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The synthesis and recognition properties of colorimetric fluoride receptors bearing sulfonamide

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Abstract

Two artificial receptors, 1,2-bis-*p*-substituted phenyl-sulfonamido-4,5-bis-nitrobenzene, have been designed and synthesized. The interactions of these receptors with halide anions are determined by UV–vis and ^{1}H NMR titration experiments. Results indicate that two receptors have strong sensitivity and selectivity for fluoride among halide anions. In addition, the visible color changes upon the addition of fluoride anion can make the receptors as convenient detection tools for fluoride anion.

Keywords: Fluoride anion; Colorimetric detection; Sulfonamide

1. Introduction

The development of design and synthesis of new artificial receptors for selective anion recognition has attracted considerable attention in the field of host–guest chemistry because of the important roles of anion in biomedicinal and chemical processes [1]. Artificial anion receptor has represented the unique application prospects in anion sensors [2], membrane transmit carrier [3] and mimic enzyme catalyst synthesis, etc. [4,5]. Because the hydrogen bond has good directionality and selectivity [6], urea, sulphur urea and amide, etc., groups that can form strong hydrogen bond ability to anions have been used extensively in the design and synthesis of the neutral anion receptors [7]. It is the key point for the molecular designs of the fluoride anion recognition that shows how to achieve the specific recognition of fluoride anion and how to convert the recognition event into a signal. In particular, the sensing of fluoride anion has attracted growing attention and several types of synthetic chemosensors have been developed to date. Shin-ichi et al. [8] have reported that sulfonamide receptors exhibit large affinity constants for acetate and dihydrogen phosphate ions. Crabtree and co-workers [9,10] also studied that the sulfonamide system had strong affinity to chloride anion. However, the recognition properties of sulfonamide receptor that can be detected by naked eyes when they act with fluoride anion are few reported. It is limited for sulfonamide receptors to use extensively and conveniently.

According to this information, we synthesized two sulfonamide receptors (see Scheme 1) and studied anion recognition properties to halide anions by UV–vis and ^{1}H NMR titration experiments. The sulfonamide receptors show the noticeable color changes and the high selectivity and affinity for fluoride ion among halide anions. The above advantages can make the receptors as convenient detection tools for fluoride anion.

2. Results and discussion

1 and **2** were synthesized according to the route shown in Scheme 2.

Briefly, *o*-phenylenediamine was reacted with *p*-substituted phenylsulfonylchloride under the conditions of pyridine and 373 K to produce 1,2-bis-*p*-substituted phenyl-sulfonamido-benzene [11]. Direct nitration [12] of 1,2-bis-*p*-substituted phenyl-sulfonamido-benzene with fuming HNO_3 gave the target compounds **1** or **2** in high yield and were characterized by IR, ^{1}H NMR spectroscopy, elemental analysis and ESI-MS.

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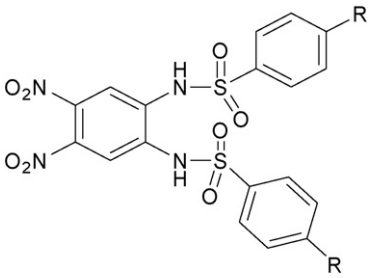


1: R=CH_3
2: R=H

Scheme 1. The structure of receptors.

UV–vis spectral titration method is applied extensively to the system of coordination reaction that can induce absorption spectrum change [13]. It is a convenient and swift method to determine the affinity constant of supramolecular complex. Recognition properties of **1** and **2** for halide anions [tetra-(*n*-butyl)-ammonium salts] were examined by UV–vis spectral titration method in DMSO.

As shown in Fig. 1, the spectra change clearly with the increase of fluoride ion concentration. Receptor **1** has a certain absorption band centered at 430 nm, and the intensity of absorbance at 430 nm decreases upon the addition of fluoride anion. At the same time, a new absorbance peak appears at 550 nm, and the intensity of this absorbance increases. The color of the solution changes from yellow to red with the increase of fluoride anion concentration (Fig. 2). When the concentration of fluoride anion is 30-fold greater than that of receptor **1**, no further change of electronic spectrum or color occurs. In addition, two clear isosbestic points appear at 400 and 475 nm. This shows that the stable complex forms with a certain stoichiometric ratio between **1** and fluoride anion. However, the additions of Cl^-, Br^- and I^- virtually lead to no spectral changes. Also there exist similar spectrum changes between **2** and F^-, Cl^-, Br^- and I^-, compared with **1**.

