Supplementary Material (ESI) for Chemical Communications

Anion-binding modes in a macrocyclic amidourea

Simon J. Brooks, Philip A. Gale* and Mark E. Light

Electronic supplementary information

Compound 2 ***1,3-Bis-(2-(3-nitro)-benzanilide-phenyl)-urea.***

Into an oven-dried 100 mL three necked round-bottomed flask was placed a solution of 3-nitrobenzoic acid (3.13 g, 18.73 mmol), triethylamine (2.81 mL, 20.60 mmol), PyBOP (9.75 g, 18.73 mmol) and HOBt (0.01g) in anhydrous dimethylformamide (40 mL) with 1,3-bis-(2-aminophenyl)urea (2.27 g, 9.37 mmol) slowly added. Following the addition the reaction was left stirring at ambient temperature for 72 hours, after which the solvent was removed using reduced pressure distillation to produce a brown solid residue. The residue was resuspended in methanol (50 mL) and filtered to afford a white solid **3** that was further washed with diethyl ether (3.70 g. 6.84 mmol, 73%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.37 (s, 2H, NH), 8.78 (s, 2H, NH), 8.52 (s, 2H, NH), 8.39 (m, 4H, ArH), 7.84 (dd, 4H, J = 8.3 & 1.5 Hz, ArH), 7.75 (t, 2H, J = 7.9 Hz, ArH), 7.40 (dd, 2H, J = 7.5 & 1.1 Hz, ArH), 7.25 (m, 2H, ArH), 7.10 (m, 2H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6) δ 163.6 (CO), 153.3 (CO), 147.7 (C), 135.7 (C), 134.1 (CH), 130.0 (CH), 128.1 (C), 127.1 (CH), 126.5 (CH), 126.1 (CH), 123.1 (CH), 122.6 (CH), 122.4 (CH). IR (cm^{-1}): 3379, 3231, 1641, 1517, 1346, 1316, 751. LRMS (ES-): 653.1 [M+TFA-H]$^-$, 1193.7 [2M+TFA-H]$^-$, 1733.4 [3M+TFA-H]$^-$. IR (cm^{-1}): 3380,3231, 1641, 1517, 1348, 1316. Anal. calcd. for $C_{27}H_{20}N_5O_7$: C, 60.00; H, 3.73; N, 15.54. Found: C, 59.70; H, 3.83; N, 15.60. mp = 217°C.

Compound 3 ***1,3-Bis-(2-(3-amino)-benzanilide-phenyl)-urea.***

Into an oven dried three necked round-bottomed flask was placed a stirring suspension of 1,3-bis-(2-(3-nitro)-benzanilide-phenyl)-urea (0.50 g, 0.93 mmol) in ethanol (150 mL), to which was added Pd/C 10% (0.01 g, cat.) and hydrazine monohydrate (0.50 mL) dropwise. The reaction was then heated to reflux and left stirring for 16 hours after which the reduced product was removed *via* filtration. The product was dissolved in dimethylformamide and filtered to remove Pd/C after which time the solvent was removed via reduced pressure distillation, resuspended in dichloromethane and washed with water to remove remaining dimethylformamide. The white precipitated product **7** was removed *via* filtration (0.40 g, 0.83 mmol, 89 %). ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.79 (s, 2H, amide NH), 8.62 (s, 2H, urea NH), 7.65 (dd, 2H, J = 7.9 & 1.5 Hz, ArH), 7.49 (dd, 2H, J = 7.5 & 1.5 Hz, ArH), 7.22-7.09 (m, 10H, ArH), 6.75 (m, 2H, ArH), 5.27 (s, 4H, NH_2). ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.1 (CO), 153.9 (CO), 148.8 (C), 135.1 (C), 132.9 (C), 129.7 (C), 128.8 (CH), 126.4 (CH), 125.7 (CH), 123.5 (CH), 123.1 (CH), 116.9 (CH), 114.5 (CH), 113.2 (CH). LRMS (ES-): 515.2 [M+Cl]$^-$, 542.1 [M+2MeOH-H]$^-$, 559.1 [M+Br]$^-$, 593.3 [M+TFA-H]$^-$, 995.4 [2M+Cl]$^-$, 1041.4 [2M+Br]$^-$, 1073.6 [2M+TFA-H]$^-$. IR (cm^{-1}): 3312, 3285, 1641, 1509, 1441, 1308, 1293, 1275, 1233. Anal. calcd. for $C_{27}H_{24}N_5O_3$ + 0.25 CH_3OH: C, 67.00; H, 5.16; N, 17.20. Found: C, 66.80; H, 5.11; N, 17.06. mp = 237°C.

