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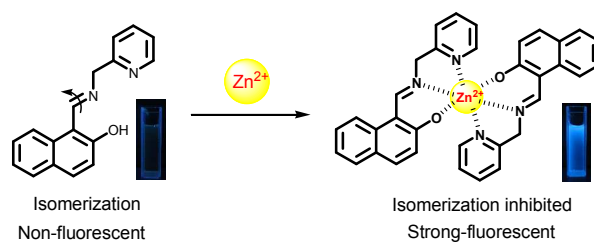


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A facile naphthalene-based Schiff base chemosensor, 1-((pyridin-2-ylmethylimino) methyl) naphthalen-2-ol, has been designed and synthesized for selective detection of  $Zn^{2+}$  ions.

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ARTICLE TYPE

# A Facile Fluorescent Chemosensor Based On Naphthalene-derived Schiff Base for Zinc Ions in Aqueous Solution

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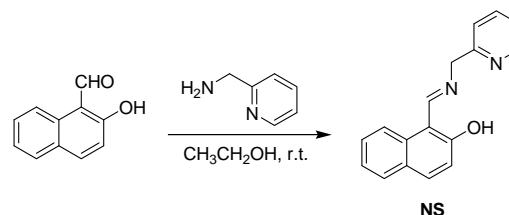
A facile naphthalene-based Schiff base chemosensor, 1-((pyridin-2-ylmethylimino) methyl) naphthalen-2-ol (NS), has been designed and synthesized for selective detection of Zn<sup>2+</sup> ions. A fluorescence enhancement of 10-fold at 446 nm can be realized upon addition of 5.0 equiv. of Zn<sup>2+</sup> with excitation at 352 nm. NS could detect as low as 1.91×10<sup>-6</sup> M Zn<sup>2+</sup> with an association constant value of 7.88×10<sup>6</sup> M<sup>-1</sup>. More importantly, it displayed specific and sensitive recognition to Zn<sup>2+</sup> and especially avoided the interference of Cd<sup>2+</sup> in aqueous solution.

Zinc, which plays crucial roles in many important biological processes such as the structural and catalytic cofactors, neural signal transmitters, and gene expression regulators, is the second most abundant transition-metal ion in human body.<sup>1</sup> The normal concentration range for zinc ions in biological systems is narrow, with both deficiencies and excesses causing many pathological states, such as Alzheimer's disease, epilepsy, Parkinson's disease, ischemic stroke, and infantile diarrhea.<sup>2</sup> Accordingly, developing fluorescent chemosensors with high selectivity and sensitivity for detecting trace amounts of Zn<sup>2+</sup> has attracted increasing attention.

In the past several years, considerable efforts have been made to develop fluorescent chemosensors for Zn<sup>2+</sup> ions based on quinoline, anthracene, coumarin, BODIPY, and fluorescein fluorophores.<sup>3</sup> However, most of them still have limitations such as poor water-solubility, laborious synthesis processes expensive chemicals, and interference from other coexisting metal ions. Therefore, for practical applications, it is still desirable to develop simple zinc sensors with good water-solubility and high selectivity and sensitivity.

Our research group is actively engaged in the development of novel selective and sensitive fluorescent probes for heavy metal ions.<sup>4</sup> Herein, we report a naphthalene-based Schiff base, 1-((pyridin-2-ylmethylimino) methyl) naphthalen-2-ol (NS), which shows high selectivity for Zn<sup>2+</sup> over other metal ions studied, and good water-solubility. More importantly, NS can be readily prepared with high yield (84%) by coupling of 2-hydroxy-1-naphthaldehyde and 2-picolylamine in ethanol (Scheme 1).

In the absence of metal ions, the fluorescence intensity of the fluorophore is greatly reduced due to C=N isomerization<sup>5</sup> which could be restricted by binding with Zn<sup>2+</sup> ions and the



Scheme 1 Synthesis of NS.

fluorescence intensity is then greatly enhanced due to rigid chelated complex formation. The introduction of the 2-picolylamine group provides not only another two metal coordination sites (naphthanol affords one site) but also a hydrophilic group.

