Supplementary Material (ESI) for Chemical Communications

Sulfate anion templated assembly of a [2]catenane

Supporting Information

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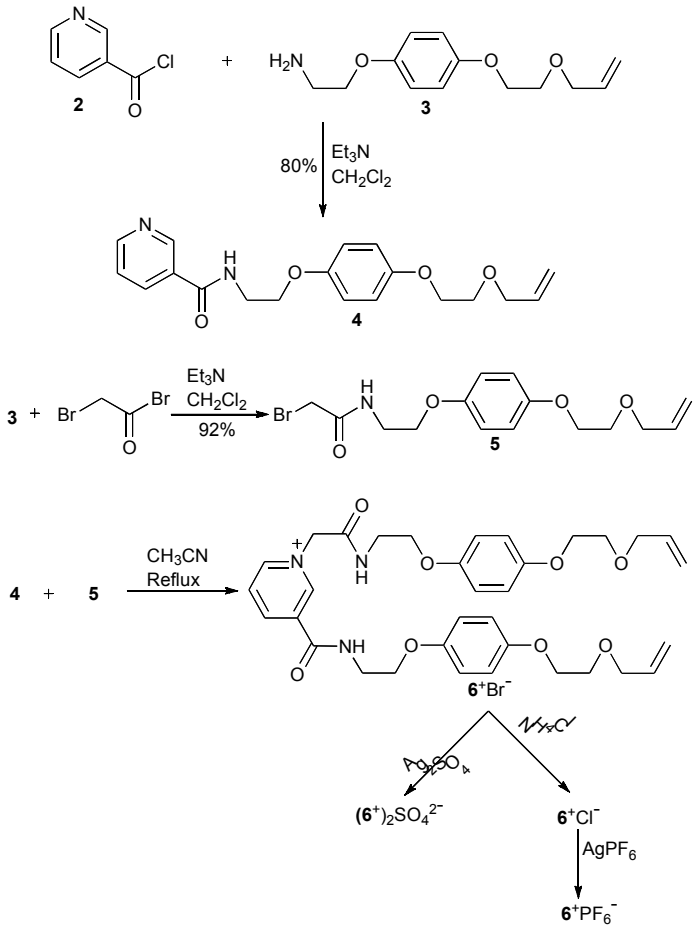
Experimental

Synthesis of precursor (**6**)

The preparation of 2-(4-(2-(allyloxy)ethoxy)phenoxy)ethanamine (**3**) has been reported elsewhere.[1] **6** was prepared via the synthetic route shown below.



Scheme S1 Synthesis of precursor **6**.

4: Acid chloride **2** (0.8g, 5.7mmol) was suspended in dry CH_2Cl_2 (30ml) and the solution cooled to 0°C. Amine **3** (1.35g, 5.7mmol) and triethylamine (1ml, 7.5mmol) were dissolved in CH_2Cl_2 (10ml) and then added dropwise into the cooled nicotinoyl chloride hydrochloride solution. The mixture was allowed to warm to room temperature and left to stir overnight under a nitrogen atmosphere. After solvent removal in vacuo, the resulting crude solid was purified by column chromatography (Silica, CH_2Cl_2/MeOH (98:2)) which gave rise to a white solid (1.6g, 80%). ^{1}H NMR (300MHz, $CDCl_3$) δ = 9.00 (1H, s, Ar*H*), 8.74 (1H, s, Ar*H*), 8.13 (1H, d, J = 4.5Hz, Ar*H*), 7.40 (1H, s, Ar*H*), 6.86 (4H, m, hydroquinone), 6.64 (1H, br, CON*H*), 5.92 (1H, qt, J_1 = 5.37Hz, J_2 = 10.74Hz, OCH_2CH), 5.29 (1H, dq, J_1 = 1.46Hz, J_2 = 17.58Hz, trans-CH_2), 5.18 (1H, dq, J_1 = 1.46Hz, J_2 =

10.74Hz, cis-C*H*$_2$), 4.11 (6H, m, C*H*$_2$), 3.87 (2H, m, C*H*$_2$), 3.78 (2H, m, C*H*$_2$). positive ESI-MS: $[C_{19}H_{22}N_2O_4 + H]^+$ *m/z* : 342.16.