Macrocycle 4

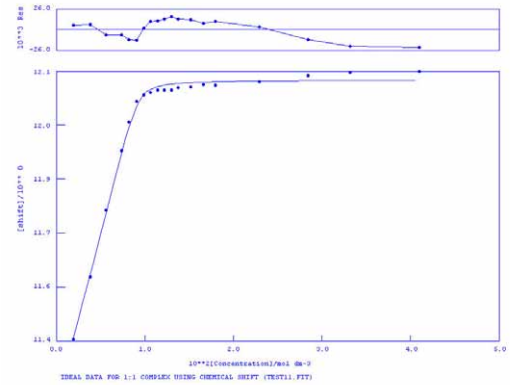
An oven-dried 1-L three-necked round-bottomed flask was filled with dry dichloromethane (500 mL) to which triethylamine (0.49 mL, 3.43 mmol) and a catalytic quantity 4-dimethylaminopyridine (0.01 g) were added. Two additional solutions were prepared, the first of **3** (1.50 g, 3.12 mmol) and tetrabutylammonium acetate (1.50 g, 4.97 mmol) in dry dichloromethane (50 mL), the second of 2,6-pyridinedicarbonyl chloride (0.64 g, 3.12 mmol) in dry dichloromethane (50 mL), with both solutions introduced into the reaction vessel using a motor-driven syringe pump over a period of 6 hours. After the addition the reaction was left stirring at ambient temperature for a further 72 hours, before the volume of solvent was reduced by approximately ¾ and reaction was extracted with water (3 × 200 mL). The retained organic phase was dried with $MgSO_4$ before removal of solvent under rotary evaporator. The light grey residue was dissolved in a small volume of 92:8 dichloromethane/methanol before purification by flash column chromatography. The white colored solid was further purified from hot ethyl acetate to give **1** as a white powder (0.32 g, 0.52 mmol, 17 %). ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.26 (s, 2H, amide NH), 9.99 (s, 2H, amide NH), 8.54 (d, 2H, J = 8.3 Hz, ArH), 8.50 (s, 2H, urea NH), 8.43-8.32 (m, 3H, ArH), 8.16 (s, 2H, ArH), 7.97 (d, 2H, J = 8.3 Hz, ArH), 7.72 (d, 2H, J = 8.3 Hz, ArH), 7.60 (t, 2H, J = 7.9 Hz, ArH), 7.31-7.21 (m, 4H, ArH), 7.07 (t, 2H, J = 7.5 Hz, ArH). ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.9 (CO), 161.6 (CO), 153.2 (CO), 148.5 (C), 140.4 (CH), 138.0 (C), 136.0 (C), 134.9 (C), 129.1 (CH), 128.3 (C), 127.3 (CH), 126.5 (CH), 125.2 (CH), 123.4 (CH), 122.9 (CH), 122.8 (CH), 120.8 (CH). LRMS (ES-): 646.3 [M+Cl]$^-$, 724.4 [M+TFA-H]$^-$. IR (cm^{-1}): 3245, 3056, 1656, 1597, 1530, 1441, 1305, 747. Anal. calcd. for $C_{34}H_{25}N_7O_5$ + 0.50 CH_2Cl_2: C, 63.35; H, 4.01; N, 14.99; Found: C, 63.19; H, 4.17; N,14.96. mp = 235°C (dec.)

Figure S1a Compound **4** in DMSO-d_6/0.5% water.

Acetate.

K_a = 16520

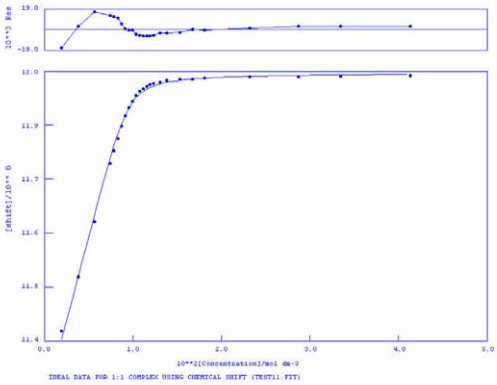
Error =3.2 %



Benzoate.

K_a = 6432

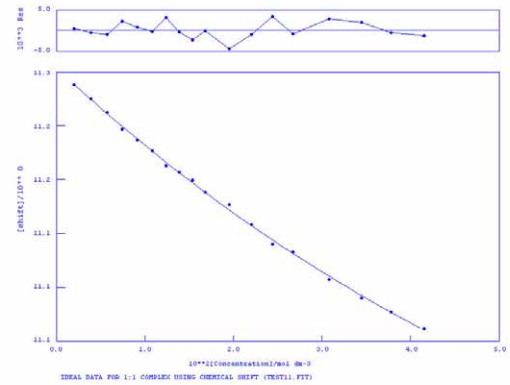
Error = 11.2 %



Bromide.

