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# Recognition and sensing of $AcO^{-}$ and $F^{-}$ using a calix[4]pyrrole-derived hydrazone: a potential molecular keypad lock

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**Abstract**：Calix[4]pyrroles based anion receptors **1** and **2** have been synthesized. The recognition and sensing process has been studied by the UV-vis absorption and partial $^{1}H$ NMR titrations experiments. Receptor **1** could act as a colorimetric sensor for fluoride anion, and receptor **2** could recognize $F^{-}$ and $AcO^{-}$ anions in DMSO solvent. Moreover, this type of sensing behaviour could successfully mimic a molecular level keypad lock stimulated by the two sequential chemical inputs ($AcO^{-}$ and $F^{-}$), which has the potential for application in security devices.

## Introduction

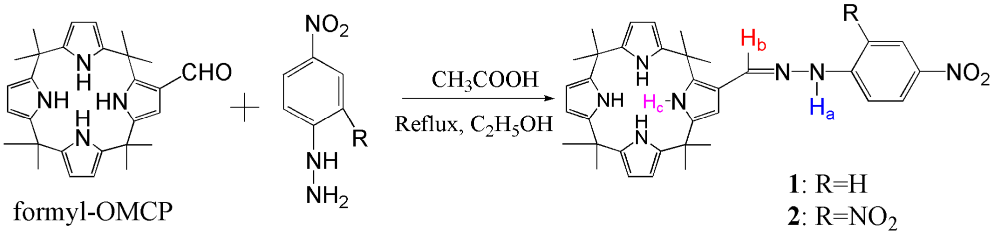
In recent years, various molecular switches, logic gates and logic circuits based on chemical systems capable of elaborating binary (Boolean) information have been proposed because of the wide variety of organic molecular designs, synthesis, and light-emitting properties that are available [1]. In particular, use of a molecular-scale keypad lock as a data security device is an attractive research goal in the area of unconventional computing, as it offers a new approach for protecting information at the molecular level, which can be opened only by the proper combination and sequence of chemical inputs [2]. Therefore, the development of such molecular devices, capable of authorizing password entries, is particularly attractive for protecting information on molecular scale.

On the other hand, the development of optical chemical sensors for ions is current interest due to their important roles in chemical and biological processes [3]. Furthermore, the integration of ion sensors into molecular level devices is an active area of research [4]. Therefore, the dual application of a single molecular system to the detection of ions and the integration of these ions as chemical-driven molecular machines would be of future interest in molecular computing.

Recently, the hydrazone functional group (-C=N-NH-) with a hydrogen bonding donor unite, has been extensively studied and used in designing optical molecular switches and sensors for biologically and environmentally important anions, cations and neutral molecules, due to its ease of synthesis, modularity, and unique structural properties[5]. In previous studies, we have developed optical chemosensors for anions with pyrrole/indole, phenyl hydroxyl and hydrazone groups as recognition sites, some of which were potential molecular switch or molecular keypad lock [6]. As part of our ongoing studies on molecular logic devices, we reported new colorimetric sensors **1** and **2** by the combination of calix[4]pyrrole and hydrazone moieties. Receptor **1** could act as a colorimetric sensor for fluoride anions, and receptor **2** could recognize $F^-$ and $AcO^-$ anions in DMSO solvent. Furthermore, receptor **2** could also behave as a molecular scale keypad lock with sequential chemical inputs of $AcO^-$ and $F^-$ anions.

## Results and Discussion

The structure and synthesis of receptors **1** and **2** were shown in Scheme 1. The intermediate Formyl-calix[4]pyrrole was synthesized according to our previous reported paper [7]. Receptors **1** and **2** were obtained by the reaction of Formyl-calix[4]pyrrole with 4-nitrophenylhydrazine and 2,4-dinitrophenylhydrazine in good yields. The purity and structure of compounds **1** and **2** were confirmed by the MS, $^1$HNMR and $^{13}$CNMR spectra.



**Scheme 1** Synthesis of receptors **1** and **2**

The anion-binding properties of receptors **1** and **2** were first studied by UV-vis spectroscopy in DMSO solution.

