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ORIGINAL PAPER

Ratiometric and Selective Fluorescent Sensor for F‾ Based on Intramolecular Charge Transfer (ICT)

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Abstract A simple colorimetric and ratiometric fluorescent anion sensor 1, was rationally designed and synthesized by facile one-step condensation on basis of the mechanism of intramolecular charge transfer (ICT). The sensor 1 shows more highly and selectively ability to F^- that induced the color changes from little yellow to purple, absorption-transferred to long wavelength and emission-transferred to short wavelength. Accordingly, ^1H NMR analysis reveals that the F^--induced colorimetric and fluorometric responses of 1 are simply driven by hydrogen bonding interaction between the NH protons and F^- ions.

Keywords Colorimetric · Ratiometric · Fluorescence · Anion sensor · Indole

Introduction

Recently, the recognition and detection of anions is a rapidly maturing field that has received considerable interest due to the fact that these species play a very important role in many chemical and biological processes [1–5]. For example, fluoride ion is drawing a special attention due to its beneficial in the clinical treatment of osteoporosis, the role it plays as an environmental pollutant, and the diseases related to its over-accumulation in the bones [6–8]. The carboxylate anions hold specific biochemical behaviors in the enzymes and antibodies and are critical components of numerous metabolic processes [9]. And phosphate is associated with a number of important biomineralization processes such as bone formation as well as pathological processes: the genesis of renal stones [10]. Nevertheless, these three kinds of anions can also cause huge damages on environments, such as toxicwastes, water eutrophication, and even in the production of nerve gases [11]. As a consequence there is in need of sensitive and easy testing methods for detecting these anions. Fortunately, fluorescent and colorimetric chemosensors for various analytes have been developed for application in physiology and medical diagnostics [12–15]. Therefore, the design and synthesis of colorimetric and fluorescent anion chemosensors is necessary for the workers. Meanwhile, the interactions between the sensor and anions give birth to color changes, absorption or fluorescence changes through intermolecular hydrogen bonds. Indeed, the great variety of hydrogen-bond donor (such as urea, thiourea, amide, and pyrrole) has been employed to bind a target anion [16–20] in this context. Accordingly, multiples (e.g. calixpyrroles) and combinations of these groups, for instance, amidopyrroles have also been successfully used [21–23]. Work from the groups of Jeong [24], Jurczak [25], Beer [26], Sessler [27], Pfeffer [28] has shown that indoles, carbazoles, indolocarbazoles and biindoles are effective components of hydrogen bond donating anion receptors [29]. Our group had reported one sensor, which can highly and effectively recognize anions. However, there are only a few examples of ratiometric fluorescent chemosensors for anions [30]. The major challenge to ratiometric fluorescence signaling is developing a system with two emitting states having both the wavelength dependent and substrate-dependent emission properties [31]. For example, Yi et al. studied a

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switchable fluorescent organogel in which the fluorescent property and gel state could be selectively controlled by F^- stimulus [32]. Accordingly, our group [33] reported a simple and efficient colorimetric anion sensor based on a thiourea group which can be highly detected fluoride anion in DMSO and DMSO—water that may be have potential application in real-life.

Herein, we report that one simple-structured molecule 1, contains the NH moiety acted as an anion binding site and one $-NO_2$ groups were an electron-withdrawing group and a chromophore, which showed ratiometric response towards anions based on the ICT mechanism. Particularly, in this molecule, an electron-donating group (−NH as an anion binding site) was conjugated to an electron withdrawing group. Accordingly, ratiometric sensing is possible due to altered ground and excited state energetics of the ICT probe upon anion complexation. Actually, the receptor 1 synthesized by facile one step condensation (Scheme 1), exhibits a highly selective F^- ions in both colorimetric and fluorometric analyses. The probe 1 shows F^--induced color changes from little yellow to purple and the responses of the colorimetric and fluorometric are ascribed to the anions-induced by hydrogen bonding interaction between NH protons and F^- anions.

Experiment

Materials

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 Sigma-Aldrich Chemical, stored in a vacuum desiccator containing self-indicating silica and dried fully before using. DMSO was dried with CaH_2 and then distilled in reduced pressure.

