

A highly efficient and selective turn-on fluorescent sensor for Cu²⁺ ion based on calix[4]arene bearing four iminoquinoline subunits on the upper rim†

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A new fluorescent chemosensor based on calix[4]arene bearing four iminoquinoline subunits on the upper rim was conveniently synthesized, which showed a remarkable enhanced fluorescent intensity in the presence of Cu²⁺ ion and a high selectivity toward Cu²⁺ ion over a wide range of tested metal ions in acetonitrile.

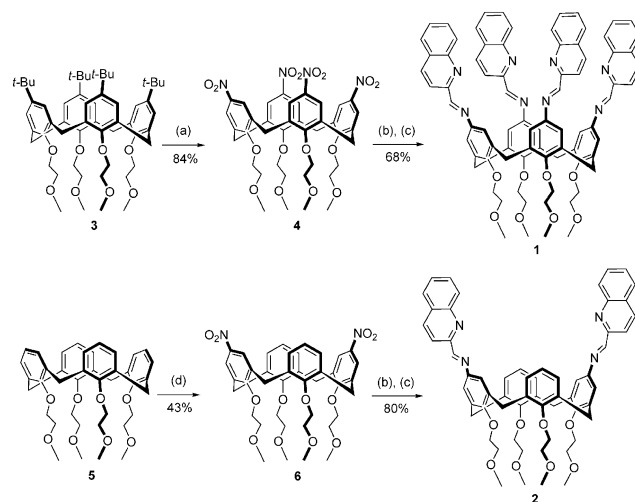
Design of artificial receptors for the sensing and recognition of transition-metal ions is currently of great interest.¹ In the past few years, much attention has been drawn to the development of fluorescent chemosensors for the detection of Cu²⁺ ion because of its importance in environmental and biological systems.² As a transition metal ion known for its efficient fluorescence quenching character,³ most of the classic and early-reported cation sensors generally undergo fluorescence quenching upon the binding of Cu²⁺ under an electron or energy transfer mechanism.⁴ Owing to sensitivity reasons, fluoroionophores showing fluorescence enhancement as a result of metal-ion binding are to be favored over those exhibiting fluorescence quenching. Recently, some examples with a selective response to Cu²⁺ ion by a copper-enhanced fluorescence emission have been reported.⁵ However, the fluorescence enhancement in most cases is fairly faint and usually has high background. Moreover, the selectivity for Cu²⁺ over other ions, such as Pb²⁺ and Fe³⁺, is not very satisfactory in some cases. So, development of new Cu²⁺-selective turn-on fluorescence sensors is still important and necessary.

Typically, fluorescent chemosensors for ions, also called fluoroionophores, consist of an ion recognition unit (ionophore) and a fluorogenic unit (fluorophore) linked together through a proper spacer.⁶ Although this methodology provides considerable flexibility of design, the recognition event is hard to be fully detected and the fluorescence quenching⁷ is usually induced because the fluorophore does not directly contact the bound metal ion. So, an ideal fluorescent chemo-

sensor will be that whose fluorescent unit is directly involved in the interaction with metal ions. On the other hand, the unsatisfactory selectivity for most of the chemosensors may be due to the single-ion recognition unit, fluoroionophores with multi-ion recognition units may overcome this disadvantage.

Calixarenes⁸ are an important class of macrocyclic compounds, and they have been widely used as an ideal platform for the development of fluorescence chemosensors⁹ for not only alkali and alkaline-earth metal ions, but also transition-metal ions including Cu²⁺.^{4i,10} However, to our knowledge, no Cu²⁺-selective turn-on fluorescent chemosensors based on calixarene derivatives were so far reported. Herein, we report a new turn-on fluorescent sensor (**1**) for Cu²⁺ ion based on calix[4]arene bearing four iminoquinoline subunits on the upper rim as not only a fluorogenic unit but also a recognition unit, which shows a remarkable fluorescent enhancement from almost zero background in the presence of Cu²⁺ and a high selectivity toward Cu²⁺ ion over a wide range of tested metal ions in acetonitrile.

