



A novel indole phenylhydrazone receptor: Synthesis and recognition for acetate anion

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ABSTRACT

A novel receptor based on phenylhydrazone derivative was developed and applied to the binding anion, showing a common preference for acetate (AcO^-) ion, and the preference was related to structure matching between the host and the guest. The receptor exhibited a dramatic color change upon the addition of acetate ions so that we could finish anion recognition by naked eye without resorting to any spectroscopic instruments. The evaluation of the receptor interaction with anions was performed by UV–vis titration experiments with a variety of structurally different anions in DMSO, and the anion binding pattern of the chemosensor was hydrogen bond interactions.

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1. Introduction

Considering the important roles that anion play in many environmental and biomedical researches, the development of chemosensors for the selective detection of biologically important anions is of great importance [1–4]. Consequently, the colorimetric receptors [5–8] having strong affinity and selectivity for specific anions are currently of major interest in supramolecular chemistry [9]. Many of the chemosensors bear carboxyamides, sulfonamides, ureas, thioureas and pyrroles [10–12] as binding moieties. Some excellent examples of compounds bearing these binding sites capable of anion recognition and sensing have been reported [13,14]. However, these approaches have often involved the synthesis of structurally complicated hosts [15,16].

Indoline-2,3-dione and 4-nitrophenylhydrazine could recognize anion by themselves accompanied with a naked-eyed color change, and the nitrophenyl hydrazine was widely used in analytical chemistry. Consequently, in this paper, we designed and synthesized a receptor through coupling 2,3-diketoindole isatin with 4-nitrophenylhydrazine only by one step. What is more, the indole phenylhydrazone receptor exhibited a naked-eyed color change upon anions binding and meanwhile showed better selectivity for acetate. So, we believe the receptor will have a better applicative foreground in the future.

2. Experimental

2.1. Reagents

All anions, in the form of tetrabutylammonium salts, were purchased from Sigma–Aldrich Chemical Co., stored in a desiccator under vacuum containing self-indicating silica, and used without any further purification. Solvents were purified prior to use and stored under nitrogen. Dimethyl sulfoxide was dried with calcium hydride and distilled in reduced pressure. Unless stated otherwise, commercial grade chemicals were used without further purification.

2.2. General methods

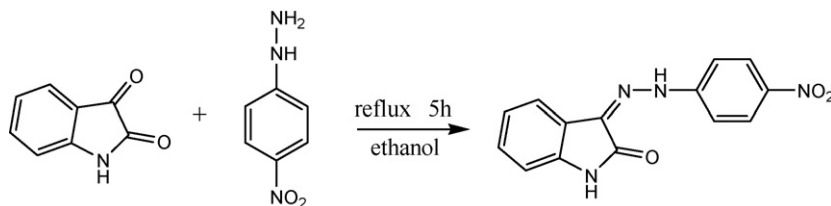
Unless otherwise specified, all of the UV–vis titration experiments were carried out at 298.2 ± 0.1 K. The ^1H NMR spectra were recorded on a Varian UNITY-plus 400MHz spectrometer using tetramethylsilane (TMS) as an internal standard. UV–vis spectra were recorded on a Shimadzu UV-2450 PC spectrophotometer.

2.3. UV–vis titration studies

The binding ability of the receptor 1 for CH_3CO_2^- , H_2PO_4^- , and halide anions (as tetrabutylammonium salts) was investigated by UV–vis spectroscopy in DMSO solution using a constant host concentration ($5.0 \times 10^{-5} \text{ mol L}^{-1}$) and increasing concentrations of anions. The change in absorbance at 592 nm for receptor was

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Scheme 1. The synthetic procedure for the anion receptor.

plotted against anion concentration and fitted by the equation as described by Connors [17].

2.4. ^1H NMR titrations

^1H NMR titration experiments were carried out in the $\text{DMSO-}d_6$ solution (TMS as an internal standard). A 5.0×10^{-3} M solution of the compound 1 in $\text{DMSO-}d_6$ was prepared. Then, the increased amount of fluoride and chloride anions (1.0 M in $\text{DMSO-}d_6$) was added to the solution above-mentioned and ^1H NMR of the host–guest system was tested.

