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Highly selective and sensitive fluorescent chemosensor for Hg^{2+} in aqueous solution

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ABSTRACT

A new indole-based fluorescent chemosensor **1** was prepared and its metal ion sensing properties were investigated. It exhibits high sensitivity and selectivity toward Hg^{2+} among a series of metal ions in H_2O–EtOH (7:1, v/v). The association constant of the 1:1 complex formation for **1**-Hg^{2+} was calculated to be $9.57 \times 10^3\ M^{-1}$, and the detection limit for Hg^{2+} was found to be 2.25×10^{-5} M. Computational results revealed that **1** and Hg^{2+} ion formed with a central tetrahedron-coordinated Hg^{2+}.

Indole-based receptor systems have recently attracted attention because an inherent fluorescent property of the indole chromophore is sensitive to change in the local environment.[1–6] Such systems, including oligoindole foldamers, macrocycles, and molecular clefts, have been prepared by Jeong[7–11] and other groups.[12,4,13–15] The receptors strongly bind anions because they contain a single hydrogen bond donor group. To the best of our knowledge, few indole derivatives have been developed as potential fluorescent chemosensors for cations, such as Hg^{2+}.[16] Mercury and its derivatives are significant environmental pollutants with inherent high toxicity. Therefore, much effort has been focused on designing Hg^{2+} sensors. Although many chemosensors specific for Hg^{2+} have been developed,[17–21] most require complicated synthesis and are aqueous unsolvable. Thus, for practical applications, it is necessary to develop aqueous soluble Hg^{2+} sensors that are easily prepared, and possess selective and sensitive signaling mechanisms. Herein, we report the design of a simple and water-soluble sensor **1**[22] that is composed of two indole fluorophores and a triaminoethylene linker. The indole-based sensor **1** exhibited selectivity and sensitivity for Hg^{2+} in aqueous solution.

The indole-based sensor **1** was synthesized by a simple one step reaction of indole-3-acetic acid (IAA) with triaminoethylene, as shown in Scheme 1. The cation screening studies for receptor **1** were established from changes in the sensor's fluorescence spectra.

The cation binding and sensing properties of **1** were investigated by UV–vis absorption and fluorescence changes upon addition of various cations in aqueous solution (H_2O: EtOH = 7:1, v/v) (Fig. 1). After addition of 10 equiv of the following 12 metal ions: Li^+, Na^+, K^+, Ca^{2+}, Mg^{2+}, Hg^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Pb^{2+}, Cd^{2+}, and Zn^{2+}, there was no meaningful absorbance change in the UV–vis spectrum. However, the fluorescence intensity of **1** was strongly quenched only in the presence of the Hg^{2+} ion. Other ions did not cause any significant changes under identical conditions. The observed quenching efficiency ($(I-I_0)/I_0 \times 100\%$) at 358 nm was nearly 100% (Fig. 2) and the other metal ions caused small enhancements in fluorescence intensity. To further investigate the chemosensor properties of **1**, we performed fluorescence titrations of **1** (74.0 μM) in the presence of different concentrations of Hg^{2+} in H_2O: EtOH (7:1, v/v). Figure 3 shows the gradual reductions in fluorescence intensity for **1** upon the addition of increasing concentrations of Hg^{2+}. From the fluorescence titration profiles, the association constant for **1**-Hg^{2+} in H_2O: EtOH (7:1, v/v) solution was $9.57 \times 10^3\ M^{-1}$, according to the Stern-Volmer plot.

Furthermore, it was found that **1** had a detection limit of 2.25×10^{-5} M for Hg^{2+}. The detection limit was sufficiently low to detect submillimolar concentrations of Hg^{2+}, which is the range found in many chemical and biological systems. In order to determine the stoichiometry of the **1**-Hg^{2+} complex, the Job's method was used. In the Job's plot (Fig. 4), a maximum fluorescence change was observed with a 0.5 M fraction of ionophore to Hg^{2+} for **1**, which indicated that only a 1:1 complex was formed.

