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Fluoride Triggered Fluorescence “Turn On” Sensor for Zn^{2+} Ions Based on Pentaquinone Scaffold That Works as a Molecular Keypad Lock

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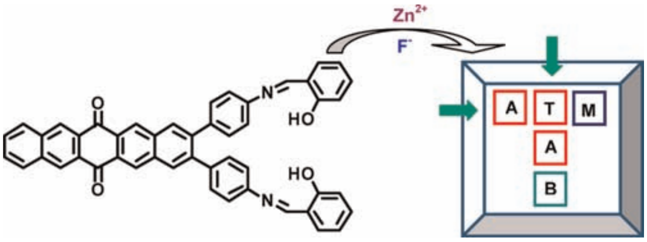
ABSTRACT



A pentaquinone based compound 3a has been synthesized which exhibits pronounced fluorescence enhancement in the presence of Zn^{2+} ions under a F^- triggered synergistic effect. Derivative 3a also behaves as a molecular keypad lock with sequential chemical inputs of Zn^{2+} and F^- ions.

Recently, fluorescent chemosensors for zinc ions have received wide attention because of vital roles played by zinc in numerous biological processes, including catalytic activity,[1] brain activity, gene transcription, immune function, and cellular transport,[2] and the lack of an adequate zinc level in the body may lead to a number of severe neurological diseases, developmental defects, and malfunctions.[3] Further, detection of zinc is also important for environmental safety as zinc is a harmful metal pollutant to the environment.[4] Thus, intensive efforts have been devoted to develop sensitive fluorescent sensors for detection of trace amounts of zinc ions in both biological and environmental systems[5] and a variety of chemosensors for zinc have been reported in the past.[6] However, most of them suffer from a turn off response, low detection limit, and cross sensitivity toward other heavy metal ions. Therefore, it remains a challenge to develop a sensitive chemosensor for Zn^{2+} ions with fluorescence enhancement exhibiting a high selectivity for Zn^{2+} ions over other metal ions.

Our research work involves the development of chemosensors for soft metal ions and evaluation of their logic behaviors for the construction of molecular switches and molecular level devices.[7] Recently, we reported a hexaphenylbenzene based derivative which showed fluorescence enhancement in the presence of Zn^{2+} ions and works as a multichannel keypad system by using Zn^{2+}, phosphate, and AMP as chemical inputs.[8] In continuation of this

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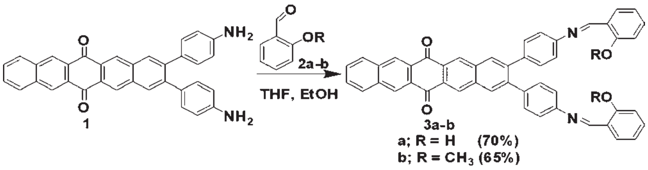
work, we have now designed and synthesized a new fluorescent chemosensor **3a** for Zn^{2+} ions based on a pentaquinone scaffold. Pentaquinone derivatives are a key precursor for the synthesis of solution processable acenes derivatives. However, their utility as a fluorescent sensor has not been explored yet, despite the fact that these derivatives emit at a higher wavelength. Derivative **3a** exhibits high sensitivity and selectivity toward Zn^{2+} ions as compared to other reported chemosensors for Zn^{2+} ions.[9] Derivative **3a** undergoes fluorescence enhancement ($\Phi = 0.23$) in the presence of zinc ions and, interestingly, exhibits more pronounced fluorescence enhancement ($\Phi = 0.80$) under a fluoride triggered synergistic effect. Such a pronounced response of a chemosensor toward Zn^{2+} ions under the F^- triggered effect has no precedent. Moreover, derivative **3a** mimics the functions of a security keypad lock on sequential addition of Zn^{2+} and F^- ions. To the best of our knowledge, this is the first report where a pentaquinone derivative senses zinc ions under the fluoride triggered synergistic effect and behaves as a molecular keypad lock with sequential chemical inputs of Zn^{2+} and F^- ions.

Scheme 1. Synthesis of Compound **3a**



The condensation of pentaquinone diamine **1**[10] with 2-hydoxybenzaldehyde **2a** in THF−ethanol furnished compound **3a** in 70% yield (Scheme 1). The structure of compound **3a** was confirmed by its spectroscopic and analytical data (Supporting Information (SI), Figures S1−S4).

