A new building block for anion supramolecular chemistry. Study of carbazolocarbazole as anion receptor†

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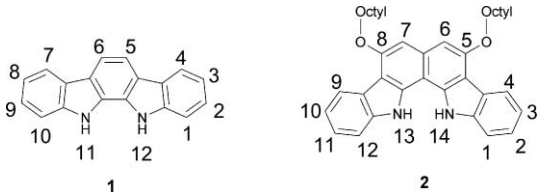
A novel carbazolocarbazole system has been evaluated as an anion receptor in DMF solution. A good affinity has been detected for oxoanions. The anion binding studies have been contrasted by different experimental techniques.

Nowadays anion recognition represents one of the most explored areas in supramolecular chemistry.[1] The important role that anionic species play in biological processes motivates the development of synthetic receptors which can contribute to their detection, quantification and/or transport. In this regard, a plethora of compounds have been described with potential application as anion sensors and carriers.[2] One of the most extended approaches to the design of host molecules is based on the use of NH units to interact through hydrogen bonds with the anionic guests. The wide range of functional groups which bear that NH unit (amides, thioamides, sulfonamides, ureas, thioureas, guanidinium salts, amines, pyrroles, *etc.*) makes the synthetic scope for anion receptors virtually unlimited. Due to our interest in the study of preorganized pyrrole-based structures[3,4] as ligands for anions, we want to report the preliminary results of a novel anion receptor based on the skeleton of carbazolo[1,2-*a*]carbazole (Fig. 1).

Since we first described the use of indolocarbazoles as host systems for anions,[3] several groups have elegantly exploited this building block in anion-based supramolecular chemistry.[5,6] In this context, we have recently reported the first synthetic route for carbazolo[1,2-*a*]carbazole derivatives[7] (Scheme 1) and now we have studied the ability of this new polyheteroaromatic molecule



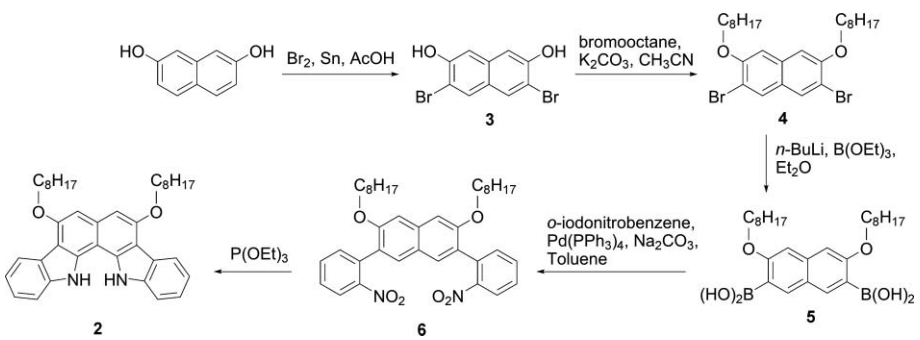
1 2

Fig. 1 Indolo[2,3-*a*]carbazole, **1**, and 5,8-dioctyloxycarbazolo[1,2-*a*]-carbazole, **2**.

to work as an anion receptor. This fused hexacyclic system is structurally related to the indolocarbazole with two pyrrole rings adequately incorporated into a rigid structure which defines a concave cavity where several hydrogen bonds might be geometrically favoured. It is worth mentioning how the bite angle defined by the NH bonds narrows considerably in the carbazolo[1,2-*a*]carbazole when compared to the indolo[2,3-*a*]carbazole.[8]

Initially, control experiments were undertaken by ^{1}H-NMR titrations, with indolocarbazole **1**, in DMF-d_7 (without any drying treatment and an estimated water content of 0.4%), in order to evaluate its aptitude as anion receptor in a highly competitive environment. The known high affinity of **1** towards oxoanions is still detected in a very polar solvent. Similarly, when aliquots of different anions, used as their tetrabutylammonium salts, were added over a solution of 5,8-dioctyloxycarbazolo[1,2-*a*]carbazole **2**, the typical downfield shift was detected for the pyrrolic protons as well as for the CHs on positions 1 and 12 of the carbazolocarbazole structure, as a result of the anion complexation (Fig. 2). This contrasts with the response detected for indolocarbazole **1**, whose CHs on positions 1 and 10 do not intervene in the complexation of the anions (see ESI).