To test the practical applicability of **1** as a Hg^{2+} selective fluorescence chemosensor, competition experiments (Fig. 5) were carried out. We found that the fluorescence intensity of **1** in the presence of 10 equiv of Hg^{2+} was unaffected by the addition of 10 equiv of

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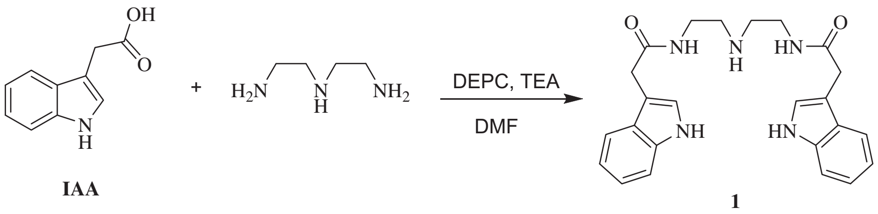


Scheme 1. Synthesis of chemosensor **1**.

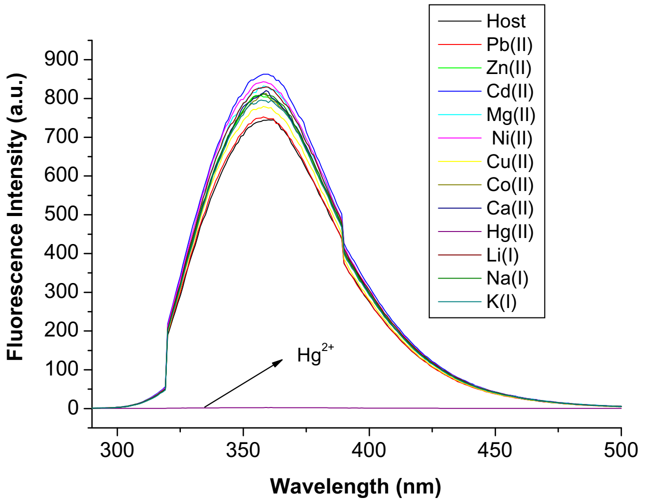


Figure 1. Fluorescent spectra of **1** (94.5 μM) upon the addition of Li^+, Na^+, K^+, Ca^{2+}, Mg^{2+}, Hg^{2+}, Co^{2+}, Ni^{2+}, Zn^{2+}, Cu^{2+}, Cd^{2+}, and Pb^{2+} (10 equiv) in H_2O: EtOH (7/1, v/v) (excitation at 279 nm).

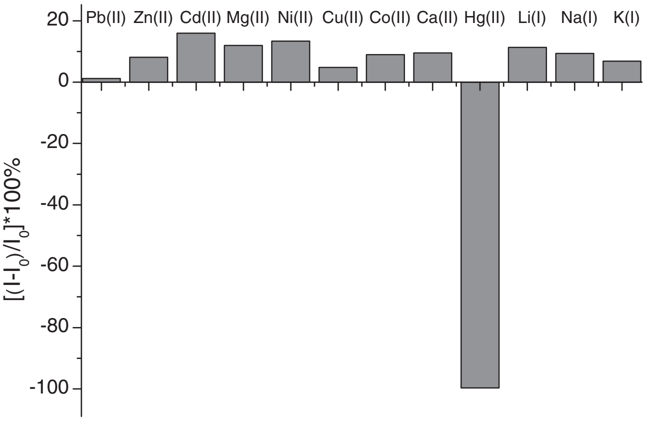


Figure 2. Fluorescence intensity changes ($(I-I_0)/I_0 \times 100\%$) of **1** (94.5 μM) upon the addition of Li^+, Na^+, K^+, Ca^{2+}, Mg^{2+}, Hg^{2+}, Co^{2+}, Ni^{2+}, Zn^{2+}, Cu^{2+}, Cd^{2+}, and Pb^{2+} (10 equiv) in H_2O:EtOH (7/1, v/v) (excitation at 279 nm).

