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## A selective "turn-on" sensor for recognizing of In<sup>3+</sup> and Zn<sup>2+</sup> in respective system based on imidazo[2,1-b]thiazole

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A new simple and easily synthesized multitarget sensor, (E)-N'-(4-(diethylamino)-2-hydroxybenzylidene)imidazo[2,1b]thiazole-6-carbohydrazide (**X**), was designed and synthesized based on imidazo[2,1-b]thiazole-6-carboxylic acid and 4-(diethylamino)-2-hydroxybenzaldehyde. **X** could be used as a sensor to detect  $In^{3+}$  in DMF-H<sub>2</sub>O buffer solution and detect  $Zn^{2+}$  in EtOH-H<sub>2</sub>O buffer solution through fluorescence enhancement with detection limits of  $1.02 \times 10^{-9}$  M and  $5.5 \times 10^{-9}$  M, respectively. **X** exhibited an efficient "off-on-off" fluorescence behavior by cyclic addition of metal ions ( $In^{3+}$  and  $Zn^{2+}$ ) and EDTA. The stoichiometry between **X** and metal ions ( $In^{3+}$  and  $Zn^{2+}$ ) was 1:1. The binding mode and sensing mechanism of **X** with metal ions ( $In^{3+}$  and  $Zn^{2+}$ ) was verified by theoretical calculations using Gaussian 09 based on B3LYP/6-31G(d) and B3LYP/LANL2DZ basis, respectively. Moreover, **X** could be applied as a potential sensor for the quantitative detection of  $In^{3+}$ and  $Zn^{2+}$  with a satisfactory recovery and the relative standard deviation (RSD) in real water samples.

## 1. Introduction

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Metal ions are widely found in nature and closely related to the physiological activities of living bodies.<sup>1-3</sup> Among diverse metal ions, zinc is the second most abundant trace element in the human body and plays an important role in various physiological activities, such as gene expression, cellular metabolism, immune function, neural signal transmission and DNA recombination or recognition.<sup>4-8</sup> Thus, zinc is vital for human health.9, 10 The permissible concentration of zinc is 2-2.5 g throughout the human body, whereas lack and excessive intake of zinc can cause a variety of diseases, such as Alzheimer, Parkinson, epilepsy, amyotrophic lateral sclerosis (ALS) and ischemia.<sup>11-15</sup> Likewise, indium is an important industrial metal with good toughness, plasticity and ductility, and has significant applications in many fields, such as manufacture of low fusion gold, bearing alloys, semiconductor devices and transparent electrically conductive films.<sup>16-18</sup> Moreover, it is generally believed that indium in pure metal form is a non-toxic and safe metal.<sup>19</sup> However, some of studies recently suggested that indium and its compounds (indium phosphide and indium tin oxide) not only interfere with iron metabolism during cell absorption, transport and storage, but also cause severe lung damage.<sup>20-23</sup> Therefore, for the above reasons, the detection of zinc and indium is crucial and urgent.

Recently, various analytical technique for detection of Zinc and indium have been reported, such as graphite furnace atomic absorption spectrometry, molecular imprinted polymer sensor and ion-selective electrodes, which are characterized by complicated operation, skilled experts and involve expensive equipment.<sup>19, 20, 24-26</sup> However, compared with these methods, fluorescence methods has attracted more and more attention due to its quick response, simple operation, high sensitivity and real application.<sup>27-30</sup> In the past, there have been many reports on the detection of zinc, but few on the detection of indium.<sup>18,</sup> <sup>31-34</sup> Detection of zinc and indium by fluorescent sensor in organic solvent or aqueous solution is often interfered by other metal ions.35-37 For example, cadmium, which has similar properties and coordination modes to zinc, will affect the detection of zinc.<sup>4</sup> Analogously, the detection of indium is often disturbed by the same group metal ions, aluminum and gallium.<sup>21</sup> In addition, the detection limit of sensor for metal ions is usually between 10<sup>-5</sup> M and 10<sup>-8</sup> M.<sup>30</sup> So, it is necessary to design the sensor with high selectivity and sensitivity for detection of In<sup>3+</sup> and Zn<sup>2+</sup>. At the present, the research of multitarget sensor is much less than that of single target sensor.<sup>20, 38,</sup> <sup>39</sup> Multi-target sensors with highly sensitivity and selectivity are valuable and should receive close attention because they could detect different metal ions in respective system.

