

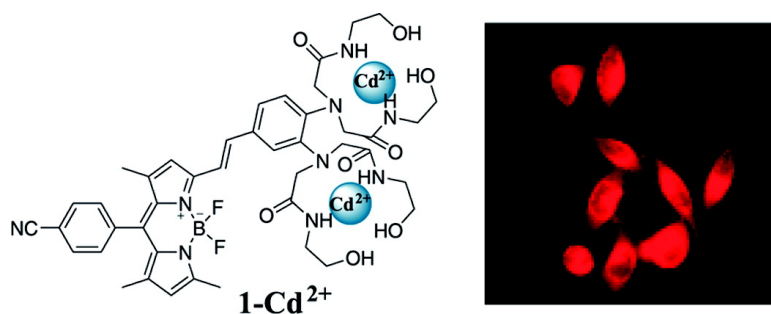
Communication

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A Highly Sensitive and Selective OFF-ON Fluorescent Sensor for Cadmium in Aqueous Solution and Living Cell

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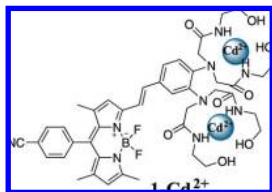
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As a result of its wide use in industry and agriculture, such as special alloys, nickel–cadmium batteries, and phosphate fertilizers, etc.,¹ the resulting high level of cadmium contamination in soil and corps has raised a great concern.² It causes serious environmental and health problems, including lung, prostatic, and renal cancers.³ Accordingly, facile techniques, enabling professionals to monitor cadmium temporally in the environment and in vivo, are of considerable significance.

Fluorescence is a powerful method to detect ions and neutral molecules owing to its operational simplicity and high sensitivity.⁴ The challenge in development of any fluorescent sensor is the induced signal change (e.g., intensity and/or emission wavelength) when a target specifically binds to the probe.⁵ Photoelectron transfer (PET)-based fluorescent sensor design has been successfully explored, which often induces alternation of fluorescence intensity. A number of such sensors have been reported including ions sensing,⁶ chemical warfare detection,⁷ and fluorescent labeling.⁸

Several methods such as atomic absorption⁹ and ICP (inductively coupled plasma) atomic emission spectroscopy¹⁰ have been employed to detect cadmium. Moreover, fluorescent sensors for the ion have also been disclosed recently; however, most of these available probes have poor selectivity between Cd²⁺ and Zn²⁺.¹¹ Peng and co-workers reported a selective sensor for Cd²⁺ which was detected in a mixture of aqueous acetone (1/9 v/v). Liu and colleagues described a water soluble cadmium sensor whose fluorescence intensity enhancement was only about 2.5-fold. Herein, we describe a novel highly selective and sensitive, based on PET mechanism, OFF–ON fluorescent Cd²⁺ sensor **1** in aqueous solution.



To obtain a truly highly sensitive and selective OFF–ON sensor for Cd²⁺ in aqueous solution with potential practical applications, we chose BODIPY as fluorophore because of its sharp absorption and fluorescence peaks, high stability, and high fluorescence quantum yield.¹² To minimize the background fluorescence of the free sensor, an electron withdrawing group of cyano was introduced^{8b,13} (Supporting Information, Figure S1) and water soluble polyamide similar to crown as the receptor was chosen to improve the solubility, selectivity, and sensitivity.

As designed, the free fluorescent probe **1** (see Supporting Information for its synthesis) in aqueous solution exhibited almost nonfluorescence (Figure S2). In addition, the sensor is relatively

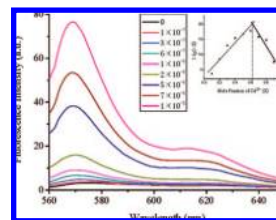


Figure 1. Emission spectra (excitation at 550 nm) of **1** (5 μM) in Tris-HCl (0.02 M) solution (containing 0.1 mM sodium phosphate, pH = 7.5) in the presence of Cd²⁺ (0–10 μM). Inset: Job's plot of **1**. The total concentration of sensor and Cd²⁺ ion was 5 μM . Excitation and emission slit widths were 5 and 2.5 nm.

inert to pH and it was found that no fluorescence intensity change was observed with pH > 3.

The fluorescent emission spectra were measured in physiological conditions (20 mM Tris-HCl solution containing 0.1 mM sodium phosphate, pH 7.5) with λ_{ex} :550 nm. Free **1** displayed very weak fluorescence (quantum yield: 0.003) because of the efficient PET quenching from polyamide to BODIPY fluorophore (Figure 1). When Cd²⁺ was added to the probe solution, a new absorption peak at 562 nm appeared, and the peak at 578 nm decreased, with an isosbestic point at 566 nm (Figure S3a). The fluorescence intensity at 570 nm significantly enhanced by about 195-fold and the quantum yield increased \sim 100-fold (up to 0.3) without change in wavelength (Figure S3b). Moreover, the sensor showed high sensitivity toward Cd²⁺ and a pronounced intensity increase was seen even with 6×10^{-7} M. More importantly, the enhancement of fluorescence intensity of **1** corresponds to the concentration of Cd²⁺ in a linear manner (linearly dependent coefficient: $R^2 = 0.99984$) (Figure S5). This indicated that sensor **1** can be potentially used to quantitatively detect Cd²⁺ concentration. A Job's plot indicated that **1** chelated Cd²⁺ ion with 1:2 stoichiometry (Figure 1). The association constants K_{11} and K_{21} were determined by a nonlinear least-squares analysis of fluorescence intensity versus Cd²⁺ ion concentration to be 7.2×10^3 and 1.3×10^5 (Figure S4).

