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Triazolyl-linked 8-Hydroxyquinoline Dimer as a Selective Turn-on Fluorosensor for Cd^{2+}

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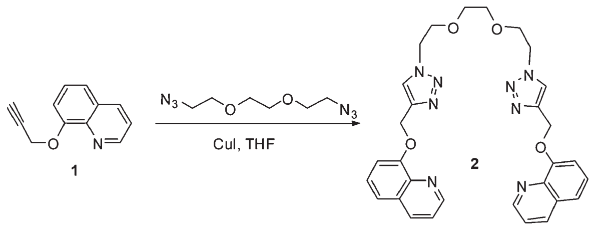
A novel 1,2,3-triazolyl-linked 8-hydroxyquinoline (8-HQ) dimer, as a selective turn-on fluorescent sensor for Cd^{2+} was efficiently synthesized from the "click" reaction and gave weaker fluorescence in protic solvents and water-based mixture solvent ($CH_3CN/H_2O = 5/95$, v/v). This sensor showed highly selective turn-on fluorescence for Cd^{2+} over Zn^{2+} within a broad pH range in aqueous solution ($CH_3CN/H_2O = 5/95$, v/v).

Fluorescent chemosensors have found wide application for the detection of various transition and heavy toxic metal ions, due to their simplicity and sensitivity.[1] Cd^{2+} is an environmental pollutant and has been widely used in nickel–cadmium batteries, special alloys, and phosphate fertilizers in industry and agriculture.[2] The high level of Cd^{2+} contamination in soil and crops causes serious environmental and health problems, including lung, prostate, and renal cancers.[3] Relatively few fluorescent chemsensors have been reported for Cd^{2+}, and most have interference from Zn^{2+}.[4,5] There is continuing research interest in the development of highly selective and sensitive analogs[6,7] that can distinguish Cd^{2+} from Zn^{2+}.

When sensitivity is considered, turn-on upon binding metal ions fluorescent sensors are more favorable. 8-Hydroxyquinoline (8-HQ) itself is weakly fluorescent due to excited-state intramolecular proton transfer (ESIPT) and has been used as a turn-on fluorescent sensor for various metal ions. However, the 8-HQ fragment lacks selectivity in binding to metal ions, and the incorporation of suitable binding scaffolds, most often the pyridine based tri- and tetradentate ligands, to 8-HQ skeletal structure at C-2 and/or C-7 positions has been extensively explored.[4–8] In addition, some effort has been devoted to derivation at the 8-position oxygen of 8-HQ,[9–11] due to high fluorescent properties of the resultant 8-HQ ethers. For example, the fluorescence quantum yield of 8-methoxyquinoline in MeCN is 0.23.[10a] Thus the metal-ion-induced fluorescence enhancement is limited. Recently, Jiang[10] and Liu[11] have introduced acetophenone and lone-pair-electron-containing atoms adjacent to the 8-position oxygen, to quench the fluorescence of 8-HQ ethers via intersystem crossing (ISC) and radiationless processes.

Inspired by the fluorescence-quenching behavior of indoline and aniline derivatives in aqueous solutions,[12] herein, using a similarly specific solute–solvent interaction as the fluorescence-quenching pathway, we report a 8-HQ-ether-based selective turn-on fluorosensor for Cd^{2+} in aqueous solution ($CH_3CN/H_2O = 5/95$, v/v). Attracted to the wide application of Cu(I)-catalyzed "click" reactions[13] and the good coordination properties of the resultant 1,2,3-triazolyl moiety,[14] highly adaptable for synthetic variations, the triazolyl-linked 8-HQ dimer **2** was used for the study.



Scheme 1. Synthesis of compound **2**.

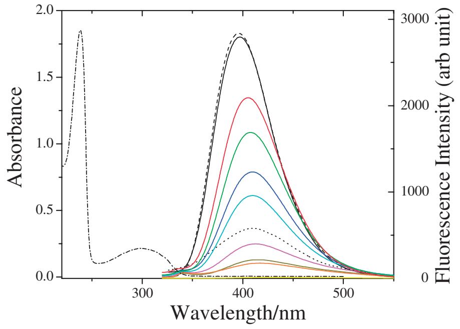


Figure 1. Representive absorption (10 µM in MeCN, dash-dot) and fluorescence spectra (1 µM, $\lambda_{ex} = 290$ nm) of compound **2** in organic solvent (black): CH_3CN (solid), CH_2Cl_2 (dash), MeOH (black); and in CH_3CN/H_2O binary solvent mixture (color): 90% (red), 60% (green), 50% (blue), 40% (cyan), 20% (pink), 10% (dark green), 5% (orange), and H_2O (yellow).

