Indolocarbazoles: a new family of anion sensors†

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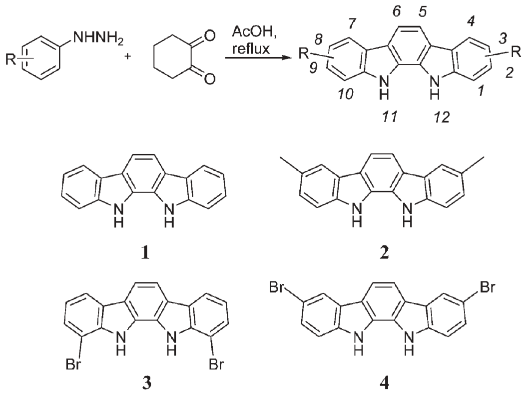
Simple preorganised indolo[2,3-a]carbazole derivatives are shown to recognise and sense anionic guest species using fluorescence spectroscopy.

As a consequence of the fundamental roles played by negatively charged species in a range of biological, chemical, medical and environmental processes, the interest shown in the syntheses of host systems designed to recognize and sense anions is ever increasing.[1] In particular, Sessler, Gale and co-workers have exploited the hydrogen bond donating pyrrole moiety in the construction of a variety of novel macrocyclic (calixpyrroles and expanded porphyrins) and acyclic anion receptors.[2,3] Surprisingly the preorganised indolocarbazole moiety which contains two pyrrole heterocyclic subunits in a conjugated planar structure has not to our knowledge been utilised for anion recognition purposes.[4] We report here the synthesis of a family of simple indolo[2,3-a]carbazoles and demonstrate their ability to recognize and sense anions using fluorescence spectroscopy. Adaptation of Fischer indolisation using appropriate aryl functionalised hydrazines and 1,2-cyclohexanedione produced the indolocarbazole derivatives **1**–**4** in 40–47% yields (Scheme 1).[5]

Initial binding studies with a series of anions F^-, Cl^-, $H_2PO_4^-$, HSO_4^- and $PhCO_2^-$ were carried out by ^{1}H-NMR titration experiments in acetone-d_6 as solvent. By monitoring the peak assigned to the pyrrole ring NH protons of the respective indolocarbazole derivative, significant downfield shifts could be detected as a result of anion complexation. Solubility problems coupled with the complexed anion induced disappearance of the NH proton due to deuterium exchange thwarted quantitative association constant data being obtained. Analogous UV-vis anion titration experiments in acetone solution revealed the evolution of new absorption maxima as well as isosbestic points suggesting the formation of strong indolocarbazole–anion complexes (Fig. 1). Job plot and Specfit analysis[6] of the titration data gave substantial association constant values for 1 : 1 complexes shown in Table 1. With all the indolocarbazoles the strongest complex is formed with benzoate anion followed by $H_2PO_4^- > F^- > Cl^- > HSO_4^-$ with the largest association constant magnitudes exhibited by **4**, containing the electron-withdrawing 3,8-functionalised bromo substituents. The observed preference towards benzoate may be indicative of complementary hydrogen bonding between the carboxylate anion guest and the two pyrrole moieties of the preorganised indolocarbazole structural unit. Table 1 also shows that bromo substituents at positions 1 and 10 of the indolocarbazole motif reduce significantly the magnitudes of the anion association constant values, presumably by sterically hindering the approach of a potential anionic guest species. By contrast, comparing the association constant values of **1** and **2** reveals appended 3,8-functionalised methyl groups have little effect on anion complex stability.

Fluorescence spectroscopy studies were also carried out in order to evaluate the ability of these systems to operate as fluorescent



Scheme 1 (**1**) Indolo[2,3-a]carbazole (40%); (**2**) 3,8-dimethylindolo[2,3-a]carbazole (47%); (**3**) 1,10-dibromoindolo[2,3-a]carbazole (42%); (**4**) 3,8-dibromoindolo[2,3-a]carbazole (41%).

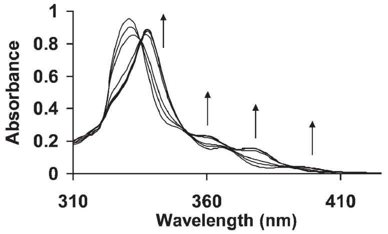


Fig. 1 Evolution of the UV-vis spectrum of 3,8-dibromoindolo[2,3-a]carbazole (3×10^{-5} M in acetone) during the titration with tetrabutylammonium (TBA) benzoate (0, 0.2, 0.4, 1, 2, 5, 7, 10 equivalents of TBA benzoate).

