

New Application of 2-(4-*N*-Phenyl-3-thiosemicarbazone)-8-hydroxyquinoline as a Sensor for Relay Recognition of Cu^{2+} and Sulfide in Aqueous Solution

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Fluorescent and colorimetric recognition properties of 2-(4-*N*-phenyl-3-thiosemicarbazone)-8-hydroxyquinoline (**1**) in buffered aqueous solution (1% DMSO, HEPES 20 mM, pH = 7.4) have been examined. Sensor **1** displays highly selective and sensitive recognition to Cu^{2+} with fluorescence “ON-OFF” performance. The in situ formed **1**- Cu^{2+} complex exhibits an excellent selectivity toward sulfide ions with fluorescence “OFF-ON” behavior *via* Cu^{2+} displacement approach. Thus, relay recognition of Cu^{2+} and sulfide by a known molecule **1** has been achieved.

Key Words : Copper detection, Sulfide recognition, Fluorescence, Quinoline, Thiosemicarbazone

Introduction

Fluorescent and colorimetric recognition of biologically and environmentally important metal cations and anions have received tremendous attention due to their crucial roles in a variety of biological and chemical processes.¹ Particularly, Cu^{2+} detection has aroused immense interest, because it plays critical roles in the fundamental physiological processes of organisms.² Whereas, overloading of copper in the neuronal cytoplasm is associated with Wilson's disease, Alzheimer's disease and Menke's disease.³ Consequently, considerable efforts have been devoted to the development of artificial Cu^{2+} probes.^{1c,4} A Cu^{2+} bound fluorophore generally behaves fluorescence quenching due to the paramagnetic nature of Cu^{2+} , however, the in situ formed ligand- Cu^{2+} complex has potential utility to act as highly selective anion sensor *via* Cu^{2+} displacement approach, which can provide an indirect approach for fluorescence “turn-on” anion detection.⁵

Sulfide is widely spread in the environment. Sulfide has many applications such as for manufacture of sulfur, sulfuric acid, dyes and cosmetics, but exposure to high level sulfide can lead to a variety of physiological and biochemical problems, including irritation in mucous membranes, unconsciousness, and respiratory paralysis.⁶ Thus, sulfide detection has received enormous interest and a number of detection strategies have been developed for sulfide anions, such as spectroscopy, titration, electrochemical methods, chemoluminescence methods, and ion chromatography, *etc.*⁷ Sulfide sensing by fluorescence spectrometry is an increasingly popular method because of its high sensitivity and easy operability.⁸ Although a vast number of S^{2-} selective fluorescent probes have been investigated, fluorescent sensing of sulfide anions in water solution still remains a challenging task due to the strong hydration nature of anions.⁹ Fortunately, the displacement (ensemble) approach has been proved to be an effective method to tackle this hurdle.^{5,10}

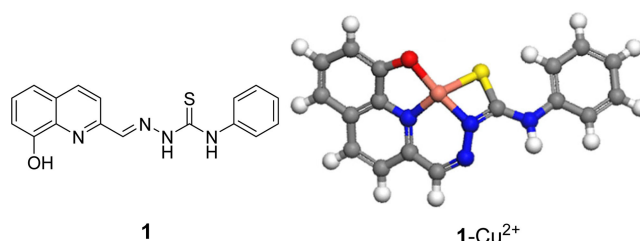


Figure 1. Structure of **1** and the schematic representation of **1**- Cu^{2+} complex.

Currently, most of metal ion and anion recognition studies are focused on design and synthesis of structural novel probes. However, exploit new applications of some known metal ion ligands have not received adequate attention. Carefully selection and screening some effective optical probes from known ligands can provide a labour and time saving approach for developing probes. Herein we report the new application of a known compound, 2-(4-*N*-phenyl-3-thiosemicarbazone)-8-hydroxyquinoline (**1**) (Figure 1), as a fluorescent and colorimetric sensor for relay recognition of Cu^{2+} and S^{2-} in aqueous solution.

