

A new hydrazone-based colorimetric chemosensor for naked-eye detection of copper ion in aqueous medium

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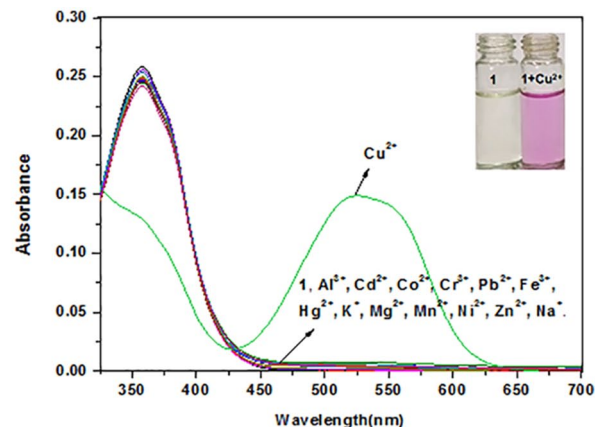
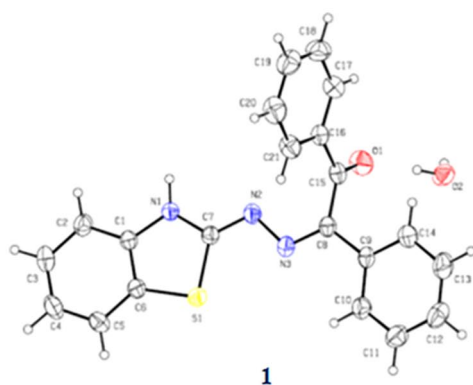
Abstract

A new hydrazone-based colorimetric Cu^{2+} chemosensor is synthesized. Its structure was confirmed by single-crystal X-ray diffraction. Its binding properties towards various metal ions are examined through absorption spectroscopy. In aqueous THF solution, the chemosensor exhibits selective recognition towards Cu^{2+} over other metal ions with a colour change from colourless to pink. The complex formed between the chemosensor and Cu^{2+} ions forms a 2:1 stoichiometry with an association constant of $2.46 \times 10^8 \text{ M}^{-2}$. The analytical detection limit for Cu^{2+} by the naked eye is as low as $10.0 \mu\text{M}$.

Keywords

chemosensors, colorimetric, copper ions, hydrazones, X-ray structure

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Introduction

In recent years, the development of highly selective and sensitive chemosensors for transition metal ions has attracted significant interest due to their vital role in various biological and environmental processes.^{1–3} Among these metal ions, copper ions play a critical role in various biological processes^{4,5} and are also significant environmental pollutant in modern society. The over-accumulation of copper ions can cause a series of severe diseases such as Alzheimer's, Wilson's and Menke's diseases.^{6,7} Therefore, it is very important to detect rapidly Cu^{2+} in environmental and biological systems.

Up to now, many fluorescent probes^{8–16} have been reported. However, most of them usually require expensive

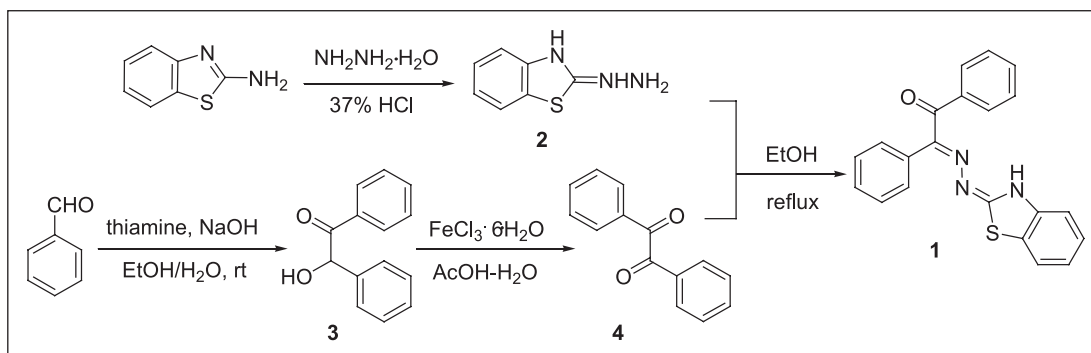
instruments, involve complicated syntheses or are insoluble in aqueous solutions. For practical applications, it is necessary to develop Cu^{2+} sensors that are easily prepared and

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Scheme 1. Synthesis of the sensor **1**.

that can be easily detected rapidly without the help of instruments. In this respect, colorimetric chemosensors would appear to be the most attractive and could be widely used owing to the low cost and lack of equipment required. Moreover, a colour change can easily be observed by the naked eye.¹⁷ However, so far, reported colorimetric Cu^{2+} probes are still relatively rare,^{18–23} and it is still a challenge to develop colorimetric chemosensing molecules to detect Cu^{2+} in aqueous solution.

