Inorganic Chemistry Communications 50 (2014) 84–87

Contents lists available at ScienceDirect

Inorganic Chemistry Communications

journal homepage: www.elsevier.com/locate/inoche

An "off–on" optical sensor for mercury ion detection in aqueous solution and living cells

Ziya Aydin [a,b], Yibin Wei [a], Maolin Guo [a,b,*]

[a] Department of Chemistry and Biochemistry, UMass Cranberry Health Research Center, University of Massachusetts Dartmouth, 285 Old Westport Road, Dartmouth, MA 02747, USA
[b] Department of Chemistry, University of Massachusetts Amherst, 710 North Pleasant Street, Amherst, MA 01003, USA

ARTICLE INFO

Article history:
Received 22 May 2014
Received in revised form 19 September 2014
Accepted 26 October 2014
Available online 28 October 2014

Keywords:
Fluorescence
Sensor
Rhodamine
Mercury ions
Live cell imaging

ABSTRACT

A rhodamine-based optical sensor Rh–3S has been developed for selective detection of Hg^{2+} in aqueous solution as well as in living cells. UV–vis and fluorescence spectroscopic studies reveal that Rh–3S shows marked sensitivity and selectivity to Hg^{2+} with a chelation-induced "off–on" response in acetonitrile (ACN)/MOPS buffer (10 mM, pH 7.3, v/v, 1:1). The Rh–3S sensor binds Hg^{2+} in a 1:1 stoichiometry with an apparent binding constant $3.71 \times 10^6\ M^{-1}$ ($\log K = 6.57$) and displays a distinct change in color and fluorescence upon the alteration of free Hg^{2+} levels in solution with a reversible response and little interference with other biological relevant metal ions. Live cell confocal imaging studies demonstrate that the sensor is also capable of imaging the presence of Hg^{2+} ions as well as its dynamic changes in live cells.

Published by Elsevier B.V.

As one of most toxic metals, mercury is widely distributed in water, air and soil, generated from both natural and artificial sources such as oceanic and volcanic eruption, mining, waste incineration and the combustion of fossil fuels, posing serious problems to human health [1]. Mercuric ion (Hg^{2+}), the ionic mercury form, shows high affinities to thiol groups, various enzymes and amino acids, leading to the dysfunction of these biomolecules and subsequently causing serious irreversible damage to the organs in cardiovascular, endocrine and central nervous systems [1–3]. It is believed that ionic mercury and its organometallic derivatives play important roles in the pathology of neurodegenerative diseases such as Amyotrophic lateral sclerosis, Parkinson's disease, and Alzheimer's disease [1–3]. Thus, there has been a tremendous interest in developing rapid, efficient and high-throughput methods for monitoring the level of Hg^{2+} in vivo and in vitro. Compared with those costly and time-consuming methods such as atomic absorption spectroscopy, inductively coupled plasma mass spectrometry (ICP-MS), and inductively coupled plasma atomic emission spectrometry (ICP-AES), optical chemosensors are greatly preferred due to its advantages in simple sample pretreatment, low need for expensive instrument as well as in-time and on-site responses.

In recent years, considerable efforts have been devoted to the development of fluorescent and colorimetric sensors for detecting Hg^{2+} ions [4,5]. Rhodamine-based sensors with "off–on" response have attracted much attention in chemosensor development due to its striking spectroscopic properties such as large molar extinction coefficients, high quantum yield and long excitation and emission wavelength suitable for live cell imaging [6–16]. However, only a few Hg^{2+} sensors have demonstrated their capability in live cell imaging [9,11,12]. It is still highly

