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A Dual-Channel Fluorescence-Enhanced Sensor for Aluminum Ions Based on Photoinduced Electron Transfer and Excimer Formation

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Sensor **1** was developed as the first example of a fluorescence-enhanced Al^{3+} sensor with unique dual-channel emissions. The addition of Al^{3+} to **1** elicits a large fluorescence enhancement by inhibition of a quenching Photoinduced electron-transfer (PET) channel and also a dramatic fluorescence enhancement due to promotion of an emissive excimer channel formation. The dual-channel fluorescence-enhanced response of the sensor contributes to its high sensitivity and selectivity.

Introduction

Lately, fluorescent chemosensors for metal ions have become particularly attractive due to their useful applications in a wide variety of fields. [1] Aluminum is the third most abundant element on earth. However, aluminum toxicity can also elicit adverse environmental problems. It is believed that almost 40% of the world's acid soils is due to the effects of aluminum toxicity, which is the key factor hampering plant (i.e., crop) performance on the acid soils. [2] In addition, aluminum is also deemed to be the primary toxicant killing fish in acidified waters.[3] Therefore, the development of fluorescent sensors for aluminum is critical in environmental monitoring. A few cases of fluorescent Al^{3+} sensors that display limited sensitivity or selectivity have been identified.[4] However, most of them exhibit changes only in fluorescence intensity but not in fluorescence wavelengths. In practical applications, a change in fluorescence intensity is often disturbed by many factors, such as concentrations of a sensor, temperature, sensitivity of an instrument, etc. However, these issues can be addressed by employing ratiometric fluorescent sensors, which allow the measurement of emission intensities at two different wavelengths to provide a built-in correction for environmental effects.[1a]

Most of the ratiometric sensors exhibit fluorescence signal amplification at one emission wavelength concomitantly with signal reduction at another emission wavelength. By contrast, a dual-channel fluorescence-enhanced sensor displays fluorescence enhancement at two emission channels simultaneously upon binding with an analyte. Although dual-channel fluorescence-enhanced sensors are exceedingly sought because of their particularly favorable features such as high sensitivity, selectivity, and convenient visible emission assays due to improved signal-to-noise ratio, they are rarely developed with success.[5]

Herein, we report coumarin **1** as the first example of a fluorescence-enhanced Al^{3+} sensor with unique dual-channel emissions. Coumarin dyes have been extensively employed in fluorescent chemosensors primarily owing to their excellent photochemical and photophysical properties. [6] Furthermore, the carbonyl oxygen atom in coumarins could participate in coordinating with metal ions, which thus effectively modulates coumarin in the fluorescence character. Therefore, coumarins could play a role both as a fluorophore and a binding unit in sensors.[6d,6e] Compound **1** was readily synthesized in a few steps. The binding of Al^{3+} to **1** concurrently switches on two distinct fluorescence emission bands by combination of two signaling mechanisms: suppression of a quenching PET channel and promotion of an emissive excimer channel formation.

Results and Discussion

Compound **1** was readily synthesized by the route as outlined in Scheme 1. Condensation of 2,4-dihydroxybenzaldehyde with propanoic anhydride afforded hydroxycoumarin **2** in modest yield,[7] which was then treated with *n*BuBr to give *n*-butoxycoumarin **3** in good yield. Reaction of **3** with NBS (1.2 equiv.) provided bromocoumarin **4** in excellent yield.[8] Finally, **1** was prepared by treating **4** (two equiv.) with ethylenediamine in anhydrous acetonitrile (yield: 44%). The structures of the intermediates and the final product were confirmed by NMR spectroscopy, ESI MS, and elemental analysis.

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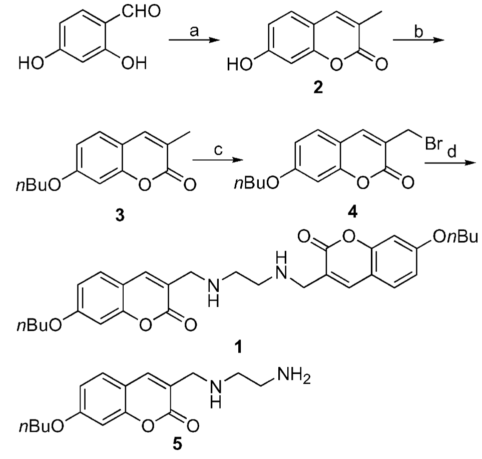

Scheme 1. Synthetic route to sensor **1**. Reagents and conditions: (a) CH_3CH_2COONa, $(CH_3CH_2CO)_2O$, triethylamine, reflux, 6 h; (b) *n*BuBr, acetone, K_2CO_3, reflux, 5 h; (c) NBS, AIBN, CCl_4, reflux, 8 h; (d) ethylenediamine, anhydrous acetonitrile, r.t., 4 h.

