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A Highly Selective Colorimetric Sensor for Cu^{2+} Based on Phenolic Group Biscarbonyl Hydrazone

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A novel copper selective sensor **2** based on hydrazide and salicylaldehyde has been designed and prepared. Sensor **2** behaves a single selectivity and sensitivity in the recognition for Cu^{2+} over other metal ions such as Fe^{3+}, Hg^{2+}, Ag^{+}, Ca^{2+}, Zn^{2+}, Pb^{2+}, Cd^{2+}, Ni^{2+}, Co^{2+}, Cr^{3+} and Mg^{2+} in DMSO. The distinct color change and the rapid changement of fluorescence emission provide naked-eyes detection for Cu^{2+}. The UV-vis data indicate that 1 : 2 stoichiometry complex is formed by sensor **2** and Cu^{2+}. The association constant K_s was 3.51×10^4 mol^{-1}•L. The detection limitation of Cu^{2+} with the sensor **2** was 2.2×10^{-7} mol•L^{-1}. The sensing of Cu^{2+} by this sensor was found to be reversible, with the Cu^{2+}-induced color being lost upon addition of EDTA.

Keywords copper ion, colorimetric sensor, biscarbonyl hydrazone, single selectivity

Introduction

In recent years, the design and exploration of chemosensors probes for the detection of transition metal ions have been received extensive attention because chemosensors have several advantages such as high selectivity, sensitivity, and real-time monitoring over other methods.[1,2] Among transition metal ions, copper is one of the important elements in humans, and is present at low levels in a variety of cells and tissues with the highest concentration in the liver.[3,4] Copper is utilized in several physiological responses and copper containing proteins are useful as redox catalysts in biological processes such as electron transfer or oxidation of various organic substrates.[5,6] However, chronic copper overload or exposure to excess copper by accidents and environmental contamination can lead to oxidative damage.[7] Therefore, the rational design and synthesis of efficient sensors to selectively recognize copper cation is an important field of supramolecular chemistry.[8-13] Although previous work developed a wide variety of chemical[14,15] and physical[16,17] sensors for the detection of Cu^{2+}, it is still a challenge to design the ion sensors with high selectivity and sensitivity in the context of interference from coexisting metal ions. Moreover, most of these methods require expensive equipment and involve time-consuming and laborious procedures that can be carried out only by trained professionals.[18] This will significantly restrict the practical applications of these Cu^{2+} sensors. For simplicity, convenience and low cost, the easily prepared Cu^{2+} colorimetric sensors are highly demanded.[19-22]

Herein, as one part of our research interest in supramolecular recognitions,[23-27] we attempted to design an easily synthesized, highly selective, and sensitive sensors for Cu^{2+}. We have designed and synthesized sensors **1**, **2** and **3** which bear phenol and carbonyl hydrazone groups. Our strategies for designing of Cu^{2+} colorimetric sensors are as follows: firstly, in order to allow the coordination capacity required to coordinate a copper ion, we introduced phenol groups into the same sensor molecule. Secondly, to achieve “naked-eye” recognition upon binding of Cu^{2+}, we introduced nitrophenyl groups as a chromophore. Thirdly, a carbonyl hydrazone structure was used to significantly enhance intramolecular charge transfer. Interestingly, sensor **2** could “naked-eye” recognize Cu^{2+} with high selectivity and sensitivity in DMSO solution; other cations such as Fe^{3+}, Hg^{2+}, Ag^{+}, Ca^{2+}, Zn^{2+}, Pb^{2+}, Cd^{2+}, Ni^{2+}, Co^{2+}, Cr^{3+} and Mg^{2+} could not cause any interference.