In this study, we reported a new hydrazone compound (**1**), 2-(benzo[d]thiazol-2(3H)-ylidene)hydrazono-1,2-diphenylethanone, which can be used as a highly selective colorimetric naked-eye sensor for Cu^{2+} in aqueous solution.

Result and discussion

The synthesis of chemosensor **1** is shown in Scheme 1; first, hydrazinobenzothiazole (**2**) is synthesized from benzothiazol-2-ylamine; second, benzil (**4**) is synthesized from benzaldehyde through two-step reaction involving benzoin condensation and further oxidation reaction; finally, the reaction of 2-hydrazinobenzothiazole (**2**) and benzil (**4**) under reflux in ethanol gives chemosensor **1**, the structure of which is identified by NMR, ESI-MS (Figure S1–S3 in the Supporting Information) and X-ray diffraction analysis. The molecular view of **1** is shown in Figure 1. The crystal packing is stabilized by the water molecules via intermolecular $\text{N-H1}\cdots\text{O2}$, $\text{O2-H(2B)}\cdots\text{N2}$ and $\text{O2-H(2A)}\cdots\text{O1}$ hydrogen bonds (Figure 2). The water molecules serve as both hydrogen-bond donors and acceptors.

The interaction of **1** ($10\ \mu\text{M}$) with various metal ions in 9:1 (v/v) THF–HEPES buffer solution (pH=7.0) was investigated by UV-Vis absorption spectrometry. As shown in Figure 3, free **1** exhibits a broad band at 358 nm. The addition of Cu^{2+} to **1** led to a red shift of its absorption maxima and formed a new absorption band at 524 nm. However, sensor **1** showed almost no change in its absorption peak on addition of other metal ions. Moreover, as shown in the insert in Figure 3, the Cu^{2+} sensing and the concomitant absorption change were clearly visible to the naked eye, which indicated that **1** can act as a colorimetric chemosensor for the naked-eye detection of Cu^{2+} in an aqueous solution.

The UV-Vis titration of **1** with Cu^{2+} was carried out. As shown in Figure 4, upon the addition of Cu^{2+} (0–5 equiv.) to

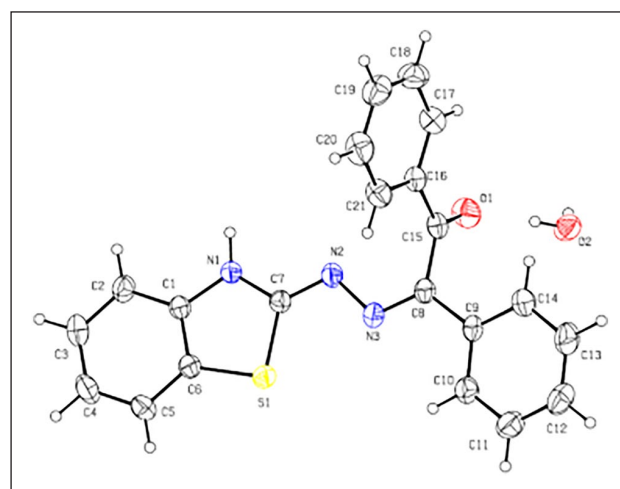


Figure 1. The molecular structure of **1** with displacement ellipsoids drawn at the 30% probability level.

a solution of **1**, the absorbance peaks at 358 nm gradually decreased and meanwhile new absorption peaks at 524 nm appeared with a clear isosbestic point at 400 nm. This red shift from 358 to 524 nm may result from the Cu^{2+} coordination-enhanced LMCT (ligand-to-metal charge-transfer) effect.²⁴