Compound **2** was synthesized in 53% isolated yield as shown in Scheme 1, from the Cu(I)-catalyzed cycloaddition compound **1**, generated in 72% yield by reacting 8-HQ with propargyl bromide in the presence of K_2CO_3 in acetone, with 1,2-bis(2-azidoethoxy)ethane[15] in THF at room temperature. Compound **2** was characterized by NMR and HRMS (see SI).[16]

Compound **2** showed two absorption bands at 238 and 298 nm (Figure 1) respectively, which are the sum of those of 8-methoxyquinoline and the 1,2,3-triazolyl moiety, indicating no ground-state interaction between these two moieties. The fluorescence emission of compound **2** was observed at 397 nm in CH_3CN, with fluorescence quantum yield (Φ) of 0.14 as summarized in Table S1,[16] similar to those of highly fluorescent 8-HQ ethers.[9–11] On the other hand, a much weaker fluorescence was observed in protic solvents, such as MeOH ($\Phi = 0.06$) and water ($\Phi = 0.01$). Similar results were observed in binary solvent mixture, CH_3CN/H_2O, with the increase of water content. For example, compound **2** gave weaker fluorescence ($\Phi =$

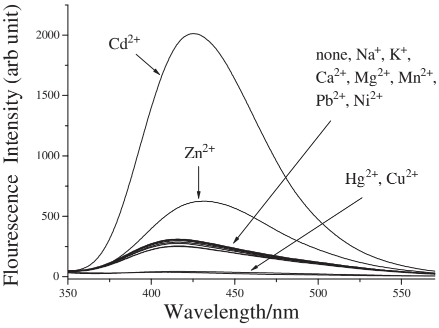


Figure 2. Fluorescence spectra of **2** (10 µM, $\lambda_{ex} = 290$ nm) and **2** (10 µM, $\lambda_{ex} = 290$ nm) in the presence of various metal ions (100 equiv of Na^+, K^+, Ca^{2+}, Mg^{2+}, Mn^{2+}, Pb^{2+}, Hg^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, and Cd^{2+}) in aqueous solution ($CH_3CN/H_2O = 5/95$, v/v).

0.017) in aqueous solution ($CH_3CN/H_2O = 5/95$, v/v) comparable to that in water. The fluorescence quenching observed in protic and water-based mixed solvent may be attributed to the increased rate constant of internal conversion resulted from the specific solute–solvent interaction, which provides an efficient excited-state-energy deactivation channel as described in the literature.[12]

Fluorescent sensors based on electron-donor/acceptor mechanisms, such as the chelation-enhanced fluorescence (CHEF) in our system, 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. Fluorescence response of compound **2** toward pH variation in the range of 4.5–11 was investigated in aqueous solution ($CH_3CN/H_2O = 5/95$, v/v) as shown in Figure S1. Compound **2** gave fluorescence emission at 417 nm at pH values above 4.30 ± 0.05, and no dramatic change is observed under basic conditions. However, under acidic conditions, the increased acidity leads to a gradual decrease in the fluorescence intensity at 417 nm and a gradual increase at 492 nm. This is a red shift of the emission maximum of about 75 nm, which may be due to the protonation of quinoline.[11]

The weak fluorescence of compound **2** observed in binary solvent, CH_3CN/H_2O, over a broad pH range may provide a simple way for enhancing the sensitivity of 8-HQ ethers toward the desired metal ions. To test our hypothesis, the fluorescence responses of compound **2** toward a range of metal ions, including Cd^{2+} and Zn^{2+} were examined in aqueous solution ($CH_3CN/H_2O = 5/95$, v/v).

A large fluorescence enhancement (6.5-fold) was observed with addition of 100 equiv of Cd^{2+} with an 11-nm red shift of the emission maximum, while no significant spectral changes were observed under the same conditions with most of the metal ions studied as shown in Figure 2, except Zn^{2+} which also gave a clear fluorescence enhancement (2.0-fold) and Cu^{2+}/Hg^{2+} which quenched the fluorescence. Furthermore, competition experiments between Cd^{2+} and selected metal ions in aqueous solution ($CH_3CN/H_2O = 5/95$, v/v) showed no significant variation in fluorescence intensity as shown in Figure 3. When 100 equiv of Cd^{2+} were added into the aqueous solution of compound **2** in the presence of 100 equiv of the other metal ions, the emission spectra displayed a similar pattern to that with Cd^{2+} only. Interestingly, although the quenching of fluorescence was observed upon addition of Cu^{2+} and Hg^{2+} as described above, the subsequent addition of Cd^{2+} still lead to a slight enhancement of the fluorescence integration (by 1.3- and 1.8-fold for Cu^{2+} and Hg^{2+}, respectively) in comparison with that with compound **2** alone.