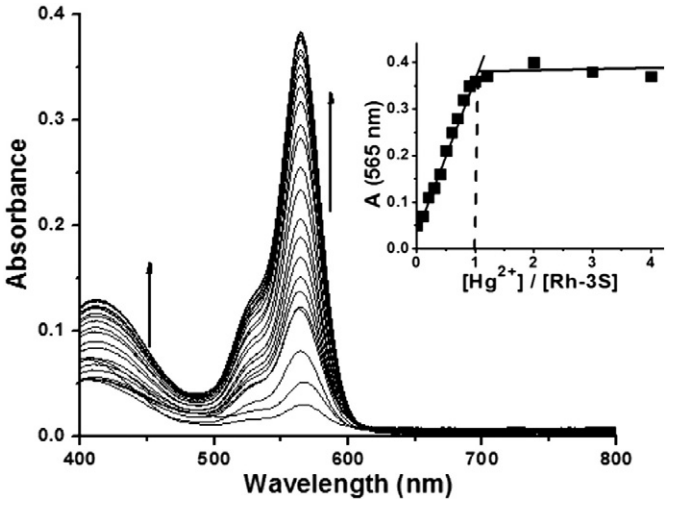


Fig. 1. Titration of 20 μM Rh–3S with increasing concentrations of $HgCl_2$ (2, 4, 6, 10, 12, 14, 16, 18, 20, 28, 36, 44, 52, 60 and 80 μM, respectively) in ACN/MOPS buffer (10 mM, pH 7.3, v/v 2:1). The absorption intensities were measured at 565 nm.

* Corresponding author at: Department of Chemistry and Biochemistry, UMass Cranberry Health Research Center, University of Massachusetts Dartmouth, 285 Old Westport Road, Dartmouth, MA 02747, USA.
E-mail addresses: mguo@umassd.edu, mguo@chem.umass.edu (M. Guo).

http://dx.doi.org/10.1016/j.inoche.2014.10.026
1387-7003/Published by Elsevier B.V.

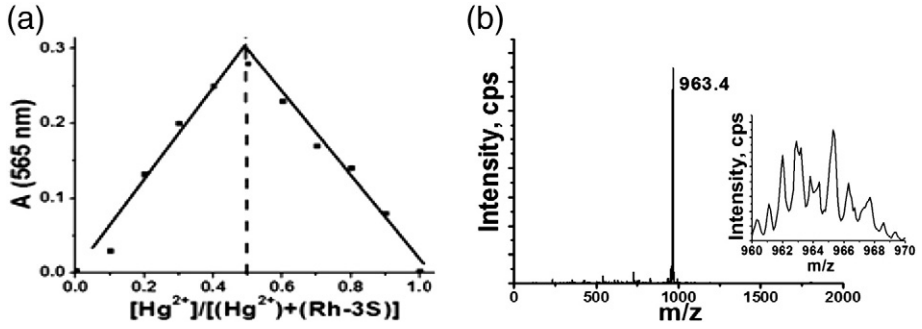
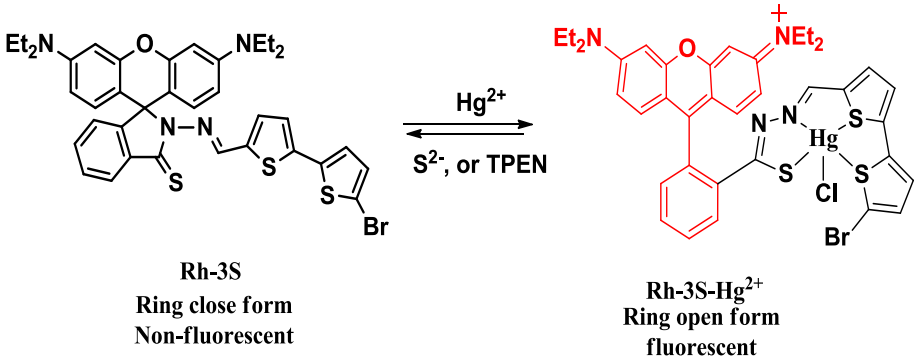


Fig. 2. (a) Job's plot of Rh–3S and Hg^{2+} in the ACN/MOPS buffer (10 mM, pH 7.3, v/v 1:1). The absorbance was collected at 565 nm. (b) ESI-MS spectrum of the solution of Rh–3S with Hg^{2+} (1 μM each in ACN).



Scheme 1. Proposed reversible 1:1 binding mode between Rh–3S and Hg^{2+}.

desirable to develop Hg^{2+} sensors with good aqueous solubility and potential applications in living cell imaging [17]. We have been devoted to designing optical sensors for detecting metal ions such as iron and copper as well reactive oxygen species (ROS) [18–22]. Herein, we have developed a novel optical chemosensor for mercury, Rh–3S, which incorporates a rhodamine fluorophore with an Hg^{2+}-binding receptor moiety composed of one nitrogen and three sulfur atoms by virtue of both the high thiophilicity of Hg^{2+} and strong nucleophilicity of sulfur.

