Coumarin Modified Rhodamine Derivative: Fluorescent Chemosensor Selectively Recognizing $\text{Al}^{3+}$ and $\text{Ca}^{2+}$

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Abstract A fluorescent probe with a coumarin moiety bound to rhodamine 6G hydrazide(1) was synthesized. Its sensing behavior toward various metal ions was investigated with fluorescence methods. Compound 1 displays different fluorescence emission responses to $\text{Al}^{3+}$ and $\text{Ca}^{2+}$ at the same excitation wavelength in the visible light region, while no changes occur after the addition of other metal ions. The binding ratios of the complexes of 1-$\text{Al}^{3+}$ and 1-$\text{Ca}^{2+}$ are both 2:1 according to the Job plot and high resolution mass spectrometer(HRMS) experiments. Moreover, emission spectrum of 1-$\text{Ca}^{2+}$ complex and absorption spectrum of the rhodamine dyes overlap largely. When $\text{Al}^{3+}$ was added to the 1-$\text{Ca}^{2+}$ system, calcium in complex 1-$\text{Ca}^{2+}$ can be displaced by $\text{Al}^{3+}$, resulting in the output of another ratiometric sensing signal, which demonstrates that the 1-$\text{Ca}^{2+}$ complex can be served as a new and effective fluorescence resonance energy transfer(FRET) donor for rhodamine derivatives.

Keywords Chemosensor; Aluminium ion; Calcium ion; Fluorescence resonance energy transfer(FRET)

1 Introduction

In recent years, fluorescent chemosensors have evoked significant interest because of the simplicity of use and high sensitivity of response[1,2]. Followed oxygen and silicon, aluminium is the third most abundant element in the earth’s crust[3]. However, mounting evidence suggests that aluminium has severe toxicity. Alzheimer’s disease, Parkinson’s disease, and amyotrophic lateral sclerosis are all induced by aluminium[4–7]. Aluminium ion($\text{Al}^{3+}$) is also suspected to be the root cause of infant liver damage[8]. Calcium ion($\text{Ca}^{2+}$) is also an important element because it modulates most physiological and pathological phenomena in the human body, including cell damage and death. $\text{Ca}^{2+}$ also performs as a vital signal transmitter[9–12]. Consequently, much attention has been paid to the development of selective $\text{Al}^{3+}$ and $\text{Ca}^{2+}$ sensors for the biological and environmental applications[13–16]. However, chemosensors which are capable to sense $\text{Al}^{3+}$, $\text{Ca}^{2+}$ or other ions and to use different signalling ways are rare in the literature[17–21]. These systems can be helpful to the design of new probes that are able to identify, not just one but multiple analytes.

Both coumarin compounds and rhodamine dyes have high molar extinction coefficients and high fluorescence quantum yields, which attract the interest of scientists to develop the rhodamine and coumarin derivative probes[22–29]. What’s more, the emission spectrum of coumarin and the absorption spectrum of rhodamine dyes overlap largely, providing the basis for the design of fluorescent probes based on the mechanism of fluorescence resonance energy transfer(FRET)[27]. Recently, several coumarin modified rhodamine derivatives have been reported[28–31] that could selectively detect metal ions. However, those sensors could only detect one or two metal ions, and the rhodamine-coumarin complexes exhibited same spectrum and rarely utilized the mechanism of FRET. Thus the design of a sensor that can detect different ions simultaneously and give different signals is still a challenging task and will be highly useful to the biological applications.

Based on the above considerations, herein we reported the synthesis and properties of a new rhodamine-based compound (1) which bears a coumarin group Schiff base derivative. Compound 1 has a capability of selective fluorescent recognition of $\text{Al}^{3+}$ or $\text{Ca}^{2+}$, giving different fluorescent signals under the same conditions. Free compound 1 shows weak fluorescence emission because of the quenching of efficient photoinduced electron transfer(PET) of coumarin moiety[31]. When $\text{Ca}^{2+}$ was added to the solution of compound 1, PET was interrupted and a strong emission was given with a peak centered at 490 nm. When $\text{Al}^{3+}$ was added to the solution of compound 1, a selective colorimetric change was observed, also the fluorescence showed a “turn-on” at 552 nm, ascribed to the rhodamine ring-opening. As expected, an FRET phenomenon occurred from the coumarin moiety to the rhodamine moiety. Adding $\text{Al}^{3+}$ to a solution of 1-$\text{Ca}^{2+}$ resulted in a decrease of the emission peak of the sensor at 490 nm. A new peak gradually
increased at around 552 nm, implying the displacement of Ca\(^{2+}\) by Al\(^{3+}\). So compound 1 is sensitive to both Al\(^{3+}\) and Ca\(^{2+}\) at the same time based on the mechanisms of FRET and PET, respectively.

