

An efficient novel receptor for sensing acetate

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Abstract A novel highly sensitive colorimetric receptor **1** for acetate based on *N*-(4-oxa-3-one-phenanthrene-2-carbonyl)-*p*-nitrophenylhydrazine was designed, synthesized and characterized. Experiments showed that the receptor **1** can selectively recognize acetate in DMSO solution and aqueous solution. The ability of recognition and the bond between receptor **1** and anions were determined using visual inspection, UV–Vis analyses and ^1H NMR experiments. In particular, the UV–Vis analyses showed the whole process included two stages: in the first step, the hydrazine form of **1** interacted with acetate through hydrogen bonding with an obvious color change from yellow to purple upon addition of a small amount of AcO^- . In the second step, as increasing the addition of AcO^- , the color changed from purple to deep yellow, which displayed the deprotonation of the receptor **1**.

Keywords Acetate · Anion recognition · Selectivity · Carbonyl hydrazine

Introduction

Many efforts have been devoted to the development of chemosensor for anions such as dihydrogenphosphate, fluoride, acetate, iodide and so on due to their fundamental role in a wide range of chemical and biological process [1–4]. It is well known that carboxylate anions [5] exhibit specific biochemical functions in the enzymes, antibodies and critical components of numerous metabolic processes. Acetate is one of the carboxylate anions with a unique trigonal chemical structure, which can form the strongest hydrogen-bond interaction with hydrogen-bond donors. A lot of examples are available about the selective receptor molecules for acetate anion in the literatures [6–8]. For instance, a set of receptors for acetate ion in dry DMSO were reported by Han et al. [9]. Ito and coworker reported that a novel Fipronil-based receptor could selectively recognize acetate among a group of anions in DMSO [10]. We also found that the phenylhydrazone-based indole receptor was an effective sensor for acetate ion in dry DMSO [11]. Despite these remarkable achievements, there are still many disadvantages recognized in many examples of the literatures. Generally speaking, the recognition studies were performed in aprotic media (e.g. DMSO, acetonitrile, CHCl_3 etc.), to avoid the competition from the protic solvent (e.g., water or alcohols) working as another hydrogen-bonding donor [12]. Thus, it is urgent to develop sensors that are able to bind anions within the competitive media, and to be simultaneously accompanied with the ‘naked-eyed’ detectable color changes.

In this paper, our research group prepared a novel colorimetric anion receptor based on 4-oxa-3-one-phenanthrene derivative. This receptor contains the hydrogen-bond-donor group (phenyl hydrazine) and the colorimetric group (nitrophenyl). The experimental results show that

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receptor **1** is highly selective and effective to recognize acetate in dry DMSO and aqueous solution.

Experimental

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. HEPES (4-(2-hydroxyethyl) piperazine-1-ethanesulfonic acid) is used as a buffer reagent.

General method

^1H NMR spectra were recorded on a Varian UNITY Plus-400 MHz Spectrometer at the Key Laboratory of Functional Polymer Materials of Ministry of Education, Nankai University, UV–Vis spectroscopy titrations were performed on a Shimadzu UV2450 Spectrophotometer at 298 K. Elemental analysis for C, H, and N were carried out on a Perkin-Elmer 240C element analyzer at the Institute of Elemento-Organic Chemistry, Nankai University.

A series of DMSO solutions having same host concentration and different anion concentrations were prepared respectively. The affinity constants K_s were obtained by the determination of absorption of the series of solutions and analysis of obtained absorption values with non-linear least square calculation method for data fitting.

