Naked Eye Fluoride Ion Chemosensors with Anthraquinone Derivatives

Eun Jin Cho, Hyoung Min Yeo, Byung Ju Ryu, Hyun Ah Jeong, and Kye Chun Nam*

Department of Chemistry, and Institute of Basic Science, Chonnam National University, Gwangju 500-757, Korea
**E-mail: kcnam@chonnam.ac.kr*
Received September 20, 2006

Key Words : Fluoride sensor, Color change, Anthraquinone, Urea derivative

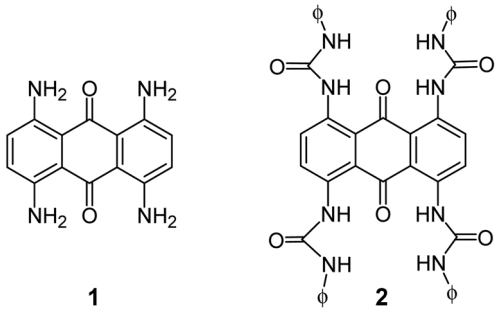
Anions play an important role in a wide range of chemical and biological processes, and considerable attention has been focused on the design of host molecules that can recognize and sense anion species selectively through the naked eye, electrochemical, and optical responses.[1,2] Among the range of biologically important anions, fluoride is of particular interest owing to its established role in preventing dental caries.[3] The fluoride anion has also been examined extensively as a treatment for osteoporosis.[4] However, excess fluoride can lead to fluorosis,[5] which is a type of fluoride toxicity that generally manifests itself clinically in terms of increasing the bone density. This diversity of its function, both beneficial and otherwise, makes the detection of fluoride anion important. Even though some receptor compounds for fluoride ions have reported,[6] there is a paucity of reports on a selective naked eye chemosensor for fluoride ions.[7]

Color changes, as signaling an event detected by naked eye, are widely used owing to the inexpensive equipment required or no equipment at all. The color variation can be related to either structural or conformational changes in the receptor structure when a complex is formed or to the formation of a charge transfer complex.[8-11]

Anthraquinones play an important role in the various photochemical and colorimetric sensor systems.[12,13] Recently Sessler and coworker[14] reported the important colorimetric anion sensors with 1,2- and 1,8-diaminoanthraquinone. They observed dramatic spectral changes with anions, particularly in the case of 1,2-diaminoanthraquinone, solutions initially yellow in color (λ_{max} = 478 nm) became dark purple (λ_{max} = 555 nm), red (λ_{max} = 519 nm), reddish orange (λ_{max} = 513 nm), orange (λ_{max} = 499 nm), purple (λ_{max} = 548 nm), and orange (λ_{max} = 493 nm) when exposed to fluoride, chloride, bromide, iodide, phosphate, and sulfate ions, respectively.

The urea moiety is powerful hydrogen bond donor and the anthraquinone group has proven to be the most versatile, redox-active chromophoric group. In pursuit of redox switchable chromogenic receptors, neutral tetra-urea receptor based on the anthraquinone moiety have been prepared and investigated its anion binding properties. The binding study was conducted with UV-Vis and color change experiment with the various anion. This novel neutral anion receptor **1** and **2** bind anions through hydrogen bonding and show a high selectivity with fluoride.

The anthraquinone urea ligand **2** was obtained by the reaction of 1,4,5,8-tetraaminoanthraquinone **1** and phenylisocyanate in THF/DMF (2 : 1 ratio). ^{1}H NMR spectrum of **2** shows two singlets at δ12.44 and 9.81 for the four urea N-H protons and a singlet at δ7.22 for the four aromatic protons of anthraquinone and at δ 7.78, 7.30 and 6.99 for the aromatic proton of phenyl group.