Experimental

Apparatus and Reagents. Unless otherwise specified, all the solvents used were of analytical grade from commercial sources. Ethanol was freshly distilled from calcium hydride. Double distilled water was used for spectral detection. Compound **1** was prepared according to literature method.¹¹ UV-vis absorption spectra were measured on a SP-1900 spectrophotometer (Shanghai, China). Fluorescence measurements were performed on a Sanco 970 CRT spectrofluorometer (Shanghai, China). pH measurements were carried out with a Model PHS-25B meter.

The salts used in stock solutions of metal ions are $\text{Ni}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$, $\text{Hg}(\text{NO}_3)_2$, $\text{Ba}(\text{NO}_3)_2$, $\text{Mg}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$,

AgNO₃, FeSO₄·7H₂O, KNO₃, Al(NO₃)₃·9H₂O, Mn(NO₃)₂, Pb(NO₃)₂, NaNO₃, Sr(NO₃)₂, Cu(NO₃)₂·3H₂O, Co(NO₃)₂·6H₂O, Zn(NO₃)₂·6H₂O, Cd(NO₃)₂, CrCl₃·6H₂O, and Fe(NO₃)₃·9H₂O, respectively. The salts used in stock solution of anions are NaF, NaCl, NaBr, KI, NaNO₃, NaHSO₄, CH₃COONa, NaH₂PO₄, Na₃PO₄, KSCN, NaNO₂, NaClO₄, KCN, K₂CO₃, NaHCO₃, Na₂SO₄, Na₂HPO₄, and Na₄P₂O₇, respectively.

Results and Discussion

1-Cu²⁺ complex has been investigated for its membrane permeability in a cultured neuronal-like cell line and subsequent potent phosphorylation of GSK3β.¹¹ However, the metal cation selectivity and sensing behaviors of **1** have not been disclosed. The combination of quinoline and thiosemicarbazone moieties make compound **1** a promising optical probe for the recognition of Cu²⁺, because both 8-hydroxy-quinoline and thiosemicarbazone are good platforms for the construction of functional metal cation receptors. Hence, we explored the new application of **1** as a sensor for relay recognition of Cu²⁺ and S²⁻.

Optical Recognition of Cu²⁺. To examine the metal ion selectivity, the fluorescence responses of **1** solution (1 μM, 1% DMSO, HEPES 20 mM, pH = 7.4) to a variety of metal ions, including Ni²⁺, Hg²⁺, Ba²⁺, Mg²⁺, Fe²⁺, K⁺, Al³⁺, Mn²⁺, Na⁺, Sr²⁺, Zn²⁺, Ca²⁺, Co²⁺, Cd²⁺, Cr²⁺, Fe²⁺, and Ag⁺ were investigated (Figure 1). Free **1** solution displays a strong emission band centered at 512 nm. Upon addition of 1 equiv. Cu²⁺, the fluorescence was almost completely quenched, which is due to the paramagnetism of Cu²⁺. No dramatic changes of the fluorescence spectra were observed for **1** solution upon addition of other metal ions. Similarly, only the addition of Cu²⁺ can induce significant changes on electronic absorption spectrum, which elicited absorption intensity decrease at 300 and 339 nm, and the appearance of new absorption band at 375 nm (Figure 3). The observed color change from colorless to yellow is ascribed to the deprotonation of phenolic hydroxyl and hydrazinic NH groups,¹¹ which result in expansion of the conjugation effect. The pH

