

A dual-model and on-off fluorescent Al³⁺/Cu²⁺-chemosensor and the detection of F[−]/Al³⁺ with 'in situ' prepared Al³⁺/Cu²⁺ complexes†

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A multifunctional fluorescent chemosensor for Al³⁺ and Cu²⁺ has been developed, which displays a dual-model and on-off fluorescence response upon addition of Al³⁺ and Cu²⁺ respectively. The fluorescence signals of the chemosensor can be restored with F[−] and ethylenediaminetetraacetic acid (EDTA) disodium for Al³⁺ and Cu²⁺, showing that the binding of the chemosensor and Al³⁺/Cu²⁺ is chemically reversible. The 'in situ' prepared Al³⁺ complex (1·Al) showed high selectivity toward F[−], which can be applied to distinguish F[−] from Cl[−], Br[−] and I[−]. Moreover, the fluorescence emission intensity of the 'in situ' prepared Cu²⁺ complex (1·Cu) is increased with the addition of Al³⁺, demonstrating that 1·Cu could be a good off-on Al³⁺ sensor candidate.

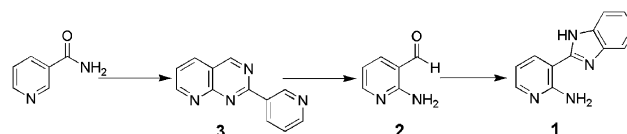
Fluorescent chemosensors with high selectivity, sensitivity and a low detection limit are widely used as powerful tools to spy on neutral and ionic species.^{1–4} As is well-known, aluminum is the third most abundant metal in the earth's crust and extensively used in modern life.⁵ The leaching of aluminum from soil by acid rain increases the free Al³⁺ in the environment and surface water, which is deadly for the growth of plants.^{6,7} On the other hand, Al³⁺ is neurotoxic to humans and could induce many health issues, such as Alzheimer's disease and Parkinson's disease.^{8–12} However, compared with other transition metal ions, the examples of Al³⁺ fluorescent chemosensors that have been reported are not many^{13–25} and the development of Al³⁺-sensors is of great importance. In addition, bifunctional probes have already emerged and have gradually become a new research focus^{26–41} because such a paradigm shift from selective to differential receptors can overcome difficulties such as cross-talk,⁴²

a larger invasive effect, *etc.* encountered with the combination of several probes.⁴³ In this work, we synthesized a bifunctional chemosensor **1** for Al³⁺ and Cu²⁺, which displays a dual-model and on-off fluorescence response upon addition of Al³⁺ and Cu²⁺ respectively. The fluorescence signals of **1** can be restored with addition of F[−] and EDTA disodium into solutions of 1·Al and 1·Cu, showing that the binding of chemosensor **1** and Al³⁺/Cu²⁺ is chemically reversible. Further experiments demonstrated that 1·Al could be applied to distinguish F[−] from Cl[−], Br[−] and I[−], and 1·Cu could be a good off-on Al³⁺ sensor candidate.

Chemosensor **1** was prepared in a yield of 70% from nicotinamide by a three-step synthetic procedure according to the synthetic route outlined in Scheme 1. The structure of **1** was confirmed by ¹H NMR, ¹³C NMR, HRMS and melting point data (ESI†).

The absorption spectrum of compound **1** in ethanol–water solution (V_{ethanol} : V_{water} = 9 : 1) exhibits a band at 345 nm in the range 300–400 nm (molar extinction coefficient ε₃₄₅ = 1.60 × 10⁴ M^{−1} cm^{−1}). This band may be assigned to electron transition from π to π*. Upon excitation at 356 nm, relatively strong fluorescence emission at 395 and 528 nm with Φ_f = 0.064 (right part of Fig. 1) was obtained in the emission spectrum of compound **1**, indicating the dual-emission behavior.

To interpret further the emission properties of **1**, we measured picosecond TRF spectra. The fluorescence decay behavior is shown in Fig. 2, and the fit results are summarized in Table 1. With emission wavelengths of 400 and 425 nm, the fluorescence decayed in a three-exponential manner with time constants of 1.0,



Scheme 1 Synthetic route of compound **1**.

