ORGANIC
LETTERS

2008
Vol. 10, No. 17
3653−3656

Design of a Semirigid Molecule as a Selective Fluorescent Chemosensor for Recognition of Cd(II)

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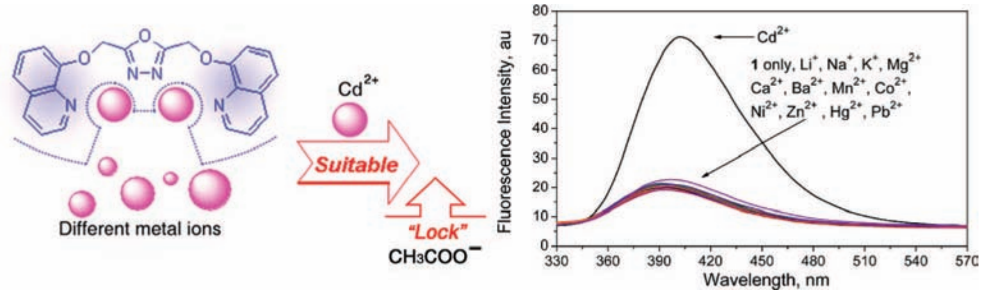
Received March 23, 2008

ABSTRACT



A new 8-hydroxyquinoline-based chemosensor possessing a semirigid structure was designed, and its fluorescent sensing behavior toward metalions was investigated. A prominent fluorescence enhancement only for Cd^{2+} was found in aqueous methanol solution. The results clearly suggest that the specific semirigid structure could selectively accommodate Cd^{2+} according to ionic radius, which would effectively suppress the intramolecular radiationless transitions from the $n\pi^*$ state to enhance the fluorescence response.

The development of selective chemosensors capable of effectively detecting the presence of transition-metal ions has received considerable current attention, mostly because these ions play important roles in living systems and have an extremely toxic impact on the environment.[1] Such sensors based on ion-induced changes in fluorescence appear to be particularly attractive due to their simplicity, high sensitivity, high selectivity, and instantaneous response.[2] Therefore, numerous excellent studies focus on the design of fluorescent chemosensors and the analysis of transition- or heavy-metal

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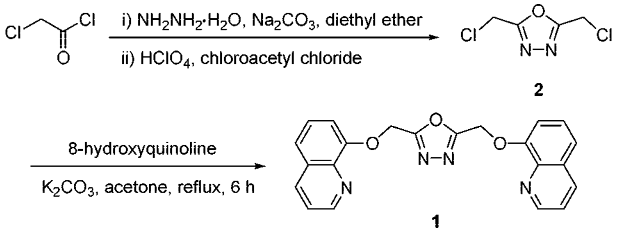
10.1021/ol801382f CCC: $40.75

ions such as Hg^{2+}, Pb^{2+}, and Cu^{2+}.[3] However, relatively few examples of fluorescent sensors for Cd^{2+} have been reported,[4] and though more research has developed rapidly in recent years.[5] It is well-known that cadmium is one of the important resources and is currently used in many processes such as electroplating, metallurgy, war industry, agriculture, etc.[6] These sources lead to cadmium exposure through various means, and there is evidence of increasing cadmium accumulation in food and organisms, which will pose severe harm for human health.[7] On the other hand, Cd^{2+} and some metal ions, especially Zn^{2+}, have many similar properties, thus it is difficult to discriminate between them.[4,5,8] Therefore, there is a great need for the design and synthesis of such chemosensors, which have high sensitivity and selectivity for detecting and monitoring Cd^{2+} by employing a simple response at physiological pH.

Based on our previous research on the recognition and separation of important metal ions,[9] it is necessary to choose an efficient fluorophore and consider the geometry of coordination sites for a certain cation. Herein, we describe a new and simple fluorescent Cd^{2+} sensor **1** based on the chelation-enhanced fluorescence (CHEF) mechanism. CHEF is an attractive design principle for developing luminescent chemical devices, which combine the ability to recognize and respond to an external input mostly with mediation of photoinduced electron transfer (PET).[10] An important part within this application is to obtain a suitable semirigid structure. Upon complexation with a certain metal ion, a large CHEF effect is observed because the stable chelation abrogates the PET process from the electron-donating group to the fluorophore ("turn-on state"). In sensor **1**, we chose the 8-hydroxyquinoline derivative as the fluorophore due to its good photostability and strong ability to complex metal ions.[11] To take advantage of the 1,3,4-oxadiazole subunit containing lone electron pairs on N, the semirigid ligand could effectively chelate Cd^{2+} according to the ionic radius and limit the geometric structure of the complex.

