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Anthracene derivatives bearing sulfur atoms or selenium atoms as fluorescent chemosensors for Cu^{2+} and Hg^{2+}: different selectivity induced from ligand immobilization onto anthracene

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Abstract—Two new selenium containing anthracene derivatives and two new sulfur containing anthracene derivatives were synthesized as fluorescent chemosensors for Hg^{2+} and Cu^{2+}. Compound **1** displayed a highly selective chelation enhanced fluorescence quenching (CHEQ) effect only with Cu^{2+}, on the other hand, compounds **3** and **4** displayed highly selective chelation enhanced fluorescence (CHEF) effects only with Hg^{2+} among the metal ions examined.

1. Introduction

Fluoroionophores chemically communicate ion concentrations and are the subjects of substantial investigation for metal ion analysis.[1] The advent of ligand engineering has introduced a more systematic approach to the design of chemosensors with new selectivities and signal transduction schemes. Selenacrown[2] or selenium containing cyclophane[3] have been studied actively by various groups due to the large covalent radius and greater polarizability of selenium compared to oxygen, nitrogen and sulfur, which could influence the conformational as well as complexation properties of these compounds. Another reason can be the accessibility of ^{77}Se NMR for the investigation of structural properties of selenium containing compounds. Selenium containing hosts have been reported to display strong affinities with Hg^{2+} or Ag^{+}.[3e,4] Recently, a calix[4](diseleno)crown ether[4] as well as organoselenium-bridged bis(β-cyclodextrin)s[5] have been also reported. However, as far as we are aware, there has not been any report regarding a fluorescent chemosensor containing selenium atoms as a binding site for metal ions.

We report herein two new selenium containing anthracene derivatives and two new sulfur containing anthracene derivatives as fluorescent chemosensors for Hg^{2+} and Cu^{2+}. Four different host compounds **1–4** have been synthesized to compare the binding affinities of sulfur containing ligand and selenium ligand towards various metal ions. Compound **1** displayed a highly selective chelation enhanced fluorescence quenching (CHEQ) effect only with Cu^{2+}, on the other hand, compounds **3** and **4** displayed highly selective chelation enhanced fluorescence (CHEF) effects only with Hg^{2+} among the metal ions examined. Especially, compounds **1** and **2**, 9,10-isomer and 1,8-isomer, respectively, showed quite different emission patterns and selectivity towards metal ions; a large CHEQ effect was observed with $\mathbf{1}\cdot Cu^{2+}$, on the other hand, a large CHEF effect along with a red shift (∼40 nm) was observed in the case of $\mathbf{2}\cdot Cu^{2+}$. We observed high selectivity for compound **1** with Cu^{2+}, which is relatively a simple host compound. Furthermore, 1,8-isomer (**2**) containing same ligand displayed quite different binding selectivity towards metal ions.

2. Results and discussion

1,8-Bis(bromomethyl)anthracene (**6**) was first synthesized following the procedures of Gunnlaugsson[6] and Nakagawa.[7] Treatment of compounds **5** and **6** with K_2CO_3 and ethanethiol in chloroform led to 9,10-bis(ethylthiamethyl)anthracene (**1**) and 1,8-bis(ethylthiamethyl)anthracene (**2**) in 83% and 72% yield, respectively, after purification by flash chromatography using ethyl acetate/hexane (1:2) (Scheme 1). For the synthesis of 1,8-diselenanthracenometacyclophane (**3**) and 1,8-diselenanthraceno-2,6-pyridinophane (**4**), 2,6-bis(selenocyanatomethyl)benzene (**7**) and 2,6-bis(selenocyanatomethyl)pyridine (**8**) were synthesized following the published procedure.[3c,d] Either compound **7** or **8** was reacted with 9,10-bis(bromomethyl)anthracene (**5**) and sodium