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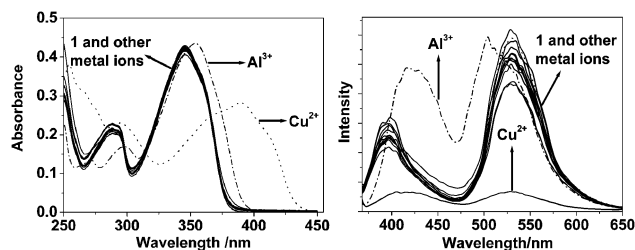


Fig. 1 Absorption (left) and emission (right) spectra of **1** (2.5×10^{-5} M, $V_{\text{ethanol}}:V_{\text{water}} = 9:1$) upon addition of different metal ions. The final ratio of metal ions to **1** is 13 and the excitation wavelength is 356 nm. The metal salts used were KCl, CaCl₂, NaCl, MgCl₂, Al(NO₃)₃, NiCl₂, CdCl₂, PbCl₂, MnCl₂, CoCl₂, HgCl₂, ZnSO₄, and CuCl₂.

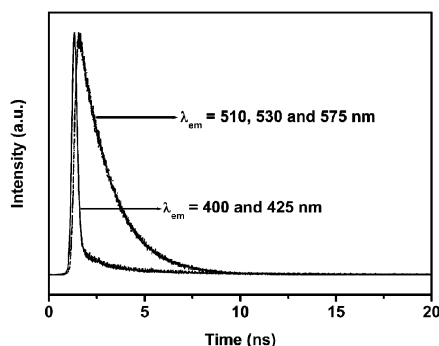


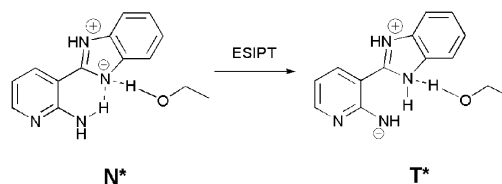
Fig. 2 Time-resolved fluorescence of **1** with an excitation at 372 nm and with different emission wavelengths.

Table 1 Fluorescence decay time constants of **1** with different emission wavelengths

$\lambda_{\text{em}}/\text{nm}$	τ_1	τ_2	τ_3	A1	A2	A3	χ^2
400	0.1	1.0	4.21	22%	30%	48%	1.250
425	0.1	1.0	5.07	17%	26%	57%	1.275
510	1.64			100%			1.111
530	1.64			100%			1.072
575	1.64			100%			1.032

0.1 and 4.21/5.07 ns, indicating that the fluorescence spectrum in a short wavelength range consist of three contributions from free **1**. With emission wavelengths of 510, 530 and 575 nm, the fluorescence decayed in a one-exponential manner with a time constant of 1.64 ns, indicating that the fluorescence spectrum in a long wavelength range consists of one contribution from free **1**. Such great difference in fluorescence decay behavior and the dual-emission behavior indicated that there exist two different excited states upon excitation at 356 nm. The dual emissions may be attributed to the excited normal (N^*) and tautomer (T^*) forms which result from an ESIPT ($N^* \rightarrow T^*$) process (Scheme 2).⁴⁴

Upon addition of 13 equiv. of different metal ions and with excitation at 356 nm, only Al(NO₃)₃ (Al³⁺) and CuCl₂ (Cu²⁺) resulted in different changes in the absorption spectrum of **1** (left part of Fig. 1). Al³⁺ led to a little red-shift from 345 nm to 355 nm ($\epsilon_{355} = 1.69 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$) (left part of Fig. 3), and Cu²⁺ brought a great red-shift from 345 to 390 nm ($\epsilon_{390} = 1.09 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$) (left part of Fig. 4). Upon addition of equal



Scheme 2 Model explaining the effect of protic solvent on the ESIPT reaction in **1**.