The binding behavior of compound **3a** toward different cations (Zn^{2+}, Cu^{2+}, Hg^{2+}, Fe^{2+}, Fe^{3+}, Co^{2+}, Pb^{2+}, Ni^{2+}, Cd^{2+}, Ag^+, Ba^{2+}, Mg^{2+}, K^+, Na^+, and Li^+) as their perchlorate salts was investigated by UV−vis and fluorescence spectroscopy. The UV−vis spectrum of compound **3a** (5 μM) exhibits absorption bands at 298 and 350 nm and a shoulder at 414 nm ascribed to a pentaquinone moiety (SI, Figure S5). Upon addition of Zn^{2+} ions (0−10 equiv), the absorption band at 350 nm decreases slightly and the band at 414 nm increases slightly along with the formation of an isosbestic point at 390 nm. However, no significant variation in the absorption spectra was observed in presence of other metal ions (SI, Figure S6). The fluorescence spectrum of compound **3a** exhibits a very weak emission at 530 nm, when excited at 350 nm which is attributed to the very fast enol-imine to keto-amine tautomerism involving the phenomenon of excited state intramolecular proton transfer (ESIPT). To confirm the phenomenon of tautomerism, we also prepared compound **3b** in which the phenolic hydroxyl groups of compound **3a** were protected by methyl groups (SI, Figure S7). On excitation at 350 nm, the compound **3b** did not exhibit any band at 530 nm (SI, Figure S8). This result confirms the presence of an ESIPT phenomenon in compound **3a**. Upon addition of Zn^{2+} ions (0−2.0 equiv) to the solution of **3a**, a new emission band appeared at 496 nm which undergoes significant fluorescence enhancement (7.6-fold) along with the appearance of a green colored fluorescence (inset A Figure 1). This blue shift (34 nm) in fluorescence emission is attributed to the interaction between compound **3a** and the Zn^{2+} ion, which inhibits the enol-imine to keto-amine tautomerism and results in the appearance of a fluorescence emission at a shorter wavelength (496 nm). The emission intensity of compound **3a** increased linearly as a function of Zn^{2+} ion concentration as shown in inset B Figure 1. The fluorescence quantum yield (Φ_{fs}) of compound **3a** in the free state was found to be 0.03 and in the Zn^{2+}-bound state to be 0.23. Fitting the changes in the fluorescence spectra of compound **3a** with Zn^{2+} ions using the nonlinear regression analysis program SPECFIT[11] gave a good fit and demonstrated that 1:1 stiochiometry (host/guest) was the most stable species in the solution with the binding constant ($\log \beta$) = 4.81 ± 0.25. The method of continuous variation (Job's plot)[12] was also used to prove the 1:1 stiochiometry (SI, Figure S9). The binding of Zn^{2+} ions with receptor **3a** is also proved by mass spectroscopy (SI, Figure S10). The mass spectrum showed a peak at m/z 763.31 corresponding to the [**3a**−Zn^{2+}] complex which not only confirms the binding of Zn^{2+} ions with receptor **3a** but also proves the 1:1 stoichiometry of host and guest species. We also carried out ^1H NMR studies to prove the

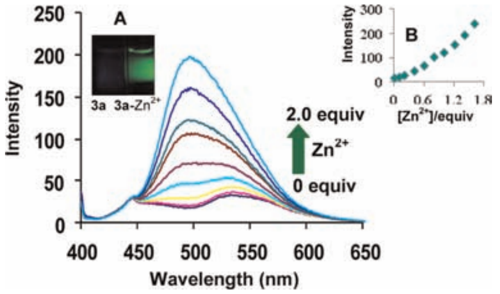


Figure 1. Fluorescence response of receptor **3a** (5 μM) on addition of Zn^{2+} ions (0−2.0 equiv) in THF; λ_{ex} = 350 nm. Inset: (A) fluorescence before and after the addition of Zn^{2+} ions; (B) change in the fluorescence intensity of receptor **3a** as a function of Zn^{2+} ion concentration.

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binding of compound **3a** with Zn^{2+} ions. On addition of Zn^{2+} ions to the receptor **3a**, broadening of the signal of the hydroxyl protons was observed which indicates interaction between Zn^{2+} and the oxygen atom of the hydroxyl group (SI, Figure S18). Under the same conditions as used above for the Zn^{2+} ions, we also tested the fluorescence response of receptor **3a** for other metal ions (SI, Figures S11–S12). No significant change in emission spectra was observed in the presence of other metal ions. To check out the practical applicability of receptor **3a** as a Zn^{2+} selective fluorescent sensor, we carried out competitive experiments in the presence of Zn^{2+} mixed with various metal ions (SI, Figure S12), no significant variation in the fluorescence intensity change was found by comparison with or without the other metal ions. Yet, compound **3b** which lacks phenolic hydroxyl groups did not exhibit any fluorescence enhancement in the presence of Zn^{2+} ions (SI, Figure S19).