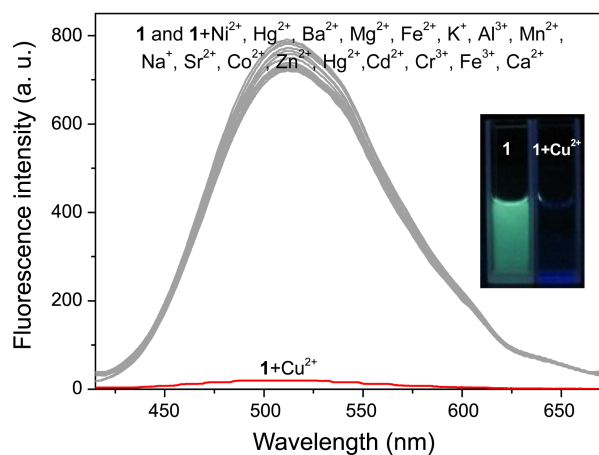


Figure 2 Fluorescence spectra changes of **1** solution (1 μM, 1% DMSO, HEPES 20 mM, pH = 7.4) upon addition 1 equiv. of different metal ions.

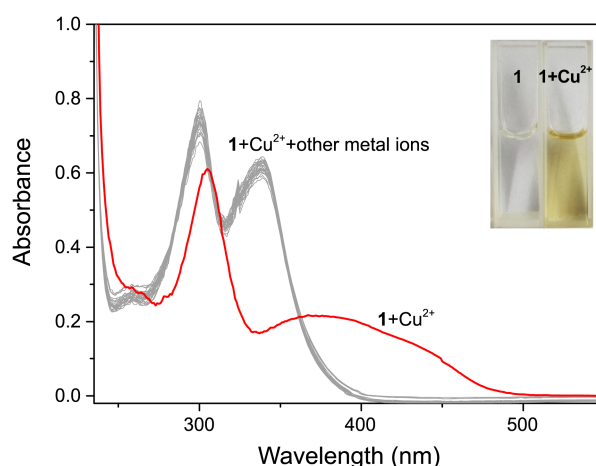


Figure 3. Absorption spectra of **1** solution (10 μM, 1% DMSO, HEPES 20 mM, pH = 7.4) in the presence of 1 equiv. of various metal ions (Cu²⁺, Ni²⁺, Hg²⁺, Ag⁺, Ba²⁺, Mg²⁺, Fe²⁺, K⁺, Al³⁺, Mn²⁺, Na⁺, Sr²⁺, Ca²⁺, Co²⁺, Zn²⁺, Cd²⁺, Cr³⁺, Fe³⁺, Pb²⁺).

effect evaluations reveal that **1** exhibits strong fluorescence emission over a wide range from 4 to 9 (Fig. S1, Supporting Information). These results demonstrate that **1** has excellent selectivity to Cu²⁺ in near neutral water solutions.

The fluorescence titration of **1** solution by incremental addition of Cu²⁺ ions (0–1 μM) was then performed (Figure 4). On stepwise increasing the added Cu²⁺ amounts, the emission intensity at 512 nm was gradually decreased and arrived tranquil as 1 equiv. of Cu²⁺ was used. Furthermore, there was a significant modification on the UV-vis spectra (Fig. S2, SI).

Previous crystal X-ray diffraction analysis disclosed the 1:1 binding stoichiometry and the detailed binding mode between **1** and Cu²⁺,¹¹ and the schematic representation of **1**-Cu²⁺ complex was illustrated in Figure 1. Based on the titration data, we conducted nonlinear least-squares fitting following 1:1 interaction equation¹² and obtained a nice smooth curve ($R^2 = 0.9994$) (Fig. S3, SI), the association constant of **1** with Cu²⁺ was evaluated to be $1.8 \times 10^8 \text{ M}^{-1}$.

