

A Phenylbenzothiazole Derived Fluorescent Sensor for Zn(II) Recognition in Aqueous Solution Through “Turn-On” Excited-State Intramolecular Proton Transfer Emission

Lijun Tang · Xin Dai · Keli Zhong · Xin Wen · Di Wu

Received: 5 May 2014 / Accepted: 21 July 2014 / Published online: 7 August 2014
© Springer Science+Business Media New York 2014

Abstract A highly selective and sensitive fluorescent Zn²⁺ sensor *N*-(2-(benzo[d]thiazol-2-yl)phenyl)-2-((pyridin-2-ylmethyl)amino)acetamide (**1**) that derived from 2-(2'-aminophenyl)benzothiazole has been developed. In aqueous solution (HEPES/CH₃CN=4/6, v/v, HEPES 20 mM, pH=7.4), sensor **1** displays highly selective recognition to Zn²⁺ over other metal ions with a distinct longer-wavelength emission enhancement. Sensor **1** binds Zn²⁺ through its amide form with a 1:1 binding stoichiometry, which switched on the excited-state intramolecular proton transfer (ESIPT).

Keywords Zinc recognition · Benzothiazole · Chemosensor · ESIPT

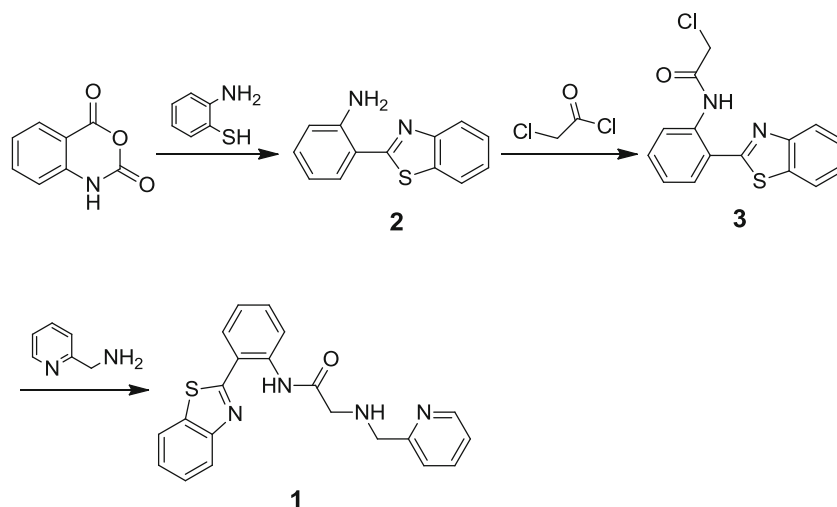
Introduction

Zinc plays crucial roles in a variety of biological processes including apoptosis, regulators of gene expression, and neural signal transmitters or modulators [1, 2]. Deficiency of Zn²⁺ can lead to unbalanced metabolism, which is responsible to some problems such as retarded growth in children, the decrease of the immunological defense, eye lesion and some skin diseases [3]. Overloading Zn²⁺ level in human body is also associated with some serious neurological disorders such as Alzheimer's and Parkinson's diseases [4–6]. As a consequence, considerable attention has been devoted to the development of fluorescent chemosensors for Zn²⁺ detection [7–13], because fluorescence techniques can offer distinct advantages such as low cost, simplicity, good sensitivity, and capability of real-time detection [14].

Although a large number of Zn²⁺ selective fluorescent sensors have been well established, many reported Zn²⁺ sensors still encountered a difficulty in distinguishing Zn²⁺ from Cd²⁺ [15–18], because Cd²⁺ is in the same group in the periodic table with Zn²⁺ and usually induces a comparable fluorescent response to that of Zn²⁺. Therefore, development of small molecular fluorescent sensors that can clearly distinguish Zn²⁺ from Cd²⁺ is still challenging and imperative. Fluorescence Zn²⁺ sensors generally contain two parts, a Zn²⁺ receptor unit that can selectively binds Zn²⁺ ion and a signaling unit that can responses the recognition event by fluorescence changes. Besides the well-known dipicolylamine (DPA) Zn²⁺ ion chelator, 2-picolylamine also has been widely used as the Zn²⁺ binding unit [19–21]. Although a number of fluorophores such as anthracene [22–25], coumarin [10, 26, 27], boron dipyrromethene [28, 29], fluorescein [30], rhodamine [31, 32], cyanine [13, 33], benzimidazole [34–36], and benzoxazole [19, 21, 37, 38] have been employed to construct Zn²⁺ selective fluorescent sensors, benzothiazole derivatized fluorescent sensors for Zn²⁺ detection are still rare [39–41]. Therefore, we are encouraged to design and synthesize a novel fluorescent sensor based on benzothiazole fluorophore.

Owing to the potential ESIPT property of 2-(2'-aminophenyl)benzothiazole (APBT) derivatives, design and synthesis of new Zn²⁺ selective fluorescent sensors based on APBT fluorophore aroused our great interest. In this work, a simple and effective APBT-based fluorescence sensor (**1**) has been designed and prepared (Scheme 1). Sensor **1** displays highly selective response to Zn²⁺ with the appearance of a strong longer-wavelength emission band, which makes **1** has an excellent ability to discriminate Zn²⁺ from Cd²⁺ and other metal ions. Sensing mechanism studies reveal that sensor **1** bind with Zn²⁺ through the amide form and the newly developed longer-wavelength emission band is attributed to the ESIPT fluorescence emission.