Apparatus

^1H NMR spectra were obtained on a Varian UNITY Plus-400 MH_Z Spectrometer. ESI-MS performed with a MARINER apparatus. C, H, N elemental analyses were made on an elementar varuo EL. UV–vis spectra were recorded on a Shimadzu UV-2450 Spectrophotometer with a quartz cuvette (path length=1 cm) at 298.2±0.1 K and the width of the slits used is 10 nm.

General method

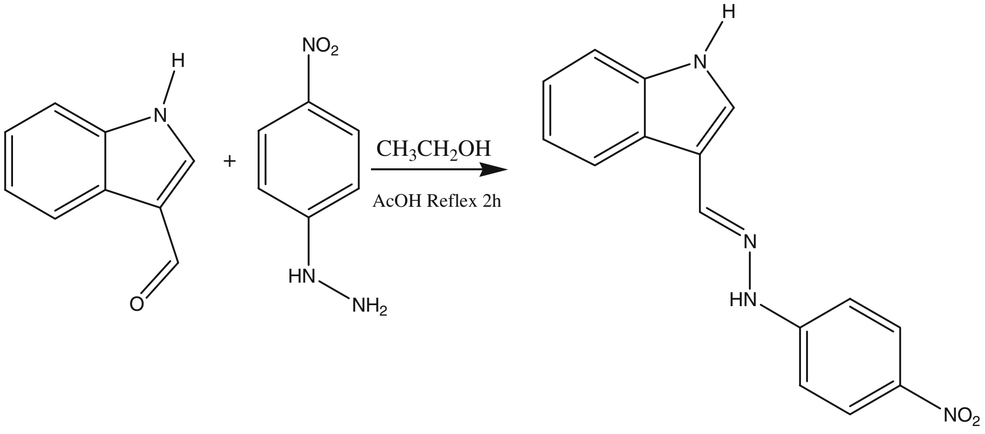
All experiments were carried out at 298.2±0.1 K, unless otherwise mentioned. UV–vis spectra were measured using an ultraviolet-visible spectrophotometer, UV-2450 (Shimadzu Corp., Kyoto, Japan). A 5.0×10^{-4} M solution of the compound 1 in DMSO was prepared and stored in the dry atmosphere. This solution was used for all spectroscopic studies after appropriate dilution. Solutions of 1.0×10^{-3} M tetrabutylammonium salt of the respective anion were prepared in dried and distilled DMSO and were stored under a dry atmosphere.

^1H NMR titration experiments were carried out in the DMSO-d_6 solution (TMS as an internal standard). Certain amount of 0.01 M solution of the compound 1 in the DMSO-d_6 was prepared, into which the increased amount of acetate anion (1.0 M in DMSO-d_6) was added and ^1H NMR of the host–guest system was recorded.

Synthesis of 1H-Indole-3-carboxaldehyde *p*-nitrophenylhydrazone

The structures and synthesis of receptor 1 are shown in Scheme 1. 0.29 g (2 mmol) 1H-Indole-3-carboxaldehyde, 0.306 g *p*-nitrophenylhydrazine (2 mmol) and four drops of acetic acid were dissolved in 40 mL CH_3CH_2OH and then the resulting solution was heated and refluxed 2 h. The mixture was cooled at room temperature after reaction.

Scheme 1 The synthesis route of receptor 1



Precipitate formed was filtered, and 0.448 g pure red solid was obtained after recrystallization by CH_3CN. Yeild= 80%. ^1H NMR (DMSO-d_6, 300 MHz) δH 7.13 (s, 1H, Ar-H), 7.22 (d, 2H Ar-H), 7.46 (s, 1H, −CH = N), 7.82 (s, 1H, Ar-H), 8.16 (s, 2H, Ar-H), 8.28 (t, 3H, Ar-H), 11.04 (s, 1H, amide NH2), 11.59 (s, 1H, NH1), Elemental analysis calcd for $C_{15}H_{12}N_4O_2$ (280.1): C: 64.28, H: 4.23, N: 19.99, Found: C: 64.26, H: 4.23, N: 19.98.

