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Tetrahedron Letters
Tetrahedron Letters 48 (2007) 5525–5529

# A novel colorimetric and fluorescent chemosensor: synthesis and selective detection for $Cu^{2+}$ and $Hg^{2+}$

Honglei Mu, Rui Gong, Qiao Ma, Yimin Sun and Enqin Fu*

*Hubei Key Laboratory on Organic and Polymeric Optoelectronic Materials, Department of Chemistry, Wuhan University, Wuhan 430072, PR China*

Received 4 April 2007; revised 23 May 2007; accepted 29 May 2007
Available online 2 June 2007

**Abstract**—A novel two-channel metal ion sensor has been synthesized from macrocyclic dioxotetraamine and 1,8-naphthalimide derivative. The metal ion-selective signaling behaviors of the sensor were investigated. The sensor presented the selective coloration for $Cu^{2+}$ and $Hg^{2+}$ that can be detected by the naked-eye, respectively. Besides, the addition of $Cu^{2+}$ and $Hg^{2+}$ quenched the fluorescence of **1** obviously and the detection limit was found to be $3 \times 10^{-7}$ M for $Cu^{2+}$ and $7 \times 10^{-7}$ M for $Hg^{2+}$. This sensor can be utilized for the visual and spectroscopic detection of $Cu^{2+}$ or $Hg^{2+}$ in the presence of the other competing metal ions.


The recognition of ions and molecules is an essential part of supramolecular chemistry. The design and synthesis of chemosensors for heavy and transition metal ions (HTM) are currently a task of prime importance for medical, environmental, and biological applications.[1] Presently, one of the most attractive approaches focuses on the research of novel colorimetric and fluorescent metal ion sensors, which allow naked eyes a real time and space detection of the change of color and fluorescent emission upon metal ion binding without any use of a spectroscopic instrument.[2] It is still a challenge to design a chemosensor, which can be used for detecting different metal ions by both the selective coloration and the change in the fluorescence spectra.

Macrocyclic dioxotetraamines have attracted increasing attention because of some interesting coordination behaviors[3] and they are well known for their ability to complex with some metal ions, such as $Cu^{2+}$, $Co^{2+}$, and $Ni^{2+}$.[4] On the other hand, the 4-amino-1,8-naphthalimide group is a well-known chromophore and fluorophore.[5] It contains an electron-donating group and an electron-withdrawing group conjugated to the π-system. When its electron donating or withdrawing character is affected, some optical changes will be expected. Keeping this in mind, we have designed a chemosensor **1**, which links 4-amino-1,8-naphthalimide as an appended group to the macrocyclic dioxotetraamine, and expected that the 4-amino-1,8-naphthalimide could chelate to different metal ions together with the macrocyclic dioxotetraamine in different coordinating modes and transmit the signal of recognition.

This Letter reports the synthesis of the novel chemosensor **1** and its optical properties for the selective detection of $Cu^{2+}$ and $Hg^{2+}$. Chemosensor **1** was synthesized as shown in Scheme 1. First, 4-bromo-*N*-butyl-1,8-naphthalimide was prepared as described in the procedure.[6] Second it reacted with ethanolamine catalyzed by copper sulfate (0.1 equiv) to yield compound **3**. Then phosphorus tribromide was added dropwise to **3** in dry chloroform at 0–5 °C and the mixture was allowed to reflux for 3 h to afford **2**. Finally, compound **1** was obtained by the reaction of **2** with **L**, which was prepared according to the literature.[7] The structures of the product were identified by using $^1$H NMR, $^{13}$C NMR, and MS.[8]

The absorption spectrum of **1** showed a typical naphthalimide absorption band at 440 nm in the methanol solution, which was responsible for its yellow-green color.[9] In the presence of $Cu^{2+}$ or $Hg^{2+}$, the color of the solution changed from yellow green to almost colorless or orange, respectively. When the other control metal ions ($Fe^{2+}$, $Co^{2+}$, $Ni^{2+}$, $Pb^{2+}$, $Zn^{2+}$, $Mg^{2+}$, $Mn^{2+}$, $Cd^{2+}$, and $Ag^{+}$) were added into the solution of **1**, no

