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# A Highly Selective and Sensitive Fluorescent Chemosensor for Detection of $Al^{3+}$ in Totally Aqueous Media

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A fluorescent chemosensor (**1**) based on 2-hydroxy-1-naphthaldehyde Schiff-base was developed for the detection of $Al^{3+}$ in 100% aqueous solution. Upon addition of $Al^{3+}$, a significant fluorescence enhancement was observed, which was not affected by other metal ions including $Na^+$, $K^+$, $Ca^{2+}$, $Mg^{2+}$, $Mn^{2+}$, $Co^{2+}$, $Ni^{2+}$, $Cu^{2+}$, $Cr^{3+}$, $Ag^+$, $Pb^{2+}$, $Zn^{2+}$, $Cd^{2+}$, $Hg^{2+}$, $Fe^{2+}$ and $Fe^{3+}$ under weak acid conditions. Moreover, the specific response to $Al^{3+}$ was visible under natural light. The binding mode between **1** and $Al^{3+}$ was clarified by ESI-MS and $^1H$ NMR.

**Keywords** fluorescence, sensor, aluminum ion, 2-hydroxynapthaldehyde, aqueous sensor

## Introduction

Aluminum is the third most abundant element and the most abundant metal in the earth's crust. By the weathering of aluminum-containing rocks, it is liable to be released to aquatic environments. Aluminum concentrations in waters are increased further by industrial discharges. In contrast with its ubiquity, it is not an essential element for either plants or animals. Moreover, aluminum is toxic to many aquatic species and excessive aluminum intake can cause damage of the function of human body, including muscle weakness, osteoporosis, delayed growth in children, altered mental abilities, *etc*.[1] The aluminum-containing food additives are the major sources of aluminum in the diet. The aluminum-containing medications such as antiperspirants, antiulcer agents and antacids are more hazardous to human health than the aluminum-containing food. Since aluminum is closely associates with human health and our exposure to it is so common, the selective recognization and detection of $Al^{3+}$ are crucial for the environment, public health and food safety.

According to Pearson acid base concept, $Al^{3+}$ is one of the hardest Lewis acids and $H_2O$ is a typical hard base. Consequently $Al^{3+}$ in water is apt to get involved in hydration instead of coordinating with sensing receptors. The high binding affinity between $Al^{3+}$ and $H_2O$ is an insurmountable difficulty for sensing $Al^{3+}$ in 100% aqueous solution. In recent years, considerable efforts have been made for fluorescent detection of metal ions in biological systems[2-9] and environmental systems[10-15] and a number of $Al^{3+}$-selective fluorescent chemosensors have been reported.[16-18] However, the fluorescent sensors with high selectivity and sensitivity to $Al^{3+}$ in 100% aqueous solution were rarely reported.[19-22] Herein, we report a Schiff-base based chemosensor (**1**) derived from 2-hydroxy-1-napthaldehyde. It exhibits a highly sensitive fluorescence turn-on response specific to $Al^{3+}$ in 100% aqueous solution. In addition, it is a visible-excited fluorescent sensor and the fluorescence response is visible under natural light.[23] All these features make the chemosensor convenient and practical for use.

## Experimental

### Reagents and apparatus

All chemicals were purchased from commercial suppliers and used without further purification. The corresponding metal nitrates were employed as the metal cation sources. HEPES buffer solution was used as solvent in all spectral measurements. $^1H$ NMR and $^{13}C$ NMR spectra were recorded on a Bruker-400 spectrometer with TMS as the internal standard. ESI-MS spectra were performed on a Bruker esquire HCT-Agilent 1200 spectrometer. Fluorescence spectra were taken on a Hitachi F-7000 fluorescence spectrometer. UV-vis absorption spectra were measured on TU-1901 spectrophotometer. The pH measurement was carried out on a PHS-3C digital pH meter.

### Synthesis of propyl 4-(2,3-dihydroxypropoxy)benzoate (3)

A mixture of 3-chloro-1,2-propanediol (3.4 g, 30.7 mmol), propyl 4-hydroxybenzoate (5 g, 27.7 mmol), potassium carbonate (5.8 g, 42.0 mmol) and a particle of potassium iodide in DMF (15 mL) was stirred at 90 ℃ under nitrogen for 30 h. After cooling, 80 mL water was

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added. Then the result mixture was extracted with chloroform and the organic extract was evaporated *in vacuo* to afford **3** as a dark red viscous oil (6.7 g, 95%).