In addition to cation binding properties, we also investigated the fluorescence behavior of compound **3a** toward different anions and biomolecules (CN^-, AcO^-, Cl^-, Br^-, I^-, NO_3^-, $H_2PO_4^-$, HSO_4^-, PPi^-, AMP, ADP, and ATP). Among the various anions and biomolecules tested, only the addition of F^- ions (0–20 equiv) slightly quenches the fluorescence emission of **3a**, indicating that the presence of F^- inhibits the ESIPT phenomenon (SI, Figure S13). This inhibition of the ESIPT phenomenon is ascribed to the intermolecular proton transfer from phenolic oxygen to F^- ions.

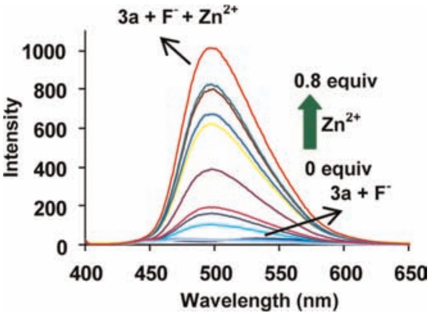

Figure 2. Fluorescence response of receptor **3a** (5 μM) + 20 equiv of F^- in THF with increasing amount of Zn^{2+} ions (0–0.8 equiv) in THF; λ_{ex} = 350 nm.

Since compound **3a** shows optical sensing toward Zn^{2+} and F^- ions in contrasting modes, we further investigated the "On–Off" switching process and sequence dependent emission output of **3a** using Zn^{2+} and F^- as chemical inputs. In the first sequence, when F^- ions were added to the solution of the **3a**–Zn^{2+} complex, the emission band at 496 nm undergoes fluorescence quenching (SI, Figure S14). This fluorescence quenching is due to the removal of Zn^{2+} from the **3a**–Zn^{2+} complex by F^- ions as the interaction between Zn^{2+} and F^- ions is stronger in comparison to Zn^{2+} and compound **3a**. However, in the reverse input sequence, the gradual addition of just 0.8 equiv of Zn^{2+} ions to the solution of **3a**–F^- led to the 31-fold fluorescence enhancement at 496 nm (Figure 2) in comparison to the 7.6-fold emission enhancement upon direct addition of Zn^{2+} ions to the solution of **3a**. This fluorescence enhancement is due to the fact that the initial addition of F^- ions results in the formation of a deprotonated species (SI, Figure S17). The deprotonated species then forms a strong complex with zinc ions leading to an increase in the rigidity of the system; as a result the nonradiative decay from the excited state becomes less possible, and consequently the emission intensity increases. The formation of deprotonated species is also confirmed by ^1H NMR studies wherein the hydroxyl protons completely disappeared on addition of F^- ions to the solution of compound **3a**. Subsequent addition of Zn^{2+} ions leads to broadening of the spectrum with a small shift in the imino protons. These ^1H NMR studies indicate that the binding is mainly through the oxygen atoms of the phenolic hydroxyl groups (SI, Figure S15). The fluorescence quantum yield of the F^- triggered **3a**–Zn^{2+} complex was found to be 0.80, which indicates the formation of highly fluorescent species. The detection limit of the F^- triggered **3a**–Zn^{2+} complex as a fluorescent chemosensor for the analysis of Zn^{2+} ions was found to be 30×10^{-9} mol L^{-1} which suggests high sensitivity as well as selectivity for Zn^{2+} recognition in the presence of F^- as a coexisting anion. We also tested the fluorescence response of receptor **3a** toward Zn^{2+} ions in the presence of other anions. No significant change in the fluorescence was observed in the presence of other anions except the CN^- ion which slightly triggers the fluorescence enhancement (Figure 3a; SI, Figure S16). To investigate the practical applicability of receptor **3a** as a Zn^{2+} selective fluorescent sensor in the presence of F^- ions, we studied the fluorescene behavior of derivative **3a** toward Zn^{2+} ions in the presence of 20 equiv of F^- ions mixed with 20 equiv of various anions (Figure 3b). These results show the chemosensing behavior of derivative

