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SHORT COMMUNICATION

Selective "naked-eye" sensing of acetate ion based on conformational flexible amide-pyridinium receptor

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Abstract A simple pincer-shape anion receptor **L1** containing amide-pyridinium as binding unit was synthesized and its anion binding properties were investigated by UV–Vis, NMR titration spectra and molecular simulation. **L1** displayed better affinity toward AcO^- ion with visible color change compared with other investigated anions, including F^-, $H_2PO_4^-$, Cl^-, Br^-, I^-, NO_3^- and HSO_4^- ions. The selectivity was ascribed to the synergistic effects arising from hydrogen bonding, electrostatic interaction and induced-fit process.

Keywords Anion sensing · Acetate recognition · Colorimetric sensor · Induced-fit

Introduction

Anions recognition and sensing continue to be a hot research topic in the area of supramolecular chemistry due to the important roles anions play in chemical, biological and environmental processes [1–5]. Among various anions, acetate ion (AcO^-) draws considerable attention because it is a critical component of numerous metabolic processes [6–11]. The rate of AcO^- production and oxidation has been frequently used as an indicator of organic decomposition in marine sediments [12]. However, until now, selective chromogenic and/or fluorescent sensors for AcO^- are quite limited [9, 13–16], compared with a large number of reported sensors for F^- and $H_2PO_4^-$, which have similar basicity to AcO^-. Most of the AcO^- sensors usually also display response to $H_2PO_4^-$ and F^-, especially the latter [7, 17–20]. In this sense, development of novel receptors having the capability to discriminate AcO^- from $H_2PO_4^-$ and F^- is of quite significance. Induced-fit theory, well-known in biological process, is an important characteristic of the interactions between enzyme and substrate, and now is widely expanding to supramolecular chemistry [21]. Inspired by the positive role of induced-fit theory in molecular recognition, in this paper, we report the selective sensing of AcO^- by cooperative functions of hydrogen-bonding, electrostatic interactions and induced-fit mechanism.

To achieve this goal, dipodal receptor **L1** was designed and prepared as the host molecule to recognize anions. **L1** comprises tri-substituted benzene as the core to control the direction of the arms and pyridinium amide as the main binding motif to bind anions, which exhibited excellent binding ability toward anions recently reported by us [22] and other groups [23–31]. Furthermore, the nitrophenyl group was chosen since it can not only enhance the hydrogen donating property of amide NH but also act as a signaling part by charge transfer mechanism [32]. It should be mentioned that the conformation of **L1** would be restricted by the intramolecular hydrogen bonds (IHB) between acidic proton at α-position of pyridinium and carbonyl group. Then, the anion-induced conformational change of **L1** via disturbing the IHB might favor the selective anion sensing, just according with the induce-fit mechanism (Fig. 1). Furthermore, the electrostatic interaction between electron–positive pyridinium ring and anions would also be expected.

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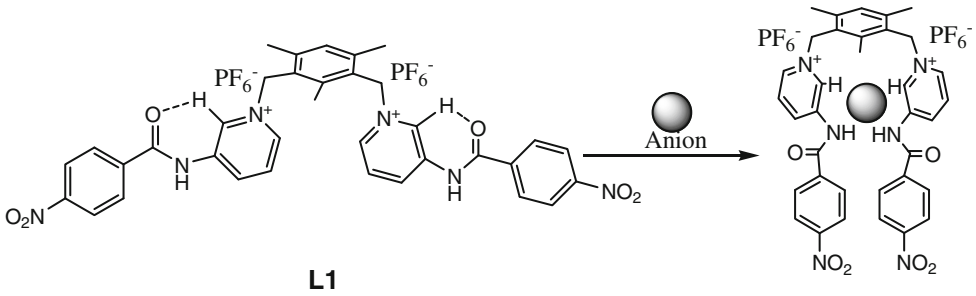


Fig. 1 Structure of receptor **L1** and expected binding mode toward anions

Experimental

Reagents

All anions existed as their tetrabutylammonium salts and were purchased from Alfa-Aesar Chemical Co. Other chemical reagents were used as received without further purification.

