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Highly sensitive and selective reversible sensor for the detection of Cr^{3+}

Aruna J. Weerasinghe, Carla Schmiesing, Ekkehard Sinn *

Department of Chemistry, Western Michigan University, Kalamazoo, MI 49008, USA

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ABSTRACT

A new fluorescent sensor capable of sensing Cr^{3+} has been synthesized. Complexing with Cr^{3+} triggers the formation of a highly fluorescent ring-open form which is pink in color. The sensor shows extremely high fluorescence enhancement upon complexation with Cr^{3+} and it can be used as a 'naked eye' sensor. Binding of Cr^{3+} was found to be reversible as the pink color disappears with excess EDTA.

Trivalent chromium, Cr^{3+}, is an important metal for human and animal biology as it is involved in several biochemical processes at the cellular level.[1] Chromium deficiency can increase the risk factors associated with diabetes and cardiovascular diseases.[2] In addition, chromium is a known environmental pollutant that accumulates due to agricultural and industrial activities.[3] Therefore, great importance is attached to developing selective chemosensors for chromium. Due to its simplicity, selective fluorimetric detection of Cr^{3+} has great advantages over other detection techniques such as electrochemical[4] and potentiometric.[5] Trivalent chromium is one of the most effective fluorescent quenchers known due to its paramagnetic nature which also makes it difficult to develop a turn-on sensor. In the recent past, several attempts have been made to develop chemosensors to detect paramagnetic species.[6]

Rhodamine B is extensively used as a chemosensor due to its remarkable properties such as a high absorption coefficient, high fluorescent quantum yield, and excitation and emission within visible wavelengths.[7] In addition, the equilibrium between the nonfluorescent spirocyclic form and the highly fluorescent ring-open form provides a better model for the development of turn-on sensors. Recently, several rhodamine B-based turn-on fluorescent sensors have been developed for metal ions.[8] Several successful attempts have been made to develop selective fluorescent sensors based on rhodamine B for Cu^{2+},[9] Pb^{2+},[8] Hg^{2+},[10]and Fe^{3+}.[11] In all these sensors, the mechanism involves the formation of a ring-open form from the spirolactam form upon the binding of the cation, resulting in fluorescence enhancement (550–600 nm).

Recently, Mao et al. developed a rhodamine-6G-based turn-on sensor for Cr^{3+}.[12] Another chemosensor was reported by Zhou et al. based on rhodamine B for the detection of Cr^{3+} in living cells.[13] Our sensor shows extremely high sensitivity compared to the above-mentioned Cr^{3+} sensors attributed to the very high association constants for the binding of Cr^{3+}-(vide infra). The sensitivity of our sensors matches that of the powerful Hg^{2+} sensor developed by Zhan et al.[10a]

We report compound **1** as a new fluorescent sensor for Cr^{3+}. Sensor **1** shows very good sensitivity as well as selectivity for Cr^{3+}. Both nitrate and perchlorate salts of chromium yielded essentially the same result. The one metal which showed interference was Hg^{2+}, for which the nitrate salt showed emission enhancement while the perchlorate did not.

As shown in Scheme 1, the rhodamine B derivative **1** was prepared in 81% yield by reacting **2**[9a] with thiophene-2-furanaldehyde in an equal molar ratio in ethanol.[14] The structure was confirmed using ^1H NMR, ^{13}C NMR, mass spectra, and X-ray crystallography (Supplementary data). Single crystal was grown from CH_3CN solution and the crystallographic data confirmed the presence of the spirolactam form of the structure (Fig. 1).

Compound **1** was designed to bind metal ions via the carbonyl O, inamine N, and thiophene S as donors. All the spectroscopic studies were performed in acetonitrile in which sensor **1** formed a colorless solution that was stable for more than one week. The solution of compound **1** was very weakly fluorescent in the absence of any analyte due to the predominant ring-closed spirolactone. This was further confirmed by the ^{13}C NMR signal at δ 66.26 corresponding to C-1 (Fig. 1). The absorption spectra showed no peak above 400 nm but upon the addition of Cr^{3+}, a new peak appeared at 559 nm with a shoulder at 520 nm (Supplementary

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* Corresponding author. Tel.: +1 269 387 2832; fax: +1 269 387 2909.
E-mail addresses: ekk.sinn@wmich.edu, esinn@mst.edu (E. Sinn).