The UV-vis experiments were carried out in a DMSO solution. A receptor solution (3×10^{-5} M) was treated with the representative anions such as tetrabutylammonium (TBA) fluoride, chloride, bromide, iodide, dihydrogen phosphate, hydrogen sulfate, benzoate and acetate. When compound **1** forms a complex with F^-, the absorption peak at 611nm and 655 nm disappears and a new peak appears at 755 nm with a red-shifted by a $\Delta\lambda_{max}$ of 100 nm as shown in Figure 1. However, any bathochromic shift of other ions was not observed at all. Figure 2 shows the absorption spectra of compound **2** in the presence of the anions. The absorption peaks at 591nm and 637 nm were shifted to 686 nm ($\Delta\lambda_{max}$ 49 nm) when fluoride was added to compound **2** in the DMSO solution. On the other hand, any bathochromic shift

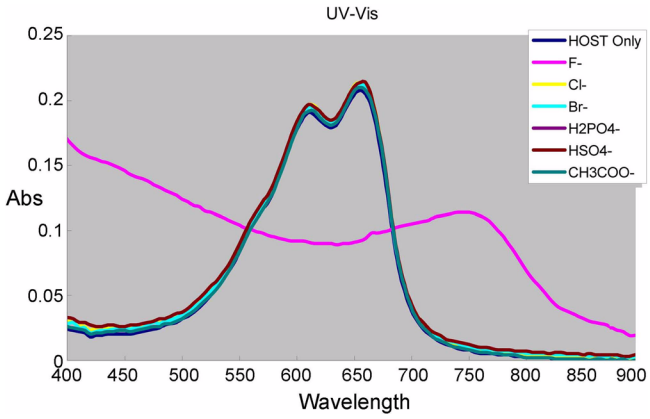


Figure 1. Absorption spectra of compound **1** (3×10^{-5} M) upon addition of tetrabutylammonium fluoride, chloride, bromide, iodide, dihydrogen phosphate, hydrogen sulfate, benzoate and acetate (1.5×10^{-2} M) in DMSO.

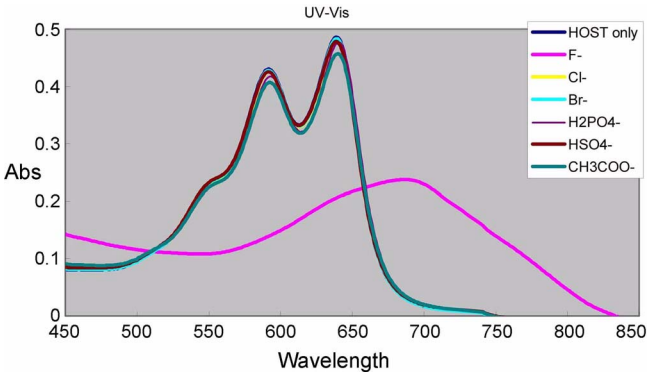


Figure 2. Absorption spectra of compound **2** (3×10^{-5} M) upon addition of tetrabutylammonium fluoride, chloride, bromide, iodide, dihydrogen phosphate, hydrogen sulfate, benzoate and acetate (1.5×10^{-2} M) in DMSO.

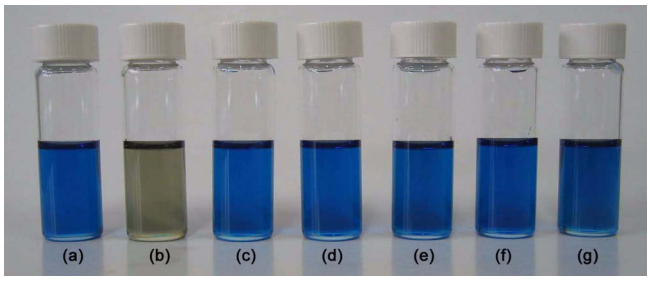


Figure 3. Color changes of ligand **1** (2.5×10^{-4} M) in DMSO with the addition of tetrabutylammonium anions (2.5×10^{-1} M). (a) = free receptor, (b) = Fluoride, (c) = Chloride, (d) = Bromide, (e) = Dihydrogen Phosphate, (f) = Hydrogen Sulfate, (g) = Acetate