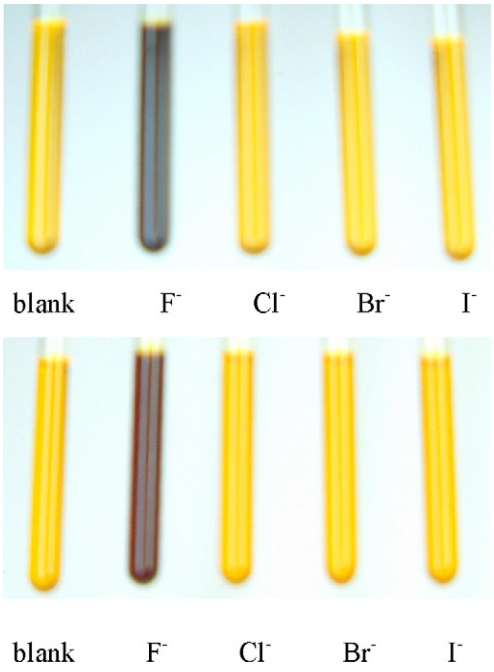
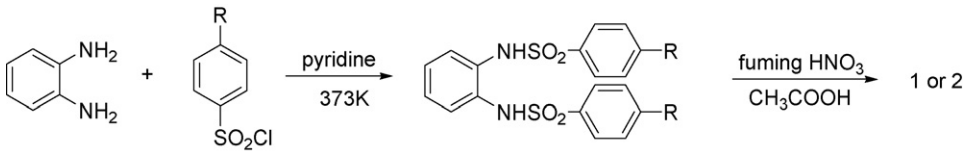


Fig. 2. Color changes observed with the addition of various anions to DMSO solution of **1** and **2**, 5 equiv. for each anion were used.



1: R=CH_3 2: R=H

Scheme 2. Synthesis route for **1** and **2**.

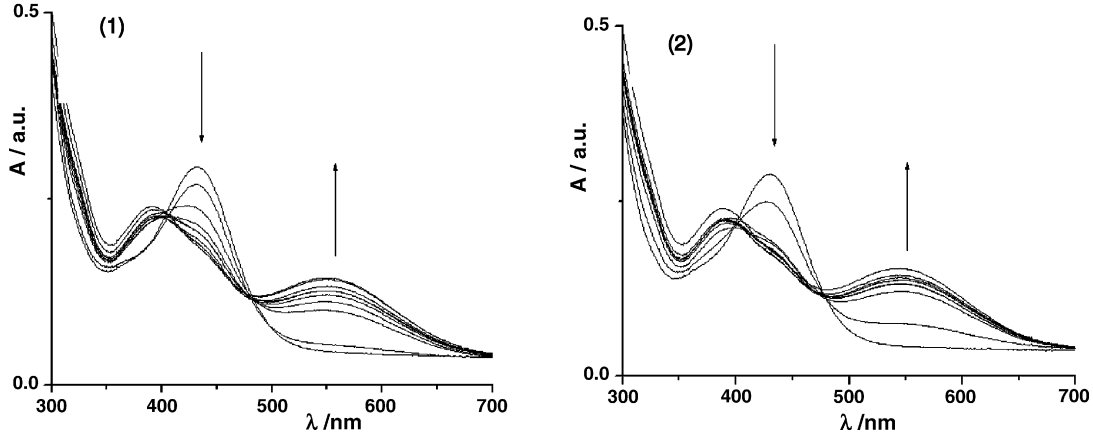


Fig. 1. UV–vis spectral changes of receptors **1** and **2** upon the addition of fluoride anion (added in the form of tetra-*n*-butylammonium salts) at 298 K, [**1**] = [**2**] = 2×10^{-5} mol/l, [F^-] = 0–160×10^{-5} mol/l. Arrows indicate the direction of increasing anion concentration.

