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Highly selective fluorescence turn-on chemosensor based on naphthalimide derivatives for detection of copper(II) ions

ABSTRACT

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HIGHLIGHTS

- It was a turn-on sensor for copper(II) ions based on naphthalimide derivatives.
- It had a good selectivity for copper(II) ions.
- The sensor had a low detection limit (0.15 μM).

G R A P H I C A L A B S T R A C T



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Introduction

Copper is an essential soft transition metal ion that plays a pivotal role in environmental, biological, and chemical systems [1–4]. In addition, excessive levels of copper could do harm to liver. As reported, copper deficiency may lead to hematological manifestations

A new fluorescent probe, DN-SB, was synthesized. DN-SB was based on the naphthalimide derivatives and exhibited high selectivity and sensitivity for Cu^{2+} ions. As a Cu^{2+} -amplified fluorescent probe, its fluorescence spectrum showed 4.5-fold enhancement in the intensity of the signal at 519 nm on binding with the Cu^{2+} . Based on the fluorescence titration spectra and job's-plot, binding mode of DN-SB with Cu^{2+} was proposed. Fluorescence intensity was linear with concentration of Cu^{2+} cation in a range from 4 μ M to 7 μ M. DN-SB was also sensitive for copper ions. The detection limit was calculated to be 0.15 μ M which indicated DN-SB was sensitive to Cu^{2+} .

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and a wide variety of neuro-logical problems [5–8]. Currently, chemosensors are widely employed as the signal output due to its high sensitivity and the simplicity of its equipment requirement [9–14]. So, the design and construction of sensory molecules of copper ions is essential because of their important roles in biological, industrial, and environmental processes. Recently, the detection and estimation of Cu^{2+} always constitutes an active area of research [15–24]. Schiff base is always used as a typical acceptor for copper ions [25–27] and a number of luminescent probes for copper ions have been reported, many of them which show enhancement in the intensity of the signal are based on the coupling of two

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Scheme 1. The synthetic path of DN-SB.

structural subunits: rhodamine derivatives (used for signal transduction) and Schiff base (used for the selective recognition of copper ions) [28–31]. Few of chemosensors for copper ions based on the other fluorophores can show fluorescence enhancement. The "off–on" type signal is superior compared to the "on–off" type due to their better overall signal processing in biosystems and specificity of mode of action [32]. With this in mind, we designed and synthesized a new fluorescent sensor for detection of copper ions based on naphthalimide derivatives. The synthesis of DN-SB started from 4-bromine naphthalene anhydride **1**, via four steps, DN-SB was obtained, as shown in Scheme 1.

Materials and methods

Experimental

General

Reagents and solvents were reagent grade, used as received unless otherwise noted. All solvents used in water-sensitive reactions were freshly distilled. Reactions were monitored by TLC. Yields were of purified product and were not optimized. ¹H NMR were recorded at 400 MHz. ¹³C NMR were recorded at 100 MHz. Fluorescence spectra was measured on a Thermo Fluorescence spectrophotometer.

Synthesis

Synthesis of synthesis of 4-bromo-N-butyl-1,8-naphthalic anhydride (2)

A mixture of compound 1 (5 g, 18 mmol), 1-aminobutane (1.7 g, 23.3 mmol) in 40 mL acetic acid was stirred under reflux in a nitro-

gen atmosphere for 6 h, After the completion of reaction, the reaction mixture was then poured into a mixture of cracked ice and water and filtered to get a pale yellow solid. The crude product was recrystallized from chlorobenzene to give 4.6 g light gray solid in a yield of 85%. ¹H NMR, (CDCl₃): 8.64 (d, 1H, J = 7.2 Hz), 8.53–8.55 (m, 1H), 8.39 (d, 1H, J = 7.6 Hz), 8.02 (d, 1H, J = 8.0 Hz), 7.81–7.85 (m, 1H), 4.17 (t, 2H, J = 7.6 Hz), 1.67–1.75 (m, 2H), 1.40–1.49 (m, 2H), 0.98 (t, 3H, J = 7.2 Hz).