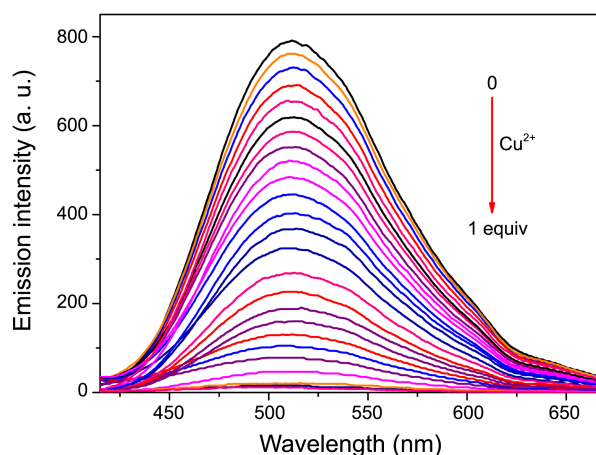


Figure 4. Fluorescence spectra changes of **1** solution (1 μM) in the presence of different amounts of Cu²⁺ (0 to 1 μM).

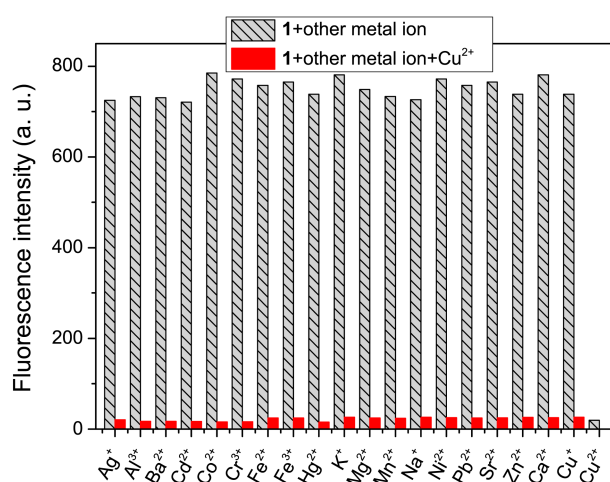


Figure 5. Fluorescence intensity changes in of **1** solution (1 μM) in the presence of miscellaneous metal ions (1 equiv. of each). The gray bars represent the fluorescence intensity of **1** solution with different metal ions; the red bars represent the fluorescence intensity of the abovementioned solution upon further addition Cu^{2+} .

The detection limit of **1** for Cu^{2+} ions was calculated to be 0.29 μM according to the reported method (Fig. S4, SI).¹³

Another momentous feature of a chemosensor is its ability to function without substantial interference from other relevant metal ions. The tolerance of sensor **1** for Cu^{2+} sensing over other metal cations was then investigated (Fig. 5). The existence of equal amount of metal ions such as Ni^{2+} , Hg^{2+} , Mg^{2+} , Fe^{2+} , Al^{3+} , Mn^{2+} , Sr^{2+} , Zn^{2+} , Ba^{2+} , Co^{2+} , Cd^{2+} , Cr^{2+} , Fe^{2+} , Ag^{+} and Pb^{2+} , or 30 equiv. of the biological important metal ions of Mg^{2+} , K^{+} , Na^{+} and Ca^{2+} do not cause noticeable interference on Cu^{2+} recognition.

Optical Recognition of S^{2-} by 1-Cu^{2+} Complex. To investigate whether the 1-Cu^{2+} complex could be used as an anion selective ensemble, the response of 1-Cu^{2+} complex toward physiologically and environmentally important anions were evaluated. On addition of 2 equiv. of S^{2-} ions to 1-Cu^{2+} (1 μM , prepared *in situ* by mixing **1** with $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ at a

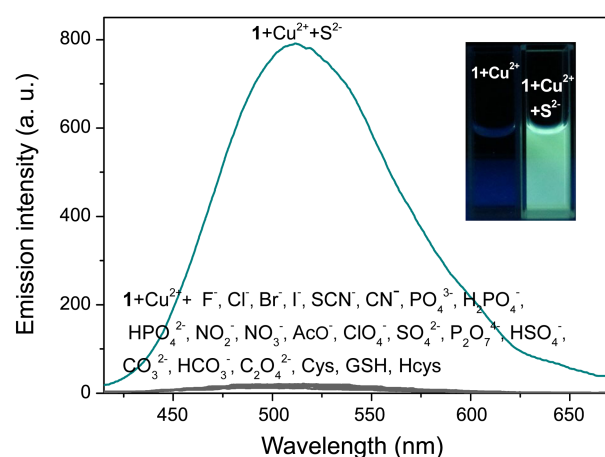


Figure 6. Fluorescence spectra changes of 1-Cu^{2+} solution (1 μM) upon addition of different anions (2 equiv. of each).

