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Highly Selective Visual Detection of Cu(II) Utilizing Intramolecular Hydrogen Bond-Stabilized Merocyanine in Aqueous Buffer Solution

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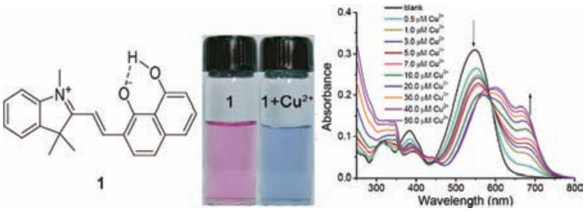
ABSTRACT



A Cu^{2+}-specific colorimetric sensor 1, which is stabilized by an intramolecular hydrogen bonding, was designed and developed. The color of 1 changes from purple to blue on addition of 1.0 μM Cu^{2+} in aqueous buffer solution, which can be detected by the naked eye. The analytical detection limit for Cu^{2+} by the naked eye is as low as 1.0 μM. The stoichiometry for 1 and Cu^{2+} in complex is 2:1 in aqueous solution.

The development of highly selective sensors for metal ions is particularly important, since metal ions can have detrimental effects on humans and the environment.[1] Copper is the third most abundant essential trace element in the human body and is commonly found as Cu^{2+} in natural water.[2] However, free Cu^{2+} is potentially very toxic to aquatic life, both acutely and chronically. For example, microorganisms are affected by even submicromolar concentrations of Cu^{2+}.[3] Excessive uptake of copper causes liver or kidney damage.[4] Several analytical methods[5] and a number of probes[6,7] have been developed for sensitive, selective, and accurate detection of Cu^{2+}. Colorimetric methods, in particular, are extremely attractive because they can be easily read with the naked eye. Most of the reported colorimetric sensors[7] for Cu^{2+} are used in mixed solvent (water/organic solvent), but only a

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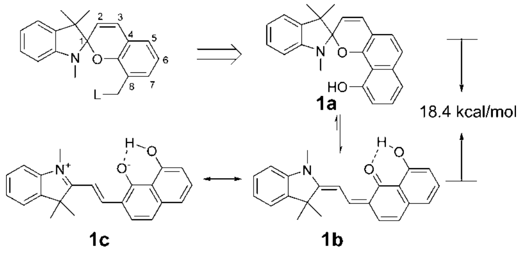
few of them are used in neat aqueous solution.[7f] Consequently, the development of nake-eyed sensors for Cu^{2+} in neat aqueous solution has the important feature that they can be used to evaluate the analyte concentration rapidly.

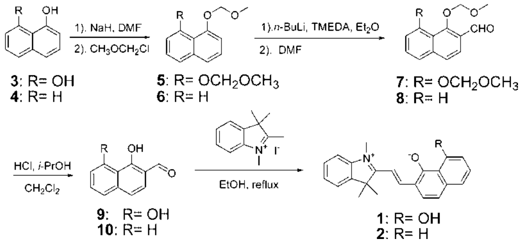
The conversion of spiropyran to merocyanine[8] was used for metal ion sensing by phenolate oxygen in the merocyanine via cooperative ligation of other chelating functionality attached at the 8-position or N-position (Scheme 1).[6a,7g,9] However, the use of organic solvents and light-black protection in the measurement limits their application. Therefore, thermo-/photostable merocyanine from spiropyran is desirable. Herein, we introduce naphthalen-1,8-diol moiety into spiropyran **1a**, which is likely to convert to merocyanine **1b** due to the formation of a six-membered-ring intramolecular hydrogen bond between hydroxyl group and carbonyl (or naphthanolate) group (Scheme 1). The formed hydrogen bonding will stabilize the zwitterion form **1c** and increase its solubility in polar solvent. Furthermore, the hydroxyl group together with naphthanolate could bind to the metal ion and act as a sensor. In this context, we present the synthesis and the spectroscopic evaluation of colorimetric chemosensor **1**, which is developed for the highly selective visual detection of Cu^{2+} in aqueous buffer solution.

