Dual Spectroscopic Responses of Pyridinium Hemicyanine Dyes to Anions

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The absorption and fluorescence spectroscopic responses of three pyridinium hemicyanine dyes to anions F^-, Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^- and OAc^- were investigated. At lower concentrations of OAc^- (less than 1 equiv.), both the absorption and the fluorescence intensities of **1**—**3** were more effectively changed than F^- at identical concentrations. At higher concentrations of OAc^- (more than 1 equiv.), the interaction was opposite for each compound. ^1H NMR results indicated the interaction between **1**, **2** or **3** and F^- proceeded through hydrogen bonding. The results showed that these dyes are promising to develop dual fluorescence and chromogenic chemosensors toward F^- and OAc^- according to the subtle difference in the affinity of F^- and OAc^-.

Keywords hemicyanine, absorption spectra, fluorescence spectra, chemosensors, anions

Introduction

As anions play important roles in a wide area of chemical, medical, industrial, environmental and biological processes, considerable attention has been focused on the design of chemosensors that can recognize and detect anion species selectively through visible, electrochemical, nuclear magnetic and optical responses.[1-5] Color changes, recognized by the naked eye, are conveniently applied because they may be used as dip-stick sensors. Color variation can be related to either structural or conformational changes in chemosensors when an interaction is happened.[2,5,6] Chemosensors are designed according to the binding of a specific anion with their receptor sites, with a chromophore on a chemosensor responsible for translating the receptor-anion association into an optical signal.

Among the biologically important anions, fluoride is of particular importance due to its crucial role in dental care[7,8] and osteoporosis.[9] The addition of fluoride in drinking water and toothpastes has become widespread due to the valuable effects of fluoride in human health. High doses of fluoride are hazardous and can lead to dental or skeletal fluorosis. Therefore, convenient methods for the detection of fluoride have become a hot topic.

We set out to choose pyridinium hemicyanine dyes as chromophores (Figure 1). Their large dipole moments originate from an intramolecular charge transfer (ICT) states. The ground state, and therefore the color of the compounds, may be modulated via hydrogen bonding or deprotonation of the hydroxy moiety by small anions possessing high electron density such as F^- and HO^-.[10] It is significant to develop simple systems without complicated synthesis. The dual action of **1**—**3** toward F^- would thus yield a combined fluorescent and colorimetric based sensor in a single molecule. The receptors containing hydroxy groups displayed the F^- and OAc^- recognition due to hydrogen bonding and/or intermolecular proton transfer in the sensor-anion complexes, but most of those receptors could not distinguish these two anions.[11-13] Detailed investigation in this work found acetate increased the absorbance of the new band and decreased the fluorescence intensity of **1**—**3** more pronounced than F^- at lower concentration (less than 1 equiv.). At higher concentrations, the interaction was opposite for each compound. Acetate could even decrease the absorbance of the newly formed absorption band in some degree, resulting in partially faded color.

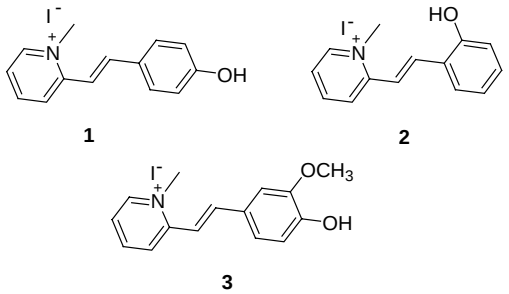

Figure 1 Pyridinium hemicyanine dyes **1**, **2** and **3**.

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Experimental

General experiments

The anion salts *n*-Bu_4NF, *n*-Bu_4NCl, *n*-Bu_4NBr, *n*-Bu_4NI, *n*-Bu_4NHSO_4, *n*-Bu_4NOAc and *n*-$Bu_4NH_2PO_4$ were purchased from Aladdin-reagent Inc. All the solvents for spectroscopic measurement were AR grade and were dried and distilled before use.

