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ORIGINAL ARTICLE

A novel anion receptor employing the pyrrole and amide moieties in the cooperative binding of anions

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Abstract A novel anion receptor 1 based on pyrrole and amide moieties was designed, synthesized and characterized by X-ray crystallography, ^{1}H NMR, ESI-MS and so on. Its anions (such as AcO^-, F^-, Cl^- and $H_2PO_4^-$) binding properties was studied in detail by the ^{1}H NMR titrations in DMSO-d_6.

Keywords Anion receptor · Pyrrole · Crystal structure · Hydrogen bond

Introduction

The design of chemosensors for a special anionic analyte is currently an expanding area in the field of supramolecular chemistry due to the amazing impact of anions in many chemical and biological processes [1, 2]. Among the anions, phosphate ion is one of most particular interest because it is involved in a number of important biomineralization processes such as bone formation. However, an excess inorganic phosphate ion is one of many reasons that lead to renal stones [3, 4]. This diversity of function, both beneficial and detrimental, necessitates the development of systems capable of detecting the anion [5–7].

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The NMR titration as the most common and convenient approach is widely used in host–guest chemistry [8–10]. Firstly, it can shed light on the nature of the interactions between the host molecule and the guest molecule (anionic, cationic and neutral) [11]. For example, L. Fabbrizzi and the other groups reported a lot of papers about two-step mechanism during the anion recognition process supported by the ^{1}H NMR titration [12–15]. In the first step, the anion exhibited a hydrogen-bonding interaction with the receptor, and in the second step, the deprotonation of binding sites of the host took place on addition of a second equivalent anion. Secondly, it can provide valuable quantitative information such as the association constant of the host with the guest [16]. In this regard, P. A. Gale and co-workers [17, 18] did large numbers of researches on the association constant determined by ^{1}H NMR titration. However, ^{1}H NMR titration is limited to K_{ass} values below ca. 10^5 M^{-1}. Above this limit, the chemical shift movements are essentially linear with concentration of guest added, halting after addition of one equivalent [19]. In addition, addition of anions can not result in deprotonation of binding sites when the association constant is calculated by the ^{1}H NMR titration method.

In this paper, a simple anion receptor based pyrrole derivative was synthesized by coupling α-pyrrolylcarbonyl chloride with 5-amino-1.10-phenanthroline in pyridine. The crystal of 1·DMF·H_2O was obtained by slow evaporation of a DMF solution of the compound 1. In the crystal structure of the receptor 1, the intermolecular hydrogen bonds and π–π stacking between 1,10-phenanthroline planes resulted in the assembly of discrete molecules into infinite supermolecule (3D). The results of ^{1}H NMR titrations indicated that 1:1 complex formed between the receptor 1 and anions tested.

Experimental

Apparatus

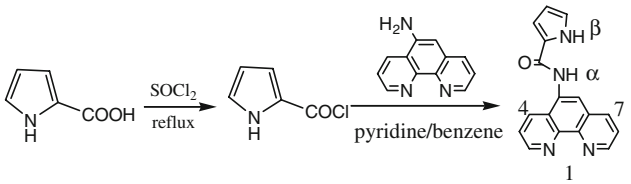
^{1}H NMR spectra were recorded on a Varian UNITY Plus-400 MHz Spectrometer in DMSO-d_6 (TMS as the internal standard). ESI-MS was performed with a MARINER apparatus. C, H, N elemental analyses were made on an elementar vario EL. X-ray single crystal diffraction dada was collected on a Rigaku Saturn CCD.

Chemicals

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-d_6 solvent was purchased from Cambridge Isotope Laboratories, Inc.

