# Colorimetric fluoride sensors based on deprotonation of pyrrole–hemiquinone compounds†

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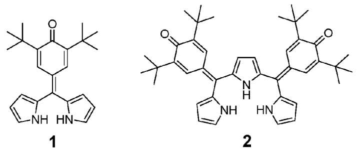
**The combination of pyrrole and hemiquinone units produced a novel prototype of efficient colorimetric fluoride sensors, and the presence of the tautomerism effect provides additional means of modulating the sensing behavior.**

The design and synthesis of anion receptors have become of increasing interest due to the important roles of anions in many biological and chemical processes.[1] Considerable attention has been focused on the design of colorimetric hosts that can selectively recognize anion species through visible color changes with the advantages that the responses can be conveniently detected by the naked eye.[2–5]

Hydrogen containing polar groups, such as ureas and thioureas, have been widely employed as hydrogen-bond donors in the design of anion receptors.[6] Pyrrole, as a versatile building unit for macrocyclic dyes, has an NH moiety, which may be utilized to bind anions. In fact, pyrrole-based macrocyclic dyes are well documented as cation and anion binding agents.[7–9] However, only a few examples have been reported utilizing easily accessible acyclic oligopyrroles incorporating chromophores or fluorophores as colorimetric or fluorometric anion receptors.[2j,10,11]

Among various anions, fluoride has caused intense interest owing to its important clinical roles and theoretical interest.[12] As the most electronegative atom, fluoride can form the strongest hydrogen bond with protons and tend to deprotonate polar NH groups. Thus, various colorimetric sensors containing NH arrays have been developed to detect fluoride based on the deprotonation mechanism.[13]

Recently, we have developed anion receptors with various binding moieties.[14] In this work, we designed acyclic oligopyrrole–hemiquinone compounds **1** and **2** (Scheme 1) as fluoride sensors utilizing the conjugated hemiquinone–pyrrole structures as novel chromophores and the oligopyrrole moieties as the recognition site.



**Scheme 1** Structures of sensors **1** and **2**.

Compounds **1** and **2** were readily synthesized and characterized by $^1$H, $^{13}$C NMR and HRMS (Scheme S1, Fig. S1–S6†). Anion sensing measurements have revealed that they can selectively recognize fluoride through vivid color changes. In view of the unique structures, the easy synthesis and the highly selective recognition of $F^-$, **1** and **2** may be developed as a novel prototype of colorimetric fluoride sensors.

Changes in electronic spectra upon adding various anions were measured in DMSO. The addition of fluoride induced a color change from orange to bright blue (Fig. 1), and the peak centered at 496 nm in the UV-vis spectra (Fig. 2) gradually decreased, with a new band developed at 568 nm, which can be ascribed to internal charge transfer (ICT) originated from the deprotonation of the N–H moiety,[15] showing the $FHF^-$ signal in the $^1$H NMR spectra (Fig. S7†). In contrast, $Cl^-$, $Br^-$, $I^-$, $CN^-$, $CH_3COO^-$ and $H_2PO_4^-$ bind **1** only through hydrogen bonds, and the addition of these anions did not induce obvious changes in the color and the UV-vis spectra of **1**. The selectivity for $F^-$ over other anions, especially $CN^-$ and $CH_3COO^-$, is important because many reported fluoride sensors suffer from the deleterious interference of these anions. The excellent selectivity of **1** for fluoride over other anions is evident from the pronounced differences in absorbance and color changes.

Compared to **1**, sensor **2** has a more complicated structure containing two kinds of NH protons with different chemical environments and its sensing behavior showed marked

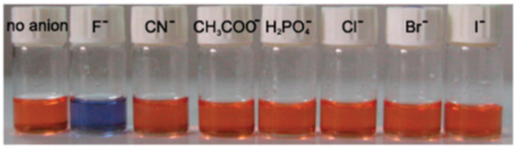


**Fig. 1** A photograph showing the color change of **1** (25 μM) in DMSO upon addition of 40 eq. of various anions.

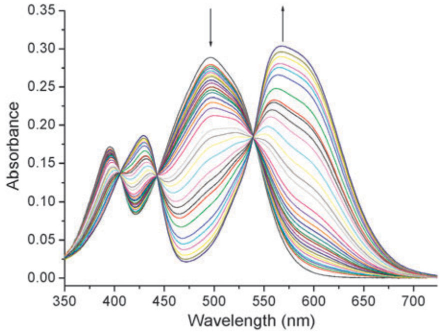


**Fig. 2** UV-vis spectral changes of **1** (10 μM in DMSO) observed upon the addition of 0–180 eq. $F^-$ (TBA salt) in DMSO.