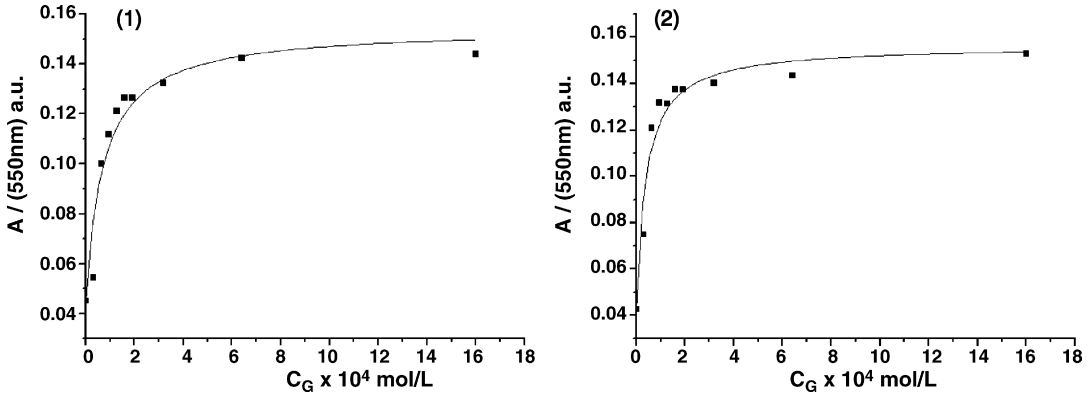


Fig. 3. Fitting curves of receptors **1** and **2** with fluoride anion using non-linear least square method.

Job's plots of receptors **1**, **2** and various anions in DMSO show the maximum at a molar fraction of 0.5. The results indicate that the receptors bind anion guest with a 1:1 ratio. Affinity constants of receptor for anionic species are calculated according to the relational expression (1) of 1:1 host–guest complexation [14]:

$$X = X_0 + 0.5\,\Delta\varepsilon\left\{c_H + c_G + \frac{1}{K_s} - \left[\left(c_H + c_G + \frac{1}{K_s}\right)^2 - 4c_H c_G\right]^{1/2}\right\} \quad (1)$$

where c_G and c_H are the concentration of guest and host, respectively, X the intensity of absorbance at certain concentrations of host and guest, X_0 the intensity of absorbance of host when the anion is not added, K_s the affinity constant of host–guest complexation and $\Delta\varepsilon$ is the change in molar extinction coefficient. Fig. 3 shows the fitting curves by non-linear least square method. The higher correlation coefficients ($r > 0.98$) of fitting curves also prove the receptors **1** and **2** bind fluoride anion for 1:1 ratio. The affinity constants obtained by the method of non-linear least square calculation are summarized in Table 1.

Obviously, the recognition function of **1** and **2** for fluoride anion are the most remarkable among halide anions. The binding abilities between **1** or **2** and various anions lie in the order: $F^- \gg Cl^- \sim Br^- \sim I^-$. The affinity constant between **1** and F^- is about 1200-fold greater than that for Cl^-, Br^- and I^-, and the affinity constant between **2** and F^- is about 1500-fold greater than that for other anions observed. The reason may be that spatial steric hindrance of oxygen atoms limits the interactions of receptors with anions in space, and only matched anion may have strong binding ability with receptors. Furthermore, the radius of fluoride anion is much smaller than the radius of Cl^-, Br^- and I^-, and easily forms hydrogen bonds between F^- and –NH. Therefore, **1** and **2** have strong recognition for fluoride anion. In addition, for F^-, the affinity constant of **2** is 1.8-fold than that of receptor **1**. Comparison with **2**, the electron-giving effection of $-CH_3$ in receptor **1** induces the increase of electron cloud density of –NH. Thus, the binding ability of **1** for fluoride anion is weaker than that of **2**.

