doi:10.1246/cl.2010.100
Published on the web January 16, 2010

A Coumarin-appended Pseudo-crown for the Selective Recognition of Fe^{3+}

Shyamaprosad Goswami* and Rinku Chakrabarty
Department of Chemistry, Bengal Engineering and Science University, Shibpur, Howrah-711 103, India

(Received October 9, 2009; CL-090909)

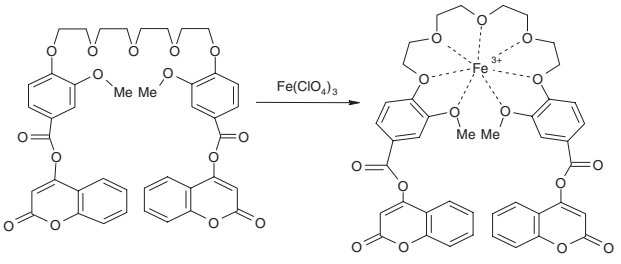
A coumarin-appended pseudo-crown (receptor **1**) demonstrates remarkable selectivity for Fe^{3+} in an acetonitrile–water (9:1 v/v) medium (which can be determined by UV–vis and fluorescence methods) over others studied e.g., Li^+, Na^+, K^+, Ca^{2+}, Mg^{2+}, Ba^{2+}, Pb^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, and Mn^{2+} which are used as their perchlorate salts.

During the recent few decades an upsurge of interest is taking place regarding the development of fluorescent probes for transition-metal ions due to their important and fundamental roles in a wide range of biological and environmental processes.[1] Although many works regarding the selective detection of transition-metal ions e.g., Cu(II), Pb(II), Zn(II), and Hg(II) have been reported, the development of receptors for the selective detection of Fe^{3+} is still rare.[2] Fluorescent sensors are particularly attractive due to their simplicity, high sensitivity, and instantaneous response. They also allow nondestructive and quick detection of ionic species by a simple fluorescence response.

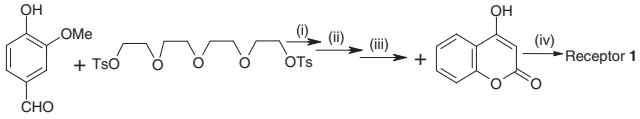
Iron is the most abundant transition-metal ion present in the earth's crust. It is an important biological element due to its diverse functions. Iron plays an indispensible role in the growth and development of living systems.[3] Iron provides the oxygen carrying capacity of heme and acts as a cofactor in many enzyme-catalyzed reactions which are involved in the mitochondrial respiratory chain. Intracellular iron level needs to be controlled because lack of iron causes severe deficiency symptoms, whereas excess iron may be equally harmful or even fatal.[4]

We report here a designed pseudo-crown based fluorescent sensor (receptor **1**) which selectively binds Fe^{3+} in CH_3CN–H_2O (9:1/v/v). The incorporated coumarin moiety acts as a fluorophore. The benzene rings attached immediately to the crown part get involved in cation–π interaction. They create a hydrophobic cavity so that the metal ions will be better encapsulated (Scheme 1) resulting in high complex stability.

Receptor **1** has been synthesized as delineated in Scheme 2. The tetraethyleneglycol ditosylate was reacted with vanillin to produce the desired dialdehyde which then after oxidation to



Scheme 1. Receptor **1** and its complexation with Fe^{3+} cation.



Scheme 2. Synthetic scheme of preparation of receptor **1**. *Reagents and conditions:* (i) K_2CO_3, TBAB, dry acetone, rt, 24 h. (ii) aq. $KMnO_4$, 3 h. (iii) oxalyl dichloride, dry CH_2Cl_2, dry DMF (cat. amount), N_2-atmosphere, 3 h. (iv) dry CH_2Cl_2, NEt_3, rt, 12 h.

carboxylic acid and acid chloride formation ultimately furnished receptor **1** upon reaction with 4-hydroxy coumarin as a colorless semisolid in an overall ca. 10.2% yield.

The preliminary UV–vis and fluorescence studies of receptor **1** were carried out with different metal cations to determine the binding ability of receptor **1** in CH_3CN–H_2O (9:1 v/v) medium. The preliminary fluorescence studies of receptor **1** shows fluorescence quenching i.e., "*switching off*" with Fe^{3+} in the presence of other interfering metal ions viz. Ni^{2+}, Zn^{2+}, Pb^{2+}, Hg^{2+}, and alkali and alkaline earth metal ions even in very large amounts in μM level (only a small quenching takes place in the case of Cu^{2+}). Therefore, for the quantitative detection of Fe^{3+}, receptor **1** can be efficiently and successfully used.