Scheme 1. Synthesis of the Chemosensor **1**



The synthesis of **1** is described in Scheme 1. Compound **2** was first prepared according to the literature.[12] Compound **1** was then synthesized as a pale brown solid via a simple one-step reaction of **2** with 2 equiv of 8-hydroxyquinoline in good yield using anhydrous potassium carbonate in refluxing acetone (91%).

Sensor **1** should have weak fluorescence on the basis of the consideration that the N lone electron pairs in the 1,3,4-oxadiazole are brought into immediate proximity to the 8-hydroxyquinoline fluorophores, as a result of a radiationless process via the $n\pi^*$ state. This interpretation is supported by the fact that **1** in the aprotic solvent acetonitrile exhibits weaker fluorescence, with quantum yield (Φ) ca. 0.01 (Table S1, Supporting Information), which obviously differs from those highly fluorescent ether derivatives, for example, $\Phi = 0.5$ for 8-(benzyloxy)quinoline.[11] Further, in the protic solvent MeOH and mixed solvent 5% H_2O−MeOH, Φ of **1** are 1.24 times and 3.09 times greater than that in acetonitrile, respectively, due to the hydrogen bonding of the solvent to the N lone electron pairs. It weakens the intramolecular radiationless transitions from the $n\pi^*$ state and makes the emission maximum (λ_{em}) undergo a gradual red shift with increasing protonation by the solvent. Therefore, **1** appears to be a promising candidate for enhancing fluorescence emission upon binding suitable metal ions if their radiationless channel could be well blocked.

Fluorescent sensors based on electron donor/acceptor are usually disturbed by protons in the detection of metal ions, so it is necessary to consider excluding the pH effect and finding optimal sensing conditions. The response of **1** toward pH was investigated in 5% H_2O−MeOH mixed solvent in search of the "turn-off state" (Figure S1, Supporting Information). The emission peak of **1** is observed at ca. 397 nm at neutral pH, and no dramatic change is expected under alkaline conditions. However, under acidic conditions, increasing the acid concentration leads to a gradual decrease

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in the fluorescence intensity at ca. 397 nm and a gradual increase at ca. 480 nm. This is a red shift of the emission maximum of about 83 nm (Figure 1). The large change in fluorescence at acidic pH is due to the protonation of quinoline, which results in the structure change of **1** and produces the new emission at ca. 480 nm. For **1**, a pK_a of 4.10 ± 0.05 was determined from these changes. Therefore, this experiment enabled us to identify the conditions (near neutral pH) under which the metal-sensing ability of **1** could be probed.

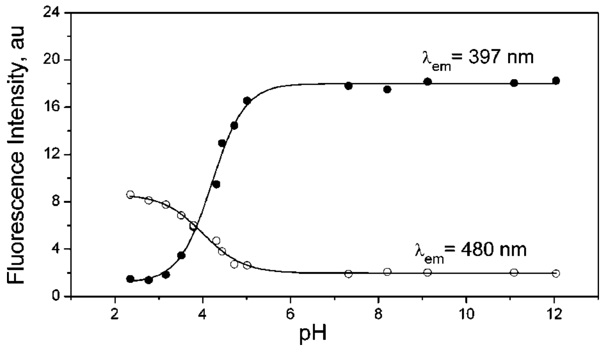

Figure 1. Plot of fluorescence emission at 397 and 480 nm of **1** versus pH in MeOH−H_2O (95:5, v/v). λ_{ex} = 302 nm, [**1**] = 2.5×10^{-5} M.

After systematically looking for selective signaling toward different metal ions for potential applications, the fluorescence measurements were carried out in 5% H_2O−MeOH solution at pH 7.0 ([**1**] = 2.5×10^{-5} M and [M^{n+}] = 2.5×10^{-3} M in HEPES buffer). As shown in Figure 2a, a clear fluorescence enhancement (ca. 2.1-fold) is observed with addition of Cd^{2+}, but no increase of fluorescent emission in the same conditions is detected with other metal ions Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Ba^{2+}, Mn^{2+}, Co^{2+}, Ni^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, and Pb^{2+} (as their Cl^- or NO_3^- salts). Moreover, the addition of Cd^{2+} causes a slight red shift of λ_{em} from 397 to 410 nm (Figure S2, Supporting Information). In this system, the binding constant log β is 5.2 ± 0.1 (Figure S3, Supporting Information) and Cd^{2+} could be detected at least down to 9.0×10^{-6} M by fluorimetric assay. In addition, fluorescence detection for all metal ions did not exhibit any appreciable time-dependent effects. ^{1}H NMR spectra of **1** and its complex system with Cd^{2+} in CD_3OD were measured as shown in Figure S4 (Supporting Information). Apparently, the signals for the methylene and heteroaromatic protons in the **1**−Cd^{2+} complex all shift to downfield in certain degrees in comparison to the ligand **1**. Furthermore, the competition experiments of Cd^{2+} mixed with the above-mentioned metal ions show that no significant variation is observed in fluorescence intensity and the **1**−Cd^{2+} system is stable (Figure 2b). To improve the sensitivity and magnify the selectivity, the anion responses to the detection systems were further investigated. The result indicates that only AcO^- can efficiently enhance the fluorescence intensity of **1**−$Cd(ClO_4)_2$ system over other anions such as F^-, Cl^-, Br^-, I^-, NO_3^-, or HSO_3^- (Figure S5 and S6, Supporting Information), and ca. 3.5-fold fluorescence enhancement can be observed (Figure 2a and Figure S7, Supporting Information). Moreover, this sensing for Cd^{2+} is also hardly interfered with by commonly coexistent ions (Figure 2b).

