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ORIGINAL ARTICLE

Anion receptor based on thiourea: via hydrogen bonding interaction and efficient deprotonation

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Abstract A new thiourea-based receptor through Schiff-based condensation of 8-hydroxyqui nolino-7-aldehyde and a phenylthiosemicarbazide was easily obtained. This novel sensor shows strong binding affinity for acetate, fluoride and phosphate ions through efficient deprotonation. We make an in-depth investigation on its anion binding prosperities and deprotonation process through Fluorescence, UV–vis and ^{1}H NMR titration experiments. Moreover, we propose the anion recognition process by assuming the existence of three-step equilibria.

Keywords ESPT · Hydrogen-bonding · Deprotonation · Chemosensor

Introduction

The synthesis of artificial receptors capable of recognizing and sensing of anionic analytes has recently been substantial progress in the field of supramolecular chemistry, due to the extensive understanding of supramolecular chemistry of anions, as well as the predomination of the sophisticated synthetic methods [1–4]. There are two main interactions, i.e. hydrogen bonding and electrostatic interaction, which, in general, make the anion sensing possible. Therefore, to well organize the H-bonds in receptor is the directionality considered, which allows the design of receptors capable of selective recognition among various anions with varied geometries and hydrogen-bonding requirements [5]. Neutral sensors containing urea or thiourea are good H-bond donors and excellent receptors for anions, through the participation of the bifurcate H-bond interaction [6–8]. And the design of receptors containing one or more urea subunits has attracted much attention. In recently years, anion chemosensors coupled with two subunits exhibiting different functions, as the binding site and the signaling subunit have been modified [9]. Moreover, the binding site takes the role of combination to certain anion, whereas the signaling unit is capable of translating the analyte-binding induced changes into the outside world through an optical signal (UV–vis and fluorescence emission spectra changes) [10].

In connection with the idea mentioned above, we synthesizes a thiourea-based receptors 1 which consists of a phenylthiourea subunit to interact with the anion and a naphthalene moiety to act as a chromogenic signaling unit through modulation of the fluorescence emission. To explore the thiourea-based molecular in anion recognition, we performed a systematic study with a number of anionic guest species by observing the change in Fluorescence, UV–vis and ^{1}H NMR titration experiments.

Experimental

Apparatus and measurements

UV–vis spectra and Fluorescent spectra were recorded with a Shimadzu UV-2450PC spectrophotometer and a

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Shimadzu RF-5301PC Spectrophotometer, respectively, at 298.2 ± 0.1 K. The ^{1}H NMR spectra were performed on a Varian UNITY-plus 400 MHz spectrometer using tetramethylsilane (TMS) as an internal standard. ESI–MS was carried out with a Mariner apparatus. Elemental analysis (C, N and H) was made on a Vario ELIII instrument.

Reagents

All reagents were of analytical grade and used without further purification unless otherwise specified. All the anions, which were purchased from Sigma–Aldrich Chemical, were added in the form of tetra-*n*-butylammonium (TBA) salts, and stored in a vacuum desiccator containing self-indicating silica. DMSO used in the titration experiments, was dried with CaH_2 and then distilled in reduced pressure.