NMR spectra were recorded with a 400 MHz Varian spectrometer. Electrospray ionization mass spectra (ESI-MS) were measured on an LC-MSD-Trap-SL system. Elemental analyses were carried on an elemental analyzer (Flash EA 1112, Thermo Electron SPA, Italy). Absorption spectra were measured on a TU1901 UV-vis spectrometer. Fluorescence spectra were collected on the SPEX Fluorolog-3 spectrometer. Stock solutions of pyridinium hemicyanine dyes **1**—**3** and anions were prepared in CH_3CN solutions. Then they were diluted to 3×10^{-5} mol•L^{-1} with CH_3CN. Titration experiments were performed by placing 3 mL of the diluted solution in a quartz cuvette of 1 cm optical path length, then adding the stock solutions of anions incrementally by means of a micro-pipette. Spectra were recorded 5 s later after each addition.

Synthesis of 1—3

Synthesis of 2-methyl-*N*-methyl pyridinium iodide 9.8532 g (105.88 mmol) of 2-methylpyridine and 14.9862 g (105.54 mmol) of iodomethane were dissolved in 20 mL of acetonitrile. The mixture was refluxed for 10 h. After cooling to room temperature, the mixture was concentrated under reduced pressure and then ethyl ether was added and stirred. The precipitate was filtered and washed twice with ethyl ether. 10.686 g of salts were resulted. The crude product was used directly without further purification.

Synthesis of (*E*)-1-methyl-2-[4-(hydroxybenzyl)-vinyl]-pyridinium iodide (1) 0.4237 g (1.79 mmol) 2-methyl-*N*-methyl pyridinium iodide and 0.2836 g (2.32 mmol) 4-hydroxybenzaldehyde were dissolved in 10 mL ethanol with three drops of triethyl amine. The mixture was refluxed for 12 h and then concentrated under reduced pressure. The precipitate was filtered and washed twice with ethyl ether. The crude product was chromatographed with dichloromethane/ethanol1 (V∶V = 2∶1) and finally get the product. ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.21 (s, 1H), 8.82 (d, J=6.8 Hz, 1H), 8.48—8.40 (m, 2H), 7.88 (d, J=16.0 Hz, 1H), 7.82 (d, J=6.0 Hz, 1H), 7.35 (d, J=16.0 Hz, 1H), 7.26 (d, J=8.4 Hz, 2H), 6.88 (d, J=8.4 Hz, 2H), 4.32 (s, 3H); MS (EI) *m/z* (%): 212.1 ($[M-I]^+$, 100). Anal. calcd for $C_{14}H_{14}NOI\cdot0.5H_2O$: C 48.29, H 4.34, N 4.02; found C 48.26, H 4.35, N 4.03.

Similar procedures were carried out for the synthesis of **2** and **3**, using 2-methyl-*N*-methyl pyridinium iodide to react with 2-hydroxybenzaldehyde and 4-hydroxy-3-methoxybenzaldehyde respectively.

(*E*)-1-Methyl-2-[2-(hydroxybenzyl)vinyl]-pyridinium-iodide (**2**): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.45 (s, 1H), 8.89 (d, J=6.0 Hz, 1H), 8.48—8.42 (m, 2H), 7.97 (d, J=16 Hz, 1H), 7.88—7.84 (m, 1H), 7.77 (dd, J=1.2, 8.0 Hz, 1H), 7.61 (d, J=16 Hz, 1H), 7.32—7.28 (m, 1H), 6.97—6.90 (m, 2H), 4.32 (s, 3H); MS (EI) *m/z* (%): 212.1 ($[M-I]^+$, 100). Anal. calcd for $C_{14}H_{14}NOI\cdot0.4H_2O$: C 48.55, H 4.31, N 4.04; found C 48.58, H 4.30, N 4.05.

