Supplementary Material (ESI) for Chemical Communications

Anion Templated Double Cyclization Assembly of a Chloride Selective [2]Catenane

Supplementary Information

*Ka-Yuen Ng, Andrew R. Cowley and Paul D. Beer**

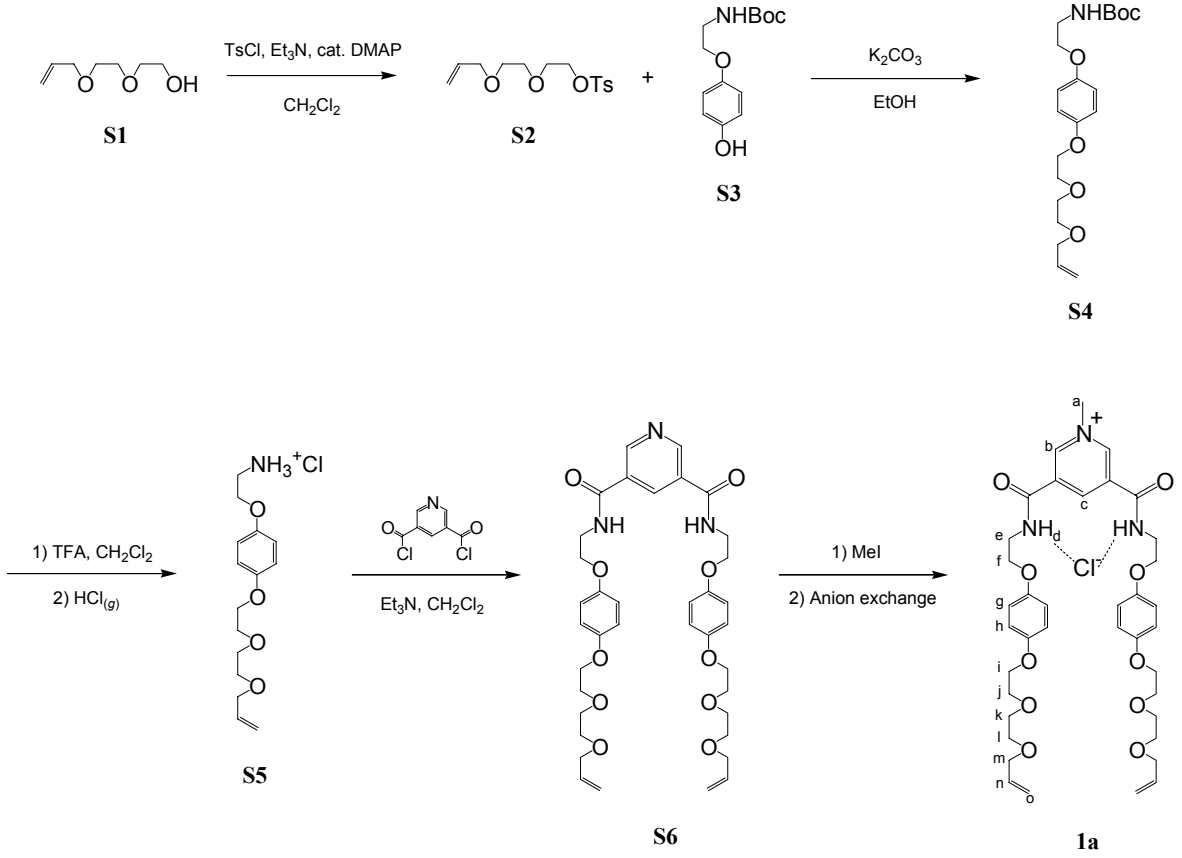
[*] Prof. P. D. Beer, K.-Y. Ng
Inorganic Chemistry Laboratory, Department of Chemistry
University of Oxford
South Parks Road, Oxford, OX1 3QR (UK)
Fax: (+44) 01865-272690
E-mail: paul.beer@chem.ox.ac.uk

Dr. A. R. Cowley
Chemical Crystallography Laboratory, Department of Chemistry
University of Oxford
Mansfield Road, Oxford, OX1 3TA (UK)

Experimental

Synthesis of precursor **1a** and **1b**

The preparation of 2-[2-(allyloxyethoxy)ethoxyl]ethanol (**S1**)[1] and 2-(4-hydroxy-phenoxy)-ethylcarbamic acid *tert*-butyl ester (**S3**)[2] have been reported elsewhere. **1a** was prepared via the synthetic route shown below.



