Supplementary Material (ESI) for Chemical Communications

Sodium and barium cation-templated synthesis and cation-induced molecular pirouetting of a pyridine *N*-oxide containing [2]rotaxane

Supplementary Information

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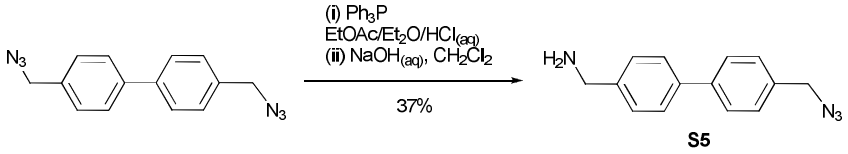
PART I: SYNTHESIS AND CHARACTERISATION

General Considerations. Commercially available solvents and chemicals were used without further purification unless stated. Where dry solvents were used, they were degassed with nitrogen, dried by passing through an MBraun MPSP-800 column and then used immediately. Water was deionized and microfiltered using a Milli-Q Millipore machine.

^{1}H and ^{13}C spectra were recorded on a Varian Mercury-VX 300 spectrometer and AVII 500 (for ^{13}C cryoprobe). Mass spectrometry was carried out on a Bruker micrOTOF spectrometer.

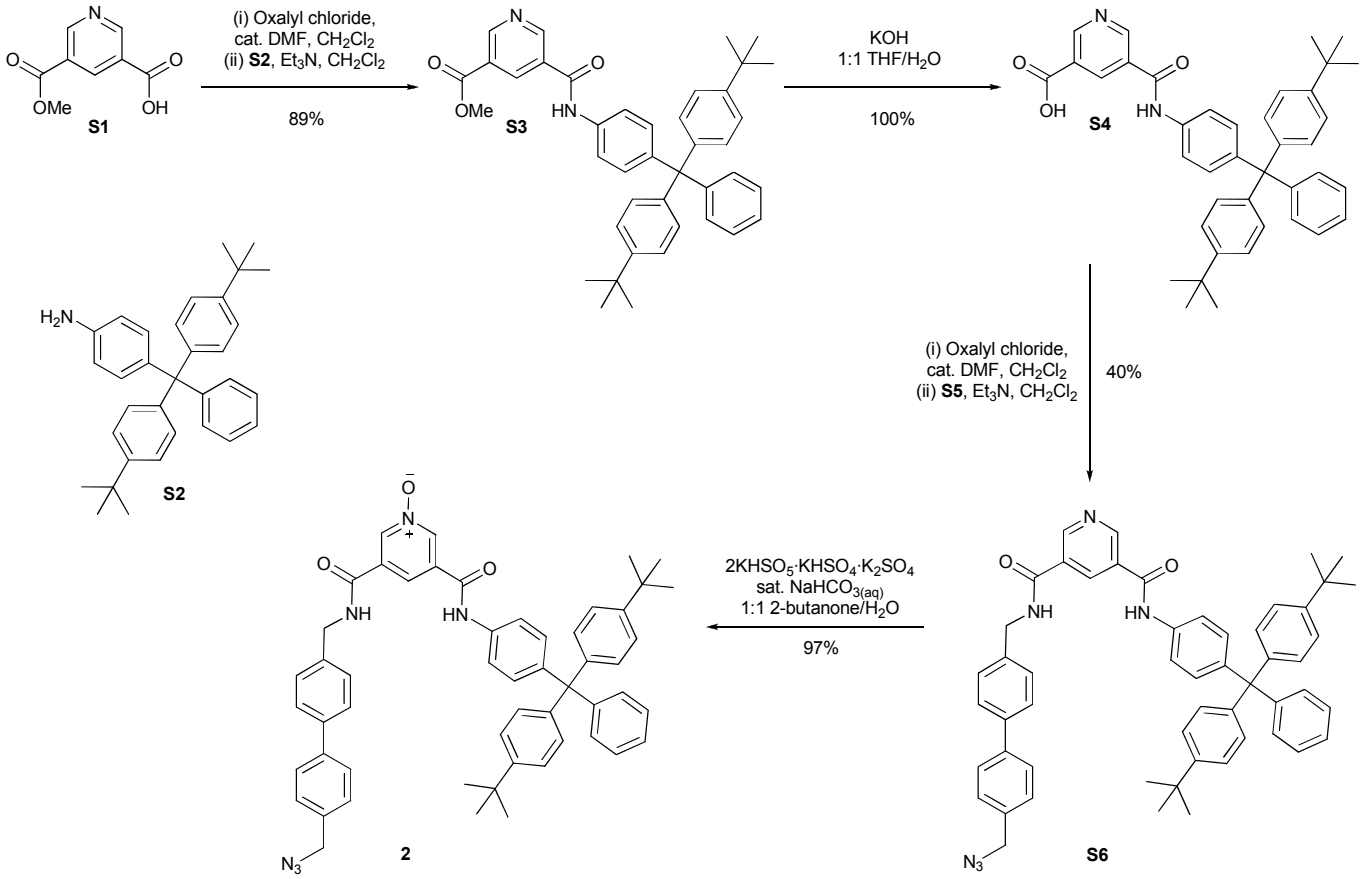
The synthesis of macrocycle **1,**[1] stopper **3,**[1] **S1 (**5-(methoxycarbonyl)nicotinic acid),[2] and stopper **S2**[3] are reported elsewhere. Compound **S5** and pyridine *N*-oxide precursor were prepared according to Schemes S1 and S2 respectively.