Experimental

Apparatus and reagents

^{1}H NMR spectra were recorded on a Mercury-400BB spectrometer at 400 MHz. ^{1}H chemical shifts were reported in ppm downfield from tetramethylsilane (TMS, δ scale with solvent resonances as internal standards). UV-vis spectra were recorded on a Shimadzu UV-2550 spectrometer. Fluorescent spectra were recorded on a Shimadzu RF-5301 spectrometer. Melting

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points were measured on an X-4 digital melting-point apparatus (uncorrected). Infrared spectra were performed on a Digilab FTS-3000 FT-IR spectrophotometer. Mass spectra were measured with a Bruker Daltonics Esquire 6000. All reagents used were of analytical grade.

Synthesis of sensors 1, 2 and 3

The syntheses of sensors **1**, **2** and **3** are outlined in Scheme 1. The compound **4** (5-hydroxy-1,3-benzenedicarboxylic dihydrazide) was prepared according to the literature reported.[28] Intermediate 5-hydroxy-1,3-benzenedicarboxylic dihydrazide (0.01 mol) and benzaldehyde derivatives (0.01 mol) were mixed in absolute ethanol solutions (50 mL) with hydrochloric acid as a catalyst. Then, the resulting solution was stirred under reflux conditions for 8 h at 80 ℃. After cooling, and removing the solvent, the residue was purified by recrystallization from DMF-EtOH to get **1**, **2** and **3**.

1: Yield 76%, m.p. 297—299 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.90 (s, 2H, NH), 10.16 (s, 1H, Ar-OH), 8.40 (s, 2H, =CH), 7.38—7.87 (m, 13H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 117.805, 127.247, 128.962, 130.288, 134.319, 135.180, 148.212, 157.987, 162.448, 162.768; IR (KBr) v: 1654.17, 1649.38, 3185.72 cm^{-1}. Anal. calcd for $C_{22}H_{18}N_4O_3$: C 68.51, H 4.53, N 14.82; found C 68.38, H 4.70, N 14.50; MS calcd for $C_{22}H_{18}N_4O_3+H$ 387.4, found 387.4.

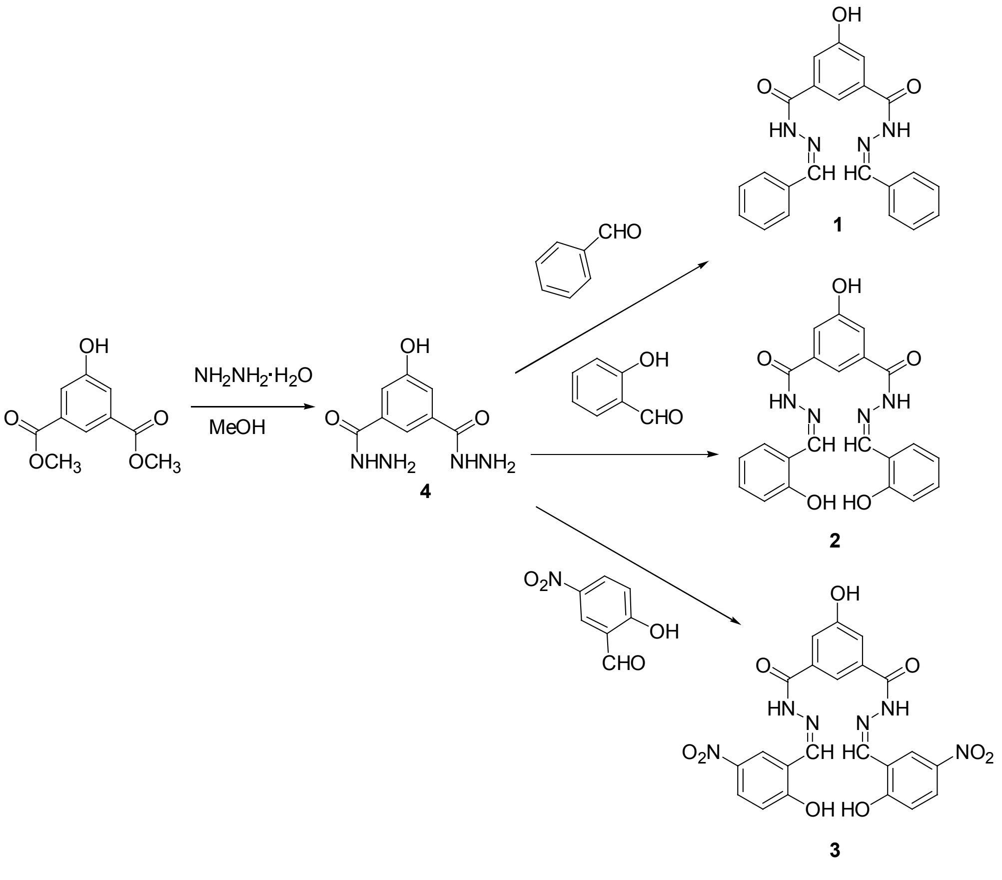
2: Yield 84%, m.p.$>$300 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 12.24 (s, 2H, Ar-OH), 11.26 (s, 2H, NH), 10.30 (s, 1H, CH), 8.68 (s, 2H, =CH), 6.92—7.96 (m, 11H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 116.479, 117.530, 117.934, 118.757, 119.451, 129.488, 131.576, 134.632, 148.509, 157.502. 162.349, 162.395; IR (KBr) v: 1665.25, 1622.88, 3317.56 cm^{-1}. Anal. calcd for $C_{22}H_{18}N_4O_5$: C 63.37, H 4.54, N 13.20; found C 63.15, H 4.34, N 13.39. MS calcd for $C_{22}H_{18}N_4O_5+H$ 419.4, found 419.3.