L. Tang (✉) · X. Dai · K. Zhong · X. Wen · D. Wu
Department of Chemistry, Liaoning Provincial Key Laboratory for the Synthesis and Application of Functional Compounds, Bohai University, Jinzhou 121013, China
e-mail: ljtang@bhu.edu.cn

Scheme 1 Synthesis of fluorescent sensor **1**

Experimental Section

General Methods and Materials

Unless otherwise stated, solvents and reagents were of analytical grade from commercial suppliers and were used as received. Compound **2** was prepared following the method previously described [42]. ¹H NMR and ¹³C NMR spectra were recorded on Agilent 400-MR spectrometer, chemical shifts (δ) were expressed in ppm and coupling constants (J) in Hertz. High-resolution mass spectroscopy (HRMS) was measured on a Bruker micrOTOF-Q mass spectrometer (Bruker Daltonik, Bremen, Germany). Low-resolution mass spectroscopy (LRMS) was measured on an Agilent 1100 series LC/MSD mass spectrometer. Fluorescence measurements were performed on a Sanco 970-CRT spectrofluorometer (Shanghai, China). The pH measurements were made with a Model PHS-25B meter (Shanghai, China).

Synthesis of Compound **3**

A solution of 2-chloroacetyl chloride (0.34 g, 3 mmol) in dry CH₂Cl₂ (5 mL) was added dropwise to a solution of compound **2** (0.44 g, 2 mmol) and 4-dimethylaminopyridine (DMAP, 0.5 g, 4.1 mmol) in dry CH₂Cl₂ (5 mL) in an ice bath. The resultant was stirred for 2 h at room temperature and then the solvent was removed by rotary evaporation. The desired product **3** was recrystallized from acetone. Yield: 70 %. m.p. 144.1–144.5 °C. ¹H NMR (400 MHz, CDCl₃) δ 13.25 (s, 1H), 8.80 (d, J =8.4 Hz, 1H), 8.04 (d, J =8.1 Hz, 1H), 7.90 (dd, J =18.5, 7.9 Hz, 2H), 7.57–7.46 (m, 2H), 7.43 (t, J =7.6 Hz, 1H), 7.22 (t, J =7.6 Hz, 1H), 4.31 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) 172.6, 170.9, 157.5, 141.7, 138.4, 137.2, 135.4, 132.2, 131.3, 129.8, 127.7, 126.0, 125.3, 48.9. LRMS

(API-ES⁺) calcd. for C₁₅H₁₂ClN₂OS [M+H]⁺, 303.0, found 303.0.

Synthesis of Sensor **1**

Compounds **3** (0.30 g, 1.5 mmol) and 2-picolylamine (0.195 g, 1.8 mmol) were dissolved in DMF and were stirred overnight at room temperature. After removing the solvent under reduced pressure, the residue was extracted with ethyl acetate. The organic layer was dried over Na₂SO₄, filtered and evaporated. The crude product was purified by silica gel column chromatography to afford sensor **1** as yellow solids (0.12 g, 65 %). ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.96 (s, 1H), 8.82 (d, J =8.4 Hz, 1H), 8.53 (d, J =4.8 Hz, 1H), 8.16 (d, J =8.0 Hz, 1H), 7.96 (d, J =8.0 Hz, 1H), 7.70 (d, J =8.0 Hz, 1H), 7.65 (t, J =8.0 Hz, 1H), 7.56 (t, J =8.0 Hz, 1H), 7.45–7.39 (m, 3H), 7.29–7.24 (m, 2H), 3.95 (s, 2H), 3.45 (s, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆):171.7, 167.5, 153.0, 149.3, 137.3, 137.0, 133.6, 132.2, 131.9, 130.6, 127.0, 126.3, 124.2, 123.0, 122.7, 122.6, 122.4, 121.0, 54.3, 53.0. HRMS (ESI⁺) calcd. for C₂₁H₁₉N₄OS [M+H]⁺ 375.1280, found 375.1270.

Procedures of ion Sensing

Doubly distilled water was used for all experiments. Sensor **1** was dissolved in aqueous solution (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES) was employed as buffer agent, HEPES/CH₃CN=4/6, v/v, HEPES 20 mM, pH=7.4) to afford the test solution (10 μ M). Titration experiments were carried out in 10-mm quartz cuvettes at 25 °C. Metal ions (as chloride or nitrate salts, 10 mM) were added to the host solution and used for the titration experiment.

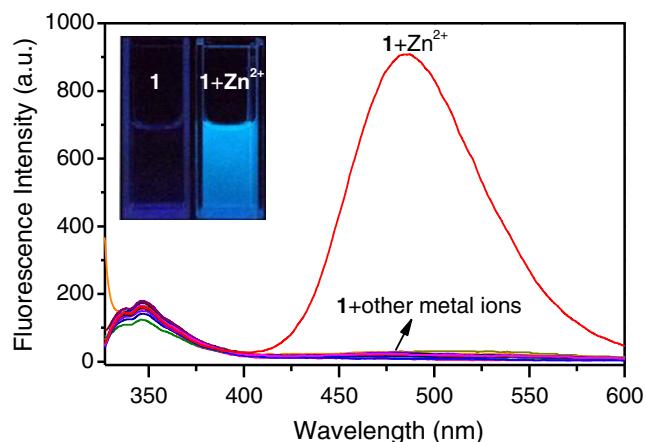


Fig. 1 The fluorescence spectra of **1** (10 μM) upon addition of various metal ions, including Zn²⁺, Cd²⁺, Cr³⁺, Mn²⁺, Hg²⁺, Ag⁺, Pb²⁺, Fe²⁺, Fe³⁺, Ni²⁺, Co²⁺, Cu²⁺, Ba²⁺, Al³⁺, Sr⁺ (3 equiv. of each) and Na⁺, K⁺, Ca²⁺, Mg²⁺ (100 equiv. of each) in aqueous solution (HEPES/CH₃CN=4/6, v/v, HEPES 20 mM, pH=7.4). Inset: Fluorescence color changes of **1** solution before and after addition of Zn²⁺ under irradiation at 365 nm

Result and Discussion

Synthesis

The synthetic route to sensor **1** is depicted in Scheme 1, which involves the synthesis of APBT (**2**), amidation of **2** with chloroacetic chloride, and nucleophilic substitution of **3** with 2-picolyamine. The obtained compound **1** is fully characterized by ¹H NMR, ¹³C NMR, and HRMS spectroscopy, and the results are in full agreement with the presented structure.

