A selective fluorescent ratiometric chemodosimeter for mercury ion†

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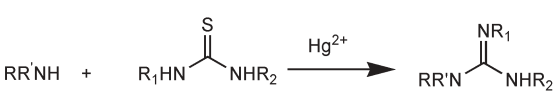
A selective fluorescent chemodosimeter for mercury ion based on the mercury-promoted intramolecular cyclic guanylation of thiourea connected on 1, 8-naphthalimide is described.

Compared to the relatively well-developed fluorescent sensors, development of fluorescent chemodosimeters has recently emerged as a research area of significant importance.[1,2] 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. Some fluorescent chemodosimeters for mercury ion have exploited an irreversible mercury-promoted desulfurization of a thioamide derivative of anthracene or naphthalene with fluorescent changes.[3] However, these fluorometric dosimeters along with most other fluorescent chemosensors for Hg(II) involved only changes in the emissive intensities.[1,3,4] In spite of this, it is generally preferable for a fluorescence sensory signal to involve a new emission at a different wavelength rather than a modulation of an existing signal.[5] New approaches should take the signal measurements at two excitation or emissive wavelengths where the intensity responses are also different.[6]

As a further advance in the field of fluorescent detective systems, here we report the first case of a ratiometric fluorescent chemodosimeter for selective detection of the mercuric ion. The design is based on the well-known reactivity of thiourea derivatives with amine under the promotion of mercuric ion. It has been reported over the last twelve years that thiourea can be easily transformed into guanidine derivatives as shown in Scheme 1.[7] Nevertheless, the conversion from thiourea to guanidine had rarely attracted attention as a potential fluorogenic reaction because most thiourea derivatives have the same color or fluorescence as that of the guanidine analogues. We envisioned that a similar molecular recognition/reactivity motif might be incorporated into fluorophores, so that Hg(II) addition would lead to a variation of fluorescent wavelengths. Our approach is depicted in Scheme 2. We hypothesized that the benzoyl thiourea group, which is known to bind Hg(II) with higher dehydrothiolazition reactivity than the thiourea analogue,[8] would provide recognition for Hg(II) and this



Scheme 1 Hg^{2+}-promoted guanylation of thiourea.

† Electronic supplementary information (ESI) available: the synthesis, NMR, MS and elemental analysis data of the system as well as the absorption and fluorescence spectra for various ions. See http://www.rsc.org/suppdata/cc/b5/b501913c/

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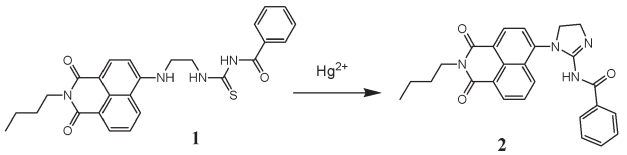

Scheme 2 Hg^{2+}-promoted intramolecular guanylation of **1**.

newly designed molecular system (**1** shown in Scheme 2) would undergo guest-induced intramolecular chemical reaction[9] coupled with suitable fluorometric and colorimetric events.

In consideration of how to best construct such a system for the selective detection of mercury ions we decided to explore the above-mentioned scheme using the unique chemical reactivity of mercuric ions with a sulfur compound. A mercury-triggered intramolecular cyclization of thioureas results in the formation of a highly blue fluorescent naphthalimide derivative, whereas the dosimeter itself fluoresces yellowish green. The variation of electron-donating ability of substitution at the 4-position of 1,8-naphthalimide could change emissive wavelengths effectively.[10] In the dosimeter reported here, the benzoyl thiourea unit as a receptor is linked to 4-amino-1,8-naphthalimide through ethylene, the receptor has much less effect on the emission of the fluorophores, this dosimeter still emits yellow-green light similar to the 1,8-naphthalimide with just one single amino group in the 4-position. Compound **1** was easily synthesized through the reaction of benzoyl isothiocyanate and *N*-butyl-4-(2-aminoethylamino)-1,8-naphthalimide, which was prepared from the corresponding 4-bromo-1,8-naphthalimide and ethylenediamine.† The addition of Hg(II) ion transforms the thiourea unit of the chemodosimeter under aqueous conditions into an imidazoline moiety that is a much less electron-donating group, which results in a significant reduction in electron delocalization within the fluorophore. The absorption and emission maximum shift accordingly from 435 nm and 530 nm (for the chemodosimeter) to 350 nm and 475 nm (for the imidazoline derivative), respectively.