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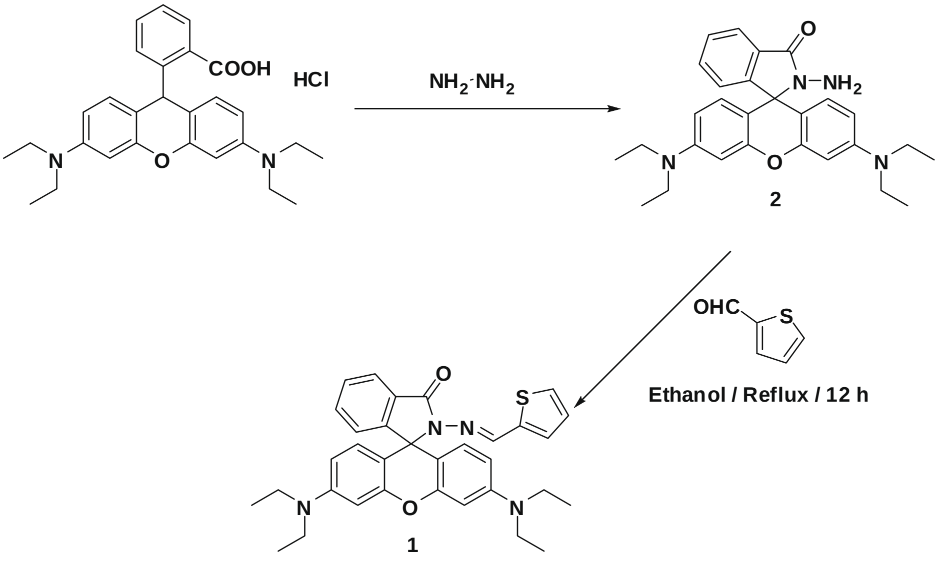

Scheme 1. Synthetic pathway of **1**.

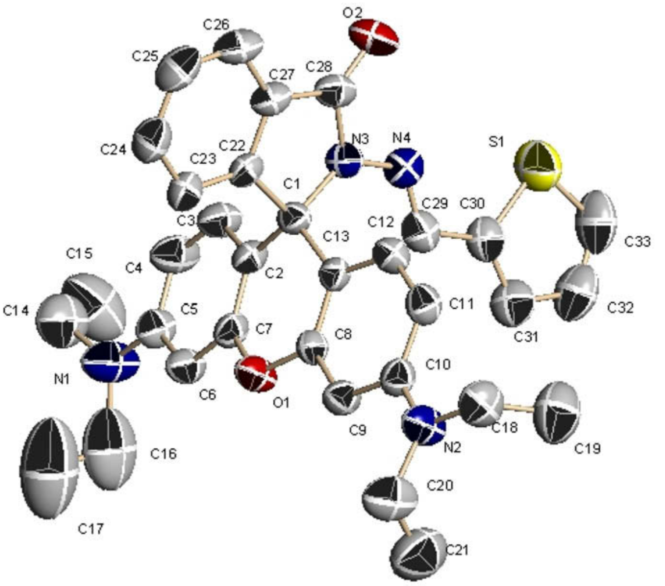

Figure 1. X-ray crystal structure of **1**.

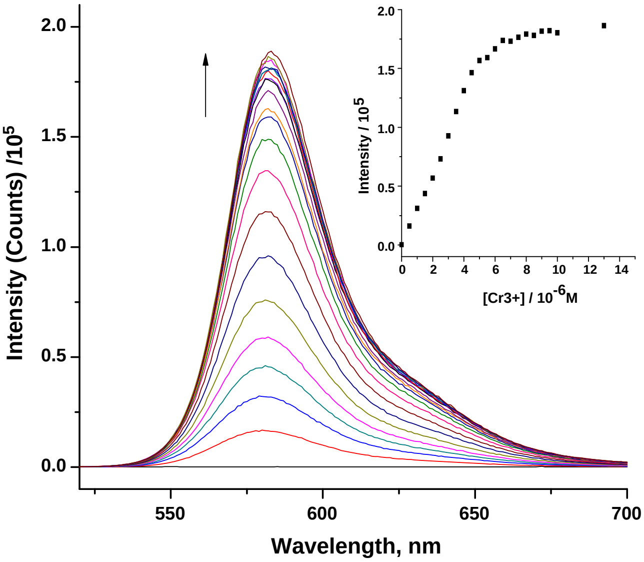

Figure 2. Fluorescence changes of **1** (10 μM) with Cr^{3+} (0–13 μM) in CH_3CN.

