

A novel neutral receptor for selective recognition of H_2PO_4^-

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Abstract A new urea-based receptor was designed to selectively recognize H_2PO_4^- among other anions (such as F^- , Cl^- , Br^- , I^- , OH^- , AcO^-) in organic solvent (DMSO) through intermolecular hydrogen bonding. Addition of anions to the receptor caused changes in UV–vis spectrum which provided the first indication of its anion binding ability.

Keywords Anion recognition · Urea · Receptor

Introduction

Anions play significant roles in chemical and biological processes and environmental systems etc. Along with these, considerable attention continues to be focused on the receptors and sensors that are capable of binding and sensing biologically important anions selectively [1]. During the last 20 years, a number of host molecules for anions were reported. With a view to binding sites, those are classified basically into electrostatic interactions, formation of hydrogen bonds, and interactions with metal

centers. In general, the positively charged receptors, which mainly contain guanidinium groups [2], quaternary ammonium groups [3] or isothiuronium groups [4], interact with anions. Metal complexes [5] as anion binding sites can bind anions forming stronger bonds than those observed using electrostatic or hydrogen-bonding interactions. In supramolecular systems of anion recognition, hydrogen-bonding groups have been widely used in binding sites and most of them are ureas [6], thioureas [7], calyx[4]pyrroles [8], pyrrole subunit [9, 10], amides [11] and so on. In contrast with merely electrostatic, H-bonds are directional, a feature which allows the design of receptors having ability to differentiate between anions with different geometries and hydrogen-bonding requirements. As an example, Luigi Fabbrizzi and other research group's [12] studies showed that urea was a good H-bonds donor and excellent receptor for tetrahedral anions and Y-shaped anions through the formation of multitopic H-bonds. Moreover, Jurczak group also reported the receptors derived from diamino-dichlorocarbazole [11b] which was shown as easily available and important substrate for the synthesis of the host molecular. But the stability constants of receptor with only three anions were determined by $^1\text{H-NMR}$ titration. All these prompted us to develop the novel receptor with urea units conjugated to diamino-dichlorocarbazole group as guest recognition sites and meanwhile introduce $-\text{NO}_2$ group as chromophore into the receptor so that UV–vis spectra titrations could be carried out. Besides, the most of urea derivatives [13] reported previously deprotonated easily and took an acid-base reaction upon addition of anions. Here we synthesized the novel receptor 1 which could form classical supramolecular systems and recognize selectively H_2PO_4^- from different anions such as F^- , Cl^- , Br^- , I^- , OH^- , AcO^- .

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Experiment section

General procedures and materials

All reagents for synthesis were obtained commercially and were used without further purification except CH_3CN , which was further dried. ^1H NMR spectra were obtained on a Varian UNITY Plus-400 MHz Spectrometer. C, H, N elemental analyses were made on a elemental vario EL. ESI-MS was performed with a MARINER apparatus. UV-vis spectra were recorded on a Shimadzu UV2550 Spectrophotometer with a quartz cuvette (path length = 1 cm) at 298.2 K. In the UV-vis titration experiment, all the anions were added in the form of tetra-n-butylammonium (TBA) salts purchased from Sigma-Aldrich Chemical and DMSO were dried with CaH_2 distilled in reduced pressure. TBAF obtained as a hydrate were dried with P_2O_5 in vacuo at 353 K.

Synthesis of 1, 8-di(4-nitrophenylurea)-3,6-dichlorocarbazole

1,8-diamino-3,6-dichlorocarbazole (0.2128 g, 0.8 mmol), whose synthesis was specified in supplementary material according to the literature (Scheme 1), was dissolved in dry CH_3CN . To this solution was added 4-nitrophenylisocyanate (0.3808 g, 3.2 mmol) dropwise slowly and stirred under inert atmosphere refluxing for 8 h. Then the reaction mixture was cooled to room temperature. Precipitate formed was filtered and washed with CH_3CN . Mass of product = 0.37 g. Yield = 78%. $^1\text{H-NMR}$ (DMSO-d_6) δ_{H} 10.7 (s 1H) 9.8 (s 2H) 9.1 (s 2H) 8.1 (m 6H) 7.7 (d 4H) 7.6 (d 2H) ESI-mass: m/z (negative ion mode) 592.38 (M-H^+) Elemental analysis calcd for $\text{C}_{26}\text{H}_{17}\text{N}_7\text{O}_6\text{Cl}_2$ ($M = 593.06$): C, 52.54; H, 2.88; N, 16.50; found: C, 52.19; H, 3.01; N, 16.07.