Synthesis of 8-hydroxy-quinolino-7-aldehyde 4-phenylthiosemicarbazone

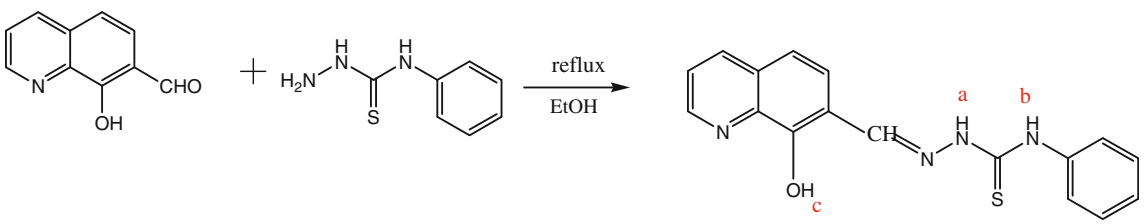
To a vigorously stirred and refluxing solution of 4-phenylthiosemicarbazide (0.835 g, 0.5 mmol) in C_2H_5OH (20 mL) in the presence of catalytical amount of acetic acid (3d), 7-formal-8-hydroxyquinoine (0.0863 g, 0.5 mmol) in C_2H_5OH (10 mL) was added in dropwise. After stirring and refluxing for 6 h, the yellow precipitate formed was filtered off and washed twice with C_2H_5OH (5 mL). The crude product was successively recrystallized from ethanol to give the pure compound 1. Yield: 56%. ^{1}H NMR (DMSO-d_6, 400 MHz, Me_4Si) δ (ppm): 11.689 (s, 1H, CS-N*H*), 10.437 (s, 1H, aromatic-O*H*), 10.023 (s, 1H, Phen-N*H*), 8.929 (s, 2H, aromatic*H*), 8.815 (s, 1H, aromatic-C*H*), 8.255 (d, 1H, aromatic*H*), 7.729 (d, 1H, Phen*H*), 7.619 (d, 2H, aromatic*H*), 7.380 (s, 2H, Phen*H*), 7.184 (s, 2H, Phen*H*); Elemental analysis calcd. (%) for $C_{17}H_{14}N_4OS$: C 63.33; N 17.38; H 4.38; Found: C 63.56 N 17.43; H 4. 91; ESI-mass: *m/z* calcd. for $C_{17}H_{14}N_4OS$ [(M + H)$^-$]: 322.09, found: 321.99.

Results and discussion

The binding properties of the compound 1 toward AcO^-, F^-, $H_2PO_4^-$, Cl^-, Br^-, and I^- were explored with the UV–vis titrations, Fluorescent titrations and the ^{1}H NMR experiment. All the anions added were in the form of tetrabutylammonium salts to 2.0×10^{-5} M solutions of the host molecule 1 in DMSO.

UV–vis experiments

In order to establish the nature of the receptor–anion interaction, we carried out spectrophotometric titration experiments by adding a standard solution of the tetrabutylammonium salt of anions to a dry DMSO solution of the sensor (2×10^{-5} mol/L) at 298.2 ± 0.1 K (Scheme 1). Figure 1a shows the UV–vis spectral changes of 1 during the titration with the Y-shaped anion AcO^-. It can be observed that, upon addition of AcO^-, the band centered at 374 nm, specific to the derivative 1, eventually with decreases its strength, while a new band at 450 nm forms and develops, which may be attributable to the intramolecular charge transfer (ICT) from the –OH and –NH units to the electron-deficient $-C_6H_5$ moiety [11]. Look more closely, acetate displays a more complex producer. Upon addition of minor of AcO^- just as Fig. 1b displays, the original absorption band at 374 nm of derivative 1 behaves subtle changes associated with the emergence of the new peak centered at 450 nm. However, when approaching 4 equiv of AcO^-, as indicated by the titration profile shown in Fig. 1c, the initial band at 374 nm descends gradually with the intensifying of the intensities of the band at 450 nm. As stated previously no major changes are seen with up to 136 equiv of acetate ions, and the equilibrium is achieved. Therefore, the titration profiles, shown in Fig. 1, clearly suggest the presence of the two distinct steps in Scheme 2 II and III: at low acetate concentration, sensor–acetate interaction is the authentic hydrogen binding, and with the further increase of the acetate ions, the excess acetate can interact with the sensor–acetate complex and induce the deprotonation of the sensor [12]. With the addition of the tetrabutylammonium salts of other common inorganic anions to DMSO solutions of the compound, the spectral changes are clearly observed in the case of F^- and $H_2PO_4^-$, which produced a family of spectra very similar to that obtained on titration with acetate. Nevertheless the addition of Cl^-, Br^-, and I^- do not result in any spectra response even added in abundance. The association