A good behaviour was obtained for acetate, benzoate and dihydrogenphosphate anions. Conversely, a weaker interaction was detected for chloride anion and no interaction was observed for hydrogensulfate, nitrate and bromide anions. Binding constant values are summarized in Table 1.[9] These experiments confirm a



2 6 5 4 3 6

Scheme 1 Synthesis of receptor **2**.

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† Electronic supplementary information (ESI) available: Titration fitplots, titration Job plots, ITC, HRMS, emission spectra, absorption spectra, diffusion NMR fitplots and X-ray data. CCDC reference number 787231. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0ob00522c

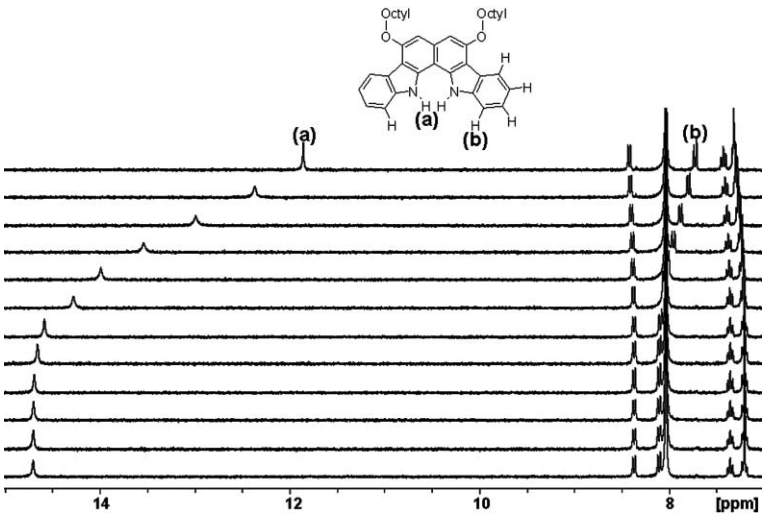

Fig. 2 Evolution of the ^{1}H-NMR spectra of **2** upon titration with TBAAcO in DMF-d_7 at r.t.

Table 1 Binding constants (Log K_a) in DMF-d_7

	AcO^-	BzO^-	$H_2PO_4^-$	Cl^-
1	4.42	4.18	—[a]	2.64
2	4.12	4.20	3.17; 6.07[b]	3.15

[Host] = 4×10^{-3} M, $T = 25$ °C; error < 10% in all cases.[a] Titration isotherm could not be fitted. [b] log K_1 and log β_2.

Table 2 ITC thermodynamic data of **2** in DMF[a]

	AcO^-	BzO^-	$H_2PO_4^-$
ΔH (cal mol^{-1})	–3583	–2720	–10860
ΔS (cal mol^{-1} K)	5.3	8.4	–20.5

[a] [Host] = 10^{-3} M, $T = 25$ °C.

higher preference of the carbazolocarbazole receptor for certain oxoanions.

The carboxylate anions form highly stable 1 : 1 complexes due to the good geometrical correspondence between the Y-shaped anion and the orientation of the hydrogen bond donor groups. Interestingly, the titration with dihydrogenphosphate revealed the formation of a stable 2 : 1 (host : guest) complex with compound **2**. This stoichiometry has also been detected for indolocarbazole with fluoride and sulfate anions in acetone and acetonitrile solution respectively.[3,5] Besides, different geometries have been determined for the 2 : 1 complexes depending on the nature of the anion and the solvent.

