Pyrrolylamidourea based anion receptors†‡

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The anion binding behaviour of a number of pyrrolylamidourea and thiourea compounds have been studied in DMSO solution. Mono-amidothioureapyrrole compounds were found to be deprotonated by basic anions such as fluoride, acetate, benzoate or dihydrogenphosphate with the structure of the deprotonated species elucidated by X-ray crystallography. 2,5-Bis-amidoureapyrroles were synthesized and found to be effective anion receptors for a range of putative anionic guests.

Introduction

The development of anion sensors and receptors has attracted a great deal of interest and effort from the supramolecular chemistry community due to the importance of anions in many biological and chemical processes.[1] Hydrogen-bond donating amide, pyrrole and urea/thiourea groups have been employed in a wide range of synthetic anion receptors and sensors and a variety of neutral hydrogen bond donor groups are employed in selective biological anion binding agents such as the sulfate binding protein.[2] Over recent years we have extensively studied the anion binding properties of 2,5-dicarboxamidopyrrole systems. These compounds have been found to be effective anion receptors showing selectivity for oxoanions in competitive solvent media (DMSO/water).[3] In the past few years, amidothiourea compounds have been used as anion receptors, and examples of selective colorimetric and fluorimetric anion sensors containing this motif have been reported.[4] Very recently Gunnlaugsson, Kruger and co-workers reported the use of a naphthalimide–amidothiourea derivative for colorimetric sensing of anions in highly competitive aqueous media.[5]

Continuing our efforts in producing new anion receptors and sensors we set out to synthesize a family of compounds containing both amidopyrrole and urea groups and to study their anion binding properties. Aspects of this work have been communicated recently.[6]

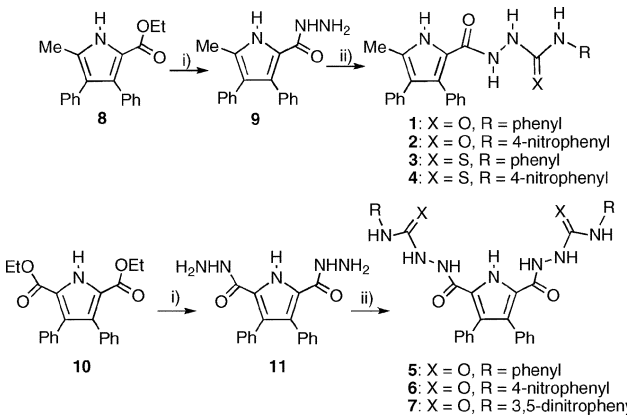
Results and discussion

Synthesis

We decided to produce a series of increasingly acidic compounds containing a 2-amido(thio)urea substituted pyrrole unit **1–4**, and also the 2,5-amidourea substituted pyrrole derivatives **5–7**. Nitroaromatic substituents were introduced in some of the hosts as chromophores which have the potential to signal the binding event by a change of colour produced by intramolecular charge transfer processes.[7] Receptors **1–7** were synthesized according to the route depicted in Scheme 1. 5-Methyl-3,4-diphenyl-1*H*-pyrrole-2-carboxylic acid ethyl ester **8**[8] and 3,4-diphenyl-1*H*-pyrrole-2,5-dicarboxylic acid diethyl ester **10**[9] were treated with an excess of hydrazine hydrate in refluxing ethanol to yield the corresponding carbohydrazide derivatives **9** and **11** as white, crystalline solids. Reaction of these compounds with the appropriate isocyanate or isothiocyanate gave receptors **1–7** in moderate to good yields.

Crystals of compound **9** were grown by slow evaporation of a methanolic solution of the receptor. In the solid state, compound **9** forms hydrogen-bonded chains by dimerization of the amidopyrrole and hydrazine groups through N–H···O interactions and N–H···N interactions (Fig. 1). Representative bond distances and angles are: N4···O1 2.844(4) Å, N1···O2 2.854(4) Å, N–H···O with bond angles being 158(3) and 159(3)°, respectively, and N2···N6^{i} 3.007(4) Å, N5···N3^{ii} 3.072(4) Å with N–H···N with bond angles of 141(3) and 142(3)°, respectively (Fig. 1).

Crystals of compound **2** were obtained by slow evaporation of a methanol solution of the receptor. In the solid state the pyrrole N–H group and the carbonyl group of the amido moiety adopt a *cis* arrangement, with a torsion angle of 94° between the planes defined by the pyrroleamido and urea functionalities (Fig. 2).[10] This receptor is further arranged



Scheme 1 Synthesis of receptors **1–7**. (i) NH_2NH_2/EtOH; (ii) RCNX (X = O or S)/$CHCl_3$.

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† The HTML version of this article has been enhanced with colour images.

‡ Electronic supplementary information (ESI) available: Additional experimental data. See DOI: 10.1039/b603223k

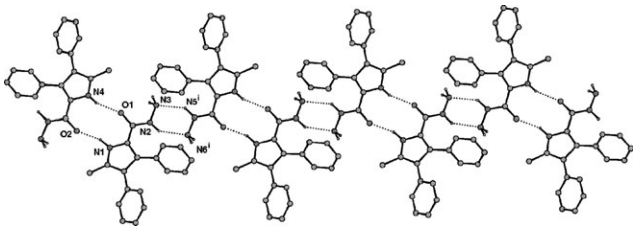

Fig. 1 Hydrogen bonded chains, running along the *a* axis, formed by compound **9** in the solid state (symmetry code: (i) $-1 + x, y, z$).

into hydrogen-bonded sheets through urea–urea and amidopyrrole–amidopyrrole interactions with N···O distances of N1···O1^{i} 2.857(2) Å, N3–H3···O2^{ii} 2.811(2) and N4···O2^{ii} 3.003(2) Å and N–H···O bond angles of 161.3, 135.5 and 151.0°, respectively (symmetry codes: (i) $-x, -y + 1, -z + 1$; (ii) $-x, y - 1/2, -z + 1/2$) (Fig. 3).