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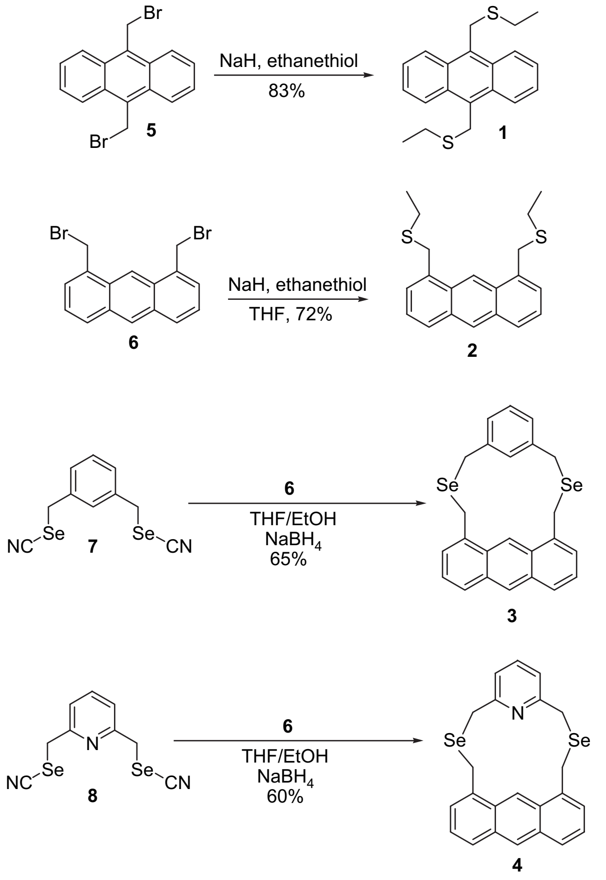
borohydride in THF/ethanol (4:1, v/v) to give compound **3** or **4**, respectively, as yellow crystalline compound after recrystallization from chloroform.



Scheme 1. Syntheses of compounds **1**, **2**, **3** and **4**.

Ag^+, Ca^{2+}, Cd^{2+}, Co^{2+}, Cs^+, Cu^{2+}, K^+, Li^+, Hg^{2+}, Mg^{2+}, Mn^{2+}, Na^+, Ni^{2+}, Pb^{2+} and Zn^{2+} ions were used to evaluate the metal ion binding properties of compounds **1**, **2**, **3** and **4** in acetonitrile/chloroform (4:1, v/v). Using these metal ions (100 equiv), compound **1** (6 μM) displayed a CHEQ effect only with Cu^{2+} (Fig. 1). As the amounts of Cu^{2+} were increased, the fluorescent intensities (Fig. 2) as well as UV absorptions (Fig. 3) of compound **1** were consequently decreased. These observations of UV along with fluorescent data support the fact that there is an additional π–Cu^{2+} interaction in the case of 9,10-isomer (**1**). Similar interaction between the silver ion and the anthracene moiety was reported by our group[8] and Desvergne group.[9] Therefore, compound **1** may provide three potential binding sites, namely two sulfur atoms and an additional π–cation interaction. From the fluorescent titrations (Fig. 2), the association constant for Cu^{2+} was calculated as 238 000 M^{-1}.[10] An overall emission change of 100-fold was observed for Cu^{2+}. Thia-anthracene derivative bearing $SCH_2CH_2CH_2S$ spacer at the 9,10-positions of anthracene was reported by Ostaszewski et al.,[11] which was reported to display a selective fluorescence change with Ag^+. The selectivity of compound **1** with Cu^{2+} can be productively compared with that of the compound reported by Ostaszewski.

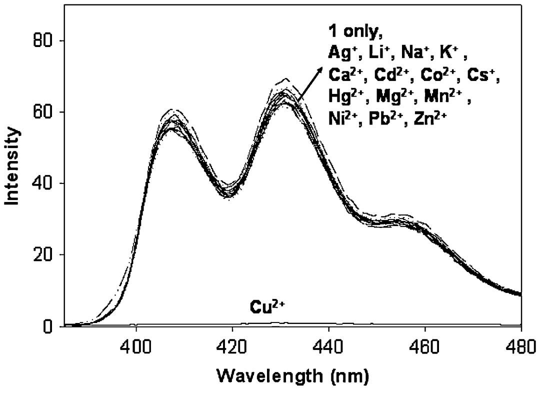


Figure 1. Changes in the fluorescence emission spectra of compound **1** (6 μM) upon the addition of 100 equiv of metal ions in $CH_3CN/CHCl_3$ (4:1, v/v) (excitation at 379 nm, excitation and emission slit width=1.5 nm).