Further analyses were carried out in order to confirm the different binding mode observed for the $H_2PO_4^-$ anion. In this regard, studies by high resolution mass spectrometry also enabled the detection of the 2 : 1 dihydrogenphosphate complex (see ESI). Additionally, isothermal titration calorimetry [10] experiments were carried out with those anions which had offered good results by ^{1}H-NMR (see ESI).[11] Binding constants determined by calorimetric measurements were in a reasonably good agreement with those calculated from NMR data. The acetate and benzoate anions showed both a sigmoid-shaped titration profile which fitted well to a 1 : 1 binding model. The thermodynamic data (Table 2) resulting from the heat measurements revealed that the binding process is exothermic, as a consequence of the hydrogen bonds formed between the receptor and the anionic guest. Moreover, the positive increment of entropy, presumably due to the desolvation of the species taking part in the equilibrium, favours the evolution of the complexation equilibria. In contrast to these results, the titration of **2** with dihydrogenphosphate displayed a different titration profile which fitted well to a 2 : 1 host : guest molar ratio. The analysis of the energetic characteristics of the equilibrium corresponded to an exothermic process accompanied, in this case, by a negative entropy change. This difference in the entropy increment, when compared to that obtained for acetate and benzoate anions, reveals the higher order of the system imposed by the structure of a complex with two molecules of **2** surrounding one molecule of the $H_2PO_4^-$ anion.

Since the diffusion coefficient could be a very informative parameter about the change in the size of the species upon anion complexation, we decided to perform diffusion NMR studies (see ESI).[12,9] Compound **2** was analyzed in the presence of acetate and dihydrogenphosphate anions to compare both of the stoichiometries observed for the carbazolocarbazole receptor. The diffusion coefficients were calculated from the attenuation of the carbazolocarbazole NMR signals. Data corresponding to the calculated diffusion coefficients for the free receptor and the anion complexes are plotted in Fig. 3.

The value for the free receptor is 0.46×10^{-9} m^2 s^{-1}. The NMR measurements carried out at different anion concentrations revealed how the diffusion coefficient determined for the acetate complex was fairly consistent throughout the experiment and did not significantly change from the value calculated for the free receptor. This is concordant with the approximate same size of the free receptor and the 1 : 1 complex with the acetate anion.[13] The results obtained for dihydrogenphosphate revealed a noticeably lower diffusion coefficient which supported the formation of a more voluminous 2 : 1 host : guest complex.

An important advantage of the fused polyheteroaromatic systems is their luminescent properties, which permit their study by the highly sensitive emission spectroscopy.[6,14] In general, when

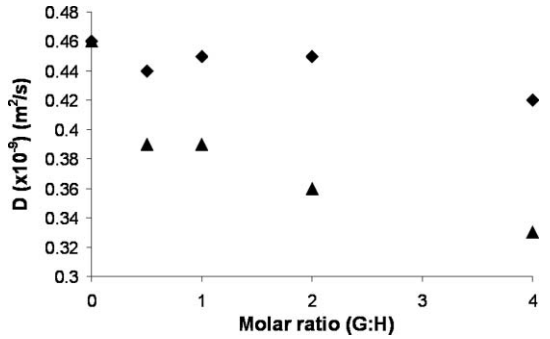

Fig. 3 Diffusion coefficients ($\times 10^{-9}$) (m^2 s^{-1}) in DMF-d_7. [Host] = 10^{-3} M. Acetate ◆, Dihydrogenphosphate ▲.

carbazolocarbazole **2** was titrated with the former series of anions, we did not observe any significant changes in the emission spectra. This was not unexpected since the binding constants previously determined by NMR and ITC might not be high enough to be accurately reproduced by the fluorescence spectroscopy titrations carried out under diluted conditions (2×10^{-5} M). Nevertheless, a noticeable emission quenching could be detected for the benzoate anion, which emphasizes the sensitivity of carbazolocarbazole for this anion when analysed by emission spectroscopy (Fig. 4). The origin of this change in the emission intensity may be ascribed to a static quenching mechanism since titrations followed by absorption spectroscopy also showed changes in the UV-vis spectra. Thus, a ground state interaction between the receptor and the anion is confirmed. This was further reinforced by the Stern–Volmer plot which displayed a good linear behaviour.[15]