**Synthesis of 4-(2,3-dihydroxypropoxy)benzohydrazide (2)**

A solution of **3** (5.0 g, 19.7 mmol) and hydrazine hydrate (2.1 g, 41.9 mmol) in ethanol (30 mL) was refluxed for 50 h. The solvent was evaporated off *in vacuo* and the residue was purified by silica gel column chromatography (eluant: EtOAc∶MeOH, 4∶1, *V*∶*V*) to give **2** as a white solid (2.4 g, 54%).

**Synthesis of 1**

2-Hydroxy-1-napthaldehyde (0.30 g, 1.7 mmol), **2** (0.58 g, 2.6 mmol) and 3 drops of glacial acetic acid were dissolved in methanol (30 mL), and then refluxed under nitrogen for 8 h. The reaction mixture was cooled to room temperature to give a precipitate. The precipitate was purified using silica gel column chromatography (eluant: petroleum ether∶ethyl acetate, 1∶4, *V*∶*V*) to afford **1** as a pale yellow solid (0.46 g, 70%). $^1$H NMR (DMSO-$d_6$, 400 MHz) $\delta$: 12.88 (b, 1H), 12.12 (b, 1H), 9.49 (s, 1H), 8.21 (d, $J$=8.4 Hz, 1H), 7.98 (d, $J$=8.0 Hz, 2H), 7.87−7.96 (m, 2H), 7.62 (t, $J$=7.2 Hz, 1H), 7.42 (t, $J$=7.2 Hz, 1H), 7.25 (d, $J$=8.4 Hz, 1H), 7.13 (d, $J$=8.0 Hz, 2H), 5.07 (d, $J$=4.8 Hz, 1H), 4.77 (b, 1H), 4.13 (dd, $J$=9.6, 3.6 Hz, 1H), 3.99 (dd, $J$=9.6, 6.2 Hz, 1H), 3.81−3.89 (m, 1H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz) $\delta$: 162.0, 161.9, 157.9, 146.2, 132.6, 131.6, 129.5, 129.0, 127.8, 127.7, 124.5, 123.5, 120.5, 118.9, 114.4, 108.6, 66.91, 69.87, 62.6; ESI-MS *m/z*: 381.5 $[M+H]^+$, 403.4 $[M+Na]^+$, 379.4 $[M-H]^-$, 415.4 $[M+H_2O+OH]^-$, 442.4 $[M+NO_3]^-$. Anal. calcd for $C_{21}H_{20}N_2O_5$: C 66.31, H 5.30, N 7.36; found C 66.18, H 5.23, N 7.32.

## Results and Discussion

**Fluorescence response to $Al^{3+}$**

Owing to a dihydroxypropoxy group in the sensor, **1** exhibits good solubility in water. All the optical properties of **1** were measured in HEPES buffered aqueous solution. The fluorescence responses of **1** to different concentrations of $Al^{3+}$ are shown in Figure 1. **1** in the absence of $Al^{3+}$ hardly exhibits any fluorescence. The addition of $Al^{3+}$ leads to a remarkably enhanced fluorescence emission with a dual-peak at 452 and 470 nm. Meanwhile, bright blue luminescence is observed (Figure 2a). Significantly, **1** is a visible-excited fluorescent sensor with the excitation wavelength at 400 nm and the fluorescence response to $Al^{3+}$ can be observed under natural light (Figure 2b). During the titration with $Al^{3+}$, a rapid fluorescence enhancement (up to 109-fold) was observed when the concentrations of $Al^{3+}$ were below 20 μmol/L (1.0 equiv.) and soon afterwards the fluorescence saturation was observed, which suggested a high-affinity binding between **1** and $Al^{3+}$ with 1∶1 stoichiometry (Figure 1, inset). A Job's plot further confirmed the 1∶1 binding stoichiometry (Figure S5). The association constant of $0.69\times10^4$ L•mol$^{-1}$ was evaluated from the Bensei-Hildebrand plot (Figure S6) and the detection limit was calculated to be $6.57\times10^{-8}$ mol/L according to the slope of calibration plot (Figure S7) between $Al^{3+}$ concentration and fluorescence intensity, which indicated a high sensitivity of **1** to $Al^{3+}$ in water. Figure S8 illustrated the change in the UV-Vis spectra of **1** with $Al^{3+}$ concentration. Upon the stepwise addition of $Al^{3+}$, a dual peak gradually took shape and a nearly linear dependence of the absorbance at 400 nm as a function of $Al^{3+}$ concentration (0−1.0 equiv.) was observed.