Experimental Details



S5

Scheme S1. Synthesis of Compound **S5.**



Scheme S2. Synthesis of pyridine *N*-oxide precursor **2.**

S3:

5-(methoxycarbonyl)nicotinic acid (**S1)** (0.2 g, 1.11 mmol) was suspended in dry CH_2Cl_2 (30 mL), oxalyl chloride (0.19 mL, 2.22 mmol) and DMF (cat.) were added, and the mixture stirred under $N_{2(g)}$ for 1 h until homogenous. The solvent was removed *in vacuo*, the residue dissolved in dry CH_2Cl_2 (20 mL) and added dropwisely to a solution of **S2** (0.52 g, 1.16 mmol), Et_3N (0.28 mL, 2.0 mmol) and DMAP (cat.) in dry CH_2Cl_2 (30 mL). The resulting solution was stirred for 1 h, washed with 10% $HCl_{(aq)}$ (2 × 50 mL) and H_2O (2 × 50 mL), dried over anhydrous $MgSO_4$ and the solvent removed *in vacuo*. The resulting brown oil was purified by column chromatography (silica; 95:5 CH_2Cl_2: MeOH) to yield an oily cream coloured solid (0.60 g, 89%).

^{1}H NMR (300MHz, $CDCl_3$) δ: 9.34-9.62 (2H, m, pyridine H^2 & H^6), 8.78 (1H, t, ^4J = 2.1 Hz, pyridine H^4), 8.05 (1H, br s, ArN*H*), 7.55 (2H, d, ^3J = 8.9 Hz, Ar*H*NH), 7.11 – 7.28 (17H, m, Ar*H*), 4.02 (3H, s, CH_3), 1.31 (18H, s, ^{t}Bu); **^{13}C NMR** (300MHz, $CDCl_3$) δ: 164.9, 162.8, 152.9, 151.9, 148.5, 146.9, 144.3, 143.5, 135.9, 134.9, 131.9, 131.1, 130.6, 127.3, 125.8, 124.3, 119.3, 63.8, 34.3, 33.3; **HRMS (ESI):** *m/z* calc. for $C_{41}H_{42}N_2O_3$ $[M + Na]^+$: 633.3088; found 633.3091.

S4:

S3 (1.81 g, 2.96 mmol) was dissolved in 1:1 THF/H_2O (50 mL), KOH (0.196 g, 3.5 mmol) was added, and the solution stirred for 16 h. 10% citric $acid_{(aq)}$ was added until the solution was pH = 7, and the aqueous mixture extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$, and the solvent removed *in vacuo*. The resulting sticky brown solid was recrystallized from $CHCl_3$ to give an off-white solid (1.77 g, 100%).