Synthesis of the calix[4]arene derivatives **1** and **2** is depicted in Scheme 1. Compounds **3**¹¹ and **5**¹² were prepared according to the literatures. Nitrocalix[4]arenes **4** and **6** were obtained through nitration of **3** and **5** with HNO₃ in glacial acetic acid.



Scheme 1 Synthesis of calix[4]arene derivatives **1** and **2**. Reagents and conditions: (a) 100% HNO₃, AcOH, CH₂Cl₂, 0 °C, 3 h; (b) NH₂NH₂, Raney Ni, THF; (c) 2-quinolinecarbaldehyde, CH₂Cl₂, C₂H₅OH; (d) 65% HNO₃, AcOH, CH₂Cl₂, r.t., 7 h.

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† Electronic supplementary information (ESI) available: Synthesis of compounds **1**, **2**, **5** and **6**; absorption and fluorescence spectra of **1** and **2** in the presence of Cu²⁺ or Zn²⁺; ESI mass spectra of **1**-Cu²⁺ and **1**-Zn²⁺. See DOI: 10.1039/b800258d

Reduction of **4** and **6** with hydrazine hydrate and Raney nickel in THF gave the corresponding aminocalix[4]arenes, which were then reacted with 2-quinolinecarbaldehyde in CH_2Cl_2 and $\text{C}_2\text{H}_5\text{OH}$ to afford the iminoquinoline derived calix[4]arenes **1** and **2** in 68 and 80% yield, respectively.

The absorption spectrum of **1** in CH_3CN exhibits two bands at 235 and 335 nm, respectively (ESI†). In the presence of $\text{Cu}(\text{ClO}_4)_2$, the band at 335 nm was decreased while a new band around 415 nm appeared. A clear isosbestic point at 385 nm was observed during the spectral titration, indicating the formation of a well-defined **1**- Cu^{2+} complex. The addition of Zn^{2+} also resulted in the decrease of the band at 335 nm, but no obvious new bands appeared at longer wavelength (ESI†).

Fig. 1 shows the fluorescence spectra (λ_{em} 335 nm) of **1** (10^{-5} M) measured in acetonitrile with respective metal cations (11 equiv.). Without cations, **1** shows a very weak fluorescence at 412 nm; however, Cu^{2+} addition creates a remarkably enhanced fluorescence (about 1200-fold). Under the same conditions, Zn^{2+} only induces an emission enhancement of **1** up to 24-fold, while no obvious fluorescence changes were observed for other tested transition-metal ions (Fe^{3+} , Mn^{2+} , Co^{2+} , Ni^{2+} , Zn^{2+} , Cd^{2+} , Ag^+ , Pb^{2+} , Hg^{2+}), alkali-metal ions (Li^+ , Na^+ , K^+), and alkaline-earth metal ions (Mg^{2+} , Ca^{2+} , Ba^{2+}). These observations indicate that compound **1** has high sensitivity and selectivity for Cu^{2+} .

The fluorescence titration of **1** with Cu^{2+} was then performed. As shown in Fig. 2, the fluorescence intensity of **1** is enhanced remarkably upon the addition of Cu^{2+} . When the concentration of Cu^{2+} is increased up to 11×10^{-5} M, the intensity is increased by about 1200-fold. The nonlinear fitting of the titration curve assumed a 1 : 1 stoichiometry for the **1**- Cu^{2+} complex, and the association constant (K_a) was thus determined to be $3.67 \times 10^7 \text{ M}^{-1}$, which indicates a high affinity of **1** to Cu^{2+} . Similarly, from the fluorescence titration of **1** with Zn^{2+} , the association constant (K_a) of the 1 : 1 complex formation for **1**- Zn^{2+} was calculated to be $1.75 \times 10^3 \text{ M}^{-1}$ (ESI†). The selectivity for Cu^{2+} is almost 21 000 fold compared to that of Zn^{2+} . Furthermore, it was found that **1** had a detection limit¹³ of $2.71 \times 10^{-8} \text{ mol L}^{-1}$ for Cu^{2+} ,

