A Simple Turn-On Schiff base Fluorescence Sensor for Aluminum Ion

Jinli Zhu, Yuhuan Zhang, Lun Wang, Tongming Sun, Miao Wang, Yipu Wang, Danyang Ma, Qingqing Yang, Yanfeng Tang

PII: S0040-4039(16)30792-4
DOI: http://dx.doi.org/10.1016/j.tetlet.2016.06.112
Reference: TETL 47839

To appear in: *Tetrahedron Letters*

Received Date: 31 May 2016
Revised Date: 22 June 2016
Accepted Date: 24 June 2016

Please cite this article as: Zhu, J., Zhang, Y., Wang, L., Sun, T., Wang, M., Wang, Y., Ma, D., Yang, Q., Tang, Y., A Simple Turn-On Schiff base Fluorescence Sensor for Aluminum Ion, *Tetrahedron Letters* (2016), doi: http://dx.doi.org/10.1016/j.tetlet.2016.06.112

A Simple Turn-On Schiff base Fluorescence Sensor for Aluminum Ion

Jinli Zhu [a], Yuhuan Zhang[c], Lun Wang[b], Tongming Sun [a], Miao Wang [a], Yipu Wang [a], Danyang Ma [a], Qingqing Yang [a] and Yanfeng Tang [a,*]

a. School of Chemistry and Chemical Engineering, Nantong University, Nantong 226019, P.R. China

b. Inspection and Quarantine Center of Shandong Exit & Quarantine Bureau, Qingdao, 266001, P.R. China

c.School of Textiles, Nantong University, Nantong 226019, P.R. China

Abstract: A simple Schiff base **L** derived from 2-hydroxy-naphthalene-1-carbaldehyde and benzene-1,2-diamine, was proved to be a turn-on fluorescent probe for the recognition of Al^{3+}, based on photoinduced electron transfer (PET) mechanism. It exhibited a high selectivity for Al^{3+} over other competing ions (e.g., Hg^{2+}, Ag^{+}, Pb^{2+}, Cu^{2+}, Ba^{2+}, Cd^{2+}, Zn^{2+}, Ni^{2+}, Co^{2+}, Fe^{2+}, Fe^{3+}, Mn^{2+}, Li^{+}, Cr^{3+}, Ca^{2+}, Mg^{2+}, K^{+}, Na^{+}) in EtOH/HEPES buffer (95:5, v/v, pH = 7.2). The complex formation of **L**-Al^{3+} was determined to be 1:1 for L and Al^{3+} in molar. This result was based on the Job plot, ^{1}H NMR titration and ESI-mass. The binding constant of the complex was 6.53×10^{3} M^{-1} with a detection limit of 1.08×10^{-7} M. The potential applications of **L** to detect Al^{3+} in live cells and in environmental water samples were also investigated. The results indicated that **L** could be a promising probe for Al^{3+} recognition.

Keywords: Al^{3+} detection, PET, Schiff base, turn-on fluorescence, live cells

Introduction

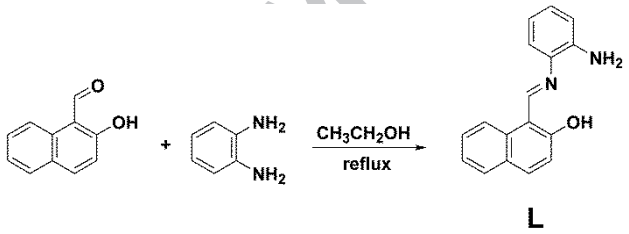
Aluminum is the third most abundant metal in the earth's crust. It is extensively useful in many fields, from the national defense to our daily lives. These fields include aerospace industry, automobiles, computers, packing materials, electrical equipment, machinery, food additives, building construction, clinical drugs and water purification [1,2]. Aluminum also plays a great role in biochemical reactions, such as enzyme-catalyzed reactions [3], biotechnological transformation [4], and others. However, nowadays, a large amount of medical research reveals that excessive absorption of aluminum is harmful to human health. It sometimes leads to diseases, such as Alzheimer's disease [5-6], Parkinson's disease [7], osteoporosis [8] and osteomalacia [9]. Therefore, it is of great importance to develop the efficient methods for the detection of aluminum, especially in drinking water.