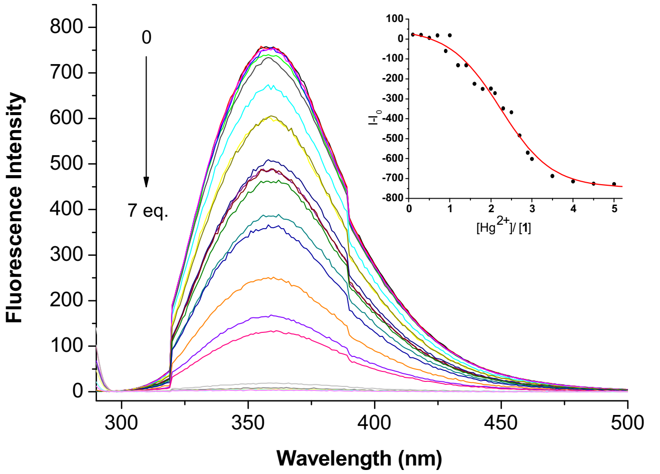


Figure 3. Fluorescence spectra of **1** (74.0 μM) in the presence of different concentrations of the Hg^{2+} ion in H_2O:EtOH (7/1, v/v) with an excitation at 279 nm.

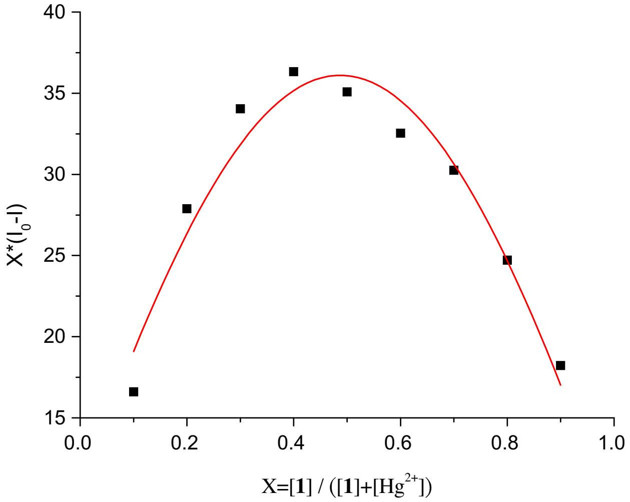


Figure 4. Job plot of **1** with $Hg(ClO_4)_2$ in H_2O: EtOH (7/1, v/v).

competing metal ions (Li^+, Na^+, K^+, Ca^{2+}, Mg^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Pb^{2+}, Cd^{2+}, or Zn^{2+}). The results suggested that **1** could potentially be used as a Hg^{2+} selective fluorescent chemosensor. The coordination behavior of **1** with Hg^{2+} was corroborated by ^1H NMR titration experiments carried out in DMSO. It was found that NH signals underwent continuous upfield shifts with increasing Hg^{2+} concentration from 0 to 2.0 equiv (Fig. 6). These observations further revealed that the NH of **1** establishes H-bond interaction with Hg^{2+}. Indole has a hydrogen bond donor group that could play a role as an anion binding motif. Therefore, in addition to the cation binding properties, we have also investigated the sensing properties of **1** for anions (F^-, Cl^-, Br^-, I^-, HSO_4^{-1}, NO_3^{-1}, and $H_2PO_4^{-1}$) using tetrabutylammonium as a counteraction in H_2O: EtOH (7:1, v/v) solution. The fluorescence intensities of the spectra of **1** did not show any changes upon addition of the above anions, probably because the conformation of the indole derivative **1** was not suitable for the recognition of these anions.

