Electronic Supplementary Information

Modulating the expression of chirality in a mechanically chiral rotaxane

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General Information

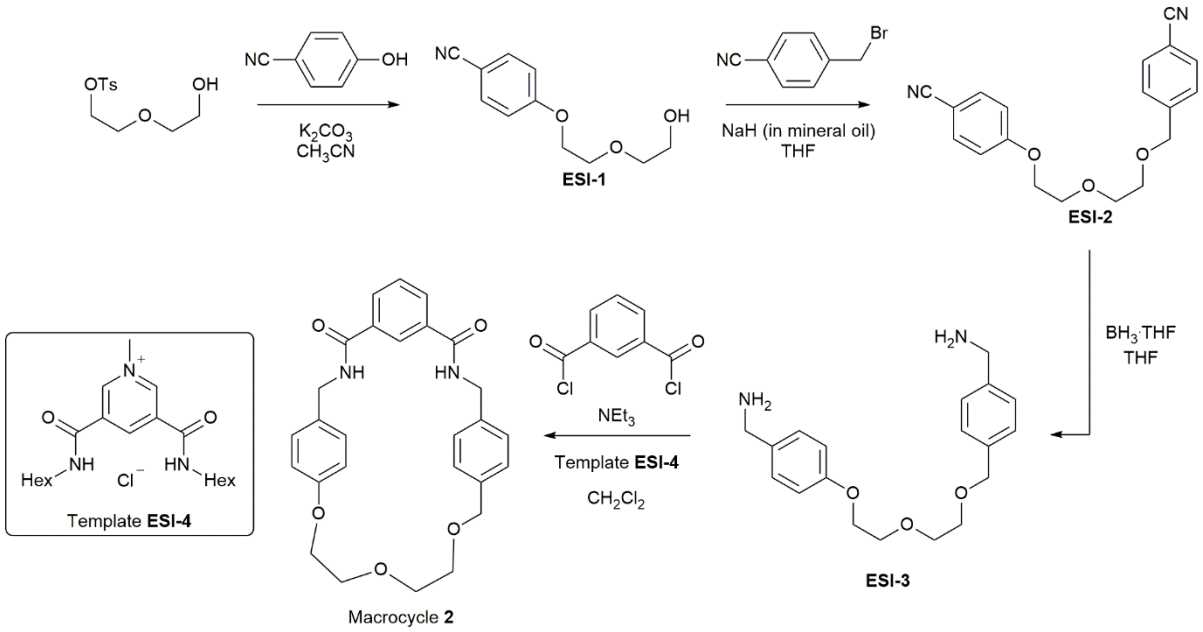
Commercially available solvents and chemicals were used without further purification unless stated. Dry solvents, NEt_3 and DIPEA were purchased dry and stored under an inert atmosphere. $Cu(CH_3CN)_4BF_4$ was stored in a desiccator over P_4O_{10}. Deionised water was used in all cases. Azide **3**,[1] alkyne **4**,[2] 2-(2-hydroxyethoxy)ethyl 4-methylbenzenesulfonate[3] and methyl pyridinium template **ESI-4**[4] were prepared according to previously reported procedures.

Silica gel with a 60 Å particle size was used as the stationary phase for column chromatography. Analytical TLC was used to monitor the progress of column chromatography and analytical TLC plates were typically examined under short wavelength (lambda = 254 nm) UV light. If required, ceric ammonium molybdate or potassium permanganate stains were used to develop the analytical TLC plates.

IR spectra were recorded on an Agilent Technologies Cary 630 FTIR spectrometer. NMR spectra were recorded on a Bruker Ultrashield 400 Plus Spectrometer at 298 K. Mass spectra were recorded on a Shimadzu LCMS IT ToF instrument. Melting points were recorded on a Gallenkamp capillary melting point apparatus and are uncorrected. HPLC was performed on a Shimdazu NexeraX2 UHPLC system.

Experimental Procedures

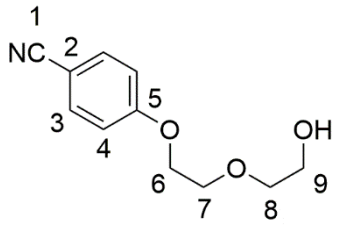
Multi-step synthesis of Macrocycle 2



*Preparation of rotationally asymmetric macrocycle **2**.*

The monotosylate of diethylene glycol was prepared by following an adapted literature procedure.[3]

Mono-nitrile **ESI-1**



4-Hydroxybenzonitrile (2.29 g, 19.2 mmol) and K_2CO_3 (3.98 g, 28.8 mmol) were added to a solution of diethylene glycol monotosylate (3.33 g, 12.8 mmol) in dry CH_3CN (50 mL). The resulting mixture was heated under reflux for 5 days, under an Ar (g) atmosphere. After cooling to RT, the suspension was filtered under suction and the solvent removed *in vacuo*. The resulting oil was re-dissolved in CH_2Cl_2 (50 mL) then washed with 1 M NaOH (aq) (25 mL) and H_2O (25 mL). The organic layer was dried ($MgSO_4$), and the solvent removed *in vacuo* to yield the product as a colourless oil (2.00 g, 82%).

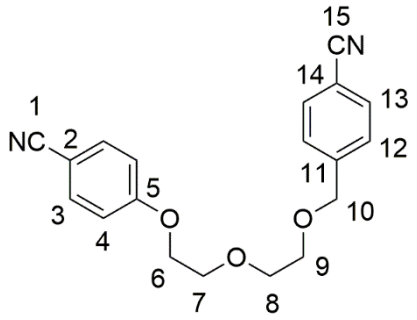
IR (neat) υ_{max}: 3500 (O–H), 2900 (C–H), 2230 (CN), 1600, 1510, 1460, 1300, 1260, 1180, 1130, 1090, 1050.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57-7.61 (2H, m, C^3H), 6.96-7.00 (2H, m, C^4H), 4.18-4.20 (2H, m, C^6H), 3.88-3.91 (2H, m, C^7H), 3.77-3.79 (2H, m, C^9H), 3.67-3.69 (2H, m, C^8H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.0 (C^5), 134.0 (C^3), 119.1 (C^1), 115.3 (C^4), 104.3 (C^2), 72.6 (C^8), 69.3 (C^7), 67.7 (C^6), 61.7 (C^9).

HRMS (ES –ve) *m/z*: 242.0618 ($[M + Cl]^-$, $C_{11}ClH_{13}NO_3$ requires 242.0589).

Bis-nitrile **ESI-2**



NaH (60% in mineral oil, 0.49 g, 12 mmol) was added to **ESI-1** (2.00 g, 10.2 mmol) in dry THF (30 mL). 4-(Bromomethyl)benzonitrile (2.20 g, 11.2 mmol) was then added and the reaction mixture stirred for 1 h at RT under an Ar (g) atmosphere. The reaction mixture was then quenched with H_2O (20 mL) and then extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude material was was purified by silica gel column chromatography (petrol 40-60/EtOAc 4:1 to 3:1), to yield the product as a white solid (2.47 g, 75%).

Mt Pt 70-72 °C

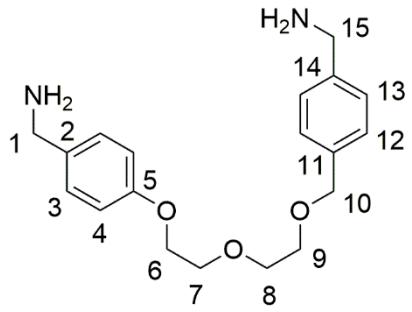
IR (neat) υ_{max}: 2940, 2920, 2870 (multiple C–H), 2220 (CN), 1610, 1510, 1480, 1300, 1260, 1180, 1130, 1030.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.61-7.64 (2H, m, $C^{13}H$), 7.56-7.60 (2H, m, C^3H), 7.45 (2H, d, ^3J = 8.6 Hz, $C^{12}H$), 6.95-6.98 (2H, m, C^4H), 4.63 (2H, s, $C^{10}H$), 4.18-4.20 (2H, m, C^6H), 3.88-3.91 (2H, m, C^7H), 3.75-3.78 (2H, m, C^8H), 3.69-3.72 (m, 2H, C^9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.0 (C^5), 143.8 (C^{11}), 134.0 (C^3), 132.2 (C^{13}), 127.7 (C^{12}), 119.1 (C^1), 118.8 (C^{15}), 115.3 (C^4), 111.3 (C^{14}), 104.2 (C^2), 72.3 (C^{10}), 70.9 (C^8), 70.0 (C^9), 69.5 (C^7), 67.7 (C^6).

HRMS (ES +ve) *m/z*: 345.1201 ($[M + Na]^+$, $C_{19}H_{18}N_2NaO_3$ requires 345.1210).

Bis-amine **ESI-3**



BH_3·THF (1 M, 20.0 mL, 20.0 mmol) was added dropwise to a solution of **ESI-2** (1.26 g, 3.91 mmol) in dry THF (20 mL) under Ar (g) atmosphere. The reaction mixture was heated under reflux for 3 h maintaining the inert atmosphere. Excess reducing agent was then quenched with CH_3OH, then conc. HCl (5 mL) was added and the mixture was allowed to stir for a further 10 minutes at RT. All solvent was then removed *in vacuo*. The resulting solid was re-dissolved in H_2O (30 mL) and washed with CH_2Cl_2 (30 mL). The aqueous layer was basified with 10% NaOH (aq), and then extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude material was purified by silica gel column chromatography (CH_2Cl_2/CH_3OH/NEt_3 93:4:2) to give the product as a waxy white solid (0.80 g, 62%).

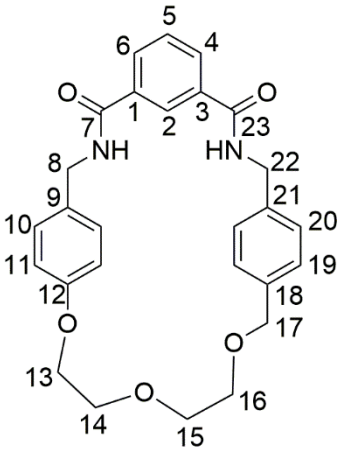
IR (neat) υ_{max}: 3360, 3020, 2860 (multiple C–H & very broad N–H), 1610, 1510, 1450, 1350, 1300, 1240, 1180, 1090.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.27-7.34 (4H, m, $C^{12}H$ & $C^{13}H$), 7.22 (2H, d, ^3J = 8.7 Hz, C^3H), 6.89 (2H, dt, ^3J = 8.7 Hz, C^4H), 4.57 (2H, s, $C^{10}H$), 4.12-4.15 (2H, m, C^6H), 3.85-3.88 (4H, m, C^7H & $C^{15}H$), 3.80 (2H, s, C^1H), 3.74-3.77 (2H, m, C^8H), 3.65-3.67 (2H, m, C^9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.7 (C^5), 142.8 (C^{14}), 136.8 (C^{11}), 135.8 (C^2), 128.2 (C^3), 128.1 (C^{12}), 127.1 (C^{13}), 114.7 (C^4), 73.1 (C^{10}), 70.9 (C^8), 69.8 (C^7), 69.4 (C^9), 67.5 (C^6), 46.3 (C^{15}), 45.9 (C^1).

HRMS (ES +ve) *m/z*: 331.2008 ($[M + H]^+$, $C_{19}H_{27}N_2O_3$ requires 331.2016).

Macrocycle **2**



ESI-3 (800 mg, 2.42 mmol) and methyl pyridinium chloride template **ESI-4** (997 mg, 2.42 mmol) dissolved in dry CH_2Cl_2 (100 mL) and isophthaloyl chloride (590 mg, 2.90 mmol) dissolved in dry CH_2Cl_2 (100 mL), were simultaneously added dropwise to NEt_3 (0.24 g, 0.33 mL, 2.4 mmol) dissolved in CH_2Cl_2 (100 mL) at RT under an Ar (g) atmosphere. The reaction was then stirred for 1 h maintaining the inert atmosphere. The mixture was concentrated *in vacuo* and then washed with 1 M HCl (aq) (2 × 25 mL) and H_2O (2 × 25 mL). The organic layer was dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude material was purified by silica gel column chromatography (EtOAc/CH_2Cl_2 4:1), with the pure product being isolated, following trituration with EtOAc (3 × 2 mL), as a white solid (286 mg, 26 %).

Mt Pt 220-221 °C

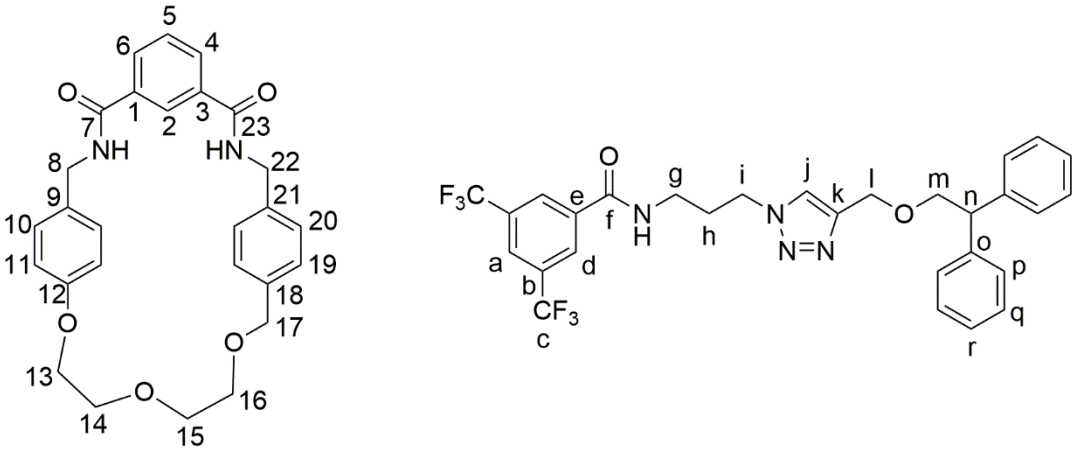
IR (neat) υ_{max}: 3260 (N–H), 3070, 2930, 2900, 2860 (multiple C–H), 1640 (C=O), 1500, 1510, 1300, 1250, 1100, 1090, 1080.

^{1}H NMR (400 MHz, 1:1 $CDCl_3$/CD_3OD) δ: 8.00-8.04 (2H, m, C^4H & C^6H), 7.95 (1H, app t, C^2H), 7.56-7.60 (1H, m, C^5H), 7.30 (4H, s, $C^{19}H$ & $C^{20}H$), 7.25 (2H, d, ^3J = 8.7 Hz, $C^{10}H$), 6.89 (2H, d, ^3J = 8.7 Hz, $C^{11}H$), 4.53 (2H, s, $C^{22}H$), 4.52 (2H, s, $C^{17}H$), 4.47 (2H, s, C^8H), 4.16-4.18 (2H, m, $C^{13}H$), 3.81-3.84 (2H, m, $C^{14}H$), 3.72-3.75 (2H, m, $C^{15}H$), 3.59-3.62 (2H, m, $C^{16}H$).

^{13}C NMR (100 MHz, 1:1 $CDCl_3$/CD_3OD) δ: 167.9 (C^{23}), 167.8 (C^7), 158.5 (C^{12}), 137.4 (C^{18}), 137.1 (C^{21}), 134.5, 134.3 (C^1 & C^3), 131.0, 130.9 (C^4 & C^6), 130.0 (C^9), 129.6 (C^{10}), 129.2 (C^5), 128.6 (C^{19}), 128.1 (C^{20}), 124.6 (C^2), 114.9 (C^{11}), 73.0 (C^{17}), 70.7 (C^{15}), 69.5 (C^{14}), 69.3 (C^{16}), 67.8 (C^{13}), 43.9 (C^{22}), 43.7 (C^8).

HRMS (ES +ve) *m/z*: 483.1881 ($[M + Na]^+$, $C_{27}H_{28}N_2O_5$ requires 483.1900).

Rotaxane **1**



Macrocycle **2** (100 mg, 0.22 mmol) and azide **3** (111 mg, 0.33 mmol) were dissolved in dry CH_2Cl_2 (6 mL) under an Ar (g) atmosphere. Then, alkyne **4** (77 mg, 0.33 mmol), DIPEA (60 μL, 46 mg, 0.36 mmol), $Cu(CH_3CN)_4BF_4$ (10 mg, 0.033 mmol) and TBTA (17 mg, 0.033 mmol) were added. The reaction was stirred at RT for 16 h under an Ar (g) atmosphere. Then, the reaction was diluted with CH_2Cl_2 (15 mL), washed with 0.02 M EDTA in 1 M NH_3 (aq) solution (10 mL) and H_2O (2 × 10 mL). The organic layer was dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. The crude material was purified by careful silica gel column chromatography ($CHCl_3$/CH_3OH 99:1 to 98:2), to yield the product as a white solid (100 mg, 44 %).

Mt Pt 79-80 °C

IR (neat) υ_{max}: 3340 (multiple N–H), 3060, 2920, 2870 (multiple C–H), 1650 (multiple C=O), 1510, 1470, 1450, 1360, 1280, 1180, 1130, 1080, 1030.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.54 (1H, s, C^2H), 8.30-8.33 (2H, m, C^4H & C^6H), 8.07 (2H, s, C^dH), 8.04 (1H, s, C^aH), 7.63 (1H, app t, C^5H), 7.17-7.29 (11H, m, C^jH, C^pH, C^qH & C^rH), 7.14 (1H, t, ^3J = 3.8 Hz, C^8H_2NH), 7.07 (1H, t, ^3J = 4.2 Hz, $C^{22}H_2NH$), 6.75 (4H, app d, $C^{10}H$ & $C^{20}H$), 6.63 (2H, d, ^3J = 7.8 Hz, $C^{19}H$), 6.56 (1H, t, ^3J = 4.2 Hz, axle NH), 6.11 (2H, d, ^3J = 8.5 Hz, $C^{11}H$), 4.68 (2H, s, C^lH), 4.40-4.48 (3H, m, C^8H & $C^{22}H$), 4.20-4.35 (5H, m, $C^{8'}H$ & $C^{17}H$, C^nH, C^iH), 4.17 (1H, d, ^2J = 9.3 Hz, $C^{17'}H$), 4.12 (2H, d, ^3J = 7.3 Hz, C^mH), 3.70-4.01 (8H, m, $C^{13}H$, $C^{14}H$, $C^{15}H$ & $C^{16}H$), 2.54-2.63 (1H, m, C^gH), 2.40-2.48 (1H, m, $C^{g'}H$), 1.94-2.08 (2H, m, C^hH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.0 (C^{23}), 165.8 (C^7), 163.7 (C^f), 157.5 (C^{12}), 145.3 (C^k), 141.9 (C^o), 137.4 (C^{21}), 135.6 (C^{18}), 135.1 (C^e), 133.7 (C^1 or C^3), 133.5 (C^1 or C^3), 132.0 (C^4 & C^6), 131.4 (quar, ^2J = 34 Hz, C^b), 130.0 (C^{10} or C^{20}), 129.6 (C^{19}), 129.3 (C^5), 129.0 (C^9), 128.8 (C^{10} or C^{20}), 128.4 (1 of C^p/C^q/C^r), 128.3 (br, C^d), 128.2 (1 of C^p/C^q/C^r), 126.5 (1 of C^p/C^q/C^r), 124.5 (br, C^a), 123.1 (quar, ^1J = 271 Hz, C^c), 122.9 (C^j), 122.7 (C^2), 113.5 (C^{11}),

74.3 (C^{17}), 73.9 (C^{m}), 70.5 (1 of C^{14}/C^{15}/C^{16}), 70.3 (1 of C^{14}/C^{15}/C^{16}), 70.2 (1 of C^{14}/C^{15}/C^{16}), 66.5 (C^{13}), 64.7 (C^{l}), 50.9 (C^{n}), 48.1 (C^{i}), 44.8 (C^{8} or C^{22}), 44.8 (sic, C^{8} or C^{22}), 38.2 (C^{g}), 28.0 (C^{h}).

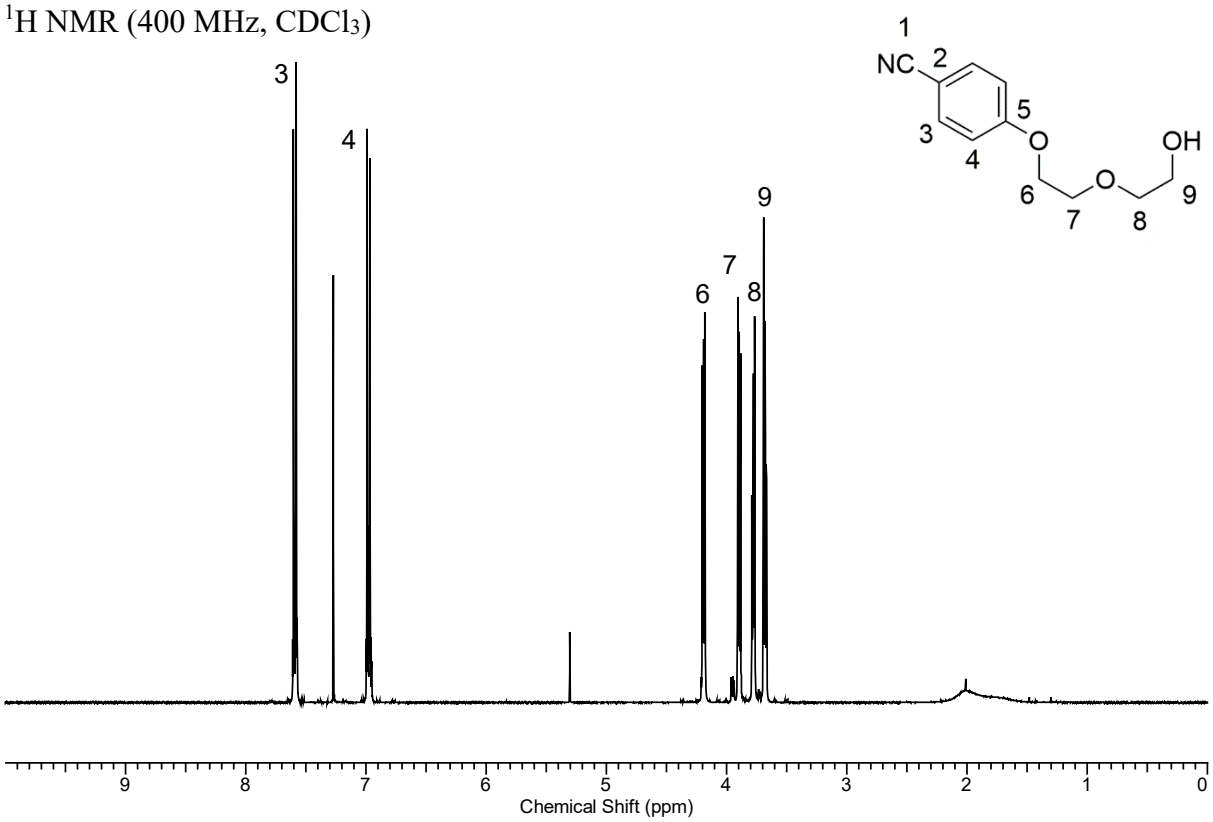
^{19}F NMR (377 MHz, $CDCl_3$) δ: –62.6.

HRMS (ES +ve) *m/z*: 1037.3949 ($[M + H]^+$, 1037.4031 requires $C_{56}H_{54}N_6O_7F_6$).