Apparatus

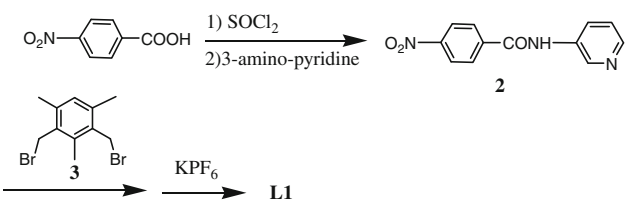
Unless otherwise specified, all of the UV–Vis titration experiments were carried out at 298.2 ± 0.1 K. ^{1}H and ^{13}C NMR spectra were recorded on AVANCE II400 spectrometer at room temperature with Me_4Si as the internal standard. HRMS were measured on UPLC/Q-Tof Microa MS apparatus. The UV–Vis spectra were measured on HITACHI U-4100 spectrophotometer.

Synthesis

The synthetic route to receptor **L1** was shown in Scheme 1.

Synthesis of intermediate compound 2

To a solid of 4-nitrobenzoic acid (334 mg, 2 mmol) was added excess of $SOCl_2$ and stirred at 70 °C for about 24 h to give clear solution. The excess of $SOCl_2$ was removed under reduced pressure, and the residue was dried under vacuum for 3 h. The obtained acid chloride was used directly without any further treatment. To a 20 mL of dry THF solution of 3-aminopyridine (190 mg, 2 mmol) was added dropwise a solution of abovementioned acid chloride in 20 ml of dry THF at 0 °C. After the solution was stirred overnight at room temperature, the THF was removed, the solid residue was dissolved in CH_2Cl_2 and the solution was washed with water. The organic layer was separated, dried over $MgSO_4$ and concentrated. The product was purified by column chromatography (silica gel, 3:1 CH_2Cl_2:AcOEt) to give white solid.



Scheme 1 Synthetic route to receptor **L1**

Yield 0.784 g (65%), ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 9.06 (s, 1H, NH), 8.87 (s, 1H,Py-H), 8.38 (d, J = 8.4 Hz, 1H, Py-H), 8.35-8.32 (d, J = 8.8 Hz,2H, Ph-H), 8.19 (d, J = 8.4 Hz,1H, Py-H), 8.17-8.16 (d, J = 8.8 Hz, 2H, Ph-H), 7.37 (m, 1H, Py-H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 164.8, 149.8, 145.5, 142.2, 140.4, 135.9, 129.8, 128.0, 124.1. HRMS (ESI^{+}) m/z:244.0731; calcd 244.0722.

*Synthesis of target compound **L1***

A mixture of **2** and **3** in dry CH_3CN was refluxed for 3 h, and gradually white precipitate was formed. After cooling to room temperature, the precipitate was filtered off and washed several times with cold CH_3CN to give pure compound **L1** with bromide as counter ion. Then, the dibromide salt (100 mg) was dissolved in 2 ml DMF. During dropwise addition of saturated aqueous KPF_6 solution (5 ml), a light white precipitate was formed. After washing the precipitate several times with distilled water, the desired chemosensor **L1** was obtained in 88% yield.

*Yield 0.*221 g (28%), ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 11.38 (s, 2H, NH), 9.24 (s, 2H, Py-H), 8.79 (d, J = 6.0 Hz, 2H, Py-H), 8.68 (d, J = 8.8 Hz, 2H, Py-H), 8.38-8.36 (d, J = 8.8 Hz, 4H, Ph-H), 8.19 (m, 2H, Py-H), 8.17-8.15 (d, J = 8.8 Hz,4H, Ph-H), 7.35 (s, 1H, Py-H),6.06 (s, 4H, –CH_2–), 2.38 (s, 6H, MePh). 2.35 (s, 3H, MePh);^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 165.3, 150.2, 142.2, 141.5, 139.9, 139.7, 138.8, 135.8, 134.6, 132.3, 129.9, 128.9, 128.3, 124.2, 20.23, 16.42 ;HRMS (ESI^{+}) m/z: 632.2410, calcd 632.2383.

