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A new fluorogenic chemodosimetric system for mercury ion recognition

Wen Xiu Ren, Sankarprasad Bhuniya, Jun Feng Zhang, Young Hoon Lee, Suk Joong Lee, Jong Seung Kim *

Department of Chemistry, Korea University, Seoul 136-701, Republic of Korea

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ABSTRACT

A new probe system for fluorogenic sensing of mercury ions has been designed and synthesized. It is the first intermolecular reaction-based fluorogenic chemodosimetric probe system for Hg(II) ion recognition. High and low concentrations of mercury ions gave different fluorescence responses that could easily be distinguished by the naked eye. This unique system allows detection of the concentration and presence of the mercury ion.

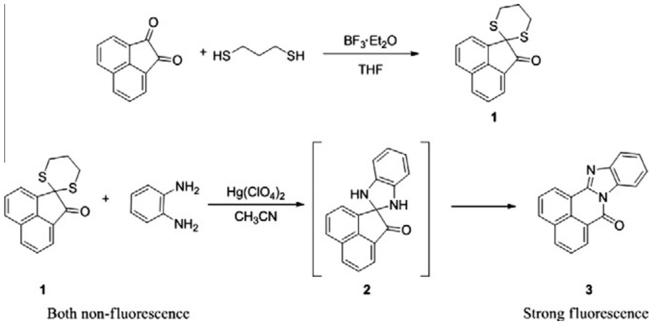
The detection and quantification of heavy- and transition-metal (HTM) ions have drawn current interest because of their detrimental effect on the living species and their adverse impact on the environment.[1]

Mercury, one of the most toxic HTM elements, represents a major source of toxicity for microorganisms and environments, even at low concentrations. When consumed by humans, mercury can trigger several serious disorders, including sensory, motor, and neurological damage.[2] In the past few decades, many sophisticated analytical tools have been developed to detect mercury ions,[3] especially fluorescent chemosensors,[4] in view of their high sensitivity. More recently, the chemodosimetric approach has attracted much attention given its great simplicity, sensitivity, selectivity, and irreversibility.[5] Most methods are designed on mercury-promoted desulfurization reactions;[5c–h] as a consequence, it increases the fluorescent intensity originating mainly from the functional group interconversion. Our major interest is the introduction of this well-known desulfurization technique towards chemodosimetric sensors for Hg^{2+} with the fabrication of a fluorescent dye triggered by an intermolecular chemical reaction.

Herein, we have designed and synthesized a novel probe system utilizing mercury-promoted desulfurization reactions as outlined in Scheme 1. The 6,10-dithiaspiro-acenaphthene quinone (**1**) was prepared in high yield (89%) and further catalyzed with *o*-phenylenediamine (*o*-PDA) to form **3** in the presence of Hg^{2+} ions and as a consequence amplified the fluorescent signal.[6] To the best of our knowledge, this is the first intermolecular reaction-based 'turn on' fluorescent sensing approach for Hg^{2+} ions.

Upon addition of Hg^{2+} ions to a mixture of **1** and *o*-PDA (both non-fluorescence),[8] it catalyzed desulfurization (Fig. S1) and promoted the formation of the unstable spiroheterocyclic intermediate **2**, which subsequently was converted to **3** through an intramolecular rearrangement.[9] Although the formation of **3** is well supported with spectroscopic data that correlates with authentic data, the corresponding mechanism remains unclear. Compound **3** is a classic dye, with strong green fluorescence, that is widely used as a basic skeleton in the design of new organic pigments, laser dyes, textile dyes, and polymer fibers.[10]

UV irradiation of a mixture of **1**, *o*-PDA, and Hg^{2+} in CH_3CN could accelerate the reaction rate. For example, upon the irradiation with a handheld UV lamp (365 nm) for 5 min,[11] the fluorescence intensity at 492 nm dramatically increased by approximately 19-fold (compared with the intensity without irradiation at 1.5 h) (Fig. S3). In addition, the molar ratio of **1** and *o*-PDA can also influence the reaction rate. To optimize the system, various molar ratios



Scheme 1. Synthesis of ligand **1** and proposed reaction mechanism.

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* Corresponding author. Tel.: +82 2 3290 3143; fax: +82 2 3290 3121.
E-mail address: jongskim@korea.ac.kr (J.S. Kim).

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of **1** and *o*-PDA were tested with a fixed concentration of 20 μM of Hg^{2+} ion in CH_3CN (Fig. S4). The system containing **1** (20 μM) and *o*-PDA (3.0 equiv) gave the best results.