2 Material and Methods

2.1 Reagents and Instruments

Anhydrous methanol, ethanol, N,N-dimethylformamide, ethyl acetate and petroleum ether were purchased from Sinopharm Chemical Reagent Co., Ltd. Metal salts (Zn\(^{2+}\), Hg\(^{2+}\), Cu\(^{2+}\), Fe\(^{3+}\), Cd\(^{2+}\), Ni\(^{2+}\), Mg\(^{2+}\), Ca\(^{2+}\), Al\(^{3+}\), La\(^{3+}\), K\(^{+}\), Na\(^{+}\), Mn\(^{2+}\), Pb\(^{2+}\) and Ag\(^{+}\)) were purchased from Aladdin Co., Ltd., and used without further purification. Methanol used for spectra detection was of high performance liquid chromatography (HPLC) purity. Double-distilled water was used throughout the experiments.

NMR spectra were recorded on a Varian 400 MHz NMR spectrometer with CDCl\(_3\) as the solvent. A Varian Cary-50 UV-Vis spectrophotometer with 1.0-cm quartz cell was used to record the absorbance spectra. The fluorescence spectra were recorded on a Varian spectrofluorometer with both the excitation and emission slit widths setting at 10.0 nm. High resolution mass spectrum (HRMS) was determined on an LCMS-IT TOF (LC30A, Shimadzu, Japan). Fourier transform infrared (FTIR) spectra were recorded on a TENSOR27 FTIR spectrometer (Bruker, Germany). Thin layer chromatography (TLC) analysis was performed on silica gel plates and column chromatography was conducted on silica gel, both of which were obtained from Qingdao Ocean Chemicals (Qingdao, China).

2.2 General Method

Stock solutions of the metal ions (10 mmol/L) were prepared with deionized water. A stock solution of compound 1 (0.2 mmol/L) was prepared with ethanol and 0.5 mL of it was diluted with ethanol to 10 \(\mu\)mol/L in 10 mL volumetric flask and then metal ions were added. During the 1-Al\(^{3+}\) titration experiments, spectral data were recorded at 5 min after the addition each time. While during the 1-Ca\(^{2+}\) titration experiments, spectral data were recorded immediately after the addition. For fluorescence measurements, excitation wavelength was 397 nm, and emission wavelengths were from 495 nm to 675 nm for 1-Al\(^{3+}\) and from 420 nm to 650 nm for 1-Ca\(^{2+}\), respectively.

2.3 Synthesis of Probe(1)

As shown in Scheme 1, 7-hydroxy-2-oxo-2H-chromene-8-carbaldehyde(3) was synthesized by the reported procedure \cite{32} with a yield of 54%. Rhodamine 6G hydrozide (0.084 g, 0.21 mmol) and compound 3 (0.04 g, 0.21 mmol) were dissolved in methanol and then the solution was heated under reflux for 3 h. After cooling, the precipitate was collected by filtration and washed with methanol three times. The crude product 1 was further purified by chromatography on silica gel (petroleum ether):ethyl acetate)=9:1] to give the light pink solid (0.065 g, yield 52%). \(^{1}H NMR(400 MHz, CDCl_3), \delta: \) 12.07(s, 1H), 9.37(s, 1H), 8.08—8.05(m, 1H), 7.58—7.55(m, 2H), 7.51(d, \(J=9.5\) Hz, 1H), 7.23(d, \(J=8.7\) Hz, 1H), 7.17—7.15(m, 1H), 6.76(d, \(J=8.7\) Hz, 1H), 6.51(s, 2H), 6.30(s, 2H), 6.17(d, \(J=9.5\) Hz, 1H), 3.55(s, 2H), 3.23(q, \(J=7.1\) Hz, 4H), 1.91(s, 6H), 1.32(t, \(J=7.1\) Hz, 6H); \(^{13}C NMR(101 MHz, CDCl_3), \delta: \) 163.97, 162.09, 159.67, 153.72, 151.77, 151.36, 147.66, 144.73, 143.25, 133.73, 129.80, 129.04, 128.53, 127.71, 124.08, 123.40, 118.00, 114.06, 112.35, 110.62, 106.65, 104.95, 96.84, 66.13, 38.21, 16.62, 14.57; HRMS-electrospray ionization (ESI), \(m/z\) 601.2442 [M+H]+ (100%). The characterization of the new compounds is listed in Fig.S1—S4 and Table S1 (see the Electronic Supplementary Material of this paper). The structure of sensor 1 (Fig.1) was further confirmed by X-ray analysis.

2.4 Quantum Yield Measurement

The fluorescence quantum yields of complexes 1-Al\(^{3+}\) and 1-Ca\(^{2+}\) were obtained with the following formula \cite{33}

\[
\phi = \phi_{\text{ad}} \left( \frac{n_{\text{sample}}^2}{n_{\text{ref}}^2} \right) \left( \frac{F_{\text{sample}}}{F_{\text{ref}}} \right)
\]

where \(\phi\) and \(\phi_{\text{ad}}\) represent the fluorescence quantum yields of the sample and reference, respectively; \(A\) and \(A_{\text{ad}}\) are the absorbance of sample and the reference, respectively. Under the same excitation wavelength, \(F_{\text{sample}}\) and \(F_{\text{ref}}\) are the corresponding...