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Simple naphthalimide-based fluorescent sensor for highly sensitive and selective detection of Cd^{2+} and Cu^{2+} in aqueous solution and living cells

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A novel naphthalimide-based fluorescent sensor bearing the *N*,*N*′-bis(salicylidene)diethylenetriamine receptor was developed, which exhibited dual signaling behaviors for Cd^{2+} and Cu^{2+}, and was applicable to the environmental and biological milieus. Upon addition of Cd^{2+}, the fluorescence intensity enhanced in a linear fashion with the maximum fluorescence intensity increase of about 4-fold. Moreover, with the sensor **1** and **1**–Cd^{2+} complex, Cu^{2+} was easily recognized by marked fluorescence quenching. The selectivity and sensitivity of the sensor **1** for Cd^{2+} were satisfactory and achieving a detection limit at the nanomolar level. The living cell image experiments demonstrated the value of sensor **1** in fluorescent visualization of Cd^{2+} ions in biological systems.

1. Introduction

Cd^{2+} has caused serious harm to the environment and human health. It can cause serious injury to the human kidney, lung, bone and nerve system, which resulted in renal dysfunction, calcium metabolism disorders and an increased incidence of certain forms of cancers.[1] However, the mechanisms involved in the Cd^{2+}-uptake and carcinogenesis remain undefined.[2] The EPA (United States Environmental Protection Agency) gives an enforceable drinking water standard for Cd of 5 ppb to prevent kidney damage and other related diseases, while the WHO (World Health Organization) provides a more strict guideline value for Cd of 3 ppb for drinking water.[3] Therefore, developing reliable methods for Cd^{2+} trace quantification in environmental samples and in living cell/tissue samples is of great significance for clarifying the Cd^{2+}-carcinogenesis and other biological effects.

In recent years, the development of fluorescent chemosensors for sensing and reporting heavy transition-metal ions has been receiving considerable attention. Fluorescence techniques have become powerful tools for sensing and imaging metal ions in trace amounts because of its simplicity, high sensitivity and real-time monitoring with a short response time. Sensitive and reliable fluorescent molecular sensors seem to be the ideal tool for evaluating and dynamically mapping the intracellular fluctuations of metal ions by using microscopy techniques to allow real-time local imaging.[4–11] Up to now, many fluorescent sensors for Cd^{2+} have been reported,[12,13] but only a few of them are applicable to cellular imaging,[14] their practical application is still restrained due to their poor water solubility, UV-excitation and pH-dependent fluorescence in physiological environments. To date, it is still a tremendous challenge to design Cd^{2+}-selective sensors, in particular, fluorescent chemosensors for the accurate detection of Cd^{2+} in aqueous solutions and biological environments.

A practical fluorescent chemosensor must produce a strong fluorescent response upon binding the analyte. 1,8-Naphthalimide derivatives are dyes extensively employed in fluorogenic-labeling and fluorescent chemosensors because of their high absorption coefficient, high fluorescence quantum yield and high photostability.[15] By virtue of these fascinating properties, the excellent examples of 1,8-naphthalimide-based fluorescent chemosensor applications in cell imaging have been reported.[16]

In this paper, we report the synthesis and fluoroionophoric properties of a novel fluorescent sensor aimed at the selective recognition of Cd^{2+} and Cu^{2+} ions in aqueous solution. Sensor **1** is composed of an aminonaphthalimide fluorophore and a receptor of the *N*,*N*′-bis(salicylidene)diethylenetriamine attached *via* a space linker. Sensor **1** exhibits Cd^{2+}-selective TURN-ON and Cu^{2+}-selective TURN-OFF type signaling behaviors that can be used to distinguish Cd^{2+} and Cu^{2+} ions. Moreover, to the best of our knowledge, this is the first example of a

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cation-induced TURN-ON and TURN-OFF type of fluorescent signal control behavior with Cd^{2+} and Cu^{2+}.

