Electronic Supplementary Information

Hydrogen bond templated synthesis of catenanes and rotaxanes from a single isophthalic acid derivative

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Part 1: Supplementary Experimental Procedures for Main Article

General Information

All reagents and solvents were used as obtained from commercial suppliers, unless otherwise stated. Dry solvents, Et_3N 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}. Petrol refers to the fractions of petroleum that boil between 40°C and 60°C. Deionised water was used in all cases. All aqueous solutions are saturated unless otherwise stated.

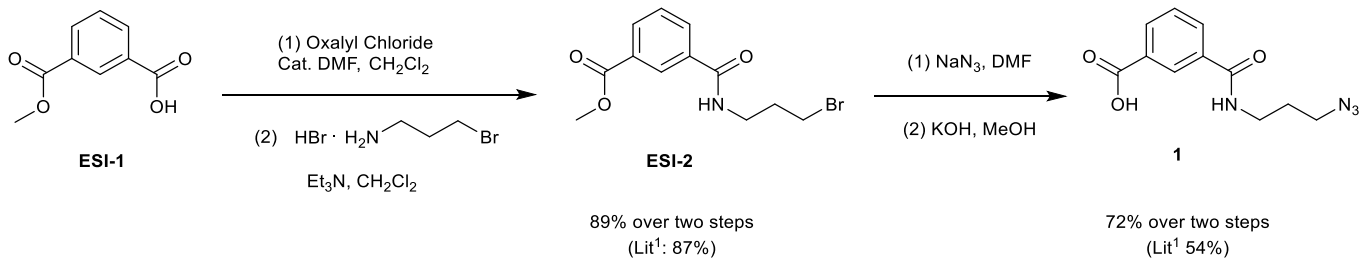
Azido-functionalized isophthalic acid derivative **1**[1] and alkyne **20**[2] were all synthesized based on previously reported procedures.

Silica gel with a 60Å particle size was used as the stationary phase for column chromatography. Analytical TLC was used to monitor the progress of column chromatography, with analytical TLC plates examined under short wavelength (254 nm) UV light or staining with potassium permanganate and phosphomolybdic acid solutions as appropriate. Preparatory TLC was carried out on silica gel possessing a fluorescent indicator to allow for examination with short wavelength UV light.

IR spectra were recorded on an Agilent Technologies Cary 630 FTIR spectrometer. NMR spectra were recorded on a Bruker AVANCE III 400 or Bruker Fourier 300 spectrometer at 298 K (unless otherwise stated). 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.

Additional Reaction Schemes

*(A) Scheme for synthesis of isophthalic acid **1***



Supplementary Scheme 1: *Synthesis of isophthalic acid derivative **1**.*

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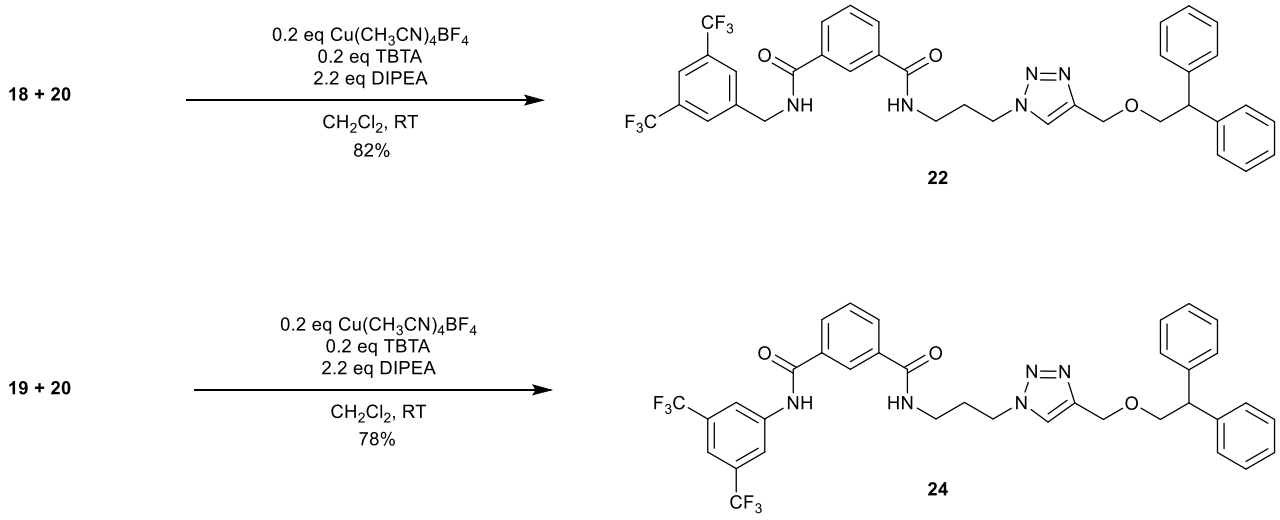
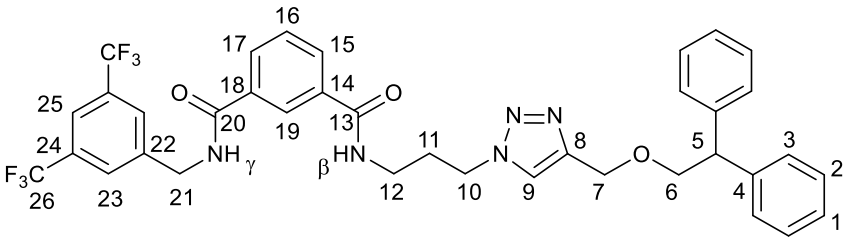
*(B) Scheme for synthesis of rotaxane axles **22** and **24***



