

A New Anthracene Based Fluorescent Turn-On Sensor for Fe<sup>3+</sup>Kyoung-Lyong An,<sup>†,‡</sup> Sang-Oh Lee,<sup>†</sup> Sun Duk Koh,<sup>†</sup> Seung-Rim Shin,<sup>†</sup> Jong-Il Shin,<sup>†</sup>  
Soo-Youl Park,<sup>†</sup> Young-A Son,<sup>§</sup> Koon Ha Park,<sup>‡,\*</sup> and Kun Jun<sup>†,\*</sup><sup>†</sup>Interface Chemistry & Engineering Research Team, Korea Research Institute of Chemical Technology,  
Daejeon 305-600, Korea. \*E-mail: kjun@kRICT.re.kr<sup>‡</sup>Department of Chemistry, Chungnam National University, Daejeon 305-764, Korea. \*E-mail: khpark@cnu.ac.kr<sup>§</sup>Department of Advanced Organic Materials Engineering, Chungnam National University, Daejeon 305-764, Korea

Received September 10, 2013, Accepted October 13, 2013

**Key Words :** Anthracene, Fluorescent sensor, Fe<sup>3+</sup>, CHEF

Fluorescent metal ion sensors have become increasingly important tools for the quantitative, real time monitoring of metal ions in biological, environmental, medical and electronics.<sup>1-7</sup> These methods have multiple advantages over other methods, such as high sensitivity, low cost, ease of application and versatility.<sup>8</sup>

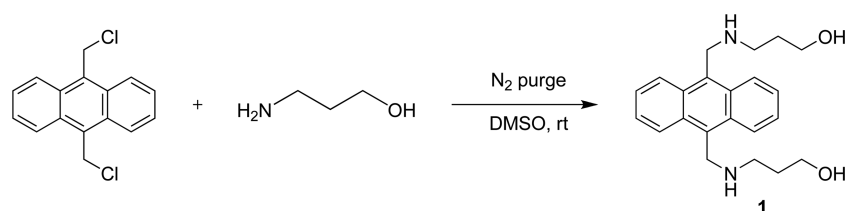
Typical fluorescent sensors consist of a receptor linked to a fluorophore directly or through a spacer. Wherein the receptor moiety is capable of selectively interacting with an analytes, the fluorophore converts the recognition proceedings into fluorescent signals. Several fluorophore based sensors such as anthracene,<sup>9a</sup> coumarin,<sup>9b</sup> rhodamine,<sup>9c</sup> BODIPY (borondipyrromethene),<sup>9d</sup> naphthalenediimide,<sup>9e</sup> pyrene,<sup>9f</sup> ferrocene,<sup>9g</sup> fluorescein,<sup>9h</sup> porphyrin,<sup>9i</sup> fluorene,<sup>9j</sup> calixarene<sup>9k</sup> and quinolone<sup>9l</sup> were reported.

Anthracene and its derivatives, a highly fluorescent fluorophore, have been investigated into a number of functions for sensing metal ions,<sup>10</sup> pH,<sup>11</sup> simple inorganic anions<sup>12</sup> and small organic molecule.<sup>13</sup> They have shown very interesting photo-physical properties. Upon complexation the CHEF (chelation enhanced fluorescence) or CHEQ (chelation enhanced fluorescence quenching) was observed for these systems.<sup>14-18</sup>

Up to now, some Fe<sup>3+</sup> selective fluorescence probe have been reported<sup>19</sup> since Fe<sup>3+</sup> is not only a biologically essential element but also a cofactor in many enzymatic reactions such as in oxygen-carrying capacity of hem.

Herein, we have synthesized and investigated a new fluorescent “turn-on” sensor that responded to Fe<sup>3+</sup> through anthracene moiety. And metal ion binding properties were investigated by <sup>1</sup>H NMR and fluorescence titration analysis.

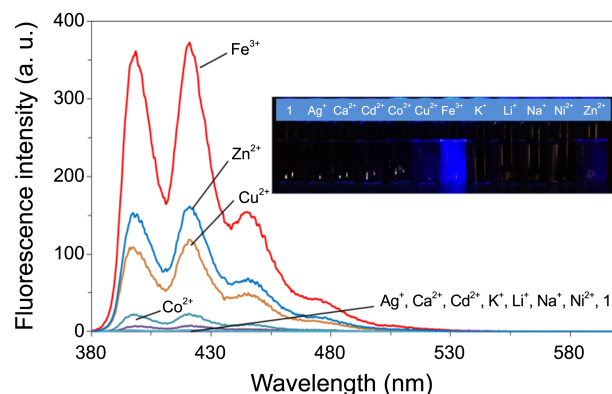
Synthetic route of 9,10-bis(3-hydroxypropylamino-methyl)anthracene (**1**), a new Fe<sup>3+</sup> sensor, was synthesized as

