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Fluorescence chemosensor containing 4-methyl-7-coumarinyloxy, acetylhydrazono and *N*-phenylaza-15-crown-5 moieties for K^+ and Ba^{2+} ions

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Abstract: A new aza-15-crown-5 derivative **1** bearing coumarin and hydrazone moieties was synthesized and characterized. The fluorescent sensing behavior and selectivity of **1** toward different metal ions in ethanol were investigated. There are 4-fold and 2-fold fluorescence enhancements of **1** at $\lambda_{em} = 406$ nm upon addition of five equivalents of K^+ and Ba^{2+}, respectively. The fluorescence titration revealed the stoichiometry of 1:1 for **1**-K^+ **1**-Ba^{2+} complexes and the binding constants ($\lg K_s$) of 4.11 for **1**-K^+ and 3.61 for **1**-Ba^{2+}. Compound **1** can be used as a fluorescent chemosensor for K^+ and Ba^{2+} through discriminable photoresponse signals. The calculated detection limits for K^+ and Ba^{2+} are 2.28 μm and 5.21 μm, respectively.

Keywords: barium ion; chemosensor; detection; fluorescence; potassium ion; synthesis.

Introduction

The design and construction of chemosensors with high selectivity and sensitivity for various metal ions have become the focus of numerous studies due to their importance in chemical, biological and environmental processes [1–7]. Of various chemosensors known to date, the fluorescence sensors are excellent tools for detecting metal ions due to their high sensitivity and real-time detection [8–13].

Potassium ion is one of the most abundant physiological metal ions in living organisms. The imbalance in K^+ in the human body is an early indicator of certain diseases. An excessive concentration of Ba^{2+} in the human body may cause heart rate change, high blood pressure, kidney problem, significant weight loss and nerve palsy. Therefore, the selective detection of K^+ and Ba^{2+} in the presence of other ions is of practical significance. However, the challenge exists in detecting and accurately measuring the concentrations of these ions in the presence of other ions, such as Na^+, Ca^{2+} and Mg^{2+} [14–21]. Few sensors have been developed for K^+ and Ba^{2+} ions [22, 23]. Sensors for other metal ions are normally composed of crown ether and/or coumarin moieties [24–30]. On the basis of the information discussed above, a new coumarin derivative **1** was synthesized and characterized (Scheme 1). Compound **1** is capable of selective fluorescent recognition of K^+ and Ba^{2+} ions, giving rise to a different fluorescent signal for each metal ion under the same conditions.

Results and discussion

The straightforward synthesis of compound **1** is shown in Scheme 1. Compound **1** was obtained in an analytically pure form and fully characterized. In order to examine the spectral sensitivity and selectivity of compound **1** as a metal ion sensor, spectroscopic studies in the presence of various metal ions were conducted in ethanol. UV-vis spectra and fluorescence emission spectra changes of **1** upon addition of five equivalents of various metal ions including Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, Al^{3+}, Fe^{3+}, Tb^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+} and Hg^{2+} are shown in Figure S1 and Figure 1, respectively. As can be seen, the addition of these metal ions does not cause significant UV-vis absorption spectral changes of **1**. By contrast, a substantial change in fluorescence of **1** is observed in the presence of K^+ or Ba^{2+}. As can be seen from Figure 1, there are 4-fold and 2-fold fluorescence enhancements of **1** at $\lambda_{em} = 406$ nm upon addition of K^+ and Ba^{2+}, respectively. Other ions cause a negligible response to fluorescence of **1**.

High selectivity is an important feature in the performance of a fluorescent sensor for the specific analyte over other competitive species. In order to evaluate the selectivity of **1** as a fluorescent chemosensor for the detection of K^+ and Ba^{2+}, the competitive spectral analysis in ethanol in the presence of other metal ions was conducted. Compound **1** (7 μm) was treated with five equivalents of K^+ or Ba^{2+} and an additional metal ion (five equivalents)