2.5. Synthesis

2.5.1. 3-(4'-Nitrophenylhydrazono) indolin-2-one (1)

To a solution of 4-nitrophenylhydrazine (0.612 g, 4 mmol) in ethanol (60 ml) a solution of Isatin (0.588 g, 4 mmol) in ethanol (20 ml) was added dropwise with magnetic stirring at reflux (see Scheme 1). After being stirred for 5 h, the solvent was removed under reduced pressure. The solid was recrystallized from ethanol to give yellow crystals. Yield 85% δ_{H} (400 MHz; $\text{DMSO-}d_6$; Me_4Si): 12.88 (s, 1H, N–H), 11.136 (s, 1H, N–H), 8.23 (d, 2H, Ar–H, $J=8$ Hz), 7.62 (d, 2H, Ar–H, $J=8$ Hz), 7.59 (d, 1H, Ar–H, $J=2$ Hz), 7.31 (t, 1H, Ar–H, $J=12$ Hz), 7.08 (t, 1H, Ar–H, $J=12$ Hz), 6.93 (d, 1H, Ar–H, $J=8$ Hz) Anal. Calcd. for $\text{C}_{14}\text{H}_{10}\text{N}_4\text{O}_3$: C 59.57%, H 3.57%, N 19.85%, Found C 59.75%, H 3.23%, N 19.93%.

3. Results and discussion

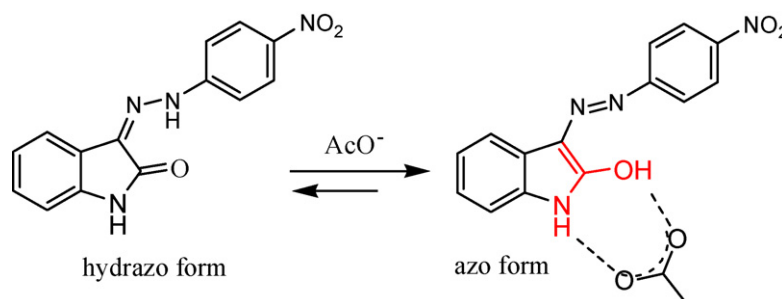
Here, we report a high selective indolehydrazone-based acetate chemosensor: a Schiff-base compound, 3-(4'-nitrophenylhydrazono) indolin-2-one. It contains an indolehydrazone group that can be transformed to phenol form in the presence of anion (see Scheme 2) [18,19].

3.1. UV–vis experiments

The recognizing ability of the receptor 1 to anions was evaluated in DMSO by monitoring the changes in the absorption spectra of the receptor 1. In the qualitative experiment, the presence of 10 equiv. of AcO^- ions resulted in visible color change of solu-

tion of the sensor 1 from yellow to blue, which could be detected by naked-eye without resorting to any spectroscopic instruments (see Fig. 1). Fig. 2 shows the changes in the UV–vis spectra of 1 at a concentration of 2×10^{-5} mol L $^{-1}$ in DMSO upon addition of acetate anion. The receptor had strong absorption band centered at 431 nm which were assigned to the intramolecular charge transfer (ICT) nature of the chromophore [20,21]. There were significant changes in absorption spectra of the host molecule upon addition of AcO^- . Just as shown in Fig. 2, the absorbance peak at 431 nm was gradually decreased with increasing addition of AcO^- and a new absorbance band centred at 592 nm was observed. A possible reason for the new absorbance band observed might be as follows (see Scheme 2). Before coordination with AcO^- ion, the receptor 1 existed as the form hydrazone and the form azo but the form hydrazone dominated in the solution. And recently the tautomeric equilibrium between hydrazone and azo was studied in detail by IR spectroscopy, DFT calculation, ^{13}C NMR spectroscopy and so on in the literatures reported [18,19,22,23]. Therefore, once 1 interacted with AcO^- , the azo isomer of the receptor 1 dominated in the solution and was coordinated with AcO^- , which was different from electronic property of the hydrazone isomer and resulted in a new peak at 592 nm. In addition, binding sites of the azo isomer are structurally similar with (thio)urea moiety (see Scheme 2) and consequently, the sensor 1 showed preference for AcO^- ion in DMSO solution because the receptor based on (thio)urea derivative have a selectivity for AcO^- (discussed in detail below) [24]. Similar changes were observed in UV–vis spectra of 1 upon addition of F^- and H_2PO_4^- ions. Nevertheless, the receptor 1 was insensitive to addition of excess equiv. of Cl^- , Br^- and I^- ions.

In addition, there was one well-defined isosbestic point at 483 nm, which indicated that there formed the stable complex having a certain stoichiometric ratio between the receptor 1 and anion tested. The Job plot suggested that there was only one type of 1:1 binding interaction between the receptor and anion added (see Fig. 3). Affinity constants of the receptor 1 with anionic species, which were shown in Table 1, were determined by non-linear fitting analyses of the titration curves according to 1:1 host–guest complexation equation [17]. Obviously shown in Table 1, the selectivity trends of binding affinities of anions for 1 were determined to be $\text{AcO}^- > \text{F}^- > \text{H}_2\text{PO}_4^- > \text{Cl}^- \sim \text{Br}^- \sim \text{I}^-$. The receptor had a high selectivity for acetate anion, which could be rationalized on basis



Scheme 2. Proposed mode of transformation of the receptor 1 in DMSO.

