A Catenane Assembled through a Single Charge-Assisted Halogen Bond

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Introduction

Interlocked molecules are attractive for their non-trivial topology and their promising potential in chemical sensor and nanotechnological applications.[1] Their synthesis is a challenge, however, and requires imaginative templation methodologies, which exploit a combination of electrostatic, Lewis acid–base and hydrogen-bonding (HB) interactions for component assembly.[2]
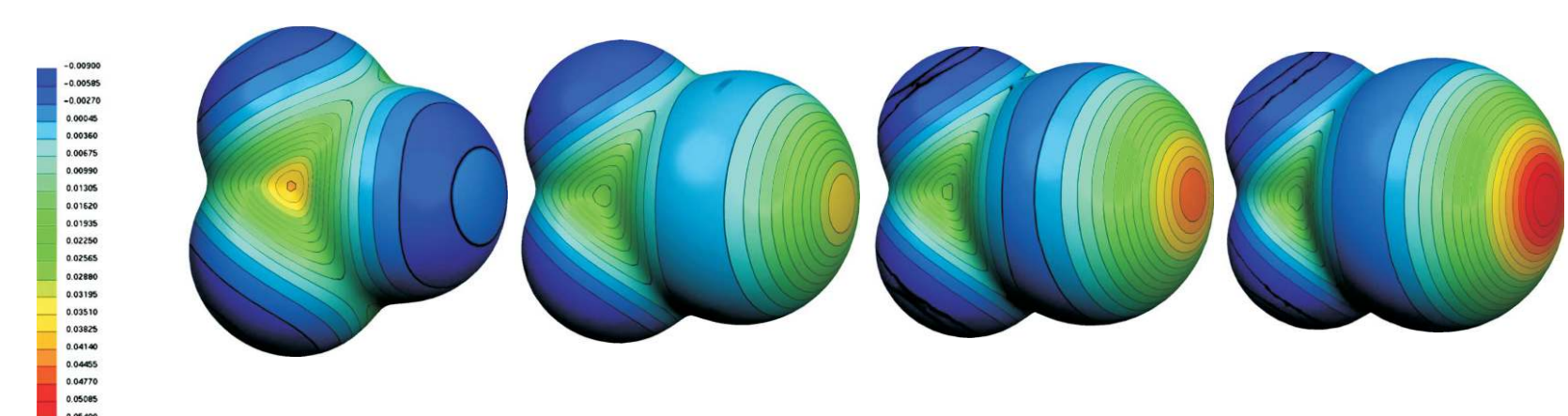

Figure 1. The molecular electrostatic potential, in Hartrees, at the 0.001 electrons Bohr[3] isodensity surface of CF_3X (where X = F, Cl, Br and I).[3]

Halogen bonding (XB) is the attractive, highly directional, non-covalent interaction between an electron-deficient halogen atom and a Lewis base.[4] The scope of XB in solid-state crystal engineering has been explored for sometime, but the exploitation of XB in solution-phase molecular recognition processes, self-assembly and catalysis is still very much in its infancy–a surprise given XB's complementary analogy to ubiquitous HB.[5]
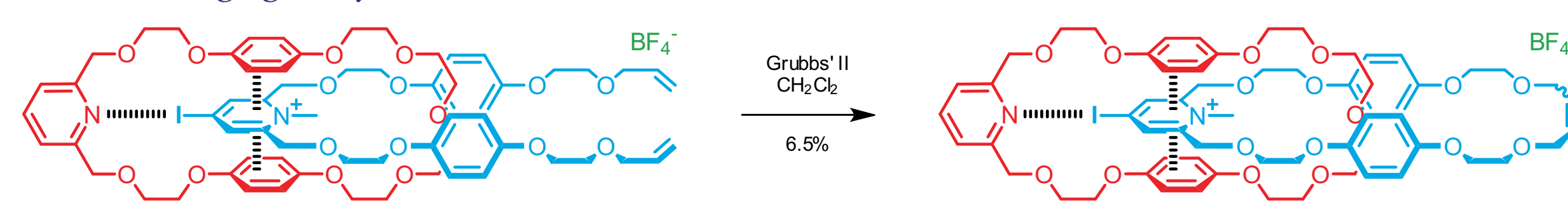
By incorporating a suitable neutral halogen-bond acceptor, such as pyridine,[6] into a macrocyclic framework, a single charge-assisted XB interaction can be exploited for pseudorotaxane assembly and, importantly, in the synthesis of a novel interlocked catenane.[7]
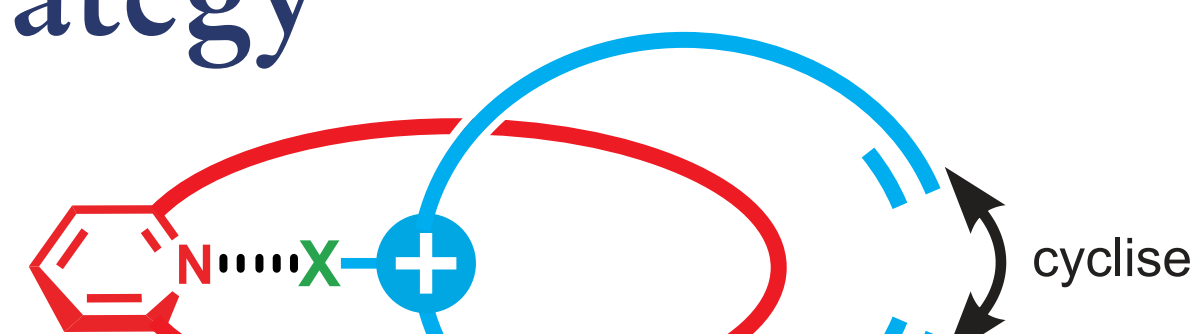
Synthetic strategy