K_a = 10

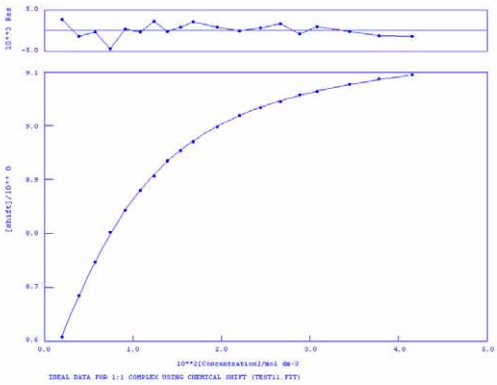
Error =13.7 %



Chloride.

K_a = 194

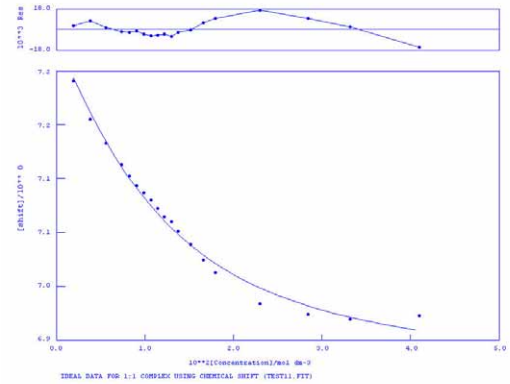
Error = 1.5 %



Dihydrogen Phosphate.

K_a = 141

Error = 13.4 %



Hydrogen Sulfate.

K_a = 115

Error = 10.3 %

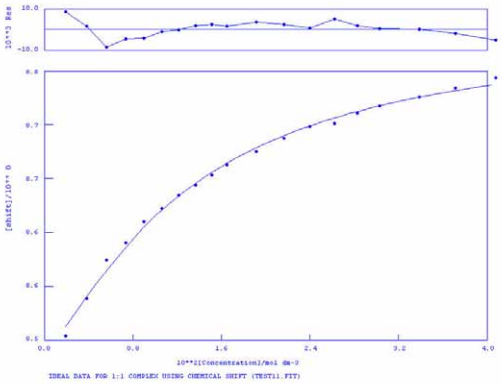


Figure S1b Compound **4** in DMSO-d_6/0.5% water.

Nitrate.

$K_a = 9$

Error = 16.2 %

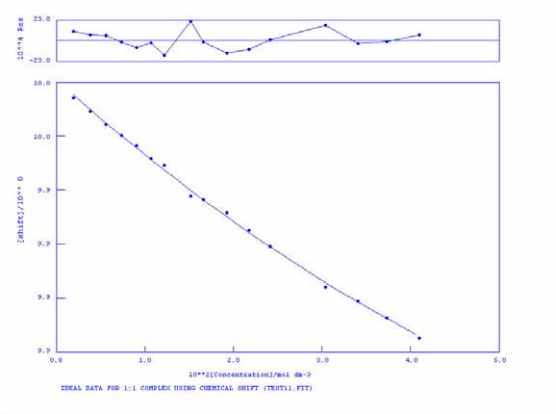
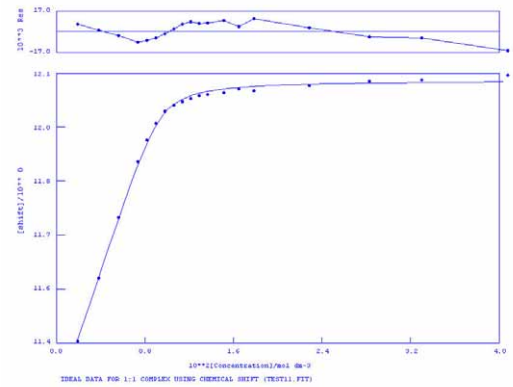


Figure S2 Compound **4** in DMSO-d_6/5.0 % water.

Acetate.

K_a = 5170

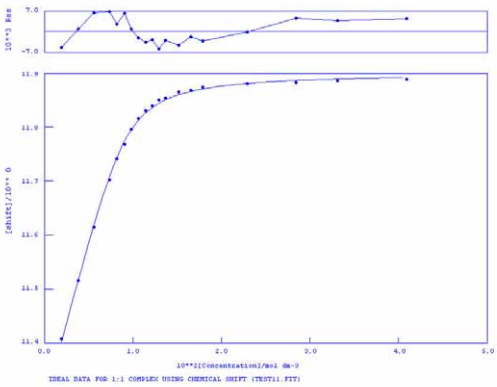
Error = 4.4 %



Benzoate.