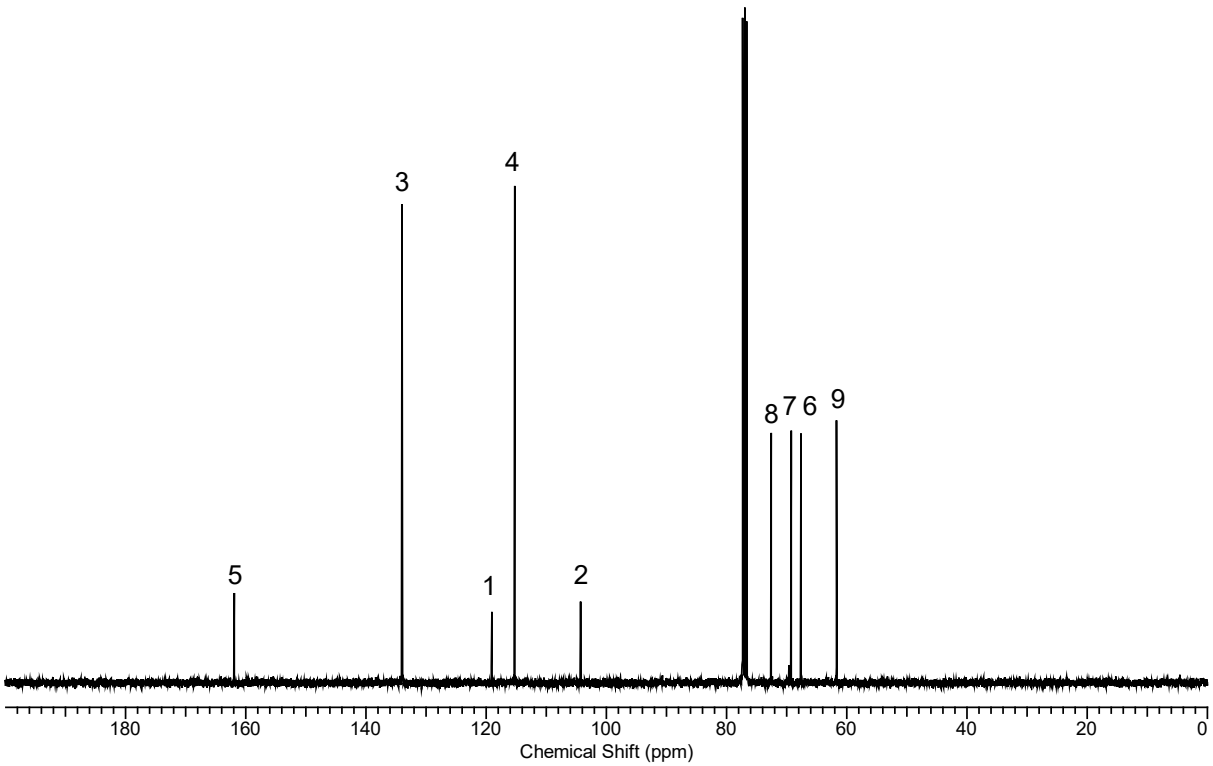
Characterisation Data

Mono-nitrile **ESI-1**

^{1}H NMR (400 MHz, $CDCl_3$)

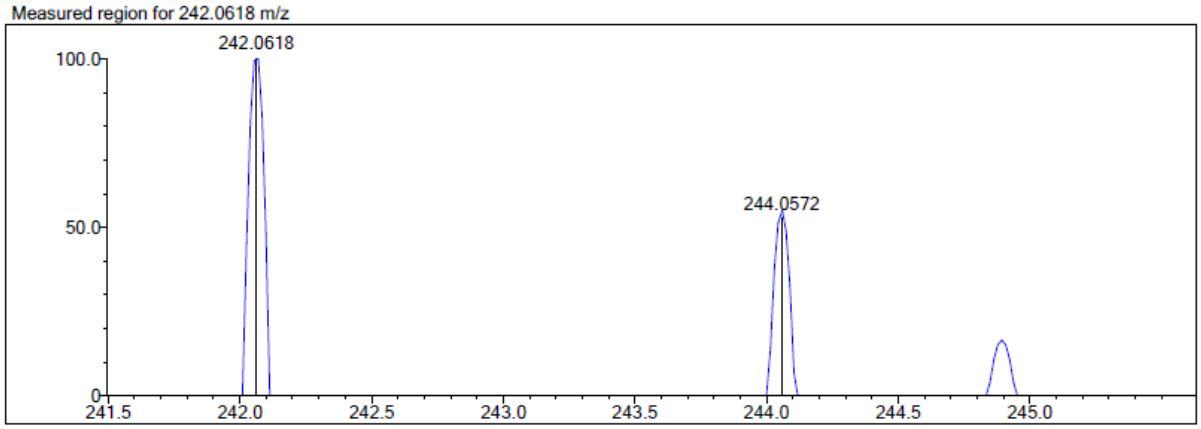


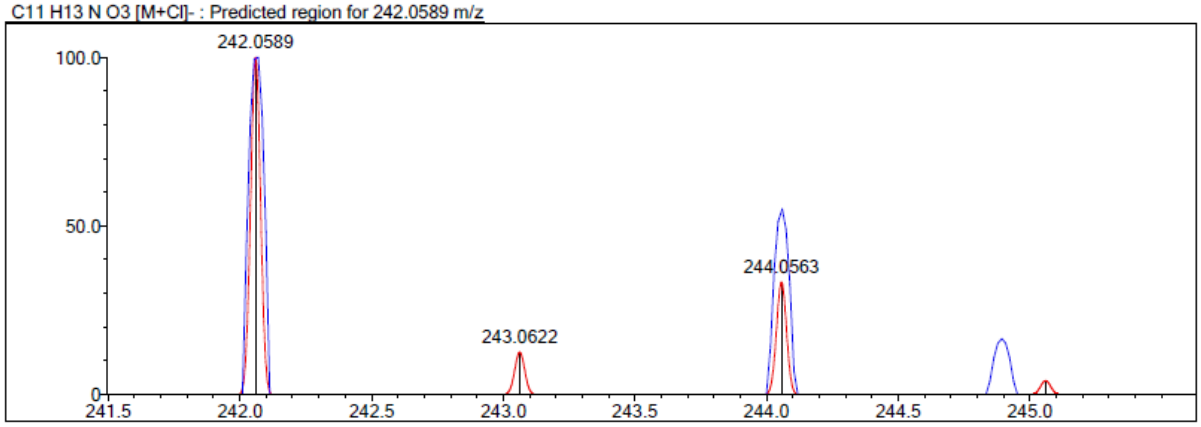
^{13}C NMR (100 MHz, $CDCl_3$)



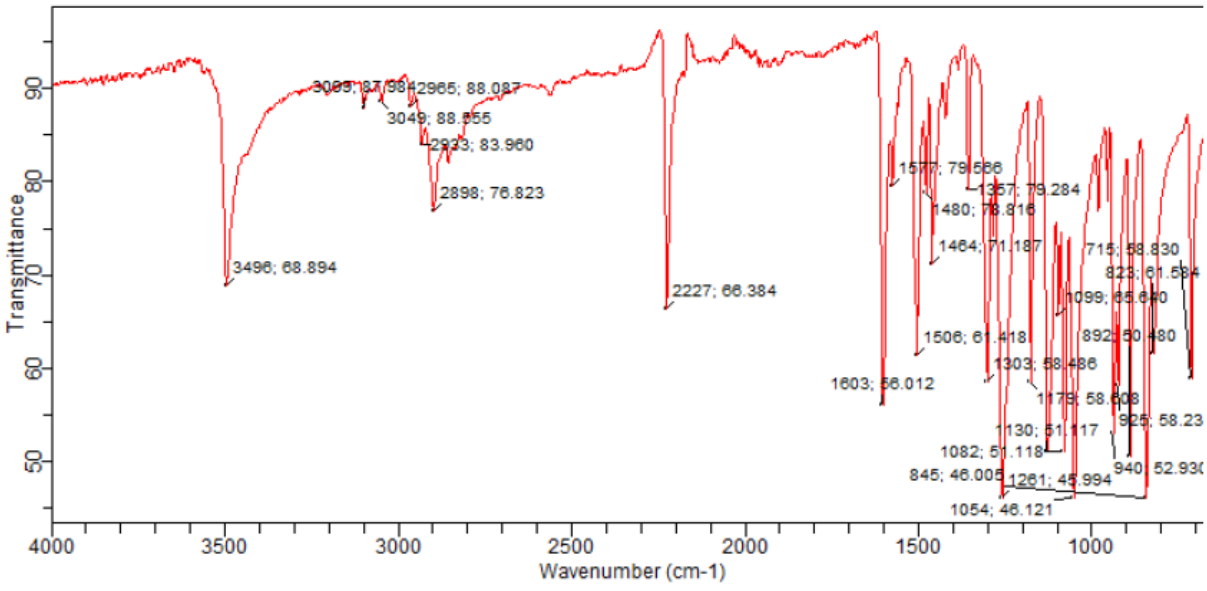
Mono-nitrile **ESI-1**

MS (ES –ve)



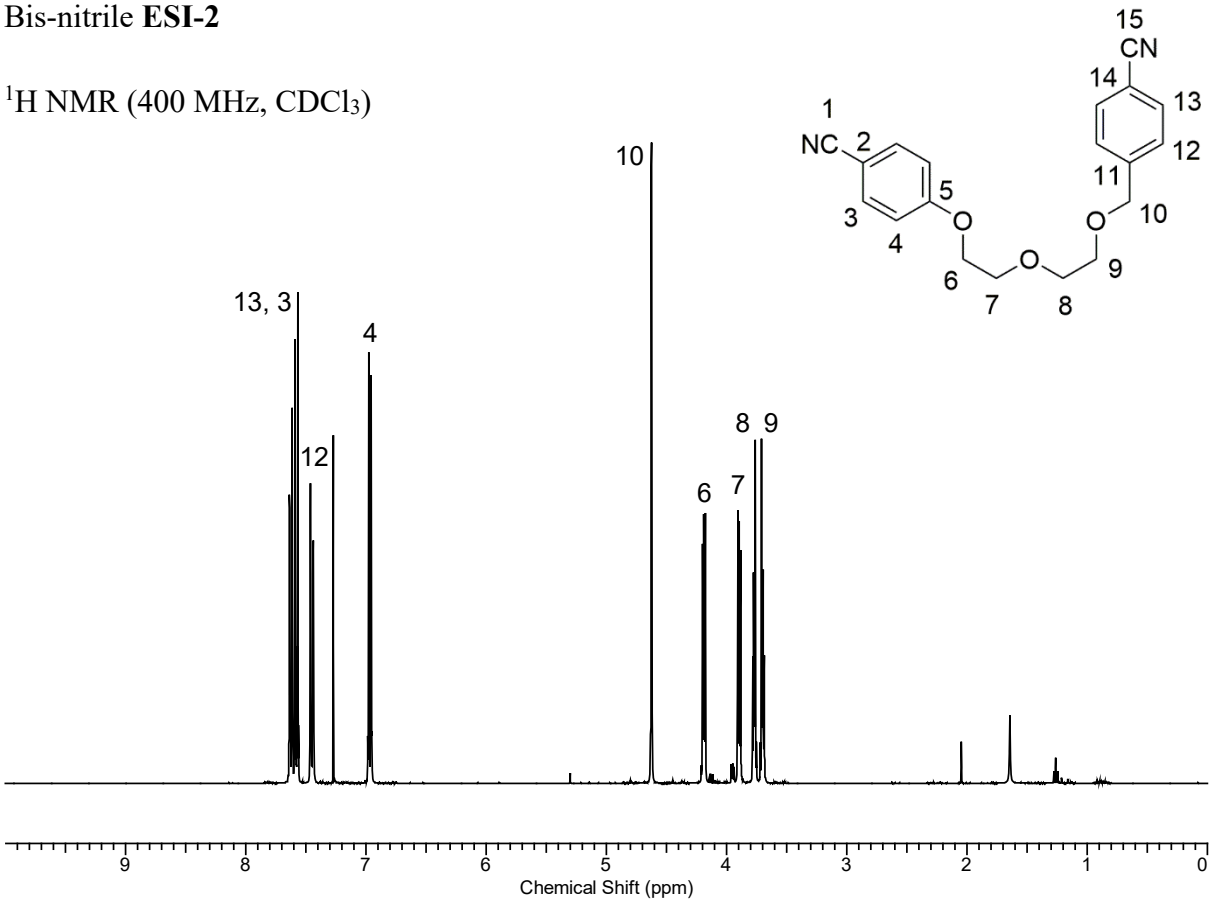


IR (neat)

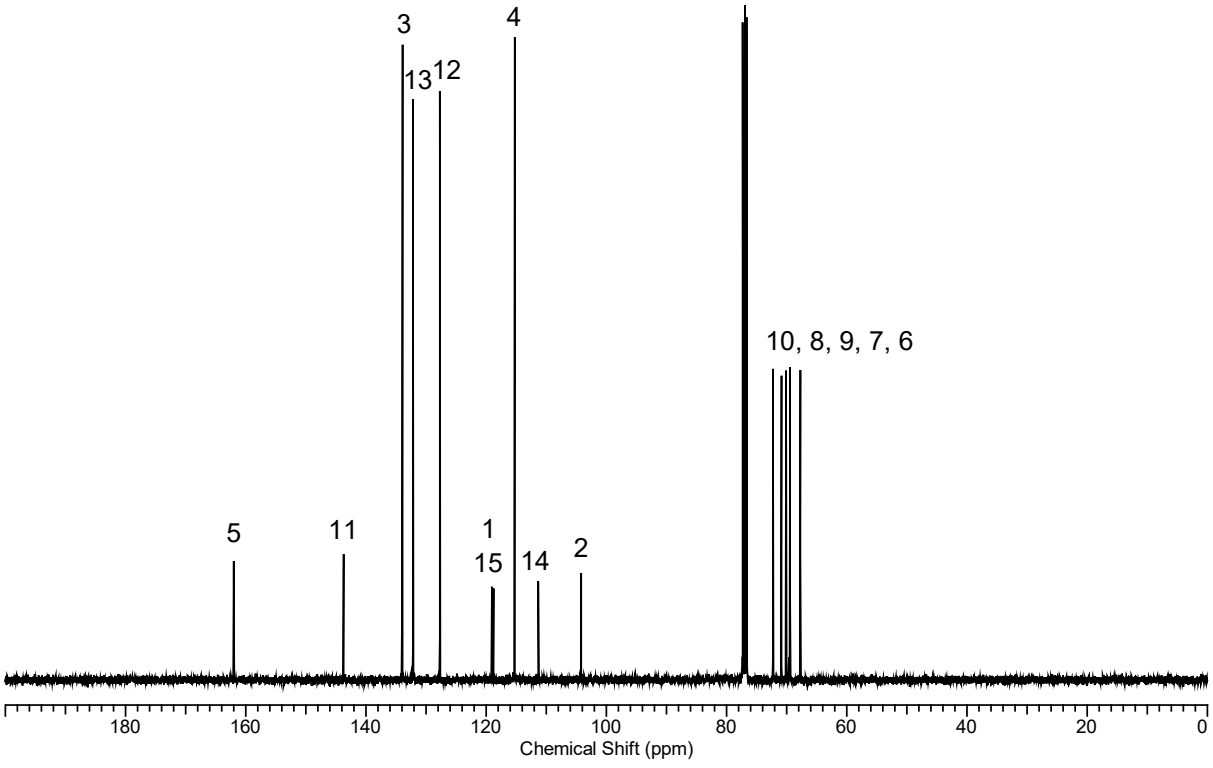


Bis-nitrile **ESI-2**

^{1}H NMR (400 MHz, $CDCl_3$)

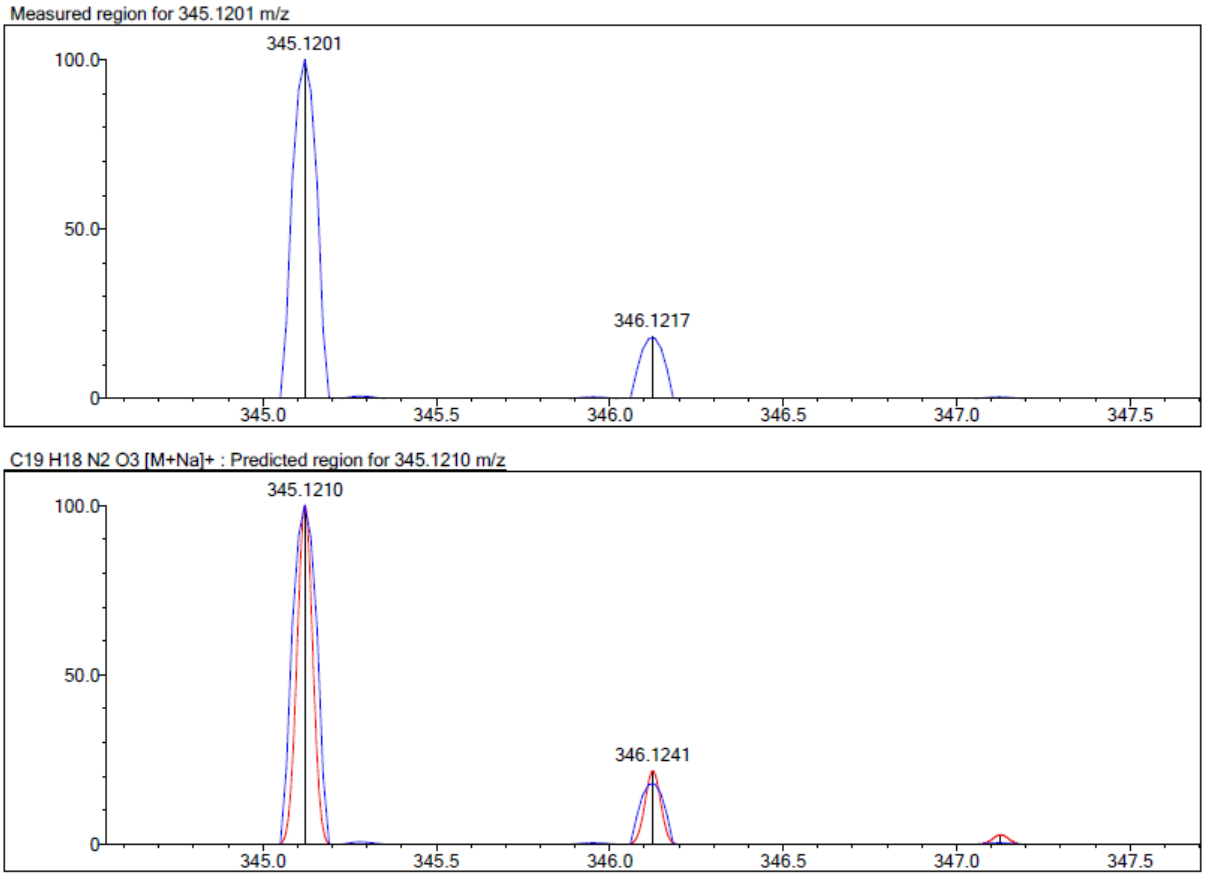


^{13}C NMR (100 MHz, $CDCl_3$)

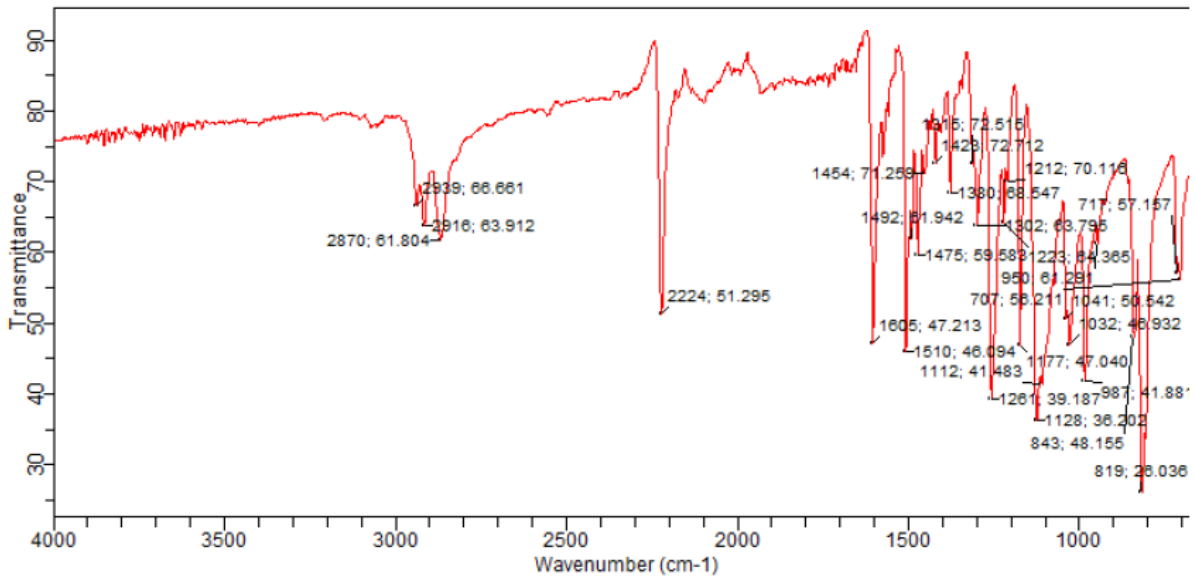


Bis-nitrile **ESI-2**

MS (ES +ve)

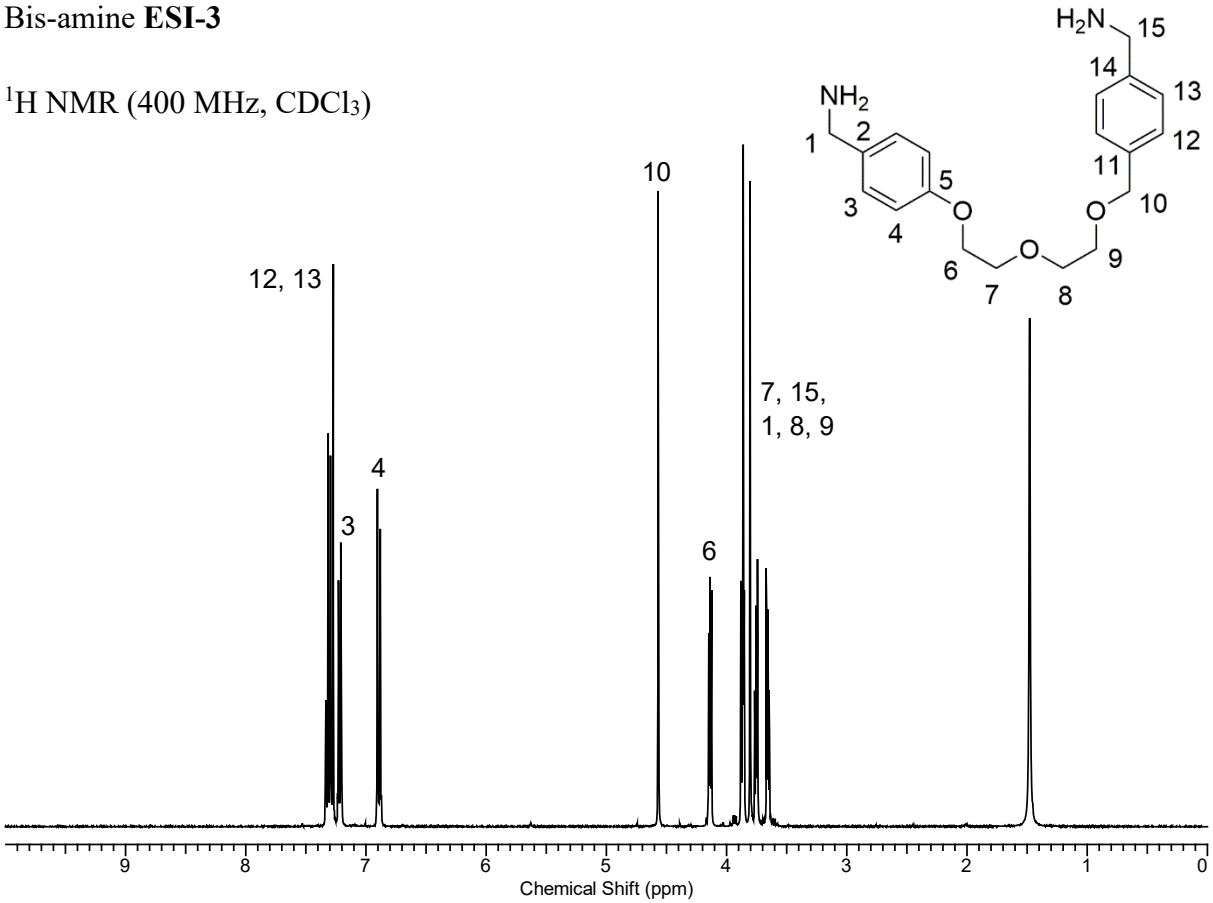


IR (neat)