3: Yield 78%, m.p.$>$300 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 12.30 (s, 2H, Ar-OH), 12.22 (s, 2H, NH), 10.21 (s, 1H, CH), 8.69 (s, 2H, =CH), 7.03—8.53 (m, 9H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 117.172, 117.697, 118.132, 120.144, 123.635, 126.752, 134.540, 139.997, 144.524, 157.715, 162.425, 162.623; IR (KBr) v: 1664.17, 1658.92, 3361.72 cm^{-1}. Anal. calcd for $C_{22}H_{16}N_6O_9$: C 51.77, H 3.24, N 16.40; found C 51.97, H 3.17, N 16.53. MS calcd for $C_{22}H_{16}N_6O_9+H$ 509.4, found 509.2.

General spectroscopic methods

All UV-vis spectroscopy and fluorescent spectroscopy were carried out just after the addition of perchlorate metal salts in DMSO solution, while keeping the ligand concentration constant (2.0×10^{-5} mol/L) on a Shimadzu UV-2550 spectrometer and a Shimadzu RF-5301 spectrometer. The solutions of metal ions were

Scheme 1 Synthetic procedures for sensors **1**, **2** and **3**



prepared from the perchlorate salts of Fe^{3+}, Hg^{2+}, Ag^{+}, Ca^{2+}, Cu^{2+}, Zn^{2+}, Pb^{2+}, Cd^{2+}, Ni^{2+}, Co^{2+}, Cr^{3+} and Mg^{2+}.

Results and Discussion

The colorimetric sensing abilities were primely investigated by adding various metal ions such as Fe^{3+}, Hg^{2+}, Ag^{+}, Ca^{2+}, Cu^{2+}, Zn^{2+}, Pb^{2+}, Cd^{2+}, Ni^{2+}, Co^{2+}, Cr^{3+} and Mg^{2+} to DMSO solutions of sensors **1**, **2** and **3**, respectively. When adding 5 equiv. of Cu^{2+} to the DMSO solution of sensors **1**, **2** and **3**, **2** and **3** responded with dramatic color changes from colorless to yellow-green. In the corresponding UV-vis spectrum, a strong and broad absorption band from 340 to 400 nm was observed for sensors **2** and **3**. To validate the selectivity of sensor **2**, the same tests were applied using Fe^{3+}, Hg^{2+}, Ag^{+}, Ca^{2+}, Zn^{2+}, Pb^{2+}, Cd^{2+}, Ni^{2+}, Co^{2+}, Cr^{3+} and Mg^{2+} metal ions, and none of these ions induced any significant changes in the UV-vis spectrum of sensor **2**. Meanwhile, the absorbance changes of sensor **1** with different metal ions are also shown in Figure 1a. No obvious changes were observed in the UV-vis spectrum upon addition of any metal, indicating that sensor **1** was not a good sensor for these metals.