Rh–3S was synthesized in two steps (Scheme S1) by refluxing rhodamine B hydrazine [23] and 5-bromo-2,2′-bithiophene-5′-carboxaldehyde in ethanol, followed by the thionation of carbonyl group of the product obtained in the first step [24]. The detailed synthetic procedures and characterization are described in the Supporting information.

First, we evaluated the optical properties of Rh–3S and its interactions with Hg^{2+} in a mixture solvent of acetonitrile (ACN)/3-(N-morpholino)propanesulfonic acid (MOPS) buffer (10 mM, pH 7.3, v/v, 1:1) (Fig. 1). Rh–3S (20 μM) in ACN/MOPS buffer solution is yellowish with only very weak absorption over 500 nm, indicating that the rhodamine moiety was dominant in the spirolactam form. When Hg^{2+} was added to the solution, the solution instantaneously turned pink with an absorption band that appeared at 565 nm and increased in intensity with the gradual addition of Hg^{2+}, suggesting the formation of ring-opened rhodamine species [18–20]. This rapid response to mercury is very important in practical application for real-time detection. The titration curve (a plot of Rh–3S versus Hg^{2+} concentration) increased linearly and plateaued at 1:1 ratio of the sensor and Hg^{2+}, suggesting the formation of a 1:1 Hg^{2+}/Rh–3S complex. The binding constant of this complex was determined to be $3.71 \times 10^6\ M^{-1}$ (log K = 6.57) by following a method reported previously [25], using absorption values at 565 nm (the equations were described in the Supplementary material). The stoichiometry of Rh–3S–Hg^{2+} complex was further confirmed by Job's method (Fig. 2a) and is supported by mass spectrometric analysis. Job's plot, using continuous variation with a total concentration of 20 μM Rh–3S and Hg^{2+}, exhibited a maximum absorbance (at 565 nm) when the molecular fraction of Hg^{2+} and Rh–3S was close to 1:1, suggesting a 1:1 binding ratio of Rh–3S

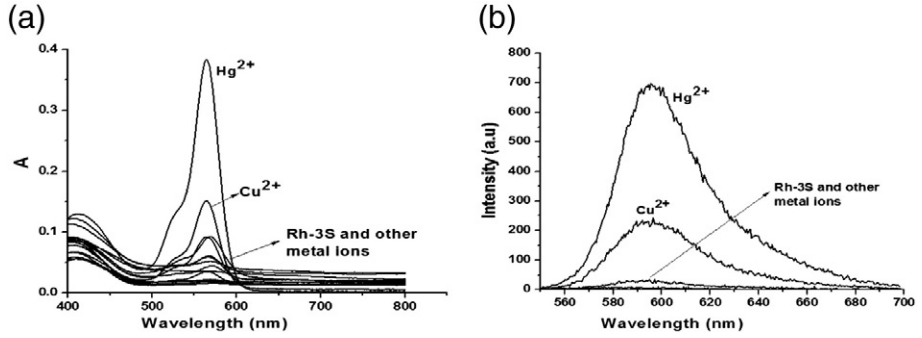


Fig. 3. (a) Absorption responses of 20 μM Rh–3S to various metal ions (20 μM for Zn^{2+}, Cr^{3+}, Ni^{2+}, Hg^{2+}, Fe^{3+}, Mn^{2+}, Ag^{+}, Pb^{2+}, Fe^{2+}, Cu^{+}, Cu^{2+}, and Co^{2+}; 100 μM for Na^{+}, K^{+}, Mg^{2+}, and Ca^{2+}) in ACN/MOPS buffer (10 mM, pH 7.3, v/v 1:1). (b) Fluorescence response ($\lambda_{Ex}/\lambda_{Em}$ 510/580 nm, filter 515 nm) of 20 μM Rh–3S to various metal ions (20 μM for Ni^{2+}, Cu^{+}, Cu^{2+}, Zn^{2+}, Pb^{2+}, Fe^{2+}, Fe^{3+} Cr^{3+}, Hg^{2+}, Mn^{2+}, Ag^{+}, and Co^{2+}; 100 μM for K^{+}, Na^{+}, Ca^{2+} and Mg^{2+}) in the ACN/MOPS buffer (10 mM, pH 7.3, v/v 1:1).