Synthesis of 4-hydrazine hydrate-N-butyl-1,8-naphthalic anhydride (**3**)

Compound **2** (5.4 g, 16.3 mmol) and 5 mL hydrazine hydrate (85%, w/w) was added into 50 mL of ethylene glycol monomethyl ether and refluxed for 6 h. After cooled to room temperature, the mixture was poured into 150 mL water, the precipitated solids were filtered, dried in vacuum to give a red solid. Yield: 80%. ¹H NMR, (DMSO-d₆): 8.60 (d, 1H, *J* = 8.4 Hz), 8.41 (d, 1H, *J* = 7.2 Hz), 8.28 (d, 1H, *J* = 8.4 Hz), 7.63–7.65 (m, 1H), 7.24 (d, 1H, *J* = 8.4 Hz), 4.60–4.67 (m, 2H), 4.01 (t, 2H, *J* = 7.2 Hz), 3.24–3.25 (m, 1H), 1.54–1.62 (m, 2H), 1.30–1.36 (m, 2H), 0.92 (t, 3H, *J* = 7.6 Hz).

Synthesis of 4-hydrazine-N-butyl-1,8-naphthalic anhydride (4)

Naphthalimide hydrazine **3** (283.0 mg, 1 mmol) was dissolved in 20 mL ethanol, then 3.0 mL aqueous glyoxal (30%, w/w) was then added to the solution. The mixture was stirred at room temperature for 5 h. The precipitated crystals were filtered and washed with ethanol to give the orange solid (217 mg, yield: 66%). ¹H NMR, (DMSO-d₆): 12.19 (s, 1H), 9.62 (s, 1H), 8.37–8.48 (m, 2H), 7.72– 7.83 (m, 3H), 6.57–6.79 (m, 1H), 4.01 (t, 2H, *J* = 7.2 Hz), 1.58–1.61 (m, 2H), 1.34–1.36 (m, 2H), 0.93 (t, 3H, *J* = 7.2 Hz).

Synthesis of DN-SB

Compound **4** (0.1 g, 0.3 mmol) and o-aminophenol (0.03 g, 0.3 mmol) was added into 15 mL ethanol and refluxed for 6 h. After the mixture cooled to room temperature, the precipitated crystals were filtered and washed with ethanol to give the red solid. yield: 93%.¹H NMR, (DMSO-d₆): 11.87 (s, 1H), 9.28 (s, 1H), 8.77 (d, 1H, *J* = 7.6 Hz), 8.48–8.53 (m, 2H), 8.27–8.40 (m, 2H), 7.81–7.84 (m, 1H), 7.71 (d, 1H, *J* = 8.4 Hz), 7.23 (d, 1H, *J* = 7.6 Hz), 7.09–7.13 (m, 1H), 6.82–6.93 (m, 1H), 6.51–6.64 (m, 1H), 4.02 (t, 2H, *J* = 7.2 Hz), 1.56–1.64 (m, 2H), 1.32–1.37 (m, 2H), 0.93 (t, 3H, *J* = 7.2 Hz). ¹³C NMR (DMSO-d₆): δ :163.52, 162.90, 157.13, 151.26, 145.13, 143.92, 137.28, 133.03, 130.94, 128.15, 128.10, 123.90, 122.05, 119.96, 119.55, 119.44, 119.05, 116.24, 114.38, 114.29, 29.70, 19.79, 18.50, 13.70. MS: m/z 414.1692[Calcd 414.1689].

The metal salts used

 $Fe_2(SO_4)_3 \cdot 9H_2O$, $ZnSO_4 \cdot 6H_2O$, $Co(CIO_4)_2 \cdot 6H_2O$, $NiSO_4 \cdot 6H_2O$, $Ca(CIO_4)_2$, $SnCl_2 \cdot 6H_2O$, $Pb(CIO_4)_2 \cdot 3H_2O$, $Cr(CIO_4)_3 \cdot 6H_2O$, $CuSO_4 \cdot CuSO_4 \cdot C$



Fig. 1. Fluorescence spectra of DN-SB (1×10^{-5} M) in acetonitrile–water (70:30, v/v) with a buffer solution of 3-(N-morpholino) propanesulfonic acid (MOPS, 10 mM, pH = 7.0). in the presence of different concentrations of Cu²⁺ (0–10equiv), $\lambda ex = 455$ nm. Inset: fluorescence intensity at 519 nm of DN-SB as a function of Cu²⁺ concentration.



