**, *44*, 847. (h) Aoki, S.; Sakurama, K.; Matsuo, N.; Yamada, Y.; Takasawa, R.; Tanuma, S.-i.; Shiro, M.; Takeda, K.; Kimura, E. *Chem. Eur. J.* **2006**, *12*, 9066. (i) Majzoub, A. E.; Cadiou, C.; Déchamps-Oliver, I.; Chuburu, F.; Aplincourt, M. *Eur. J. Inorg. Chem.* **2007**, 5087. (j) Aoki, S.; Sakurama, K.; Ohshima, R.; Matsuo, N.; Yamada, Y.; Takasawa, R.; Tanuma, S.-i.; Takeda, K.; Kimura, E. *Inorg. Chem.* **2008**, *47*, 2747. (k) Zeng, Z.; Spiccia, L. *Chem. Eur. J.* **2009**, *15*, 12941.
16. (a) Kodama, M.; Kimura, E. *J. Chem. Soc. Dalton Trans.* **1977**, 2269. (b) Amorim, M. T. S.; Chaves, S.; Delgado, R.; Frausto, J. J. R. J. *Chem. Soc. Dalton Trans.* **1991**, 3065. (c) Mizukami, S.; Nagano, T.; Urano, Y.; Odani, A.; Kikuchi, K. *J. Am. Chem. Soc.* **2002**, *124*, 3920.
17. Wu, Q.; Anslyn, E. V. *J. Am. Chem. Soc.* **2004**, *126*, 14682.
18. Shiraishi, Y.; Sumiya, S.; Kohno, Y.; Hirai, T. *J. Org. Chem.* **2008**, *73*, 8571.
19. Shinoda, S.; Okazaki, T.; Player, T. N.; Misaki, H.; Hori, K.; Tsukube, H. *J. Org. Chem.* **2005**, *70*, 1835.
20. (a) Lakowicz, J. R. *Principles of Fluorescence Spectroscopy*, 3rd ed.; Springer: New York, 2006; pp 67-69. (b) Ramette, R. W.; Sandell, E. B. *J. Am. Chem. Soc.* **1956**, *78*, 4872. (c) Valdes-Aguilera, O.; Neckers, D. C. *Acc. Chem. Res.* **1989**, *22*, 171. (d) Dujols, V.; Ford, F.; Czarnik, A. W. *J. Am. Chem. Soc.* **1997**, *119*, 7386.
21. (a) Yang, Y.-K.; Yook, K.-J.; Tae, J. *J. Am. Chem. Soc.* **2005**, *127*, 16760. (b) Ko, S.-K.; Yang, Y.-K.; Tae, J.; Shin, I. *J. Am. Chem. Soc.* **2006**, *128*, 14150. (c) Yang, Y.-K.; Ko, S.-K.; Shin, I.; Tae, J. *Nat. Protoc.* **2007**, *2*, 1740. (d) Bae, S.; Tae, J. *Tetrahedron Lett.* **2007**, *48*, 5389. (e) Yang, Y.-K.; Lee, S.; Tae, J. *Org. Lett.* **2009**, *11*, 5610. (f) Yang, Y.-K.; Ko, S.-K.; Shin, I.; Tae, J. *Org. Biomol. Chem.* **2009**, *7*, 4590. (g) Yang, Y.-K.; Cho, H. J.; Lee, J.; Shin, I.;

Tae, J. *Org. Lett.* **2009**, *11*, 859. (h) Kang, S.; Kim, S.; Yang, Y.-K.; Bae, S.; Tae, J. *Tetrahedron Lett.* **2009**, *50*, 2010. (i) Moon, K.-S.; Yang, Y.-K.; Ji, S.; Tae, J. *Tetrahedron Lett.* **2010**, *51*, 3290. (j) Yang, Y.-K.; Shim, S.; Tae, J. *Chem. Commun*. **2010**, *46*, 7766.
22. (a) Benniston, A. C.; Gunning, P.; Peacock, R. D. *J. Org. Chem*. **2005**, *70*, 115. (b) Kimura, E.; Aoki, S.; Koike, T.; Shiro, M. *J. Am. Chem. Soc*. **1997**, *119*, 3068.
23. Vosburgh, W. C.; Cooper, G. R. *J. Am. Chem. Soc.* **1941**, *63*, 437.
24. Connors, K. A. *Binding Constants-The Measurement of Molecular Complex Stability*; John Wiley & Sons: New York, 1987; Chapter 4.
25. Liu, Z.; Zhang, C.; He, W.; Yang, Z.; Gao, X.; Guo, Z. *Chem. Commun*. **2010**, *46*, 6138.