Synthesis

N-(1′,10′-phenanthrolin-5′-yl)-1H-pyrrolyl-2-amide (1) was synthesized according to Scheme 1. α-Pyrrolylcarboxylic acid (1.0 g, 9.0 mmol) was added to $SOCl_2$ (6.0 ml), the suspension was refluxed for 10 min. The mixture was concentrated in vacuum by evaporation $SOCl_2$ until a grayer solid precipitated (α-pyrrolylcarbonyl chloride). The solution of the α-pyrrolylcarbonyl chloride in benzene was added dropwise to 5-amino-1.10-phenanthroline (1.9 g, 9.0 mmol) in pyridine (15.0 ml) and the resulting mixture was stirred over-night at RT. The crude product precipitated, was filtered and crystallized from EtOH–H_2O to give the yellow powder. Mp: 272–274°C. ^{1}H NMR (400 MHz, DMSO-d_6) 11.74 (s, 1H, pyrrole-N*H*), 10.20 (s, 1H, CON*H*), 9.14–9.09 (d, 2H, phen*H*, J = 8.0 Hz), 8.52–8.50 (d, 2H, phen*H*, J = 8.8 Hz), 8.09 (s, 1H, phen*H*), 7.84–7.78 (m, 2H, phen*H*, J = 8.0 Hz), 7.23(d, 1H, pyrrole-C*H*, J = 4.2 Hz), 7.03(t, 1H, pyrrole-C*H*, J = 4.6 Hz), 6.25–6.24(d, 1H, pyrrole-C*H*, J = 3.2 Hz); ESI-mass: m/z calcd. for $C_{17}H_{12}N_4O$ $[M + H]^+$:289.11, found: 289.09. Anal. Calcd for $C_{17}H_{12}N_4O$: C 70.82, H 4.20, N 19.43, Found C 71.12, H 3.85, N 19.50.



Scheme 1 General synthetic routes to the target compound 1

X-ray crystallography

Single crystal suitable for X-ray crystallographic analysis was obtained by slow evaporation of a DMF solution of the compound 1. A yellow block crystal of **1** with dimensions of 0.20 mm × 0.14 mm × 0.06 mm was mounted on a glass fiber. X-ray single-crystal diffraction data were collected on a Rigaku Saturn CCD area detector at 113(2) K with Mo-Ka radiation (λ = 0.71073 Å). The structure was solved by direct methods and refined on $F2$ by full-matrix least squares methods with SHELXL-97 [20]. Crystal data for 1·DMF·H_2O: $C_{20}H_{21}N_5O_3$, Mr = 379.42, T = 113(2) K, triclinic, space group P-1, a = 7.8559(4) Å, b = 9.1681(6) Å, c = 14.6818(9) Å, α = 73.254(10), β = 88.938(15), γ = 68.080(10), V = 934.66(7) Å^3, D_{calc} = 1.348 g cm^{-3}, Z = 2, Reflections collected/unique: 7175/3259 (R_{int} = 0.0598), $R1$/$wR2$ [$I > 2.00\sigma$(I)]: $R1$ = 0.0680, $wR2$ = 0.1427, $R1$/$wR2$ (all dada): $R1$ = 0.1084, $wR2$ = 0.1653, GoF on : 1.087 (CCDC No.: 640696) [21].

Results and discussion

X-ray crystallographic study

The perspective view of the receptor 1 with atomic labeling was shown in Fig. 1. The dihedral angles of O(1)–C(13)–N(3)–C(6) and N(3)–C(6)–C(7)–C(11) were −1.3° and −177.1°, respectively indicating the two planes (amide and 1,10-phenanthroline planes) were almost parallel. In addition, the dihedral angle of the O(1)–C(13)–C(14)–N(4) plane was −12.2°, which was almost parallel with the amide plane and the pyrrole plane. In other words, the groups: amide, pyrrole and phenanthroline were nearly coplanar. Particularly, the hydrogen bonds between the units and solvent molecules and π–π stacking between 1,10-phenanthroline planes gave rise to the assembly of discrete molecules into infinite supermolecule (3D) (see Fig. 2). The supermolecular structure was clustered by

