Sulfate anion templation of a neutral pseudorotaxane assembly using an indolocarbazole threading component†

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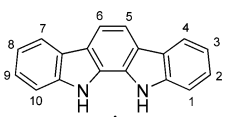
The first example of anion templated pseudorotaxane formation between two neutral components in solution and in surface assembled monolayers is described.

In spite of the enormous progress made in the field of anion recognition in recent years,[1] the use of anions as templating agents[2] is still in its infancy. In particular, the strategic use of anion binding as a driving force for templated assembly is extremely rare. The challenges encountered in the use of anion templation can be attributed to their diffuse nature (small charge/radius ratio), pH dependence and relatively high solvation energies as compared to that of cations. Hydrogen bonds formed by anions are weaker and more difficult to control as compared to metal cation coordinative bonds.

We have recently developed a general method of using anions to template the formation of a range of interpenetrated structures.[3] The assembly process is based on coupling anion recognition with ion-pairing, where, in non competitive solvent media, a coordinatively unsaturated chloride anion of a tight ion-pair threading component facilitates the interpenetration of a pyridinium, imidazolium or guanidinium cationic thread through the annulus of an isophthalamide macrocycle. This strategy has been successfully applied to the preparation of a range of rotaxanes and catenanes.[3]

A desirable extension of this methodology, however, is the use of discrete anions to template the assembly of two *neutral* components which is obviously more challenging and has no precedent in interpenetrative assembly.



Here we report the first example of anion templated pseudorotaxane formation between two neutral components. This was achieved by combining the strongly coordinating anion sulfate with the potent indolocarbazole uncharged anion receptor. Indolo[2,3-*a*]carbazoles are a new family of anion receptors which have been demonstrated to bind anions strongly *via* their two preorganised hydrogen bond donating pyrrole groups.[4] They are attractive building blocks for the potential construction of interpenetrative assemblies because of their rod-like shape and provision of only two hydrogen bonds which will leave anions coordinatively unsaturated - a prerequisite for anion templation. In search of potent anionic templates we turned our attention to the usually overlooked sulfate anion.[5]

Sulfate binding by indolocarbazole **1** was studied in acetonitrile-d_3 by ^{1}H NMR titration experiments. As expected, the addition of $(TBA)_2SO_4$ to the solution of indolocarbazole results in very large downfield shifts of the pyrrole NH protons (>5 ppm) due to strong hydrogen bonding with the anion. The NH peak remains sharp throughout the titration, indicating that no deprotonation occurs. The shifts of the other aromatic protons, not involved directly in anion binding, are much smaller (<0.35 ppm), but reveal interesting features; these signals move upfield until 0.5 equivalent, and then go downfield (Fig. 1). The resulting sharp minima of the titration curves reveal the initial formation of a strong 2 : 1

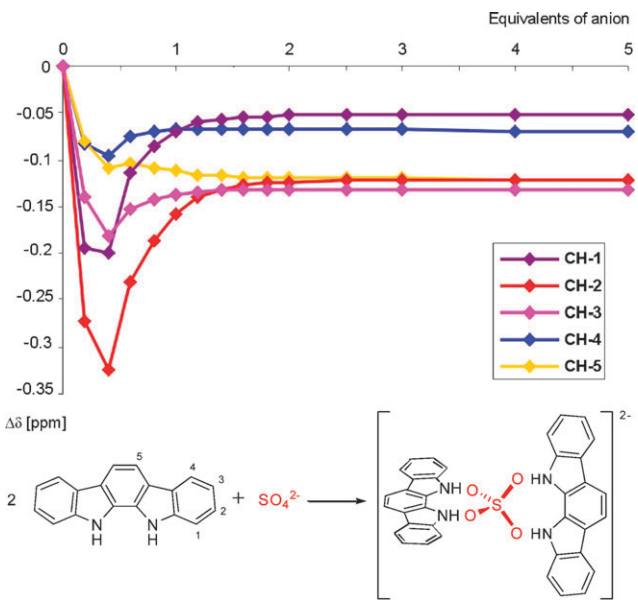


Fig. 1 ^{1}H NMR titration of 0.002 M solution of indolocarbazole **1** with $(TBA)_2SO_4$ in acetonitrile-d_3.

