Fluoride-selective Colorimetric Sensors Based on Hydrazone Functionality

Lili Zhou, Xiaohong Zhang,* and Shikang Wu*
Nano-Organic Photoelectronic Labsoratory, Technical Institute of Physics and Chemistry,
Chinese Academy of Sciences, Beijing, 10010, P. R. China

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Hydrazone derivatives **2**, **3**, **5**, **6** with H-bond donor and color-reporting chromophore were synthesized to be used as chemosensors for selective detecting anionic species via naked eye and absorption spectroscopy. The results revealed that these compounds exhibited good selectivity to fluoride anion (F^-). In order to clarify the mechanism of interaction between anionic species and sensors, compound **4** was synthesized for comparative study.

The design and synthesis of systems that are capable of sensing various biologically and/or chemically negative charged species is an area of the current interest.[1] This is due to the crucial roles anions play in biological processes, medicine, catalysis, and molecular assembly.[2] Moreover, various anions are believed to have deleterious effect on the environment.[3] Redox and photoactive sensor molecules have been developed to coordinate with anions and report their presence via changes of physical properties (such as redox potential, fluorescence, or phosphorescence) of hosts.[4] A more attractive approach in this field involves the construction of colorimetric anion sensors[5] which have considerable advantages over others,[6] because it can be carried out without potentiostat or spectrometer. However, few cases in such system have been reported so far.[7] For example, aminoanthraquinone has been used to monitor various anions in organic solution through the color changes with poor selectivity.[8] Recently, we discovered that hydrazone function group could act as powerful colorimetric sensors selective to F^- anions over other anionic species and its derivatives are very easy to be synthesized in high yield by reacting *p*-nitrophenylhydrazine with substituted benzaldehyde in ethanol.

The structures of the six compounds studied as colorimetric sensors for detecting anionic species are listed in Figure 1. Because there exist several different binding sites in these molecules, it is necessary to clarify where the key site is for the recognition of anions.

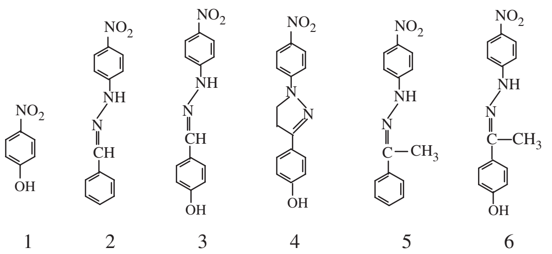

Figure 1. The molecular structures of the hydrazone compounds.

The color of the solution changed when the effective interaction between sensors and anions occurred. Figure 2 displays the UV–vis absorption spectra of compound **2**, **3** upon addition of 100 equivalents of diverse anions in acetonitrile, respectively (anions were added in the form of tetrabutylammonium salts). The most remarkable effect was observed when F^- was added. The colors of both compounds **2** and **3** solutions changed from yellow to purple upon addition of F^-. For compound **2**, the peak at 396 nm disappeared while a new peak appeared at 562 nm in absorption spectra, no significant color change was observed upon addition of $H_2PO_4^-$, Cl^-, Br^-, I^-, HSO_4^-, NO_3^-, AcO^-, or ClO_4^- anions. This hints that there is no interaction between compound **2** and anionic species listed above except for F^-. However, the color of compound **3** solution changed from yellow to dark yellow upon addition of $H_2PO_4^-$, while it was similar to compound **2** when other anionic species were added. The absorption spectra also indicate that the addition of $H_2PO_4^-$ can induce significant bathochromic shift, though less dramatic than that induced by addition of F^-. These results indicate that compounds **2** and **3** (especially, compound **2**) could be used as a naked-eye sensor for effective recognition of F^-.

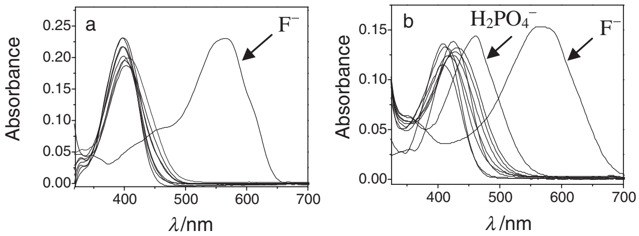

Figure 2. UV–vis absorption spectra of compound **2**(a), **3**(b) (1×10^{-5} mol/L) after addition of 100 equiv. of anions (F^-, $H_2PO_4^-$, Cl^-, AcO^-, HSO_4^-, Br^-, NO_3^-, ClO_4^-, and I^-) in acetonitrile, respectively.