Results and discussion

UV-vis spectral titrations

The qualitative evaluation of the anion sensing capability of 1 was performed in DMSO solutions containing a series of anions, namely, F^-, AcO^-, $H_2PO_4^-$, Cl^-, Br^- and I^-. Figure 1 shows changes in UV-vis absorption spectra of 1 (1.0×10^{-5} M) upon addition of 8 equiv. of respective anions as the *n*-tetrabutylammonium (*n*-bu_4N^+) salt. As shown in Fig. 1, without anions, 1 exhibits a strong band centered at 447 nm, as the concentration of F^- increased stepwise, leads to a gradually decrease in this absorption at 447 nm, along with a new broadly band centered at 570 nm. As seen from Fig. 2, the solution color changes from little yellow to purple upon addition of F^- ions. Meanwhile, on addition equivalent anions of AcO^- and $H_2PO_4^-$, the solution induces less color changes than of F^-. In contrast, addition of any other halide anions does not show any spectra and color changes.

To further evaluate anion binding behavior of the receptor 1, the UV-vis titrations were carried out in DMSO. A solution of the host 1 (1.0×10^{-5} M) was added with various kinds of anions such as fluoride, chloride, bromide, iodide, dihydrogen phosphate, and acetate. Figure 3 shows the results of absorption titration of 1 with F^-. The gradually added the F^- leads to the band centered at 447 nm decrease, while the bond centered at 570 nm increase. The spectra change almost stops upon addition of 40 equiv. of F^-, which were ascribed to the intramolecular charge transfer (ICT) between the electron rich −NH moiety and the electron deficient $-NO_2$ moiety [34, 35]. Therefore, the results testified the host interacted with anionic guests through hydrogen bond, which would affected the electronic properties of the chromophore so that a new charge transfer mechanism established between the electron rich −NH moiety and the electron deficient $-NO_2$ moiety along with a color change. The clear isosbedtic points at 486 nm and 384 nm indicate that a single component is produced in response to the interaction between 1 and F^-. In addition, the spectral responses of 1 toward AcO^- and $H_2PO_4^-$ exhibited similar changes as with F^- while the changes is smaller than that of fluoride ions (see Fig. 3a and b); on the contrary, the spectral absorption hardly changed upon addition of a large amount of Cl^-, Br^- and I^- anions. Consequently, the receptor 1 may be highly selective with the fluoride anions.

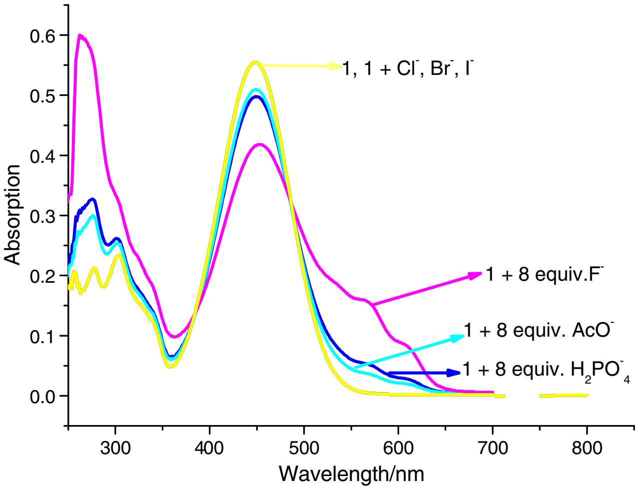


Fig. 1 UV-vis spectra spectra of **1** (1×10^{-5} M) in DMSO in the presence of 8 equiv of F^-, AcO^-, $H_2PO_4^-$, Cl^-, Br^- and I^-

Fig. 2 Color changes of the receptor **1** in DMSO (5.0×10^{-4} M) in absence and presence of 10 equiv of anions (from the left to the right: **1** only, **1**+F^- (the color changes of the AcO^- and $H_2PO_4^-$ is similar with F^-), **1**+ Cl^- (the color changes of the I^- and Br^- is similar with Cl^-)

Fluorescent titrations

The interactions of the anions with the receptor 1 (1.0×10^{-5} M) were determined by the fluorescent spectroscopic titrations in DMSO solution. Figure 4 shows the results of fluorescence titration (I_{ex}=428 nm) of 1 with F^-. Upon addition of F^- leads to continuous decrease in the band centered at 626 nm, along with an increase in the 515 nm band and the clear isoemission points at 591 nm indicate that a component is formed in response to the interaction between 1 and F^-, (See Fig. 4). Interesting, such a significant blue-shift 0 ~110 nm emission band shift from 626 to 514 nm was rarely seen in the ever-reported ICT anion sensors. Meanwhile, the band centered at 514 nm is