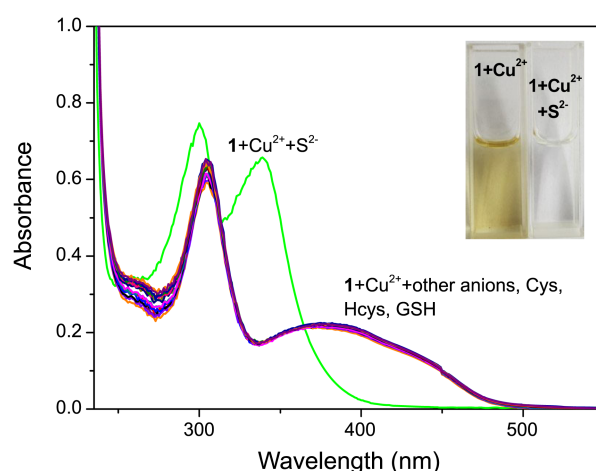


Figure 7. Changes of absorption spectrum of 1-Cu^{2+} solution (10 μM) in the presence of 20 μM of various anions and thiol-containing amino acids.

1:1 ratio in HEPES buffered (1% DMSO, HEPES 20 mM, pH = 7.4) solution), a remarkable fluorescence enhancement was observed (Fig. 6). Whereas no noticeable fluorescence emission changes were observed upon addition of anions such as F^{-} , Cl^{-} , Br^{-} , I^{-} , SCN^{-} , CN^{-} , PO_4^{3-} , $\text{H}_2\text{PO}_4^{-}$, HPO_4^{2-} , NO_2^{-} , NO_3^{-} , AcO^{-} , ClO_4^{-} , SO_4^{2-} , $\text{P}_2\text{O}_7^{4-}$, HSO_4^{-} , CO_3^{2-} , HCO_3^{-} , $\text{C}_2\text{O}_4^{2-}$, as well as some thiol-containing amino acids such as L-Cysteine (Cys), reduced glutathione (GSH), and L-homocysteine (Hcys). Similarly, only the addition of S^{2-} exerted a distinct absorption spectrum change, which result in absorption spectrum restoration to the shape of **1** (Fig. 7). These fluorescence and absorption spectra recoveries strongly advocate the Cu^{2+} removing event. These results show that 1-Cu^{2+} complex has an excellent selectivity toward S^{2-} .

The sensing behavior of 1-Cu^{2+} solution toward S^{2-} was then examined by fluorescence titration. As shown in Figure 8, upon incremental addition of S^{2-} , the 1-Cu^{2+} solution displays stepwise fluorescence enhancement, the fluorescence changes terminated when 2 equiv. of S^{2-} was employed,

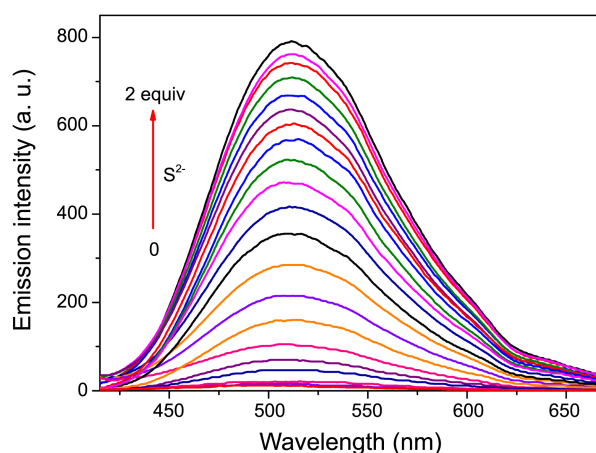


Figure 8. Fluorescence spectra changes of 1-Cu^{2+} solution (1 μM) in the presence of different amounts of S^{2-} .

