Anion templated double cyclization assembly of a chloride selective [2]catenane†

Ka-Yuen Ng,[a] Andrew R. Cowley[b] and Paul D. Beer*[a]

Received (in Austin, TX, USA) 8th May 2006, Accepted 5th June 2006
First published as an Advance Article on the web 19th June 2006
DOI: 10.1039/b606503a

The interweaving of two identical acyclic positively charged anion recognizing units around a chloride anion template leads to the formation of an orthogonal supramolecular ensemble which upon subsequent double ring cyclization gives a chloride selective [2]catenane in very high yield.

Stimulated by the potential uses mechanically bonded molecules may have as molecular switches, sensors and machines,[1] the interest being shown in discovering new imaginative and strategic high yielding templation methods for their construction is ever increasing.[2] In the majority of cases cationic and neutral species have been used to assemble these interlocked structures[3] whereas by contrast, manipulating anions to direct supramolecular assembly remains largely under-developed.[4,5] With the ultimate objective of constructing novel anion receptor systems with increasingly superior binding behaviours we have undertaken the challenge of exploiting anions to template the formation of interlocked supramolecular assemblies. Indeed we have recently shown that pseudorotaxane,[6] rotaxane[7] and catenane[8] formation can be templated selectively by a chloride anion which facilitates the interpenetration of a pyridinium, imidazolium or guanidinium threading component through the annulus of an isophthalamide macrocycle.

Inspired by Sauvage's metal-directed synthesis of a pseudo-tetrahedral copper(I) bis-1,10-phenol-phenanthroline complex as a precursor to catenane structures,[9] we describe herein the first example of an anion directed interweaving of two identical acyclic positively charged anion recognizing motifs into an orthogonal assembled structure which upon a subsequent double cyclization reaction using ring closing metathesis (RCM)[10] produces a novel [2]catenane in very high yield (Fig. 1).

The catenane precursor compound 1^+ (Fig. 2) is designed to incorporate complementary supramolecular interactions which assist the molecule to assemble around a chloride anion template in a 2 : 1 stoichiometric host to guest fashion. Each precursor molecule provides two amide hydrogen bond donating groups for anion binding such that a pseudo-tetrahedral amide hydrogen bonding association of two molecules of 1^+ around the spherical chloride anion can occur.

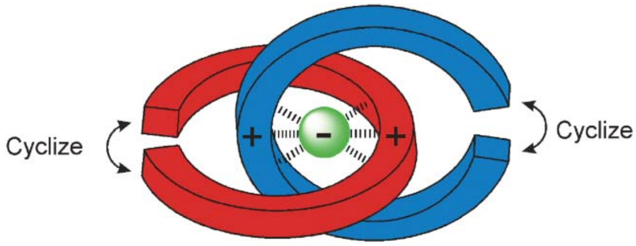

Fig. 1 The anion templated double cyclization strategy leading to catenane formation.

The new compounds, **1a**, **1b** were prepared using standard synthetic procedures described in the supplementary information. The targeted [2]catenane $2^{2+}(Cl^-)(PF_6^-)$ shown in Fig. 3 was prepared by mixing an equimolar solution of **1a** and **1b** in dry dichloromethane followed by the addition of Grubbs' 1st generation catalyst (10% by weight). Purification by column chromatography afforded the product in 78% yield. The analogous RCM reaction with **1a** gave the catenane $2^{2+}(Cl^-)_2$ in 34% yield. The significant reduction in yield is attributed to competition from a 1 : 1 binding mode, which favors the formation of the macrocyclic structure. Interestingly, RCM of **1b** afforded $2^{2+}(PF_6^-)_2$[11] in only 16% yield. The low yield is explained by the lack of an anion templation effect from chloride, however catenane formation demonstrates that π–π stacking and pyridinium CH···O hydrogen bonding effects also play a role in the catenation formation process. All the catenane cations displayed characteristic

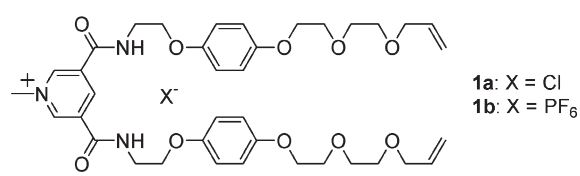

Fig. 2 Structure of the catenane precursor.

