ORGANIC LETTERS

2007
Vol. 9, No. 22
4515−4518

Selectively Chemodosimetric Detection of Hg(II) in Aqueous Media

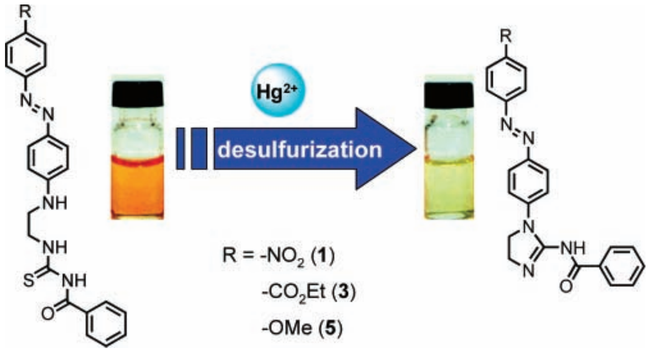
Min Hee Lee,[†] Byoung-Ki Cho,[†] Juyoung Yoon,[‡] and Jong Seung Kim*,[§]

Department of Chemistry and Institute of Nanosensor and Biotechnology, Dankook University, Seoul 140-714, Korea, Division of Nano Science and Department of Chemistry, Ewha Womans University, Seoul 120-750, Korea, and Department of Chemistry, Korea University, Seoul 136-701, Korea

jongskim@korea.ac.kr

Received August 16, 2007

ABSTRACT



A new series of benzoylthiourea derivatives of 1, 3, and 5 were prepared, and their chemodosimetric behaviors toward metal cations were investigated in aqueous media at room temperature. Among various metal cations tested, exclusively Hg^{2+} ion responses to irreversible color changes of receptors, along with distinctive blue shifts in UV/vis spectra. The receptors can be applicable for the monitoring of Hg^{2+} ion in aqueous solution with a pH span 4–9.

Development of chemosensors for heavy-transition metal ions, such as Hg^{2+}, Cu^{2+}, Pb^{2+}, and Cd^{2+} ions, has received considerable attention because the metals have an extremely toxic impact on the environment.[1] Among them, Hg^{2+} ion is considered to be highly dangerous to human beings when it is ingested or inhaled. Elemental mercury is converted into methyl mercury by microbial action on the sediments or soil. Once formed, methyl mercury can be taken up in the food chain of aquatic organisms.[2] Although, of course, all forms of mercury can bioaccumulate, methyl mercury particularly accumulates to a greater extent than other forms. Thus, its accumulation in the human body affects a wide variety of diseases even with a low concentration, such as prenatal brain damage, serious cognitive and motion disorders, and Minamata disease.[3] Therefore, in recent years, many efforts have been made to develop various chemosensors specifically for Hg^{2+} ion detection.[4−9] The most attractive approach in this field involves highly selective reactions induced by a specific metal cation. Some selective chemodosimeters for the Hg^{2+} ion have been designed to adopt mercury-promoted desulfurization, leading to an irreversible chemical event between

---

[†] Dankook University.

[‡] Ewha Womans University.

[§] Korea University.

(1) (a) Czarnik, A. W. *Fluorescent Chemosensors for Ion and Molecule Recognition*; American Chemical Society: Washington, D.C., 1993. (b) de Silva, A. P.; Fox, D. B.; Huxley, A. J. M. *Coord. Chem. Rev.* **2000**, *205*, 41. (c) 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. (d) Desvergne, J. P.; Czarnik, A. W. *Chemosensors of Ion and Molecule Recognition*; Kluwer: Dordrecht, 1997.

(2) (a) Boening, D. W. *Chemosphere* **2000**, *40*, 1335. (b) Benoit, J. M.; Fitzgerald, W. F.; Damman, A. W. *Environ. Res.* **1998**, *78*, 118. (c) Queen, H. L. *Chronic Mercury Toxicity: New Hope Against An Endemic Disease*; Queen and Company Health Communications, Inc.: Colorado Springs, 1998. (d) Renzoni, A.; Zino, F.; Franchi, E. *Environ. Res.* **1998**, *77*, 68.