5: Amine **3** (1.0g, 4.2mmol) and triethylamine (0.63g, 6.3mmol) were dissolved in 30ml dry CH_2Cl_2 and solution cooled to 0^{o}C. Bromoacetyl bromide (0.84g, 4.2mmol) in 10ml dry CH_2Cl_2 was then added dropwise into the cooled **3** and triethylamine solution. The mixture was allowed to warm to room temperature and was left to stir overnight under a nitrogen atmosphere. The organic layer was then washed with H_2O (2 x 15 ml) and brine (15 ml) before being dried over $MgSO_4$, filtered and the solvent removed *in vacuo* to give a dark oil **5** in 90% yield. ^{1}H NMR (300MHz, $CDCl_3$) δ = 6.93 (1H, br, CON*H*), 6.89 – 6.81 4H, m, Ar*H*), 5.92 (1H, qt, J_1 = 5.37Hz, J_2 = 10.74Hz, OCH$_2$C*H*), 5.29 (1H, dq, J_1 = 1.46Hz, J_2 = 17.58Hz, *trans*-C*H*$_2$), 5.18 (1H, dq, J_1 =1.46Hz, J_2 = 10.74Hz, *cis*-C*H*$_2$), 4.10 (4H, t, *J* = 4.88Hz, C*H*$_2$OArOC*H*$_2$), 4.07 (2H, t, *J* = 4.88Hz, OC*H*$_2$CH), 3.90 (2H, s, BrCH$_2$CONHC*H*$_2$) 3.75 (2H, t, *J* = 5.13Hz, ArOCH$_2$C*H*$_2$), 3.02 (2H, t, *J* = 5.37Hz, C*H*$_2$CH$_2$). positive ESI MS $[C_{15}H_{20}BrNO_4 + H]^+$ *m/z*: 359.39.

6$^+$Br$^-$: **5** (1.0g, 2.8mmol) was stirred under reflux in acetone (40ml) with 1.0 equivalents of **4** (0.95g, 2.8mmol) for 24 hours. The solution was cooled to room temperature and poured into ether to form a off white precipitate. The suspension was stirred for twenty minutes and then filtered to give the product as a white power (0.98g, 49%). ^{1}H NMR (500MHz, $CDCl_3$) δ = 10.19 (1H, s, Ar*H*), 8.95 (1H, d, J = 7.99Hz, Ar*H*), 8.77 (1H, d, J = 6.42Hz, Ar*H*), 8.43 (1H, br, CON*H*), 8.22 (1H, br, CON*H*), 7.94 (1H, t, J = 14.10Hz, Ar*H*), 6.90 – 6.72 (8H, m, hydroquinone), 5.98 – 5.90 (2H, m, OCH$_2$C*H*), 5.61 (2H, s, N$^+$C*H*$_2$), 5.34 – 5.19 (4H, m, OC*H*$_2$CH), 4.16 – 4.01 (8H, m, C*H*$_2$), 3.83 – 3.76 (8H, m, C*H*$_2$), 3.60 (12H, m, C*H*$_2$). ^{13}C NMR (75.5 MHz, $CDCl_3$), δ = 160.6, 145.7, 145.0, 144.1, 135.1, 128.0, 62.2, 40.7, 31.8, 31.5, 31.0, 29.1, 26.8, 25.7, 22.6, 22.3, 14.1, 13.9. positive ESI MS $[C_{34}H_{42}N_3O_8 - Br]^+$ *m/z*: 620.70. Elemental analysis calculated for $C_{34}H_{42}BrN_3O_8$: C 58.3, H 6.0, N 6.0; found C 58.3, H 6.1, N 5.9.

Anion exchange from **6**$^+$Br$^-$ to (**6**$^+$)$_2$SO$_4^{2-}$
Silver sulfate (0.30g) was dissolved in water (100ml). **6**$^+$Br$^-$ (0.25g, 0.36mmol) dissolved in CH2Cl2 915ml) was extracted with 10 mM AgSO4(aq) (3x30ml). Solvents were removed in *vacuo* to yield a white solid (0.2g, 90%). ^{1}H NMR (500MHz, $CDCl_3$) δ = 10.04 (1H, br, Ar*H*), 9.81 (1H, br, N*H*), 9.62 (1H, br, N*H*), 8.83 (1H, br, Ar*H*), 8.71 (1H, br, Ar*H*), 7.83 (1H, br, Ar*H*), 6.71 (8H, s, hydroquinone), 5.93 (2H, m, =C*H*), 5.50 (2H, s, N$^+$C*H*$_2$), 5.27 (4H, m, =C*H*$_2$), 4.07-3.98 (8H, m, C*H*$_2$), 3.73 (12H, m, C*H*$_2$). positive ESI MS $[C_{34}H_{42}N_3O_8 – SO_4^{2-}]^+$: *m/z* observed 620.70, calcd 620.70.