Result and discussion

The interactions of host molecular 1 with a variety of anions were investigated in a DMSO solution through

Scheme 1

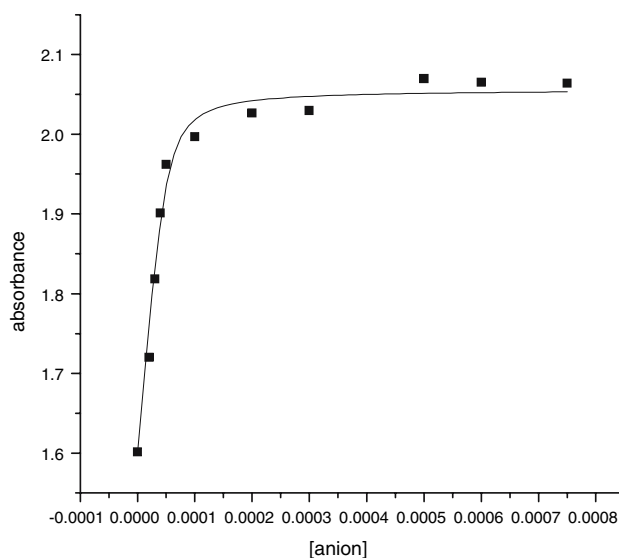
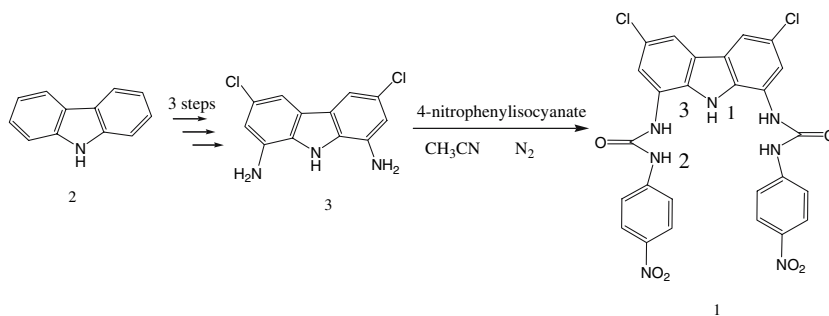
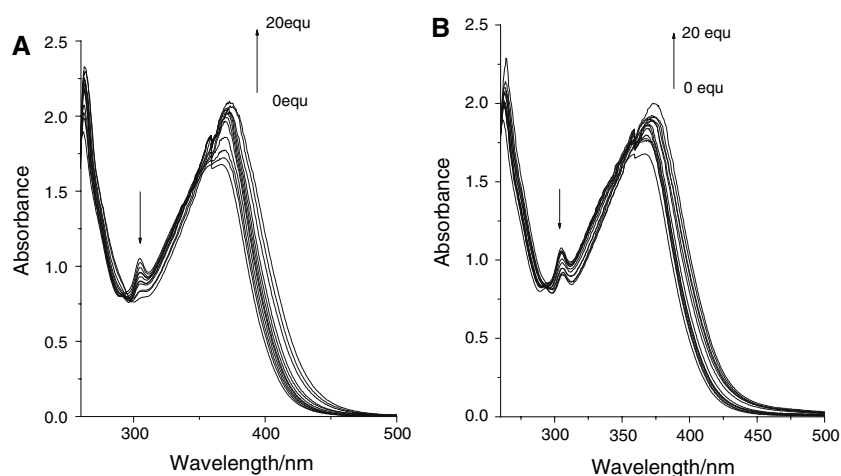


Fig. 1 UV-vis spectrum changes of receptor 1 (5×10^{-5} M) at room temperature in DMSO upon addition of (A) H_2PO_4^- and (B) AcO^-

UV-vis spectra titrations. In particular, a standard solution of the tetrabutylammonium salt of the investigated anions was added stepwise to a 5×10^{-5} M solution of 1 at 298 K. Figure 1 showed the family of spectra taken in the course of the titration, and the addition of H_2PO_4^- resulted in changes in the spectrum obtained during the titration. The peak at 375 nm increased while the peak at 304 nm decreased upon addition of the anion. This could be explained by the intramolecular charge-transfer interaction between the electron rich urea bond anion and the electron deficient carbazole/ NO_2 moiety. In addition, there were two well-defined isosbestic points at 293 nm and 350 nm, which indicated that there formed the stable complex having a certain stoichiometric ratio between the receptor 1 and H_2PO_4^- anion. Figure 2 showed that there were changes of absorbance of 1 at 373 nm upon addition of H_2PO_4^- . The addition of AcO^- led to similar spectral changes, but the addition of F^- , Cl^- , Br^- , I^- and OH^- resulted in neglectable and/or out-of-order spectral changes (see supplementary material). Firstly, H_2PO_4^- and AcO^- could be recognized selectively from the other

Fig. 2 The plot of the change in absorbance at 373 nm as a function of H_2PO_4^- anion



anions tested according to the dissimilar changes of spectra caused by various anions.

To further investigate the anion binding properties of the receptor 1, ^1H NMR titrations, which were shown in Fig. 3 were obtained upon addition of H_2PO_4^- as its TBA^+ salt to the DMSO-d_6 solution of the receptor 1 (0.01 M). Upon addition of H_2PO_4^- , the NH proton signals of urea and carbazole underwent a continuous downfield shift and the other proton resonance did not move nearly, indicating the formation of a host–guest hydrogen-bonding complex, in which H_2PO_4^- ion interacted merely with the N–H fragment. As mentioned above, the proposed binding mode was shown in Fig. 4.