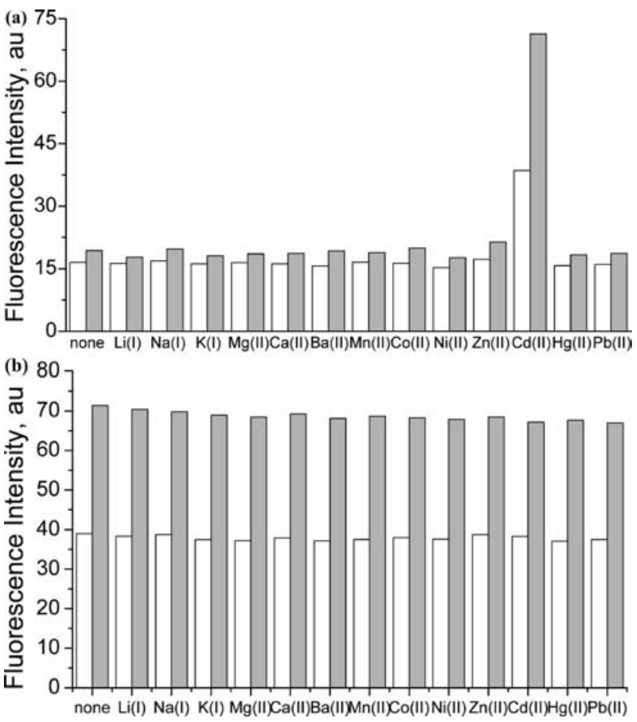

Figure 2. (a) Fluorescence enhancement of **1** at 410 nm in the presence of different metal ions in HEPES-buffered (10 mM, pH = 7.0) MeOH−H_2O (95:5, v/v). λ_{ex} = 302 nm, white bars, [**1**] = 2.5×10^{-5} M, [M^{n+}] = 2.5×10^{-3} M; black bars, [**1**] = 2.5×10^{-5} M, [M^{n+}] = 2.5×10^{-3} M, [AcO^-] = 5.0×10^{-3} M. (b) The fluorescence responses of **1** at 410 nm containing Cd^{2+} to different metal ions in HEPES-buffered (10 mM, pH = 7.0) MeOH−H_2O (95:5, v/v). λ_{ex} = 302 nm, white bars, [**1**] = 2.5×10^{-5} M, [Cd^{2+}] = 2.5×10^{-3} M, [M^{n+}] = 2.5×10^{-3} M; black bars, [**1**] = 2.5×10^{-5} M, [Cd^{2+}] = 2.5×10^{-3} M, [AcO^-] = 5.0×10^{-3} M, [M^{n+}] = 2.5×10^{-3} M.

To gain more insight into the chemosensing properties and mechanism of **1** toward Cd^{2+} ions, a fluorescence titration (Figure 3) and absorption titration (Figure S8, Supporting Information) with $Cd(ClO_4)_2$ in acetonitrile were carried out. In the fluorescence emission, free **1** exhibits a maximum at 384 nm. Upon the gradual addition of the $Cd(ClO_4)_2$ from 0 to 7 equiv, the λ_{em} undergoes a red shift to 410 nm. An isoemissive point at 375 nm and 2.5-fold fluorescence enhancement are also observed. The emission intensity at 410 nm (F_{410}, Figure S9, Supporting Information) and the intensity ratio, *R* (F_{410}/F_{360}, Figure S11, Supporting Information), increase upon the addition of Cd^{2+}, which allows the detection of Cd^{2+} by direct fluorescence and the ratiometric

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fluorescence method. From these sigmoidal curves, binding constant log β (8.9 ± 0.1) and log β' (8.7 ± 0.1) are obtained, respectively.[13] In addition, the absorption titration also shows small change in the spectral traces, indicative of the formation of a **1**−Cd^{2+} complex. Job's plots of fluorescence obtained for **1**−Cd^{2+} system in acetonitrile clearly suggest a formation of 1:2 stoichiometry (Figure 3, inset), which is also supported by fitting a Hill coefficient of 2 (1.9473 in Figure S10 and 2.0519 in Figure S12, Supporting Information).