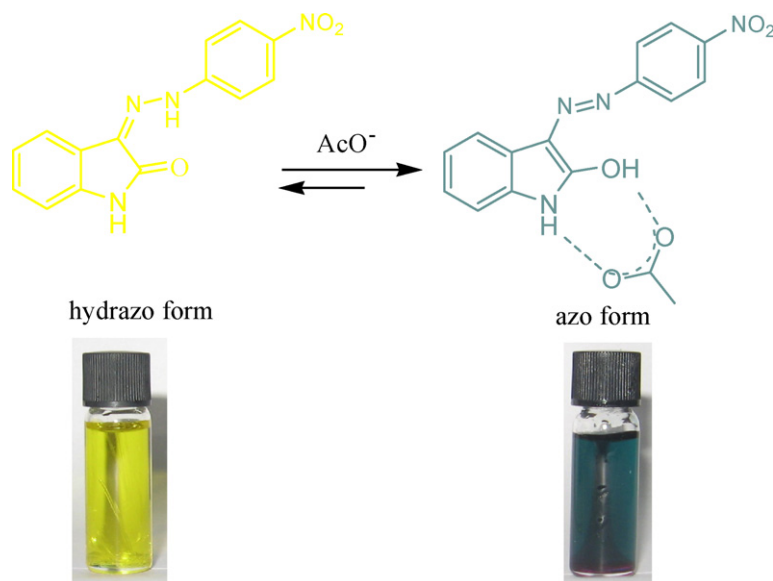


Fig. 1. The color change of the receptor 1 ($2 \times 10^{-5} \text{ mol L}^{-1}$) in the absence and the presence of acetate ions ($2 \times 10^{-4} \text{ mol L}^{-1}$) in DMSO. (For interpretation of the references to color in text, the reader is referred to the web version of the article.)

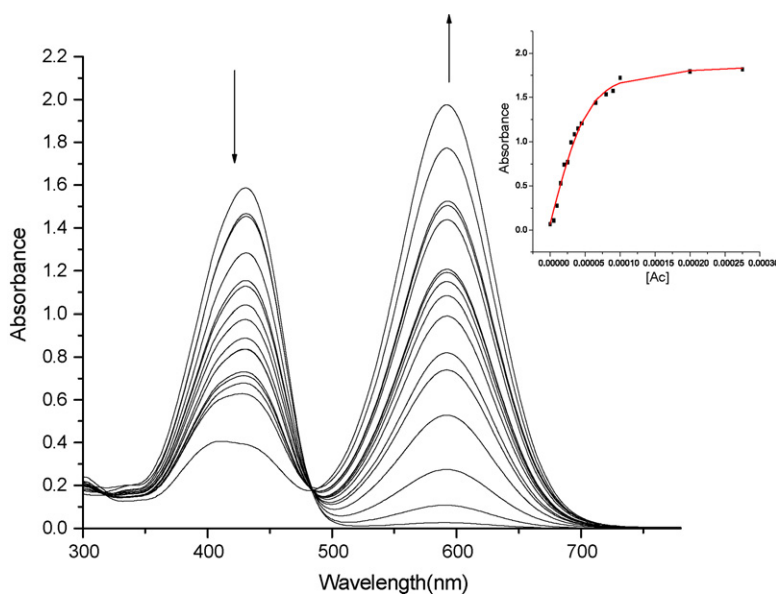


Fig. 2. The UV-vis spectra of the receptor 1 ($2 \times 10^{-5} \text{ mol L}^{-1}$) in DMSO solution during the titration with tetrabutylammonium (TBA) acetate. Inset: titration plots (observed binding profiles and corresponding non-linear fit plots monitored by the absorbance increase at 592 nm).

Table 1
Association constants K_{ass} ($\text{mol}^{-1} \text{ L}$) of the receptor 1 with anions in DMSO at $298.2 \pm 0.1 \text{ K}$

Anion ^a	K_{ass} (M^{-1}) ^b
AcO^-	1.20×10^5
F^-	2.31×10^3
H_2PO_4^-	1.14×10^3
Cl^-	ND ^c
Br^-	ND
I^-	ND

^a The anions were added as their tetrabutylammonium salts.

^b All errors are $\pm 10\%$.

^c The association constant could not be determined due to very weak complexation.

of shape complementarity between the host and the anionic guests and the basicity of the anion. Basic acetate anion was a plane, the angle of O–C–O was about 120° , but the angle of O–P–O was only about 108° , so the two oxygen atoms of acetate could match well with the receptor 1. In case of F^- , it had the smaller radius and therefore did not also match well with binding sites of the receptor 1. Consequently, acetate ion could be recognized selectively, sensitively and conveniently from the other anions tested.

