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PAPER

Pyridinium/urea-based anion receptor: methine formation in the presence of basic anions†

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The influence of the positively charged *N*-methylpyridinium substituent on the anion binding tendencies of urea-based receptors has been investigated by comparing molecules **1** and **2**. These receptors have been studied in acetonitrile, by performing UV-vis. and ^{1}H NMR titrations with several anions. UV-vis. titrations have also been performed in DMSO, MeOH and $CHCl_3/CH_3CN$ mixture (1/1, v/v). In the case of **1**, the presence of both H-donor and H-acceptor groups (urea and pyridine, respectively) favours aggregation and the formation of dimers in the solid state. In solution, this tendency to aggregate reduces affinity for anions with respect to the similar urea-based receptor **3**. The methylation of the pyridyl group of **1** leads to the pyridinium-containing receptor **2**. The pyridinium positive charge enhances the acidity of urea and increases anion affinity, as evidenced by the comparison of the binding constants. Both receptors (**1–2**) form stable adducts with all investigated anions. However, in the case of **2**, the formation of 1 : 1 adducts with basic anions, such as acetate and fluoride, is followed by a proton transfer process. Quite interestingly, deprotonation does not involve the urea group, thus preserving the 1 : 1 adduct, as demonstrated by the ^{1}H NMR measurements. In particular, the proton transfer process takes place at the methylene group linking the pyridinium fragment to the receptor's skeleton. ^{1}H NMR studies indicate the formation of a stable neutral methine species, characterised by the loss of aromaticity by the pyridyl ring. These results open new perspectives in the field of anion recognition, as receptor **2** may by applied to the monitoring of both bound anion (through the urea unit) and excess anion in solution (through the development of the yellow methine species).

Introduction

Over the past decades, anion recognition has attracted the interest of many scientists, as attested by the large number of publications on the topic. Anion recognition by neutral receptors is generally based on H-bonding interactions, involving polarized N–H fragments of ureas, thioureas, squaramides, pyrroles, amides and sulfonamide binding groups.[1] The affinity towards anions is increased and tuned by providing the receptor with several H-bond donor groups, placed at well-defined distance and geometry, according to the size and shape of the target anion.[2] The H-bonding donor ability of N–H groups can be increased by introducing electron-withdrawing substituents (EWG) on the receptor. Powerful EWGs effectively polarise the N–H groups, thus favouring the formation of stable H-bonded receptor:anion adducts.[3] In particular, EWGs affect the acidity of the H-donor moiety, thus favoring proton transfer processes in the presence of basic anions (*e.g.* acetate, fluoride). As the H-bond interaction can be considered as a "frozen" proton transfer from the receptor to the anion,[4] the higher the acidic properties of the receptor and the basic features of the anion, the more advanced the proton transfer and the more stable the receptor:anion adduct.[5] The polarization effect on N–H donor groups can be also obtained by introducing positive charges on the receptor's skeleton, in the proximity of the N–H.[6]

Herein, we present two new urea-based anion receptors, **1** and **2** (see Scheme 1). Both may potentially behave as ditopic receptors, employing the urea and the pyridyl unit in the formation of H-bonds with opposite behaviour: pyridine as H-acceptor, pyridinium as H-donor.[7] Due to the EWG effect of the pyridinium unit on the N–H donor groups of urea, receptor **2** might undergo proton transfer processes in the presence of basic substrates (*e.g.* acetate and fluoride). In this situation, the proton transfer process would compete with anion complexation as, on deprotonation, the urea unit would lose its H-binding capability. It has to be noted that also the *N*-methylene and 2-methylene groups of the 1,2-disubstituted pyridinium in receptor **2** might give proton transfer processes with basic anions, leading to methylide and methine species, respectively.[8] However, in this latter case, deprotonation would not involve the urea group, thus preserving the anion binding capability of the receptor even in the presence of basic

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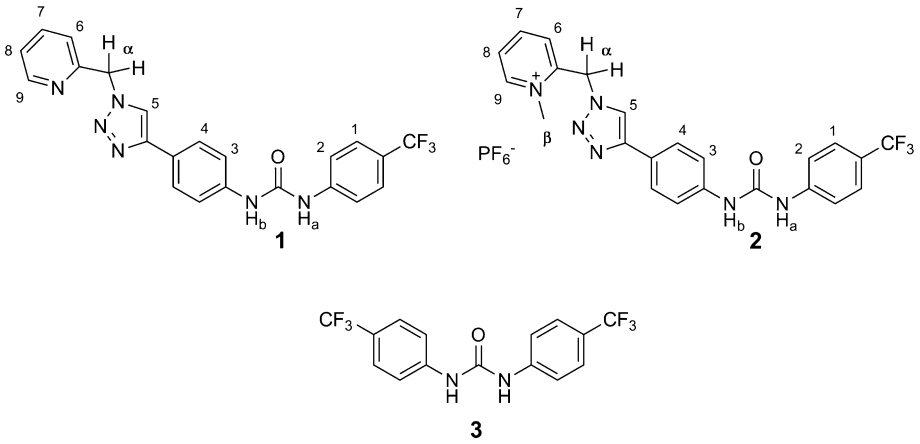


Scheme 1 Formulae of receptors **1–3**.

substrates. These results could open new perspectives in the field of anion recognition, as **2** would represent, to our knowledge, the first example of anion receptor in which the presence of an EWG at the same time activates the H-donor group and prevents the effect of proton transfer processes on adduct formation.

