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Synthesis of Schiff Base Bearing Phenolic Hydroxy Group and Its Anion Recognition

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A new anion receptor bearing phenolic hydroxy group based on 3,5-ditertbutylsalicylaldehyde-p-nitrophenylhydrazone (**1**) was designed and synthesized. Upon addition of AcO^- and F^-, the receptor exhibited visible color changes from deep yellow to purple. However, no obvious color changes were observed on addition of the other anions tested ($H_2PO_4^-$, Cl^-, Br^-, I^-). The binding properties of the receptor with anions such as AcO^- and F^- were investigated by UV-Vis and fluorescent titrations. The result indicated that the receptor **1** had a higher affinity to AcO^- and F^- and a 1:1 host-guest complex was formed through H-bond interactions between **1** and anions.

Key words: Schiff-base receptor, Anion recognition, Fluorescence, Intramolecular charge transfer

I. INTRODUCTION

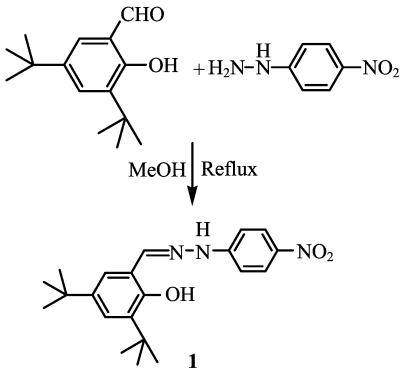
More and more attentions have been paid to the design and synthesis of the receptors that selectively recognize specific anions such as fluoride [1], carboxylate [2], iodide [3], and phosphate [4, 5] as anions are ubiquitous throughout biological systems and play crucial roles in the areas of medicinal, catalysis, biochemistry, and environmental chemistry [6]. For example, the carboxylate anions exhibit specific biochemical behaviors in the enzymes and antibodies and are also critical components of numerous metabolic processes [7]. In general, the anion binding event can be transduced into observable signals: color changes, UV-Vis spectral changes, fluorescent spectral changes and so on [8]. The fluorescent response has gained more considerable attentions because it is advantageous in terms of the low detection limit. Commonly, the design of fluorescent chemosensors is mainly based on photoinduced electron/energy transfer (PET) [9], metal-ligand transfer (MLCT) [10], intramolecular charge transfer (ICT) [11], guest-induced changes in the rigidity of the host molecules [12−15] and so on.

In supramolecular systems of anion recognition, hydrogen-bonding groups have been widely used in bingding sites such as ureas [16], thioureas [17], pyrroles [18], amides [19], imidazo [20], and so on. Some excellent examples of compounds bearing these binding sites capable of anion recognition and sensing have been reported [21, 22]. Kandaswamy reported a Schiff base which was condensed by 3,5-ditertbutylsalicylaldehyde and nitrophenyl hydrazinee, and the compound successfully recognized fluoride by colorimetric method in acetonitrile solution [23]. Bearing these in mind, we developed a novel receptor with Schiff base units as guest recognition sites conjugated to 4-nitrophenyl hydrazine as a signal unit, which was responsible for UV-Vis spectral changes and fluorescent changes. The compound **1**, which could recognize selectively AcO^- and F^- from different anions including $H_2PO_4^-$, Cl^-, Br^-, I^-, was easily prepared through one step (scheme 1).

II. EXPERIMENTS

A. Apparatus

^{1}H NMR spectra were obtained on a Varian UNITY Plus-400 MHz Spectrometer. ESI-MS (electrospray



Scheme 1 Synthetic route for the receptor **1**.

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ionization-mass spectrometry) was performed with a MARINER apparatus. C, H, N elemental analyses were made on an elementary vario EL. UV-Vis spectra were recorded on a TU-1810 Spectrophotometer made by Beijing Puxi Tongyong apparatus company with quartz cuvette (path length=1 cm), and fluorescence spectra were recorded on a F96 Spectrophtometer made by Shanghai Lengguang Technology Co., Ltd. The width of the slits is 10 nm.

B. Chemicals

All reagents for synthesis obtained commercially were used without further purification. In the titration experiments, all the anions were added in the form of tetrabutylammonium (TBA) salts, which were purchased from Alfa Aesar Chemical, stored in a vacuum desiccator containing self-indicating silica and dried fully before using. DMSO was dried with CaH_2 and distilled in reduced pressure.

