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Single sensor for multiple analytes: chromogenic detection of I^- and fluorescent detection of Fe^{3+}

Hee Jung Jung [a], Narinder Singh [b], Doo Youn Lee [a], Doo Ok Jang [a,*]

[a] Department of Chemistry, Yonsei University, Wonju, Gangwon 220-710, Republic of Korea
[b] Department of Chemistry, Indian Institute of Technology Ropar, Rupnagar, Punjab 140 001, India

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ABSTRACT

A novel receptor, designed with a combination of oxygen and nitrogen-binding sites for metal ions and hydrogen bond donor sites for anion binding, was synthesized. The receptor has been explored for the selective detection of I^- against a range of physiologically relevant anions and cations through changes in its UV–vis spectra. On the other hand, receptor-binding selectivity for Fe^{3+} over a wide linear concentration range was observed through changes in the emission spectra. This is the first Letter of a sensor capable of detecting both I^- and Fe^{3+} using two different detection modes.

Development of new synthetic receptors for the detection of physiologically important cations and anions is of considerable importance.[1] High sensitivity and easy operational use have encouraged the recent interest in UV–vis and fluorescence spectroscopy-based analytical techniques. Numerous chromogenic and fluorescent receptors which are selective for a particular analyte have been reported in the literature.[2] However, few receptors have been designed based on the concept of 'single sensor for multiple analytes', that is, analysis of more than one analyte by one receptor using a single detection method, or alternatively, an array of detection methods.[3] Currently, molecular diagnostics is moving towards the development of tests that are capable of detecting different analytes simultaneously.[4] Because a number of complex molecular events and several micronutrient deficiencies are responsible for the progression of human diseases, such parallel analyses are needed. For instance, iodine is integral to thyroid function, and its deficiency results in a spectrum of disorders including goitre, cognitive impairment and congenital abnormalities.[5] In human physiology, iron and iodine are closely associated with each other. Iron is required not only to combat anaemia but also to increase the efficacy of iodine prophylaxis.[6] The development of sensors that can recognize physiologically deleterious conditions caused by abnormal concentrations of iodine and/or iron is required. Furthermore, screening samples for multiple targets with a single sensor would lead to faster analytical processing and potential cost reductions.

To realize such a multiple-analyte sensor, it is not necessary for a synthetic receptor to possess very selective binding to a particular analyte. Instead, the receptor must incorporate different binding patterns and binding affinities to various analytes, which can be monitored by changes in the physical properties of the receptor.[7] A receptor for this purpose was engineered utilizing binding sites that are found in siderophores and abiotic Fe^{3+} sensors.[8] As depicted in Scheme 1, these binding sites comprise a phenol substituent adjacent to a nitrogen donor, such that iron binding leads to the formation of a six-membered chelate ring. In addition, this receptor offers a second binding mode consisting of an array of hydrogen bond donors.

We designed receptor **2** to actualize the 'single sensor for multiple analytes' concept. The binding sites of the receptor are directly attached to a naphthalene moiety, such that binding of anions or cations could be monitored by changes in the photophysical properties of the receptor by either UV–vis or fluorescence spectroscopy. The coordination sphere offered by the receptor is different for metal binding and anions. Therefore, dissimilar photophysical properties were expected from cation and anion binding, which would enable the sensor to operate as a single receptor for multiple analytes.

Compound **1** was synthesized by the condensation reaction of naphthalene-2,3-diamine with 2-hydroxynaphthalene-1-carbaldehyde in the presence of a catalytic amount of $Zn(ClO_4)_2$ (Scheme 2).

* Corresponding author. Tel.: +82 337602261; fax: +82 337602182.
E-mail address: dojang@yonsei.ac.kr (D.O. Jang).