3.2. ^1H NMR titrations

To further shed light on the nature of the interactions between 1 and the anions, as an example, ^1H NMR spectral changes upon addition of AcO^- as their tetrabutylammonium salts to the solution of 1 ($5 \times 10^{-3} \text{ mol L}^{-1}$) were investigated. Due to insufficient solubility (for NMR measurements) of receptor in CHCl_3 , CH_2Cl_2 , CH_3CN , ace-

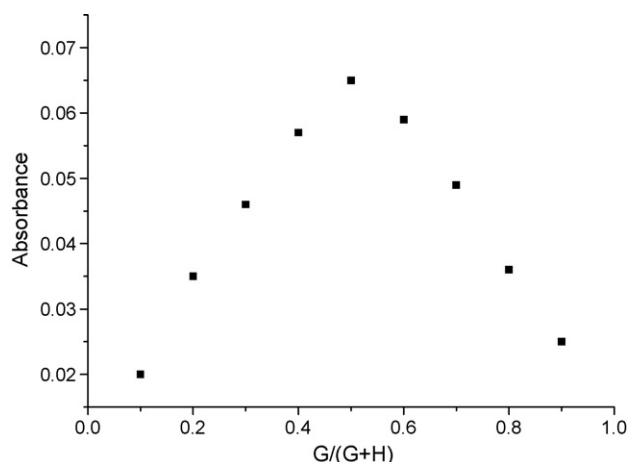


Fig. 3. A Job plot of the receptor 1 with tetrabutylammonium acetate.

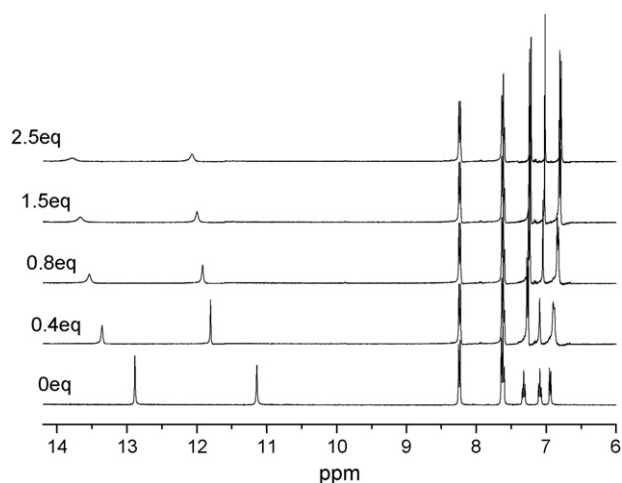


Fig. 4. Plots of ^1H NMR spectra of the receptor 1 ($5.0 \times 10^{-3} \text{ mol L}^{-1}$) upon addition of tetrabutylammonium acetate in $\text{DMSO}-d_6$.

tone, and THF, all NMR studies were performed in $\text{DMSO}-d_6$. Fig. 4 shows changes in the ^1H NMR spectra of 1 upon gradual addition of acetate anions. Upon addition of 0.4 molar equiv. of AcO^- , the signals of the indole and phenylhydrazone subunit protons (12.88 and 11.136 ppm) exhibited a downfield shift. At the same time, the peaks of the recognition points broadened. According to the spectral changes induced by further addition of the AcO^- from 0.4 to 2.5 molar equiv., the proton signals of indole and phenylhydrazone continued to broaden and moved downfield. These results indicated that the interactions between the host and guest were through multiple hydrogen bonding [25,26]. However, some of the protons of aromatic ring upfield shifted with the increase of acetate, for the protons that are far from the hydrogen bonds, the through-bond effects which increased the electron density of the phenyl ring and promoted upfield shifts. According to the results from UV–vis titrations and ^1H NMR titrations, the proposed anion recognition process in solution is shown in Scheme 2.

4. Conclusion

In summary, a simple colorimetric anion receptor was synthesized only by one step, where 4-nitrophenyl was treated as a signaling unit and phenylhydrazone and indole moieties acted as binding sites. The anion recognition via hydrogen-binding interactions could be easily monitored by anion-induced changes in

UV–vis absorption spectra. Moreover, the unique color change was observed from yellow to blue upon the presence of AcO^- ion in DMSO , which was convenient in qualitative detection of acetate. In addition, the presence of AcO^- tautomerized the sensor 1 from the isomer hydrazo to the isomer azo and accordingly UV–vis spectral changes and color changes were seen during the titrations. The novel design strategy would help to extend the development of fluorescent sensors for biologically inorganic anions.

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Biographies

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