The conditions of this reaction can be chosen to yield high selectivity for Hg(II) ion. To a solution of the chemodosimeter (3 μM), 1 equiv of metal salts are added, and the fluorescence intensity is monitored with time. The salts tested are Ag(I), Co(II), Cu(II), Hg(II), Ni(II), Pb(II) and Zn(II). After 1 h, only the solution containing Hg(II) showed a change in fluorescence color (Fig. 1). Optimization of assay conditions requires 80% acetonitrile. The analogous reaction with Ag(I) requires 20 h to achieve completion with the changes in the emissive intensity. The cyclization reaction is irreversible and produces a time-dependent dosimetric response that is controlled by the reaction kinetics. The reaction with Hg(II) affords the changes in both the fluorescence and absorption

Fig. 1 The fluorescence emission response of **1** (3×10^{-6} M) on addition of 3×10^{-6} M cations in the form of acetate salts in aqueous solution of acetonitrile excited at 254 nm using UV lamp. Left to right: free metal, Cu^{2+}, Co^{2+}, Ni^{2+}, Zn^{2+}, Pb^{2+}, Ag^{+}, Hg^{2+}.

spectra, so that both fluorometric and colorimetric analyses are obtained.

Upon addition of Hg(II), the 435 nm band for free dosimeter **1** (log ε = 4.13) in the solution (acetonitrile:H_2O = 80:20, v:v) decreased significantly along with the growth of a new absorption band at ~350 nm (Fig. 2).‡ An isosbestic point at ~391 nm throughout the titration was attributed to the formation of benzoyl imidazoline derivative of naphthalimide in equilibrium with the free chemodosimeter, benzoyl thiourea derivative of naphthalimide. The measured absorbance [$A_0/(A–A_0)$] as a function of the inverse of mercury ion concentrations in a linear relationship, indicating the ~1:1 stoichiometry of the mercury-promoted cyclic guanylation of the chemodosimeter. Therefore, chemodosimeter **1** is also a colorimetric ratiometer for Hg(II) since the reaction with Hg(II) in aqueous solution effects a cyclic guanylation of chemodosimeter **1** leading to imidazoline derivative **2** in a stoichiometric process.‡

Dual spectral features were observed in the fluorescence titration study (Fig. 3). The results in combination with different excitation spectra between monitoring at, *e.g.* 475 nm and 530 nm, led us to conclude that dual fluorescence originated from different precursors, namely, the unreacted **1** and product **2**, respectively. The clear isoemissive point appeared at 510 nm. The presence of Hg(II) shifts the equilibrium toward product **2**, which is confirmed by ^{1}H NMR and mass spectrometry data.† Moreover, the emission change from yellow-green to blue is

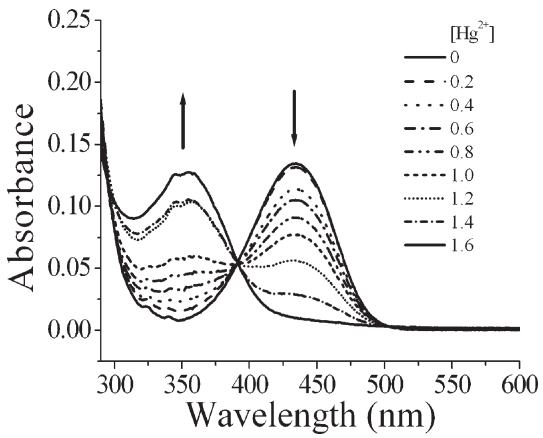

Fig. 2 UV-Vis spectra of **1** (1×10^{-5} M) and Hg^{2+} (2×10^{-6} to 1.6×10^{-5} M) in acetonitrile:H_2O (80:20, v:v), at room temperature. Each spectrum was acquired 10 min after Hg^{2+} addition. As the concentration of Hg^{2+} increases, a blue shift from 435 nm to 350 nm is observed.