The absorption spectrum of receptor **1** in DMSO solution ($5\times10^{-5}$) has a strong absorption band with maxima 455 nm. When various anions ($F^-$, $Cl^-$, $Br^-$, $I^-$, $AcO^-$, $ClO_4^-$, $HSO_4^-$, $H_2PO_4^-$) were added to the solution, only fluoride anions could cause obvious change in absorption. As shown in Fig. 1a, a new broad absorption band between 500 and 600 nm appeared upon addition of fluoride anions. Titration of receptor **1** with fluoride anions (0~30 equiv.), the band at 425 nm progressively decreases, while two new peaks at 540 and 570 nm appears and develops (Fig. 1b), and the color of the solution changed from yellow to purple accordingly. During the titration process, apart from the original absorption specta of receptor **1**, two clear isosbestic points at 375 and 475 nm was observed, indicating a single component was produced. The new absorption bands induced by fluoride anions matched well with band formed in the presence of [TBA] OH, suggesting that it can be respond to the deprotonation of NH proton of receptor **1**.

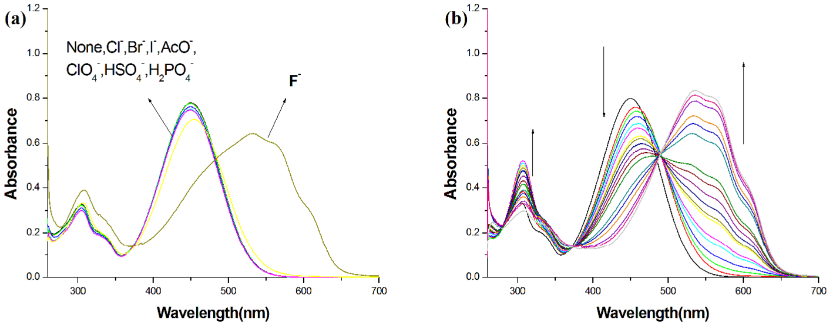


**Fig. 1** Changes in the UV/vis absorption spectrum of receptor **1** ($5\times10^{-5}$ M) upon addition of anions in TBA salts in DMSO solvent: (a) 10 equiv. of various anions ($F^-$, $Cl^-$, $Br^-$, $I^-$, $AcO^-$, $ClO_4^-$, $HSO_4^-$, $H_2PO_4^-$); (b) $F^-$ ( 0~30 equiv.).

Fig. 2a shows the spectral changes of receptor **2** in response to various anions. The absorption spectrum of receptor **2** in DMSO solution ($5\times10^{-5}$) has a strong absorption band with maxima at 434 nm. Titration of receptor **2** with $AcO^-$ and $F^-$ anions resulted in new absorption band at 470 and 510 nm, respectively. In contrast, the addition of other anions ($Cl^-$, $Br^-$, $I^-$, $ClO_4^-$, $HSO_4^-$, $H_2PO_4^-$) did not cause obvious changes in absorption. The new absorption band at 510 nm induced by fluoride anions match well with band formed in the presence of [TBA] OH, suggesting that it can be respond to the deprotonation of receptor **2**. On the other hand, the band at 470 nm could be attributed to hydrogen bonding interaction between receptor **2** and $AcO^-$.

Upon the addition of 5% water to the solution of receptor **2** in the presence of $AcO^-$ and $F^-$ anions, respectively, the absorption of the system with $AcO^-$ recovered. However, the system with $F^-$ did not recover until over 25% $H_2O$ was added (Fig. 2b). So, receptor **2** was an efficient sensor for fluoride anions in aqueous medium. And yet, development of chemosensors capable of efficient recognition and quantification of anions in aqueous solution remains a challenge.

