



A highly selective and sensitive colorimetric chemosensor for Fe²⁺ based on fluoran dye

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ABSTRACT

A highly selective chemosensor based on fluoran dye for Fe²⁺, 2'-anilino-3'-methyl-6'-dibutylamino-N-((2'-(2''-ethylimino) methyl) naphthalen-2-yl) iso-indolin-1-one-fluoran (**5**), was designed and synthesized. The chemical structures of all the intermediates and the fluoran dye **5** are characterized by ¹H NMR, ¹³C NMR, Ms and elemental analysis. Upon addition of Fe²⁺, the fluoran dye **5** shows a new peak around 658 nm in its absorption spectra, and the color of solution changed from colorless to greenish black. Whereas other ions including Mg²⁺, Pb²⁺, Ni²⁺, Hg²⁺, Cd²⁺, Fe³⁺, Cu²⁺, Zn²⁺ and Al³⁺ and so on induced basically no spectral change, which constituted a Fe²⁺ highly sensitive and selective colorimetric chemosensor by “naked eyes”.

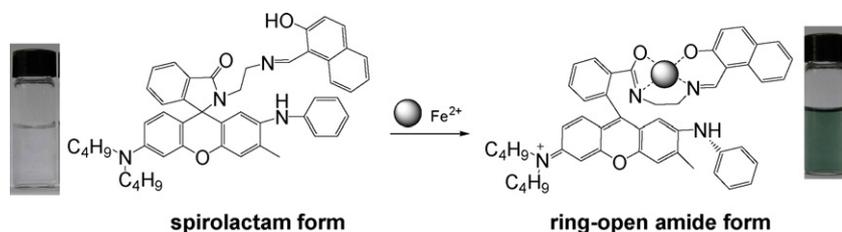
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1. Introduction

The development of sensitive chromogenic probes has been receiving much attention in recent years because of the potential application in clinical biochemistry and environment. There are already many chromogenic chemosensors developed for selective recognition of different species so far due to their high selectivity, sensitivity and simplicity [1–3]. Iron is one of the most important elements among heavy metal for metabolic processes, being indispensable for plants and animals and therefore it is extensively distributed in environmental and biological materials [4]. If iron concentration exceeds the normal level it may become potential health hazard. Iron deficiency leads to anemia. Therefore, it is important to explore new chromogenic chemosensors for selective detection of iron. Over the past years, some examples for iron detection, including chromogenic [5] and fluorescent [6–10] chemical sensors, electrochemical devices [11] have been reported. Currently, colorimetric sensors are popular due to their capability to detect analyses by naked eye without resorting to any expensive instruments [12]. Therefore, to develop simple-to-use and naked eye diagnostic tool for selective detection of iron is a hot and interesting topic.

Fluoran dyes have the remarkable feature of giving a wide variety of colors depending on their substituents [13]. In particular, fluoran type dyes are very important in their ability to yield singly black color on the addition of an acidic compound. The fluoran dyes as a color former are only applied for use in thermosensitive recording paper. The color formers used in thermal paper are essentially colorless organic compounds that develop an intense color when brought into contact with an acid. Black is the most important color in thermal printing, and the most widely used color formers for producing a black color are fluoran derivatives. No one almost care about the fluoran chromophore as metal recognition chromophore. The structure of fluoran dye is very resemble the rhodamine dye. Rhodamine is a dye used extensively as a chemosensor reagent due to its excellent photophysical properties, such as long absorption and emission wavelengths elongated to visible region, high absorption coefficient and high fluorescence quantum yield [14]. Various rhodamines fluorescent probes for heavy metal have been developed [15,16]. Several organic dye-based chemosensors for Fe³⁺ have recently been reported. However, despite the urgent need for Fe²⁺ sensing, there have been only limited studies on Fe²⁺ selective sensors. We designed and synthesized a highly selective chemosensor based on fluoran dye **5** for Fe²⁺ as shown in Scheme 1. To the best of our knowledge, this is the first example of fluoran dye as colorimetric chemosensor that show the greenish black color for highly sensitive and selective Fe²⁺ metal cation.