C. Synthesis of receptor 1

To a solution of 3, 5-ditertbutylsalicylaldehyde (0.2 mmol) in ethanol (20 mL) was added p-nirophenylhydrazine (0.2 mmol). The mixture was stirred and heated to reflux for 2 h. The solvent was removed under reduced pressure and the crude was obtained. Then, the crude product was purified by chromatography on a silica gel column to give 1.0 g as orange solid in 56% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ in ppm: 10.70 (s, ^{1}H, OH), 8.25 (s, ^{1}H, NH), 8.22 (s, ^{1}H, N=CH), 8.00 (s, ^{1}H, ArH), 7.83 (s, ^{1}H, ArH), 7.39 (s, ^{1}H, ArH), 7.03 (s, 2H, Ar), 7.00 (s, ^{1}H, Ar), 1.48 (s, 9H, *t*-Bu), 1.32 (s, 9H, *t*-Bu); ESI-MS: $C_{21}H_{27}N_3O_3$, m/z=368.26; Element analysis for $C_{21}H_{27}N_3O_3$, Calc. C, 68.27; H, 7.37; N, 11.37; Found: C, 68.32; H, 7.62; N, 11.19.

III. RESULTS AND DISCUSSION

A. UV-Vis spectral responses of receptor 1

The binding ability of the receptor **1** via hydrogen-bonding interactions could be easily followed by monitoring the changes in the UV-Vis spectra induced by presence of anions. The interaction of **1** with various anions was evaluated through UV-Vis titrations, by adding a solution of the tetrabutylammonium salt of anions to a dry DMSO solution of receptor **1**. Real-time color changes were observed upon addition 10 equivalence of F^- or AcO^- anions to DMSO solutions of the receptor **1** (0.04 mmol/L). On the contrary, addition of 10 equivalence of $H_2PO_4^-$, Cl^-, Br^-, or I^- could not result in any detectable color changes (see Fig.1). These

FIG. 1 Color changes observed in receptor **1** in DMSO (0.04 mmol/L) in the presence of 10 equivalence of anions as TBA salts (from left to right: **1** only, **1**+AcO^-, **1**+$H_2PO_4^-$, **1**+F^-, **1**+Cl^-, Br^- and I^-). For clarity of the color change in this figure legend, the reader can refer to the web version of this article.

results observed showed that the receptor could strongly bind F^- or AcO^- and had very weak binding ability for $H_2PO_4^-$, Cl^-, Br^-, or I^-. Just as Fig.2 shows, the receptor **1** (0.02 mmol/L) was characterized by very strong absorption band at 420 nm, which decreased gradually and a new broad band centered at 560 nm simultaneity appeared with increasing amounts of AcO^-, F^-, or $H_2PO_4^-$. This new band could be attributed to the intramolecular electron transfer between the electron donor groups including $-$NH, $-$OH, $-CH_3$, and the electron withdrawing group such as $-NO_2$ [24]. In addition, there were two well-defined isosbestic points at approximately 360 and 468 nm, which indicated that the stable complex having a certain stoichiometric ratio between the receptor **1** and AcO^-, F^-, or $H_2PO_4^-$ formed. The Job plot indicated the formation of a 1:1 **1**-to-anion complex (as an example see Fig.3). In addition, receptor **1** was found to be insensitive to the addition of a large excess of Cl^-, Br^-, or I^- in UV-Vis spectral (see Fig.4).

B. Fluorescence titration

To corroborate well with those obtained during the UV-Vis titrations described above, the fluorescence titration experiment was carried out. This observation was illustrated in Fig.5, which showed the fluorescence spectra of the receptor **1** in the absence and presence of various concentrations of AcO^- or F^-. The fluorescence properties of the free **1** (0.02 mmol/L) were determined in DMSO showing a weak emission band centered at 405 nm, which mainly resulted from Schiff base unit [25]. However, upon the addition of AcO^- or F^- to DMSO solutions of **1**, the fluorescence emission intensity of the sensor enhanced drastically at about 417 nm (λ_{exc}=367 nm). The proposed mechanism for the enhancement was based upon binding-induced conformational restriction of a fluorophore. Before the addition of anions, the structure of receptor molecule vibrated and rotated freely, resulting in a weak emission of **1**. As a consequence of the anion coordination, the rigidity of the formed complex increased rendering the non-radiative decay from the excited state less proba-