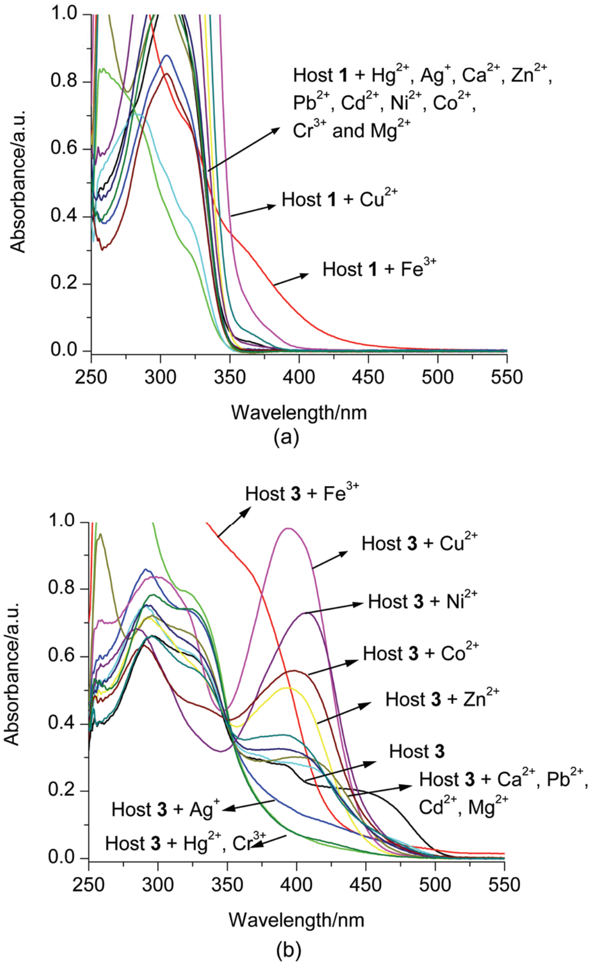


Figure 1 Absorption changes of sensors **1** and **3** (c=2.0×10^{-5} mol/L) in DMSO upon addition of 5 equiv. of different metal perchlorate salts.

To further exploit the utility of sensor **2** as ion-selective sensor for Cu^{2+}, competitive experiments were carried out in the presence of 5.0 equiv. of Cu^{2+} and various metal ions in the DMSO. As shown in Figure 3, sensor **2** (2.0×10^{-5} mol/L) shows an obvious color change from colorless to yellow green upon addition of 5 equiv. of Cu^{2+} in DMSO solution; the peak at 333 nm disappeared in the UV-vis spectrum and a new signal appeared at 400 nm. On the other hand, a variety of other metal ions, such as Fe^{3+}, Hg^{2+}, Ag^{+}, Ca^{2+}, Zn^{2+}, Pb^{2+}, Cd^{2+}, Ni^{2+}, Co^{2+}, Cr^{3+} and Mg^{2+}, did not cause such a significant change, indicating that the sensor **2**-Cu^{2+} was hardly affected by these coexistent cations. Accordingly these results suggested that sensor **2** still displayed an excellent selectivity toward Cu^{2+}.