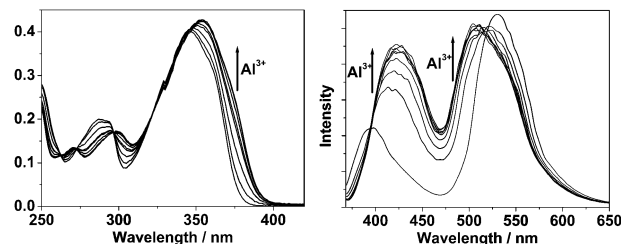


Fig. 3 Absorption (left) and emission (right) spectra of **1** (2.5×10^{-5} M, $V_{\text{ethanol}}:V_{\text{water}} = 9:1$) upon titration of Al³⁺ (the final ratio of Al³⁺ to **1** is 2). The excitation wavelength is 356 nm.

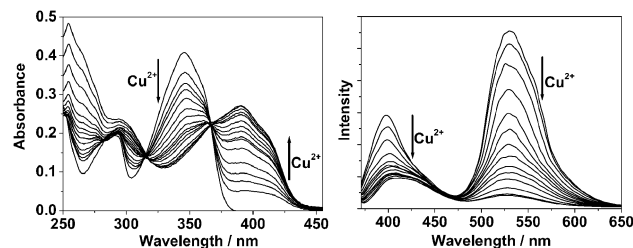


Fig. 4 Absorption (left) and emission (right) spectra of **1** (2.5×10^{-5} M, $V_{\text{ethanol}}:V_{\text{water}} = 9:1$) upon titration of Cu²⁺ (the final ratio of Cu²⁺ to **1** is 13). The excitation wavelength is 356 nm.

amounts of various metal ions (13 equiv.), only Al³⁺ and Cu²⁺ can cause a change in the emission spectrum of **1** (right part of Fig. 1). Such absorption and emission spectral changes may be ascribed to the newly formed complexes (**1**·Al and **1**·Cu).

With titration of Al³⁺, the fluorescence of **1** was enhanced ($\Phi_f = 0.089$) with a change in fluorescence emission wavelength from 395 and 528 nm to 430 and 504 nm, respectively (right part of Fig. 3), indicating efficient Al³⁺-selective dual-model fluorescent behaviour. As for Cu²⁺, because of its paramagnetic property and unfilled d shell, Cu²⁺ could strongly quench the fluorescence of the fluorophore **1** through electron and/or energy transfer processes.⁴⁵ As expected, Cu²⁺ decreased the emission of **1** (right part of Fig. 4), demonstrating effective on-off fluorescent behaviour. However, under identical conditions, nearly no fluorescence changes were observed in the emission spectrum of **1** with K⁺, Ca²⁺, Na⁺, Mg²⁺, Ni²⁺, Cd²⁺, Pb²⁺, Co²⁺, Mn²⁺, Hg²⁺, or Zn²⁺ (right part of Fig. 1, dark bars in Fig. 5 and Fig. S1, ESI†). That is, sensor **1** can readily distinguish Al³⁺/Cu²⁺ from environmentally and biologically relevant metal ions using fluorescent spectroscopy. Job's plots indicated that **1** chelates Al³⁺ (left part of Fig. 6)/Cu²⁺ (right part of Fig. 6) with 1:1 stoichiometry, and the binding constants of **1** with Al³⁺

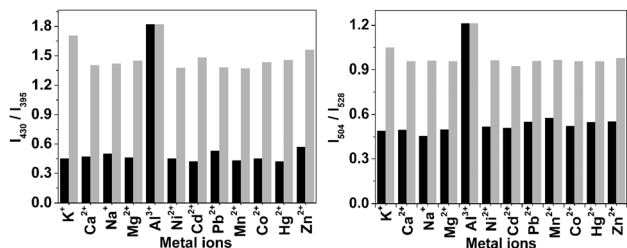


Fig. 5 Fluorescence responses of **1** (2.5×10^{-5} M, $V_{\text{ethanol}}:V_{\text{water}} = 9:1$) upon addition of different metal salts (2 equiv. of salt ion relative to **1**) (dark bars) and fluorescence changes of the mixture of **1** and Al^{3+} after addition of an excess of the indicated metal ions (6 equiv. relative to **1**) (light gray bars). The excitation wavelength was 356 nm. I_{430} , I_{395} , I_{504} , and I_{528} represent the emission intensities at 430, 395, 504, and 528 nm in the fluorescence spectrum of compound **1** after addition of the metal ion to the solution of **1** (dark bars) and of the mixture of **1** and Al^{3+} after addition of an excess of the metal ion (light gray bars). The metal salts used were KCl, CaCl_2 , NaCl, MgCl_2 , $\text{Al}(\text{NO}_3)_3$, NiCl_2 , CdCl_2 , PbCl_2 , MnCl_2 , CoCl_2 , HgCl_2 , and ZnSO_4 .