To further investigate the Hg^{2+} accurate coordinating mode of the **1**-Hg^{2+} complex, computation for **1**-Hg^{2+} was conducted at the B3LYP/LanL2DZ theory level with a Gaussian 03 package. On the basis of these calculations, we found four stationary points that could be verified as genuine minima via vibrational frequency analyses. The optimized structure for the most stable isomer of

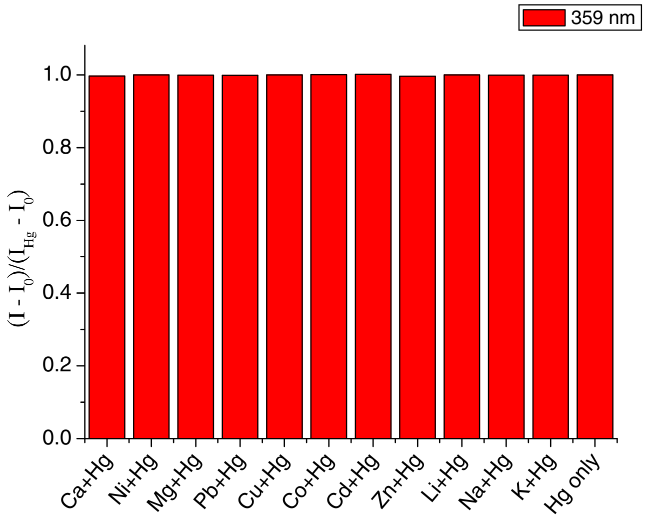


Figure 5. Competitive experiments in the **1**+Hg^{2+} system with interfering metal ions. [**1**] = 4.2×10^{-6} M, [Hg^{2+}] = 4.2×10^{-5} M, and [M^{n+}] = 4.2×10^{-5} M in H_2O:EtOH (7/1, v/v). λ_{ex} = 279 nm.

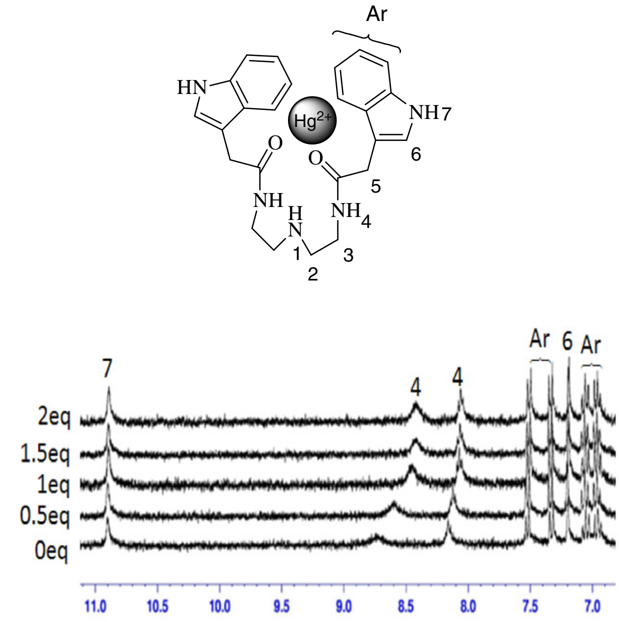


Figure 6. ^{1}H NMR spectra of **1** (4.1 mM) in the presence of 0–2.0 equiv of $Hg(ClO_4)_2$ in DMSO-d_6.

1-Hg^{2+} is illustrated in Figure 7. It is clear that the Hg^{2+} occupied the coordination center of **1**, surrounded by two carbonyl groups and two anti-parallel indole rings. The average of the two bond lengths of Hg–O$=_{\mathrm{C}}$ was estimated at 2.43 Å and the lengths of those for Hg–C of the indole ring in **1**-Hg^{2+} were 2.47 Å and 2.46 Å, respectively. These results indicated that a tetrahedron Hg^{2+} center was nearly formed, where all the neighboring ligands (i.e., two carbonyl oxygen atoms and two indole rings) were involved in binding with Hg^{2+}, and the triaminoethylene linker spacer acted as a scaffold to bring these functional ligands into a suitable geometry.