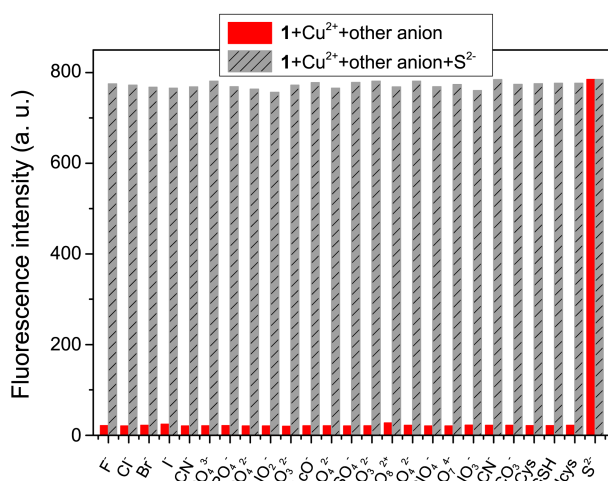


Figure 9. Fluorescence intensity changes in of **1**-Cu²⁺ solution (1 μM) in the presence of miscellaneous anions. The gray bars represent the fluorescence intensity of **1**-Cu²⁺ solution with different anions; the red bars represent the fluorescence intensity of the abovementioned solution upon further addition S²⁻.

indicative of its good sensing property to S²⁻. The electronic absorption spectrum also behaves significant change during the S²⁻ addition process (Fig. S5, SI). The absorption spectrum of **1**-Cu²⁺ solution in the presence of 2 equiv. of S²⁻ reverted to the original state of free **1** solution, indicating that the supposed S²⁻ induced Cu²⁺ displacement was complete.¹⁴ Based on the fluorescence titration profile, the detection limit of **1**-Cu²⁺ for S²⁻ was evaluated to be 0.19 μM (Fig. S6, SI), implying that **1** is sensitive enough to detect S²⁻ concentration in real water.

To further investigate the anti-jamming ability of **1**-Cu²⁺ for S²⁻ recognition, competition experiments were explored (Fig. 9). The fluorescence intensity of **1**-Cu²⁺ solution was not affected by the potential competitive anions such as F⁻, Cl⁻, Br⁻, I⁻, SCN⁻, CN⁻, PO₄³⁻, H₂PO₄⁻, HPO₄²⁻, PO₄³⁻, P₂O₇⁴⁻, NO₂⁻, NO₃⁻, AcO⁻, ClO₄⁻, SO₄²⁻, HSO₄⁻, CO₃²⁻, HCO₃⁻, C₂O₄²⁻ and the thiol-containing amino acids of Cys, GSH, and Hcys. Subsequent addition of 2 equiv. of S²⁻ to the aforementioned test solution elicited a dramatic fluorescence enhancement (red bars), which further confirms the excellent selectivity of **1**-Cu²⁺ to S²⁻. Additionally, time course study reveals that both of the Cu²⁺ and S²⁻ recognition processes can complete within 1 minute (Fig. S7, SI).

Conclusions

In summary, a new application of 2-(4-*N*-phenyl-3-thiosemicarbazone)-8-hydroxyquinoline (**1**) as a fluorescent and colorimetric sensor was described. Sensor **1** behaves relay recognition ability to Cu²⁺ and S²⁻ in buffered (1% DMSO, HEPES 20 mM, pH = 7.4) aqueous solution through fluorescent and colorimetric dual channel responses. Both of the Cu²⁺ and S²⁻ detection processes are reversible with rapid response, high selectivity and sensitivity. This highly

selective and sensitive Cu²⁺ and S²⁻ relay recognition make sensor **1** has potential applicability in real water samples.

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