Crystals of compound **5** were grown by slow evaporation of an acetonitrile solution of the receptor and was also characterized by means of X-ray diffraction. The molecule lies about a twofold axis through the pyrrole N–H bond. The pyrrole N–H and carbonyl groups adopt a similar *cis* conformation to receptor **2** in the solid state (Fig. 4). In this case, the urea groups form hydrogen-bonded chains through DDA contacts, with N···O bond distances of N1···O1^{ii} 2.8975(19) Å and

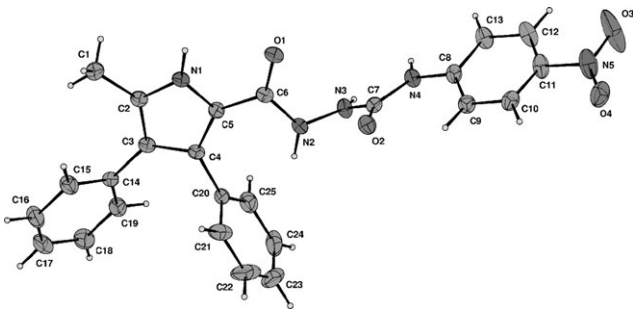

Fig. 2 X-ray crystal structure of compound **2**. Thermal ellipsoids are drawn at the 50% probability level.

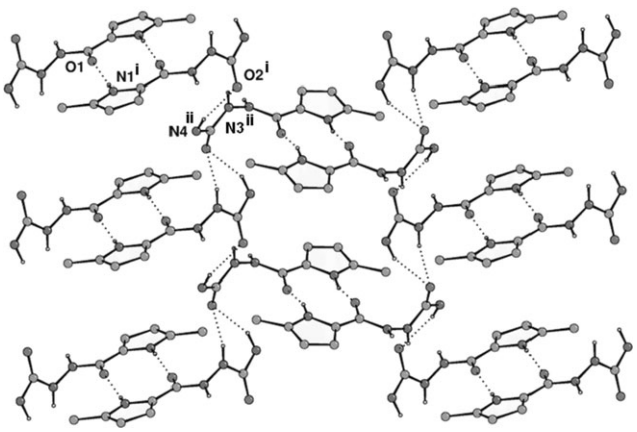

Fig. 3 Hydrogen bonded sheets formed by compound **2** in the solid state viewed looking down the *a* axis. Non-acidic hydrogen atoms, phenyl and nitrobenzene groups are omitted for clarity (symmetry codes: (i) $-x, 1 - y, 1 - z$; (ii) $x, 0.5 - y, 0.5 + z$).

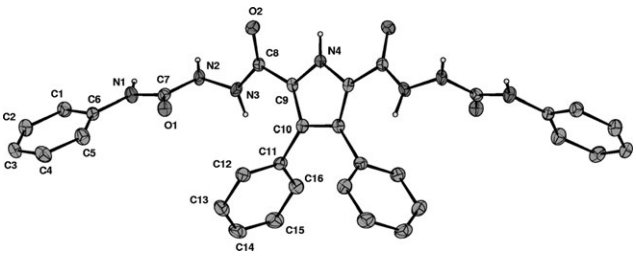

Fig. 4 X-Ray crystal structure of compound **5**. Thermal ellipsoids are drawn at the 50% probability level.

N2···O1^{ii} 2.8744(18) Å and N–H···O bond angles N1–H1A···O1 156.5° and N2–H2A···O1^{ii} 142.0°, preventing the participation of the 2,5-amidopyrrole moiety in any hydrogen bond (Fig. 5) (symmetry codes: (ii) $x, -y, z - 1/2$).

Anion binding studies

The anion binding abilities of the new receptors were studied by means of UV-Vis and ^{1}H NMR titration experiments using DMSO and DMSO-d_6 as solvents, respectively. Upon addition of anions to compound **1**, no significant changes were observed in either UV/Vis or ^{1}H NMR spectra, indicating that the receptor is not interacting significantly with the putative anionic guests in this competitive solvent medium. The ^{1}H NMR spectra of the more acidic 4-nitrophenyl substituted derivative **2** showed a significant broadening of all the NH signals upon addition of tetrabutylammonium fluoride, acetate, benzoate and dihydrogenphosphate, indicating an interaction between the receptor and the anions through hydrogen bonds. These changes are accompanied by a gradual but visible change of colour from an almost colourless solution to dark yellow. UV-Vis spectra reflected these changes with an increase of the absorbance in the 450 nm region and appearance of two isosbestic points at *ca.* 280 and 340 nm (Fig. 6). The changes in the absorbance as function of the concentration of anion added can be fitted to a 1 : 1 binding equilibrium model,[11] giving association constants of 3010 M^{-1} (F^{-}), 5580

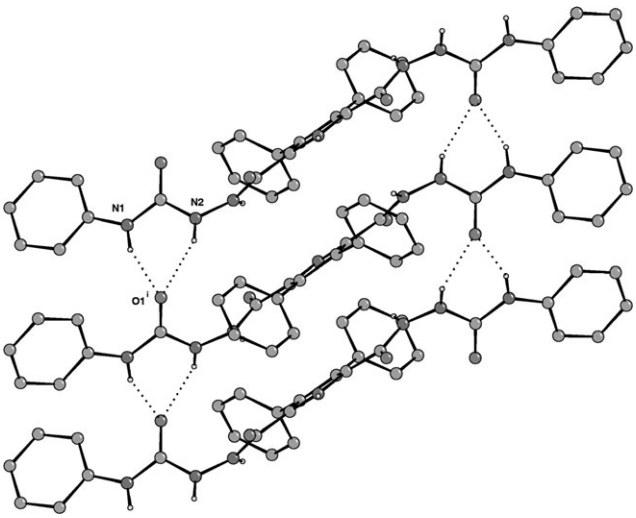

Fig. 5 Hydrogen bonded chain defined by compound **5** along the crystallographic *c* axis (symmetry code: (i) $x, -y, -0.5 + z$).