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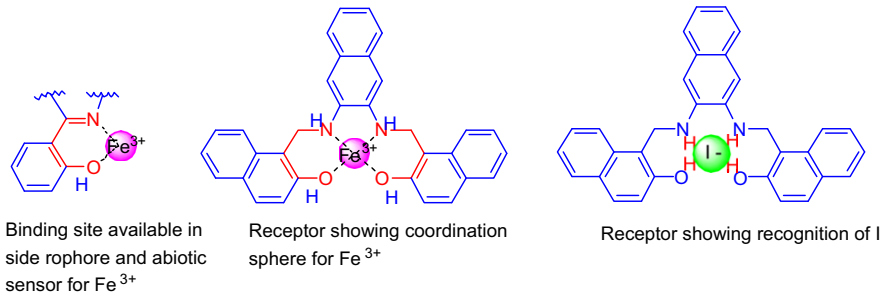
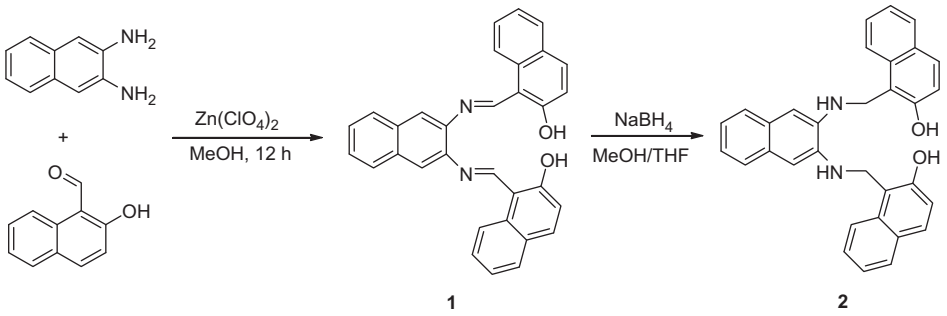


Scheme 1.



Scheme 2.

The imine linkages (CH=N) of compound **1** were reduced with $NaBH_4$. The final product **2** was characterized by elemental analysis and spectroscopic techniques.[9]

The anion and cation recognition profiles for receptor **2** were established from changes in its UV–vis and fluorescence spectra. Absorption spectra were recorded with solutions composed of 10 μM of receptor **2** and 40 μM of a particular anion. Changes in the absorption spectra of receptor **2** upon anion binding are shown in Figure 1. The graph clearly shows a selectivity of receptor **2** for iodide. Similarly, the metal-binding ability of receptor **2** was investigated from changes in its absorption spectra upon addition of metal ions. It was observed that among the metal ions examined with Fe^{3+}, Cu^{2+} and Ag^{+} binding, the bands of receptor **2** were changed with no ion selectivity (Supplementary Fig. S1). Various solvent systems and compositions to improve the selectivity of receptor **2** towards metal ions were tried unsuccessfully.

In general, metal complexation leads to changes in the photophysical properties of a receptor, which depend upon the coordination sphere, oxidation state and binding sites. Thus, one can expect different profiles for absorption and emission spectroscopy. In this context, we explored the metal and anion-binding ability of receptor **2** by fluorescence spectroscopy. Fluorescence spectra were recorded with CH_3CN solutions composed of 10 μM of receptor **2** and 10 μM of a particular cation. Although initial results were discouraging, it was found that changes in the fluorescence profile caused by metal binding depended on the solvent system. After experimenting with solvent systems and compositions, it was determined that the solvent system (THF/H_2O (1:99, v/v) HEPES buffered (pH 7.0 ± 0.1)) was ideal, showing high receptor selectivity for Fe^{3+} (Fig. 2). The UV–vis spectra of receptor **2** in this solvent system with λ_{max} = 225 nm is not presentable due to instrument limitations (Supplementary Fig. S2).