As shown in Figure 1, the fluorescence titration profile of **1** and *o*-PDA (3.0 equiv) versus Hg^{2+} demonstrated that the concentration of Hg^{2+} could impact emission intensity and emission wavelength. In the presence of a low concentration of Hg^{2+} ions (0–1.4 equiv), the fluorescence emission at 492 nm (same with **3**) and emission intensity were enhanced with gradually increased Hg^{2+} ions. Upon further addition of Hg^{2+} ions (>1.4 equiv), the emission band at 492 nm gradually decreased and concomitantly blue shifted to 454 nm. This may be caused by either: (1) interaction of Hg^{2+} with **3** and/or; (2) the decrease in concentration of free *o*-PDA in a solution of excess Hg^{2+} ion due to ligation of *o*-PDA to Hg^{2+}, which disrupts the formation of **3** and consequently decreases emission intensity (Fig. S5). To rationalize this change in the presence of excess Hg^{2+} ions, we examined spectral changes upon the gradual addition of Hg^{2+} to a solution of **3** (Fig. S6). There was a strong emission at 492 nm of **3** that gradually blue shifted and reached λ_{max} = 454 nm in a 150 μM concentration of Hg^{2+}, with a significant increased emission intensity due to internal charge transfer (ICT). NMR titration experiments were performed to verify the coordination mechanism between **3** and Hg^{2+}. Comparison of the ^1H NMR spectra of **3** before and after the addition of Hg^{2+} revealed that all the proton signals were shifted downfield (Fig. S7). These changes were likely due to metal ion complexation, in which Hg^{2+} was bound to an imidazole nitrogen in **3**.[10a,c] Furthermore, complexation of Hg^{2+} with **3** was weaker than with *o*-PDA (Fig. S8). Thus, control of the emission intensity and wavelength of a sample is possible by controlling the concentration of *o*-PDA. This Hg^{2+} concentration dependence of fluorescent spectral changes implied that this unique system allows detecting the presence and concentration of the Hg^{2+} ion.

To understand the role of other metals ions in this chemical transformation, identical experiments were carried out with other heavy, alkaline, and alkaline earth metals, such as Ag^+, Ba^{2+}, Ca^{2+}, Cd^{2+}, Co^{2+}, Cu^{2+}, Cs^{2+}, K^+, Li^+, Mg^{2+}, Na^+, Rb^+, and Sr^{2+}; however, these ions did not influence any fluorescence changes, even at very high concentrations. Only the addition of Fe^{2+}, Pb^{2+}, and Zn^{2+} gave relatively slight fluorescence enhancements (Fig. S9).

From a practical application point of view, the interference from other metal ions should be taken into account; hence, the fluorescence change in this Hg^{2+} ion-catalyzed reaction in the presence of other competitive metal ions was investigated as illustrated in Figure 2. Some transition and post transition metal ions like Ag^+, Co^{2+}, and Zn^{2+} slightly reduced the fluorescence intensity because of their complexation ability with *o*-PDA (Fig. S10).

The UV–vis absorption behavior of the probe system toward representative metal ions was investigated by treatment with physiologically important alkali, alkaline earth, and transition-metal perchlorates in CH_3CN, as presented in Figure 3. Upon interaction with various metal ions, significant changes in absorption spectra were immediately observed, particularly with Cu^{2+}, because Cu^{2+} can easily interact with *o*-PDA and produce a $CuPDA_x(ClO_4)_2$ (*x* = 1 or 2) complex in solution, resulting in a concomitantly chromogenic change from colorless to brown.[12]

It is to be noted that due to the strong interactions between Cu^{2+} with *o*-PDA, the existence of high concentrations of Cu^{2+} can

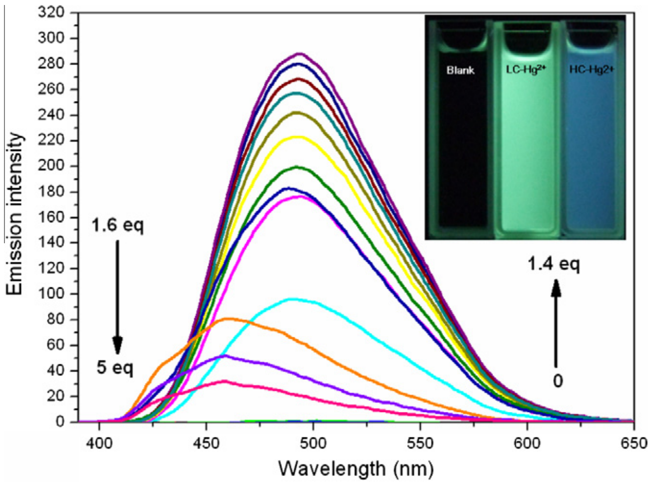

Figure 1. Fluorescence response of the probe system (1 (20 μM) and *o*-PDA (3.0 equiv)) upon addition of the Hg2+ ion (0–100 μM) in CH3CN, λ_{ex} = 380 nm. Inset: fluorescence images in the absence of the Hg^{2+} ion (left); in the presence of the Hg^{2+} ion (low concentration, middle; high concentration, right).