^{1}H NMR (300MHz, d_6-DMSO) δ: 11.70 (1H, s, COO*H*), 10.63 (1H, s, ArN*H*), 9.27 (1H, d, ^4J = 2.0 Hz, pyridine H^2), 9.21 (1H, d, ^4J = 2 Hz, pyridine H^6), 8.74 (1H, t, ^4J = 2 Hz, pyridine H^4), 7.68 (2H, d, ^3J = 8.8 Hz, Ar*H*NH), 7.10 – 7.34 (17H, m, Ar*H*), 1.26 (18H, s, *t*Bu); **^{13}C NMR** (300MHz, d_6-DMSO) δ: 165.8, 163.1, 152.3, 147.9, 146.9, 143.6, 142.5, 136.4, 136.0, 130.7, 130.4, 130.1, 127.7, 126.4, 125.8, 124.5, 119.6, 34.9, 31.1; **HRMS (ESI):** *m/z* calc. for $C_{40}H_{40}N_2O_3$ $[M - H]^+$: 596.2966; found: 595.2980.

S5:

4,4'-bis(azidomethyl)biphenyl (**S5**) (300 mg, 1.14 mmol) was dissolved in 1:1 Et_2O/EtOAc (10 mL), 5% $HCl_{(aq)}$ (20 mL) was added and the biphasic mixture cooled to 0 ºC. A solution of Ph_3P (295 mg, 1.13 mmol) in 1:1 Et_2O/EtOAc (10 mL) was added dropwise over 30 min, and the solution stirred for 18 h at RT. The precipitate was collected by vacuum filtration and washed with 1:1 Et_2O/EtOAc (2 × 50 mL). The resulting solid was suspended in CH_2Cl_2, 10% $NaOH_{(aq)}$ added and the biphasic mixture stirred for 30 min until all solid had dissolved. The organic layer was separated, washed with H_2O (2 × 50 mL), dried over $MgSO_4$, and the solvent removed *in vacuo* to give a white waxy solid (100 mg, 37%).

^{1}H NMR (300 MHz, CD_3OD) δ: 7.59 – 7.66 (4H, m, Ar*H*), 7.42 (4H, d, ^3J = 8.2 Hz, Ar*H*), 4.40 (2H, s, CH_2N_3), 3.83 (2H, s, CH_2NH_2); **^{13}C NMR** (75.5 MHz, CD_3OD) δ: 142.6, 141.9, 140.3, 135.9, 129.8, 128.9, 128.1, 128.0, 55.1, 46.2. **HRMS (Probe FI)** calculated for $C_{14}H_{14}N_4$ $[M]^{+}$: 238.1218; found 238.1212.

S6:

S4 (192 mg, 1.06 mmol) was suspended in dry CH_2Cl_2 (20 mL), then oxalyl chloride (0.190 mL, 2.12 mmol) and DMF (cat.) were added. The mixture was stirred for 1 h until all solid had dissolved. The solvent was removed *in vacuo*, then redissolved in dry CH_2Cl_2 (15 mL) and added dropwise to a solution of compound **S5** (253 mg, 1.06 mmol) and Et_3N (0.42 mL, 3 mmol) in CH_2Cl_2 (20 mL). The resulting solution was stirred for 1 h, washed with 10 % $HCl_{(aq)}$ (2 x 50 mL) and H_2O (2 x 50 mL), dried over anhydrous $MgSO_4$, and the solvent removed *in vacuo*. The resulting brown oil was purified by column chromatography (silica; 95:5 CH_2Cl_2/MeOH) giving an oily orange solid (306 mg, 72 %).