In past reports, Schiff base, derived from 4-(diethylamino)-2-hydroxybenzaldehyde, is often used as a "off-on" sensor to detect single target in a particular system because they have simple synthesis method, ideal solubility and strong complexing

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ability of metal ions.<sup>40-45</sup> Moreover, imidazo[2,1-b]thiazole, which contains two conjugated rings and eight central atoms in its molecule, was a potential fluorescent nucleus.<sup>46</sup> In this study, a new simple schiff base (X) with a distinct "acceptor-donor" structure was designed and synthesized based on imidazo[2,1*b*]thiazole-6-carboxylic acid and 4-(diethylamino)-2hydroxybenzaldehyde.<sup>47-49</sup> The sensor showed strong ability to recognize metal ions because of the oxygen atom of -OH and the nitrogen atoms of -CH=N- and -N=. As expected, X could be used as a highly selective and sensitive fluorescent sensor to detect zinc and indium by fluorescence enhancement in ethanol-water and DMF-water buffer system and could quantitatively assess zinc and indium in tap water samples. As shown in Table S1, the comparison of some different reported sensors for the detection of In<sup>3+</sup> and Zn<sup>2+</sup> were summarized. Compared with these reported sensors, comprehensively speaking, our sensor had a lower LOD for In<sup>3+</sup> and Zn<sup>2+</sup>. On the whole, the **X** could serve as a sensor for  $In^{3+}$  and  $Zn^{2+}$ .

#### 2. Experimental section

#### 2.1. Materials and sample preparation

All reagents and solvents were commercially available AR and CP and were used without further treatment. All metal ionic solution are corresponding chloride, sulfate and nitrate solutions, including InCl<sub>3</sub>, Ga(NO<sub>3</sub>)<sub>3</sub>, ZnCl<sub>2</sub>, Li<sub>2</sub>SO<sub>4</sub>, AlCl<sub>3</sub>·6H<sub>2</sub>O, CdCl<sub>2</sub>·2.5H<sub>2</sub>O, CoCl<sub>2</sub>·6H<sub>2</sub>O, FeCl<sub>3</sub>, MgCl<sub>2</sub>·6H<sub>2</sub>O, CrCl<sub>3</sub>·6H<sub>2</sub>O, MnCl<sub>2</sub>·4H<sub>2</sub>O, AgCl, KCl, CuCl<sub>2</sub>·2H<sub>2</sub>O, NiCl<sub>2</sub>·6H<sub>2</sub>O, HgCl<sub>2</sub>. The anion solution is the corresponding sodium salt solutions. Stock solutions of the ions mentioned above were prepared with a concentration of 0.03 M in distilled water. The probe **X** was dissolved in ethanol/H<sub>2</sub>O (v/v = 9 : 1) buffer solution (10 mM tris, pH = 7.4) and DMF/H<sub>2</sub>O (v/v = 9 : 1) buffer solution of 1 × 10<sup>-5</sup> M.

#### 2.2. Measurements

UV-vis spectra were obtained on a Shimadzu 3100 spectrometer. Fluorescence spectral data was recorded on an Edinburgh Instruments Ltd-FLS920 Fluorescence Spectrophotometer. Fluorescence measurements were recorded using excitation at 365 nm. The slits of excitation and emission were 10 nm and 10 nm, respectively. <sup>1</sup>H NMR measurement was performed on a Bruker AV III 400 MHz NMR spectrometer with tatramethysilane (TMS) as internal standard and CDCl<sub>3</sub> as solvent. <sup>13</sup>C NMR spectra data was taken on a Bruker AV III 100 MHz NMR spectrometer with tatramethysilane (TMS) as internal standard and DMSO as solvent. Infrared spectral data was obtained on a Bruker Vertex 70 FT-IR spectrometer using samples as KBr pellets. Thin layer chromatography (TLC) analyses were performed to monitor all the reactions.

#### 2.3. Calculation of quantum yield and association constant

Quantum yield was calculated according to the following formula (1):

$$\Phi_u = \Phi_s \frac{F_u A_s n_u^2}{F_s A_u n_s^2} \text{View Article Online} \\ F_s A_u n_s^2 \text{OI: 10.1039/C9PP00408E}$$

 $\Phi$ , *F*, *A*, and *n* represent the quantum yield, the integrated area under the corrected emission spectra, the absorbance intensity at the excitation wavelength and the refractive index of solvent, respectively. In addition, s refers to rhodamine B as the standard, and u refers to the target. The quantum yield ( $\Phi$ ) of rhodamine B dissolved in anhydrous ethanol is 0.97.

The association constant between  $\mathbf{X}$  and metal ions was calculated by the Benesi-Hildebrand eqn (2):

$$\frac{1}{F - F_0} = \frac{1}{M^{n+}} \times \frac{1}{K_a [F_{max} - F_0]} + \frac{1}{F_{max} - F_0}$$

where *F* is the fluorescence intensity of the  $X[M^{n+}]$  complex, which is in accordance with the concentration of  $M^{n+}$ . *F*<sub>0</sub> is the fluorescence intensity of free **X**. *F*max is the fluorescence intensity of  $X[M^{n+}]$  complex in the presence of the maximum concentration of  $M^{n+}$ .

#### 2.4. Theoretical calculations

Density functional theory (DFT) structural optimizations were performed with the Gaussian 09 program. In all cases, the structures were optimized using the B3LYP functional and the mixed basis set 6-31+G (d) and LANL2DZ. Each structure was subsequently subjected to TD-DFT calculation using the B3LYP functional.<sup>50</sup> For all optimized structures, frequency calculations were performed to confirm the absence of imaginary frequencies. The molecular orbitals were visualized and plotted with the GaussView 5.0 program.

