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A novel ratiometric probe based on rhodamine B and coumarin for selective recognition of Fe(III) in aqueous solution

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ABSTRACT

We have developed a new ratiometric fluorescence probe based on rhodamine B and coumarin to monitor the Fe^{3+} with high sensitivity and selectivity. Upon addition of Fe^{3+} to aqueous solution of the probe, two fluorescence peaks at 580 nm and 460 nm were observed, which belong to rhodamine B and coumarin, respectively. This is a novelty design of ratiometric probe of Fe^{3+}, due to CHEF process generated along with the PET process suppressed simultaneously. The fluorescence intensity at 580 nm was significantly increased about 120-fold with 5 equiv. of Fe^{3+} added in aqueous solution.

1. Introduction

Fe^{3+} plays a major role in many biochemical processes at the cellular level. High levels of Fe^{3+} within the body have been associated with increasing incidence of certain cancers and dysfunction of certain organs, such as the heart, pancreas, and liver [1,2]. Accordingly, the development of methods, enabling professionals to spatially and temporally track intracellular Fe^{3+}, is challenging but essential to address these issues and has become the subject of current chemical research.

Optical cellular imaging with fluorescent probes might be the best choice for visualizing the intracellular Fe^{3+} ion by virtue of its high sensitivity, high-speed spatial analysis, and less cell-damaging. However, most reported examples of fluorescent sensing of Fe^{3+} ions in living cells were functioned through the enhancement of fluorescence signals [3–5]. As the change in fluorescence intensity is the only detection signal, factors such as instrumental efficiency, environmental conditions, and the probe concentration can interfere with the signal output [6,7]. Ratiometric probes can eliminate most or all interferences by built-in correction of two emission bands and seem to be more favorable for imaging intracellular metal ions in comparison with fluorescence enhancement probes.

Ratiometric probes can be designed to function following two mechanisms: intramolecular charge transfer (ICT) [8–11] and fluorescence resonance energy transfer (FRET) [12–16]. Relatively broad fluorescence spectra are often observed for ICT fluorophores; in a significant number of cases the broad fluorescence spectra before and after binding target ions have a high degree of overlap (or in an extreme case, a broad spectrum with high intensity completely covers one with lower intensity, which makes it difficult to accurately determine the ratio of the two fluorescence peaks. However, probes based on FRET can avoid these disadvantages in a certain extent [7,17]. Although some fluorescent probes for detecting Fe^{3+} have been reported [18–21], up to now, only a few ratiometric probe for Fe^{3+} was reported [19,22] based on cyclodextrin supramolecular complex and quinoline, respectively. Moreover, the synthesis process of the probe based on cyclodextrin superamolecular is complex, and the fluorescence intensity of quinoline acted as donor is week.

Thus, we designed a coumarin-rhodamine system **L** as a ratiometric probe for Fe^{3+}.

Two fluorescence peaks which belong to coumarin and rhodamine exist simultaneously. Upon addition of Fe^{3+}, a new fluorescence emission peak appeared at 580 nm. This wavelength change allows the ratiometric detection of Fe^{3+} ions in ethanol/water solution. To the best of our knowledge, this is a novelty design of ratiometric probe of Fe^{3+} based on the conjugated link of the rhodamine and coumarin. Herein, we develop a new

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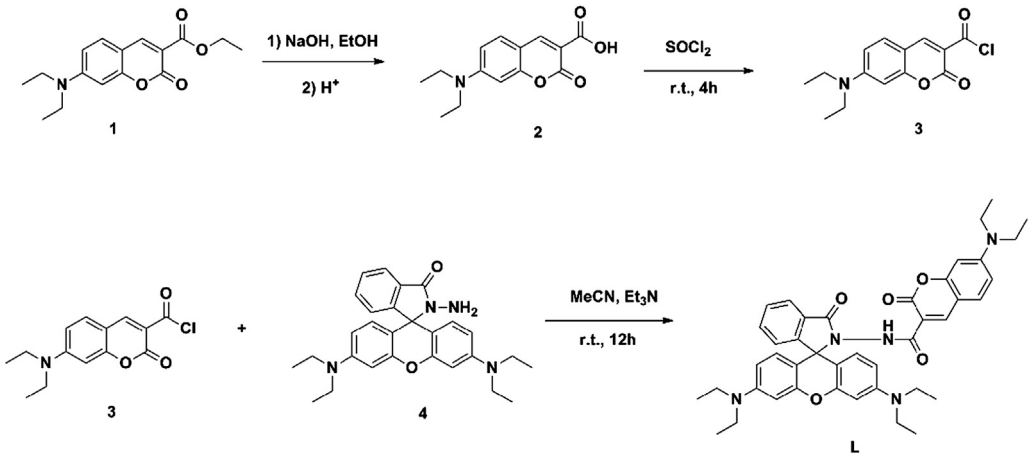

Scheme 1. Synthesis of probe **L**.

ratiometric probe **L** for Fe^{3+}, which differs from reported ratiometric probe.