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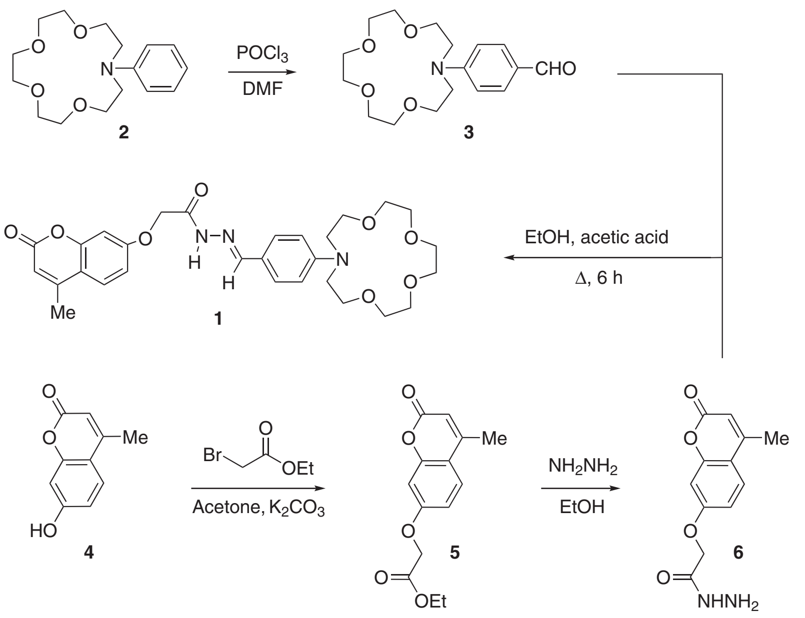

Scheme 1 The synthetic route to fluorescent sensor **1**.

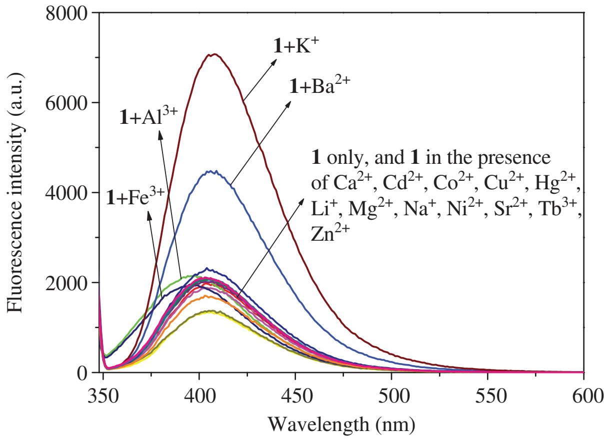

Figure 1 Fluorescence emission spectra of **1** (7 μM) in ethanol in the presence of five equivalents of different metal ions ($\lambda_{ex} = 343$ nm).

and fluorescence at 406 nm was recorded. The results are summarized in Figure 2A and B. As can be seen, the corresponding fluorescence responses of **1** to K^+ and Ba^{2+} in the absence and presence of other ions are similar. The addition of K^+ to the mixture of **1** and Ba^{2+} results in an enhancement of fluorescence intensity at 406 nm of **1** compared with the spectrum in the presence of Ba^{2+} alone (Figure 2B). This result is in agreement with the data in Figure 1 and demonstrates that **1** shows a preference to K^+ relative to any other metal ion.

The sensitivity of sensor **1** was estimated by changing amounts of K^+ and Ba^{2+} from 0–7.5 equivalents and 0–9.5 equivalents, respectively (Figure 3A and B). When **1** was titrated with K^+ or Ba^{2+}, the fluorescence emission intensity of **1** gradually increased. The maximum intensity was obtained for 7.5 equivalents of K^+ and 9.5 equivalents of Ba^{2+}, leading to 4.2-fold and 2.8-fold fluorescence enhancement, respectively, at $\lambda_{em} = 406$ nm. This result is consistent with the superior binding ability of **1** towards K^+, as already discussed. The observed fluorescence enhancement might be attributed to the inhibition of the photo-induced electron transfer (PET) process upon complexation of sensor **1** with K^+ and Ba^{2+} [31]. The Benesi-Hildebrand equation was used to analyze the complexation ratio and binding constants. The results in Figure 3A and B indicate a 1:1 binding stoichiometry of **1** towards K^+ and Ba^{2+}. The calculated binding constants ($\lg K_s$) for K^+ and Ba^{2+} are 4.11 and 3.61, respectively.

For practical applications, the detection limit is also an important parameter. The limits of detection of **1** for the analysis of K^+ and Ba^{2+} were calculated to be 2.28 μM and 5.21 μM, respectively. A good linear relationship between the fluorescence emission intensity at 406 nm of **1** and the concentration of K^+ and Ba^{2+} in the respective ranges of 2.2 μM–50 μM and 5.0 μM–66 μM were obtained. In both cases, the coefficients of linearity were 0.99. The recognition reversibility of sensor **1** to K^+ and Ba^{2+} were further verified by adding sodium tetraphenylborate (NaTPB) to the solution of **1**-K^+ complex and Na_2EDTA to the solution of **1**-Ba^{2+} complex. The addition of NaTPB to a mixture of **1** with K^+ or the addition of Na_2EDTA to a mixture of **1** with Ba^{2+} both resulted in the return of the original fluorescence at 406 nm, for free compound **1**. These results demonstrate that **1** is as a reversible chemosensor for K^+ and Ba^{2+} ions.