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indolocarbazole–anion complex subsequently replaced by a 1 : 1 complex.[6]

X-Ray structural analysis[7] of crystals obtained by slow diffusion of pentane or ether into a solution of a 2 : 1 mixture of indolocarbazole and $(TBA)_2SO_4$ in dichloromethane confirms the expected stoichiometry and binding mode: each of the two indolocarbazoles bind one pair of oxygen atoms of the sulfate dianion so that their planes form a $\sim 48^\circ$ angle (Fig. 2). Taken together these results demonstrate that the sulfate anion has the ability to bring two neutral receptors together and direct them roughly in an orthogonal manner.

Encouraged by the formation of the stable homodimer $[\mathbf{1}\cdot SO_4\cdot\mathbf{1}]^{2-}$ we moved on to the interpenetration experiments, hoping to achieve threading of indolocarbazole **1** through the annulus of macrocycle **2**. A solution of macrocycle **2** in acetonitrile-d_3 was titrated with a 1 : 1 mixture of indolocarbazole and $(TBA)_2SO_4$. In view of the very strong affinity and 1 : 1 ratio, the titrant may be treated to a first approximation as a solution of complex anion $[\mathbf{1}\cdot SO_4]^{2-}$. In analogy to all our previous threading experiments with ion-pair components,[3] pseudorotaxane formation was expected to manifest itself by significant upfield shifts of hydroquinone protons caused by π-stacking with indolocarbazole. Fig. 3 compares the changes of chemical shifts of the macrocycle's hydroquinone protons during macrocycle **2** titration with $[\mathbf{1}\cdot SO_4]^{2-}$and SO_4^{2-} alone.

As was hoped, large upfield shifts ($\Delta\delta_{max} = -0.28$ ppm for HQ1, $\Delta\delta_{max} = -0.49$ ppm for HQ2) of both hydroquinone signals of **2** were observed upon binding with $[\mathbf{1}\cdot SO_4]^{2-}$, confirming the formation of the pseudorotaxane assembly $[\mathbf{2}\cdot SO_4\cdot\mathbf{1}]^{2-}$ and its interpenetrative nature. This is in contrast to the titration of **2** with sulfate alone, where the two hydroquinone protons close to the bound anion move slightly downfield (~ 0.15 ppm) during titration, whereas the other, more distant pair, move slightly upfield (< 0.07 ppm). Threading of the indolocarbazole through the annulus of macrocycle **2** was further confirmed by a series of intermolecular 1D NOE effects between the indolocarbazole thread and the macrocyclic wheel measured in 1 : 1 : 1 mixture of **2**, $(TBA)_2SO_4$ and **1**. In particular, protons NH, CH-2 and CH-3 of the indolocarbazole are in close proximity to hydroquinone protons of the macrocycle (see ESI†).

Importantly, analogous titration experiments with the chloride anion, which has been very successful as a template for pseudorotaxane formation with cationic threads, gave no indication of threading (see ESI†). On the other hand, fluoride

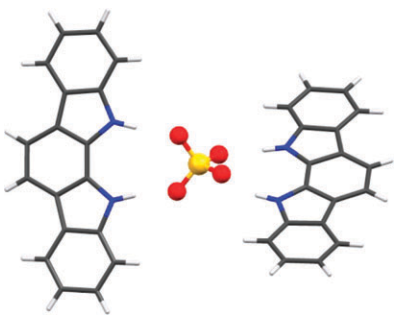


Fig. 2 X-Ray structure of 2 : 1 indolocarbazole–sulfate complex. Only one of two crystallographically independent complexes is shown.

