Thiazole-based Orange-emitting Excited-State Intramolecular Proton Transfer Chemosensors for Selective and Ratiometric Sensing of Zn^{2+} Ions

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Received June 26, 2019, Accepted June 18, 2019, Published online September 16, 2019

Keywords: Chemosensor, Thiazole, Zn^{2+} ion, Excited-state intramolecular proton transfer, Specific binding

Investigation of highly sensitive and selective fluorescent materials for transition metal ions has attracted significant interest because of their important roles in biological and environmental importances.[1–3] Because the second most plentiful transition metal ion in human body, Zn^{2+} plays various critical roles in biological functions including neuronal signal transmission, enzymatic regulations, influencing DNA synthesis, and numerous cellular functions.[4,5] In this respect, sensitive and noninvasive technique to detect free zinc ions, which are spectroscopically silent due to its $3d^{10}$ electron configurations, is one of the important research areas.[6–8] However, most of the reported wavelengths of the chemosensors and their emissions are still lies in blue or green region, and only a few molecules showed red or orange emissions, which are better wavelengths in cellular bioimaging.[9–11]

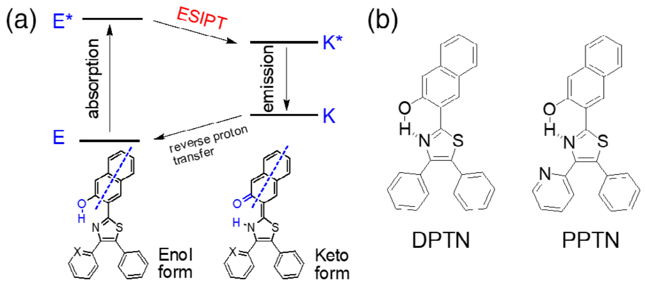
To generate bathochromic shifted emission, we have designed and synthesized novel class of excited-state intramolecular proton transfer (ESIPT) fluorescent molecules, 3-(4,5-diphenylthiazol-2-yl)naphthalen-2-ol (DPTN) and 3-(5-phenyl-4-(pyridin-2-yl)thiazol-2-yl)naphthalen-2-ol (PPTN). ESIPT is a fast enol (*E*)-to keto (K) phototautomerization which occurs in the excited states of intramolecularly hydrogen (H)-bonded molecules.[12] Because they are more stable in E forms in ground states and in K* forms in excited states, the ESIPT molecules have the characteristic four-level cyclic proton transfer processes (E → E* → K* → K → E) (see Scheme 1(a)). Therefore, an unusually large Stokes' shift without self-absorption is observed in ESIPT molecules.[13] Moreover, color tuning of ESIPT molecules is possible by the strategy known as a "nodal plane model", which introduces an arbitrary nodal plane to the molecule (see the dashed lines in Scheme 1(a)).[13]

According to the "nodal plane" strategy, in this work, thiazole-based novel ESIPT molecules, DPTN and PPTN, were designed and synthesized (Scheme 1(b)). The molecular structures were fully confirmed by ^1H NMR, ^{13}C NMR, and elemental analyses. A brief synthetic scheme was shown in Scheme 2 and the detailed experimental procedures were included in File S1 (Supporting Information).

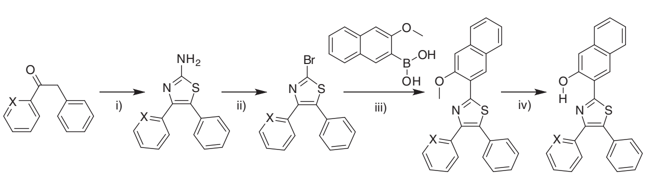
Both of the prepared molecules showed orange ESIPT emission at λ_{max} = 578 and 585 nm, respectively. For the selective sensing of the cation, pyridine was substituted instead of normal phenyl group. The presence of pyridine in **PPTN** molecule caused fluorescence enhancement at 585 nm because of selective binding with zinc ion. All the prepared molecules were soluble in a mixture of polar organic solvents and water, suggesting that they have a proper amphiphilic property due to the hydroxyl group as well as pyridine fragment.

The emission spectra of PPTN and DPTN, and their fluorescence evolutions, were recorded in EtOH/H_2O (9:1, v/v)-HEPES buffer solutions (20 mM, pH 7.4). In polar solvents, the PPTN and DPTN showed dual emissions of approximately 430 and 550 nm, which are originated from the enol (E) form and keto (K) form, respectively. As depicted in Figure 1(a), upon addition of zinc ion (Zn^{2+}) to the PPTN solution, emission at 578 nm was increased while the emission at 418 and 558 nm were decreased. However, other cations such as K^+, Na^+, Ba^{2+}, Cd^{2+}, Hg^{2+}, Ni^{2+}, Ca^{2+}, Cu^{2+}, Co^{2+}, Cr^{3+}, NH_4^+, Fe^{2+} showed no significant fluorescence enhancement at 578 nm compare to the initial state. According to the screening test for the PPTN molecule, the cations such as K^+, Ca^{2+}, Ni^{2+}, Hg^{2+}, Cu^{2+}, Cr^{2+}, and NH_4^+ quenched the fluorescence over approximately 553–578 nm region (see Figures S6 and S7). From the Job's plot analysis, PPTN displayed 1:1 stoichiometry with Zn^{2+} ion.