(3) (a) Grandjean, P.; Weihe, P.; White, R. F.; Debes, F. *Environ. Res.* **1998**, *77*, 165. (b) Takeuchi, T.; Morikawa, N.; Matsumoto, H.; Shiraishi, Y. *Acta Neuropathol.* **1962**, *2*, 40. (c) Harada, M. *Crit. Rev. Toxicol.* **1995**, *25*, 1.

10.1021/ol7020115 CCC: $37.00

thioamide derivatives and Hg^{2+} ion.[5−9] For example, Czarnik et al. reported anthracene-containing thioamide derivative.[6] Sonnenschein et al. developed a fluorescent 1,2,4-thiadiazole derivative (oxidized form) and an iminoyl thiourea (its reduced form).[7] Chang et al. also devised an 8-hydroxyquinoline scaffold bearing benzothiazole group.[8] Interestingly, Tian et al. expoited mercury-promoted intramolecular cyclic guanylation of thiourea connected on 1,8-naphthalimide inducing UV/vis and fluorescence spectral changes, but the mostly they paid attention to the fluorescence ratiometric chemodosimeter.[9a]

Most chemodosimeters developed so far have been known to be related to their fluorescence changes upon metal ion introduction. However, chemodosimeters inducing color changes, accompanied with their UV band shifts, are very rare.[9b−e]

In this context, we have designed azo-component containing chemodosimeters responsible for the Hg^{2+} ion-induced desulfurization which involves a cyclization leading to irreversible and unique color changes. The azo unit herein is very useful because its color change is remarkably responsive to an electronic effect of the substrate species in the event of the Hg^{2+} ion-induced chemodosimetric cyclization. In this paper, we report the syntheses of chemodosimeters (**1**, **3**, and **5**) and their photochemical elucidation of their selective color changes toward Hg^{2+} ion.

Scheme 1 shows reaction pathways for **1**−**9**. In order to investigate an electronic effect on the chemodosimetric behavior, various substituents (**1**, $-NO_2$; **3**, $-CO_2Et$; **5**, $-OMe$) were introduced to the para position of the azobenzene unit. To make sure the mercury-induced desulfurization happened in this event, **2** (90% yield), **4** (93% yield), and **9** (95% yield) were isolated from the reaction of **1**, **3**, and **5** with 1 equiv (1:1 stoichiometry) of $Hg(ClO_4)_2$ in DMSO at room temperature, respectively. To obtain insight into a role of the benzoylthiourea on desulfurization reaction, reference **8** was also prepared. In the Supporting Information, there are synthetic details and all spectroscopic data for compounds **1**−**9**.

In the UV/vis spectra (see Figure S1, Supporting Information) of the receptors, we observed a solvatochroism depending on solvents such as DMSO (λ_{max} = 490 nm, red) and CH_3CN (λ_{max} = 448 nm, orange). For the studies on chemodosimetric response to metal cations, we here chose DMSO because it provides more distinctive color changes of receptors than CH_3CN does. For further application necessary to be carried out in water media, DMSO/H_2O (4:1, volume ratio) as a solvent was employed in all experiments.