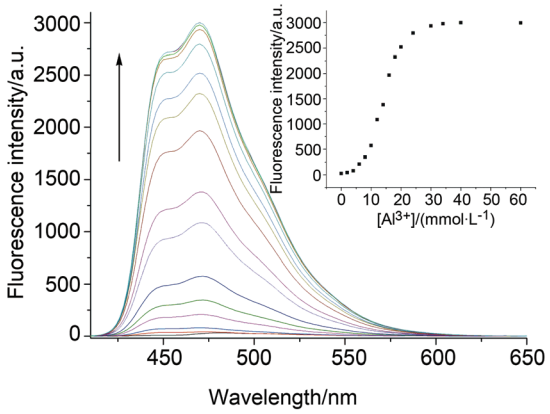


**Figure 1** Fluorescence spectra of **1** (20 μmol/L) in the presence of different concentrations of $Al^{3+}$ (0−60 μmol/L) in HEPES buffer solution (10 mmol/L, pH=7.2), $\lambda_{ex}$=400 nm. Inset: the emission intensity as a function of $Al^{3+}$ concentration.

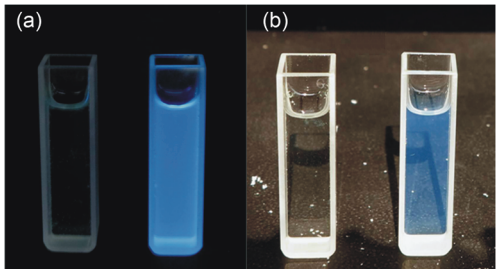


**Figure 2** The photos of fluorescence response of **1** to $Al^{3+}$, (a) in the absence (left) and presence (right) of $Al^{3+}$ excited at 395−400 nm, (b) in the absence (left) and presence (right) of $Al^{3+}$ under natural light.

Since the ionization of the phenolic hydroxyl group of **1** and the hydrolysis of $Al^{3+}$ are very sensitive to the pH value, it is necessary to consider the pH effect on the fluorescence enhancement upon addition of $Al^{3+}$. As shown in Figure 3, **1** exhibits good fluorescence sensing ability to $Al^{3+}$ over a wide range of pH values (4.5−8.0). Nevertheless it shows no appreciable fluorescence response to $Al^{3+}$ at a pH value above 10.0 or below 3.0, respectively due to the hydrolysis of $Al^{3+}$ and the failure of the phenolic OH deprotonation. These results indicated that **1** is applicable to detect $Al^{3+}$ in weak acidic and neutral condition.

  

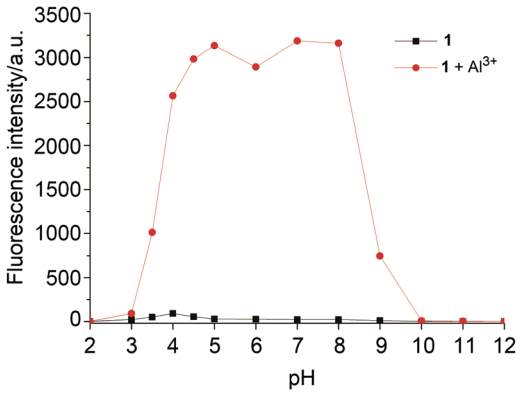


**Figure 3** pH-dependent emission intensities of **1** in the absence (black) and presence (red) of $Al^{3+}$ in aqueous solution.