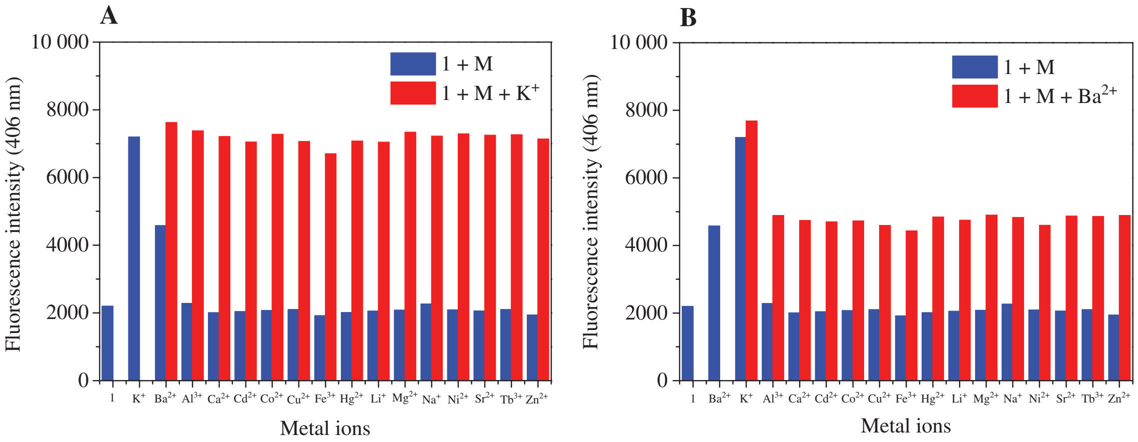

Figure 2 Panels (A) and (B) show the results of interference tests in ethanol of **1**-K^+ and **1**-Ba^{2+} by other metal ions. Blue bar: **1** (7 μM) in the presence of five equivalents of another metal ion. Red bar: **1** (7 μM) in the presence of five equivalents of K^+ or Ba^{2+} and five equivalents of another metal ion. Response of **1** (7 μM) is included as control. The excitation was at 343 nm and fluorescence at 406 nm was measured in all cases.

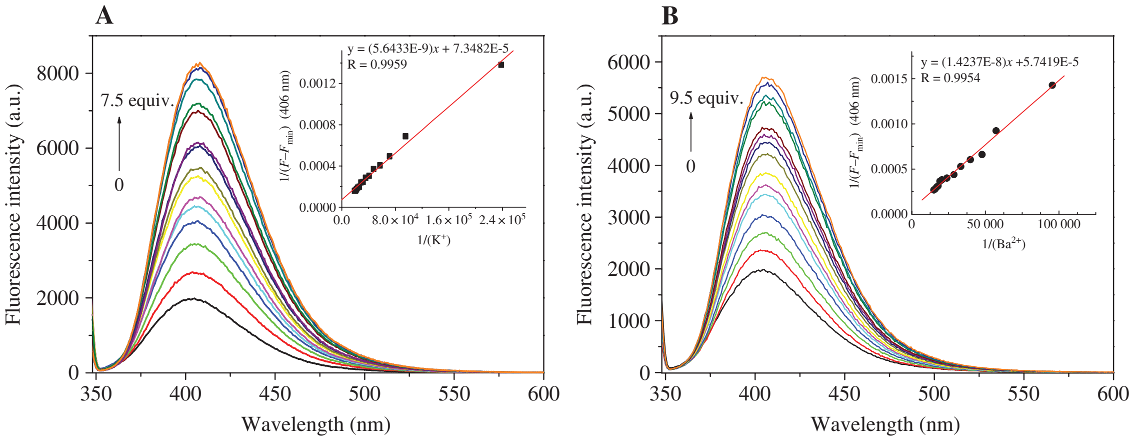

Figure 3 Fluorescence emission changes of **1** (7 μM) in ethanol upon addition of 0–7.5 equivalents of K^+ (A) and addition of 0–9.5 equivalents of Ba^{2+} (B) upon excitation with $\lambda_{ex} = 343$ nm. Inserts are Benesi-Hildebrand plots of fluorescence emission at 406 nm versus the equivalents of K^+ (A), Ba^{2+} (B) added.

Conclusion

A new fluorescent chemosensor **1** was synthesized and used to detect K^+ and Ba^{2+} ions at the respective concentrations in ethanol as low as 2.28 μM and 5.21 μM. Sensor **1** shows a preferential selectivity to K^+ relative to other metal ions. The 1:1 binding stoichiometry of **1** towards K^+ and Ba^{2+} was obtained by linear fitting analyses to the Benesi-Hildebrand equation. The binding constants ($\lg K_s$) of 4.11 for **1**-K^+ and 3.61 for **1**-Ba^{2+} were obtained.