Results and discussion

The synthesis of receptor **1** involves the Cu(I)-catalyzed 1,3-dipolar cycloaddition[9] between 2-(azidomethyl)pyridine and the ethynyl group of 1-(4-ethynylphenyl)-3-(4-(trifluoromethyl)phenyl)urea. Receptor **2** has been obtained from **1**, by methylation of the pyridine nitrogen with methyl iodide (see the ESI†). The binding tendencies of **1** and **2** towards anions have been investigated through spectrophotometric and, in some cases, by ^{1}H NMR titration experiments. The obtained results have been compared to those already reported by our group for the symmetric receptor **3**, presenting two 4-trifluorophenyl groups appended to the urea fragment.[10] Receptor **1** was isolated as a crystalline solid and its molecular structure was determined by single crystal X-ray diffraction studies.

Spectrophotometric studies

The affinity of receptors **1** and **2** towards anions was first investigated by UV-vis. spectroscopy. Receptor solutions in acetonitrile were titrated with standard solutions of the tetrabutylammonium (TBA) salt of the tested anion. The titration profiles (as absorbance at a fixed wavelength *vs.* equivalents of anion, X^-) were fitted by means of a non-linear least-squares program,[11] obtaining the association constants shown in Table 1. The interaction with weakly basic anions (*i.e.* X^-: Cl^-, Br^-, I^-, NO_3^-, and HSO_4^-) significantly shifts the absorption maximum of the investigated urea-based receptors ($\mathbf{R}H_2$) to longer wavelengths, as expected from the formation of H-bonded adducts. Single equilibria are involved, corresponding to a 1 : 1 binding stoichiometry: $\mathbf{R}H_2 + X^- \leftrightharpoons [\mathbf{R}H_2 \cdots X]^-$.

Among the investigated receptors, anion affinity decreases along the series: **2** > **3** > **1**. The high binding constants observed for **2** show that the presence of positive charges on the receptor's skeleton, albeit not directly conjugated to the urea group, enhances anion affinity. In the literature, many examples of pyridinium-based anion receptors are reported.[7] In most cases, the pyridinium moiety itself provides H-bonding interactions with anions, involving the C–H bonds of the aromatic ring as H-donor. However, for receptor **2**, at the concentrations used for the UV-vis. titrations (10^{-4}–10^{-3} M), only a single equilibrium was observed, involving the urea fragment. Titrations of **1** and **2** with TBA–Cl are shown in the ESI (Fig. S1 and S2, respectively).† With respect to **2** and **3**, receptor **1** displays lower binding constants with all investigated anions (see Table 1). The scarce binding tendencies of **1** may be attributed to the simultaneous presence of H-donor and H-acceptor groups on the receptor's skeleton. As a matter of fact, the urea and the pyridine groups belonging to different receptor molecules may interact with each other, leading to the formation of stable H-bonded aggregates.[12]

The unfavourable enthalpic contribution, associated with the disruption of these interactions in the formation of anion adducts, may be responsible for the lower binding tendencies of **1** with respect to **3**. The tendency of **1** to form intermolecular H-bonding interactions, involving both urea and pyridine groups, was observed in the solid state by diffraction studies (see further). It should be noted that, at the low concentration employed for titrations, only a small fraction of **1** in solution is present as a dimer, therefore the titration curves exhibit close adherence to the binding isotherm for 1 : 1 association.

Table 1 Association constants (as log K values) for the interaction of receptors **1–3** with anions (as TBA salts) in pure acetonitrile at 25 °C, determined *via* UV-vis. spectroscopy

X^-	$\mathbf{R}H_2$	Log K_{11}[a]	X^-	$\mathbf{R}H_2$	Log K_{11}[a]	Log K_{12}[a]
Cl^-	**1**	3.93(1)	$H_2PO_4^-$	**1**	4.44(1)	
	2	4.52(1)		**2**	///	
	3[b]	4.14(1)		**3**[b]	3.37(1)	
Br^-	**1**	2.88(1)	$CH_3CO_2^-$	**1**	5.24(1)	
	2	3.61(1)		**2**	6.7(1)	4.8(1)
	3[b]	3.37(1)		**3**[b]	5.88(1)	
I^-	**1**	<2	HSO_4^-	**1**	2.77(1)	
	2	2.58(1)		**2**	3.41(1)	
	3[b]	<2		**3**[b]	3.10(1)	
NO_3^-	**1**	2.44(1)	F^-	**1**	5.24(2)	
	2	3.15(1)		**2**	6.8(1)	5.6(1)

[a] In parentheses, the standard deviations on the last figure are reported. [b] Ref. 10