Scheme 1. Chemical Structure of the Spironaphthanopyran **1** and the Interconversion of Spiropyran to Merocyanine



Theoretical calculations are performed to evaluate the sum of electronic and zero-point energies of spiro-form **1a** and mero-form **1b** on the isolated gas phase by using the Gaussian 03 program (b3lyp/6-31+G(d,p)).[10] The result shows the energy of mero-form **1b** is 18.4 kcal/mol lower than that of spiro-form **1a**. This demonstrates **1** exists mainly in mero-form **1b** in the equilibrium and is in accordance with our design. Compound **1** can be obtained by condensation of 1,8-dihydroxy-2-naphthaldehyde **9** with 1,2,3,3-tetramethyl-3*H*-indolium iodide in ethanol (shown in Scheme 2).[8]

Scheme 2. Synthesis of **1** and **2**



Compound **9** was obtained in three steps starting from commercially available naphthalen-1,8-diol **3**.[11] In the same procedure, compound **2**, without an additional chelating hydroxyl group, was also synthesized in control. The detailed experimental procedures can be found in the Supporting Information.

Compound **1** exists mainly as merocyanine in solution. In its ^{1}H NMR spectrum in CDCl$_3$, a singlet at 14.58 ppm is assigned to the proton of the hydroxyl group involved in a strong intramolecular hydrogen bonding; two doublets (6.18 and 8.66 ppm) with a coupling constant of 14.2 Hz are assigned to the protons of *trans*-CH=CH bond and a singlet at 3.48 ppm is assigned to the proton of N−CH$_3$. In contrast, compound **2** exists as the spiro-form in chloroform due to chemical shifts at 2.73 ppm for N−CH$_3$ and a coupling constant of 10.2 Hz for *cis*-CH=CH. The results demonstrate the intramolecular hydrogen bonding in molecule **1** makes the equilibrium shift to merocyanine and stabilizes the merocyanine. About 20% intramolecular proton tranfer tautormer existing in CDCl$_3$ and CD$_3$CN vanished when CD$_3$OD and DMSO-d_6 were used as solvent (Figure 1). When an equivalent of Cu(OAc)$_2$ was added to a solution of **1** in DMSO-d_6, the naphtholate together with hydroxy group bind to Cu^{2+}, which results in the peaks broadening and shifting in the ^{1}H NMR spectrum.

The intramolecular hydrogen bond-stabilized merocyanine exhibits a strong absorption band in the range of 500−650 nm in selected solvents. (Figure 2). The absorption maximium of **1** in methanol appears at 603 nm with a extinction coefficient (ε) of 7.4 × 10^4 M^{-1} cm^{-1}, which is assigned to the transition to the intramolecular charge transfer state from

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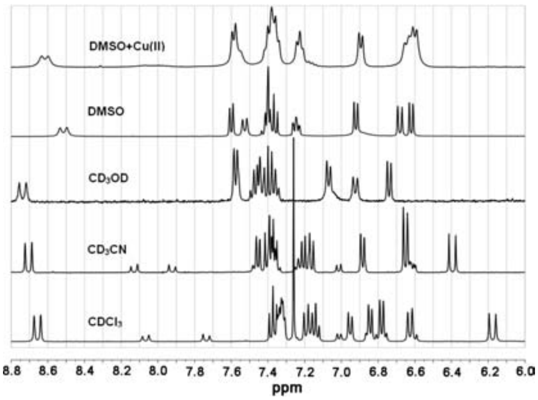