Supplementary Scheme 2: *Synthesis of non-interlocked axles **22** and **24**.*

Supplementary Experimental Procedures

Axle 22



Azide **18** (32 mg, 0.067 mmol) and alkyne **20**[2] (16 mg, 0.067 mmol) were dissolved in dry CH_2Cl_2 (3 mL) and place under an argon atmosphere. $Cu(CH_3CN)_4BF_4$ (1 mg, 0.001 mmol), TBTA (1.5 mg, 0.001 mmol) and DIPEA (11 μL, 7.2 mg, 0.06 mmol) were added and then the reaction was stirred for 16 hours at room temperature maintaining the argon atmosphere. The reaction mixture was diluted to 10 mL, washed with 0.02 M EDTA in aq. 1 M NH_3 (2 x 10 mL) and brine (1 x 10 mL). The organic layer was dried ($MgSO_4$), filtered and solvent removed *in vacuo*. The crude material was purified by silica gel column chromatography (CH_2Cl_2/CH_3OH 98:2) to afford the *title product* as a colourless glassy film (39 mg, 82%).

***R*$_f$** 0.80 (CH_2Cl_2:CH_3OH 96:4).

ν_{max} / cm^{-1} (neat): 3315 (N-H), 2924 (C-H), 1641 (C=O), 1533 (C-N), 1276 (C-O).

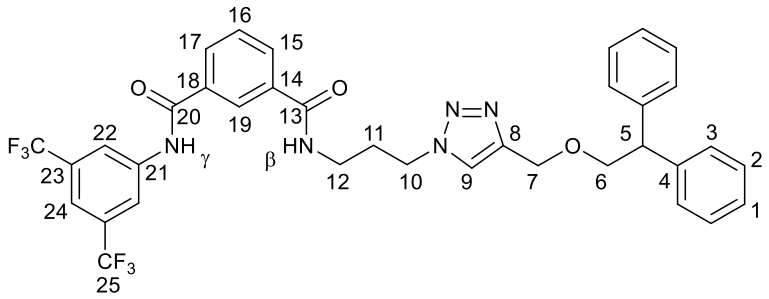
δ_H (400 MHz, $CDCl_3$): 8.31 (1H, bs, NH^{γ}), 8.14 (1H, d, *J* = 7.7 Hz, $H^{15/17}$), 8.10 (1H, s, H^{19}), 8.05 (1H, d, *J* = 7.8 Hz, $H^{15/17}$), 7.88 (2H, s, H^{23}), 7.80 (1H, s, H^{25}), 7.54 (1H, t, *J* = 7.8 Hz, H^{16}), 7.32-7.13 (12H, m, H^1, H^2, H^3, H^9 & NH^{β}), 4.77 (2H, d, *J* = 5.7 Hz, H^{21}), 4.50-4.46 (2H, m, H^{10}), 4.43 (2H, s, H^7), 4.19 (1H, t, *J* = 7.2 Hz, H^5), 3.89 (2H, d, *J* = 7.3 Hz, H^6), 3.69-3.60 (2H, m, H^{12}), 2.27-2.18 (2H, m, H^{11}).

δ_C (100 MHz, $CDCl_3$): 166.7 (C^{20}), 166.0 (C^{13}), 146.0 (C^8), 141.7 (C^4), 141.5 (C^{22}), 133.8 ($C^{14/18}$), 133.7 ($C^{14/18}$), 131.6 ($C^{15/17}$), 131.5 ($C^{15/17}$), 131.0 (C^{26}), 129.4 (C^{16}), 128.4 (C^2), 128.2 (C^3), 128.1 (C^{23}), 128.0 (C^{24}), 126.5 (C^1), 123.9 (C^{19}), 123.5 (C^9), 121.2 (C^{25}), 73.8 (C^6), 64.1 (C^7), 50.9 (C^5), 49.6 (C^{10}), 43.1 (C^{21}), 38.6 (C^{12}), 29.0 (C^{11}).