*Keywords*: Macrocyclic dioxotetraamine; 1,8-Naphthalimide; Selective coloration; Recognition; $Cu^{2+}$; $Hg^{2+}$.
* Corresponding author. Tel.: +86 27 87219044; fax: +86 27 68756757; e-mail: fueq@whu.edu.cn

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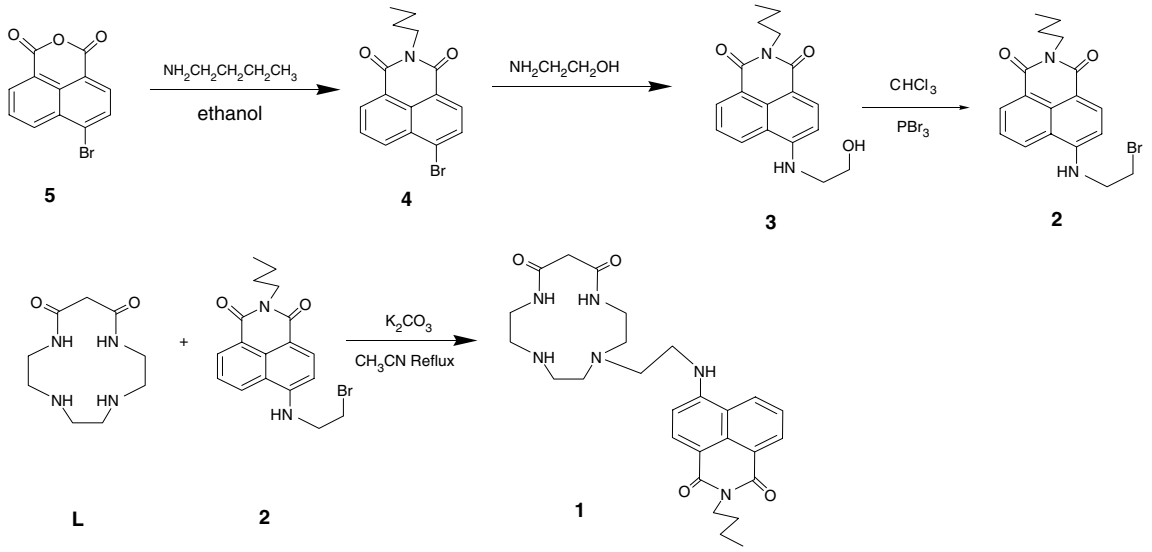
doi:10.1016/j.tetlet.2007.05.155




**Scheme 1.** The synthetic route of **1**.

observable color changes of the solution (Fig. 1) could be detected. These results indicated that **1** could be used as a potential candidate of colorimetric chemosensor for $Cu^{2+}$ and $Hg^{2+}$ with very high selectivity.

Then, the influence of water on the absorption of **1** in the presence of $Cu^{2+}$ or $Hg^{2+}$ was investigated. With the addition of water, the absorption at 483 nm of **1**–$Hg^{2+}$ system disappeared gradually and transformed into the original absorption at 438 nm of free **1** (Fig. S1, Supplementary data). This is probably due to the small stability constant of **1**–$Hg^{2+}$. In the presence of water, the $Hg^{2+}$ ion tended to form the hydrate ion instead of forming a complex with compound **1**. As for the absorption of **1**–$Cu^{2+}$ system, it had little change with the increasing water content. This means that the chemosensor can be used for the detection of the $Cu^{2+}$ in aqueous solution, which is very important for the application of **1** in biological systems.