A Job plot²⁵ analysis was used to determine the stoichiometry of **1**– Cu^{2+} . Figure 5 shows a plot of absorbance at 524 nm against the mole fractions of Cu^{2+} at a constant concentration of **1** + $[\text{Cu}^{2+}]$. As shown in Figure 5, when the molar fraction $[\text{Cu}^{2+}]/([\text{1}] + [\text{Cu}^{2+}])$ was about 0.33, the concentration of the **1**– Cu^{2+} complex reached a maximum value, which indicated a 2:1 stoichiometric complexation of **1** with Cu^{2+} ions. The association constant (K_{ass}) between compound **1** and Cu^{2+} was calculated to be $2.46 \times 10^8 \text{ M}^{-2}$ by non-linear fitting of the titration curve of a 2:1 binding model (Figure 6).

The analytical detection limit of Cu^{2+} , defined as the lowest concentration of Cu^{2+} at which the colour change of **1** ($10\ \mu\text{M}$) in 9:1 (v/v) THF–HEPES buffer solution can be detected by the naked eye,¹⁸ is as low as $10.0\ \mu\text{M}$ (Figure 7), which is lower than the limit of copper in drinking water ($\sim 20\ \mu\text{M}$).

The mode of interaction between **1** and Cu^{2+} ions was investigated through ^1H NMR spectroscopy and mass spectrometry upon the addition of Cu^{2+} . The ^1H NMR spectra of sensor **1** revealed that the imine proton (Ha) signal at

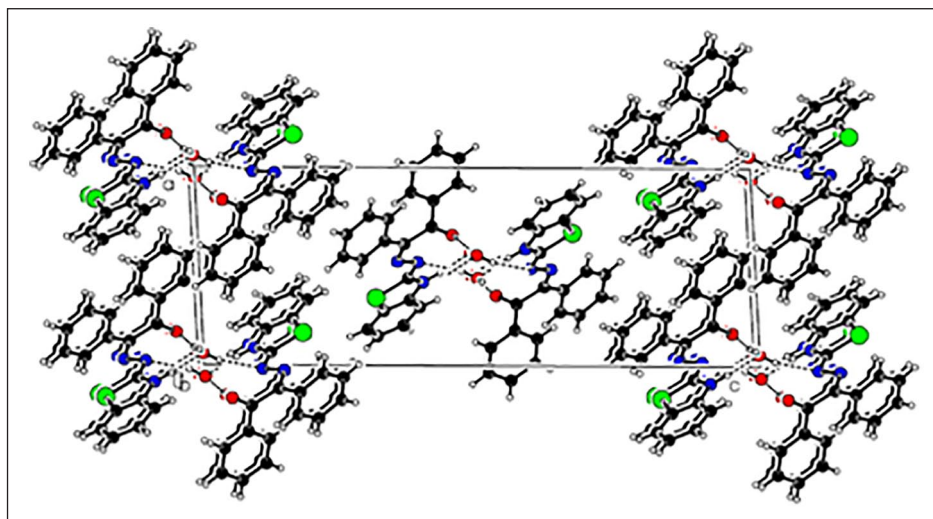


Figure 2. A packing diagram for **I** viewed along the c-axis. Dashed lines show arrays of hydrogen bonds.

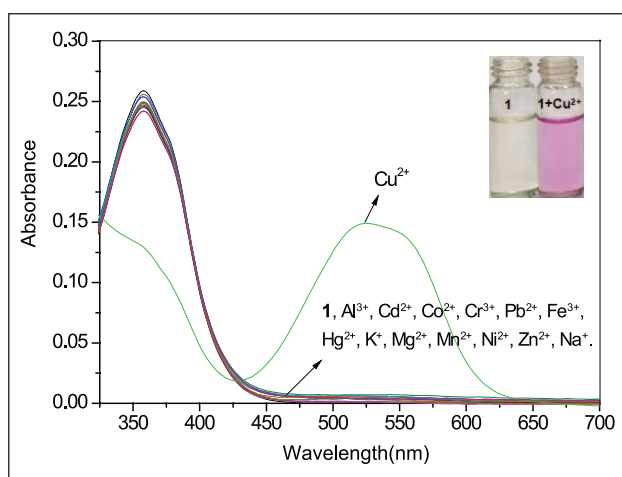


Figure 3. UV-Vis spectral changes of compound **I** ($10\ \mu\text{M}$) in 9:1 (v/v) THF-HEPES buffer solution (10 mM, pH=7.0) upon addition of various metal ions ($20\ \mu\text{M}$). Insert: Visual colour change of **I** ($10\ \mu\text{M}$) upon addition of 2.0 equiv. of Cu^{2+} .