δ_F (377 MHz, $CDCl_3$): − 62.7.

***m/z* (ESI):** 732.2380 ($[M+Na]^+$ $C_{37}H_{33}F_6N_5O$ requires 732.2385).

Axle 24



Azide **19** (32 mg, 0.070 mmol) and alkyne **20**[2] (16 mg, 0.070 mmol) were dissolved in dry CH_2Cl_2 (3 mL) and placed under an argon atmosphere. $Cu(CH_3CN)_4BF_4$ (1 mg, 0.001 mmol), TBTA (1.5 mg, 0.001 mmol) and DIPEA (12 μL, 7.8 mg, 0.07 mmol) were added and then the reaction was stirred for 16 hours at room temperature maintaining the argon atmosphere. The reaction mixture was diluted to 10 mL, washed with 0.02 M EDTA in aq. 1 M NH_3 (2 x 10 mL) and brine (1 x 10 mL). The organic layer was dried ($MgSO_4$), filtered and solvent removed *in vacuo*. The crude material was purified by silica gel column chromatography (CH_2Cl_2/CH_3OH 98:2) to afford the *title product* as a colourless glassy film (38 mg, 78%).

***R*$_f$** 0.83 (CH_2Cl_2:CH_3OH 96:4).

ν_{max} / cm^{-1} (neat): 3063 (N-H), 2922 (C-H), 1638 (C=O), 1541 (C-N), 1276 (C-O).

δ_H (400 MHz, $CDCl_3$): 10.15 (1H, s, NH^{γ}), 8.38 (2H, s, H^{22}), 8.18-8.04 (2H, m, $H^{15/17}$ & H^{19}), 7.95 (1H, d, *J* = 7.8 Hz, $H^{15/17}$), 7.64 (1H, s, H^{24}), 7.42 (1H, t, *J* = 7.8 Hz, H^{16}), 7.35-7.08 (12H, m, H^1, H^2, H^3, H^9 & NH^{β}), 4.43 (2H, s, H^7), 4.38 (2H, t, *J* = 5.9 Hz, H^{10}), 4.12 (1H, t, *J* = 7.2 Hz, H^5), 3.85 (2H, d, *J* = 7.3 Hz, H^6), 3.52 (2H, app. q, *J* = 5.7 Hz, H^{12}), 2.27-2.18 (2H, m, H^{11}).

δ_C (100 MHz, $CDCl_3$): 166.0 (C^{13}), 165.6 (C^{20}), 145.6 (C^8), 141.6 (C^4), 133.9 ($C^{14/18}$), 133.5 ($C^{14/18}$), 132.2 (C^{25}), 131.8 ($C^{15/17}$), 131.6 ($C^{15/17}$), 129.5 (C^{16}), 128.5 (C^{22}), 128.4 (C^2), 128.1 (C^3), 126.5 (C^1), 124.6 (C^{21}), 124.0 (C^{19}), 123.5 (C^9), 120.2 (C^{23}), 117.1 (C^{24}), 73.9 (C^6), 64.0 (C^7), 50.8 (C^5), 49.8 (C^{10}), 38.6 (C^{12}), 28.9 (C^{11}).