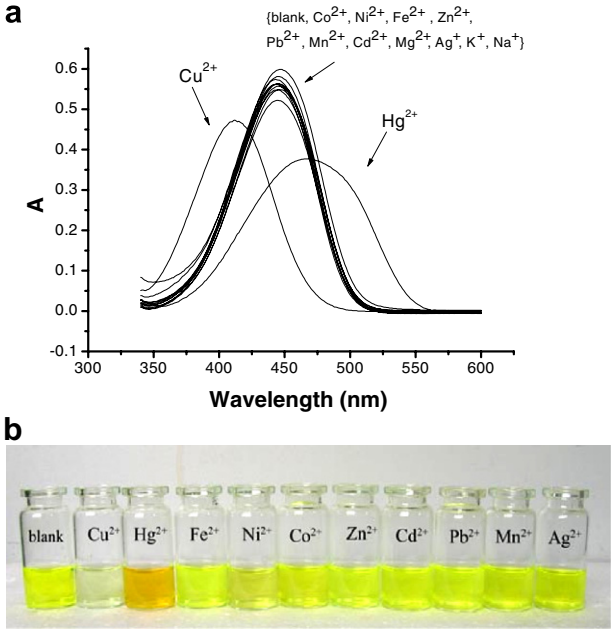



**Figure 1.** (a) UV–vis spectra of **1** in methanol solution in the presence of different metal ions (1 equiv of $Cu^{2+}$, 1 equiv of $Hg^{2+}$, 5 equiv of other metal ions). (b) The color response of **1** to different transition metal ions.

In order to have the optimum condition for the realization of peak selectivity and practicability for the target metal ions, the further UV–vis titration of **1** with $Cu^{2+}$ was carried out in aqueous methanol solution and UV–vis titration of **1** with $Hg^{2+}$ was carried out in methanol solution. The changes in the absorption spectra of **1** upon the addition of $Cu^{2+}$ are shown in Figure 2a. The absorption at 437 nm ($\varepsilon = 16{,}000\ M^{-1}\ cm^{-1}$) decreased sharply with the gradual addition of $Cu^{2+}$ to the solution of **1**. At the same time the high-energy bond at 403 nm increased prominently ($\varepsilon = 12{,}500\ M^{-1}\ cm^{-1}$) with two isosbestic points at 417 nm and 305 nm. This was attributed to the formation of a **1**–$Cu^{2+}$ complex.[10] The presence of $Cu^{2+}$ induced a color change from yellow green to almost colorless. From the absorption spectra of **1**–$Cu^{2+}$, we can see that not only was the absorption band at 438 nm blue shifted but also the developed new band at 403 nm had a smaller molar absorption coefficient than the original one. The possible reason is that the lone pair electron of the 4-amino group in the chromophore may perpendicularly coordinate to the $Cu^{2+}$, which was located in the cavity of macrocyclic dioxotetraamine. The coordination has raised the energy of the charge transfer from the amino group to the carbonyl fragment in the 1,8-naphthalimide group. This five-coordinated complex had been confirmed in some similar macrocyclic derivatives.[11]

However, with the gradual addition of $Hg^{2+}$ to the methanol solution of **1**, the absorption at 438 nm ($\varepsilon = 12{,}600\ M^{-1}\ cm^{-1}$) was reduced in intensity and a new absorption band at ca. 483 nm ($\varepsilon = 13{,}400\ M^{-1}\ cm^{-1}$) was developed (Fig. 2b). The color of solution changed from yellow green to orange. The appear-