2. Experimental

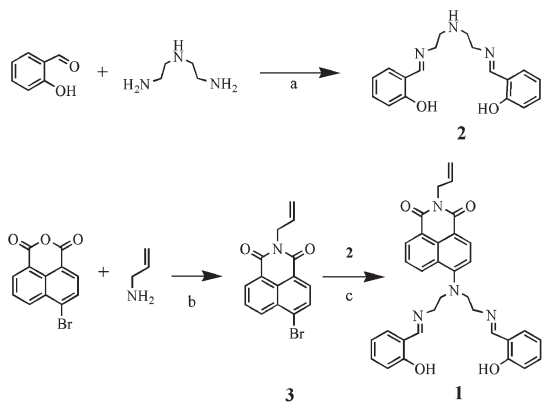
2.1 Materials

4-Bromo-1,8-naphthalic anhydride (98% purity, Beijing Hengyue Zongyuan Chemical CO., LTD) was purified by recrystallization from acetic acid. Allyl amine (XinHua Chemical Reagent Co.) was distilled and then stored at −20 °C prior to use. *N*,*N*-Dimethylformamide (DMF) was distilled and dried by anhydrous magnesium sulfate. Diethylenetriamine (99% purity), salicylaldehyde, and all other reagents were purchased from Sinopharm Chemical Reagent Co., Ltd., and used as received. The solutions of metal ions were prepared from NaCl, KCl, $CaCl_2$, $MgSO_4$, $FeCl_3$, $Mn(NO_3)_2{\cdot}6H_2O$, $CoCl_2{\cdot}6H_2O$, $NiCl_2{\cdot}6H_2O$, $Zn(NO_3)_2$, $C_4H_6CdO_4{\cdot}2H_2O$, $CuCl_2{\cdot}2H_2O$, $Hg(NO_3)_2$, $AgNO_3$, $Pb(NO_3)_2$, respectively, and were dissolved in deionized water. Aqueous HEPES–NaOH (0.1 mol L^{-1}) solution was used as a buffer to maintain the pH value (pH = 7.14), and the ionic strength of all solutions used in the experiments.

2.2 Characterization

^{1}H NMR spectra were measured on a Bruker AV-400 spectrometer with chemical shifts reported as parts per million (in $CDCl_3$, TMS as internal standard). IR spectra were recorded on a Bruker Vector-22 spectrometer. The pH values of the test solutions were measured with a glass electrode connected to a Mettler-Toledo Instruments DELTA 320 pH meter (Shanghai, China) and adjusted if necessary. Fluorescence spectra were determined on a Hitachi F-4500. UV-Vis spectra were recorded on a Hitachi U-3010 UV-Vis spec. All of the measurements were performed at about 298.0 ± 0.2 K.

The synthesis of sensor **1** is shown in Scheme 1. The intermediate, compound **2**, was synthesized from salicylaldehyde and diethylenetriamine following a literature procedure.[17] Compound **3** was prepared in 50.8% yield by coupling 4-bromo-1,8-naphthalic anhydride with allyl amine. Sensor **1** was easily synthesized by compounds **2** and **3** in 36.9% yield, all compounds were characterized by ESI-MS and ^{1}H NMR.



Scheme 1 Synthesis and structure of **1–3**. (a) C_2H_5OH, room temperature, 3 h, 92.5%; (b) allyl amine, C_2H_5OH, reflux, 1 h, 50.8%; (c) CH_2CN, K_2CO_3, reflux, 6 h, 36.9%.

3. Synthesis

Synthesis of intermediate 2

To 20 mL anhydrous ethanol containing diethylenetriamine (1.0 g, 10 mmol), an excess of 2-hydroxy-4-methoxybenzaldehyde (2.6 g, 21 mmol) was added and the mixture was stirred vigorously at room temperature for 24 h. The reaction progress was monitored by thin-layer chromatography (TLC). After completion of the reaction, the formed precipitate was filtered, washed with cold ethanol (3 × 10 mL) and then dried in vacuum, affording 0.17 g crude product, which was further purified by silica gel column chromatography using CH_2Cl_2/EtOH (20/1, v/v) containing 1% (v/v) triethylamine as eluent. 2.88 g of intermediate **2** as a yellow viscous liquid was obtained, yield: 92.5%. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.34 (s, 2H), 7.30–7.26 (m, 2H), 7.20 (dd, J = 1.5 Hz, 7.8 Hz, 2H), 6.93 (d, J = 8.1 Hz, 2H), 6.87–6.82 (m, 2H), 5.28 (s, 2H), 3.70 (t, J = 5.7 Hz, 4H), 2.98 (t, J = 5.7 Hz, 4H), 1.23 (t, J = 6.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 300 MHz) d 49.5, 59.26, 116.7, 118.2, 131.0, 118.2, 136.7, 160.9, 165.8. IR (KBr, cm^{-1}): 3427, 2917, 2846, 2107, 1732, 1633, 1455, 1382, 1280, 1230, 1105, 905, 888, 818, 753, 699, 665, 620, 569. HRMS calcd for $C_{18}H_{21}N_3O_2$. [MH^+]: 311.

