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A new sensitive and selective chromogenic and fluorescent chemodosimeter for Hg(II) in aqueous media and its application in live cell imaging

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ABSTRACT

A new rhodamine-based chemodosimeter(**L2**) was synthesized and characterized, which contained a tosyl group acted as a strong electron acceptor. As expected, **L2** exhibited high selectivity and excellent sensitivity in both absorbance and fluorescence detection of Hg^{2+} in aqueous solution. The coordination of **L2** with Hg^{2+} was chemically nonreversible and it was based on the fact that Hg^{2+} exhibited a strong thiophilic affinity. Addition of Hg^{2+} to an ethanol aqueous solution of **L2** resulted in a color change from color-less to obvious pink color, these significant changes in color could be used for naked-eye detection. Furthermore, fluorescence imaging experiments of Hg^{2+} ions in living MGC803 cells demonstrated its value of practical applications in biological systems.

1. Introduction

Recently, the design and development of fluorescent chemodosimeters for the detection of heavy- and transition- metals ions have received considerable attentions because fluorescent chemodosimeters have several advantages over other methods such as high sensitivity, selectivity, and real-time monitoring [1]. Mercury is one of the most prevalent toxic metals in both the environment and biological system [2]. Mercury can cause serious and irreversible DNA damage, mitosis impairment and nervous system defects [3]. Therefore, there is a high demand for developing artificial receptors with high selectivity and sensitivity for chemical and biochemical agents for determination of the Hg^{2+} ion in both the environment and biological systems.

As is well known, rhodamine derivatives having a spirolactam structure is non-fluorescent and colorless, whereas ring-opening of the spirolactam give rise to a strong fluorescence emission and a pink color [4–9]. As their excellent photochemical properties, such as high fluorescence quantum yields, large molar extinction coefficient, long excitation and emission wavelengths, rhodamine derivatives have been actively utilized as fluorescent or colorimetric chemodosimeters for detection of Hg^{2+} [10–14]. According to the strong thiophilic affinity of Hg^{2+}, many chemodosimeters based on rhodamine contained an “S” group [11–15]. As the reported mechanism, with the leaving of HgS, the intramolecular nucleophilic reaction is accomplished, which triggered a domino reaction to bring about the opened-ring form of the rhodamine spirolactam. However, there were only a few chemodosimeters that can be used in biological systems [12], there is still an intense demand for new efficient Hg^{2+} optical chemodosimeters, especially those that can work in biological systems with high selectivity and sensitivity.

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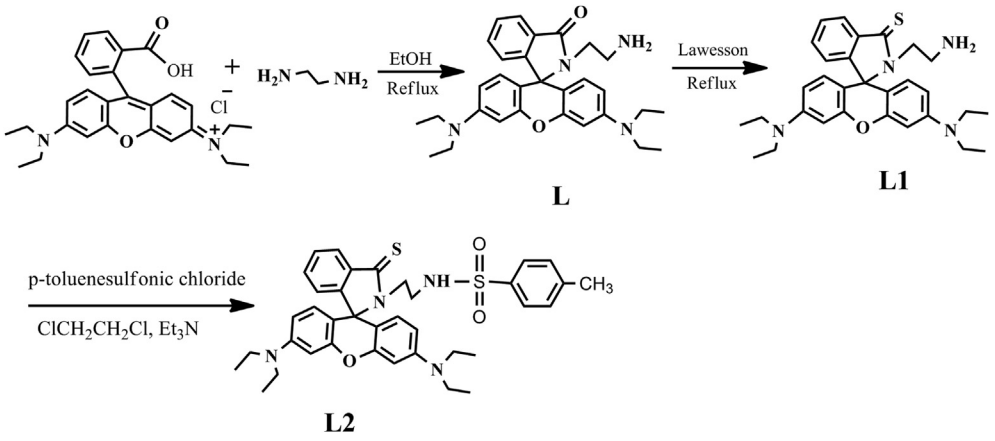

Scheme 1. Synthetic route of **L2**.

Herein, we reported a novel chemodosimeter **L2** which bearing a rhodamine and sulfonamide group (Scheme 1). Chemodosimeter **L2** contained a "C═S" group, and as expected, it exhibited a nonreversible, highly selective and sensitive recognition toward Hg^{2+} over other examined metal ions in CH_3CH_2OH–H_2O (1/1, v/v). Additionally, the significant changes in the fluorescence color could be used for naked-eye detection, and according to the fluorescence imaging experiments of Hg^{2+} ions in living MGC803 cells, **L2** could be used for detecting Hg^{2+} in biological samples.