Figure 2. Cartoon representation of the orthogonal halogen-bond-templated pseudorotaxane species (where X = Br or I).

The synthetic strategy employed is outlined in Figure 2. An acyclic positively charged XB-donor threads through a halogen-bond-accepting, pyridine-containing macrocycle, forming an orthogonal interpenetrated assembly that is stabilised by a charge-assisted XB interaction. Macrocycle **1** contains electron-rich hydroquinone units to facilitate secondary aromatic donor–acceptor interactions with an electron-poor pyridinium motif. Vinyl-appended bromo- and iodo-functionalised triazolium and pyridinium compounds were chosen as potential threading components which, after successful pseudorotaxane assembly with **1**, could be used in a RCM cyclisation to form the target catenane.
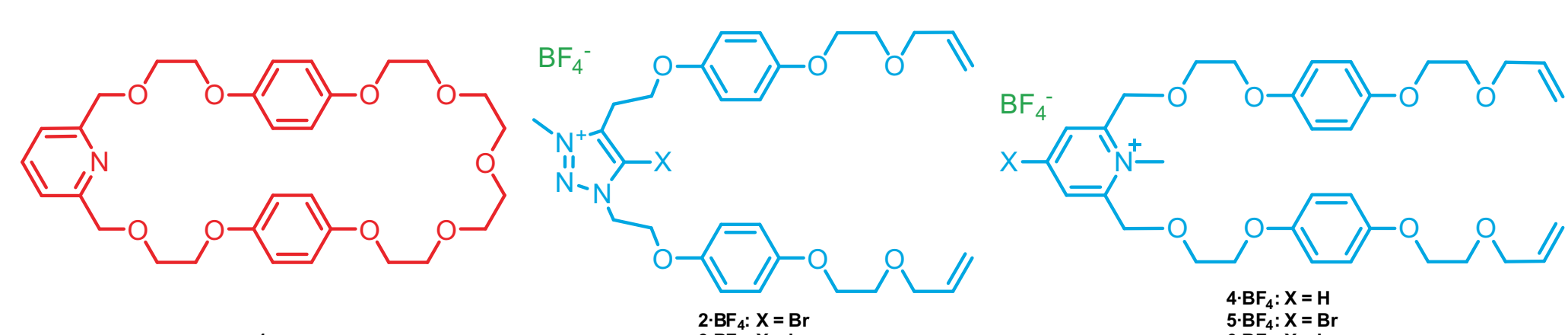
Pseudorotaxane assembly

Figure 3. Structures of macrocycle **1** and threading components **2–6·BF₄** (where X = H, Br or I).