Scheme 1 The synthetic procedure for an anion receptor 1

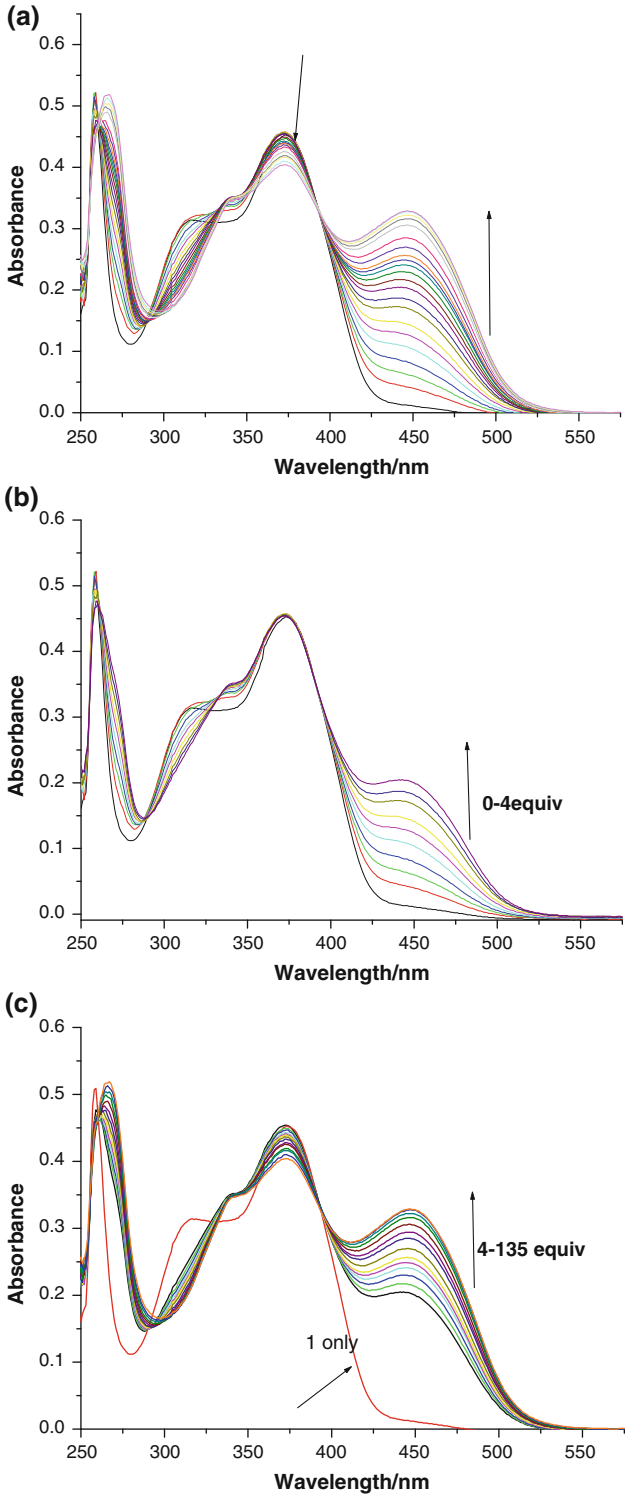


Fig. 1 **a** Family of spectra taken in the course of the titration of the receptor 1 (2×10^{-5} mol/L) in the presence of AcO^- ion (as its tetrabutylammonium salt) in DMSO. **b** Addition of 0–4 equiv of AcO^-. **c** Addition of 4–135 equiv of AcO^-

