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A simple sensitive ESIPT on-off fluorescent sensor for selective detection of Al^{3+} in water†

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Junfeng Wang[a] and Yi Pang*[ab]

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A highly selective and sensitive fluorescent sensor for Al^{3+} has been developed. The sensor shows great fluorescence turn-on upon binding Al^{3+} in complete water, giving strong blue emission. In addition, the sensor's turn-on exhibits excellent selectivity to the Al^{3+} cation, with only a slight interference from Zn^{2+}. These findings suggest that the developed Al^{3+} sensor could be a useful molecular probe for practical applications.

Aluminum is the most abundant metal in the Earth's crust and extensively used in modern life.[1] The soluble form of aluminum (Al^{3+}), however, is highly toxic to plant growth.[2] Excessive aluminum, especially when deposited in the brain even in small amounts, has also been shown to be toxic to humans, and is believed to cause neurodementia such as Parkinson's disease, Alzheimer's disease and dialysis encephalopathy, osteoporosis, *etc.*[3] For these reasons, the development of Al^{3+} sensors for its facile detection is of great importance in both environmental monitoring and biological assays.

Despite the strong interest, the fluorescent detection for Al^{3+} cations remains to be a challenging problem. Owing to its weak coordination with ligands and strong hydration ability in water,[4] the detection of Al^{3+} cation is often affected by the existence of interfering metal ions. So far, very few fluorescent chemosensors have been reported for detection of Al^{3+} with moderate success to date compared to the transition metal ions.[5–25] The majority of the reported Al^{3+} sensors, however, have limitations such as tedious synthetic efforts and/or lack of practical applicability in aqueous solutions.[11] Today, almost all the reported dyes for Al^{3+} have been tested in organic solvents or mixed solvents. In order to enable evaluation of Al^{3+} ions in aqueous environments, it is highly desirable to develop new sensors, which not only recognize Al^{3+} ions selectively but also compete effectively with the strong hydration of Al^{3+} ion during the application in aqueous.

One option is to integrate the Al^{3+} binding event with the excited state intramolecular proton transfer (ESIPT) in the sensor design. Recently, ESIPT has attracted attention from both theoretical and experimental viewpoints, because it shows a uniquely large Stokes' shifted fluorescence emission (6000–12 000 cm^{-1}).[26] In addition, the ESIPT turn-on or turn-off events will usually lead to a large change in fluorescence wavelength,[27] which is of great importance in their practical applications. In general, the ESIPT process requires a proton donor (–OH, $–NH_2$) and a proton acceptor (–C═O, –N═) group in close proximity in order to form the intramolecular hydrogen bond (a necessary condition for ESIPT).[28]

In order to demonstrate the concept of using ESIPT in Al^{3+} sensing, we decide to explore the synthesis of Schiff base **1**. In the sensor design, the hydroxyl group in **1** forms an intramolecular hydrogen bond with the adjacent imine bond (–CH═N–), which gives ESIPT. The hydroxyl and adjacent "acetohydrazide" groups also provide a strong binding cavity to host the Al^{3+} cation. As a consequence, the new sensor integrates the following functions into a single molecule: (a) containing sufficient polar groups to improve water solubility; (b) including an amine group for photoinduced electron transfer (PET) effect to suppress the background signal; and (c) utilizing the Al^{3+} binding to switch the excited-state intramolecular proton transfer (ESIPT), thereby inducing a large spectral shift. Herein, we report the fluorescence response of sensor **1**, which exhibits remarkable fluorescence turned on (by ~73 fold) upon binding Al^{3+} ion. In addition, the Al^{3+} binding also induced a large spectral shift (by 40 nm) (Fig. 1), as the cation binding turned off the ESIPT.