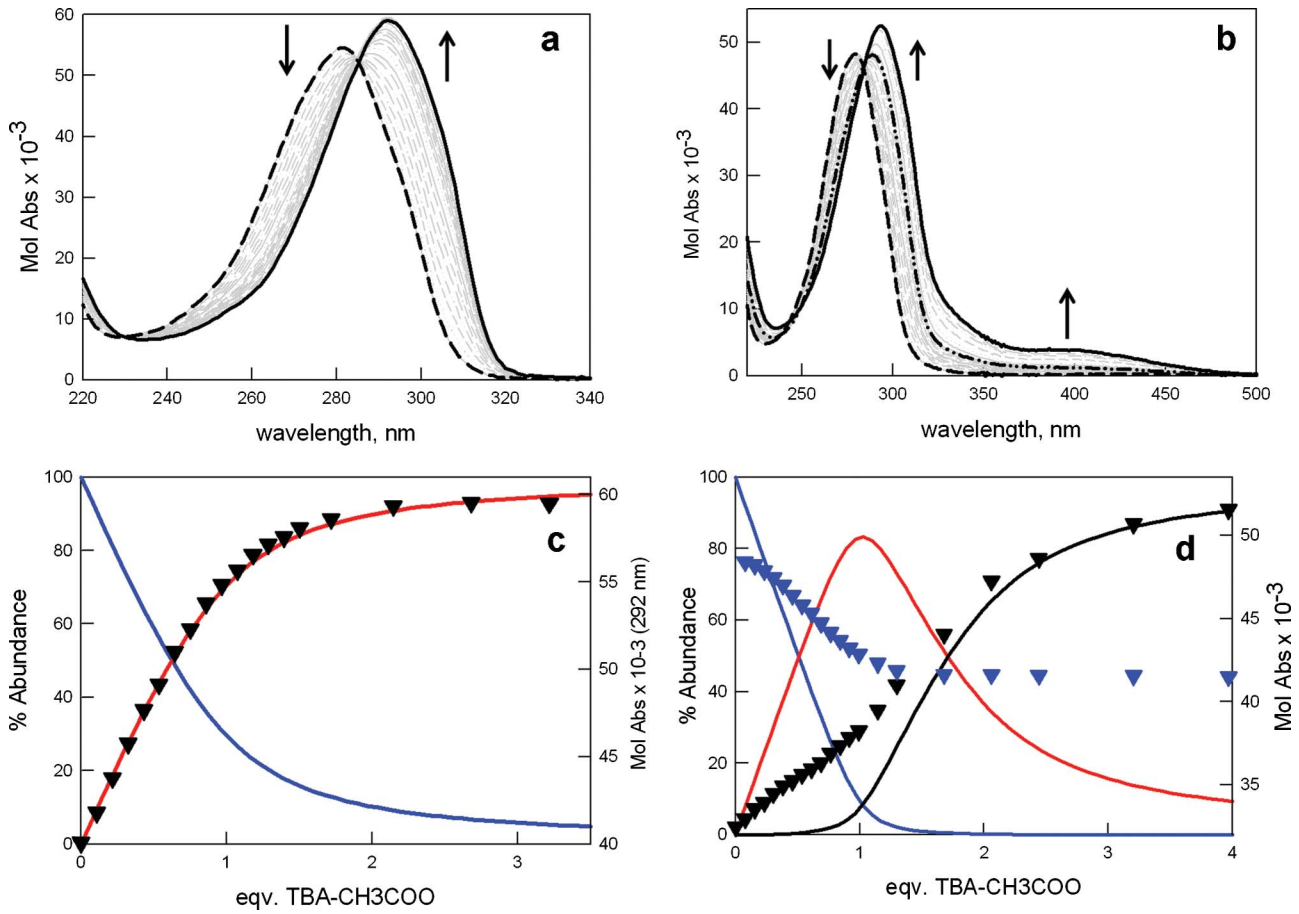


Fig. 1 Absorption spectra taken over the course of (a) the titration of a 4.6×10^{-5} M solution of **1** in acetonitrile, with a 4.9×10^{-3} M solution of the TBA–CH_3COO (l = 0.1 cm); (b) the titration of **2** (8.7×10^{-5} M) with TBA–CH_3COO (3.3×10^{-2} M), l = 0.1 cm. Diagrams (c) and (d) show the distribution of the species present at the equilibrium in titration (a) and (b), respectively. In diagram (c): blue line, free receptor; red line, 1 : 1 adduct; black triangles, superimposed plot of molar absorbance *vs.* equiv. of TBA–CH_3COO. In diagram (d): blue line, free receptor; red line, 1 : 1 adduct; black line: deprotonated receptor; black and blue triangles, superimposed plot of molar absorbances (at 406 and 280 nm, respectively) *vs.* equiv. of TBA–CH_3COO.

Receptors **1** and **2** were also investigated in the presence of basic anions (*i.e.* CH_3COO^-, $H_2PO_4^-$, F^-). In the case of **1**, only one equilibrium was observed, corresponding to the formation of 1 : 1 adducts, as suggested by the red shift of the receptor's absorption maximum (see Fig. 1a and 1c for the titration of **1** with TBA–CH_3COO). From the point of view of anion affinity, receptor **3** mainly prevails over **1**, as already observed for weaker basic anions (see Table 1). The only exception is represented by dihydrogen phosphate (see Fig. S3† for the titration of **1** with TBA–H_2PO_4), for which receptor **1** displays higher affinity. This singular behaviour could depend on the contribution of the pyridine group in the interaction with the anion. Indeed, pyridine may accept H-bonds from dihydrogen phosphate, while urea acts as H-donor towards the anion oxygen atoms. The understanding of this aspect was deepened by means of ^{1}H NMR titrations (see further).

Studies on receptor **2** showed the presence of two equilibrium steps, with both acetate (see Fig. 1b and 1d) and fluoride; due to precipitation, the interaction with dihydrogen phosphate could not be studied. In the first step, the urea band shifts towards higher wavelengths, due to the establishment of receptor:anion H-bonding interactions. In the second step, further red shift of the absorption maximum is observed, accompanied by the development of a new band at about 400 nm and yellow colour of the solution. The effect of excess anion on receptor **2** may be attributed to the receptor's deprotonation. This hypothesis is confirmed by recording the UV-vis. spectrum of the deprotonated species, generated on addition of 1 equiv. 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to a solution of **2** in acetonitrile: the obtained yellow solution shows a band at 400 nm, similar to that observed with excess acetate (see in Fig. S4† the UV-vis. spectra taken over the course of the titration of **2** with DBU). The nature of this deprotonated species was further investigated by ^{1}H NMR. It has to be noted that no deprotonation occurs when DBU is added to solutions of **1** or **3**, therefore confirming that deprotonation does not involve the urea moiety.

