

2-Hydroxy-naphth-1-aldehyde phenyl-thiosemicarbazone: effective thiourea-based sensor for acetate anion

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Abstract A novel urea-based sensor displaying selective recognition for AcO^- had been designed and synthesized. Experiments showed that sensor 1 can selectively recognize acetate in DMSO. The evaluation of the sensor's interaction with a variety of structurally different anions was performed by UV–vis titration experiments in DMSO. In addition, the nature of interaction between sensor 1 and AcO^- was investigated by ^1H NMR titrations.

Keywords Anion recognition · Hydrogen-bonding · Deprotonation · Thiourea

Introduction

Anions, such as CH_3COO^- , F^- and H_2PO_4^- , play a fundamental role in a wide range of biological, chemical, medical and environmental process as well as in agricultural fertilizers and food additives [1–3]. Thus, considerable attention has been focused on the search for chemosensors that recognize and detect these anionic analytes. Full charged host molecules, such as protonated polyamines, guanadinium [4], transition metal, and azamacrocycles based complexes were first employed in the anion recognition. More recently neutral sensors such as

pyrroles [5, 6] indoles [7, 8] calixpyrroles, urea and thioureas [9] have been cited as anion recognition moieties. For example, the construction of anion sensors consisted of urea and thiourea motifs have been demonstrated to be good hydrogen bond donors and excellent sensors for “Y-shaped” acetate ion. A selective sensor molecule is mostly composed of a component specific for a selected analyte and a signaling unit capable of translating the analyte-binding induced changes into an output signal [10]. Furthermore, the information of the anion binding process can be detected, as optical signals, by simple spectroscopic methods, such as UV–vis and NMR titration experiments.

Spherical ions (e.g., halide ions), tetrahedral-shaped phosphate, and planar carboxylate anions are easy to form hydrogen bonds with urea/thiourea based sensor molecules [11–13]. In this paper, we synthesized a naphthalene-based thiourea molecule and performed a systematic study with a number of anionic guest species such as halides, carboxylate and phosphate anions. UV–vis and ^1H NMR titration experiments were carried out to investigate the binding properties of the sensor 1 in the presence of various anions in dry DMSO.

Experimental

Apparatus and measurements

UV–vis spectra were recorded with a Shimadzu UV-2450PC spectrophotometer at 298.2 ± 0.1 K. The ^1H 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.

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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-indication silica. DMSO used in the titration experiments, was dried with CaH_2 and then distilled in reduced pressure.

Synthesis

Synthesis of 2-hydroxynaphthalene-1-carbaldehyde [14]

2-Naphthol (22.2 g, 130 mmol) and hexamethylenetetramine (23.8 g, 170 mmol) were added slowly to acetic acid (30 mL) in a 200 mL three-necked round flask equipped with a magnetic stir bar. The mixture was reacted in 60 °C water bath for 20 min. And then the solution was heated to 90 °C, 98% H_2SO_4 (33 mL) was added dropwise to the mixture with stirring. After the addition, the temperature of the solution was elevated to 95–98 °C for next 3 h. The reaction mixture was cooled to room temperature and then poured into water (100 mL). At 30 °C, additional water (200 mL) was added and the solution was stirred for another 1 h, which was cooled to room temperature and left to stand for 24 h. The solid was filtered off, washed with water until the pH = 7, and then dried at 50 °C. The crude product was filtered and 18.5 g pure product was obtained after recrystallization from $\text{C}_2\text{H}_5\text{OH}$. (70%) mp: 79–80 °C (lit. 78–79 °C).