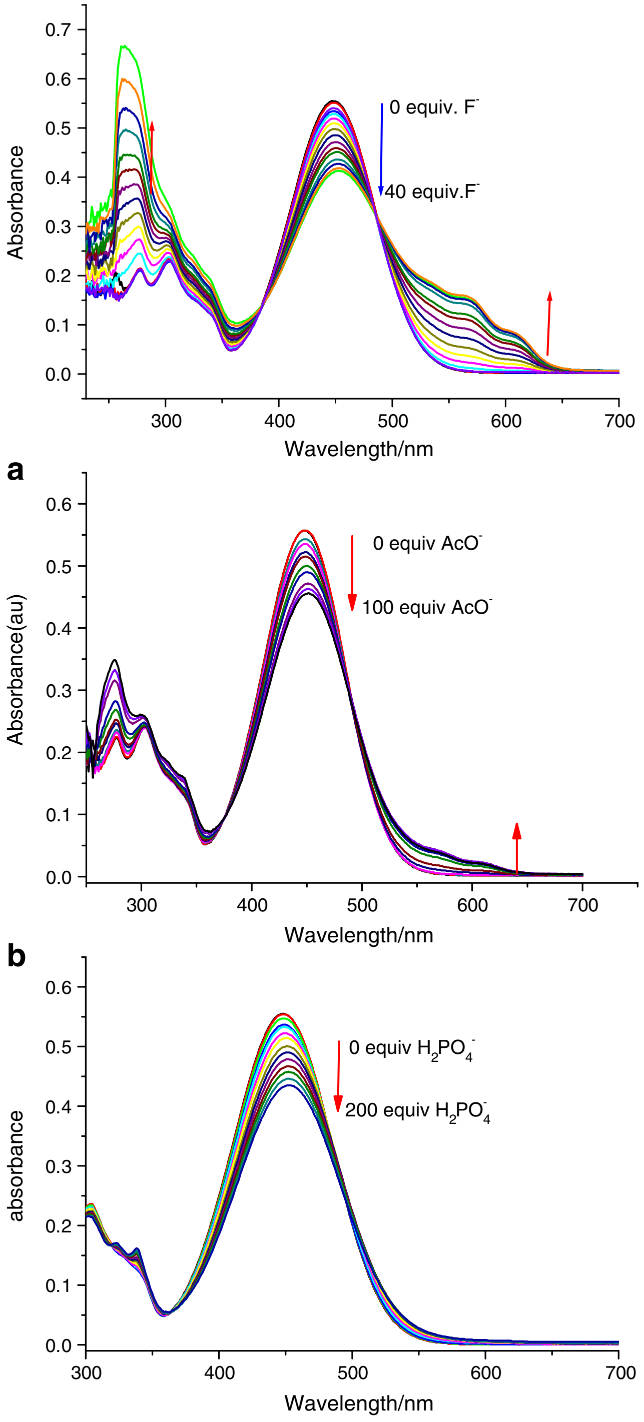


Fig. 3 UV-vis spectral changes of receptor **1** (1.0×10^{-5} M) upon addition of fluoride ion (0 to 40 equiv) in DMSO at 298.2±0.1 K. **a** UV-vis spectral changes of receptor **1** (1.0×10^{-5} M) upon addition of acetate ion (0 to 100 equiv) in DMSO at 298.2±0.1 K. **b** UV-vis spectral changes of receptor **1** (1.0×10^{-5} M) upon addition of $H_2PO_4^-$ ion (0 to 200 equiv) in DMSO at 298.2±0.1 K