Experimental

Solutions of metal ions (Li^+, Na^+, K^+, Ca^{2+}, Mg^{2+}, Ba^{2+}, Sr^{2+}, Fe^{3+}, Co^{2+}, Cu^{2+}, Ni^{2+}, Al^{3+}, Cd^{2+}, Hg^{2+}, Tb^{3+} and Zn^{2+}) were prepared from the corresponding metal chloride salts. Proton nuclear magnetic resonance (^1H NMR) spectra (500 MHz) were recorded on a Bruker Advance III 500 spectrometer with tetramethylsilane (TMS) as internal standard. Elemental analyses were done on a Vario micro-elemental analyzer. UV-vis and fluorescence spectra were recorded on Hitachi U-2900 and F-4600 spectrophotometers. Mass spectra were obtained using Thermo LCQ Advantage LC-MS instrument operating in electrospray ionisation (ESI) mode. *N*-Phenylaza-15-crown-5 (**2**), *N*-(4-formylphenyl)-aza-15-crown-5 (**3**) and 7-hydroxy-4-methylcoumarin (**4**) have been described in the literature and are commercial products.

Coumarin derivative 5

A mixture of compound **4** (880 mg, 5 mmol) and anhydrous potassium carbonate (691 mg, 5 mmol) in dried acetone (40 mL) was stirred and treated dropwise with ethyl bromoacetate (0.55 mL, 835 mg, 5 mmol) for 15 min. The mixture was heated under reflux for 10 h, then filtered, and the filtrate was concentrated. The residue was washed with water and crystallized from ethanol to give colorless flakes; yield 93%; mp 98.4–99.5°C; ^{1}H NMR ($CDCl_3$): δ 1.33 (t, 3H, J = 7.0 Hz), 2.43 (s, 3H), 4.29 (q, 2H, J = 7.0 Hz), 4.71 (s, 2H), 6.19 (s, 1H), 6.81 (d, 1H, J = 2.5 Hz), 6.93 (dd, 1H, J_1 = 8.5 Hz, J_2 = 2.5 Hz), 7.56 (d, 1H, J = 8.5 Hz). Anal. Calcd for $C_{14}H_{14}O_5$: C, 64.12; H, 5.38. Found: C, 64.17; H, 5.28.

Coumarin derivative 6

A solution of compound **5** (524 mg, 2 mmol) in ethanol (4 mL) was stirred and treated dropwise for 15 min with hydrazine hydrate (80%, 0.17 mL, 2.7 mmol) and then the mixture was heated under reflux for an additional 3 h. The resultant white precipitate was filtered, crystallized from methanol and dried *in vacuo*; yield 59%; mp 201.4–203.0°C; ^{1}H NMR (DMSO-d_6): δ 2.40 (s, 3H), 4.35 (m, 2H), 4.62 (s, 2H), 6.23 (s, 1H), 6.97 (d, 1H, J = 2.5 Hz), 7.01 (dd, 1H, J_1 = 8.5 Hz, J_2 = 2.5 Hz), 7.70 (d, 1H, J = 8.5 Hz), 9.43 (s, 1H). Anal. Calcd for $C_{12}H_{12}N_2O_4$: C, 58.06; H, 4.87; N, 11.29. Found: C, 58.17; H, 4.78; N, 11.19.

Sensor 1

A solution of compound **6** (212 mg, 0.85 mmol) in absolute ethanol (23 mL) under a nitrogen atmosphere was stirred and treated dropwise for 30 min with a solution of aza-15-crown-5 derivative **3** (276 mg, 0.85 mmol) in absolute ethanol (23 mL) and then with two drops of glacial acetic acid. Upon stirring, the mixture was heated under reflux for 6 h. The resultant white precipitate was filtered, crystallized from *n*-heptane and dried *in vacuo*: white needles; yield 70%; mp 177.1–178°C; ^{1}H NMR (DMSO-d_6): δ 2.41 (s, 3H), 3.51–3.56 (m, 16H), 3.64–3.66 (m, 4H), 4.76 and 5.24 (2s, 2H), 6.22–6.25 (m, 1H), 6.68–6.71 (m, 2H), 6.95–7.06 (m, 2H), 7.48–7.51 (m, 2H), 7.69–7.75 (m, 1H), 7.87 and 8.15 (2s, 1H), 11.32 and 11.38 (2s, 1H); ESI-MS: *m/z* 576.30 ($M + Na^+$). Anal. Calcd for $C_{29}H_{35}N_3O_8$: C, 62.92; H, 6.37; N, 7.59. Found: C, 62.68; H, 6.30; N, 7.43.

Supporting information

Supplementary data for this article can be found in the online version.

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