#### 2.5. Synthesis of X

Compound **1** (ethyl imidazo[2,1-b]thiazole-6-carboxylate) and compound **2** (imidazo[2,1-b]thiazole-6-carbohydrazide) were prepared according to a previous report.<sup>46</sup> Firstly, compound **1** was obtained by the reaction of thiazol-2-amine with ethyl 3bromo-2-oxopropanoate (80%) in THF solution. Then, compound **1** and hydrazide hydrate (80%) were stirred overnight in ethanol solution at room temperature to produce compound **2** (white solid).

Synthesis of (E)-N'-(4-(diethylamino)-2-hydroxybenzylidene) imidazo[2,1-b]thiazole-6-carbohydrazide (X). imidazo[2,1-



 $\label{eq:scheme1.synthesis routes of X. Conditions: (a) THF/ethanol, r.t./refluxed, 20 h/4 h; (b) ethanol, r.t., overnight; (c) ethanol, refluxed, 2 h.$ 

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**Fig. 1**. (a) Fluorescence responses of X in DMF/H<sub>2</sub>O buffer solution (v/v = 9:1, tris = 10 mM, pH = 7.4) with 7.5 equiv. of various metal ions (In<sup>3+</sup>, Ag<sup>+</sup>, Zn<sup>2+</sup>, Ni<sup>2+</sup>, Mg<sup>2+</sup>, Cd<sup>2+</sup>, Cu<sup>2+</sup>, K<sup>+</sup>, Cr<sup>3+</sup>, Fe<sup>3+</sup>, Mn<sup>2+</sup>, Ga<sup>3+</sup>, Al<sup>3+</sup>, Hg<sup>2+</sup>, Li<sup>+</sup> and Co<sup>2+</sup>). Inset: the color of **X** and **X**[In<sup>3+</sup>] system under UV lamp. (b) changes in the fluorescence intensity of **X** in the presence of various metal ions.

b]thiazole -6-carbohydrazide (compound **2**, 84 mg, 0.461 mmol) and 4-(diethylamino)-2-hydroxybenzaldehyde (101 mg, 0.523 mmol) were mixed and stirred in 10 ml ethanol at room temperature for 6 hours. Then the mixture was refluxed for 2 hours. The solvent was removed by rotary evaporation. The residue was washed with methanol to obtain the pure yellow solid **X**. Yield: 102 mg, 62.1%. Ms (ESI): m/z = 358.13 [M + H]<sup>+</sup>. FTIR (KBr, cm<sup>-1</sup>): 3312 (N–H), 1670 (C=O), 1547 (C=N). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  11.12 (s, 1H), 9.90 (s, 1H), 8.21 (s, 1H), 8.15 (s, 1H), 7.51 (d, *J* = 4.5 Hz, 1H), 7.01 (d, *J* = 8.6 Hz, 1H), 6.97 (d, *J* = 4.5 Hz, 1H), 6.26 – 6.20 (m, 2H), 3.37 (q, *J* = 7.0 Hz, 4H), 1.18 (t, *J* = 7.0 Hz, 6H). <sup>13</sup>C NMR (101 MHz, DMSO)  $\delta$  160.20, 157.87, 150.49, 149.30, 140.90, 132.18, 120.69, 116.75, 115.86, 107.05, 104.05, 98.05, 44.25, 13.01.

#### 3. Results and discussion

As shown in scheme 1, **X** was designed and synthesized in medium yield according to the synthetic route. Compound 1 (ethyl imidazo[2,1-b]thiazole-6-carboxylate) and compound 2 (imidazo[2,1-b]thiazole-6-carbohydrazide) were synthesized according to a previous report. The structure of **X** was characterized by <sup>1</sup>H NMR (Fig. S1), <sup>13</sup>C NMR (Fig. S2), FTIR (Fig. S3), ESI-MS (Fig. S4). All the data in the spectra were in good accordance with the structure.

#### 3.1. The sensing behavior of X to In<sup>3+</sup> in DMF buffer solution

The sensing behavior of **X** to  $In^{3+}$  was studied by UV-vis and fluorescence emission spectra. Primitively, the fluorescence sensing behavior of **X** ( $1 \times 10^{-5}$  M) to various metal ions ( $In^{3+}$ ,  $Ag^+$ ,  $Zn^{2+}$ ,  $Ni^{2+}$ ,  $Mg^{2+}$ ,  $Cd^{2+}$ ,  $Cu^{2+}$ ,  $K^+$ ,  $Cr^{3+}$ ,  $Fe^{3+}$ ,  $Mn^{2+}$ ,  $Ga^{3+}$ ,  $Al^{3+}$ ,  $Hg^{2+}$ ,  $Li^+$  and  $Co^{2+}$ ) were explored in DMF/H<sub>2</sub>O buffer solution (v/v =9:1, tris = 10 mM, pH = 7.4). As shown in Fig. 1(a), **X** exhibited a relatively weak fluorescence intensity with excitation at 365 nm. When various metal ions (7.5 equiv.) were added into **X**, only  $In^{3+}$  could lead to a significant increase in fluorescence at 463 nm. From Fig. 1 insert, the color of **X** was easy observed in the absence and presence of  $In^{3+}$  under UV lamp. After addition of  $In^{3+}$ , the fluorescence intensity of **X** changed from dim blue ( $\Phi =$  0.11) to bright blue ( $\Phi$  = 0.42). As shown in Fig. 1(b), when In<sup>3+</sup> were added, the fluorescence intensity of **X** was significantly increased (about 9 times), displaying an efficient "turn-on" behavior. In addition, the fluorescence intensity of **X** was almost unchanged in the presence of other metal ions, except for Ni<sup>2+</sup> and Co<sup>2+</sup>. Both Ni<sup>2+</sup> and Co<sup>2+</sup> could quench the fluorescence of **X**.