1a: ^{1}H NMR (500 MHz, $CHCl_3$, 298 K): δ = 10.150 (1H, s, H_c), 9.482 (2H, s, H_d), 9.383 (2H, s, H_b), 6.715 (4H, d, J = 9.1 Hz, H_g), 6.583 (4H, d, J = 9.1 Hz, H_h), 5.820 (2H, m, H_n), 5.189 (2H, d, J = 17.2 Hz, H_o), 5.094 (2H, d, J = 10.5 Hz, H_o), 4.390 (3H, s, H_a), 4.091 (4H, m, H_j), 3.916-3.972 (8H, m, H_f and H_m), 3.726-3.755 (8H, m, H_e and H_i), 3.583-3.672 (8H, m, H_k and H_l); positive ESI-MS: $[C_{38}H_{50}N_3O_{10}]^{2+}$ m/z: 708.3; elemental analysis (%) calcd for $C_{38}H_{50}N_3O_{10}Cl\cdot1.5H_2O$ (found): C 59.17 (59.21), H 6.93 (7.03), N 5.45 (5.53).

Anion exchange from **1a** to **1b**

To a methanol solution of **1a** (280 mg, 0.38 mmol) was added silver triflate (116 mg, 0.45 mmol) and white precipitate was observed to form immediately. The solution was stirred for 30 min in darkness, filtered and excess AgOTf was removed by column chromatography on

9:1 dichloromethane:methanol to afford **1**$^{+}$OTf (250 mg, 77%). ^{1}H NMR (300 MHz, $CHCl_3$, 298 K): δ = 9.273 (1H, s, Ar*H*), 9.065 (2H, s, Ar*H*), 8.507 (2H, s, N*H*), 6.654 (4H, d, *J* = 9.0 Hz, Ar*H*), 6.550 (4H, d, *J* = 9.0 Hz, Ar*H*), 5.815 (2H, m, *H*C=CH_2), 5.186 (2H, d, *J* = 15.8 Hz, HC=CH_2), 5.092 (2H, d, *J* = 10.5 Hz, HC=CH_2), 4.377 (3H, s, $N^{+}CH_3$), 3.597-4.029 (28H, m, OCH_2CH_2NH and OCH_2); ^{19}F NMR (300 MHz, $CHCl_3$, 298 K): δ = -78.250 (3F, s, C$F_3SO_3^{-}$); positive ESI-MS: $[C_{38}H_{50}N_3O_{10}]^{2+}$ *m*/*z*: 708.3; negative ESI-MS: $[CF_3SO_3]^{-}$ *m*/*z*: 149.0.

To a 9:1 methanol:water solution of **1**$^{+}$OTf (250 mg, 0.29 mmol) was added NH_4PF_6 (236 mg, 1.45 mmol) dissolved in minimal amount of 9:1 methanol:water. The solution was well stirred prior to addition of large excess of water to precipitate the hexafluorophosphate salt, which is extracted from chloroform to give **1b** in quantitative yield. ^{1}H NMR (300 MHz, $CHCl_3$, 298 K): δ = 9.086 (1H, s, Ar*H*), 8.978 (2H, s, Ar*H*), 7.935 (2H, s, N*H*), 6.640 (4H, d, *J* = 9.1 Hz, Ar*H*), 6.537 (4H, d, *J* = 9.1 Hz, Ar*H*), 5.774 (2H, m, *H*C=CH_2), 5.155 (2H, d, *J* = 17.0 Hz, HC=CH_2), 5.066 (2H, d, *J* = 10.6 Hz, HC=CH_2), 4.238 (3H, s, $N^{+}CH_3$), 3.585-3.977 (28H, m, OCH_2CH_2NH and OCH_2); ^{19}F NMR (300 MHz, $CHCl_3$, 298 K): δ = -71.863 (6F, d, *J* = 755 Hz, PF_6^{-}); positive ESI-MS: $[C_{38}H_{50}N_3O_{10}]^{2+}$ *m*/*z*: 708.3; negative ESI-MS: $[PF_6]^{-}$ *m*/*z*: 145.0.