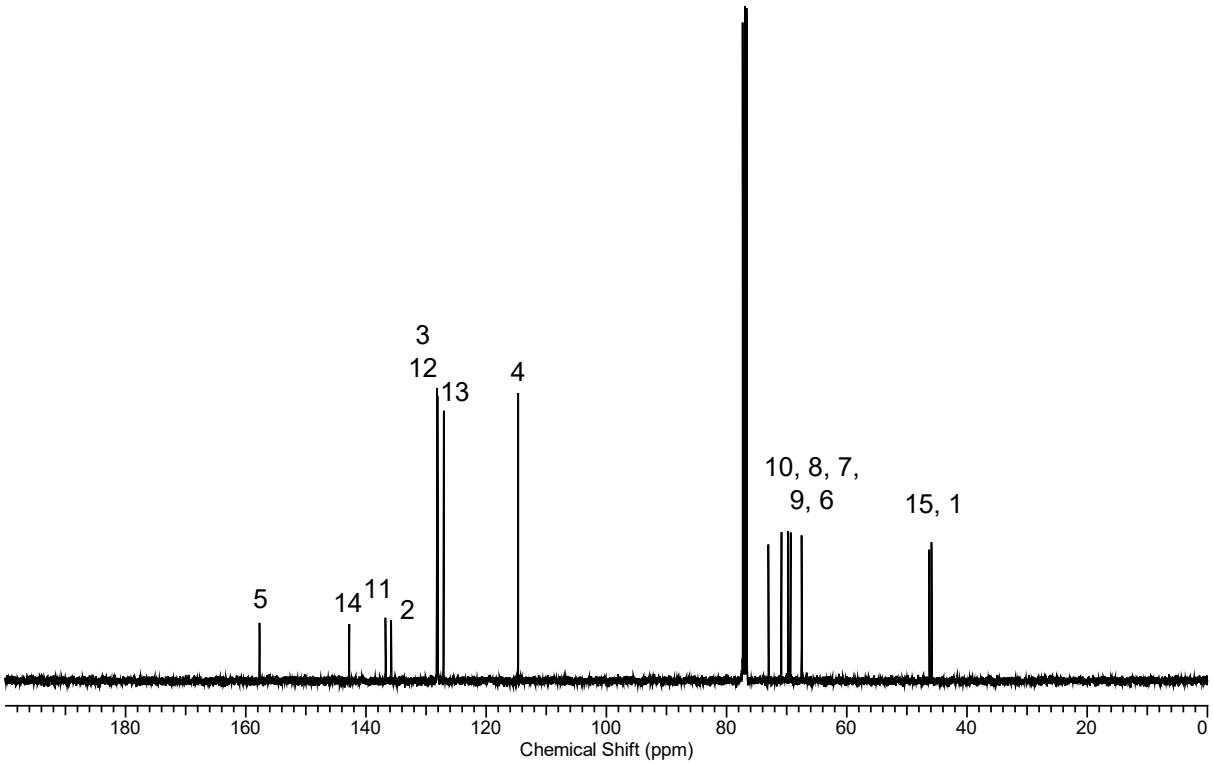


Bis-amine **ESI-3**

^{1}H NMR (400 MHz, $CDCl_3$)

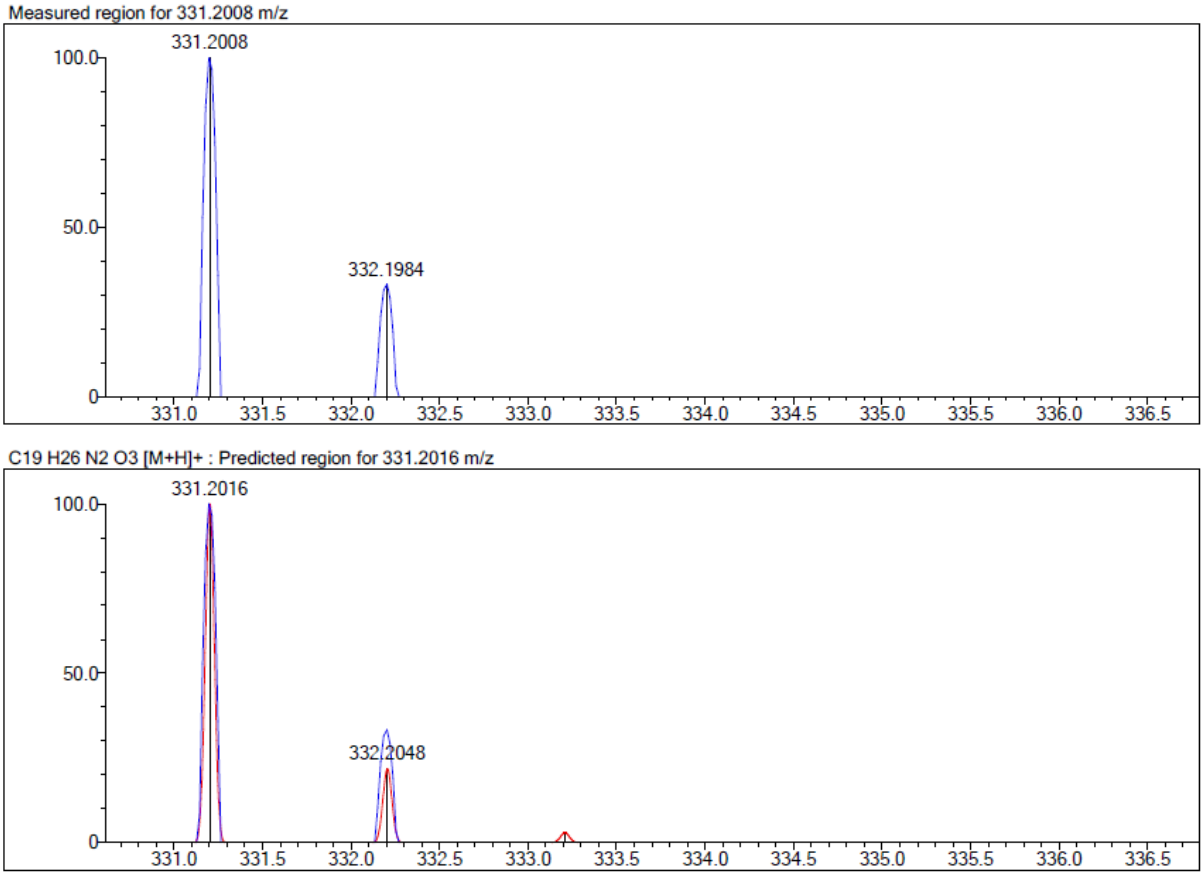


^{13}C NMR (100 MHz, $CDCl_3$)

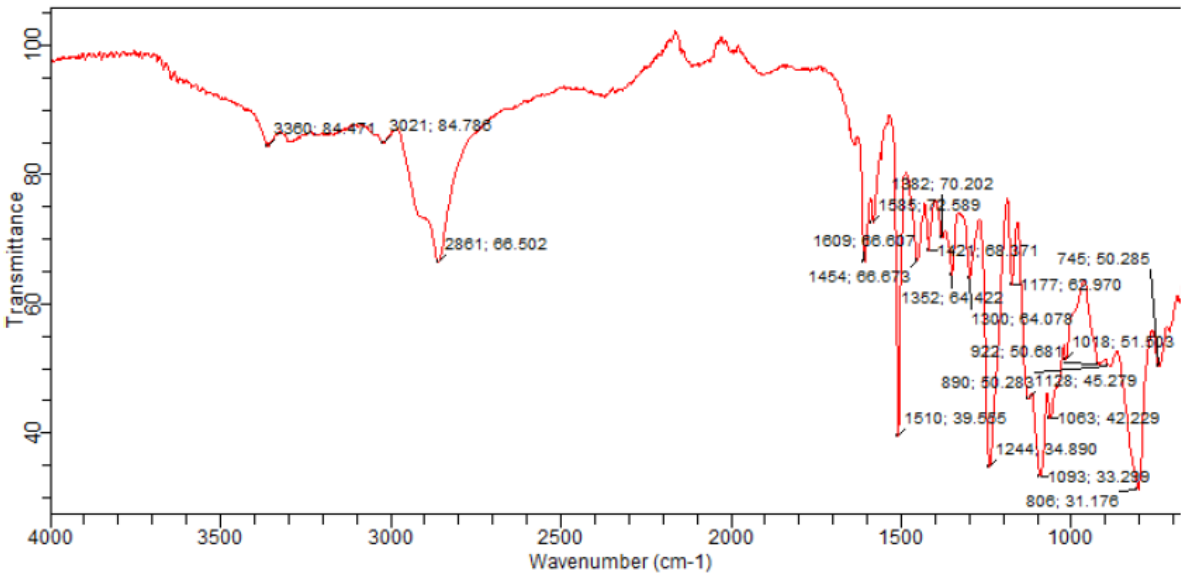


Bis-amine **ESI-3**

MS (ES +ve)

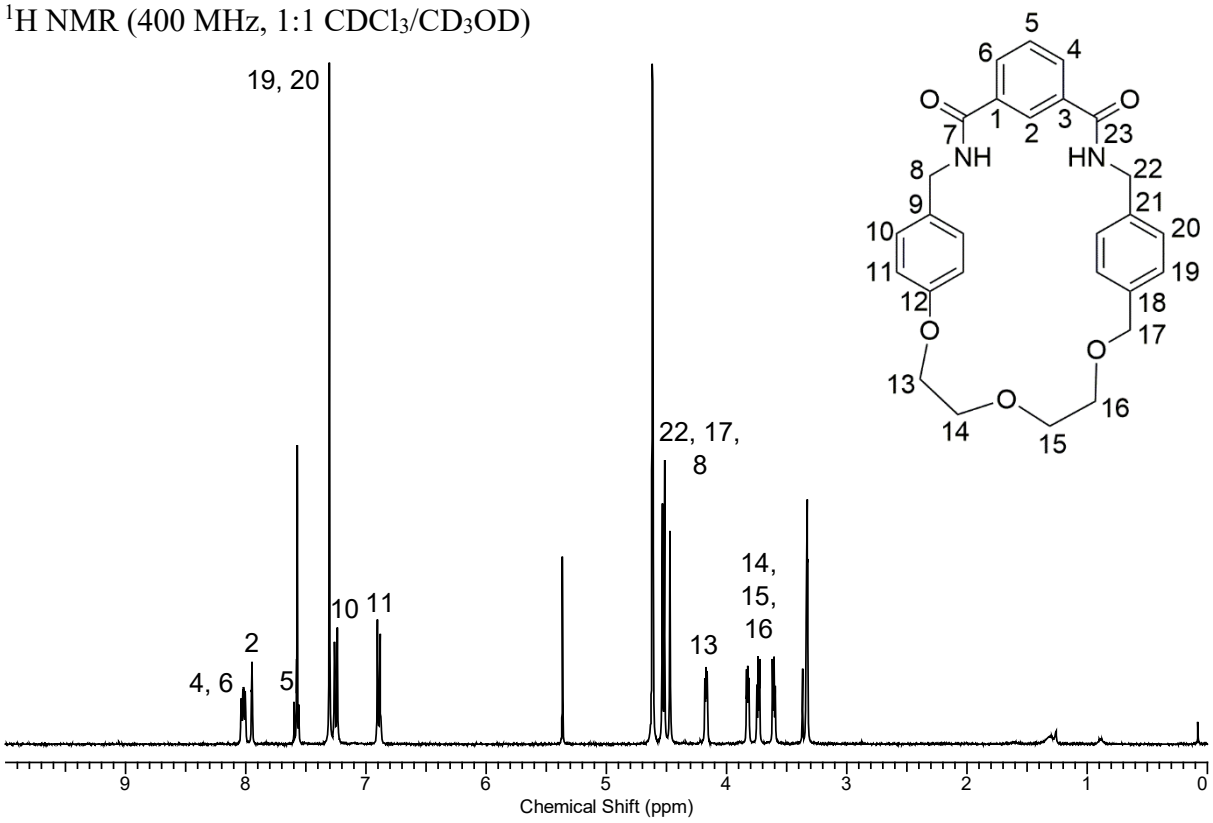


IR (neat)

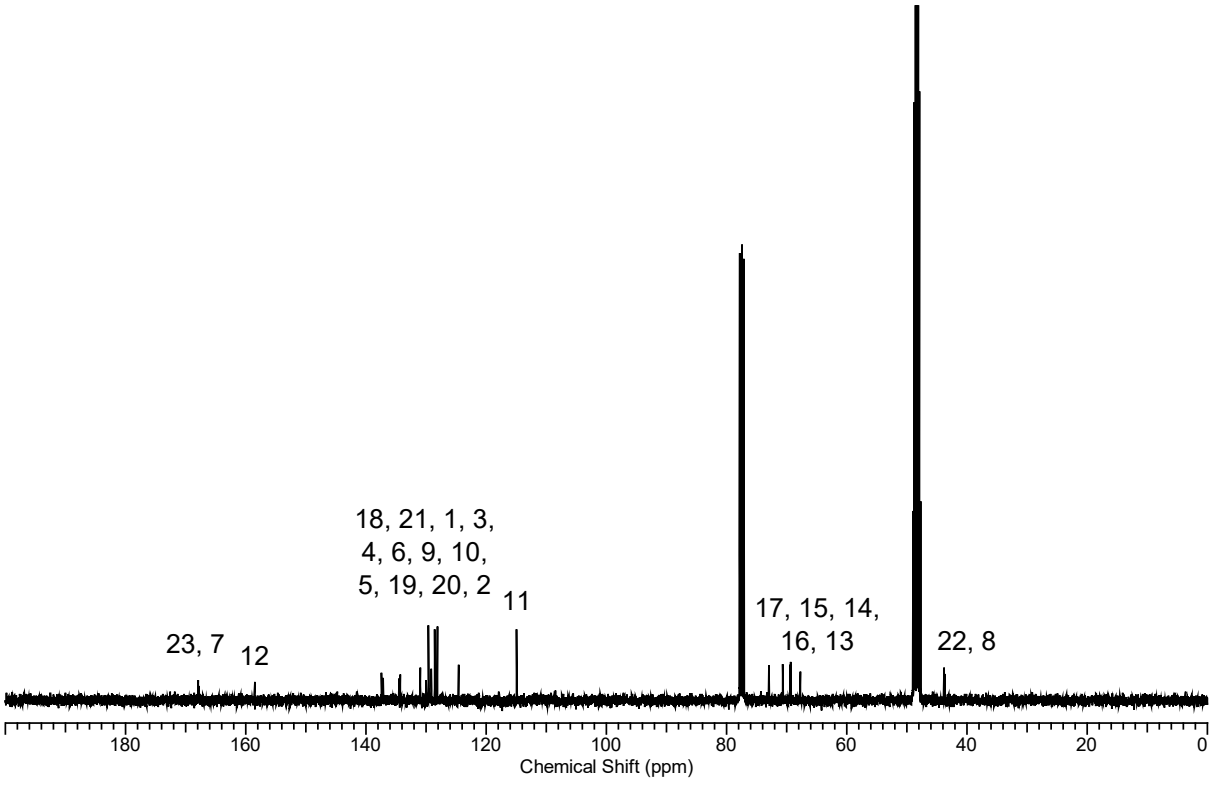


Macrocycle **2**

^{1}H NMR (400 MHz, 1:1 $CDCl_3/CD_3OD$)

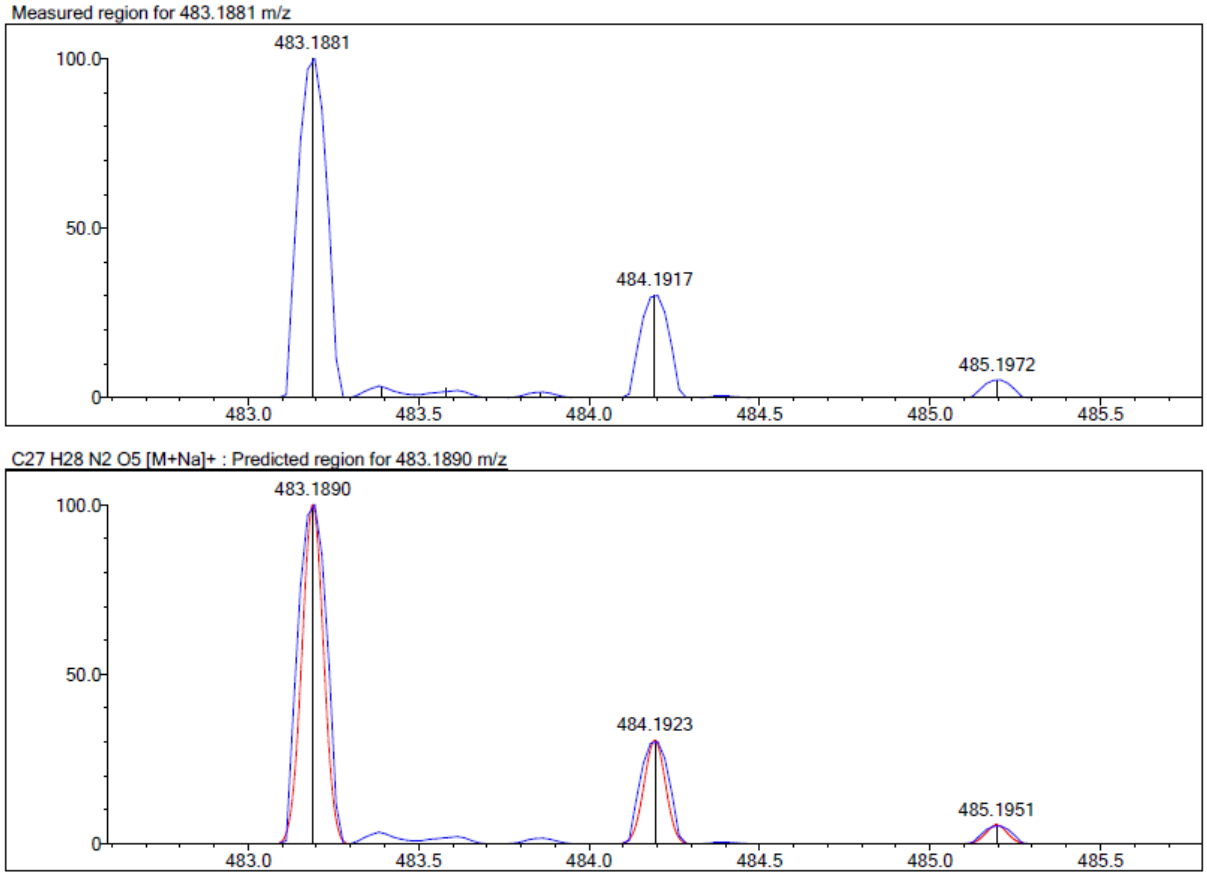


^{13}C NMR (100 MHz, 1:1 $CDCl_3/CD_3OD$)

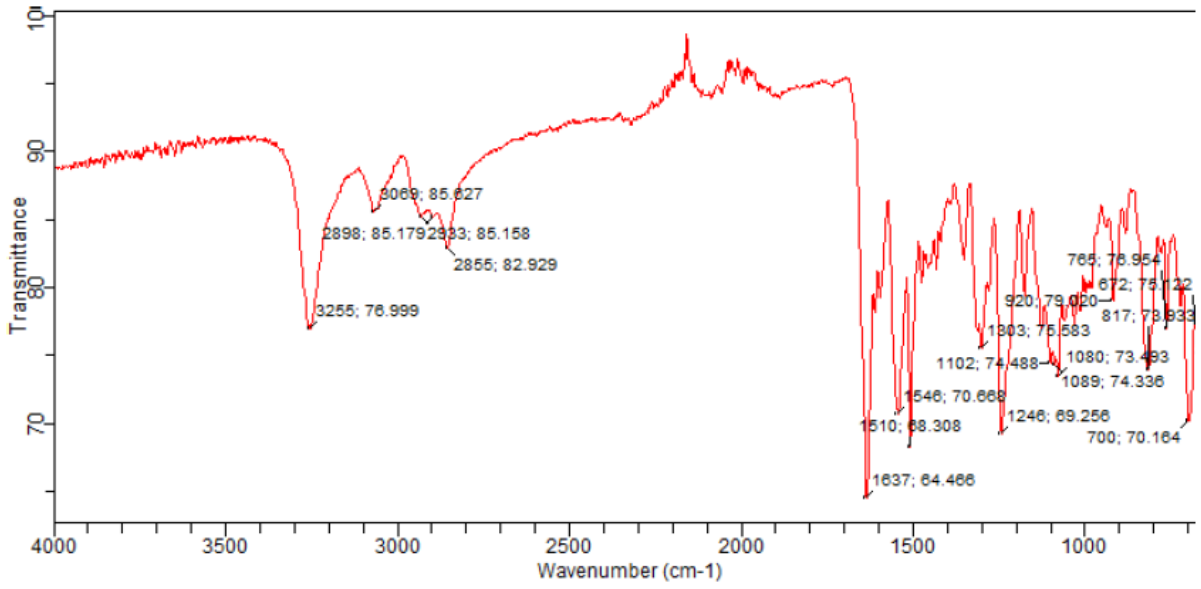


Macrocycle **2**

MS (ES +ve)

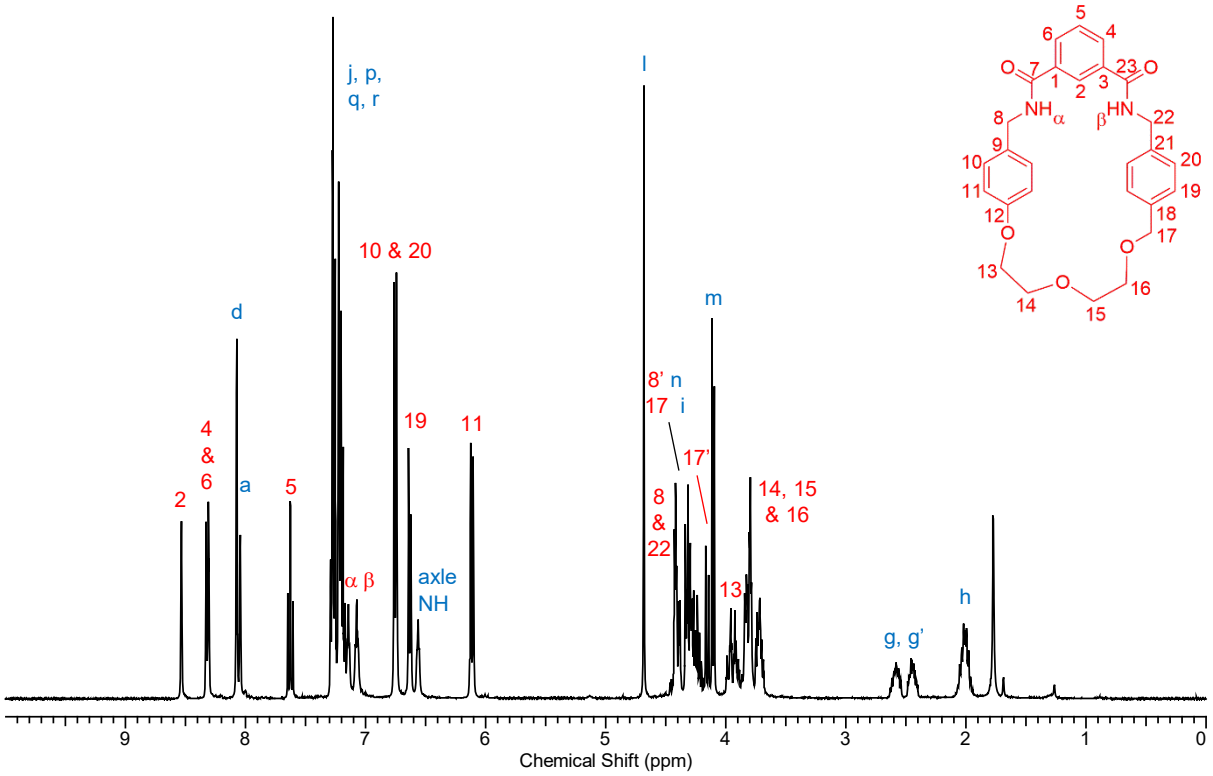


IR (neat)

