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Fluoride-selective chromogenic sensors based on azophenol

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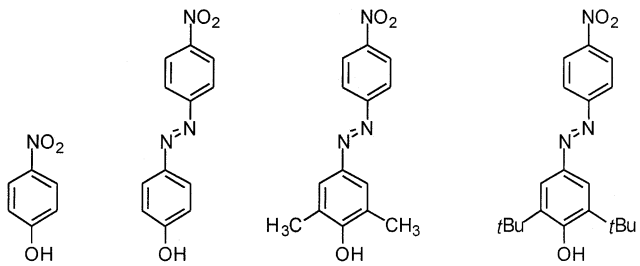
Abstract—Azophenol dyes were used as an optical-signaling chromophoric unit to selectively trigger color change upon complexation with fluoride anion among various anions.

Of the classes of artificial anion receptors reported to date, few are capable of selectively sensing anions via optical methods.[1] In particular, the number of chromogenic sensors for fluoride anion[2] is still quite small in spite of its importance in clinical treatment for osteoporosis[3] and detection of fluoride toxicity resulting from overaccumulation of fluoride in bone.[4]

Selective complexation and coloration of azophenol hosts with alkali,[5] alkaline earth metal ions[5] and amines[6] have been reported. However, fluoride anion-selective coloration with azophenol derivatives has not yet been reported in spite of their potential affinity to anions through hydrogen bonding interaction or salt complex in organic phase.[7] Therefore, 2,6-dialkyl azophenol derivatives can be used to trigger color change upon complexation with anions. In this paper we report the selective complexation of fluoride anion in organic solution and signaling its presence via marked color changes using azophenols (**2**, **3**, **4**) as an optical-signaling chromophoric unit. Azophenol based anion sensors (**2**–**4**) contain an azophenolic OH that could function as an anion binding site capable of naked-eye anion sensing, and alkyl groups (H, methyl, *tert*-butyl) on 2 and 6 positions which may affect anion selectivity by exerting steric effects on incoming anions.

The binding ability of compounds **1**–**4** for anions was investigated using the UV–vis absorption method.[8] The molar ratio analysis of the signal change exhibits a 1:1 complex formation. Analysis of the UV–vis data for the complex with **3** gives the binding constants in the order $F^- \gg H_2PO_4^- > AcO^- > N_3^- > HSO_4^- > Cl^- > Br^- > I^-$ in chloroform.[9] Extremely tight binding of fluoride anion to **2**, **3**, and **4** results from the formation of the salt complex. A linear increase in absorbance at 562 nm for **2**, 615 nm for **3** and 632 nm for **4** is observed respectively until each chromophore is saturated with 1 equiv. of fluoride anion, and after that almost no absorbance change is observed. The control system, *p*-nitrophenol **1** without an extended π-conjugating *p*-nitroazophenyl group, shows lower selectivity toward anions. It turns out that the hydrogen bonding ability and basicity of the anions are the main factors in anion binding to compounds **1**–**4**.



The UV–vis spectra of compound **3** after addition of 1 equiv. of each anion are presented in Fig. 1. All anions

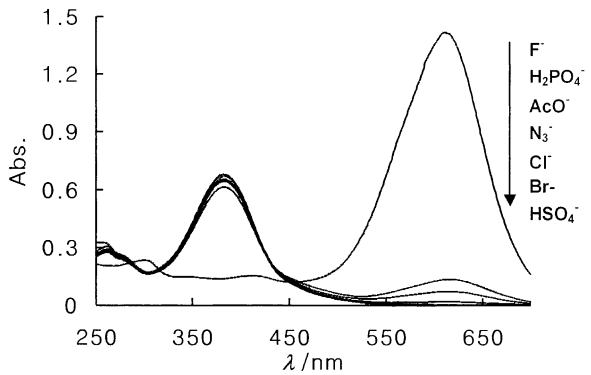


Figure 1. UV–vis absorption spectra of **3** after addition of 1 equiv. of anions (F^-, $H_2PO_4^-$, AcO^-, N_3^-, Cl^-, Br^-, HSO_4^-).

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added to compounds **1**, **2**, **3** and **4** cause red shifts due to the increase of the donor ability of the chromophore. In fact, compounds **3** and **4** undergo a dramatic fluoride anion-induced color change from yellow to blue upon the addition of 1 equiv. of tetrabutylammonium fluoride. However, in chloroform, the addition of protic polar solvents (water and methanol) results in turning the blue solution into yellow. This is presumably because protic solvents compete for F^- at the phenolic OH hydrogen bond site.

