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A single fluorescent chemosensor for multiple target ions: Recognition of Zn^{2+} in 100% aqueous solution and F^- in organic solvent

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ABSTRACT

A structurally simple 2-((1-hydroxynaphthalene-2-yl)methyleneamino)acetic acid (**1**) was used as a turn-on fluorescent sensor for both Zn^{2+} and F^-. This receptor **1** showed a significant fluorescence enhancement in the presence of zinc ion over most other competitive metal ions in 100% aqueous solution. In particular, this chemosensor could clearly distinguish Zn^{2+} from Cd^{2+}. The spectroscopic studies suggested that the selective response to zinc ion involved the disruption of the internal charge transfer (ICT), and the inhibition of the C=N isomerization and the excited-state proton transfer (ESIPT). *In vitro* studies with fibroblasts showed fluorescence when sensor **1** and Zn^{2+} were present. The receptor **1** could also sense F^- selectively in DMSO. The fluorescence, UV–vis titration and ^1H NMR titration indicated that F^- ion enhanced the fluorescence of **1** through deprotonation.

1. Introduction

Zinc ion is one of the most abundant transition-metal ions present in living cells, owing to its rich coordination chemistry [1,2]. In addition to its well-described vital role in catalytic centers and structural cofactors of many Zn^{2+}-containing enzymes and DNA-binding proteins, it plays important roles in various biological processes such as apoptosis, regulators of gene expression, and neural signal transmitters or modulators [3–8]. However, the deficiency of zinc causes unbalanced metabolism, which in turn can induce retarded growth in children, brain disorders and high blood cholesterol, and also be implicated in various neurodegenerative disorders such as Alzheimer's disease, epilepsy, ischemic stroke, and infantile diarrhea [9,10]. Nevertheless, the mechanism of action of free zinc ion still remains poorly understood [11].

In the last decade, numerous scientific endeavors have focused on the development of fluorescent chemosensors for Zn ion [12–17] based on quinoline, anthracene, coumarin, BODIPY, and fluorescein fluorophores [18–33]. Some of them have well overcome the Zn^{2+} sensor's limitations such as low water-solubility, poor selectivity, and/or few with fluorescent enhancements [34–36], while others still confront the problems [37]. Moreover, there has been a challenge to develop chemosensors that can discriminate Zn^{2+} from Cd^{2+} because they are in the same group of the Periodic table and have similar properties [9,38]. Thus, a technique to trace and visualize free zinc ions would be highly demanded [39].

As the most electronegative atom, fluoride being the smallest anion with high charge density plays an important role in biological, medical and chemical processes [40–48]. Proper ingestion of fluoride can prevent and cure dental problems and osteoporosis. Hence, it is necessary to add fluoride to toothpaste and drinking water [49]. However, fluoride is absorbed easily by the body and excreted slowly from the body [50]. Therefore, the presence of excess fluoride ions resulted in dental and skeletal fluorosis, bone diseases, mottling of teeth, lesions of the thyroid, liver and other organs [51–57]. The U.S. Environment Protection Agency (EPA) has set a maximum contaminant level (MCL) of 4 mg L^{-1} (4 ppm or 211 μM) in drinking water, but many people still regularly drink the water containing fluoride above this level all over the world [58]. Hence, new probes for its powerful recognition and detection are necessary [46].

Quite recently, the development of fluorescence sensors for detection of analytes has made remarkable progress due to their immense analytical application in many areas including biology and chemistry [51]. Therefore, fluorescent chemosensors of single-ion responsive systems are common in the literature. In contrast, multi-ion responsive unimolecular systems are still rare [59],

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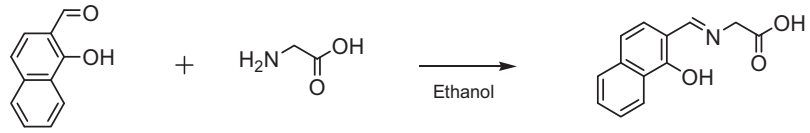


Scheme 1. The synthetic procedure for receptor **1**.

although their use has the advantages such as faster analytical processing and potential cost reductions [60].

With these considerations in mind, we sought out a chemosensor, which could be water-soluble, have an easy synthetic property, and sense both zinc ion and fluoride by fluorescence. Therefore, we found 2-((1-hydroxynaphthalene-2-yl)methyleneamino)acetic acid (**1**) with a hydroxynaphthalene group as chromogenic signaling subunit and a carboxylic group as a water-soluble subunit which shows a dual sensing property for Zn^{2+} and F^-.

Herein, we report that the receptor **1** has intense fluorescence in the presence of zinc ion in contrast to other metal ions in 100% aqueous solution, could distinguish Zn^{2+} from Cd^{2+} selectively, and sense Zn^{2+} ion in the cells for application to bioimaging. Moreover, receptor **1** can detect fluoride anion through the emission enhancement. The addition of fluoride to receptor **1** exhibits an unique 'turn-on' fluorescence with high selectivity in a DMSO solution.

2. Experimental

2.1. Materials and Instrumentation

All the solvents and reagents (analytical grade and spectroscopic grade) were obtained from Sigma-Aldrich and used as received. NMR spectra were recorded on a Varian 400 spectrometer. Chemical shifts (δ) are reported in ppm, relative to tetramethylsilane $Si(CH_3)_4$. Absorption spectra were recorded at room temperature using a PerkinElmer model Lambda 2S UV/vis spectrometer. Electrospray ionization mass spectra (ESI-mass) were collected on a Thermo Finnigan (San Jose, CA, USA) LCQTM Advantage MAX quadrupole ion trap instrument. Fluorescence measurements were performed on a PerkinElmer model LS45 fluorescence spectrometer.