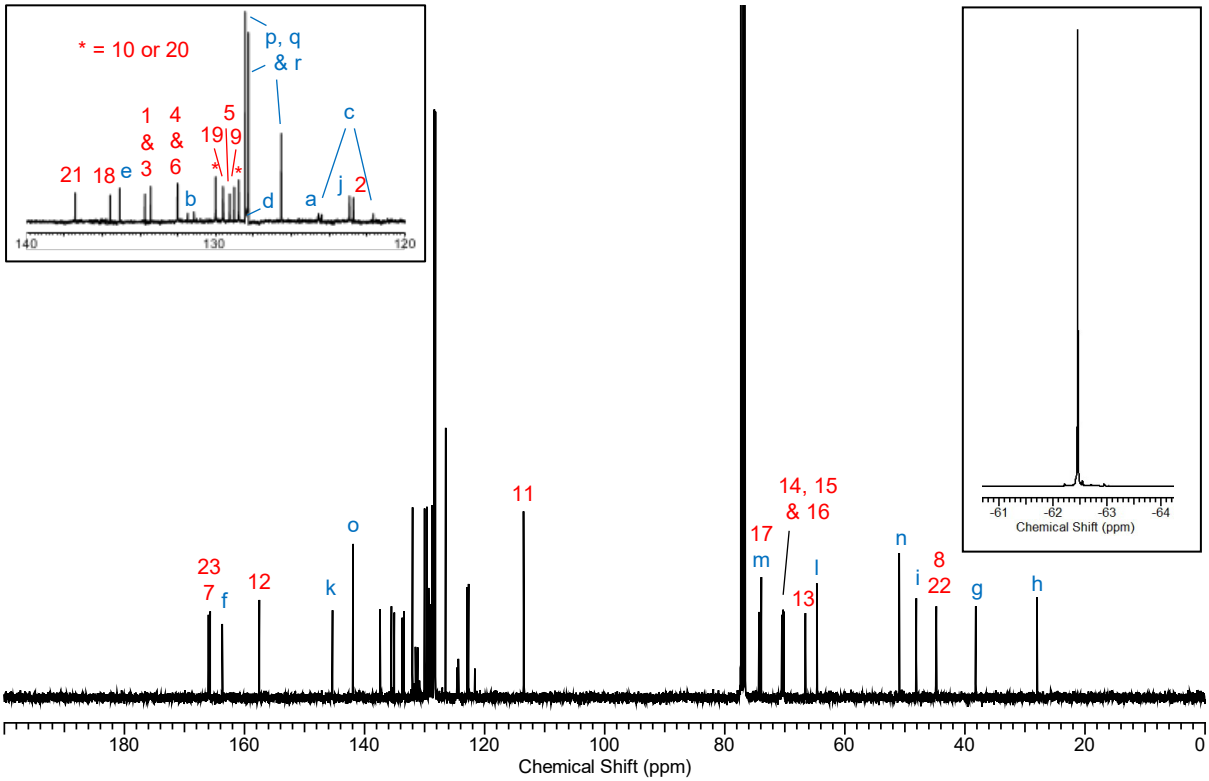


Rotaxane **1**

^{1}H NMR (400 MHz, $CDCl_3$)



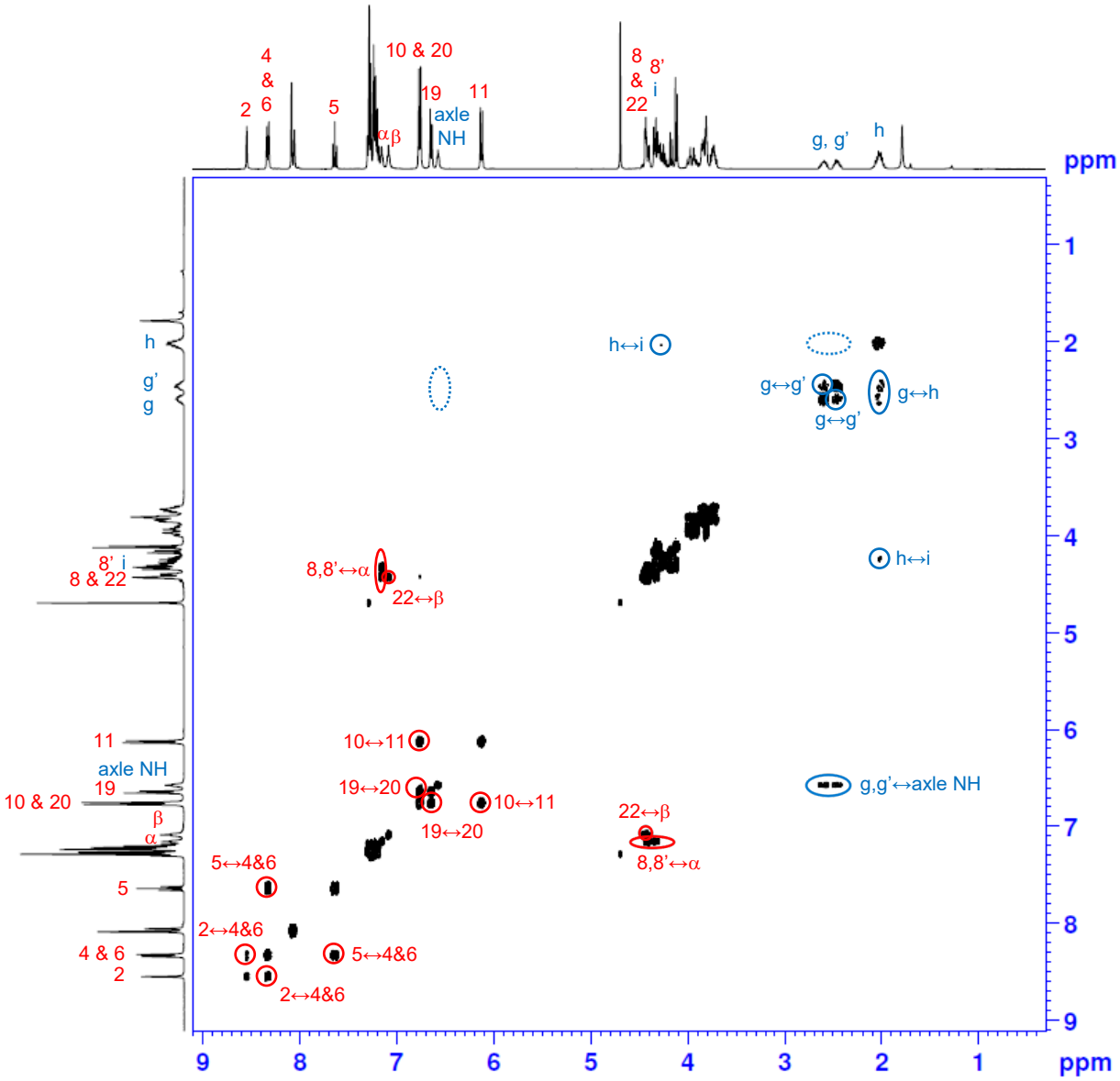
^{13}C NMR
(100 MHz, $CDCl_3$)



^{19}F NMR
(377 MHz, $CDCl_3$)

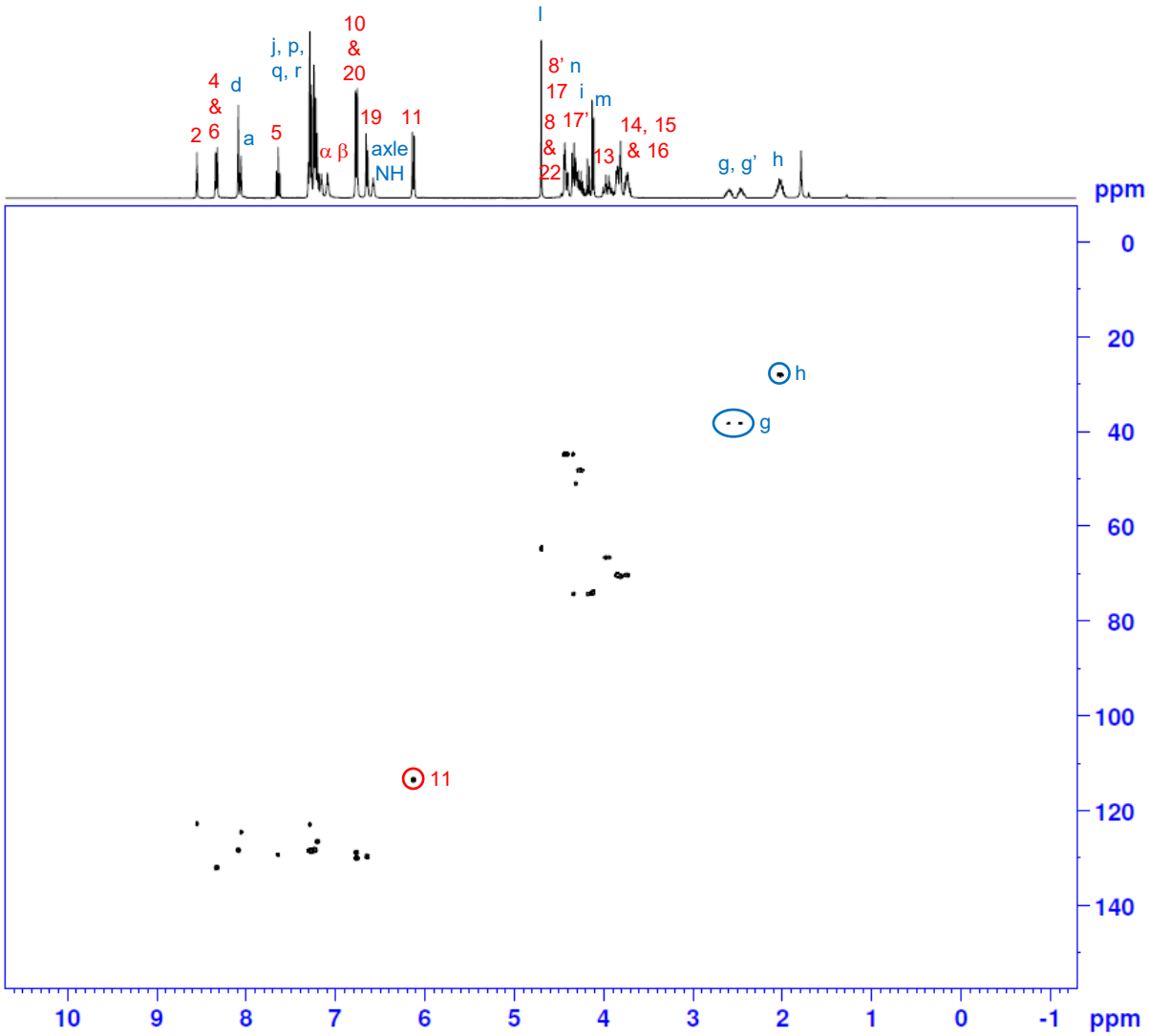
Rotaxane **1**

^{1}H-^{1}H COSY NMR (400 MHz, $CDCl_3$) – *Key peaks & cross-peaks labelled*



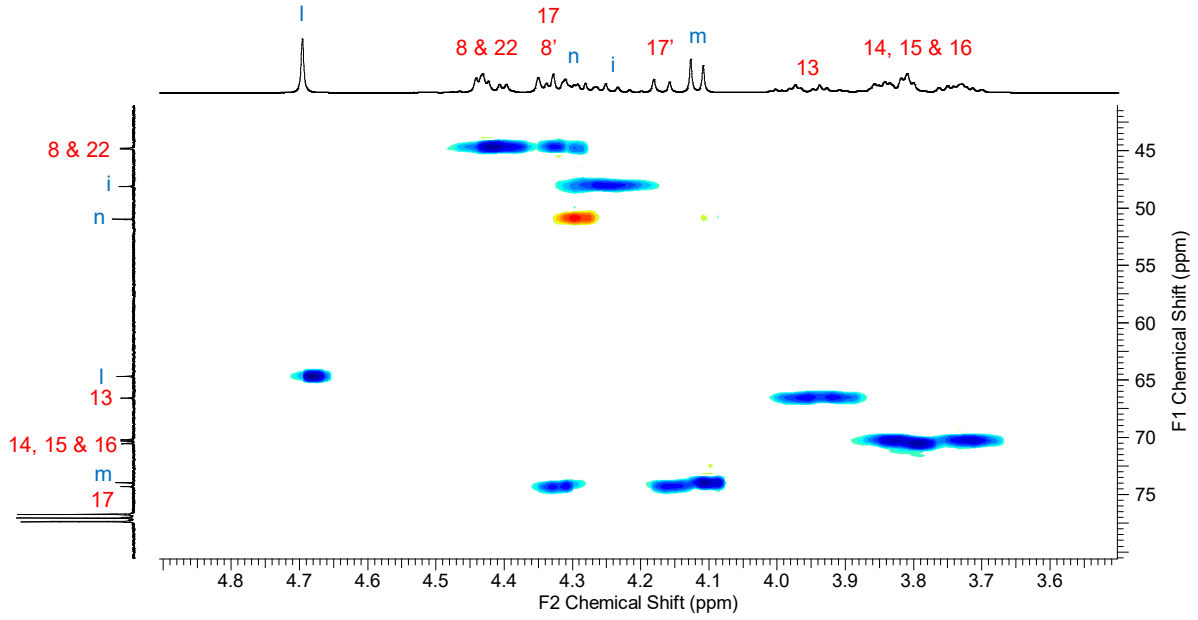
Rotaxane **1**

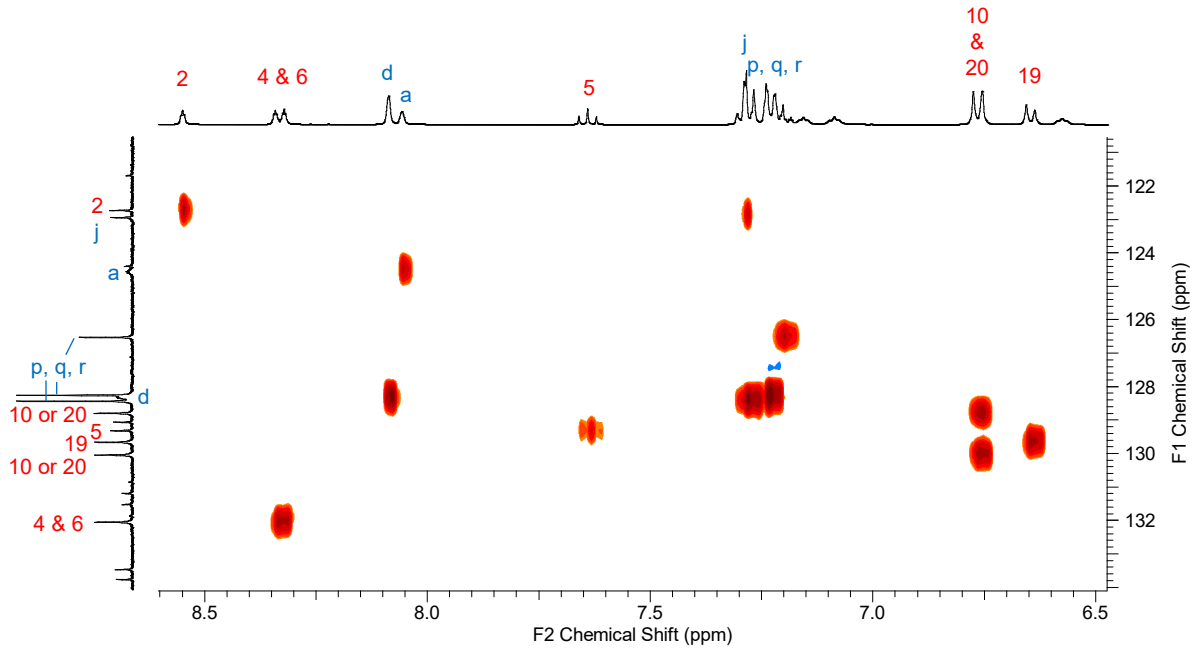
^{1}H-^{13}C HSQC NMR (400 MHz, $CDCl_3$) – *Peaks (& correlations for 11, g & h) labelled*



Rotaxane **1**

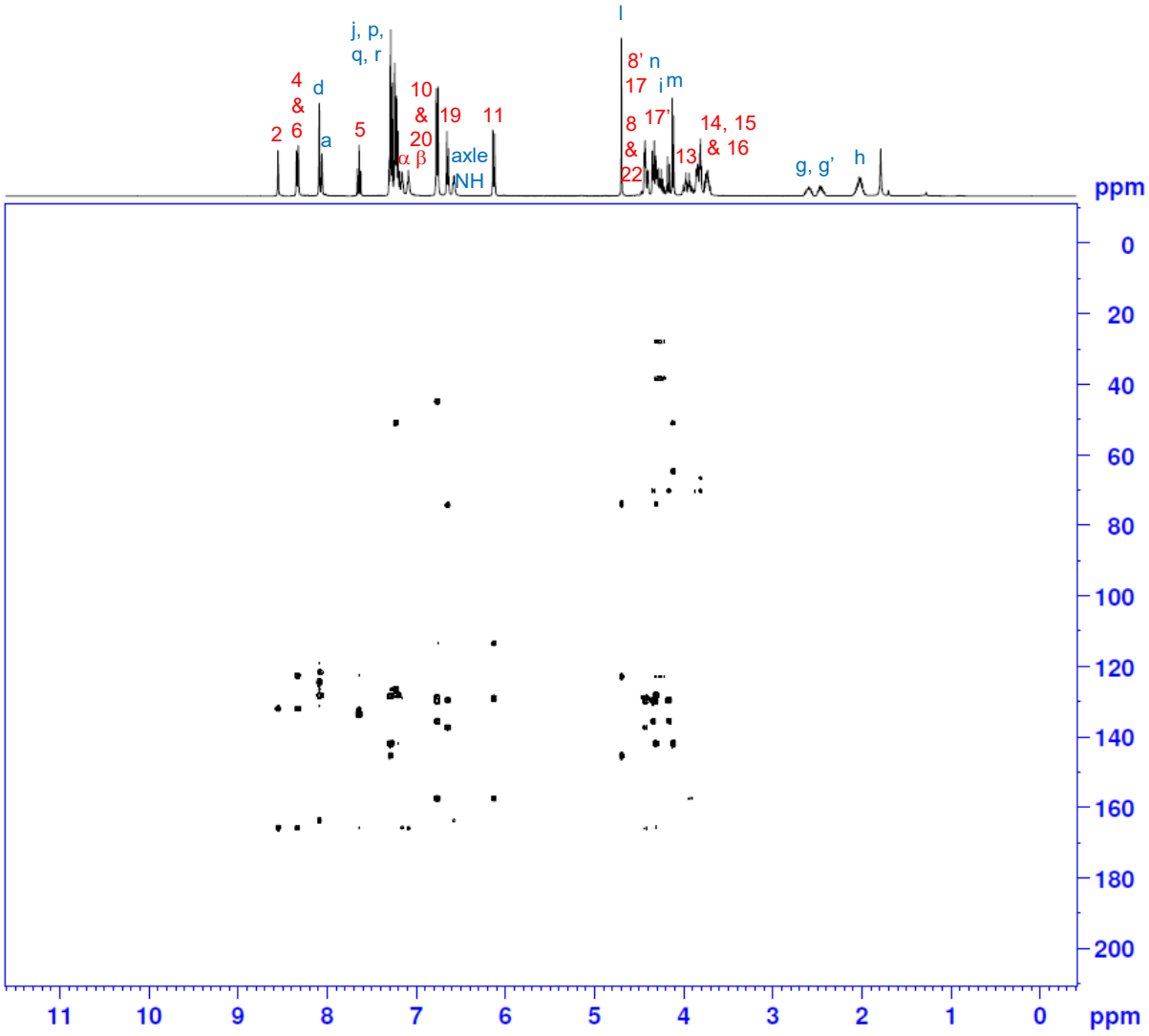
^{1}H-^{13}C HSQC NMR (400 MHz, $CDCl_3$) – *Zoomed sections, peaks with correlations labelled*