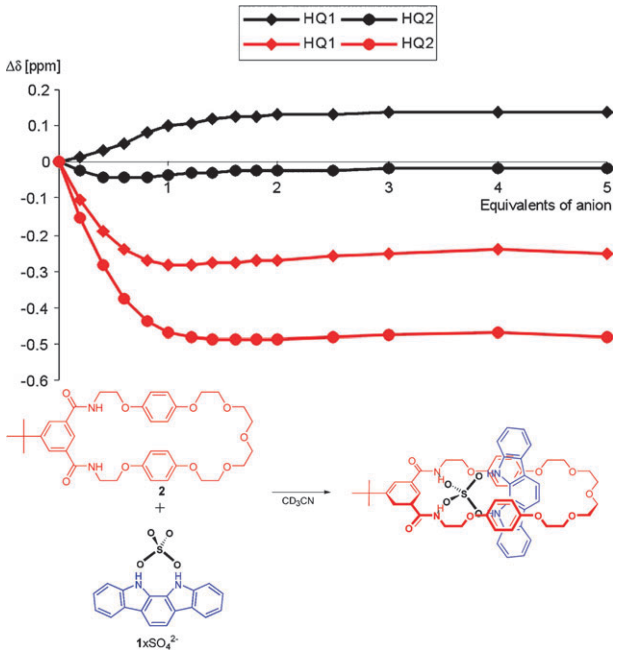
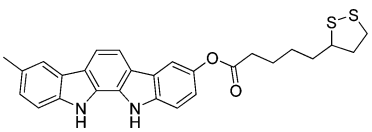


Fig. 3 The comparison of titration curves obtained by following two signals from hydroquinone protons (HQ1 and HQ2) during ^{1}H NMR titration of 0.002 M solution of macrocycle **2** with $(TBA)_2SO_4$ (black) and a 1 : 1 mixture of $(TBA)_2SO_4$ and indolocarbazole **1** (red). Solvent: acetonitrile-d_3, $T = 298$ K.

does template pseudorotaxane formation, but also deprotonates indolocarbazole, as evidenced by broadening and disappearance of the NH signal and appearance of the FHF^- anion triplet in the ^{1}H NMR spectra. Furthermore, binding is weaker for fluoride than for sulfate, as judged from the shallower minima on titration curves and smaller upfield shifts of hydroquinone protons (see ESI†).

Additional evidence for sulfate-templated pseudorotaxane formation was provided by surface plasmon resonance (SPR) analyses utilising the robust chemisorption of the disulfide functionalised indolocarbazole derivative **3** on gold. FTIR reflectance, ellipsometric and electrochemical analyses of SAMs formed by the axle **3** were fully consistent with a vertical orientation and good homogeneity (see ESI†).

The sulfate anion templated threading of **2** over surface immobilised axles can be readily monitored through changes in surface refractive index, where anion mediated surface assembly, pseudorotaxane stability and (water) triggered dethreading can be observed (Fig. 4). In the absence of the templating anion macrocycle association with the axle adlayer is minimal, physical and largely ($> 70\%$) reversible by washing in acetonitrile.



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A more detailed insight into the dynamic behaviour of $[\mathbf{2}\cdot SO_4\cdot\mathbf{1}]^{2-}$ in CH_3CN was accomplished by means of molecular dynamics (MD) simulations with the AMBER9[8] software, using the GAFF force field.[9] The assessment of the