Compared to **2**, compound **3** shows excellent discrimination for fluoride anion due to steric hindrance by the dimethyl groups at 2 and 6 positions, which prohibits the formation of effective hydrogen bonds and salt complexes for the larger anions. Compounds **2**–**4** exhibit little color change upon addition of 1 equiv. of various anions except F^-, while the addition of excess anions ($H_2PO_4^-$, AcO^-, N_3^-) to azophenols causes a detectable color change from yellow to yellow–green. Although sensor **4** is expected to show better selectivity for F^- due to the larger steric bulkiness of the *t*Bu groups *ortho* to the phenolic OH, it does not show better discrimination in color for fluoride anion than **3**. This may result from the existence of hydrazone–azophenol equilibrium in **4**.[10]

UV–vis spectra of **3** in the presence of anions ($H_2PO_4^-$, AcO^-, N_3^-, HSO_4^-) show the absorption maxima at 615 nm for the phenolate formation (salt complex) and at 470 nm for the hydrogen bonded complex. Especially, titration spectra of fluoride anion display both a linear decrease of the absorption band at 386 nm and a linear increase of the absorption band at 615nm without the appearance of the hydrogen bonded complex at 470 nm, as shown in Fig. 2. Treating **3** with increasing amount of $n\text{Bu}_4\text{N}^+\text{OH}^-$ (1.0 M solution in methanol) in $CHCl_3$ shows a similar increase of a new peak at $\lambda_{max}=607$ nm indicating the phenolate formation. Similarly, ^{19}F NMR for a mixture of **3** (25 mM) and 1 equiv. of $n\text{Bu}_4\text{N}^+\text{F}^-$ in $CHCl_3$ ($CFCl_3$ as an internal reference) shows a peak at −139 ppm due to HF hydrogen bonded to the phenolate formed from a proton transfer to F^- (free HF in $CFCl_3$ resonates at −192 ppm),[12] and the fluorine resonance of $n\text{Bu}_4\text{N}^+\text{F}^-$ in $CHCl_3$ appears at −124 ppm in the absence of **3**, implying that the phenolic proton of **3** is completely transferred to the fluoride anion. ^1H NMR data for the mixture of **3** (22 mM) and excess $n\text{Bu}_4\text{N}^+\text{F}^-$ in $CHCl_3$ display new peaks corresponding to the salt complex. In contrast, anions Cl^-, Br^-, I^- show only hydrogen-bonded complexes with a newly emerging peak at $\lambda_{max}=470$ nm.

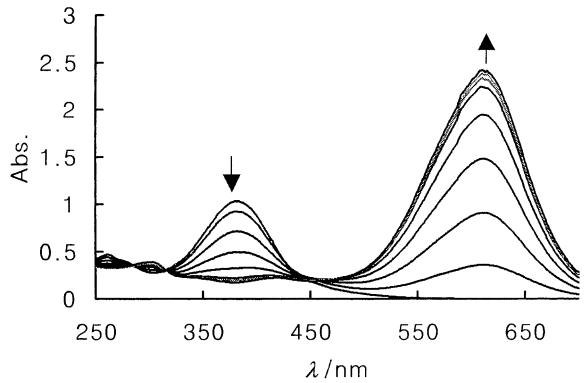

Figure 2. UV–vis spectra of **3** (4.5×10^{-5} M) after addition of fluoride anion (0, 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.7, 1.9, 2.8, 3.6 equiv.).

Azophenols **2**, **3**, **4** undergo naked-eye detectable changes in color, from yellow to bluish purple (**2**) or blue (**3**, **4**), in the presence of F^- ions in chloroform. In particular, **3** causes a most pronounced, selective color change from yellow to blue upon addition of fluoride anion, among various anions.

In conclusion, azophenol dyes provide a simple unexplored class of anion receptors which are capable of selectively reporting the presence of fluoride anion in chloroform by color changes. The present study illustrates that azophenol chromophores can be used as a colorimetric anion sensor.

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9. Binding constants (M^{-1}) of **3** with anions in $CHCl_3$ at rt: F^- (1 000 000), $H_2PO_4^-$ (1400), N_3^- (140), AcO^- (250), Cl^- (40), Br^- (30), I- (13), HSO_4^- (70).
10. An ^1H NMR study reveals that **2** and **3** exist only as the azophenol isomer, but **4** consists of a hydrazone–azophenol equilibrium mixture (hydrazone:azophenol = 1:1.7 in $CDCl_3$), which is in contrast to a marked preference for the hydrazone isomer exceeding 95% in the dinitrophenylazo-2,6-dialkylphenol derivatives.[11] Also, an IR spectrum of **4** displays both NH and OH signals due to hydrazone–azophenol equilibration in comparison to **2** and **3**. UV–vis spectrum of **4** shows λ_{max} values at 425 and 445 nm indicating the presence of two isomers of hydrazone and azophenol.
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