To establish evidence for interpenetrative assembly in solution and also determine the strength of any association between XB-acceptor and potential XB-donor components, the pseudorotaxane assembly between macrocycle **1** and threading components **2–6·BF₄** in CD_2Cl_2 was studied using ^{1}H NMR spectroscopy. Addition of **3·BF₄**, **5·BF₄** and **6·BF₄** to macrocycle **1** induced upfield shifts in the macrocycle's hydroquinone proton signal, consistent with the formation of aromatic donor–acceptor interactions as the XB-donor species thread through the macrocyclic ring (Figure 4). The Δδppm values and 1:1 association constants (Table 1) reveal the most stable interpenetrative assembly is found with the iodopyridinium thread **6·BF₄** with an association constant value double that with the bromopyridinium species **5·BF₄**. This can be attributed to the greater halogen-bond-donor ability of the more polarisable iodine substituent compared with bromine. Importantly, the pseudorotaxane assembly with the protic pyridinium analogue **4·BF₄** is significantly weaker, thus highlighting the essential contribution of the XB interaction in stabilising the overall pseudorotaxane assembly. Table 1 shows that although the iodotriazolium compound **3·BF₄** forms a measurable pseudorotaxane association with macrocycle **1**, the extremely small chemical shift perturbations noted in the titration experiment with the bromotriazolium analogue **2·BF₄** suggest interpenetration is not occurring. The reduced supplementary secondary aromatic donor–acceptor interactions of the triazolium motif with the macrocycle's hydroquinone groups in comparison with pyridinium will also be a contributing factor.

Thread	3·BF₄	4·BF₄	5·BF₄	6·BF₄
Δβ (ppm)[a]	0.03[b]	0.03	0.07	0.10
K_{app} (M⁻¹)	55(3)	30(2)	80(2)	180(20)

Table 1. Observed chemical shift perturbations (Δδ) of hydroquinone protons and association constants, K_a, for macrocycle **1** with thread components **2–6·BF₄**. Estimated standard errors are given in parentheses. [a] After ten equiv. [b] After five equiv. (CD_2Cl_2, 293 K).
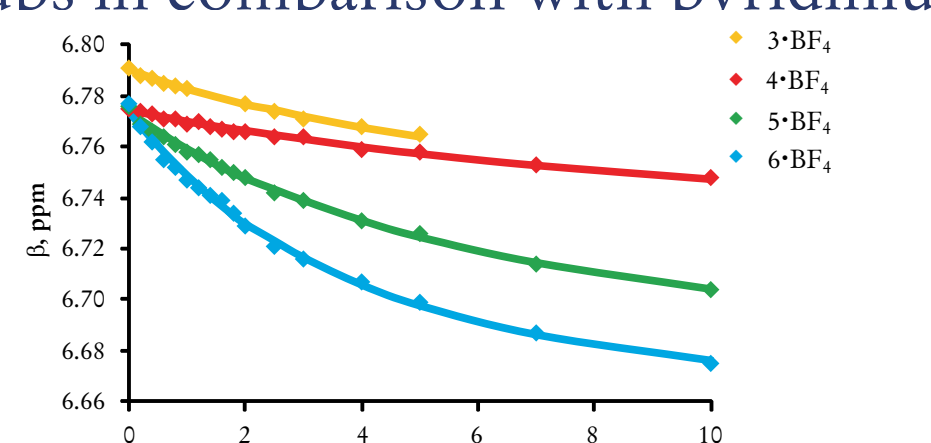

Figure 4. Titration curves for pseudorotaxane assembly between macrocycle **1** and thread components **3·BF₄**, **4·BF₄**, **5·BF₄** and **6·BF₄**.

Synthesis of the target catenane

Encouraged by the favourable association between macrocycle **1** and iodopyridinium thread **6·BF₄**, the synthesis of a novel [2]catenane using a Grubbs'-catalysed RCM clipping reaction was undertaken (Scheme 1).

Macrocycle **1** and 1.1 equivalents of iodopyridinium thread component **6·BF₄** in anhydrous CH_2Cl_2 solution were stirred at r.t. under N_2 in the presence of Grubbs'(II) catalyst (10% wt). Following purification using repeated preparative thin layer chromatography the target [2]catenane **7·BF₄** was isolated in 6.5% yield.

The synthesis of the related protic- and bromopyridinium-containing catenanes were also attempted with threading components **4·BF₄** and **5·BF₄** using analogous Grubbs'-catalysed RCM reaction conditions. Although no evidence of catenane formation was observed with proticpyridinium thread **4·BF₄**, with the bromopyridinium thread **5·BF₄** a peak at $m/z = 1213.4$, corresponding to the [2]catenane species, was detected by electrospray mass spectrometry. In spite of numerous attempts, however, the catenane could not be isolated which suggests it is produced in negligible yield.