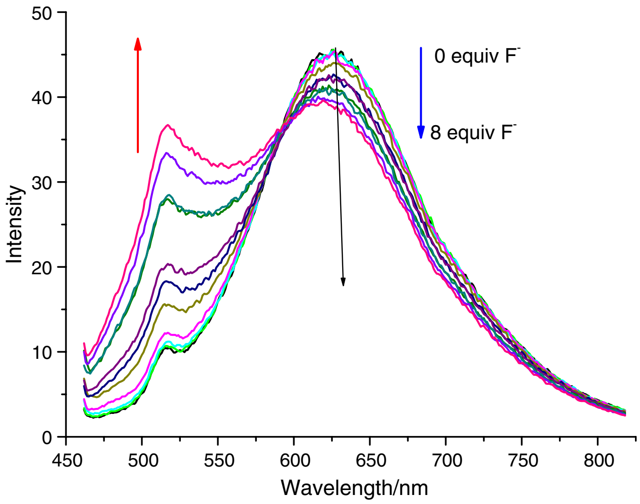


Fig. 4 Fluorescent changes of the sensor 1 in DMSO (1×10^{-5} M) upon addition of F^- ions

shown in the UV-vis absorption spectra of 1 with addition of the F^-. This would indicate that the blue-shift of fluorescence spectra was caused by a change of the charge transfer character of the emissive species [36–38]. When the anion interacted with the binding site, the excited state was more strongly destabilized by the anion than the ground state, and consequently, a blue-shift of the emission spectra was expected. In addition, the presence of AcO^- and $H_2PO_4^-$ induced similar changes in fluorescent spectrum with F^-, but addition of excess equiv. Cl^-, Br^- and I^- ions had slight effects on fluorescence intensity.

Determination of affinity constants

To determine the stoichiometry of the host-guest complex, Job plots were obtained according to the method reported by K.A. Connors [39]. As an example (for F^-), Fig. 5 demonstrates the formation of 1:1 stoichiometry host-fluoride complex. The association constants of the host 1 for anionic species, which are shown in Table 1,

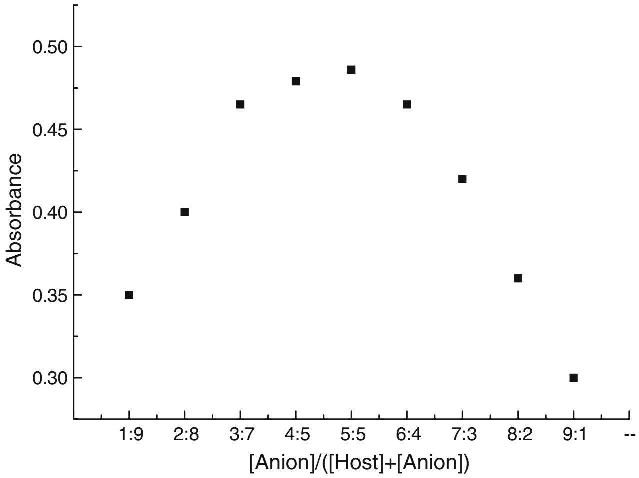


Fig. 5 The stoichiometry analysis of complex 1•F^- by Job plot analysis

Table 1 Association constants for various anions toward receptor **1** in DMSO at 298.2±0.1 K, respectively

Anions[a]	AcO^-	$H_2PO_4^-$	F^-	Cl^-	Br^-	I^-
$K_{ass}(M^{-1})$[b]	$1.09(\pm0.71)\times10^3$	$0.78(\pm0.16)\times10^3$	$3.89(\pm0.31)\times10^3$	ND[d]	ND	ND

[a] The anions were added as their tetrabutylammonium salts

[b] K_{ass} was determined in dry DMSO

[d] ND indicated that the spectra showed little or no change with the addition of anion so that the association constants can not be determined using the spectra