Compound **5** containing one coumarin fluorophore was used as a monomer control. As shown in Figure S1 (Supporting Information), monomer **5** only displays a weak fluorescent emission band around 395 nm owing to a quenching photoinduced electron-transfer (PET) process from the amino group to the coumarin fluorophore.[1] By contrast, **1**, which possesses two coumarin moieties, shows not only a monomer emission band at 395 nm, but also a broad and redshifted emission peak around 500 nm, which indicates that some excimer is already present in the apolar solvent CH_2Cl_2.[9,10] Moreover, the excimer formation in **1** is dependent on the polarity of solvents as indicated in Figure 1, which is in good agreement with the characteristics of the excimer as reported in the literature.[10] As **1** has minimum excimer fluorescence background around 500 nm in $CH_3OH/CH_2Cl_2/H_2O$ (2:3:0.01), this solvent system was chosen in the subsequent examination of the fluorescence response of the sensor toward metal ions in order to maximize the detection sensitivity.

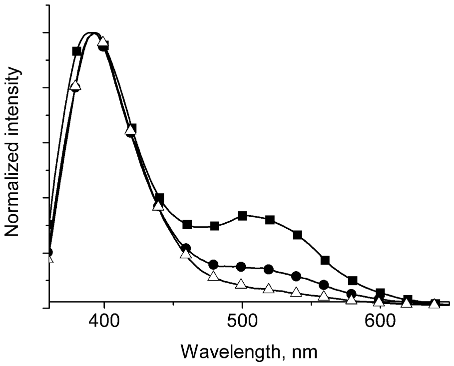

Figure 1. Solvent effect on the excimer fluorescence of **1**. Normalized at the monomer emission. The excitation wavelength was 340 nm: (■) CH_2Cl_2, (●) $CH_3OH/CH_2Cl_2/H_2O$ (1:4:0.01), (△) $CH_3OH/CH_2Cl_2/H_2O$ (2:3:0.01).

The metal recognition properties of **1** were initially evaluated by UV/Vis analysis. Figure 2a shows the absorption spectra of **1** in the absence and presence of different amounts of Al^{3+}. Free sensor **1** displays an absorption peak with a maximum around 327 nm, which is slightly redshifted (by about 7 nm) to 334 nm with a small decrease in the absorbance intensity upon addition of increasing concentrations of Al^{3+} ions. In addition, the spectra also exhibit a distinct isosbestic point at 340 nm, which is indicative of complex formation. Fluorescence emission was further investigated to determine the fluorescence response of **1** toward Al^{3+} ions under excitation at 340 nm (Figure 2b). The addition of Al^{3+} ions elicits not only a drastic increase in the monomer emission intensity around 395 nm owing to inhibition of the quenching PET process,[1] but also a dramatic fluorescence enhancement around 500 nm as a result of the promotion of an emissive excimer channel formation. The fluorescence enhancement factors (FEF) at 395 and 500 nm were determined as 15.7- and 56.8-fold, respectively. Thus, sensor **1** displays striking fluorescence amplification at two emission bands. Furthermore, the excitation spectra of the Al^{3+}-bound sensor (Figure S2, Supporting Information) suggest that the two emission bands at 395 and 500 nm originate from the same ground state.[5a]