The absorbance sensing behavior of **X** ( $1 \times 10^{-5}$  M) to various metal ions ( $In^{3+}$ ,  $Ag^+$ ,  $Zn^{2+}$ ,  $Nl^{2+}$ ,  $Mg^{2+}$ ,  $Cd^{2+}$ ,  $Cu^{2+}$ ,  $K^+$ ,  $Cr^{3+}$ , Fe<sup>3+</sup>, Mn<sup>2+</sup>, Ga<sup>3+</sup>, Al<sup>3+</sup>, Hg<sup>2+</sup>, Li<sup>+</sup> and Co<sup>2+</sup>) were also explored in DMF/H<sub>2</sub>O buffer solution (v/v = 9:1, tris = 10 mM, pH = 7.4). As shown in Fig. S5, the absorption spectrum of free **X** exhibited a maximum peak centred at 366 nm. When 7.5 equiv. of various metal ions were added, the absorption of **X** was basically unchanged, except for  $In^{3+}$ ,  $Ni^{2+}$ ,  $Co^{2+}$  and  $Cu^{2+}$ . All four metal ions could from stable complexes with **X**. In order to explore the anti-interference ability of **X**, the competitive experiments were carried out in presence of various metal ions. As shown in Fig. S6, the fluorescence response of **X** to  $In^{3+}$  was disturbed to varying degrees and maintained significant enhancement in the presence of Ni<sup>2+</sup>,  $Cu^{2+}$ , Fe<sup>3+</sup>, Hg<sup>2+</sup> and Co<sup>2+</sup>. These results indicated that **X** could be used as a sensor to detect  $In^{3+}$  in



Fig. 2. UV-vis spectral changes of  $\boldsymbol{X}$  in the presence of different concentrations of  $\mathsf{In}^{3*}$  ions.

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Fig. 3. (a) Fluorescence spectral changes of X in the presence of different concentrations of  $In^{3+}$  ions. (b) Plot of the fluorescence intensity at 463 nm as a function of  $In^{3+}$  concentration. Insert: linear relationship between the fluorescence intensity at 463nm and concentration of  $In^{3+}$  (0 - 1  $\times$  10<sup>-7</sup> M).

 $\mathsf{DMF/H}_2\mathsf{O}$  buffer solution with good selectivity and anti-interference ability.

In order to further investigate the chemosensing properties of X, relevant titration experiments of X with In<sup>3+</sup> were carried out in DMF/H<sub>2</sub>O buffer solution (v/v = 9:1, tris = 10 mM, pH = 7.4). As shown in Fig. 2, the free X ( $1 \times 10^{-5}$  M) exhibited an absorption peak at 366 nm. Upon gradual addition of In<sup>3+</sup> (0 - 8  $\times$  10<sup>-5</sup> M) to X solution, the absorption peak at 366 nm decreased obviously, whereas new prominent absorption peaks at 401 nm and 420 nm were appeared with an isosbestic point at 385 nm. The results indicated that X could form a stable complex (X[In<sup>3+</sup>]) with In<sup>3+</sup>. In addition, the fluorescence titration experiments were also shown in Fig. 3. As mentioned above, the free X maintained a concentration of  $1 \times 10^{-5}$  M and exhibited weak fluorescence. With the increased gradually of  $In^{3+}$  concentrations from 0 to 8 × 10<sup>-5</sup> M, the fluorescence intensity of X increased steadily (Fig. 3(a)) and reached a plateau (Fig. 3(b)) at 463 nm, indicating that the fluorescence intensity reached the maximum. As shown in Fig. 3(b) insert, a good linear relationship between the fluorescence intensity of X and the low concentration of  $In^{3+}$  (0 - 1 × 10<sup>-7</sup> M) with  $R^2 = 0.9864$ and Y = 14.63X + 377.54 was obtained. The detection limit of X for In<sup>3+</sup> was calculated to be 1.02 × 10<sup>-9</sup> M based on 3 $\sigma/s$  equation, which is lower than that had been reported.<sup>17, 21</sup> The association constant (Ka) of **X** with In<sup>3+</sup> was calculated to be 1.01 × 10<sup>5</sup> M<sup>-1</sup> (Fig. S7) based on eqn (2). These results indicated that **X** could be used as a sensitive sensor to detect In<sup>3+</sup> in DMF/H<sub>2</sub>O buffer solution.