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† Electronic supplementary information (ESI) available: Full experimental and crystallographic data and Fig. S1–S13. CCDC 740202. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c001509a

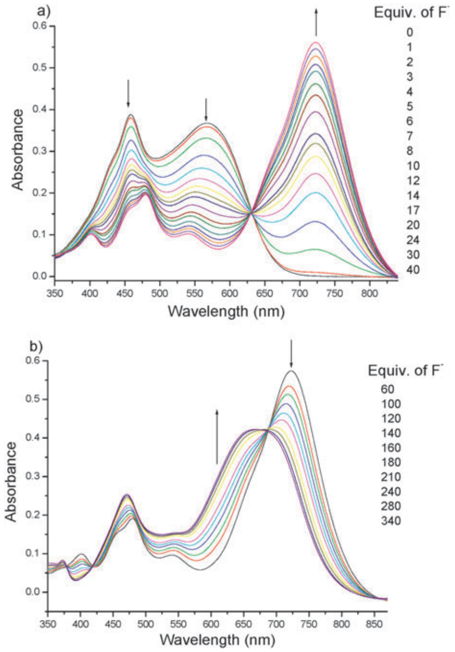
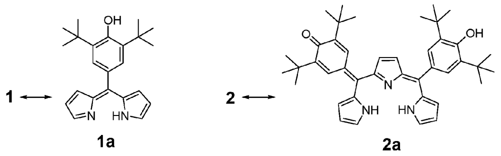


**Fig. 3** UV-vis spectral changes of **2** (10 μM in DMSO) observed upon addition of $F^-$ (TBA salt) in DMSO.

difference from that of **1**. The spectral changes of a DMSO solution of **2** upon addition of $F^-$ are shown in Fig. 3. The initial addition (< 40 eq.) resulted in a decrease of the bands at 459 and 571 nm and an increase of a new band at 740 nm, meanwhile the color changed from wine-red to gray. Upon further addition (> 40 eq.), the band at 740 nm decreased and a new band developed at 624 nm. The solution color further changed from gray to green (Fig. S8†), which can be ascribed to the second deprotonation process. The blue shift from 740 to 624 nm can be rationalized by the different energy levels for the mono- and di-deprotonated species, as indicated by the DFT calculations (Fig. S9 and Table S1†). $Cl^-$, $Br^-$, and $I^-$ can be readily discriminated from $F^-$ based on the fact that no obvious change in the UV-vis spectra could be observed even when large equivalents of these anions were added.

On the other hand, the addition of $CN^-$, $CH_3COO^-$ or $H_2PO_4^-$ to a DMSO solution of **2** could induce only mono-deprotonation, with a new band developed at 740 nm (Fig. S10†). The difference between these anions and $F^-$ may be ascribed to the unique stability of the hydrogen bonded complex $[HF_2]^-$.[13a,16] Thus, $F^-$ may be discriminated from these anions based on the further color change from gray to green caused by dideprotonation. These observations are in sharp contrast to the fact that $F^-$ could induce only monodeprotonation of **1**. This may be ascribed to the difference in NH acidity between **1** and **2**, *i.e.*, the molecule of **1** contains only one electron-withdrawing hemiquinone group, whereas, **2** has two hemiquinone groups, which induce stronger acidity. The detection limits for $F^-$ in DMSO are $2 \times 10^{-4}$and $2 \times 10^{-5}$ M for **1** and **2**, respectively.

When $H_2O$-containing solvents such as DMSO–$H_2O$, were used, similar sensing behavior (Fig. S11–Fig. S15†) was observed, but the deprotonation processes are associated with larger equivalents of $F^-$ due to the competition effect of $H_2O$, as observed for most fluoride chemosensors based on the H-bonding mechanism.



**Scheme 2** Tautomerism of sensors **1** and **2**.

When we further checked the solvent-dependence of the sensing behavior, interesting solvent-induced tautomerism was observed for both **1** and **2** (Scheme 2). In $CDCl_3$, the molar fractions of isomers **1** and **1a** are 88.5 and 11.5%, respectively (Fig. S16†). With the addition of DMSO-$d_6$, the peaks for **1a** gradually disappeared to afford the spectra of pure **1**, and the NH peaks were shifted downfield, indicative of intermolecular hydrogen-bonding interactions, which may be the driving force for the tautomerism shift.[17] The conversion of **1a** into **1** with increasing solvent polarity is consistent with DFT calculations, which have indicated that the energy difference between **1** and **1a** in polar solvents are much larger than that in nonpolar solvents (Table S2†). Molar fractions of **2** and **2a** in $CDCl_3$ are 68.2 and 31.8%, respectively (Fig. S17†). Similar tautomerism behavior was also observed when DMSO-$d_6$ was added.