The binding abilities of receptor **1** toward cations have been studied by UV–vis as well as fluorescence methods in acetonitrile–water (9:1/v/v) medium with metal ions e.g., Li^+, Na^+, K^+, Ca^{2+}, Mg^{2+}, Ba^{2+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, Mn^{2+}, and Pb^{2+} as their perchlorate salts. The UV–vis titration spectra of receptor **1** ($c = 1.21 \times 10^{-5}$ M) exhibits a broad absorption peak at 280 nm. Upon the addition of perchlorate salts of metal ions, the titration spectra almost remain unchanged except in the case of Fe^{3+}. In this case, a remarkable and continuous increase is observed with the concomitant increase of two newly generated peaks at 309 and 359 nm (Figure 1a). The concentration of the guest cations was taken in the order of 10^{-4} M. The value of association constant (K_a) determined by this method has been found to be 5.23×10^5 (see Supporting Information).[6] The strong peaks at higher energy region are well-resolved and the peak at 359 nm can be assigned due to the pseudo-crown oxygen atoms and the guest Fe^{3+} charge-transfer transitions.[5]

The 1:1 stoichiometry of complexation is further confirmed from the value of mole fraction (0.5) in Job plot (Figure 1b).

The fluorescence titration was also performed for receptor **1** using all the perchlorate salts stated earlier to confirm the selective binding ability of receptor **1** with Fe^{3+}. Except for Cu^{2+} and Fe^{3+}, other metal ions show very little influence on the spectrum of receptor **1** (λ_{max} for receptor **1** is 343 nm). After addition of Cu^{2+} a small decrease takes place in the spectrum of **1**. Prominent and remarkable decrease takes place in the case of Fe^{3+}. This probably happens owing to the strong complex

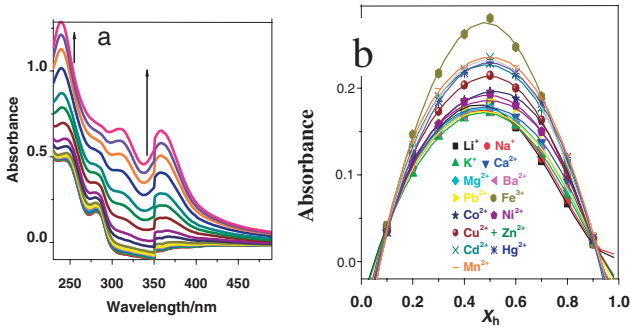


Figure 1. (a) Change in absorbance of **1** ($c = 1.21 \times 10^{-5}$ M) in the presence of increasing amounts of Fe^{3+} ($c = 2.4 \times 10^{-4}$ M) in acetonitrile–water medium; (b) Job plot of receptor **1** with different metal ions by UV–vis method, where X_h represents the mole fraction of the particular metal ions.

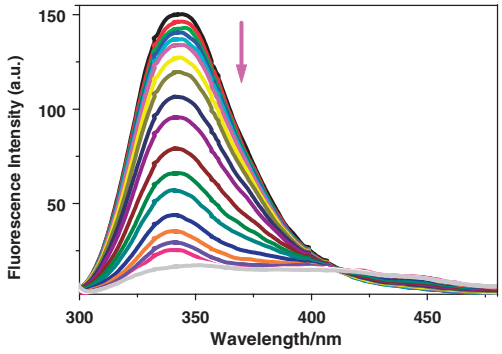


Figure 2. Fluorescence spectral changes of receptor **1** ($c = 1.21 \times 10^{-5}$ M) upon addition of iron(III) perchlorate ($c = 2.4 \times 10^{-4}$ M) in CH_3CN–H_2O (9:1 v/v).

formation between the host and the guest cation due to which the pseudo-cavity becomes more like a 21-crown-7 system resulting in a remarkable decrease in fluorescence intensity in the case of Fe^{3+} ion (Figure 2). Figure 3 depicts the response of **1** to Fe^{3+}. This instrumental read-out (Figure 3) helps us to conclude that the response of **1** toward Fe^{3+} is highest and for other cations it remains almost unchanged. For alkaline earth metal (Ba^{2+}, Ca^{2+}, and Mg^{2+}) ions the host–guest complexation leads to the molecular rigidification and thereby slight increase in the fluorescence intensity for receptor **1** is observed in those cases.