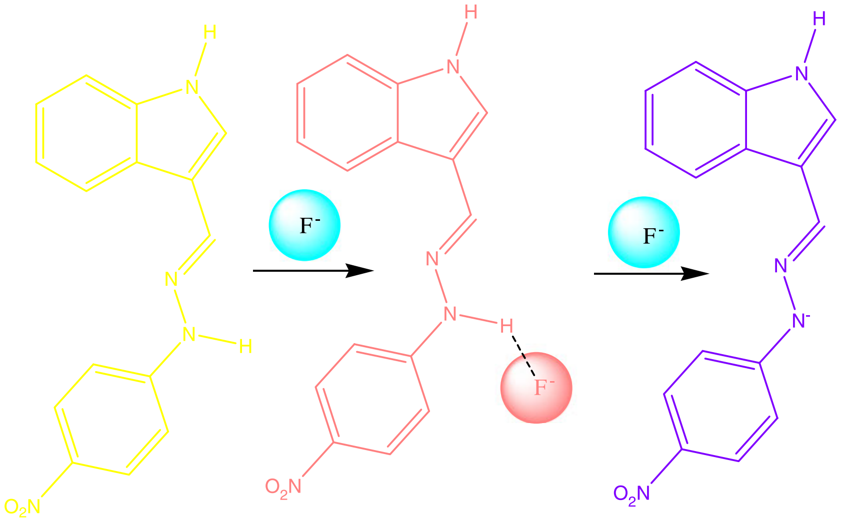
were determined by the non-linear fitting analyses of the titration curves according to Eq. 1, which is applied to the 1:1 host-guest complexation and reported by B. Valeur [40],

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

Where, c_G and c_H are the concentrations of guest and host, respectively, and A is the intensity of absorbance at the monitored wavelength at certain concentrations of the host and the guest. A_0 is the intensity of absorbance of host only and A_{lim} is the maximum intensity of absorbance of host when gust is added. K is the affinity constant. As clearly shown from Table 1, the order of selectivity or the binding affinity of anions for 1 in DMSO is $F^- > AcO^- > H_2PO_4^- >> Cl^- \sim Br^- \sim I^-$. The main reasons can be ascribed to the basicity of the guest molecule and the shape complementarity between the host and the anionic guests [41]. Particularly, the presence of multiple hydrogen bonding interactions are necessary to generate the high-affinity anion binding sites. Among the anions tested, the basicity of AcO^-, F^- and $H_2PO_4^-$ anions are stronger than other anions. Furthermore, the fluoride anions are global and the smallest atoms radius might be the best to fit for the sensor 1 with hydrogen-bonding interactions (Scheme 2) that the receptor 1 has better selectivity and higher affinity constants with fluoride anions than others examined by present work.

^{1}H NMR titrations

To further study the nature of host-guest interactions, ^{1}H NMR spectra changes upon addition of F^- as their tetrabutylammonium salts to the DMSO-d_6 solution of 1 (1×10^{-2} mol L^{-1}) were investigated. Obviously, the proton signals at 11.58 ppm and 11.04 ppm, which were assigned to the −NH moiety of the Indole-3-carboxaldehyde and the amide of the *p*-nitrophenylhydrazine, respectively, were observed in the absence of the fluoride ions (see Fig. 5). Upon addition of 0.5 equiv. of F^- ions, the signals of the NH moiety were broadened and the signals on phenyl rings changed slightly. This result indicated that a hydrogen-bonding complex was formed at this stage. With further addition of F^- ions, the phenyl protons especially for H1 shifted downfieds significantly, due to the increase of the electron density on the phenyl rings by the through-bond effect. At the same time, the signals from binding sites of the receptor 1 downshifted and the proton of the *p*-