So far, several methods are available for the detection of aluminum, including atomic absorption spectrometry (AAS) [10], atomic emission spectrometry (AES) [11], voltammetry [12]

* Corresponding author

and electrochemical methods [13-15]. However, most of them require expensive instruments and are time-consuming [16-19]. Compared to these methods, fluorescent chemical sensors have attracted enormous attention due to their faster-response and lower-cost properties [20-23]. A few of fluorescent sensors for detecting Al^{3+} have been developed with good selectivity and sensitivity [24-28]. However, some of them require complicated synthetic protocols and others are not sensitive enough to detect Al^{3+} [29-32]. Thus, for practical applications, it is of great significance to design readily synthesized Al^{3+} sensors with simple structures and high selectivity and sensitivity [33-34].

Sun et al synthesized a symmetric Schiff base for Al^{3+} from benzene-1,2-diamine and 2-hydroxy-1-naphthaldehyde [35]. This sensor showed stable complexation with Al^{3+} in DMF, but it also gave an obvious turn-on signal in the presence of Mg^{2+}. Herein, to avoid the disturbance of Mg^{2+}, we prepared an asymmetric Schiff base **L**, (1-[(2-Amino-phenylimino)-methyl]-naphthalen-2-ol), from the above mentioned two compounds, as shown in Scheme 1. L showed better selectivity to Al^{3+} without disturbance of Mg^{2+} and other metals. Moreover, **L** has the potential use of detecting Al^{3+} in living cells and real water samples.



L

Scheme 1. The synthesis of Schiff base **L**.

Results and discussion

The fluorescence responses of receptor **L** on various metal ions were investigated in EtOH/HEPES buffer (95:5, v/v, pH 7.2) (Fig. 1). Upon excited at 273 nm, **L** (10 μM) showed barely-detectable emissions at 473 nm and 499 nm. And there were no obvious changes in the spectra after adding other metal ions to the **L** solution, including Hg^{2+}, Ag^{+}, Pb^{2+}, Cu^{2+}, Ba^{2+}, Cd^{2+}, Zn^{2+}, Ni^{2+}, Co^{2+}, Fe^{2+}, Fe^{3+}, Mn^{2+}, Li^{+}, Cr^{3+}, Ca^{2+}, Mg^{2+}, K^{+} and Na^{+} (100 μM)（Fig. S1）. However, the addition of Al^{3+} (100 μM) led to significant fluorescence enhancement (63 fold) at 473 nm and 499 nm, which indicated that an Al^{3+}-selective "off-on" fluorescent signaling behavior had occurred. Among these metal ions and L solutions excited by UV at 273 nm, only the solution mixed with both Al^{3+} and **L** (Al^{3+}-**L**) showed a dramatic color change from green to fluorescent blue. This change could be easily detected by the naked-eye (Fig. S2). The observed fluorescence enhancement was attributed to blocking the photoinduced electron transfer (PET) process when **L** is bound with Al^{3+} (Scheme 2) [35-36].

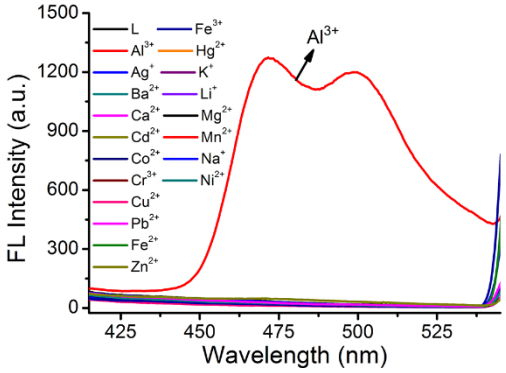
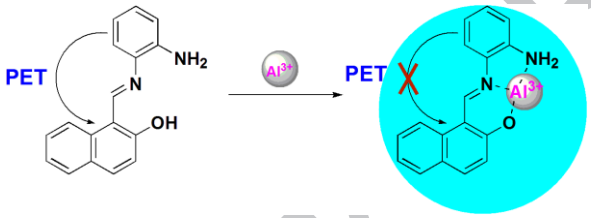