The anion binding tendency was also studied in DMSO, CH_3OH and $CHCl_3/CH_3CN$ (1/1, v/v) mixture, by performing UV-vis. titrations of **1–3** with TBA–Cl and TBA–CH_3COO (see Table 2). The obtained results demonstrate that highly polar and competitive solvents, such as DMSO and CH_3OH, deeply affect anion affinity. In particular, in CH_3OH solution, affinity constants are too low to be safely determined with both chloride and acetate. Anion:receptor interaction is also affected by scarcely polar solvents, such as $CHCl_3$, probably due to the stabilization

Table 2 Association constants (as log K values) for the interaction of receptors **1–3** with TBA–Cl and TBA–CH_3COO in DMSO and $CHCl_3/CH_3CN$ (1/1, v/v) mixture determined by UV-vis. spectroscopy (at 25 °C). The experiments in CH_3OH solution gave log $K < 2$ with both receptors and anions. In parentheses, the standard deviations on the last figure are reported

Anion	RH_2	Log K_{11} DMSO	Log K_{12} DMSO	Log K_{11} $CHCl_3$/CH_3CN	Log $K_{12}CHCl_3$/CH_3CN
Cl^-	**1**	<2		2.97(1)	
	2	<2		3.78(1)	
	3	<2		3.29(1)	
$CH_3CO_2^-$	**1**	3.80(1)		4.78(1)	
	2	4.64(1)	3.12(3)	5.68(4)	4.0(1)
	3	4.18(1)		5.04(1)	

of ion pairs (*e.g.* TBA–anion) and to the consequent high energy required for ion pair disaggregation. Due to the receptors' low solubility, anion affinity could not be investigated in other media.

^{1}H NMR studies

Further investigations on the interaction of receptors **1** and **2** with anions were performed by ^{1}H NMR measurements in CD_3CN. ^{1}H NMR titrations of receptor **1** with TBA–Cl and TBA–CH_3COO evidenced the formation of H-bonded adducts, involving the N–H protons of the urea group. Fig. 2 shows the family of ^{1}H NMR spectra taken on a solution of **1** in CD_3CN, in the presence of increasing amounts of TBA–CH_3COO. The urea protons (H_a and H_b) are the most affected by the formation of the adduct, undergoing downfield shift ($\Delta\delta_{Ha} \cong +5.0$ ppm). As already observed for receptor **3**, also the phenyl groups conjugated to urea feel the effect of the interaction with the anion, with the C–H in the α-position shifting downfield.[10] Similar behaviour was observed in the ^{1}H NMR titration of **1** with TBA–Cl, see Fig. S5.†

Quite interestingly, the ^{1}H NMR titration of **1** with TBA–H_2PO_4 revealed the occurrence of two stepwise equilibria, corresponding to the formation of 1 : 1 and 2 : 1 receptor:anion adducts (see Fig. S6,†); whereas, the UV-vis. titration evidenced only a single equilibrium in solution, leading to the 1 : 1 adduct.

The formation of the 2 : 1 (receptor:anion) adduct could be followed only by ^{1}H NMR because of the higher molar concentration used for both receptor and anion; in the conditions used for the UV-vis. titration, the percentage of the developed 2 : 1 adduct was too low to be detected. ^{1}H NMR titrations on receptor **2** were performed with TBA–Cl and TBA–CH_3COO (measurements in the presence of TBA–H_2PO_4 gave no results due to precipitation). Upon chloride addition (see Fig. S7†), the N–H protons, as well as the C–H_α protons of the conjugated aromatic rings, are downfield shifted. This result is consistent with the interaction of chloride with the urea unit, leading to a 1 : 1 adduct. After 1 equiv., both triazole and methylene protons (at 8.23 and 6.05 ppm, respectively) start to feel the effect of the anion, probably due to the interaction of excess chloride with the pyridinium moiety.

The titration of **2** with TBA–CH_3COO shows a peculiar trend (see Fig. 3). The downfield shift of the urea protons ($\Delta\delta_{Ha} = +4.94$ ppm) is consistent with the formation of a 1 : 1 adduct (**2**–**A**, see Scheme 2). However, with respect to the titration with TBA–Cl, acetate addition promotes the enlargement and disappearance of the peaks corresponding to the triazole/pyridinium unit. The complete attribution of the ^{1}H NMR signals in spectra 1 and 9 is reported in Table 3. Quite interestingly, the deprotonation process