Furthermore, the favorable reversibility was an important characterization of sensor. EDTA was an ideal metal chelating agent, which could extract metal ions from the complex (sensormetal ions) and restore the fluorescence of sensor. The cycle test was carried out by successively adding In<sup>3+</sup> and EDTA to X. As shown in Fig. 4, free X exhibited weak fluorescence intensity. In the presence of In<sup>3+</sup> (7.5 equiv.), the fluorescence intensity of X increased significantly at 463 nm. When the same concentration (7.5 equiv.) of EDTA were added to X[In<sup>3+</sup>] system, the fluorescence was completely quenched, indicated the regeneration of free X. Then continue to add In<sup>3+</sup> (10 equiv.) to the system above, the fluorescence intensity was significantly increased again. Moreover, keep adding EDTA, the fluorescence disappeared completely. In addition, X still maintains a good response to In<sup>3+</sup> after two cycles with a negligible fluorescence loss at 463 nm and exhibited efficient "on-off-on" behavior



Fig. 4. The reversibility experiment of X towards  $In^{3+}$  by adding EDTA in DMF/H<sub>2</sub>O solution (v:v = 9:1, tris = 10 mM, pH = 7.4).



Fig. 5. The pH effect on the fluorescence intensity of X in the absence/presence of  $\mbox{In}^{3+}.$ 



Fig. 6. Energy diagram of HOMO and LUMO orbital X and  $X[{\rm In^{3+}}].$ 

indicated that  $\boldsymbol{X}$  could be used as a reversible sensor to detection of  $\mathsf{In}^{\mathsf{3+}}.$ 

Moreover, the fluorescence response of **X** to  $In^{3+}$  at different pH value (from 3 to 11) were shown in Fig. 5. The free **X** (1 × 10<sup>-5</sup> M) exhibited a stable and weak fluorescence between pH value from 3 to 11. In the presence of  $In^{3+}$  (7.5 equiv.), the fluorescence intensity did not change in the range of 3 to 5 and gradually increased with the pH changed from 5 to 7.4. When pH > 7.4, the fluorescence intensity of **X**[In<sup>3+</sup>] gradually decreased over the pH range of 7.4 to 10 and reached a stable value (pH>10). These results indicated that sensor responded best to In<sup>3+</sup> at pH = 7.4.

Otherwise, the possible binding mode between **X** and In<sup>3+</sup> was also proposed and demonstrated. As shown in Fig. S7, an ideal linear relationship (R<sup>2</sup> = 0.9952) between 1 / (I - I<sub>0</sub>) and 1 / In<sup>3+</sup> suggested that the stoichiometry between **X** and In<sup>3+</sup> may be 1:1. In addition, the binding model was further demonstrated by mass spectrometry. As shown in Fig. S8, a peak at m/z

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506.8572 corresponded to  $[\mathbf{X} + \ln^{3+} + Cl^{-} - H^{+}]^{+}$  and a peak at m/z 472.8330 corresponded to  $[\mathbf{X} + \ln^{3+}]^{3+}$ , respectively. All off the experimental data indicated that the binding ratio between **X** and  $\ln^{3+}$  ions was 1:1. Thus, the possible binding mechanism between **X** and  $\ln^{3+}$  ions were proposed in scheme 2 according to experiments data and relevant literatures.<sup>17, 20, 23, 38</sup> The oxygen atom on -OH, the nitrogen atoms on C=N bond were involved in the complexation of  $\ln^{3+}$  ions.

Moreover, in order to prove the feasibility of the proposed binding mechanism between **X** and In<sup>3+</sup>, structure optimization and energy calculation of X and  $X[In^{3+}]$  were investigated using density functional theory (DFT) combined with time-dependent density functional theory (TDDFT) calculations, as implemented in the Gaussian 09 package based on B3LYP/LANL2DZ basis.<sup>50</sup> The optimal structure of **X** and **X**[In<sup>3+</sup>] were shown in Fig. S9. For and Х, imidazo[2,1-b]thiazole 4-(diethylamino)-2hydroxybenzaldehyde maintained good planar property, respectively. After binding with In<sup>3+</sup>, X[In<sup>3+</sup>] had good planarity and structural rigidity. Besides, the spatial distributions and orbital energies of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) of **X** and **X**[In<sup>3+</sup>] were shown in Fig. 6. For free **X**, the HOMO and distributed 4-(diethylamino)-2-**LUMO** were around hydroxybenzaldehyde and C=N group. There was no obvious electron transfer. For X[In<sup>3+</sup>], the HOMO was still around 4-(diethylamino)-2-hydroxybenzaldehyde and C=N group, while electrons in LUMO were mostly concentrated around the 4-(diethylamino)-2-hydroxybenzaldehyde and marginally distributed over the C=N group and the imidazole ring. Obviously, after binding with In<sup>3+</sup>, the degree of intramolecular charge transfer was increased when excited. Moreover, the energy gap of X and X[In<sup>3+</sup>] were calculated to be 4.31 eV and 3.35 eV. Thus, theoretical calculation results proved the binding model between X and In<sup>3+</sup> was feasible and indicated that the response of **X** to In<sup>3+</sup> may be the joint result of photo-induced electron transfer (PET) and chelation enhanced fluorescence mechanism (CHEF).11, 31, 38, 51, 52