Synthesis of catenane **2**$^{2+}$(Cl^{-})(PF_6^{-}), **2**$^{2+}$(Cl^{-})$_2$ and **2**$^{2+}$(PF_6^{-})$_2$

2^{2+}(Cl^{-})(PF_6^{-}): To a well stirred mixture of **1a** (47 mg, 0.063 mmol) and **1b** (53 mg, 0.063 mmol) 1st Generation Grubbs' catalyst (10 mg, 10% by weight) was added. The reaction was left to stir under N_2 overnight followed by column chromatography on 9:1 dichloromethane : methanol to elute the catenane (76mg, 78%). ^{1}H NMR (500 MHz, $CHCl_3$, 298 K): δ = 9.761 (2H, s, Ar*H*), 9.058 (4H, s, Ar*H*), 8.689 (4H, s, N*H*), 6.618 (8H, d, *J* = 9.0 Hz, Ar*H*), 6.186 (8H, d, *J* = 9.0 Hz, Ar*H*), 5.879 (3.3H, s, *trans*-*H*C=C*H*), 5.802 (0.7H, s, *cis*-*H*C=C*H*), 4.566 (6H, s, $N^{+}CH_3$), 4.058-4.076 (16H, m, OCH_2CH_2NH), 3.696-3.804 ppm (40H, m, OCH_2); positive ESI-MS: $[C_{72}H_{92}N_6O_{20}]^{2+}$ *m*/*z*: 680.32, $[C_{72}H_{92}N_6O_{20}Cl]^{+}$ *m*/*z*: 1395.61; elemental analysis (%) calcd for $C_{72}H_{92}N_6O_{20}ClPF_6 \cdot 0.5CHCl_3$ (found): C 54.37 (54.35), H 5.82 (5.92), N 5.25 (5.20).

The catenane **2**$^{2+}$(Cl^{-})$_2$ and **2**$^{2+}$(PF_6^{-})$_2$ were synthesized from an analogous procedure as **2**$^{2+}$(Cl^{-})(PF_6^{-}) except pure **1a** (or **1b**) were used instead of 1:1 mixture of the two.

2^{2+}(Cl^{-})$_2$: Yield: 34%. ^{1}H NMR (500 MHz, $CHCl_3$, 298 K): δ = 9.939 (2H, s, Ar*H*), 9.326 (4H, s, Ar*H*), 9.235 (4H, s, N*H*), 6.653 (8H, d, *J* = 8.9 Hz, Ar*H*), 6.407 (8H, d, *J* = 8.9 Hz, Ar*H*), 5.890 (4H, s, *trans*- and *cis*-*H*C=C*H*), 4.579 (6H, s, $N^{+}CH_3$), 3.708-4.092 (56H, m, OCH_2CH_2NH and OCH_2); positive ESI-MS: $[C_{72}H_{92}N_6O_{20}]^{2+}$ *m*/*z*: 680.32, $[C_{72}H_{92}N_6O_{20}Cl]^{+}$ *m*/*z*: 1395.60.

2^{2+}(PF_6^-)$_2$: Yield: 16%. ^{1}H NMR (500 MHz, $CHCl_3$, 298 K): δ = 9.766 (2H, t, J = 14.3 Hz, Ar*H*), 9.073 (4H, s, Ar*H*), 8.687 (4H, s, N*H*), 6.606 (8H, t, J = 9.0 Hz, Ar*H*), 6.205 (8H, d, J = 9.0 Hz, Ar*H*), 5.874 (2.9H, s, *trans*-*H*C=C*H*), 5.794 (1.1H, s, *cis*-*H*C=C*H*), 4.570 (6H, s, N^+CH_3), 4.053-4.061 (16H, m, OCH_2CH_2NH), 3.691-3.805 (40H, m, OCH_2); positive ESI-MS: $[C_{72}H_{92}N_6O_{20}]^{2+}$ *m*/*z*: 680.32.