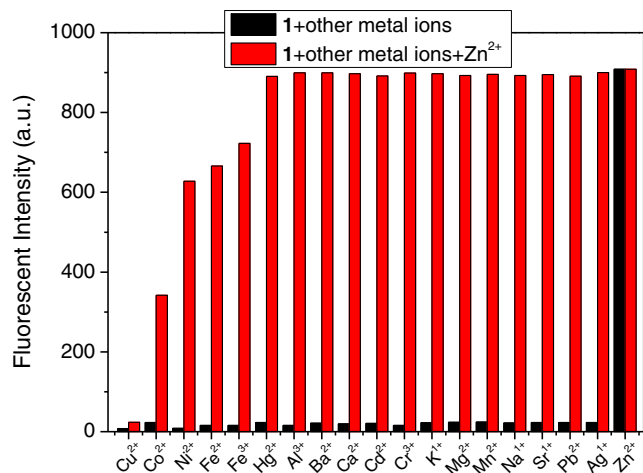


Fig. 2 Fluorescence intensity changes of **1** (10 μM) to various metal ions in aqueous solution (HEPES/CH₃CN=4/6, v/v, HEPES 20 mM, pH=7.4) at 485 nm. The black bars represent the fluorescence intensity of **1** solution in the presence of 3 equiv. of miscellaneous metal ions; the red bars represent the fluorescence intensity of the above solution upon further addition of 3 equiv. of Zn²⁺

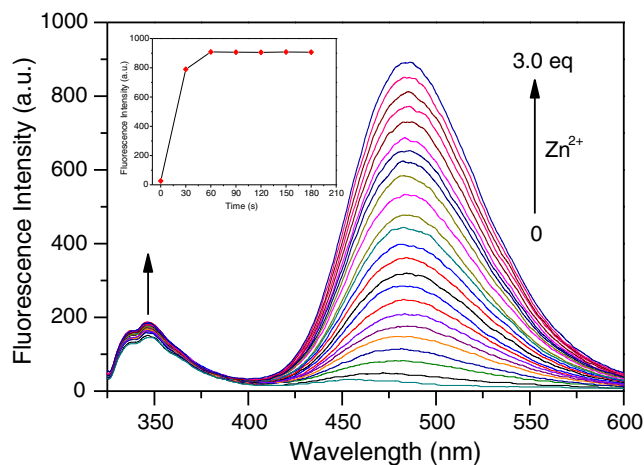


Fig. 3 Fluorescence spectra of **1** (10 μM) in aqueous solution (HEPES/CH₃CN=4/6, v/v, HEPES 20 mM, pH=7.4) in the presence of different amounts of Zn²⁺. Inset: Time-dependence fluorescence intensity of **1** solution in the presence of 3 equiv. of Zn²⁺

Fluorescence Recognition of Zn²⁺

The metal ion binding behavior of **1** was examined by fluorescence spectroscopic studies. As shown in Fig. 1, sensor **1** showed a weak fluorescence in HEPES/CH₃CN=4/6 (v/v, HEPES 20 mM, pH=7.4) solution at 348 nm, which is assigned to the normal excited state emission of **1**. Upon addition of Zn²⁺, a new strong emission band centered at 485 nm was observed. Concomitantly, the original emission at 348 nm enhanced slightly. In addition, the Zn²⁺ induced fluorescence change is naked eye detectable (Fig. 1, inset). However, other tested cations promoted no distinct emission shift and enhancement. These results indicate that sensor **1** has an excellent selectivity to Zn²⁺ and can clearly discriminate Zn²⁺ from Cd²⁺ and other metal ions. The influences of other potential competitive metal ions on Zn²⁺ recognition were then evaluated. In the presence of some metal ions such

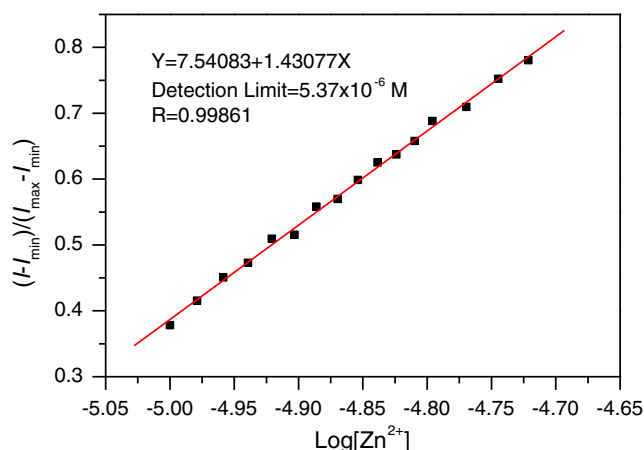


Fig. 4 Normalized intensity of **1** solution (10 μM) against Log[Zn²⁺] in the low Zn²⁺ concentration range