2.2. Synthesis of 1

The receptor **1** was prepared by the condensation reaction of 1-hydroxy-2-naphthaldehyde with glycine according to the literature method (Scheme 1) [61]. To a ethanol (15 mL) solution of 1-hydroxy-2-naphthaldehyde (0.35 g, 2 mmol), two drops of HCl and glycine (0.15 g, 2 mmol) in ethanol (5 mL) was added slowly while being stirred vigorously. After 1 day, the solution was filtered and the filtrate was recrystallized with hexane. Yellow solid was filtered and dried (0.25 g, 56%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.79 (s, 1H), 8.28 (d, 1H), 8.13 (d, 1H), 7.61 (d, 1H), 7.55 (t, 1H), 7.37 (t, 1H), 7.03 (d, 1H), 6.69 (d, 1H), 4.37 (s, 2H). ESI-MS m/z $[M-H]^-$: calcd, 228.07; found, 228.07.

2.3. UV–vis and fluorescence studies of 1with various metal ions

Compound **1** (0.37 mg, 0.0016 mmol) was dissolved in buffer (10 mM HEPES, pH 7.4, 40 mL) to make concentration of 40 μM. Stock solutions (0.02 M) of the nitrate salts of Al^{3+}, Ca^{2+}, Cd^{2+}, Co^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Ga^{3+}, Hg^{2+}, In^{3+}, K^+, Mg^{2+}, Mn^{2+}, Na^+, Ni^{2+} and Zn^{2+} ions were prepared in buffer (10 mM HEPES, pH 7.4). 15 μL of the stock solutions (0.02 M) of the metal nitrate salts were transfered to 3 mL of compound **1** solution (40 μM) prepared above. After mixing them for a few seconds, the absorption and fluorescence spectra of **1** were taken at room temperature.

2.4. Fluorescence titration of 1

Compound **1** (0.73 mg, 0.0032 mmol) was dissolved in buffer (10 mM HEPES, pH 7.4, 80 mL) to make the concentration of 40 μM. $Zn(NO_3)_2$ (30.0 mg, 0.1 mmol) was dissolved in distilled water (D.W.; 5 mL). 3–54 μL of the zinc nitrate (20 mM) were added to each receptor solution (40 μM, 3 mL) prepared above. After mixing them for a few seconds, fluorescence spectra were taken at room temperature.

2.5. UV–vis titration of 1

Compound **1** (1.46 mg, 0.0064 mmol) was dissolved in buffer (10 mM HEPES, pH 7.4, 80 mL) to make the concentration of 80 μM. $Zn(NO_3)_2$ (30.0 mg, 0.1 mmol) was dissolved in D.W (5 mL). 1.7–51 μL of the zinc nitrate (20 mM) was added to each receptor solution (80 μM, 1.5 mL) prepared above. After mixing them for a few seconds, UV–vis spectra were taken at room temperature.

2.6. Job plot measurement

Compound **1** (0.73 mg, 0.0032 mmol) was dissolved in buffer (10 mM HEPES, pH 7.4, 40 mL) to make the concentration of 80 μM. 5, 4.5, 4, 3.5, 3, 2.5, 2, 1.5, 1 and 0.5 mL of the compound **1** solution were taken and transferred to vials. Zinc nitrate (0.97 mg, 0.0032 mmol) was dissolved in buffer (10 mM HEPES, pH 7.4, 40 mL) to make the concentration of 80 μM. 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5 and 5 mL of the zinc solution were added to each compound **1** solution. Each vial had a total volume of 5 mL. After shaking the vials for a few seconds, UV–vis spectra were taken at room temperature.

2.7. Quantum yield measurements

Fluorescence quantum yield was measured by using quinine hemisulfate monohydrate as a standard. Compound **1** (0.73 mg, 0.0032 mmol) was dissolved in buffer (10 mM HEPES, pH 7.4, 80 mL) to make the concentration of 40 μM. $Zn(NO_3)_2$ (30.0 mg, 0.1 mmol) was dissolved in distilled water (D.W.; 5 mL). Quinine hemisulfate monohydrate (21.7 mg, 0.05 mmol) was dissolved in 0.1 M H_2SO_4 (10 mL). UV–vis spectra of **1** (40 μM) were taken with and without $Zn(NO_3)_2$ (240 μM) in HEPES buffer (10 mM HEPES, pH 7.4, 3 mL). UV–vis spectra of quinine hemisulfate monohydrate (5, 10, 15, 20, 25 μM) were taken in 0.1 M H_2SO_4 solution. Fluorescence spectra of **1** (40 μM) were taken with and without $Zn(NO_3)_2$ (240 μM) in HEPES buffer (10 mM HEPES, pH 7.4, 3 mL) after being excited at 389 nm. Fluorescence spectra of quinine hemisulfate monohydrate (20.8, 33.1 μM) were taken in 0.1 M H_2SO_4 solution after being excited at 389 nm.