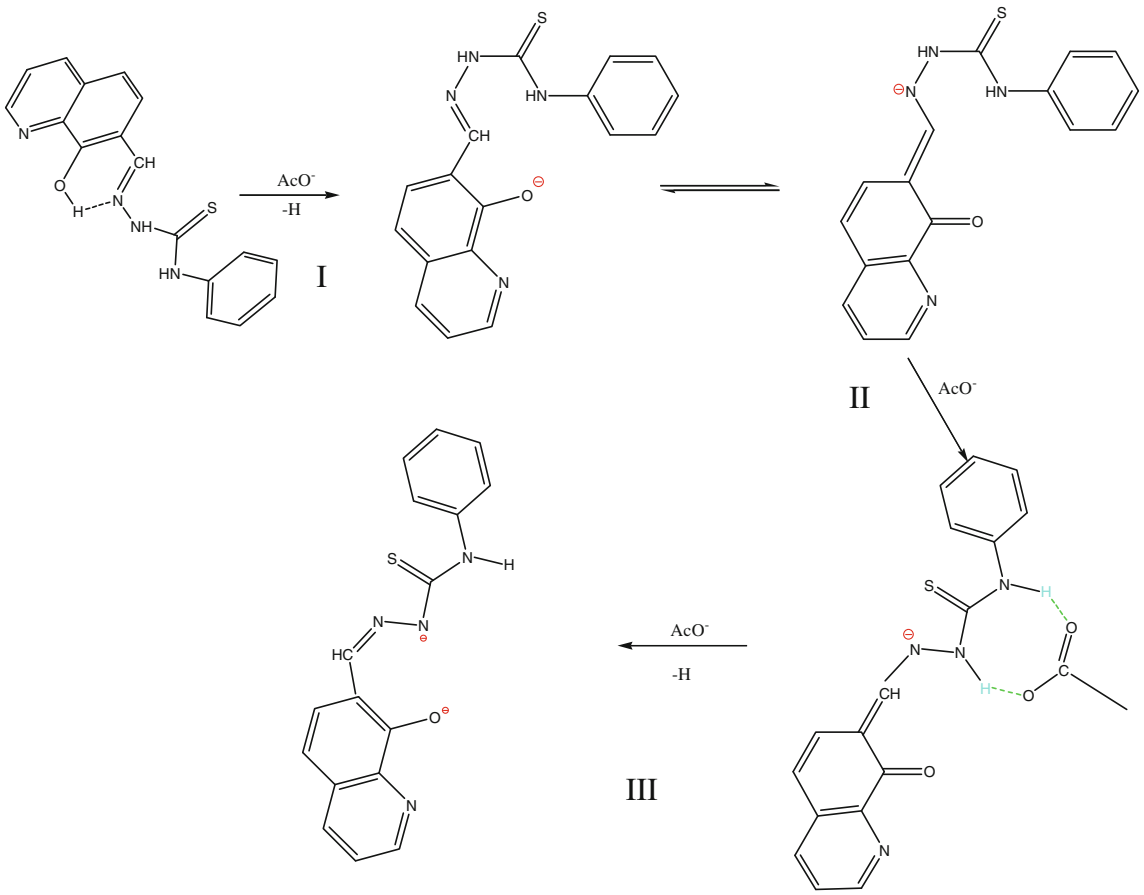
constants (K_a) can be calculated by non-linear fitting analyses of the titration curves and the absorbance at 449 nm of the receptor against anion concentration, assuming a 1:1 equilibrium. The latter is further confirmed by the Job plot analysis in Fig. 2 [13, 14] and the nice fitting curves (Supporting information, S1).

Obviously from Fig. 3 and Table 1, the selective trend of the anions for the sensor was determined to be $AcO^- > F^- > H_2PO_4^- > Cl^- \sim Br^- \sim I^-$. Although the principles that governing the anion recognition have not been completely found, it is apparently that the selectivity for specific anions can be rationalized on the basis of the guest basicity and the shape complementarity [15]. Particularly, multiple hydrogen-bond interaction was also a necessary factors in anion binding process. As to the basicity of anions, $H_2PO_4^-$, F^-, and AcO^- can offer much stronger interactions with host than other halogen anions. Furthermore, thiourea is an appropriate receptor for oxoanions because of the formation of two N–H···O bonds with the two consecutive oxygen atoms of the anion. Consequently, the triangular acetate anion with an O–C–O angle of ca. 120° (e.g., matching of the distance of the N atoms of the thiourea subunit and the distance of the O atoms of the oxoanion) [16] and may be the best fitting for the curvature shape of the binding sites of receptor among the anions tested. So AcO^- might be selectively recognized from other anions.

Fluorescence response of anions

The fluorescence responses on the interactions of the receptor 1 with anions are also conducted by observing emission spectra with excitation band centered at isosbestic point of 394 nm in DMSO (Fig. 4a). The free 1 exhibit an emission maximum centered at 468 nm with a shoulder band at 677 nm. With the introduction of acetate ions, a new emission band at 546 nm as well as the drastic increase of fluorescent intensity of acetate ions turns up. This phenomenon may be ascribed to the formation of intermolecular excited state proton transfer (ESPT) in the senor–anion complexes based on the previously reported similar cases [17–19]. Among the anions investigated, only F^- and $H_2PO_4^-$ induces similar spectral changes contrasted with other anions, such as Cl^-, Br^-, and I^-, they dot not induce any fluorescence response because of their relatively lower basicity. Consequently, the receptor 1 has the potential to be a sensing agent for anions due to the unique change of their fluorescence upon binding certain anions via ESPT mechanism.