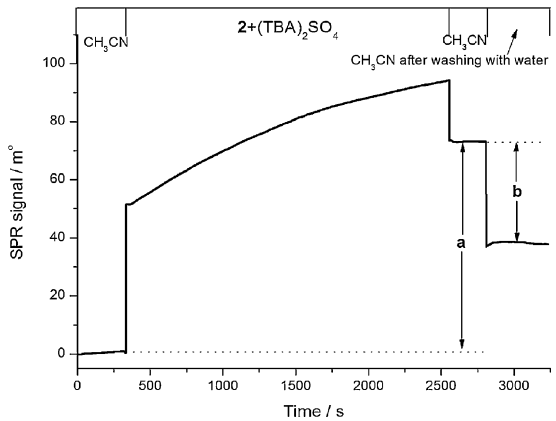

Fig. 4 SPR sensorgram showing the threading of **2** over surface confined **3** on the addition of a 1 : 1 molar equivalence of the macrocycle and $(TBA)_2SO_4$. Physically adsorbed macrocycle can be removed by flushing the surface with acetonitrile solvent to give a stable pseudorotaxane coverage of $\sim$0.6 ng mm^{-2}, a value corresponding to $\sim$30% of axle threading (a). In washing the surface with water approximately 50% of the pseudorotaxanes are triggered to dethread (b). The top axis represents a continuous flow of the indicated solutions.

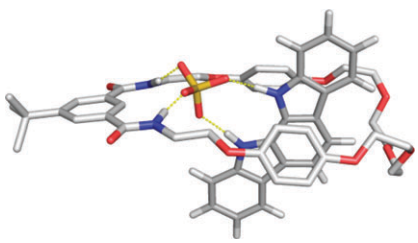

Fig. 5 Co-conformation of $[\mathbf{2}\cdot SO_4\cdot\mathbf{1}]^{2-}$ in CH_3CN (solvent molecules have been omitted for clarity). This conformation corresponds to the average structure obtained from a 5 ns trajectory. Hydrogen bonds are presented as yellow dashes; C–H hydrogen atoms of **2** have been omitted for clarity.

lowest energy conformations of the complex was performed by gas-phase simulated annealing methods (see ESI†). The lowest energy gas-phase co-conformation obtained for $[\mathbf{2}\cdot SO_4\cdot\mathbf{1}]^{2-}$ (see Fig. S5 in ESI†) presents the indolocarbazole molecule unthreaded and partially wrapped by **2** and parallel to the isophthalamide moiety. This arrangement allows for the establishment of hydrogen bonds to two oxygens of the sulfate anion, whereas the NH groups from the isophthalamide unit only establish hydrogen bonds to one sulfate oxygen. This co-conformation, however, was found to be unstable in acetonitrile relative to the pseudorotaxane assembly (Fig. 5).

Solvation effects lead to the partial unwrapping of the indolocarbazole unit during the first stages of the equilibration step, leaving it solely hydrogen bonded to the sulfate oxygen donor atoms. In the pseudorotaxane co-conformation, **1** and **2** were both kept hydrogen bonded to the sulfate anion during the entire course of the simulation, with N–H$\cdots$O distances ranging from 1.52 to 2.50 Å, having **1** establishing π–π stacking interactions with the hydroquinones of **2**, in either face-to-face or face-to-edge dispositions. Interestingly, two simultaneous face-to-face interactions were never encountered, suggesting that the macrocyclic cavity is not large enough to accommodate the SO_4^{2-} anion, and simultaneously withstand these face-to-face π–π interactions. Further insights into the enthalpic and entropic contributions to the free energy difference between the two co-conformations in acetonitrile were obtained from MM-PBSA (molecular mechanics-Poisson–Boltzmann surface area) calculations[10] and normal mode analysis,[11] based on 5 ns long simulations. Results showed that pseudorotaxane formation is favoured ($\Delta G = -5.95$ kcal mol^{-1}) mainly by enthalpic effects ($\Delta H = -6.30$ kcal mol^{-1}) with negligible entropic contributions ($\Delta S = -1.17 \times 10^{-3}$ kcal mol^{-1} K^{-1}). The overall results consistently support the formation of the pseudorotaxane entity, and are in total agreement with the extensive ^{1}H NMR binding investigations.

In summary, the sulfate anion has been shown to be capable of templating the formation of pseudorotaxane assembly between a neutral indolocarbazole thread and an isophthalamide macrocycle. This finding serves to further illustrate the tremendous potential anions have in directing the assembly of mechanically bonded molecular structures.

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