^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.34 (1H, s, pyridine H^2), 9.26 (1H, s, pyridine H^6), 8.69 (1H, s, pyridine H^4), 7.61 (4H, d, ^3J = 8.2 Hz, Ar*H*), 7.47 (2H, d, ^3J = 8.2 Hz, Ar*H*), 7.41 (2H, d, ^3J = 8.2 Hz, Ar*H*), 6.61 (1H, br s, N*H*), 4.72 (2H, d, ^3J = 5.9 Hz, NHCH_2), 4.40 (2H, s, CH_2N_3), 3.99 (3H, s, OCH_3); **^{13}C NMR**

(75.5 MHz, $CDCl_3$) δ: 164.9, 164.4, 153.0, 151.9, 140.5, 140.2, 136.7, 135.7, 134.6, 129.8, 128.7, 128.6, 127.6, 127.5, 125.9, 54.5, 52.7, 44.0; **HRMS (ESI)** *m/z* calc.for $C_{54}H_{52}N_6O_2$ $[M + Na]^+$: 839.4044; found: 839.4038.

Pyridine *N*-oxide axle precursor (2):

Compound **S5** (0.198 g, 0.24 mmol) and $NaHCO_3$ (1.03 g, 7.26 mmol) were dissolved in 1:1 2-butanone/H_2O (50 mL) and a saturated solution of Oxone® (0.446 g, 0.726 mmol) in H_2O (3 mL) was added dropwisely. The solution was stirred vigorously for 2 h before addition of NaCl (1.70 g, 29.0 mmol) and extraction with $CHCl_3$ (3 × 50 mL). The organic layer was dried over anhydrous $MgSO_4$ and the solvent removed *in vacuo* to give a white solid (0.196 g, 97%).

^{1}H NMR (300MHz, $CDCl_3$) δ (ppm): 9.71 (1H, s, ArHN*H*), 8.88 (1H, s, pyridine H^6), 8.84 (1H, s, pyridine H^2), 8.38 (2H, br s, CH_2NH & pyridine H^4), 7.63 (2H, d, ^3J = 8.8 Hz, Ar*H*NH), 7.55 (2H, d, ^3J = 8.2 Hz, biphenyl ArH), 7.49 (2H, d, ^3J = 8.2 Hz, biphenyl ArH), 7.15 – 7.35 (19H, m, stopper Ar*H*), 4.53 (2H, d, ^3J = 4.7 Hz, CH_2NH), 4.35 (2H, s, CH_2N_3), 1.36 (18H, s, ^{t}Bu*H*) **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ (ppm): 162.0, 160.4, 148.5, 146.9, 144.5, 143.5, 140.2, 139.8, 136.3, 135.0, 134.5, 133.6, 131.8, 131.0, 130.6, 128.6, 128.3, 127.4, 127.3, 127.2, 125.8, 124.3, 119.5, 63.8, 54.4, 44.0, 34.3, 31.3. **HRMS (ESI):** *m/z* calc. for $C_{54}H_{52}N_6O_3$ $[M + Na]^+$: 855.3993; found: 855.3994.

Calixdiquinone *N*-oxide rotaxane (4):

General procedure: calixdiquinone macrocycle **1** (30 mg, 0.0285 mmol), compound **2** (24 mg, 0.0285 mmol), and stopper **3** (14 mg, 0.0285 mmol) were dissolved in degassed CH_2Cl_2 (20 mL), (a solution of $M(ClO_4)_x$ (0.0285mmol) in) CH_3CN (0.25 mL) was added and the solution stirred for 15 min. DIPEA (5 μL, 0.0293 mmol) and $Cu(CH_3CN)_4PF_6$ (2 mg, 0.0054 mmol) were added and the solution stirred under N_2 for 16 h. The solvent was removed *in vacuo* and the crude material purified by preparative TLC (silica; 1:1 acetone/hexane & CH_3CN → 93:7 CH_3CN/MeOH) to obtain a yellow solid.

Without cation: Neat CH_3CN added i.e. no $M(ClO_4)_x$, giving a yield of 10% (7 mg).

With Barium: M = Ba x = 2, giving a yield of 28% (18 mg). N.B. $Ba(ClO_4)_2$ mostly suspended throughout reaction

With Sodium: M = Na, x = 1, giving a yield of 50% (34 mg).