The different modes of complex formation between the host and the guest cations have also been studied using MMX method. These theoretical results are found to be similar with the experimental findings. The energy of complexation of receptor **1** and Fe^{3+} is much more lowered compared to the other ones studied (see Supporting Information)[6] i.e., inclusion of Fe^{3+} within the pseudo-crown cavity of receptor **1** is also very much energetically favorable.

Thus the designed coumarin-appended pseudo crown, receptor **1** has been synthesized which selectively binds Fe^{3+} in CH_3CN–H_2O (9:1 v/v) medium over other metal ions studied

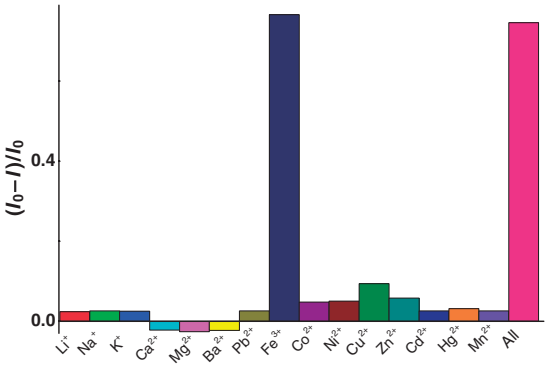


Figure 3. Fluorescence response of receptor **1** ($c = 1.21 \times 10^{-5}$ M) toward metal ion upon addition of 50 micromolar solutions of individual metal ions; all means the presence of Fe^{3+} ca. 10^{-7} M plus coexisting metal ions at ca. 10^{-5} M.

viz. Li^+, Na^+, K^+, Ca^{2+}, Mg^{2+}, Ba^{2+}, Pb^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, and Mn^{2+} as their perchlorate salts. The selectivity can be determined by UV–vis as well as by fluorescence methods.

We wish to express our appreciation to the CSIR and DST, Govt. of India for financial supports. R. C. thanks the CSIR, Govt. of India for a Senior Research Fellowship.

References and Notes

1 a) V. Amendola, L. Fabbrizzi, M. Licchelli, C. Mangano, P. Pallavicini, L. Parodi, A. Poggi, *Coord. Chem. Rev.* **1999**, *190–192*, 649. b) L. Prodi, F. Bolletta, M. Montalti, N. Zaccheroni, *Coord. Chem. Rev.* **2000**, *205*, 59.

2 a) G. E. Tumambac, C. M. Rosencrance, C. Wolf, *Tetrahedron* **2004**, *60*, 11293. b) R. Kikkeri, H. Traboulsi, N. Humbert, E. Gumienna-Kontecka, R. Arad-Yellin, G. Melman, M. Elhabiri, A.-M. Albrecht-Gary, A. Shanzer, *Inorg. Chem.* **2007**, *46*, 2485. c) X. Zhang, Y. Shiraishi, T. Hirai, *Tetrahedron Lett.* **2008**, *49*, 4178, and the references cited therein. d) A. Mitra, B. Ramanujam, C. P. Rao, *Tetrahedron Lett.* **2009**, *50*, 776. e) H. J. Jung, N. Singh, D. O. Jang, *Tetrahedron Lett.* **2008**, *49*, 2960. f) X. Zhang, Y. Shiraishi, T. Hirai, *Tetrahedron Lett.* **2007**, *48*, 5455. g) J. Mao, L. Wang, W. Dou, X. Tang, Y. Yan, W. Liu, *Org. Lett.* **2007**, *9*, 4567. h) Y. Xiang, A. Tong, *Org. Lett.* **2006**, *8*, 1549. i) S. Bae, J. Tae, *Tetrahedron Lett.* **2007**, *48*, 5389. j) M. Zhang, Y. Gao, M. Li, M. Yu, F. Li, L. Li, M. Zhu, J. Zhang, T. Yi, C. Huang, *Tetrahedron Lett.* **2007**, *48*, 3709.

3 P. Aisen, M. Wessling-Resnick, E. A. Leibold, *Curr. Opin. Chem. Biol.* **1999**, *3*, 200.

4 D. Touati, *Arch. Biochem. Biophys.* **2000**, *373*, 1.

5 L. Lopes, J. d. Laat, B. Legube, *Inorg. Chem.* **2002**, *41*, 2505.

6 Supporting Informatuion is also available online electronically on CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