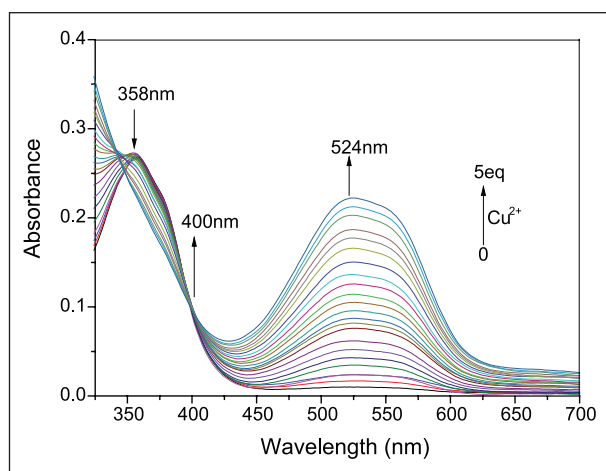


Figure 4. UV-Vis absorption spectra of **I** ($10\ \mu\text{M}$) in 9:1 (v/v) THF-HEPES buffer solution (10 mM, pH=7.0) upon the addition of Cu^{2+} (0– $50\ \mu\text{M}$) at $25\ ^\circ\text{C}$. Each spectrum is obtained 5 min after Cu^{2+} addition.

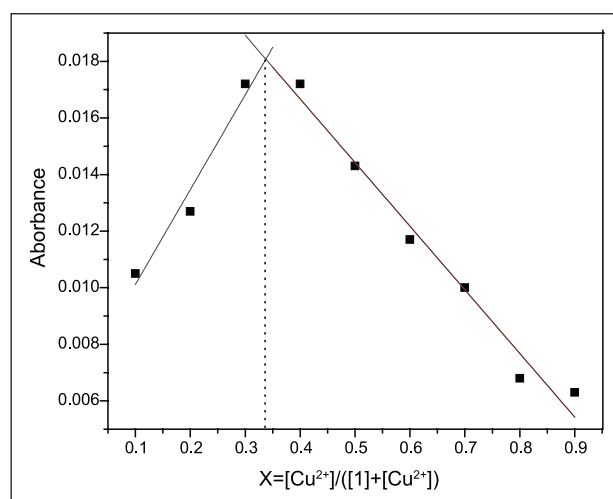


Figure 5. Job plot of a 2:1 complex of **I** and Cu^{2+} . $[\text{I}] + [\text{Cu}^{2+}] = 10\ \text{mM}$. The absorbance is monitored at 524 nm.

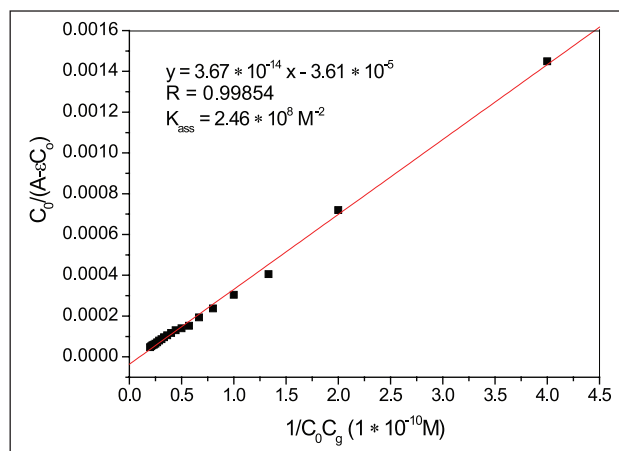


Figure 6. Plot of $C_0/(A_{524}-\epsilon_m C_0)$ against $1/C_0 C_g$ at 524 nm. See text for a definition of the parameters.

9.33 ppm almost completely disappeared upon the addition of 5 equiv. of Cu^{2+} (Figure 8), which indicates that Cu^{2+}

induces deprotonation of the active NH of the imine group. The appearance of a peak at m/z 776.00 (calcd for 776.12, $[(2 \text{ receptor } \mathbf{1} + \text{Cu}^{2+} - 2\text{H}^+) + \text{H}^+]$) in the electrospray ionization mass spectrum (Figure S4) further confirmed the formation of a 2:1 complex between $\mathbf{1}$ and Cu^{2+} ions.