In accordance well with UV–vis titration experiment, the fluorescence acetate titration spectra of sensor 1 also displays stepwise changes. The detailed fluorescence titration results of the sensor 1 upon addition of various molar ratios of acetate ions are plotted in Fig. 4b and c. When the ratio between AcO^- and the receptor 1 is <4, the



Scheme 2 The proposed host–guest binding mode in solution

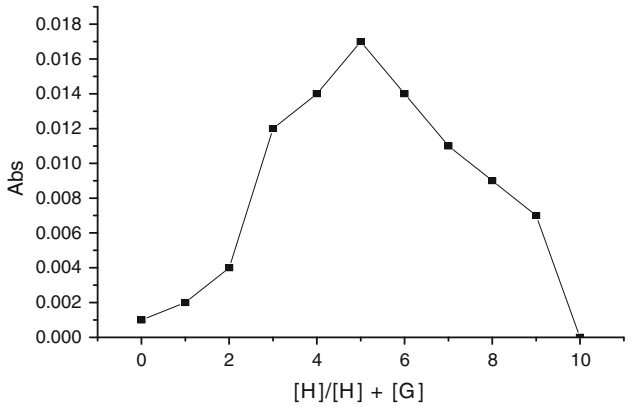


Fig. 2 The stoichiometry analysis of complex 1·AcO^- by Job plot analysis ([H] + [G] = 2×10^{-5} mol/L)

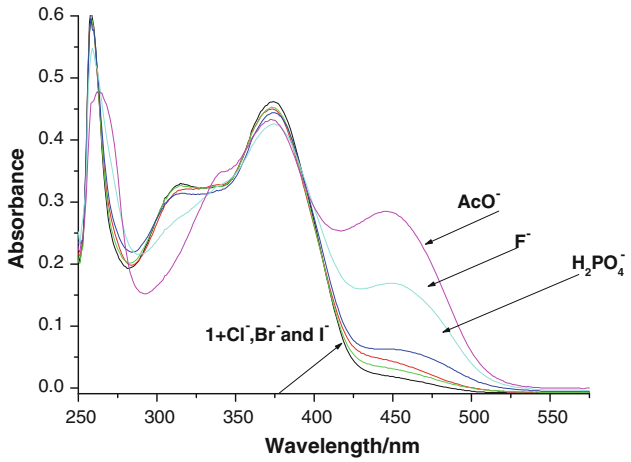


Fig. 3 Changes in absorption spectra of the compounds 1 (2×10^{-5} mol/L) in DMSO upon addition of 10 equiv of various anions

fluorescence switch-off gradually with small red shift, and then a new fluorescent switch-on band centered at 546 nm develops with the further excess of acetate due to intermolecular proton transfer from –NH units to AcO^- ion. The same phenomenon can also be observed with the introduction of F^- and $H_2PO_4^-$ ions into the receptor 1 of DMSO solution.

^{1}H NMR titrations

^{1}H NMR titration experiment is conducted to investigate the interaction of the receptor 1 with anion (added as

Table 1 Association constants (K_a) and correlation coefficients (R) of the receptor 1 with various anions in DMSO

Anion[a]	K_a (M^{-})[b]	R^{2}[d]
AcO^{-}	2.2×10^{4}	0.99398
F^{-}	2.5×10^{3}	0.98902
$H_2PO_4^{-}$	7.1×10^{2}	0.98908
Cl^{-}	ND[c]	ND
Br^{-}	ND	ND
I^{-}	ND	ND

[a] The anion were added as their tetrabutylammonium salts

[b] K_a was determined in dry DMSO

[c] *ND* indicated that the spectra showed little or no change with the addition of anion so that the association constants cannot be determined using the spectra

[d] Correlation coefficient (R^2) determined by non-linear fitting analyses

tetrabutylammonium salt). Detailed ^{1}H NMR spectra of 1 upon addition of increasing amount of AcO^{-} are displaced in Fig. 5 and F^{-} (Supporting information, S4). Before examining the spectroscopic features in detail, we firstly bring forward two effects which would be responsible for spectral shifts of the aromatic protons of the phenyl rings linked to the thiourea moiety as well as the deprotonation of O–H and one N–H fragement. (1) through-bond effects, which increase the electron density of the benzene ring and promote upfield shifts in ^{1}H NMR spectrum, (2) through-space effects, which polarize C–H bond in proximity to hydrogen bond, create the partial positive charge on the proton and cause downfield shifts [20].

