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Tuning the Selectivity of Two Chemosensors to Fe(III) and Cr(III)

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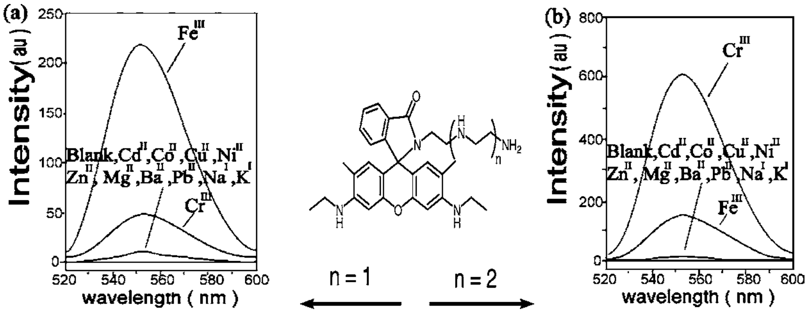
ABSTRACT



Two rhodamine-based chemosensors (1 and 2) were designed, and their sensing behavior toward metal ions was investigated by fluorescence spectroscopies. 1 and 2 achieved tuning the selectivity to Fe(III) and Cr(III) in 100% aqueous solution, whereas other ions including Cd(II), Co(II), Cu(II), Ni(II), Zn(II), Mg(II), Ba(II), Pb(II), Na(I), and K(I) induced basically no spectral change, which constituted a Fe(III)-selective and a Cr(III)-selective fluorescent chemosensor, respectively.

The development of fluorescent chemical devices is a promising field.[1] An important area within this field is the design of fluorescent chemosensors for various metal ions.[2] Ions play a fundamental role in a wide range of chemical and biological processes, and numerous efforts have been made in the development of effective fluorescent chemosensors. Sensors based on ion-induced changes in fluorescence appear to be particularly attractive due to their simplicity, high sensitivity, and instantaneous response.[1,2] The trivalent form of iron is an essential element in man. It provides the oxygen-carrying capacity of heme and acts as a cofactor in many enzymatic reactions involved in the mitochondrial respiratory chain. Meanwhile, the trivalent form of chromium is also an essential nutrient for humans, and its deficiency causes disturbances in the glucose levels and lipid metabolism. On the other hand, chromium is an environmental pollutant, and its build-up due to various industrial and agricultural activities is a matter of concern.[3] Thus, there is an urgent need to develop chemical sensors that are capable of detecting the presence of iron and chromium ions in environmental and biological samples at a physiological pH value. Considerable efforts have been devoted to developing fluorescent chemosensors for various metal ions over the last few decades. To date, some Fe(III)-selective fluorescent chemosensors have been achieved;[4] however very few fluorescent sensors for Cr(III) have been reported mainly owing to the lack of a proper selective ligand system for Cr(III), and only Sarkar et al. reported one

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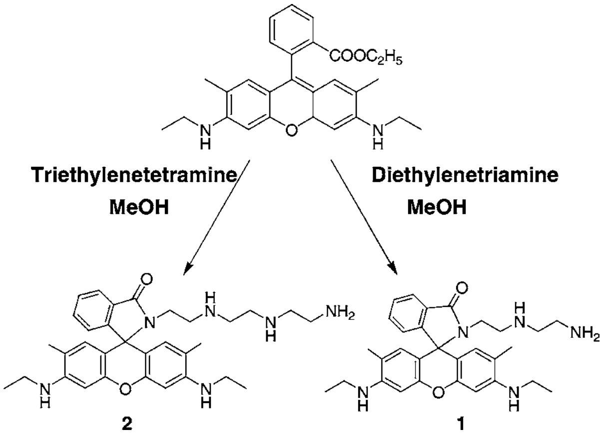
containing di(2-ethylsulfanylethyl)amine as a selective receptor moiety for Cr(III) in tetrahydrofuran.[5] Furthermore, no Cr(III) fluorescent sensors in aqueous system have been successfully designed so far.