**Fig. 7.** (a) Fluorescence responses of **X** in EtOH/H<sub>2</sub>O buffer solution (v/v = 9:1, tris = 10 mM, pH = 7.4) with 5 equiv. of various metal ions ( $Zn^{2+}$ ,  $Li^+$ ,  $K^+$ ,  $Mg^{2+}$ ,  $Al^{3+}$ ,  $Mn^{2+}$ ,  $In^{3+}$ ,  $Ga^{3+}$ ,  $Hg^{2+}$ ,  $Ag^+$ ,  $Cd^{2+}$ ,  $Fe^{3+}$ ,  $Cr^{3+}$ ,  $Ni^{2+}$ ,  $Cu^{2+}$  and  $Co^{2+}$ ). Inset: the color of **X** and **X**[ $Zn^{2+}$ ] system under UV lamp. (b) changes in the fluorescence intensity of **X** in the presence of various metal ions.

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Fig. 8. UV-vis spectral changes of  ${\bf X}$  in the presence of different concentrations of  $Zn^{2*}$  ions.

In order to explore the practical application of **X**, **X** was used as a sensor to detect  $In^{3+}$  in tap water. The various concentrations of  $In^{3+}$  were prepared in tap water and measured by fluorescence assay method. As shown in Table S2,  $In^{3+}$  in tap water samples could be accurately measured with a satisfactory recovery (91.2%, 92.3%, 92.8% and 94.1%) and the relative standard deviation (RSD) of three measurements was less than 3.51%. Ultimately, these results indicated that **X** could be applied as a potential sensor for the quantitative detection of  $In^{3+}$  in real water samples.

#### 3.2. The sensing behavior of X to Zn<sup>2+</sup> in EtOH buffer solution

Furthermore, the properties of **X** in EtOH buffer solution were also explored by fluorescence and ultraviolet absorption. Primarily, the fluorescence response of **X** to various metal ions  $(Zn^{2+}, Li^+, K^+, Mg^{2+}, Al^{3+}, Mn^{2+}, In^{3+}, Ga^{3+}, Hg^{2+}, Ag^+, Cd^{2+}, Fe^{3+}, Cr^{3+}, Ni^{2+}, Cu^{2+} and Co^{2+})$  was shown in Fig. 7. In Fig. 7(a), the free **X** displayed a weak fluorescence intensity in EtOH buffer solution (v/v = 9:1, tris = 10 mM, pH = 7.4) with excitation at 365 nm. Upon addition of various metal ions (5 equiv.), only Zn<sup>2+</sup> could immediately cause a significant increase in fluorescence intensity at 463 nm while other metal ions lead to either no. or slight change in the emission intensity relative to the XVP from Fig. 7 insert, the color of **X** was direct observed to be dim blue ( $\Phi = 0.11$ ) and medium blue ( $\Phi = 0.26$ ) in the absence and presence of Zn<sup>2+</sup> under UV lamp. As shown in Fig. 7(b), in the presence of Zn<sup>2+</sup>, the fluorescence intensity of **X** was increased by about 6.5 times, showing an obvious fluorescence "off - on" behavior. Moreover, some metal ions could cause a slight increase in the fluorescence intensity of **X**, such as In<sup>3+</sup> and Cd<sup>2+</sup>. On the contrary, Ni<sup>2+</sup>, Cu<sup>2+</sup> and Co<sup>2+</sup> could quench the emission intensity due to intrinsic quenching nature.<sup>53-55</sup> These results indicated that **X** could be used as a fluorescence enhancement sensor for recognizing of Zn<sup>2+</sup>.

The UV absorption spectra of **X** (1 × 10<sup>-5</sup> M) in EtOH/H<sub>2</sub>O buffer solution (v/v = 9:1, tris = 10 mM, pH = 7.4) was also investigated in the absence and presence of various metal ions, including Zn<sup>2+</sup>, Li<sup>+</sup>, K<sup>+</sup>, Mg<sup>2+</sup>, Al<sup>3+</sup>, Mn<sup>2+</sup>, In<sup>3+</sup>, Ga<sup>3+</sup>, Hg<sup>2+</sup>, Ag<sup>+</sup>, Cd<sup>2+</sup>, Fe<sup>3+</sup>, Cr<sup>3+</sup>, Ni<sup>2+</sup>, Cu<sup>2+</sup> and Co<sup>2+</sup>. As shown in Fig. S10, the absorption spectrum of free **X** exhibited a maximum peak centered at 371 nm. When 5 equiv. of various metal ions were added, both Cu<sup>2+</sup> and Co<sup>2+</sup> could induce a distinct change in the ultraviolet absorption spectrum except for Zn<sup>2+</sup>, indicating that they could also form complexes with **X**.

