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Rhodamine-Based Hg^{2+}-Selective Chemodosimeter in Aqueous Solution: Fluorescent OFF–ON

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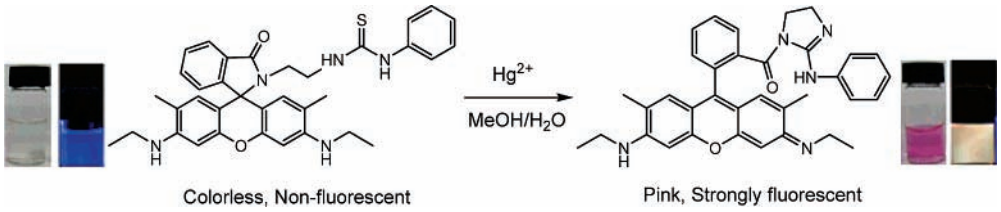
ABSTRACT



***N*-(Rhodamine-6G)lactam-*N'*-phenylthiourea-ethylenediamine (1) was developed as a fluorescent and colorimetric chemodosimeter in aqueous solution with a broad pH span (5∼10) and high selectivity toward Hg^{2+} but no significant response toward other competitive cations, such as Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Pb^{2+}, Cd^{2+}, Ca^{2+}, Mg^{2+}, K^{+}, Na^{+}, etc. The Hg^{2+}-promoted ring opening of spirolactam of the rhodamine moiety induced cyclic guanylation of the thiourea moiety, which resulted in the dual chromo- and fluorogenic observation (OFF–ON).**

Mercury contamination is widespread and arises from a variety of natural sources.[1] As we know, once introduced into the marine environment, bacteria convert inorganic Hg^{2+} ions into methylmercury, which is neurotoxic and has been implicated as a cause of mercury pollution related to serious irreversible neurological damage.[2] Thus, the pollution by Hg^{2+} ions will have severe effects on human health and the environment. Recently, many fluorescent chemosensors for Hg^{2+}-selective detection have become available.[3] However, most of them have shortcomings in practical application, such as cross-sensitivities toward other metal cations, low water solubility, a narrow pH span, and delayed response, etc. Accordingly, the demand for analytical methods for the selective and sensitive determination of Hg^{2+} ions is of topical interest, especially in the presence of miscellaneous competitive metal cations and a wide pH span in practical use.

Recently, a particularly attractive alternative presented herein is the use of chemodosimeters as analytes through a specific chemical reaction between dosimeter molecules and target species, leading to the formation of a fluorescent or colored product. One of the more attractive approaches in this field involves the use of highly selective reactions (usually irreversible) induced by target analytes, in which an accumulative effect is directly related to the analyte concentration. Thus, high selectivity toward the analyte is a welcome feature of chemodosimeters, which is preferable for the detection of the Hg^{2+} ion. However, only a few Hg^{2+} chemodosimeters are available to date.[4]

Herein, we report a rhodamine-based Hg^{2+} chemodosimeter (compound **1**) as a new advance in this field. Our design

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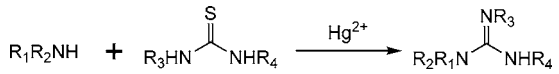
is based on the well-known reaction that thiourea derivatives with amine can easily be transformed into guanidine derivatives with the promotion of the Hg^{2+} ion, as depicted in Scheme 1.[5] First, we chose the typically mercury-promoted

Scheme 1. Hg^{2+}-Induced Guanylation of the Thiourea Derivative



desulfurization reaction as the recognition event for its high selectivity (the strong thiophilic affinity toward the Hg^{2+} ion). On the other hand, the rhodamine framework as the signaling moiety is attached to the recognition moiety with a spirolactam structure (nonfluorescent). When the Hg^{2+}-promoted desulfurization reaction takes place, a ring-opening process of spirolactam of rhodamine (strongly fluorescent) is the first step, followed by the intramolecular guanylation. Actually, this desulfurization reaction was applied for the design of a chemodosimeter for the Hg^{2+} ion. Recently, Tae et al. reported that a rhodamine-based thiosemicarbazide was easily transformed into 1,3,4-oxadiazole in the presence of a Hg^{2+} ion.[4e] Tian et al. used this desulfurization reaction to develop a naphthalimide-based chemodosimeter for the Hg^{2+} ion with an insensitive ratiometric signal from green to blue emission.[4f] To get a better signal response, we used the rhodamine chromophore to give rise to a sensitive dual chromo- and fluorogenic observation (OFF−ON).