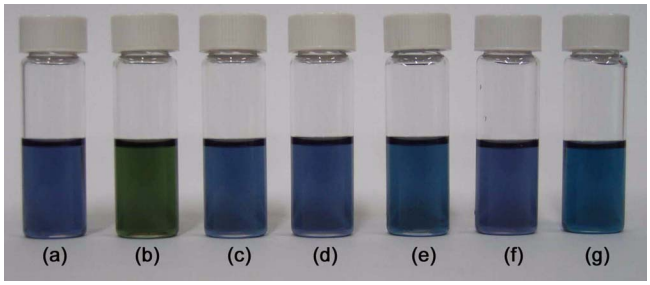


Figure 4. Color changes of ligand **2** (2.5×10^{-4} M) in DMSO with the addition of tetrabutylammonium anions (6.25×10^{-1} M). (a) = free receptor, (b) = Fluoride, (c) = Chloride, (d) = Bromide, (e) = Dihydrogen Phosphate, (f) = Hydrogen Sulfate, (g) = Acetate

of other ions was not observed at all. A color change could be observed easily by mixing the ligand and anion as shown in Figure 3. A receptor solution was simply treated with various anions such as F^-, Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^-, CH_3COO^- and $C_6H_5COO^-$. Noticeable color changes were observed when ligand **1** was treated with fluoride ions. It was remarkable that a blue ligand solution became black-green when fluoride ions were added to compound **1** in DMSO, but no color changes were observed when the other anions were added. A similar green color was observed when the urea ligand **2** was treated with fluoride ions.

Fluoride ion binding properties were investigated from ^{1}H NMR titration. When fluoride ions were added, a broad singlet at 7.62 ppm for -NH_2 resonance for ligand **1** slowly shifted to downfield with more than two equivalents of fluoride ions. Also, a new singlet at 6.42 ppm was appeared, indicating that ligand anion was formed.

In conclusion, chromogenic anthraquinones which have tetra urea moieties as a anion binding site were prepared by the selective reaction of amino groups with phenyliso-cyanate. But urea derivative **2** showed a similar UV-Vis spectral change with **1**, suggesting that fluoride binding occurred at the amino site as well as urea moiety. Anthraquinone group might increase the acidity of amine, which can afford to bind with fluoride ions. An electrochemical investigation should be carried out to reveal the redox properties of ligand **2**.

Acknowledgment. This work was supported by the Ministry of Education of Korea (BK 21 project).