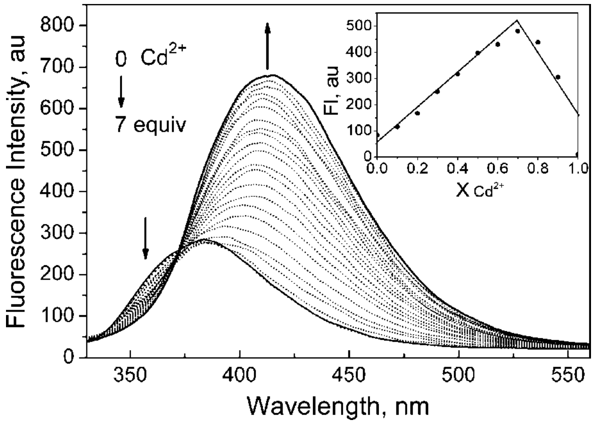

Figure 3. Fluorescence spectra of **1** in acetonitrile in the presence of increasing concentration of $Cd(ClO_4)_2$. λ_{ex}= 319 nm, [**1**] = 1.0 × 10^{-5} M. Each spectrum was acquired 2 min after Cd^{2+} addition. Inset: Job's plots according to the method for continuous variations, indicating the 1:2 stoichiometry for **1**−Cd^{2+} (the total concentration of **1** and Cd^{2+} is 20 μM).

However, compared with a fluorescence titration with Cd^{2+}, we also find that the λ_{em} of **1** undergoes a similar red shift and fluorescence enhancement uponaddition of $Zn(ClO_4)_2$ in acetonitrile (Figure S13, Supporting Information), which does not appear in aqueous methanol solution. This result indicates that the semirigid structure of **1** plays an important role in recognition of Cd^{2+}. In aprotic solvents, **1** can self-assemble with Cd^{2+} and Zn^{2+} to form complexes by modulating the flexible part despite different ion radii (0.74 Å for Zn^{2+}, 0.97 Å for Cd^{2+}). However, the complex of Zn^{2+} without suitable ion radius is easily disrupted by protic solvent molecules and the fluorescence of this complex is easily quenched because of solvent's O−H high energy oscillation. Accordingly, there is no obvious change for **1** in the fluorescence intensity upon addition of Zn^{2+} in protic solvents.

To understand the selectivity and the configuration of **1**−Cd^{2+}, we carried out density functional theory (DFT) calculations with B3LYP exchange functionals using the Gaussian 98 package. The 6-31G basis sets were used except for Cd^{2+}, where LANL2DZ effective core potential (ECP) was employed. The optimized configuration is shown in Figure 4, which shows that two Cd^{2+} ions well occupy the coordination centers of **1** and the whole molecule forms a planar structure. The Cd−O bond length is 2.25 Å, and the Cd−N bond lengths are 2.17 Å (Cd−$N_{quinoline}$) and 2.44 Å (Cd−$N_{oxadiazole}$), respectively. Based on these data, it is indicated that the design of semirigid structure can effectively create suitable space to better match corresponding ions and influence the emission of fluorophore itself with the help of protic solvent.

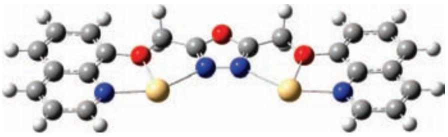

Figure 4. Calculated energy-minimized structureof **1** with Cd^{2+}.

In summary, we have designed and prepared an 8-hydroxyquinoline-based chemosensor possessing a semirigid structure and investigated its chemosensing properties. It was found that the selectivity experiment of this sensor for Cd^{2+} ion mostly relies on a specific space of the semirigid ligand, sensitive fluorophore, and suitable protic solvent. Compound **1**, with a specific semirigid framework, exhibits a selective coordinate with Cd^{2+} at pH 7.0 in H_2O−MeOH solution, which causes a CHEF effect by suppressing the intramolecular radiationless transitions from the nπ* state. The strategy will help us in the design of more chemosensors for some specific ions.

Acknowledgment. This study was supported by the NSFC (Grant Nos. 20771048, 20431010, 20621091, J0630962). We thank Dr. Wen-Hao Chen (Lanzhou University) for NMR measurements.

Supporting Information Available: Experimental details, characterization for the compound, and selected fluorescence data are reported. This material is available free of charge via the Internet at http://pubs.acs.org.

OL801382F