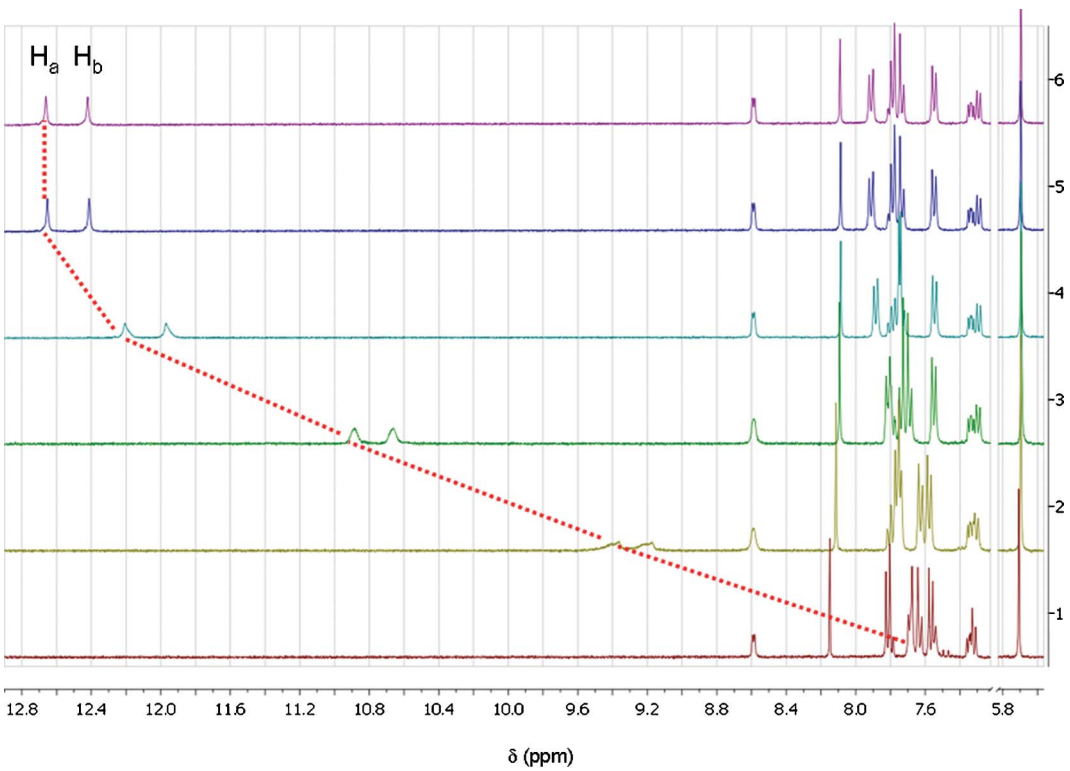


Fig. 2 ^{1}H NMR spectra taken over the course of the titration of a 7.9×10^{-3} M solution of **1** in CD_3CN with a 8.9×10^{-2} M solution of the TBA–CH_3COO. Spectra 1–6 correspond to the addition of 0, 0.3, 0.6, 0.9, 1.4 and 2.0 equiv. of TBA–CH_3COO, respectively.

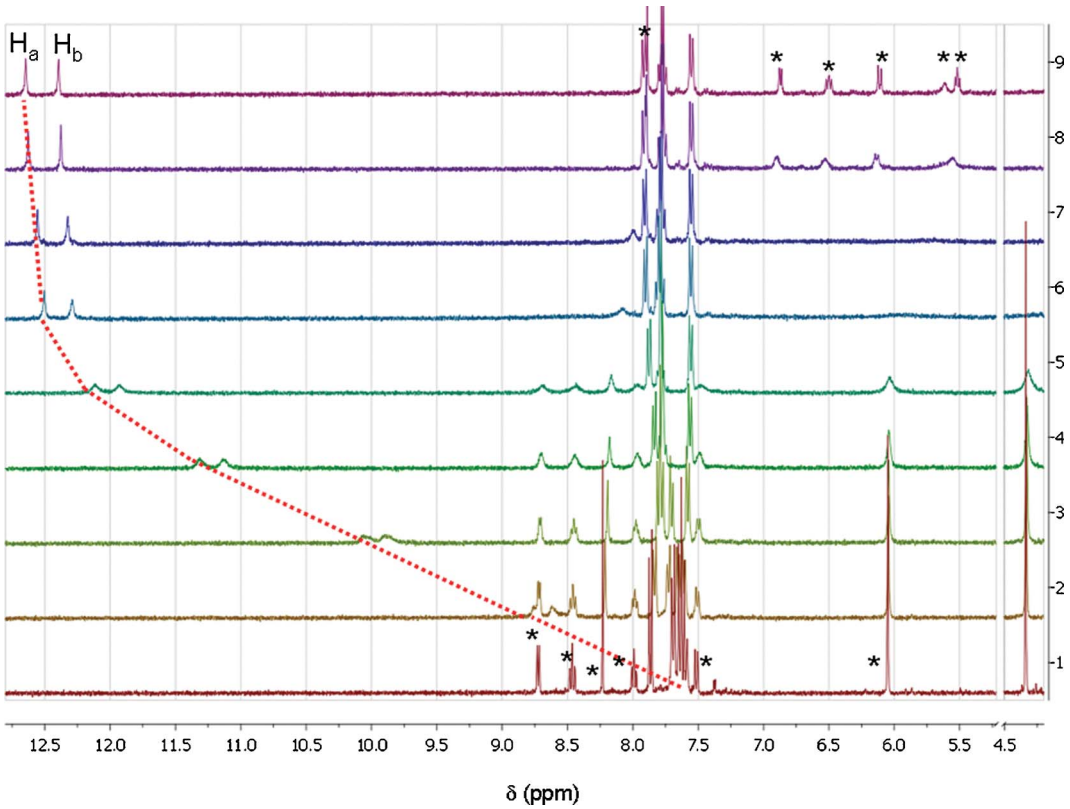
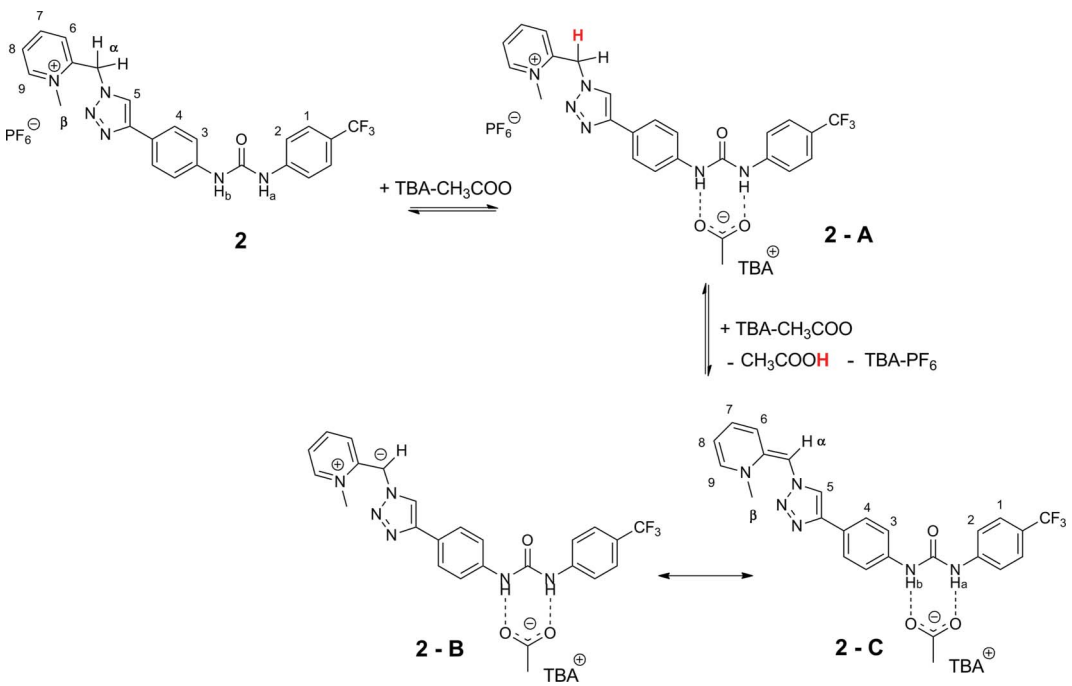