Synthesis of *N*-allyl-4-bromo-1,8-naphthalimide (intermediate 3)

Compound **3** was synthesized from 4-bromo-1,8-naphthalimide *via* a literature procedure.[15] Allyl amine (57 mg, 1.00 mmol) in ethanol (10 mL) was added dropwise, under mechanical stirring, to a solution of 4-bromo-1,8-naphthalic anhydride (270 mg, 0.97 mmol) in ethanol (40 mL). The reaction mixture was refluxed for 1 h and then cooled. After the removal of the solvent, the crude product was purified by column chromatography (silica gel, CH_2Cl_2–EtOH, 20 : 1) to give compound **2** as a white solid (160 mg, 50.8%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.66 (dd, J = 0.8 Hz, 7.9 Hz, 1H), 8.58 (dd, J = 0.8 Hz, 7.9 Hz, 1H), 8.45 (d, J = 7.6 Hz, 1H), 8.05 (d, J = 7.6 Hz, 1H), 7.83–7.88 (m, 1H), 5.93–6.06 (m, 1H), 5.32 (dd, J = 0.7 Hz, 6.2 Hz, 1H), 5.22 (dd, J = 0.8 Hz, 8.2 Hz, 1H), 4.80 (d, J = 5.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 300 MHz) d 37.1, 112.6, 122.7, 123.3, 125.8, 125.9, 126.3, 126.6, 126.8, 127.9, 128.0, 128.8, 129.4, 157.9. IR (KBr, cm^{-1}): 3341, 3069, 2021, 1786, 1787, 1735, 1703, 1659, 1592, 1571, 1460, 1426, 1402, 1730, 1345, 1332, 1236, 1222, 1153, 1134, 1019, 950, 932, 849, 777, 746, 718, 568, 556. HRMS calcd for $C_{15}H_{10}BrNO_2$. [MH^+]: 316.

Synthesis of sensor 1

Sensor **1** was synthesized as shown in Scheme 1. Intermediate **2** (430 mg, 1.38 mmol) in acetonitrile (10 mL) was added dropwise, under mechanical stirring, to a solution of intermediate **3** (300 mg, 0.95 mmol) in acetonitrile (40 mL). The reaction

mixture was refluxed for 6 h and then cooled. After removal of the solvent, the crude product was purified by column chromatography (silica gel, CH_2Cl_2–EtOH, 10 : 1) to give compound **1** as a yellow solid (202 mg, 36.9%). ^{1}H NMR (DMSO-d_6, 300 MHz) δ 9.90 (s, 2H), 8.67 (dd, J = 1.2 Hz, 7.3 Hz, 1H), 8.58 (dd, J = 1.1 Hz, 8.5 Hz, 1H), 8.44–8.36 (m, 1H), 8.05 (d, J = 7.9 Hz, 1H), 7.85 (dd, J = 8.5 Hz, 7.3 Hz, 2H), 7.58–7.50 (m, 2H), 7.32–7.20 (m, 2H), 7.21 (dd, J = 1.8 Hz, 7.8 Hz, 1H), 6.94–6.82 (m, 2H), 6.11–5.93 (m, 1H), 5.30–5.25 (m, 2H), 4.82–4.80 (m, 2H), 3.75–3.71 (m, 2H), 3.32–3.20 (m, 4H), 3.08–3.02 (m, 4H). ^{13}C NMR ($CDCl_3$, 300 MHz) δ 42.4, 49.5, 59.3, 116.9, 117.5, 117.8, 118.5, 119.7, 122.0, 128.0, 128.5, 130.3, 130.6, 130.9, 131.0, 131.2, 131.6, 131.9, 132.0, 132.2, 133.1, 133.3, 133.6, 134.0, 134.6, 136.9, 161.0, 161.5, 163.2, 166.1. IR (KBr, cm^{-1}): 3419, 2923, 2843, 2728, 2023, 1732, 1644, 1458, 1832, 1312, 1233, 1109, 905, 883, 818, 753, 694, 671, 615, 505. HRMS calcd for $C_{33}H_{30}N_4O_4$. [MH$^+$]: 547.

4. Results and discussion

pH-titration and spectral responses

Fluorophores are usually disturbed by protons in the detection of metal ions, so their low sensitivity to the operational pH value is expected and investigated. Fig. 1 shows the fluorescence response of sensor **1** without and with Cd^{2+} ions as a function of pH. Experimental results showed that for the Cd^{2+}-free sensor **1**, under acidic conditions (pH < 7.0), an obvious increase of the emission spectra was observed with the decrease of pH from 7.0 to 4.5, which was attributed to the inhibition of the PET (photoinduced electron transfer) process. In a pH range from 7.0 to 13.5, almost negligible fluorescence signal (excited at 525 nm) could be observed for the Cd^{2+}-free sensor **1**, suggesting that protonation of **1** takes place under neutral aqueous media in the ground state. Upon the addition of Cd^{2+} ions, there was a remarkable fluorescence enhancement of sensor **1** at different pH values. And the pH-control emission measurements revealed that sensor **1** could respond to Cd^{2+} ions in a pH range from 7 to 13.5 with little change of the fluorescent intensity, suggesting that sensor **1** facilitated the quantification of the concentration of Cd^{2+} ions in aqueous solution in a pH range from 7.0 to 13.5. In consideration of most samples for sensor **1** analysis of Cd^{2+} ions being neutral, the medium for Cd^{2+} ions quantification was then buffered at pH 7.2.