Anion exchange from **2**$^{2+}$(Cl^-)(PF_6^-) to **2**$^{2+}$(PF_6^-)$_2$

2^{2+}(Cl^-)(PF_6^-) (40 mg, 0.026 mmol) was stirred with silver triflate (6.7 mg, 0.026 mmol) in 9:1 methanol:dichloromethane overnight. The solution was filtered through celite to obtain **2**$^{2+}$(OTf^-)(PF_6^-) quantitatively. ^{1}H NMR (300 MHz, $CHCl_3$, 298 K): δ = 9.317 (1H, s, Ar*H*), 8.971 (2H, s, Ar*H*), 8.234 (2H, s, N*H*), 6.553 (4H, d, J = 9.0 Hz, Ar*H*), 6.420 (4H, br, Ar*H*), 5.746-5.841 (2H, m, *trans*- and *cis*-*H*C=C*H*), 4.478 (3H, s, N^+CH_3), 3.674-4.036 (28H, m, OCH_2CH_2NH and OCH_2); ^{19}F NMR (300 MHz, $CHCl_3$, 298 K): δ = -72.763 (6F, d, J = 758 Hz, PF_6^-), -78.711 (3F, s, C$F_3SO_3^-$).

The triflate was exchanged for hexafluorophosphate in an analogous way as previous exchange from **1**$^+$OTf to **1b**. Nearly quantitative yield was obtained. Disappearance of the singlet at -78 ppm from ^{19}F NMR indicated removal of triflate. ^{19}F NMR (300 MHz, $CHCl_3$, 298 K): δ = -72.649 (6F, d, J = 714 Hz, PF_6^-).

^{1}H NMR titrations

All titration results were acquired by a Varian 500 MHz NMR spectrometer and performed with the starting concentration of hosts **1b** at 2.5×10^{-3} M or **2**$^{2+}$(PF_6^-)$_2$ at 1.25×10^{-3} M and the addition of appropriate aliquots of titrant with a microsyringe. The amide and pyridinum aryl protons were followed during the course of the titration and the data fitted and analysed to give association constants using the program EQNMR.[3] Binding stoichiometries were confirmed by the use of Job Plots.

The NMR titration curves are shown below.