2.8. Cell test

The cell imaging test was carried out by the same method as our previous study [62]. Human dermal fibroblast cells in low passage were cultured in FGM-2 medium (Lonza, Switzerland) supplemented with 10% fetal bovine serum, 1% penicillin/streptomycin in the in vitro incubator with 5% CO_2 at 37 °C. Cells were seeded onto a 12 well plate (SPL Lifesciences, Korea) at a density of 2×10^5 cells per well and then incubated at 37 °C for 4 h after addition

of two different concentrations (500 and 5000 μM) of $Zn(NO_3)_2$. After washing with phosphate buffered saline (PBS) three times to remove the remaining $Zn(NO_3)_2$, the cells were incubated with 50 μM of **1** at room temperature for 30 min. Subsequent to washing of the incubated cells with PBS, the cells were observed by using a microscope (Olympus, Japan). The fluorescent images of the cells were obtained by using a fluorescence microscope (Leica DMLB, Germany) at the excitation wavelength of 515–560 nm. Fluorescence visualization of the cell viability previously exposed to the $Zn(NO_3)_2$ was performed with the live and dead viability/cytotoxicity kit for mammalian cells (Invitrogen, USA). After in vitro incubation and exposure to the $Zn(NO_3)_2$, a live and dead viability/cytotoxicity assay was prepared by adding 1.2 μL ethidium homodimer-1 (EthD-1) solution (2 mM) and 4 mM calcein AM solution (0.3 μL) into 600 μL PBS. After letting the cells react with the prepared assay solution for 30 min in the in vitro incubator, cell viability was observed by a fluorescence microscope (Leica DMLB, Germany), where the live cells were observed to be blue and the dead ones as red.

2.9. UV–vis and fluorescence studies of *1* with various anions

Compound **1** (0.37 mg, 0.0016 mmol) was dissolved in DMSO (160 mL) to make concentration of 10 μM. Stock solutions (0.10 M) of the tetraethylammonium salts of F^-, Cl^-, Br^-, I^-, OAc^- and CN^- anions were prepared in DMSO. 15 μL of the stock solutions (0.10 M) of the anions were transfered to 3 mL of compound **1** solution (10 μM) prepared above. After mixing them for a few seconds, the absorption and fluorescence spectra of **1** were taken at room temperature.

2.10. Fluorescence titration of *1* with F^-

Compound **1** (0.73 mg, 0.0032 mmol) was dissolved in DMSO (80 mL) to make the concentration of 40 μM. The stock solution (0.10 M) of the tetraethylammonium fluoride was prepared in DMSO. 6–96 μL of the tetraethylammonium fluoride (100 mM) were added to each receptor solution (40 μM, 3 mL) prepared above. After mixing them for a few seconds, fluorescence spectra were taken at room temperature.

2.11. UV–vis titration of *1* with F^-

Compound **1** (0.73 mg, 0.0032 mmol) was dissolved in DMSO (80 mL) to make the concentration of 40 μM. 1.2–66 μL of the tetraethylammonium fluoride (100 mM) were added to each receptor solution (40 μM, 3 mL) prepared above. After mixing them for a few seconds, UV–vis spectra were taken at room temperature.

2.12. NMR titration with F^-

Six NMR tubes of **1** (2.29 mg, 0.01 mmol) dissolved in DMSO-d_6 (0.5 mL) were prepared, and six different equiv (0, 1, 5, 15, 20, and 25 equiv) of the tetraethylammonium fluoride dissolved in DMSO-d_6 (0.5 mL) were added to **1** solution separately. After shaking them for a minute, their ^1H NMR spectra were taken.

3. Results

3.1. Spectroscopic studies toward Zn^{2+}

The fluorescence response of **1** toward various metal ions was investigated in the buffer solution (10 mM HEPES, pH 7.4) at room temperature. As shown in Fig. 1, receptor **1** alone has a very weak fluorescence emission with an excitation of 389 nm. The addition of various metal ions such as Ca^{2+}, Cd^{2+}, Co^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Hg^{2+}, In^{3+}, K^+, Mg^{2+}, Mn^{2+}, Na^+ to the solution of **1** exhibited no or small significant increase of the fluorescence. In contrast, the addition of Zn^{2+} resulted in a drastic enhancement (105-folds) of the emission intensity at 463 nm. In particular, the receptor **1** could selectively distinguish Zn^{2+} from Cd^{2+}. The fluorescence titration of compound **1** with Zn^{2+} was measured with an excitation at 389 nm for the quantitative study in buffer solution (Fig. 2). Upon the addition of Zn^{2+} to **1**, fluorescence intensity increased gradually and was saturated with 10 equiv of Zn^{2+}.

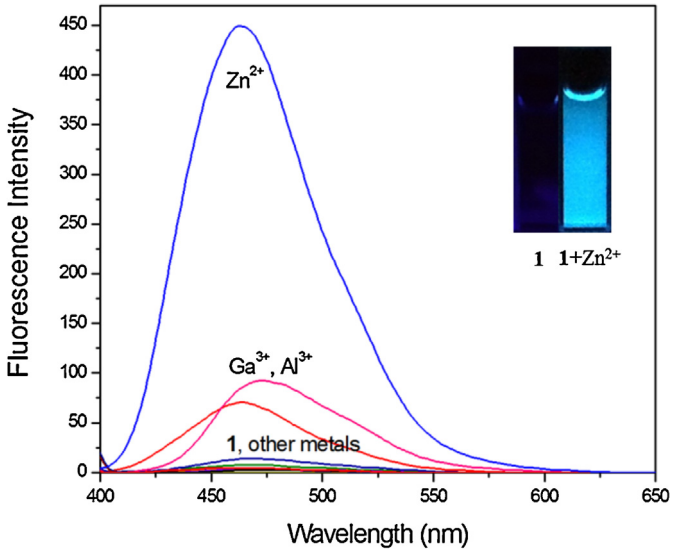


Fig. 1. Fluorescence spectra (λ_{ex} = 389 nm) of receptor **1** (40 μM) upon the addition of different metal ions (6 equiv) in buffer (10 mM HEPES, pH 7.4).