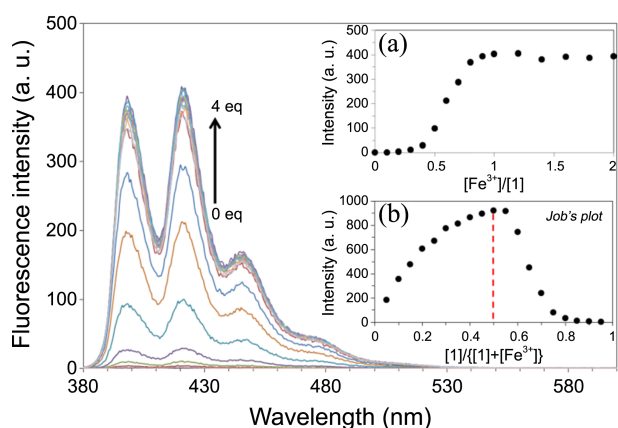
**Scheme 1.** Synthetic Route to compound **1**.

shown in Scheme 1.

Upon addition of Fe<sup>3+</sup> (10 μM, 1.0 equiv., nitrate salt) to the solution of compound **1**, colorless and non-fluorescent in acetonitrile solution, the fluorescence intensity increased rapidly, peaking at λ<sub>em</sub> = 421 nm. However, no changes were observed by Ag<sup>+</sup>, K<sup>+</sup>, Li<sup>+</sup>, Na<sup>+</sup>, Ca<sup>2+</sup>, Cd<sup>2+</sup>, Co<sup>2+</sup> and Ni<sup>2+</sup> (10 μM, 1.0 equiv., nitrate salt). On the other hand, the addition of Cu<sup>2+</sup> or Zn<sup>2+</sup> induced a small emission increment in acetonitrile solution (Figure 1). These photophysical data also indicated that anthracene derivative compound **1** had high selectivity and sensitivity to Fe<sup>3+</sup>.

The fluorescence titration of **1** (10 μM) was then conducted by different Fe<sup>3+</sup> amounts (0 to 4.0 equiv.). As shown in Figure 2(a), the fluorescence intensity at 421 nm increased as sigmoidal curve and reached saturation by addition of

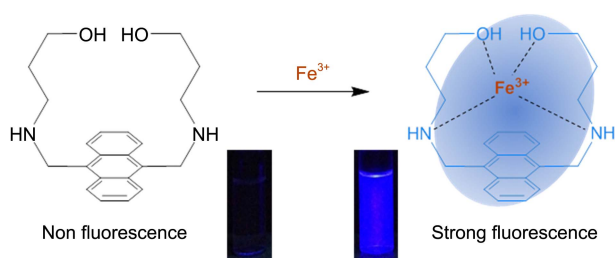
**Figure 1.** (a) Fluorescence intensity spectra of **1** ( $c = 1.0 \times 10^{-5}$  M) in the presence of various metal ions ( $c = 1.0 \times 10^{-5}$  M). Inset: The fluorescence image of a solution of **1** with metal ions excited by UV lamp ( $\lambda = 365$  nm). Conditions: CH<sub>3</sub>CN, λ<sub>ex</sub> = 373 nm, λ<sub>em</sub> = 421 nm.



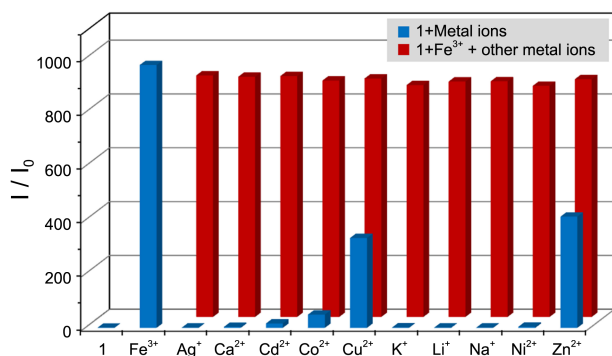
**Figure 2.** Emission spectra of **1** ( $c = 1.0 \times 10^{-5}$  M) during titration of 0–4 equivalent of  $\text{Fe}^{3+}$ . Inset (a): The fluorescence intensity as a function of  $[\text{Fe}^{3+}]$ . Inset (b): Job's plot data for evaluating the stoichiometry of  $1+\text{Fe}^{3+}$  complex. Conditions:  $\text{CH}_3\text{CN}$ ,  $\lambda_{\text{ex}} = 373$  nm,  $\lambda_{\text{em}} = 421$  nm.