Table 1 Association constants (log K_a)[a] in acetone solution

	1	2	3	4
F^-	4.7	4.7	3.6	5.0
Cl^-	4.5	4.1	4.0	4.9
$PhCO_2^-$	5.3	5.4	4.4	5.9
$H_2PO_4^-$	4.9	5.2	4.1	5.3
HSO_4^-	—[b]	—[b]	—[b]	—[b]

[a] Determined by UV-vis spectroscopy; T = 25 °C; [Host] = 3×10^{-5} M. [b] Very weak complexation. Binding constant could not be determined; error <10%.

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† Electronic supplementary information (ESI) available: characterisation data. See http://www.rsc.org/suppdata/cc/b4/b412363h/

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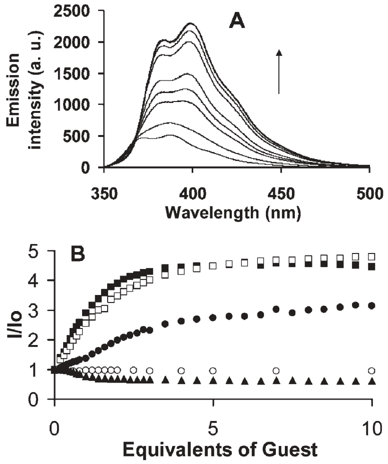

Fig. 2 (A) Fluorescence enhancement upon titration of receptor **2** (3 × 10^{-5} M in acetone) with TBAF (λ_{exc} = 320 nm); 0, 0.2, 0.5, 0.7, 1, 2, 3, 5, 10 equivalents of TBAF. (B) Titrations curves: ■ TBAF, □ TBACl, ● TBAH_2PO_4, ▲ TBA benzoate and ○ TBAHSO_4.

anion sensors. Remarkable emission responses were obtained upon anion titration. Significant enhancement of emission was observed with F^- (Fig. 2A), Cl^- and $H_2PO_4^-$ whereas addition of benzoate resulted in quenching of fluorescence[7] and HSO_4^- caused no effect.[8] Bathochromic shifts (10–15 nm) of the emission maxima were also noted in the presence of the former anions (Fig. 2A). Specfit analysis of the resulting titration curves (Fig. 2B) gave very similar anion association constant values for **1** and **2** to those determined by UV-vis titration experiments (Table 1).

Attempts were made to provide solid state evidence for anion complexation by setting up a series of crystallisation experiments of indolocarbazole derivatives and tetrabutylammonium fluoride and chloride salts in 1 : 1 and 2 : 1 receptor : halide stoichiometric ratios. In two cases crystals of sufficient quality for single crystal X-ray structural analysis were obtained.‡§ From a 2 : 1 mixture of **2** : TBAF, the determined crystal structure (Fig. 3) reveals a novel complex which has a self-assembled helical structure in which four indolocarbazole molecules surround two fluoride anions (F···F, 2.910 Å). These anions are bound by four pyrrole hydrogen bonds, each one belonging to a different indolocarbazole molecule, which defines an almost square planar coordination geometry around the fluoride anion.

A 1 : 1 complex was obtained with **2** and TBACl (Fig. 4). In this case the chloride anion is complexed by two pyrrole hydrogen bonds and is located between the two NH groups of **2**.

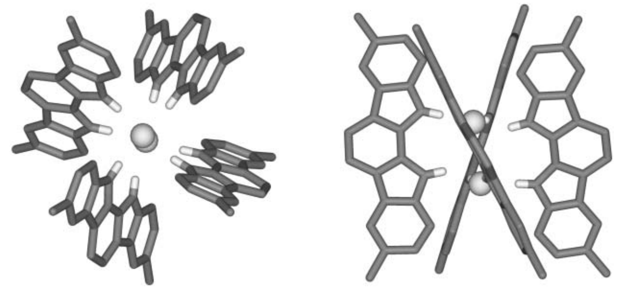

Fig. 3 Different views of the crystal structure of a 1 : 2 complex, TBAF : receptor **2**. TBA counter-cation is omitted for clarity.‡