In order to clarify the linker effect in a different site of **1,** an analogue **2** was synthesized and tested. From the screening experiments, we found that **2** exhibited the same binding behavior with the Hg^{2+} ion as that of **1**. Similarly, sensor **2** showed significant fluorescence quenching in the presence of the Hg^{2+} ion (Figs. S8–S13). These results provided support for the calculated binding mode of **1** derived in the computational study. The results also showed that the site of the linker in receptor **1** or **2** does not affect the recognition of the Hg^{2+} ion. The formation of 1:1 complex between **2** and Hg^{2+} was further confirmed by the appearance of a peak at m/z 591, assignable to [**2**+Hg^{2+}] in the ESI/MS (Fig. S14).

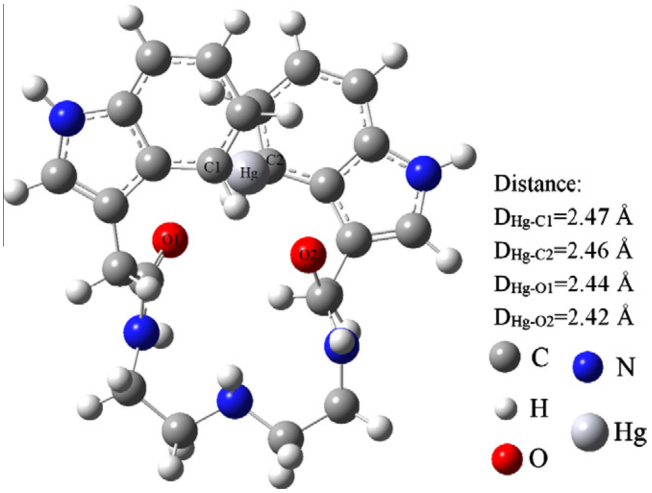
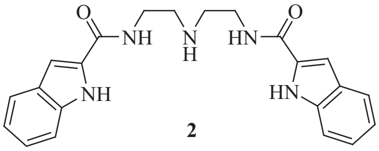


Figure 7. Conformation of **1**/Hg^{2+} optimized by the density functional theory.



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In summary, an aqueous indole-based, Hg^{2+}-selective, fluorescent sensor **1** was designed and synthesized by coupling indole and triaminoethylene moieties. Fluorescent sensor **1** showed selectivity for Hg^{2+} over other metal ions that was sufficiently low for the detection of trace amounts of Hg^{2+} ion present in many chemical and biological systems. Computational calculations provided evidence that a tetrahedron coordinated Hg^{2+} center was formed and the triaminoethylene linker spacer acted as a scaffold to bring functional ligands into a suitable geometry.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.12.110.

References and notes

1. Adams, P. D.; Chen, Y.; Ma, K.; Zagorski, M. G.; Sonnichsen, F. D.; McLaughlin, M. L.; Barkley, M. D. *J. Am. Chem. Soc.* **2002**, *124*, 9278–9286.
2. Liu, B.; Thalji, R. K.; Adams, P. D.; Fronczek, F. R.; McLaughlin, M. L.; Barkley, M. D. *J. Am. Chem. Soc.* **2002**, *124*, 13329–13338.
3. Shizuka, J.; Serizawa, M.; Kobayashi, J.; Kameta, K.; Sugiyama, H.; Matsuura, T.; Saito, I. *J. Am. Chem. Soc.* **1988**, *110*, 1726–1732.
4. Sessler, J. L.; Cho, D. G.; Lynch, V. *J. Am. Chem. Soc.* **2006**, *128*, 16518–16519.