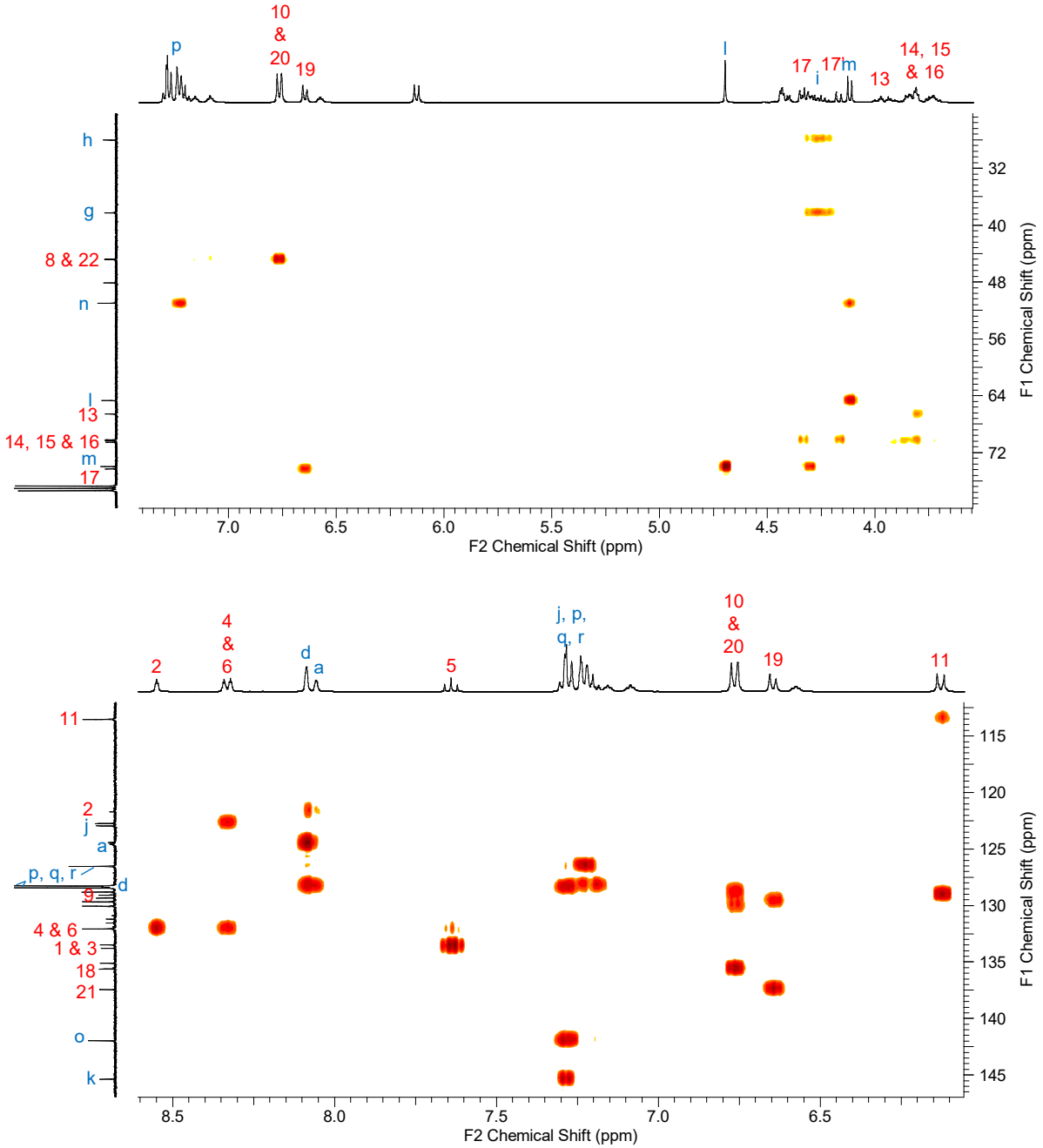
Rotaxane **1**

^{1}H-^{13}C HMBC NMR (400 MHz, $CDCl_3$) – *Peaks labelled*



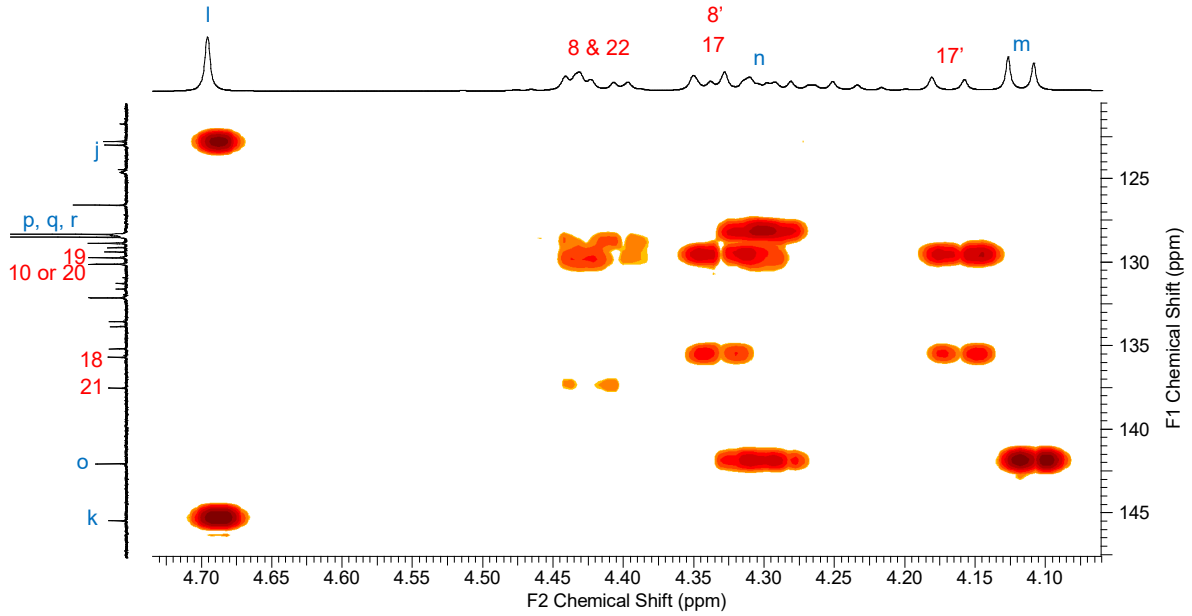
Rotaxane **1**

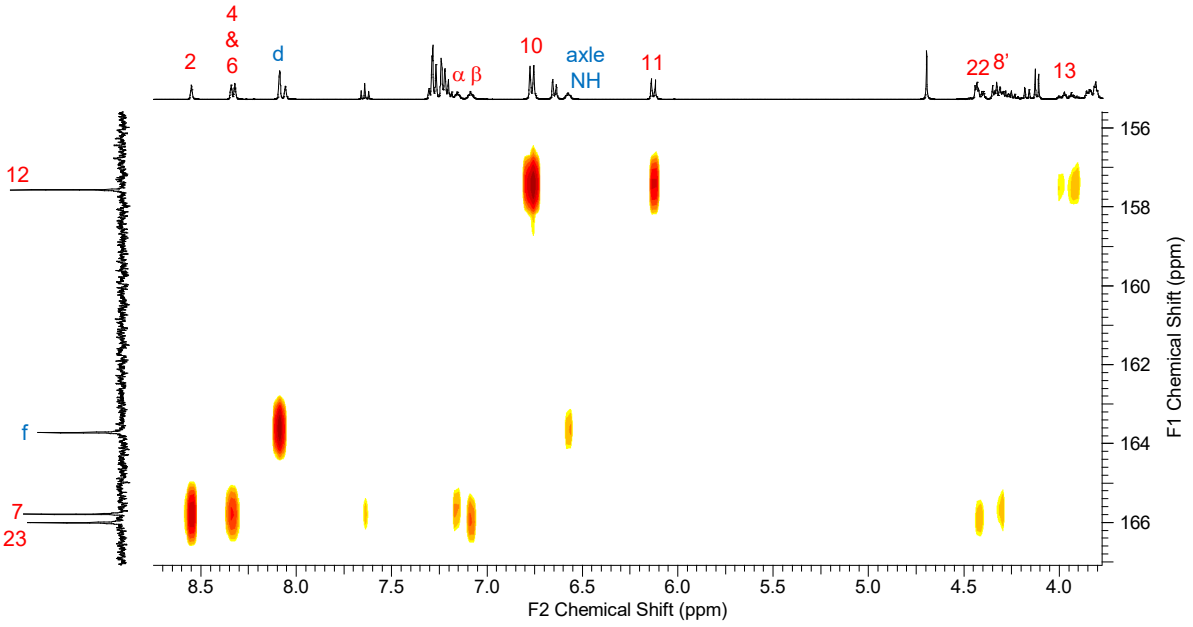
^{1}H-^{13}C HMBC NMR (400 MHz, $CDCl_3$) – *Zoomed sections, peaks with correlations labelled*



Rotaxane **1**

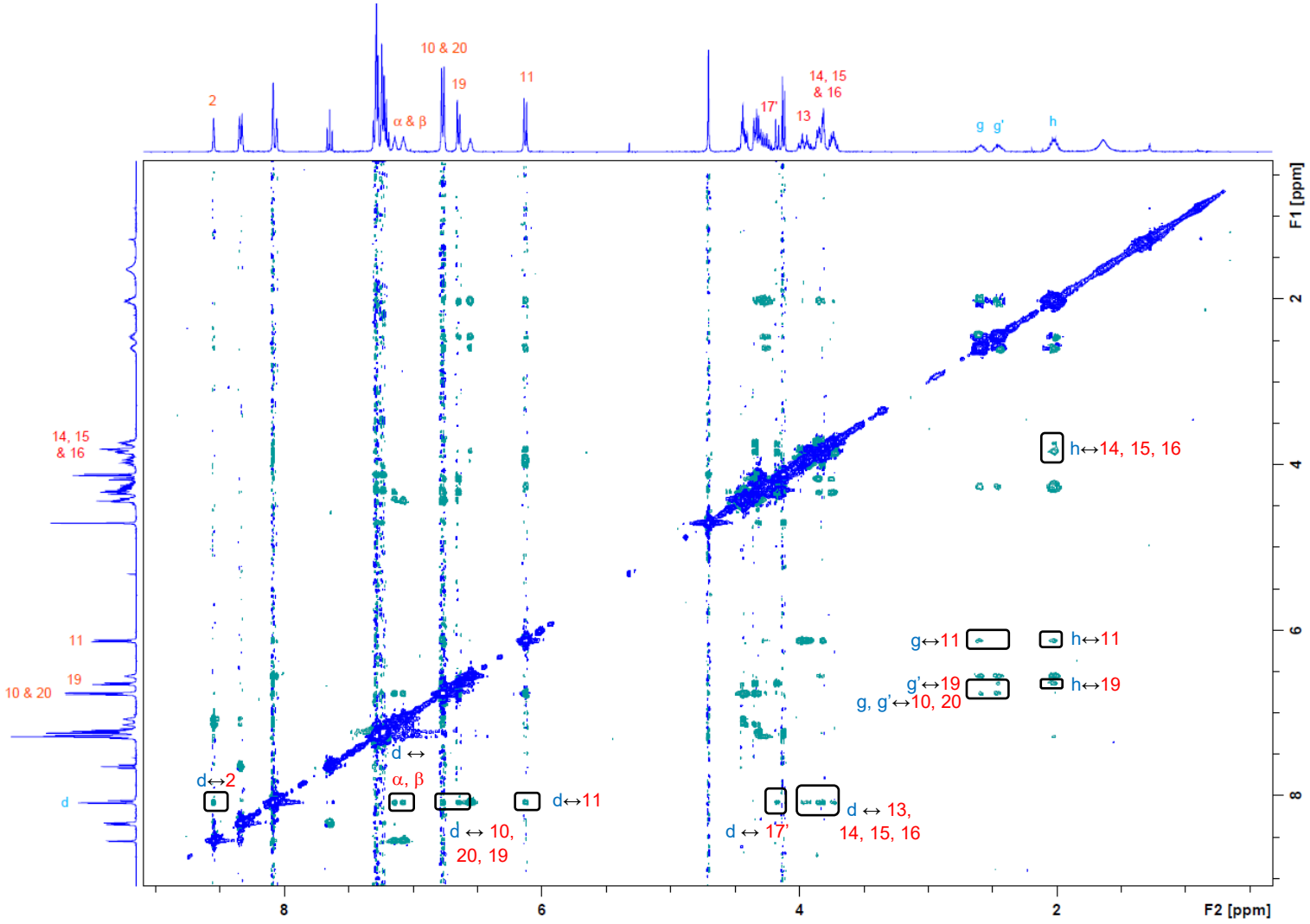
^{1}H-^{13}C HMBC NMR (400 MHz, $CDCl_3$) – *Zoomed sections, peaks with correlations labelled*





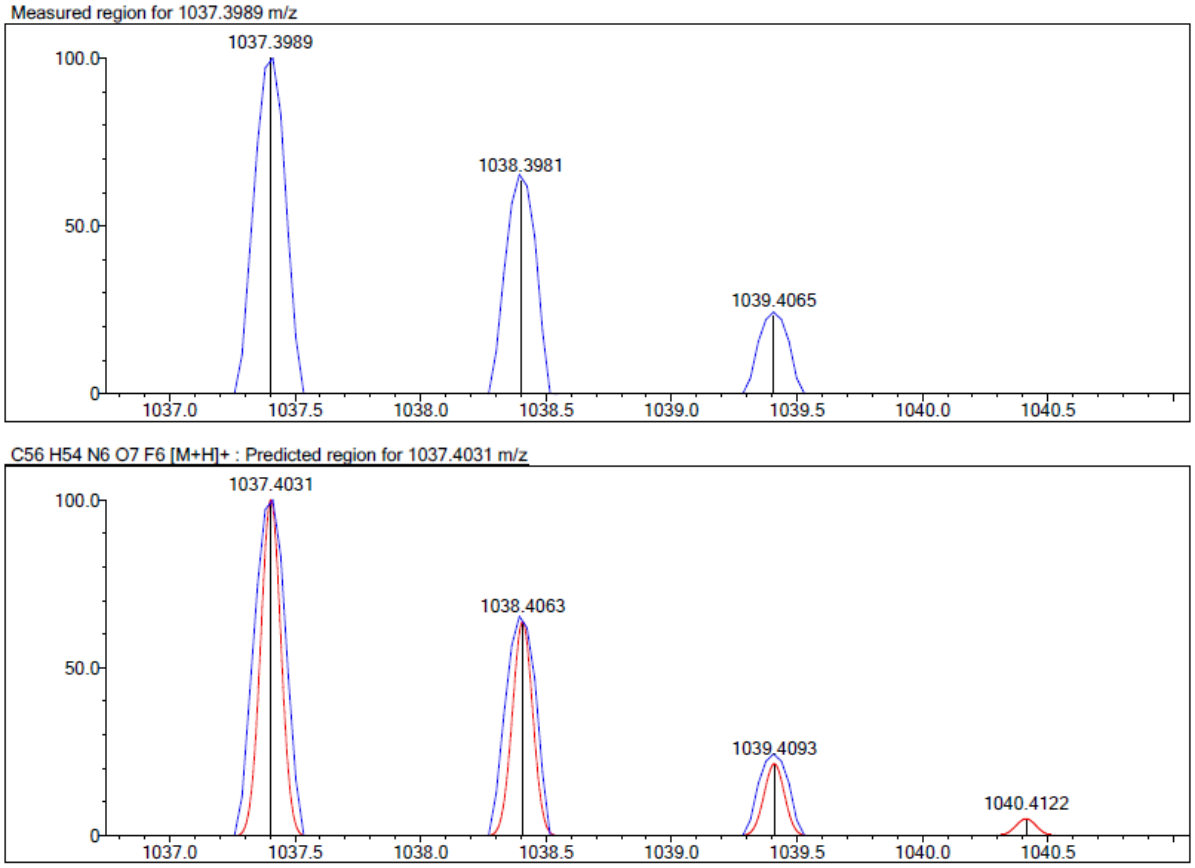
Rotaxane **1**

^{1}H-^{1}H ROESY NMR (400 MHz, $CDCl_3$) - *Inter-component couplings highlighted by boxes.*

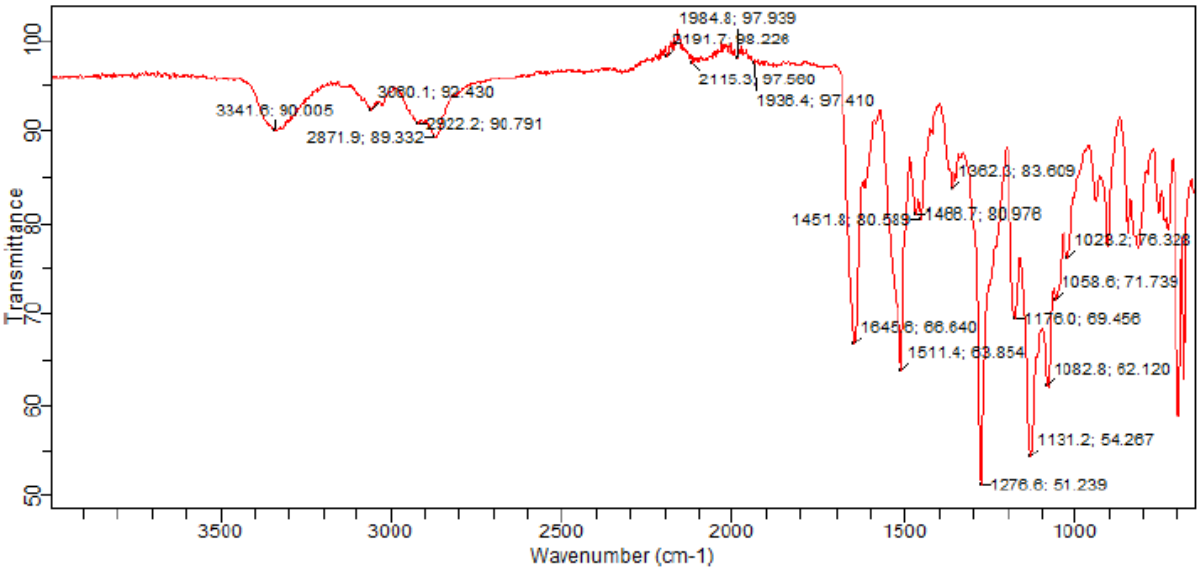


Rotaxane **1**

MS (ES +ve)



IR (neat)

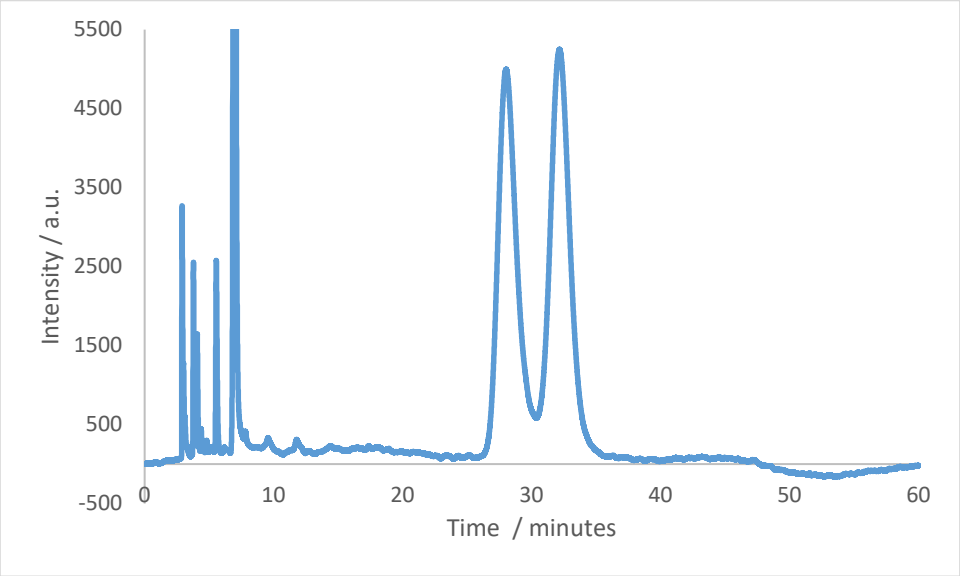


Rotaxane **1**

HPLC

Samples were analysed using a CHIRALPAK AD-H (4.6 mm × 250 mm) column.
Sample concentration was ~ 1×10^{-4} mol cm^{-3} in 9:1 hexane:IPA, with an injection volume of 2 μL. (Initial injections at lower concentrations failed to produce an unambiguous response in the HPLC trace.)
The eluent used was 4:1 hexane:IPA at a flow rate of 1.5 mL min^{-1}.
Detection was by measuring absorption at a range of wavelengths (204-240 nm).

Full HPLC trace
(CHIRAL-PAK AD-H 4.6 × 250 mm, 4:1 hexane:IPA, 1.5 mL/min, λ_{abs} = 240 nm)

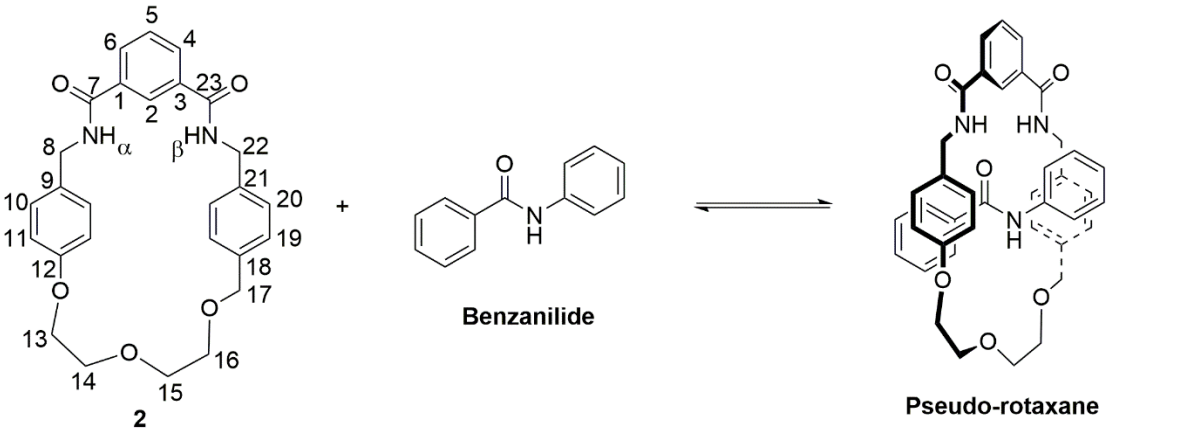


Titrations

Protocols

NMR spectra were recorded on a Bruker Ultrashield 400 Plus Spectrometer.

Pseudo-Rotaxane Study



(only 1 enantiomer shown for clarity)

A 0.05 M solution of benzanilide was added to 500 μL of a 2.00 mM solution of macrocycle **2** at 298 K. *Low solubility of macrocycle **2** in $CDCl_3$ necessitated a very low concentration to be used.*

In $CDCl_3$ the volumes of benzanilide added were 10 × 4 μL, 2 × 10 μL, 2 × 20 μL, 2 × 40 μL, 1 × 60 μL (i.e. in total 10 equivalents of benzanilide).

In D_6-acetone and D_6-DMSO, fewer spectra were recorded and only up to 5 equivalents of benzanilide was added, as no perturbation in macrocycle resonances was observed.

Rotaxane 1

Acid/Base Titrations

A 0.25 M solution of TFA was added to 500 μL of a 2.50 mM $CDCl_3$ solution of rotaxane **1** at 298 K. The volumes added were 5, 5, 15, 25, 50, 50, 50 & 50 μL (i.e. in total 50 equivalents of TFA). Then 50 equivalents of base (dissolved in 125 μL of $CDCl_3$) were added.

Cation Titrations

A 0.25 M solution of salt was added to 500 μL of a 2.50 mM CD_3CN solution of rotaxane **1** at 298 K.

In the case of $LiPF_6$, the volumes added were 5, 5, 15, 25, 50 & 50 μL (i.e. in total 30 equivalents of $LiPF_6$). Then 30 equivalents of 12-crown-4 (dissolved in 75 μL of CD_3CN) were added.

In the case of $LiClO_4$, the volumes added were, 5, 5, 15, 25, 50, 50 & 100 μL (i.e. in total 50 equivalents of $LiClO_4$). Then 50 equivalents of 12-crown-4 (dissolved in 125 μL of CD_3CN) were added.

In the case of $Zn(ClO_4)_2$, the volumes added were, 2.5, 2.5, 5, 15 & 25 μL (i.e. in total 10 equivalents of $Zn(ClO_4)_2$). Then 10 equivalents of 12-crown-4 (dissolved in 25 μL of CD_3CN) were added.

ROESY Study (with TFA)

A 9.62 mM $CDCl_3$ solution of rotaxane **1** was prepared and a ^1H-^1H ROESY NMR spectrum recorded (number of scans = 4).

To this solution, 50 μL of 165 mg of TFA in 300 μL of $CDCl_3$ solution was added. By recording a ^{19}F NMR spectrum with sufficient delay time to relax all F nuclei, it was possible to calculate ~ 40 equivalents of TFA had been added. A ^1H-^1H ROESY NMR spectrum was then recorded using the same settings as above.

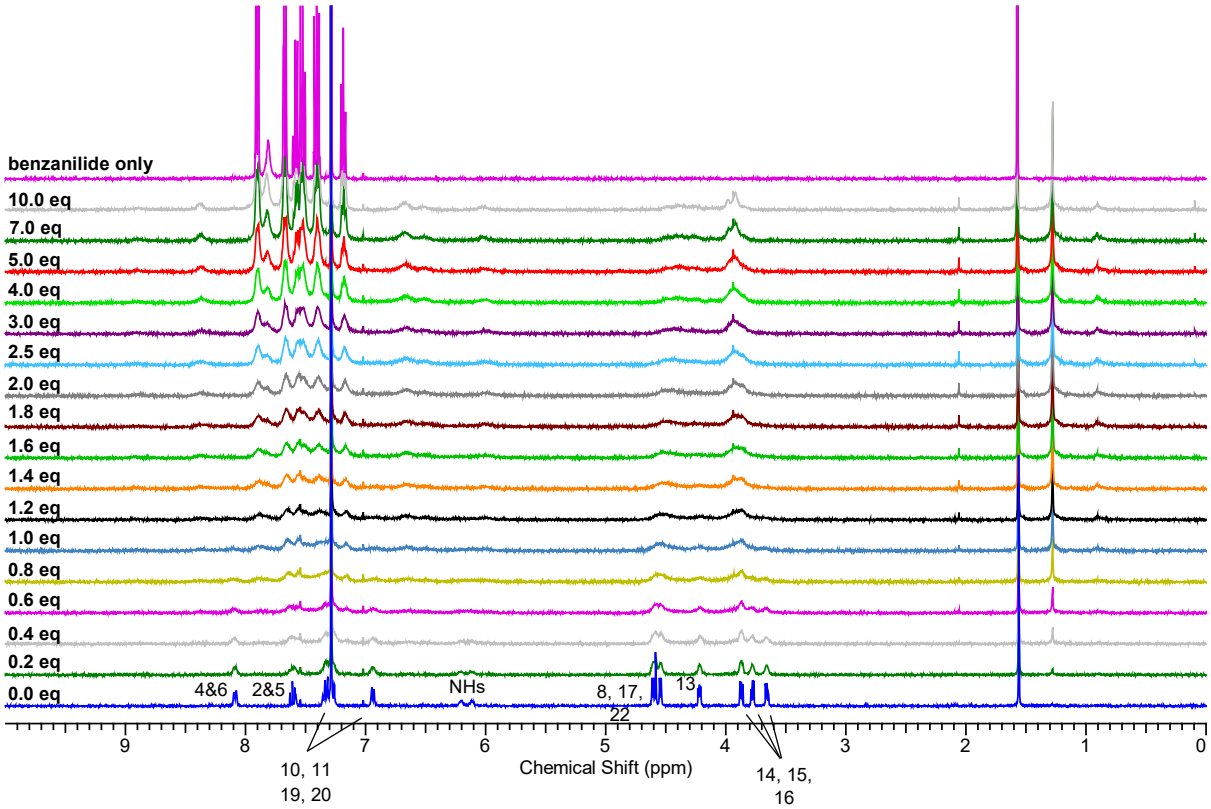
Due to a poor signal-nose ratio, a second ^1H-^1H ROESY NMR spectrum was recorded, which is presented here, after adding sufficient TFA solution to restore ~ 40 equivalents of TFA (*losses due to evaporation*). In this case the number of scans were increased to 64.