Synthesis of receptor **1**

The receptor **1** was synthesized in four steps (see Scheme 1) starting from compound 4-oxo-3-one-phenanthrene-2-carboxylic acid (**3**) that was prepared by the literature [13]. 0.48 g (**3**) (2.0 mmol), 20 mL SOCl_2 and 3 drops of DMF were refluxed for 5 h, then evaporated the SOCl_2 , and dried in vacuum, faint yellow solid 4-oxo-3-one-phenanthrene-2-carbonyl chloride (**2**) was obtained. It can be used for further reaction directly without purification. The solution of 0.306 g *p*-nitrophenylhydrazine (2.0 mmol) in dry CHCl_3 was added dropwise to the mixture of compound (**2**) (0.5 mmol), 1 mL triethylamine and 20 mL CHCl_3 in 10 min. After continuous stirring for about 24 h, the mixture was filtrated and the precipitate was recrystallized by DMF, and the pure receptor **1** *N*-(4-oxa-3-one-phenanthrene-2-carbonyl)-*p*-nitrophenylhydrazine was gained. This procedure yields 0.555 g (76%). ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ_{H} : 6.93 (dd, 2H, Ar-H), 7.67 (t, 2H, Aromatic-H), 7.79 (t, 1H, Aromatic-H), 8.10 (t, 3H, Aromatic-H), 8.36 (t, 1H, Aromatic-H), 8.67 (t, 1H, Aromatic-H), 9.36 (s, 1H, N-H), 9.43 (s, 1H, Aromatic-H), 10.45 (s, 1H, N-H). ESI-MS (m/z): calcd. for $\text{C}_{20}\text{H}_{13}\text{N}_3\text{O}_5$ $[\text{M}]^+$: 375.33, found: 375.21. Elemental analysis calcd. for $\text{C}_{20}\text{H}_{13}\text{N}_3\text{O}_5$: C, 64.00; H, 3.49; N, 11.20. Found: C, 64.57; H, 4.01; N, 11.61.

Results and discussion

UV–Vis anion titration studies

The tetrabutylammonium salts of anions were used to evaluate the anions binding properties of receptor **1** in DMSO. As shown in Fig. 1, there was a distinct change in UV–Vis spectra when 1.0 equiv. AcO^- was added. The

Scheme 1 The synthesis of receptor **1**

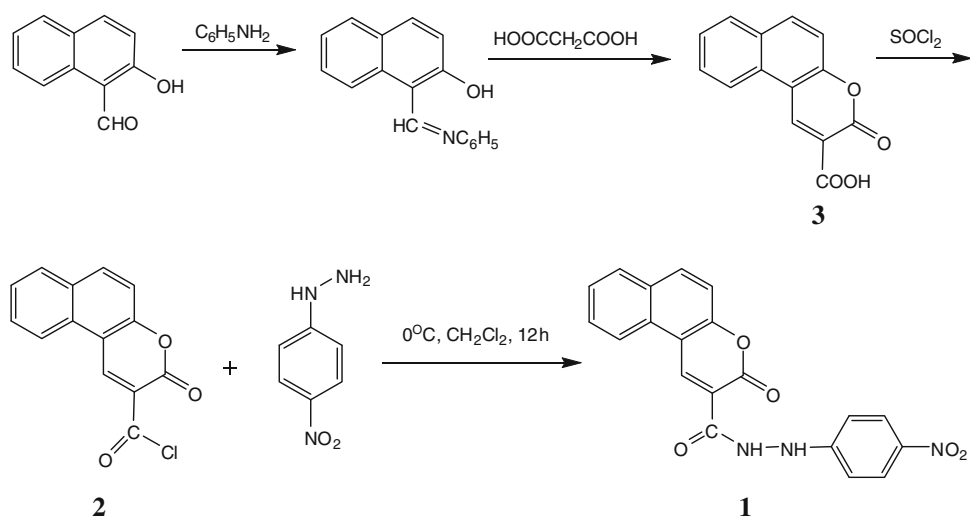


Fig. 1 *Left*: Absorption spectra of receptor **1** (2×10^{-5} M) on the addition of 1.0 equiv. of various anions such as AcO^- , H_2PO_4^- , F^- , Cl^- , Br^- , and I^- in DMSO. *Right*: Color changes of receptor **1** in DMSO. $[\mathbf{1}] = 2.0 \times 10^{-5}$ M, $[\text{anion}] = 1.0$ equiv.: A = free receptor, B = AcO^- , C = F^- , D = H_2PO_4^- , E = Cl^- , F = Br^- and G = I^-