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Scheme 1. Proposed binding mode and color change of fluoran dye 5 with Fe^{2+} .

2. Experimental

2.1. Materials and methods

Most of chemicals were purchased from Aldrich Chemical Co. and TCI. Solvents were purified by normal procedures and used under moisture free atmosphere. The other materials were commercial products and were used without further purification.

2.2. Instruments and spectral measurements

Melting points were determined using an Electrothermal IA 900 and are uncorrected. Elemental analyses were recorded on a Carlo Erba Model 1106 analyzer. UV–vis absorption spectra were measured on an Agilent 8453 spectrophotometer. Mass spectra were recorded on a Shimadzu QP-1000 spectrometer using electron energy of 70 eV and the direct probe EI method. ^1H NMR, ^{13}C NMR spectra were recorded using a Varian Inova 400 MHz FT-NMR spectrometer with TMS as internal standard.

2.3. Synthesis of fluoran dye 3

The fluoran dye 3 was synthesized according to the literature method [17].

^1H NMR Yield: 58%, m.p. 187 °C; mass (m/z) 532(M^+); ^1H NMR (400 MHz, DMSO- d_6): δ (ppm) 7.93 (d, $J=7.56$, 1H), 7.76 (t, $J=7.56$, 1H), 7.66 (t, $J=7.36$, 1H), 7.41 (s, 1H), 7.26 (t, $J=7.84$, 1H), 7.22 (s, 1H), 6.99 (t, $J=7.84$, 2H), 6.62 (t, $J=7.04$, 1H), 6.55 (d, $J=7.6$, 2H), 6.49 (d, $J=8.08$, 2H), 6.43 (s, 1H), 6.41 (d, $J=9.08$, 1H), 3.25 (t, $J=7.6$, 4H), 2.21 (s, 3H), 2.07 (s, 1H), 1.48 (m, 4H), 1.29 (m, 4H), 0.87 (t, 6H).

^{13}C NMR (400 MHz, DMSO- d_6): δ (ppm), 13.78, 17.84, 19.63, 28.86, 30.59, 49.89, 83.55, 96.98, 104.1, 108.5, 114.63, 116.99, 118.32, 118.53, 119.49, 123.92, 124.45, 126.24, 128.59, 128.77,

129.94, 134.92, 135.40, 136.85, 145.25, 146.58, 149.63, 152.43, 152.49 and 168.66.

2.4. Synthesis of fluoran dye 4

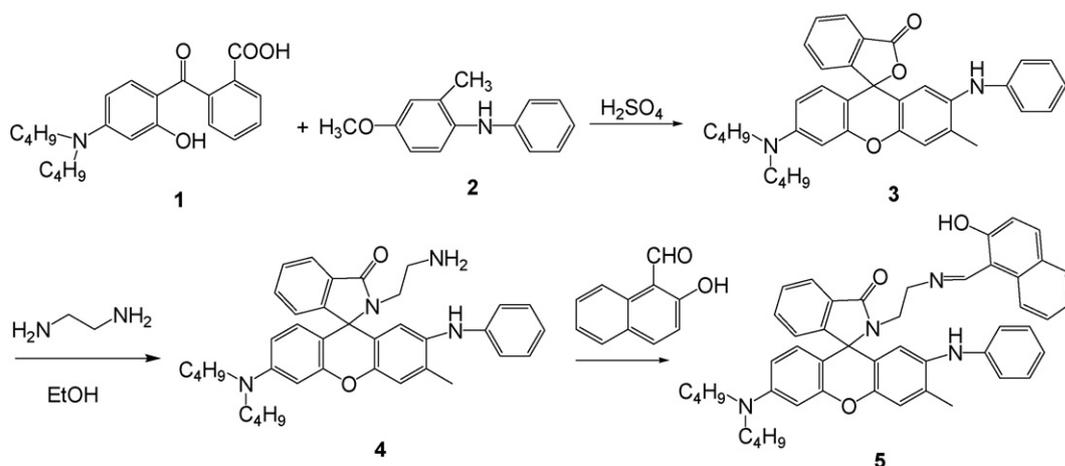
Fluoran dye 3 (1.0 g, 1.9 mmol) was dissolved in 100 mL of ethanol solution, followed by addition of ethylenediamine (2.0 mL, 24.7 mmol). The reaction mixture was refluxed for 12 h. After cooling to the room temperature, the solvent was evaporated in vacuum. The CH_2Cl_2 and water (200 mL) were added, and the organic layer was separated, washed twice with water and dried over anhydrous sodium sulfate. After filtration of sodium sulfate, the solvent was removed under reduced pressure. Then 1 M HCl (50 ml) was added to the solid in the flask to generate a clear red solution. After that, 2 M NaOH was added slowly with stirring until the pH of the solution reached 7–8. The resulting pink solid was filtered and obtained 1.1 g of fluoran dye 4.

