A Highly Efficient and Selective Turn-on Fluorescent Sensor for Cu^{2+} Ion[†]

Wang, Xuehua(王学花)　　Cao, Jing(曹菁)　　Chen, Chuanfeng*(陈传峰)

Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China

A new fluorescent chemosensor based on an open-chain azacrown bearing a quinoline subunit was conveniently synthesized, which showed a remarkable enhanced fluorescent intensity in the presence of Cu^{2+} ion and a high selectivity toward Cu^{2+} ion over a wide range of tested metal ions in acetonitrile.

Keywords Cu^{2+} recognition, fluorescent chemosensor, turn-on, selective

Introduction

In recent years, the development of fluorescent chemosensors for the detection of Cu^{2+} ion has drawn much attention owing to its importance in environmental and biological systems.[1] Since Cu^{2+} has efficient fluorescence quenching character,[2] it has been used in many classic and early-reported cation sensors, which undergo fluorescence quenching upon the binding of Cu^{2+} ion under an electron or energy transfer mechanism.[3] Because of 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 have been reported, which have a selective response toward Cu^{2+} ion by a copper-enhanced fluorescence emission.[4] In most cases, however, the fluorescence enhancement is faintish and usually has high background. Furthermore, the selectivity for Cu^{2+} over other ions, such as Pb^{2+} and Fe^{3+}, is not very satisfactory in some cases. Thus, development of new Cu^{2+}-selective turn-on fluorescence sensors is still important and necessary.

Recently, we reported a highly efficient and selective turn-on fluorescent sensor for Cu^{2+} ion based on calix[4]arene bearing four iminoquinoline subunits on the upper rim.[5] Herein, we report a new easily available turn-on fluorescent sensor for Cu^{2+} ion based on an open-chain azacrown bearing a quinoline subunit, which shows a remarkable fluorescent enhancement from almost zero background in the presence of Cu^{2+} and a high selectivity toward Cu^{2+} ion over a wide range of tested metal ions in acetonitrile.

Experimental

^1H NMR spectra were recorded on a Bruker 300 (300 MHz) spectrometer. The fluorescence experiments at room temperature reported in this paper were carried out in CH_3CN. The resolution was set at 1 nm, and λ_{ex} was 315 nm. The samples were prepared with a series of 1.0×10^{-5} mol•L^{-1} HPLC acetonitrile solutions of compound **1**. Metal perchlorates were performed with 1.0×10^{-3} mol•L^{-1}. The sample was performed with 1.0×10^{-5} mol•L^{-1}. Starting material and solvents were purchased from Beijing Chemical Company. Compound **3** was synthesized according to the published procedure.[6]

Synthesis of compound 1

Under N_2 atmosphere, a mixture of **3** (0.6 g, 3.92 mmol) and 2-quinolinecarboxaldehyde (0.62 g, 3.92 mmol) in ethanol (80 mL) was stirred for 4 h. The solvent was removed under the reduced pressure, and the residue was then recrystallized from methanol to give the imine as a yellow solid, which was not purified and used for the further reaction. To the solution of the imine (0.3 g, 1 mmol) in methanol (150 mL) at 0 ℃ was slowly added $NaBH_4$ (0.8 g, 20 mmol). After the mixture was stirred at room temperature for 24 h, the solvent was removed *in vacuo*. The residue was treated with 1 mol•L^{-1} aqueous NaOH, and then extracted with CH_2Cl_2. The organic layer was dried over anhydrous Na_2SO_4, and concentrated to give the residue, which was purified by recrystallization from methanol to give the product **1** (0.25 g, 83%) as a yellow solid. m.p. 107—108 ℃; ^1H NMR ($CDCl_3$, 300 MHz) δ: 8.12 (d, J=8.4 Hz, 2H), 7.81 (d, J=6.8 Hz, 1H), 7.72 (t, J=7.4 Hz, 1H), 7.52 (d, J=8.3 Hz, 2H), 6.85 (t, J=8.3 Hz,

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* E-mail: cchen@iccas.ac.cn; Tel.: 0086-010-62588936; Fax: 0086-010-62554449

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2H), 6.67—6.56 (m, 2H), 5.72 (brs, 1H), 4.69 (s, 2H), 4.23 (t, *J*=4.6 Hz, 2H), 3.83 (t, *J*=4.6 Hz, 2H), 3.49 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 159.7, 146.2, 138.6, 136.6, 129.5, 128.9, 127.6, 127.4, 126.1, 122.0, 119.5, 116.7, 112.0, 110.6, 71.3, 68.5, 59.2, 49.9. MALDI-TOF MS *m/z*: 308 (M^+). Anal. calcd for $C_{19}H_{20}N_2O_2$: C 74.00, H 6.54, N 9.08; found C 73.81, H 6.55, N 9.02.