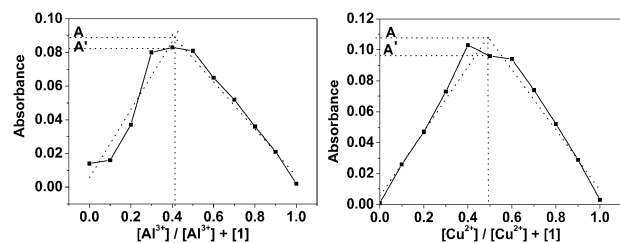


Fig. 6 Job's plot of compound **1** with Al^{3+} (left) and Cu^{2+} (right) obtained by absorption spectroscopy measurements and the wavelength used is 382 nm (left) and 400 nm (right).

and Cu^{2+} were calculated to be $1.35 \times 10^6 \text{ L mol}^{-1}$ and $6.53 \times 10^5 \text{ L mol}^{-1}$, respectively, indicating that **1** has higher binding affinity for Al^{3+} than for Cu^{2+} .

Competition experiments were also conducted for **1** (light gray bars in Fig. 5 and Fig. S1, ESI†). When 2 equiv. of Al^{3+} was added into the solution of **1** in the presence of 6 equiv. of other metal ions, a similar fluorescent spectroscopy change was displayed to that with Al^{3+} ions only. As for the competition experiments using Cu^{2+} , under similar conditions as those for Al^{3+} (13 equiv. of Cu^{2+} and 39 equiv. of other metal ions), the fluorescence emission spectrum displayed a similar pattern to that with Cu^{2+} only, except for that with Al^{3+} . Under such conditions, Al^{3+} leads to disturbance in the detection of Cu^{2+} , which was ascribed to the higher binding affinity of **1** for Al^{3+} than for Cu^{2+} (Fig. 6). Because the amount of Na^+ , Mg^{2+} , K^+ , or Ca^{2+} is much more than that of Al^{3+} and Cu^{2+} biologically, it is necessary to measure the disturbance when the amount of these metal ions is much higher than that of $\text{Al}^{3+}/\text{Cu}^{2+}$. The measurement experiments show that no fluorescence change was found even when the amount of these alkali and alkaline earth metal ions was at a high concentration of 6 mM. Such results turned out to be applicable in environmental technology.

Experiments to explore the counterion effect on the Cu^{2+} -selective properties of **1** were also performed (left part of Fig. 7). Acetate, sulfate, and nitrate counter anions had similar

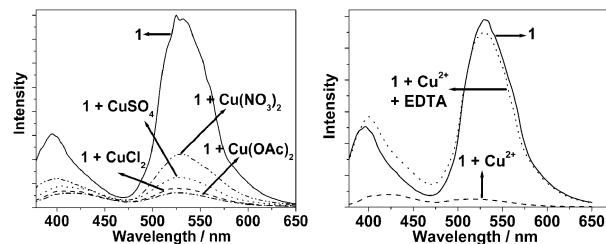


Fig. 7 Fluorescence emission spectrum of **1** (2.5×10^{-5} M, $V_{\text{ethanol}}:V_{\text{water}} = 9:1$) upon addition of different copper salts (the ratio of metal ion to **1** is 13) with excitation at 356 nm (left); fluorescence emission spectrum of **1** (2.5×10^{-5} M, $V_{\text{ethanol}}:V_{\text{water}} = 9:1$) under different conditions with excitation at 356 nm.