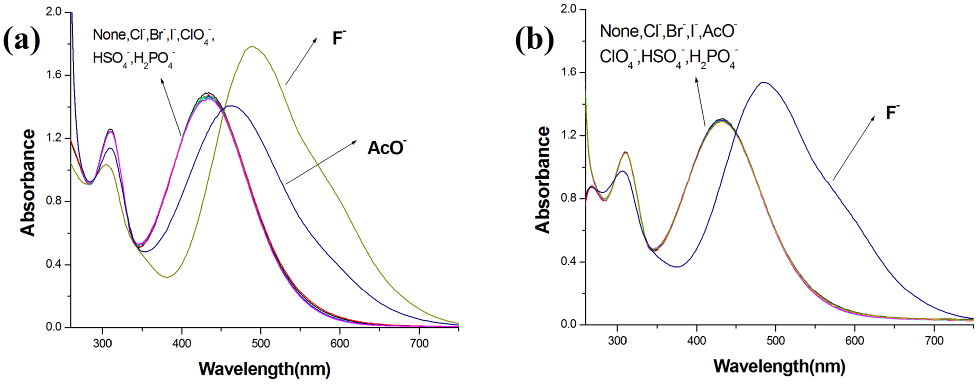


**Fig. 2** Changes in the UV/vis absorption spectrum of receptor **2** ($5\times10^{-5}$ M) upon addition of anions (25 equiv.) in TBA salts (a) in DMSO solvent and (b) in DMSO-$H_2O$ (V/V, 80/20) medium.

The corresponding titrations experiment of receptor **2** with fluoride anions were carried out in DMSO-$H_2O$ (v/v, 90/10), as shown in Fig. 3. Titration of receptor **2** with fluoride anions resulted in a red shift of the spectrum with two isosbestic points at 300 and 450 nm and the formation of a new red-shift absorption band with a maximum at 510 nm. The detection limit is an important factor for an optical chemosensor to be practical application. The absorption response of receptor **2** toward the fluoride anions in DMSO-$H_2O$ medium covered a linear rang 20–150 μM (Supplementary Information, fig. s1), with a detection limit of 0.89 μM (based on S/N=3).

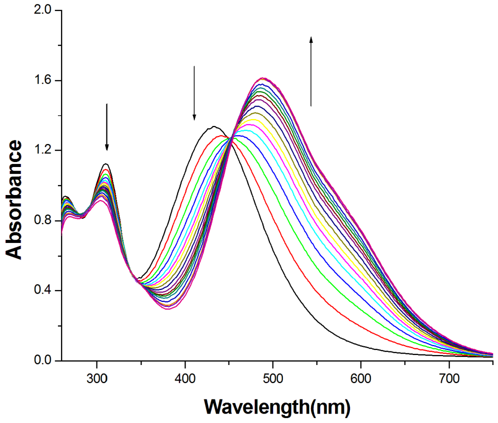


**Fig. 3** Changes in the UV/vis absorption spectrum of receptor **2** ($5\times10^{-5}$ M) upon addition of F⁻ ( 0~50 equiv.) anions in TBA salts in DMSO-$H_2O$ (V/V, 90/10 ) solution.

The binding stoichiometry of receptors **1** and **2** with F⁻ were calculated through the Benesi-Hildebrand equation. As shown in Fig. s2 and s3 (Supplementary Information), the plot of $1/(A-A_0)$ against $1/[F^-]_0$ shows a linear relationship (R =0.99), indicating that receptor **1** associates with F⁻ in a 1:1 stoichiometry. The association constant, K, between **1** and F⁻, is determined from the ratio of intercept / slope to be 3550 $M^{-1}$ in DMSO solvent. And receptor **2** associates with F⁻ in a 1:1 ratio with an association constant, K=3201$M^{-1}$ in DMSO-$H_2O$ medium.

In order to clarify the sensing mechanism, a $^1$H NMR titrations experiment was carried out with receptor **2**. Fig. 4 shows the $^1$HNMR spectral changes of receptor **2** upon addition of fluoride in DMSO-$d_6$ at room temperature. Upon addition of 0.5~1 equiv. F⁻ to receptor **2** in DMSO-$d_6$, the hydrazone proton $H_a$ signal showed a little downfield and $H_b$ and $H_c$ signal became broad, the four pyrrole NHs showed down shift, split by interaction with F⁻, In presence of 4 equiv. F⁻, the $H_a$ , $H_b$ and $H_c$ signal disappeared, the pyrrole NH complex [8] appears at ca.12~13, and a new signal $[FHF]^-$ appears at ca.16. From above titration results, F⁻ indeed interacted with pyrrole NH protons and hydrazone (-CH=N-NH-) NH and CH protons, and a deprotonation process has been involved in the titration process.