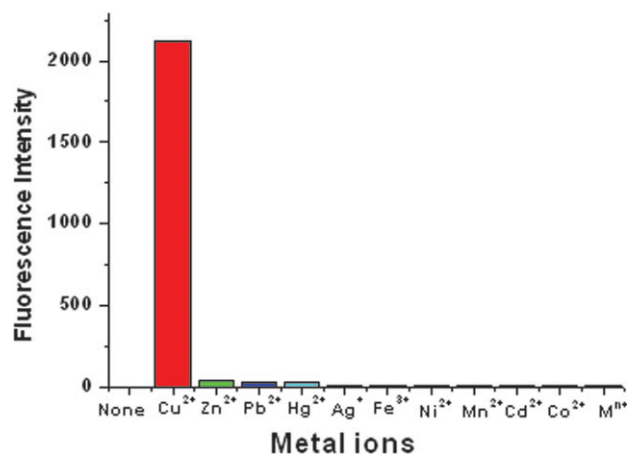


Fig. 1 Fluorescent intensity of **1** (1.0×10^{-5} M) in MeCN upon the addition of 11.0 equiv. metal ions (M^{n+} denotes Li^+ , Na^+ , K^+ , Mg^{2+} , Ca^{2+} , Ba^{2+}).

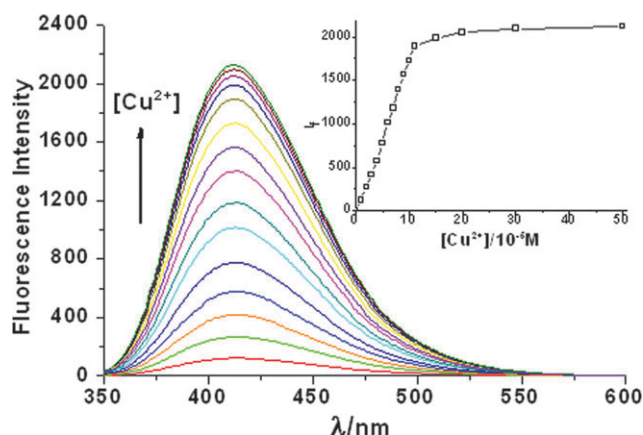


Fig. 2 Fluorescence titration of **1** (10^{-5} M) with $\text{Cu}(\text{ClO}_4)_2$ in CH_3CN . $[\text{Cu}^{2+}]$: 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0, 9.0, 10.0, 11.0, 15.0, 20.0, 30.0, 50.0 $\times 10^{-5}$ M. $\lambda_{\text{ex}} = 335$ nm. Inset: plot of I_f vs. $[\text{Cu}^{2+}]$.

which is sufficiently low for the detection of the submillimole concentration range of Cu^{2+} ions found in many chemical and biological systems.

The 1 : 1 binding mode between **1** and Cu^{2+} was also supported by the Job plot evaluated from the fluorescence spectra of **1** and Cu^{2+} with a total concentration of $10.0 \mu\text{M}$ (ESI†). A more direct evidence for formation of the 1 : 1 complex **1**- Cu^{2+} was obtained by the ESI mass spectrum (ESI†). Consequently, the peak at m/z 717.73 (calc. = 717.71) corresponding to $[\text{1-Cu}^{2+} + \text{ClO}_4^- + \text{H}^+]^2+$ was clearly observed when an excess of Cu^{2+} was added to **1** in CH_3CN . Similarly, the peak at m/z 729.23 (calc. = 729.21) corresponding to $[\text{1-Zn}^{2+} + \text{ClO}_4^- + \text{Na}^+]^2+$ provided an evidence for formation of the complex **1**- Zn^{2+} (ESI†).

To explore the utility of **1** as an ion-selective fluorescence chemosensor for Cu^{2+} , competition experiments were further carried out. Consequently, compound **1** (10^{-5} M) was treated with 11 equiv. Cu^{2+} in the presence of different background metal ions (100 equiv.). As shown in Fig. 3, the tested background metal ions showed small or no interference with the detection of Cu^{2+} ion, indicating that **1** could be used as a potential practical Cu^{2+} -selective turn-on fluorescent sensor.