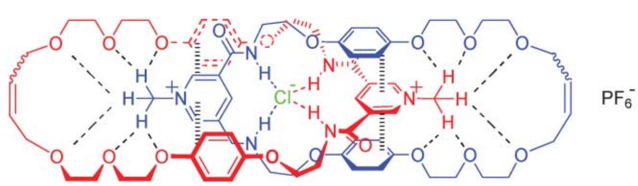

Fig. 3 Structure of the [2]catenane $2^{2+}(Cl^-)(PF_6^-)$.

[a]*Inorganic Chemistry Laboratory, Department of Chemistry, University of Oxford, South Parks Road, Oxford, UK OX1 3QR. E-mail: paul.beer@chem.ox.ac.uk; Fax: (+44) 01865-272690; Tel: (+44) 01865-285142*
[b]*Chemical Crystallography Laboratory, Department of Chemistry, University of Oxford, Mansfield Road, Oxford, UK OX1 3TA*

† Electronic supplementary information (ESI) available: Synthesis and characterisation data for compounds **1** and **2**, general procedures for ^1H NMR titration and competitive mass spectrometry binding experiments, single X-ray crystal data for $2^{2+}(Cl^-)(PF_6^-)$. See DOI: 10.1039/b606503a

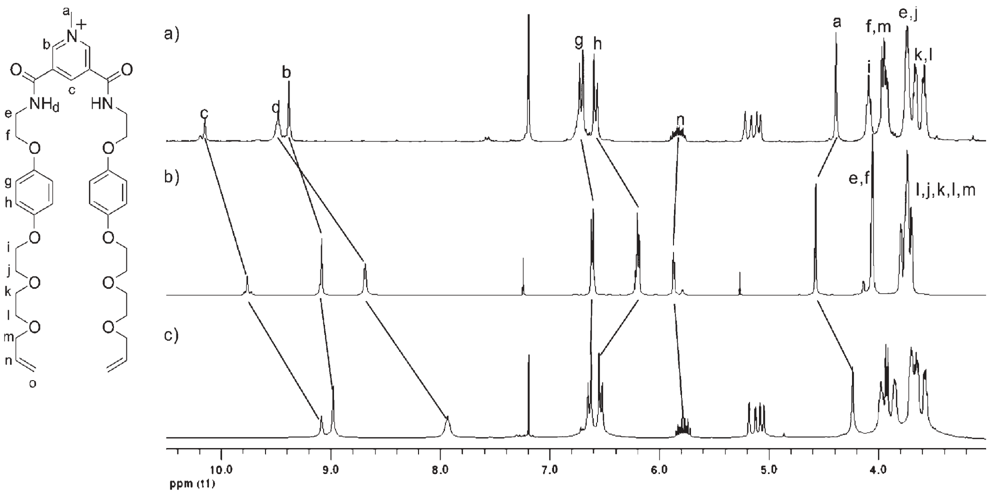

Fig. 4 ^{1}H NMR spectra ($CDCl_3$, 298 K) of a) **1a**, b) $\mathbf{2}^{2+}(Cl^-)(PF_6^-)$ and c) **1b**.

intense doubly charged ion peaks in electrospray mass spectrometry at m/z = 680.3. For $\mathbf{2}^{2+}(Cl^-)(PF_6^-)$ and $\mathbf{2}^{2+}(Cl^-)_2$ a weaker singly charged ion peak occurred at m/z = 1395.6, corresponding to the catenane chloride complex $[\mathbf{2}^{2+}(Cl^-)]$.