Table 1
Affinity constants of **1** and **2** with various anions

	Anion			
	F^-	Cl^-	Br^-	I^-
K_s (**1**) (M^{-1})	$(1.4 \pm 0.4) \times 10^4$	11	12	14
K_s (**2**) (M^{-1})	$(2.5 \pm 0.6) \times 10^4$	20	14	19

The sulfonamide system of Crabtree and co-workers [9,10] have strong affinity to chloride anion because the coordination space of two –NH locating meta-site is fit for the size of chloride anion. While, the two –NH of our sulfonamide system is located ortho-site. We speculate the space of anionic coordination in this system is fit for the size of fluoride anion according to the affinity constants (see Table 1). Therefore, sulfonamide receptor with –NH located ortho-site may have strong affinity to fluoride anion, and Crabtree's sulfonamido with –NH located meta-site may have strong selectivity for chloride anion.

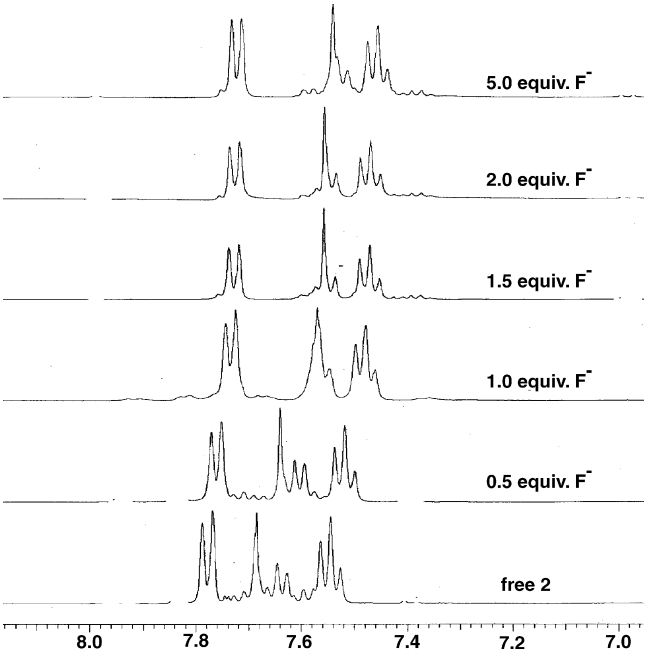


Fig. 4. Plots of ^1H NMR spectra of receptor **2** in DMSO-d_6 upon the addition of various quantities of Bu_4NF.

On the other hand, the synthesis route for **1** and **2** were short and simple. The materials were cheap and easily obtained. It is convenient and available for us to make **1** and **2** as good chemosensors.

Very recently, a number of fluorogenic and/or chromogenic anion sensors comprising recognition moieties with acidic protons, such as urea, thiourea, or amide have been reported to undergo an anion-induced deprotonation [15–17]. According to these reports, one triplet resonance appears at 16.1 ppm, the characteristic resonance of bifluoride (F–H–F) and the non-interacted protons undergo upfield shift. To look into the anion binding properties of receptors for halide anions, the ^{1}H NMR titration experiment in DMSO-d_6 between receptor **2** and F^- is shown in Fig. 4. Upfield proton shift are observed in the phenyl rings signals (δ = 7.8–7.54 ppm) with the addition of 1 equiv. F^-. That suggests that the amides of receptor **2** occur deprotonation according to reported literature [18]. In fact, the negative charge of nitrogen atom, after the amides occur deprotonation, causes a shielding effect and should promote an upfield shift. In addition, the chemical shift of phenyl rings signals are stopped after addition of 1 equiv. F^-. This also explains the binding between receptor **2** and fluoride anion is 1:1. As for receptor **1**, the amides may occur deprotonation due to the similar system with receptor **2** only the difference of substituent group.