^{1}H NMR (300MHz, $CDCl_3$) δ (ppm): 9.12 (1H, s, axle ArHN*H*), 8.68 (2H, s, pyridine H^6 & isophthalamide H^2), 8.54 (1H, s, pyridine H^2), 8.52 (1H, t, ^3J = 5.6 Hz, axle CH_2NH), 8.39 (2H, br s, macrocycle NH), 8.23 (2H, dd, ^3J = 7.9 Hz, ^4J = 1.9 Hz, isophthalamide H^4 & H^6), 8.03 (1H, s, pyridine H^4), 7.92 (2H, d, ^3J = 8.8 Hz, Ar*H*NH), 7.64 (1H, s, triazole, C*H*), 7.59 (2H, d, ^3J = 7.5 Hz, biphenyl Ar*H*), 7.50 (2H, d, ^3J = 8.2 Hz, biphenyl Ar*H*), 7.37 – 7.41 (4H, m, biphenyl Ar*H*), 7.06 – 7.29 (31H, m, isophthalamide H^5 & stopper Ar*H*), 6.85 (2H, d, ^3J = 8.8 Hz, Ar*H*OCH_2), 6.55 – 6.56 (4H, m, calix Ar*H*), 6.50 (4H, d, ^3J = 9.1 Hz, hydroquinone Ar*H*), 6.32 – 6.37 (8H, m, calix & hydroquinone Ar*H*), 5.60 (2H,

s, axle OCH_2), 5.17 (2H, s, CH_2N), 4.59 (2H, d, ^3J = 5.6 Hz, axle CH_2NH), 4.29 (2H, d, ^2J = 12.9 Hz, calix CH_2), 4.21 (2H, t, ^3J = 8.7 Hz, macrcocycle CH_2), 4.09 (2H, d, ^2J = 12.9 Hz, calix CH_2) 3.96 – 3.99 (2H, m, macrocycle CH_2), 3.89 – 3.94 (6H, m, macrocycle CH_2), 3.82 – 3.85 (2H, m, macrocycle CH_2), 3.71 – 3.77 (4H, m, macrocycle CH_2), 2.92 (2H, ^2J = 12.9 Hz, calix CH_2), 2.73 (2H, ^2J = 12.9 Hz, calix CH_2), 1.32 (18H, s, axle ^{t}Bu), 1.29 (18H, s, axle ^{t}Bu), 0.95 (18H, s, calix ^{t}Bu); **^{13}C NMR** (125 MHz, $CDCl_3$) δ (ppm): 187.9, 187.5, 185.0, 184.9, 167.9, 167.8, 161.6, 159.4, 156.4, 153.3, 152.8, 152.0, 149.0, 148.7, 148.2, 148.0, 147.5, 147.3, 147.0, 145.0, 144.4, 144.1, 143.5, 141.3, 140.9, 140.3, 140.2, 139.7, 137.9, 136.2, 134.1, 134.0, 132.5, 132.2, 132.1, 131.8, 131.4, 131.2, 130.9, 130.8, 129.5, 129.4, 129.2, 129.0, 128.0, 127.7, 127.7, 127.5, 127.0, 126.3, 125.9, 125.4, 125.3, 124.9, 124.7, 124.5, 124.4, 122.9, 118.7, 115.4, 114.2, 113.5, 74.4, 67.7, 67.0, 634.0, 63.7, 62.3, 54.2, 53.7, 43.4, 41.0, 34.6, 34.5, 34.2, 31.6, 31.6, 31.4. **HRMS (ESI):** *m/z* calc. for $C_{154}H_{154}N_8O_{16}$ $[M + Na]^+$: 2395.1414; found 2395.1450