The interaction between **1** and Zn^{2+} was further investigated through UV–vis titration (Fig. 3). Upon the addition of Zn^{2+} ion to a solution of **1**, the absorption peaks at 270, 284, and 412 nm gradually decreased while the absorption intensities at 218 and 337 nm increased with blue shift. The clear isosbestic points were observed at 263, 274, 281, 311, 388 and 459 nm, which means that only one product was generated from **1** upon binding Zn^{2+} [63].

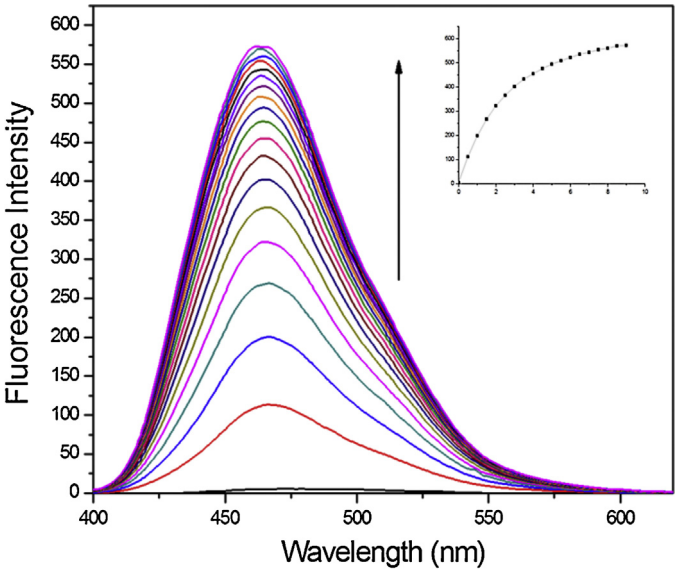


Fig. 2. Fluorescence spectra (λ_{ex} = 389 nm) of receptor **1** (40 μM) upon the addition of Zn^{2+} (0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, 8.5 and 9.0 equiv) in buffer (10 mM HEPES, pH 7.4).

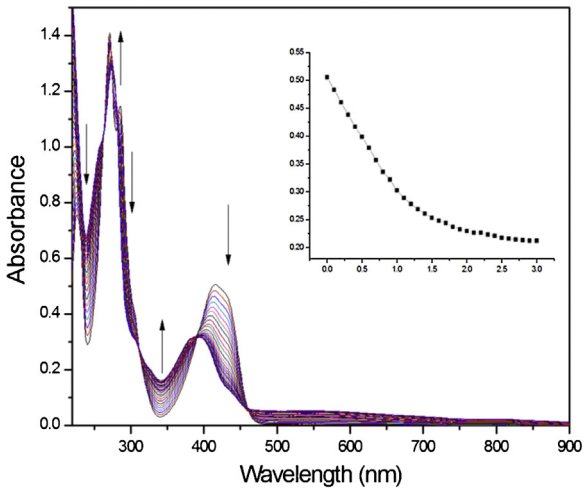
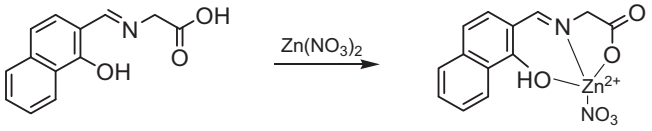


Fig. 3. UV–vis spectra of receptor **1** (40 μM) upon the addition of Zn^{2+} from 0.1 to 3.0 equiv in buffer (10 mM HEPES, pH 7.4).



Scheme 2. Proposed structure of **1**–Zn^{2+} complex.

In order to determine the binding mode between compound **1** and Zn^{2+}, Job plot analysis was carried out. As shown in Fig. S1, the Job plot showed a 1:1 complexation stoichiometry between **1** and Zn^{2+}. The binding mode was further confirmed by the ESI-mass spectrometry analysis (Fig. S2). The negative-ion mass spectrum of **1** upon addition of 1 equiv of Zn^{2+} showed the formation of **1** + Zn^{2+} + NO_3^- complex [*m*/*z*: 352.87; calcd, 352.98]. Based on Job plot and ESI-mass spectrometry analysis, we propose the structure of **1**–Zn^{2+} complex (Scheme 2).

From the result of UV–vis titration, the association constant of the **1**–Zn^{2+} complex was determined to be $1.25 \times 10^4\ M^{-1}$ by

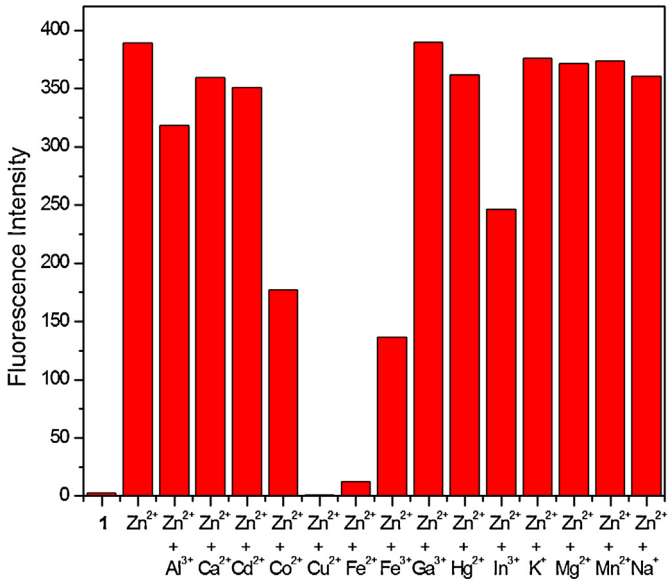


Fig. 4. Effect of competitive metal ions (240 μM) on the interaction between receptor **1** (40 μM) and Zn^{2+} ion (240 μM) in buffer (10 mM HEPES, pH 7.4).