In order to gain further insight into receptor **2** as a sensor for Fe^{3+} and I^{-}, titrations were performed. Changes in the UV–vis spectrum of receptor **2** upon continuous addition of I^{-} are shown in Figure 3, and changes in the fluorescence spectrum of receptor **2** upon the addition of Fe^{3+} are presented in Figure 4. Upon addition of a 10 μM solution of Fe^{3+}, the intensity of the emission band at

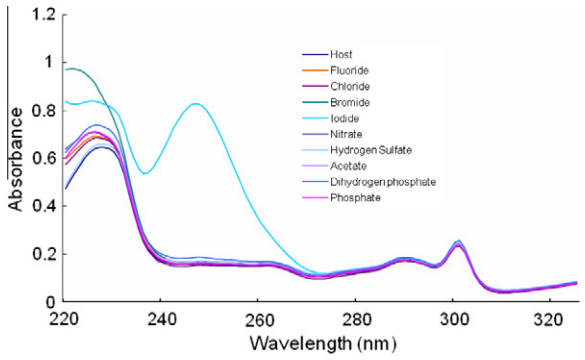


Figure 1. Changes in UV–vis spectra of receptor **2** (10 μM) upon addition of a particular tetrabutylammonium salt of anion (40 μM) in CH_3CN.

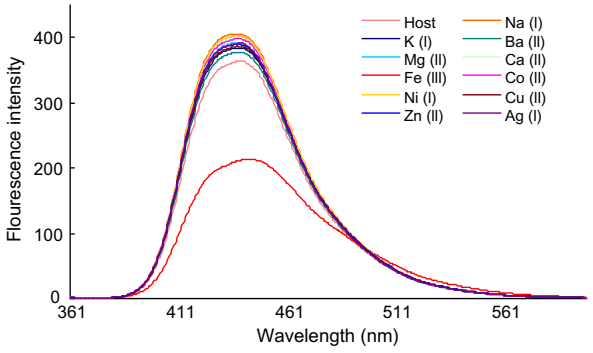


Figure 2. Changes in fluorescence intensity of receptor **2** (10 μM) upon addition of a particular metal salt (40 μM) in a THF/H_2O (1:99, v/v) HEPES buffered (pH 7.0 ± 0.1) solution (λ_{ex} = 351 nm).

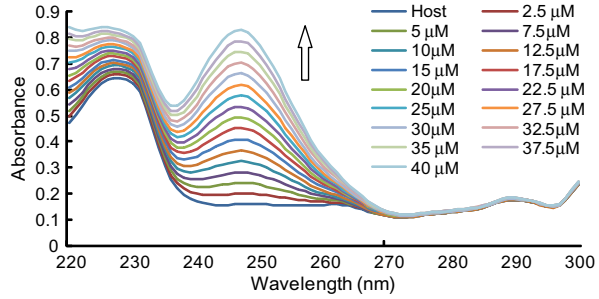


Figure 3. Changes in UV–vis spectrum of receptor **2** (10 μM) upon addition of tetrabutylammonium iodide (0–40 μM) in CH_3CN.

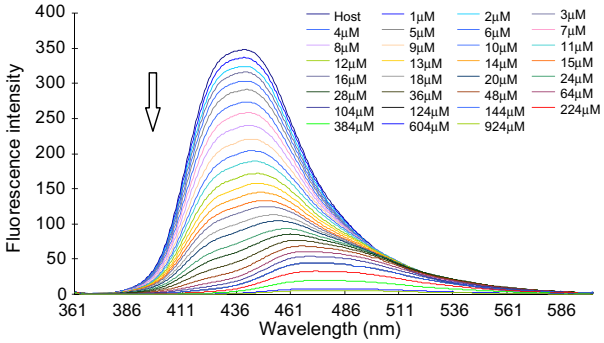


Figure 4. Changes in fluorescence spectrum of receptor **2** (10 μM) upon addition of Fe^{3+} (0–92.4 μM) in a THF/H_2O (1:99, v/v) HEPES buffered (pH 7.0 ± 0.1) solution.

438 nm decreased significantly (~90%) with a noticeable shift in the λ_{max} from 438 nm to 478 nm.