Scheme 1. Synthetic Routes to **1**−**9**

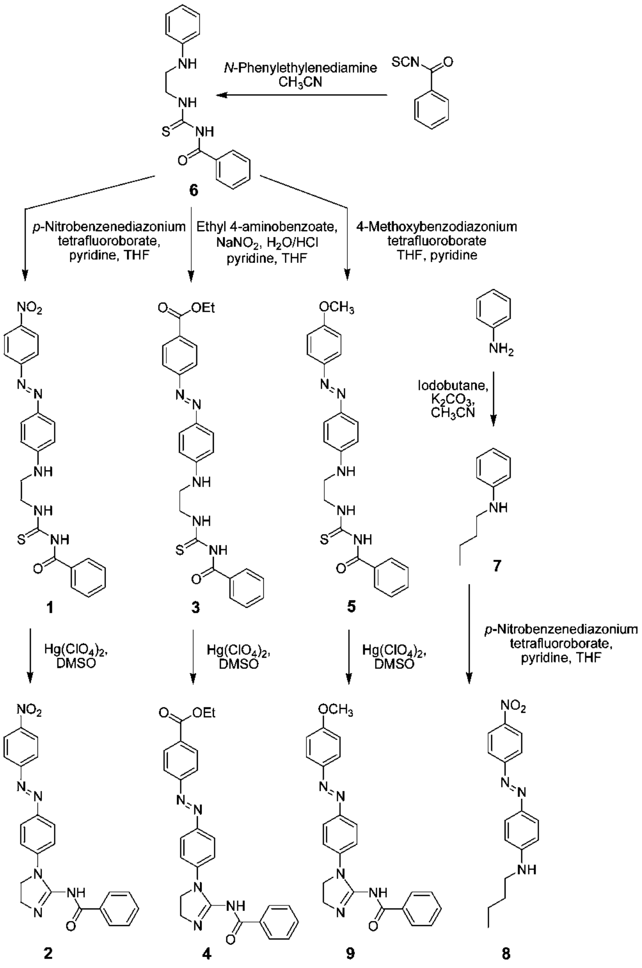


Figure 1 shows UV/vis spectral and visual color changes of **1** in aqueous solutions upon addition of 1 equiv of various

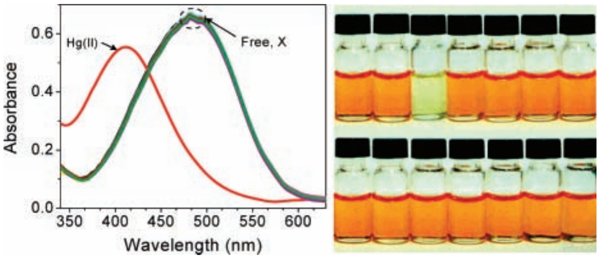


Figure 1. UV/vis spectra and photographs of **1** (20.0 μM) upon addition of ClO_4^- salts of X = Al^{3+}, Pb^{2+}, Hg^{2+}, Zn^{2+}, Cu^{2+}, Cd^{2+}, Co^{2+}, Ca^{2+}, Ba^{2+}, Sr^{2+}, Mg^{2+}, Na^+, K^+, and Cs^+ (1 equiv) in aqueous solution (DMSO/H_2O = 4:1, v/v).

---

(4) (a) Coskun, A.; Yilmaz, M. D.; Akkaya, E. U. *Org. Lett.* **2007**, *9*, 607. (b) Lee, M. H.; Wu, J.-S.; Lee, J. W.; Jung, J. H.; Kim, J. S. *Org. Lett.* **2007**, *9*, 2501. (c) Wang, J.; Qian, X. *Org. Lett.* **2006**, *8*, 3721. (d) Yoon, S.; Albers, A. E.; Wong, A.; Chang, C. J. *J. Am. Chem. Soc.* **2005**, *127*, 16030. (e) Guo, X.; Qian, X.; Jia, L. *J. Am. Chem. Soc.* **2004**, *126*, 2272. (f) Song, K. C.; Kim, J. S.; Park, S. M.; Chung, K.-C.; Ahn, S.; Chang, S.-K. *Org. Lett.* **2006**, *8*, 3413. (g) Nolan, E. M.; Lippard, S. J. *J. Am. Chem. Soc.* **2003**, *125*, 14270.

(5) (a) Manimala, J.; Anslyn, E. V. *Eur. J. Org. Chem.* **2002**, 3909. (b) Kim, K. S.; Qian, L. *Tetrahedron Lett.* **1993**, *34*, 7677. (c) Batey, R. A.; Powell, D. A. *Org. Lett.* **2000**, *2*, 3237. (d) Boeglin, D.; Cantel, S.; Heitz, A.; Martinez, J.; Fehrentz, J. A. *Org. Lett.* **2003**, *5*, 4465.

(6) Chae, M.-Y.; Czarnik, A. W. *J. Am. Chem. Soc.* **1992**, *114*, 9704.