K_a = 1834

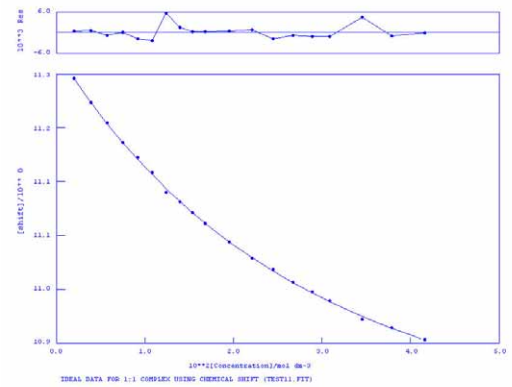
Error = 5.4 %



Chloride

K_a = 42

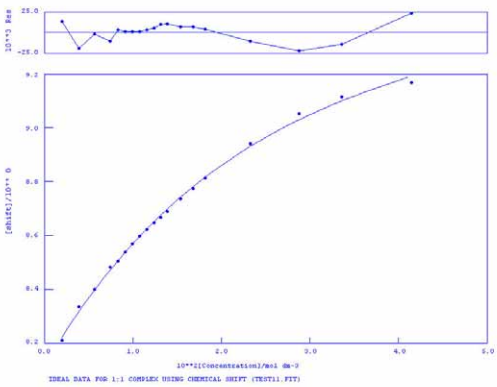
Error =3.7 %



Dihydrogen Phosphate.

