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A Novel Coumarin Schiff-base Fluorescent Probe for Mg^{2+}

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ABSTRACT

A novel fluorescent probe for Mg^{2+} based on coumarin Schiff-base was synthesized and characterized. The sensor displayed high selectivity toward Mg^{2+} in acetonitrile, and shows 1:1 complex formation with Mg^{2+} in acetonitrile.

KEYWORDS

Coumarin, Schiff-base, fluorescent probe, magnesium ion.

1. Introduction

The design and synthesis of fluorescent probes with selectivity and sensitivity is an active field of supramolecular chemistry for biological as well as analytical and environmental problems. Mg^{2+} is one of the most abundant divalent ions in the cell, and it plays a critical role in many biological activities, such as cell proliferation[1,2], cell death[3], signal transduction[4], transporters[5] and ion channels.[6,7] To date, several fluorescence-based probes for Mg^{2+} have been developed; however, most of them have shortcomings in practical application, such as difficult synthesis, insufficient selectivity or sensitivity, or interference problems from other metal ions.[8,9] Therefore, development of highly sensitive and selective fluorescent probes is necessary.

Coumarin and its derivatives have been widely used as desirable fluorophore and binding moiety. However, there are few reports about the derivatives of coumarin as fluorescent sensors for Mg^{2+}.[10–12] In this paper, a highly sensitive and selective fluorescent chemosensor **3** for Mg^{2+} based on coumarin Schiff-base is demonstrated (Scheme 1), which displays remarkable fluorometric enhancement upon the addition of Mg^{2+}.

2. Experimental

All chemicals were purchased from commercial suppliers and used without further purification. The solvents purified with standard methods. ^1H and ^{13}C NMR spectra were recorded in a Broker 400 spectrometer. Chemical shifts are reported in ppm using tetramethylsilane (TMS) as the internal standard. Mass spectra were obtained in Agilent 1100-Bruker Esquire HCT liquid chromatograph-mass spectrometer. UV-vis absorption and fluorescence spectra were measured with a TU-1901 double-beam UV-vis spectrophotometer, RF-53010 PC fluorescence spectrophotometer, respectively.

Synthesis of 8-((1,3,4-Thiadiazol-2-ylimino)methyl)-7-hydroxy-4- methyl-2H-chromen-2-one (**3**)

1,3,4-Thiadiazol-2-amine (**1**) was synthesized according to literature.[13] 8-Formyl-7-hydroxy-4-methylcoumarin (**2**) was synthesized according to literature.[14]

Compound **1** (2.45 mmol, 0.500 g) was dissolved in ethanol (20 mL), and compound **2** (2.45 mmol, 0.247 g) was added to the solution. The reaction mixture was refluxed for 8 h under N_2 atmosphere, cooled to room temperature. The pale yellow precipitate was filtered and washed with cold ethanol. The crude product was recrystallized from ethanol to give **3** (90 %) as yellow solid; m.p. 226–228 °C; δ_H (400 MHz, $CDCl_3$): 2.43(3H, s), 6.21(1H, s), 6.91(1H, d, *J* 9.2 Hz,), 7.73(1H, d, *J* 8.8 Hz), 10.62(1H, s),12.22(1H, s) ppm; δ_C (100 MHz, $CDCl_3$): 18.95, 108.66, 111.96, 112.06, 114.27, 132.88, 152.63, 156.14, 159.19, 165.25,193.40 ppm; *m/z*: 286.1 $[M-H]^+$ (Found: C, 54.40; H, 3.11; N, 14.78; S, 11.10 %. Calc. for $C_{13}H_9N_3O_3S$(287.29): C, 54.35; H, 3.16; N, 14.63; S 11.16 %).

3. Results and Discussion

As shown in Fig. 1, the free ligand **3** (10 μM) alone had a weak fluorescence intensity at 456 nm when it was excited at 343 nm, due to isomerization of the C=N double bond and effect of intramolecular charge transfer (ICT) in Schiff base. Compound with an unbridged C=N structure is often nonfluorescent due to the C=N isomerization, but it may be inhibited by complexation with metal ions.[15] Upon addition of Mg^{2+} (0–300 μM) into the

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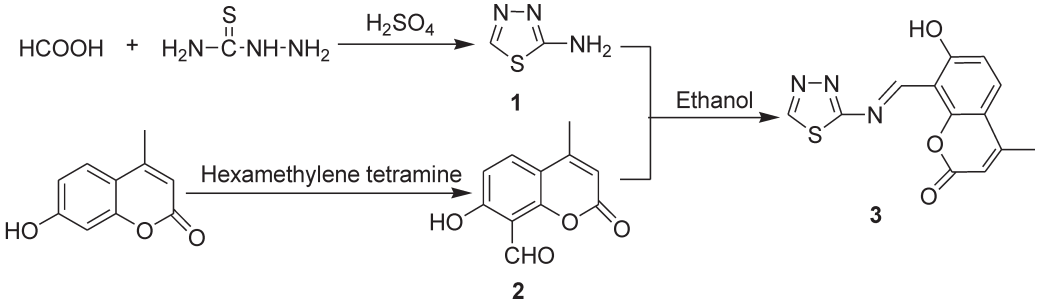

Scheme 1
Synthetic route of chemosensor **3**.