Anion binding behavior of **1** and **2** in $CHCl_3$ and $CH_2Cl_2$ shows a significant difference from that in DMSO due to the coexistence of the two tautomers. For example, when chloride was added to a DMSO solution of **2**, the hydrogen bonding interactions induced very small electronic spectra changes (Fig. S18†), and the NH peaks in the $^1H$ NMR spectra shifted very little (from 11.45 to 11.54 ppm) when 1 equivalent of $Cl^-$ was added to a DMSO-$d_6$ solution of **2** (Fig. S19†). In contrast, when chloride was added to a $CH_2Cl_2$ solution of **2**, the binding was accompanied with a tautomerism shift, showing much larger electronic spectra changes (Fig. S18†), and the signal of the peripheral NH protons of **2** in the $^1H$ NMR spectra shifted significantly downfield from 8.60 to 12.31 ppm (Fig. 4), indicative of the binding at these NH moieties.

The proposed binding of chloride at the peripheral NH moieties was further evidenced by X-ray diffraction analyses of a single crystal of $\mathbf{2}\cdot 2MeOH\cdot H_2O$ (Fig. 5).‡ In this crystal, the O atom of water was hydrogen-bonded to two NH donors. For the quinone oxygens O1 and O2, the C–O bond lengths are 1.255(5) and 1.247(5), respectively, indicative of C=O

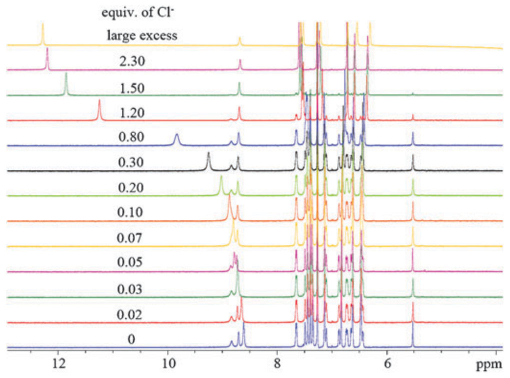


**Fig. 4** $^1H$ NMR spectral changes of **2** (6.4 mM) upon addition of chloride anion (TBA salt) in $CDCl_3$.

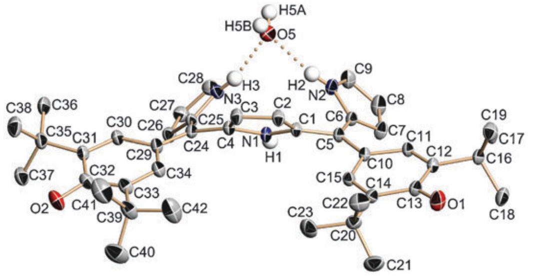


**Fig. 5** Crystal structure of **2**·2MeOH·$H_2O$ with ellipsoids shown at the 25% probability level. Hydrogen atoms attached to carbons have been omitted for clarity.

double bonds. It is noteworthy that the three pyrrole rings are not coplanar. The dihedral angles between the central ring and the peripheral ones are 54.86(2) and 57.07(2)°, respectively, and the tilt of the rings facilitates the cooperative binding of a water molecule at the peripheral NH donors.

In summary, we have developed a novel prototype of highly efficient colorimetric fluoride sensors **1** and **2** incorporating various numbers of hemiquinones and pyrroles. For receptor **1** in DMSO, only the addition of fluoride results in vivid color change from orange to blue due to deprotonation, which makes it a promising colorimetric fluoride sensor. **2** also can be used to selectively discriminate fluoride from other anions based on a unique dideprotonation process.

These results indicate that the combination of hemiquinone group and pyrrole is an effective approach to designing novel colorimetric fluoride sensors, and the variation in the number of quinone and pyrrole units has a great influence on the sensing behavior. The presence of a tautomerism effect provides additional means of modulating the sensing behavior. Furthermore, the unsubstituted pyrrole α-positions in **1** and **2** can be readily functionalized to introduce other chromophores or fluorophores with the purpose to further modify the sensing properties, which is under research in our group.

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## Notes and references

‡ *Crystal data* for **2**·2$CH_3OH$·$H_2O$: $C_{44}H_{61}N_3O_5$, $M_r$ = 711.96 g $mol^{-1}$, 0.45 × 0.43 × 0.40 $mm^3$, monoclinic, $P2_1/c$, $a$ = 9.9033(8), $b$ = 23.558(2), $c$ = 18.9225(17) Å, $\beta$ = 102.366(2)°, $V$ = 4312.2(7) $Å^3$, $F(000)$ = 1544, $D_c$ = 1.097 g $cm^{-3}$, $\mu$(Mo-Kα) = 0.071 $mm^{-1}$, $T$ = 298(2) K, 18262 data measured on a Bruker SMART Apex diffractometer, of which 7471 were unique ($R_{int}$ = 0.0678); 484 parameters refined against $F_o^2$ (all data), final w$R_2$ = 0.2487, $S$ = 1.069, $R_1$ ($I > 2\sigma(I)$) = 0.0820, largest final difference peak/hole = 0.413 and −0.353 e $Å^{-3}$. Structure solution by direct methods and full-matrix least-squares refinement against $F^2$ (all data) using SHELXTL.

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