It can be observed in Fig. 5 that the peak assigned to –OH is not clearly present due to the intramolecular hydrogen bonding [21]. Upon addition of minor of acetate, the signal disappeared completely, which may be ascribed to the one-step Bronsted acid–base reaction transformation between the strong acid and strong base (Scheme 2 I).The downfield shift and broadness of the protons CS-N*H* and CS-N*H* signals (the peaks at 11.689 and 10.023 ppm, respectively) are also observed, indicating the presence of hydrogen bonding between host and guest at this stage. And it might be ascribed to the through-space effects, polarization C–H bond in proximity to hydrogen bond (Scheme 2 II). With the further introduction of acetate ions, deprotonation of one –NH fragment takes place, and the majority of signals on the phenyl rings shift upfield clearly, which illustrate the increase of the electron density on the aromatic rings owing to the through-bond effects. (Scheme 2 III). According to the results of UV–vis spectral, fluorescent and ^{1}H NMR titrations, the anion binding mode of the receptor—AcO^{-} is shown in Scheme 2 [22].

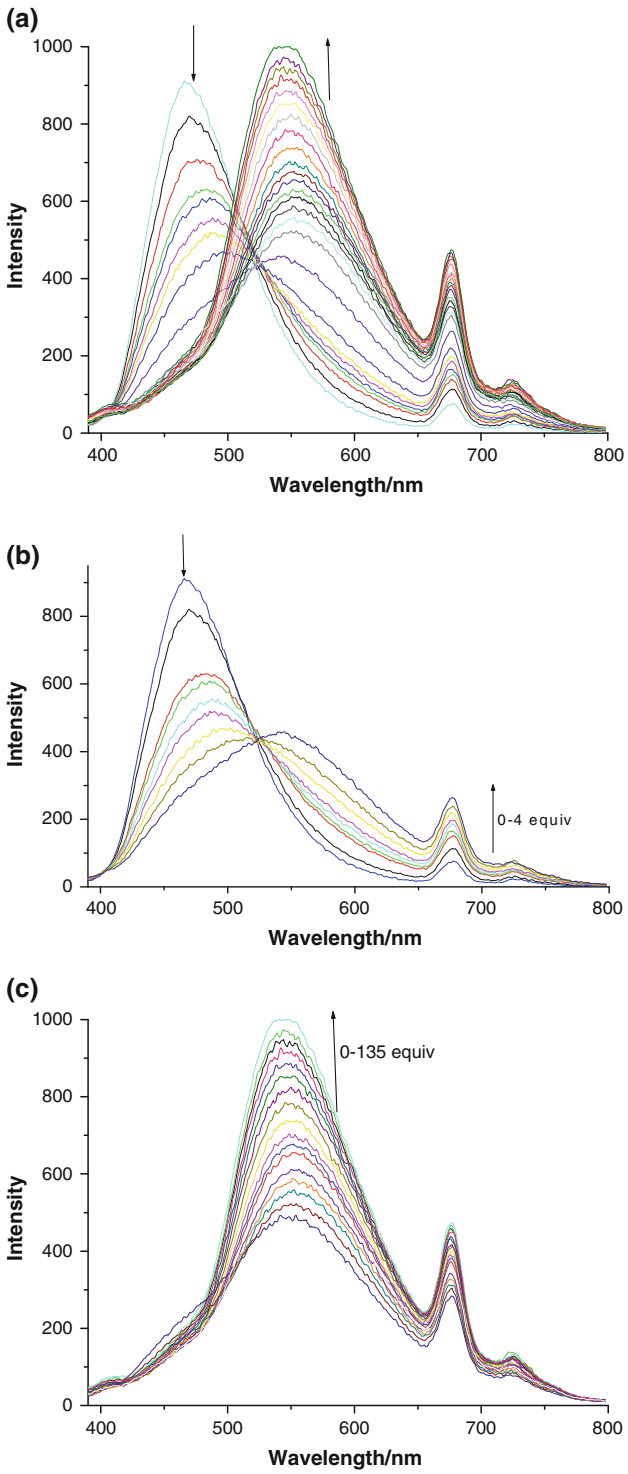


