Acridinone-based anion receptors and sensors†

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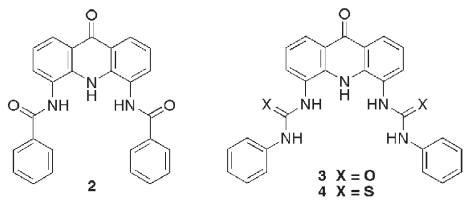
The interaction of a variety of acridinone derivatives containing hydrogen-bond donor groups in the 4- and 5-positions with anions demonstrate the potential of this new scaffold in anion receptor and sensor design.

Anion recognition and sensing is currently an area of intense interest and effort within the supramolecular chemistry community.[1] Compounds that contain neutral hydrogen bond donor groups such as amide,[2] urea[3] or thiourea[4] groups, have been shown to be particularly effective anion receptors in organic solution.[1–4] The acridinones[5] are a group of heterocyclic aromatic compounds that possess strong absorption and emission in the UV-vis region.[6–8] We decided to investigate the interaction of anions with a series of acridinone derivatives containing a convergent array of hydrogen bond donor groups (amides, ureas or thioureas) (**2–4**), and evaluate their potential as both anion receptors and sensors. Whilst this work was in progress, Morán and co-workers reported chloride selective sensing by a mixed amide/urea functionalised acridinone.[9]



4,5-Diamino-9(10H)-acridinone (**1**) was synthesised according to literature procedures.[10] The reaction of **1** with 3.0 equivalents of benzoyl chloride gave the 4,5-dibenzamido-9(10H)-acridinone (**2**) in 49% yield. Similarly, the urea and thiourea derivatives **3** and **4** were prepared in *ca.* 85% yield by the treatment of **1** with an excess of phenylisocyanate or phenylisothiocyanate respectively (see ESI for more details†).

The interactions of these compounds with anions were initially studied by ^{1}H NMR titration experiments. Aliquots of the tetrabutylammonium salts of the putative anionic guest (0.1 mol dm^{-3}) were added to a solution of acridinones **2–4** (0.01 mol dm^{-3}) in DMSO-d_6–0.5% water. The ^{1}H NMR spectra of the amide derivative **2** showed a significant broadening of all the NH signals upon addition of tetrabutylammonium fluoride, acetate, benzoate and dihydrogen phosphate. In all these cases the spectra obtained after the addition of only one equivalent of the corresponding anion salt are nearly identical to those obtained after the addition of one equivalent of tetrabutylammonium hydroxide to a DMSO-d_6–0.5% water solution of compound **2** (see ESI†), evidence that leads us to suggest that these four anions deprotonate the amide derivative **2** in DMSO solution.[11] Only small changes in the ^{1}H NMR spectra were observed upon addition of less basic anions (Cl^-, Br^- or HSO_4^-) suggesting that these anions interact weakly with compound **2**.

During the ^{1}H NMR experiments a gradual change of colour from a pale to dark yellow was observed. UV-vis absorption spectrophotometric titrations of **2** with tetrabutylammonium salts of acetate, benzoate, dihydrogen phosphate and fluoride in DMSO reflected these changes with an increase of the absorbance in the 350, 435 and 460 nm regions of the spectrum and the appearance of two isosbestic points at approximately 370 and 410 nm. Following the changes in the absorbance as a function of the concentration of anion resulted in a well defined steep curve, which suggests that the deprotonation process occurs after the addition of one equivalent of the basic anion salt (see ESI†).

The structure of the deprotonated derivative tetrabutylammonium **2**$-H^+$ was confirmed by X-ray crystallography‡ (Fig. 1). Crystals of **2**$-H^+$ were obtained by evaporation of a heated DMSO–0.5% water solution of compound **2** in the presence of an excess of tetrabutylammonium chloride.[12] The structure of **2**$-H^+$ in the solid state shows the two amide units coplanar with respect the acridinone moiety, with the NH groups orientated to the deprotonated central nitrogen N2. Notably the proton NMR of the **2**$-H^+$ crystals obtained in DMSO-d_6 gave an identical spectrum to those obtained after the addition of one equivalent