Fig. 3 ^{1}H NMR spectra taken over the course of the titration of a 4.4×10^{-3} M solution of **2** in CD_3CN with a 8.9×10^{-2} M solution of the TBA–CH_3COO. Spectra 1–9 correspond to the addition of 0, 0.3, 0.6, 0.9, 1.1, 1.6, 3.2, 4.3 and 5.5 equiv. of TBA–CH_3COO, respectively. Spectrum 5 corresponds to the 1 : 1 adduct (**2**–**A**).



Scheme 2 Effect of excess TBA–CH_3COO on receptor **2**.

Table 3 Attribution of the ^{1}H NMR peaks from spectra 1 and 9, Fig. 3. $\Delta\delta$ corresponds to the chemical shift variation upon formation of the final methine species. Standard deviation: ±0.01 on the last represented figure.[a]

	Spectrum 1	Spectrum 9	
	δ, ppm	δ, ppm	Δδ, ppm
H_1	7.85	7.75	–0.10
H_2	7.61	7.79	+0.18
H_3	7.69	7.91	+0.22
H_4	7.63	7.55	–0.08
H_5[a]	8.23	7.91	–0.32
H_6[a]	7.50	6.12	–1.38
H_7[a]	8.46	6.52	–1.94
H_8[a]	7.99	5.54	–2.45
H_9[a]	8.74	6.90	–1.84
H_α[a]	6.06	5.55	–0.51
H_β	4.34	3.18	–1.16
H_a	7.69	12.63	+4.94
H_b	7.63	12.38	+4.75

[a] See asterisks in Fig. 3

does not involve the urea unit; thus, the 1 : 1 receptor:acetate adduct is preserved, as evidenced by the N–H signals (see H_a and H_b, spectrum 9, Fig. 3). The $\Delta\delta$ values reported in Table 3 indicate that the pyridinium unit (from H_6 to H_9) is the most affected by deprotonation and its signals are strongly upfield shifted, as expected from a loss of aromaticity by the heterocyclic ring. It has to be noted that the formation of the methine species[13] **2**–**C** is consistent with the second equilibrium step observed in the UV-vis. titration and, in particular, with the development of a new band at about 400 nm in the absorption spectrum (see Fig. 1b), typical of a polyconjugated chromophore. Similar results were obtained by performing the ^{1}H NMR titration of **2** with acetate in d^6-DMSO.

The interaction of acetate with **2** is pictorially illustrated in Scheme 2.

The acidity of receptor **2** was also investigated in water solution, by performing potentiometric and pH-spectrophotometric titrations on **2** in CH_3CN/water mixture (9/1 v/v, 0.1 M TBA–PF_6).

In Fig. S8,† the family of the UV-vis. spectra, taken over the course of the pH-spectrophotometric titration of **2**, and the distribution diagram with the superimposed pH-spectrophotometric profile (at 400 nm) are reported. Only one deprotonation step is observed, corresponding to pK_a = 13.1(2), attributable to the formation of the methine species **2**–**C**. On the contrary, no deprotonation was observed on performing analogous titrations on receptors **1** and **3**.

X-Ray diffraction studies

The crystal and molecular structure of receptor **1** has been assessed through X-ray diffraction study of a colourless crystal obtained by slow evaporation of a solution of **1** in CD_3CN. As shown by the ORTEP view in Fig. 4(a), the two aromatic rings linked to the urea group are not placed according to a coplanar arrangement. In particular, the dihedral angle between the urea group and the 4-(trifluoromethyl)phenyl arm is 21.4(2)°, whereas the dihedral angle between urea and the other aromatic ring is 37.4(2)°. However, the 4-(trifluoromethyl)phenyl is bent with respect to the urea group in a way that maintains the *ortho* C–H fragment at a distance suitable to establish a single intramolecular C(aryl)–H···O interaction. The observed 2.35(1) Å H···O distance is lower than the value of 2.40 Å, which can be considered as an upper limit to reveal the presence of an intramolecular C(aryl)–H···O hydrogen bond.[14]

Intramolecular C(aryl)–H···O interactions occur frequently in planar diaryl-ureas and often result in the exclusion of the C=O group from intermolecular N–H···O urea–urea H-bonds.[15]

Therefore, the urea N–H groups are available for the interaction with other molecular moieties having H-bond acceptor groups (*e.g.*, the N atom of pyridyl groups). As a consequence, the common urea tape bifurcated N–H···O hydrogen bond motif disappears and other supramolecular synthons, also involving acceptor groups different from the carbonyl atoms, can be identified.[12] Actually, in the crystal structure of **1**, the bifurcated N–H···O urea tape is not present, whereas the two hydrogen bond motifs shown in Scheme 3 can be recognized; they can be