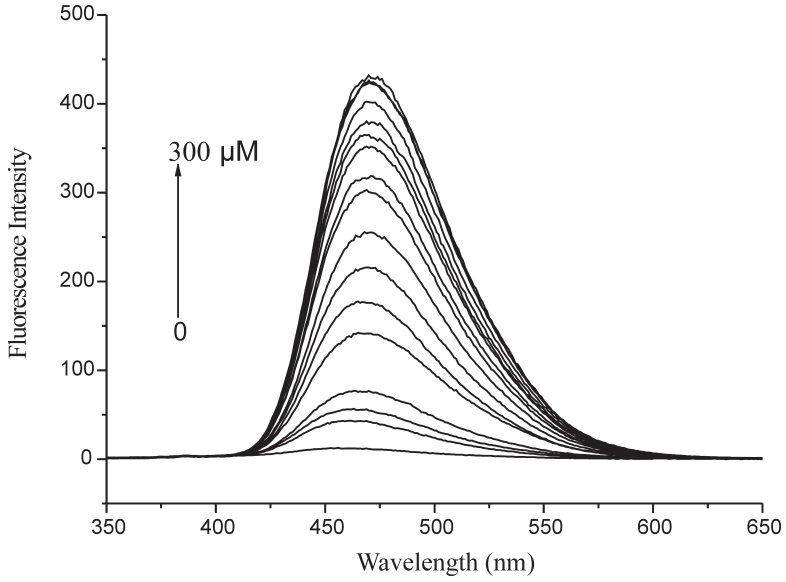

Figure 1 Fluorescence spectra (λ_{ex} = 343 nm) of **3** (10 μM) upon the titration of Mg^{2+} (0–300 μM) in acetonitrile.

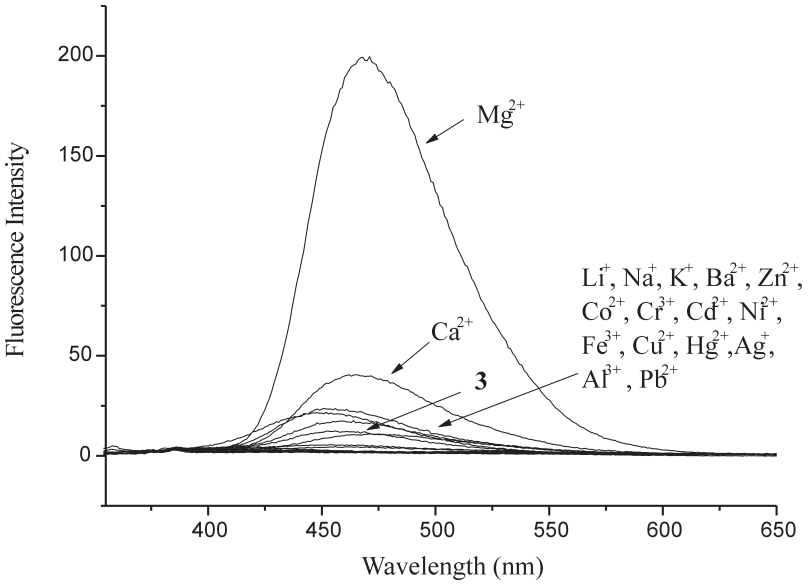

Figure 2 Fluorescence spectra of **3** (10 μM, λ_{ex} = 343 nm) with addition of various general metal ions (1 equiv, respectively) in acetonitrile.

solution of **3** (10 μM), the fluorescence intensity was increased, and λ_{em} red-shifted to 470 nm. At a Mg^{2+} concentration of 150 μM, the fluorescence intensity reached a maximum and showed a 33.3-fold enhancement, which suggested that **3** may serve as a 'turn-on' sensor for Mg^{2+}.

The selectivity of **3** (10 μM) to various metal ions was examined in acetonitrile. As shown in Fig. 2, upon addition of 1 equiv. of Li^+, Na^+, K^+, Ca^{2+}, Ba^{2+}, Zn^{2+}, Co^{2+}, Cr^{3+}, Cd^{2+}, Ni^{2+}, Fe^{3+}, Cu^{2+}, Hg^{2+}, Ag^+, Al^{3+}, Pb^{2+} and Mg^{2+}, the sensor **3** (10 μM, λ_{ex} = 343 nm) showed large fluorescence enhancement with Mg^{2+}, the other metal cations showed relatively little influence on the fluorescence intensity of **3**.