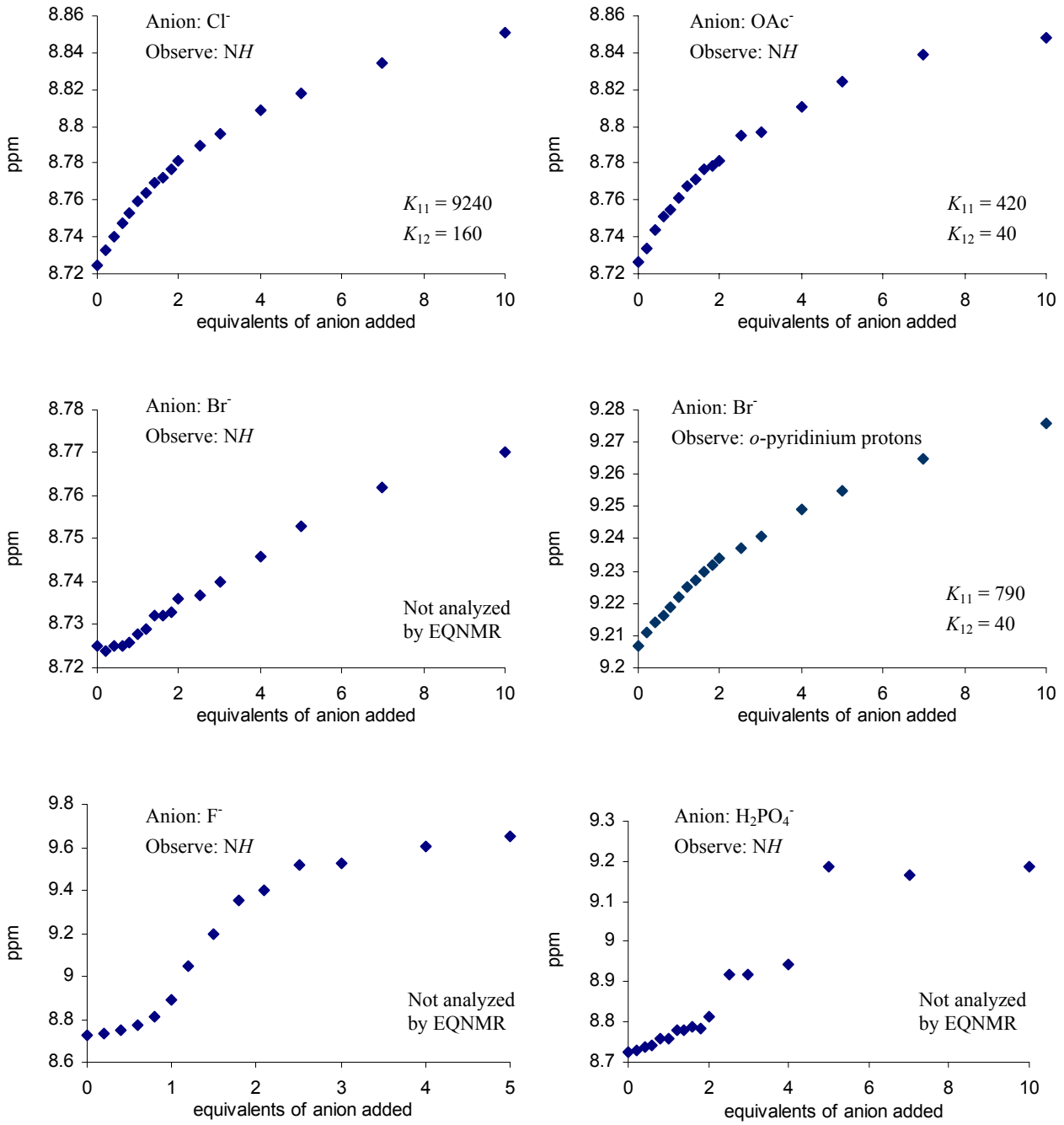


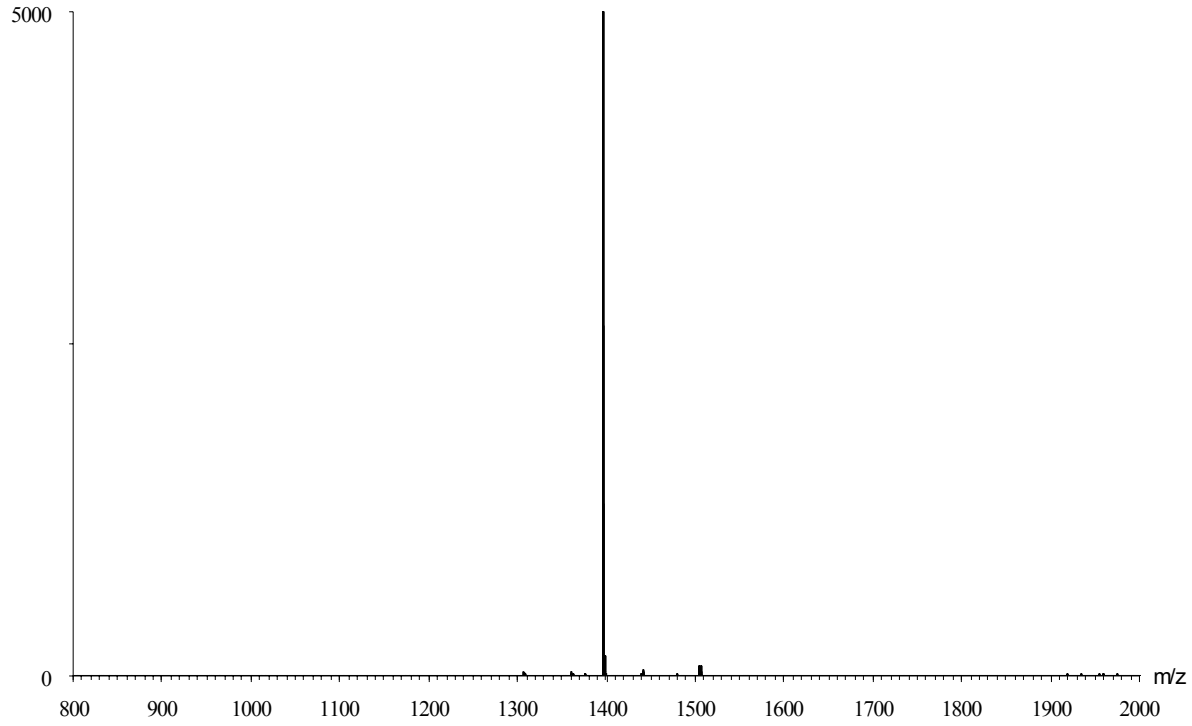
Figure S1 The NMR titration curves of $\mathbf{2}^{2+}(PF_6^-)_2$ with TBA salts of different anions. The association constants (M^{-1}) as obtained by EQNMR for each anion is also shown. In the titration experiment against fluoride, the amide peak broadens into the baseline after addition of 5 equivalents of anion.