Results and discussion

Synthesis of compound **1** is depicted in Scheme 1. According to the literature method,[6] compound **3** was first prepared by reaction of *o*-nitrophenol **2** with 2-methoxyethyl tosylate in 1 : 1 (*V* : *V*) CH_3CN and CH_2Cl_2 in the presence of K_2CO_3, and then catalytic hydrogenation in methanol in the presence of Pd/C. Reaction of **3** with 2-quinolinecarboxaldehyde in ethanol, and then reduction with sodium borohydride in methanol gave the target molecule **1** in a total 83% yield for the two steps. Compound **1** was characterized by ^{1}H NMR, ^{13}C NMR, MALDI-TOF MS, and elemental analysis.

Scheme 1 Synthesis of compound **1**

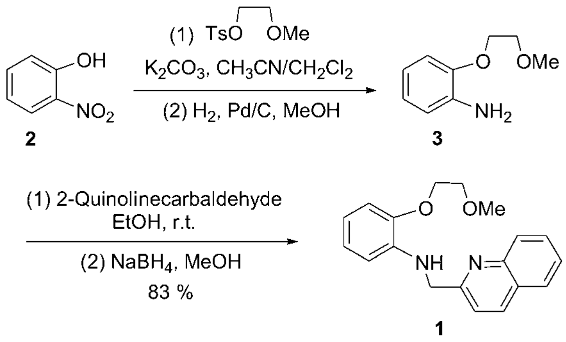

Figure 1 shows the fluorescence spectra (λ_{em}=315 nm) of **1** (10^{-5} mol•L^{-1}) measured in acetonitrile with respective metal cations (40 equiv.). Without cations, **1** shows a very weak fluorescence at 412 nm; however, the addition of Cu^{2+} creates a remarkably enhanced fluorescence. Under the same conditions, no obvious fluorescence change was observed for other tested transition-metal ions (Ni^{2+}, Pb^{2+}, Hg^{2+}, Cd^{2+}, Zn^{2+}, Co^{2+}, Mn^{2+}), and alkali metal and alkaline earth metal ions (Li^+, Na^+, K^+, Mg^{2+}). These observations indicate that compound **1** has high sensitivity and selectivity for Cu^{2+} ion.

The Cu^{2+} induced selective fluorescence enhancement of **1** might be mainly attributed to formation of the stable complex between compound **1** and Cu^{2+} ion, and the subsequent block photoinduced electron transfer of the quinoline group by the lone-pair electron of the amine nitrogen atom in the presence of Cu^{2+}.[5] Consequently, when Cu^{2+} ion coordinates with the amine and quinoline nitrogen atoms, the energy of the nπ* state would be raised so that the $\pi\pi$* state of the emission of the quinoline group becomes the lowest excited state, which thus resulted in the increase of the fluorescence intensity.

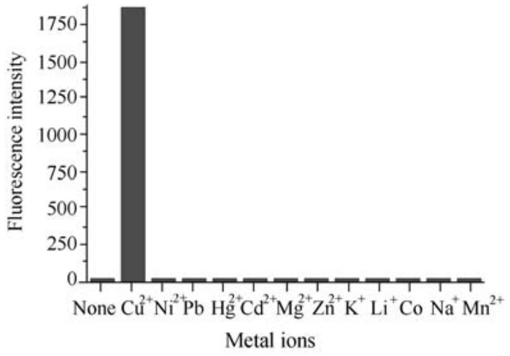

Figure 1 Fluorescent intensity of **1** (1×10^{-5} mol•L^{-1}) in CH_3CN upon the addition of 40.0 equiv. metal ions.

