'Twisted' isophthalamide analogues†

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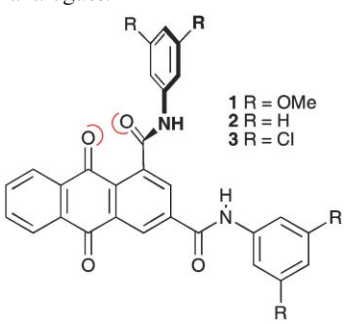
Steric interactions in 1,3-dicarboxamidoanthraquinones have been employed to 'twist' isophthalamide-like anion binding sites; the crystal structure of the fluoride complex of a bis-3,5-dichlorophenylamide derivative shows the receptor acting as a 'hydrogen-bonding corner' in a '2 + 2' fluoride containing molecular box.

Anion complexation,[1] sensing[2] and templated assembly[3] are currently areas of intense interest. In the late 1990s, Crabtree and co-workers demonstrated that isophthalamides are excellent anion receptors in organic solution.[4] This motif has been used by a number of researchers in both anion and ion-pair receptors.[5] Recently, we reported that two 3,5-dinitrophenylisophthalamide ligands were found to form a double helix around two fluoride anions in the solid state.[6] This was the first example of a fluoride templated double helix and the first anion templated helix containing neutral anion binding groups. We wished to investigate further the assembly properties of isophthalamide-like compounds with fluoride and other anions. Specifically, we wished to induce a twist in an isophthalamide-like ligand in order to make the formation of higher order anion : receptor complexes more likely. To achieve this, we synthesised several 1,3-dicarboxamido-9,10-anthraquinone derivatives.

Anthraquinones containing hydrogen bond donor groups have previously been reported to bind and sense anions *via* colour changes.[7] Compounds **1–3** were designed to use the steric interaction between the amide in the 1-position and the anthraquinone oxygen in the 9-position to twist the amide out of the anthraquinone plane and hence disfavour the *syn–syn* conformation previously observed in 1 : 1 halide complexes of isophthalamides.[4] We therefore studied the structural properties in the solid state and anion complexation properties of the 'twisted' isophthalamide analogues.



† Electronic supplementary information (ESI) available: ^{1}H and ^{13}C NMR data for **1–3**, synthetic details, NMR titration curves and packing diagrams of the structures presented in the paper. See http://www.rsc.org/suppdata/cc/b4/b413654c/

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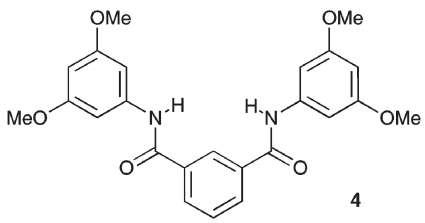
Receptors **1–3** were synthesised from 1,3-dicarboxyanthraquinone synthesised *via* literature procedures.[8] This was converted to the acid chloride by heating at reflux in thionyl chloride and then condensed with the relevant aniline in dichloromethane solution in the presence of Et_3N and a catalytic quantity of DMAP to afford receptors **1–3** in 43, 36 and 6% respective yields. Crystals of receptors **1**‡ and **2**§ were obtained from solutions of the compounds in acetonitrile and DMSO respectively (Fig. 1). In both crystals, there are extensive hydrogen bonding arrays (see ESI for more information†). The structures illustrate the twist in the amide in the 1-position out of the plane of the anthraquinone ring system. There are two crystallographically distinct molecules in the unit cell of compound **1**. The amide in the 1-position is twisted out of the plane by 87.14(51) and 86.89(50)° in compound **1** and 73.35(86)° in compound **2** whilst the amides in the 3-position are only twisted out of the plane by 15.10(49) and 23.61(52)° for compound **1** and 35.78(65)° for compound **2**.

Compound **4** was synthesised in order to compare the effect of the 'twist' on the binding properties of compound **1**. The anion binding ability of receptors **1–4** were investigated using ^{1}H NMR titration techniques in DMSO-d_6/0.5% water. The results shown in Table 1.