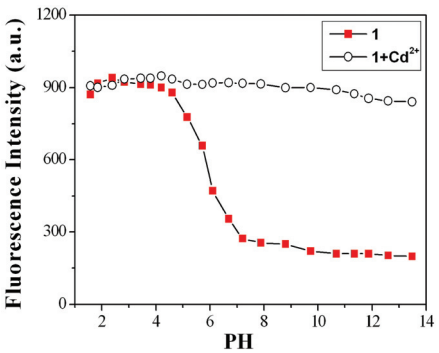


Fig. 1 Fluorescence intensity of sensor **1** in ethanol–water (1 : 10, v/v) with and without Cd^{2+} ions measured as a function of pH.

Cd^{2+}-titration and spectral responses

In order to gain an insight into the signaling properties of the sensor **1** toward Cd^{2+}, fluorescence titration was conducted. Fluorescence titration of the sensor **1** was investigated in ethanol–water (1 : 10, v/v) solution ([Cd^{2+}] = 0–2.0 × 10^{-6} mol L^{-1}, 0.1 M HEPES–NaOH buffer at pH = 7.2, λ_{ex} = 445 nm, λ_{em} = 525 nm). Upon addition of Cd^{2+}, about a 4-fold increase in fluorescence intensity was observed (Fig. 2b), but the absorbance at 445 nm did not change (Fig. 2a). When more than 1.0 equiv. Cd^{2+} was added, the maximum fluorescence intensity was retained. The reaction responsible for these changes reached completion well within the time frame (<30 s) of the measurement. Significantly, the enhancement of fluorescence intensity of sensor **1** corresponded to the concentration of Cd^{2+} in a linear manner (linearly dependent coefficient: R^2 = 0.9902) (Fig. 3c), which indicated that sensor **1** had potential use for the quantitative determination of Cd^{2+}. It should be noted that this switch on sensing process could be readily detected not only by fluorescence spectroscopy but also by the naked eye. As shown in Scheme 2 sensor **1** (5.0 × 10^{-5} M) alone exhibited very weak fluorescence, but gave a strong pale green fluorescence in the presence of Cd^{2+} (5.0 × 10^{-5} M). Moreover, a Job's plot, which exhibited a maximum at 0.5 mole fraction of sensor **1**, indicated the 1 : 1 stoichiometry between Cd^{2+} and sensor **1** (Fig. 3). Therefore, on the basis of 1 : 1 stoichiometry and fluorescence titration data, the association constant of sensor **1** with Cd^{2+} ions was found to be 2.4 × 10^7 M^{-1}, the detection limit was found to be 5.2 × 10^{-7} mol L^{-1} (based on S/N = 3).

The response of sensor 1 to various metal ions

The selectivity is one of the essential requirements for a chemosensor to signal a specific species in a complex system. The fluorescence responses of the sensor **1** to various cations and its selectivity for Cd^{2+} were illustrated in Fig. 4. The fluoroionophoric behavior of sensor **1** was investigated in ethanol–water (1 : 10, v/v) solution ([sensor **1**] = 1 μM, [M^{n+}] = 1 mM, 0.1 M HEPES–NaOH buffer at pH = 7.14). As expected, sensor **1** showed a weak fluorescence in aqueous solution. Upon addition of different metal ions, only with Cd^{2+}, did sensor **1** show remarkable fluorescence enhancement (Fig. 4b), the absorbance at 442 nm did not change (Fig. 4a). Moreover, the Cu^{2+} induced a fluorescence decrease effect of sensor **1**, and a slight blue shift in the excitation maximum from 442 to 435 nm was observed. Fig. 5 explained the fluorescent excitation and emission changes of sensor **1** (1 μM) upon the addition of various concentrations of Cu^{2+} solutions (0–2.0 μM). Excitation spectra revealed a feeble blue shift with the gradual increasing of Cu^{2+} concentration, also the decrease of fluorescent emission intensity of sensor **1** corresponded to the concentration of Cu^{2+} in a linear manner (linearly