In the UV-vis absorption spectra (Fig. 1), NS exhibits two broad bands from 350 to 450 nm with its maximum centered at 399 and 412 nm, which is assigned to the C=N isomerization of the Schiff base. Upon addition of Zn<sup>2+</sup> (0-10 equiv.), these peaks merged to one and blue-shifted to 381 nm, accompanying six clear isosbestic points at 385, 346, 322, 310, 289, and 234 nm, respectively, indicating that NS formed a complex with Zn<sup>2+</sup> and therefore the transform of *cis-trans* isomerization has been restricted.

As expected, NS alone is almost nonfluorescent in neutral aqueous solution (0.01 M HEPES buffer, pH 7.2). However, addition of 5.0 equiv. of Zn<sup>2+</sup> triggered a ca. 10-fold increase

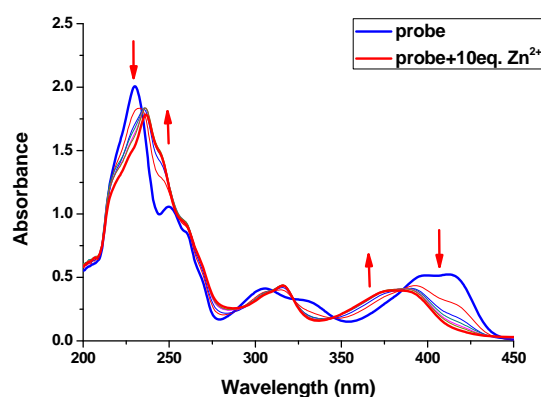
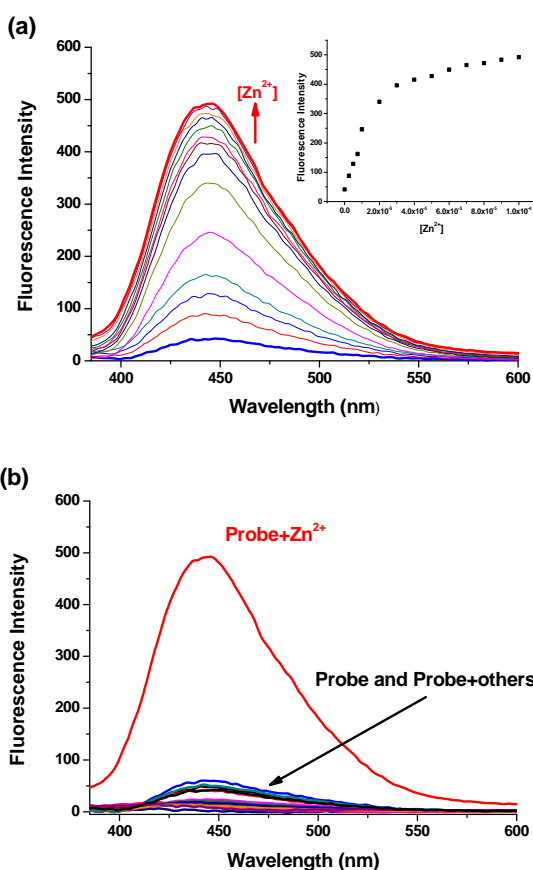


Fig. 1 Absorption spectra of NS (50 μM) in HEPES buffer (0.01 M, pH 7.2) in the presence of different concentrations of Zn<sup>2+</sup> (0-10 equiv.).

