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A catenane host system containing integrated triazole C–H hydrogen bond donors for anion recognition†

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A 3,5-bis(triazole)-pyridinium motif is integrated into a catenane structural framework *via* chloride anion templation. The catenane host system displays a high degree of selectivity for halide anions over dihydrogen phosphate.

The ease of synthesis of 1,2,3-triazoles *via* the copper(I)-catalysed cycloaddition of azides and terminal alkynes (CuAAC) has led to this reaction being widely exploited across the chemical sciences.[1] Notably, the efficacy, mild reaction conditions and range of functional group tolerance has proven ideal for use in the construction of mechanically bonded architectures.[2–8]

The triazole group itself has also been utilised in anion binding applications as the polarised heterocycle provides an effective C–H hydrogen bond donor, which is able to bind anions in organic solvents.[9–14] Herein, we demonstrate that the integration of a new 3,5-bis(triazole)-pyridinium functionality into a catenane structural framework results in a potent anion host system that exhibits a pronounced selectivity for halide anions over dihydrogen phosphate. To the best of our knowledge, a triazole-containing catenane anion receptor is unprecedented.[15]

Proton NMR pseudorotaxane assembly investigations were initially undertaken to establish whether the 3,5-bis(triazole)-pyridinium motif was capable of penetrating the cavity of an isophthalamide macrocycle *via* chloride anion templation.

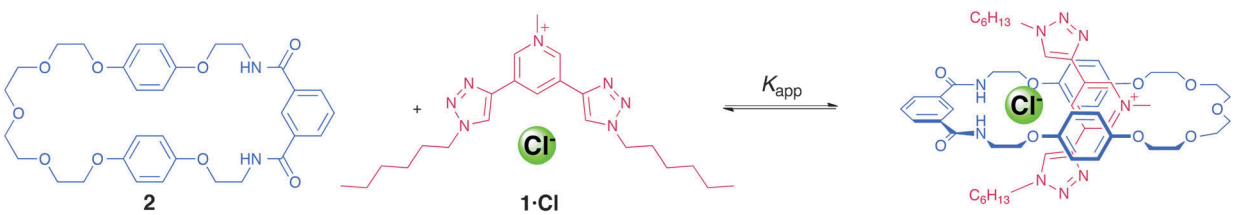
Aliquots of a solution of the novel compound **1**·Cl were titrated into a 1 : 1 $CDCl_3$: d_6-acetone solution of the isophthalamide macrocycle **2**[16] (Scheme 1, see ESI† for synthesis). Substantial upfield shifts in the macrocycle's hydroquinone resonances were observed, consistent with the formation of an anion-templated pseudorotaxane,[16,17] with these perturbations being caused by donor–acceptor interactions between electron-rich hydroquinone groups and the electron-deficient pyridinium threading component. Further evidence for pseudorotaxane formation was provided by 2D ROESY NMR (see ESI†).

In the analogous titration experiment with **1**·PF_6, only very minor shifts of the macrocycle's hydroquinone signals were observed, demonstrating the crucial importance of the chloride anion template in stabilising the interpenetrated assembly. Apparent 1 : 1 stoichiometric association constants were calculated for pseudorotaxane formation, monitoring the hydroquinone proton data, using WINEQNMR2.[18] For comparison purposes, titration experiments were also undertaken with the amide thread analogue, *N*-methyl-3,5-bis(hexylcarbamoyl)-pyridinium chloride, **3**·Cl.[17] As shown in Table 1, the bis(triazole)-pyridinium receptor **1**·Cl forms a significantly stronger pseudorotaxane assembly with **2** than does the bis(amide)-pyridinium analogue **3**·Cl. Also it is noteworthy that with the corresponding hexafluorophosphate pyridinium salts, the bis-amide **3**·PF_6 undergoes a significant degree of interpenetration, whereas the pseudorotaxane assembly with **1**·PF_6 is extremely weak.

Table 1 Apparent association constants, K_{app} (M^{-1})[a] for pseudorotaxane formation with isophthalamide macrocycle **2**

Anion	Triazole thread $\mathbf{1}^+$	Amide thread $\mathbf{3}^+$
Cl^-	800(70)	420(15)
PF_6^-	38(3)	170(25)

[a] Calculated using WINEQNMR2[18] monitoring the hydroquinone signal; estimated standard errors are given in parentheses (293 K, solvent: 1 : 1 $CDCl_3$: acetone-d_6).



Scheme 1 Formation of chloride-templated pseudorotaxane between isophthalamide macrocycle and threading component **1**·Cl.