2. Experimental

2.1. Apparatus

A Lambda 35 UV/VIS spectrometer (Perkin Elmer) was used for absorption spectra measurements. Fluorescence spectra measurements were performed on a HITACHI F-4500 fluorescence spectrophotometer, and the excitation and emission wavelength band passes were both set at 3.0 nm. The melting points were determined by an X-4 microscopic melting point apparatus with a digital thermometer (Shanghai, China). The pH was measured with a Model pHs-3C meter (Shanghai, China). ^1H and ^{13}C NMR spectra were recorded using a Bruker DTX-400 spectrometer. Samples were dissolved in $CDCl_3$ and placed in 5 mm NMR tubes. TMS was used as internal reference. ESI mass spectra were carried out on an HPLC Q-Tof HR-MS spectrometer (Waters Micromass) by using methanol as mobile phase. Fluorescence images experiments were carried out with a Nikon-80i inverted fluorescence microscope.

2.2. Materials

All chemicals and reagents were used as received from commercial sources without further purification. Solvents for chemical synthesis and analysis were purified according to standard procedures. Chloride salts of metal ions (K^+, Na^+, Ca^{2+}, Mg^{2+}, Ba^{2+}, Zn^{2+}, Fe^{2+}, Fe^{3+}, Mn^{2+}, Pb^{2+}, Cu^{2+}, Co^{2+}, Ni^{2+}, Cd^{2+}, Cr^{3+}, Hg^{2+}) and the nitrate salt of Ag^+ ions were used to evaluate the metal ion binding properties by synthesized compounds. The metal ions were prepared as 10.00 mmol/L in water solution. Double distilled water was used throughout the experiment.

2.3. Synthesis

Compound **L** and **L1** were synthesized by reported methods [13,14]. Compound **L2** was synthesized by a similar way described in a reported method [16]. The concrete way was described as follows:

To a stirred solution of compound **L1** (500 mg, 1 mmol) and Et_3N (204 mg, 2 mmol) in dry $ClCH_2CH_2Cl$ (20 ml), a solution of p-toluene sulfonyl chloride (190 mg, 1 mmol) in 10 ml dry $ClCH_2CH_2Cl$ was added in dropwise and the mixture was stirred at 0 °C for 5 h, and then stirred at room temperature for 5 h. After completion of reaction, monitored by TLC, solvent was evaporated off and water was added to the residue. The aqueous layer was extracted with $CHCl_3$(25 ml × 3) and dried over anhydrous $MgSO_4$. Purification of the crude product by silica gel column chromatography with CH_3OH/CH_2Cl_2(1/25, v/v), gave 356 mg of white solid in a yield of 54.4%. ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 1.19–1.22 (t, 12H, J = 7.0 Hz), 2.34(s, 3H), 2.84–2.88 (q, 2H, J = 5.3 Hz), 3.35–3.40(q, 8H, J = 6.7 Hz), 3.56–3.63(t, 2H, J = 6.0 Hz), 5.15–5.18(t, 1H, J = 6.0 Hz), 6.20–6.27(m, 4H), 6.43–6.33(d, 2H, J = 2.0 Hz), 7.08–7.10(q, 1H, J = 2.7 Hz), 7.21–7.23(d, 2H, J = 8.0 Hz), 7.49–7.51(t, 2H, J = 4.0 Hz), 7.60–7.62(d, 2H, J = 8.0 Hz), 8.11–8.14(t, 1H, J = 4.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): 12.56, 14.15, 18.43, 21.45, 29.71, 41.89, 43.92, 44.46, 50.86, 58.46, 73.74, 97.93, 99.98, 103.07, 108.31, 123.29, 125.05, 127.03, 128.47, 128.60, 129.51, 129.61, 132.73, 137.14, 137.59, 142.93, 149.23, 150.99, 153.20, 191.92. ESI-MS: m/z = 655.4 $[M + H]^+$; HR-MS: Calcd for $C_{37}H_{43}N_4O_3S_2^+$, Exact Mass: 655.2777 $[M + H]^+$, Found: 655.2784$[M + H]^+$, 677.2595$[M + Na]^+$, 693.2341 $[M + K]^+$, M.p: 178–180 °C.

3. Results and discussion

The UV–vis and Fluorescence studies were performed using a 10 μM CH_3CH_2OH solution of **L2** in CH_3CH_2OH–H_2O solution with appropriate amounts of metal ions. Solutions were shaken for about 25 min before measuring the absorption and fluorescent intensity in order to make the metal ions chelate with the sensors sufficiently. The solution of **L2** was colorless and found to be very stable in the above-mentioned solution system for more than one week. In addition, a very weak fluorescence signal was observed at 590 nm (Fig. 1) upon excitation at 520 nm, confirming the presence of ring-closed spirolactone.

3.1. Fluorescence spectral responses of L2

Considering the strong thiophilic affinity of Hg^{2+}, we investigated the color and fluorescence response of **L2** to Hg^{2+}. As shown in Fig. 1, the fluorescence spectra (λ_{ex} = 520 nm) of **L2** measured in CH_3CH_2OH–H_2O (1/1, v/v) with the addition of respective metal cations. There was very weak fluorescence signal (at 590 nm) in the