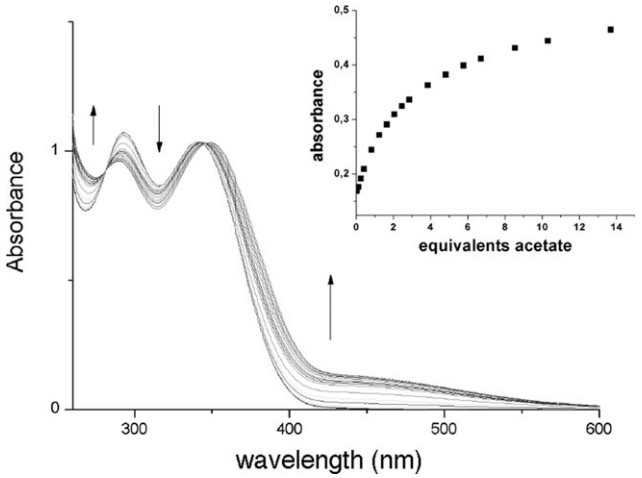

Fig. 6 UV-Vis absorption spectrophotometric titration of compound **2** with tetrabutylammonium acetate in DMSO at 25 °C. Inset: increase of absorbance at 390 nm *vs*. equivalents of acetate.

Table 1 Association constants K_a (M^{-1}) for receptors **2** and **5–7** with different anions (added as tetrabutylammonium salts) at 298 K in DMSO[a] as determined by UV/Vis titration techniques

	2	**5**	**6**	**7**
F^-	3010	3890	8590	15 300
$C_6H_5COO^-$	1440	5000	9630	16 600
CH_3COO^-	5880	3610	6830	13 800
$H_2PO_4^-$	1060	4010	8220	13 000

[a] Errors estimated to be no more than ±10%.

M^{-1} ($CH_3CO_2^-$), 1440 M^{-1} ($PhCO_2^-$) and 1060 M^{-1} ($H_2PO_4^-$) (Table 1). Smaller changes in the UV/Vis spectra were observed upon addition of less basic anions (Cl^-, Br^- or HSO_4^-) that were insufficient to provide a reliable value of the association constant.

The analogous thiourea receptors **3** and **4** were evaluated, and addition of F^-, CH_3COO^-, $PhCO_2^-$ or $H_2PO_4^-$ as tetrabutylammonium salts to solutions of compound **3** or **4** in DMSO resulted in dramatic changes in the UV-vis spectra of the receptors, with new intense absorption bands appearing at 330 and 430 nm, respectively. Following the changes in the absorbance as function of the concentration of anion resulted in a steep curve, preventing the calculation of an apparent stability constant. In the case of compound **4**, a distinctive change of colour from yellow to red is observed (see Fig. 7 and 8).

Proton NMR titration experiments in DMSO-d_6 shed light on the interaction of the anions and receptor **4**. Instead of a broadening of the NH signals, as was observed with compound **2**, a new set of three sharp signals at 11.3, 9.6 and 8.7 ppm, corresponding to three NH groups appeared (Fig. 9) upon addition of F^-, CH_3COO^-, $PhCO_2^-$ or $H_2PO_4^-$, suggesting the formation of a new compound.

Red crystals were formed upon slow evaporation of a dichloromethane–diethyl ether solution compound **4** containing one equivalent of tetrabutylammonium fluoride. The X-ray crystal structure showed that the crystals were the tetrabutylammonium salt of $(\mathbf{4} - H^+)^-$ and that deprotonation of the thiourea had occurred at N103 (NH hydrogens were located in the X-ray crystal structure, see Fig. 10). A proton NMR the tetrabutylammonium salt of $(\mathbf{4} - H^+)^-$ in DMSO-d_6 gave an identical spectrum to those obtained after the addition of one equivalent of tetrabutylammonium fluoride, acetate, benzoate or dihydrogen phosphate, evidence that leads us to suggest that these four anions deprotonate compound **4** in DMSO solution. Crystallisation of compound **4**

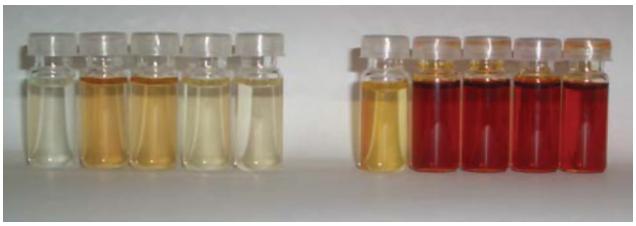

Fig. 7 DMSO solutions (2×10^{-3} M) of compounds **2** (left group) and **4** (right group). From left to right within each group: solution of receptor, and solution of receptor in the presence of one equivalent of tetrabutylammonium fluoride, acetate, benzoate and dihydrogen phosphate.

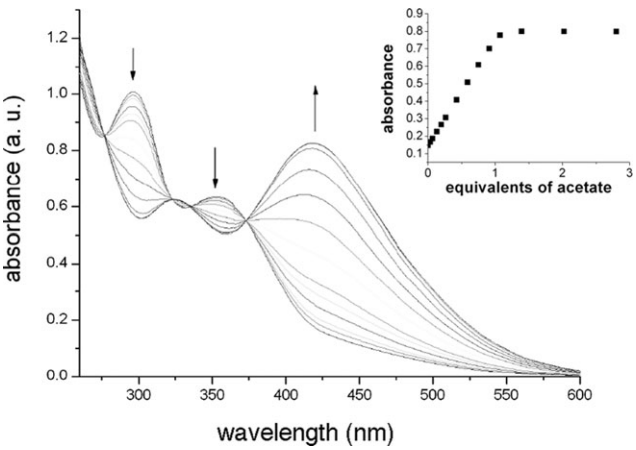

Fig. 8 UV-Vis absorption spectrophotometric titration of compound **4** with tetrabutylammonium acetate in DMSO at 25 °C. Inset: variation of absorbance at 450 nm *vs*. equivalents of acetate.