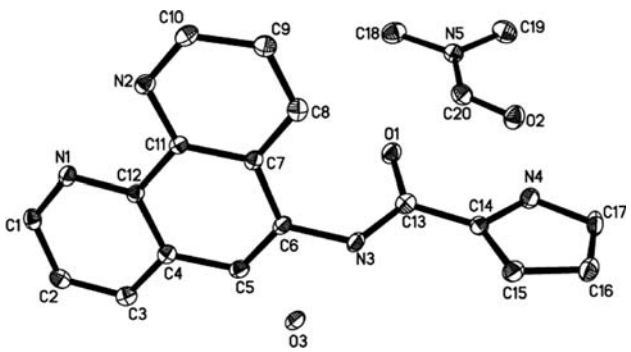


Fig. 1 OETEP plot of the molecular structure of 1·DMF·H_2O and atomic number (H atoms were omitted for clarity)

water molecule, *N*,*N*-dimethylform amide and the compound 1 through hydrogen bonds. The H(3B) and H(3C) atoms of water molecule linked two nitrogen atoms of 1,10-phenanthroline of adjacent units, and the amide N(3)–H(3A) of the compound linked with the O(3) of water and meanwhile the pyrrole N(4)–H(4A) was linked to *N*,*N*-dimethylform amide O(2). Moreover, there existed π–π stacking between 1,10-phenanthroline planes as the distance between the 1,10-phenanthroline planes was about 3.6 Å (the range of the distance of π–π stacking is from 3.3 to 3.8 Å). However, the distance between pyrrole planes exceeded 4 Å, suggesting no π–π stacking exists between the pyrrole rings.

^{1}H NMR titration

The ^{1}H NMR spectra were recorded on a Varian UNITY Plus-400 MHz Spectrometer in the DMSO-d_6 solution (TMS as an internal standard). A 1.0 M solution of the compound 1 in DMSO-d_6 was prepared. Then, aliquots of acetate anion (1.0 M in DMSO-d_6) were added to the solution above-mentioned and then, ^{1}H NMR of the host–guest system was tested [22].

The anion binding ability of the receptor 1 was invested through ^{1}H NMR technique. Figure 3 showed partial ^{1}H NMR spectra of the receptor 1 (1.0 M) in DMSO-d_6 in the absence and the presence of different equiv of $[(Bu)_4N]AcO$. Obviously, the peaks at 11.74 ppm and 10.20 ppm, which were ascribed to $-NH_\alpha$ and $-NH_\beta$, respectively, exhibited a gradual downfield shift and broadened along with successive addition of AcO^-. The result suggested that formation of intermolecular hydrogen bonds between NH_α and $-NH_\beta$ of the host molecule 1 and AcO^- ion [23, 24]. In addition, the signals of the hydrogen atoms of the aromatic ring and the pyrrolyl ring shifted upfield, which indicated the increase of the electron density on the phenyl ring owing to the through-bond effects [25, 26]. Particularly, C–H4 and C–H7 had the same chemical shift before 1 coordinated with AcO^-. Once 1 interacted with AcO^- ion through H-bonds, which induced changes in electronic properties of the receptor, the signals of C–H4 and C–H7 were split to two peaks (see Fig. 3: the right). On the contrary, two CH resonances of pyrrolyl ring incorporated together upon formation of the hydrogen bonding complex. Similar changes were observed in ^{1}H NMR spectra of 1 upon addition of F^- and $H_2PO_4^-$ ions.

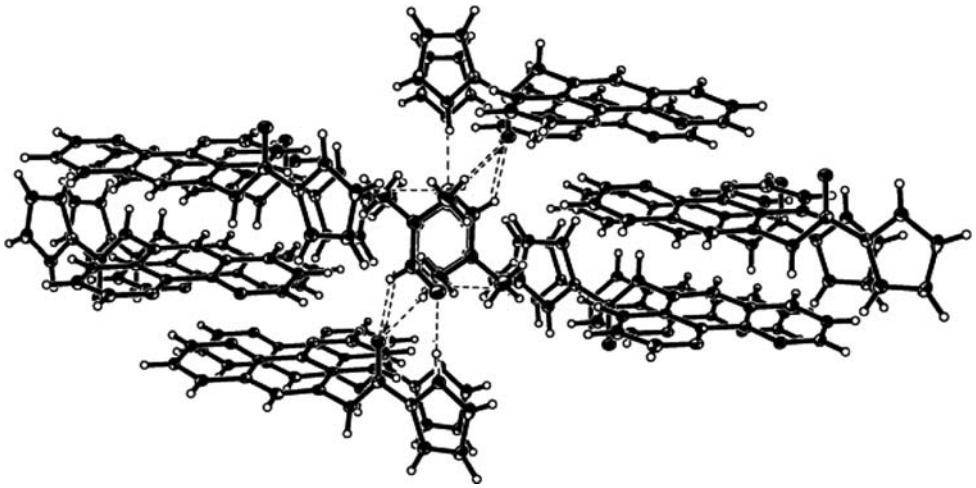


Fig. 2 Packing of the molecule in a unit cell (H-bonds were shown as dotted lines)