As described in Scheme 2, **1** was synthesized from the simple reaction of rhodamine 6G and ethylenediamine, followed by the reaction with phenyl isothiocyanate in 60% overall yield. The structure of **1** was confirmed by ^1H NMR, ^{13}C NMR, MS, and X-ray analysis (Supporting Information). The single crystal of **1** suitable for X-ray diffraction studies was grown by the vapor diffusion of *n*-hexane into a CH_3CN solution of **1** for 5 days (Figure 1). The crystal structure clearly represents the unique spirolactam ring formation.[6]

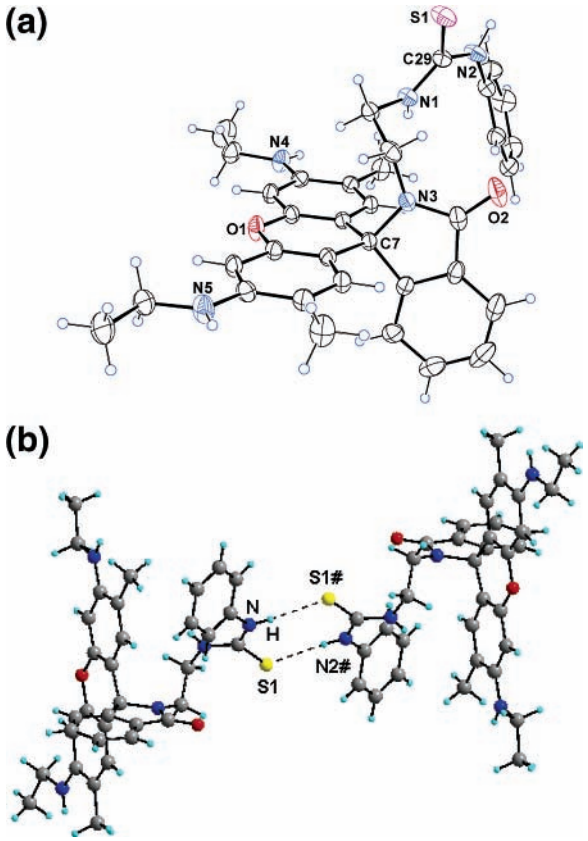
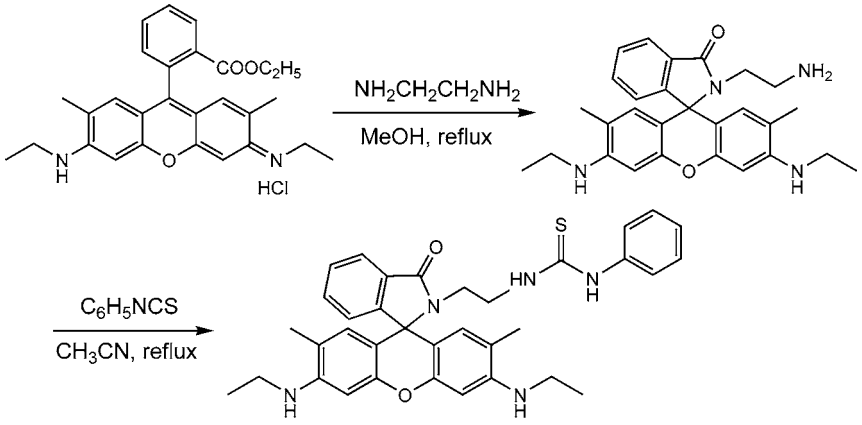


Figure 1. (a) View of the structure of **1** with displacement atomic ellipsoids drawn at the 30% probability level. (b) View of the enantiomer and dimer structures with intermolecular double NH···S hydrogen bondings distances (d(H···S1#) = 2.458 Å, d(N2···S1#) = 3.293 Å).

Two planes of the spiro of the rhodamine framework are coordinated in a mutually vertical position. The enantiomer and dimer structures of **1** were assembled through the intermolecular double NH···S hydrogen bondings. To the

Scheme 2. Synthetic Route of Chemodosimeter **1**



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best of our knowledge, only a few crystal structures have been reported based on the rhodamine spirolactam.[7]

Figure 2 shows a spectral variation of **1** upon the gradual addition of $Hg(ClO_4)_2$. The UV−vis titration of the Hg^{2+} ion was conducted using 10 μM **1** in 90% methanol aqueous solution at pH ∼ 7. Upon the addition of increasing concentrations of the Hg^{2+} ion, a new absorption band centered at 532 nm appeared with increasing intensity, which induced a clear color change from colorless to pink (Figure 2A). According to the linear Benesi−Hildebrand expression,[8] the measured absorbance [$1/(A - A_0)$] at 532 nm varied as a function of $1/[Hg^{2+}]$ in a linear relationship ($R = 0.9992$), indicating the ∼1:1 stoichiometry between the Hg^{2+} ion and **1** (Figure S1, Supporting Information). On the other hand, for the fluorescence titration spectra of **1**, in the presence of the Hg^{2+} ion, there was also a new emissive peak at 555 nm (Figure 2B), which was consistent with the results of UV−vis spectra. Both UV−vis and fluorescence data lead to a significant OFF−ON signal. From the molecular structure and spectral results of **1**, it is concluded that the addition of the Hg^{2+} ion induced the N atom of spirolactam to attack the C atom of thiourea, and thus a ring opening of the spirolactam of rhodamine took place, followed by the removal of HgS and the formation of intramolecular guanylation. Finally, a stable cyclic product **2** was formed through an irreversible desulfurization reaction, as depicted in Scheme 3.