2. Experimental sections

2.1. Materials and methods

Deionized water was used throughout the experiment. All the reagents were purchased from commercial suppliers and used without further purification. All samples were prepared at room temperature, shaken for 10 s and waited for 18 h before UV–vis and fluorescence determination. The solutions of metal ions were prepared from $NaNO_3$, $Mg(NO_3)_2{\cdot}6H_2O$, KNO_3, $Ca(NO_3)_2{\cdot}4H_2O$, $Cr(NO_3)_3{\cdot}9H_2O$, $Fe(NO_3)_3{\cdot}9H_2O$, $Co(NO_3)_2{\cdot}6H_2O$, $Ni(NO_3)_2{\cdot}6H_2O$, $Cu(NO_3)_2{\cdot}3H_2O$, $Zn(NO_3)_2{\cdot}6H_2O$, $AgNO_3$, $Cd(NO_3)_2{\cdot}4H_2O$, $Ba(NO_3)_2$, $HgCl_2{\cdot}H_2O$, $Pb(NO_3)_2$, respectively, and were dissolved in distilled water. Thin-layer chromatography (TLC) was conducted on silica gel $60F_{254}$ plates (Merck KGaA). HEPES buffer solutions (pH 7.2) were prepared using 20 mM HEPES, and proper amount of aqueous sodium hydroxide under adjustment by a pH meter. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 300 spectrometer, using DMSO as solvent and tetramethylsilane (TMS) as internal standard. Melting points were determined on an XD-4 digital micro melting point apparatus. IR spectra were recorded with an IR spectrophotometer VERTEX 70 FT-IR (Bruker Optics). HRMS spectra were recorded on a Q-TOF6510 spectrograph (Agilent). UV–vis spectra were recorded on a U-4100 (Hitachi). Fluorescent measurements were recorded on a PerkinElmer LS-55 luminescence spectrophotometer.

2.2. Synthesis of ethyl 7-(diethylamino)-2-oxo-2H-chromene-3-carboxylic acid (2)

A mixture of **1** (1.15 g, 4 mmol) and NaOH (0.48 g 12 mmol) in EtOH (20 mL) was refluxed for 1 h, after which an orange solid was precipitated. When the reaction was cooled to room temperature, the mixture was added to a breaker containing 150 mL water. The orange solid was dissolved and adjust the pH of the solution to 3 ~ 4. An orange solid 7-(diethylamino) coumarin-3-carboxylic acid **2** (0.845 g) was obtained in 81% yield; m.p. 90–92 °C.

2.3. Synthesis of 7-(diethylamino)-2-oxo-2H-chromene-3-carbonyl chloride (3)

The acid chloride **3** was synthesized by the reaction of the 7-(diethylamino) coumarin-3-carboxylic acid **2** with thionyl chloride at room temperature in 80% yield.

2.4. Synthesis of N-(3′,6′-bis(diethylamino)-3-oxo-4a',9a'-dihydrospiro [isoindoline-1,9′-xanthen]-2-yl)-7-(diethylamino)-2-oxo-2H-chromene-3-carboxamide (L)

Compound **3** (0.279 g, 1.0 mmol) and **4** (0.547 g, 1.2 mmol) was dissolved in 20 mL of acetonitrile. The mixture was stirred for 8 h under nitrogen at room temperature. Concentration of the mixture under reduced pressure gave a yellow solid. The residue was purified by silica gel column using petroleum ether: ethyl acetate = 1:1 as eluent to obtain an orange solid **L** (0.51 g) in 73% yield; m.p. 305 °C. IR (KBr, cm^{-1}): 3461.7, 2971.4, 2928.4, 1725.4, 1692.3, 1615.9, 1582.3, 1512.7, 1353.4, 1215.8, 1117.1, 819.0, 787.6; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm) 1.05–1.15 (18H, m, CH_3), 3.30–3.38 (8H, m CH_2), 3.44–3.51 (4H, m, CH_2), 6.33 (2H, d, J = 2.4 Hz, ArH), 6.37–6.40 (2H, m, ArH), 6.57 (1H, d, J = 1.8 Hz, ArH), 6.62 (1H, s, ArH), 6.65 (2H, s, ArH), 6.78–6.82 (1H, m, ArH), 7.02–7.05 (1H, m, ArH),7.51–7.56 (2H, m, ArH), 7.57-7.65 (1H, m, ArH), 7.84–7.87 (1H, m, NH), ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 12.4, 43.6, 65.2, 97.2, 103.8, 107.0, 118.0, 128.5, 132.0, 145.0, 148.4, 149.0, 152.8, 157.5, 161.1, 162.2, 164.0; HRESIMS calcd for $[M + H]^+$ $C_{42}H_{46}N_5O_5^+$: 700.3499 found: 700.3422.

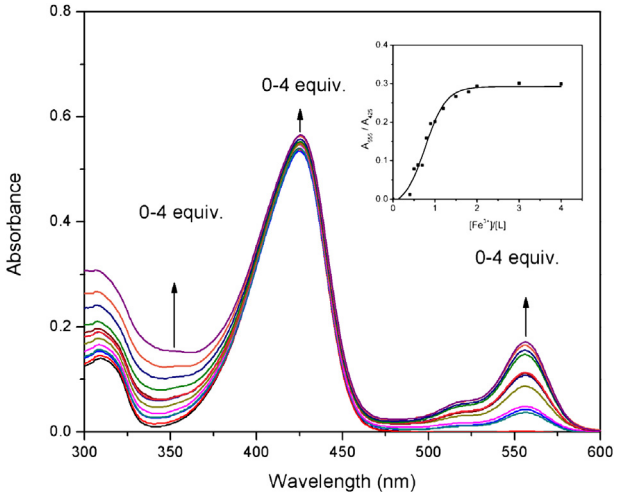

Fig. 1. Absorption spectra of 10 μM **L** upon the addition of Fe^{3+} (0–4 equiv.) in buffered EtOH/HEPES = 99:1 solution at pH 7.2. The inset shows the ratio of the absorbance (555 nm/425 nm) as a function of Fe^{3+} concentration.