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Titrations were conducted with various anions and stability constants obtained using the EQNMR computer program.[9] In all cases, fluoride gave titration curves which could not be fitted to simple 1 : 1 or 1 : 2 receptor : anion binding models.[6] Bromide, hydrogen sulfate and, in the cases of compounds **1** and **2**, chloride caused insignificant changes to the ^{1}H NMR spectra of the ligands. Compounds **1** and **2** have very similar affinities for anions whilst compound **3** binds anions significantly more strongly presumably due to the electron withdrawing chlorine substituents. Interestingly, this compound binds two equivalents of dihydrogen phosphate with high affinity in this competitive solvent mixture (K_1 = 1520 M^{-1} and K_2 = 65 M^{-1}). The binding mode of the oxo-anion to this compound has yet to be determined. We expected that the anion complexation properties of **1–3** would be weaker than analogous isophthalamides due to the steric constraints present in these systems. However we found that whilst compound **4** binds chloride more strongly than any of the anthraquinone derivatives, interestingly dihydrogen phosphate is

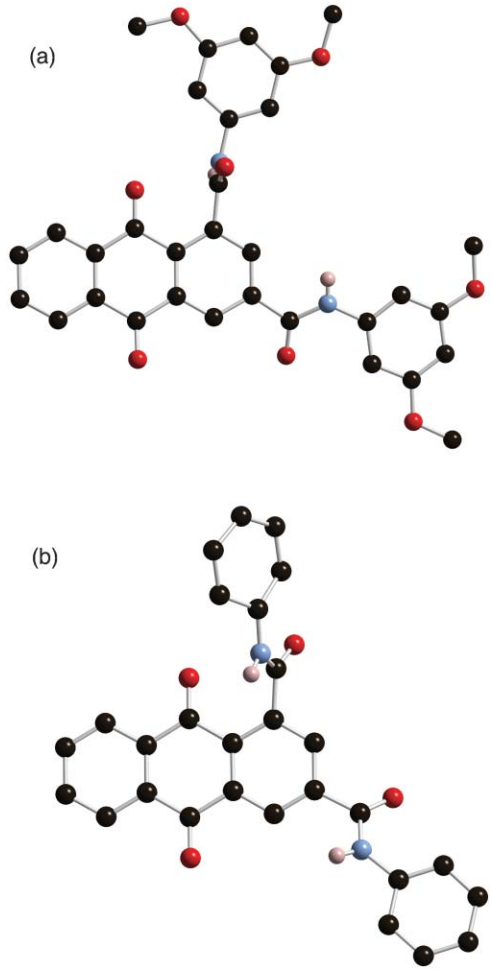

Fig. 1 The X-ray crystal structures of (a) compound **1** (only one molecule shown) and (b) the DMSO solvate of compound **2**. In both cases the amide in the 1-position is twisted out of the plane of the anthraquinone ring (and involved in the hydrogen bonding interactions in the crystal). Non-acidic hydrogen atoms (and solvent in the case of **2**) have been omitted for clarity.

Table 1 Stability constants K_a/M^{-1} for the reaction of **1–4** with anions determined by ^1H NMR titrations[a]

	Cl^-	$H_2PO_4^-$	$C_6H_5CO_2^-$
1	—	214	26
2	—	198	17
3	13	$K_1 = 1520$ $K_2 = 65$	160
4	20	120	42

[a] Titrations performed in DMSO/0.5% H_2O with anions added as the tetrabutylammonium salts. All titration plots fitted to a 1 : 1 binding model unless otherwise stated. Stability constants are given with <10% error.

bound more strongly by compound **1** than compound **4**. This may be due to the oxo-anion bridging between the amide groups in the anthraquinone derivatives. The compounds also give a colorimetric response to the presence of anions in solution (see ESI†).

Crystals of the tetrabutylammonium fluoride complex of **3**¶ were obtained from an acetonitrile solution of receptor **3** in the presence of excess tetrabutylammonium fluoride (Fig. 2). The

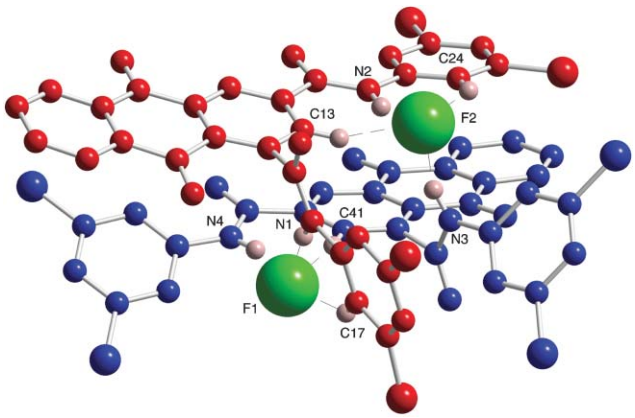

Fig. 2 The X-ray crystal structure of the fluoride complex of compound **3** (various hydrogen atoms, counter cations and disorder have been removed for clarity).