The same metal cation screening test was performed using DPTN at same condition. However, there was no significant change in fluorescence spectra of DPTN in contrast to the PPTN which showed bathochromic shifted emission from 558 to 578 nm. As shown in Figure 1(b), almost all of the fluorescence were similar at approximately 548 nm without any bathochromic or hypsochromic shifts compare



Scheme 1. (a) Schematic representation of the ESIPT photocycle. (b) Molecular structure of DPTN and PPTN.



Scheme 2. Synthetic routes for the ESIPT-based chemosensor molecules.

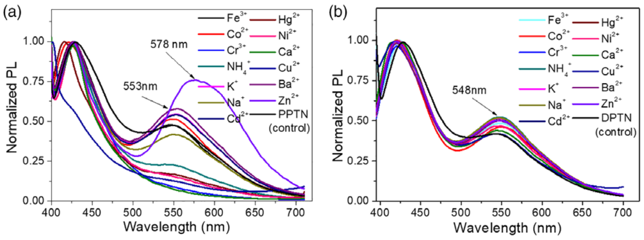


Figure 1. Emission spectra of (a) PPTN and (b) DPTN (10 μM) with various metal ions (100 μM) in EtOH/H_2O (9:1, v/v)-HEPES buffer (0.02 M, pH 7.4).

to the initial emission, which implies the metal cation binding is not effective with DPTN molecule and the pyridine unit in PPTN plays a critical role in Zinc ion binding. The characteristic fluorescence changes to the binding of Zn^{2+} can be ascribed to (a) deprotonation of naphtholic –OH and successive restriction of the ESIPT process, (b) prohibition of intramolecular charge transfer process, and (c) chelation-enhancement of fluorescence as a result of vibrational loss due to the rigid molecular conformation of the complex.[7,9]

Figure 2 shows absorption and emission spectra of PPTN during their fluorescence titrations. The titration was performed with an excitation wavelength of 360 nm in EtOH/H_2O (9:1) containing HEPES buffer (20 mM, pH 7.4) upon addition of Zn^{2+} ion at room temperature. PPTN showed absorption $\lambda_{max,abs}$ at 315 nm and fluorescent emission $\lambda_{max,ems}$ at 558 nm in the absence of Zn^{2+}, whereas in the presence of Zn^{2+} it revealed the absorption and emission bands at 244 and 578 nm, respectively. As a consequence of complexation with zinc ion, PPTN showed hypsochromic shift in absorption and bathochromic shift in emission spectrum. From the fluorescence titrations, the association constants were calculated as 4.7×10^5 M^{-1} for Zn^{2+}.

Moreover, PPTN showed ratiometric fluorescence change upon addition of zinc ion into the solution, buffered at pH 7.4. Also, due to the presence of pyridine ring, PPTN has significant changes in absorption and fluorescence emissions than DPTN upon addition of zinc ion. The colorimetric experiment was carried out with PPTN visualized by irradiation at wavelength 360 nm UV light and the optical response was measured by UV–Visible spectroscopy. Under the UV irradiation, the probe PPTN showed dramatic color change from colorless to fluorescent yellow orange according to addition of Zn^{2+} ion whereas the other metal ions did not show any significant color changes (Figures S5 and S7).

In summary, a novel ESIPT-based selective and ratiometric chemosensor for Zn^{2+} ion was developed in this work. The synthesized molecule, PPTN showed bathochromic shifted fluorescence ($\lambda_{max,ems}$ = 585 nm) due to the ESIPT process as well as extended conjugation by introduced naphthalene unit, which is known as nodal plane. Due to the deliberately introduced pyridine group, synthesized PPTN senses Zn^{2+} ion in aqueous ethanol system at pH 7.4, while the molecule without pyridine unit, 3-(4,5-diphenylthiazol-2-yl)naphthalen-2-ol (DPTN), shows no significant detection of Zn^{2+} under same conditions. The selective detection of Zn^{2+} ion using ESIPT-active fluorescent materials can provide a potential guideline in environmental or biological application-related sensor research.

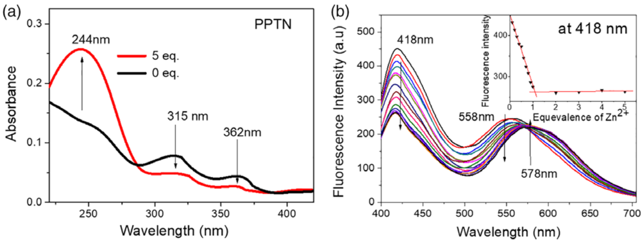


Figure 2. (a) Absorption change and (b) emission titrations of PPTN (20 μM) with Zn^{2+} in EtOH/H_2O(9:1.v/v) containing HEPES buffer (20 mM, pH 7.4) (λ_{ex} = 360 nm).

Acknowledgments. This work was supported by the grant from Kongju National University, South Korea.

Supporting Information. Additional supporting information is available in the online version of this article.

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