Synthesis of 2-hydroxy-naphth-1-aldehyde phenylthiosemicarbazone (see Scheme 1)

To a vigorously stirred and refluxing solution of 4-phenylthiosemicarbazide (0.835 g, 0.5 mmol) in $\text{C}_2\text{H}_5\text{OH}$ (20 mL) in the presence of catalytical amount of acetic acid, 2-hydroxynaph-1-aldehyde (0.0865 g, 0.5 mmol) in $\text{C}_2\text{H}_5\text{OH}$ (10 mL) was added dropwise. After stirring and refluxing for 2 h, yellow precipitate formed and filtered off and washed twice with $\text{C}_2\text{H}_5\text{OH}$ (5 mL). The crude product was successively recrystallized from ethanol to give the pure sensor 1. Yield: 67%. ^1H NMR (DMSO- d_6 , 400 MHz, Me_4Si) δ (ppm): 11.749 (s, 1H, CS-NH), 10.678 (s, 1H, aromatic-OH), 10.062 (s, 1H, Phen-NH), 9.158 (s, 1H, aromatic-CH), 8.499 (d, 1H, aromatic-H), 7.892 (s, 2H, aromatic-H), 7.570 (s, 3H, aromatic-H) 7.377 (s, 3H, Phen-H), 7.230 (s, 2H, Phen-H); Elemental analysis calcd (%), for $\text{C}_{18}\text{H}_{15}\text{N}_3\text{OS}$: C 67.27; N 13.07; H 4.70; Found: C 67.31; N 13.32; H 4.91; ESI-mass: m/z calcd. For $\text{C}_{18}\text{H}_{15}\text{N}_3\text{OS}$ [(M + H) $^+$]: 321.09, Found: 321.11.

Results and discussion

The binding properties of the sensor 1 toward AcO^- , F^- , H_2PO_4^- , Cl^- , Br^- , and I^- were explored with UV–vis titrations, the ^1H 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

UV–vis titrations were conducted to investigate the interaction of the sensor 1 with anions by adding a standard solution of the tetrabutylammonium salt of anions to dry DMSO solution of sensor (2×10^{-5} M) at 298.2 ± 0.1 K. Figure 1 shows the UV–vis spectral changes of the sensor 1 during the titration with acetate ion. With the addition of various molar of acetate ions, the strong absorbance peak at the λ_{max} of 430 nm resulting from the π – π^* transition of the chromophore, disappeared gradually, while a new band at 458 nm with two shoulder bands at 429 and 488 nm formed and developed [15, 16], and the phenomenon may be owing to the intramolecular charge transfer (ICT) from the –OH and –NH units to the electron-deficient $-\text{C}_6\text{H}_5$ moiety. At the same time, the pale yellow of the solution became deeper. Also, four well-defined isosbestic points indicating the formation of stable complex presented at 303, 335, 345 and 398 nm, respectively, and the stoichiometry of the sensor–acetate interaction was confirmed to be 1:1 by Job plot (Fig. 1 inset).

Similar changes were also observed in UV–vis spectra of the sensor 1 upon addition of H_2PO_4^- , and F^- , nevertheless the addition of Cl^- , Br^- , and I^- did not result in any spectra response even in abundance.

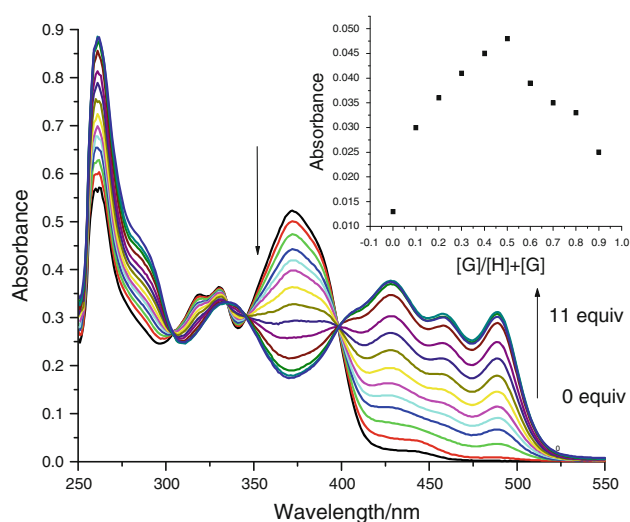


Fig. 1 UV–vis spectrum of the sensor 1 (2×10^{-5} M) in the presence of AcO^- ion in DMSO. Inset: The stoichiometry analysis of complex 1- AcO^- by Job plot analysis ($[\text{H}] + [\text{G}] = 4 \times 10^{-5}$ M)