K_a = 51

Error = 8.3 %



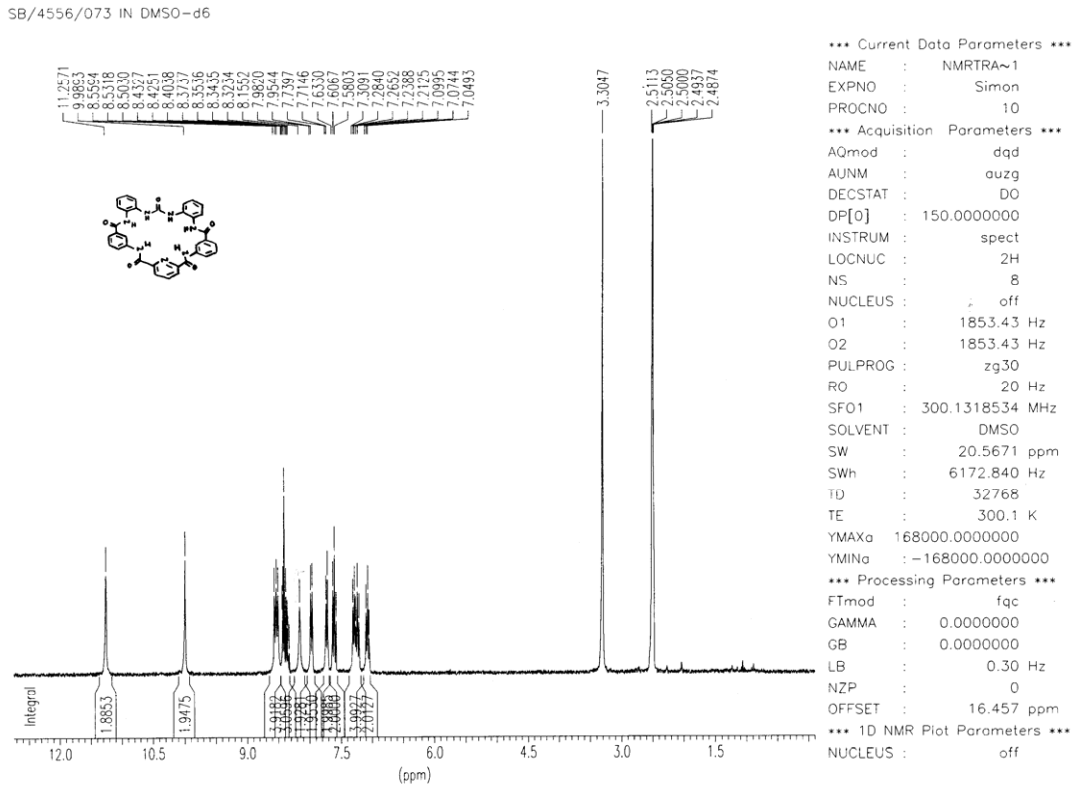


Figure S3 ^{1}H NMR of compound **4** in DMSO-d_6

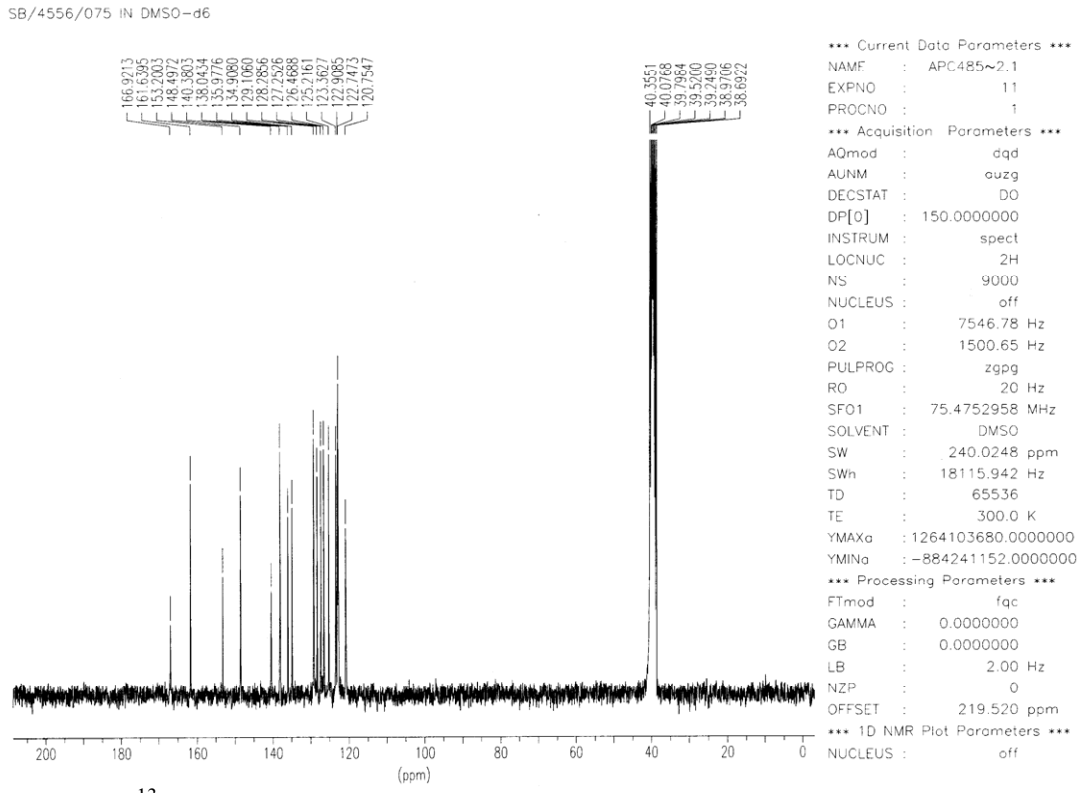


Figure S4 ^{13}C NMR of compound **4** in DMSO-d_6

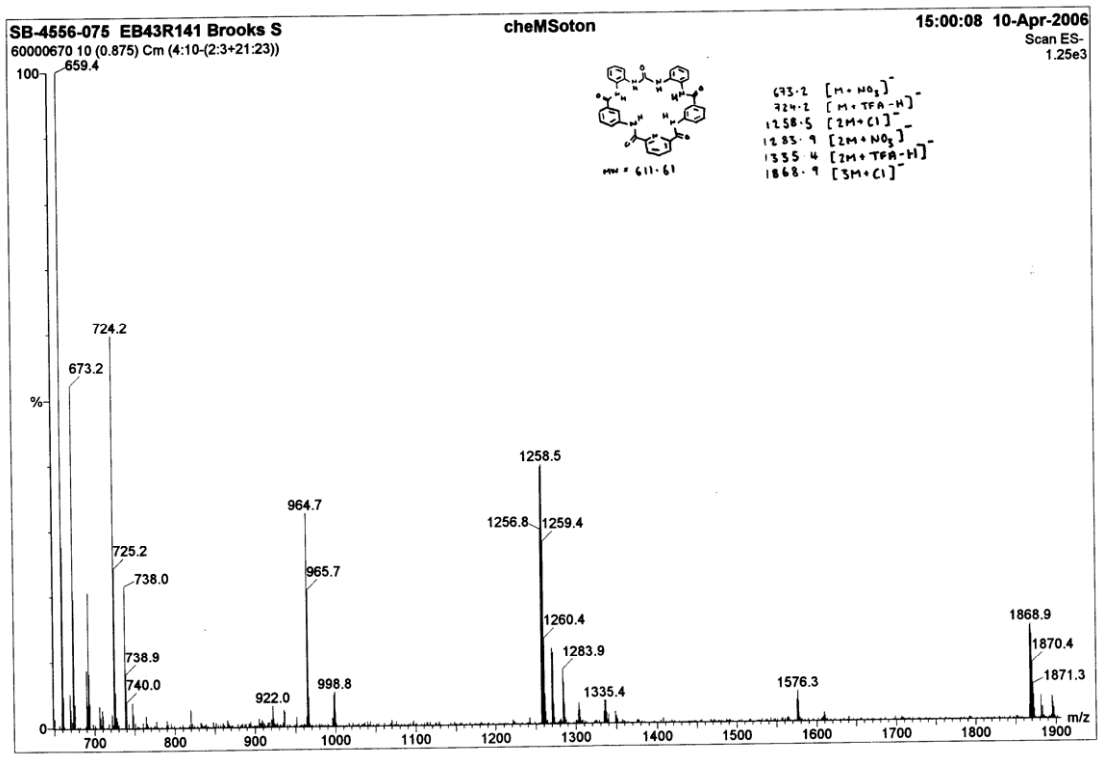


Figure S5 ESMS of compound **4**

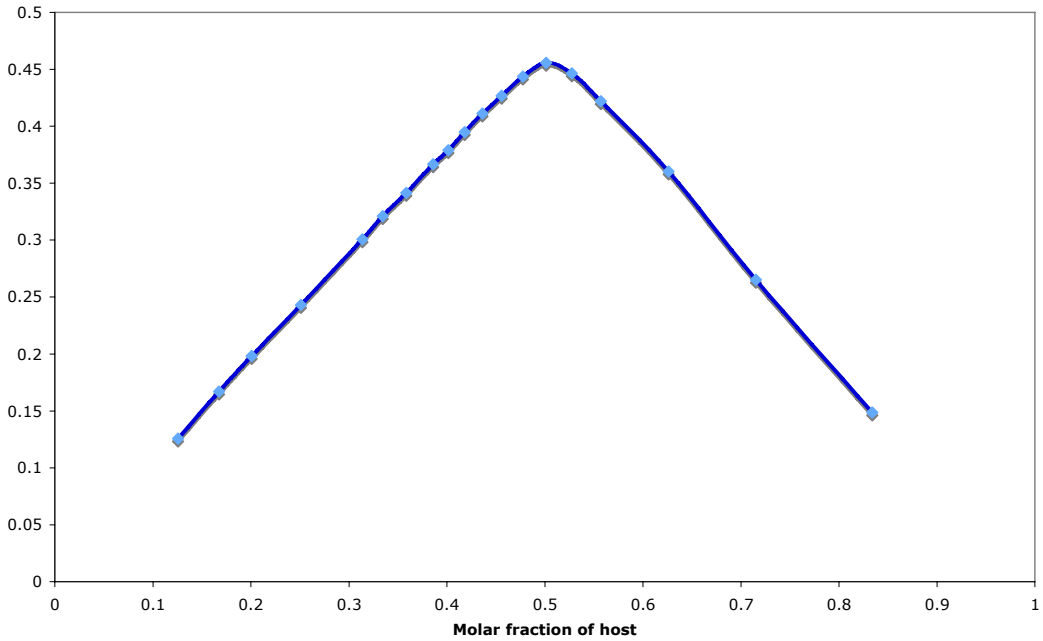


Figure S6 Job plot of compound **4** with acetate in DMSO-d_6/0.5% water

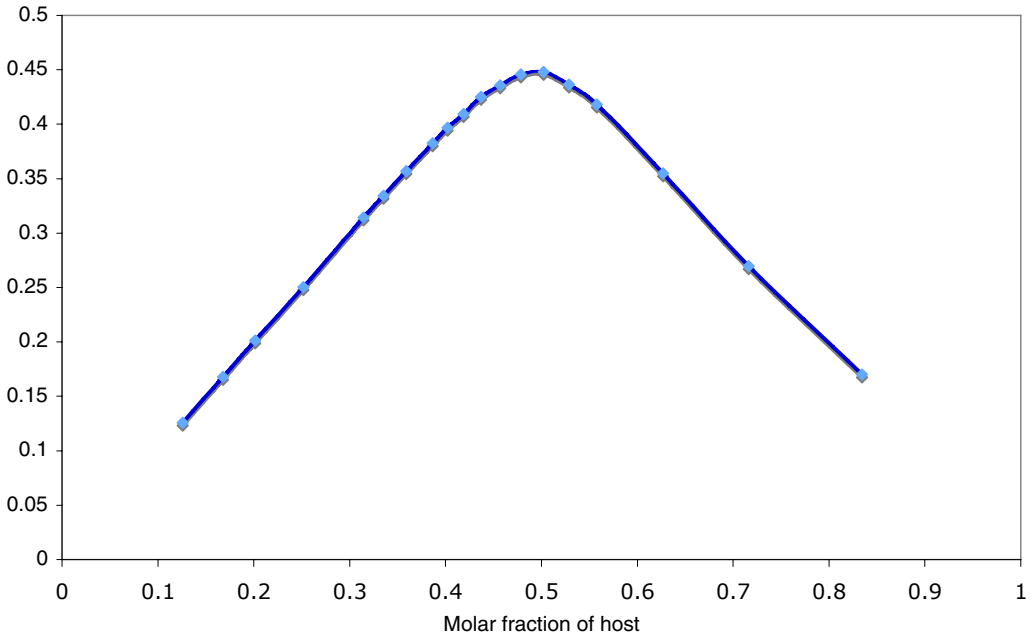