equivalent  $\text{Fe}^{3+}$  (1 equiv.). The results revealed that sensor **1** behaved a good sensitivity toward  $\text{Fe}^{3+}$  and combined  $\text{Fe}^{3+}$  through a 1:1 stoichiometry. This result was further confirmed by the Job's plot (Figure 2(b)). In the Job's plot, the maximum fluorescence change was observed when the molar ratio of compound **1** versus  $\text{Fe}^{3+}$  was 0.5. Thus, in accordance with the 1:1 stoichiometry, the possible binding mode between **1** toward  $\text{Fe}^{3+}$  could be proposed in Scheme 2.

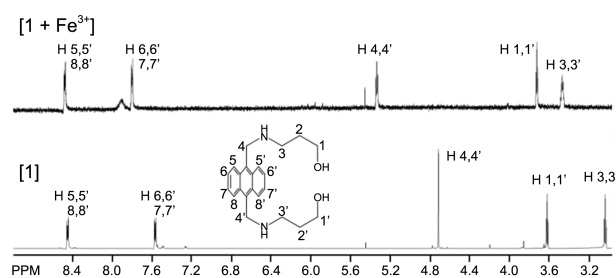
Competitive recognition of  $\text{Fe}^{3+}$  in the presence of various other metal ions, even in equal concentration, was also studied and shown in Figure 3. It was observed that  $\text{Fe}^{3+}$  detected in presence of the other metal ions like  $\text{Ag}^+$ ,  $\text{K}^+$ ,



**Scheme 2.** Proposed binding mode of compound **1** with  $\text{Fe}^{3+}$ .



**Figure 3.** Fluorescence intensity ratio of **1** ( $c = 1.0 \times 10^{-5}$  M) with various metal ions ( $c = 1.0 \times 10^{-5}$  M) in the absence (blue bar) and presence (red bar) of  $\text{Fe}^{3+}$  ( $c = 1.0 \times 10^{-5}$  M). Conditions:  $\text{CH}_3\text{CN}$ ,  $\lambda_{\text{ex}} = 373$  nm,  $\lambda_{\text{em}} = 421$  nm.



**Figure 4.** The partial  $^1\text{H}$  NMR spectra of compound **1** ( $c = 1.0 \times 10^{-4}$  M) [**1**] and in the presence of 1.0 equiv. of  $\text{Fe}(\text{NO}_3)_3$  [ $1+\text{Fe}^{3+}$ ] in  $\text{CD}_3\text{CN}$ .

$\text{Li}^+$ ,  $\text{Na}^+$ ,  $\text{Ca}^{2+}$ ,  $\text{Cd}^{2+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Co}^{2+}$  and  $\text{Ni}^{2+}$ . From the bar diagram, we could find out that the intensity negligibly change in presence of other metal ions. Therefore we could make it sure that other ions' interferences were insignificantly small during the detection of  $\text{Fe}^{3+}$ , which obviously strongly indicated the excellent selectivity of compound **1**.

To approve the nature of the complexation between **1** and  $\text{Fe}^{3+}$ , the  $^1\text{H}$  NMR spectrum of **1** was recorded in the absence and presence of  $\text{Fe}^{3+}$  (Figure 4). The  $^1\text{H}$  NMR spectrum of **1** in  $\text{CH}_3\text{CN}$  showed two aromatic protons (H5, H6) as multiplets in the region between  $\delta$  7.5 and 8.5, whereas the hydroxyalkylamine protons appeared as singlet and triplets  $\delta$  3.0 to 4.7, respectively. With an increase by the addition of  $\text{Fe}^{3+}$ , the aromatic and alkyl protons exhibited downfield shifts in the range  $\Delta\delta = 0.0$ –0.54. These observations effectively recommended the prospect of coordination between the donor set (HO, -NH) in **1** and the  $\text{Fe}^{3+}$ . Chemical shift change ( $\Delta\delta$ ) decreased in the following order;  $\text{H4} > \text{H3} \gg \text{H1}$ , indicating that the  $\text{Fe}^{3+}$  connected more strongly to the bridgehead nitrogen atoms than to oxygen atoms.

In conclusion, we have developed a new fluorescent sensor for  $\text{Fe}^{3+}$  based on anthracene moiety of hydroxyalkylamine. Fluorescent sensor **1** displayed highly selective and sensitive fluorescent “turn-on” toward  $\text{Fe}^{3+}$  in acetonitrile solution. The 1:1 stoichiometry of sensor complex  $1+\text{Fe}^{3+}$  was confirmed by Job's plots based on fluorescence emission titration. Furthermore, the binding sites of sensor complex  $1+\text{Fe}^{3+}$  was properly identified from  $^1\text{H}$  NMR study.