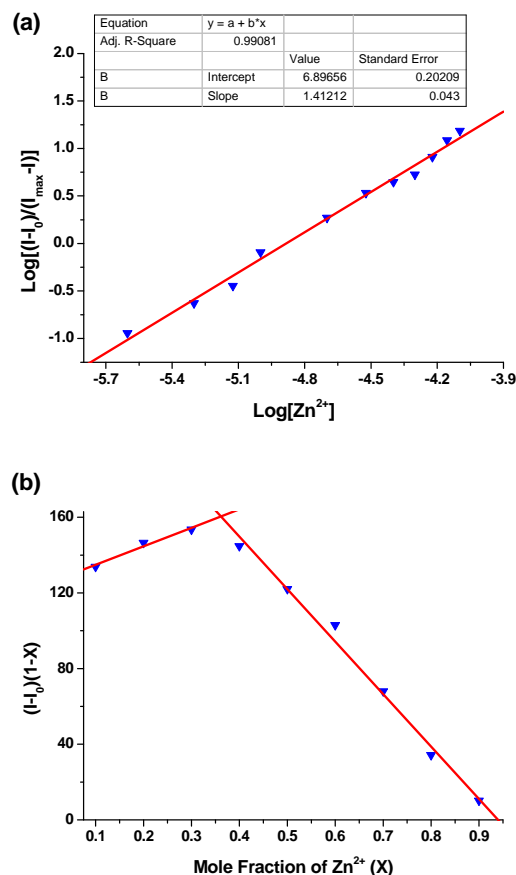


**Fig. 2** (a) Fluorescence spectra of NS (10  $\mu\text{M}$ ) in HEPES buffer (pH 7.2) in the presence of different concentrations of  $\text{Zn}^{2+}$  (0-100  $\mu\text{M}$ ) ( $\lambda_{\text{ex}} = 352$  nm). Inset: fluorescence intensity changes as a function of  $\text{Zn}^{2+}$  concentration. (b) Emission spectra of NS (10  $\mu\text{M}$ ) in HEPES buffer (pH 7.2) in the presence of various metal ions ( $\lambda_{\text{ex}} = 352$  nm, 10.0 eq. of  $\text{Li}^+$ ,  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$ ,  $\text{Cd}^{2+}$ ,  $\text{Hg}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Mn}^{2+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Pb}^{2+}$ ,  $\text{Cr}^{3+}$ ,  $\text{Fe}^{3+}$ , and  $\text{Zn}^{2+}$ , respectively).

in fluorescence intensity for NS (Fig. 2a), which was attributed to the  $\text{Zn}^{2+}$  chelation of the nitrogen atom on the Schiff base moiety.

The fluorescence titration of NS with various metal ions was conducted to examine the selectivity (Fig. 2b). As expected, other metal ions such as  $\text{Li}^+$ ,  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Cd}^{2+}$ ,  $\text{Hg}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Mn}^{2+}$ ,  $\text{Fe}^{3+}$ ,  $\text{Cr}^{3+}$ ,  $\text{Cu}^{2+}$ , and  $\text{Pb}^{2+}$  did not induce a nominal response under otherwise identical conditions. The competing experiments were then tested in the presence of  $\text{Zn}^{2+}$  and other competing metal ions (Fig. S2, ESI $^\dagger$ ). Interestingly, except  $\text{Co}^{2+}$ ,  $\text{Cu}^{2+}$ , and  $\text{Ni}^{2+}$ , other background metal ions had small or no obvious interference with the detection of  $\text{Zn}^{2+}$  ions. It should be noted that NS has displayed a considerable ability to distinguish  $\text{Zn}^{2+}$  from  $\text{Cd}^{2+}$  which has similar properties with  $\text{Zn}^{2+}$  and generally causes a strong interference.<sup>7</sup>

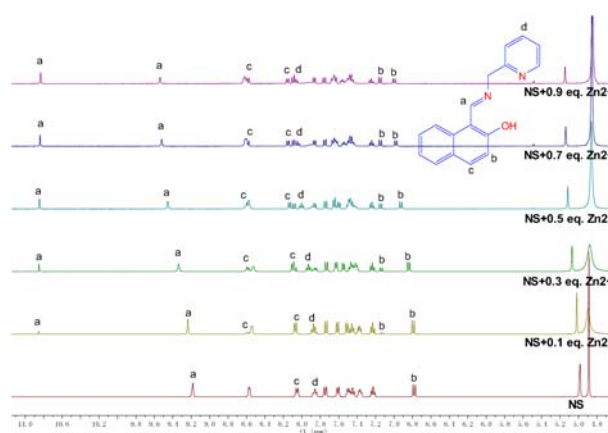
Subsequently, the  $\text{Zn}^{2+}$ -sensing ability of NS at a wide range of pH values was investigated. As depicted in Fig. S3, ESI $^\dagger$ , NS had no fluorescence response to  $\text{Zn}^{2+}$  in the highly acidic environment due to the protonation of the nitrogen atoms of NS. However, satisfactory  $\text{Zn}^{2+}$ -sensing abilities were exhibited in the range of pH from 6 to 10, indicating that