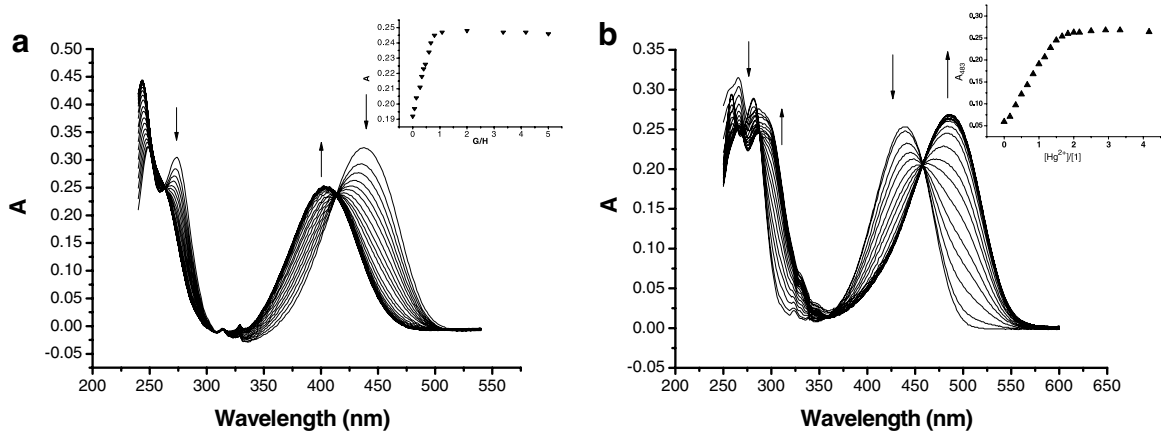



**Figure 2.** (a) UV–vis titration of **1** ($2\times10^{-5}$ M) in the presence of different concentrations of $Cu^{2+}$ in $H_2O$–$CH_3OH$ (3:1, v/v, Britton–Robinson buffer, pH = 7.1). The inset shows absorbance at 402 nm versus equivalents of $Cu^{2+}$. (b) UV–vis titration of **1** ($2\times10^{-5}$ M) in the presence of different concentrations of $Hg^{2+}$ in methanol solution. The inset shows absorbance at 483 nm versus equivalents of $Hg^{2+}$.

ance of the new absorption band and the isosbestic points at 458 nm and 360 nm indicated the presence of a unique complex in equilibrium with the free ligand. When $Hg^{2+}$ was coordinated to chemosensor **1**, it could not enter into the macrocyclic cavity completely due to the large radius of $Hg^{2+}$.[12] The 4-aminonaphthalimide in chemosensor **1** must be together with the macrocyclic dioxotetraamine to coordinate $Hg^{2+}$. The complexation was evidenced by the $^1H$ NMR spectrum of **1** with $Hg^{2+}$ (Fig. S2, Supplementary data). The addition of $Hg^{2+}$ ion resulted in not only a significant broadening of the proton peaks of the macrocyclic dioxotetraamine moiety but also an upfield shifting of the 7-ArH proton signal from 8.69 ppm to 8.50 ppm. Compared with $Cu^{2+}$, the polarization of $Hg^{2+}$ was easier; in this case the intramolecular d–π interaction between $Hg^{2+}$ and the chromophore in chemosensor **1** was probably existent so as to form a **1**–$Hg^{2+}$ complex. This similar phenomenon of d–π interaction in some coordinated systems had also been reported before.[13] Till now there is not enough evidence to completely exclude another possibility, that is, the deprotonation of the secondary amine conjugated to 1,8-naphthalimide may occur in the complex of **1**–$Hg^{2+}$. Further investigations are necessary to confirm the accurate coordinating mode of the **1**–$Hg^{2+}$ complex.

The Job plots of **1** with $Cu^{2+}$ and $Hg^{2+}$ showed a maximum of absorption at $X = 0.5$ (Fig. S3, Supplementary data), which indicated that a 1:1 complex was formed.[14] The stability constants $K_s$ were measured from the Benesi–Hildebrand plot of $A_0/(A_0-A)$ against $[M]^{-1}$, which showed a linear relationship, with the characteristic of a 1:1 binding.[15] The stability constants of **1**–$Cu^{2+}$ and **1**–$Hg^{2+}$ were 10,074 $M^{-1}$ and 5018 $M^{-1}$, respectively. The $K_s$ values obtained suggested that the $Cu^{2+}$ formed more stable complexes with compound **1** than did $Hg^{2+}$. This fact was also confirmed by the competition experiments carried out for the complexation of **1** between $Cu^{2+}$ and $Hg^{2+}$. The absorption of the **1**–$Hg^{2+}$ system was only influenced by $Cu^{2+}$ ion, but $Hg^{2+}$ did not interfere with the absorption of **1**–$Cu^{2+}$ in the aqueous solution (Fig. S4, Supplementary data). Therefore **1** could be used for the detection of $Cu^{2+}$ in the presence of other competing metal ions, including $Hg^{2+}$ in neutral aqueous solution. In addition chemosensor **1** can be also utilized for the qualitative analysis (color change) of $Hg^{2+}$ in the presence of other competing ions except $Cu^{2+}$ in methanol (Fig. S5, Supplementary data).