Based on the above results of the Job plot analysis, the mass spectrum, and the ^1H NMR study, a possible coordination mode of receptor $\mathbf{1}$ with Cu^{2+} is proposed in Scheme 2.

Conclusion

In conclusion, a new hydrazone-based colorimetric Cu^{2+} chemosensor $\mathbf{1}$ was synthesized and its structure was confirmed by X-ray diffraction analysis. The recognition of Cu^{2+} brought about colour changes from colorless to pink. The analytical detection limit for Cu^{2+} by the naked eye is as low as $10.0 \mu\text{M}$, which suggests chemosensor $\mathbf{1}$ has great potential in colorimetric Cu^{2+} detection.

Experimental

Infrared (IR) spectra were recorded on a Perkin-Elmer PE-983 IR spectrometer as KBr pellets. NMR spectra were



Figure 7. Visual colour change of $\mathbf{1}$ ($10 \mu\text{M}$) in 9:1 (v/v) THF-HEPES buffer solution (10 mM, pH=7.0) upon addition of 10–50 μM of Cu^{2+} ions.

recorded on a Varian Mercury 300 spectrometer. Electrospray ionization mass spectra were measured on a Finnigan LCQ Advantage Max spectrometer. Absorption spectra were measured on a Hitachi U-3010 spectrometer. The crystal structure of $\mathbf{1}$ was determined on a Bruker SMART APEX CCD system. HEPES buffer solution (pH=7.0) was prepared using 4-(2-hydroxyethyl)-1-piperazine ethanesulfonic acid (HEPES) and aqueous sodium hydroxide. 2-Hydrazinobenzothiazole ($\mathbf{2}$)²⁶ and benzil ($\mathbf{4}$)²⁷ were prepared according to reported procedures.

Synthesis of 2-(benzo[d]thiazol-2(3H)-ylidene)hydrazone-1,2-diphenylethanone ($\mathbf{1}$)

A solution of 2-hydrazinobenzothiazole ($\mathbf{2}$) (1.0 mmol) and benzil ($\mathbf{4}$) (1.0 mmol) in ethanol (40 mL) was heated under reflux for 3 h. After cooling, the solvent was evaporated and the desired product $\mathbf{1}$ (0.25 g) was obtained in 70% yield via flash chromatography with petroleum as the eluent; m.p.: 94–95 °C. IR (ν_{max} , KBr, cm^{-1}): 3450, 1666, 1606, 1575, 1539, 1471, 1441, 1271, 1223, 1130, 1075, 731, 519; ^1H NMR ($\text{DMSO}-d_6$): δ 12.10 (s, 1H, NH), 7.85–7.88 (m, 2H, Ar-H), 7.55–7.71 (m, 6H, Ar-H), 7.43–7.49 (m, 3H, Ar-H), 7.20–7.25 (m, 1H, Ar-H), 6.99–7.08 (m, 2H, Ar-H), ^{13}C NMR ($\text{DMSO}-d_6$): δ 191.2, 155.1, 147.6, 144.0, 138.5, 138.0, 131.8, 130.5, 129.8, 129.6, 129.5, 128.9, 127.8, 117.9, 108.4. ESI-MS: m/z 358.02 [$M + \text{H}$]⁺; M^+ calculated 357.09.

X-ray diffraction study of compound $\mathbf{1}$

A yellow crystal of the compound $\mathbf{1}$, obtained by slow evaporation from 95% ethanol solution, was mounted on a glass fibre in a random orientation at 295(2)K. The determination of the unit cell and the data collection were performed with MoK α radiation ($\lambda=0.71073 \text{ \AA}$) on a Bruker Smart Apex-CCD diffractometer with a ω -(θ) scan mode. The structure was solved by direct methods with SHELXS-97 and expanded by the Fourier technique. The non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were placed at calculated