Scheme 2 The proposed host–guest binding mode in solution

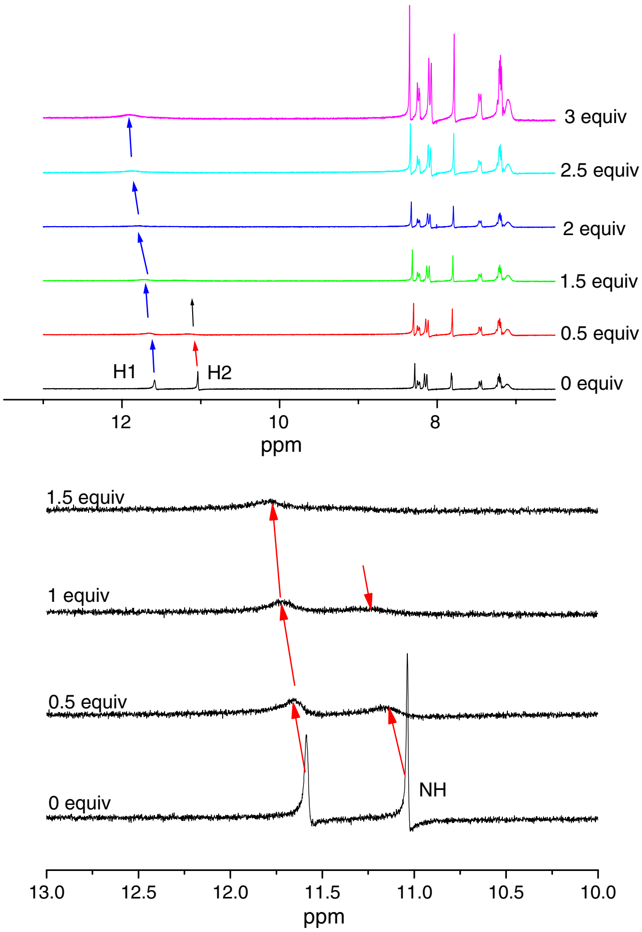


Fig. 6 ^{1}H NMR spectra of the receptor 1 in DMSO-d_6 (1×10^{-2}) upon addition of molar equiv. of F^-

nitrophenylhydrazine eventually disappeared with the F^- up to 1.5 equiv., while the −NH proton of the indole shifted downfields and the peaks broadened, which was ascribed to the deprotonation of the amide proton that induced the increase of the electron density on the indole rings through bond effect. So, the process of anion recognition had two steps, firstly, the NH binding parts of the *p*-nitrophenylhydrazine formed supermolecule through hydrogen bond, secondly, the NH proton of the *p*-nitrophenylhydrazine was deprotonated by adding fluoride ions. Consequently, the results of the UV-vis titrations and ^{1}H NMR titrations have testified the above supposition of the H-bond interactions between the host and the F^- ions (Fig. 6).

Analytical applications

As a good anion sensor, the high selectivity for anions in the analyte has great interest over the practical analytical. Recently, inspired by Koide and coworkers [42, 43] who reported qualitative detection of palladium and fluoride in real-life application, respectively. Although, the sensor 1 didn't induce the UV-vis spectrum, a sample that contained commercially available toothpaste and F^- (as tetrabutylammonium salts) was prepared in DMSO solution. Adding proper amount of the sample to the solution of the receptor 1 in DMSO forming mixture solutions, which were made up of 0.1 $mgmL^{-1}$ toothpaste, 4×10^{-4} mol L^{-1} F^- ions, was obtained. Then, the UV-vis absorbance method for the mixture solutions were measured and compared to a toothpaste-free F^- solution. As shown in the Fig. 7, the intensity containing toothpaste was stronger than that without it, which is ascribed to fluoride of the toothpaste so that the receptor 1 may be used in qualitative detecting fluoride in toothpaste. But detecting fluoride in the protic solution is called for further research.

Conclusions

In summary, we have successfully designed and synthesized a colorimetric and ratiometric fluorescent anion sensor which recognizes anions through hydrogen bonding between −NH protons and F^-, AcO^- and $H_2PO_4^-$ shows more selective to F^- in DMSO solution based on an intermolecular charge transfer mechanism. The changes in absorption and fluorescence spectra upon addition F^-, AcO^- and $H_2PO_4^-$ anions were attributed to the conjugation of the host and the guest. For practical application, the ratiometric sensor displays distinct color changes for fast and efficient sensing. The anion recognition and sensing processes are supported by UV–vis spectral titration, fluorescent titration and ^{1}H NMR titration. More important, the remarkable photophysical properties of the sensor would help to extend the development of fluorescent sensors for biologically inorganic anions.

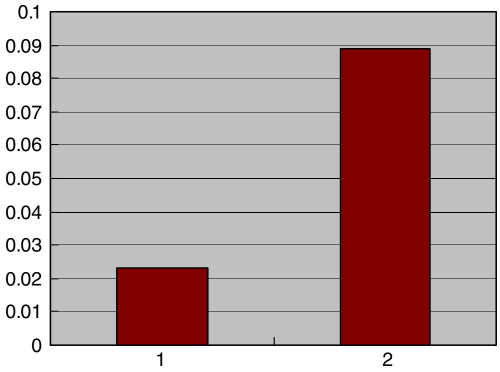


Fig. 7 The proof of concept for fluoride detection in toothpaste (1) sensor + tetrabutylammonium fluoride; (2) sensor + tetrabutylammonium fluoride + toothpaste (_*A* = *A*host + guest − *A*host only)

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