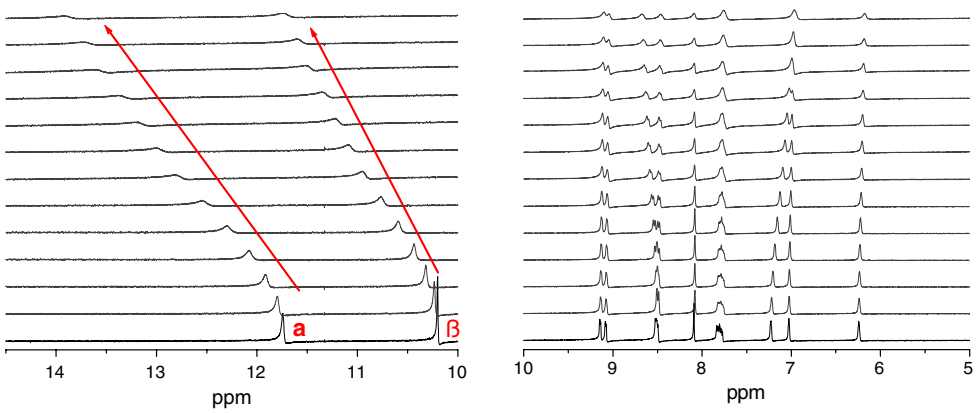


Fig. 3 Stack plots of ^{1}H NMR of the receptor 1 (1.0 M) on addition of AcO^- in DMSO-d_6. The chemical shifts of the binding sites were shown on the left and the chemical shifts of phenanthrolinyl or pyrrolyl ring were shown on the right

Nevertheless, the receptor 1 was insensitive to addition of excess equiv. Cl^-.

Association constants

The association constants of the receptor 1 for anionic species, K_{ass}, which were shown in Table 1, were calculated by non-linear least-square analysis using the Eq. 1 derived from the 1:1 host–guest complexation [27].

$$\delta = \delta_0 + \left(\delta_{\lim} - \delta_0\right) \cdot \left\{ K^{-1} + c_G + c_H - \left[\left(K^{-1} + c_G + c_H \right) * - > \psi_G \cdot \psi_H \right]^{-0.5} \right\} \Big/ 2c_H \quad (2)$$

where, c_G and c_H are the concentration of guest and host, respectively and δ is the chemical shifts of the bind site at certain concentration of host and guest. δ_0 is the chemical shifts of the binding site of host only and $\delta_{\lim}$ is the maximum chemical shifts of the binding site when guest is added. K is the affinity constant of host–guest complexation. The good correlation coefficient (R^) obtained by non-linear fitting analyses also indicated the stoichiometry of the host–guest interaction was confirmed to be 1:1 (Host:Guest).

The receptor 1 bore two different groups (amide and pyrrole) as binding sites with diverse resonance signals. Therefore, the association constant could be determined according to chemical shifts of two binding sites, respectively. Figure 4 showed changes in chemical shifts of pyrrole NH and amide NH upon addition of AcO^- ion in DMSO-d_6. Evidently, the association constants of 1 with the anions (such as $H_2PO_4^-$ and AcO^-) calculated according to chemical shifts of pyrrole NH were nearly consistent with those obtained according to chemical shifts of amide NH (see Table 1). Different from other anions tested, the association constant of 1 with F^- determined by chemical shits of pyrrole (1,010 M^{-1}) was larger than that obtained by chemical shifts of amide (710 M^{-1}). The results could be likely rationalized on basis of the facts as follow: (1) The acidity of the pyrrole moiety is stronger than that of the amide moiety; and (2) the ionic radius of F^- ion is small and its basicity is strong. Hence, the fluoride interacted easily with the pyrrole NH with stronger acidity, which would make the distance of F^- with the amide NH far and make the hydrogen binding interaction between amide-NH and F^- weak. In other words, the changes in the chemical shift of the pyrrole were larger than those in the chemical shifts of the amide induced by the same equiv of F^-. In contrast, two oxygen atoms of AcO^- and $H_2PO_4^-$ ions could interact with the pyrrole and the amide moieties, respectively, through intermolecular hydrogen bonding (see Scheme 2). Namely, anions-induced changes of two binding sites were almost same (as an example see Fig. 4). Therefore, the association constant of 1 with F^- obtained by analysis of chemical shifts of pyrrole was larger than that determined according to chemical shifts of amide. And the association constants of 1 with AcO^- and $H_2PO_4^-$, which were calculated by chemical shifts of two different binding sites, were almost identical. Particularly, with the receptor 1 the stronger complex was formed with AcO^- than $H_2PO_4^-$. It has been clear that the selectivity for special analyte can be rationalized on basis of the guest basicity and shape complementarity between the host and the anionic guests. However, multiple hydrogen-bonding interactions are also necessary in high-affinity anions binding sites [28]. The