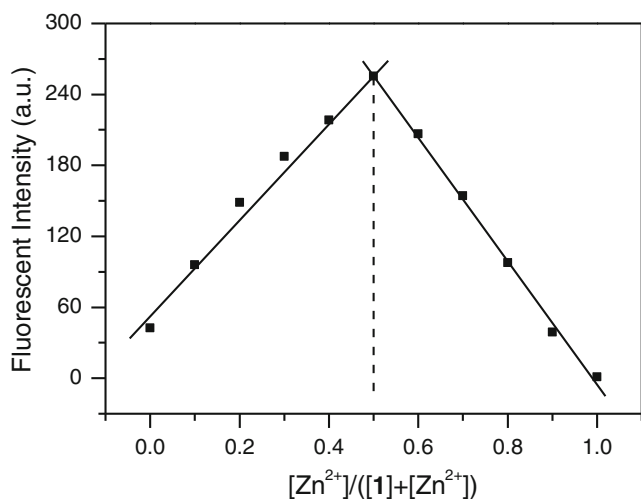


Fig. 5 Job's plot for **1** and Zn^{2+} solution with a total concentration as $10 \mu\text{M}$ in aqueous solution (HEPES/ CH_3CN =4/6, v/v, HEPES 20 mM, pH=7.4). The fluorescence intensity was monitored at 485 nm

Ag^+ , Pb^{2+} , Sr^{2+} , Ba^{2+} , Cd^{2+} , Mn^{2+} , Cr^{3+} , and Al^{3+} , further addition of Zn^{2+} ion still generated the similar fluorescence changes (Fig. 2). Co-existence of some metal ions including Co^{2+} , Ni^+ , Fe^{2+} , and Fe^{3+} could quench the fluorescence intensity of **1**- Zn^{2+} solution at 485 nm to different extent. Notably, Cu^{2+} can completely quench the fluorescence emission of **1**- Zn^{2+} solution at 485 nm. This phenomenon is often encountered in many fluorescent sensors due to the paramagnetic nature of Cu^{2+} [43, 44]. In addition, the biologically abundant metal ions of Na^+ , K^+ , Ca^{2+} , and Mg^{2+} displayed no hinder effects on Zn^{2+} recognition even they were used in high concentration as 1 mM. Thus, sensor **1** has a good anti-jamming ability to other metal ions except Cu^{2+} .

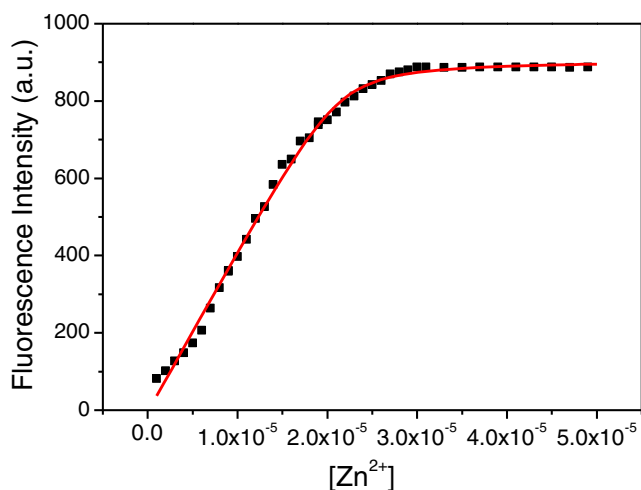


Fig. 6 Nonlinear fitting of fluorescence intensity of **1** solution ($10 \mu\text{M}$) against Zn^{2+} concentration (emission at 485 nm)

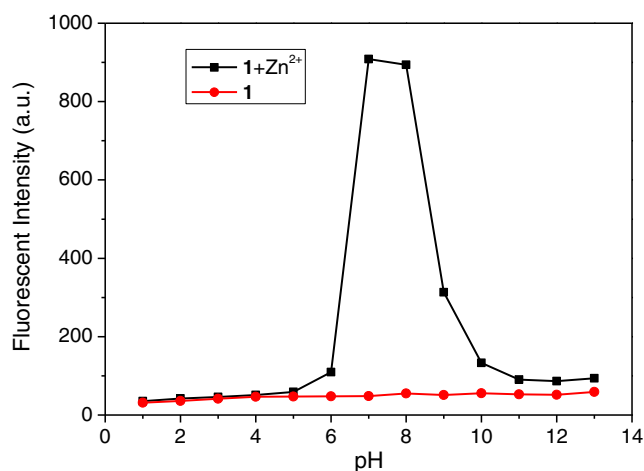


Fig. 7 Fluorescence intensity (at 485 nm) of **1** and **1**+ Zn^{2+} at various pH values in aqueous solution (HEPES/ CH_3CN =4/6, v/v)

Fluorescence Titrations and Detection Limit

To obtain a better insight into the Zn^{2+} sensing property of **1**, fluorescence titration experiments with addition of increasing amounts of Zn^{2+} were carried out (Fig. 3). Upon stepwise increasing in Zn^{2+} concentration, the fluorescence intensity of **1** solution at 348 nm increased slowly, but the intensity at 485 nm increased sharply. The fluorescence spectra changes stopped when 3 equiv. of Zn^{2+} was added. Moreover, time course examination reveals that the response of **1** to Zn^{2+} can finish within 1 min (Fig. 3, inset), indicating its rapid response to Zn^{2+} .