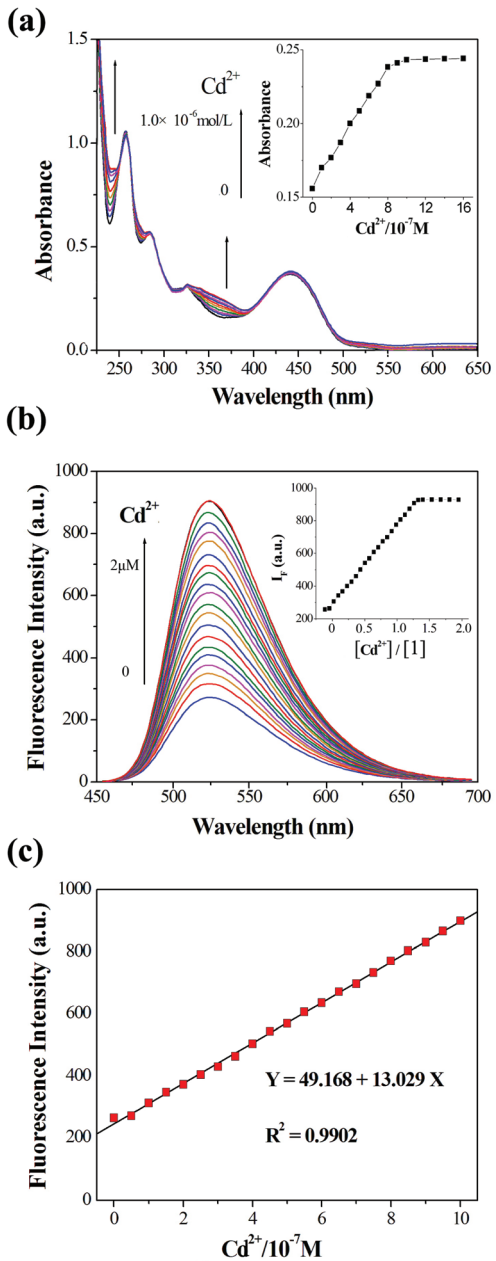


Fig. 2 UV spectra (a) and fluorescence spectra (b) of sensor **1** (1 μM) in the presence of increasing concentrations of Cd^{2+} (0–2 equiv.) in HEPES–NaOH (0.1 M) solution (ethanol–water = 1 : 10, v/v, pH = 7.14). Inset shows fluorescence intensity as a function of the molar ratio ([Cd^{2+}]/[**1**]). (c) Curve of fluorescence intensity at 525 nm of sensor **1** *versus* increasing concentrations of Cd^{2+}.

dependent coefficient: R^2 = 0.9984) (Fig. 5c). Therefore, on the basis of fluorescence titration data, the association constant of sensor **1** with Cu^{2+} ions was found to be 6.5 × 10^8 M^{-1}. Other representative metal ions, such as Na^+, K^+, Ca^{2+}, Mg^{2+}, Mn^{2+}, Ni^{2+}, Fe^{3+}, Cd^{2+}, Co^{2+}, Pb^{2+}, Zn^{2+} ions, particularly some metal ions like Hg^{2+} and Pb^{2+} induced very slight fluorescence enhancement, whereas Ni^{2+} and Ca^{2+} slightly quenched the fluorescence. However, when the concentrations of Hg^{2+} and Pb^{2+} solutions were lowered to 10^{-3} mol L^{-1}, these ions did not induce any obvious interference in fluorescence, which

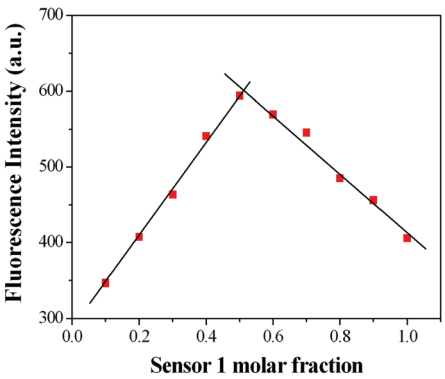
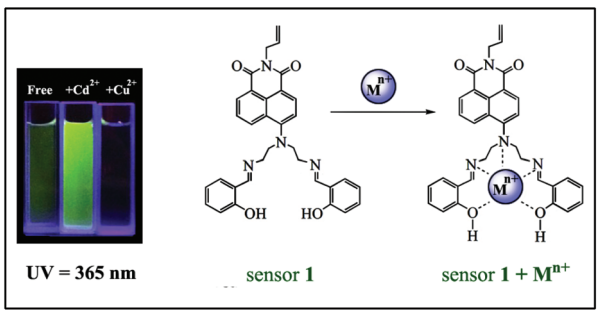


Fig. 3 Job's plot for sensor **1** (forms 1 : 1 complexes) in 0.1 M HEPES–NaOH solution (ethanol–water = 1 : 10, v/v, pH = 7.14). The total concentration of **1** and Cd^{2+} is 1 μM.