The interlocked nature and presence of various supramolecular interactions in $\mathbf{2}^{2+}(Cl^-)(PF_6^-)$ are revealed in the ^{1}H NMR spectrum, which is compared to that of **1a** and **1b** in Fig. 4. The spectra of **1a** and **1b** show little discrepancy apart from the anion binding region that involves the amide and *para*-pyridinium protons. This is to be expected in view of their similarity in structure. Upon catenation, however, the hydroquinone protons, pyridinium N^+–CH_3 methyl protons and hydrogen atoms on the polyether chain all display significant NMR perturbations.

In particular the downfield shift of the amide proton signal for $\mathbf{2}^{2+}(Cl^-)(PF_6^-)$ as compared with **1b** is indicative of chloride binding in the amide cleft. The extent of the shift ($\Delta\delta$ = 0.80 ppm) is not as large as in **1a** ($\Delta\delta$ = 1.64 ppm), since two anion binding moieties are competing for one chloride in the catenane. The *para*-pyridinium protons, which are also involved in anion coordination, exhibit similar trends. The large splitting ($\Delta\delta$ = 0.43 ppm) of the hydroquinone proton signals is suggestive of extensive π–π stacking interactions with the pyridinium ring. Hydrogen bonds between the pyridinium N^+–CH_3 methyl protons and the polyether chain are signified by the downfield shifts of the methyl protons and perturbation of the –OCH_2– protons.

Single crystals of $\mathbf{2}^{2+}(Cl^-)(PF_6^-)$‡ suitable for X-ray diffraction analysis were grown by the slow diffusion of diisopropyl ether into a dichloromethane solution of the [2]catenane. The structure (Fig. 5) confirms the interlocked nature of the molecule in the solid state and highlights the crucial importance of the templating role of the chloride anion, which sits in the middle of a distorted octahedral binding cavity formed by the four amide protons and two *para*-pyridinium protons. These six hydrogens all point towards the chloride anion and the X–H···Cl (where X = C or N) bond distances range from 3.288 Å to 3.518 Å. Each pyridinium ring is sandwiched between the hydroquinone units from the other macrocycle, forming parallel face to face stacks of the aromatic planes. Hydrogen bonding probably exists between the N^+–CH_3 methyl protons and the polyether chain but these interactions were not properly defined due to disorder of the latter.

The anion binding properties of the catenane cation were investigated by titrating $\mathbf{2}^{2+}(PF_6^-)_2$ with TBA salts of F^-, Cl^-, Br^-, $H_2PO_4^-$ and OAc^- in 1 : 1 *d*-chloroform : d_6-acetone and the ^{1}H NMR shifts of the pyridinium and amide protons were monitored. With chloride and acetate guest anions EQNMR[12] analysis of the respective amide proton titration curves gave association constant values shown in Table 1, where both anions are bound by the catenane in a major 1 : 1 host : guest stoichiometric complex together with a minor 1 : 2 host : guest complex stoichiometric component. The catenane binds chloride much more strongly (K_{11} > 20 fold) than the basic acetate anion which reflects the halide anion's complementary match of size and geometry to the catenane's unique interlocked binding cavity. With bromide, although EQNMR could not determine association

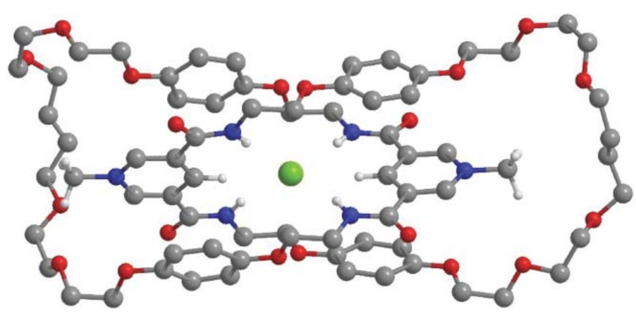

Fig. 5 The crystal structure of the [2]catenane with a chloride ion in the binding cavity. Hydrogen atoms have been omitted except for those involved in hydrogen bonding.