The fluorescence titration experiments of **1** with Cu^{2+} ion were then performed. As shown in Figure 2, the fluorescence intensity of **1** is gradually enhanced upon the addition of Cu^{2+} ion. When the concentration of Cu^{2+} ion is increased up to 40.0×10^{-5} mol•L^{-1}, the intensity is increased by about 1000-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 4.87×10^5 L•mol^{-1}, which indicates a high affinity of **1** to Cu^{2+}. Furthermore, it was found that **1** had a detection limit of 2.06×10^{-6} mol•L^{-1} for 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.

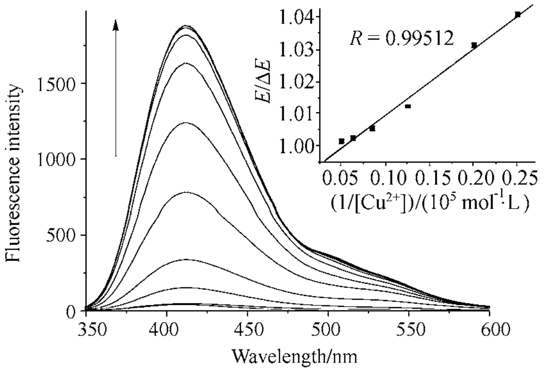

Figure 2 Fluorescence titration of **1** (10^{-5} mol•L^{-1}) with $Cu(ClO_4)_2$ in CH_3CN. [Cu^{2+}]/(10^{-5} mol•L^{-1}): 1.0, 4.0, 8.0, 12.0, 16.0, 20.0, 24.0, 28.0, 32.0, 36.0, 40.0. λ_{ex}=315 nm. Inset: plot of $F/\Delta F$ vs. 1/[Cu^{2+}].

The Job's plot shown in Figure 3 was evaluated from the fluorescence spectra of **1** and Cu^{2+} with a total concentration of 10.0 μmol/L, which further support the 1 : 1 binding mode between **1** and Cu^{2+} ion.

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} mol•L^{-1}) was treated with 30 equiv. of

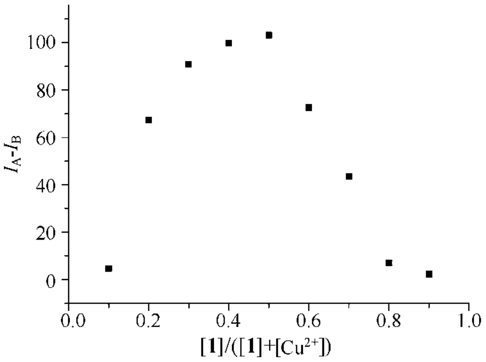

Figure 3 Job plot of **1** vs. $Cu(ClO_4)_2$.

Cu^{2+} ion in the presence of different background metal ions (100 equiv.). As shown in Figure 4, except for Hg^{2+} and Co^{2+} ions, other 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.

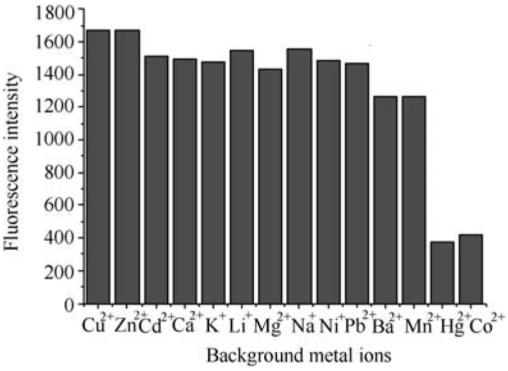

Figure 4 Fluorescent intensity of **1** (10^{-5} mol•L^{-1}) upon the addition of 30 equiv. Cu^{2+} in the presence of 100 equiv. background metal ions in CH_3CN. $\lambda_{ex}=315$ nm.

Conclusion

In conclusion, we have developed a new easily available turn-on fluorescent chemosensor **1** based on an open-chain azacrown bearing a quinoline subunit, which showed a remarkable enhanced fluorescent intensity (about 1000-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 2.06×10^{-6} mol•L^{-1}, and most tested 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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