The specificity of the probe **1** toward Cd²⁺ was determined next, as shown in Figure 2. Nearly no fluorescence intensity changes were observed in emission spectra with Zn²⁺, Pb²⁺, Cr³⁺, Fe³⁺, Cu²⁺, Hg²⁺, Ag⁺, Ba²⁺, Mg²⁺, Co²⁺, Cs⁺, Na⁺, K⁺, Ca²⁺ and Ni²⁺. However, under identical conditions, fluorescence intensity enhanced significantly in the presence of Cd²⁺. Moreover, notably, sensor **1** can readily distinguish Cd²⁺ from Zn²⁺ by both naked eye and fluorescence (Figure S6).

The competition experiments were also conducted for **1** (Figure 2). When 1 equiv of Cd²⁺ was added into the solution of **1** in the presence of 2 equiv of other ions, the emission spectra displayed a similar pattern at near 570 nm to that with Cd²⁺ ion only. Hg²⁺ induced very slight fluorescence enhancement, whereas Pb²⁺ and Cr³⁺ slightly quenched the fluorescence.

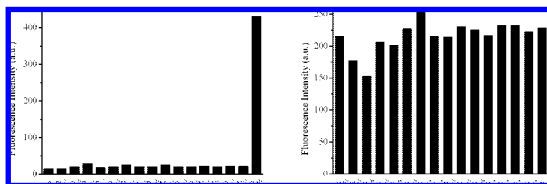


Figure 2. Left: The fluorescence intensity of **1** ($5 \mu\text{M}$) in the presence of different metal ions ($10 \mu\text{M}$); (right) the fluorescence intensity of sensor **1** ($5 \mu\text{M}$) at 570 nm with 2 equiv M^{n+} , followed by 1 equiv Cd^{2+} . In Tris-HCl (0.02 M) solution (containing 0.1 mM sodium phosphate, $\text{pH } 7.5$). Slit widths were 5 nm .

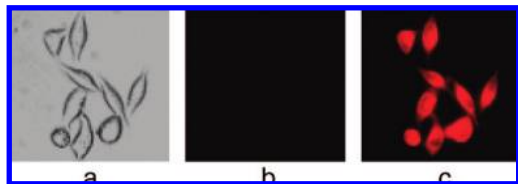


Figure 3. Fluorescent images of Cd^{2+} in HeLa cells. (a) Bright-field transmission image of HeLa Cells incubated with **1** ($5 \mu\text{M}$). (b) Fluorescence image of HeLa cells incubated with **1** ($5 \mu\text{M}$). (c) Fluorescence image of HeLa cells incubated with **1** for 30 min, washed three times, and then further incubated with $5 \mu\text{M}$ Cd^{2+} for 30 min.

To further demonstrate the practical application of the probe, we carried out experiments in living cells. Incubation of HeLa cells with **1** ($5 \mu\text{M}$) for 0.5 h at $37 \text{ }^\circ\text{C}$ was followed by the addition of Cd^{2+} ($5 \mu\text{M}$) and then was incubated for another 0.5 h . The enhancement of fluorescence was observed (Figure 3). The results suggest that sensor **1** can penetrate the cell membrane and can be used for imaging of Cd^{2+} in living cells and in vivo potentially.

Most reported fluorescent sensors containing BODIPY fluorophore are based on intramolecular charge transfer (ICT) mechanism^{11,14} with few exceptions.¹⁵ In our case, the high fluorescence intensity enhancement of sensor **1** might be due to the interception of PET process when binding to Cd^{2+} . The preliminary computational simulation study also revealed that the receptor twisted with the BODIPY fluorophore remarkably and resulting ICT was blocked.

In conclusion, we have developed a new fluorescent sensor **1** based on BODIPY fluorophore. It shows high sensitivity and selectivity toward Cd^{2+} in aqueous solution. The fluorescence intensity was significantly enhanced about 195-fold and the quantum yield increased almost 100-fold. Moreover, its fluorescence intensity enhanced in a linear fashion with concentration of Cd^{2+} and thus can be potentially used for quantification of Cd^{2+} . The living cell image experiments further demonstrate its value in the practical applications of biological systems.

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Supporting Information Available: Synthesis, experimental details, and additional spectroscopic data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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