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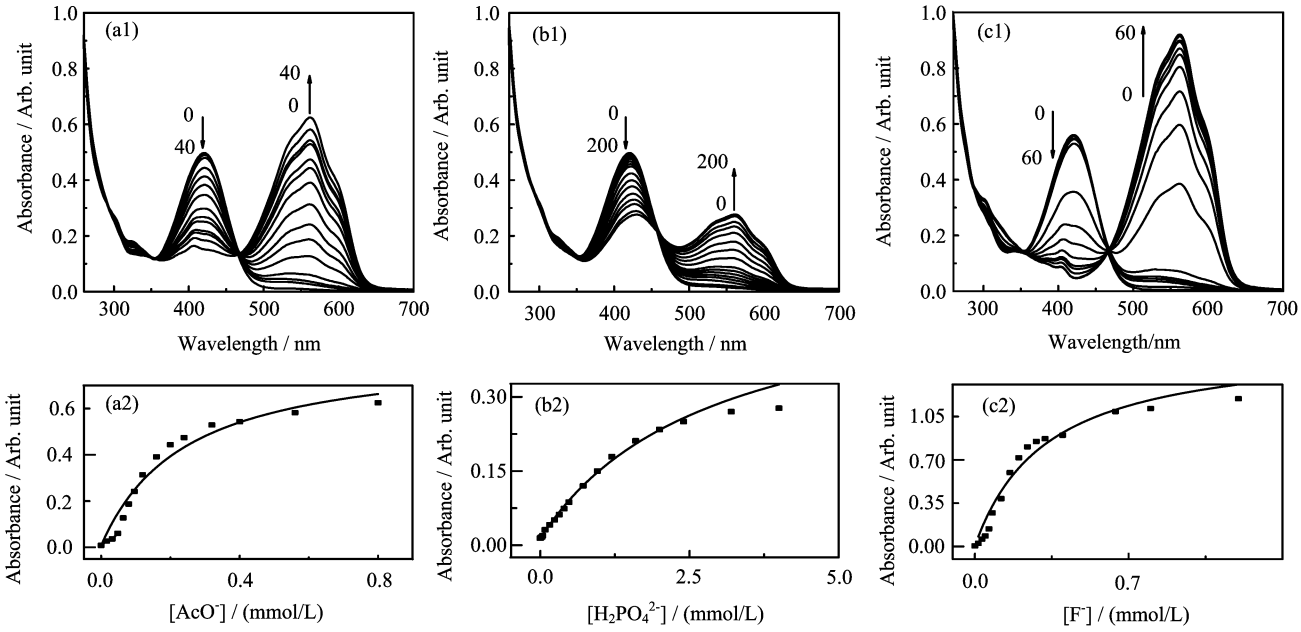

FIG. 2 UV-Vis spectra ((a1), (b1), and (c1)) and the plot of the UV-Vis absorbance ((a2), (b2), and (c2)) at 560 nm of **1** (0.02 mmol/L) in DMSO during the titration with AcO^- (a), $H_2PO_4^-$ (b) and F^- (c), (arrow direction with different equivalence).

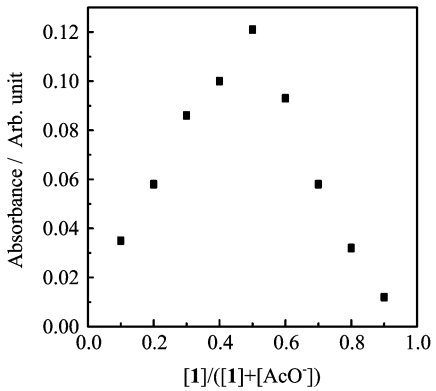

FIG. 3 The stoichiometry analysis of complex **1**+AcO^- by Job plot analysis.