Results and discussion

UV–Vis experiments

Due to the presence of nitro-benzene group as signal-reporting unit, UV–Vis spectral change of **L1** (2×10^{-5} M in CH_3CN) upon addition of different anions was monitored firstly. The corresponding result was shown in Fig. 2. As seen from this figure, **L1** in the absence of anions exhibited a broad absorption region centered about 275 nm coming from substituted phenyl group. When AcO^- anion was added, a new peak centered at 360 nm induced by complexation of **L1** with AcO^- appeared. It might be due to the intramolecular charge transfer (ICT) from electron-rich anion binding part to relative electron-deficient nitro-benzene fragment [17]. In contrast, other investigated anions (F^-, Cl^-, Br^-, I^-, HSO_4^-, NO_3^-, $H_2PO_4^-$) showed negligible effect, which demonstrated the excellent selectivity of **L1** toward AcO^-.

As a result, after interaction with AcO^-, the maximum absorption peak of **L1** was shifted from UV to visible region, which rationalized the corresponding color change from colorless to yellow-green, realizing a naked-eye detection of AcO^- in solution (Fig. 3). It should be pointed out that using stronger base such as OH^- instead of AcO^- also induce the same 'naked-eye' sensing results. But, it is still meaningful that receptor **L1** has the capability to discriminate AcO^- from $H_2PO_4^-$ and F^- by changing the solution color, considering most of the reported anion receptors using hydrogen bonds to complex anions can not discriminate OH^- and other basic anions.

The result of Job plot shown in Fig. 4, identified the 1:1 complexation between **L1** and AcO^-, because the receptor-anion complex concentration approaches a maximum when the molar fraction of host {[H]/([H]+G])} is about 0.50. Furthermore, the binding constant of **L1** toward AcO^- was

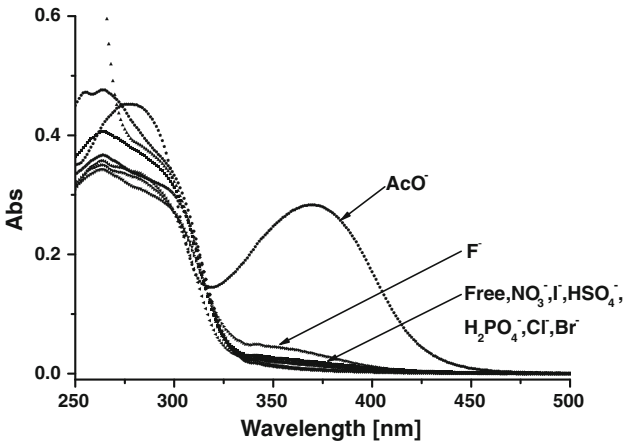


Fig. 2 UV–Vis spectral changes of receptor **L1** (2×10^{-5} M in CH_3CN) upon addition of various anions (5 equiv.)

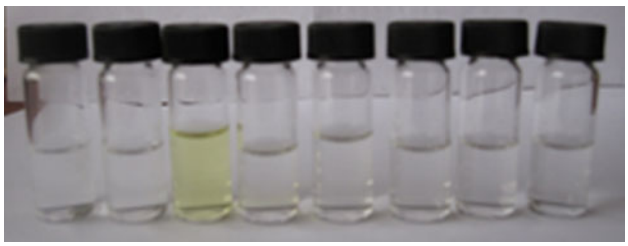


Fig. 3 Color changes of receptor **L1** (2.0×10^{-5} M) in CH_3CN after addition of 10 equiv. anions

calculated to be $(1.1 \pm 0.1) \times 10^5$ from the nonlinear curve fitting based on the detailed titration of **L1** (Fig. 5).