Because paramagnetic Fe(III) and Cr(III) are described as two of the most efficient fluorescence quenchers among the transition metal ions, the signal transduction occurrence via chelation enhanced fluorescence (CHEF) with these inherent quenching metal ions is a challenging task. The rhodamine framework is an ideal mode to construct CHEF OFF−ON fluorescent chemosensors due to its particular structural property; i.e., it undergoes equilibrium between nonfluorescent spirocyclic ("off" signal) and strongly fluorescent ring-open ("on" signal) forms, and the two forms always behave with completely different fluorescent properties.[6] Heretofore, some studies on rhodamine-based chemosensors have been reported.[4d,7]

In this study, we synthesized two rhodamine-based chemosensors (**1** and **2**) with a similar structure and were able to alter their selectivity to certain ions by tiny structural alterations of the recognition moiety. The selectivity of **1** and **2** was switched between Fe(III) and Cr(III) at biological pH value in 100% aqueous solution, depending on their structures of the recognition moiety.

Scheme 1. Synthetic Pathways of **1** and **2**



As depicted in Scheme 1, compounds **1** and **2** were facilely synthesized from the reaction of rhodamine 6G with diethylenetriamine or triethylenetetriamine. Their molecular structures were confirmed by NMR and MS.[8] Although **1** and **2** are derivatives of rhodamine 6G, they form nearly colorless solutions in HEPES aqueous buffer solution (pH = 7.2), indicating that the spirocyclic forms exist predominantly. The characteristic peak near 65.0 ppm (9-carbon) in the ^{13}C NMR spectra of **1** and **2** also supports this consideration.[9] Besides, the fluorescence characteristic of rhodamine could not be observed for **1** and **2** between pH 6.0 and 8.0 in water, suggesting that the spirocyclic form was still preferred in this range. As the solution became even more acidic (pH < 5), however, an obvious enhancement of color and fluorescence appeared due to the formation of the open-ring state.[4d]

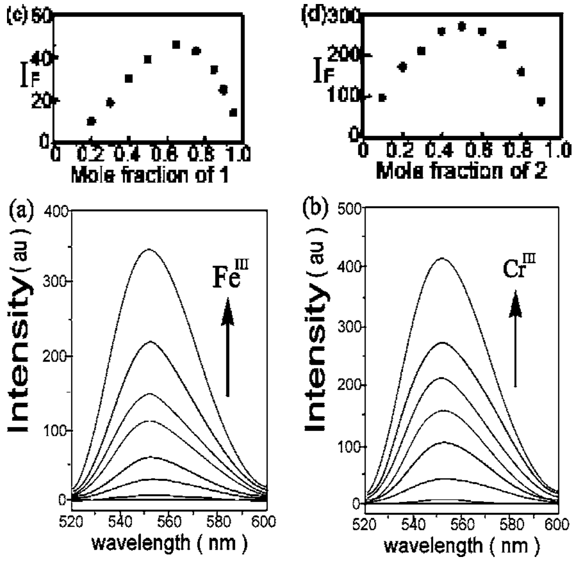


Figure 1. Fluorescence spectra of (a) **1** (10 μM) with addition of various concentrations of Fe(III) and (b) **2** (10 μM) with addition of various concentrations of Cr(III) [(a) 0, 5, 10, 20, 30, 50, and 100 μM Fe(III), respectively; (b) 0, 1, 3, 5, 7, 10, and 20 μM Cr(III), respectively] in HEPES buffer (20 mM, pH = 7.2) with an excitation at 500 nm. (c) and (d): plots according to the method for continuous variations, indicating (c) the 1:2 stoichiometry [Fe(III)/**1**] and (d) the 1:1 stoichiometry [Cr(III)/**2**] (the total concentration of either **1** and Fe(III) or **2** and Cr(III) is 20 μM).

Figure 1 shows the fluorescence emission changes of **1** in HEPES aqueous solution at pH 7.2 upon the addition of Fe(III) and of **2** upon the addition of Cr(III) in the same conditions. The fluorescence spectra were obtained by excitation at 500 nm.[10] When no metal ion was added to the solution of **1** or **2**, almost no fluorescence signal in the range

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(10) Excitation was performed at 500 nm rather than at 527 nm (the peak of the absorption spectra) to obtain a full view of the fluorescence spectra from 520 to 600 nm.