Obviously from Fig. 2, the order of the sensor's selectivity toward different anions was determined to be $\text{AcO}^- > \text{H}_2\text{PO}_4^- \gg \text{F}^- > \text{Cl}^- \sim \text{Br}^- \sim \text{I}^-$. Although the principles that govern anion recognition have not been completely understood, it is apparently that the selectivity for specific anions can be rationalized on the basis of the shape complementarity and the guest basicity [17]. Urea is an appropriate sensor for oxoanions because of the easy formation of $\text{N-H}\cdots\text{O}$ bonds with two neighboring oxygen atoms of the anion [18]. The distance between two oxygen atoms of AcO^- might be more fits to two $-\text{NH}$ of sensor 1 than those spherical and tetrahedral anions (see Scheme 1). This shows that sensor 1 has a high selectivity for anions that with a two- or three-dimensional structure of space, rather than globular.

^1H NMR titrations

We conducted ^1H NMR titrations experiments in $\text{DMSO}-d_6$ to investigate the nature of the new peaks formed in UV–vis spectra. The ^1H NMR titrations course listed in

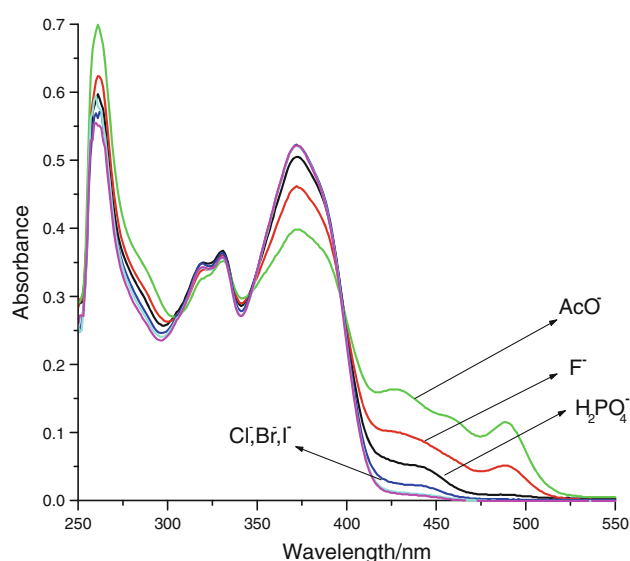


Fig. 2 Changes in absorption spectra of the sensors 1 (2×10^{-5} mol/L) in DMSO upon addition of five equiv of various anions

Scheme 1 The synthetic procedure for an anion sensor 1

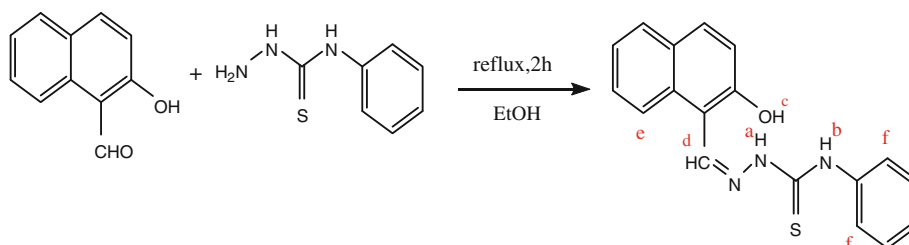


Fig. 3 interpreted the spectral shifts of the aromatic protons of the phenyl rings linked to the thiourea moiety when adding acetate. It is well known that, two effects might be responsible for the formation of hydrogen bonds between the thiourea subunit and anion. Through-bond effects, which increase the electron density of the benzene ring and promote upfield shifts in ^1H NMR spectrum, 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 [19].