^{1}H NMR spectroscopic titration

In order to know more about the nature of the interaction between **L1** and AcO^- and disclose the origin of better selectivity toward AcO^-, ^{1}H NMR titration was carried out (Fig. 6). Due to the disappearance of amide proton of **L1** in CD_3CN, DMSO-d_6 was utilized as the solvent in this sense. When addition of small amount of AcO^- (0.1 equiv.) into **L1** solution, the spectrum showed almost no change expect for broadening of amide NH. This indicated that small amount of anion lack the ability to disturb the conformation of **L1** controlled by IHB mentioned above in Fig. 1. The presence of such kind of IHB was partially supported by our previous work [22, 33–36]. Continuous addition of AcO^- induced the disappear of amide NH peak, and shifting to downfield of acidic proton H_g implying the hydrogen bonding interactions between them and AcO^-. Additionally, other protons on pyridinium rings were found to shift to upfield, which proved the presence of the electrostatic interaction between electron–positive pyridinium ring and AcO^- as expected. Accordingly, the excellent selectivity of **L1** toward AcO^-, especially better for more basic F^-, was ascribed to the synergistic effects arising from, hydrogen

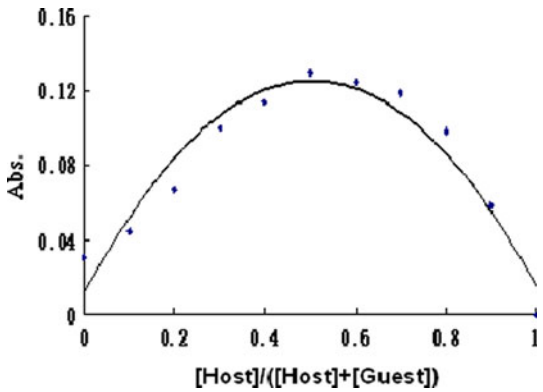


Fig. 4 Job plot of receptor **L1** with $Bu_4N^+AcO^-$

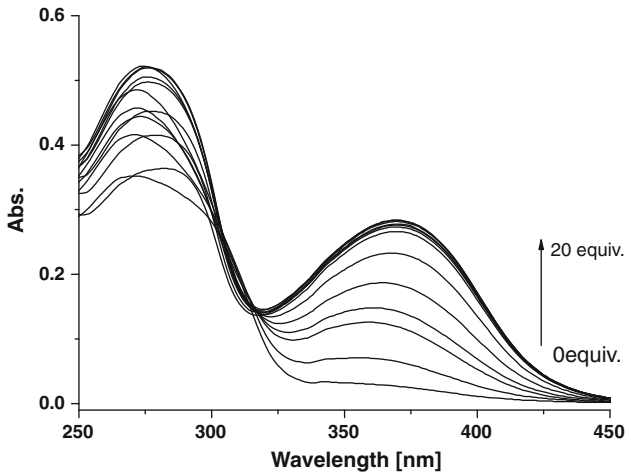


Fig. 5 UV–Vis spectral changes of receptor **L1** (2.0×10^{-5} M) in CH_3CN upon addition of $Bu_4N^+AcO^-$ (0–20 equiv.)

bonding, electrostatic interaction and induced-fit process, which exclude the possible deprotonation process.

Actually, the binding phenomena of **L1** for other anions were also checked via ^{1}H NMR. $H_2PO_4^-$ and F- induced the similar but smaller changes of NMR peaks compared with that of AcO^-, implying relative weaker interactions between it and receptors. However, they did not induce any color change of the solution indicating the selective sensing of **L1** toward AcO^-. As for other anions, no changes were observed at all.