Fig. 1. Fluorescent selectivity of **L** (10 μM) upon the addition of various mental ions (100 μM) in EtOH/HEPES buffer (95:5, v/v, pH 7.2) at 473 nm and 499nm. λ_{ex} = 273 nm.



Scheme 2. Proposed binding mechanism between the receptor **L** and Al^{3+}.

The selectivity toward Al^{3+} was further ascertained by the competitive experiment. As shown in Fig. 2, when the Al^{3+}-**L** solution was mixed with one of following metal ions, including Ag^{+}, Cd^{2+}, Co^{2+}, Li^{+}, Mn^{2+}, Na^{+}, Pb^{2+}, Zn^{2+}, K^{+} , Ca^{2+} and Mg^{2+}, the emission intensities were almost identical to that of Al^{3+}-**L** solution. In the case of other metal ions, including Ba^{2+}, Cr^{3+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Hg^{2+}, Ni^{2+}, the emission intensities diminished to a different extent, like those obtained in the presence of Al^{3+} alone, and they still had a sufficient turn-on ratio for the detection of Al^{3+}. Therefore, L displayed a promising selective fluorescent sensor for Al^{3+} in the presence of competing mental ions.

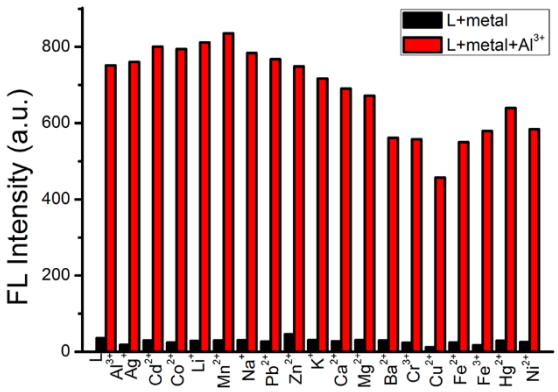


Fig. 2. Fluorescent selectivity of **L** (10 μM) at 473nm upon addition of various metal ions ((100 μM) Al^{3+}, Ag^{+}, Cd^{2+}, Co^{2+}, Li^{+}, Mn^{2+}, Na^{+}, Pb^{2+}, Zn^{2+}, K^{+} , Ca^{2+}, Mg^{2+} , Ba^{2+}, Cr^{3+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Hg^{2+}, Ni^{2+}) in EtOH/HEPES buffer (95:5, v/v, pH 7.2), λ_{ex} = 273nm.

To further investigate the chemosensing properties of **L**, a fluorescence titration of **L** was done by increasing the concentration of Al^{3+}. As calculated from the fluorescence titration profile shown in Fig. 3A, the fluorescence quantum yield of **L** changed from 0.007 to 0.053 after the addition of 20 equivalent of [Al^{3+}] (i.e., 200 μM). Benesi–Hildebrand analysis of the titration profiles based on 1:1 binding model resulted in a linear relationship of intensity to concentration (Fig. 3C). This indicated a 1:1 binding stoichiometry of Al^{3+} and **L**, and the binding constant was estimated to be 6.53 $\times 10^3$ M^{-1}. The 1:1 binding ratio was also supported by Job's plot investigation (Fig. 4). In addition, the formation of 1:1 complex between receptor **L** and Al^{3+} was further confirmed by the appearance of a peak at m/z 350.22, assignable to [**L**+ Al^{3+} + NO_3^-] in the ESI/MS (Fig. 5). By using the above-mentioned fluorescence titration results, the detection limit for Al^{3+} was determined to be 1.08×10^{-7} M (Fig. 3D). The detection limit was sufficiently low to detect a submicromolar concentration of Al^{3+}.