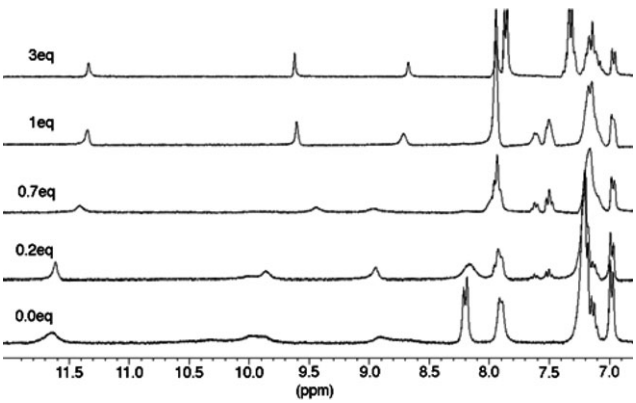

Fig. 9 Stack plot of the ^1H NMR spectra of compound **4** in the presence of increasing amounts of tetrabutylammonium benzoate recorded in DMSO-d_6.

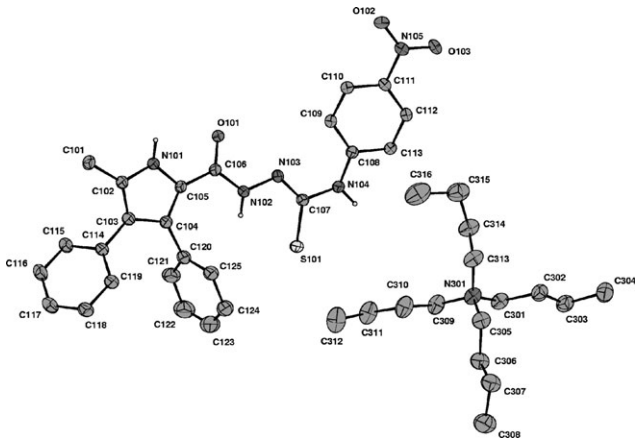

Fig. 10 X-Ray crystal structure of the tetrabutylammonium salt of deprotonated compound **4**. Thermal ellipsoids are drawn at the 35% probability level. The deprotonated species adopts an essentially planar conformation. Only part of the asymmetric unit is shown; the full unit comprises two anions in general positions, one cation in a general position, one half cation ordered about a twofold axis, and another half cation disordered about a twofold axis.

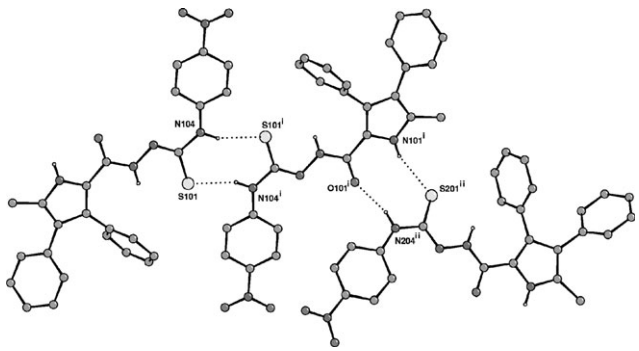

Fig. 11 Part of the hydrogen-bonded chain defined by the deprotonated amidothiourea $(\mathbf{4} - H^+)^-$ in the solid state (symmetry codes: (i) $1 - x, 1 - y, -z$, (ii) $1 + x, y, z$).

from a solution containing one equivalent of tetrabutylammonium benzoate also led to the formation of identical red crystals and also colourless needles which proved to be benzoic acid. The deprotonated species appears to be stabilized by an intramolecular hydrogen bond from the CH at the *ortho*-proton of the 4-nitrophenyl group (N103···C109 2.823 Å) with the deprotonated species now adopting an essentially planar arrangement (Fig. 10). In the solid state the receptor forms hydrogen-bonded chains through interactions of the amidopyrrole and thiourea groups (Fig. 11) with N102···S101 2.881(5) Å, N101···$S201^i$ 3.311(5) Å, N204···$O101^i$ 2.894(6) Å and N201···$O201^{ii}$ 2.826(6) Å; N102–H102···S101 11.7°, N101–H101···$S201^i$ 157.9°, N204–H204···$O101^i$ 163.3° and N201–H201···$O201^{ii}$ 159.8° (symmetry codes: (i) $-x, y, -z + 1/2$; (ii) $-x + 1, y, -z - 1/2$).

The increased acidity of the thiourea N–H groups resulted in the deprotonation of the receptor upon addition of anions with the red colour the result of the formation of the amidourea anion and not the formation of a receptor–anion complex. This may be due to the non-convergent nature of the hydrogen bonding array in this system which fails to adopt a geometry suitable for the stabilization of a hydrogen-bonded complex, leading to a neat deprotonation. We[12] and other research groups[13] have reported colour changes in different receptors identified as deprotonation processes, however, in previous studies, two equivalents of anion (frequently fluoride) have been necessary to achieve deprotonation (the formation of HF_2^- drives the deprotonation process in these cases). This is not the case with compound **4**, as deprotonation is complete after addition of only one equivalent of anionic guest. Receptor **3** shows the same behaviour in the ^{1}H NMR titration experiments, but complete deprotonation is not achieved until an excess of the anion is added (presumably due to this compound being less acidic than **4**). When UV-Vis titration experiments of compound **4** were performed employing a 9 : 1 mixture of DMSO–water a virtually equivalent family of spectra was obtained, indicating that the same 'neat' deprotonation process is occurring in this solvent media. Solubility problems prevented the use of more water-rich mixtures.