In order to further explore the selectivity of **X** for  $Zn^{2+}$ , the competitive experiments were carried out in presence of various metal ions (Li<sup>+</sup>, K<sup>+</sup>, Mg<sup>2+</sup>, Al<sup>3+</sup>, Mn<sup>2+</sup>, In<sup>3+</sup>, Ga<sup>3+</sup>, Hg<sup>2+</sup>, Ag<sup>+</sup>, Cd<sup>2+</sup>, Fe<sup>3+</sup>, Cr<sup>3+</sup>, Ni<sup>2+</sup>, Cu<sup>2+</sup> and Co<sup>2+</sup>). As shown in Fig. S11, most metal ions, except for Cu<sup>2+</sup> and Co<sup>2+</sup>, did not have much effect on the fluorescence response of **X** to Zn<sup>2+</sup>. Thus, the **X** was less efficient in detecting Zn<sup>2+</sup> in the presence of Cu<sup>2+</sup> and Co<sup>2+</sup>. These results indicated that **X** could be used as a sensor to detect Zn<sup>2+</sup> in EtOH/H<sub>2</sub>O buffer solution without interference from most metal ions.

To further explore the binding property of **X** with  $Zn^{2+}$ , relevant titration experiments were carried out in EtOH/H<sub>2</sub>O buffer solution (v/v = 9:1, tris = 10 mM, pH = 7.4). Primarily, the UV-vis titration was shown in Fig. 8. The free **X** (1 × 10<sup>-5</sup> M) showed an absorption peak at 371 nm. It can be obviously observed that the absorption peak gradually decreased at 371



**Fig. 9.** (a) Fluorescence spectral changes of **X** in the presence of different concentrations of  $Zn^{2+}$  ions. (b) Plot of the fluorescence intensity at 463 nm as a function of  $Zn^{2+}$  concentration. Insert: linear relationship between the fluorescence intensity at 463nm and concentration of  $Zn^{2+}$  (1 × 10<sup>-7</sup> M - 6 × 10<sup>-7</sup> M).

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Fig. 10. The reversibility experiment of X towards  $Zn^{2+}$  by adding EDTA in EtOH/H<sub>2</sub>O solution (v:v = 9:1, tris = 10 mM, pH = 7.4).

nm and increased at 399 nm with the addition of Zn<sup>2+</sup> from 0 to  $5 \times 10^{-5}$  M. In addition, a clear isosbestic point was found at 386 nm, indicating that X could form a stable complex (X[Zn<sup>2+</sup>]) with Zn<sup>2+</sup>. Moreover, the fluorescence titration experiments for the binding of X with Zn<sup>2+</sup> were also shown in Fig. 9. As mentioned above, the free X maintained a concentration of  $1 \times 10^{-5}$  M and exhibited weak fluorescence. With the increased gradually of  $Zn^{2+}$  concentrations from 0 to 5 equiv., the fluorescence intensity of X increased gradually (Fig. 9(a)) and reached a plateau at 463 nm (Fig. 9(b)) when the concentration was 5  $\times$ 10<sup>-5</sup> M, indicating that the fluorescence intensity reached the maximum. As shown in Fig. 9(b) insert, a good linear relationship between the fluorescence intensity of X and the low concentration of  $Zn^{2+}$  (1 × 10<sup>-7</sup> M - 6 × 10<sup>-7</sup> M) with R<sup>2</sup> = 0.9858 and Y = 26X + 235.5 was obtained. The detection limit of **X** for Zn<sup>2+</sup> was calculated to be 5.5  $\times$  10<sup>-9</sup> M based on 3 $\sigma/s$ equation, which is lower than detection of Zn<sup>2+</sup> that had been reported.<sup>13, 15</sup> The association constant (Ka) of X with Zn<sup>2+</sup> was calculated to be  $2.65 \times 10^5$  M<sup>-1</sup> (Fig. S12) based on eqn (2).

Furthermore, the reversible binding of **X** to Zn<sup>2+</sup> was also verified by adding EDTA. As shown in Fig. 10, free X exhibited weak fluorescence intensity. When Zn<sup>2+</sup> (5 equiv.) were added, the fluorescence intensity of X increased significantly at 463 nm. When EDTA (5 equiv.) were added to X[Zn<sup>2+</sup>] system, the fluorescence signal was completely disappeared. Then continue to add Zn<sup>2+</sup> (10 equiv.) to the system above, the fluorescence intensity was significantly increased again. Moreover, keep adding EDTA, the fluorescence disappeared completely. X still maintained well response to Zn2+ after two cycles with a small fluorescence loss at 463 nm and exhibited efficient "on-off-on" behavior.