Anion exchange from $\mathbf{6}^{+}Br^{-}$ to $\mathbf{6}^{+}Cl^{-}$

$\mathbf{6}^{+}Br^{-}$ (0.2g, 0.29mmol) was dissolved in chloroform (25) and stirred vigorously with 1M aqueous NH4Cl solution (10ml) for 15 minutes. The aqueous layer was decanted off and the procedure repeated five more times. The organic layer was then dried over magnesium sulfate and the solvent removed to give the product as a white solid (0.16g, 85%). ^{1}H NMR (500MHz, $CDCl_3$) δ = 10.44 (1H, s, Ar*H*), 9.36 (1H, br, CON*H*), 9.26 (1H, br, CON*H*), 8.96 (1H, d, *J* = 9.45Hz, Ar*H*), 8.62 (1H, s, Ar*H*), 7.88 (1H, t, *J* = 11.59Hz, Ar*H*), 6.84 – 6.70 (8H, m, hydroquinone), 5.98 – 5.90 (2H, m, OCH_2CH), 5.62 (2H, s, $N^{+}CH_2$), 5.34 – 5.19 (4H, m, OCH_2CH), 4.16 – 4.01 (8H, m, CH_2), 3.83 – 3.76 (8H, m, CH_2), 3.60 (4H, m, CH_2). positive ESI MS $[C_{34}H_{42}ClN_3O_8 - Cl]^{+}$ *m/z*: 620.70. Elemental analysis calculated for $C_{34}H_{42}ClN_3O_8$: C 62.2, H 6.4, N 6.4; found C 62.2, H 6.2, N 6.4.

Anion exchange from $\mathbf{6}^{+}Cl^{-}$ to $\mathbf{6}^{+}PF_6^{-}$

Chloride salt $\mathbf{6}^{+}Cl^{-}$ (0.10g, 0.15mmol) was dissolved in dry CH_2Cl_2 (35ml) and $AgPF_6$ (0.15g, 0.30mmol) added. This solution was stirred in the absence of light under a night atmosphere for 2 hours and then filtered. The solid residue was then triturated with CH_3CN, filtered and the resulting filtrate concentrated in *vacuo* gave a yellow solid (0.10g, 89%). ^{1}H NMR (500MHz, $CDCl_3$) δ = 8.98 (2H, s, br, Ar*H*), 8.81(1H, br, Ar*H*) 8.04 (1H, br, Ar*H*), 7.64 (1H, br, N*H*), 7.42 (1H, br, N*H*), 6.71 (8H, m, hydroquinone), 5.92 (2H, m, =C*H*), 5.31 (2H, s, $N^{+}CH_2$), 5.27 (4H, m, $=CH_2$), 4.10-3.98 (8H, m, CH_2), 3.73 (12H, m, CH_2). ^{19}F NMR (300 MHz, $CHCl_3$, 298 K): δ = -71.863 (6F, d, *J* = 755 Hz, PF_6^{-}); positive ESI MS $[C_{34}H_{42}PF_6N_3O_8 - PF_6]^{+}$ *m/z*: 620.70.

Synthesis of catenane $\mathbf{1}^{2+}\,SO_4^{2-}$

To a well stirred solution of $(\mathbf{6}^{+})_2SO_4^{2-}$ (99.5 mg, 0.13 mmol) in dry CH_2Cl_2 (20ml) 2st Generation Grubbs' catalyst (5 mg, 5% 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, 80%). ^{1}H NMR (500MHz, $CDCl_3$) δ = 10.04 (2H, br, Ar*H*), 9.81 (2H, br, N*H*), 9.69 (2H, br, N*H*), 8.83 (2H, s, Ar*H*), 8.71 (2H, s, Ar*H*), 7.83 (2H, t, *J* = 12.45Hz, Ar*H*), 6.92 (4H, s, hydroquinone), 6.83 (4H, s, hydroquinone), 6.73 (4H, s, hydroquinone), 6.64 (4H, s, hydroquinone), 5.93 (4H, s, C*H*=C*H*), 5.41 (4H, s, $N^{+}CH_2$), 4.21 (4H, s, CH_2), 4.09-4.06 (12H, m, CH_2), 3.99 (4H, s, CH_2), 3.84-3.76 (12H, m, CH_2), 3.58 (8H, s, CH_2). ^{13}C NMR (75.5 MHz, $CDCl_3$), δ = 161.78, 153.95, 153.76, 147.07, 134.30, 131.28, 130.63, 116.15, 115.89, 71.78, 70.25, 69.35, 67.05, 50.87, 41.57. positive ESI MS $[C_{64}H_{76}N_6O_{16}]^{2+}$ *m/z*: 592.65. Elemental analysis calculated for $C_{64}H_{76}N_6O_{20}S$: C, 59.99; H, 5.98; N, 6.56; observed: C, 60.01; H, 6.02; N, 6.53.