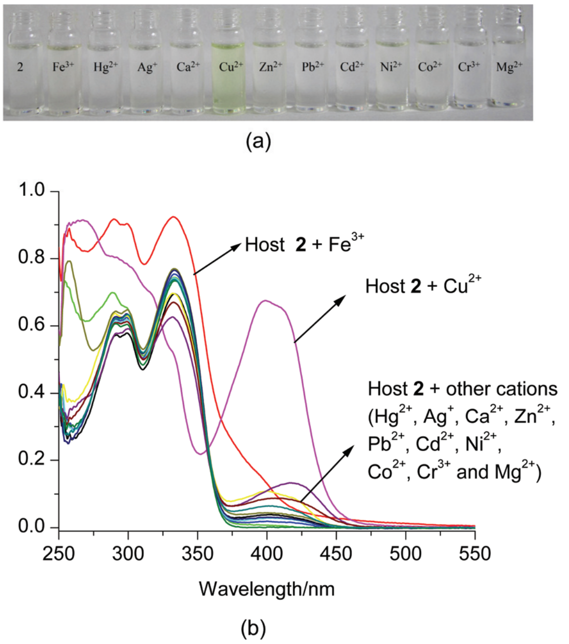


Figure 2 (a) Solutions of sensor **2** upon addition of different metal ions. (b) Absorption changes of sensor **2** (c=2.0×10^{-5} mol/L) in DMSO upon addition of 5 equiv. of different metal perchlorate salts.

The stoichiometry between the sensor **2** and Cu^{2+} was determined by Job's plot. As expected, when the molar fraction of sensor **2** was 0.35, the absorbance value approached a maximum, which demonstrated the formation of 1∶2 complex between sensor **2** and Cu^{2+}.

In order to estimate the specific properties for selective recognition of Cu^{2+} and colorimetric changes associated with the sensor **2**, the sensor **2** toward Cu^{2+} was studied by UV-vis absorption spectra titration experiments. Along with the increasing of concentration of Cu^{2+}, a significant decreasing of the UV-vis absorbance at 332 nm and a new band centered at 400 nm were observed. Such a red shift led to the solution color changing from colorless to yellow green. On the other hand,

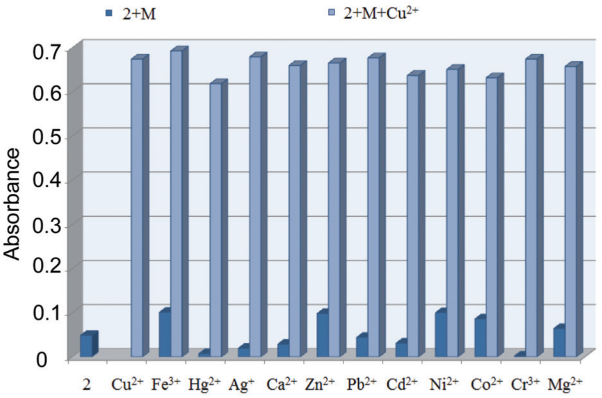


Figure 3 Optical density of sensor **2** at 400 nm with addition of Cu^{2+} in the presence of 5 equiv. of other metal ions.

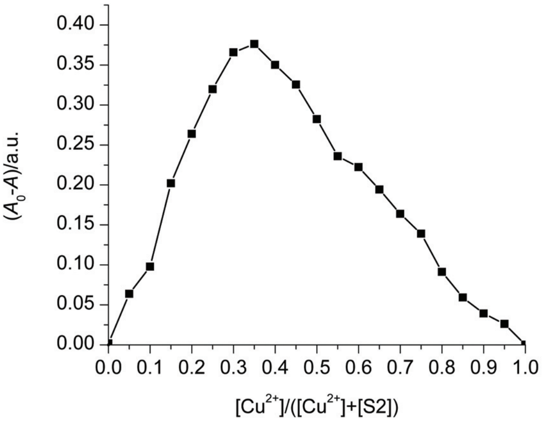


Figure 4 Job's plot analysis for Cu^{2+} versus receptor **2** in DMSO solution measured at 400 nm.