Competitive mass spectrometry binding experiment

Ammonium salts of acetate, chloride, dihydrogenphosphate, fluoride, hydrogensulfate and nitrate were made up to 1×10^{-2} M in water. A 100 μL sample of 1×10^{-4} M $\mathbf{2}^{2+}(PF_6^-)_2$ in 98:2 methanol:dichloromethane was prepared. 5 μL aliquots of each anion were added to the catenane solution and the mass spectrometry was run using standard procedures.

Control experiments were also undertaken to determine the mass spectrum signal count for each potential anion-catenane adduct. 5 μL aliquot of an anion solution ($1x10^{-2}$ M) was added into the 100 μL $1x10^{-4}$ M catenane solution and the mass spectrometry was run using standard procedures. Peaks corresponding to the catenane anion complexwere only observed in the case of chloride and nitrate (Figure S2). For acetate there is no detectable anion complexation peak, whereas for dihydrogenphosphate, fluoride and hydrogensulfate only the bromide adduct is observed, which originates from the tetraoctylammonium bromide that acts as the mass reference in ESMS.

(a)



(b)

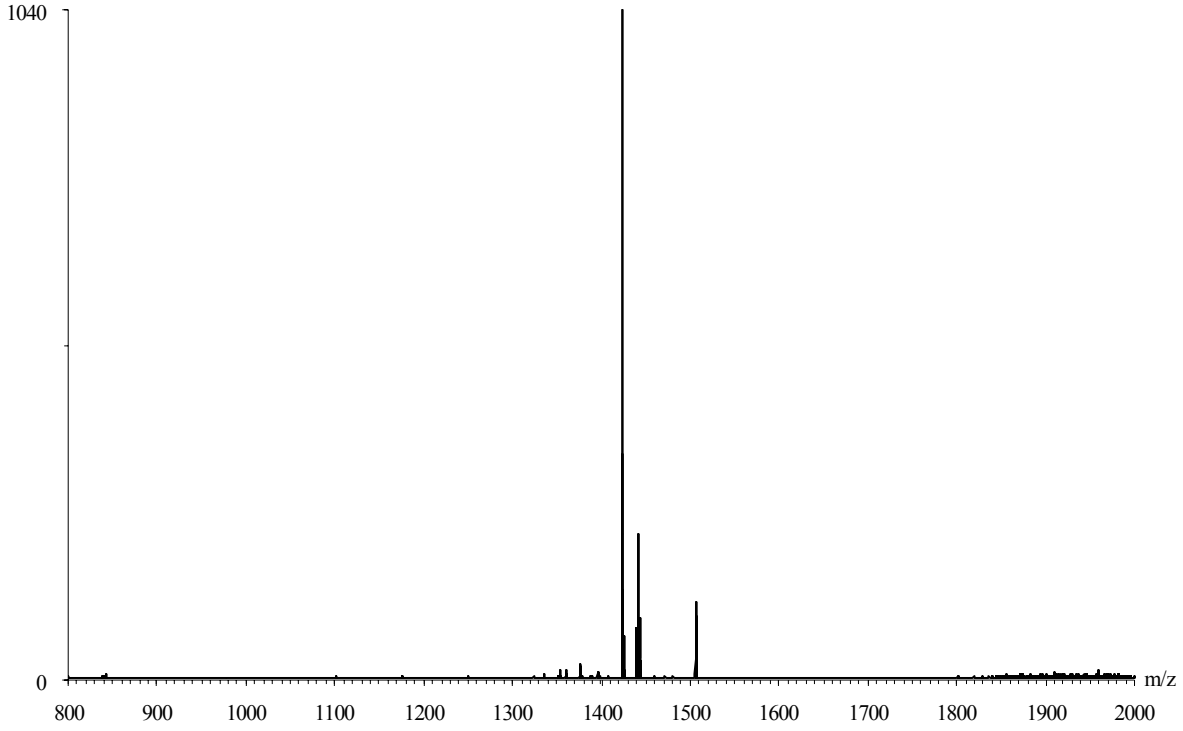


Figure S2 Electrospray mass spectrum for a) the catenane chloride complex and b) the catenane nitrate complex. A small signal corresponding to the catenane bromide adduct is observed in (b).

Repeating the experiment at 10 times the concentration leads to the enhancement of the above mentioned chloride, nitrate and bromide complex peaks but there is still no detectable host-guest ensemble signal for acetate, dihydrogenphosphate, fluoride or hydrogensulfate.

1422.91
(nitrate adduct)

The overwhelming chloride-catenane adduct peak in the resultant spectrum of the competitive MS experiment (Figure S3) suggests the catenane host binds preferentially to chloride.

1441.82
(bromide adduct)