Yield: 91%, m.p. 223–225 °C; mass (m/z) 574(M^+); ^1H NMR (400 MHz, DMSO- d_6): δ (ppm) 7.72 (d, $J=7.08$, 1H), 7.54 (t, $J=6.8$, 1H), 7.48 (t, $J=7.32$, 1H), 7.16 (s, 1H), 7.04 (d, $J=7.32$, 1H), 6.99 (d, $J=7.84$, 2H), 6.61 (t, $J=7.32$, 1H), 6.49 (d, $J=7.84$, 2H), 6.38 (s, 1H), 6.33 (d, $J=7.56$, 4H), 3.42 (m, 2H), 3.22 (t, $J=6.8$, 4H), 3.0 (m, 2H), 2.17 (s, 3H), 2.08 (s, 1H), 1.48 (m, 4H), 1.30 (m, 4H), 0.9 (t, 6H).

^{13}C NMR (400 MHz, DMSO- d_6): δ (ppm), 13.89, 17.76, 18.59, 19.69, 25.24, 28.95, 32.14, 43.58, 49.88, 63.89, 97.11, 103.91, 108.41, 114.48, 117.35, 118.32, 118.18, 118.60, 119.70, 122.38, 123.57, 128.38, 128.86, 130.14, 132.81, 133.81, 136.58, 145.43, 146.32, 146.86, 152.39, 153.35 and 167.10.

2.5. Synthesis of fluoran dye 5

Fluoran dye 4 (0.2 g, 0.35 mmol) was dissolved in 15 mL absolute ethanol. An excessive 2-hydroxy-1-naphthaldehyde (0.171 g, 1.4 mmol) was added then the mixture was refluxed for 6 h. After



Scheme 2. The synthetic route of fluoran dye 5.

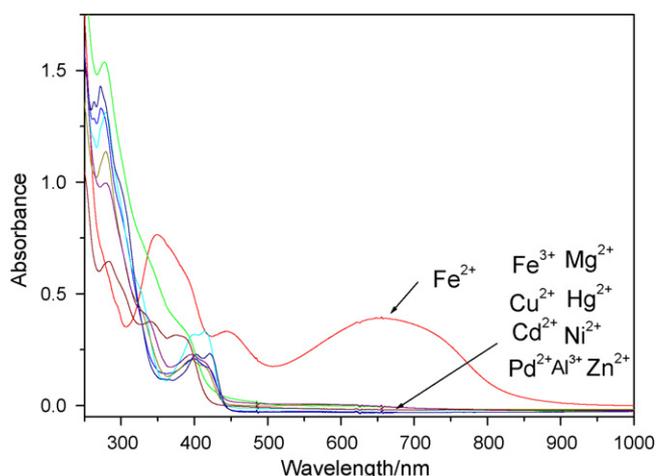


Fig. 1. The UV-vis spectra of fluoran dye **5** ($1.0 \times 10^{-5} \text{ mol L}^{-1}$) upon addition of ClO_4^- salt of $\text{X} = \text{Cd}^{2+}, \text{Mg}^{2+}, \text{Pd}^{2+}, \text{Hg}^{2+}, \text{Ni}^{2+}, \text{Cu}^{2+}, \text{Fe}^{2+}, \text{Fe}^{3+}, \text{Zn}^{2+}$ and Al^{3+} (10 equiv.) in CH_3CN solution.

that, the solution was cooled (concentrated to 10 mL) and allowed to stand at room temperature overnight. The precipitate was filtered and washed 3 times with 10 mL cold ethanol to obtain the crude product. Then, the crude product was purified by column chromatography on silica gel ($\text{CHCl}_3/\text{EtOH}$: 8/1 (v/v)) to give 0.14 g white powder of fluoran dye **5**.