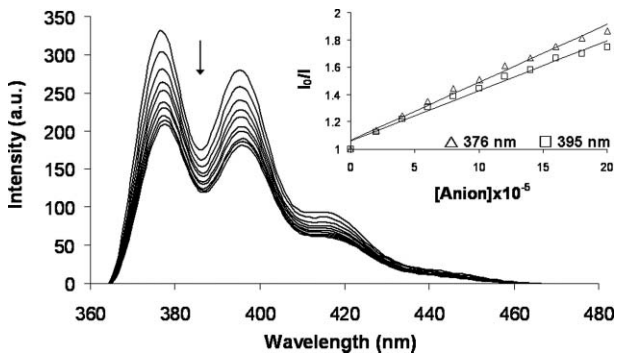

Fig. 4 Evolution of the emission spectra upon titration of **2** with TBAbenzoate in DMF. [Host] = 2×10^{-5} M, r.t., λ_{exc} = 348 nm. Inset: Stern–Volmer plot at 376 and 395 nm.

Despite being the anion with a weaker host–guest interaction, the crystal structure of the chloride complex could be obtained (Fig. 5). The X-ray analysis shows the anion stabilized by two hydrogen bonds with the pyrrole NHs. The spherical chloride is located slightly out of the plane defined by the carbazolocarbazole unit. Subtle differences were measured for both hydrogen bond distances, NH $\cdots$ Cl, ranging from 2.265 Å to 2.302 Å.

In conclusion, several experimental techniques (^{1}H-NMR, ITC, absorption spectroscopy, emission spectroscopy and diffusion NMR) have been employed to contrast the validity of the binding studies performed with the novel carbazolo[1,2-*a*]carbazole. These studies have demonstrated a higher affinity of carbazolocarbazole towards Y-shaped carboxylate anions, as was reported for the

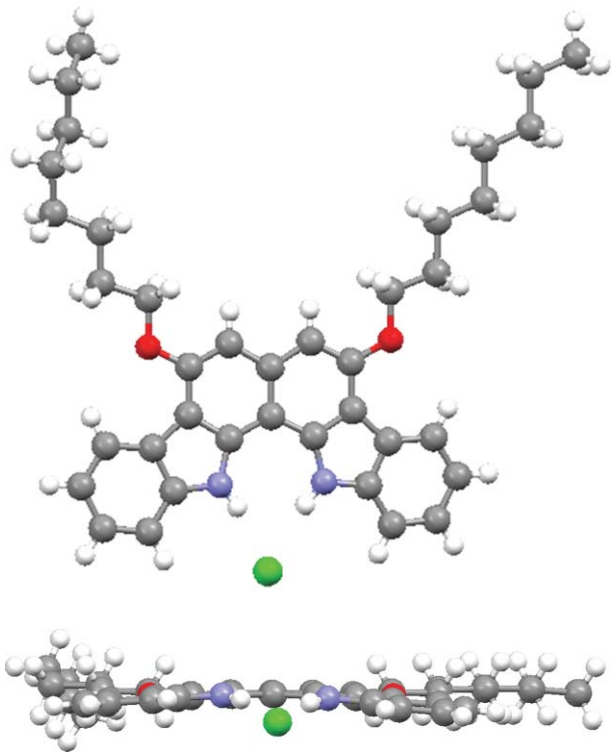

Fig. 5 Two views of the X-ray structure of **2**·Cl^- complex. Tetrabutylammonium countercation has been omitted for the sake of clarity.

structurally related indolo[2,3-*a*]carbazole. Nevertheless, it is likely that different binding modes can operate in solution as a result of the dissimilar geometries defined by the rigid polyheteroaromatic systems. The hydrogen bonds formed by the pyrrole NHs, with a more acute bite angle for the carbazolocarbazole, are additionally assisted by interactions with the CHs on positions 1 and 12. This circumstance highlights the better design of the arch-shaped carbazolocarbazole and opens up the possibility of further improving its anion binding ability by an adequate functionalisation.

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