(*E*)-1-Methyl-2-[4-(hydroxyl-3-methoxybenzyl)-vinyl]-pyridinium iodide (**3**): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 9.82 (s, 1H), 8.82 (d, J=6.4 Hz, 1H), 8.47—8.40 (m, 2H), 7.88 (d, J=16.0 Hz, 1H), 7.83—7.79 (m, 1H), 7.46 (d, J=1.6 Hz, 1H), 7.38 (d, J=16.0 Hz, 1H), 7.29 (dd, J=1.6, 8.4 Hz, 1H), 6.88 (d, J=8.0 Hz, 1H), 4,34 (s, 3H), 3.87 (s, 3H); MS (EI) *m/z* (%): 242.1 ($[M-I]^+$, 100). Anal. calcd for $C_{15}H_{16}NO_2I\cdot0.8H_2O$: C 46.96, H 4.62, N 3.65; found C 46.99, H 4.61, N 3.66.

Results and discussion

Absorption responses of 1—3 to F^- and OAc^-

The absorption spectra displayed maximum peaks at 371, 353 and 383 nm for **1**, **2** and **3** in CH_3CN solutions respectively. The 12 nm red shift for **3** compared to **1** is due to electron donating effect of the methoxy group on the benzene ring. The electron donating effect on the benzene ring would decrease the energy gap from π to π* transition, leading to red-shift in the absorption spectra of **3**. The 18 nm blue shift for **2** compared to **1** is due to steric effect of the hydroxyl group in 2-position on the benzene ring, which can be proved by the density functional theory (DFT) calculations performed with the Gaussian 03 software (Table S1). The results showed that the dihedral angle of **1** (1.6°) is less than that of **2** (4.7°). And the energy difference between the HOMO orbital and LUMO orbital for **1** is slightly lower than that for **2**.

The binding ability of **1**, **2** and **3** for anions was investigated using the UV-vis absorption method.[14] Figure 2 shows the absorption spectra of **1**, **2** or **3**, with the concentration of 3.0×10^{-5} mol/L in CH_3CN upon titration with F^- or OAc^- respectively. For **1**, the absorbance at 371 nm decreased with the increase of F^- concentration, at the same time a new absorption band at about 543 nm appeared and enhanced (Figure 2a). The changes of absorption spectra indicated obvious interaction between F^- and **1**. The relationship between the absorbance at 543 nm and the equivalents of F^- was almost linear for **1** within 2 equiv. of F^- (Figure 3a). Non-linear fitting could not get a good fitting in the whole range. The modulation in the electron-donating capabilities of the hydroxyl group in the presence and absence of F^- directly influences the ICT from the benzene ring to the pyridinium ring. In the presence of F^-, the ICT effect was enhanced. The color of the solution changed from light yellow to strong pink upon addition of 6 equiv. of F^- (Figures 4 and 5). The absorption at 371 nm was almost switched off and that at 543

nm was switched on. However, the response of **1** to OAc^- is quite different. Upon titration of 1 equiv. OAc^- to **1**, a pink color was generated. The absorbance of **1** at 543 nm reached its maximum (Figure 2b, Figure 3a). Further titration of OAc^- gradually decreased the absorbance. The absorption band at 371 nm was red-shifted to 400 nm. And new absorption bands between 400 to 500 nm became stronger and stronger (Figure 2b). After addition 6 equiv. of OAc^- to **1**, the color of the solution became weaker. This is possibly due to aggregation induced by tetrabutylammonium acetate. Upon addition of less than 1 equiv. of OAc^-, the interaction between **1** and OAc^- became stronger than the interaction between **1** and F^-. However, upon addition of more than 1 equiv. of OAc^-, the results were opposite. Whereas addition of other anions such as Cl^-, Br^-, I^-, $H_2PO_4^-$ and HSO_4^- almost did not induce obvious color change and absorption change of **1**.