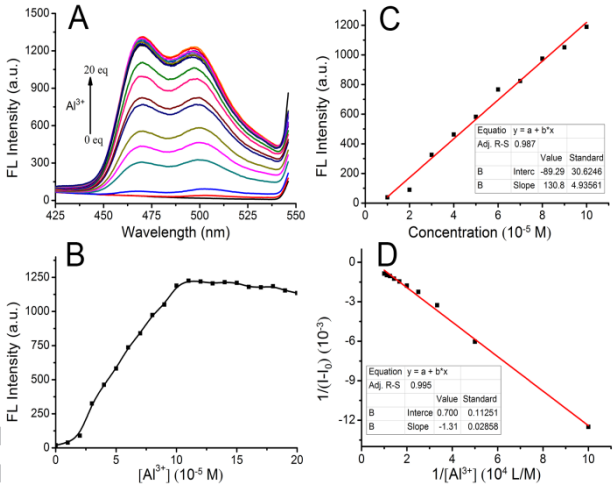


Fig. 3. (A) Fluorescence emission spectra of L (10 μM) upon the addition of Al^{3+} with different [Al^{3+}] in EtOH/HEPES buffer (95:5, v/v, pH = 7.2), λ_{ex} = 273nm. (B) A plot of intensity changes versus the concentrations of Al^{3+} added. (C) Calculation of detection limit of **L** for Al^{3+}. The spectra were recorded in EtOH/HEPES buffer (95:5, v/v, pH 7.2) with excitation at 273 nm and emission at 499 nm. FL Intensity is the fluorescence intensity of sample **L** solution (10 μM) upon addition of different amounts of Al^{3+}. (D) Calculation of binding constant between L and Al^{3+}. The spectra were recorded in EtOH/HEPES buffer (95:5, v/v, pH = 7.2) with excitation at 273 nm and emission at 499 nm. I_0 is the fluorescence intensity of sample **L** solution (10 μM) upon addition of different amounts of Al^{3+}; I is the fluorescence intensity of free **L** solution.

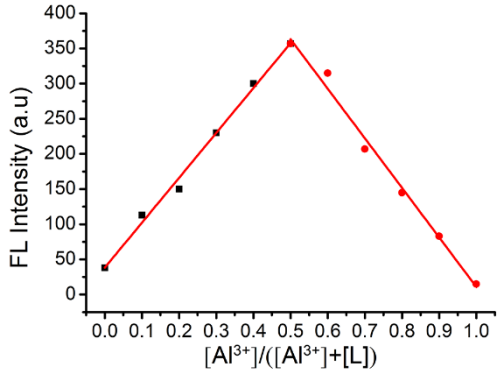


Fig. 4. The Job's plot of fluorescence intensity response of **L** at 500 nm to the mole fraction of Al^{3+} in EtOH/HEPES buffer (95:5, v/v, pH = 7.2), λ_{ex}=273nm.

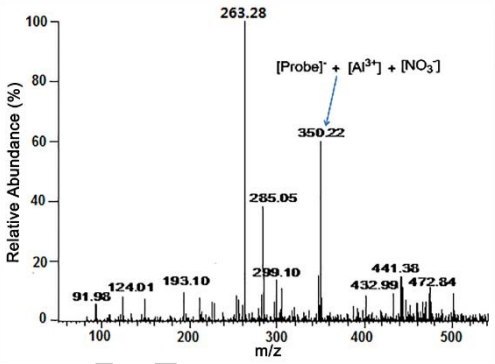


Fig. 5. ESI Mass spectrum of L-Al^{3+}-NO_3^- complex.