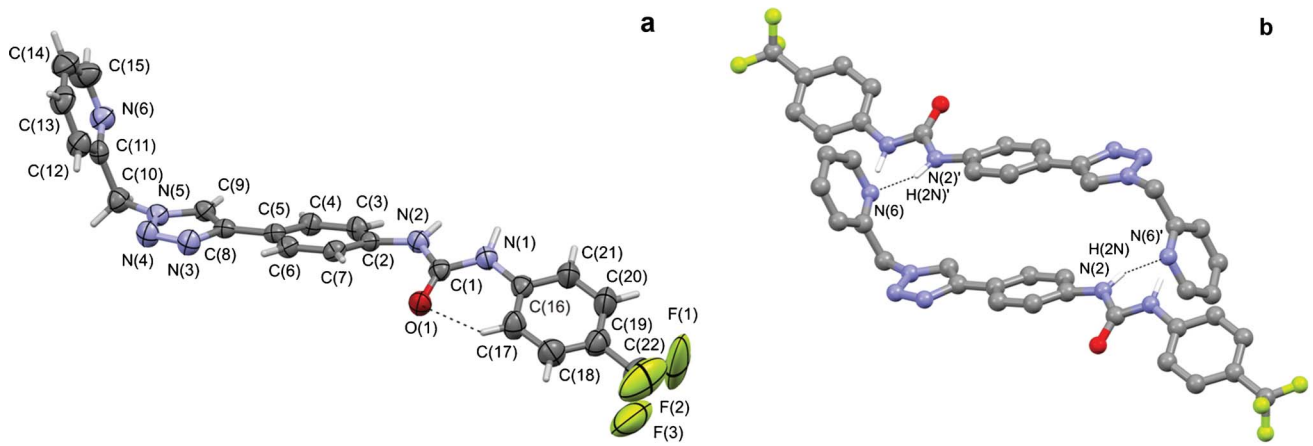
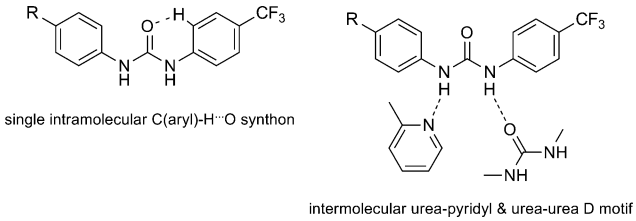


Fig. 4 (a) An ORTEP view of the molecular structure of the **1** receptor (ellipsoids are drawn at the 50% probability level, atom names are shown only for non-hydrogen species). Dashed line indicates the intramolecular C(aryl)–H···O hydrogen bond involving the carbonyl oxygen and the proton of the *ortho* C–H aromatic group; the distance between the aromatic proton and the carbonyl oxygen is 2.35(1) Å. (b) A simplified sketch of the molecular dimer that forms between two molecules of **1** related by a centre of inversion (names are only reported for atoms involved in hydrogen bonds; only H atoms belonging to the urea groups are shown). Features of the N–H···N urea–pyridyl interactions are: N(2)···N(6)′ 3.07(1) Å, H(2 N)···N(6)′ 2.16(2) Å, N(2)–H(2 N)···N(6)′ 158.3(15)°; symmetry code: (′) = –*x*, 1–*y*, 1–*z*.



Scheme 3 The hydrogen bond motifs occurring in the crystal of **1**.

described as a single intramolecular C(aryl)–H···O synthon and an intermolecular urea–pyridyl and urea–urea D motif.[12]

In particular, the single N–H···N urea–pyridyl interaction involves as the H-donor group one of the two N–H groups of the urea moiety and, as H-acceptor, the N atom of a 2-pyridyl terminal group of another receptor's molecule. On the basis of the donor···acceptor separation ($d_{D\cdots A}$ = 3.07(1) Å), the urea–pyridyl interaction turns out to be the strongest intermolecular H-bonding interaction of the crystal structure and leads to the formation of a molecular dimer, in which two molecules of **1** are related by a center of inversion, Fig. 4(b). Actually, the urea–urea D motif involving the carbonyl oxygen as H-acceptor and the N–H group not interacting with the pyridyl moiety as H-donor is characterized by a donor···acceptor separation ($d_{D\cdots A}$ = 3.18(1) Å) longer than that observed for the urea–pyridyl interaction. These weak urea–urea H-bonds lead to the formation of rows of overlapping **1** molecular receptors, extending along the direction of the *a* crystallographic axis (see Fig. S9†).

Conclusions

The comparison of the anion binding tendencies of receptors **1–3** has brought some significant results. In the case of receptor **1**, the presence of the H-acceptor pyridyl group in the proximity of urea promotes the formation of H-bonding interactions in the solid state, responsible for the aggregation of the receptor molecules which self-assemble into dimers. These intermolecular interactions are likely to be present also in solution and may be responsible for the lower anion binding constants measured for **1** with respect to **3**. The pyridyl fragment may also take part in the interactions with anions, acting as H-bond acceptor, thus leading to adducts of different stoichiometries. This behavior was observed in the ^{1}H NMR titration with dihydrogen phosphate, with which **1** forms both 1 : 1 and 2 : 1 receptor:anion adducts. As expected, the methylation of the pyridyl group enhances anion affinity, as evidenced by the comparison of the binding constants of **2** with those of **1**. The increased anion affinity of **2** is connected to the higher acidity of the urea group. As a matter of fact, pyridinium is a stronger EWG with respect to pyridine and, by consequence, its polarization effect on the N–H bonds of urea is more effective. Even if the C–H bonds of the pyridinium unit are potentially H-donors, no clear evidence for the participation of pyridinium in the interaction with the anions has been found.