Fig. 4 **a** Change in fluorescent spectra for sensor (2×10^{-5} mol/L) in DMSO upon the addition of a standard solution of $[(Bu)_4N]AcO^{-}$. **b** Addition of 0–4 equiv of AcO^{-}. **c** Addition of 4–135 equiv of AcO^{-}

And the mechanism should also be applicable to phosphate and fluoride ions, which include similar spectral patterns as acetate (Supporting information, S2 and S3).

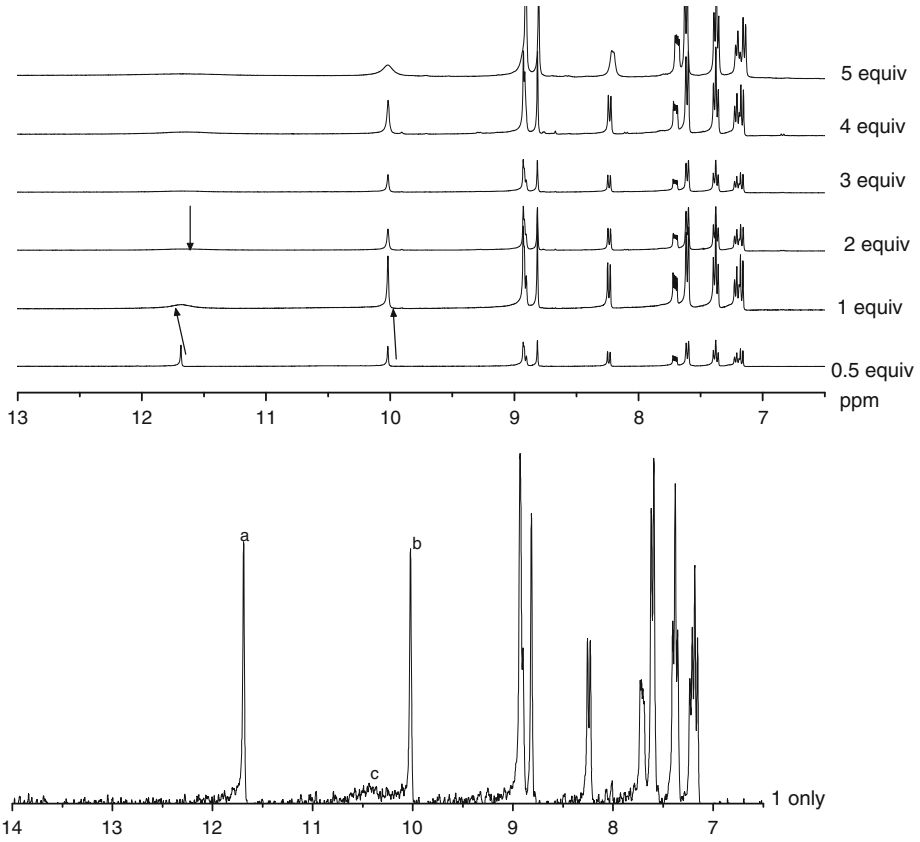


Fig. 5 ^{1}H NMR titration of a 1×10^{-2} mol/L solution of the receptor 1 in DMSO-d_6 with tetrabutylammonium acetate

Conclusions

In conclusions, we put up a study for the interaction of receptor with anions by UV–vis, fluorescence and ^{1}H NMR titration experiments. Summing up all the titration data, we can claim that: (I) the host interacts with anions to induce the deprotonation of –OH, (II) the compound interacts with anions to bring on the formation of sensor–anion hydrogen bonds and (III) the continuous addition of anions results in the urea deprotonation. Besides, during combining process a tautomeric equilibrium occurred and the different electronic properties of the tautomer are responsible for the observed spectral changes.

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