## Selectivity to $Al^{3+}$

For investigating the selectivity of **1** for $Al^{3+}$, the fluorescence spectra in the presence of different mental ions were performed under same experimental conditions. As shown in Figure 4, no significant fluorescence responses were observed towards $Na^+$, $K^+$, $Ca^{2+}$, $Mg^{2+}$, $Mn^{2+}$, $Co^{2+}$, $Ni^{2+}$, $Cu^{2+}$, $Cr^{3+}$, $Ag^+$, $Pb^{2+}$, $Zn^{2+}$, $Cd^{2+}$, $Hg^{2+}$, $Fe^{2+}$ and $Fe^{3+}$ except a $Fe^{3+}$-induced faint enhancement effect. In contrast, the addition of $Al^{3+}$ gives rise to a remarkable fluorescence enhancement. However, UV-Vis spectral changes were observed when added some metal ions (such as $Zn^{2+}$, $Ni^{2+}$, $Ag^+$ and $Pb^{2+}$), indicating that besides $Al^{3+}$ some other metal ions could also coordinate with **1** (Figure S9). The $Al^{3+}$-specific fluorescence response of **1** might be attributed to the strong Lewis acidic character of $Al^{3+}$, which leads to a more ionic Al—O bond and thereby reinforces the propensity towards a quinoid-type resonance structure that emits strong fluorescence. For further evaluating the effects of complex backgrounds on the $Al^{3+}$-selectivity, competing experiments were carried out by measuring the fluorescence response to $Al^{3+}$ in the presence of other metal ions. It was found that pH value was crucial for the $Al^{3+}$-selectivity against other coexisting metal ions. When the pH is below 6.0, **1** can selectively recognize $Al^{3+}$ from the mixture of $Al^{3+}$ and each competing metal ion. As shown in Figure 5, at pH 6.0 the $Al^{3+}$-induced fluorescence enhancement was little affected by other coexisting metal ions excluding $Cu^{2+}$ which lead to a 30% quenching of fluorescence. But fortunately, the depressing effect of $Cu^{2+}$ can be entirely eliminated via adding 3 mol equiv. of *L*-cysteine. When the pH value rises above 7.0, the $Al^{3+}$-induced fluorescence was still not affected by alkali and alkaline earth metal ions, but most of the transition metal ions caused fluorescence quenching to different levels (Figure S10). The negative effect of alkaline medium on the $Al^{3+}$-selectivity is because $HO^-$ is a harder base than $H_2O$, and consequently, exhibits a higher affinity to the hard acid ion $Al^{3+}$ than to transition metal ions.

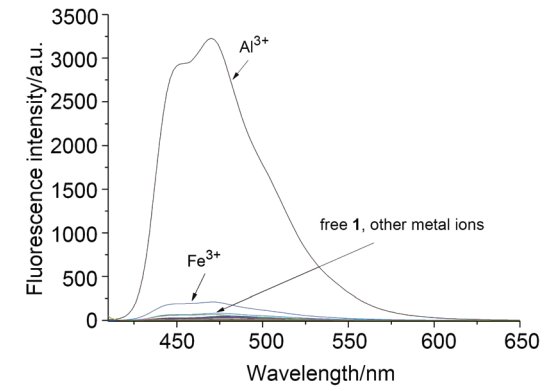


**Figure 4** Fluorescence spectra of **1** in the presence of various cations (2.0 equiv.) in HEPES buffer solution (10 mmol/L, pH = 7.2).

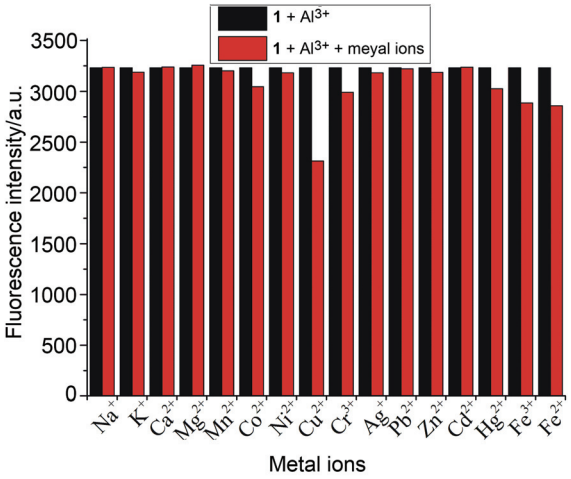


**Figure 5** The selective responses of **1** to $Al^{3+}$ (2.0 equiv.) in the presence of other different cations (2.0 equiv.) at pH 6.0.