^{1}H and ^{13}C spectra of Compounds 2 and 4

Compound 2

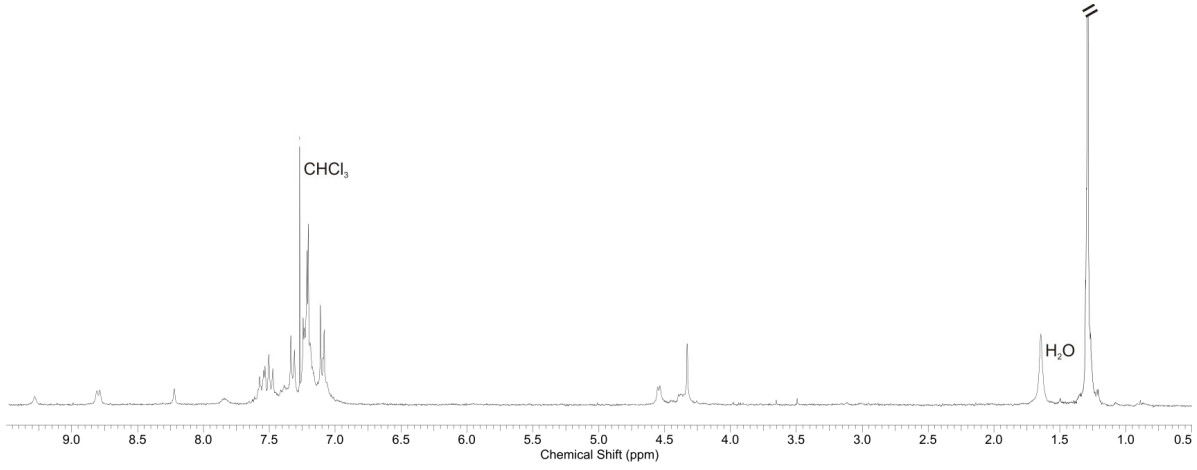


Figure S1. ^{1}H NMR spectrum of **2** ($CDCl_3$, 300 MHz, 293 K)

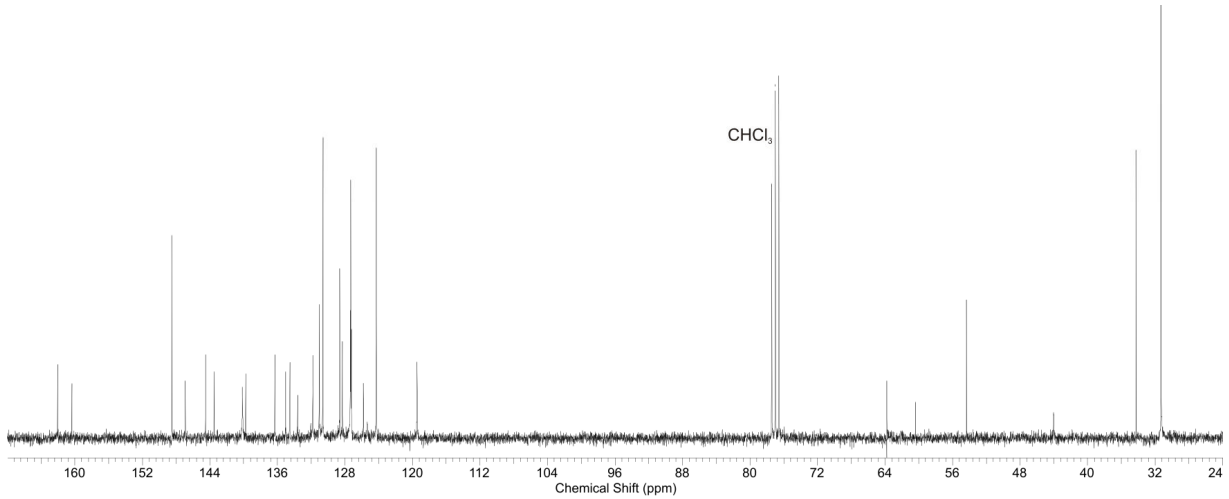


Figure S2. ^{13}C NMR spectrum of **2** ($CDCl_3$, 75.5 MHz, 293 K)