Yield: 59%, m.p. 193–195 °C; mass (m/z) 728 (M^+); ^1H NMR (400 MHz, CDCl_3) δ : 0.95 (t, $J = 7.32 \text{ Hz}$, 6H), 1.33 (sextet, $J = 7.32 \text{ Hz}$, 4H), 1.56 (quintet, $J = 7.32 \text{ Hz}$, 4H), 2.10 (s, 3H) 3.22 (t, $J = 7.8 \text{ Hz}$, 4H), 3.42 (m, 4H), 5.23 (s, 1H), 6.25 (d, $J = 9.08 \text{ Hz}$, 1H), 6.38 (m, 4H), 6.45 (s, 1H), 6.66 (t, $J = 7.32 \text{ Hz}$, 1H), 6.86 (d, $J = 7.32 \text{ Hz}$, 1H), 6.99 (d, 2H), 7.09 (m, 2H), 7.23 (t, $J = 7.08 \text{ Hz}$, 1H), 7.44 (m, 3H), 7.59 (d, $J = 7.84 \text{ Hz}$, 1H), 7.66 (d, $J = 9.32 \text{ Hz}$, 1H), 7.80 (d, $J = 8.60 \text{ Hz}$, 1H), 7.87 (m, 1H), 8.52 (d, $J = 7.08 \text{ Hz}$, 1H), 13.98 (s, 1H, -OH).

^{13}C NMR (400 MHz, CDCl_3) δ : 14.18, 18.13, 20.50, 29.53, 32.36, 38.26, 41.28, 50.86, 50.94, 65.10, 97.91, 103.92, 107.08, 108.69, 114.77, 117.67, 118.29, 119.14, 121.99, 122.93, 123.33, 123.90, 125.00, 126.40, 128.16, 128.59, 128.72, 129.23, 129.32, 130.77, 132.98, 133.92, 135.18, 136.29, 137.28, 145.18, 148.41, 149.61, 153.35, 153.47, 158.71, 168.79, 172.00 and 176.02.

Anal. Calcd. for $\text{C}_{48}\text{H}_{48}\text{N}_4\text{O}_3$: C 79.09, H 6.64, N 7.68; found: C 78.61, H 6.80, N 7.68.

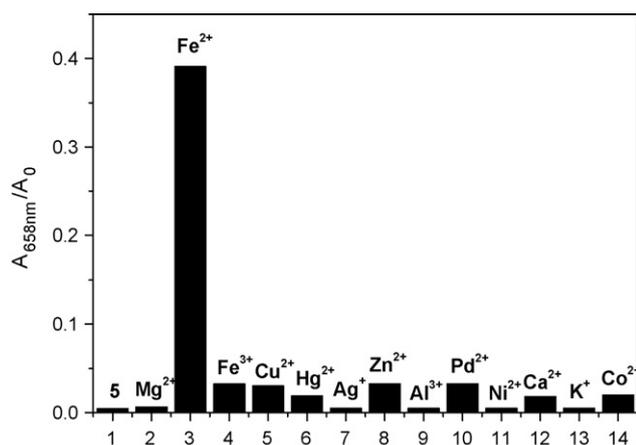


Fig. 2. The absorbance response of fluoran dye **5** to $1.0 \mu\text{M}$ of various cations in CH_3CN solution. The bar represent the absorbance intensities at 653 nm ($A_{653 \text{ nm}}$) over the absorbance intensity of the blank dye **5** solution. From left to right: (1) dye **5**, (2) Mg^{2+} , (3) Fe^{2+} , (4) Fe^{3+} , (5) Cu^{2+} , (6) Hg^{2+} , (7) Ag^+ , (8) Zn^{2+} , (9) Al^{3+} , (10) Pb^{2+} , (11) Ni^{2+} , (12) Ca^{2+} , (13) K^+ and (14) Co^{2+} .