Data

Pseudo-rotaxane studies

Macrocycle **2** + Benzanilide

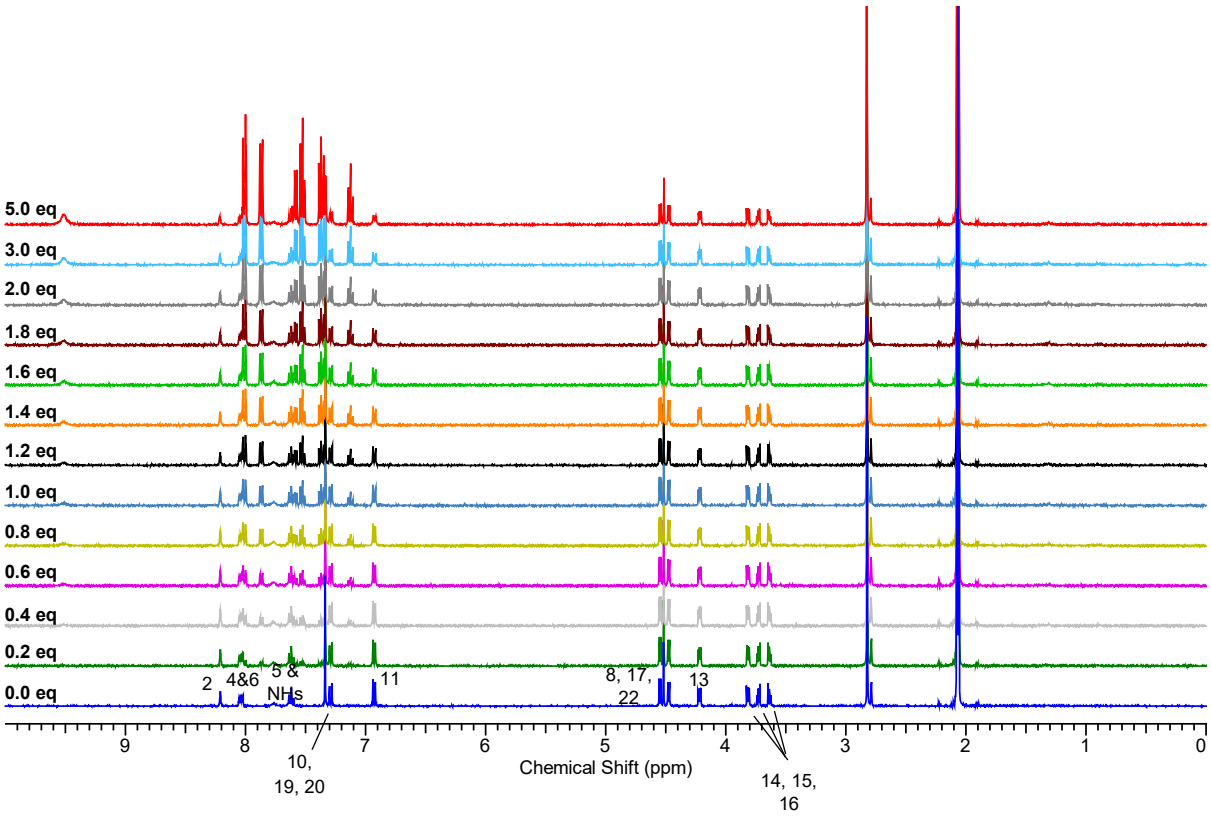
^{1}H NMR **in $CDCl_3$**
(Eq. of benzanilide added: 0, 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.4, 1.6, 1.8, 2.0, 2.5, 3.0, 4.0, 5.0, 7.0, 10.0. Top spectrum benzanilide only for comparison).



Broadening of (macrocycle) peaks indicates formation of pseudo-rotaxane is occurring but with intermediate exchange on the NMR timescale.

Macrocycle **2** + Benzanilide

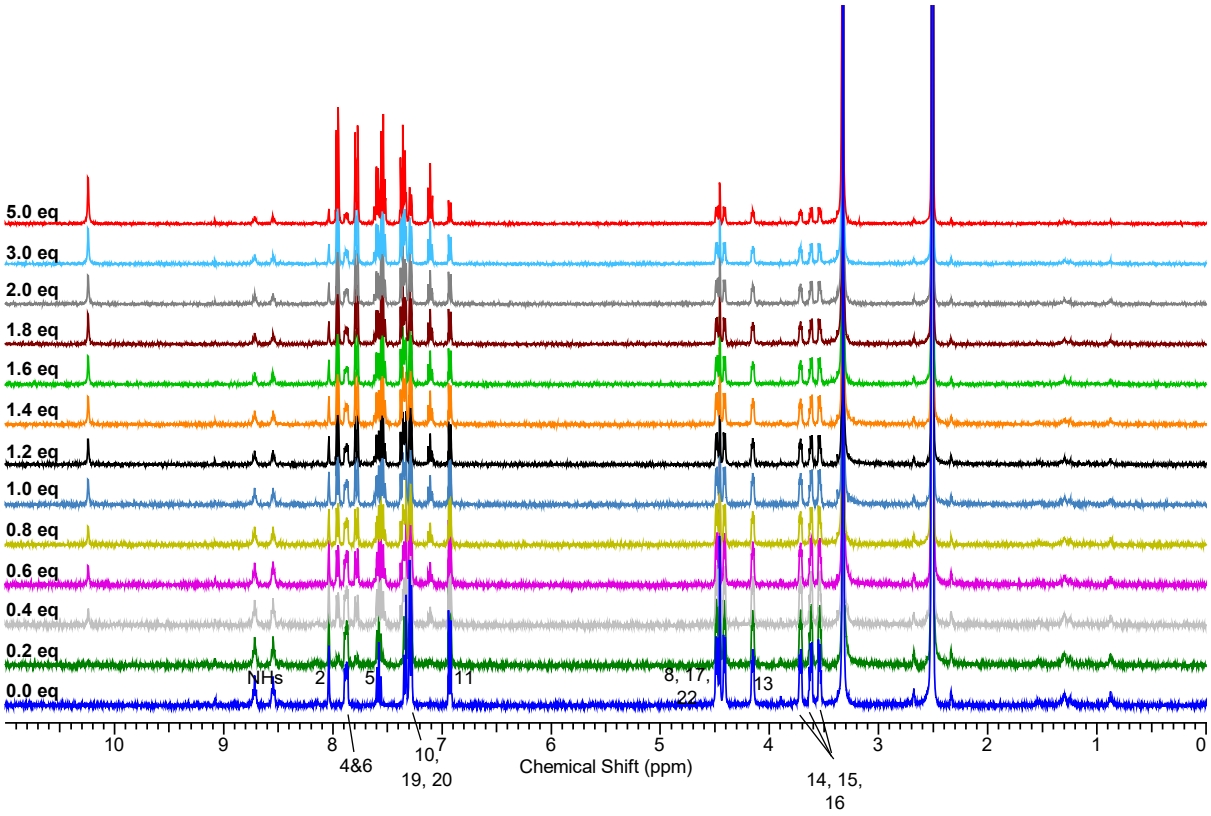
^{1}H NMR **in D_6-acetone**
(Eq. of benzanilide added: 0, 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.4, 1.6, 1.8, 2.0, 3.0, 5.0)



Lack of perturbation of macrocycle resonances indicative of no pseudo-rotaxane formation.

Macrocycle **2** + Benzanilide

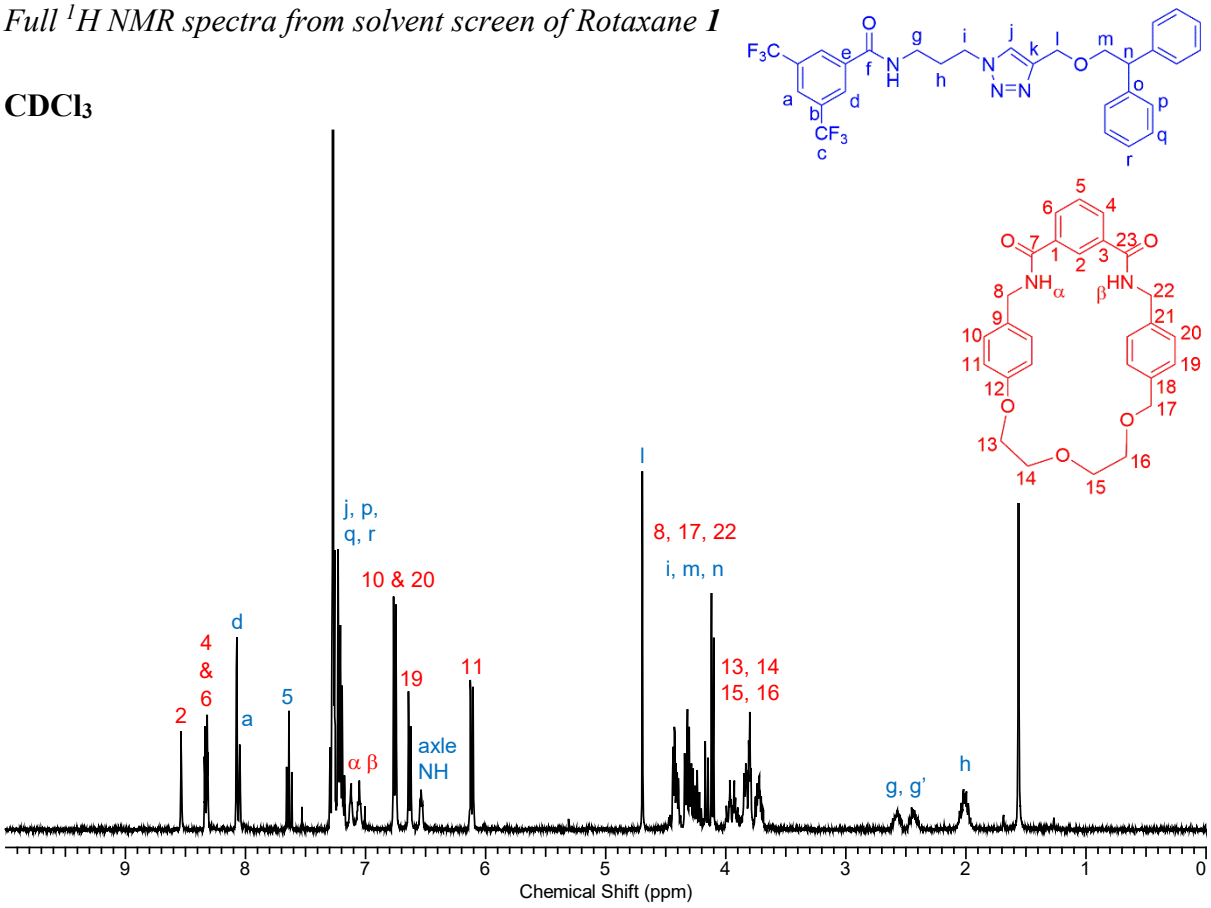
^{1}H NMR **in D_6-DMSO**
(Eq. of benzanilide added: 0, 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.4, 1.6, 1.8, 2.0, 3.0, 5.0)



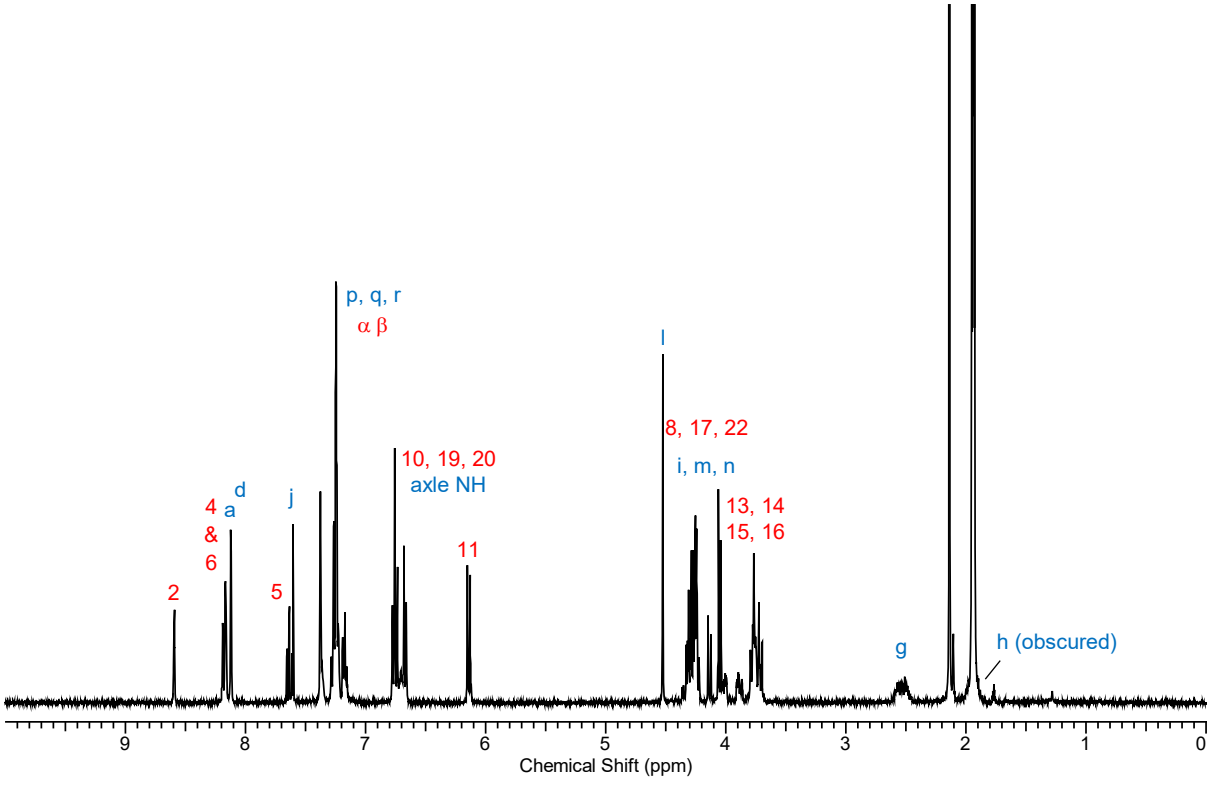
Lack of perturbation of macrocycle resonances indicative of no pseudo-rotaxane formation.

*Full ^{1}H NMR spectra from solvent screen of Rotaxane **1***

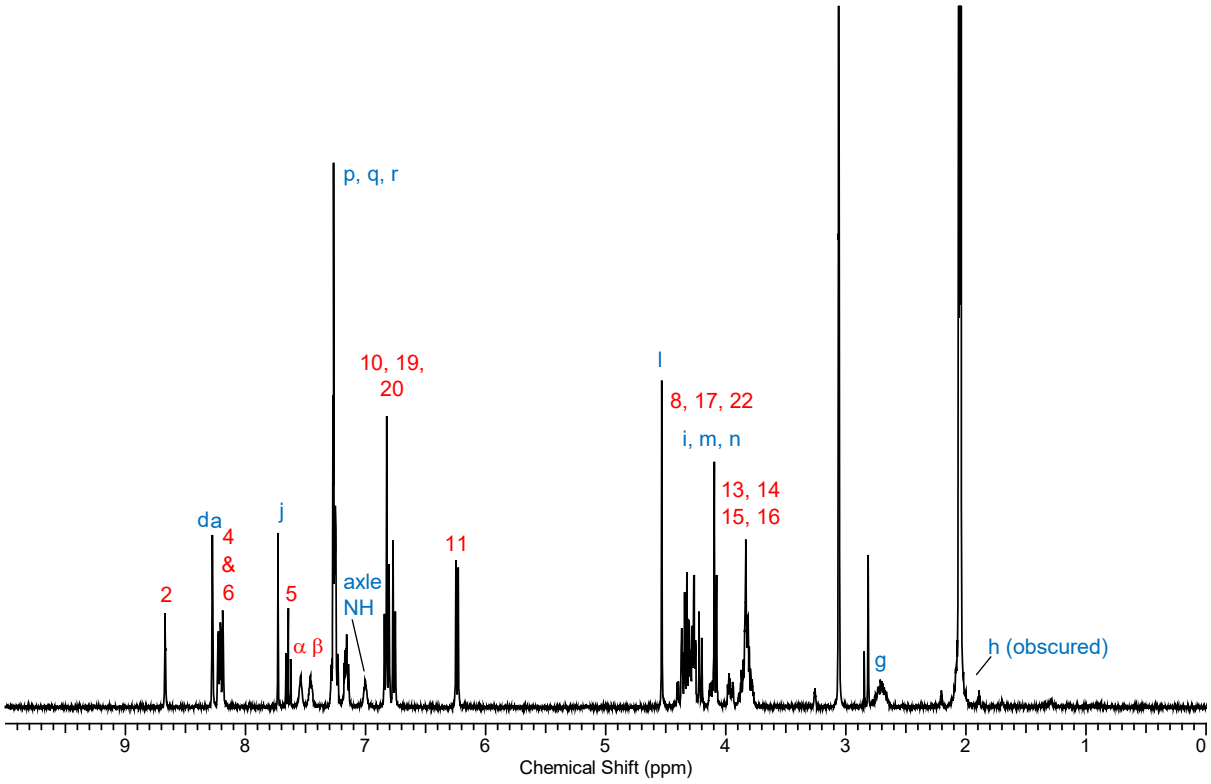
$CDCl_3$



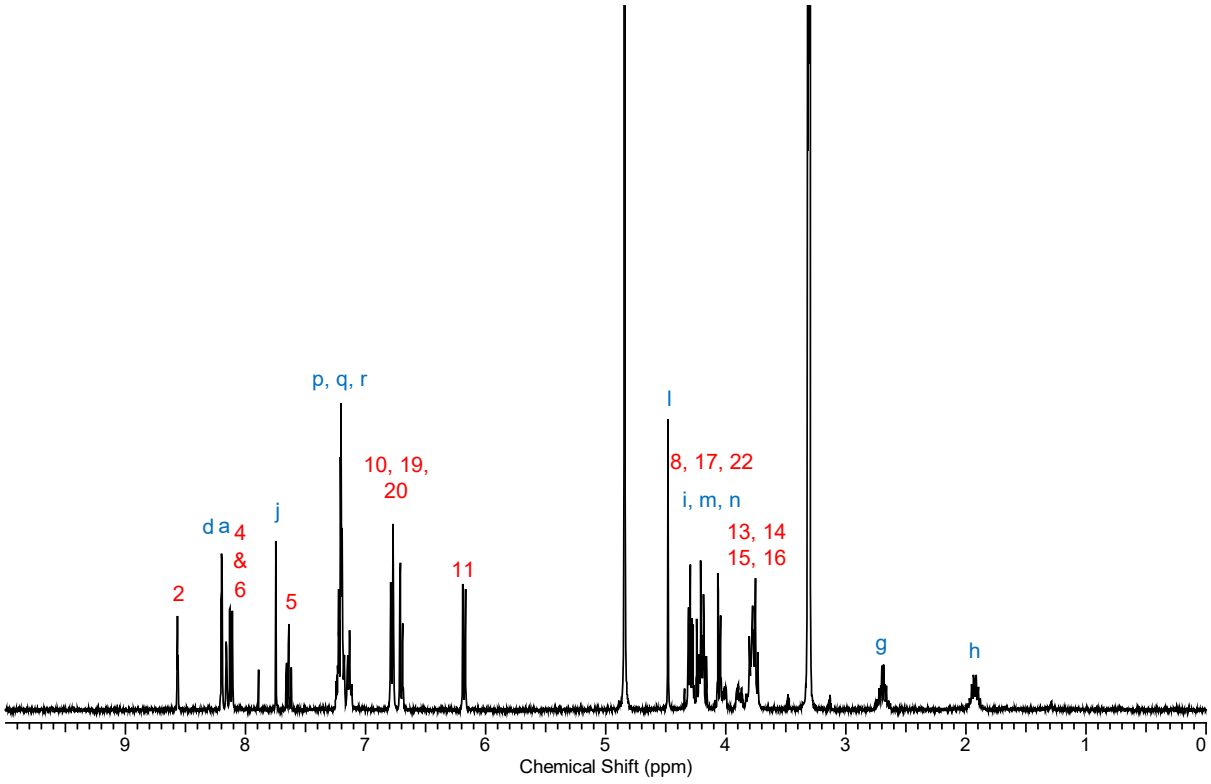
CD_3CN



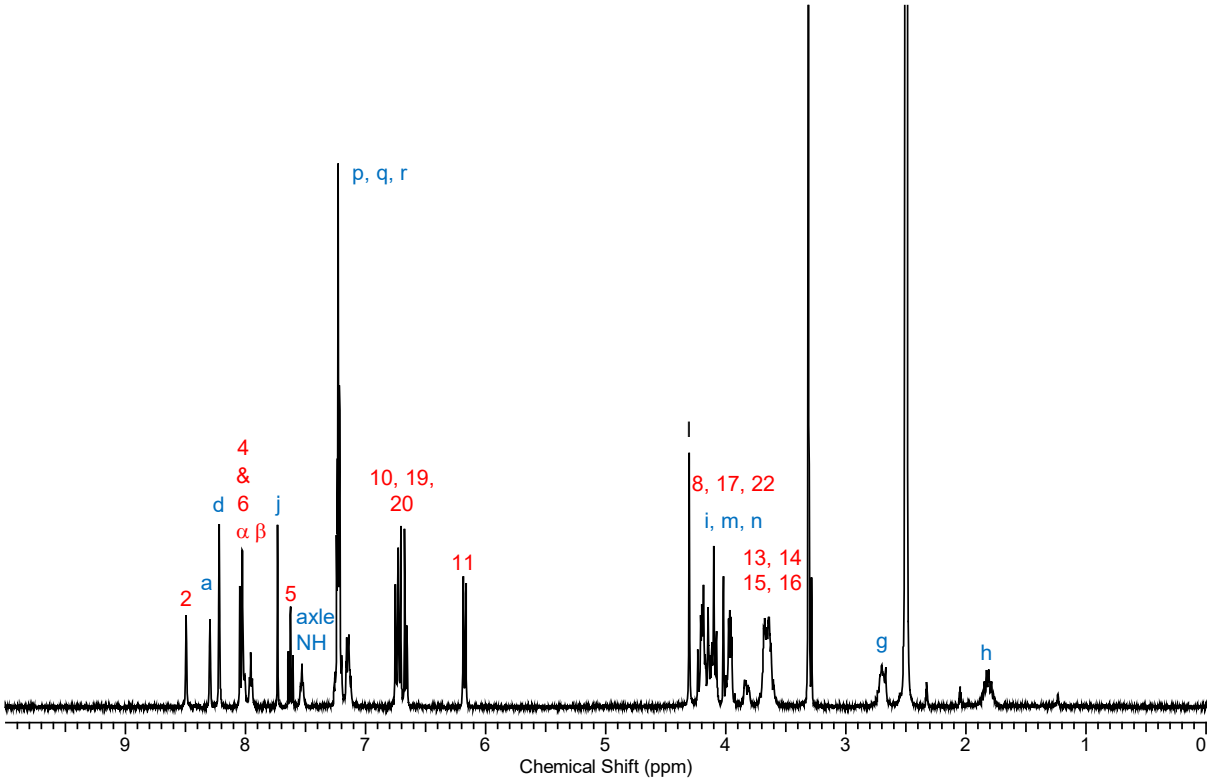
D_6-acetone



CD_3OD



D_6-DMSO


p, q, r
4
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6
α β
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6
5
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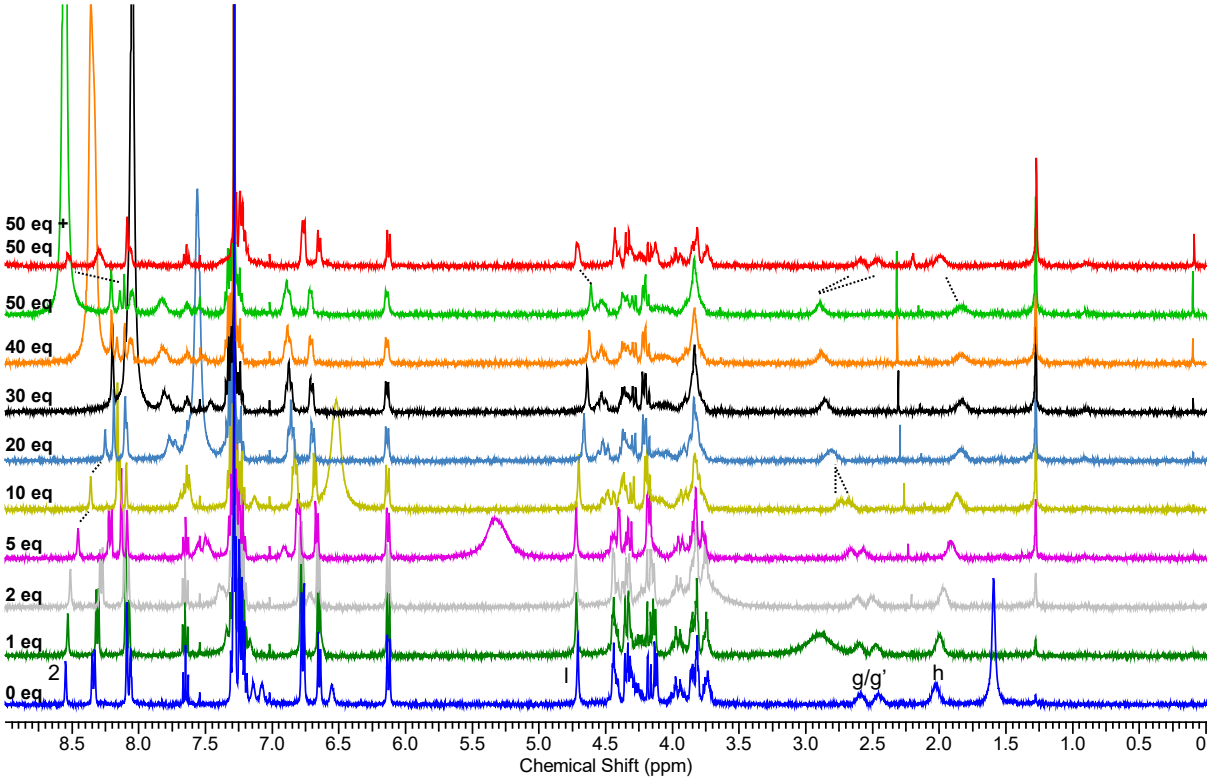
3
2
1
0
Chemical Shift (ppm)