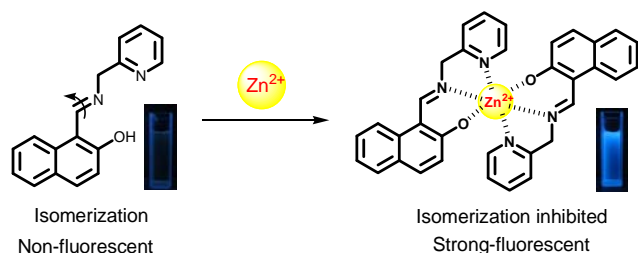
**Fig. 3** (a) Hill plot of sensor NS. Fluorescence responses as a function of  $\text{Zn}^{2+}$  concentration (HEPES buffer, pH 7.2,  $\lambda_{\text{ex}} = 352$  nm). The solid line represents a linear fit to the experimental data. (b) Job's plot of sensor NS, the total concentration of the sensor and  $\text{Zn}^{2+}$  is 30.0  $\mu\text{M}$  (HEPES buffer, pH 7.2,  $\lambda_{\text{ex}} = 352$  nm).

NS could be used in neutral natural systems, or a mildly acidic or basic environment.

The binding ratio and association constant ( $K_a$ ) of complex were determined by titration experiment of NS with  $\text{Zn}^{2+}$ .  $K_a$  of NS/ $\text{Zn}^{2+}$  was determined to be  $7.88 \times 10^6 \text{ M}^{-1}$  by a Hill plot



**Fig. 4**  $^1\text{H}$  NMR titration experiment of NS in the presence of different concentrations of  $\text{Zn}^{2+}$  ions (in  $\text{CD}_3\text{OD}$ ).



**Scheme 2** A proposed structure of NS-Zn<sup>2+</sup> complex.

analysis (Fig. 3a).<sup>6</sup> Moreover, a Job's plot, which exhibited a maximum at 0.34 M fraction of Zn<sup>2+</sup>, indicated that a 2:1 complex was formed between NS and Zn<sup>2+</sup> (Fig. 3b).

To clarify the actual NS/Zn<sup>2+</sup> interactions, <sup>1</sup>H NMR titration experiment was conducted. As shown in Fig. 4, the olefinic proton attributed to the C=N bond was dramatically downfield shifted from  $\delta$  9.18 ppm to 10.83 ppm after the addition of Zn<sup>2+</sup> due to the chelation of the lone-pair electrons of nitrogen of Schiff base by Zn<sup>2+</sup>, which was in agreement with the optical responses. Meanwhile, the chemical shifts of the six resonances attributed to the naphthalene protons (H<sub>b</sub>, H<sub>c</sub>) and pyridine protons also experienced a similar shift ( $\delta$  = 0.2-0.5 ppm), indicating that the nitrogen of pyridine and oxygen of naphthol were involved in the chelation to Zn<sup>2+</sup> ion. Accordingly, the structure of NS/Zn<sup>2+</sup> complex was proposed as shown in scheme 2.

For practical purposes, the detection limit of NS for the analysis of Zn<sup>2+</sup> ion was also an important parameter. Thus, according to the fluorescence titration curve, the detection limit was calculated to be  $1.91 \times 10^{-6}$  M, which reveals the high sensitivity for the analysis of zinc ion. The low detection limit might fully meet the requirements in biosensing.

In conclusion, we have successfully designed a simple naphthalene-based fluorescent chemosensor for Zn<sup>2+</sup> and investigated its selectivity and binding abilities towards Zn<sup>2+</sup>. It has the unique advantage of easy-preparation, good water solubility, and excellent selectivity and sensitivity toward zinc ion. Moreover, it can distinguish Zn<sup>2+</sup> from Cd<sup>2+</sup> in aqueous solution, which is usually a technique problem for other related probes. We anticipate that the experimental results of this study will inspire in the future design of metal-ion sensors in water for a variety of chemical and biological applications.

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## Notes and references

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<sup>50</sup> † Electronic Supplementary Information (ESI) available: Experimental details, synthetic details of NS, additional spectroscopic data, and copies of NMR spectra. See DOI: 10.1039/b000000x/

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