## Binding mode and signaling mechanism

Toward understanding the binding mode between **1** and $Al^{3+}$, ESI-MS spectra of **1** in the presence of $Al^{3+}$ were performed (Figure 6). The spectrum in positive ion mode exhibits the base peak at *m*/*z* 468.3 which was assigned to $[Al(\mathbf{1})–H+NO_3]^+$ (calcd 468.11). That confirmed the 1∶1 binding stoichiometry and indicated the deprotonation of the phenolic hydroxyl group upon coordination with $Al^{3+}$. In the negative ion mass spectrum, the base peak was observed at *m*/*z* 529.2 corresponding to $[Al(\mathbf{1})–2H+2NO_3]^-$ (calcd 529.09), which implied the deprotonation of the amido NH besides the phenolic OH.

To further illustrate the binding mode of **1** with $Al^{3+}$, $^1H$ NMR spectra of **1** in the absence and presence of $Al^{3+}$ (1.0 equiv.) were carried out in $CD_3OD/D_2O$ (9∶1). It is pity that the signals of phenolic hydroxy proton ($H_i$) and amido proton ($H_k$) do not appear as a result of the fast proton-exchange between **1** and solvent. However, the spectral changes in the aromatic region upon the addition of $Al^{3+}$ clearly demonstrated the binding mode between **1** and $Al^{3+}$ (Figure 7). The imine peak

  

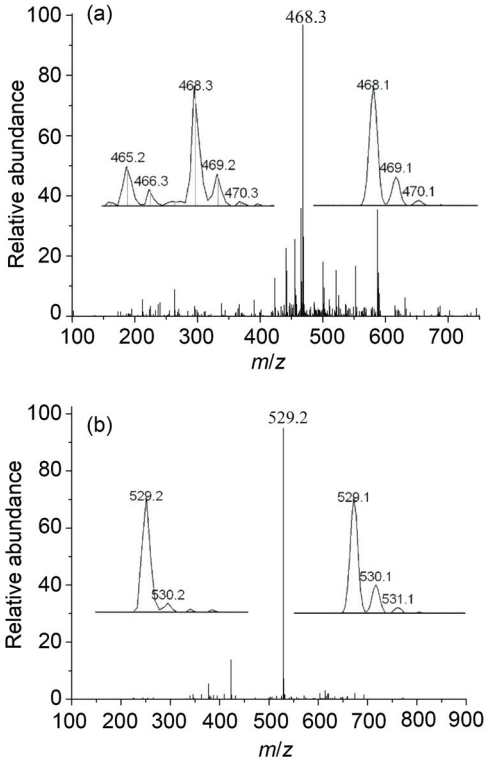


**Figure 6** ESI-MS spectra of **1** in the presence of $Al^{3+}$: (a) in positive ion mode, $[Al(\mathbf{1})–H+NO_3]^+$ $m/z=468.3$. Inset: observed (left) and calculated (right) isotopic patterns for the $[Al(\mathbf{1})–H+NO_3]^+$; (b) in negative ion mode, $[Al(\mathbf{1})–2H+2NO_3]^-$ $m/z=529.2$. Inset: observed (left) and calculated (right) isotopic patterns for the $[Al(\mathbf{1})–2H+2NO_3]^-$.