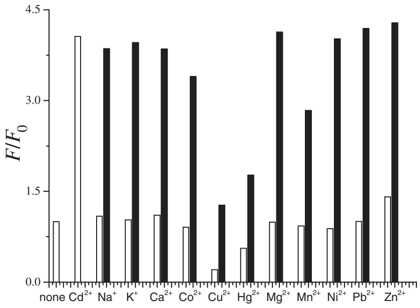


Figure 3. Metal ion selectivity profiles of **2** (5 µM): white bars, fluorescence of **2** alone and **2** in the presence of 100 equiv of Cd^{2+}, Na^+, K^+, Ca^{2+}, Co^{2+}, Cu^{2+}, Hg^{2+}, Mg^{2+}, Mn^{2+}, Ni^{2+}, Pb^{2+}, and Zn^{2+} ions; black bars, fluorescence of **2** in the presence of 100 equiv of various metal ions, followed by 100 equiv of Cd^{2+} (500 µM). All samples were measured in aqueous solution ($CH_3CN/H_2O = 5/95$, v/v) at 25 °C. Bars represented the final integrated fluorescence response (F) over the initial integrated emission of **2** (F_0).

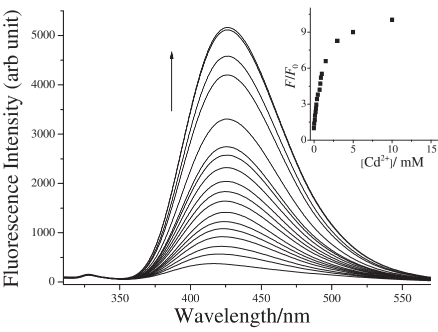


Figure 4. Fluorescence spectra of **2** (10 µM, $\lambda_{ex} = 290$ nm) upon the titration of Cd^{2+} (0, 5, 10, 15, 20, 25, 30, 40, 50, 70, 80, 90, 100, 150, 300, 500, 1000, and 2000 equiv) in aqueous solution ($CH_3CN/H_2O = 5/95$, v/v) at 25 °C. Inset: the ratio of integrated fluorescence (F/F_0) of **2** as a function of Cd^{2+} concentration.

Subsequently, a fluorescence titration of compound **2** toward various amounts of Cd^{2+} was performed as shown in Figure 4. It only requires 50 equiv of Cd^{2+} to induce a large (6-fold) increase of the fluorescence intensity with a red shift of the emission maximum from 416 to 427 nm. Further addition of Cd^{2+} (up to 2000 equiv) brings only the increase of fluorescence intensities with no further red shift of the spectra. A Job's plot as shown in Figure 5 indicated that compound **2** chelated with Cd^{2+} in a 1:1 stoichiometry, with an association constant (K) at $9.2 \times 10^3\,M^{-1}$ based on the Hill plot[17] result as shown in Figure S2.

Furthermore, in binary solution ($MeCN/H_2O = 95/5$, v/v), compound **2** showed a ratiometric fluorescence spectrum upon addition of Zn^{2+} with a 32-nm red shift of the emission maximum and an enhancement of the fluorescence intensity as shown in Figure S3; while it showed a decreased fluorescence

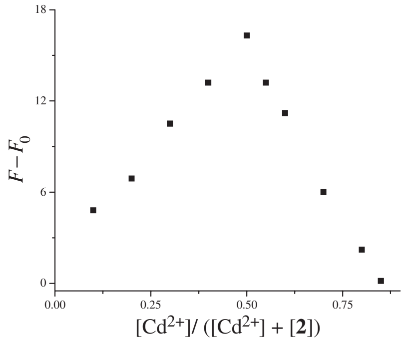


Figure 5. Job plot of changes in fluorescence intensity at 427 nm at varying mole ratio of **2** and Cd^{2+}, $[\mathbf{2}] + [Cd^{2+}] = 10\,\mu M$ in aqueous solution ($CH_3CN/H_2O = 5/95$, v/v) at 25 °C.

intensity with a 16-nm red shift of the spectrum upon addition of Cd^{2+} as shown in Figure S4. This result indicates that compound **2** may take different binding mode in chelating with Cd^{2+} and Zn^{2+}.

In summary, the application of the Cu(I)-catalyzed Huisgen cycloaddition reactions has efficiently generated a triazolyl-linked 8-HQ dimer **2**, which shows weaker fluorescence in protic solvent and water-based binary mixture solvent and gives a selective turn-on fluorescence to Cd^{2+} over a range of other metal ions, including Zn^{2+} in 5% aqueous CH_3CN solution over a broad pH range.

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