For the sake of comparison with **1**, diiminoquinoline derived calix[4]arene **2** was synthesized (Scheme 1). Similar to **1**, the fluorescence enhancement of **2** in the presence of Cu^{2+} could also be observed, but it is obviously less than that of **1** induced by Cu^{2+} in the same conditions. The association constant (K_a) of the 1 : 1 complex **2**- Cu^{2+} was calculated to be $3.7 \times 10^5 \text{ M}^{-1}$ (ESI†), which is only about one-hundredth of that of the 1 : 1 complex **1**- Cu^{2+} . The results indicated that tetraiminoquinoline derived calix[4]arene **1** might have a pre-organized and multi-coordinated complexing site for Cu^{2+} ion.

For rationalizing the observed fluorescence enhancement, two factors may be considered. First, the low fluorescence intensity of **1** in CH_3CN in the absence of Cu^{2+} ion may be attributed to radiationless channel from the $n\pi^*$ state of the emission of the quinoline group by the lone-pair electron of the imine nitrogen atom (photo-induced electron transfer,

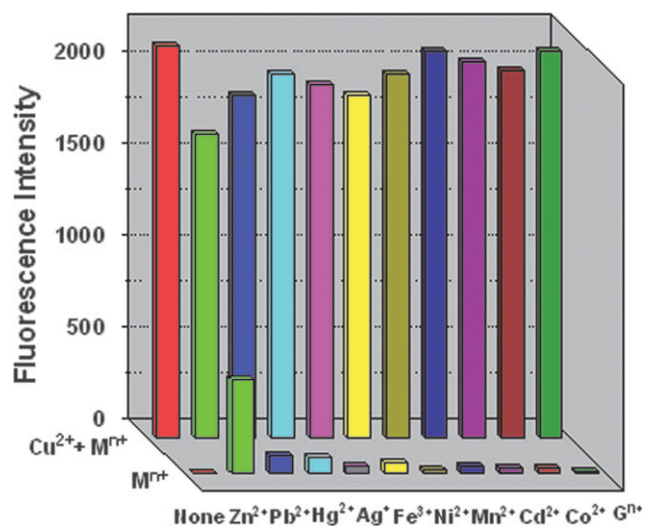


Fig. 3 Fluorescent intensity of **1** (10^{-5} M) upon the addition of 11 equiv. Cu^{2+} in the presence of 100 equiv. background metal ions in CH_3CN . $\lambda_{\text{ex}} = 335$ nm, $\lambda_{\text{em}} = 412$ nm. G^{n+} denotes Li^+ , Na^+ , K^+ , Mg^{2+} , Ca^{2+} , Ba^{2+} .

PET).¹⁴ When Cu^{2+} ion coordinates with the lone pair of the imine and quinoline nitrogens, the energy of the $n\pi^*$ state would be raised so that the $\pi\pi^*$ state of the emission of the quinoline group becomes the lowest excited state, leading to a substantial increase in the fluorescence intensity (block PET).¹⁵ Secondary, Cu^{2+} binding to **1** induced its conformation restriction, which could also result in the increased fluorescence intensity.¹⁶

In conclusion, we have presented a new easily available turn-on fluorescent chemosensor **1** based on calix[4]arene bearing four iminoquinoline subunits on the upper rim, which showed a remarkable enhanced fluorescent intensity (about 1200-fold) in the presence of Cu^{2+} ion and a high selectivity toward Cu^{2+} ion over a wide range of metal ions in acetonitrile. Moreover, the detection limit for Cu^{2+} was found to be 2.71×10^{-8} mol L^{-1} , and background metal ions showed small or no interference with the detection of Cu^{2+} , indicating that compound **1** could be used as an efficient Cu^{2+} -selective turn-on fluorescent chemosensor, and subsequently found practical applications in chemical and biological systems.

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