Chemosensor **1** was synthesized in over 90% yield by simple coupling of 2-hydroxybenzaldehyde with acetohydrazide (**A**) (Scheme 1). Compound **1** could exist in the isomers **1a** and **1b**, whose ratio was dependent on the equilibrium in different solvents (See ESI Fig. S1–S3†). The structure of the major isomer

[a]*Department of Chemistry, The University of Akron, Akron, Ohio 44325, USA*
[b]*Maurice Morton Institute of Polymer Science, The University of Akron, Akron, Ohio 44325, USA. E-mail: yp5@Uakron.edu*

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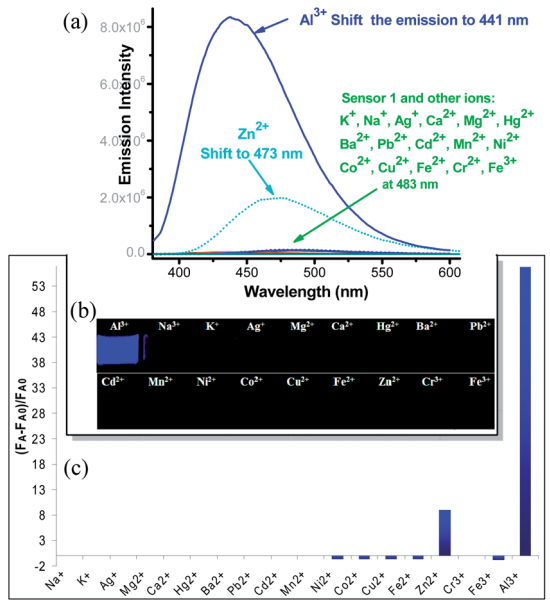
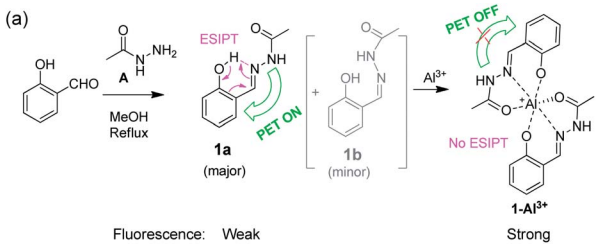


Fig. 1 (a) Fluorescent spectra of **1** (20.0 μM) with 5.0 equiv. of various metal ions in pure water: Na^+, K^+, Ag^+, Mg^{2+}, Ca^{2+}, Hg^{2+}, Ba^{2+}, Pb^{2+}, Cd^{2+}, Mn^{2+}, Ni^{2+}, Co^{2+}, Cu^{2+}, Fe^{2+}, Zn^{2+}, Cr^{3+}, Fe^{3+}. (b) Fluorescent images of **1** in the presence of different cations. (c) Change ratio ($(F_A - F_{A0})/F_{A0}$) of fluorescence of **1** (20.0 μM) in pure water containing various metal ions (5.0 equiv.): Na^+, K^+, Ag^+, Mg^{2+}, Ca^{2+}, Hg^{2+}, Ba^{2+}, Pb^{2+}, Cd^{2+}, Mn^{2+}, Ni^{2+}, Co^{2+}, Cu^{2+}, Fe^{2+}, Zn^{2+}, Cr^{3+}, Fe^{3+}, Al^{3+}.



Scheme 1 Synthesis of **1** and its Al^{3+} complex.

1a was determined by X-ray diffraction (ESI Fig. S14†). In aqueous, the free ligand **1** gave very weak green fluorescence (the emission $\lambda_{em} = 485$ nm, $\phi_{fl} = 0.01$), partly attributing to the PET effect from the amine. As expected, the emission of **1** exhibited a large Stocks' shift in water ($\Delta\lambda = 495$ (λ_{em}) − 317 (λ_{max}) ≈ 168 nm), as a consequence of ESIPT process. Upon addition of Al^{3+} cation, however, the solution gave bright blue fluorescence, with its quantum efficiency reaching as high as $\phi_{fl} = 0.73$ (Fig. 1a). In addition, the Al^{3+} binding also shifted the emission signal (around 40 nm shift from the weak green fluorescence to strong blue fluorescence), which could be used for naked eye detection (See Fig. 1a and b). Clearly, two "oxygen" and one "nitrogen" atoms in sensor **1** provided a strong Al^{3+} binding (*via* hard acid–base interaction) to compete with the Al^{3+} hydration, thereby allowing the reliable fluorescence turn-on in the aqueous solution.