Scheme 1. Synthesis of novel, halogen-bond-templated catenane **7·BF₄**.

Characterisation of novel catenane 7·BF₄

The ^{1}H NMR spectrum of the [2]catenane together with those for the component macrocycle and vinyl-appended precursor for comparison are shown in Figure 5. The disappearance of the vinylic multiplet μ and the convergence of multiplet λ into a pseudo-singlet in the catenane spectrum are attributed to cyclisation of the acyclic precursor. Most importantly, the upfield shift and splitting of the macrocycle hydroquinone protons f and g is indicative of aromatic donor–acceptor interactions between the electron-rich macrocycle hydroquinone units and the electron-poor pyridinium group. The downfield shift of pyridine protons a and b is consistent with the withdrawal of electron density by the formation of the halogen bond. Finally, the upfield shift of pyridinium proton signal β is a result of catenane inter-ring halogen-bond-formation between the pyridine nitrogen and the iodine substituent.
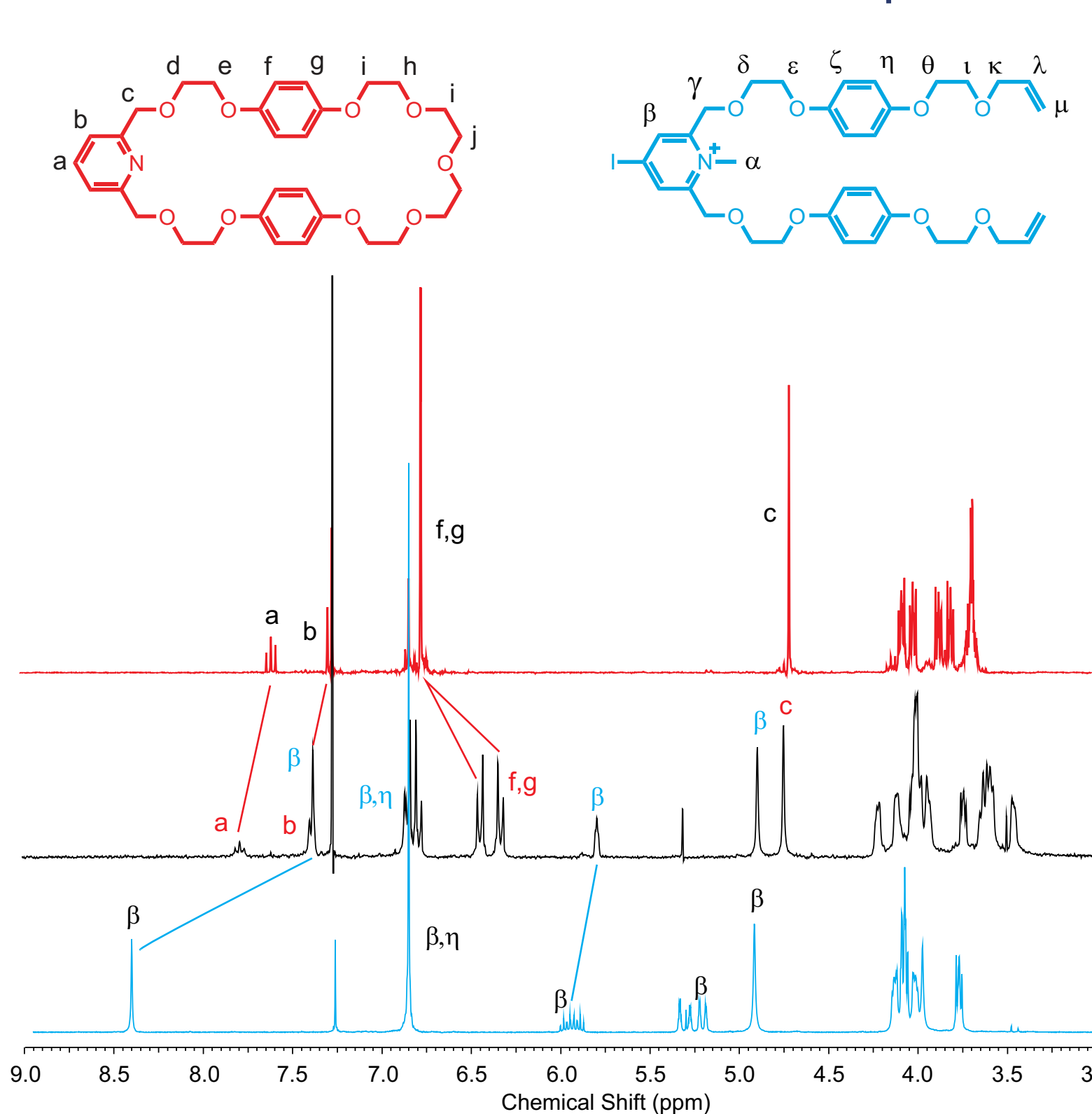