Fig. 2. Curve of fluorescence intensity at 519 nm of DN-SB $(1\times 10^{-5}\,M)$ versus increasing concentrations of Cu^{2*} (4–7 $\mu M).$



Fig. 3. Job's plot for determining the stoichiometry of DN-SB ([DN-SB] + $[Cu^{2+}] = 40 \ \mu\text{M}$) and Cu^{2+} in acetonitrile–water (70:30, v/v) with a buffer solution of 3-(N-morpholino) propanesulfonic acid (MOPS, 10 mM, pH = 7.0). $\lambda ex = 455 \text{ nm}$.



Fig. 4. Fluorescent response of DN-SB $(1 \times 10^{-5} \text{ M})$ to various metal ions at 10 equiv concentration in acetonitrile–water (70:30, v/v) with a buffer solution of 3-(N-morpholino) propanesulfonic acid (MOPS, 10 mM, pH = 7.0).

 $5H_2O$, $Mn(ClO_4)_2 \cdot 6H_2O$, $Na_2SO_4 \cdot 10H_2O$, K_2SO_4 , $AgClO_4 \cdot H_2O$, $Hg(ClO_4)_2 \cdot 3H_2O$, $Cd(ClO_4)_2 \cdot 6H_2O$.

Result and discussion

The interaction of sensor DN-SB with the cations was investigated through fluorescence spectra. All the fluorescence behavior of sensor DN-SB was studied in acetonitrile–water (70:30, v/v) with a buffer solution of 3-(N-morpholino) propanesulfonic acid (MOPS, 10 mM, pH = 7.0). Fluorescence titrations of DN-SB with Cu^{2+} were performed and the responding spectra are shown in Fig. 1. Free DN-SB exhibited very slight fluorescence response in the range from 495 to 650 nm, which was due to efficient photoinduced electron transfer (PET) process from the electron-rich receptor to the excited DN-SB fluorophore. Upon addition of Cu^{2+} , the PET mechanism was quenched. Thus, the emission band peaked at 519 nm significantly increased in intensity, and a continuous increase of fluorescence intensity could be observed with Cu^{2+} concentration increasing (Fig. 1).

This fact meant that DN-SB could act as an off-on fluorescent probe for Cu²⁺. The fluorescence peak no longer changed when



Fig. 5. Fluorescent emission changes of DN-SB $(1 \times 10^{-5} \text{ M})$ upon addition of 10 equiv of each relevant analyte $(Cu^{2+}, Mg^{2+}, Hg^{2+}, Na^+, K^+, Zn^{2+}, Fe^{2+}, Cr^{3+}, Co^{2+}, Ni^{2+}, Ca^{2+}, Pb^{2+}, Cd^{2+}, Sn^{2+}, Mn^{2+})$ in acetonitrile–water (70:30, v/v) with a buffer solution of 3-(N-morpholino) propanesulfonic acid (MOPS, 10 mM, pH = 7.0). λ ex = 455 nm.



Fig. 6. The fluorescent intensity at 533 nm of DN-SB $(1 \times 10^{-5} \text{ M})$ with 10 equiv of Cu²⁺ and 10 equiv of various metal ions in acetonitrile–water (70:30, v/v) with a buffer solution of 3-(N-morpholino) propanesulfonic acid (MOPS, 10 mM, pH = 7.0). λ ex = 455 nm.

the concentration of Cu^{2+} increased from 1 to 10 equiv (Fig. 1, inset), implicating a 1:1 complexation of DN-SB with the Cu^{2+} .