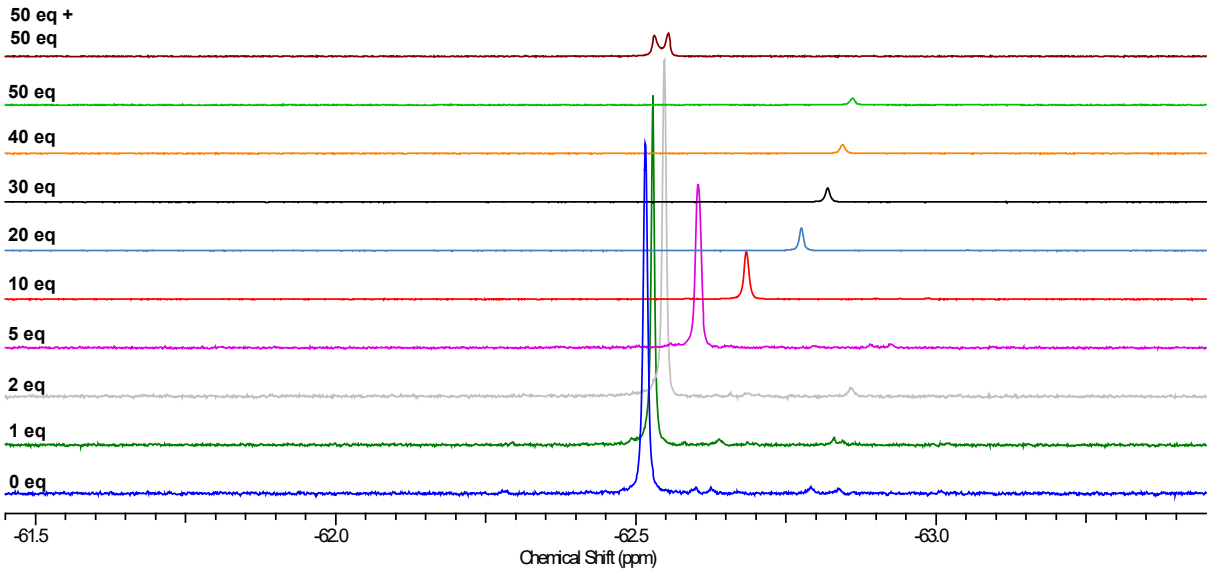
Acid/Base Titrations

Rotaxane **1** + *TFA, then D₅-pyridine*

^{1}H NMR (Equivalents of TFA added: 0, 1, 2, 5, 10, 20, 30, 40, 50, 50 + 50 of D_5-pyridine)

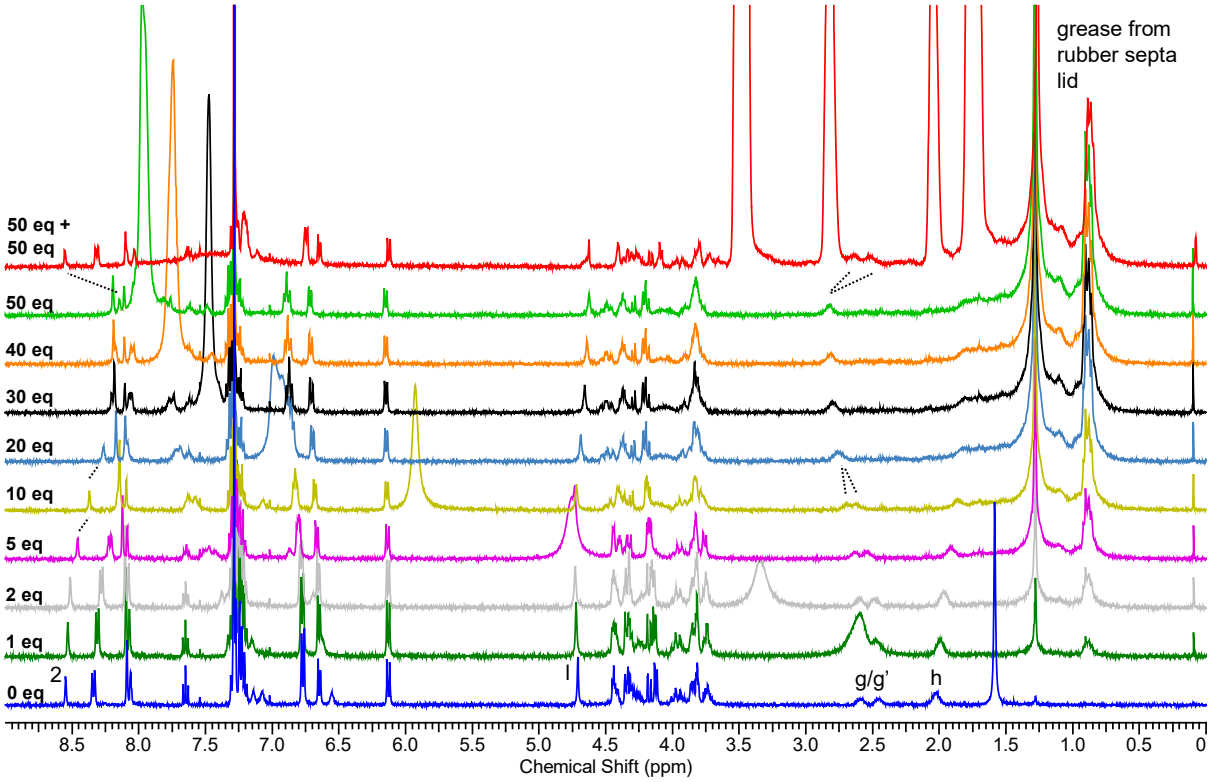


^{19}F NMR (Equivalents of TFA added: 0, 1, 2, 5, 10, 20, 30, 40, 50, 50 + 50 of D_5-pyridine)

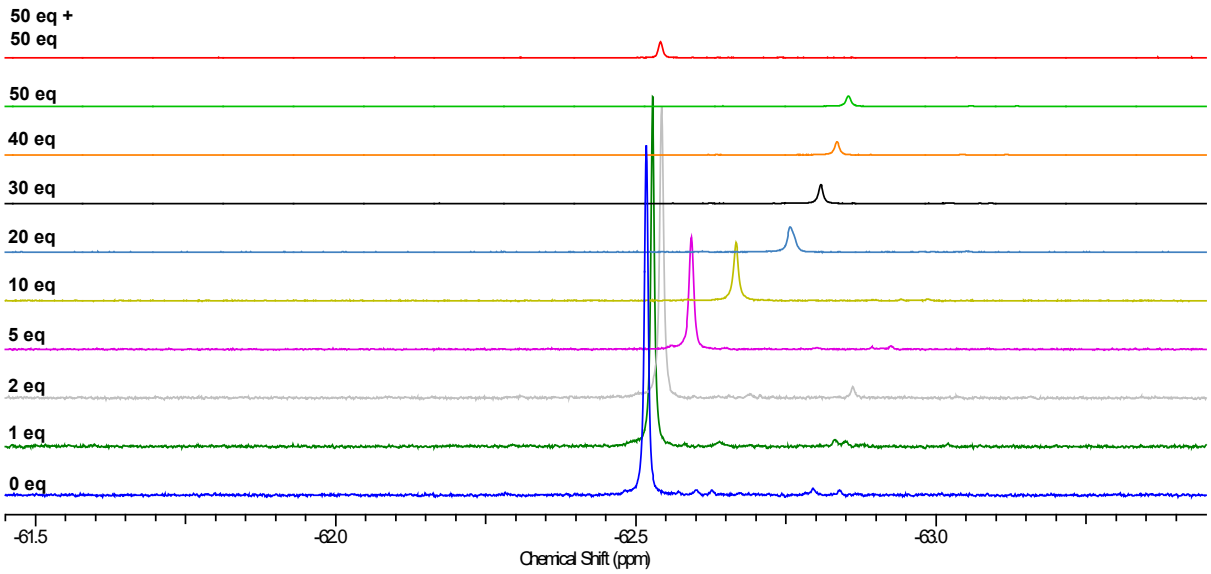


Rotaxane **1** + *TFA, then DBU*

^{1}H NMR (Equivalents of TFA added: 0, 1, 2, 5, 10, 20, 30, 40, 50, 50 + 50 of DBU)



^{19}F NMR (Equivalents of TFA added: 0, 1, 2, 5, 10, 20, 30, 40, 50, 50 + 50 of DBU)

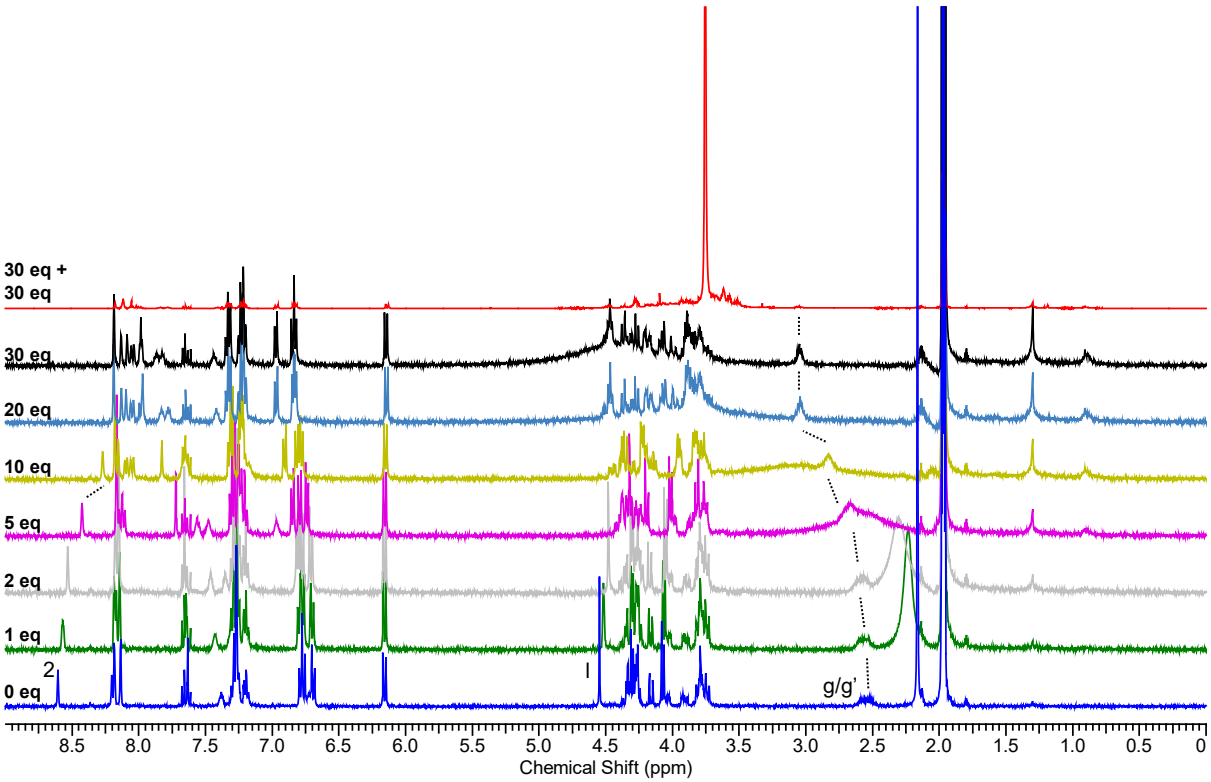


NB: Upfield shift of the CF_3 resonance in the ^{19}F NMR spectrum was observed during the course of both titrations above. Addition of D_5-pyridine resulted in a reversal of this shift but a broad peak shape implies an intermediate exchange process is occurring on the NMR timescale. Notably, addition of DBU (in an equivalent titration) results in no such intermediate exchange behaviour in the ^{19}F NMR spectrum.

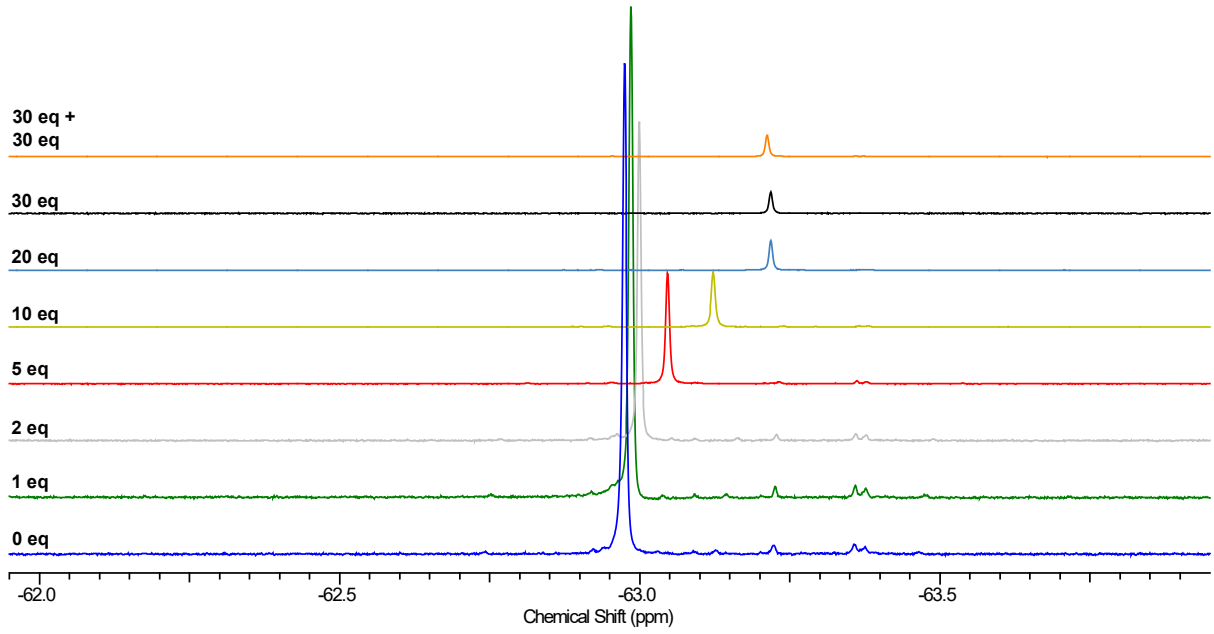
Cation Titrations

Rotaxane **1** + *$LiPF_6$*

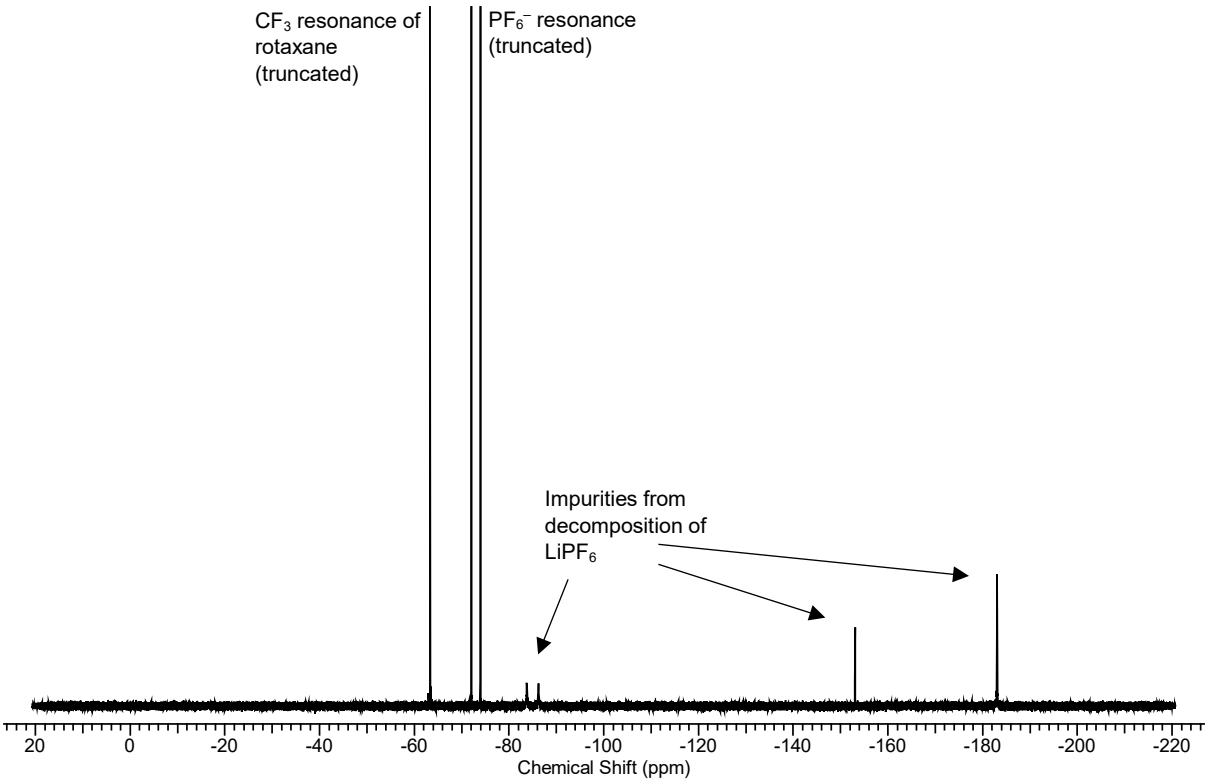
^{1}H NMR (Equivalents of $LiPF_6$ added: 0, 1, 2, 5, 10, 20, 30, 30 + 30 of 12-crown-4)



^{19}F NMR (Equivalents of $LiPF_6$ added: 0, 1, 2, 5, 10, 20, 30, 30 + 30 of 12-crown-4)

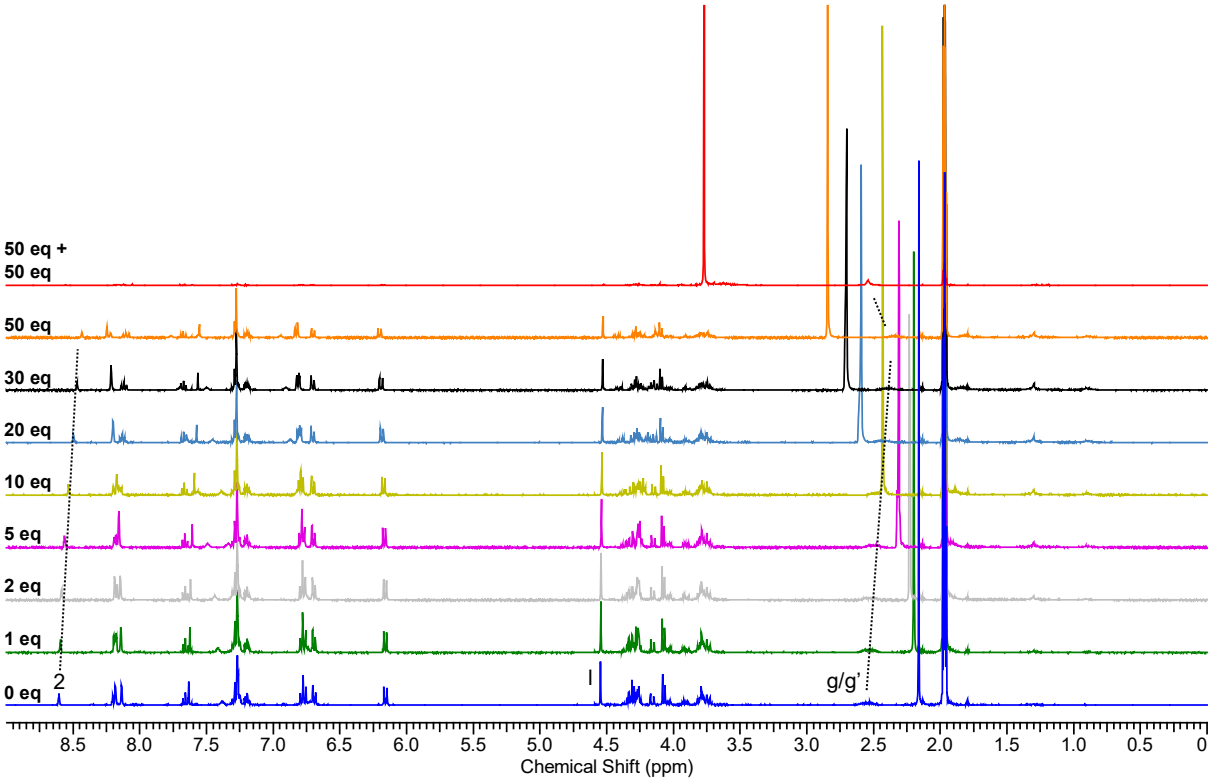


^{19}F NMR spectrum for 30 equivalents of added $LiPF_6$:

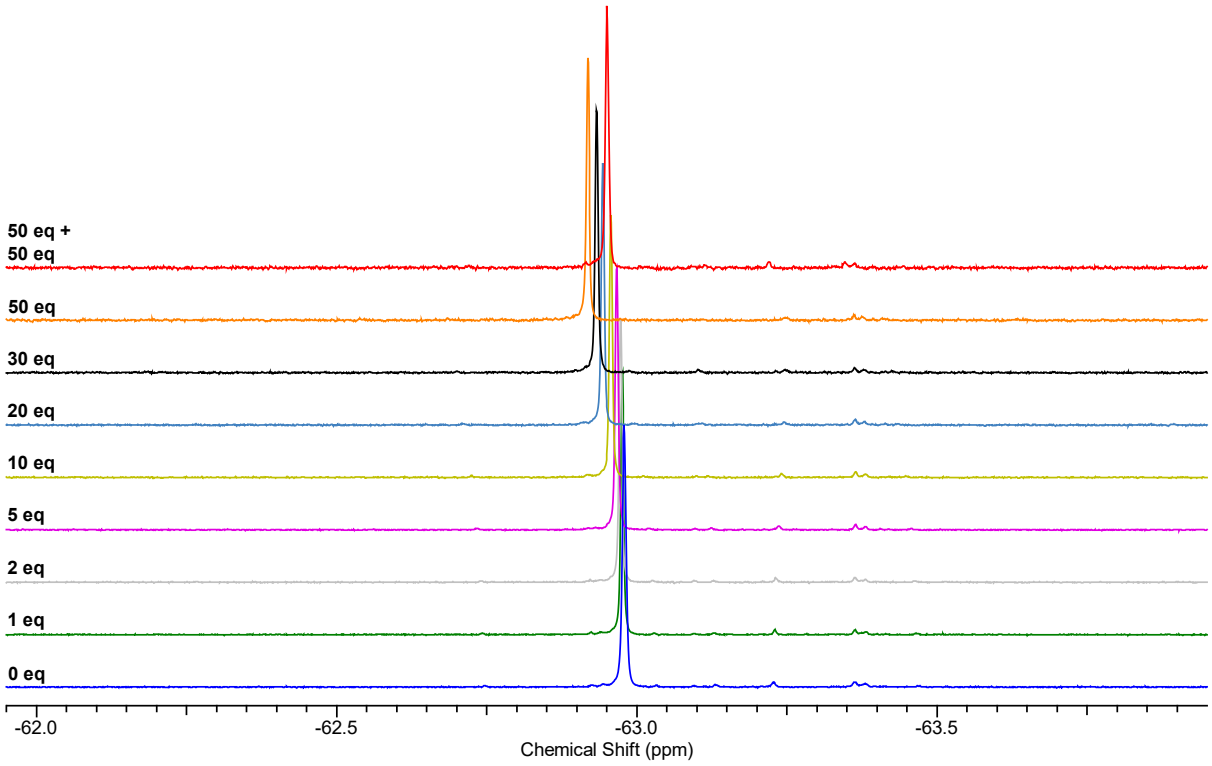


Rotaxane **1** + *LiClO₄*

^{1}H NMR (Equivalents of $LiClO_4$ added: 0, 1, 2, 5, 10, 20, 30, 50, 50 + 50 of 12-crown-4)