Table 1 Association constants (M^{-1}) for $\mathbf{2}^{2+}(PF_6^-)_2$ with Cl^-, OAc^- and Br^- at 298 K in 1 : 1 *d*-chloroform : d_6-acetone[a]

	Cl^-	OAc^-	$Br^{-\,b}$
K_{11}	9240	420	790
K_{12}	160	40	40

[a] Errors less than 10%. [b] Determined by *ortho*-pyridinium protons.

constant values from the amide proton titration curve data, analysis of the *ortho*-pyridinium proton titration data, which interestingly displayed comparatively larger magnitudes of downfield perturbations, proved successful (Table 1). Taking into account the larger size of the bromide anion, the topologically constrained binding cavity of the catenane and the greater perturbation of the *ortho*-pyridinium protons, association of bromide with the catenane may occur outside of the amide binding pocket, possibly *via* favourable electrostatic interactions with the positively charged pyridinium ring. Downfield shifts of the amide and *ortho*-pyridinium protons signals were also observed in catenane titrations with fluoride and dihydrogenphosphate, however the data could not be analysed by any EQNMR binding models. These results suggest the [2]catenane is able to interact with various anions but importantly, only chloride is bound strongly and specifically inside the amide binding cavity, whose size and geometry are suitably designed to accommodate this anionic guest.

Indeed competitive anion complexation studies using electrospray mass spectrometry (ESMS) further corroborate the catenane's selectivity for chloride. An equimolar aqueous mixture of the ammonium salts of chloride, fluoride, acetate, dihydrogenphosphate, hydrogensulfate and nitrate was mixed with $\mathbf{2}^{2+}(PF_6^-)_2$ in methanol and the resulting ESMS spectrum revealed only the chloride adduct $[\mathbf{2}^{2+}(Cl^-)]$ and the catenane dication $\mathbf{2}^{2+}$ signal. This selectivity for chloride has to be attributed to the unique interlocked chelating structure of the topologically interesting binding compartment.

In conclusion, we have developed a high yielding anion templated synthesis of a chloride selective [2]catenane *via* an unprecedented novel anion directed interweaving strategy which assembles two identical anion recognizing motifs into an orthogonal structure. Catenane formation resulting from a double RCM reaction is critically dependent on the molar equivalence of chloride anion template present. ^{1}H NMR, electrospray mass spectrometry and single crystal X-ray analysis all provide evidence for the formation of the catenane. The application of mechanically interlocked cavities as potential binding domains for the selective recognition and sensing of a range of anionic guest species is currently under investigation in our laboratories.

We thank the Clarendon Fund and the Overseas Research Student (ORS) Awards Scheme for a scholarship (K.-Y. N.). Oxford Diffraction Ltd is thanked for the generous loan of a Gemini diffractometer.

Notes and references

‡ Crystal data for $\mathbf{2}^{2+}(Cl^-)(PF_6^-)\cdot 2CH_2Cl_2$: $C_{74}H_{96}Cl_5F_6N_6O_{20}P$, M_r = 1711.83, crystal dimensions 0.20 × 0.40 × 0.42 mm, monoclinic, space group *C c*, a = 21.5488(19), b = 13.3481(9), c = 27.620(3) Å, β = 92.313(7)°, V = 7938.0(11) Å^3, Z = 4, ρ_{calcd} = 1.432 g cm^{-3}, $\mu(CuK_\alpha)$ = 2.615 mm^{-1}, F_{000} = 3584, T = 150 K. Final R = 0.0770, wR = 0.0914 with $I > 2\sigma(I)$, GOF = 1.009 for 1010 parameters and a total of 26601 reflections, of which 13870 were independent (R_{int} = 0.030). Oxford Diffraction Gemini diffractometer, graphite-monochromated CuK_α radiation (λ = 1.54248 Å); collection range 5.0° ⩽ θ ⩽ 74.2°. Details of the structure have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 602960. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b606503a