Compound 4

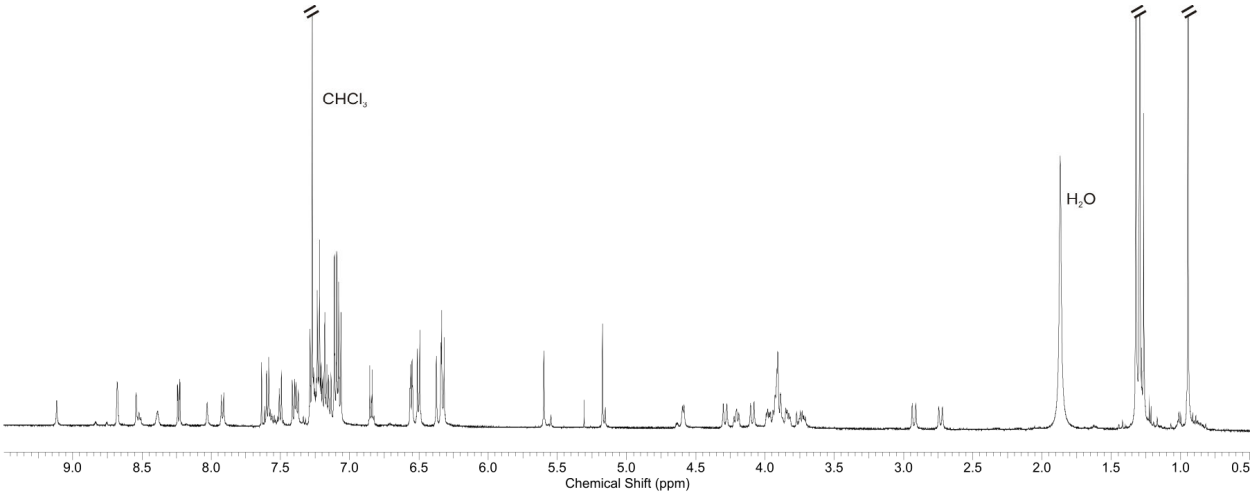


Figure S3. ^{1}H NMR spectrum of **4** ($CDCl_3$, 300 MHz, 293 K)

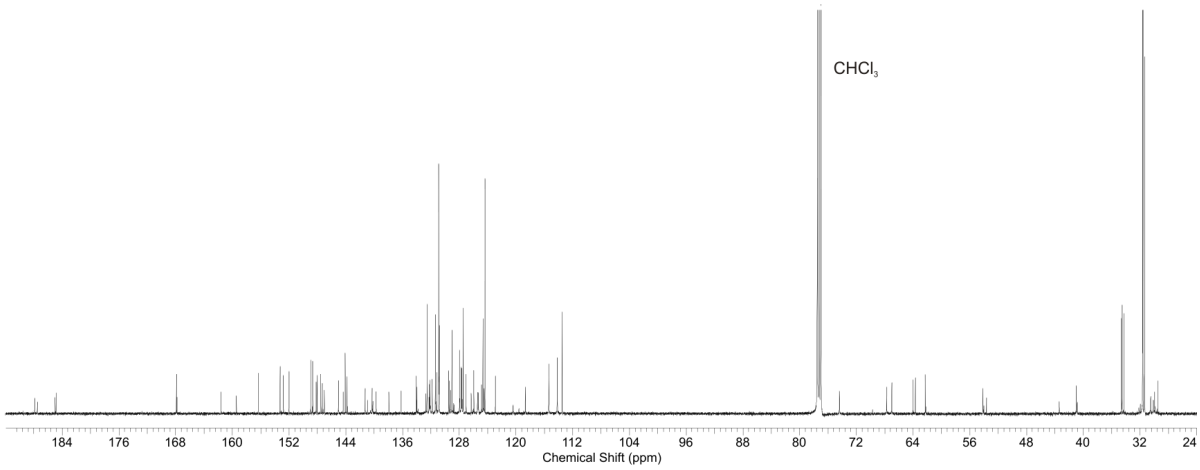


Figure S4. ^{13}C NMR spectrum of **4** ($CDCl_3$, 125 MHz, 293 K)