two clear isosbestic points are observed at 340 and 380 nm, which indicates the formation of **2**-Cu^{2+}complex.[29] The binding constant K of the metal complex was determined by Equation (1), assuming that the concentration of free metal is about equal to its total concentration ($[M] \approx [M]_t$), where F_0, F and F_m are the corrected emission intensities of the complex at initial, interval, and the final states at which the complex was fully formed upon addition of metal ion, respectively. The binding constant K was determined from the plot of the linear regression of $\lg[(F-F_0)/(F_m-3F)]$ vs. $\lg[M]$ in Equation (2), derived from Equation (1), to obtain the intercept as $\lg K$ and the slope as n.[30] Thus, the association constant K of the sensor **2** toward Cu^{2+} was calculated as $3.51 \times 10^4\ mol^{-1} \cdot L$. Furthermore, with the probe concentrations employed in our studies, interactions of sensor **2** with Cu^{2+} could be detected down to at least concentrations of 2.2×10^{-7} mol/L in DMSO,[31] showing that this sensor could potentially be used as a probe for monitoring Cu^{2+} levels in physiological and environmental systems.

$$\frac{F-F_0}{F_m-F}=\frac{[C]}{[D]}=K[M]^n \quad (1)$$

$$\lg\frac{F-F_0}{F_m-F}=\lg K+n\lg[M] \quad (2)$$

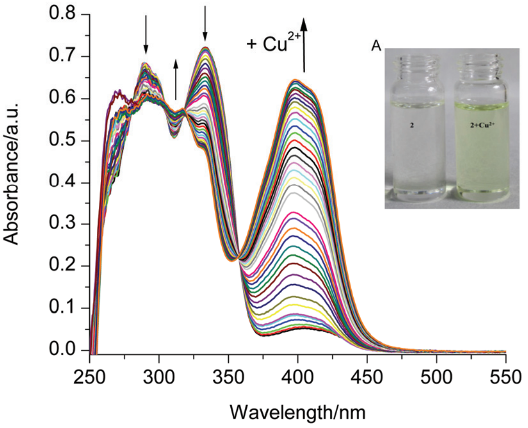


Figure 5 Titration curves of sensor **2** in DMSO ($c=2.0\times10^{-5}$ mol/L) upon addition of Cu^{2+}. Inset: A. Color change of sensor **2** in DMSO solution.

Similarly, the fluorescence spectra of sensor **2** change significantly along with the increase of Cu^{2+} concentration as shown in Figure 6. The intensity of the fluorescence band centered at 500 nm of sensor **2** decreased progressively along with the increase of Cu^{2+} concentration, and it was quenched almost completely after the addition of 2 equiv. Cu^{2+}.

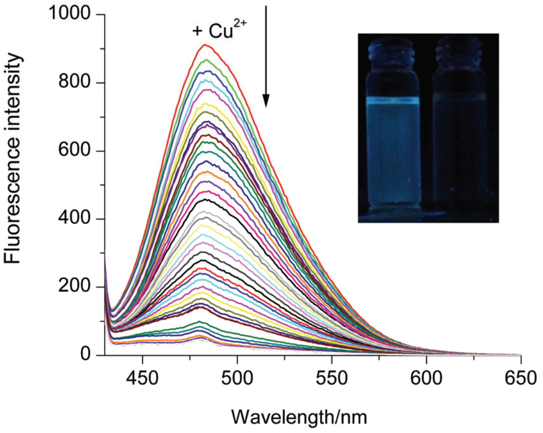
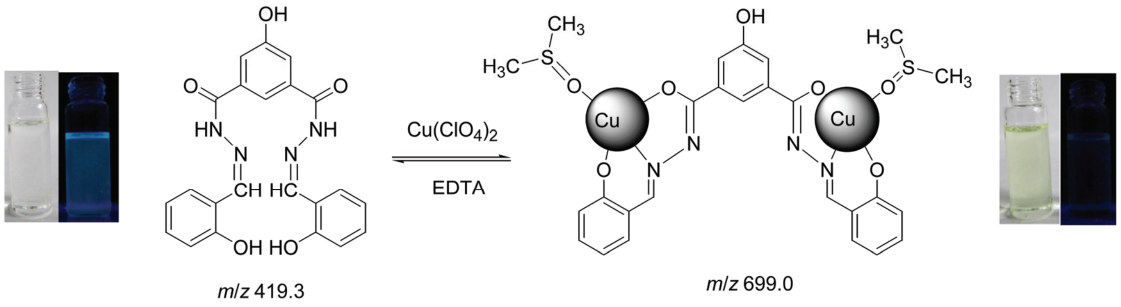


Figure 6 Fluorescent intensity ($\lambda_{ex}=420$ nm) changes of sensor **2** in DMSO upon the additio of Cu^{2+} ions. Inset: Fuorescent change of sensor **2** under 365 nm lamp excitation.