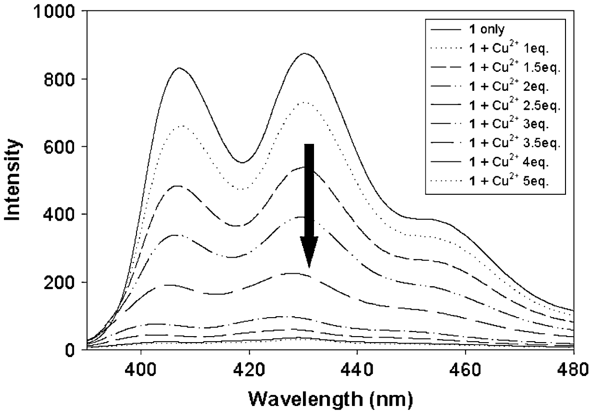


Figure 2. Fluorescent titrations of compound **1** (1 μM) with Cu^{2+} in $CH_3CN/CHCl_3$ (4:1, v/v). (excitation at 379 nm, excitation and emission slit width=5 nm).

On the other hand, 1,8-isomer (**2**) (6 μM) showed CHEF effects with Cu^{2+}, Hg^{2+} and Ag^+ among the metal ions examined (Fig. 4). In the absence of metal ions, compound **2** displayed its maximum intensity at 417 nm. Upon the addition of these metal ions, significant red shifts (Cu^{2+}, 40 nm; Hg^{2+}, 13 nm; Ag^+, 17 nm) were observed in their fluorescent spectra. Unlike 9,10-isomer (**1**), 1,8-isomer (**2**) displayed a similar red shift (367–390 nm) in its UV spectra upon the addition of Cu^{2+}. The red shift of fluorescence emission

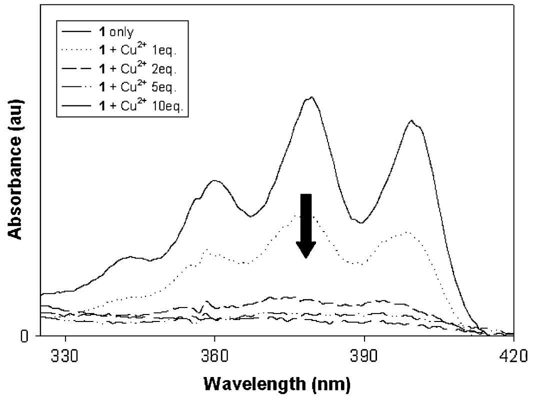


Figure 3. Changes in the UV absorption spectra of compound **1** (20 μM) upon the addition of Cu^{2+} in $CH_3CN/CHCl_3$ (4:1, v/v).

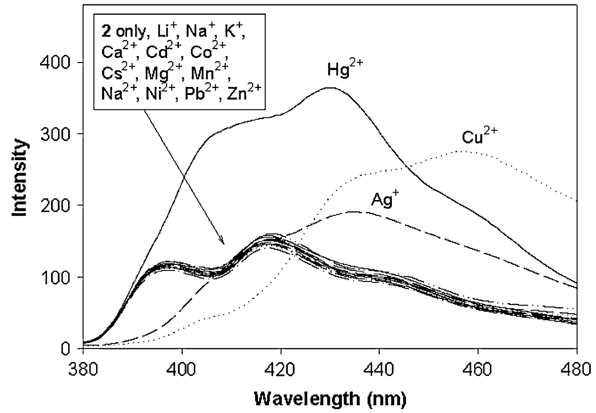


Figure 4. Changes in the fluorescence emission spectra of compound **2** (6 μM) upon the addition of 100 equiv of metal ions in $CH_3CN/CHCl_3$ (4:1, v/v) (excitation at 368 nm, excitation and emission slit width=5 nm).

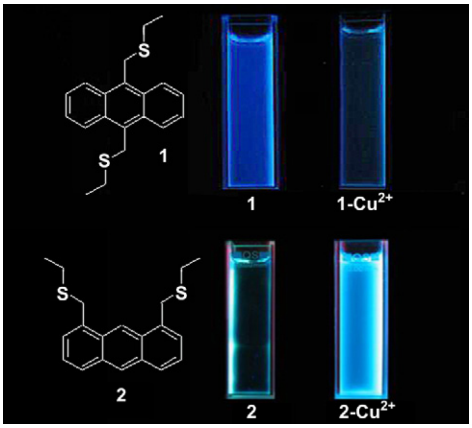


Figure 6. Changes in the fluorescence compounds **1** and **2** (10 μM) upon the addition of 50 equiv of $Cu(ClO_4)_2$ in $CH_3CN/CHCl_3$ (4:1, v/v).

is closely related to the red shift of absorption peak upon the addition of Cu^{2+} ion because the less excitation energy will induce the less emission energy.