Benesi–Hildebrand equation (Fig. S3) [64]. This constant is in the range of those (10^4–$10^{12}\ M^{-1}$) reported for Zn^{2+}-chemosensors [65]. The detection limit of receptor **1** for the analysis of Zn^{2+} ion was calculated to be 18.2 nM (Fig. S4). Furthermore, the quantum yields of **1** and **1**–Zn^{2+} complex in buffer were found to be 0.00432 and 0.30611, respectively.

To explore the ability of **1** as a fluorescence sensor for Zn^{2+}, the competition experiments were conducted in the presence of Zn^{2+} mixed with other relevant metal ions, such as Al^{3+}, Ca^{2+}, Cd^{2+}, Co^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Ga^{3+}, Hg^{2+}, In^{3+}, K^+, Mg^{2+}, Mn^{2+}, Na^+. When **1** was treated with 6 equiv of Zn^{2+} in the presence of the same concentration of other metal ions (Fig. 4), the coexistent metal ion had a small and negligible effect on the emission intensity of the complexation, except for Cu^{2+} and Fe^{2+}. Fe^{2+} inhibited about 90% of the fluorescence of **1**–Zn^{2+} complex and Cu^{2+} did completely. In particular, Cd^{2+} ion hardly inhibited the emission intensity of **1**–Zn^{2+}. These

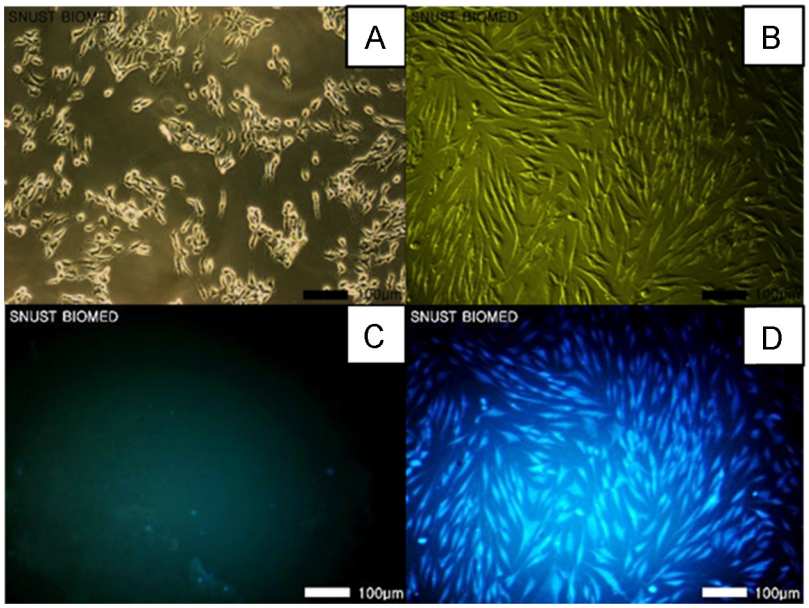


Fig. 5. Fluorescence images of fibroblasts cultured with Zn^{2+} and **1**. Cells were exposed to 500 (A and C) and 5000 (B and D) μM $Zn(NO_3)_2$ for four hours and then later with 50 μM **1** for 30 min. The top images (A and B) were observed with the light microscope and the bottom images (C and D) were taken with a fluorescence microscope.

Table 1
Emission properties of **1** in various solvents.

Solvent	λ_{ex}	λ_{em}
Buffer[a]	389	467
DMSO	409	463
MeOH	400	461
Toluene	400	459

[a] 10 mM HEPES, pH 7.4.

results indicate that **1** could be a good Zn^{2+} sensor which could distinguish Zn^{2+} from Cd^{2+} commonly having similar properties.

In order to understand the fluorescence enhancement of **1** in the presence of Zn^{2+}, the responsive mechanism was investigated. As shown in Scheme 1, compound **1** contains the naphthol and imine groups as a chromophore moiety. From this structure, the C=N isomerization could be considered as a responsive mechanism. It has been known that the C=N isomerization of the imine group is the predominant decay process of excited states in compounds

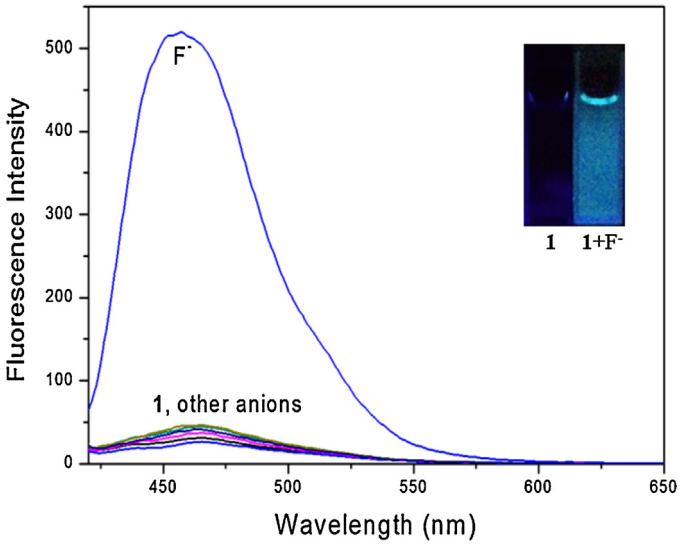


Fig. 6. Fluorescence spectra (λ_{ex} = 409 nm) of receptor **1** (40 μM) upon the addition of different anions (50 equiv) in DMSO.