3. Results and discussion

The fluoran dye **5** was synthesized according to the Scheme 2. At first, the intermediate the fluoran dye **3** was synthesized from 2-(4-(dibutylamino)-2-hydroxybenzoyl) benzoic acid **1** and 4-methoxy-2-methyl-N-phenylbenzenamine **2** as starting materials using H_2SO_4 as catalyst. Then, the fluoran dye **3** was transferred to the fluoran dye **4** via condensation reaction. At last, the fluoran dye **5** was prepared from the fluoran dye **4** and 2-hydroxy-1-naphthaldehyde by Schiff's base condensation. The chemical structures of all the intermediates and the dye **5** are characterized by ^1H NMR, ^{13}C NMR, MS and elemental analysis.

The recognition between the fluoran dye **5** and different metal cations were investigated by UV-vis spectroscopy in the CH_3CN solution. The solution of the fluoran dye **5** is at a concentration of $1.0 \times 10^{-5} \text{ mol/L}$. From the absorption spectrum of the fluoran dye **5** in the CH_3CN solution, it was not found that an absorption band appeared in visible region, the fluoran dye **5** solution is colorless. Variation of absorption spectra of the fluoran dye **5** upon addition of different metal cations including $\text{Cd}^{2+}, \text{Mg}^{2+}, \text{Pd}^{2+}, \text{Hg}^{2+}, \text{Ni}^{2+}, \text{Cu}^{2+}, \text{Fe}^{2+}, \text{Fe}^{3+}, \text{Zn}^{2+}, \text{Al}^{3+}$, alkali metal and alkaline earth metal cations, are shown in Figs. 1 and 2. Fig. 1 show the UV-vis spectra of fluoran dye **5** ($1.0 \times 10^{-5} \text{ mol L}^{-1}$) upon addition of ClO_4^- salt of $\text{X} = \text{Mg}^{2+}, \text{Cu}^{2+}, \text{Hg}^{2+}, \text{Ag}^+, \text{Zn}^{2+}, \text{Fe}^{3+}, \text{Fe}^{2+}, \text{Pb}^{2+}, \text{Al}^{3+}, \text{Ni}^{2+}$ (10 equiv.) in CH_3CN solution. The absorption maximum show no obvious change upon the addition of the metal ions $\text{Cd}^{2+}, \text{Mg}^{2+}, \text{Pd}^{2+}, \text{Hg}^{2+}, \text{Ni}^{2+}, \text{Fe}^{3+}, \text{Ca}^{2+}$ and Co^{2+} . While upon addition of Fe^{2+} , we found new absorption bands appeared including the absorption at wavelength peaked at around 658 nm. The color changed from colorless to greenish black. While upon addition of Fe^{3+} , we do not found new absorption bands appeared including the absorption at wavelength peaked. Fig. 2 shows the absorbance intensities at 658 nm ($A_{658 \text{ nm}}$) over the absorbance intensity of the blank fluoran dye **5** solution. With the addition of Fe^{2+} , the absorbance intensity of the fluoran dye **5** at around 658 nm was increased. With the addition of the other metal ion, the absorbance intensity of the dye **5** at 658 nm was almost no evidently changed.