The fluorometric behaviour of **1** was further investigated by addition of the other metal ions Na^+, K^+, Ag^+, Mg^{2+}, Ca^{2+}, Hg^{2+}, Ba^{2+}, Pb^{2+}, Cd^{2+}, Mn^{2+}, Ni^{2+}, Co^{2+}, Cu^{2+}, Fe^{2+}, Zn^{2+}, Cr^{3+}, and Fe^{3+} in pure water. As shown in Fig. 1a and c, the addition of 5.0 equiv. of Na^+, K^+, Ag^+, Mg^{2+}, Ca^{2+}, Hg^{2+}, Ba^{2+}, Pb^{2+}, Cd^{2+}, Mn^{2+} and Cr^{3+} has no obvious effect on the fluorescence emission. The metal ions Ni^{2+}, Co^{2+}, Cu^{2+}, Fe^{2+} and Fe^{3+} quenched the fluorescence. Although sensor **1** responded to Zn^{2+} cation with a slight increase in the fluorescent intensity, the emission wavelength of **1**-Zn was only shifted to 473 nm (around 10 nm blue shift). Therefore, sensor **1** is highly selective and sensitive for Al^{3+} detection, which makes it feasible for biological and environmental applications.

The absorption peak of **1** ($\lambda_{max} = 317$ nm) was progressively decreased upon addition of Al^{3+} (Fig. 2a), which was accompanied with a new band at about 352 nm. The large spectral bathochromic shift indicated the deprotonation, as a consequence of Al^{3+}-binding to phenol. Observation of the distinct isosbestic point at 333 nm suggests the complex formation with one new chemical species. On the basis of Job plot, the complex was assumed to have a ligand-to-metal ratio of 2 : 1. The assumption was supported by high resolution mass spectroscopy (HRMS), which detected *m*/*z* 381.1135, corresponding to $[2(\mathbf{1}\text{-}H^+)+Al^{3+}]^+$ (See Fig. 4: the calcd mass for $C_{18}H_{18}AlN_4O_4$: 381.1143). Furthermore, mass spectra detected no Al^{3+} complex with 1 : 1 ligand-to-metal ratio from the aqueous solution of **1** and Al^{3+} (ESI Fig. S5†).

The cation binding was further examined by ^1H NMR titration. The free ligand exhibited two imine (–CH=N–) signals at 8.25 and 8.15 ppm, corresponding to the major and minor isomers **1a** and **1b** respectively (Fig. 3). Upon addition of Al^{3+} cation, a broad imine signal was developed at 8.45 ppm, attributing to the formation of **1**-Al^{3+} complex. The triplet signal

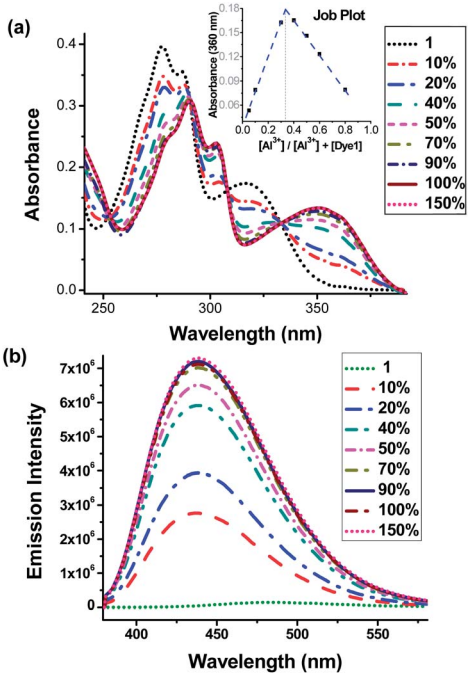


Fig. 2 Titration of **1** (10 μM) in water by addition of different amount of Al^{3+}.