($H_g$) is markedly shifted downfield region supporting the coordination of the imine nitrogen to $Al^{3+}$. In addition, the inductive effect of coordinative imine group causes a downshift of the $H_b$ and $H_f$ peaks. The peak for *ortho* hydrogen ($H_a$) of hydroxyl group moves towards the upfield region which confirmed the deprotonation of the phenolic hydroxyl group. It is worth noting that the $H_h$ and $H_i$ peaks are shifted downfield. This observation indicated that the carbonyl group strongly coordinates to $Al^{3+}$ and the deprotonation process of the amido NH does not occur. However, the deprotonation of the amido NH was suggested in the negative ion mass spectrum. It may be attributed to only trace amount of NH-deprotonated complex that is detectable for ESI-MS but undetectable for $^1H$ NMR. In order to directly see the changes of the signals of $H_j$ and $H_k$, DMSO-$d_6$ was used as solvent for $^1H$ NMR experiments. As shown in Figure S11, the OH ($H_j$) and NH ($H_k$) signals in free **1** appear at $\delta$ 12.8 and 12.1, respectively. The presence of $Al^{3+}$ results in a rapid disappearance of the $H_i$ signal and a gradual decrease of the $H_k$ signal. The observations affirmed the possibility of NH deprotonation upon coordination with $Al^{3+}$. The solvent may be a critical influence factor on the NH deprotonation process. In view of the above, we would propose the binding mode between **1** and $Al^{3+}$ in water as shown in Figure 8.

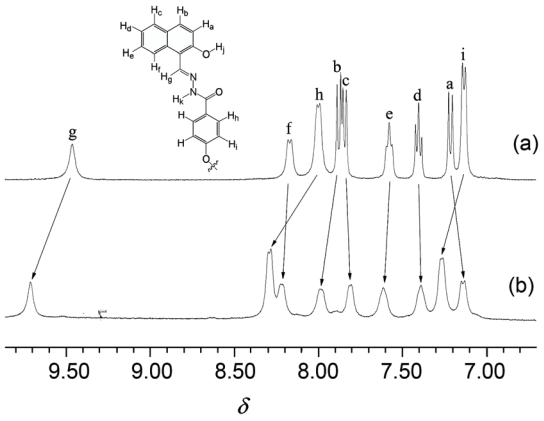


**Figure 7** $^1H$ NMR spectra of **1** in the absence (a) and presence (b) of $Al^{3+}$ (1.0 equiv.) in $CD_3OD$ ∶ $D_2O$ (9 ∶ 1).

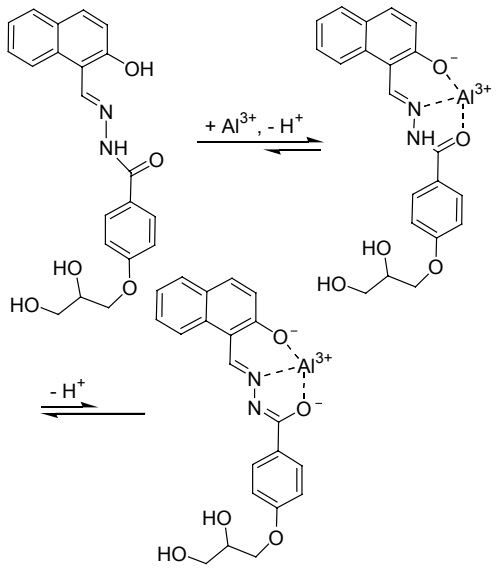


**Figure 8** The proposed binding mode between **1** and $Al^{3+}$.

It is generally known that $Al^{3+}$ shows very high binding affinity to O-donor atom.[24] Consequently, the sensor **1** containing O, N, O donor atoms displays the higher affinity to $Al^{3+}$ than to the other test metal ions. Thanks to the much stronger Lewis acidic character of $Al^{3+}$, the Al—O bond takes on a more ionic character and thereby the sensor **1** is likely to take on a quinoid-type resonance structure. The quinoid-type structure probably is the reason why the complex between **1** and $Al^{3+}$ shows high absorption and emission ability.

## Conclusions

In summary, we have developed a fluorescent chemosensor based on 2-hydroxy-1-naphthaldehyde Schiff-base, which shows a highly sensitive response to $Al^{3+}$ in water over a wide range of pH values (4.5—8.0). Other coexisting metal ions have little or no effect on its specific response to $Al^{3+}$ under weak acid conditions. Moreover, the specific response to $Al^{3+}$ is visible under natural light. Based on ESI-MS and $^1H$ NMR,

  

The binding mode between **1** and $Al^{3+}$ was proposed.

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