from 520 to 600 nm could be observed, whereas a significant enhancement of the characteristic fluorescence of rhodamine 6G emerged quickly, either after Fe(III) was injected into the HEPES buffer solution of **1** or after Cr(III) was injected into the HEPES solution of **2**. However, other ions, such as Co(II), Ni(II), Zn(II), Cd(II), Ag(I), Pb(II), Ba(II), Mg(II), Ca(II), K(I), and Na(I), gave no distinct response to the solution of both **1** and **2** in fluorescence spectra. For the buffer solution of **1** (10 μM), there was a large (22-fold) fluorescence enhancement (FE) at $\lambda_{em} = 552$ nm upon the addition of 5 equiv of Fe(III) (50 μM). A mild increase of fluorescence at 552 nm was also detected after addition of Cr(III) (50 μM, causing 5-fold FE) due to its low binding affinity to **1**. Other cations of interest gave no response (Figure 2a). For the buffer solution of **2** (10 μM), there was a large enhancement factor (61-fold) of fluorescence at $\lambda_{em} = 552$ nm upon the addition of 5 equiv of Cr(III) (50 μM). A moderate enhancement of fluorescence at 552 nm was also detected when the same amount (50 μM) of Fe(III) (causing 17-fold FE) was added because of the low binding affinity between Fe(III) and **2**. Other cations of interest failed to respond (Figure 2b). This interesting feature reveals that **1** and **2** can serve as selective fluorescent chemosensors for Fe(III) and Cr(III), respectively, in a 100% aqueous system.

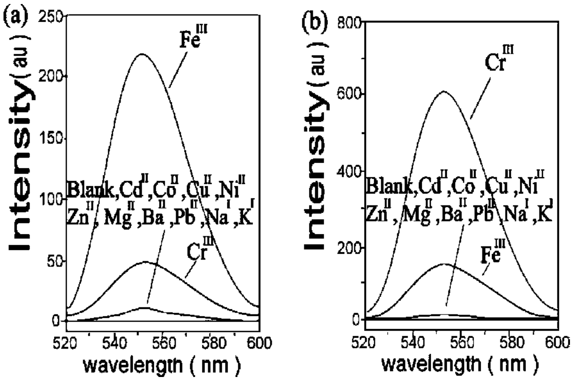

Figure 2. Fluorescence spectra of (a) **1** (10 μM) and (b) **2** (10 μM) in the absence and presence of 5 equiv of different metal ions in HEPES buffer (20 mM, pH = 7.2) with an excitation at 500 nm.

Achieving high selectivity for the analyte of interest over a complex background of potentially competing species is a challenging task in sensor development. Figure 3 illustrates the fluorescence response of **1** to Fe(III) and of **2** to Cr(III) in the presence of alkali, alkaline earth, and other transition metal ions. A background of most selected metals does not interfere with Fe(III) coordination to **1** and Cr(III) to **2** and subsequent fluorescence turn-on. The characteristics of Fe(III) and Cr(III) are so similar that, generally speaking, Cr(III) is able to affect the Fe(III)-selective chemosensor to a certain extent and vice versa.[4d,5]

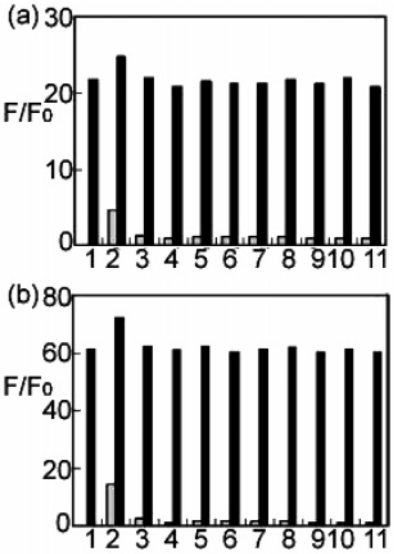

Figure 3. Metal−ion selectivity of (a) **1** and (b) **2** at pH 7.2 (20 mM HEPES). The light bars represent the fluorescence emission of a solution of **1** or **2** and 5 equiv of the cation of interest. The dark bars show the fluorescence change that occurs upon addition of (a) 5 equiv of Fe(III) to the solution containing **1** and the cation and (b) 5 equiv of Cr(III) to the solution containing **2** and cation. 1, blank; (a) 2, Cr,(III); (b) 2, (Fe); 3, Cd(II); 4, Cu(II); 5, Ni(II); 6, Zn(II); 7, Mg(II); 8, Ba(II); 9, Pb(II); 10, Na(I); 11, K(I). The response (F) is normalized with respect to the emission of the free dye (F_0).