Figure 1. ^1H NMR spectra of **1** in selected solvent in the range of 6.0−8.8 ppm: (a) $CDCl_3$; (b) CD_3CN; (c) CD_3OD; (d) DMSO-d_6; and (e) DMSO-d_6 with 1.0 equiv of $Cu(OAc)_2$

the ground state. The absorption maximium shifts to 548 nm with $\varepsilon = 3.1 \times 10^4$ M^{-1} cm^{-1} in phosphate-buffered saline (PBS, pH 9.18) solution, and 547 nm with $\varepsilon = 5.1 \times 10^4$ M^{-1} cm^{-1} in hexane. In contrast, there was no absorption at 500−650 nm for **2** in hexane, but the absorption intensity of the band increased as the solvent polarity increased (Figure S1, Supporting Information). The results indicate compound **1** shows strong solvatochromism due to the solute−solvent interaction, and for compound **2**, solvatochromism was governed by the shift of the equilibrium.[8]

The metal ions binding properties and selectivity of compound **1** were first investigated in methanol solutions with use of metal acetate salts. Chemosensor **1** response to Cu^{2+}, Fe^{2+}, and Fe^{3+} lead to absorption variation (Figure S2, Supporting Information). The absorption peak at 565 nm vanished for **1** in methanol gradually with the addition of Cu^{2+}, while a new absorption band appeared at 636 nm. The color of the solution changed from blue to cyan (Figure S3, Supporting Information). The stoichiometry for **1** and Cu^{2+} is 1:1 in methanol determined by a Job's plot[12] (Figure S4, Supporting Information). Ascribed to the equilibrium, **1c** existing in methanol, two oxygen atoms were both partially negatively charged and easily chelated to Cu^{2+}.

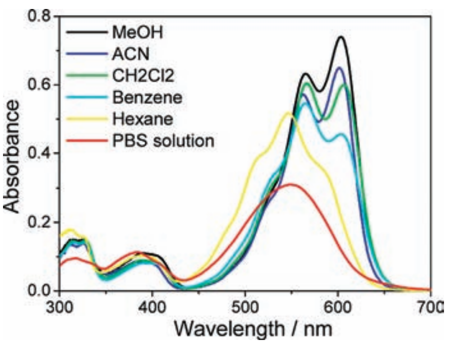

Figure 2. Absorption spectra of **1** (10 μM) in selected solvents.

The selective interaction of sensor **1** with Cu^{2+} in methanol encourage us to further investigate its binding property in aqueous solution. Fortuanately, compound **1** can be dissolved in basic solution due to the probable deprotonation. The changes in the absorption spectra of **1** upon addition of Cu^{2+} in PBS solution (pH 9.18) are shown in Figure 3a. The intensity of the absorption maximum at 548 nm was gradually reduced with the addition of Cu^{2+}, while a new absorption band appeared at 670 nm with a red shift of 122 nm. The absorption change at 670 nm gradually increased with the concentration of Cu^{2+} increasing (inset in Figure 3a). The analytical detection limit of Cu^{2+} by the naked eye is as low as 1.0×10^{-6} M. The association constant is $(1.0 \pm 0.15) \times 10^{10}$ M^{-2} (Supporting Information). The stoichiometry of Cu^{2+} and **1** is 1:2 determined by a Job's plot (Figure 3b).[12]