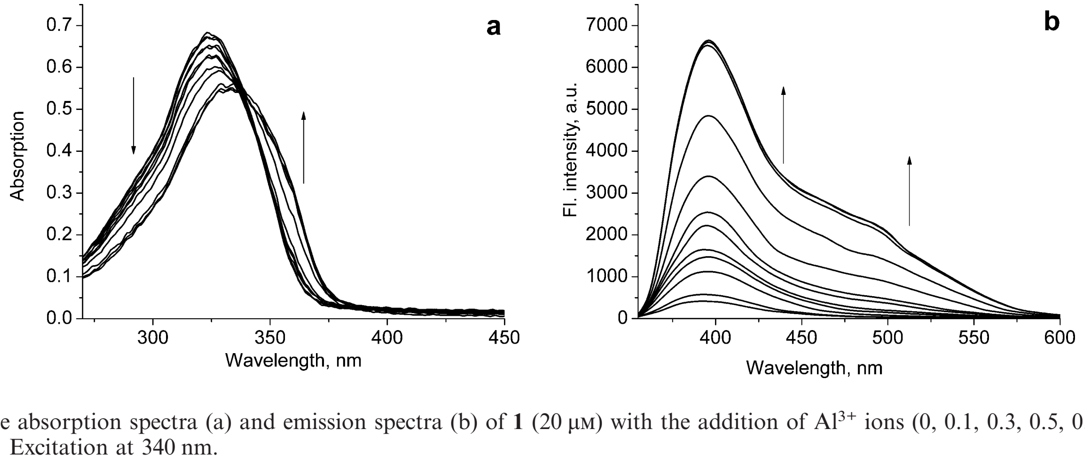

Figure 2. The absorption spectra (a) and emission spectra (b) of **1** (20 μM) with the addition of Al^{3+} ions (0, 0.1, 0.3, 0.5, 0.7, 1, 3, 5, 7, 9, 12 equiv.). Excitation at 340 nm.

To determine the stoichiometry of sensor **1** and Al^{3+} in the complex, Job's method [11] was employed by using emission changes at 395 nm as a function of molar fraction of Al^{3+}. A maximum emission was observed when the molar fraction of Al^{3+} reached 0.5 (Figure 3), which is indicative of a 1:1 stoichiometry complexation between **1** and Al^{3+} (the same stoichiometry value was obtained by using the emission changes at 500 nm, Figure S3). The stability constant of the complex was then calculated to be 1.23×10^5 M^{-1} with a good linear relationship (R = 0.993) by a 1:1 binding mode (Figure S4, Supporting Information).[12] As expected, the binding of Al^{3+} to sensor **1** is reversible, as evidenced by the complete reversal of the fluorescence signal to free sensor **1** when an excess amount of ethylenediamine was added to Al^{3+}-bound sensor **1** (Figure S5, Supporting Information). The proposed binding mode of sensor **1** with Al^{3+} is shown in Figure 4. This proposed mechanism is consistent with the dual-channel emissions of the complex at 395 and 500 nm. Coordination of Al^{3+} with the nitrogen atoms may effectively decrease their electron-donating ability, so the quenching PET process from the nitrogen atoms to the coumarin rings is inhibited, which results in a large increase in fluorescence intensity at 395 nm. In addition, the binding of Al^{3+} with two carbonyl oxygen atoms of the coumarin rings (consistent with the report that the carbonyl oxygen atom in the coumarin could be involved in an interaction with metal ions [6d,6e]) and the nitrogen atoms could elicit the folding of the sensor and the π–π* stacking of the coumarin dyes for the intramolecular excimer formation, consequently promoting the emission channel at 500 nm. In line with the proposed mechanism, the coordination of Al^{3+} with the nitrogen and two carbonyl oxygen atoms is further supported by the observation that addition of Al^{3+} induces significant changes in the NMR spectrum of sensor **1** (Figure 5). For example, upon the addition of Al^{3+}, the resonance signals corresponding to H^a on the –NH–, H^b on the –NCH_2–, and H^c on the coumarin rings become slightly broad and shift downfield to 0.81, 0.62, and 0.21 ppm, respectively.

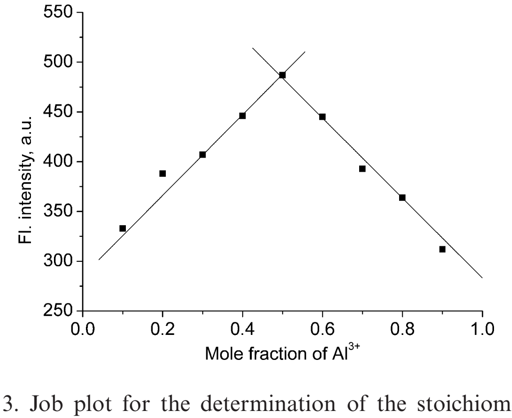

Figure 3. Job plot for the determination of the stoichiometry of sensor **1** and Al^{3+}. The total concentration of **1** and Al^{3+} was kept constant (25 μM). Excitation and emission was at 340 and 395 nm, respectively.

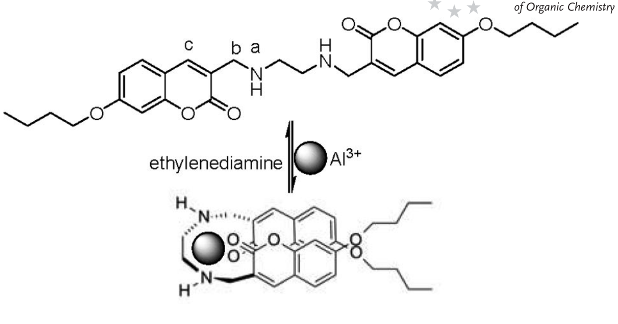

Figure 4. Proposed binding mode of **1** with Al^{3+}.