X-ray crystal structure revealed that the strategy of using a 'twisted' binding site had indeed resulted in the formation of a 2 : 2 anion : receptor complex. As in the structures of the free ligands **1** and **2**, the amide in the 1-position of compound **3** is twisted out of the plane of the anthraquinone ring. This NH group forms a hydrogen bond to the fluoride anion bound by the amide in the 3-position of the other receptor in the complex with N–F distances in the range 2.574(6)–2.615(6) Å. Additionally there are CH–F close contacts in the solid state with C–F distances ranging between 2.789(8) and 3.062(9) Å (Fig. 2).

The design principle of restricting the possible conformations of the amide in the 1-position has been successful with the formation of a '2 + 2' complex with fluoride in the solid state. We are continuing to investigate the anion complexation chemistry of these interesting new anion complexation agents.

Data were collected on a Bruker Nonius Kappa CCD area detector diffractometer with a rotating molybdenum anode following standard procedures‡¶ or on a Bruker Nonius SMART APEX2 CCD diffractometer at Daresbury SRS station 9.8.§

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Notes and references

‡ Crystal data for **1**: $C_{32}H_{26}N_2O_8$, $M_r = 566.55$, $T = 293(2)$ K, triclinic, space group $P\bar{1}$, $a = 10.634(5)$, $b = 14.312(6)$, $c = 17.706(13)$ Å, $\alpha = 95.07(7)$, $\beta = 104.67(4)$, $\gamma = 91.17(4)°$, $V = 2594(3)$ Å^3, $\rho_{calc} = 1.451$ g cm^{-3}, $\mu = 0.105$ mm^{-1}, $Z = 4$, reflections collected: 37176, independent reflections: 8983 ($R_{int} = 0.1592$) final R indices [$I > 2\sigma(I)$]: $R1 = 0.0801$, $wR2 = 0.1592$, R indices (all data): $R1 = 0.1727$, $wR2 = 0.1986$. CCDC 246437. See http://www.rsc.org/suppdata/cc/b4/b413654c/ for crystallographic data in .cif or other electronic format.
§ Crystal data for **2**·DMSO: $C_{30}H_{24}N_2O_5S$, $M_r = 524.57$, $T = 120(2)$ K, monoclinic, space group $P2_1/c$, $a = 15.3919(17)$, $b = 4.9065(5)$,

c = 33.175(4) Å, β = 102.202(2)°, V = 2448.8(5) Å^3, ρ_{calc} = 1.423 g cm^{-3}, μ = 0.179 mm^{-1}, Z = 4, reflections collected: 16177, independent reflections: 4263 (R_{int} = 0.0402) final R indices [$I > 2\sigma(I)$]: $R1$ = 0.0586, $wR2$ = 0.1294, R indices (all data): $R1$ = 0.0738, $wR2$ = 0.1351. CCDC 246438. See http://www.rsc.org/suppdata/cc/b4/b413654c/ for crystallographic data in .cif or other electronic format.

¶ Crystal data for **3**·TBAF: $C_{44}H_{50}Cl_4FN_3O_4$, M_r = 845.67, T = 120(2) K, orthorhombic, space group *Pbca*, a = 18.133(5), b =24.621(5), c = 37.774(5) Å, V = 16864(6) Å^3, ρ_{calc} = 1.332 g cm^{-3}, μ = 0.331 mm^{-1}, Z = 16 (2 assemblages in the asymmetric unit), reflections collected: 95521, independent reflections: 14874 [R_{int} = 0.1075], final R indices [$I > 2\sigma(I)$]: $R1$ = 0.1082, $wR2$ = 0.2511, R indices (all data): $R1$ = 0.1695, $wR2$ = 0.2893. CCDC 246439. The presence of the NH hydrogen atoms was confirmed from the difference map. The atoms were placed in idealised positions and refined using a Riding model. See http://www.rsc.org/suppdata/cc/b4/b413654c/ for crystallographic data in .cif or other electronic format.

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