Moreover, the fluorescence response of X to Zn2+ at different pH value (from 2 to 11) were shown in Fig. 11. The free X (1 imes 10<sup>-5</sup> M) exhibited a stable and weak fluorescence between pH value from 2 to 11. In the presence of  $Zn^{2+}$  (5 equiv.), the fluorescence intensity did not change in the range of 2 to 4.5 and gradually increased with the pH changed from 4.5 to 7.4. When pH>7.4, the fluorescence intensity of X[Zn<sup>2+</sup>] gradually decreased over the pH range of 7.4 to 9.5 and reached



Fig. 11. The pH effect on the fluorescence intensity of **X** in the absence/presence of  $7n^{2+}$ 

a stable value (pH>9.5). These results indicated that X could be used as a sensor to detect Zn<sup>2+</sup> in physiological conditions for biological samples.

The possible binding mode between **X** and Zn<sup>2+</sup> was also proposed and demonstrated. The stoichiometry between X and  $Zn^{2+}$  may be 1:1, which was proved by B-H equation (Fig. S12) and mass spectrometry (a peak at m/z 422.9017 corresponded to [X + Zn<sup>2+</sup>]<sup>2+</sup>, Fig. S13). Thus, the possible binding model between X and Zn<sup>2+</sup> ions was proposed in scheme 3 according to experiments data and relevant literatures.<sup>38, 47-49</sup> The oxygen atom on -OH and the nitrogen atoms on C=N bond were involved in the complexation of Zn<sup>2+</sup> ions.

Moreover, in order to prove the feasibility of the proposed binding mechanism between X and Zn<sup>2+</sup>, structure optimization and energy calculation of X and X[Zn<sup>2+</sup>] were also investigated using ab initio density functional theory (DFT) combined with time-dependent density functional theory (TDDFT) calculations, as implemented in the Gaussian 09 package based on B3LYP/6-31G(d) basis.<sup>50</sup> The optimal structure of X and X[Zn<sup>2+</sup>] were



Fig. 12. Energy diagram of HOMO and LUMO orbital X and X[Zn<sup>2+</sup>].

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shown in Fig. S14. For X[Zn<sup>2+</sup>], from vertical view, the whole molecule was basically in the same plane after binding with Zn<sup>2+</sup>. Otherwise, the spatial distributions and orbital energies of HOMO and LUMO of X and X[Zn<sup>2+</sup>] were shown in Fig. 12. For X[Zn<sup>2+</sup>], the HOMO was still around 4-(diethylamino)-2hydroxybenzaldehyde and C=N group, while electrons in LUMO were uniformly distributed throughout the whole molecule, including imidazo[2,1-b]thiazole and 4-(diethylamino)-2hydroxybenzaldehyde parts. The role of  $Zn^{2+}$  ions was to increase the degree of intramolecular charge transfer.<sup>38</sup> The energy gap of  $X[Zn^{2+}]$  were calculated to be 3.24 eV. Thus, theoretical calculation results proved the binding model between  $\boldsymbol{X}$  and  $Zn^{2\ast}$  was feasible and indicated that the response of **X** to Zn<sup>2+</sup> may also be the joint result of PET and CHEF. The calculated results and experimental phenomena were highly consistent with the theoretical basis.

Furthermore, in order to explore the practical application of **X**, **X** was used as a sensor to detect  $Zn^{2+}$  in tap water. The various concentrations of  $Zn^{2+}$  were prepared in tap water and were measured by fluorescence assay method. As shown in Table S3,  $Zn^{2+}$  could also be accurately measured in tap water samples. Suitable recoveries (97.3%, 104.1% and 106.2%) and RSD (1.50%, 2.39% and 3.01%) were observed. Ultimately, these results indicated that **X** could be applied as a potential sensor for the quantitative detection of  $Zn^{2+}$  in real water samples.

## Conclusions

In summary, A new simple and easily synthesized multitarget sensor(X), was designed and synthesized based on imidazo[2,1*b*]thiazole-6-carboxylic acid and 4-(diethylamino)-2hydroxybenzaldehyde. The structure of **X** was characterized by NMR, FTIR and ESI-MS spectroscopy. X could be used as a sensor to detect In<sup>3+</sup> in DMF-H<sub>2</sub>O buffer solution and detect Zn<sup>2+</sup> in EtOH-H<sub>2</sub>O buffer solution through fluorescence enhancement. X exhibited an efficient "off-on-off" fluorescence behavior by cyclic addition of metal ions (In<sup>3+</sup> and Zn<sup>2+</sup>) and EDTA. The binding mode and sensing mechanism of X with metal ions (In<sup>3+</sup> and Zn<sup>2+</sup>) was verified by theoretical calculations using Gaussian 09. Moreover, X could be applied as a potential sensor to detect In<sup>3+</sup> and Zn<sup>2+</sup> in real water samples.

## **Conflicts of interest**

There are no conflicts to declare.

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## Short statement:

An imidazo[2,1-*b*]thiazole based compound (X) was designed and synthesized as an "off-on-off" sensor for the multiple recognition of  $In^{3+}$  and  $Zn^{2+}$  in different system.