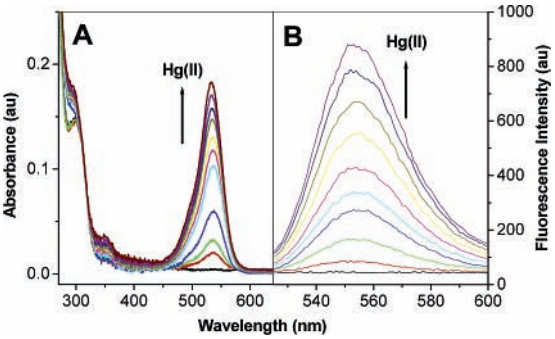
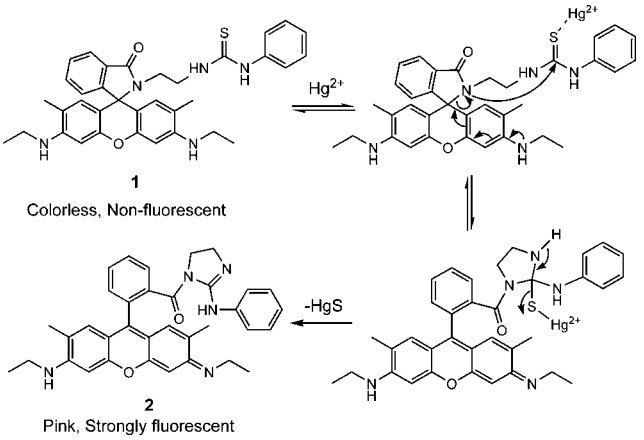


Figure 2. (A) UV−vis and (B) fluorescence titration spectra of **1** (10 μM) in 9:1 CH_3OH/H_2O (v/v) at pH ∼ 7 upon gradual addition of $Hg(ClO_4)_2$ (excitation wavelength at 520 nm; Hg^{2+} concentrations, (A) 0, 20, 50, 80, 100, 150, 200, 250, 300, 400, 500 μM, respectively, and (B) 0, 10, 20, 40, 60, 80, 100, 200, 300, 400, 500 μM, respectively). All spectral data were recorded at 10 min after the Hg^{2+} addition.

Scheme 3. Proposed Hg^{2+}-Promoted Ring Opening of Spirolactam and Intramolecular Guanylation



Further evidence for the above process came from the independent synthesis of **2** from the direct reaction of **1** and $Hg(ClO_4)_2$ in ethanol (Supporting Information). ^1H NMR, ^{13}C NMR, and MS data clearly confirmed the structure of **2**. Comparing the ^{13}C NMR data of **1** and **2**, we found that the chemical shift of **2** at 178 ppm was kept intact, whereas that at 167 ppm disappeared, indicating that the C═O group of **1** was retained and the C═S group vanished during the guanylation progress from **1** to **2**. In addition, the ^{13}C chemical shift of tetra-C of **1** (64 ppm) changed to the aryl region of **2**, implying the occurrence of ring opening of spirolactam upon the promotion of the Hg^{2+} ion.

An important feature of the chemodosimeter is its high selectivity toward the analyte over the other competitive species. Variations of UV−vis and fluorescence spectra of **1** caused by miscellaneous cations including Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Pb^{2+}, Cd^{2+}, Ca^{2+}, Mg^{2+}, K^+, and Na^+ in a 90% methanol aqueous solution at pH ∼ 7 are recorded in Figure 3 (counteranions of the used cations are all perchlorate). The miscellaneous competitive cations did not lead to any significant absorption in the visible region and fluorescence changes. Moreover, in the presence of miscellaneous competitive cations, the Hg^{2+} ion still resulted in the similar absorption and fluorescence changes. In addition, the increases of absorbance and fluorescence intensity resulting from the addition of the Hg^{2+} ion were not influenced by the subsequent addition of miscellaneous cations. All this

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(6) The crystal data of **1**·(CH_3CN) are a colorless stick form and have dimensions of: 0.35 × 0.25 × 0.21 Å^3; triclinic; space group P-1, a = 12.173(1), b = 12.299(1), c = 12.909(1) Å, α = 98.22°, β = 112.03°, γ = 101.33°, V = 1706.2 Å^3, Z = 2, σ = 1.232 Mg/m^3, R1 = 0.0693, wR2 = 16.17, GOF = 1.176. Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC No. 632879. Copies of the data can be obtained free of the charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data centre, 12 Union Road, Cambridge CB21EZ, UK; fax (+44)1223−33603.3; e-mail deposit@ccdc.cam.ac.uk).