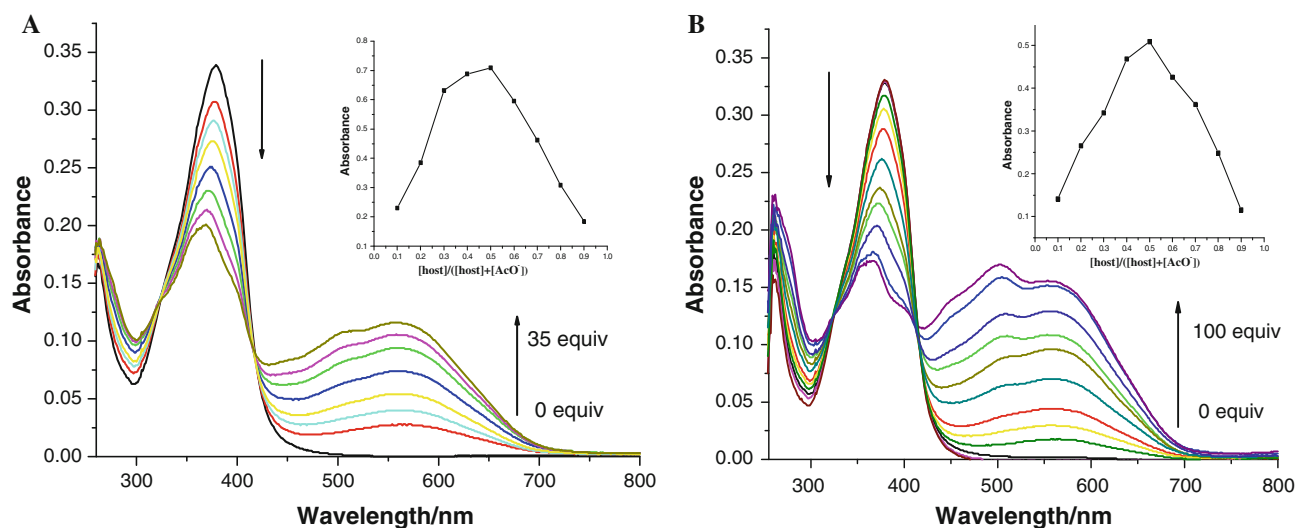
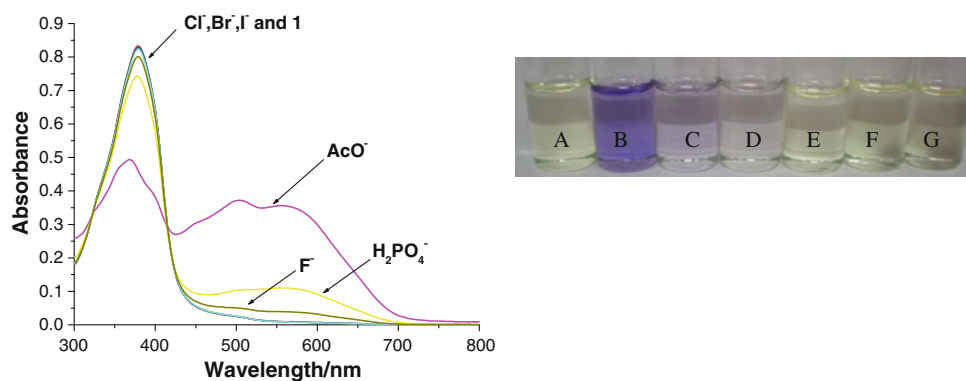
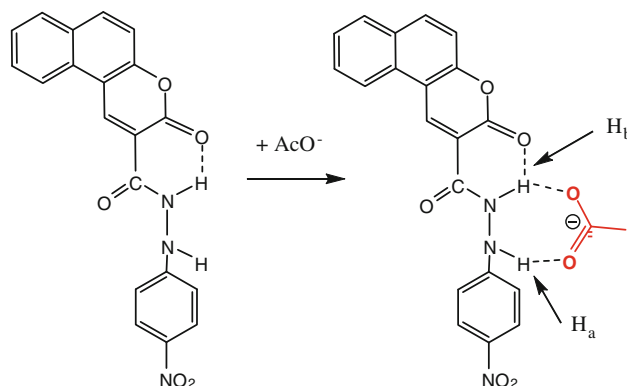