On the other hand, both UV-vis. and ^{1}H NMR titrations indicate a strong interaction between the anion and the urea moiety, leading to 1 : 1 adducts. The effect of pyridinium on the receptor's acidity is observed with basic anions (*e.g.* acetate and fluoride). In the titration with acetate, the first equivalent is bound by the urea unit, leading to a 1 : 1 adduct. After the equivalence, excess anion promotes a proton transfer process involving the methylene group connecting the pyridinium unit to the receptor's skeleton, thus leading to the formation of a neutral methine derivative. Quite interestingly, deprotonation does not affect the urea moiety, thus preserving the 1 : 1 adduct, as evidenced by the chemical shifts of the N–H protons in the final ^{1}H NMR spectrum.

In conclusion, among anion receptors, for the first time deprotonation does not involve the H-donor moiety (*e.g.* urea), but occurs on a different acidic site of the receptor's skeleton (*e.g.* a –CH_2– fragment).

Moreover deprotonation (i) takes place in the presence of excess anion, (ii) preserves the 1 : 1 adduct and (iii) is accompanied by the development of an intense yellow colour. These findings offer the prospect of applying receptor **2** to monitoring both bound anion (through the urea unit) and excess anion in solution (through the development of the methine species).

Experimental section

General

All reagents for syntheses were purchased form Aldrich/Fluka and used without further purification. All reactions were performed under dinitrogen. Mass spectra were acquired on a Thermo-Finnigan ion trap LCQ Advantage Max instrument equipped with an ESI source. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker ADVANCE 400 spectrometer (operating at 9.37 T, 400 MHz). UV-vis. spectra were run on a Varian Cary 50 SCAN spectrophotometer, with quartz cuvettes of the appropriate path length (1 or 0.1 cm) at 25.0 ± 0.1 °C under inert conditions. Solvents were dried by common methods. Syntheses of receptors **1** and **2** are available in the ESI.† The synthesis **3** has been already reported.[10]

Spectrophotometric titrations

All titrations were performed at 25 °C. For the determination of binding constants, the solution of receptor was titrated with a 100-fold more concentrated solution of the anion, as its TBA salt. After each addition of a sub-stoichiometric amount of anion, the UV-vis. spectrum was recorded. The concentration of the receptor solution was chosen on the basis of the *p*-parameter (p = [concentration of complex]/[maximum possible concentration of complex]), which should range between 0.2 and 0.8.[16] Titration data were processed with the Hyperquad package[11] to determine the equilibrium constants.

^{1}H NMR titrations

All measurements were performed at 25 °C in CD_3CN. For the determination of binding constants, receptor was titrated with a 100-fold more concentrated solution of the anion, as its TBA salt. After each addition of a sub-stoichiometric amount of anion, the ^{1}H NMR spectrum was recorded.

Potentiometric and pH-spectrophotometric titrations

All measurements were performed at 25 °C in CH_3CN : water mixture (1 : 1 v:v, 0.1 M TBA–PF_6). Titrations were performed under nitrogen atmosphere. In a typical experiment, 15 mL of a 5.0×10^{-4} M solution of the receptor were treated with an excess of a

1.0 M HNO_3 standard solution. Titrations were run by addition of 10 μL portions of standard 0.1 M NaOH, collecting 80–100 points for each titration. On each addition of standard 0.1 M NaOH, the UV-vis. spectrum of the solution was recorded. Prior to each potentiometric titration, the standard electrochemical potential ($E°$) of the glass electrode was determined in CH_3CN/water mixture (9/1 v/v, 0.1 M TBA–PF_6), by a titration experiment according to the Gran method.[17] Titration data (emf *vs.* mL of NaOH) were processed with the Hyperquad package to determine the equilibrium constants.[11]

X-Ray crystallographic studies

Diffraction data were collected at room temperature by means of an Enraf-Nonius CAD4 four-circle diffractometer, working with graphite monochromated Mo-Kα X-radiation ($\lambda = 0.71073$ Å). Crystal data for the receptor **1**: $C_{22}H_{17}F_3N_6O$; M 428.42; colourless; monoclinic, $P2_1/a$ (no. 14); $a = 8.751(3)$, $b = 10.633(2)$, $c = 21.676(6)$ Å; $V = 1983.2(9)$ Å^3; $T = 293$ K; $Z = 4$; $\rho_c = 1.468$ g cm^{-3}; μMo-Kα = 0.115 mm^{-1}; 3915 measured reflections, 3517 unique reflections (R_{int} 0.0258), 2637 strong reflections [$I_O > 2\sigma(I_O)$]; refined parameters = 295; R_1 and wR_2 (strong data) 0.0737 and 0.1688; R_1 and wR_2 (all data) 0.0992 and 0.1916. Data reductions (including intensity integration, background, Lorentz, and polarization corrections) were performed with the WinGX package.[18] Absorption effects were evaluated with the psi-scan method,[19] and absorption correction was applied to the data (0.926 and 0.990 min and max transmission factor). Crystal structure was solved by direct methods (SIR 97)[20] and refined by full-matrix least-squares procedures on F^2 using all reflections (SHELXL 97).[21] Anisotropic displacement parameters were refined for all non hydrogen atoms. Hydrogens belonging to C atoms were placed at calculated positions with the appropriate AFIX instructions and refined using a riding model. Hydrogens of the urea group were located in the final ΔF map and their position refined restraining the N–H distance to be 0.96 ± 0.01 Å.

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