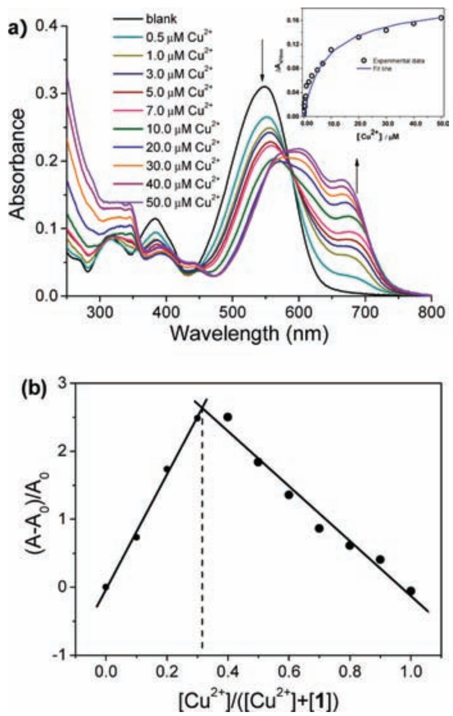

Figure 3. (a) Absorption spectra of **1** (10 μM) in pH 9.18 PBS buffer solution in the presence of different concentrations of Cu^{2+}. Inset: The absorption change of **1** at 670 nm upon the initial concentration of $[Cu^{2+}]$. (b) Job's plot for determing the stoichiometry for **1** and Cu^{2+} in PBS buffer solution. Total concentration $= 1.0 \times 10^{-5}$ mol/L.

Furthermore, we investigated the metal ions binding property and selectivity of compound **1** in PBS solutions (pH 9.18). Figure 4a (the black bar portion) illustated the absorption resopnse of **1** to metal ions Na^+, K^+, Ag^+, Mg^{2+}, Cu^{2+}, Ca^{2+}, Cd^{2+}, Co^{2+}, Hg^{2+}, Ni^{2+}, Pb^{2+}, Zn^{2+}, Fe^{2+}, and Fe^{3+} in aqueous solution. No significant absorption changes were observed with common interferences, the purple color of **1** showed no change when other metal ions were added

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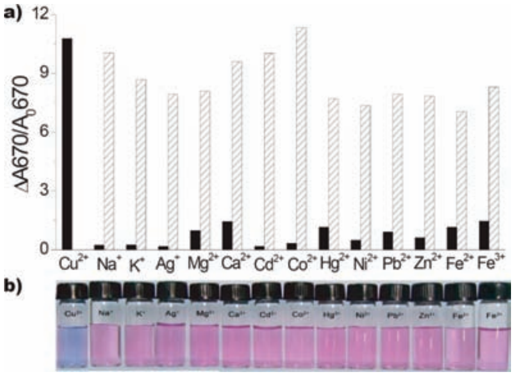

Figure 4. (a) Absorption responses of **1** (10 μM) to 10 μM Cu^{2+} or 50 μM other metal ions (the black bar portion) and to the mixture 50 μM other metal ions with 10 μM Cu^{2+} (the shaded bar portion). (b) Photograph of sensor **1** containing 50 μM metal ions in PBS buffer solutions.

except for Cu^{2+}. However, with the addition of 1 equiv of Cu^{2+}, the color changed from purple to blue (Figure 4b). These results indicated that our proposed sensor exhibited high selectivity to Cu^{2+} over other metal ions. In river water and seawater, the concentrations of some other contaminating metal ions, such as Zn^{2+}, Ni^{2+}, and Pb^{2+}, are significantly higher than that of Cu^{2+}; selective detection of Cu^{2+} in the presence of these metal ions with high concentration is a challenge to the application of most common sensors. To test the practical applicability of our visual chemosensor for Cu^{2+}, competition experiments were also carried out. Five times the concentration of the above-mentioned metal ions (50 μM) was added to 10 μM **1** followed by addition of Cu^{2+} (10 μM). The results are also shown in Figure 4a (the shaded bar portion). Our sensor showed a small change response to Cu^{2+} with or without addition of other interfering metal ions. These experimental results showed that the response of the sensor to Cu^{2+} is little affected by the presence of the other possible contaminating metal ions.

In conclusion, a highly sensitive and selective merocyanine-based colorimetric chemosensor **1** was developed for the detection of Cu^{2+} in PBS solution (pH 9.18). The recognition of Cu^{2+} gave rise to color changes from purple to blue that were clearly visible to the naked eye. Such Cu^{2+} selective colorimetric chemosensors could meet the sensitive and selective requirements for biomedical and environmental application and be of great importance for real-time and instrument free detection.

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Note Added after ASAP Publication. In the version published ASAP April 19, 2010 two doublet values were incorrect in the paragraph describing Figure 1; the correct version published on the web May 14, 2010.

Supporting Information Available: Experimental procedures and characterization data of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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