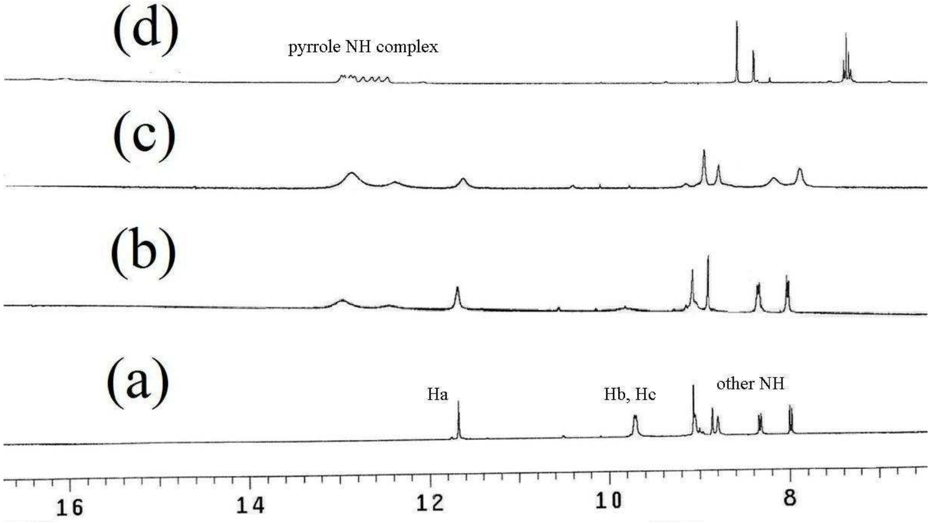


**Fig. 4** Partial $^1$H NMR spectra of receptor **2** on addition of F⁻ (TBA salts) in DMSO-$d_6$: (a) 0 equiv. F⁻; (b) 0.5 equiv. F⁻; (c) 1 equiv. F⁻; (d) 4 equiv. F⁻.

The hydrazone group intergated with anions recognition unites such as phenyl OH, indolic NH and et al., have been developed to recognize and sense anions. Hydrzaone based anions receptors and sensors with different types functional groups has shown various sensing ability and optical behaviours[9]. For comparison, the anions recognition and sensing properties of naphthalene-derived hydrazone **N1** and **N2** (see supporting information, scheme s1) without additional recognition unites were also studied by UV-vis spectroscopy in DMSO solution. The absorption spectrum of **N1** in DMSO solution has a strong absorption band with maxima 412 nm, only fluoride anions could cause obvious change in absorption. Titration of **N1** with $F^-$ anions resulted in a new absorption band at 576 nm, as shown in fig. S4. The absorption anions titration results of **N1** was similar with that of receptor **1**. The absorption spectrum of **N2** in DMSO solution has a strong absorption band with maxima at 392 nm. Upon addition of various anions, both the $F^-$ and $AcO^-$ could cause the obvious changes in the absorption, inducing a new band at 500 nm (Fig.S5). Then 3% and 7% $H_2O$ was added to the system, the absorption with $AcO^-$ or $F^-$ recovered, respectively. As for the control compound **N2**, it could not distinguish $AcO^-$ from $F^-$ anions through absorption spectrum compared to receptor **2**. On the other hand, calix[4]pyrroles with four NHs cooperated with NH of Hydrazone moiety, making receptor **2** an efficient colorimetric sensor for fluoride anions in aqueous medium.