## Experimental

**Synthesis of 1.** To a solution of 3-amino-1-propanol 1.28 g (17 mmol) in anhydrous dimethylsulfoxide (30 mL) under nitrogen atmosphere, was added slowly 9,10-bis(chloromethyl)anthracene 0.90 g (3.3 mmol) at room temperature. After stirring for 6 h, water (70 mL) was poured into the reaction mixture. Then the product was extracted by dichloromethane. The combined organic layer was dried with anhydrous sodium sulfate and the solution was evaporated to dryness. The crude product washed with acetone to give 0.65 g (56%, pale yellow solid) of **1**.  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  1.63 (4H, qt), 2.83 (4H, t), 3.47 (4H, t), 4.58 (4H, s), 7.53 (4H, dd), 8.41 (4H, dd), MS (m/e): 352, HRMS: calcd. for  $\text{M}^+$  ( $\text{C}_{22}\text{H}_{28}\text{N}_2\text{O}_2$ ) 352.2151, found 352.2147.

**Acknowledgments.** This work was supported by Institutional Research Program of Korea Research Institute of Chemical Technology (KRICT) and the R&D Program of Small & Medium Business Administration (SMBA).

## References

1. Valeur, B.; Leray, I. *Coord. Chem. Rev.* **2000**, *205*, 3.
2. Quang, D. T.; Kim, J. S. *Chem. Rev.* **2010**, *110*, 6280.
3. de Silva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515.
4. Que, E. L.; Domaille, D. W.; Chang, C. *Chem. Rev.* **2008**, *108*, 1517.
5. Robinson, N. J.; Winge, D. R. *Annu. Rev. Biochem.* **2010**, *79*, 537.
6. Rurack, K. *Spectrochim. Acta* **2001**, *57A*, 2161.
7. Amendola, V.; Fabbrizzi, L.; Forti, F.; Licchelli, M.; Mangano, C.; Pallavicini, P.; Poggi, A.; Sacchi, D.; Taglietti, A. *Coord. Chem. Rev.* **2006**, *250*, 273.
8. Callan, J. F.; de Silva, A. P.; Magri, D. C. *Tetrahedron* **2005**, *61*, 8551.
9. (a) Kumar, S.; Singh, P.; Kaur, S. *Tetrahedron* **2007**, *63*, 11724. (b) Li, K.; Li, N.; Chen, X.; Tong, A. *Anal. Chim. Acta* **2012**, *712*, 115. (c) Zhou, Z.; Yu, M.; Yang, H.; Huang, K.; Li, F.; Yi, T.; Huang, C. *Chem. Commun.* **2008**, *29*, 3387. (d) Peng, X.; Du, J.; Fan, J.; Wang, J.; Wu, Y.; Zhao, J.; Sun, S.; Xu, T. *J. Am. Chem. Soc.* **2007**, *129*, 1500. (e) Shen, L. J.; Lu, X. Y.; Tian, H.; Zhu, W. H. *Macromolecules* **2011**, *44*, 5612. (f) Shellaiah, M.; Wu, Y. H.; Singh, A.; Ramakrishnam Raju, M. V.; Lin, H. C. *J. Mater. Chem. A* **2013**, *1*, 1310. (g) Chen, S.; Lu, L.; Sun, C.; Ma, H. *Analyst* **2010**, *135*, 577. (h) Chen, X.; Li, Z.; Xiang, Y.; Tong, A. *Tetrahedron Lett.* **2008**, *49*, 4697. (i) Li, C. Y.; Zhang, X. B.; Dong, Y. Y.; Ma, Q. J.; Han, Z. X.; Zhao, Y.; Shen, G. L.; Yu, R. Q. *Anal. Chim. Acta* **2008**, *616*, 214. (j) Ding, L.; Zou, Q.; Su, J. *Sens. Actuators B* **2012**, *168*, 185. (k) Chen, Q. Y.; Chen, C. F. *Tetrahedron Lett.* **2005**, *46*, 165. (l) Zhou, X.; Yu, B.; Guo, Y.; Tang, X.; Zhang, H.; Liu, W. *Inorg. Chem.* **2010**, *49*, 4002.