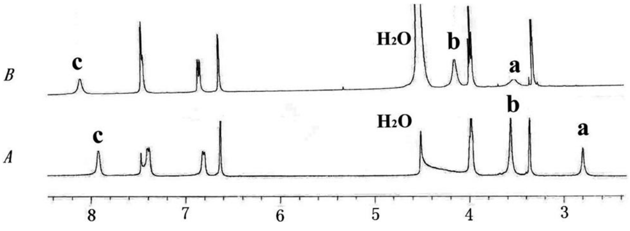

Figure 5. Partial ^1H NMR (400 MHz) spectrum of **1** in CD_3OD/$CDCl_3$ (2:3). (A) **1** only; (B) **1** + Al^{3+} (2 equiv.).

The sensor was treated with various metal ions to investigate the selectivity. Representative metal ions such as Na^+, K^+, Ca^{2+}, Mg^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Hg^{2+}, Cd^{2+}, Mn^{2+}, and Zn^{2+} only induce minimum perturbation in fluorescence spectra of sensor **1**, whereas Fe^{3+} gives a modest fluorescence enhancement (Figures S6 and S7, Supporting Information). However, the addition of Al^{3+} to sensor **1** causes the largest fluorescence enhancement, both around 395 and 500 nm. Thus, emissions from two channels are metal-ion dependent. This contributes considerably to the high selectivity of the sensor, supporting the benefit of dual-channel fluorescence-enhanced emissions. Furthermore, the visible emission of sensor **1** is also metal-ion dependent (Figure 6; for a color version, see Figure S8 in the Supporting Information); thus, the sensor could be employed for convenient visual sensing of Al^{3+}. To further explore the effective applications of the sensor, the fluorescence response of **1** to Al^{3+} in the presence of typical competing ions was studied. As shown in Figure 7, when Al^{3+} (12 equiv.) was added to sensor **1** in the presence of a wide variety of competing metal ions (12 equiv.) most exhibited minimum interference in the

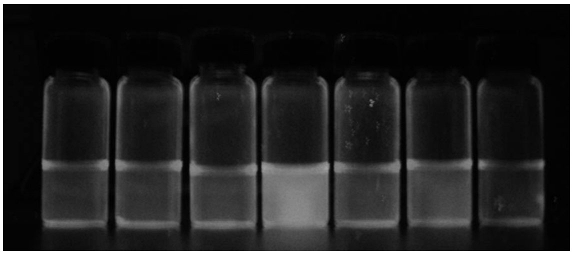

Figure 6. The visual fluorescence emissions of sensor **1** (20 μM) to metal ions (12 equiv.) on excitation at 365 nm by using a UV lamp at r.t. From left to right: free, Mg^{2+}, Co^{2+}, Al^{3+}, Hg^{2+}, Zn^{2+}, and Ni^{2+}.

detection of Al^{3+}. The observation that Fe^{3+} has no marked influence on Al^{3+} detection indicates that **1** has a higher binding affinity to Al^{3+} than Fe^{3+}. Thereby, sensor **1** is useful for selectively sensing Al^{3+} even under competition from other related metal ions.

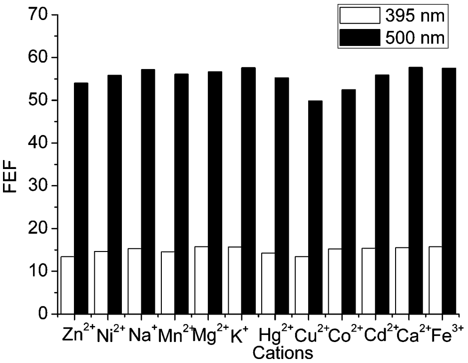

Figure 7. Fluorescence enhancement response of **1** (20 µm) to Al^{3+} (12 equiv.) in the presence of different competing metal ions (12 equiv.). Excitation at 340 nm.

Conclusions

Sensor **1** was developed as the first example of fluorescence-enhanced Al^{3+} sensor with unique dual-channel emissions. The addition of Al^{3+} to **1** results in not only a large fluorescence enhancement at 395 nm because of inhibition of a quenching PET channel, but also a dramatic fluorescence enhancement around 500 nm as a result of the promotion of an emissive excimer channel formation. The metal-ion-dependent dual-channel fluorescence-enhanced response contributes substantially to the high sensitivity and selectivity of **1**. Although sensor **1** is potentially useful in nonaqueous settings (environmental applications), it could also be extended to function in aqueous systems by incorporating hydrophilic groups. The work toward this end is in progress in our laboratory. In addition, we believe that the dual-channel signaling mechanism of sensor **1** should lead to the development of powerful sensors for other metal ions with fluorescence-enhanced dual-channel emissions for exciting applications in diverse fields.