To check its practical utility, the fluorescence detection limit of **1** for Zn^{2+} was evaluated. Based on the fluorescence titration data at 485 nm, plotting of the normalized

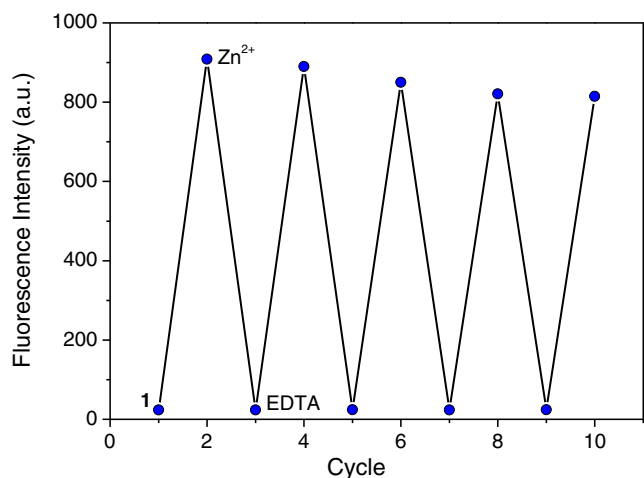
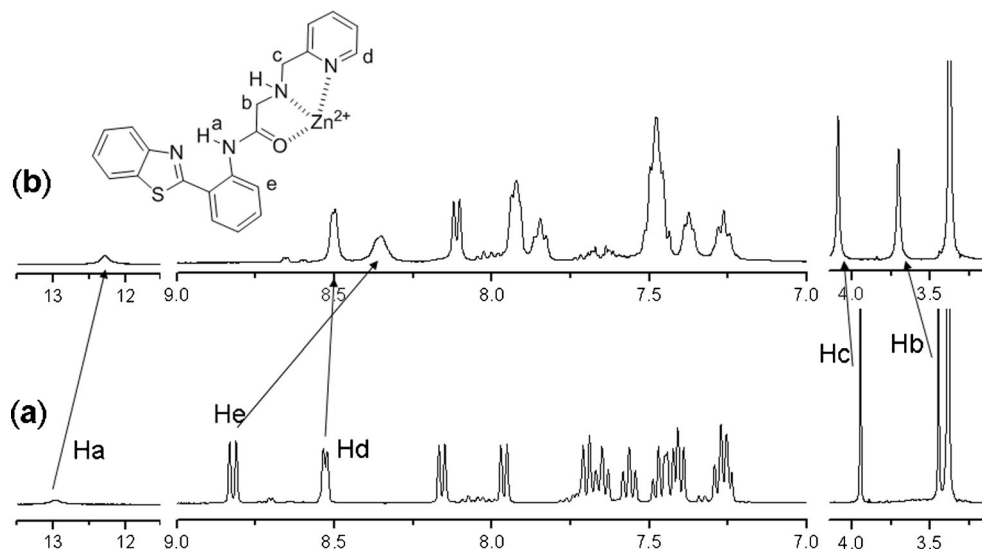


Fig. 8 Fluorescence intensity changes of **1** solution ($10 \mu\text{M}$) at 485 nm upon alternative addition of Zn^{2+} and EDTA

Fig. 9 ^1H NMR spectra of **1** in $\text{DMSO-}d_6$ in the absence and presence of 1.0 equiv. of Zn^{2+}

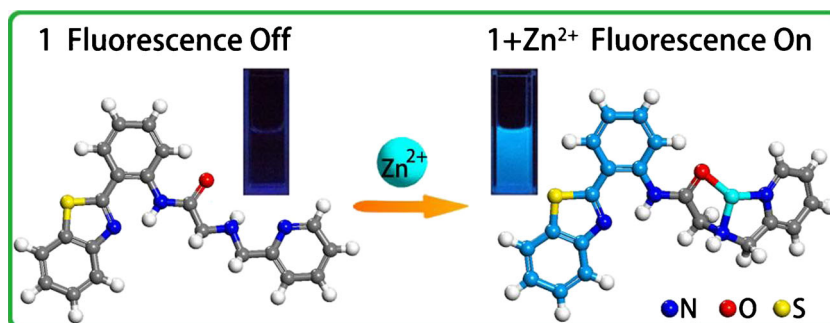


fluorescence intensity of $(I_{\min}-I)/(I_{\min}-I_{\max})$ versus $\log[\text{Zn}^{2+}]$ afforded a nice linear relationship ($R=0.99861$), the point at which this line crossed the ordinate axis was regarded as the detection limit [45, 46], which was calculated to be 5.37×10^{-6} M (Fig. 4). This result demonstrates that sensor **1** is highly sensitive for Zn^{2+} recognition with micromolar level detection limit.

Determination of Binding Stoichiometry

To determine the binding stoichiometry of **1** and Zn^{2+} , Job's plot analysis was conducted. As depicted in Fig. 5, a maximum fluorescence intensity was observed when the mole fraction of Zn^{2+} is 0.5, indicating the 1:1 binding stoichiometry of **1** and Zn^{2+} . Meanwhile, nonlinear least-squares fitting of the titration profiles (Fig. 6) employing a 1:1 binding mode equation led to a nice nonlinear curve ($R^2=0.9969$) [47], which also strongly supports the 1:1 interaction between **1** and Zn^{2+} , and the association constant K_a was calculated to be $2.97 \times 10^6 \text{ M}^{-1}$.