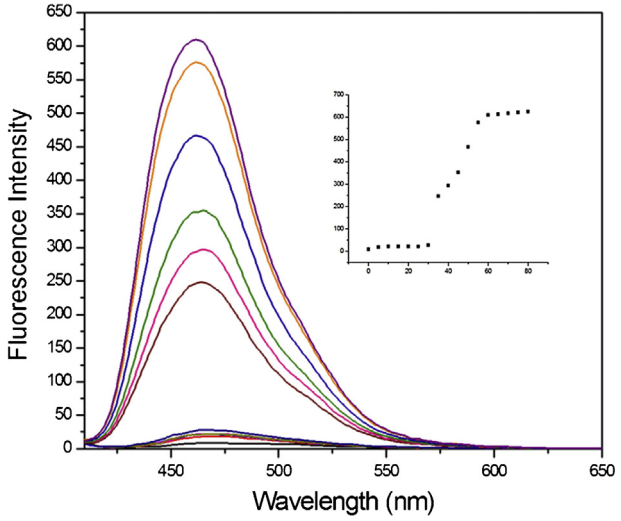


Fig. 7. Fluorescence spectra (λ_{ex} = 409 nm) of receptor **1** (40 μM) upon the addition of F^- (5.0, 10.0, 15.0, 20.0, 25.0, 30.0, 35.0, 40.0, 45.0, 50.0, 55.0 and 60.0 equiv) in DMSO.

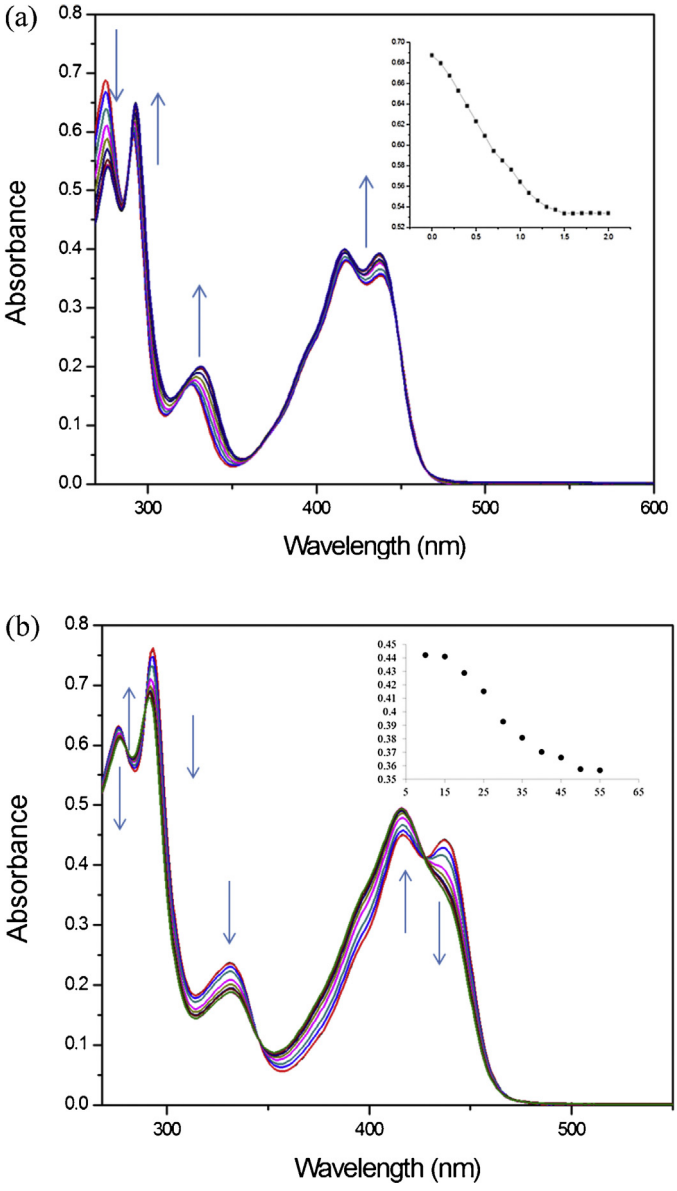


Fig. 8. UV–vis spectra of receptor **1** (40 μM) upon the addition of F^- in DMSO; (a) 0.1–2.0 equiv; (b) 10.0–55 equiv.

with an unbridged C=N structure, which usually result in non-fluorescence of chromophore. In contrast, compounds containing a covalently bridged C=N structure have been known to exhibit the fluorescence owing to the suppression of C=N isomerization in the excited states. Likewise, the binding of Zn^{2+} to **1** prevents the C=N isomerization, thus resulting in a dramatic increase of the fluorescence intensity [66]. In addition to the C=N isomerization, the strong intramolecular hydrogen bond between imine and hydroxyl moieties of the naphthol group in **1**, the excited-state proton transfer (ESIPT), could be also considered as an another responsive mechanism. Upon the stable chelation with Zn^{2+} ion, the ESIPT might be inhibited, resulting in increase of the fluorescence intensity of the **1**–Zn^{2+} complex [67].