To better understand the complexation of the receptor **L** with Al^{3+}, ^{1}H NMR was carried out. Fig. 6A showed ^{1}H NMR spectrum of **L** receptor. The peaks at 15.66 and 5.11 ppm were assigned to –OH (H_a) and NH_2 (H_c) of **L**, respectively. Fig. 6B and Fig. 6C showed the ^{1}H NMR spectra of the **L** receptor upon the addition of Al^{3+} with 1.0 and 2.0 equiv concentrations, respectively. It was clearly found that the peaks of H_a at 15.66 ppm and H_c at 5.11 ppm disappeared, demonstrating that –OH (H_a) and –NH_2 (H_c) were involved in the complexation of Al^{3+} and **L**. The peak of –CH=N– (H_b) was shifted to downfield from 9.61 ppm to 9.96 ppm after complexation. Similarly, the aromatic proton peaks including naphthalenyl and phenyl rings also underwent a downfield shift from a range of 6.70-8.51 ppm to that of 6.96-8.71 ppm, which further proved the complexation formation of **L** with Al^{3+}. Furthermore, there were no obvious differences between the spectra shown in Fig. 6B and Fig. 6C corresponding to 1:1 of Al^{3+}/**L** and 2:1 of Al^{3+}/**L** in molar, respectively. It revealed that the combination of **L** and Al^{3+} was 1:1, which was consistent with the Job's plot result.

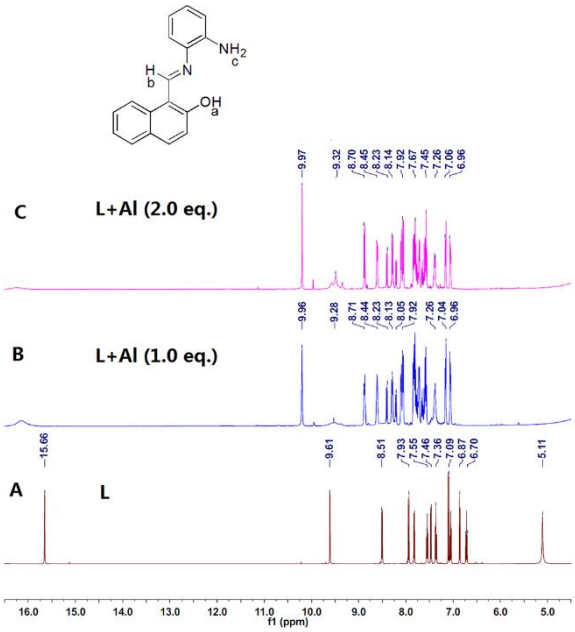


Fig. 6. ^{1}H NMR spectra in DMSO-d6 of (A) **L** only, (B) **L** with 1.0 equiv of Al^{3+}, and (C) **L** with 2.0 equiv of Al^{3+}.

For a practical application of **L** under different environment and physiological conditions, it is necessary to verify the pH-stability of **L**-Al^{3+}. As expected, no obvious fluorescence emission of L was observed under different pH values. The fluorescence of **L**-Al^{3+} complex was stable from pH 2 to 10, which demonstrated that **L** and **L**-Al^{3+} complex are steady and work well over this wide pH range (Fig. 7).

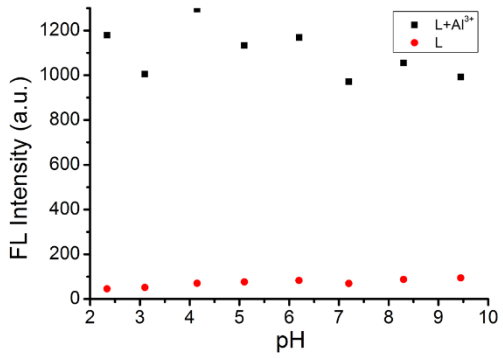


Fig. 7. The fluorescence intensity response of L (10 μM) and L with 10 eq of Al3+ at emission of 473 nm to different pH values in Ethanol-H2O (95:5, V/V), λex=273 nm.

Before studying the use of **L** as a bio-imaging probe, the cytotoxicity of **L** was assessed. The HeLa cells were incubated with different concentrations of L (from 20 up to 100 μg/mL) for 24 h. Subsequently, MTT assay was carried out [37-40]. Fig. 8A showed that over 90% of cells were alive, even when treated at a high concentration of **L** at 100 μg/mL. This revealed that **L** had very low cytotoxicity and is a good potential for an intracellular imaging probe.