(7) Hennrich, G.; Walther, W.; Resch-Genger, U.; Sonnenschein, H. *Inorg. Chem.* **2001**, *40*, 641.

(8) Song, K. C.; Kim, J. S.; Park, S. M.; Chung, K.-C.; Ahn, S.; Chang, S.-K. *Org. Lett.* **2006**, *8*, 3413.

(9) (a) Liu, B.; Tian, H. *Chem. Commun.* **2005**, 3156. (b) Yang, Y.-K.; Yook, K.-J.; Tae, J. *J. Am. Chem. Soc.* **2005**, *127*, 16760. (c) Ko, S.-K.; Yang, Y.-K.; Tae, J.; Shin, I. *J. Am. Chem. Soc.* **2006**, *128*, 14150. (d) Wu, J.-S.; Hwang, I.-C.; Kim, K. S.; Kim, J. S. *Org. Lett.* **2007**, *9*, 907. (e) Ros-Lis, J.; Marcos, M. D.; Martínez-Máñez, R.; Soto, J. *Angew. Chem., Int. Ed.* **2005**, *44*, 4405.

metal ions, Al^{3+}, Pb^{2+}, Hg^{2+}, Zn^{2+}, Cu^{2+}, Cd^{2+}, Co^{2+}, Ca^{2+}, Ba^{2+}, Sr^{2+}, Mg^{2+}, Na^{+}, K^{+}, and Cs^{+}. Remarkably, we observed a selective blue shift from 486 to 406 nm upon the addition of only Hg^{2+} ion, but no spectral change was detected in other metal ions. For the chemodosimetric mechanism of the blue-shift in UV/vis spectra, we envision that the addition of the thiophilic Hg^{2+} ion induces a cyclization of **1** followed by desulfurization into an imidazoline moiety which can decrease the intramolecular charge-transfer property of the azo chromophore.

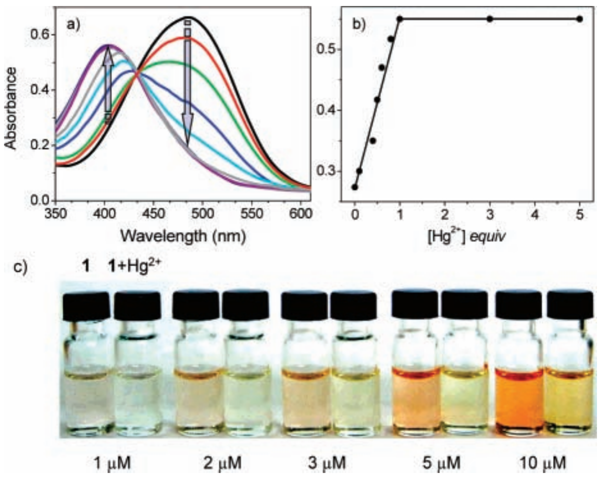


Figure 2. UV/vis titration spectra (a) of **1** (20.0 μM) and titration profile (b) at 406 nm upon addition of various amounts of $Hg(ClO_4)_2$ (0, 0.2, 0.4, 0.5, 0.6, 0.8, 1.0, 3.0, and 5.0 equiv). Color changes (c) of **1** in the presence of 1 equiv of Hg^{2+} in aqueous solution ($DMSO/H_2O$ = 4:1, v/v).

From the Hg^{2+} titration to a solution of **1** (Figure 2a), we noticed a definite ratiometry with one isosbestic point at 433 nm and an 1:1 reaction stoichiometry. To corroborate 1:1 ratio between **1** and Hg^{2+} ion, Job's plot analysis was also executed. The measured absorbance variation ($\Delta = A_{obs} - A_i$) reaches to a maximum when the molar fraction of ([**1**]/[Hg^{2+}] + [**1**]) is 0.5, confirming the 1:1 stoichiometry (Figure S2, Supporting Information).