As shown in Figure 4, there was a unique change in the emission spectrum upon the addition of Cu^{2+}. A new red-shifted peak at 457 nm was observed and ratiometric changes were observed as the amount of Cu^{2+} was increased. A ratiometric sensor allows a calibration curve, which is independent of the sample condition e.g. the concentration of the sensor, etc. Furthermore, ratiometric fluorescence measurements can increase the selectivity and the sensitivity of the detection. The addition of Ag^+ caused similar changes in the fluorescent emission spectra of compound **2**; the λ_{max} at 417 moved to 434 nm upon the addition of Ag^+. The job plots indicate 1:1 binding between these hosts and Hg^{2+} (S-Figure 1). From the fluorescent titrations, the association constants for Cu^{2+} (Fig. 5), Ag^+ and Hg^{2+} were calculated as 146 000, 71 200 and 24 000 M^{-1}, respectively.[10]

Figure 6 explains the opposite fluorescence changes of compounds **1** and **2** upon the addition of Cu^{2+}. These results explain that relatively simple hosts, such as compounds **1** and **2**, can display effective selectivity towards metal ions. Even though there have been many reports regarding fluorescent chemosensors for Cu^{2+}, relatively few examples are available as OFF–ON type sensors or ratiometric sensors for Cu^{2+}.[12]

On the other hand, compounds **3** and **4** displayed highly selective CHEF effects with Hg^{2+} among the metal ions examined (Figs. 7 and 8). The association constants were

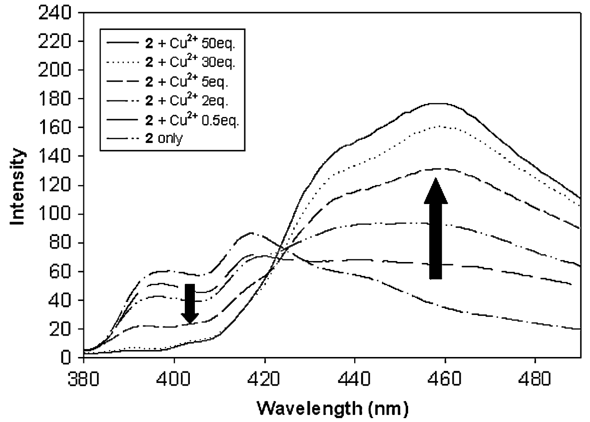


Figure 5. Fluorescent titrations of compound **2** (3 μM) with Cu^{2+} in $CH_3CN/CHCl_3$ (4:1, v/v). (excitation at 368 nm, excitation and emission slit width=5 nm).

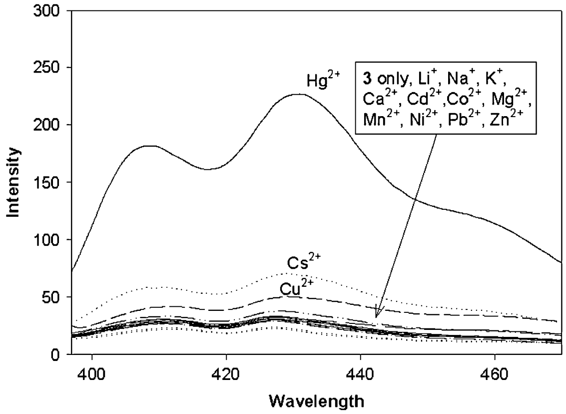


Figure 7. Changes in the fluorescence emission spectra of compound **3** (6 μM) upon the addition of 100 equiv of metal ions in $CH_3CN/CHCl_3$ (4:1, v/v) (excitation at 377 nm, excitation and emission slit width=5 nm).

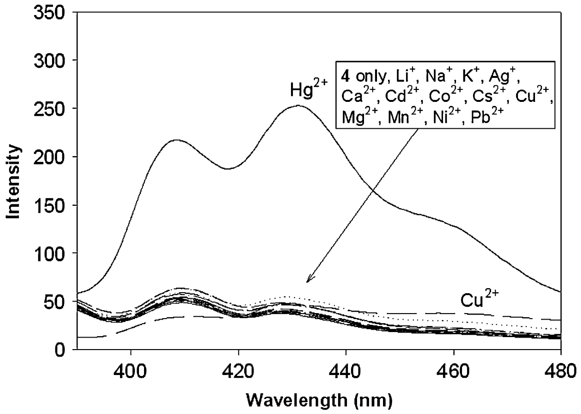


Figure 8. Changes in the fluorescence emission spectra of compound **4** (6 μM) upon the addition of 100 equiv of metal ions in $CH_3CN/CHCl_3$ (4:1, v/v) (excitation at 377 nm, excitation and emission slit width=5 nm).

calculated as 36 000 and 44 000 M^{-1}, respectively.[10] The job plots indicate 1:1 binding between host compounds **3** and **4** and Hg^{2+} (S-Figure 1). Even though pyridine moiety contains additional nitrogen for the binding with Hg^{2+}, the association constants turned out to be very similar.