The interference of other metal ions to the detection of Mg^{2+} was also investigated. Mg^{2+} (10 μM) was added to the solution of **3** (10 μM) in the presence of 1 equiv. of the other metal ions. As shown in Fig. 3, with the addition of Hg^{2+}, Co^{2+}, Zn^{2+} and Ni^{2+}, the fluorescence intensity of Mg^{2+} complex at 470 nm decreased, but it still had strong fluorescence intensity. The fluorescence intensity increased with the addition of Li^+, Na^+, K^+, Ca^{2+}, Ba^{2+}, Ag^+, Pb^{2+} and Cd^{2+}. Although Cu^{2+}, Al^{3+} and Fe^{3+} could quench fluorescence of **3** *via* energy or electron transfer[16], the quenched fluorescence intensity could be enhanced to 8-fold, 4.5-fold and 4.75-fold, respectively. Therefore, **3** showed a high selectivity for Mg^{2+} in the presence of these coexistent metal ions in acetonitrile.

To determine the stoichiometry of the **3**/Mg^{2+} complex, Job's method was used. By keeping the total concentration of Mg^{2+} and **3** at 20 μM, and changing the molar ratio of Mg^{2+} (X_M; X_M=[Mg^{2+}]/{[**3**]+[Mg^{2+}]}) from 0 to 0.9, the fluorescence intensity of **3** in the absence (F_0) and presence (F) of Mg^{2+} ion was determined, respectively. A plot of ($F-F_0$) *versus* X_M shows that the value goes through a maximum at a molar fraction of about 0.5, indicating a 1:1 stoichiometry complex formation exactly (Fig. 4).

4. Conclusion

A novel coumarin Schiff-base fluorescent probe **3** for Mg^{2+} has been designed and synthesized. It displayed high selectivity and sensitivity for Mg^{2+} over the other metal ions. The chemosensor **3** shows 1:1 complex formation with Mg^{2+} in acetonitrile.

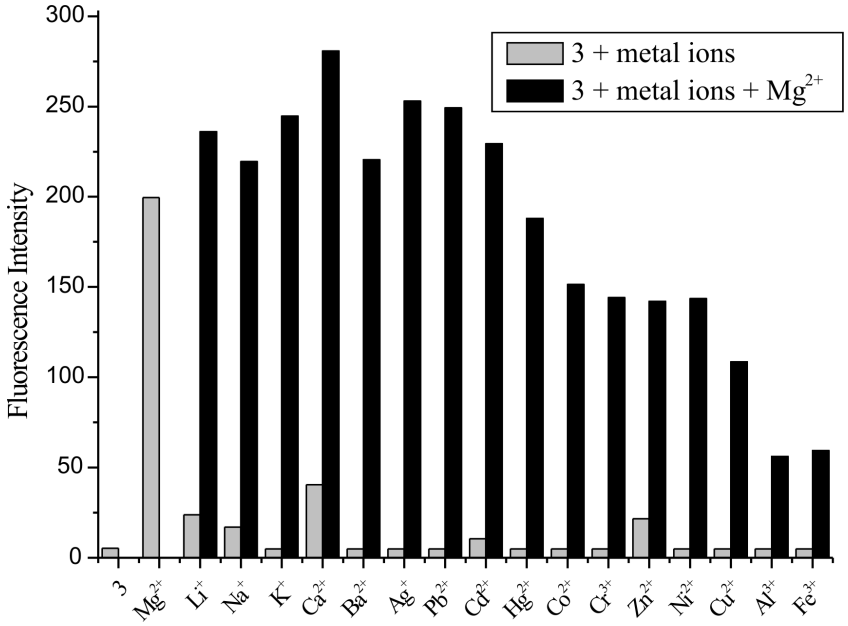

Figure 3 Fluorescence responses of **3** (10 μM, λ_{ex} = 343 nm) to various metal ions (10 μM) in acetonitrile. Light grey bars represent the addition of metal ions to a 10 μM solution of **3**, respectively. Black bars represent emission intensity of a mixture of **3** (10 μM) with metal ions (10 μM) followed by addition of 10 μM Mg^{2+} to the solutions, respectively.

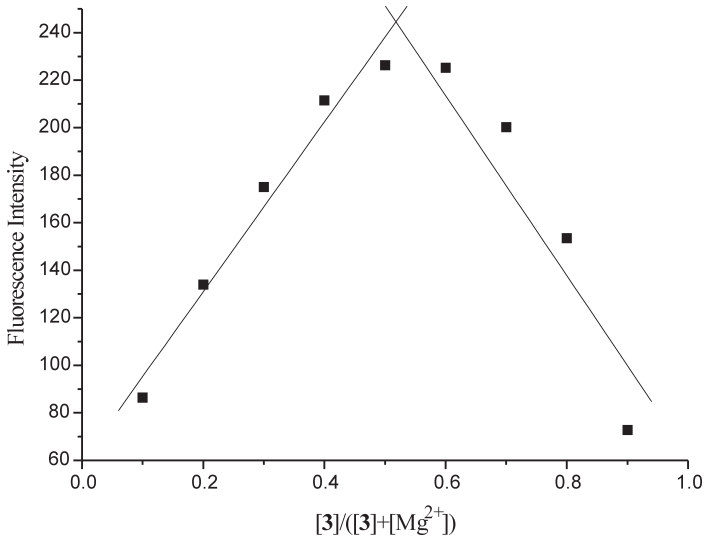

Figure 4 Job's plot of the complexation between **3** and Mg^{2+}, total concentration of **3** and Mg^{2+} is 20 μM.

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