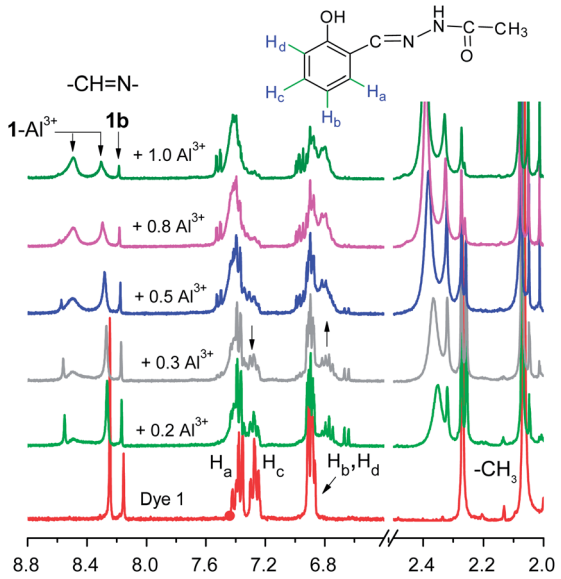


Fig. 3 ^{1}H NMR of **1** in CD_3OD upon addition of various equiv. of Al^{3+} cation.

at 7.27 ppm (aromatic H_c) disappeared when ~0.5 equiv. molar Al^{3+} was added, indicating that all ligand was consumed to bind Al^{3+} cation, forming **1**-Al^{3+} complex. Further addition of Al^{3+} (0.5–1.0 equiv. molar) did not reveal significant change. Since all the ligand was used to bind Al^{3+}, the broad peak at 8.28 ppm was also attributed to **1**-Al^{3+}, in addition to the peak at 8.45 ppm. The two peaks at 8.28 and 8.45 ppm suggested possible existence of two different isomers in the metal complex, as the mass spectra detected only **1**-Al^{3+} complex in 2 : 1 ligand-to-metal ratio.

In order to further evaluate the selectivity of **1** for Al^{3+} sensing, competition experiments were carried out with other metal cations. The fluorescence response of **1** to Al^{3+} in pure water in the presence of 5 equiv. of various cations including Na^+, K^+, Ag^+, Mg^{2+}, Ca^{2+}, Hg^{2+}, Ba^{2+}, Pb^{2+}, Cd^{2+}, Mn^{2+}, Ni^{2+}, Co^{2+}, Cu^{2+}, Fe^{2+}, Zn^{2+}, Cr^{3+} and Fe^{3+} are given in Fig. 4, respectively.

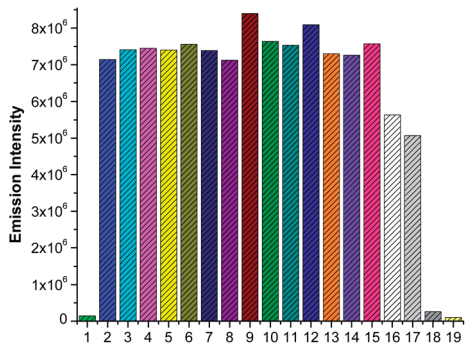


Fig. 4 Fluorescence intensity of **1** (20.0 μM) in pure water (column 1), and sensor **1** in the presence of different metal ion(s) (5.0 equiv.): (2) Al^{3+}; (3) Al^{3+} + Na^+; (4) Al^{3+} + K^+; (5) Al^{3+} + Ag^+; (6) Al^{3+} + Mg^{2+}; (7) Al^{3+} + Ca^{2+}; (8) Al^{3+} + Hg^{2+}; (9) Al^{3+} + Ba^{2+}; (10) Al^{3+} + Pb^{2+}; (11) Al^{3+} + Cd^{2+}; (12) Al^{3+} + Mn^{2+}; (13) Al^{3+} + Ni^{2+}; (14) Al^{3+} + Co^{2+}; (15) Al^{3+} + Zn^{2+}; (16) Al^{3+} + Cr^{3+}; (17) Al^{3+} + Fe^{2+}; (18) Al^{3+} + Cu^{2+}; (19) Al^{3+} + Fe^{3+}.