3. Conclusion

In conclusion, two new selenium containing anthracene derivatives (**3**, **4**) and two new sulfur containing anthracene derivatives (**1**, **2**) were synthesized as fluorescent chemosensors for metal ions. Compound **1**, which contains three potential binding sites, two sulfur atoms and an additional π–cation interaction, displayed a selective fluorescent quenching effect with Cu^{2+}. On the other hand, the 1,8-isomer (**2**) displayed a unique red-shifted and enhanced fluorescent effects upon the addition of Cu^{2+}. Compounds **3** and **4** displayed a highly selective CHEF effect with Hg^{2+} among the metal ions examined. It is worth noting that the anthracene moiety in these hosts acts not only as a fluorescent source but also as a template for introducing the binding selectivity.

4. Experimental

4.1. General methods

Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. Flash chromatography was carried out on silica gel 60 (230–400 mesh ASTM; Merck). Thin layer chromatography (TLC) was carried out using Merck 60 F_{254} plates with a thickness of 0.25 mm. Preparative TLC was performed using Merck 60 F_{254} plates with the thickness of 1 mm.

Melting points were measured using a Büchi 530 melting point apparatus. ^1H NMR and ^{13}C NMR spectra were recorded using Bruker 250 MHz or Varian 500 MHz. Chemical shifts were given in parts per million and coupling constants (J) in Hertz. UV absorption spectra were obtained on UVIKON 933 Double Beam UV–vis Spectrometer. Fluorescence emission spectra were obtained using RF-5301/PC Spectrofluorophotometer (Shimadzu).

4.1.1. 9,10-Bis(ethylthiamethyl)anthracene (1). *Procedure A*. To a reaction mixture of ethanethiol (62 mg, 1.0 mmol) in THF (20 mL) was added NaH (48 mg, 2.0 mmol) at 0 °C. After stirring for 20 min at 0 °C, 9,10-bis(bromomethyl)anthracene (**5**)[6] (100 mg, 0.28 mmol) was added to the reaction mixture. After additional stirring for 1 h at room temperature, the reaction mixture was poured into 50 mL of water and extracted with $CHCl_3$. The organic layer was then separated, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. Purification by flash chromatography on silica gel (2:1, hexane/ethyl acetate) afforded compound **1** (76 mg, 83%) as a yellow solid: mp 75–78 °C; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.41 (d, J=8.8 Hz, 2H), 8.35 (d, J=8.8 Hz, 2H), 7.56 (m, 4H), 4.78 (s, 4H), 2.74 (q, J=7.8 Hz, 4H), 1.40 (t, J=7.8 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 134.4, 133.4, 128.3, 127.5, 35.6, 29.9, 15.1; HRMS (FAB) m/z=326.1166 $(M+H)^+$, Calcd for $C_{20}H_{22}S_2$=326.1163. Anal. Calcd for $C_{20}H_{22}S_2$: C, 73.57; H, 6.79. Found: C, 73.44; H, 6.83.

4.1.2. 1,8-Bis(ethylthiamethyl)anthracene (2). Application of procedure A to 1,8-bis(bromomethyl)anthracene (**6**)[7] (100 mg, 0.28 mmol) afforded compound **2** (66 mg, 72%) as a yellow solid: mp 80–83 °C; ^1H NMR ($CDCl_3$, 500 MHz) δ 9.03 (s, 1H), 8.45 (s, 1H), 7.91 (d, J=4.0 Hz, 2H), 7.38 (m, 4H), 4.33 (s, 4H), 2.56 (q, J=7.3 Hz, 4H), 1.33 (t, J=7.3 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 134.5, 132.4, 129.8, 128.3, 128.2, 126.6, 125.0, 120.0, 34.6, 29.9, 14.8; HRMS (FAB) m/z=349.1062 $(M+H+Na)^+$, Calcd for $C_{20}H_{22}S_2Na$=349.1061.