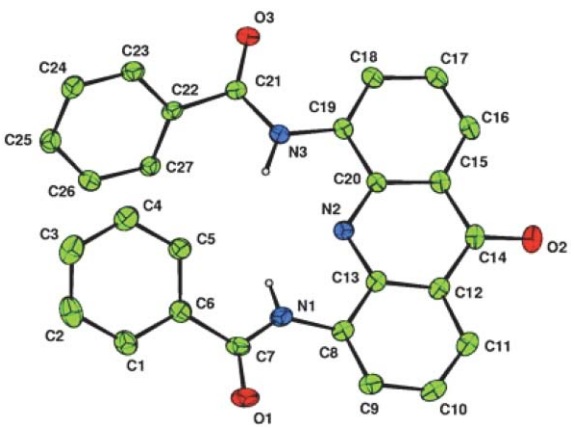


Fig. 1 X-Ray crystal structure of the anion **2**$-H^+$. Thermal ellipsoids are drawn at the 35% probability level. Non-acidic hydrogen atoms and the tetrabutylammonium counter cation have been omitted for clarity.

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† Electronic supplementary information (ESI) available: Synthesis and characterization of compounds **2–4**, UV-vis and ^{1}H NMR titration profiles and further details of X-ray crystallography. See DOI: 10.1039/b618072h

of tetrabutylammonium acetate, benzoate, dihydrogen phosphate or fluoride, evidence that confirms that these four anions deprotonate compound **2** in DMSO solution.

In contrast to the results obtained for the amide derivative **2**, the spectra of compounds **3** and **4** obtained after the addition of one equivalent, as well as an excess of the corresponding anion salts, are different to those obtained after the addition of one equivalent of tetrabutylammonium hydroxide to a DMSO-d_6–0.5% water solution of compounds **3–4**. Analysis of the titration profile of the inner NH *vs.* outer NH groups of the urea and thiourea moieties upon addition of basic anions such as acetate, benzoate or dihydrogen phosphate shows that the inner NH group resonances shift with a similar titration profile to those seen in the NMR spectrum of compound **2** upon addition of these anions, but that the outer NH group resonance has a more complex profile (see Fig. 2). This behaviour is consistent with initial deprotonation of the acridinone by the first added equivalent of basic anion (and intramolecular hydrogen bond formation with the inner amide NH groups or enhanced intramolecular hydrogen bonding—see below) followed by hydrogen bonding of further added anion with the outer NH groups.[13] Smaller changes of the ^{1}H NMR spectra were observed upon addition of less basic anions (Cl^-, Br^- or HSO_4^-) that were fitted to 1 : 1 binding using the EQNMR computer program,[14] giving association constants of 273 M^{-1} (Cl^-), 28 M^{-1} (Br^-) and 69 M^{-1} (HSO_4^-) for compound **3** and 53 M^{-1} (Cl^-) for compound **4** (all errors less than 15%, 298 K, DMSO-d_6–0.5% water solution).

Crystals of tetrabutylammonium chloride complex of receptor **3** were grown by slow evaporation of an acetonitrile solution of the receptor in the presence of excess tetrabutylammonium chloride§ (Fig. 3). Interestingly, the crystal structure reveals that compound **3** adopts the hydroxyacridine form in the chloride complex (see Fig. 3).[15] The urea groups are coplanar with the acridine core, with the inner NH groups (N4 and N2) within hydrogen bonding distance of the central nitrogen N3. Moreover the structure reveals two bound chloride atoms, one coordinated *via* a hydrogen bond to the O2 atom (O2···Cl2 2.965(4) Å) and the other coordinated to the four urea NH groups but being significantly closer to the outer hydrogen bond donors (N1···Cl1 3.198(4) Å, N2···Cl1 3.460(4) Å, N4···Cl1 3.364(4) Å and N5···Cl1 3.154(4) Å).