Bio-imaging experiments were then conducted to prove the ability of **L** to detect Al^{3+} in the Hela cells. As shown in Fig. 8B, only a very weak green luminescence signal was detected inside the Hela cells when the cells treated with **L** without Al^{3+}. However, after the Hela cells pretreated with **L** were incubated with Al^{3+} (0.2 μM, for 15 min), a much brighter green luminescence was observed inside the cells (Fig. 8C). These results demonstrated that L was capable of imaging Al^{3+} in the live cells.

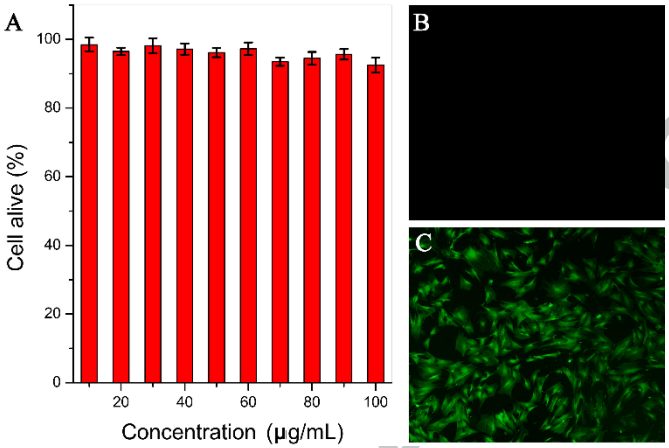


Fig. 8. (A) Cell viability of HeLa cells treated with different concentrations of L. Confocal fluorescence micrograph of L loaded HeLa cells (B) without and (C) with Al^{3+}.

The potential application of **L** in the detection of Al^{3+} in water samples was also investigated, following the protocol published previously [41]. Three water samples were used in the experiments including distilled water, lake and river water, which were collected from our lab, Tongda Lake in Nantong University and Haohe River in Nantong, respectively. Al^{3+} (0-100 μM) was dissolved in these water samples following the addition of L (1 μM). As shown in Fig. 9, the fluorescence intensities of all these samples displayed good linear properties with the concentrations of Al^{3+}. Particularly, the intensities of both the lake and river samples were only slightly lower than that of distilled water samples. The interesting result showed that **L** can be applied for the detection of Al^{3+} in environmental water systems.

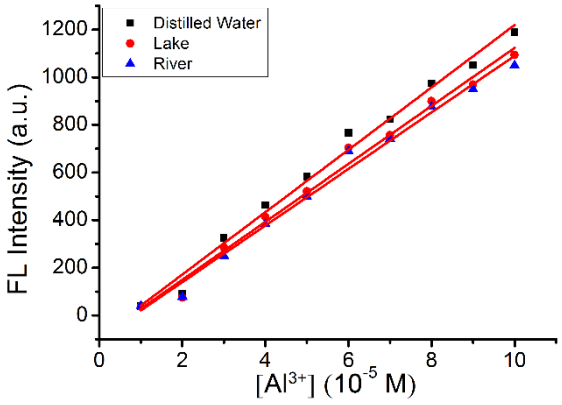


Fig. 9. Linear fluorescence intensities of **L** (10 μM) upon addition of Al^{3+} (0-100 μM) in the three natural water samples.

Conclusions

In summary, we synthesized a very simple fluorescence sensor **L**, which was based on the blocking PET process from the nitrogen donor to the 2-hydroxy-1-naphthaldehyde fluorophore. **L** exhibited high selectivity for Al^{3+} over other metal ions with 63-fold fluorescence enhancement, and high sensitivity with the detection limit at 10^{-7} M level in EtOH/HEPES buffer (95:5, v/v, pH = 7.2). The predicted configuration of the **L**-Al^{3+} complex was well-characterized to be 1:1 by the Job plot, ^{1}H NMR titration and ESI-mass. Moreover, **L** showed a good linear property in detecting Al^{3+} in real water samples. Beyond that, **L** was employed to detect the Al^{3+} in live cells sensitively by emitting visible fluorescence. These results indicated that **L** could be served as an excellent fluorescence chemosensor for Al^{3+} in water and cells.