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† Electronic supplementary information (ESI) available: Synthetic procedures and characterisation of all new compounds, crystallographic data for **1**·Cl·$\mathbf{2}^{tBu}$ and **5**·Cl, NMR titration protocols and data. CCDC 885861, 885862. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2cc34210c

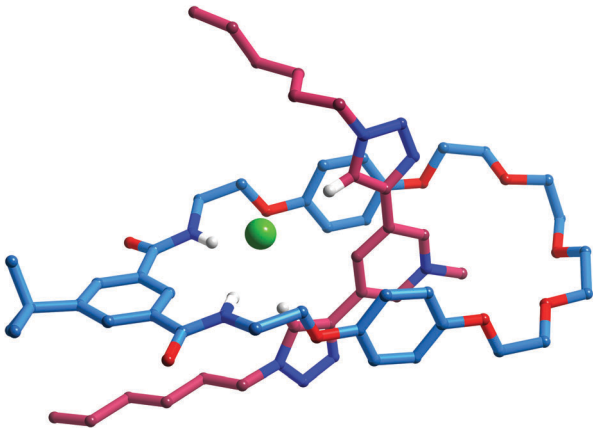


Fig. 1 X-ray crystal structure of **1**·Cl·**2**$^{t\mathrm{Bu}}$.

The solid state structure of the pseudorotaxane **1**·Cl·**2**$^{t\mathrm{Bu}}$ [19] was determined by single crystal X-ray crystallography (Fig. 1). The pseudorotaxane is stabilised by hydrogen bonds between the chloride anion and amide and triazole groups, with additional close hydroquinone···pyridinium···hydroquinone contacts and hydrogen bonding between the pyridinium methyl group and macrocycle polyether chain.

The synthesis of the new catenane **5**·Cl was achieved by chloride anion templated Grubbs' catalysed ring-closing metathesis reaction of 1.2 equivalents of **4**·Cl and one equivalent of isophthalamide macrocycle **2** in dichloromethane (Scheme 2). The catenane was isolated in 64% yield (following purification by preparative thin layer chromatography) – significantly higher than the 45% reported for the analogous bis(amide)-pyridinium catenane.[20] No catenane formation was detected when **4**·PF_6 was used in place of **4**·Cl, demonstrating the importance of the templating halide anion.

Catenane **5**·Cl was characterised by ^{1}H, ^{13}C and 2D ROESY NMR (see ESI†), as well as by high resolution ESI mass spectrometry and single crystal X-ray crystallography (Fig. 2). The solid state structure of **5**·Cl shows that both amide and both triazole groups form hydrogen bonds to the chloride anion, with the structure stabilised by the packing of electron-poor and electron-rich aromatic rings, and hydrogen bonding between the pyridinium methyl group and macrocycle polyether chain.

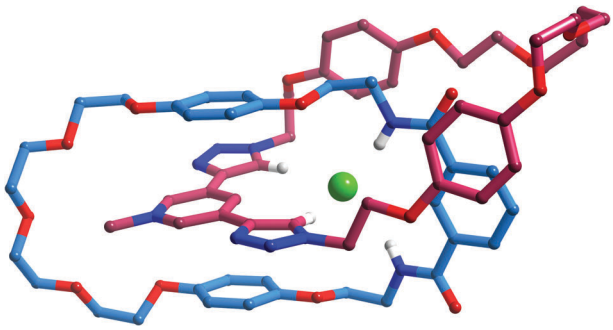
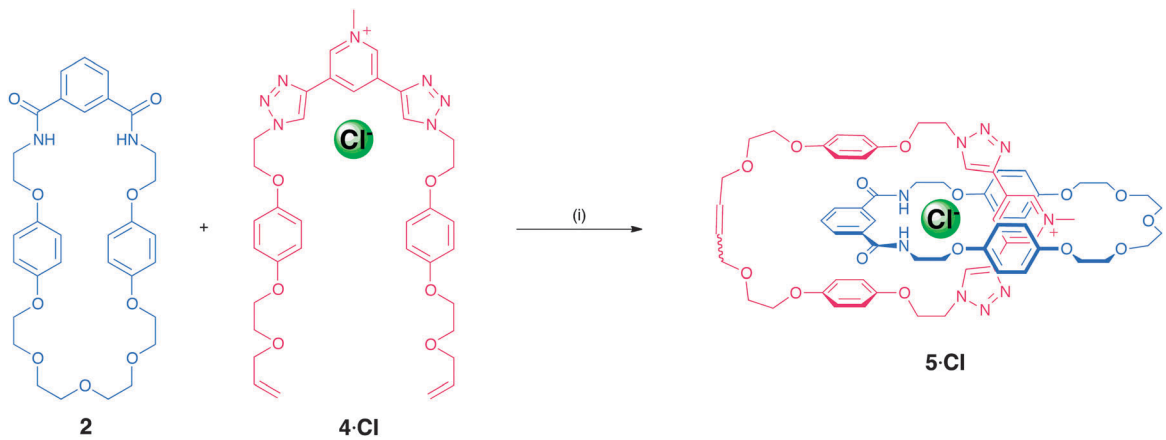


Fig. 2 X-ray crystal structure of **5**·Cl.