4.1.3. 1,8-Diselenanthracenometacyclophane (3). *Procedure B*. 2,6-Bis(selenocyanatomethyl)benzene (**7**) (158 mg, 0.5 mmol) and 1,8-bis(bromomethyl)anthracene (**6**) (181 mg, 0.5 mmol) were each dissolved separately in a mixture of 80% freshly distilled THF and 20% absolute ethanol to a total volume of 50 mL and thoroughly degassed with Ar. They were added separately but simultaneously from two constant addition funnels over 20 h into 95 mL freshly distilled THF and 5 mL of absolute ethanol containing an excess (150 mg) of $NaBH_4$ at room temperature under Ar. The resulting solution was filtered and concentrated to dryness. The solid was treated with 100 mL of benzene. The benzene solution was evaporated to dryness to yield a yellow crystalline solid, which was recrystallized from $CHCl_3$ (152 mg, 65%): mp 196–200 °C; ^1H NMR ($CDCl_3$, 250 MHz) δ 8.37 (s, 1H), 8.30 (s, 1H), 7.92 (br s, 7.92), 7.79 (d, J=8.3 Hz, 2H), 7.44 (d, J=6.8 Hz, 2H), 7.44 (dd, J=8.4 Hz, J=6.8 Hz, 2H), 7.20 (t, hidden, 1H), 7.11 (d, partially hidden, 2H), 4.15 (s, 4H), 3.91 (s, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 141.4, 133.9, 132.2, 129.6, 129.3, 128.3 128.2, 128.0, 127.8, 125.3, 118.9, 29.0, 24.9 ($^2J_{Se-C}$=23.6 Hz); ^{77}Se NMR ($CDCl_3$, 95 MHz) δ 330.9; HRMS (FAB) m/z=467.9909 $(M+H)^+$, Calcd for $C_{24}H_{20}Se_2$=467.9900. Anal. Calcd for $C_{24}H_{20}Se_2$: C, 61.18; H, 4.32. Found: C, 60.96; H, 4.52.

4.1.4. 1,8-Diselenanthraceno-2,6-pyridinophane (4). Application of procedure B to 2,6-bis(selenocyanatomethyl)pyridine (150 mg, 0.5 mmol) and 1,8-bis(bromomethyl)anthracene (**6**) (181 mg, 0.5 mmol) gave compound **4** as a yellow crystalline solid after recrystallization from $CHCl_3$ (140 mg, 60%): mp ~250 °C, decomposed; ^1H NMR ($CDCl_3$, 250 MHz) δ 8.89 (s, 1H), 8.29 (s, 1H), 7.79 (d, J=8.4 Hz, 2H), 7.54 (t, J=7.6 Hz, 1H), 7.40 (d, J=6.6 Hz, 2H), 7.23 (dd, J=8.4 Hz, J=6.6 Hz, 2H), 7.04 (d, J=7.6 Hz, 2H), 4.40 (s, 4H), 4.05 (s, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 160.85, 137.3, 134.4, 132.3, 129.5, 128.3, 127.7, 127.2, 125.4, 121.8, 120.9, 30.4, 26.1 ($^2J_{Se-C}$=24.7 Hz); ^{77}Se NMR ($CDCl_3$, 95 MHz) δ 319.2; HRMS (EI) m/z=468.9852 $(M)^+$, Calcd for $C_{23}H_{19}NSe_2$=468.9845. Anal. Calcd for $C_{23}H_{19}NSe_2$: C, 59.11; H, 4.10; N, 3.00. Found: C, 59.13; H, 4.26; N, 2.83.

4.2. Preparation of fluorometric metal ion titration solutions

Stock solutions (1 mM) of the metal perchlorate salts (for Cd(II), chloride salt was used) were prepared using CH_3CN. Stock solutions of compound **1** or **2** (0.6 mM) were prepared in $CHCl_3$. Test solutions were prepared by placing 40 μL of the probe stock solution into a test tube, adding an appropriate aliquot of each metal stock and diluting the solution to 4 mL with $CH_3CN/CHCl_3$ to make 4:1 ratio.

For all measurements, excitation was at 379 nm (for compound **1**), 368 nm (for compound **2**) or 377 nm (for compounds **3** and **4**). Both excitation and emission slit widths were either 1.5 nm or 5 nm.

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2006.10.001.

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