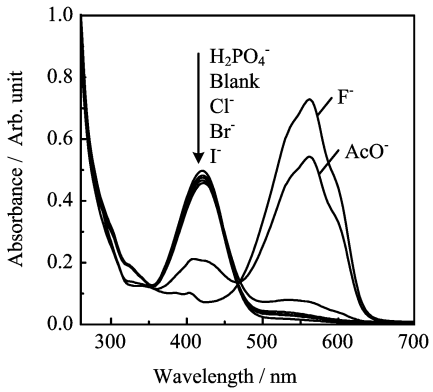

FIG. 4 The UV-Vis spectra changes of receptor **1** (0.02 mmol/L in DMSO) upon addition of 50 equivalence different anions.

ble; consequently, the emission intensity increased [26]. Fluorescence spectral profiles and the intensities of **1** were found to be unsusceptible to the addition of other anions such as $H_2PO_4^-$, Cl^-, Br^-, or I^- (see Fig.6). As expected, the analytical results of the fluorescence titration were very consistent with those of the UV-Vis titrations.

C. Association constants

Association constants of receptor **1** for anionic species, which were shown in Table I, were determined by non-linear fitting analyses of the titration curves according to the Eq.(1) and Eq.(2), 1:1 host-guest complexation [27], respectively.

$$A = A_0 + \frac{A_{\lim} - A_0}{2c_H}\left\{c_H + c_G + \frac{1}{K_{ass}} - \left[\left(c_H + c_G + \frac{1}{K_{ass}}\right)^2 - 4c_H c_G\right]^{1/2}\right\} \quad (1)$$

$$I = I_0 + \frac{I_{\lim} - I_0}{2c_H}\left\{c_H + c_G + \frac{1}{K_{ass}} - \left[\left(c_H + c_G + \frac{1}{K_{ass}}\right)^2 - 4c_H c_G\right]^{1/2}\right\} \quad (2)$$

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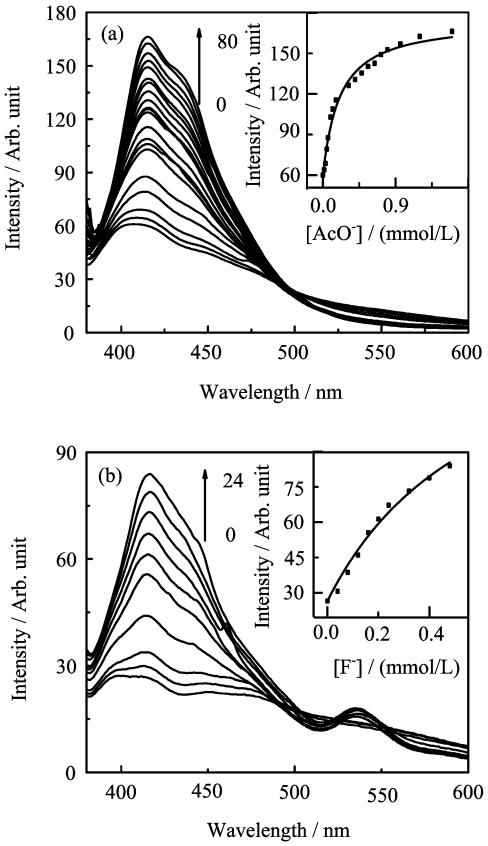

FIG. 5 Fluorescence spectra changes of receptor **1** (0.02 mmol/L) upon addition of AcO^- (a) and F^- (b) in DMSO.

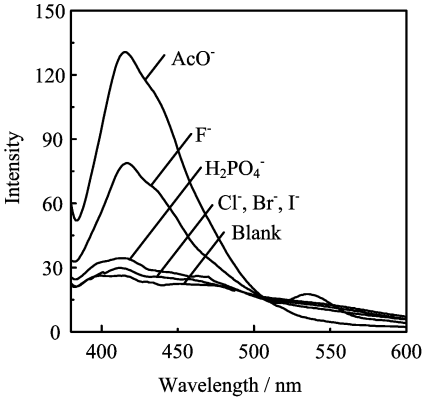

FIG. 6 Fluorescence spectra changes of receptor **1** (0.02 mmol/L) upon addition 20 equivalence different anions.

where c_G and c_H are the concentration of guest and host, respectively. A or I is the absorption of UV-vis or intensity of emission at certain concentration of host and guest. A_0 or I_0 is the absorption of UV-Vis or intensity of emission of host only. K_{ass} is the affinity constant of host-guest complexation. Obviously shown in Table I, the selectivity trends of binding affinities of anions for **1** were determined to be $AcO^->F^->H_2PO_4^->Cl^-\approx Br^-\approx I^-$. The rationalization of the selectivity trends of binding affinities of anions for **1** could be based on the guest basicity and shape complementarity between the host and the anionic guests. Accordingly, the sensor **1** had higher binding affinities for anions with strong basicity (AcO^- and F^-) than the anions with weak basicity (Cl^- and Br^-).