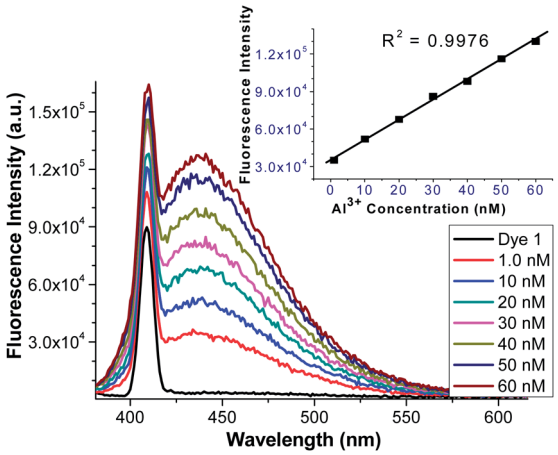


Fig. 5 Fluorescent intensity of Dye **1** (120 nM) upon addition of different concentration of Al^{3+}. The sharp signal at ~410 nm was from the scattering of water. The inset at the top right shows that the linear response of **1** to Al^{3+} concentration.

There were insignificant changes in the fluorescence of "**1** + Al^{3+}" in the presence of other competing metal cations. Except for Fe^{3+} and Cu^{2+}, most competing metal ions did not interfere with detection of Al^{3+} by **1** in H_2O (Fig. 4), indicating that **1** can be used as a selective chemosensor for the Al^{3+} cation.

When using **1** in low concentration (120 nM), the water scattering signal and the background noise could be brought to a observable level (Fig. 5) to evaluate the detection limit. Sensor **1** exhibited a good linear response towards Al^{3+} in the concentration range of 1.0 to 60 nM in water, showing its analytical value. The detection limit for Al^{3+} was determined to be as low as 5.0×10^{-11} M (0.5 nM) in pure water (ESI Fig. S15†), which was defined as the three-fold standard deviation of the fluorescence obtained from a blank sample (dye **1** in the absence of Al^{3+}).[29,30a] The detection limit of **1** for Al^{3+} cation was about 3 times lower than the highest detection limit reported in DMSO,[30b] representing a significant advance in sensing Al^{3+} cation in water.

In an effort to seek the potential biological application, sensor **1** was applied to zebrafish. When zebrafish was exposed to dye **1** and Al^{3+} in fish tank, bright fluorescence was observed in the fish head and tail (Fig. 6 and ESI Fig. S6†), suggesting that this molecule could be used in organisms at certain conditions.

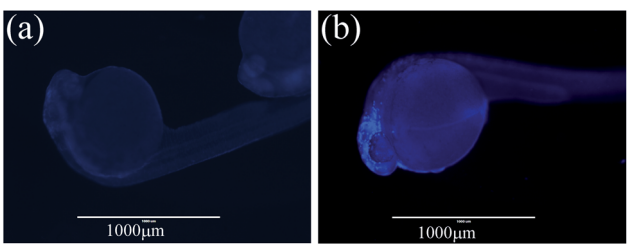


Fig. 6 Fluorescent images of Al^{3+} in Zebrafish (a) fish exposed to dye **1** only in the fish tank at the concentration of 10 μM for 2 hours and (b) fish exposed to 10 μM dye **1** and Al^{3+} for 2 hours.

In conclusion, a highly selective and sensitive fluorescent sensor for Al^{3+} has been developed. The sensor shows great fluorescence turn-on upon binding Al^{3+} in aqueous solution, giving strong blue emission. In addition, the sensor's turn-on exhibits excellent selectivity to Al^{3+} cation, with only a slight turn-on effect observed from Zn^{2+}. These findings suggest that the developed Al^{3+} sensor could be a useful probe for the application in the biological systems.

Acknowledgements

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