From above results, we can find receptor **1** could recognize fluoride anions selectively; and receptor **2** could recognize $AcO^-$ and $F^-$ in DMSO solvent. Additionally, receptor **2** could sense $AcO^-$ and $F^-$ at two different wavelengths (470 and 510 nm). Sequentially adding $AcO^-$ and $F^-$ to the solution can induce a 470 nm and then a 510 nm absorption band; however, only a 510 nm absorption band was observed when reverse the adding sequence. These studies inspire us to utilize receptor **2** to develop a molecular keypad lock for a molecular traffic signal with two inputs: $AcO^-$ and $F^-$ as input-1 and input-2. The absorption bands were observed at 470 and 510 nm when $AcO^-$ were added to receptor **2** followed by the addition of $F^-$. In another sequence, the absorption band at 510 nm was observed when $AcO^-$ was added after the addition of $F^-$ in receptor **2**.

To simplify the input sequence as a password of the molecular keypad lock, two inputs of $AcO^-$ and $F^-$ are designated as “**A**”and “**F**”. Two outputs at 470 and 510 nm are designated as “**X**” and “**Y**”. And the “ON” state of the lock was designated as “**S**” When the input “**A**” was added first and followed by “**F**”, both of the absorption band at 470 and 510 nm could be detected by the system, the lock was in the “ON” state and it created secret password “**AXFYS**”, and the keypad lock opens (Fig. 5). All the other sequences could not produce absorption band at 470 and 510 nm simultaneously, failed to open the lock. So this type of system may be applicable to protect information at the molecular level as it requires the correct order of inputs.

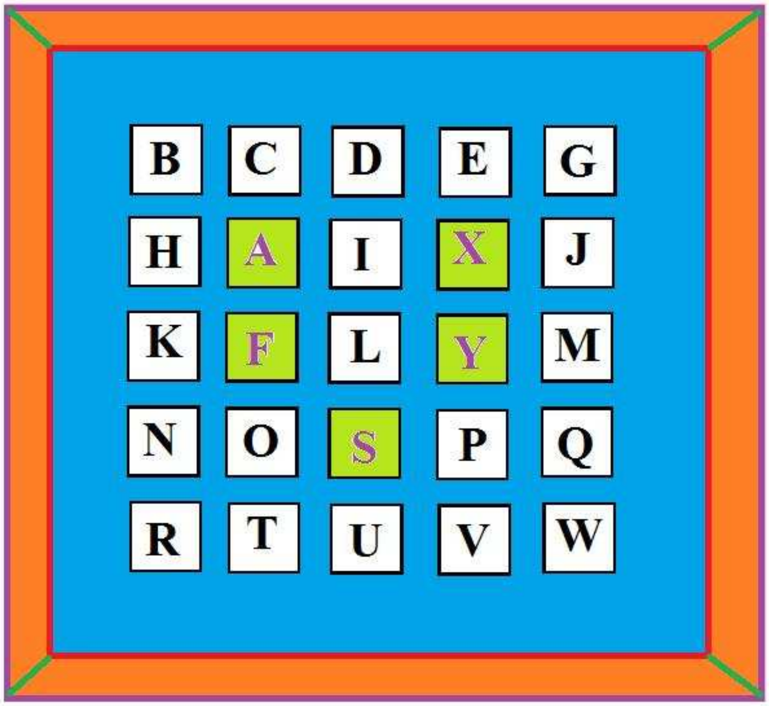


**Fig. 5** Uv-vis absorption keypad lock with the inputs of AcO$^-$ and F$^-$ to access a secret code at 470 and 510 nm.

## Conclusion

In summary, we have developed new colorimetric sensors **1** and **2** for anions sensing based on calix[4]pyrrole-derived hydrazone. Receptor **1** could recognize fluoride anion in DMSO solvent, and receptor **2** could recognize AcO$^-$ and F$^-$ anion in DMSO solvent and F$^-$ anion in DMSO-H$_2$O medium. Furthurmore, receptor **2** has been used to construct a molecular keypad lock with AcO$^-$ and F$^-$ as inputs. Therefore, this molecular keypad lock has the potential for protecting information at the molecular scale. This work provides new insights for the design of anions sensors as multifunctional logic devices.

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## Notes and References:

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† *Electronic Supplementary Information (ESI) available: Experimental details and other data.*

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