The changes in the fluorescence properties of **1** caused by different metal ions, including $Cu^{2+}$, $Hg^{2+}$ $Fe^{2+}$, $Co^{2+}$, $Ni^{2+}$, $Zn^{2+}$, $Mn^{2+}$, $Cd^{2+}$, $Pb^{2+}$, $Ag^{+}$, $Na^{+}$, $K^{+}$, and $Mg^{2+}$ were measured, respectively, in methanol. The fluorescence of **1** quenched markedly with the gradual addition of $Cu^{2+}$ or $Hg^{2+}$, but the fluorescence properties of **1** was only slightly influenced by other metal ions (Fig. 3).

The fluorescence titration of **1** with $Cu^{2+}$ was carried out in an aqueous methanol solution, which is shown in Figure 4. The fluorescence intensity of **1** at 538 nm was linearly reduced with the increasing concentration of $Cu^{2+}$.

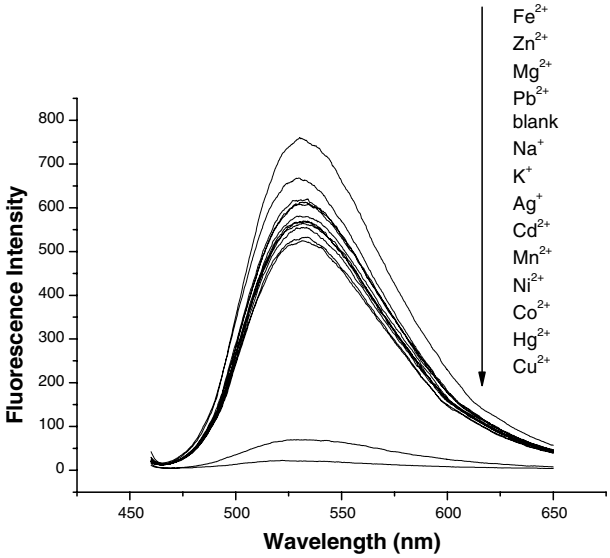



**Figure 3.** Fluorescence spectrum of **1** ($5\times10^{-6}$ M) in methanol in the presence of several metal ions ($[Cu^{2+}] = 5\times10^{-6}$ M, $[Hg^{2+}] = 10^{-5}$ M, $[M] = 2.5\times10^{-5}$ M). $\lambda_{ex} = 451$ nm.

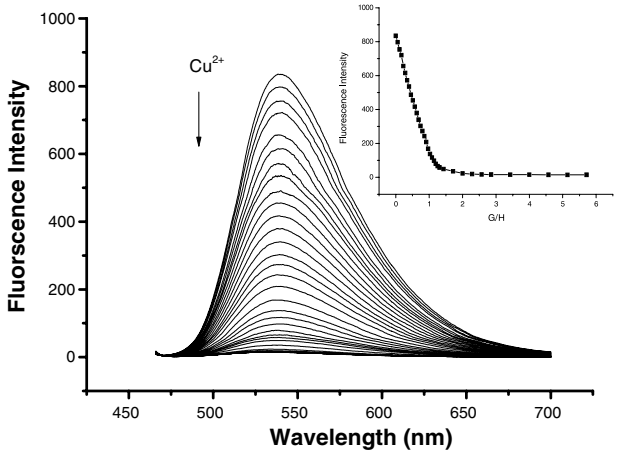



**Figure 4.** Fluorescence titration of **1** ($5 \times 10^{-6}$ M) in the presence of different concentrations of $Cu^{2+}$ in $H_2O$–$CH_3OH$ (3:1, v/v, Britton–Robinson buffer, pH = 7.1). The inset shows fluorescence intensity at 538 nm versus equivalents of $Cu^{2+}$.