Similar responses to F^- or OAc^- for **2** or **3** were observed (Figures 2c—2g). Job's plot exhibited a 1∶1 complex formation for each compound toward F^- or OAc^-. Upon titration with F^-, the color of **2** turned from colorless to purple (Figure 5). The absorption band at 353 nm decreased and a new band at 546 nm evolved and reached its limiting value upon addition of 4 equiv. of F^- (Figure 2c). The largest red-shift (193 nm) in the

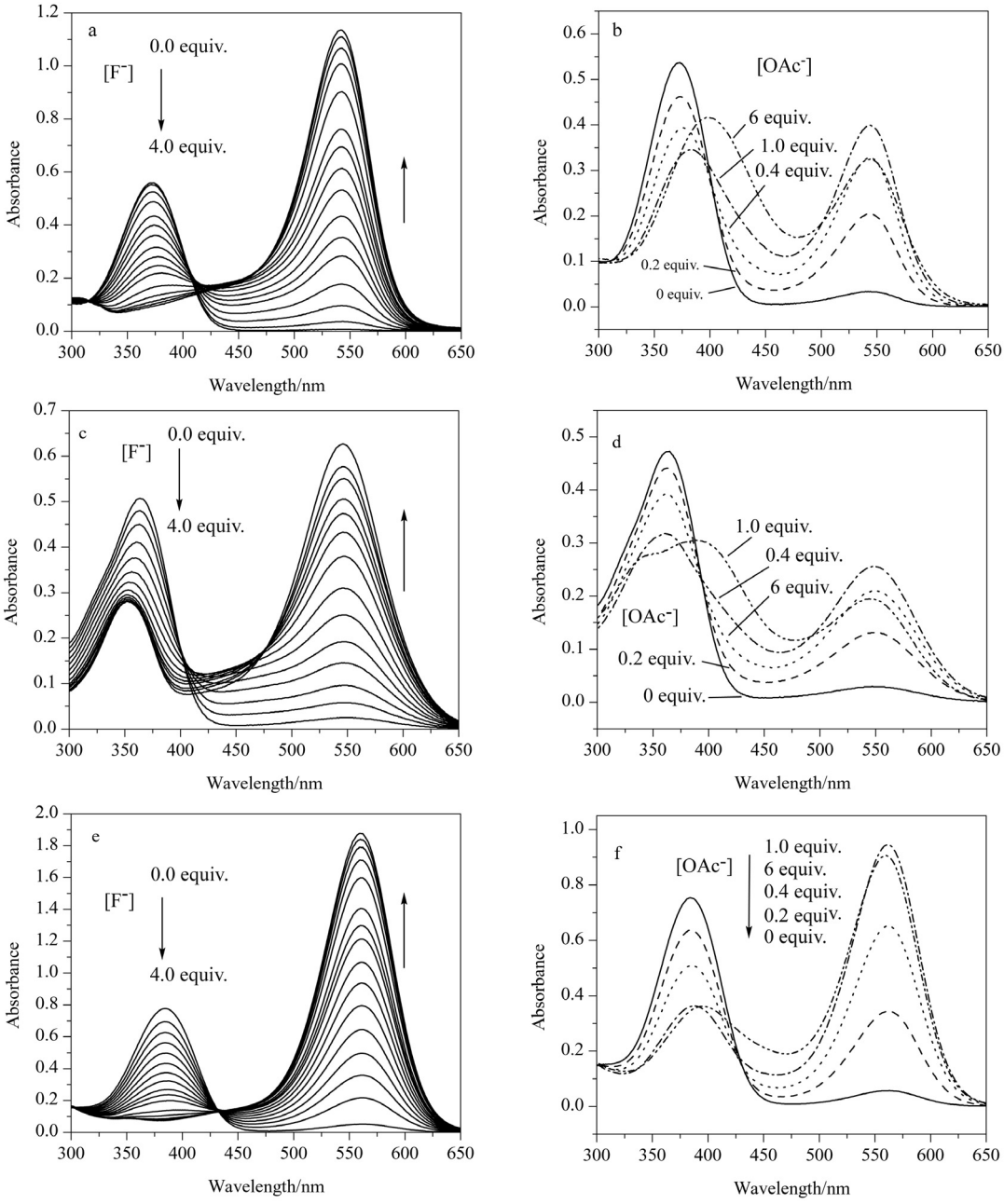

Figure 2 Absorption spectra of **1**, **2** and **3** (3.0×10^{-5} mol/L) in CH_3CN upon titration of F^- and OAc^-. (a) addition of F^- to **1**, (b) addition of OAc^- to **1**, (c) addition of F^- to **2**; (d) addition of OAc^- to **2**, (e) addition of F^- to **3**, (f) addition of OAc^- to **3**.