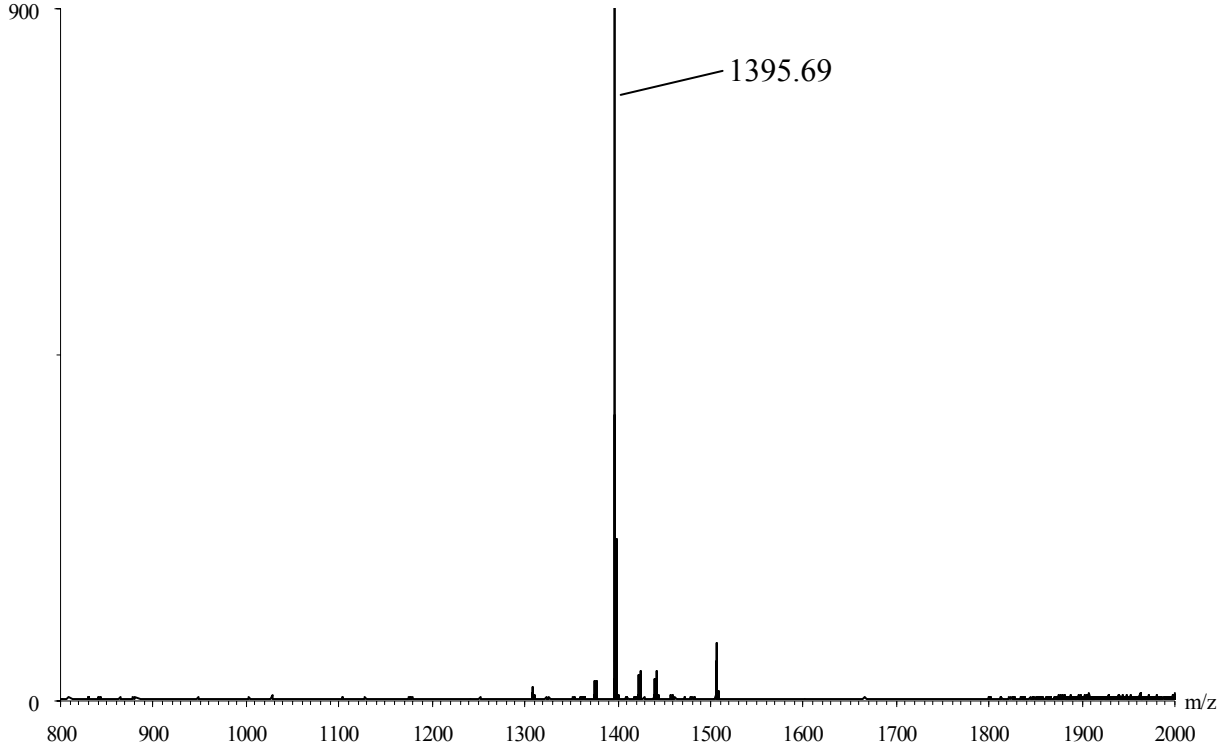


Figure S3 The predominance of the chloride adduct peak in the competitive mass spectrometry binding experiment.

Single crystal X-ray structure analysis

Crystals of $\mathbf{2}^{2+}(Cl^-)(PF_6^-)$ were grown by slow diffusion of diisopropyl ether into a dichloromethane solution of the [2]catenane. A polycrystalline aggregate was cut to give a fragment having dimensions approximately 0.20 x 0.40 x 0.42 mm. This was mounted on a glass fibre using perfluoropolyether oil and cooled rapidly to 150K in a stream of cold N_2 using an Oxford Cryosystems CRYOSTREAM unit. Diffraction data were measured using an Oxford Diffraction Gemini diffractometer (graphite-monochromated CuK_α radiation, λ = 1.54248 Å). Intensity data were processed using the Crysalis package.[4] Examination of the diffraction pattern showed the crystal to be a twin, with two components related by a 180° rotation about the *a* axis.

Examination of the systematic absences of the intensity data showed the space group to be either *C c* or *C* 2/*c*. The structure was solved in the space group *C c* using the direct-methods program SIR92,[5] which located most of the non-hydrogen atoms. Subsequent full-matrix least-squares refinement was carried out using the CRYSTALS program suite.[6] The remaining atoms were located in difference Fourier maps. Coordinates and anisotropic thermal parameters of all non-hydrogen atoms were refined. The polyether fragments were seen to have unusually large thermal parameters and abnormal geometry, indicative of disorder. Attempts to model this did not lead to any improvement in the agreement with the X-ray data and were abandoned. Geometric restraints were applied to these frements: the C-O bond lengths were restrained to 1.42(2) Å, C-C bonds to 1.52(2) Å and C=C bonds to 1.32(2) Å; the angles at sp^3 carbon atoms

to 112(2)°and those at sp^2 carbon atoms to 122(2)°. Similarity restraints were applied to the thermal parameters of directly-bonded atoms.

The relative contributions of the two twin components to those reflections for which the diffraction patterns overlapped were included in the refinement. In addition, an attempt to determine the absolute structure of the crystal was made by including two additional twin components related by inversion. The relative contributions of the latter to the diffraction pattern refined to values not distinguishable from zero. It was therefore concluded that the crystal contained only the two components related by rotation.

Hydrogen atoms were positioned geometrically after each cycle of refinement. A 3-term Chebychev polynomial weighting scheme was applied. Refinement converged satisfactorily to give R = 0.0770, wR = 0.0914.

---

[1] M. P. Doyle, W. H. Hu, *J. Org. Chem.* **2000**, *65*, 8839.
[2] M. R. Sambrook, P. D. Beer, J. A. Wisner, R. L. Paul, A. R. Cowley, *J. Am. Chem. Soc.* **2004**, *126*, 15364.
[3] M. J. Hynes, *J. Chem. Soc., Dalton Trans.* **1993**, 311.
[4] Crysalis, v 1.78, Oxford Diffraction, 2005.
[5] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori and M. Camalli, *J. Appl. Cryst.* **1994**, *27*, 435.
[6] P. W. Betteridge, J. R. Carruthers, R. I. Cooper, K. Prout and D. J. Watkin, *J. Appl. Cryst.* **2003**, *36*, 1487.