Table 1 Association constants K_{ass} (M^{-1}) of the receptors 1 with anions in DMSO-d_6

Anoins	AcO^-	$H_2PO_4^-$	F^-	Cl^-
K_{ass} (*pyrrole*)	812	369	1010	ND[c]
K_{ass} (*amide*)	758	241	710	ND
R^	0.98	0.97	0.98	–

[a] The anions were added as their tetrabutylammonium salts

[b] Correlation coefficient (R^) determined by non-linear fitting analyses

[c] Very weak complexation. The association constant could not be determined

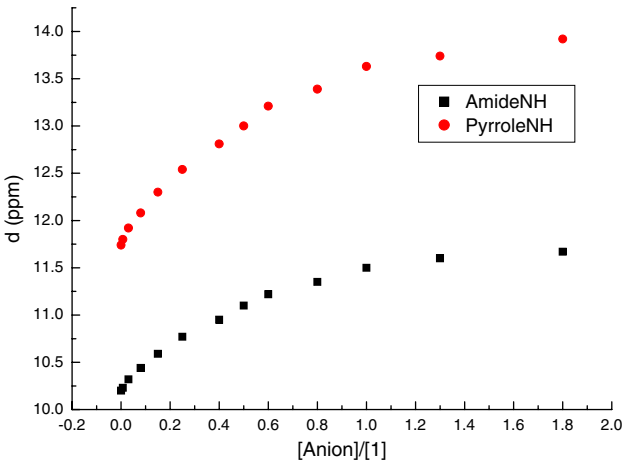
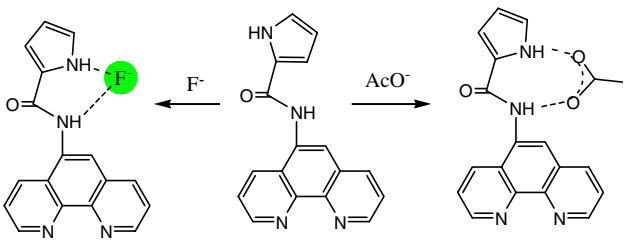


Fig. 4 The plots of chemical shifts δH of the pyrrole and the amide NH protons of the receptor 1 (1.0 M) versus addition of equivalent of AcO^-as its tetrabutylammonium (TBA) salts in DMSO-d_6



Scheme 2 The proposed host–guest binding mode in solution

acetate anion with an O–C–O angle of ca. 120° is a triangular anion and might be the fitter for the two hydrogen atoms on the binding sites of the receptor 1 to form multiple hydrogen-bonding interactions with 1 (see Scheme 2). Consequently, the association constant of the receptor 1 with AcO^- was larger than $H_2PO_4^-$.

Conclusion

In conclusion, we have successfully shown a novel anion receptor employing the pyrrole and amide moieties in the cooperative binding of anions. Crystal structure of 1 demonstrated the assembly of discrete molecules into infinite supermolecule (3D) induced by the hydrogen bonds between the units and solvent molecules and π–π stacking between 1,10-phenanthroline planes. The anion binding property of the host molecule 1 (1.0 M) was studied in detail by the ^{1}H NMR titration technique in DMSO-d_6.

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