In order to clarify the interaction between sensing molecules and anionic species, a series of similar compounds with differential functionalities were synthesized (seen in Figure 1). Compared to compound **2**, compound **3** possesses a hydroxy group at para-position of phenyl group. The specific ability of compound **2** to recognize the F^- and the recognition ability of compound **3** to both F^- and $H_2PO_4^-$ imply that hydrazone function group prefers to interact with F^-. In order to determine whether the hydrogen on carbon or on nitrogen of hydrazone function group participates in the F^- recognition, compound **5** and **6** in which a methyl group replaces the hydrogen on carbon were synthesized. The color of compounds **5** and **6** solutions similarly changed from yellow to purple when F^- was introduced. This hints that the hydrogen on nitrogen is response for the recognition of F^-. To further verify the role of the hydrogen on nitrogen played on the recognition of F^-, compound **4**, a pyrazolin derivative in which an alkyl group replaces both hydrogens of hydrazone function group were synthesized and investigated upon addition of anions. It is very interesting to note that the addition of either F^- or $H_2PO_4^-$ induces a little color change and the apparent color change requires the large amount of anion (the absorption peak, originally at 405 nm, shifts to 438 and 422 nm upon addition of 100 equivalents of tetrabutylammonium fluoride and dihydrogen phosphate, respectively). These results corroborate that the hydrogen on nitrogen in this series of hydrazone derivatives is the specific site for the recognition of F^-. Unfortunately, in our case, attempts to acquire complex stability constants from titration absorption experiments were unsuccessful. The absorption bands of these hydrazone derivatives kept shifting to the red when anions were added (data not shown). This hints that the interactions between hydrazone derivatives and anions are very complicated. However competitive assays indicate that the system is selective to F^-. For instance, the addition of a mixture of F^-, $H_2PO_4^-$, Cl^-, AcO^-, HSO_4^-, Br^-, NO_3^-, ClO_4^-, and I^- to the solutions of compounds **2**, **5**, or **6** in acetonitile resulted in the absorbance shift in UV–vis absorption spectra similar to that obtained from the addition of F^-.

In order to understand the mechanism of the interaction between anionic species and sensors, the binding properties of receptor **2** to different anions were further investigated by using ^{1}H NMR experiments in DMSO-d_6. The complexation-induced chemical shifts can be used to infer a quite detailed picture of anions binding. Although the ^{1}H NMR spectrum of **2** shown a signal at 8.15 ppm for the NH proton, this signal became broad and undetectable upon addition of 5 equivalence of F^- anion. However, the addition of F^- led to significant downfield shifts (up to 0.52 ppm) for the signals arising from the protons of the phenyl group. In contrast, no shift was observed for receptor **2** upon addition of other anions, suggesting that the interaction between receptor **2** and other anions is energetically unfavorable. These findings indicate that the proton on nitrogen is strongly perturbed by added F^-.[9] In addition, treating **2** with increasing amount of n-$Bu_4N^+OH^-$ (1.0 M solution in methanol) in CH_3CN showed a similar increase of a new peak at $\lambda_{max} = 562$ nm, indicating that the observed red-shift absorbance is possibly correlated to the deprotonated hydrazone species. Whether the color change arises from the formation of hydrogen bonding between NH in hydrazone and F^-, N^- in hydrazone and HF, or other possible complex need to be further investigated. Both hydrogen bonding between NH in hydrazone and F^-, and N^- in hydrazone and HF were proposed to extend π-conjugated system of hydrazone derivatives which accounts for large red shift in Fabbrizzi et al. recent work.[10] The consideration of large color change resulted from decomposed hydrazone derivatives is not taken since the hydrazone derivatives are relative stable in non-acidic condition, and moreover, the absorption band of decomposed species should be in the blue region in comparison to those of hydrazone derivatives.