Experimental Section

General Information and Materials: Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. Solvents used were purified and dried by standard methods prior to use. Twice-distilled water was used throughout all experiments. Melting points were determined with a Beijing taike XT-4 microscopy and are uncorrected. ESI MS analyses were performed by using a Waters Micromass ZQ-4000 spectrometer. Electronic absorption spectra were recorded with a SHIMADZU UV-2450 spectrometer. The emission spectra were measured with a HITACHI F4500 fluorescence spectrophotometer. ^{1}H NMR spectra were measured with an INOVA-400 spectrometer by using TMS as an internal standard. Elemental analyses were obtained with a Vario El III Elemental Analyzer. TLC analyses were performed on silica-gel plates and column chromatography was conducted on silica gel (mesh 200–300), both of which were obtained from Qingdao Ocean Chemicals.

4: To a solution of **3** (1.0 g, 4.3 mmol) in CCl_4 (35 mL) was added NBS (0.96 g, 5.4 mmol) and a trace amount of AIBN, and the mixture was then heated to reflux. After reaction for 8 h, the solvent was removed under reduced pressure, and the residue was then purified by chromatography on silica gel (CH_2Cl_2/petroleum ether, 1:1) to afford **4** as a colorless powder. Yield: 1.08 g (81.1%). M.p. 92–94 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.00 (t, 3 H), 1.51 (m, 2 H), 1.81 (m, 2 H), 4.03 (t, 2 H), 4.43 (s, 2 H), 6.81 (d, J = 2.0 Hz, 1 H), 6.86 (dd, J = 8.4 Hz and J = 2.4 Hz, 1 H), 7.38 (d, J = 8.8 Hz, 1 H), 7.79 (s, 1 H) ppm. MS (ESI): m/z = 311.2 $[M + H]^+$. $C_{14}H_{15}BrO_3$ (311.17): calcd. C 54.04, H 4.86; found C 53.89, H 4.92.

1: To a solution of **4** (73.8 mg, 0.30 mmol) in anhydrous CH_3CN (3 mL) was added ethylenediamine (0.01 mL, 0.15 mmol) in CH_3CN (1 mL). The reaction was kept at room temperature for 4 h, and the precipitate was collected and washed with Na_2CO_3 solution and CH_3CN to afford **1** as a colorless powder. Yield: 49.6 mg (43.6%). M.p. 176–178 °C. ^{1}H NMR (400 MHz; $CDCl_3$/CD_3OD, 3:2): δ = 1.00 (m, 6 H), 1.53 (m, 4 H), 1.80 (t, 4 H), 2.80 (s, 2 H), 3.57 (s, 4 H), 3.99 (t, 4 H), 6.64 (d, J = 2.0 Hz, 2 H), 682 (d, J = 8.0 Hz, 2 H), 7.40 (d, J = 7.6 Hz, 2 H), 7.93 (s, 2 H) ppm. MS (ESI): m/z = 520.2 $[M + H]^+$. $C_{30}H_{36}N_2O_6$ (520.62): calcd. C 69.21, H 6.97, N 5.38; found C 69.57, H 6.62, N 5.78.

General Procedures for the Metal-Ion Binding Studies: Metal chlorate (Hg^{2+}, Ni^{2+}, Ca^{2+}, Mg^{2+}, Cd^{2+}, Cu^{2+}, Co^{2+}, Zn^{2+}, Na^+, K^+, Al^{3+}, Fe^{3+}) or sulfate (Mn^{2+}) stock solutions were prepared in twice-distilled water. Sensor **1** was dissolved in CH_3OH/CH_2Cl_2 (2:3) at room temperature to afford the sensor stock solution (50 µm). Test solutions were prepared by placing 2 mL of the sensor stock solution and an appropriate aliquot of each metal stock into a 5-mL volumetric flask and diluting the solution to 5 mL with methanol/CH_2Cl_2 (2:3). The resulting solution was shaken well and left to stand at room temperature for 10 min before recording the absorption and emission spectra of the metal-complexed sensor. Unless otherwise noted, for all measurements, the excitation wavelength was at 340 nm and both the excitation and emission slit widths were 5 nm.

Supporting Information (see footnote on the first page of this article): Detailed experimental procedures and full characterization data for all compounds synthesized; some spectra of the sensor.

Acknowledgments

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