Anion exchange from $\mathbf{1}^{2+}\,SO_4^{2-}$ to $\mathbf{1}^{2+}\,(PF_6^{-})_2$

Removal of the sulfate templating anion from the catenane was achived via exchange upon addition of $BaCl_2$, followed conversion to PF_6^{-} salt using silver hexafluorophosphate. ^{1}H

NMR (500MHz, $CDCl_3$) δ = 8.66 (4H, br, Ar*H*), 8.38 (2H, br, s, Ar*H*), 7.78 (2H, br, N*H*), 7.46 (2H, br, s, N*H*), 7.38 (2H, br, s, Ar*H*), 6.79-6.60 (16H, m, hydroquinone), 5.78 (4H, s, C*H*=C*H*), 5.08 (4H, s, N^+CH_2), 4.01 (4H, s, CH_2), 4.07-3.95 (12H, m, CH_2), 3.91-3.72 (24H, m, CH_2). ESI MS $[C_{64}H_{76}N_6O_{16}]^{2+}$ *m/z*: 592.66.

^{1}H NMR titrations

All titration results were acquired by a Varian 500 MHz NMR spectrometer and performed with the starting concentration of hosts $\mathbf{6}^+PF_6^-$ at 2.5×10^{-3} M or $\mathbf{1}^{2+}(PF_6^-)_2$ at 1.25×10^{-3} M and the addition of appropriate aliquots of titrant with a microsyringe. The ortho-pyridinum nicotinamide proton were followed during the course of the titration and the data fitted and analysed to give association constants using the program EQNMR.[2] Binding stoichiometries were confirmed by the use of Job Plots.

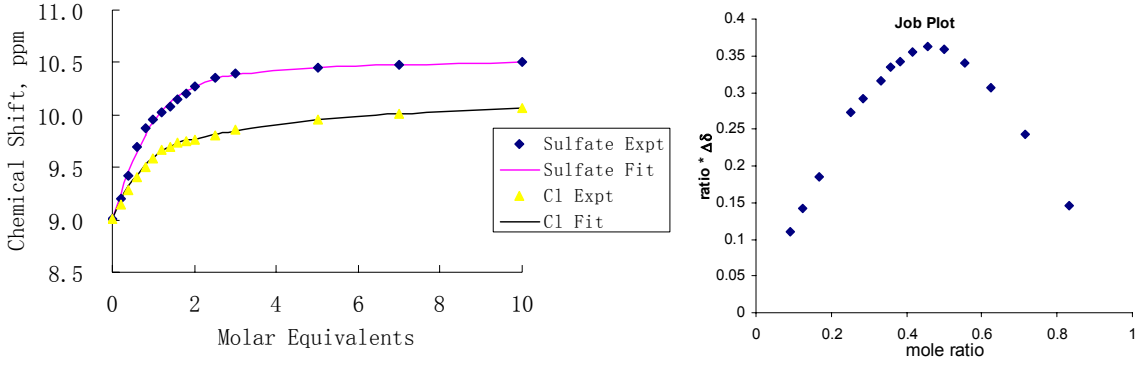


Fig S1 Experimental data and fitted binding curves for the ^{1}H NMR titration of $\mathbf{1}^{2+}(PF_6^-)_2$ with TBASO4 and TBACl.