As shown in ^1H NMR titration spectra of sensor 1 in Fig. 3, upon addition of 0.2 molar equiv of acetate ions, the downfield shift and broadness of the protons H_a and H_b signals (the peaks at 11.749 and 10.062 ppm, respectively) were observed, which indicated the formation of hydrogen bonds between host and guest for two $-\text{NH}$ at this stage. And it might be ascribed to through-space effects, polarization C–H bond in proximity to hydrogen bond. With the further addition of acetate ions, deprotonation of one $-\text{NH}$ fragment took place, and the majority of signals on the phenyl rings especially for H_c (8.499 ppm) and H_f (7.230 ppm) shifted upfield clearly, which indicated the increase of the electron density on the aromatic rings owing to the through-bond effects. As mentioned above, the proposed anion recognition process was illustrated in

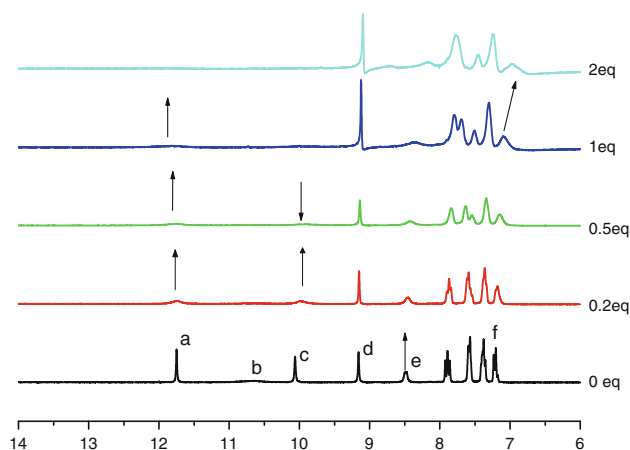
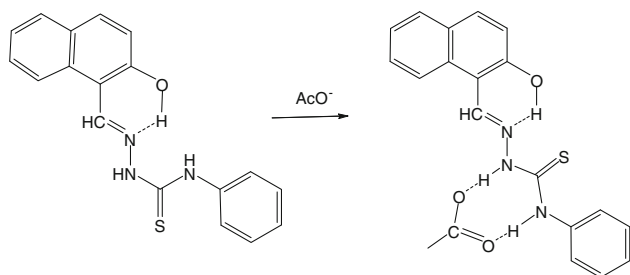


Fig. 3 ^1H NMR titration of a 1×10^{-2} M solution of the sensor 1 in $\text{DMSO}-d_6$ with tetrabutylammonium acetate



Scheme 2 The proposed host–guest binding mode in solution

Scheme 2. It was noteworthy that excess acetate ion added results the deprotonation of sensor 1, which agreed well with the Fabbri paradigm for anion-induced urea deprotonation process [20].

The calculation of K_a from UV–vis titration spectra

For a complex of 1:1 stoichiometry, the constants (K_a) can be calculated by non-linear fitting analyses of the titration curves according to the following Eq. 1 reported before [21], where C_G and C_H represent the corresponding concentration of the guest and host, and A is the intensity of absorbance at certain concentration of the host and guest. A_0 represents the intensity of absorbance of host only and A_{lim} is the maximum intensity of absorbance of host when guest is added. K_{ass} is the affinity constant of host–guest complexation.

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

The non-linear curve fitting results of the absorbance of the interaction between sensor 1 and guests were shown in Table 1. The disassociation constants (K_a) illustrated in Table 1 showed that K_a (AcO^-) was much higher than other anions.

Conclusions

In conclusion, the thiourea-based sensor 1 which shows good recognition for acetate ion has been successfully synthesized. UV–vis spectral titration experiments showed that the sensor formed 1:1 stoichiometric complexes with anions in DMSO solution and it is an excellent sensor for AcO^- . Furthermore, the proposed binding mode of sensor 1 with acetate was shown in Scheme 2 according to the proton NMR titration experiments.

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Table 1 The constants (K_a) and correlation coefficients (R) of sensor 1 with various anions in DMSO

Anion ^a	K_a (M^{-}) ^b	R^d
AcO^-	7.83×10^4	0.97161
$H_2PO_4^-$	7.89×10^3	0.98661
F^-	2.72×10^3	0.96512
Cl^-	ND ^c	ND
Br^-	ND	ND
I^-	ND	ND

^a The anion were added as their tetrabutylammonium salts at 298.2 ± 0.1 K

^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^d) determined by non-linear fitting analyses

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