Scheme 2 The proposed binding mode of sensor **1**/Cd^{2+} system and aqueous solutions of sensor **1** with and without Cd^{2+} illuminated with a UV lamp at 365 nm ([**1**] = 1 × 10^{-6} mol L^{-1}; [Cd] = 1 × 10^{-6} mol L^{-1}).

were probably due to several combined influences cooperating to achieve the unique selectivity for Cd^{2+}.

^{1}H NMR spectroscopy of sensor **1**, **1**–Cd^{2+}, and **1**–Cu^{2+} in DMSO-d_6 was undertaken to determine the complexation mode of **1** for metal cations, which results in the excimer emission changes. The spectral differences are depicted in Fig. 6. Some significant spectral changes are observed in the ^{1}H NMR spectra on addition of both of the cations. For the aliphatic region, upon interaction with Cd^{2+}, H_1 (Fig. 6) on the receptor (*N*,*N*′-bis(salicylidene)diethylenetriamine) undergoes a downfield shift by 0.16 ppm to 3.04, the H_2 peak is shifted from 3.38 to 3.42 ppm. Similarly, in the presence of Cu^{2+}, the H_1 peak is downfield shifted by 0.03 ppm and the H_2 peak is downfield shifted by 0.16 ppm. These spectral changes suggest that both Cd^{2+} and Cu^{2+} are bound by the nitrogen atom of the receptor (*N*,*N*′-bis(salicylidene)diethylenetriamine). This putative binding mode is further elucidated by additional changes in the spectra which point to the metal being bound by the under part of the fluorophores with the aid of two phenol groups. In particular, the phenol-H_8 is downfield shifted by 0.10 and by 0.29 ppm with Cd^{2+} and Cu^{2+}, respectively, whereas the Ha peak proximal to the naphthalimides moiety does not undergo a significant change in the presence of the metal cations, further corroborating 1 : 1 complex formation

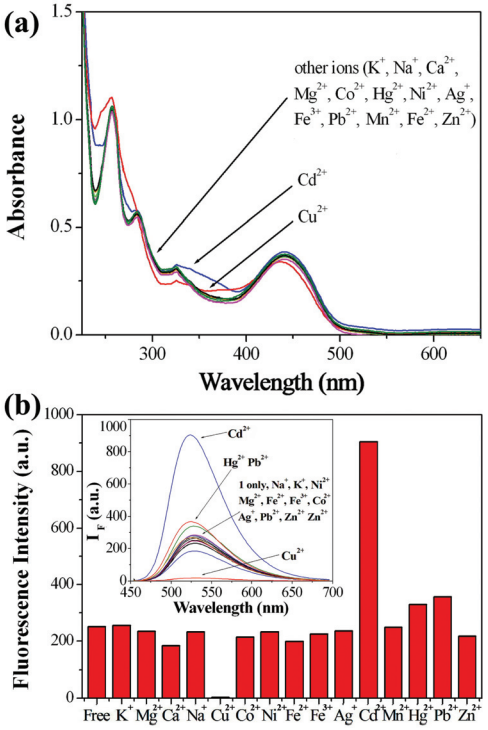


Fig. 4 (a) The absorption change and (b) the fluorescence intensity change profile of **1** (1 μM) to different metal ions (1 mM) in 0.1 M HEPES–NaOH solution (ethanol–water = 1 : 10, v/v, pH 7.14, λ_{ex} = 445 nm). Inset: corresponding fluorescent spectra of **1** in the presence of different metal ions.

that we have concluded based on the spectral titration profile. It is interesting to note that the extent of chemical shift change is in agreement with the association constants (Cu^{2+} > Cd^{2+}) calculated from the fluorescence spectrometry results suggesting that Cu^{2+} is likely to interact with the receptor of **1** more strongly than the Cd^{2+} cation.

The result of metal-ion competition experiments

In order to further test the interference of other common cations in the determination of Cd^{2+}, competition experiments were performed in which the fluorescent sensor was added to a solution of Cd^{2+} in the presence of other metal ions (Fig. 7). Experimental results indicated that these ions showed no obvious interference in the Cd^{2+} detection, but the enhanced fluorescence signal of the **1**–Cd^{2+} complex was obviously quenched with an increasing amount of Cu^{2+} (Fig. 7), which was contributed to a binding competition between Cu^{2+} and the **1**–Cd^{2+} complex.[18] Thus, the sensor **1** exhibited excellent selectivity toward Cd^{2+} and Cu^{2+}, which is its practical application.