We also considered the internal charge transfer (ICT) mechanism as the responsive mechanism for fluorescence enhancement of **1**–Zn^{2+} complex because the hydroxyl moiety of naphthol of **1** could provide electron pair to the naphthalene moiety of naphthol [68]. To investigate the ICT properties of **1**, we have checked the change of the emission spectra in polar and non-polar solvents such as buffer solution, DMSO, MeOH, and toluene, because it has

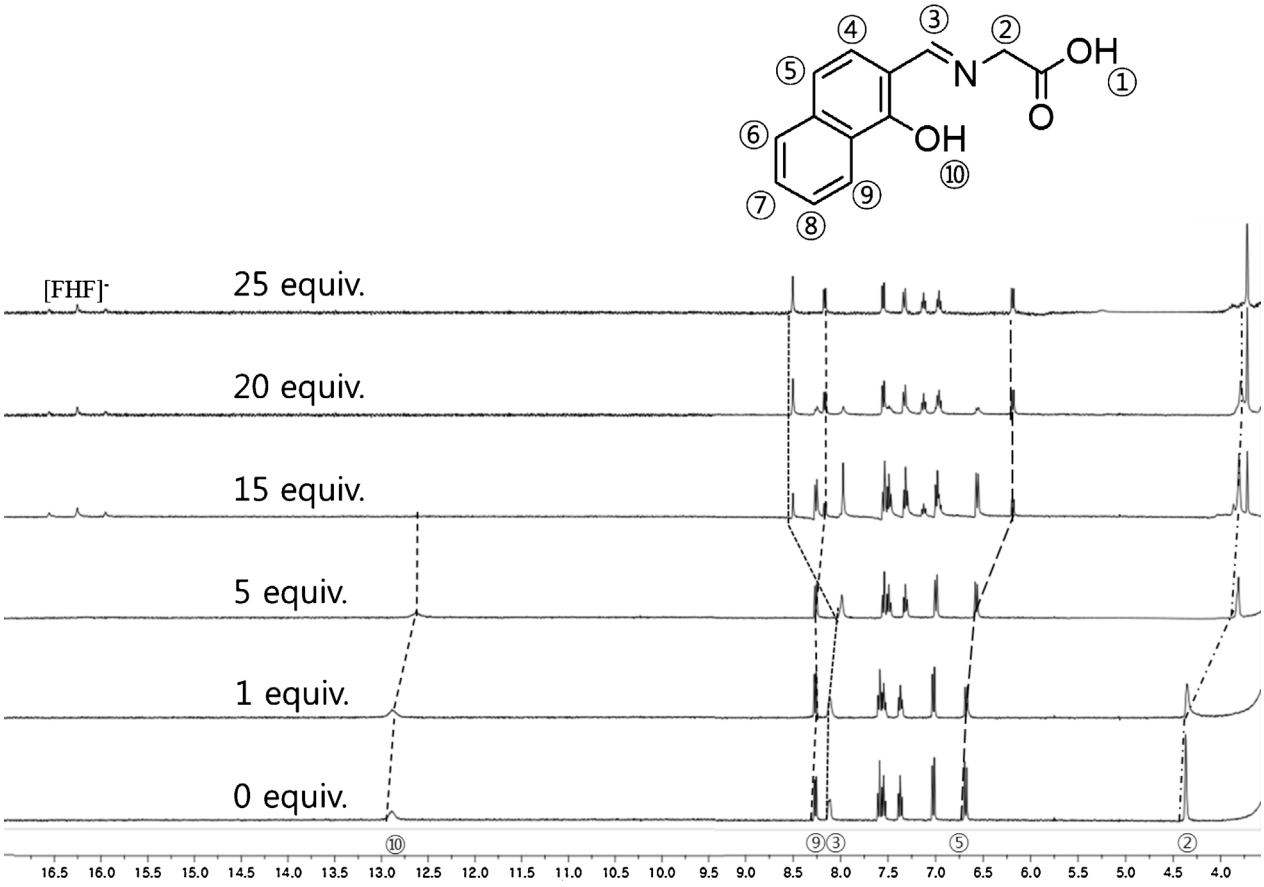


Fig. 9. ^{1}H NMR spectra of receptor **1** with F^- in DMSO-d_6: (a) only **1**; (b) **1** + F^- (1.0 equiv); (c) **1** + F^- (5.0 equiv); (d) **1** + F^- (15.0 equiv); (e) **1** + F^- (20.0 equiv); (f) **1** + F^- (25.0 equiv).

been known that the solvent dipoles can relax the ICT excited state in response to the charge separation, thus showing red-shifted fluorescence induced by polar solvents [69–71]. The emission spectra of compound **1** obtained in the various solvents are shown in Fig. S5 and summarized in Table 1. As shown in Table 1, the fluorescence spectra of **1** were red-shifted to the green region with increase of the solvent polarity. This solvatochromic behavior suggests the occurrence of ICT transition in compound **1** [69–71]. Therefore, the binding of Zn^{2+} to **1** induced the disruption of ICT, leading to the increase of the fluorescence intensity of the **1**–Zn^{2+} complex.