The fluorescence intensity was quenched more than 95% while the concentration of $Cu^{2+}$ reached that of **1**. The fluorescence titration of **1** with $Hg^{2+}$ was achieved in a methanol solution. The change in the fluorescence intensity of **1** at 538 nm with the increasing concentration of $Hg^{2+}$ is similar to the case of $Cu^{2+}$. After the addition of 2 equiv of $Hg^{2+}$, the fluorescence intensity was quenched more than 90% and maintained the constant minimum. The sensor was found to have detection limits of $3 \times 10^{-7}$ M and $7 \times 10^{-7}$ M for $Cu^{2+}$ and $Hg^{2+}$, respectively,[16] which was sufficiently low for the detection of $Cu^{2+}$ and $Hg^{2+}$ in many chemical and biological systems.

The possible reason for the fluorescence quenching is the formation of a ground-state non-fluorescent complex, which is supported by the change in the absorption spectra. The enhancement of the spin–orbit coupling[17] for **1**-$Hg^{2+}$ and energy or electron transfer[18] for **1**–$Cu^{2+}$ is presumed resulting in the fluorescence quenching.

In conclusion, we have designed and synthesized a highly selective and sensitive chemosensor for the detection of $Cu^{2+}$ and $Hg^{2+}$. The complex of macrocyclic dioxoteraamine derivative with $Hg^{2+}$ has seldom been reported in the previous literature. The chemosensor can be utilized for the detection of $Cu^{2+}$ in the presence of other competing metal ions in neutral aqueous solution by both the selective coloration and the change in the fluorescence spectra. Besides, chemosensor **1** can also be utilized for the qualitative analysis (color change) and quantitative analysis (fluorescence quenching) of $Hg^{2+}$ in the absence of $Cu^{2+}$. So chemosensor **1** is a novel and unique colorimetric and fluorescent chemosensor for the optical detection of $Cu^{2+}$ or $Hg^{2+}$.

## Acknowledgement

We gratefully acknowledge the financial support from the Natural Science Foundation of China (No. 20272045 and No. 20672085).

## Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.05.155.

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8. *4-(4-Ethylamino-N-butyl-1,8-naphthalimide)-1,4,7,10-tetraazacyclotridecane-11,13-dione* (**1**) in 37% yield: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 8.84 (d, $J = 7.2$ Hz, 1H, 7-Ar*H*), 8.53 (d, $J = 9.0$ Hz, 1H, 5-Ar*H*), 8.36 (d, $J = 8.1$ Hz, 1H, 2-Ar*H*), 7.66–7.61 (m, $J = 8.1$ Hz, 2H, 6-Ar*H*, N*H*), 6.64–6.61 (m, $J = 8.1$ Hz, 2H, 3-Ar*H*, N*H*), 6.51 (s,1H, N*H*), 4.10 (t, $J = 7.2$ Hz, 2H, $NHCH_2CH_2N$), 3.48 (m, 2H, $CH_2CH_2CH_2CH_3$), 3.48–3.37 (m, 4H, $CONHCH_2CH_2$), 3.23 (s, 2H, $COCH_2CO$), 2.88 (m, 2H, $NHCH_2CH_2N$), 2.64–2.57 (m, 8H, $CH_2NHCH_2CH_2NCH_2$), 1.70–1.62 (m, $J = 7.5$ Hz, 2H, $CH_2CH_2CH_2CH_3$), 1.46–1.38 (m, $J = 7.2$ Hz, 2H, $CH_2CH_2CH_2CH_3$), 0.96 (t, $J = 7.2$ Hz, 3H, $CH_2CH_2CH_2CH_3$). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta =$ 169.3, 167.5, 164.8, 164.3, 150.3, 134.6, 131.3, 129.5, 128.3, 124.7, 122.7, 120.7, 109.9, 104.2, 54.0, 53.8, 52.9, 49.5, 46.9, 46.4, 42.1, 40.1, 38.8, 37.6, 30.5, 20.6, 14.1; IR(KBr): $\nu$/cm$^{-1}$ 3341.2, 2956.3, 1678.4, 1639.1, 1580.0, 1550.4, 1393.7, 1358.8, 1299.2, 1244.0, 1112.6, 775.2; ESI MS found: $m/z = 509.3$ $(M+H)^+$; Anal. Calcd for $C_{27}H_{36}N_6O_4$: C, 63.76; H, 7.13; N, 16.52. Found: C, 63.61; H, 7.15; N, 16.49.
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