Acknowledgements

This work was supported by National Natural Science Foundation of China (No. 21376124, 21476117) and Qing Lan Project 2014.

Supporting information

Detailed the experimental methods and characterizations can be found in the supporting information.

References and notes

1. J. R. Lakowicz, Topics in Fluorescence Spectroscopy: Probe Design and Chemical Sensing, Kluwer Academic Publishers, New York, **2002**, p. 4.
2. M. G. Soni, S. M. White, W. G. Flamm and G. A. Burdock, Regul. *Toxicol. Pharmacol.*, **2001**, 33, 66.
3. N. J. Baxter, G. M. Blackburn, J. P. Marston, A. M. Hounslow, M. J. Cliff , W. Bermel, N. H. Williams, F. Hollfelder, D. E. Wemmer and J. P. Waltho, *J. Am. Chem. Soc.* , **2008**, 130, 3952.
4. W. Poot-Poot and S. M. T. Hernandez-Sotomayor, Iubmb. Life., **2011**, 63, 864.
5. D.P. Perl and A.R. Brody, *Science*, **1980**, 208, 297.
6. C. S. Cronan, W. J. Walker and P. R. Bloom, *Nature*, **1986**, 324, 140.
7. D.P. Perl, D.C. Gajdusek, R.M. Garruto, R.T. Yanagihara and C.J. Gibbs. *Science*, **1982**, 217, 1053.
8. S. Polizzi, E. Pira, M Ferrara, M. Bugiani, A. Papaleo, R. Albera and S. Palmi, *Neurotoxicology*, **2002**, 23, 761.
9. J.R. Walton, *Neurotoxicology*, **2006**, 27, 385.