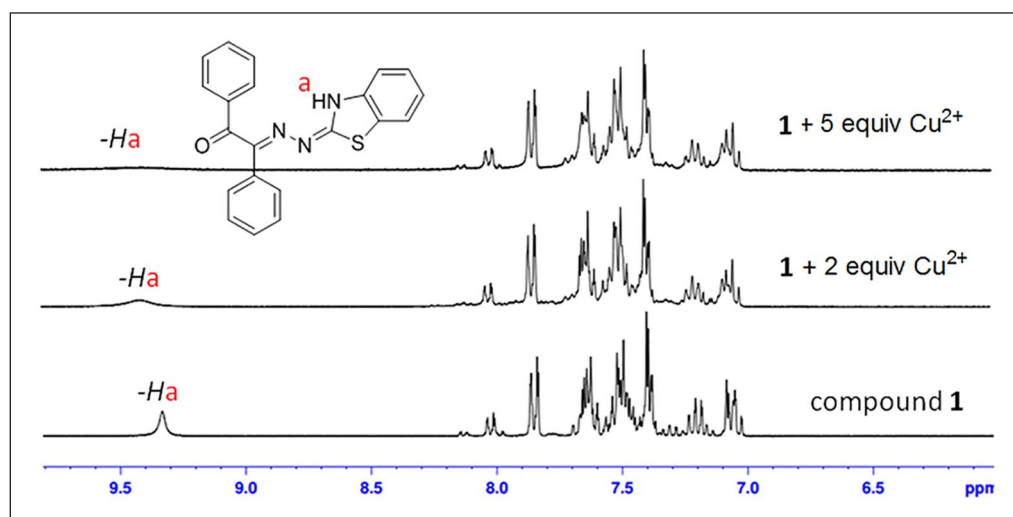
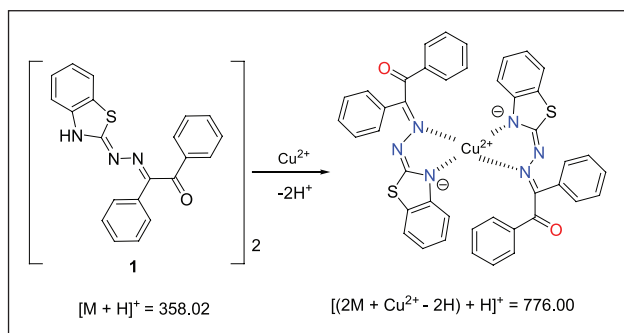


Figure 8. ^1H NMR (300 MHz) spectra of $\mathbf{1}$ in the presence of Cu^{2+} in CDCl_3 .



Scheme 2. Proposed coordination mode of sensor **1** with Cu^{2+} .

positions. Crystal data for $\text{C}_{21}\text{H}_{15}\text{N}_3\text{OS} \cdot \text{H}_2\text{O}$: crystal size: $0.2 \times 0.1 \times 0.1$ mm, $M = 375.44$, Monoclinic, space group $\text{P}2(1)/n$. $a = 9.253(2)$ Å, $b = 7.983(2)$ Å, $c = 25.931(7)$ Å, $V = 1912.3(8)$ Å³, $Z = 4$, $T = 298(2)$ K, $\theta_{\text{max}} = 30.00^\circ$, 18,963 reflections measured, 5544 unique ($R_{\text{int}} = 0.0559$). Final R indices ($I > 2\sigma(I)$): $R_1 = 0.0524$, $wR_2 = 0.1273$ and $\text{GOF} = 1.029$. CCDC 924965 contains the supplementary crystallographic data for this article. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Binding studies

A stock solution of compound **1** was prepared by dissolution in 9:1 (v/v) THF–HEPES buffer solution (10 mM, $\text{pH} = 7.4$) (1.0×10^{-5} M). The solutions of metal ions were prepared from $\text{Al}_2(\text{SO}_4)_3$, $\text{Pb}(\text{NO}_3)_2$ and the chlorides of Na^+ , K^+ , Co^{2+} , Cr^{3+} , Fe^{3+} , Hg^{2+} , Cd^{2+} , Mg^{2+} , Cu^{2+} , Zn^{2+} , Ni^{2+} and Mn^{2+} , respectively, and were dissolved in water (3.0×10^{-3} M). Fluorescence titrations were performed on a 3-mL solution of compound **1** in a quartz cell of 1-cm optical path length, by adding portionwise different stock solutions of cations into the quartz cell using a microsyringe.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Supplemental material

Supplemental material for this article is available online.

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