References

1. *Supramolecular Chemistry of Anions*; Bianchi, E.; Bowman-James, K.; Garcia-Espana, E. Eds.; Wiley-VCH: New York, 1997.
2. Martinez-Manez, R.; Sancenon, F. *Chem. Rev.* **2003**, *103*, 4419.
3. Kirk, K. L. *Biochemistry of the Halogens and Inorganic Halides*; Plenum Press: New York, 1991; p 58.
4. Kleerekoper, M. *Endocrinol. Metab. Clin. North Am.* **1998**, *27*, 441.
5. (a) Wiseman, A. *Handbook of Experimental Pharmacology XX/2*, Part 2; Springer-Verlag: Berlin, 1970; pp 48-97. (b) Weatherall, J. A. *Pharmacology of Fluorides* in *Handbook of Experimental Pharmacology XX/1*, Part 1; Springer-Verlag: Berlin, 1969; pp 141-172. (c) Dreisbuch, R. H. *Handbook of Poisoning*; Lange Medical Publishers: Los Altos, CA, 1980.
6. (a) Dusemund, C.; Sandanayake, K. R. A. S.; Shinkai, S. *J. Chem. Soc. Chem. Commun.* **1995**, 333. (b) Yamamoto, H.; Ori, A.; Ueda, K.; Dusemund, C.; Shinkai, S. *Chem. Commun.* **1996**, 407. (c) Scherer, M.; Sessler, J. L.; Gebauer, A.; Lynch, V. *Chem. Commun.* **1998**, 85. (d) Anzenbacher, Jr. P.; Jursíková, K.; Lynch, V. M.; Gale, P. A.; Sessler, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 11020. (e) Nicolas, M.; Fabre, B.; Simonet, J. *Chem. Commun.* **1999**, 1881. (f) Camiolo, S.; Gale, P. A. *Chem. Commun.* **2000**, 1129. (g) Lee, D. H.; Im, J. H.; Lee, J. H.; Hong, H. I. *Tetrahedron Lett.* **2002**, *43*, 9637. (h) Yun, S.; Ihm, H.; Kim, H. G.; Lee, C. W.; Indrajit, B.; Oh, K. S.; Gong, Y. J.; Lee, J. W.; Yoon, J.; Lee, H. C.; Kim, K. S. *J. Org. Chem.* **2003**, *68*, 2467. (i) Ilioudis, C. A.; Tocher, D. A.; Steed, J. D. *J. Am. Chem. Soc.*, **2004**, *126*, 12395.
7. (a) Boiocchi, M.; Boca, L. D.; Gomez, D. E.; Fabbrizzi, L.; Licchelli, M.; Monzani, E. *J. Am. Chem. Soc.* **2004**, *126*, 16507. (b) Miaji, H.; Sessler, J. L. *Angew. Chem. Int. Ed.* **2001**, *40*, 154. (c) Jose, D. A.; Kumar, D. K.; Ganguly, B.; Das, A. *Org. Lett.* **2004**, *6*, 3445. (d) Zhang, B. G.; Cai, P.; Duan, C. Y.; Miao, R.; Zhu, L. G.; Niitsu, T.; Inoue, H. *Chem. Commun.* **2004**, 2206.
8. Dietrich, B. *Pure Appl. Chem.* **1993**, *65*, 1457.
9. Atwood, J. L.; Holman, K. T.; Steed, J. W. *Chem. Commun.* **1996**, 1401.
10. Gale, P. A. *Coord. Chem. Rev.* **2001**, *213*, 79.
11. Beer, P. D.; Gale, P. A. *Angew. Chem. Int. Ed.* **2001**, *40*, 486.
12. (a) Delgado, M.; Gustowski, D. A.; Yoo, H. K.; Gatto, V. J.; Gokel, G. W.; Echegoyen, L. *J. Am. Chem. Soc.* **1988**, *110*, 119. (b) Chen, Z.; Schall, O. F.; Alcala, M.; Gokel, G. W.; Echegoyen, L. *J. Am. Chem. Soc.* **1992**, *114*, 444. (c) Jose, D. A.; Kumar, D. K.; Ganguly, B.; Das, A. *Org. Lett.* **2004**, *6*, 3445.
13. (a) Miyaji, H.; Sato, W.; Sessler, J. L. *Angew. Chem. Int. Ed.* **2000**, *39*, 1777. (b) Brooks, S. J.; Birkin, P. R.; Gale, P. A. *Electrochem. Comm.* **2005**, *7*, 1351.
14. Miyaji, H.; Sessler, J. L. *Angew. Chem. Int. Ed.* **2001**, *40*, 154.
15. Spectroscopic data. **2**. mp 198-201 °C; ^{1}H NMR (DMSO-d_6) δ 12.44 (s, 4H, NH), 9.81 (s, 4H, NH), 7.78 (d, 8H, ArH, J = 7.8 Hz), 7.30 (t, 8H, ArH, J = 7.5 Hz), 7.22 (s, 4H, ArH), 6.99 (t, 4H, ArH, J = 7.2 Hz); ^{13}C NMR (DMSO) δ184.9, 153.1 (-CO), 147.1, 140.2, 136.9, 129.4, 129.0, 125.7, 119.2, 119.0, 108.2 (Ar).