Scheme 2 The proposed sensing mechanism of **1** for Zn^{2+}



pH Effect and Reversibility

To apply **1** in more complicated systems, the influence of pH on the fluorescence of **1** and 1+Zn^{2+} was examined (Fig. 7). As for sensor **1**, the fluorescence intensity was barely affected when the pH ranged from 1 to 14. Upon addition of Zn^{2+} , **1** solution exhibited strong fluorescence emission between pH 7 and 8. This result demonstrates that sensor **1** is especially suitable to detect Zn^{2+} at near neutral pH conditions. The reversible Zn^{2+} binding behavior was further evaluated by alternative addition of Zn^{2+} and EDTA to **1** solution. The fluorescence intensity of the solution exhibited alternative enhancing and quenching processes (Fig. 8), indicating that the Zn^{2+} recognition event is reversible.

Recognition Mechanism

The weak fluorescence emission of **1** at 385 nm can be attributed to the emission of its normal excited state, and the photoinduced electron transfer (PET) from aliphatic amine

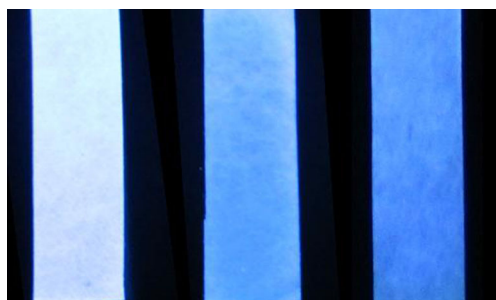


Fig. 10 Photographs of **1** on test strips after addition of HEPES buffered (pH 7.4) ZnCl_2 solutions (left to right: no Zn^{2+} , 5 μM and 50 μM Zn^{2+}) under irradiation at 365 nm

nitrogen to the excited state of phenylbenzothiazole moiety decreased its emission intensity. Binding with Zn^{2+} could suppress the PET process and allows fluorescence enhancement. The remarkable enhancement of longer-wavelength emission with a large Stokes shift (170 nm) of the **1**- Zn^{2+} complex can be inferred as Zn^{2+} coordination promoted turn-on ESIPT emission [48].

To elucidate the proposed sensing mechanism and clarify the binding mode between **1** and Zn^{2+} , ^1H NMR spectra of **1** and **1**- Zn^{2+} were compared (Fig. 9). In free **1**, the NH protons signal for amide (H_a) and 2-picolylamine (H_a) appeared at 12.96 ppm (Fig. 9a). In the presence of 3.0 equiv. of Zn^{2+} , this signal up-field shifted to 12.29 ppm (Fig. 9b), suggesting that **1** coordinates with Zn^{2+} through an amide form [26, 49]. The signal appeared at 8.82 ppm (Fig. 9a) can be tentatively assigned to H_c due to the possible existence of hydrogen bonding between H_c with amide O atom [35]. On addition of Zn^{2+} , this signal up-field shifted to about 8.35 ppm (Fig. 9b), indicating the coordination of amide O atom with Zn^{2+} , which weakened the hydrogen bonding. The signal of protons neighboring pyridine N atom (H_d) at 8.53 ppm up-field shifted to 8.50 ppm on addition of Zn^{2+} . The methylene protons (H_b and H_c) signaling at 3.45 and 3.95 ppm, respectively. These signals down-field shifted to 3.70 and 4.09 ppm, respectively, on addition of Zn^{2+} (Fig. 9b), indicating that the alkyl amine nitrogen atom also coordinated with Zn^{2+} . The proposed binding mode of **1** and Zn^{2+} was depicted in Scheme 2. Coordination of amide O atom with Zn^{2+} greatly increased the acidity of amide NH, which thus promotes H-transferred excited state efficiently.

Application of Sensor **1** to Test Strips

To demonstrate the practical applicability of sensor **1** for the detection of Zn^{2+} , we carried out a preliminary paper test strip experiment, as shown in Fig. 10. After immersing neutral filter papers into the acetonitrile solution of **1** (1 mM) and dried, Zn^{2+} solutions of with concentrations of 5×10^{-6} M and 5×10^{-5} M were prepared in buffered water (HEPES 20 mM, pH 7.4). When the dried test strips were dipped in different

concentration solutions of Zn^{2+} for 1 min and dried in air respectively, the observed color change of test strips from non-fluorescent to be blue under UV light at 365 nm clearly. Therefore, the test strips experiment demonstrates the potential utility of **1** to detect Zn^{2+} ion.

Conclusions

A new off-on fluorescent phenylbenzothiazole derivative (**1**) has been synthesized and proved to be a highly selective, sensitive and rapid recognition Zn^{2+} sensor. Sensor **1** binds Zn^{2+} via a 1:1 stoichiometry with an association constant of $2.97 \times 10^6 \text{ M}^{-1}$, and the detection limit is evaluated to be 5.37×10^{-6} M. Binding of Zn^{2+} at the receptor moiety leads to the quenching of PET state emission at 348 nm and the enhancing of ESIPT state emission at 485 nm, which is responsible for the fluorescence enhancement at the shorter-wavelength and longer-wavelength. We expect that this example will serve as practical tool for environmental samples analysis and biological studies.

Acknowledgments We are grateful to the NSFC (No. 21176029), the Natural Science Foundation of Liaoning Province (No. 20102004) and the Program for Liaoning Excellent Talents in University (LJQ2012096) for financial support.