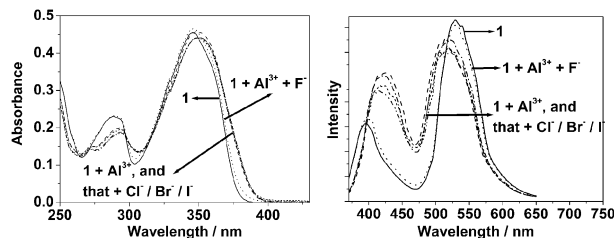


Fig. 8 Absorption (left) and emission (right) spectra of **1** (2.5×10^{-5} M, $V_{\text{ethanol}}:V_{\text{water}} = 9:1$) under different conditions.

influence to that of chloride, demonstrating that anions do not coordinate with the metal ions while compound **1** reacts with Cu^{2+} . This indicates that compound **1** as a fluorescent sensor has a much wider application range in sensing of Cu^{2+} .

To examine the reversibility of the binding of chemosensor **1** to Al^{3+} and Cu^{2+} , an ethanol solution containing 6 and 24 equiv. of NaF and EDTA disodium were added to **1-Al** and **1-Cu** solutions, respectively. Absorption (left part of Fig. 8) and fluorescence signals identical to those of **1** were restored (right part of Fig. 7 and 8), demonstrating that $\text{Al}^{3+}/\text{Cu}^{2+}$ is removed from **1-Al** and **1-Cu** by NaF and EDTA disodium, respectively, and the binding constant of $\text{Al}^{3+}/\text{Cu}^{2+}$ with F^-/EDTA is larger than that with **1**. That is, the binding of **1** and $\text{Al}^{3+}/\text{Cu}^{2+}$ is really chemically reversible. Further experiments demonstrate that **1-Al** showed high selectivity toward F^- , which can be applied to distinguish F^- from Cl^- , Br^- and I^- (Fig. 8).

Based on the fluorimetric experiments (Fig. 6), we realized that **1** would have higher binding affinity for Al^{3+} than for Cu^{2+} . As expected, addition of Al^{3+} into **1-Cu** solution resulted in quick absorption and emission spectral changes. The absorption peak at about 392 nm decreased with that at about 354 nm appearing and increasing (left part of Fig. 9). The emission intensity at about 430 and 504 nm of **1-Cu** underwent a gradual increase (right part of Fig. 9). Such spectral change indicates that Al^{3+} can displace Cu^{2+} to form the **1-Al** complex and **1-Cu** could be a good off-on Al^{3+} sensor candidate.

In summary, a dual-model and on-off fluorescent chemosensor **1** for Al^{3+} and Cu^{2+} was synthesized, which displays high selectivity and antidisturbance property for Al^{3+} and Cu^{2+} among environmentally and biologically relevant metal ions. With F^- and EDTA disodium for Al^{3+} and Cu^{2+} , respectively,

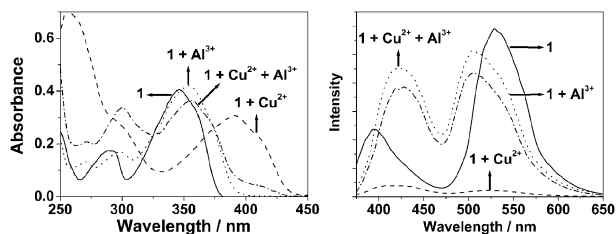


Fig. 9 Absorption (left) and emission (right) spectra of **1** (2.5×10^{-5} M, $V_{\text{ethanol}} : V_{\text{water}} = 9 : 1$) + 13 equiv. of Cu^{2+} upon titration of Al^{3+} (0–12 equiv.) with excitation at 356 nm (right).

the fluorescence spectrum of **1** can be restored, which shows that the binding of **1** and $\text{Al}^{3+}/\text{Cu}^{2+}$ is chemically reversible. The high selectivity of **1**-Al toward F^- can be applied to distinguish F^- from Cl^- , Br^- and I^- . Moreover, the fluorescence emission intensity of **1**-Cu is increased with the addition of Al^{3+} , demonstrating that **1**-Cu could be a good “off-on” Al^{3+} sensor candidate.

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