To determine the stoichiometry of the complex formed between **2** and Fe^{3+}, Stern–Volmer plot[10] and Job plot methods[11] were employed. When the quenching effect caused by Fe^{3+} complexation was evaluated using the Stern–Volmer equation, the equation for 1:1 (host/guest) stoichiometry was found to give an excellent fit (Supplementary Fig. S3). The quenching effect caused by the complexation of Fe^{3+} with receptor **2** is most likely due to an electron/energy transfer process occurring between the excited naphthalene fluorophore and the redox active metal ions, which allows a non-radiative deactivation pathway to occur.[12] To determine the stoichiometry of the complex formed between receptor **2** and I^- and to confirm the stoichiometry of the complex formed between receptor **2** and Fe^{3+}, Job plots were analyzed for each case (Fig. 5). The Job plot analyses confirm a 1:1 stoichiometry in both cases. The association constant, K_a, was calculated using the Benesi–Hildebrand equation[13] for a 1:1 complex giving $(2.7 \pm 0.3) \times 10^4\ M^{-1}$ and $(4.5 \pm 0.3) \times 10^3\ M^{-1}$ for Fe^{3+} and I^-, respectively, (Supplementary Figs. S4 and S5).

The minimum detection limits for Fe^{3+} and I^- were found to be 3.53×10^{-5} M and 4.25×10^{-7} M, respectively.[14] Since receptor **2** has a dual capacity to act as a sensor for both Fe^{3+} and I^- using different spectroscopic methods, it was of the utmost importance to investigate the extent of interference between I^- and Fe^{3+} in the analysis. Thus, the ability of receptor **2** to operate in solutions containing equimolar concentrations of both I^- and Fe^{3+} was examined. Figure 6 (A) shows overlay plots of fluorescence intensity at λ_{max} = 438 nm for solutions containing receptor **2** and Fe^{3+} with those containing receptor **2**, Fe^{3+} and equimolar I^-. Similarly, Figure 6 (B) presents an overlay of the absorption at λ_{max} = 245 nm for solutions containing receptor **2** and I^- with those containing receptor **2**, I^- and equimolar Fe^{3+}. These interference studies suggest that photophysical changes in the fluorescence intensity of **2** upon addition of Fe^{3+} and changes in the absorbance of receptor **2** due to I^- binding are free from I^- and Fe^{3+} interference, respectively. Figure 6 (A and B) also revealed that receptor **2** can be used for the estimation of iodide along a linear concentration range of 30–180 μM. However, for Fe^{3+} this range is in-between 5–20 μM.

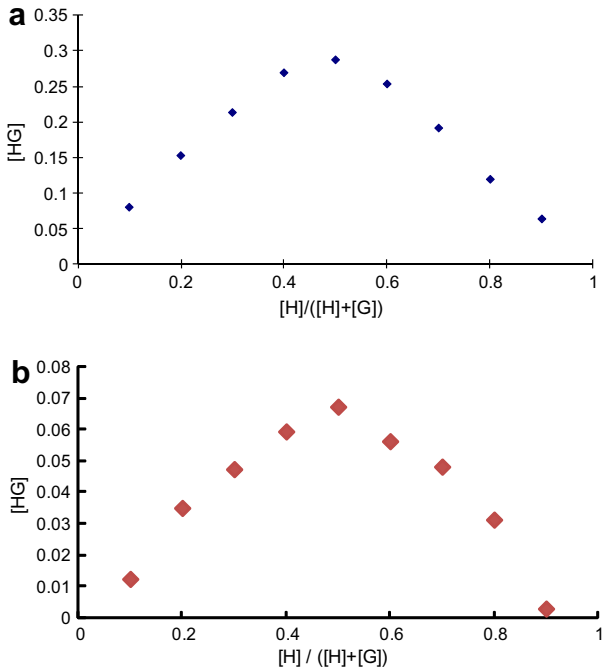


Figure 5. Job plots showing the stoichiometry formed between: (a) receptor **2** and Fe^{3+} (blue diamond); (b) receptor **2** and I^- (red square).