Disubstitution of the pyrrole ring in compounds **5–7**, should result in a more favourable cleft-like binding mode and increased affinity for anions was anticipated. In order to avoid deprotonation processes in the bis-substituted pyrrole compounds, only urea derivatives were prepared. Unlike monosubstituted derivative **1**, addition of tetrabutylammonium fluoride, acetate, benzoate and dihydrogenphosphate to compound **5** produced a significant broadening of all the NH signals in the ^{1}H NMR spectrum (Fig. 12) with similar changes being observed in the case of receptors **6** and **7**. This broadening of signals in the ^{1}H NMR spectra precluded the calculation of association constants of anions with these receptors using this technique.

Changes in the UV/Vis spectra of the bis-substituted compounds were seen upon addition of tetrabutylammonium anion salts, consisting in an increase of the absorbance in the 330 nm region for derivatives **5** and **7** and in the 400 nm region for the 4-nitrophenyl substituted compound **6** (Fig. 13) with all the putative anionic guests (see ESI‡ for more details). The UV/Vis titrations all fit satisfactorily to a 1 : 1 receptor : anion binding model and the stability constants are calculated on this basis. It is however possible that other equilibria are present in solution and hence these values should be treated with caution (Table 1). Nonetheless, the results show that while compounds **5–7** show an enhanced affinity for anions as compared to the mono-substituted derivative **2**, they are not selective under these experimental conditions.

Conclusions

There has been intense interest recently in the use of amido (thio)ureas as anion sensors and also in the interaction of basic anions with neutral hydrogen-bond donor systems as in some cases deprotonation occurs after addition of two equivalents of basic anion. In this paper we have shown that a pyrrolylamidothiourea is deprotonated upon addition of only *one* equivalent of anions such as acetate and dihydrogen phosphate. This work serves to illustrate that care must be taken when studying anion receptors containing acidic neutral hydrogen bond donor groups as deprotonation processes can

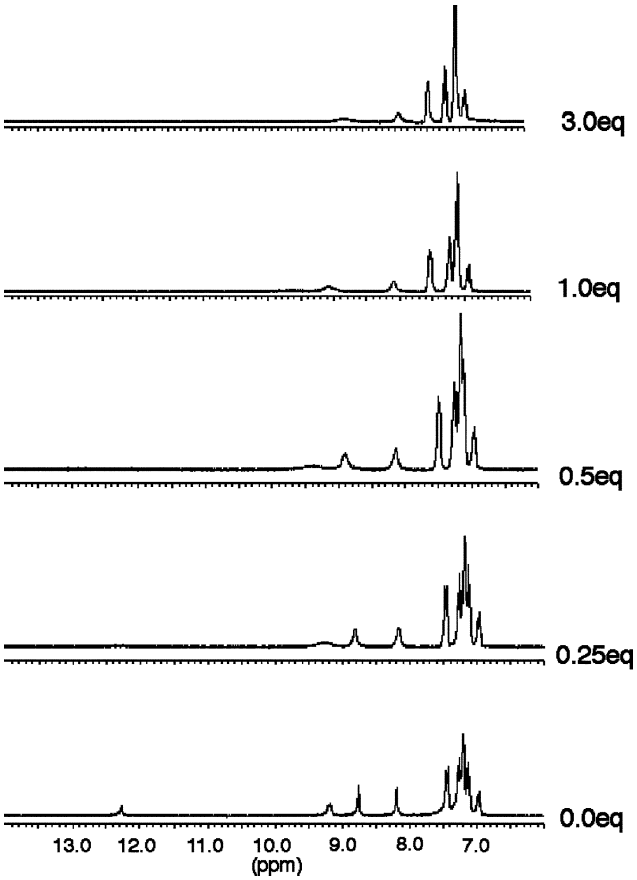

Fig. 12 Stack plot of the ^{1}H NMR spectra of compound **5** in the presence of increasing amounts of tetrabutylammonium fluoride recorded in DMSO-d_6.

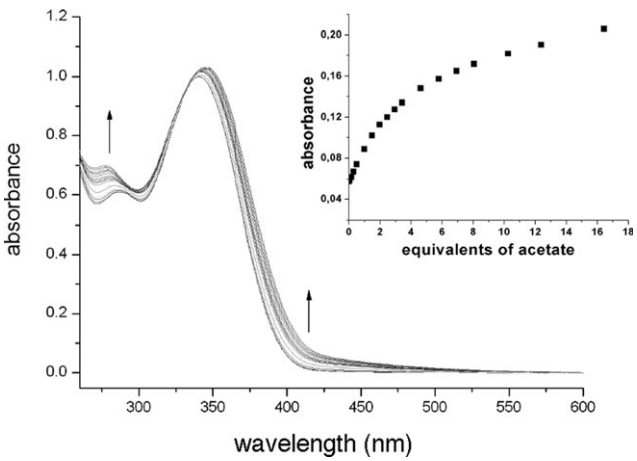

Fig. 13 UV-Vis absorption spectrophotometric titration of compound **6** with tetrabutylammonium acetate in DMSO at 25 °C. Inset: change of absorbance at 390 nm *vs.* equivalents of acetate.

occur with a range of different anions. Pyrroles functionalised with two amidourea groups function as anion receptors in DMSO but are not selective in their anion complexation properties.

Experimental

General

^{1}H and ^{13}C NMR experiments were recorded on a Bruker AV-300 NMR spectrometer. Chemical shifts are reported in ppm and referenced to solvent. Deuterated solvents were purchased from Apollo Ltd. Reagents were purchased from the Aldrich Chemical Co. and used without further purification. Elemental analyses were conducted by Medac Ltd. Mass spectrometry was carried out at the University of Southampton Mass Spectrometry Service. UV-Vis absorption spectra were recorded on a Shimadzu UV-1601 spectrometer.