3. Conclusions

In summary, we synthesized and studied the recognition properties of 1,2-bis-(*p*-methylphenylsulfonamido)-4,5-bis-nitrobenzene (**1**) and 1,2-bis-(phenyl-sulfonamido)-4,5-bis-nitrobenzene (**2**) with halide anions by UV–vis and ^{1}H NMR titration experiments. The studies of UV–vis spectra clearly show that the affinity constants of **1** and **2** to F^- are about 1.4×10^4 and 2.5×10^4 M^{-1}, respectively, almost 1200- and 1500-fold greater than that for Cl^-, Br^- and I^-. Thus, these receptors (**1** and **2**) have strong sensitivity and selectivity for fluoride anion over other anions examined. What's more, the visible color changes of the interactions between **1** or **2** and fluoride anion may make **1** and **2** as colorimetric sensors. Accordingly, it is possible to conceive the use of **1** and **2** in various sensing applications as well as in other situations, such as anion transport and purification, where the availability of cheap and easy-to-make anion receptors would be advantageous. Therefore, **1** and **2** not only have the important theory significance, but also have the significant economic and social efficiency. The above conclusion may have inspiring meaning for us to research new kinds of color receptors and may provide experimental method for the monitoring of fluoride anion in biological system. However, we only study the interactions of receptors and spherical anions. As for other type anions (linear, trigonal, tetrahedral anions), further studies on this line are in progress.

4. Experimental

Most of the starting materials were obtained commercially and all reagents and solvents used were of analytical grade. All anions, in the form of tetrabutylammonium salts, were purchased from Sigma–Aldrich Chemical Co., stored in a desiccator under vacuum containing self-indicating silica, and used without any further purification. Dimethyl sulfoxide (DMSO) was distilled in vacua after dried with CaH_2. Tetra-*n*-butylammonium salts (such as $(n\text{-}C_4H_9)_4NF$, $(n\text{-}C_4H_9)_4NCl$, $(n\text{-}C_4H_9)_4NBr$ and $(n\text{-}C_4H_9)_4NI$) need to be dried 24 h in vacuum with P_2O_5 at 333 K before use. C, H, N elemental analyses were made on Vanio-EL. ^{1}H NMR spectra were recorded on Varian UNITY Plus-400 MHz Spectrometer. UV–vis spectroscopy titrations were made on Shimadzu UV2550 Spectrophotometer at 298 K. IR spectra were obtained of KBr pellets on a 560E.S. PFT spectrophotometer spectrum. ESI-MS was performed with a MARINER apparatus.

1,2-Bis-*p*-substituted phenyl-sulfonamido-benzene were synthesized according to the reported process [11].

1,2-Bis-(*p*-methylphenylsulfonamido)-4,5-bis-nitrobenzene (**1**) [12]. 1,2-Bis-phenyl-sulfonamido-benzene (50 g, 0.25 mol) was put in 500 ml three-neck flask and CH_3COOH (250 ml) was added. Then the mixture acid with 11 ml fuming HNO_3 and 13 ml CH_3COOH was added dropwise at 333 K with stirring. After the addition was completed, the mixture solution was reacted again for 0.5 h at 333 K, then was cooled, filtrated and obtained shallow yellow solid. The product was washed with acetic acid, alcohol, recrystallized from ethyl acetate and dried in vacuum. mp 248–250 °C; IR (KBr): ν = 3264 (NH), 1357 and 1335 cm^{-1} (NO_2). ^{1}H NMR (400 MHz DMSO-d_6), δ: 7.75 (s, 2H), 7.68 (d, 4H), 7.36 (d, 4H), 2.37 (s, 6H). Elemental analysis calcd. for $C_{20}H_{18}N_4O_8S_2$: C, 47.4; H, 3.6; N, 11.1; found: C, 47.9; H, 3.5; N, 11.3. ESI-MS (*m*/*z*): 504.8 $(M - H)^-$.

1,2-Bis-(phenylsulfonamido)-4,5-bis-nitrobenzene (**2**) was synthesized according to the above procedure only the replacement of 1,2-bis-(*p*-methylphenylsulfonamido)-benzene with 1,2-bis-(phenylsulfonamido)-benzene. mp 246–248 °C; IR (KBr): ν = 3261 (NH), 1358 and 1335 cm^{-1} (NO_2). ^{1}H NMR (400 MHz DMSO-d_6), δ: 7.78 (d, 2H), 7.66 (s, 2H), 7.62 (s, 2H), 7.55 (d, 4H). Elemental analysis calcd. for $C_{18}H_{14}N_4O_8S_2$: C, 45.2; H, 3.0; N, 11.7; found: C, 45.6; H, 2.9; N, 11.6. ESI-MS (*m*/*z*): 476.6 $(M - H)^-$.

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