PART II: SULFATEABSTRACTION OF BARIUM CATION

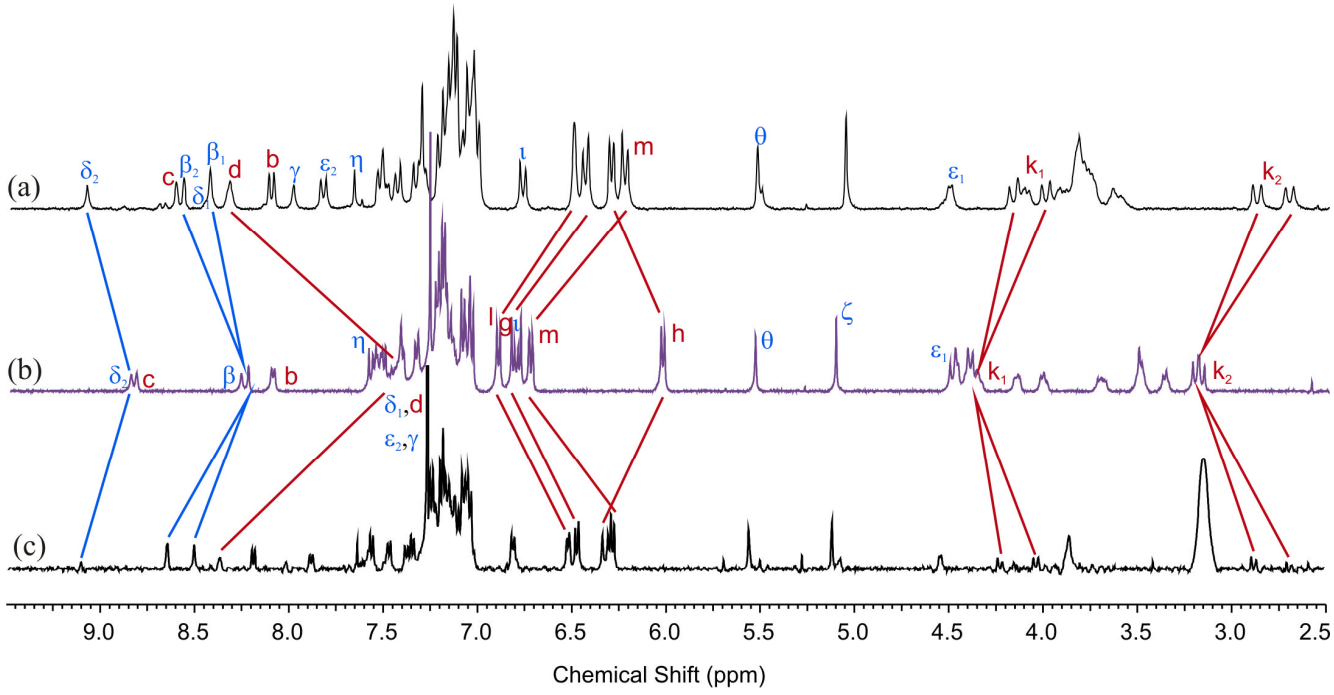


Figure S5. Partial ^{1}H NMR spectra in 5:1 $CDCl_3/CD_3CN$ of (a) rotaxane **4**, (b) rotaxane **4** + 1 eq. $Ba(ClO_4)_2$ and (c) rotaxane **4** + 1 eq. $Ba(ClO_4)_2$ + 1 eq. $(TBA)_2SO_4$.

PART III: REFERENCES

1. A. V. Leontiev, C. A. Jemmett and P. D. Beer, *Chem. Eur. J.*, 2011, **17**, 816-825.
2. K. M. Broadus and S. R. Kass, *J. Am. Chem. Soc.*, 2000, **122**, 9014-9018.
3. H. W. Gibson, S.-H. Lee, P. T. Engen, P. Lecavalier, J. Sze, Y. X. Shen and M. Bheda, *J. Org. Chem.*, 1993, **58**, 3748-3756.