The reversibility of the chemosensor function was tested by titration of the copper-sensor complex with EDTA, which is a well-known chelator of Cu^{2+}. Addition of EDTA into a solution of sensor **2**-Cu^{2+} complex induced the opposite trend in the absorption spectra to that observed on titration with Cu^{2+}. Upon addition of 2 equiv. of EDTA, the optical absorbance intensity returned to the levels observed for the free sensor **2** (Figure 7). This shows that the process of titrating sensor **2** with Cu^{2+} is reversible, and that sensor **2** could therefore be used as an off-on switch chemosensor.

Scheme 2 Proposed complexation mechanism of sensor **2** with Cu^{2+}



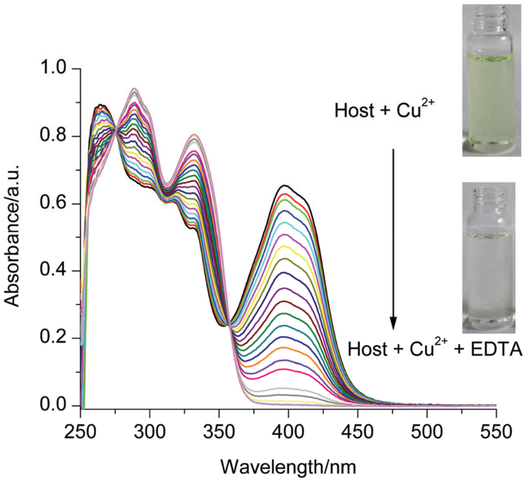


Figure 7 UV-vis spectra of sensor **2**-Cu^{2+} ($c=2.0\times10^{-5}$ mol/L) in DMSO solution upon addition of EDTA. Inset: Color changes of sensor **2**-Cu^{2+} upon the addition of EDTA.

By mass spectral analyses, the ion peaks were detected at *m*/*z* 419.3, which are corresponding to $[\mathbf{2}+H]^+$. The peak at *m*/*z* 699.0 also demonstrated the presence of $[\mathbf{2}+Cu\text{-}H]^+$. Thus, in accordance with the 1 ∶ 2 stoichiometry, sensors are most likely to chelate with metal ions via its carbonyl O, imino N, and hydroxyl O atoms (Scheme 2).

Conclusions

A new double carbonyl hydrazone derivative sensor **2** was synthesized and characterized. Sensor **2** exhibits reversible and highly selective and sensitive recognition toward Cu^{2+} over other metal ions. Upon addition of Cu^{2+}, sensor **2** exhibits remarkably enhanced absorbance intensity and color change from colorless to yellow green in DMSO solution. And the fluorescence spectra of sensor **2** change significantly along with the concentration increase of Cu^{2+} and it was quenched almost completely after the addition of 2 equiv. Cu^{2+}. The researches of recognition mechanism indicated that sensor **2** recognize Cu^{2+} by forming a stable 1 ∶ 2 sensor **2**-Cu^{2+} complex. The coexisting of other cations could not interfere the Cu^{2+} recognition process, moreover, the detection limit of sensor **2** toward Cu^{2+} is 2.2×10^{-7} mol/L, which indicated that the sensor **2** could potentially be useful as a probe for monitoring Cu^{2+} levels in physiological and environmental systems. In addition, the sensor also displayed a Cu^{2+}-induced off-on type of signaling pattern (tested by titration of the copper-sensor complex with EDTA), which means that the sensor could be used as a supramolecular switching system.

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