Figure S7 Job plot of compound **4** with benzoate in DMSO-d_6/0.5% water

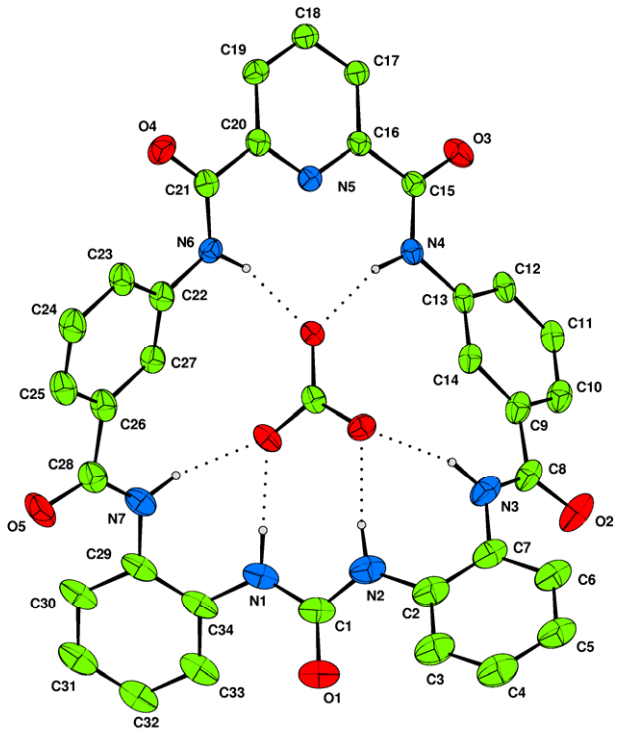


Figure S8 X-ray crystal structure of the mixed fluoride/carbonate complex of macrocycle **1**. Only the macrocycle and carbonate are shown. Thermal ellipsoids are shown at the 30% probability level.

Table S1. Hydrogen bonds [Å and °] in the X-ray crystal structure of the mixed fluoride/carbonate complex of macrocycle **4**.

D–H···*A*	*d*(*D*–H)	*d*(H···*A*)	*d*(*D*···*A*)	∠(*D*H*A*)
N1–H1···O8	0.88	1.87	2.725(13)	163.5
N2–H2···O6	0.88	1.90	2.767(13)	167.8
N3–H3···O6	0.88	1.91	2.750(13)	160.0
N4–H4···O7	0.88	1.99	2.840(11)	162.4
N6–H6···O7	0.88	1.95	2.806(11)	163.2
N7–H7···O8	0.88	1.97	2.831(12)	165.8
O9–H98···F1	0.839(12)	1.81(3)	2.621(7)	163(11)

Symmetry transformations used to generate equivalent atoms:
(i) –y+1,x–1/2,–z+1 (ii) –x+3/2,–y+1/2,z (iii) y+1/2,–x+1,–z+1