Molecular dynamic simulations

Experimental section

Conventional Molecular Dynamic (MD) simulations were carried out with the AMBER9[3] software package. Parameters for $\mathbf{1}^{2+}$, $\mathbf{6}^+$, SO_4^{2-} and $CH_3CO_2^-$ were taken from GAFF[4]; methanol and chloroform molecules were described using a full atoms model with parameters taken from ref. [5] and [6], respectively. Van der Waals parameters for Cl^- were taken from reference [7]. Partial RESP[8] fitted charges for $\mathbf{1}^{2+}$, $\mathbf{6}^+$ and $CH_3CO_2^-$ were obtained from HF/6-31G* level calculations using Gaussian03[9]. The RESP charges of SO_4^{2-} were calculated at HF/6-31++G* level.

Starting models for $\mathbf{1}^{2+}SO_4^{2-}$, $\mathbf{1}^{2+}Cl^-$, and $\mathbf{1}^{2+}CH_3CO_2^-$ and were obtained through assembly of the adequate individual moieties, and were then submitted to gas phase simulated annealing, consisting on the heating of the structures up to 1000K followed by slow cooling to 0 K, thus yielding its lowest energy conformations. The procedure was repeated ten times for each model, with the total heating time varying from 100 to 1000 ps. At least three

equivalent co-conformations, having simillar energy, were obtained for each model, thus validating the procedure. No bond or angle parameters between the anions and the N-H binding sites of $\mathbf{1}^{2+}$ were applied, for what the attractive interactions were primarily electrostatic.

For all systems, the lowest energy binding arrangement was then immersed in separated cubic boxes (typically *ca*. 50 Å in size after equilibration) containing approximately 1200 molecules of a 1:1 $CH_3OH/CHCl_3$ solvent. MD simulations of the several systems started with an initial solvent and solute relaxation, followed by 50 ps NVT heating to 300 K and 500 ps NPT equilibration periods. The final densities of the equilibrated boxes were in close agreement with the experimental density of the solvent mixture, and remained constant during, at least, the final 300 ps of the NPT equilibration period. The SHAKE[10] algorithm was employed in all condensed phase simulations to constrain all hydrogen involving bonds, thus allowing the usage of 2 fs time steps. Non-bonded van der Waals interactions were restrained to a 12 Å cutoff, while the particle mesh Ewald method was used to describe the long range electrostatic interactions. The temperature of the systems was controlled by the Langevin thermostat, using a collision frequency of 1.0 ps^{-1}.

The relative binding free energies ($\Delta\Delta G$) of the catenane to the anions were calculated from the relative free energies obtained for the solvated free anions (solvation free energy – $\Delta G_{solvation}$) and for the solvated catenane bounded anions (interaction free energy – $\Delta G_{interaction}$) by means of thermodynamic integration[11] as (eq. 1):

$$\Delta\Delta G = \Delta G_{solvation} - \Delta G_{interaction} \qquad (1).$$

With the purpose of calculating $\Delta G_{solvation}$ and $\Delta G_{interaction}$, anion *X* was mutated into anion *Y*, by coupling its Hamiltonian *H* to a mutation variable λ which spanned from 0 to 1 along the transformation $X_{\lambda=0} \rightarrow Y_{\lambda=1}$. The corresponding free energy difference was then obtained by calculating the following integral (eq. 2):

$$\Delta G = \int_{\lambda=0}^{\lambda=1} \left\langle \frac{\delta H}{\delta \lambda} \right\rangle d\lambda \qquad (2).$$

which can be estimated by a trapezoidal integration scheme at a large number of discrete values of λ. In our calculations, the mutations were divided into 21 windows (λ = 0, 0.05, 0.10, … , 1), each consisting on a 50 ps MD equilibration step and a 500 ps data collection step, both carried out at 300K and 1atm using the previously equilibrated systems. The $SO_4^{2-} \rightarrow Cl^-$ transformation, for which annihilation of the oxygen atoms and mutation of sulphur into chlorine was required, was divided into two stages comprising charge change and van de Waals parameters transformation, each treated as stated above. Relative entropy

differences ($\Delta\Delta S$) were estimated by trapezoidal integration of the following integral[11],[12] (eq. 3):

$$\Delta S = \frac{1}{k_B T^2}\int_0^1 \left(\left\langle \frac{\delta H}{\delta \lambda} \right\rangle_\lambda \left\langle H + pV \right\rangle_\lambda - \left\langle \frac{\delta H}{\delta \lambda}\left(H + pV\right) \right\rangle_\lambda \right) d\lambda \qquad (3)$$

Were T is the absolute temperature, k_B is the Boltzmann constant, p is the pressure at which the simulations were performed and V is the system's volume.

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