Fig. 2 UV absorption changes of **1** (2×10^{-5} M) with AcO^- in **a** DMSO and **b** DMSO/ H_2O (90:10, v/v; HEPES 20 mM). *Inset*: Job's plot of complexation of **1** with AcO^- determined by UV-Vis in DMSO, $[\mathbf{1}] + [\text{AcO}^-] = 2.0 \times 10^{-2}$ M

color of the solution was changed from light yellow to purple. While minor responses were observed when adding the same amount of H_2PO_4^- , F^- , Cl^- , Br^- and I^- ions to the solution. These results suggest that receptor **1** can distinguish AcO^- from other anions.

Then UV-Vis titrations were carried out in DMSO at a concentration of 2.0×10^{-5} M by adding tetrabutylammonium salt of AcO^- (see Fig. 2). The presence of acetate resulted in the intensity of the absorbance band at 376 nm decreasing gradually and that at 561 nm increasing gradually, accompanied by the formation of an isosbestic point at 405 nm. The significant color changes from light yellow to purple upon addition a small amount of anions, which indicates the intramolecular charge-transfer (ICT) between the anion binding with $-\text{NH}$ moiety and the electron-deficient $-\text{NO}_2$ moiety [14]. Specifically, the changes in UV-Vis spectra are attributed to the interactions between the $-\text{NH}$ sites of the hydrazine subunits and acetate ions via H-bond (see Scheme 2). Additionally, as the intensity of the polarization is increased by the $-\text{NO}_2$ substituent, the



Scheme 2 The possible binding model of the receptor **1** with AcO^- and its signaling transduction mechanism

electron density of the hydrazine is transferred to the nitro moiety resulting in the possibility of realizing visual inspection. Of particular note in this process, as increasing the addition of AcO^- , two new absorption bands at about 450 and 489 nm appeared, and red-shifted, the absorbance



Fig. 3 Color changes of the receptor **1** (2×10^{-5} M) with different acetate concentrations in DMSO. From left to right: (a) only **1**; (b) 1.0 equiv. of AcO^- ; (c) excess equivalent of AcO^-

band at 561 nm decreasing gradually, accompanied with a color change from purple to dark yellow of the solution (see Fig. 3). It means a new complex was obtained. A rational explanation for this is that increased concentration of acetate will caused the deprotonation of receptor **1**.

In order to examine the potential application in analytical chemistry, the selectivity of receptor **1** for AcO^- in aqueous medium has been investigated. Specifically, 5%, 10% aqueous system (DMSO/ H_2O = 95:5, 90:10, v/v; buffer solution: HEPES, pH 7.4, 20 mM) were further adopted for UV–Vis study, and similar changes in UV absorption spectra was also observed (see Fig. 2).

Determination of the binding constant and stoichiometry

A Job's plot is used to determine the stoichiometry of a binding event. In this method, the total molar concentration of host and guest are held constant, but their mole fractions are varied. A measurable parameter that is proportional to complex formation (such as absorption signal) is plotted against the mole fractions of these two components.

In Fig. 4, Job's plot [15] of receptor **1** and AcO^- in DMSO and 9/1 DMSO/ H_2O (v/v) shows the maximum at a molar fraction of 0.5. This result indicates that receptor **1** binds acetate anion guest with a 1:1 ratio (see Fig. 2).

For a complex of 1:1 stoichiometry, the relation in Eq. 1 could be derived easily, where X is the absorption intensity, and C_H or C_G is the concentration of the host or the