References

- Xie X, Smart TG (1991) A physiological role for endogenous zinc in rat hippocampal synaptic neurotransmission. *Nature* 349:521–524
- Oутten CE, O'Halloran TV (2001) Femtomolar sensitivity of metalloregulatory proteins controlling zinc homeostasis. *Science* 292:2488–2492
- Scherz H, Kirchoff E (2006) Trace elements in foods: zinc contents of raw foods—a comparison of data originating from different geographical regions of the world. *J Food Compos Anal* 19:420–433
- Cuajungco MP, Lees GJ (1997) Zinc metabolism in the brain: relevance to human neurodegenerative disorders. *Neurobiol Dis* 4:137–169
- Koh JY, Suh SW, Gwag BJ, He YY, Hsu CY, Choi DW (1996) The role of zinc in selective neuronal death after transient global cerebral ischemia. *Science* 272:1013–1016
- Bush AI, Pettingell WH, Paradis MD, Tanzi RE (1994) Modulation of a beta adhesiveness and secretase site cleavage by zinc. *J Biol Chem* 269:12152–12158
- Nolan EM, Lippard SJ (2009) Small-molecule fluorescent sensors for investigating zinc metalloneurochemistry. *Acc Chem Res* 42:193–203
- Xu Z, Yoon J, Spring DR (2010) Fluorescent chemosensors for Zn^{2+} . *Chem Soc Rev* 39:1996–2006
- Song EJ, Kim H, Hwang IH, Kim KB, Kim AR, Noh I, Kim C (2014) A single fluorescent chemosensor for multiple target ions: recognition of Zn^{2+} in 100 % aqueous solution and F^- in organic solvent. *Sensors Actuators B* 195:36–43
- Sarkar D, Pramanik AK, Mondal TK (2014) Coumarin based fluorescent 'turn-on' chemosensor for Zn^{2+} : an experimental and theoretical study. *J Lumin* 146:480–485