data). Meanwhile the solution turned pink instantaneously as a result of the ring-open structure formation caused by Cr^{3+} binding. Job's plot indicated a 1:1 binding stoichiometry between sensor and Cr^{3+} with association constant[15] $2.0 \times 10^4\ M^{-1}$.

The fluorescence spectrum of **1** showed a peak at 583 nm upon the addition of Cr^{3+} corresponding to the delocalization in the xanthene moiety of rhodamine. There was a significant emission intensity enhancement (>1200-fold) with 1.0 equiv of Cr^{3+} (Fig. 2), which indicates that compound **1** is an excellent turn-on sensor for Cr^{3+}.

It is very important to have a high selectivity for a good sensor system. We tested our sensor with possible interferences including nitrate salts of Na^+, K^+, Ni^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, and Pb^{2+} and chloride salts of Ca^{2+}, Mn^{2+}, Fe^{3+}, Co^{2+}, and Cu^{2+} (Fig. 3). Sensor **1** showed a certain emission enhancement with Hg^{2+} (<600-fold), while Zn^{2+} and Pb^{2+} showed very weak responses (Fig. 4). The association constant (K) was determined using Benesi–Hildebrand method[16] to be $1.0 \times 10^4\ M^{-1}$. The fluorescent enhancement of sensor **1** with Cr^{3+} peaked at 583 nm, while that with Zn^{2+} peaked at 576 nm, indicating a hypsochromic shift of 7 nm compared with that with Cr^{3+}. The hypsochromic shift w.r.t Cr^{3+} is 10 nm for Pb^{2+} where the fluorescence intensity peaked at 573 nm. All these observations indicate that sensor **1** has high sensitivity and selectivity towards Cr^{3+} over other metal ions tested. Furthermore, the prominent color change allows Cr^{3+} to be detected by the naked eye (Fig. 5).

Similar to most rhodamine-based spirolactam chemosensors, the binding of Cr^{3+} must be due to the ring-opening mechanism. Chromium can chelate with carbonyl oxygen, inamine nitrogen, and thiophene sulfur. The other three coordination sites can be occupied by nitrate ligands. Furthermore, the sensing mechanism is found to be reversible as the pink color of the complex disappears with the addition of excess EDTA.

In conclusion, we have synthesized in a very high yield the new fluorescent chemosensor **1** which is very stable in CH_3CN for more than one week. Sensor **1** showed high sensitivity and selectivity towards Cr^{3+} over other interference cations except Hg^{2+}, which showed a significant but smaller effect. We were able to use the

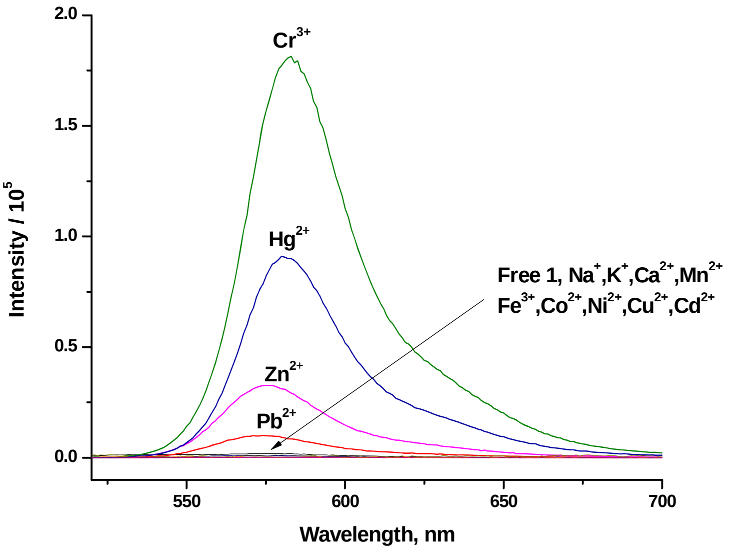

Figure 3. Fluorescence changes of **1** (10 μM) with Na^{+}, K^{+}, Ca^{2+}, Cr^{3+}, Mn^{2+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, and Pb^{2+} (10 μM) in CH_3CN (excitation at 510 nm).