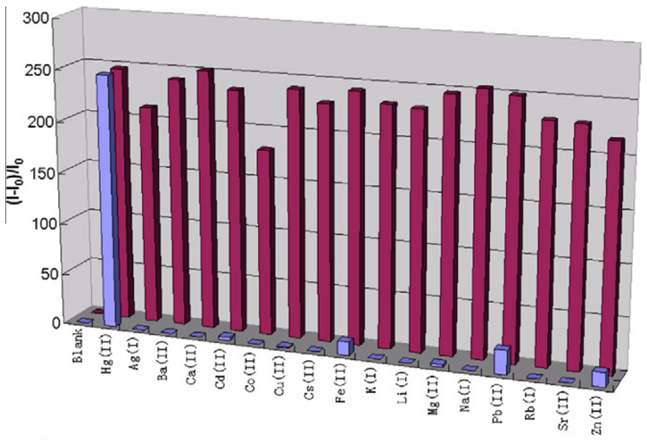

Figure 2. Fluorescence enhancement $(I - I_0)/I_0$ of the probe system (**1** (20 μM) and *o*-PDA (3.0 equiv)) in CH_3CN, λ_{max} = 492 nm. (Front line) upon the addition of different metal ions (10 equiv, except Cu^{2+} (5.0 equiv)) and Hg^{2+} (1.0 equiv); (back line) competitive selectivity of the sensor system toward Hg^{2+} ions (1.0 equiv) in the presence of other metal ions (10 equiv, except Cu^{2+} (1.0 equiv)), λ_{ex} = 380 nm.

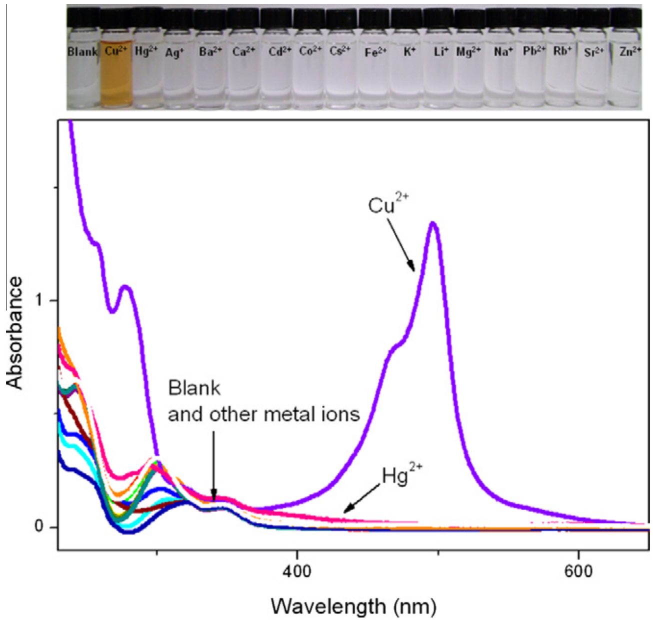

Figure 3. (a) The color response of the probe system upon the addition of different metal ions. (b) UV–vis spectra of **1** (20 μM) and *o*-PDA (3.0 equiv) in the presence of different metal ions (Ag^+, Ba^{2+}, Ca^{2+}, Cd^{2+}, Co^{2+}, Cu^{2+}, Cs^{2+}, Fe^{2+}, K^+, Li^+, Mg^{2+}, Na^+, Pb^{2+}, Rb^+, Sr^{2+}, Zn^{2+} (10 equiv); Hg^{2+} (1.0 equiv)) in CH_3CN.

interfere with the formation of **3** and consequently quench fluorescence. Further addition of *o*-PDA can recover its strong signal, allowing Hg^{2+} interactions (Fig. S11).

In summary, we developed a Hg^{2+}-catalyzed intermolecular reaction-based probe system which demonstrated high selectivity for Hg^{2+}. This is a new and unconventional chemodosimeter strategy to detect Hg^{2+} ions, even in the presence of other competitive metal ions.

Acknowledgment

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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.2010.08.088.

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6. *General*: Compound **1** was synthesized according to a literature process[7]. All reagents and solvents for syntheses were of commercial grade and used without further purification. All reactions were performed under a highly pure nitrogen or argon atmosphere. Synthesized products were purified by column chromatography on silica gel (100–200 mesh). All fluorescence and UV–vis absorption spectra were recorded with RF-5301PC and S-3100 spectrophotometers, respectively. NMR and mass spectra were recorded with a Varian instrument (300 MHz) and HRMS mass spectra.
   Preparation of benzo[de]-benzo[4,5]imidazo[2,1-a]isoquinolin-7-one (**3**). Mixture of **1** (0.027 g, 0.1 mmol), *o*-PDA (32 mg, 0.3 mmol), and $Hg(ClO_4)_2{\cdot}xH_2O$ (0.060 g, 0.14 mmol) in CH_3CN (3.0 mL) were stirred under UV irradiation at 365 nm for 5 min. After the reaction was finished, the mixture was filtered and the solvent removed in vacuo. The reaction mixture was purified by column chromatography with methylene chloride to give pure **3** (10.2 mg, 38%) as a yellowish green solid. MP = 192–193 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 7.46–7.49 (m, 2H), 7.76–7.83 (m, 2H), 7.86–7.90 (m, 1H), 8.12 (d, *J* = 8.6 Hz, 1H), 8.21 (d, *J* = 8.2 Hz, 1H), 8.54–8.57 (m, 1H), 8.75–8.83 (m, 1H). HRMS (FAB): calcd for $C_{18}H_{11}N_2O$ $[M+H]^+$ 271.0871; found 271.0871.
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