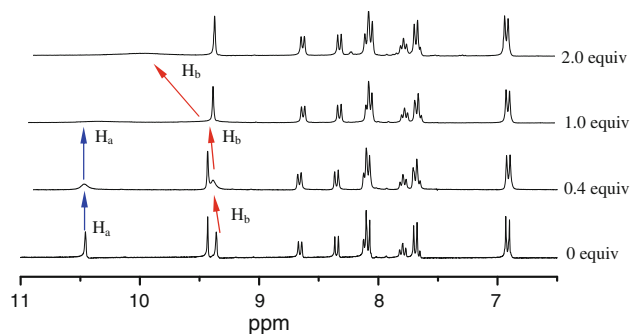


Fig. 4 ^1H NMR titration of **1** in DMSO- d_6 with AcO^-

Table 1 The affinity constants of receptor **1** with anions at 298.2 ± 0.1 K

Anions (M^{-1})	AcO^-	H_2PO_4^-	F^-	Cl^-	Br^-	I^-
$\log K_{\text{ass}}^a$	4.67	3.46	ND ^d	ND	ND	ND
$\log K_{\text{ass}}^b$	3.82	2.29	ND	ND	ND	ND
$\log K_{\text{ass}}^c$	2.73	1.85	ND	ND	ND	ND

^a The affinity constants determined by UV–Vis in dry DMSO

^b The affinity constants determined by UV–Vis in DMSO/ H_2O (95:5, v/v; HEPES, pH 7.4, 20 mM)

^c The affinity constants determined by UV–Vis in DMSO/ H_2O (90:10, v/v; HEPES, pH 7.4, 20 mM)

^d ND = cannot determined

anion guest correspondingly, K_{ass} is the affinity constant of host–guest complexation [16].

$$X = X_0 + (X_{\text{lim}} - X_0) \left\{ C_H + C_G + 1/K_{\text{ass}} - \left[(C_H + C_G + 1/K_{\text{ass}})^2 - 4C_H C_G \right]^{1/2} \right\} / 2C_H \quad (1)$$

Affinity constants of receptor **1** for anionic species are calculated and listed in the Table 1 below.

According to the results from Job's plot, the proposed mode for the host–guest bonding in solution was depicted in Scheme 2. In the structure, anions are located on one side of receptor **1** via N–H... anion hydrogen bonds. Receptor **1** could selectively recognize AcO^- ascribed to the relatively strong basicity of AcO^- and the shape complementarity between the receptor and the anionic guests [17]. Due to its triangular shape, the angle of O–C–O in AcO^- is about 120° while the angle of O–P–O in H_2PO_4^- is about 108° . The distance between two oxygen atoms of AcO^- might be more fit to the distance between the two recognition sites of receptor **1**, forming a seven-member ring structure. That is, the configuration of AcO^- is more matching with **1** than F^- and H_2PO_4^- .

^1H NMR titrations

To further elucidate the nature of intermolecular interactions between anions and receptor **1**, ^1H NMR spectral changes upon addition of AcO^- in DMSO- d_6 solution of **1** (1.0×10^{-2} M) were investigated. Figure 4 showed ^1H NMR spectral changes of receptor **1** (1.0×10^{-2} M) in DMSO- d_6 in the absence and presence of different equivalent of acetate ions. Obviously, the proton signal at 9.36 and 10.85 ppm which were assigned to the –NH group can be observed in the absence of the AcO^- . Upon addition of 0.4 equiv. of AcO^- , the signals of the –NH moiety broadened, and aromatic rings exhibited upfield shift slightly, it is showed that a hydrogen-bond complex is

formed at this stage [18]. As increasing the addition of AcO^- , the signals of $-\text{NH}$ group (10.85 ppm) downshifted and eventually disappeared, the $-\text{NH}$ group (9.36 ppm) shifted to low-field, and a broad peak formed, which displayed the complete deprotonation of receptor **1**. The results of the ^1H NMR titrations also supported the hypothesis obtained according to the results of UV–Vis titrations.

Analytical application

The potential application of receptor **1** in the analytical chemistry field was evaluated in aqueous solution (Table 1). The results show that **1** can be applied in detection of acetate ion in organic solvent, even in aqueous solution, so it may provide a potential way to recognize and detect acetate.

Conclusions

To sum up, a novel and colorimetric charge-neutral receptor has been successfully exploited, which could recognize acetate among the anions investigated. The whole processes can be observed by the ‘naked-eye’, for its sharply color changes from light yellow to purple. So it is expected to be applied for detection of acetate in analytical chemistry for its easy synthesis and highly selective sensing ability.

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