10. A. Taylor, S. Branch, D. Halls, M. Patriarca and M. White, *J. Anal. At. Spectrom*., **2002**, 17, 414.
11. J. Quinonero, C. Mongay and M.D. Guardia, *Microchem. J*., **1991**, 43, 213.
12. Q.T. Cai and S.B. Khoo, *Anal. Chim. Acta.*, **1993**, 276, 99.
13. W.J.R. Santos, A.L. Sousa, R.C.S. Luz, F.S. Damos, L.T. Kubota, A.A. Tanaka and S.M.C.N. Tanaka, *Talanta*, **2006**, 70, 588.
14. J.E. Newbery and M.P.L. de Haddad, *Analyst*, **1985**, 110, 81.
15. M. Trojanowicz, W. Matuszewski and B. Szostek, *Anal. Chim. Acta.*, **1992**, 261, 391.
16. M.I.H. Helaleh and T. Korenaga, *J. Chromatogr. B*, **2000**, 744, 433.
17. M. J. Blew and S. R. Goode, *J. Chem. Educ.*, **2008**, 85, 854.
18. I. L. S. Almeida and N. M. M. Coelho , *Energ Fuel.*, 2012, 26, 6003.
19. C. Zhu, S. W. Yang, J. Sun, P. He, N. Y. Yuan, J. N. Ding, R. W. Mo, G. Wang, G. Q. Ding and X. M. Xie, *Synth. Met.*, **2015**, 209, 468 .
20. S. W. Yang and F. Liao, *Synth. Met.*, **2012**, 162, 1343.
21. S. W. Yang, S. Q. S Huang, D. Liu and F. Liao, *Synth. Met.*, **2012**, 162, 2228.
22. F. Liao, S. W. Yang, X. B. Li, L. J. Yang, Z. H. Xie, C. S. Hu,S. A. Yan, T. Y. Ren and Z. D. Liu, *Synth. Met.*, **2014**, 189, 126.
23. F. Liao, S.W. Yang, X. B. Li, L. J. Yang, Z. H. Xie, C. S. Hu, L. He, X. Y. Kang, X. Song and T. Y. Ren, *Synth. Met.*, **2014**, 189, 135.
24. Y. W. Wang, M. X. Yu, Y. H. Yu, Z. P. Bai，Z. Shen, F. Y Li and X. Z. You, *Tetrahedron Lett.*, **2009**, 50, 6169.
25. T. J. Jia, W. Cao, X. J. Zheng and L. P. Jin, *Tetrahedron Lett.*, **2013**, 54, 3471.
26. L. Fan, T. R. Li, B. D. Wang, Z. Y. Yang and C. J. Liu, *Spectrochim. Acta. A*, **2014**, 118, 760.
27. J. Y. Jung, S. J. Han, J. Chun, C. Lee and J. Yoon, *Dyes Pigm.*, **2012**, 94, 423.
28. M. M. Yu, R. L. Yuan, C. X. Shi, W. Zhou, L.H. Wei and Z. X. Li, *Dyes Pigm.*, **2013**, 99, 887.
29. D. Zhou, C. Y. Sun, C. Chen, X. N. Cui and W. J. Li, *J. Mol. Struct.*, **2015**, 1079, 315.
30. J. Y. Noh, S. Kim, I. H. Hwang, G. Y. Lee, J. Kang, S. H. Kim, J. Min, S. Park, C. Kim and J. Kim, *Dyes Pigm*., **2013**, 99, 1016.
31. X. X. Fang, S. F. Zhang, G. Y. Zhao, W. W. Zhang, J. W. Xu, A. M. Ren, C. Q. Wu and W. Yang, *Dyes Pigm*., **2014**, 101, 58.
32. O. Adegoke and T. Nyokong, *Synth. Met.*, **2014**, 188, 35.
33. S. W. Yang, J. Sun, X. B. Li,W. Zhou, Z. Y. Wang, P. He, G. Q. Ding, X. M. Xie, Z. H. Kang and M. H. Jiang, *J. Mater. Chem. A*, **2014**, 2, 8660.
34. X. Song, H. Y. Sun, S. W. Yang, S. Z. Zhao and F. Liao, *J. Lumin.*, **2016**, 169, 186.
35. D. Zhou, C. Y. Sun, C. Chen, X. N. Cui and W. J. Li, *J. Mol. Struct.*, **2015**, 1079, 315.
36. F. Liao, X. Song, S. W. Yang, C. Y. Hu, L. He, S. A. Yan and G. Q. Ding, *J. Mater. Chem. A*, **2015**, 3, 7568.

37. J. Sun , S. W. Yang , Z. Y. Wang , H. Shen , T. Xu , L. T. Sun , H. Li ,W. W. Chen , X. Y. Jiang , G. Q. Ding , Z.H. Kang , X. M. Xie and M. H. Jiang, *Part. Syst. Char.*, **2015**, 32, 434.
38. S. W. Yang, J. Sun, P. He, X. X. Deng, Z. Y. Wang, C. Y. Hu, G. Q. Ding and X. M. Xie, *Chem. Mater.*, **2015**, 27, 2004.
39. C. Zhu, S. W. Yang, G. Wang, R. W. Mo, P. He, J. Sun, Z. F. Di, Z. H. Kang, N.Y. Yuan, J.N. Ding, G. Q. Ding and X. M. Xie, *J. Mater. Chem. B*, **2015**, 3, 6871.
40. S. W. Yang, J. Sun, C. Zhu, P. He, Z. Peng and G. Q. Ding, *Analyst*, **2016**, 141, 1052.
41. H. Zhu, J. Fan, J. Lu, M. Hu, J. Cao, J. Wang, H. Li, X. Liu and X. Peng, *Talanta*, **2012**, 93, 55.

Highlights

1. A simple Schiff-based fluorescence sensor for Al^{3+}, was synthesized.
2. This sensor was of good selectivity and sensitivity for Al^{3+}.
3. This sensor can be used in real water and live cells.