Figure 5. 1H NMR spectra of a) pyridine macrocycle 1, b) halogen-bonded [2]catenane **7·BF₄**, c) iodopyridinium RCM precursor **6·BF₄**. (300 MHz, CDCl3, 293 K).

Conclusions

Through the design of a suitable XB-acceptor pyridine-containing macrocycle, we have demonstrated the formation of pseudorotaxane assemblies with a series of XB-donor iodo-functionalised triazolium, bromo- and iodo-functionalised pyridinium threading components, which are stabilised by a charge-assisted XB interaction. The strength of the XB interpenetrative assembly between the pyridine macrocycle and iodo-pyridinium thread was exploited in the Grubbs'-catalysed RCM clipping synthesis of a novel [2]catenane. The crucial importance of the single charge-assisted XB interaction between the two components was highlighted by the fact that no evidence of catenane formation was observed in an analogous RCM reaction of the pyridine macrocycle with the corresponding protic-pyridinium reactant. Hence we have illustrated that XB has real potential in templating the construction of mechanically bonded molecular architectures.

References

1. a) S. Saha, J. F. Stoddart, *Chem. Soc. Rev.* **2007**, 36, 77-92; b) J. J. Gassensmith, S. Matthys, J.-J. Lee, A. Wojcik, P. V. Kamat, B. D. Smith, *Chem. Eur. J.* **2010**, 16, 2916-2921; c) N. H. Evans, P. D. Beer, *Org. Biomol. Chem.* **2011**, 9, 92-100; d) M. J. Chmielewski, J. J. Davis, P. D. Beer, *Org. Biomol. Chem.* **2009**, 7, 415-424.
2. a) C. O. Dietrichbuchecker, J. P. Sauvage, J. M. Kern, *J. Am. Chem. Soc.* **1984**, 106, 3043-3045; b) M. Fujita, F. Ibukuro, H. Hagihara, K. Ogura, *Nature* **1994**, 367, 720-723; c) J. A. Wisner, P. D. Beer, M. G. B. Drew, M. R. Sambrook, *J. Am. Chem. Soc.* **2002**, 124, 12469-12476
3. T. Clark, M. Hennemann, J. S. Murray, P. Politzer, *J. Mol. Model.* **2007**, 291-296.
4. P. Metrangolo, F. Meyer, T. Pilati, G. Resnati, G. Terraneo, *Angew. Chem. Int. Ed.* **2008**, 47, 6114-6127.
5. a) D. Cinčić, T. Friščćić, W. Jones, *Chem. Eur. J.* **2008**, 14, 747-753; b) R. Liantonio, P. Metrangolo, T. Pilati, G. Resnati, A. Stevenazzi, *Cryst. Growth Des.* **2003**, 3, 799-803; c) M. T. Johnson, Z. Džolić, M. Cetina, O. F. Wendt, L. Öhrström, K. Rissanen, *Cryst. Growth Des.* **2011**, 12, 362-368; d) M. Erdelyi, *Chem. Soc. Rev.* **2012**, 41, 3547-3557; e) T. M. Beale, M. G. Chudzinski, M. G. Sarwar, M. S. Taylor, *Chem. Soc. Rev.* **2013**, 1667-1680.
6. a) L. C. Roper, C. Prasang, V. N. Kozhevnikov, A. C. Whitwood, P. B. Karadakov, D. W. Bruce, *Cryst. Growth Des.* **2010**, 10, 3710-3720; b) F. Zordan, L. Brammer, P. Sherwood, *J. Am. Chem. Soc.* **2005**, 127, 5979-5989.
7. L. C. Gilday, T. Lang, A. Caballero, P. J. Costa, V. Felix, P. D. Beer, *Angew. Chem. Int. Ed.* **2013**, 52, 4356-4360.

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