Fig. 2 also showed the good linearity between the emission at 519 nm and concentrations of Cu²⁺ in the range from 4 μ M to 7 μ M, indicating that sensor DN-SB can detect quantitatively relevant concentrations of Cu²⁺. The linear equation was found to be $y = 292.6 \times 10^5 x - 804.5$ (R = 0.9986), where y was the emission

at 519 nm measured at a given Cu²⁺ concentration and x represented the concentration (10^{-5} mol/L) of Cu²⁺ added. According to IUPAC, the detection limit was determined from three times the standard deviation of the blank signal (3s) as 0.15 μ M. The result indicated that DN-SB was sensitive to Cu²⁺.

In order to further understand the coordination of DN-SB with Cu²⁺, Job's-plot analysis was carried out (Fig. 3). The results also indicated that DN-SB formed a 1:1 stoichiometrical complex with Cu²⁺, and the association constant between DN-SB and Cu²⁺ was determined to be 1.1×10^{10} M⁻¹ in acetonitrile by using nonlinear least-square analysis.

To evaluate the selectivity of DN-SB in acetonitrile–water (70:30, v/v) with a buffer solution of 3-(N-morpholino) propanesulfonic acid (MOPS, 10 mM, pH = 7.0). Various metal ions such as Na⁺, Ag⁺, Ca²⁺, Mg²⁺, Zn²⁺, Pb²⁺, Hg²⁺, Ni²⁺, Mn²⁺, Co²⁺, Cd²⁺, K⁺, Fe³⁺ and Cr³⁺ were used (Fig. 4). As expected, DN-SB showed a weak fluorescence. Upon addition of Cu²⁺ (10 equiv) to a solution of DN-SB, significant enhancement of fluorescence with an emission maximum at 519 nm was observed and the fluorescence increased by about 4.5-fold, illustrated in Fig. 5. However, other metal ions were added, the fluorescence behavior of DN-SB showed almost negligible effects. In addition, the fluorescence increase took place immediately after Cu²⁺ addition (within 10 s), indicating that DN-SB enables rapid detection of Cu²⁺.

To examine whether sensor DN-SB could still retain the sensing response to Cu^{2+} under the potential competition of relevant analytes, the sensor was treated with Cu^{2+} in the presence of other metal ions. As displayed in Fig. 6, all the relevant analytes tested had virtually no influence on the detection of Cu^{2+} . Thus, sensor DN-SB seemed to be useful for selectively sensing Cu^{2+} , even with these relevant analytes.

The above-mentioned findings clearly indicated that DN-SB behaved as a highly selective turn-on fluorescent probe for Cu^{2+} . As for the highly selectivity for Cu^{2+} , we thought that the following two factors might play critical role for high selectivity of DN-SB. On one hand, the avoidance of using sulfur atom in our scaffold would avoid interference from other metal ions especially mercury. On the other hand, the receptor of DN-SB was relatively rigid and had a cavity-like, which probably fitted Cu^{2+} best compared to other metal ions.

Based on the fluorescence titration spectra, although Cu²⁺ could induce an increasing fluorescence, it could not cause shift in emission maximum. This phenomenon usually occurred when the nitrogen, which was also the donor of push–pull system, did not chelates to metal ions. Therefore, we believed that the nitrogen that linked to the naphthalimide ring did not involve in Cu²⁺ chelation. In addition to that, some reports indicated that Cu²⁺ ions were coordinated to Shift base nitrogen atoms and the phenol oxygen atom preferably [33,34]. According to these factors and Job'splot, we proposed a plausible binding mode of the probe DN-SB with Cu²⁺ as shown in Scheme 2.



Scheme 2. Proposed binding mode of DN-SB with Cu2+.

Conclusion

Naphthalimid-based fluorescent probe DN-SB was successfully developed. DN-SB exhibited "turn-on" fluorescence, which displayed a fluorescence enhancement response to Cu^{2+} via a 1:1 binding mode. Fluorescence intensity was linear with concentration of Cu^{2+} cation in a range from 4 μ M to 7 μ M. Its selectivity toward Cu^{2+} was very high and little interference was observed for other commonly coexistent metal ions. As a chemosensor, DN-SB was also sensitive for copper ions. The detection limit was calculated to be 0.15 μ M.

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