It is difficult to distinguish the tautomeric forms of compounds **2–4** present in solution as both have similar spectroscopic properties. It has been proposed that simpler acridinones can co-exist in both forms in solution with the nature of the solvent playing a critical role in stabilizing one or other tautomer.[15] In the compounds studied here, intramolecular hydrogen bonding may stabilize the hydroxyacridine form of the receptor (Scheme 1) as was observed in the chloride complex of compound **3** in the solid state. However, upon deprotonation both forms may be stabilized by these interactions and localisation of the negative charge on the acridinone nitrogen may lead to a greater degree of stabilization

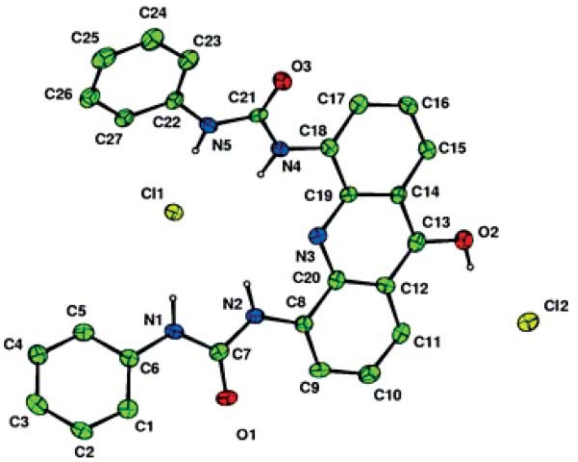


Fig. 3 X-Ray crystal structure of compound **3**·(TBA chloride)$_2$. Thermal ellipsoids are drawn at the 35% probability level. Non-acidic hydrogen atoms and the tetrabutylammonium counter cations have been omitted for clarity.

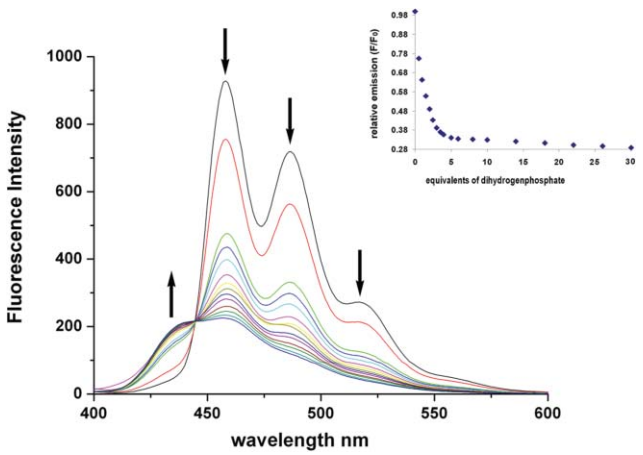


Fig. 4 Fluorescence quenching of **3** in MeCN/DMSO (96/4 v/v) upon the addition of tetrabutylammonium dihydrogen phosphate.

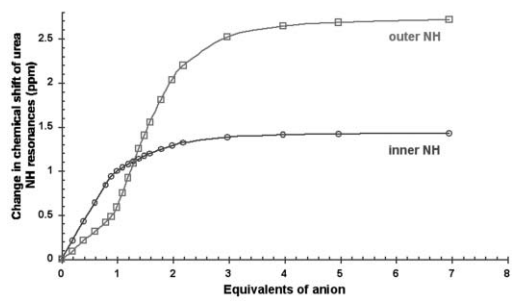
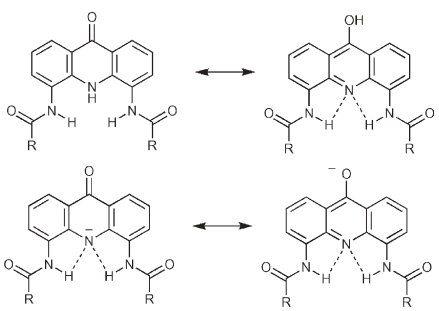


Fig. 2 Shifts of the NH groups of compound **3** upon the addition of tetrabutylammonium acetate in DMSO-d_6–0.5% water.



Scheme 1 Acridinone-hydroxyacridine tautomerism in compounds **2–4** and their deprotonated forms.