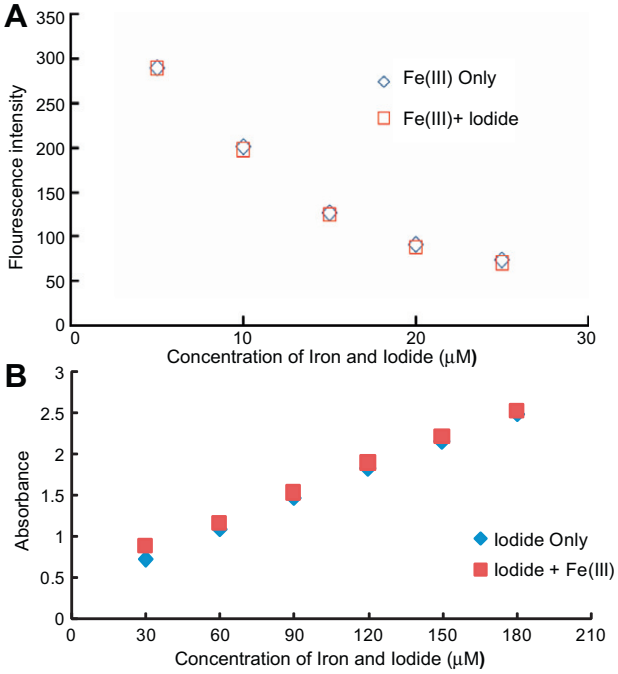


Figure 6. (A) Fluorescence intensity of receptor **2** at 438 nm in the presence of (i) Fe^{3+} (open blue diamond), (ii) Fe^{3+} with the same amount of I^- (open red square); (B) Absorbance of receptor **2** at 245 nm in the presence of (i) I^- (solid blue diamond), (ii) I^- with the same amount of Fe^{3+} (solid red square).

In conclusion, we have developed a receptor on the concept of 'one sensor for multiple analytes'. Receptor **2** exhibits selective recognition of I^- with UV–vis spectroscopy and selective analysis of Fe^{3+} with fluorescence spectroscopy. Thus, this sensor exhibits a new method to assay both I^- and Fe^{3+} using two different detection modes.

Acknowledgement

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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.2010.05.105.

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9. *Synthesis of receptor* **2**: A solution of naphthalene-2,3-diamine (80 mg, 0.51 mmol) and 2-hydroxynaphthalene-1-carbaldehyde (219.5 mg, 1.28 mmol) in MeOH (20 mL) in the presence of a catalytic amount of $Zn(ClO_4)_2$ was allowed to stir at room temperature for 12 h. A yellow solid product separated out. The solid material was washed with CH_2Cl_2 (50 mL) affording a light orange solid in 85% yield (203.9 mg). $NaBH_4$ (40.6 mg, 1.07 mmol) was added to a solution of the above-mentioned compound (100 mg, 0.21 mmol) in 30 mL of MeOH/THF (8:2, v/v). The mixture was stirred for 4 h at room temperature. Upon completion of the reaction, the solvent was evaporated and water was added to the reaction mixture. Organic material was extracted into dichloromethane (3×50 mL), and the combined organic layers were dried over anhydrous $MgSO_4$. After filtration and evaporation, the compound was obtained as a greenish white solid (79 mg, 78%). mp: 235–237 °C, IR (KBr) 3387, 3222, 1305, 1230 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 4.56 (s, 4H, $-CH_2$), 5.03 (b, 2H, –OH), 6.96–7.02 (m, 4H, Ar), 7.05–7.09 (m, 3H, Ar), 7.21–7.23 (m, 2H, Ar), 7.58–7.64 (m, 5H, Ar), 7.79–7.81 (m, 2H, Ar), 8.09–8.12 (m, 2H, Ar), 10.16 (b, 2H, –NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 42.4, 114.3, 117.7, 118.6, 121.1, 122.0, 122.6, 124.1, 125.3, 127.4, 127.7, 128.0, 128.5, 133.9, 134.8, 151.7 Anal. Calcd for $C_{32}H_{26}N_2O_2$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.67; H, 5.55; N, 5.95.
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