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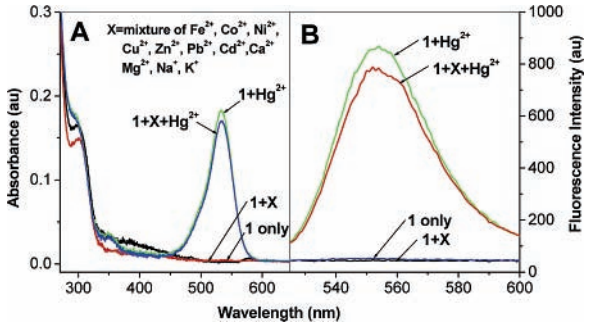

Figure 3. (A) UV−vis spectra and (B) fluorescence spectra of **1** (10 μM) in 9:1 CH_3OH/H_2O (v/v) at pH ~ 7 in the presence of the Hg^{2+} ion and miscellaneous cations including Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Pb^{2+}, Cd^{2+}, Ca^{2+}, Mg^{2+}, K^+, and Na^+ (50 equiv, respectively; excitation wavelength at 520 nm). All spectral data were recorded at 10 min after Hg^{2+} addition.

indicates that the selectivity of **1** for the Hg^{2+} ion over other competitive cations in the water medium is remarkably high. The above color changes from colorless to pink (OFF−ON) and fluorescence changes from colorless to yellow (OFF−ON) are shown in Figure 4.

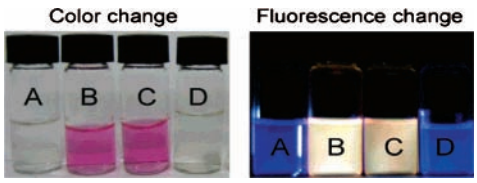

Figure 4. Color changes (left) and fluorescence changes (right) (A, **1** only; B, **1** + Hg^{2+}; C, **1** + X + Hg^{2+}; D, **1** + X; X denotes miscellaneous cations including Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Pb^{2+}, Cd^{2+}, Ca^{2+}, Mg^{2+}, K^+, and Na^+).

For practical applicability, the proper pH condition of this new chemodosimeter was also evaluated. Figure 5 shows that for free **1**, at acid conditions (pH < 5), the ring opening of rhodamine took place because of the strong protonation. When pH > 5, no significant ring opening was observed. However, in the presence of the Hg^{2+} ion, there was an obvious fluorescence OFF−ON change between pH 5 and 10. Thus, chemodosimeter **1** can detect the Hg^{2+} ion with a wide pH span (5~10) because in this region **1** with the Hg^{2+}

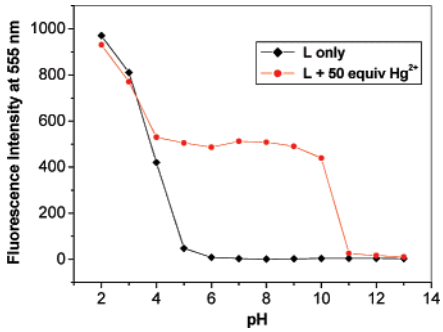

Figure 5. Fluorescence intensity (555 nm) of free **1** (5 μM) and **1** + 50 equiv of Hg^{2+} ion in 9:1 CH_3OH/H_2O (v/v) with different pH conditions.

ion induces a remarkable fluorescence OFF−ON, whereas **1** without the Hg^{2+} ion does not lead to such a change. A similar result also arises from the UV−vis spectra with the change of pH conditions (Figure S2, Supporting Information). This property of chemodosimeter **1** suggests that no buffer solutions are required for the detection of the Hg^{2+} ion, which is convenient for the practical application.

The cyclization reaction was irreversible and produced a time-dependent dosimetric response which was controlled by the reaction kinetics. Optimization of assay conditions for reaction time in 10% aqueous solution required more than 10 min to complete the reaction (Figure S3 and S4, Supporting Information), whereas in 30% and 50% aqueous solutions, it needs about 30 min and more than 1 h, respectively.

In summary, we utilized an irreversible desulfurization reaction to develop a novel chemodosimeter, which would be applied to the detection of Hg^{2+} ions in aqueous solution. Two good features of this system, a remarkably high selectivity toward Hg^{2+} ions over miscellaneous competitive cations and a wide pH span (5~10), make it promising to determine Hg^{2+} ions in aqueous solution for practical analysis.

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

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