Affinity constants of receptor 1 for anionic species, which were shown in Table 1, were determined by non-linear fitting analyses of the titration curves according to the Eq. (1), 1:1 host–guest complexation [11b, 14]

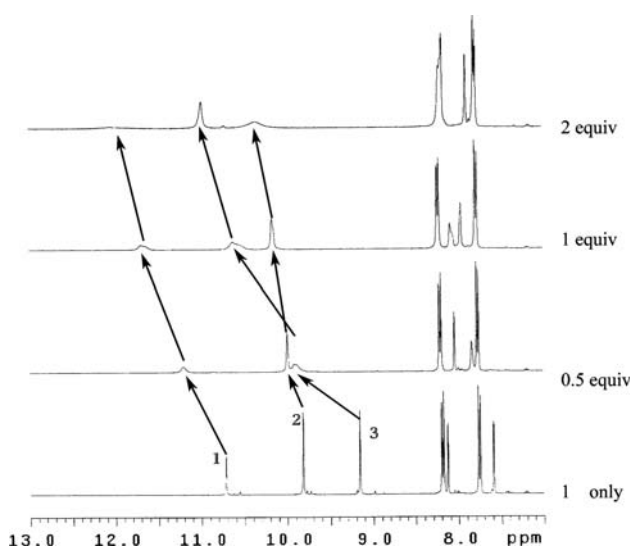


Fig. 3 ^1H NMR titrations of 1 in DMSO-d_6 (0.01 M) with H_2PO_4^-

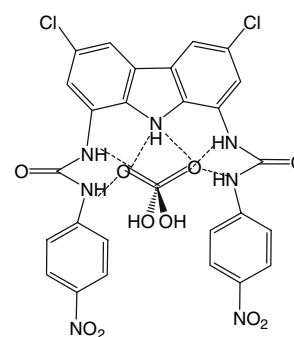


Fig. 4 The proposed host–guest binding mode in solution

$$A = A_0 + (A_{\text{lim}} - A_0) \left\{ c_{\text{H}} + c_{\text{G}} + 1/K_{\text{s}} - [(c_{\text{H}} + c_{\text{G}} + 1/K_{\text{s}})^2 - 4 c_{\text{H}}c_{\text{G}}]^{1/2} \right\} / 2c_{\text{H}} \quad (1)$$

where, c_{G} and c_{H} are the concentration of guest and host, respectively and A is the intensity of absorbance at certain concentration of host and guest. A_0 is the intensity of absorbance of host only and A_{lim} is the maximum intensity of absorbance of host when guest is added. K_{s} is the affinity constant of host–guest complexation.

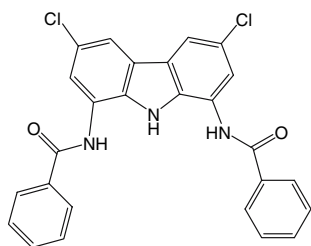
Obviously shown in Table 1, the selectivity trends of binding affinities of anions for 1 were determined to be $\text{H}_2\text{PO}_4^- > \text{AcO}^- \gg \text{F}^- \sim \text{Cl}^- \sim \text{Br}^- \sim \text{I}^- \sim \text{OH}^-$. The selectivity for H_2PO_4^- and AcO^- could be rationalized on the basis of the guest basicity and structure of the complex. As expected from the basicity [15] of anions, H_2PO_4^- and AcO^- could interact with the host molecular 1 more strongly than other anions tested. Moreover, H_2PO_4^- with four oxygens formed the strongest 1-anion complex via multitopic hydrogen-bonding interactions. F^- was also more basic anion compared with other anions, but its volume was smaller than the rest anions and there was big spacer between two urea moieties just as the crystal structure of its analogue 4 (in Fig. 5) reported by Jurczak group [11b]

Table 1 Affinity constants of receptor 1 with various anions^a in DMSO

Anion	H ₂ PO ₄ ⁻	AcO ⁻	F ⁻	Cl ⁻	Br ⁻	I ⁻	OH ⁻
K _s (M ⁻¹)	(2.04(±0.6) × 10 ⁵)	(2.67 ± 0.30) × 10 ⁴	ND ^b	ND	ND	ND	ND

^a Tetrabutylammonium salt of respective anions were used for studies

^b Can't be determined

**Fig. 5** The analogue of the receptor 1

suggested that the cleft was too wide for chloride anion. So we speculated that there couldn't form the stable complex having a certain stoichiometric ratio between the receptor 1 and F⁻ anion. That was why H₂PO₄⁻ could be recognized selectively among the anions tested. Secondly, affinity constants also provided us with the indication that H₂PO₄⁻ was differentiated selectively from various anions.

Conclusion

In summary, we have designed a novel receptor with two urea moieties as anions binding sites and studied its interaction with various anions by the method of UV–vis spectra titration. In DMSO solvent, 1 can interact with tetrahedral anions and Y-shaped anions more strongly than spherical anions. So host molecular 1 can differentiate H₂PO₄⁻, AcO⁻ anions from spheric anions such as haloid anions. To our knowledge, only a few receptors for H₂PO₄⁻ [16] were reported to date in the literature.

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