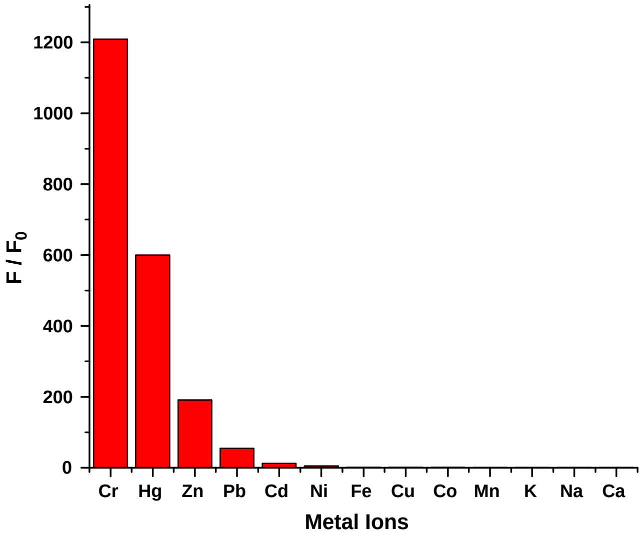

Figure 4. Fluorescence intensity of **1** (10 μM) at 583 nm with metal ions (10 μM) in CH_3CN (excitation at 510 nm).

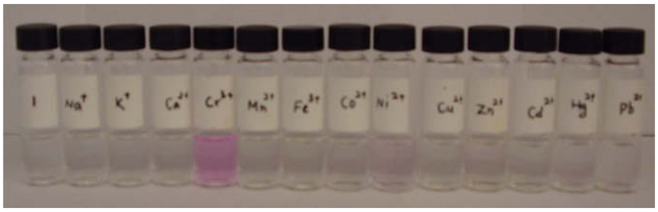

Figure 5. A photograph of compound **1** (10 μM) with different metal ions (6 μM), from left to right: 1 free, Na^{+}, K^{+}, Ca^{2+}, Cr^{3+}, Mn^{2+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, and Pb^{2+}.

ring-opening mechanism of the new rhodamine B derivatives to develop a new sensor for Cr^{3+}. Our future work will focus on developing sensors for toxic metals using the same mechanism employed in this work.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.08.025.

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14. *Preparation of* **1**: A solution of **2** (0.5 g, 1.1 mmol) and thiophene-2-carboxaldehyde (0.16 g, 1.4 mmol) in 25 ml of ethanol was refluxed for 12 h. The mixture was allowed to cool down to room temperature and the red crystals formed were separated by filtration, washed with ethanol, and dried in air (0.49 g), yield 81%. ^{1}H NMR (400 MHz, CDCl$_3$): 1.14 (12H, t, J = 6.9 Hz), 3.31 (8H, q, J = 6.9 Hz), 6.23 (2H, dd, J = 8.8 Hz, 2.6 Hz), 6.43 (2H d, J = 2.2 Hz), 6.50 (2H, d, J = 8.8 Hz), 6.90 (1H, dd, J = 4.9 Hz, 3.7 Hz), 7.06 (1H, d, J = 2.9 Hz), 7.12 (1H, dd, J = 6.2 Hz, 1.4 Hz), 7.22 (1H, d, J = 5.1 Hz), 7.47 (2H, m), 7.96 (1H, dd, J = 6.2 Hz, 1.4 Hz), 8.90 (1H, s). ^{13}C NMR (100 MHz, CDCl$_3$): δ 12.71, 44.41, 66.26, 97.98, 106.17, 108.00, 123.37, 123.98, 127.04, 127.88, 128.07, 128.39, 129.47, 129.74, 133.31, 141.42, 142.25, 148.99, 151.44, 153.40, 164.69. ESI MS: 551.33 $[M+1]^+$.
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