- Xu Z, Baek KH, Kim HN, Cui J, Qian X, Spring DR, Shin I, Yoon J (2010) Zn²⁺-triggered amide tautomerization produces a highly Zn²⁺-selective, cell-permeable, and ratiometric fluorescent sensor. *J Am Chem Soc* 132:601–610
- Wang F, Moon JH, Nandhakumar R, Kang B, Kim D, Kim KM, Lee JY, Yoon J (2013) Zn²⁺-induced conformational changes in a binaphthyl-pyrene derivative monitored by using fluorescence and CD spectroscopy. *Chem Commun* 49:7228–7230
- Kiyose K, Kojima H, Urano Y, Nagano T (2006) Development of a ratiometric fluorescent zinc ion probe in near-infrared region, based on tricarbocyanine chromophore. *J Am Chem Soc* 128:6548–6549
- Basabe-Desmonts L, Reinhoudt DN, Crego-Calama M (2007) Design of fluorescent materials for chemical sensing. *Chem Soc Rev* 36:993–1017
- Xu H, Miao R, Fang Z, Zhong X (2011) Quantum dot-based “turn-on” fluorescent probe for detection of zinc and cadmium ions in aqueous media. *Anal Chim Acta* 687:82–88
- Ciupa A, Mahon MF, De Bank PA, Caggiano L (2012) Simple pyrazoline and pyrazole “turn on” fluorescent sensors selective for Cd²⁺ and Zn²⁺ in MeCN. *Org Biomol Chem* 10:8753–8757
- Li M, Lu HY, Liu RL, Chen JD, Chen CF (2012) Turn-on fluorescent sensor for selective detection of Zn²⁺, Cd²⁺, and Hg²⁺ in water. *J Org Chem* 77:3670–3673
- Sun Young Park JHY, Hong CS, Souane R, Kim JS, Matthews SE, Vicens J (2008) A pyrenyl-appended triazole-based calix arene as a fluorescent sensor for Cd²⁺ and Zn²⁺. *J Org Chem* 73:8212–8218
- Chen M, Lv X, Liu Y, Zhao Y, Liu J, Wang P, Guo W (2011) An 2-(2'-aminophenyl)benzoxazole-based OFF-ON fluorescent chemosensor for Zn²⁺ in aqueous solution. *Org Biomol Chem* 9:2345–2349
- Tang L, Cai M, Zhou P, Zhao J, Huang Z, Zhong K, Hou S, Bian Y (2014) Relay recognition by modulating ESIP: a phenylbenzimidazole derived sensor for highly selective ratiometric fluorescent recognition of Zn²⁺ and S²⁻ in water. *J Lumin* 147:179–183
- Taki M, Wolford JL, O'Halloran TV (2003) Emission ratiometric imaging of intracellular zinc: design of a benzoxazole fluorescent sensor and its application in two-photon microscopy. *J Am Chem Soc* 126:712–713
- Kubo K, Mori A (2005) PET fluoroionophores for Zn²⁺ and Cu²⁺: complexation and fluorescence behavior of anthracene derivatives having diethylamine, N-methylpiperazine and N, N-bis(2-picolyl)amine units. *J Mater Chem* 15:2902–2907
- Kim JH, Noh JY, Hwang IH, Kang J, Kim J, Kim C (2013) An anthracene-based fluorescent chemosensor for Zn²⁺. *Tetrahedron Lett* 54:2415–2418
- Zhang G, Yang G, Wang S, Chen Q, Ma JS (2007) A highly fluorescent anthracene-containing hybrid material exhibiting tunable blue–green emission based on the formation of an unusual “T-shaped” excimer. *Chem Eur J* 13:3630–3635
- Lee HG, Kim KB, Park GJ, Na YJ, Jo HY, Lee SA, Kim C (2014) An anthracene-based fluorescent sensor for sequential detection of zinc and copper ions. *Inorg Chem Commun* 39:61–65
- Xu Z, Liu X, Pan J, Spring DR (2012) Coumarin-derived transformable fluorescent sensor for Zn²⁺. *Chem Commun* 48:4764–4766
- Mizukami S, Okada S, Kimura S, Kikuchi K (2009) Design and synthesis of coumarin-based Zn²⁺ probes for ratiometric fluorescence imaging. *Inorg Chem* 48:7630–7638
- Zhu S, Zhang J, Janjanam J, Vegesna G, Luo FT, Tiwari A, Liu H (2013) Highly water-soluble bodipy-based fluorescent probes for sensitive fluorescent sensing of zinc(II). *J Mater Chem B* 1:1722–1728
- He H, Ng DKP (2013) Differential detection of Zn²⁺ and Cd²⁺ ions by bodipy-based fluorescent sensors. *Chem Asian J* 8:1441–1446
- Jiang L, Wang L, Guo M, Yin G, Wang RY (2011) Fluorescence turn-on of easily prepared fluorescein derivatives by zinc cation in water and living cells. *Sensors Actuators B* 156:825–831
- Xu L, Xu Y, Zhu W, Zeng B, Yang C, Wu B, Qian X (2011) Versatile trifunctional chemosensor of rhodamine derivative for Zn²⁺, Cu²⁺ and His/Cys in aqueous solution and living cells. *Org Biomol Chem* 9:8284–8287
- Han ZX, Zhang XB, Li Z, Gong YJ, Wu XY, Jin Z, He CM, Jian LX, Zhang J, Shen GL, Yu RQ (2010) Efficient fluorescence resonance energy transfer-based ratiometric fluorescent cellular imaging probe for Zn²⁺ using a rhodamine spirolactam as a trigger. *Anal Chem* 82:3108–3113
- Guo Z, Kim GH, Shin I, Yoon J (2012) A cyanine-based fluorescent sensor for detecting endogenous zinc ions in live cells and organisms. *Biomaterials* 33:7818–7827
- Kim MJ, Kaur K, Singh N, Jang DO (2012) Benzimidazole-based receptor for Zn²⁺ recognition in a biological system: a chemosensor operated by retarding the excited state proton transfer. *Tetrahedron* 68:5429–5433
- Tang L, Cai M, Zhou P, Zhao J, Zhong K, Hou S, Bian Y (2013) A highly selective and ratiometric fluorescent sensor for relay recognition of zinc(II) and sulfide ions based on modulation of excited-state intramolecular proton transfer. *RSC Adv* 3:16802–16809
- Henry MM, Wu Y, Fahmi CJ (2004) Zinc(II)-selective ratiometric fluorescent sensors based on inhibition of excited-state intramolecular proton transfer. *Chem Eur J* 10:3015–3025
- Xu Y, Pang Y (2011) Zn²⁺-triggered excited-state intramolecular proton transfer: a sensitive probe with near-infrared emission from bis(benzoxazole) derivative. *Dalton Trans* 40:1503–1509
- Shiraishi Y, Matsunaga Y, Hirai T (2013) Phenylbenzoxazole–amide–cyclen linkage as a ratiometric fluorescent receptor for Zn(II) in water. *J Phys Chem A* 117:3387–3395
- Tanaka K, Kumagai T, Aoki H, Deguchi M, Iwata S (2001) Application of 2-(3,5,6-trifluoro-2-hydroxy-4-methoxyphenyl)benzoxazole and -benzothiazole to fluorescent probes sensing pH and metal cations. *J Org Chem* 66:7328–7333
- Komatsu K, Urano Y, Kojima H, Nagano T (2007) Development of an iminocoumarin-based zinc sensor suitable for ratiometric fluorescence imaging of neuronal zinc. *J Am Chem Soc* 129:13447–13454
- Nguyen DM, Frazer A, Rodriguez L, Belfield KD (2010) Selective fluorescence sensing of zinc and mercury ions with hydrophilic 1,2,3-triazolyl fluorene probes. *Chem Mater* 22:3472–3481
- Fadda AA, Refat HM, Zaki MEA, Monir E (2001) Reaction of isataic anhydride with bifunctional reagents: synthesis of some new quinazolone fused heterocycles, 2-substituted anilinoheterocyclic derivatives and other related compounds. *Synth Commun* 31:3537–3545
- Jung HS, Kwon PS, Lee JW, Kim JI, Hong CS, Kim JW, Yan S, Lee JY, Lee JH, Joo T, Kim JS (2009) Coumarin-derived Cu²⁺-selective fluorescence sensor: synthesis, mechanisms, and applications in living cells. *J Am Chem Soc* 131:2008–2012
- Chen W, Tu X, Guo X (2009) Fluorescent gold nanoparticles-based fluorescence sensor for Cu²⁺ ions. *Chem Commun* 45:1736–1738
- Lin W, Yuan L, Cao Z, Feng Y, Long L (2009) A sensitive and selective fluorescent thiol probe in water based on the conjugate 1,4-addition of thiols to α , β -unsaturated ketones. *Chem Eur J* 15:5096–5103
- Shortreed M, Kopelman R, Kuhn M, Hoyland B (1996) Fluorescent fiber-optic calcium sensor for physiological measurements. *Anal Chem* 68:1414–1418
- Connors KA (1987) Binding constants: the measurement of molecular complex stability. Wiley, New York
- Shiraishi Y, Matsunaga Y, Hongpitakpong P, Hirai T (2013) A phenylbenzoxazole–amide–azacrown linkage as a selective fluorescent receptor for ratiometric sensing of Pb(II) in aqueous media. *Chem Commun* 49:3434–3436
- Cai Y, Meng X, Wang S, Zhu M, Pan Z, Guo Q (2013) A quinoline based fluorescent probe that can distinguish zinc(II) from cadmium(II) in water. *Tetrahedron Lett* 54:1125–1128