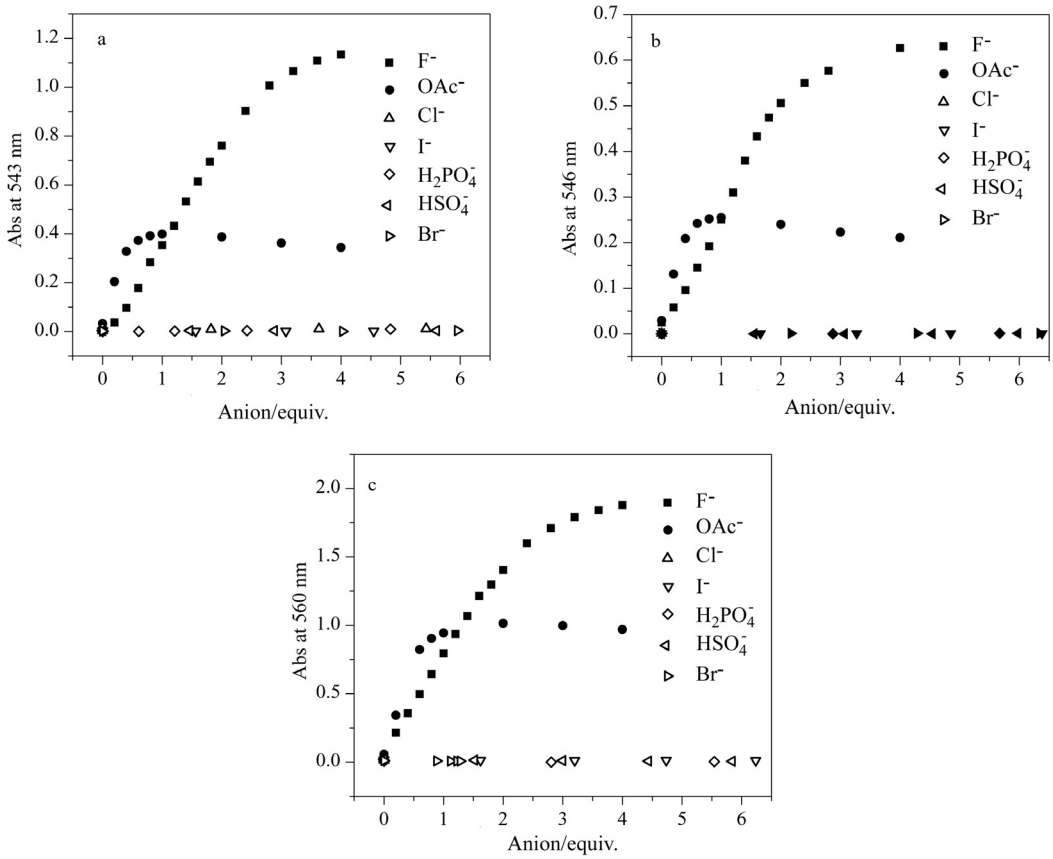

Figure 3 Titration curves of different anions to **1** (a), **2** (b) and **3** (c) in CH_3CN respectively.