TABLE I Association constants of receptor **1** with ainions in DMSO.

Anions[a]	AcO^-	F^-	$H_2PO_4^-$	Cl^-[d]	Br^-[d]	I^-[d]
K_{ass}[b]	4404	3210	348.1	Nd	Nd	Nd
K_{ass}[c]	5084	1672	Nd	Nd	Nd	Nd

[a] All anions were added in the form of tetra-*n*-butylammonium (TBA) salts.
[b] The association constant was determined by the UV-Vis spectra.
[c] The association constant was determined by the fluorescent spectra.
[d] The association constants could not be determined due to slight spectral changes.

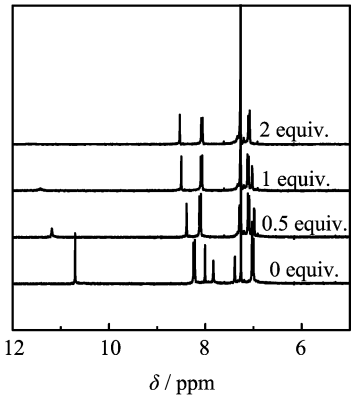

FIG. 7 ^{1}H NMR spectra of the receptor **1** in $CDCl_3$ (10 mmol/L) upon addition of different equivalence of F^-.

D. ^{1}H NMR titration

The interactions of **1** with F^- were further validated by ^{1}H NMR titration experiments, which were carried out in $CDCl_3$. Figure 7 showed plots of ^{1}H NMR spectra of receptor **1** (10 mmol/L) on addition of different equivalence of F^- in $CDCl_3$. Obviously observed from Fig.7, the peaks at 10.70 and 8.25 ppm, which could be assigned to −OH and −NH, respectively, broadened and exhibited a downfield shift to 11.35 and 8.58 ppm, respectively, upon addition of **1** equivalence F^-, implying the hydrogen bonding interactions between fluoride and the −NH and −OH units. However, when 2 equivalence of fluoride ion was added, the peak of

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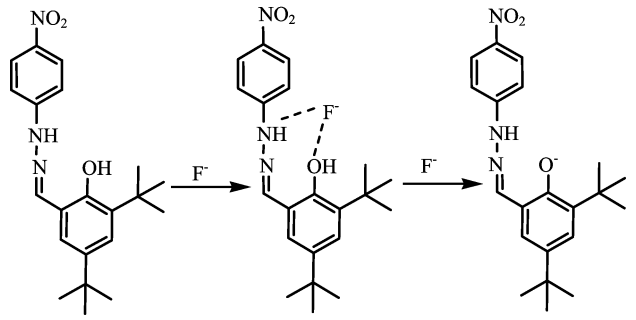

Scheme 2 The proposed binding mode of receptor **1** and F^- in solution.

11.35 ppm disappeared, indicating that the −OH moiety with strong acidity deprotonated [28]. In addition, the phenyl protons signal exhibited a slight upfield shift which indicated the increase of the electron density on the phenyl ring resulting from the through-bond effects after deprotonation of −OH moiety. The results obtained from ^{1}H NMR titrations demonstrated that the sensor **1** bond fluoride ion through hydrogen bonding interactions upon exposure to low concentration of fluoride (for example 1 equivalence). Upon addition of 2 equivalence fluoride, the anion binding sites with strong acidity such as −OH deprotonated. According to the results from UV-Vis spectral titration, fluorescent titration and ^{1}H NMR titration, the proposed host-guest binding mode in solution was depicted in Scheme 2.

IV. CONCLUSION

In summary, we have successfully presented a colorimetric and fluorescent anion sensor based on an intramolecular charge transfer mechanism. The obvious red-shift maximum length of absorption and turn-on emission upon addition of AcO^- and F^- to **1** can be observed, indicating it was attributed to the capture of anions by the OH and NH in conjugation. For practical applications, signal detecting is effective in the sensor **1**. Even better is the sensor that display distinct color changes for fast and efficient sensing. There is an anion-assisted of the host molecule in DMSO, which is supported by UV-Vis spectral titration, fluorescent titration and ^{1}H NMR titration.

V. ACKNOWLEDGMENT

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