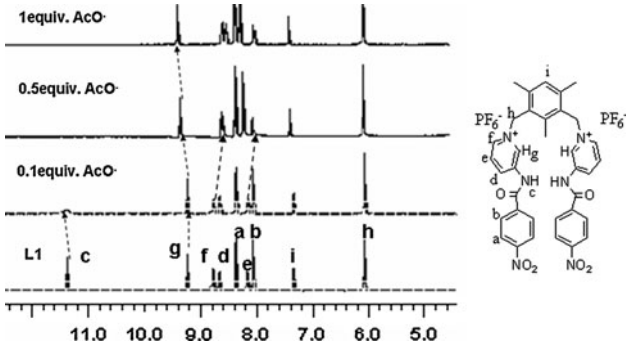


Fig. 6 Partial ^{1}HNMR titration spectra of receptor **L1** (3.0×10^{-3} M) upon addition of $Bu_4N^+AcO^-$ in DMSO-d_6

Computational studies

We tried to clarify the proposed binding geometry by means of DFT calculations. The DFT-calculated structures of **L1** and the complex between **L1** and AcO− are shown in Fig. 7. It is clear from the models that the calculation reproduces well our expectation shown in Fig. 1. Before acetate complexation, **L1** adopted an open conformation (Fig. 7a) due to the presence of IHB of C–H···O=C intramolecularly. After complexation with acetate, the IHB was accordingly destroyed and the conformation of the complex was changed to close form (Fig. 7b) due to the presence the NH···anion, CH···anion as well as the electrostatic interactions. In this sense, we deduced that the better affinity of **L1** toward AcO^- was not only ascribed to the effects arising from hydrogen bonding and electrostatic interaction, but also from the induced-fit process.

Conclusion

In conclusion, a simple pincer-shape anion receptor **L1** containing amide-pyridinium as binding unit was designed

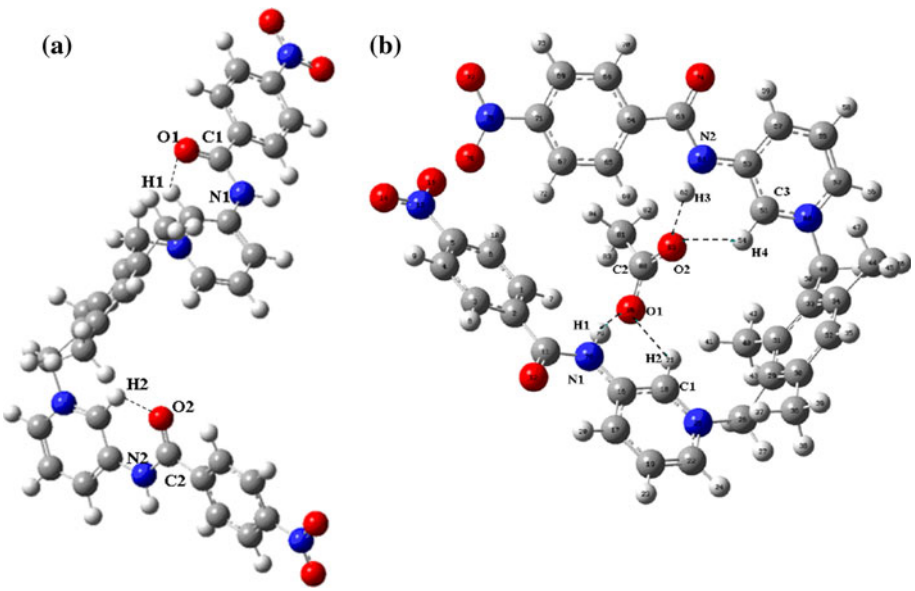


Fig. 7 DFT-calculated models of host **L1** (**a**) and host **L1** bound to 1 equiv. of acetate (**b**)

and synthesized via simple procedures. The binding and sensing behaviors of **L1** toward various anions were easily monitored by anion-induced absorption spectral changes. Only AcO^- induced remarkable visible color change of **L1** solution, realizing "naked-eye" sensing of AcO^-. Assisted by NMR experiments, the excellent selectivity of **L1** toward AcO^- might be ascribed to the multiple functions, including hydrogen bonding, electrostatic interaction and induced-fit mechanism. It is rather meaningful and suggestive for designing other efficient anion binding and sensing agents. The relative work is now on-going in our lab.

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