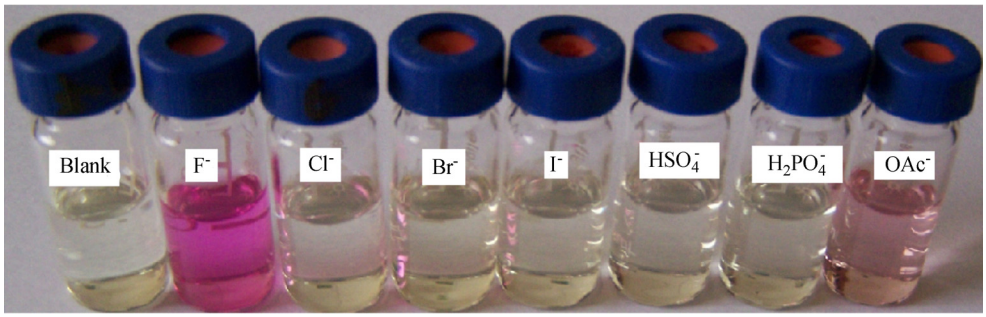

Figure 4 Color changes of **1** (2×10^{-5} mol•L^{-1}) in CH_3CN upon addition of 6 equiv. of different anions.

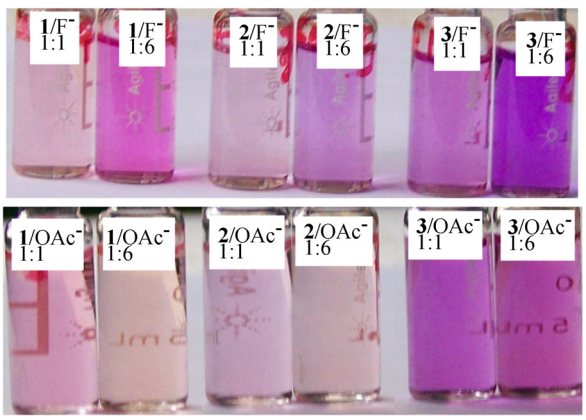

Figure 5 Color changes of **1**, **2** and **3** (3×10^{-5} mol•L^{-1}) to different equivalents of F^- and OAc^- in CH_3CN.

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absorption maxima was observed after F^- was added to the solution of **2**. This was attributed to the steric effect of the hydroxyl group on the benzene before interaction with F^-. The deprotonated form of **2** is more delocalized than the protonated form. With the increase of F^- concentration, the color of **3** turned purple (Figure 5). The absorption band at 383 nm decreased gradually and a new band at 560 nm evolved and reached its maximum upon addition of 4 equiv. of F^- (Figure 2e). One isosbestic point at 430 nm was observed. The larger red-shift and deeper color of **3** than **1** upon titration of F^- is due to electron-donating substituent of the methoxy group *ortho* to the hydroxyl group on the benzene ring of **3**. Compounds **1**, **2** and **3** have a much better selectivity and sensitivity to F^- than OAc^- upon titration of more than one equivalent, while they have a slightly better selectivity and sensitivity to OAc^- than F^- upon titration of less than one equivalent (Figures 3 and 5).

Fluorescence responses of 1, 2 and 3 to F^- and OAc^-

The fluorescence intensity of **3** at 517 nm was substantially quenched upon titration of 3.2 equiv. of F^-, with the maximum band slightly blue-shifted (Figure 6a).