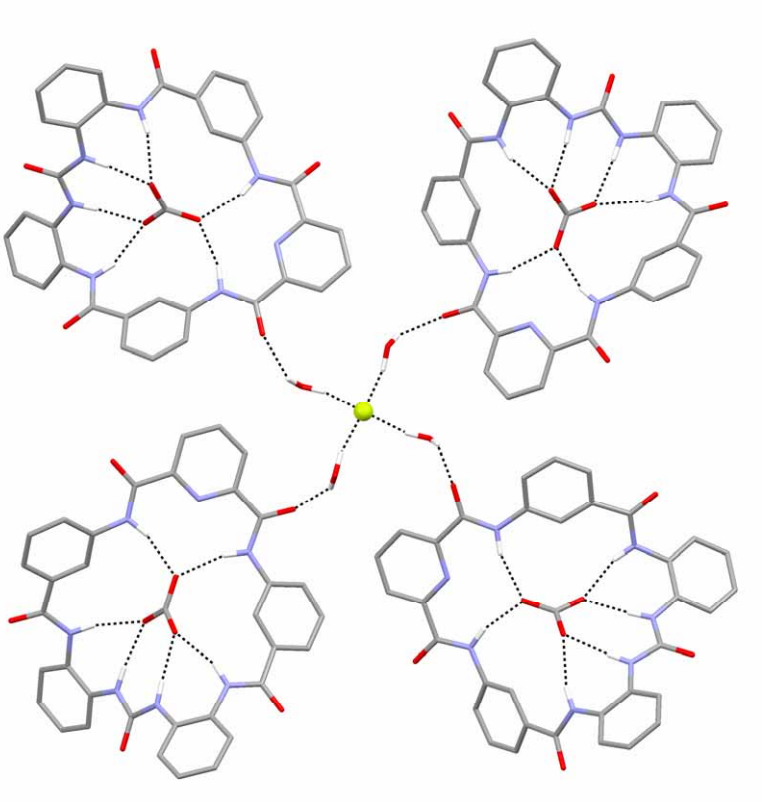


Figure S9 The coordination environment around the exocyclic fluoride anion (shown in green) in the mixed carbonate/fluoride salt is shown with four water molecules forming hydrogen bonds to the 2,6-diamidopyridine amide CO groups. The fluoride anion sits on a 4-fold axis and is surrounded by four water molecules in a square planar arrangement. The O-H…F hydrogen bond interaction has a donor-acceptor distance of 2.621(7) Å. The second hydrogen of the water forms an interaction to one of the oxygen atoms adjacent to the pyridine ring of the macrocycle and forms a tetramer through the central hub of the hydrated fluoride. This unit is surrounded by eight nearest neighbour tetrabutylammoniums in the plane with additional tetrabutylammoniums sitting above and below the plane centred over the carbonate and the fluoride.

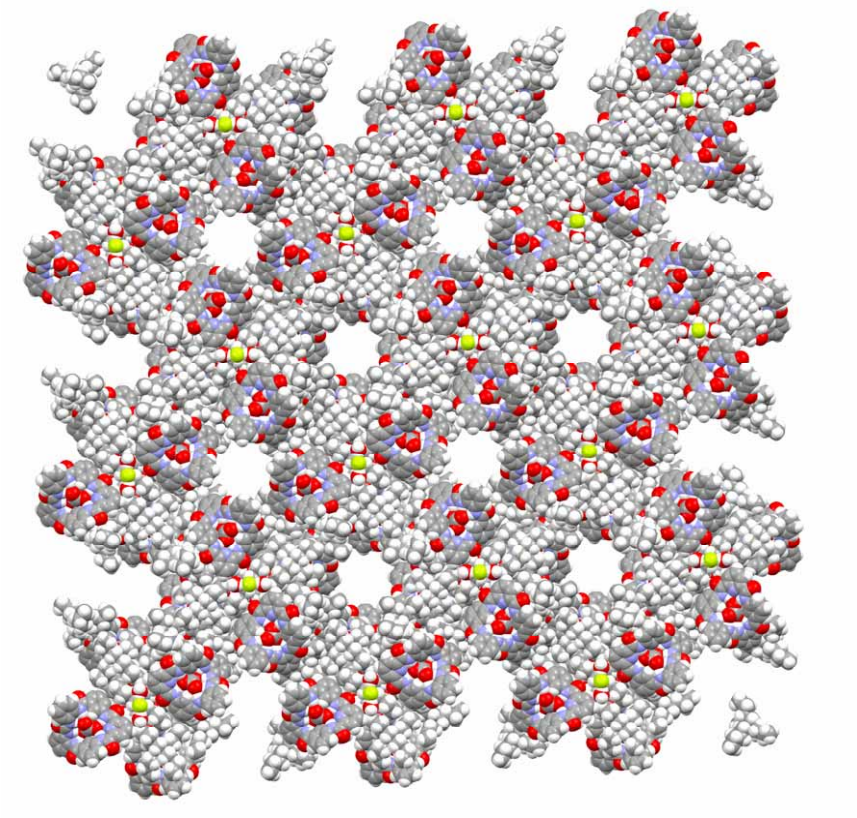


Figure S10 A space-filling packing diagram showing the *ab* plane in the carbonate/fluoride complex. When the packing is extended in the *ab* plane channels with an approximate diameter of 11Å are revealed. These form a hexagonal array and run down the *c* direction. From the presence of diffuse electron density it can be concluded that these channels are partially occupied by solvent.