Detection of Cd^{2+} in living cells

To further explore the potential biological application of this sensor, we explored the capability of the sensor **1** to track the change in Cd^{2+} levels in live MCF-7 (human breast cancer cells) and SH-SY-5Y (human neuroblastoma cells) cell lines. The live cell was first incubated with 5 μM sensor **1** (from

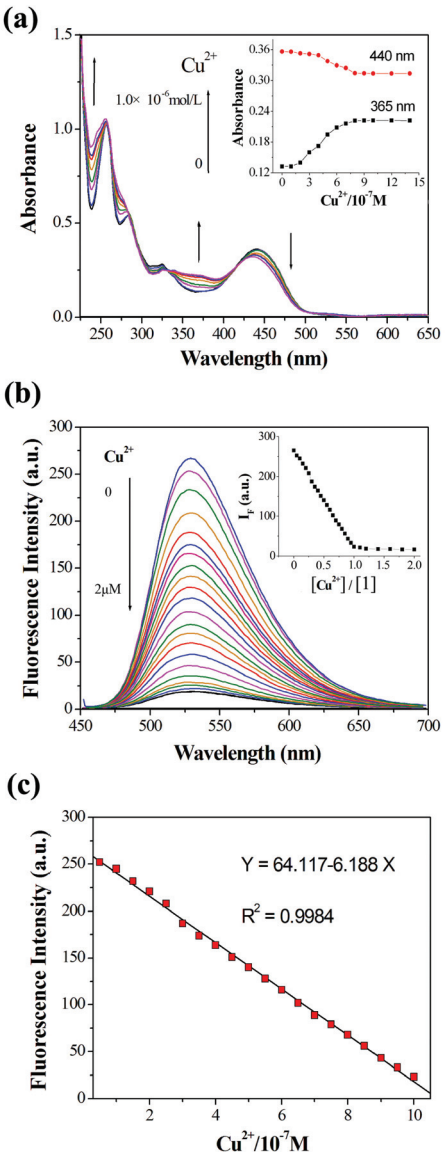


Fig. 5 UV spectra (a) and fluorescence spectra (b) of sensor **1** (1 μM) in the presence of increasing concentrations of Cu^{2+} (0–2 equiv.) in HEPES–NaOH (0.1 M) solution (ethanol–water = 1 : 10, v/v, pH 7.14). Inset shows fluorescence intensity as a function of the molar ratio ([Cu^{2+}]/[**1**]). (c) Curve of fluorescence intensity at 525 nm of sensor **1** *versus* increasing concentrations of Cu^{2+}.

1 mM solution in DMSO) for 30 min at 37 °C in 5% CO_2 atmosphere, then the cells were washed with phosphate buffered saline (PBS, pH = 7.4) 3 times, which was sufficient time for the intracellular accumulation of sensor **1** judging from its weak self-fluorescence inside a living cell (Fig. 8a and 8d). Moreover, no intracellular fluorescence was detected for cells supplementing cells with 10 μM $CdCl_2$ in the growth medium for 5 h at 37 °C. However, as shown in Fig. 8b and 8e, bright intracellular fluorescence was observed for supplementing cells with 10 μM $CdCl_2$ in the growth medium for 5 h at 37 °C and then staining with **1** under the same loading conditions. Fig. 8 displayed the fluorescence images for the two kinds of cells stained with the sensor before and after being