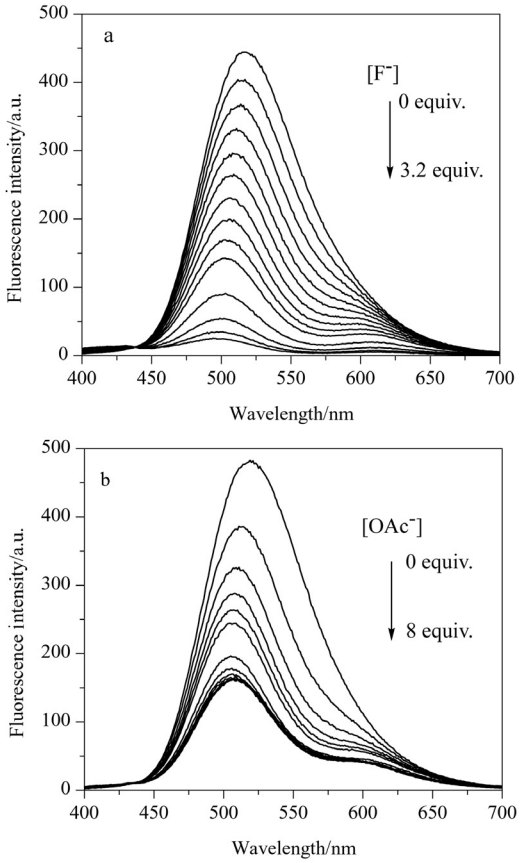


Figure 6 (a) Fluorescence spectra of **3** (3.0×10^{-5} mol/L) in CH_3CN solutions upon addition of F^- (from up to down the equivalents of F^- are 0, 0.2, 0.4, 0.6, 0.8, 1, 1.2, 1.4, 1.6, 1.8, 2, 2.4, 2.8, 3.2; (b) fluorescence spectra of **3** titrated with OAc^- (from up to down the equivalents of OAc^- are 0, 0.2, 0.4, 0.6, 0.8, 1, 2, 3, 4, 5, 6, 7, 8. λ_{ex}=383 nm, ex slit=5 nm, em slit=10 nm).

The absorption effect of newly-formed species to free dye **3** was attributed to the reduced intensity of fluorescence and the blue-shifted peaks with the increase of F^- concentration. The fluorescence of **3** was more efficiently quenched within less than 1 equiv. of OAc^- compared to F^-. Then it was slightly quenched until 4 equiv. of OAc^- were added. Further addition of OAc^- did not change the fluorescence spectra at all (Figure 6b).

Similar effects were observed in the fluorescence spectra of **1** or **2** upon addition of F^- or OAc^- (Figure 7). The fluorescence of **1** or **2** was also more effectively quenched by OAc^- within less than 1 equiv. compared to F^-, then slightly quenched with more than 1 equiv. of OAc^-. Further addition of OAc^- did not change the fluorescence spectra at all. However, further addition of F^- quenched the fluorescence of **1** or **2** more efficiently than OAc^- (with more than 1 equiv.). The relationship between fluorescence intensities of **1**, **2** or **3** and the equivalents of F^- was almost linear, while the relationship between fluorescence intensities and equivalents of OAc^- was nonlinear. The variation trends of the fluorescence intensities coincided with the absorbance upon addition of F^- or OAc^-. Other anions investigated in this paper did not induce any obvious fluorescence quenching.

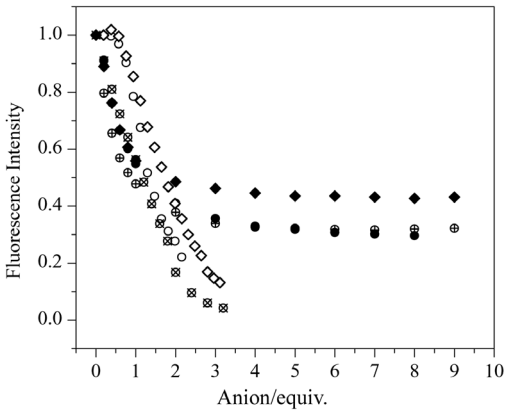


Figure 7 Relationship between fluorescence intensity of **1**, **2** and **3** and the equivalents of F^- or OAc^-. **1**-F^- (○); **1**-OAc^- (●); **2**-F^- (◊); **2**-OAc^- (♦); **3**-F^- (⊗); **3**-OAc^- (⊕). The original fluorescence was normalized for each compound.

Plotting the fluorescence changes at fluorescence maximum as a function of −lg[anion] gave sigmoidal curves in each case that switched off within one log unit.[15] These changes were fitted using a non-linear least squares regression algorithm, giving the binding constants lg K=(4.75±0.02), (4.84±0.02) and (4.83±0.03) toward OAc^- for **1**, **2** and **3** respectively and lg K=(4.12±0.01), (4.31±0.01) and (4.54±0.01) toward F^- for **1**, **2** and **3** respectively. The results indicated the affinity ability of **1**, **2** or **3** is indistinguishable toward OAc^-.