5. He, X.; Hu, S.; Liu, K.; Guo, Y.; Xu, J.; Shao, S. *Org. Lett.* **2006**, *8*, 333–336.
6. Li, L.; Dang, Y. Q.; Li, H. W.; Wang, B.; Wu, Y. *Tetrahedron Lett.* **2010**, *51*, 618–621.
7. Chang, K. J.; Moon, D.; Lah, M. S.; Jeong, K. S. *Angew. Chem., Int. Ed.* **2005**, *44*, 7926–7929.
8. Chang, K. J.; Chae, M. K.; Lee, C.; Lee, J. Y.; Jeong, K. S. *Tetrahedron Lett.* **2006**, *47*, 6385–6388.
9. Kwon, T. H.; Jeong, K. S. *Tetrahedron Lett.* **2006**, *47*, 8539–8541.
10. Chang, K. J.; Kang, B. N.; Lee, M. H.; Jeong, K. S. *J. Am. Chem. Soc.* **2005**, *127*, 12214–12215.
11. Lee, J. Y.; Lee, M. H.; Jeong, K. S. *Supramol. Chem.* **2007**, *19*, 257–263.
12. Curiel, D.; Cowley, A.; Beer, P. D. *Chem. Commun.* **2005**, 236–238.
13. Hu, X.; Hu, S.; Liu, K.; Guo, Y.; Xu, J.; Shao, S. *Org. Lett.* **2006**, *8*, 333–336.
14. Pfeffer, F. M.; Lim, K. F.; Sedgwick, K. *Org. Biomol. Chem.* **2007**, *5*, 1795–1799.
15. Wang, T.; Bai, Y.; Ma, L.; Yan, X. P. *Org. Biomol. Chem.* **2008**, *6*, 1751–1755.
16. Hsieh, Y. C.; Chir, J. L.; Yang, S. T.; Chen, S. J.; Hu, C. H.; Wu, A. T. *Carbohydr. Res.* **2011**, *346*, 978–981.
17. Kao, T. L.; Wang, C. C.; Pan, Y. T.; Shiao, Y. J.; Yen, J. Y.; Shu, C. M.; Lee, G. H.; Peng, S. M.; Chung, W. S. *J. Org. Chem.* **2005**, *70*, 2912–2920.
18. Chen, Q. Y.; Chen, C. F. *Tetrahedron Lett.* **2005**, *46*, 165–168.
19. Moon, S. Y.; Cha, N. R.; Kim, Y. H.; Chang, S. K. *J. Org. Chem.* **2004**, *69*, 181–183.
20. Cha, N. R.; Kim, M. Y.; Kim, Y. H.; Choe, J. I.; Chang, S. K. *J. Chem Soc Perkin Trans. 2* **2002**, 1193–1196.
21. Kumar, A.; Pandey, P. S *Tetrahedron Lett.* **2009**, *50*, 5842–5845.
22. Compound **1**: DEPC (3.29 mL, 17.9 mmol), TEA (4.1 mL, 18.3 mmol), and triaminoethylene (1.01 g, 1.5 mmol) were added to a stirred solution of 3-indolacetic acid (3.99 g, 3.7 mmol) in dry DMF (30 mL). The reaction mixture was stirred overnight at room temperature. After removal of the solvent under reduced pressure, the residue was dissolved in MeOH (4 mL). As the mixture cooled, a solid white precipitate formed. The precipitate was purified by filtration and the pure white product **1** (3.8 g, 80%) was obtained. $R_f = 0.62$ (hexane/EtOAc = 1:10); ^{1}H NMR (300 MHz, DMSO-d_6) δ: 11.00 (s, 1H), 9.38 (s, 1H), 8.43 (s, 1H), 7.55 (d, $J = 7.8$ Hz, 1H), 7.33 (d, $J = 7.8$ Hz, 1H), 7.23 (s, 1H), 7.05 (dt, $J = 7.2$, 7.2 Hz, 1H), 6.95 (dt, $J = 7.2$, 6.6 Hz, 1H), 3.56 (s, 2H), 3.38 (s, 2H), 2.98 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): 171.91, 136.46, 127.62, 124.38, 121.29, 119.08, 118.71, 111.74, 108.84, 46.63, 35.67, 33.05 HRMS (FAB): Calcd for $C_{24}H_{28}N_5O_2$ (M+H), m/z 418.2243, found m/z 418.2240.