As with many reported rhodamine-based spirolactam chemosensors, the selected cation-induced fluorescence enhancement of the chemosensor (**1** or **2**) is most likely the result of the spiro ring-opening mechanism (Figure 4). That is, the chelation of Fe(III) or Cr(III) with the oxygen atoms of the amide groups of **1** or **2** results in the formation of the

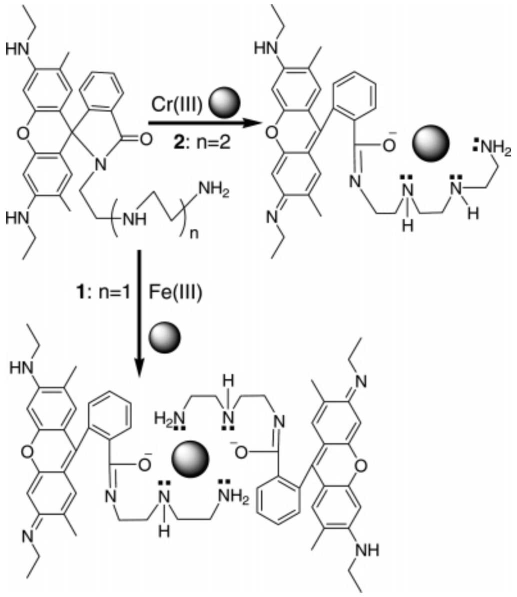

Figure 4. Proposed mechanism for the fluorescence enhancement of **1** upon the addition of Fe(III) and **2** upon the addition of Cr(III).

open-ring form. The fluorescence titration experiments were performed by means of mixing various amounts of metal ions with a HEPES buffer solution of **1** or **2** (Figure S2a−d, Supporting Information). Figure 1c,d indicates that a 1:2 stoichiometry is most possible for the binding mode of Fe(III) and **1** and that a 1:1 stoichiometry is most possible for the binding mode of Cr(III) and **2**. The stability constant (K) of **1** and **2** with Fe(III) and Cr(III) was calculated (Table 1[11]). We speculated that the distinct binding modes lead to the difference in affinity to Fe(III) and Cr(III). **1** provides only three coordination sites and thus tends to form 2:1 stoichiometry with metal ions. Yet it shows higher affinity to Fe(III) [$K_{\mathrm{Fe-}\mathbf{1}}/K_{\mathrm{Cr-}\mathbf{1}} \approx 6$], as discussed above. **2** was obtained by a tiny structure alteration of **1** and increases by one nitrogen coordination site, resulting in 1:1 stoichiometry with metal ions. Interestingly, **2** displays the opposite outcome, relative to **1**; i.e., the affinity of **2** to Cr(III) is stronger than to Fe(III) [$K_{\mathrm{Cr-}\mathbf{2}}/K_{\mathrm{Fe-}\mathbf{2}} \approx 9$]. Accordingly, **1** and **2** tune the selectivity between Fe(III) and Cr(III).

Table 1. Stability Constant (K) of **1** and **2** with Fe(III) and Cr(III)[a]

chemosensor	metal ions	K (M^{-1})
1	Fe(III)	6428
1	Cr(III)	1057
2	Fe(III)	4731
2	Cr(III)	41600

[a] K values were estimated from the fluorescence spectral data. These values of other ions including Cd(II), Cu(II), Ni(II), Zn(II), Mg(II), Ba(II), Pb(II), Na(I), and K(I) were too low to detect.

In conclusion, we synthesized two fluorescent chemosensors using rhodamine as a fluorophore and were able to alter their selectivity to Fe(III) and Cr(III) by tiny structure alterations of the recognition moiety. The selectivity of **1** and **2** was switched between Fe(III) and Cr(III) at a neutral pH value (7.2) in 100% aqueous solution, depending on their structures. Commonly coexistent metal ions, e.g., Co(II), Ni(II), Zn(II), Cd(II), Ag(I), Pb(II), Ba(II), Mg(II), Ca(II), K(I), and Na(I), displayed little interference for both **1** and **2**. To the best of our knowledge, this is an excellent example of a fluorescent sensor for Cr(III) in aqueous solution.

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Supporting Information Available: Experimental procedures, characterization data for the compounds described, and selected spectroscopic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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[11] For the details to calculate the binding stoichiometries and the binding constants, see: (a) Connors, K. A. *Binding Constants*; Wiley: New York, 1987. (b) Polster, J.; Lachmann, H. *Spectrometric Titrations*; WCH: Weinheim, 1989.