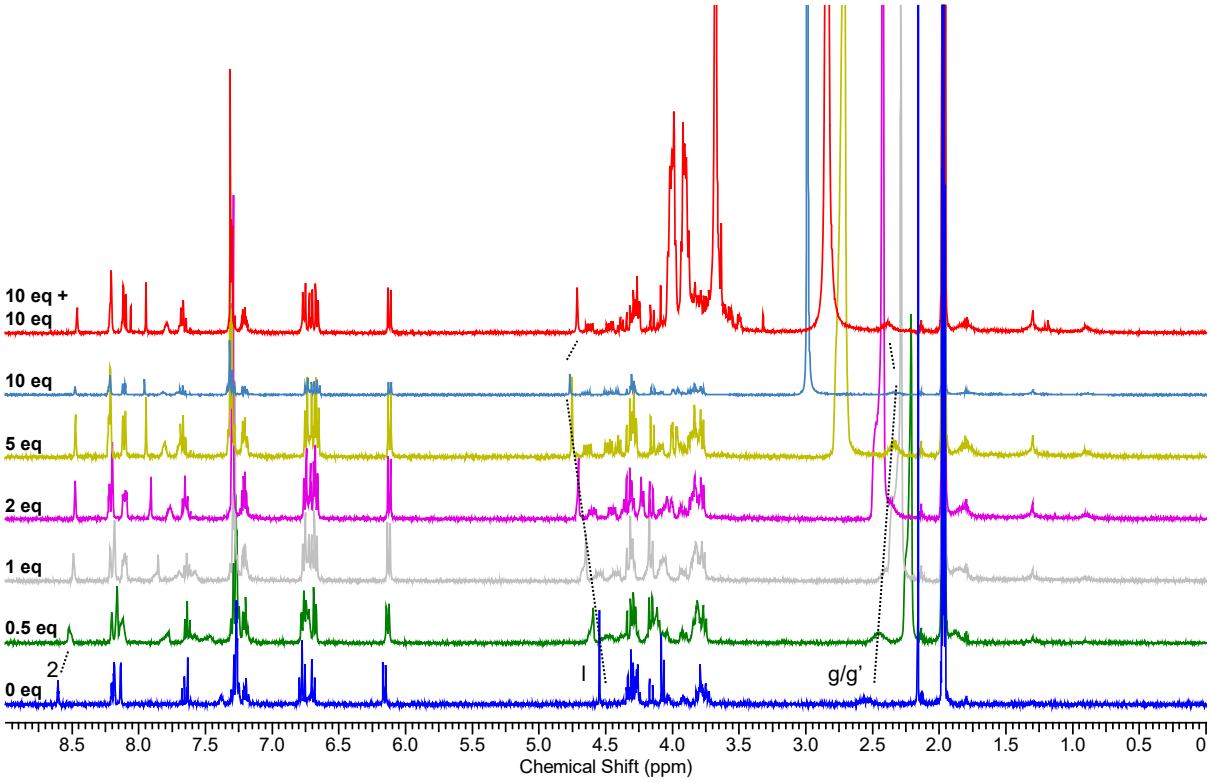


^{19}F NMR (Equivalents of $LiClO_4$ added: 0, 1, 2, 5, 10, 20, 30, 50, 50 + 50 of 12-crown-4)

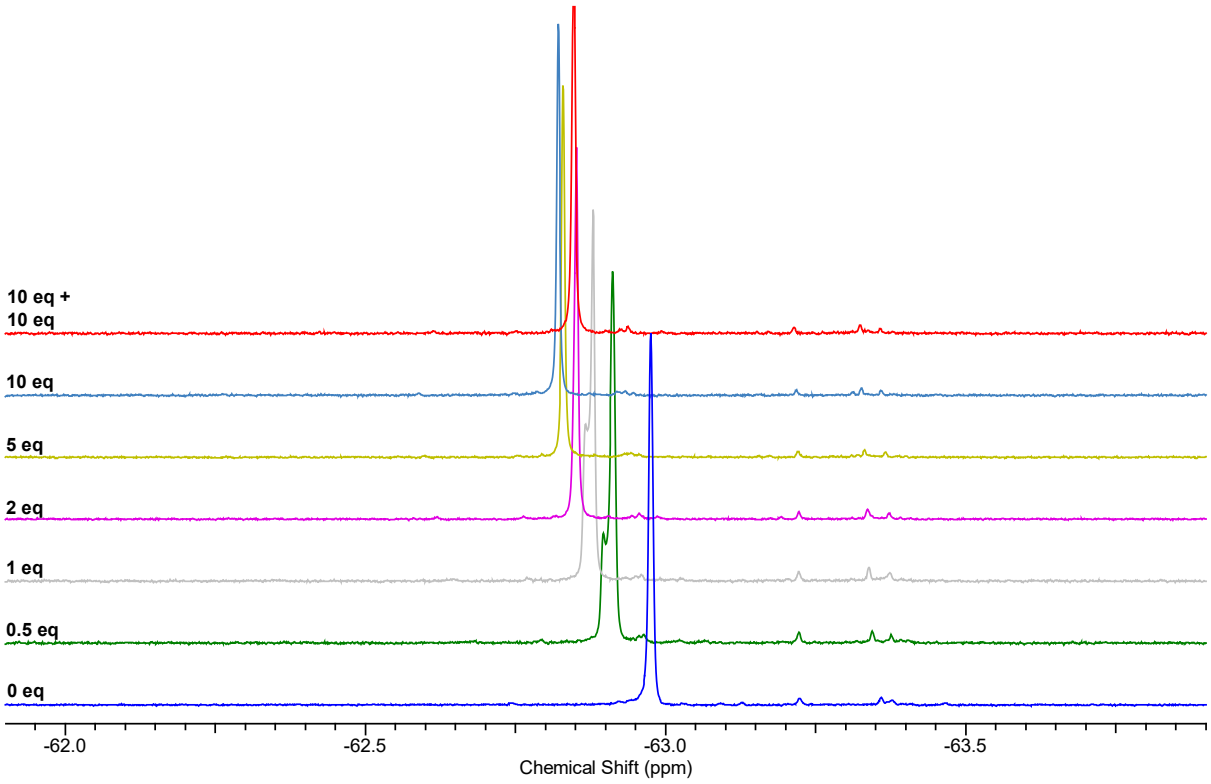


Rotaxane **1** + *Zn(ClO$_4$)$_2$*

^{1}H NMR (Equivalents of Zn(ClO$_4$)$_2$ added: 0, 0.5, 1, 2, 5, 10, 10 + 10 of 12-crown-4)

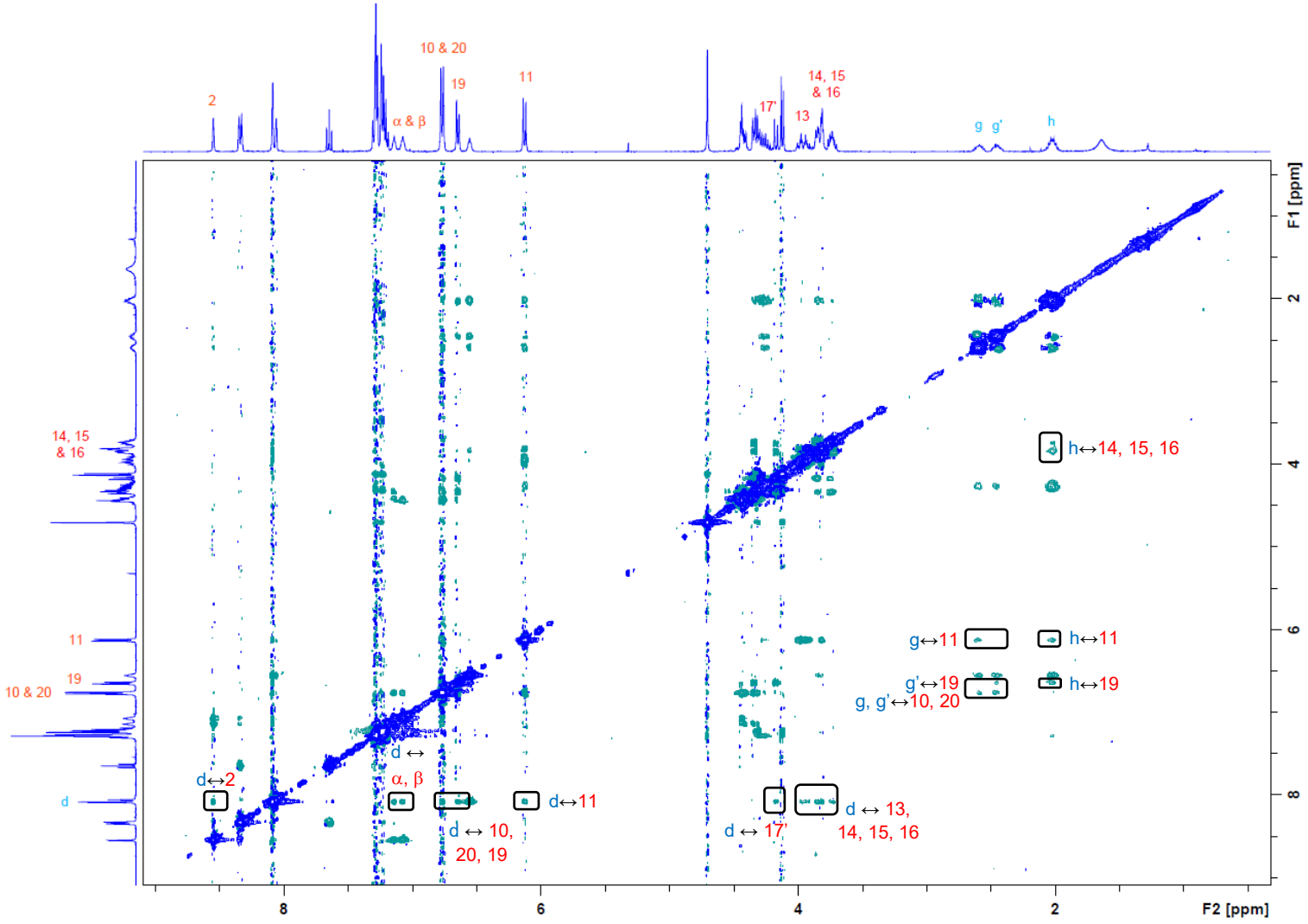


^{19}F NMR (Equivalents of Zn(ClO$_4$)$_2$ added: 0, 0.5, 1, 2, 5, 10, 10 + 10 of 12-crown-4)

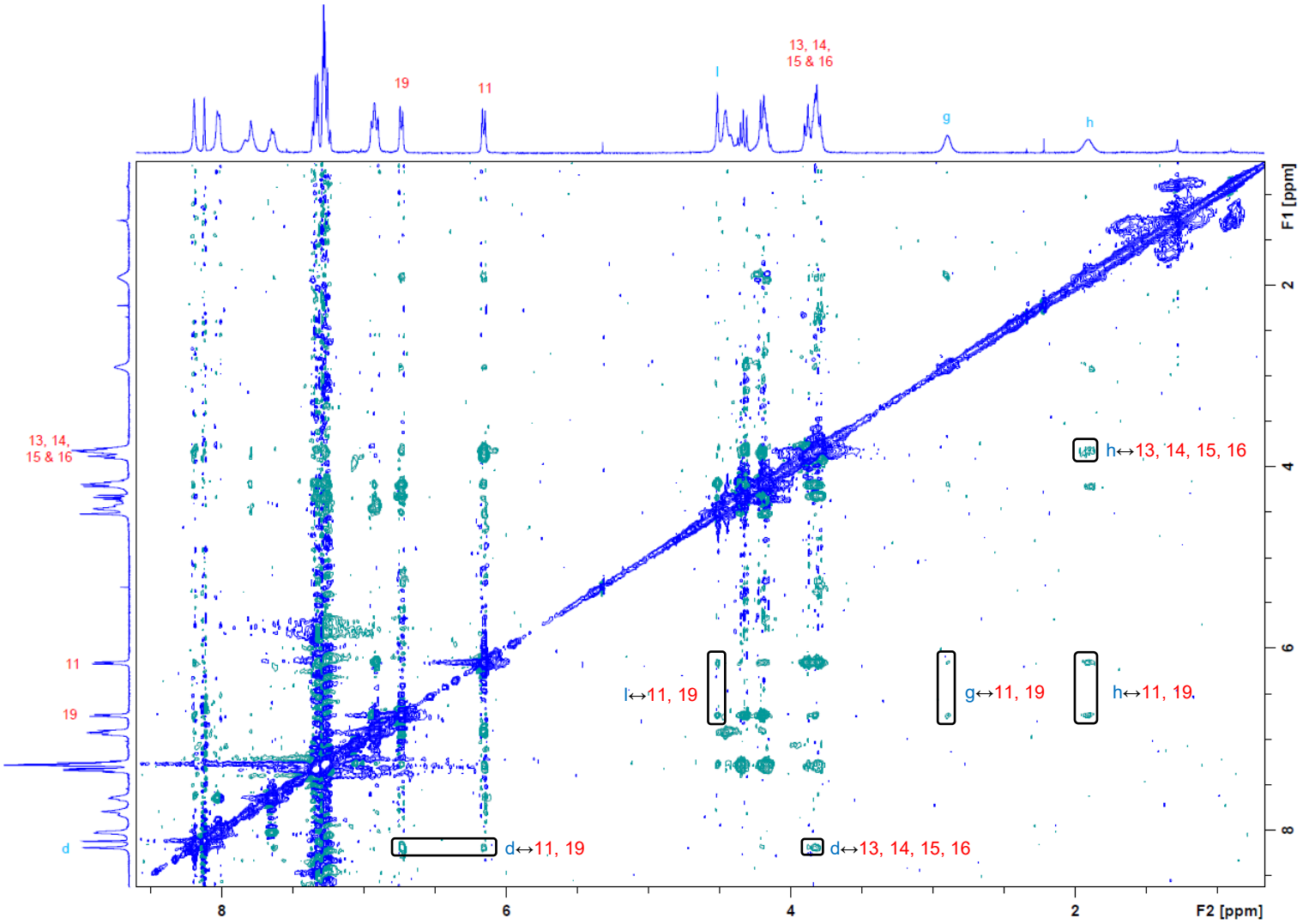


ROESY Study

*Pure Rotaxane **1** – Inter-component couplings highlighted by boxes.*



*Rotaxane **1** + ~ 40 eq of TFA – Inter-component couplings highlighted by boxes.*



Computational Modelling

The Gaussian 09 program was used to conduct all density functional theory calculations.[5]

For geometry optimisations B3LYP/6-31G* was used,[6-9] with solvent effects (chloroform) modelled using the default polarisable continuum model (and default solvent cavity parameters) as defined in Gaussian 09. Dispersion effects were approximated using the D3 approach of Grimme.[10] To obtain reasonable starting structures, structures were pre-optimised using semi-empirical PM6 methods. Several "starting points" were considered for the optimisations, to minimise bias in the final structures.

The log output files were converted to .xyz files using Avogadro software, before the figures presented belowed were generated using Mercury 4.00.

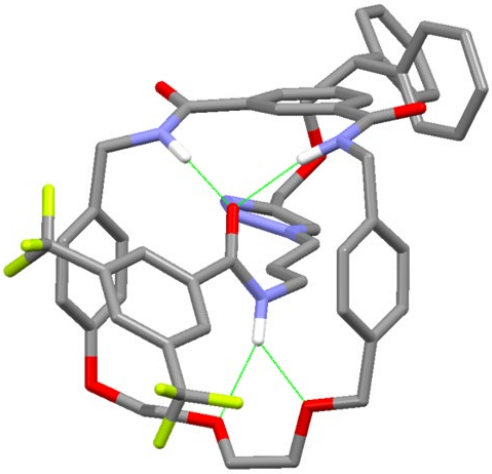
Neutral Rotaxane 1

The minimum energy structures for each co-conformation are presented on the next page.

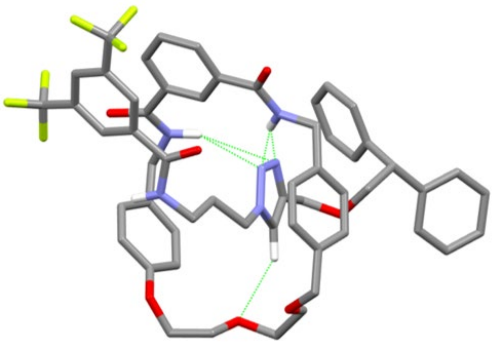
Co-conformation	Station	Isophthalamide	Energy / a.u.
A	Amide	*syn-syn*	-3620.84475653
B	Amide	*syn-anti*	-3620.84234338
C	Amide	*anti-syn*	-3620.84136406
D	Triazole	*syn-syn*	-3620.83295368
E	Triazole	*syn-anti*	-3620.83234009
F	Triazole	*anti-syn*	-3620.83202009

Key conclusions:
* Macrocycle residing at axle amide "station" is energetically favoured over residence at triazole "station".
* For both stations, *syn-syn* conformation of isophthalamide most energetically favoured.

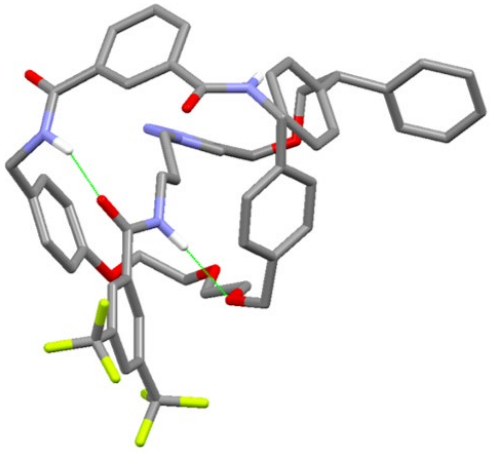
*Minimum Energy Structures of Neutral Rotaxane **1***



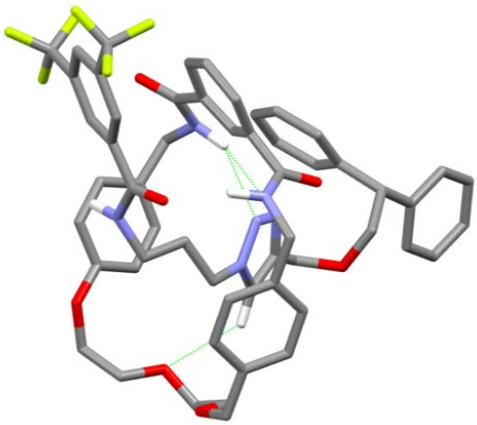
Co-conformation A



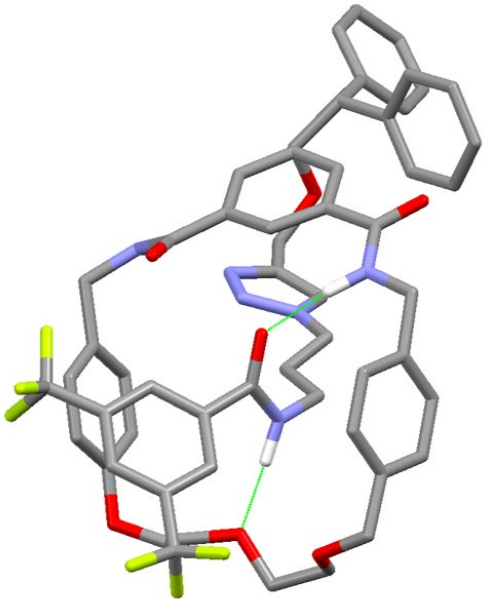
Co-conformation D



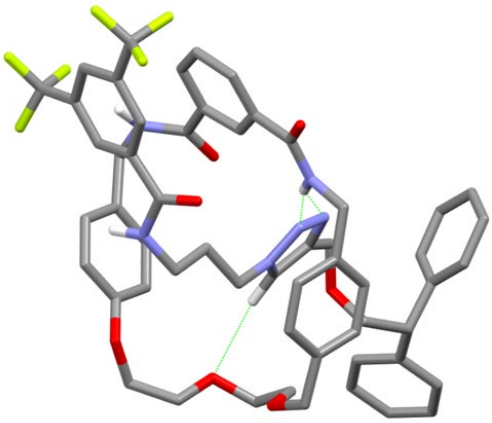
Co-conformation B



Co-conformation E



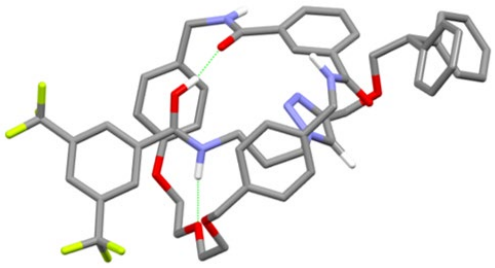
Co-conformation C



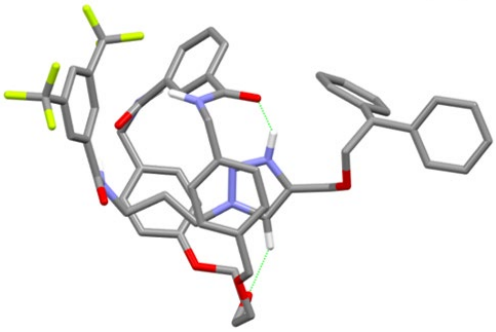
Co-conformation F

Protonated Rotaxane 1

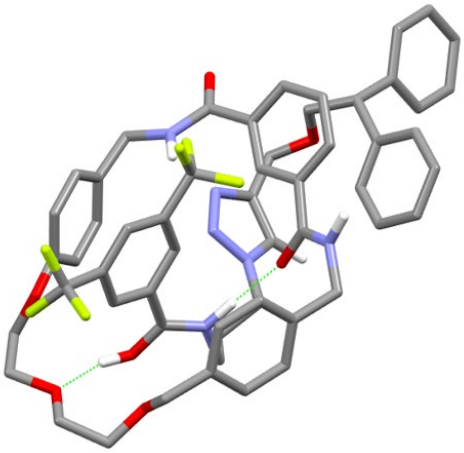
Plausible Protonated Hydrogen Bond Templated Co-conformations of Rotaxane ***1***



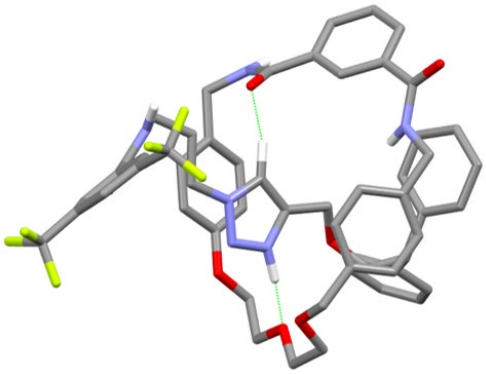
Co-conformation Alpha 1
Amide protonation



Co-conformation Beta 1
Triazole protonation (shuttled)



Co-conformation Alpha 2
Amide protonation (with pirouetting)



Co-conformation Beta 2
Triazole protonation (shuttled)

Please note: These structures are from calculations assuming mono-protonation events. An excess of TFA was added in the experiments. This may lead to (a) to multiple protonation events and/or (b) significant variation in solvent properties.

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