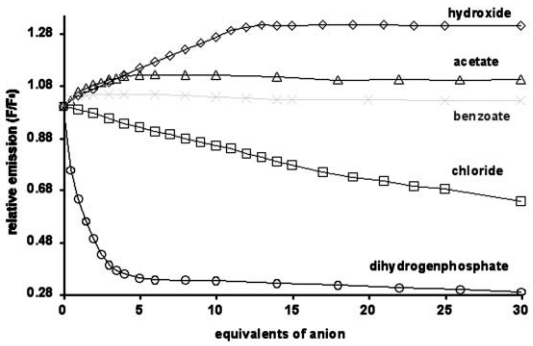


Fig. 5 Effect of increasing anion concentration upon the relative fluorescence emission of receptor **3** in MeCN/DMSO (96/4 v/v).

(the deprotonated form of compound **2** has a shorter acridinone C=O bond length (1.259(1) Å) than the acridine C–OH bond length (1.338(6) Å) in the chloride complex of compound **3**). More work is required to fully understand the tautomerism processes occurring in these systems in the absence and presence of anions.

Preliminary fluorescence titrations were performed by adding aliquots of anion (as the tetrabutylammonium salt) in MeCN (5×10^{-4} M) to a solution of receptors in a mixture of MeCN/DMSO (96/4 v/v) (1×10^{-6} M). Under these conditions only receptor **3** shows a fluorescence emission when excited at 353 nm. The fluorescence spectrum of **3** exhibits an intense band at 458 nm, and two less intense bands at 486 and 520 nm. Upon addition of increasing amounts of tetrabutylammonium dihydrogen phosphate a selective quenching of the fluorescence is observed (I_{res} = 28%) as shown in Fig. 4.

Upon addition of the tetrabutylammonium salts of acetate, benzoate and chloride a slight increase of the fluorescence emission followed by a plateau with the two former, and a slight and monotonic decrease with the latter (I_{res} = 68%) is observed (Fig. 5). Titration of **3** with tetrabutylammonium hydroxide causes an increase of the fluorescence emission evidence which leads us to suggest that the excited state complexation of acetate and benzoate also involves a deprotonation process.

Under the experimental conditions reported here, receptor **3** functions as an ON–OFF fluorescent chemosensor for the selective recognition of dihydrogen phosphate. The combination of anion-complexation, acid–base chemistry and tautomerism gives us three mechanisms by which anions may perturb the electronic properties of this scaffold, making this an attractive group upon which to base new anion sensors systems. We are continuing to study the anion recognition processes occurring in these systems.

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Notes and references

‡ Crystal data for **2**−H^+: $C_{43}H_{54}N_4O_3$, M_r = 674.9, T = 120(2) K, triclinic, space group $P\bar{1}$, a = 11.0115(7), b = 13.5609(7), c = 13.9492(7) Å, α =86.153(3), β = 73.058(3), γ = 72.371(2)°, V = 1898.49(18) Å^3, ρ_{calc} = 1.181 g cm^{-3}, μ = 0.074 mm^{-1}, Z = 2, reflections collected: 29200, independent reflections: 8676 (R_{int} = 0.0809), final R indices [$I > 2\sigma I$]: $R1$ = 0.0695, w$R2$ = 0.1579, R indices (all data): $R1$ = 0.1800. w$R2$ = 0.1800. CCDC 629281. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b618072h

§ Crystal data for **3**(TBA chloride)$_2$: $C_{59}H_{93}Cl_2N_7O_3$, M_r = 1019.30, T = 120(2) K, triclinic, space group $P\bar{1}$, a = 8.6137(6), b = 16.7161(14), c = 20.8520(16) Å, α =104.273(4), β = 93.257(4), γ = 93.788(4)°, V = 2895.1(4) Å^3, ρ_{calc} = 1.169 g cm^{-3}, μ = 0.161 mm^{-1}, Z = 2, reflections collected: 39582, independent reflections: 12741 (R_{int} = 0.1696), final R indices [$I > 2\sigma I$]: $R1$ = 0.1080, w$R2$ = 0.1831, R indices (all data): $R1$ = 0.2402. w$R2$ = 0.2258. CCDC 629282. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b618072h

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