These results indicate that fluoran dye **5** has high-sensitive and selective toward Fe^{2+} . The dependence of absorption spectroscopy of dye **5** in CH_3CN solution on the concentration of Fe^{2+} was investigated by the absorption spectroscopy titration method. With the

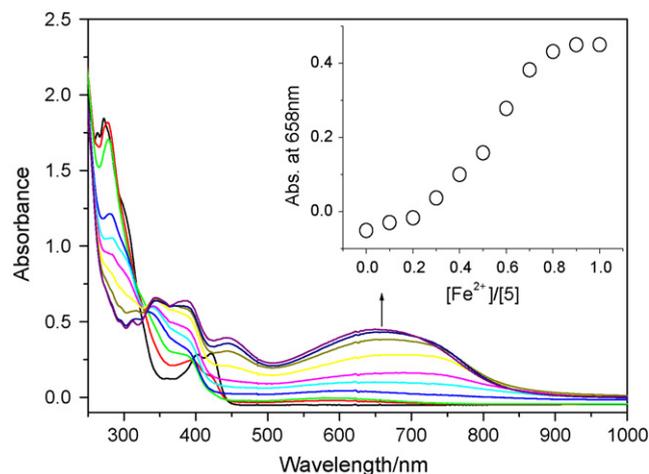


Fig. 3. The absorbance spectra of fluoran dye **5** (cal. $10^{-5} \text{ mol L}^{-1}$) in the presence of Fe^{2+} in CH_3CN solution. The Fe^{2+} concentration is 0, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9 and 1.0 equiv., respectively. Inset: absorbance at 658 nm change with Fe^{2+} concentration change.

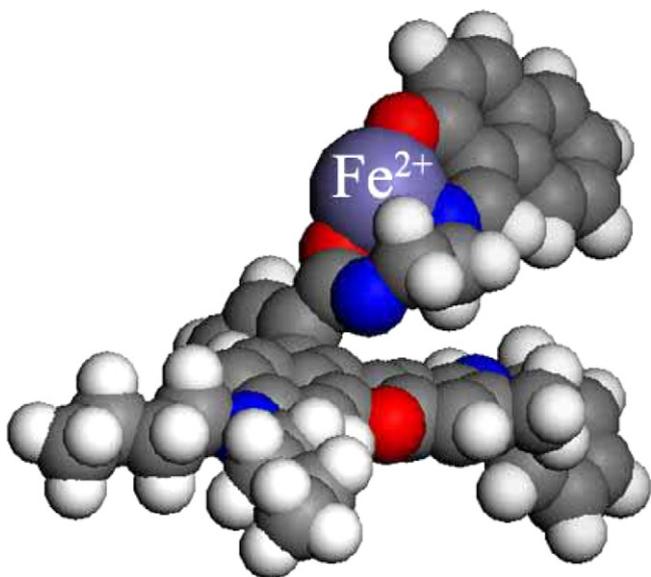


Fig. 4. The calculated results (in CPK model) for the interaction between fluoran dye **5** and Fe^{2+} based on DMol³ program in the Materials Studio 4.2 package.

addition of Fe^{2+} , the 290 nm was decreased accompanied with the increase of the wavelength at around 658 nm. An isosbestic point in the titration curves shows new specie appeared with the addition of Fe^{2+} , which could be assigned to the formation of the Fe^{2+} complex of the dye **5** as shown in Fig. 3. Fig. 3 in set shows the absorbance intensities change at 658 nm ($A_{658\text{ nm}}$) over the absorbance intensity of the blank fluoran dye **5** solution. With the addition of Fe^{2+} , the absorbance intensity of fluoran dye **5** at around 658 nm was all increased. So the color of solution gradually becomes greenish black from the colorless. Actually, an obvious color change from colorless to greenish black was observed by the naked eyes.

The molecular modeling calculation based on DMol³ program in the Materials Studio 4.2 package is performed [18–20]. The CPK model of the energy-minimized structure of fluoran dye **5** with Fe^{2+} are shown in Fig. 4, which shows the recognition of fluoran dye **5** with Fe^{2+} to form a stable complex.

4. Conclusions

In conclusion, a new chromogenic chemosensor based on fluoran derivative was developed. It shows a good selectivity and sensitivity for Fe^{2+} . An obvious color change from colorless to greenish black was observed by the naked eyes, in other words, a signal could be easily read by the naked eye without resort to any spectroscopic instrumentation. This is a very simple and effective method for detecting the Fe^{2+} .

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