According to the basicity of anions, F^-, $H_2PO_4^-$, and AcO^- should form stronger hydrogen bonding with hydrogen donor group and result in noticeable color change compared to other anions.[11] As mentioned above, only F^- does induce a pronounced color change of compound **3** solution, while $H_2PO_4^-$ induces a relatively weaker effect on the color change. Provided that the basicity of anionic species was identical, the $H_2PO_4^-$ would be able to form hydrogen bonding with the hydrogen on nitrogen equally as F^-. The disparity of results may be owing to the subtle electron affinity of these anions, which determinedly influences the proton transfer or the formation of hydrogen bonding between $H_2PO_4^-$ and H donor of hydrazone derivatives. This is further confirmed from results that no significant color change was observed in compound **2** (without OH) solution upon addition of $H_2PO_4^-$, while color change occured when $H_2PO_4^-$ was added into compound **3** (with OH) solution.

In these compounds, the hydrazone function group is the most important part for the recognition of anionic species. It can be illustrated from the interaction between the control compound **1** and different anions. There is no significant color change observed upon addition of 100 equivalents diverse anions. It displays that the hydrazone function group is necessary for the color-reporting resulted from its sensitivity to anions.

In summary, a new family of easy-to-prepare reagents used as anionic sensors has been synthesized and studied. It was found that compounds **2**, **5**, **6** are highly selective to F^-, in concomitant with color change and compound **3** can interacts with both $H_2PO_4^-$ and F^-. The present study demonstrates that hydrazone derivatives can be used as powerful and effective colorimetric anion chemosensor.

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References

1 a) F. P. Schmidtchen and M. Berger, *Chem. Rev.*, **97**, 1609 (1997). b) M. M. G. Antonisse and D. N. Reinhoudt, *Chem. Commun.*, **1998**, 443. c) P. Piatek and J. Jurczak, *Chem. Commun.*, **2002**, 2450.

2 a) P. A. Gale, *Coord. Chem. Rev.*, **199**, 181 (2002). b) P. A. Gale, *Coord. Chem. Rev.*, **213**, 79 (2001). c) P. D. Beer and P. A. Gale, *Angew. Chem., Int. Ed.*, **40**, 486 (2001).

3 P. D. Beer, P. K. Hopkins, and J. D. McKinney, *Chem. Commun.*, **1999**, 1273.

4 a) P. D. Beer, *Chem. Commun.*, **1996**, 689. b) H. Z. Xie, S. Yi, and S. K. Wu, *J. Chem. Soc., Perkin Trans. 2*, **1999**, 2751. c) H. Miyaji, P. Anzenbacher, Jr., J. L. Sessler, E. R. Bleasdate, and P. A. Gale, *Chem. Commun.*, **1999**, 1723.

5 a) P. Anzenbacher, Jr., A. C. Try, H. Miyaji, K. Jursikova, V. M. Lynch, M. Marquez, and J. L. Sessler, *J. Am. Chem. Soc.*, **122**, 10268 (2000). b) C. Lee, D. H. Lee, and J. I. Hong, *Tetrahedron Lett.*, **42**, 8665 (2001). c) K. H. Lee, H. Y. Lee, and J. I. Hong, *Tetrahedron Lett.*, **42**, 5447 (2001). d) R. Kato, S. Nihizawa, T. Hayashita, and N. Teramae, *Tetrahedron Lett.*, **42**, 5053 (2001). e) F. Sancenon, R. Martinez-Manaez, and J. Soto, *Angew. Chem., Int. Ed.*, **41**, 1416 (2002).

6 Y. Kubo, S. Maeda, S. Tokita, and M. Kuto, *Nature*, **382**, 522 (1996).

7 a) P. Chakrabarti, *J. Mol. Biol.*, **234**, 463 (1993). b) M. H. Mei and S. K. Wu, *New J. Chem.*, **2001**, 471.

8 H. Miyaji, W. Sato, and J. L. Sessler, *Angew. Chem., Int. Ed.*, **40**, 154 (2001).

9 G. Xu and M. A. Tarr, *Chem. Commun.*, **2004**, 1050.

10 M. Vázquez, L. Fabbrizzi, A. Taglietti, R. M. Pedrido, A. M. González-Noya, and M. R. Bermejo, *Angew. Chem., Int Ed.*, **43**, 1962 (2004).

11 a) S. Nishizawa, P. Bühlmann, M. Lwao, and Y. Umezawa, *Tetrahedron Lett.*, **36**, 6483 (1995). b) T. R. Kelly and M. H. Kim, *J. Am. Chem. Soc.*, **116**, 7072 (1994).

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