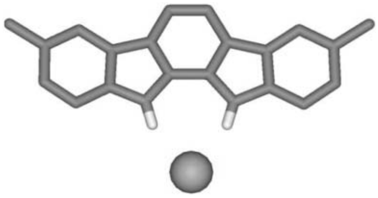

Fig. 4 Crystal structure of a 1 : 1 complex TBACl : receptor **2**. TBA counter-cation is omitted for clarity.§

In summary the simple preorganised indolocarbazole molecule has been shown to be a new efficient complexing and sensing motif for anionic guest species. The relatively straightforward functionalisation of the indolocarbazole structural framework bodes well for its future exploitation in anion supramolecular chemistry.

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Notes and references

‡ Crystals were grown by slow diffusion of diisopropyl ether into a solution of **2** and TBAF in acetone and chloroform. A single crystal having dimensions approximately 0.16 × 0.16 × 0.38 mm was mounted on a glass fibre using perfluoropolyether oil and cooled rapidly to 150 K in a stream of cold N_2 using an Oxford Cryosystems CRYOSTREAM unit. Diffraction data were measured using an Enraf-Nonius KappaCCD diffractometer (graphite-monochromated Mo Kα radiation, λ = 0.71073 Å). Intensity data were processed using the DENZO-SMN package.[9] The structure was solved in the space group $P\bar{1}$ using the direct-methods program SIR92,[10] which located all non-hydrogen atoms. Subsequent full-matrix least-squares refinement was carried out using the CRYSTALS program suite.[11] Crystal data: $C_{124}H_{164}F_2N_{10}O_2$, M = 1864.73, triclinic, a = 14.1678(2) Å, b = 14.5150(2) Å, c = 28.0396(4) Å, α = 104.5255(8)°, β = 94.2109(8)°, γ = 92.3985(5)°, U = 5555.98(14) Å^3, T = 150 K, space group $P\bar{1}$, Z = 2, μ(Mo Kα) = 0.068 mm^{-1}, 89631 reflections measured, 24984 unique (R_{int} = 0.078), 11480 observed reflections with $I > 2\sigma(I)$ which were used in the least-squares calculation. The final $wR(F)$ was 0.08939 (observed data). CCDC 247741. See http://www.rsc.org/suppdata/cc/b4/b412363h/ for crystallographic data in .cif or other electronic format.

§ Crystals were grown by slow diffusion of diisopropyl ether into a solution of **2** and TBACl in acetone and chloroform. Single crystal dimensions: 0.06 × 0.24 × 0.36 mm. Crystal data: $C_{36}H_{52}ClN_3$, M = 562.28, monoclinic, a = 8.3402(2) Å, b = 16.5722(5) Å , c = 23.5914(7) Å, α = 90°, β = 90.7479(13)°, γ = 90°, U = 3260.42(16) Å^3, T = 150 K, space group $P2_1/c$, Z = 4, μ(Mo Kα) = 0.145 mm^{-1}, 31120 reflections measured, 7394 unique (R_{int} = 0.052), 4418 observed reflections with $I > 3\sigma(I)$ which were used in the least-squares calculation. The final $wR(F)$ was 0.0566 (observed data). CCDC 247742. See http://www.rsc.org/suppdata/cc/b4/b412363h/ for crystallographic data in .cif or other electronic format.

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7 The pK_as of pyrrole (23.0) and carbazole (19.9) have been reported in DMSO, see: F.G. Bordwell, X. Zhang and J.-P. Cheng, *J. Org. Chem.*, 1991, **56**, 3216. No evidence of benzoate deprotonating the indolocarbazole NH groups was observed from UV-vis spectroscopy. Fluorescence intensity enhancement may be explained by the formation of the indolocarbazole–anion complex increasing the rigidity of the receptor, thereby disfavouring the non-radiative vibrational/rotational decay processes. The fluorescence quenching caused by benzoate suggests an energy transfer mechanism between the fluorophore and the aromatic guest since titration with acetate along with all the other titrated anions resulted in fluorescence intensity enhancement.

8 As far as compounds **3** and **4** are concerned, they did not display a good fluorescent response, possibly due to a heavy atom effect caused by the presence of bromo substituents.

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