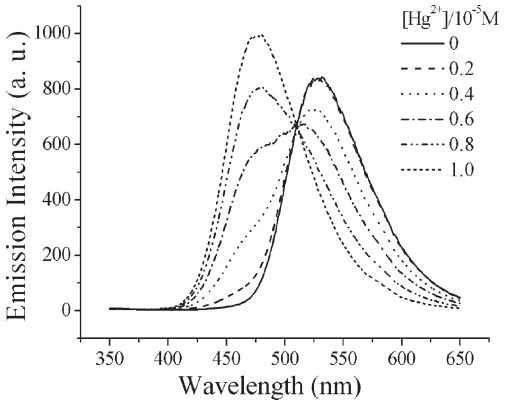

Fig. 3 Fluorescence spectra of **1** (3×10^{-6} M) and Hg^{2+} (0.2 μM–10 μM) excited at 290 nm in acetonitrile:H_2O (80:20, v:v, at room temperature). The spectra show the growth of a 475 nm emission band on complexation, accompanied by decrease of 530 nm band.

Table 1 Fluorescent emission data in acetonitrile/H_2O (80:20, v:v)

Compound	λ_{abs} (nm)	λ_{em} (nm)	Φ_F[a]	τ[b] (ns) ± 0.2
1	435	530	0.35	11.6
2	350	475	0.48	9.9

[a] Determined with *N*-butyl-4-butylamino-1,8-naphthalimide in absolute ethanol (Φ_F = 0.81)[11] as a reference. [b] Fluorescence lifetimes are performed with an Edinburgh FL900 single-photon counting system with a nitrogen laser as the excitation source.

readily detected visually. The results indicate that addition of Hg(II) ion results in a very significant changes in the spectroscopic properties (both wavelengths and the intensities) of the chemodosimeter with a thiourea group as the appended indicator. The fluorescent lifetimes and the spectral data for these compounds are listed in Table 1.

In summary, we have synthesized a new naphthalimide chemodosimeter with high selectivity for Hg(II) in aqueous solution based upon the reactivity of thiourea derivatives toward Hg(II) ion. In contrast to most mercury sensor schemes that rely on changes of emission intensity, this chemodosimetry system utilized two fluorescent variations at different wavelength, which can be used as a ratiometric chemodosimeter. Because of the simplicity and sensitivity of the analysis, this chemodosimeter should have potential application in a variety of settings requiring rapid and accurate Hg(II) ion analysis. This preliminary understanding on the cation sensing mechanism would actually help to find possible structural modification to achieve new probes that show cation sensing capacity at least in water-containing organic solvents. Investigations are continuing to figure out the methods of structural modifications of the dosimeters with water-solubilising substituents such as carboxylate or sulfonate and to design related receptors with photochemical signalling capacity.

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Notes and references

‡ Selected data for **1**: m.p. 207–209 °C. ^{1}H NMR (DMSO-d6) δ(ppm): 0.90 (t, 3H), 1.32 (m, 2H), 1.57 (m, 2H), 3.70 (m, 2H), 4.00 (m, 4H, NCH_2CH_2N), 7.02 (d, 1H, J = 8.65Hz), 7.49 (t, 2H, J = 7.80 Hz), 7.62 (t, 1H, J = 7.47 Hz), 7.88 (m, 3H), 7.93 (t, 1H, Ar–NH), 8.26 (d, 1H, J = 8.51 Hz), 8.43 (d, 1H, J = 6.74 Hz), 8.73 (d, 1H, J = 8.27 Hz), 11.07 (t, 1H, J = 5.77 Hz, –CS–NH), 11.40 (s, 1H, –CONH). EI-MS, *m*/*z*: 474 (M^+). Anal. calcd. for $C_{26}H_{26}N_4O_3S$: C 65.80, H 5.52, N 11.81. Found: C 65.69, H 5.54, N 11.90%. Selected data for **2**: m.p. 233–235 °C. ^{1}H NMR (DMSO-d6) δ(ppm): 0.85 (t, 3H), 1.39 (m, 2H), 1.65 (m, 2H), 3.93 (t, 2H), 4.11 (m, 4H, N–CH_2–CH_2–N), 7.19 (t, 2H, J = 7.74 Hz), 7.33 (t, 1H, J = 7.34 Hz), 7.61 (d, 2H, J = 8.42 Hz), 7.86 (t, 1H, J = 7.88 Hz), 7.96 (d, 1H, J = 7.87 Hz), 8.51 (d, 1H, J = 8.50 Hz), 8.56 (d, 1H, J = 7.28 Hz), 8.58 (d, 1H, J = 7.90 Hz), 9.43 (s, 1H, –CONH). EI-MS, *m*/*z*: 440 (M^+). Anal. calcd. for $C_{26}H_{24}N_4O_3$: C 70.89, H 5.49, N 12.72. Found: C 70.84, H 5.60, N 12.80%.

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