10. (a) Gunnlaugsson, T.; Lee, T. C.; Parkesh, R. *Tetrahedron* **2004**, *60*, 11239. (b) Lohani, C. R.; Kim, J. M.; Lee, K. H. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 6069. (c) Lu, D.; Lei, J.; Tian, Z.; Wang, L.; Zhang, J. *Dyes Pigm.* **2012**, *94*, 239. (d) Ocak, Ü.; Ocak, M.; Baçoğlu, A.; Parlayan, S.; Baþaran, D.; Alp, H.; Kantekin, H. *Polyhedron* **2010**, *29*, 1069. (e) Kim, K. S.; Jun, E. J.; Kim, S. K.; Choi, H. J.; Yoo, J.; Lee, C. H.; Hyun, M. H.; Yoon, J. *Tetrahedron Lett.* **2007**, *48*, 2481. (f) Huang, S.; Clark, R. J.; Zhu, L. *Org. Lett.* **2007**, *9*, 4999. (g) Chang, K. C.; Su, I. H.; Senthilvelan, A.; Chung, W. S. *Org. Lett.* **2007**, *9*, 3363.
11. Ihmels, H.; Meiswinkel, A.; Mohrschladt, C. J.; Otto, D.; Waidelich, M.; Towler, M.; White, R.; Albrecht, M.; Schnurpfeil, A. *J. Org. Chem.* **2005**, *70*, 3929.
12. (a) Gunnlaugsson, T.; Davis, A. P.; O'Brien, J. E.; Glynn, M. *Org. Biomol. Chem.* **2005**, *3*, 48. (b) Bohne, C.; Ihmels, H.; Waidelich, M.; Yihwa, C. *J. Am. Chem. Soc.* **2005**, *127*, 17158. (c) Ghosh, K.; Sarkar, A. R.; Masanta, G. *Tetrahedron Lett.* **2007**, *48*, 8725.
13. Ojida, A.; Yasuko, M. O.; Inoue, M. A.; Hamachi, I. *J. Am. Chem. Soc.* **2002**, *124*, 6256.
14. Witulski, B.; Weber, M.; Bergstrasser, U.; Desvergne, J. P.; Bassani, D. M.; Bouas-Laurent, H. *Org. Lett.* **2001**, *3*, 1467.
15. Zong, G.; Lu, G. *Sens. Actuators B* **2008**, *133*, 617.
16. Kumar, S.; Singh, P.; Kaur, S. *Tetrahedron* **2007**, *63*, 11724.
17. Witulski, B.; Zimmermann, Y.; Darcos, V.; Desvergne, J. P.; Bassani, D. M.; Bouas-Laurent, H. *Tetrahedron Lett.* **1998**, *39*, 4807.
18. Chang, J. H.; Kim, H. J.; Park, J. H.; Shin, Y. K.; Chung, Y. *Bull. Korean Chem. Soc.* **1999**, *20*, 796.
19. (a) Sikdar, A.; Panja, S. S.; Biswas, P.; Roy, S. *J. Fluoresc.* **2012**, *22*, 443. (b) Bai, R.; Gao, W.; Bai, S.; Yang, F.; Chen, H. *Opt. Mater.* **2013**, *35*, 833. (c) Singh, N.; Kaur, N.; Dunn, J.; MacKay, M.; Callan, J. F. *Tetrahedron Lett.* **2009**, *50*, 953. (d) Jung, H. J.; Singh, N.; Lee, D. Y.; Jang, D. O. *Tetrahedron Lett.* **2010**, *51*, 3962. (e) Weerasinghe, A. J.; Schmiesing, C.; Varaganti, S.; Ramakrishna, G.; Sinn, E. *J. Phys. Chem. B* **2010**, *114*, 9413. (f) Praveen, L.; Reddy, M. L. P.; Varma, R. L. *Tetrahedron Lett.* **2010**, *51*, 6626. (g) Kumar, M.; Kumar, R.; Bhalla, V. *Org. Lett.* **2011**, *13*, 366. (h) Zhang, M.; Gao, Y.; Li, M.; Yu, M.; Li, F.; Li, L.; Zhu, M.; Zhang, J.; Yia, T.; Huang, C. *Tetrahedron Lett.* **2007**, *48*, 3709. (i) Mao, J.; Wang, L.; Dou, W.; Tang, X.; Yan, Y.; Liu, W. *Org. Lett.* **2007**, *9*, 4567. (j) Lim, N. C.; Pavlova, S. V.; Brückner, C. *Inorg. Chem.* **2009**, *48*, 1173. (k) Bricks, J. L.; Kovalchuk, A.; Trieflinger, C.; Nofz, M.; Büschel, M.; Tolmachev, A. I.; Daub, J.; Rurack, K. *J. Am. Chem. Soc.* **2005**, *127*, 13522. (l) Xu, M.; Wu, S.; Zeng, F.; Yu, C. *Langmuir* **2010**, *26*, 4529.