The templating chloride anion was removed by repeatedly washing a dichloromethane solution of **5**·Cl with aqueous ammonium hexafluorophosphate to afford **5**·PF_6 (see ESI†). The ^{1}H NMR spectra of **2**, **5**·Cl and **5**·PF_6 are shown in Fig. 3. A large upfield shift of the hydroquinone proton resonances, *e* and *f*, is observed in the interlocked species compared to the free macrocycle, consistent with inter-ring stacking interactions. Significant downfield shifts are observed for triazole and amide signals in the catenane's cavity, due to deshielding of these protons by hydrogen bonding interactions with the encapsulated chloride anion.

Preliminary anion binding studies of **5**·PF_6 were conducted in the competitive solvent mixture 1 : 1 $CDCl_3$: CD_3OD. Stoichiometric association constants (1 : 1) were calculated using WINEQNMR2,[18] monitoring the triazole proton resonance. Importantly, while little difference is observed between the bis-triazole containing catenane and the all-amide catenane analogue in terms of chloride association strength, dihydrogen phosphate is bound much more weakly by **5**·PF_6, with an impressive selectivity of more than an order of magnitude between the halides and the basic oxoanion (Table 2).[21] Presumably, the tetrahedrally shaped dihydrogen phosphate anion is too large to penetrate the catenane's unique interlocked bis-triazole bis-amide hydrogen bond donating cavity.

In summary, we have demonstrated the capability of a new 3,5-bis(triazole)-pyridinium group to form a stronger chloride anion-templated pseudorotaxane assembly with an isophthalamide macrocycle than the 3,5-bis(amide)-pyridinium analogue. This enhanced stability of interpenetration has been exploited in the



Scheme 2 Synthesis of catenane **5**. Conditions and reagents: (i) Grubbs' II catalyst, CH_2Cl_2, 64%.

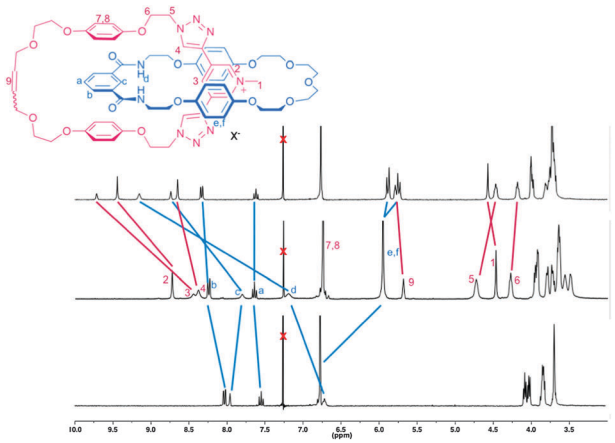


Fig. 3 Truncated ^{1}H NMR spectra of **5**·Cl (top), **5**·PF_6 (middle) and **2** (bottom) (300 MHz, 293 K, solvent: $CDCl_3$, all species 8 mM).

Table 2 Association constants, K_a (M^{-1})[a] for amide and triazole-based catenanes

Anion	Triazole catenane **5**·PF_6	Amide catenane·PF_6[19]
Cl^-	680(20)	730
Br^-	630(50)	—
I^-	510(10)	—
$H_2PO_4^-$	49(4)	K_1 = 480, K_2 = 520

[a] Calculated using WINEQNMR2[18] monitoring triazole protons; estimated standard errors are given in parentheses (293 K, solvent: 1 : 1 $CDCl_3$: CD_3OD).

synthesis of the first triazole-containing catenane anion receptor in an impressive yield of 64%. The triazole catenane host system binds halides strongly in the competitive 1 : 1 $CDCl_3$: CD_3OD solvent mixture, and importantly exhibits a high degree of selectivity for the halides over dihydrogen phosphate, superior to that of an amide catenane analogue. This serves to illustrate that the integration of triazole C–H hydrogen bond donor groups into interlocked host structural design has the exciting potential to influence significantly the host's anion recognition properties.

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