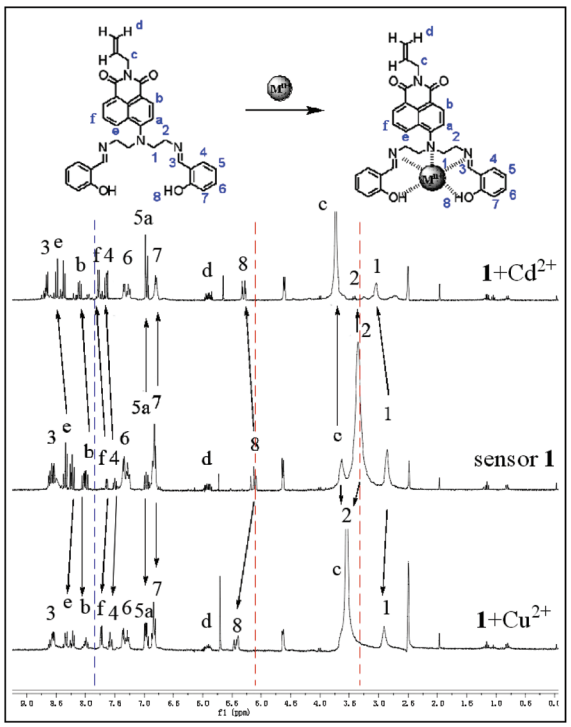


Fig. 6 The proposed structure for sensor **1** + metal ions, and ^{1}H NMR spectra of **1** (5 mM) in DMSO-d_6 and in the presence of $CdCl_2$ and $CuCl_2$ in a 1 : 1 ratio.

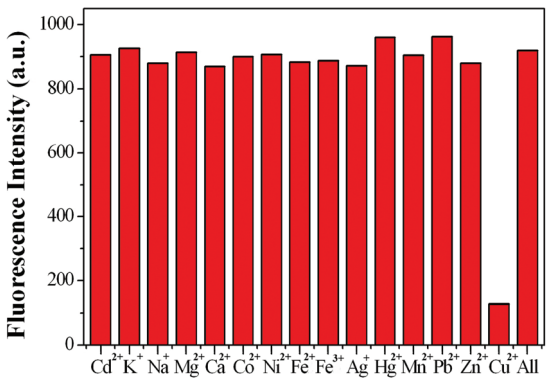


Fig. 7 The fluorescence intensity of **1** (μM) with 1.5 equiv. of Cd^{2+}, followed by 100 equiv. of M^{n+}. Conditions: 0.1 M HEPES–NaOH solution (ethanol–water = 1 : 10, v/v, pH = 7.14).

treated with Cd^{2+}. These facts implied that sensor **1** was membrane-permeable and could sense intracellular Cd^{2+} in living cells. The living cells image also demonstrated it could be a useful molecular probe for studying biological processes involving Cd^{2+} ions within living cells.

Conclusions

In conclusion, a simple naphthalimide-based fluorescent sensor **1** for detection Cd^{2+} has been developed, which displayed very high sensitivity and selectivity for Cd^{2+} over other

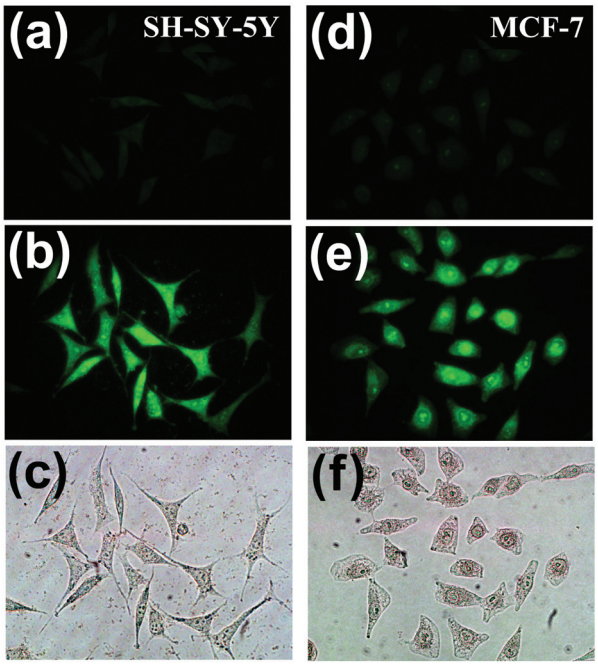


Fig. 8 Fluorescence microscope imaging of MCF-7 and SH-SY-5Y cells stained with 5 μM of sensor **1** before (a, d) and after (b, e) treating with 10 μM of Cd^{2+}. Bright-field transmission image of MCF-7 and SH-SY-5Y cells incubated with sensor **1** (1 ppm) are shown in (c, f).

trace transition metal ions and abundant cellular cations. Its fluorescence intensity enhanced in a linear fashion with the concentration of Cd^{2+} and thus can be used potentially for quantification of cadmium ions. Furthermore, the **1**–Cd^{2+} complex also behaves as a specific fluorescent sensor for Cu^{2+}. The selective Cd^{2+}/Cu^{2+}-induced OFF–ON–OFF type fluorescent signal control behavior described herein could prove useful in terms of constructing functional molecules switching systems. Moreover, the cell-permeable experiment showed it can indeed visualize the changes of intracellular Cd^{2+} in living cells. It can thus be predicted that the design strategy of cadmium-induced inhibition of the resonance process allows one to design new ratiometric sensors for other metal ions of biological interest.

Acknowledgements

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