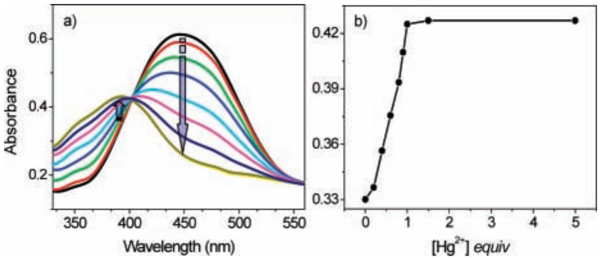


Figure 3. UV/vis titration spectra (a) of **3** (20.0 μM) and titration profile (b) at 390 nm upon addition of various amounts of $Hg(ClO_4)_2$ in aqueous solution ($DMSO/H_2O$ = 4:1, v/v).

Colorimetric detection limit of **1** for Hg^{2+} ion was also tested. In the solvent system of $DMSO/H_2O$ (4:1, v/v), the detection limit within visual color changes is allowable to 1.0 μM level of Hg^{2+} ion in 1.0 μM solution of **1** as presented in Figure 2c. In addition, the reaction responsible for these changes reaches completion within the time frame (<1 min) of these measurements.

In addition, we investigated a substituent effect on the Hg^{2+} ion-induced chemodosimetric cyclization in **1**, **3** and **5** (Figures S3 and S6, Supporting Information). In fact, **3** and **5** show similar photochemical changes to **1** upon Hg^{2+} ion introduction, but do different wavelengths from **1**. Compound **3** shows absorption spectral changes from 444 to 384 nm with one isosbestic point at 401 nm. The titration profile and Job's plot analysis indicate 1:1 stoichiometry (Figure S4, Supporting Information) between **3** and Hg^{2+} ion. The visual color changes from deep yellow to colorless in the presence of Hg^{2+} ion are also shown in Figure S3 and its detection limit in Figure S5 (Supporting Information).

Table 1. Summarized Photochemical Properties of **1**, **3**, and **5** for Hg(II) Ion, Such as Maximum Absorption Wavelength (λ_{abs}) and Absorption Coefficients (ϵ)

compd	λ_{abs} (nm)	ϵ ($M^{-1}\,cm^{-1}$)
1	486	3.3×10^4
3	444	2.9×10^4
5	412	2.9×10^4
1·Hg(II)	406	2.7×10^4
3·Hg(II)	384	2.0×10^4
5·Hg(II)	396	2.5×10^4

Table 1 summarizes photochemical features of **1**, **3**, and **5** for Hg^{2+} ion, respectively. Regarding the Hg^{2+} detection by a naked eye, **1** seems to be the best among three receptors.

To clarify a role of the benzoyl isothiocyanate unit in the receptors in the color changes, reference **8** was tested. It does not give any spectral changes upon addition of even 100 equiv of metal ions (Figure S7, Supporting Information), suggesting that the benzoylthiourea unit plays a critical role in mercury-induced desulfurization.

With respect to counteranion effects on the UV/vis spectral changes of the chemodosimeters, reactions of receptors with $HgCl_2$ were also implemented. They gave the same changes as the cases of **1**−$Hg(ClO_4)_2$ and **3**−$Hg(ClO_4)_2$, demonstrating that counteranion effect in the chemodosimeteric response is negligible (Figures S9 and S10, Supporting Information).

Figure 4 indicates competitive chemodosimetric reactions performed by using 20.0 μM of receptors and Hg^{2+} in the presence of miscellaneous cations such as Al^{3+}, Pb^{2+}, Zn^{2+}, Cu^{2+}, Cd^{2+}, Co^{2+}, Ca^{2+}, Ba^{2+}, Sr^{2+}, Mg^{2+}, Na^{+}, K^{+}, and Cs^{+} (1 equiv). The selectivity of **1** or **3** toward mercury ion is not interfered even in the presence of other various cations. This observation is quite interesting by considering that Cu^{2+} and Pb^{2+} ions can interfere with the Hg^{2+} ion selectivity to cause a serious problem in sensory application.[10] As shown in Figure 4, colorimetric chemodosimeters **1** and **3** in this