Data obtained from UV-Vis titration experiments were processed using Origin 7.0 software package. For further details and titration curves see ESI.‡

Syntheses

5-Methyl-3,4-diphenyl-1*H*-pyrrole-2 carbohydrazide 9. 5-Methyl-3,4-diphenyl-1*H*-pyrrole-2 carboxylic acid ethyl ester (1 g, 3.46 mmol) was added to a large excess of hydrazine hydrate (5 mL, 100 eq.). Enough ethanol to produce dissolution was added and the reaction was heated at reflux for 48 h, and then allowed to cool to room temperature. 100 mL of water was added, inducing precipitation of the product as a white crystalline solid. This was collected by filtration, washed with water (3 × 10 mL) and dried (717 mg, 71%). Microanalysis: Calc. for $C_{18}H_{17}N_3O$: C, 74.2; H, 5.9; N, 14.4. Found: C, 74.1; H, 5.9; N, 14.2%. ^{1}H NMR ($CDCl_3$): δ 9.67 (br s, 1H, pyrrole NH), 7.26–6.91 (m, 10H, Ar H), 6.62 (br s, 1H, NH), 3.79 (br s, 2H, NH_2), 2.29 (s, 3H, CH_3). Solubility problems precluded the acquisition of a ^{13}C NMR spectrum. MS (ES^+): m/z 605.1 ($2M + Na^+$). Suitable crystals for X-ray diffraction were obtained by slow evaporation of a methanol solution of the compound.

3,4-Diphenyl-1*H*-pyrrole-2-dicarbohydrazide 11. 3,4-Diphenyl-1*H*-pyrrole-2,5-dicarboxylic acid diethyl ester (334 mg, 0.92 mmol) was mixed with a large excess of hydrazine hydrate (8 mL) and enough ethanol was added to achieve dissolution (approx. 10 mL). The reaction was heated at reflux for 48 h and then allowed to cool. Water was then added (100 mL) and a precipitate formed. This was collected, washed with water (3 × 10 mL) and dried to give a white solid (234 mg, 76%). Microanalysis: Calc for $C_{18}H_{17}N_5O_2$: C, 64.5; H, 5.1; N, 20.9. Found: C, 64.3; H, 5.0; N, 21.0%. ^{1}H NMR (DMSO-d_6): δ 11.75 (br s, 1H, pyrrole NH), 8.41 (s, 2H, NH), 7.18 (m, 6H, Ar H), 7.06 (m, 4H, Ar H), 4.32 (s, 4H, NH_2). Solubility problems precluded the acquisition of a ^{13}C NMR spectrum. MS (ES^+): m/z 336.4 ($M + H^+$).

2-(5-Methyl-3,4-diphenyl-1*H*-pyrrole-2-carbonyl)-*N*-phenylhydrazinecarboxamide 1. Phenyl isocyanate (76 μL, 0.70 mmol) was dissolved in chloroform, and the solution degassed for 10 min. 5-Methyl-3,4-diphenyl-1*H*-pyrrole-2-carbohydrazide (203 mg, 0.70 mmol) was added, and the reaction stirred at room temperature for 24 h. A precipitate formed, which was collected by filtration, washed with dichloromethane (3 × 10 mL) and dried affording a white solid, 137 mg, yield 46%. Microanalysis: Calc. for $C_{25}H_{22}O_2N_4 \cdot H_2O$: C, 70.1; H, 5.65;

N, 13.1. Found: C, 70.1; H, 5.2; N, 13.1%. ^{1}H NMR (DMSO-d_6): δ 11.67 (s, 1H, NH), 8.72 (s, 1H, NH), 8.30 (br s, 1H, NH), 8.10 (s, 1H, NH), 7.48 (m, 2H, Ar H), 7.25 (m, 10H, Ar H), 7.04 (m, 2H, Ar H), 2.31 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 180.5, 160.6, 138.9, 134.8, 134.6, 130.7, 129.8, 128.9, 128.2, 127.9, 127.0, 126.6, 125.6, 124.9, 122.4, 118.7, 11.7. MS ES$^+$: m/z 433.2 (M + Na$^+$), 843.4 (2M + Na$^+$), 1253.8 (3M + Na$^+$). ES$^-$: m/z 409.3 (M − H$^+$)$^-$.

2-(5-Methyl-3,4-diphenyl-1*H*-pyrrole-2-carbonyl)-*N*-(4-nitrophenyl)hydrazinecarboxamide 2. 4-Nitrophenyl isocyanate (115 mg, 0.70 mmol) was dissolved in chloroform (10 mL) and degassed for 10 min. 5-Methyl-3,4-diphenyl-1*H*-pyrrole-2-carbohydrazide (204 mg, 0.70 mmol) was added and the reaction stirred at room temperature for 24 h. A precipitate formed, which was collected by filtration, washed with dichloromethane (3 × 10 mL) and dried. A cream powder was produced, 280 mg, 87% yield. Microanalysis: Calc. for: $C_{25}H_{21}N_5O_4$: C, 65.9; H, 4.65; N, 15.4. Found: C, 65.5; H, 4.6; N, 15.05%. ^{1}H NMR (DMSO-d_6): δ 11.62 (s, 1H, NH), 9.43 (br s, 1H, NH), 8.43 (br s, 1H, NH), 8.33 (br s, 1H, NH), 8.17 (d, 2H, Ar H, J = 9.15 Hz), 7.71 (d, 2H, Ar H, J = 9.15 Hz), 7.18 (m, 8H, Ar H), 6.99 (m, 2H, Ar H), 2.27 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 160.9, 146.2, 141.1, 134.8, 134.7, 130.6, 129.8, 129.0, 127.8, 126.8, 126.6, 125.6, 125.0, 122.3, 118.6, 117.7, 11.7. MS ES$^+$: m/z 478.2 (M + Na$^+$), 933.5 (2M + Na$^+$). MS ES$^-$: m/z 454.3 (M − H$^+$)$^-$, 909.5 (2M − H$^+$)$^-$. Crystals suitable for X-ray crystallographic analysis were obtained by slow evaporation of a methanol solution of the product.