1 A. R. Pease, J. O. Jeppesen, J. F. Stoddart, Y. Luo, C. P. Collier and J. R. Heath, *Acc. Chem. Res.*, 2001, **34**, 433; C. A. Schalley, K. Beizai and F. Vogtle, *Acc. Chem. Res.*, 2001, **34**, 465.
2 J.-P. Sauvage and C. Dietrich-Buchecker, *Molecular catenanes, rotaxanes and knots: a journey through the world of molecular topology*, Wiley-VCH, Weinheim; Chichester, 1999.
3 A. L. Vance, N. W. Alcock, J. A. Heppert and D. H. Busch, *Inorg. Chem.*, 1998, **37**, 6912; S. J. Loeb and J. A. Wisner, *Chem. Commun.*, 2000, 845; C. A. Hunter, *J. Am. Chem. Soc.*, 1992, **114**, 5303; C. J. Easton, S. F. Lincoln, A. G. Meyer and H. Onagi, *J. Chem. Soc., Perkin Trans. 1*, 1999, 2501.
4 For some examples, see: C. Seel and F. Vogtle, *Chem.–Eur. J.*, 2000, **6**, 21; C. M. Keaveney and D. A. Leigh, *Angew. Chem., Int. Ed.*, 2004, **43**, 1222; S. J. Coles, J. G. Frey, P. A. Gale, M. B. Hursthouse, M. E. Light, K. Navakhun and G. L. Thomas, *Chem. Commun.*, 2003, 568; D. A. Beauchamp and S. J. Loeb, *Supramol. Chem.*, 2005, **17**, 617; E. A. Katayev, C. D. Pantos, M. D. Reshetova, V. N. Khrustalev, V. M. Lynch, Y. A. Ustynyuk and J. L. Sessler, *Angew. Chem., Int. Ed.*, 2005, **44**, 7386.
5 P. D. Beer and P. A. Gale, *Angew. Chem., Int. Ed.*, 2001, **40**, 487; P. A. Gale, *Coord. Chem. Rev.*, 2003, **240**, 191; J. L. Sessler, S. Camiolo and P. A. Gale, *Coord. Chem. Rev.*, 2003, **240**, 17.
6 J. A. Wisner, P. D. Beer and M. G. B. Drew, *Angew. Chem., Int. Ed.*, 2001, **40**, 3606; D. Curiel, P. D. Beer, R. L. Paul, A. Cowley, M. R. Sambrook and F. Szemes, *Chem. Commun.*, 2004, 1162; M. R. Sambrook, P. D. Beer, J. A. Wisner, R. L. Paul, A. R. Cowley, F. Szemes and M. G. B. Drew, *J. Am. Chem. Soc.*, 2005, **127**, 2292.
7 J. A. Wisner, P. D. Beer, M. G. B. Drew and M. R. Sambrook, *J. Am. Chem. Soc.*, 2002, **124**, 12469; D. Curiel and P. D. Beer, *Chem. Commun.*, 2005, 1909.
8 M. R. Sambrook, P. D. Beer, J. A. Wisner, R. L. Paul and A. R. Cowley, *J. Am. Chem. Soc.*, 2004, **126**, 15364.
9 C. O. Dietrich-Buchecker, J. P. Sauvage and J. P. Kintzinger, *Tetrahedron Lett.*, 1983, **24**, 5095; C. O. Dietrich-Buchecker, J. P. Sauvage and J. M. Kern, *J. Am. Chem. Soc.*, 1984, **106**, 3043; C. O. Dietrich-Buchecker and J. P. Sauvage, *Chem. Rev.*, 1987, **87**, 795.
10 R. H. Grubbs, S. J. Miller and G. C. Fu, *Acc. Chem. Res.*, 1995, **28**, 446.
11 The compound could also be obtained from exchange of chloride in $\mathbf{2}^{2+}(Cl^-)(PF_6^-)$ to hexafluorophosphate. See supporting information.
12 M. J. Hynes, *J. Chem. Soc., Dalton Trans.*, 1993, 311.