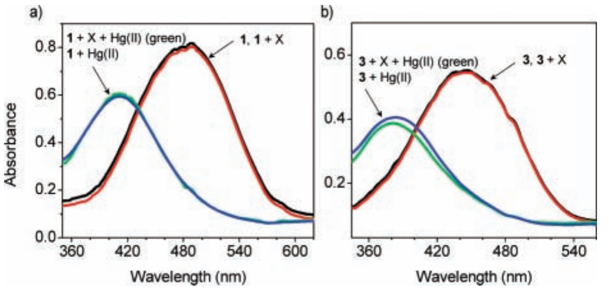


Figure 4. UV/vis spectra of (a) **1** (20.0 μM) and (b) **3** (20.0 μM) in aqueous solution (DMSO/H_2O = 4:1, v/v) in the presence of the Hg^{2+} ion (1 equiv) and miscellaneous cations (X) including Al^{3+}, Pb^{2+}, Zn^{2+}, Cu^{2+}, Cd^{2+}, Co^{2+}, Ca^{2+}, Ba^{2+}, Sr^{2+}, Mg^{2+}, Na^{+}, K^{+}, and Cs^{+} (1 equiv, respectively).

report still show a remarkable selectivity toward Hg^{2+} ion in a solution containing Cu^{2+} and Pb^{2+} ions.

Absorption intensity changes of the receptors as a function of pH in the presence and absence of Hg^{2+} ion are also noticeable (Figure 5). We found that in a solution of DMSO/water (4:1) the suitable pH span for Hg^{2+} determination is between pH 4−9. In this region, the free **1** and **3** have no response, while addition of Hg^{2+} ion can lead to a remarkable response, suggestive of efficient complexation between chemodosimeters and Hg^{2+} ion. As a result, our Hg^{2+}-selective receptors would be an ideal colorimetric chemodosimeter for monitoring Hg^{2+} in aqueous solution in the pH range of 4−9.

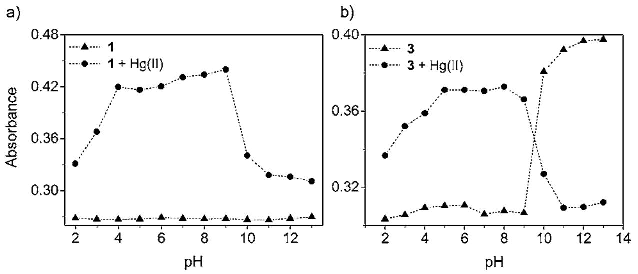


Figure 5. Variation of absorbance of **1** (20.0 μM) and **3** (20.0 μM) in aqueous solution (DMSO/H_2O = 4:1, v/v) with and without Hg^{2+} (1 equiv) ion as a function of pH: (a) λ_{abs} = 406, (b) λ_{abs} = 384 nm.

In conclusion, we here report azo-component containing chemodosimeters (**1**, **3**, and **5**) responsible for the Hg^{2+} ion-induced cyclization and desulfurization. Addition of only 1 equiv. of Hg^{2+} ion to an aqueous solution of **1**, **3**, or **5** gives an instantaneous color change along with the blue-shifted absorption band. The colorimetric chemodosimeters we have developed can be applicable for the practical usage for the monitoring of Hg^{2+} ion in aqueous solution with a pH span 4−9.

Acknowledgment. This work was supported by the SRC program (R11-2005-008-02001-0(2007)) and Basic Science Research of KOSEF (R01-2006-000-10001-0).

Supporting Information Available: Synthetic details, NMR copies, and additional spectra data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL7020115

---

(10) (a) Martinez, R.; Espinosa, A.; Tarraga, A.; Molina, P. *Org. Lett.* **2005**, *7*, 5869. (b) Kim, S. H.; Kim, J. S.; Park, S. M.; Chang, S.-K. *Org. Lett.* **2006**, *8*, 371. (c) Feng, K.; Hsu, F.-L.; Bota, K.; Bu, X. R. *Microchem. J.* **2005**, *81*, 23. (d) Yoon, J.; Ohler, N. E.; Vance, D. H.; Aumiller. W. D.; Czarnik, A. W. *Tetrahedron Lett.* **1997**, *38*, 3845.