2-(5-Methyl-3,4-diphenyl-1*H*-pyrrole-2-carbonyl)-*N*-phenylhydrazinecarbothioamide 3. 5-Methyl-3,4-diphenyl-1*H*-pyrrole-2 carbohydrazide (200 mg, 0.686 mmol), was added to a degassed solution of phenyl isothiocyanate (82 μL, 0.69 mmol) in chloroform (10 mL). The reaction was stirred at room temperature for 72 h after which time a white precipitate had formed. This was collected by filtration, washed with dichloromethane and dried to produce 214 mg of product as a white powder, 73% yield. Microanalysis: Calc. for: $C_{25}H_{22}N_4OS$: C, 70.4; H, 5.2; N, 13.1. Found: C, 70.6; H, 5.3; N, 13.05%. ^{1}H NMR (DMSO-d_6): δ 11.60 (s, 1H, pyrrole NH), 9.62 (br s, 1H, NH), 9.52 (br s, 1H, NH), 8.86 (br s, 1H, NH), 7.46 (d, 2H, CH, J = 7.92 Hz), 7.33 (m, 2H, Ar H), 7.19 (m, 9H, Ar H), 6.97 (d, 2H, Ar H, J = 6.78 Hz), 2.26 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 180.5, 160.6, 138.9, 134.8, 134.6, 130.7, 129.8, 128.9, 128.2, 127.9, 127.0, 126.6, 125.6, 124.9, 122.4, 118.7, 11.7. MS ES$^+$: m/z 449.1 (M + Na$^+$), 875.3 (2M + Na$^+$).

2-(5-Methyl-3,4-diphenyl-1*H*-pyrrole-2-carbonyl)-*N*-(4-nitrophenyl)hydrazinecarbothioamide 4. 5-Methyl-3,4-diphenyl-1*H*-pyrrole-2-carbohydrazide (400 mg, 1.37 mmol) was added to a degassed solution of 4-nitrophenylisothiocyanate (248 mg, 1.38 mmol) in chloroform (15 mL). The reaction was stirred at room temperature for 24 h during which time a yellow precipitate formed. The solution was filtered and the precipitate washed with dichloromethane (3 × 10 ml) and dried *in vacuo* affording 550 mg of product as a yellow solid, 85% yield. Microanalysis: Calc. for: $C_{25}H_{21}N_5O_3S$: C, 63.7; H, 4.5; N, 14.85. Found: C, 63.7; H, 4.5; N, 14.9%. ^{1}H NMR (acetone-d_6): δ 11.92 (s, 1H, pyrrole NH), 9.60 (s, 1H, NH), 9.02 (s, br, 1H, NH), 8.09 (m, 5H, CH and NH), 7.21 (m, 10H, CH), 2.37 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 161.4, 146.3, 144.6, 135.8, 135.7, 131.7, 131.5, 131.0, 129.7, 128.8, 128.5, 128.0, 126.7, 124.8, 124.5, 123.3, 119.7, 12.0. MS ES$^+$: m/z 471.9 (M$^+$), 535.0 (M + Na$^+$ + CH_3CN), 965.1 (2M + Na$^+$).

***N*,*N*-Bis((phenylcarbomoyl)hydrazine)-3,4-diphenyl-1*H*-pyrrole-2,5-carboxamide 5.** 3,4-Diphenyl-1*H*-pyrrole-2-dicarbohydrazide **11** (75 mg, 0.22 mmol) was dissolved in DMSO (2.5 mL) and the solution degassed for 10 min. Phenyl isocyanate (49 μL, 0.45 mmol) was added and the reaction stirred at room temperature for 24 h. The reaction mixture was poured onto water and a fine white precipitate was formed. Gentle heating induced more precipitate to form which was collected by filtration giving an overall yield of product of 40.62 mg, 32%. X-Ray quality crystals were obtained by slow evaporation of an acetonitrile solution of the receptor. Microanalysis: Calc. for $C_{32}H_{27}N_7O_4 \cdot H_2O$: C, 65.0; H, 4.9; N: 16.6. Found: C, 65.4; H, 4.65; N, 16.55%. ^{1}H NMR (DMSO-d_6): δ 12.27 (br s, 1H, pyrrole NH), 9.18 (br s, 2H, NH), 8.76 (s, 2H, NH), 8.19 (s, 2H, NH), 7.45 (m, 4H, Ar H), 7.19 (m, 14H, Ar H), 6.97 (m, 2H, Ar H). ^{13}C NMR (DMSO-d_6): δ 160.5, 155.4, 139.4, 133.4, 130.6, 128.6, 127.6, 126.7, 122.8, 122.0, 118.7. MS ES$^+$: m/z 596.3 (M + Na$^+$), 1170.7 (2M + Na$^+$). ES$^-$: m/z 572.4 (M − H$^+$)$^-$, 1145.8 (2M − H$^+$)$^-$.