^{1}H NMR responses to F^- of 2

As an example, the interaction of **2** with excess F^- was proved by ^{1}H NMR experiments in DMSO-d_6 (Figure 8). It was found that the aromatic proton signals and the methyl group signals underwent upfield shifts upon addition of excess F^-. Such an effect was resulted from the through-bond propagation onto the aromatic framework of the electronic charge generated on O—H deprotonation,[16] thus leading to a shielding effect and inducing upfield shift. The signal of the hydroxyl group disappeared. An obvious triplet peak at about δ 16 appeared, indicating the formation of HF_2^- [17] as the driving force, implying that the phenolic proton of **2** is completely transferred to F^-.

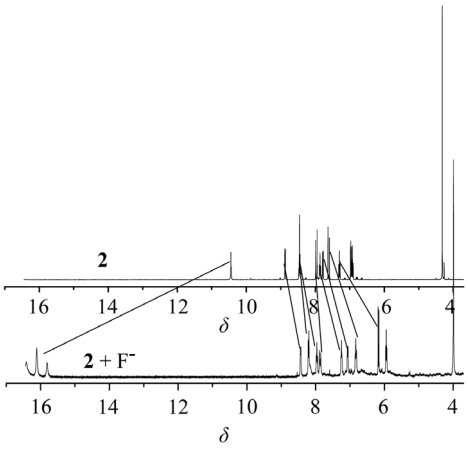
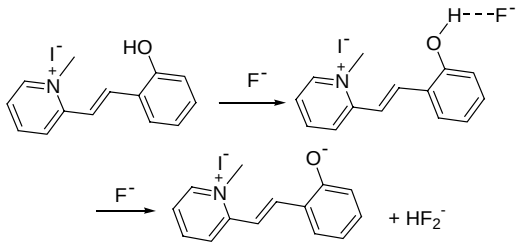


Figure 8 Partial ^{1}H NMR spectra of **2** before and after addition of F^- in DMSO-d_6.

The F^- induced deprotonation process was fully reversible. The addition of polar protic solvents such as H_2O and CH_3OH resulted in a reverse color change from purple to yellow. This is presumably because protic solvent competed for F^- with the hydroxy moiety, moreover, the presence of a relatively high amount of protic solvent disfavors the formation of the deprotonated form of **2**. However, in water-containing medium, the excess addition of strong base $[Bu_4N]OH$ could still deprotonate the hydroxyl group of **2** and induce a color change.

Compounds **1**, **2** and **3** underwent naked-eye detectable changes in color, from almost colorless to purple in the presence of F^- in CH_3CN. The spectroscopic changes signify the interaction of F^- with the hydroxy moiety which is through strong hydrogen bonding between O—H···F with less than 1 equiv., then through complete deprotonation with more than 1 equiv. (Scheme 1). The high electron density of F^- leads to further deprotonation, making the electron transfer more feasible and forming the more stabilized HF_2^-, so that at higher concentrations of F^-, the interaction is much more efficiently than OAc^-. Upon the addition of low concentration of OAc^-, both of its two resonance oxygens can interact with the hydroxyl moiety besides its basicity. The interaction between OAc^- and **1**, **2** or **3** was found slightly stronger than F^-. At higher concentrations of OAc^-, aggregation effects became more and more effective.

Scheme 1 Possible interaction mechanism of **2** and F^-



Conclusions

Pyridinium hemicyanine dyes bearing hydroxyl groups on the benzene ring provide a simple class of anion receptors which are capable of selectively reporting the presence of F^- and OAc^- in CH_3CN by color changes. The interactions between OAc^- and **1**, **2** or **3** were found slightly stronger than F^- at lower concentrations (less than 1 equiv.). But the interactions between F^- and **1**, **2** or **3** were found much more efficiently than OAc^- at higher concentrations (more than 1 equiv.). Unlike most fluorescent sensors for F^- that cannot tell F^- from OAc^-, compounds **1**, **2** and **3** showed good selectivity for F^- over OAc^- at higher concentrations (more than 1 equiv.). The interaction through hydrogen bonding and further deprotonation at the hydroxyl moiety of hemicyanine chromophores resulted in dual colorimetric and fluorescent response toward F^-.

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