To examine the pH effect on the emission, the fluorescence intensity of compound **1** with Zn^{2+} was observed at various pH. The **1**–Zn^{2+} complex was very sensitive to the pH changes as shown in Fig. S6, and showed the highest emission between 7 and 10. The pH effect of the complex might be due to the deprotonation of the hydroxyl group coordinated to zinc ion as shown in the proposed structure (Scheme 2) [37]. At higher pH than 10, the complex might decompose, thus resulting in no fluorescence.

Based on pH dependence, we tested whether **1** could be used to visualize Zn^{2+} ion in biological system (Fig. 5). Adult human dermal fibroblasts were first incubated for 4 h after additions of two different concentrations (500 and 5000 μM) of $Zn(NO_3)_2$. The cells were exposed to **1** (50 μM) and then incubated at room temperature for 30 min before imaging. The Fibroblast cells cultured under the high concentration of zinc ion (5000 μM) with **1** exhibited fluorescence, while the cells cultured under the low concentration of zinc ion (500 μM) with **1** showed little fluorescence. These results indicate that **1** could be used to detect Zn^{2+} ion in cells.

3.2. Spectroscopic studies toward F^-

We have also examined the selectivity of a variety of anions toward **1** in various solvent systems, because the receptors with both the imine and phenol groups showed sometimes the sensing properties of anions [50,53–55]. Interestingly, **1** displayed the specific sensing ability to fluoride through fluorescence in DMSO at room temperature. As shown in Fig. 6, the receptor **1** exhibited a very weak fluorescence emission (λ_{ex} = 409 nm) in DMSO. The addition of some anions such as Cl^-, Br^-, I^-, OAc^- and CN^- to the **1** solution also showed no enhancement in the emission intensity. In contrast, the addition of F^- resulted in a remarkable increase (75-fold) of the fluorescence intensity at 462 nm. In order to study the binding interaction of **1** and F^-, the fluorescence titration experiments were performed (Fig. 7). The fluorescence intensity slightly increased up to 30 equiv of F^- and further addition of F^- from 35 to 60 equiv showed a progressive enhancement of fluorescence.

In order to further understand the interaction between receptor **1** and F^-, the UV–vis titration was performed (Fig. 8). Upon addition of F^- up to 2 equiv, the absorbance in the range of 289–470 nm increased while the absorption peak at 274 nm decreased with an isosbestic point at 289 nm (Fig. 8(a)). The addition of F^- from 2 to 10 equiv showed no change in absorbance. However, the addition of F^- from 10 to 55 equiv resulted in decrease of the absorption peaks at 275, 328 and 435 nm and increase of the absorbance intensities at 285 and 412 nm (Fig. 8(b)). The isosbestic points were observed at 279, 289, 342 and 425 nm. These results suggest that the proton of the carboxylic acid moiety might be eliminated with the addition of F^- up to 2 equiv, and next, the proton of the naphthol group be

also removed upon the further addition of 20 equiv of F^-. Therefore, the deprotonation of the naphthol group led to the significant enhancement in the fluorescence intensity.

From the Benesi–Hildebrand equation, the association constants were calculated to be 2.57×10^4 and $1.99 \times 10^3\ M^{-1}$ for the deprontonation of the carboxylic acid and the naphthol group, respectively. The detection limit was also determined to be 1.80 μM, based on the fluorescence titration measurement. This value is far below the guideline (211 μM) of the U.S Environment Protection Agency. In addition, the quantum yields of **1** and **1**–F^- in DMSO were found to be 0.00726 and 0.14790, respectively.

To examine the interaction behavior between receptor **1** and fluoride anion, the ^1H NMR titration of **1** was investigated in the absence and the presence of F^- in DMSO-d_6 (Fig. 9). Upon addition of 5 equiv of F^-, all protons of **1** were shifted to upfield due to deprotonation of carboxylic acid moiety. With the increasing of the fluoride concentration, the proton of hydroxyl group at 12.8 ppm disappeared and a new peak at 16 ppm appeared, indicating the formation of [HF_2^-] species [72]. This deprotonation also caused significant upfield shifts of the protons of naphthalene moiety, whereas the signal at 8.11 ppm gradually shifted to downfield due to through-space effects which polarize C–H bond in proximity to hydrogen bond, create partial positive charge on the proton, and cause a downfield shift [73,74].

4. Conclusion

We have reported a simple imine-based dual sensor **1** for Zn^{2+} and F^-. In particular, the receptor **1** has ability to detect Zn^{2+} ion selectively over competitive metal ions, especially Cd^{2+}, in 100% aqueous solution. Moreover, it showed a good sensitivity towards Zn^{2+} ion with nM-level detection limit in aqueous solution. The proposed mechanism of receptor **1** for detecting Zn^{2+} is based on the inhibition of C=N isomerization and the excited-state proton transfer (ESIPT), and the disruption of the internal charge transfer (ICT). In the practical application, *In vitro* studies with fibroblasts showed fluorescence in the presence of both sensor **1** and Zn^{2+}. The receptor **1** also detected F^- anion selectively in DMSO. Fluoride enhanced the fluorescence intensity of receptor **1** through deprotonation. The process of deprotonation consists of two steps, which are suggested through fluorescence and UV–vis titration experiments. This type of highly sensitive and selective fluorescent sensor will be useful for development of new chemosensors for multiple targets such as cations and anions.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.snb.2014.01.009.

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