***N*,*N*-Bis((4-nitrophenylcarbomoyl)hydrazine)-3,4-diphenyl-1*H*-pyrrole-2,5-carboxamide 6.** 3,4-Diphenyl-1*H*-pyrrole-2-dicarbohydrazide **11** (50 mg, 0.15 mmol) was dissolved in DMSO (2.5 mL) and the solution degassed for 10 min. 4-Nitrophenyl isocyanate (50 mg, 0.30 mmol) was then added and the reaction stirred at room temperature for 72 h. The solution was poured onto water, left to stand and a white precipitate was formed. This was collected by filtration, washed repeatedly with dichloromethane and dried, affording a cream coloured solid as a DMSO solvate. Yield 75 mg, 74%. Microanalysis: Calc. for $C_{32}H_{25}N_9O_8 \cdot 2/3C_2H_6SO$: C, 55.9; H, 4.1; N, 17.6. Found: C, 56.1; H, 4.0; N, 17.4%. ^{1}H NMR (DMSO-d_6): δ 12.32 (br s, 1H, pyrrole NH), 9.57 (s, 2H, NH), 9.35 (br s, 2H, NH), 8.64 (s, 2H, NH), 8.23 (d, 4H, Ar H, J = 9.15 Hz), 7.77 (d, 4H, Ar H, J = 9.15 Hz), 7.22 (m, 10H, Ar H). ^{13}C NMR (DMSO-d_6): δ 160.4, 154.8, 146.2, 141.2, 133.3, 130.6, 127.8, 127.6, 126.7, 125.0, 122.8, 117.8. MS ES$^+$: m/z 686.3 (M + Na$^+$), 1349.9 (2M + Na$^+$). ES$^-$: m/z 662.3 (M − H), 1325.9 (2M − H$^+$)$^-$.

***N*,*N*-Bis((3,5-dinitrophenylcarbomoyl)hydrazine)-3,4-diphenyl-1*H*-pyrrole-2,5-carboxamide 7.** DMSO (2.5 mL) was degassed for 10 min and 3,4-diphenyl-1*H*-pyrrole-2-dicarbohydrazide **11** (69 mg, 0.21 mmol) and 3,5-dinitrophenyl isocyanate (86 mg, 0.41 mmol) were added. The solution, which initially turned an orange colour, was stirred at room temperature for 24 h. The reaction was poured onto water and a yellow precipitate formed. This was collected by filtration, affording 105 mg of the product as a yellow powder, 65% yield. Microanalysis: Calc. for $C_{32}H_{23}N_{11}O_{12} \cdot 3/2H_2O$: C, 49.2; H, 3.4; N, 19.7. Found: C, 49.3; H, 3.1; N, 19.3%. ^{1}H NMR (DMSO-d_6): δ 12.26 (br s, 1H, pyrrole NH), 9.80 (s, 2H,

NH), 9.32 (br s, 2H, NH), 8.84 (s, 4H, ArH), 8.84 (br s, 2H, NH), 8.42 (s, 2H, ArH), 7.14 (m, 10H, Ar H). ^{13}C NMR (DMSO-d_6): δ 160.36, 135.31, 148.21, 142.12, 133.28, 130.60, 127.91, 127.61, 126.75, 122.85, 117.84, 110.88. MS ES$^+$: m/z 776.2 (M + Na$^+$). ES$^-$: m/z 375.8 1/2(M − 2H$^+$), 752.3 (M − H$^+$)$^-$.

Crystallography

Data for **2**, **5** and **9** were collected on a BrukerNonius KappaCCD diffractometer mounted at the window of a Mo rotating anode. Data for the tetrabutylammonium salt of (**4** − H$^+$)− were collected on a Bruker SMART APEX2 CCD diffractometer at Daresbury SRS station 9.8 using a wavelength of 0.6814.[14]

Crystal data for 9. $C_{18}H_{17}N_3O$, M_r = 291.35, T = 120(2) K, monoclinic, space group $P2_1/n$, a = 10.990(4), b = 18.366(9), c = 15.123(4) Å, V = 3033(2) Å^3, D_c = 1.276 g cm^{-3}, μ = 0.081 mm^{-1}, Z = 8 (2 molecules in the asymmetric unit), reflections collected: 27627, independent reflections: 6610 (R_{int} = 0.1582), final R indices [$I > 2\sigma I$]: $R1$ = 0.0685, $wR2$ = 0.1249, R indices (all data): $R1$ = 0.2330. $wR2$ = 0.1765.

Crystal data for 2. $C_{25}H_{21}N_5O_4$, M_r = 455.47, T = 120(2) K, monoclinic, space group $P2_1/c$, a = 18.0210(4), b = 8.0777(2), c = 16.7769(4) Å, β = 115.5230(10)°, V = 2203.86(9) Å^3, D_c = 1.373 g cm^{-3}, μ = 0.096 mm^{-1}, Z = 4, reflections collected: 20202, independent reflections: 5054 (R_{int} = 0.0486), final R indices [$I > 2\sigma I$]: $R1$ = 0.0548, $wR2$ = 0.1218, R indices (all data): $R1$ = 0.0834. $wR2$ = 0.1352.

Crystal data for 5. $C_{32}H_{27}N_7O_4$, M_r = 573.61, T = 120(2) K, monoclinic, space group $C2/c$, a = 31.1616(11), b = 10.9342(4), c = 8.3276(3) Å, β = 104.131(2)°, V = 2751.58(1) Å^3, D_c = 1.373 g cm^{-3}, μ = 0.096 mm^{-1}, Z = 4, reflections collected: 18483, independent reflections: 3160 (R_{int} = 0.0560), final R indices [$I > 2\sigma I$]: $R1$ = 0.0481, $wR2$ = 0.1073, R indices (all data): $R1$ = 0.0695. $wR2$ = 0.1168.

Crystal data for the tetrabutylammonium salt of (4 − H$^+$)$^-$. $C_{41}H_{56}N_6O_3S$, M_r = 712.98, T = 120(2) K, monoclinic, space group $P2/c$, a = 22.9059(19), b = 8.5806(7), c = 40.738(3) Å, β = 93.308(2)°, V = 7993(11) Å^3, D_c = 1.185 g cm^{-3}, μ = 0.125 mm^{-1}, Z = 8, reflections collected: 43492, independent reflections: 9695 (R_{int} = 0.0869), final R indices [$I > 2\sigma I$]: $R1$ = 0.0901, $wR2$ = 0.2368, R indices (all data): $R1$ = 0.1344. $wR2$ = 0.2735.

CCDC reference numbers 292339–292341 and 602690.

For crystallographic data in CIF or other electronic format see DOI: 10.1039/b603223k

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