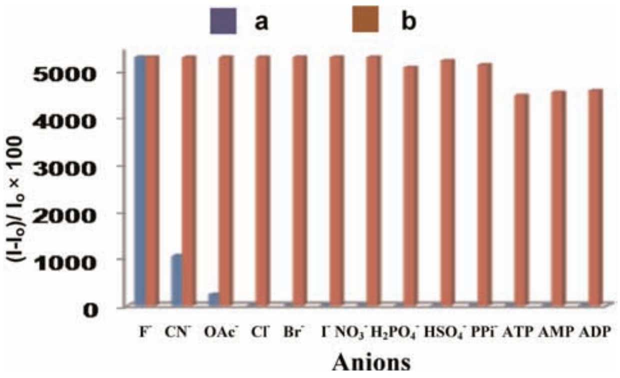

Figure 3. (a) Selectivity of receptor **3a** (5 μM) toward Zn^{2+} ions in the presence of various anions and biomolecules. (b) Competitive selectivity of receptor **3a** (5 μM) toward Zn^{2+} ions in the presence of 20 equiv of F^- ions mixed with 20 equiv of various anions and biomolecules in THF, λ_{ex} = 350 nm.

3a toward Zn^{2+} ions under F^- triggered conditions is not influenced by the presence or absence of other anions. We also carried out the fluorescence studies of compound **3a** toward various cations and anions in a mixed aqueous medium, but no significant change in the emission behavior was observed.

Recently, there has been a lot of interest in the development of molecular logic systems for the construction of molecular devices.[13] Different types of molecular devices such as moleculators, multiplexers, and demultiplexers have been reported in literature.[14] Most of the devices reported in literature were based on combinatorial logic circuits. However, present sophisticated digital electronic devices are based on sequential logic circuits i.e. circuits whose output depends upon both the inputs of the circuit and its previous state. In other words, we need circuits that have memory elements. The memory elements are devices capable of storing binary information. The binary information stored in the memory elements at any given time defines the state of the sequential circuit. The input and the present state of the memory element determine the output. All digital microprocessors are designed on such sequential systems. Thus, to meet the recent demands of digital electronics we need molecular systems which can store information. We recently reported two sequential molecular devices, molecular traffic lights and a molecular keypad lock which provide a way of protecting information at the molecular level.[15] In continuation of our research program to construct electronic devices at the molecular level, we examined our system as a molecular keypad lock.

To acquire a molecular keypad lock system based on Boolean arithmetic from the fluorescence behavior of **3a**, we envisaged Zn^{2+} and F^- as inputs. To simplify the input sequence as a password of the molecular keypad lock, inputs F^- and Zn^{2+} were designated as "**A**" and "**T**". When the input "**A**" was added first and followed by "**T**", the emission at 496 nm was in the "On" state and it created secret password "**ATM**" (**M** defines the On state); see Figure 4. Reversal of the input sequence, i.e. the first input is **T** and the second input is **A**, gave fluorescence quenching (Off, designated as letter **B**). Thus, the wrong password "**TAB**" fails to open the lock (Figure 4). Therefore, only the exact password "**ATM**" can open the lock, and such types of chemical systems may be applicable to protect information at the molecular level as it requires the correct order of inputs.

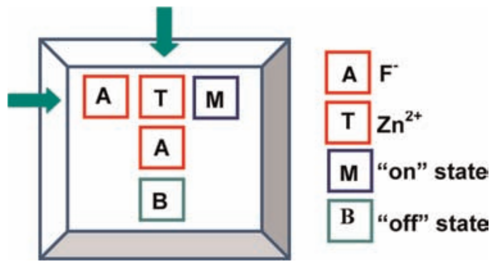

Figure 4. Molecular keypad lock to access a secret code at 496 nm.

In conclusion, we designed and synthesized a pentaquinone based fluorogenic receptor **3a** for Zn^{2+} ions. Derivative **3a** exhibits significant fluorescence enhancement in the presence of Zn^{2+} ions with a detection limit up to a nanomolar range under the F-triggered synergistic effect. In addition, derivative **3a** behaves as a molecular keypad with sequential chemical inputs of Zn^{2+} and F^- ions.

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Supporting Information Available. Experimental data and synthetic detail of compound **3a**–**b**. This materials is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

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