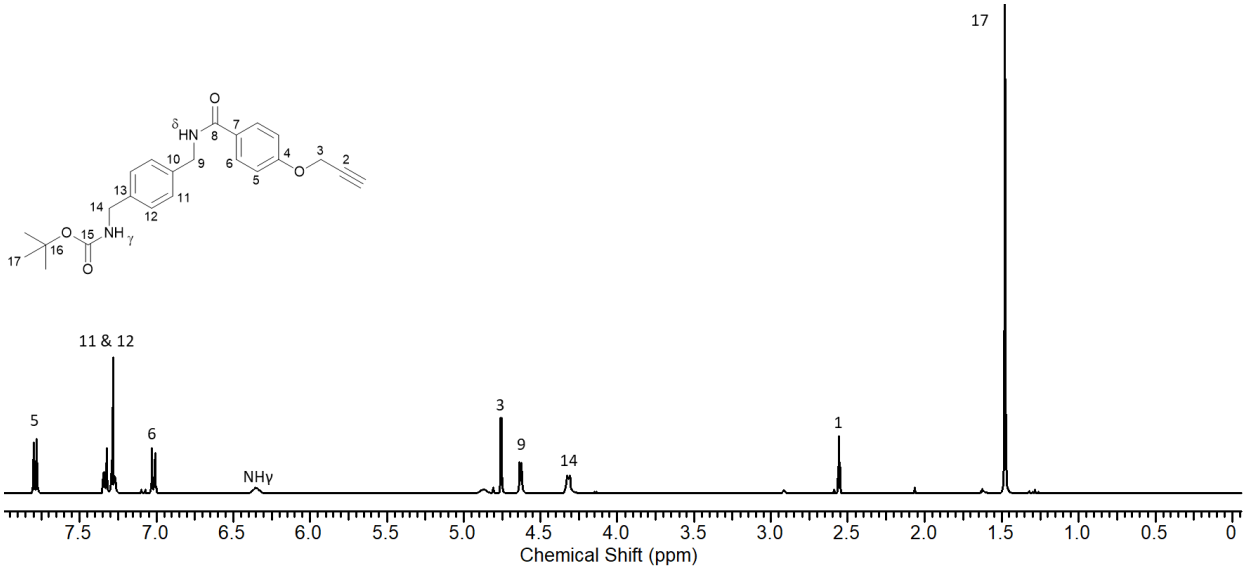
δ_F (377 MHz, $CDCl_3$): − 62.8

***m/z* (ESI):** 718.2256 ($[M+Na]^+$ $C_{36}H_{31}F_6N_6O$ requires 718.2229).

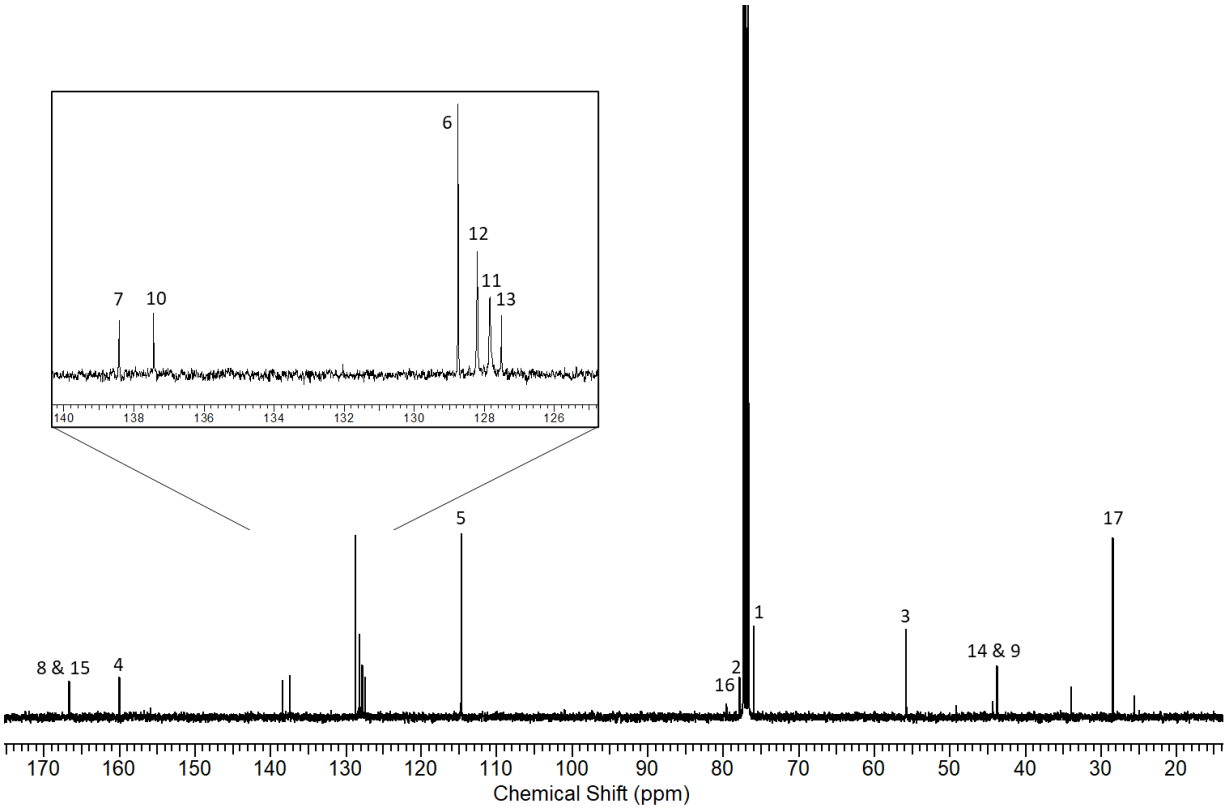
Part 2: Spectral Data for Main Article

Alkyne 5

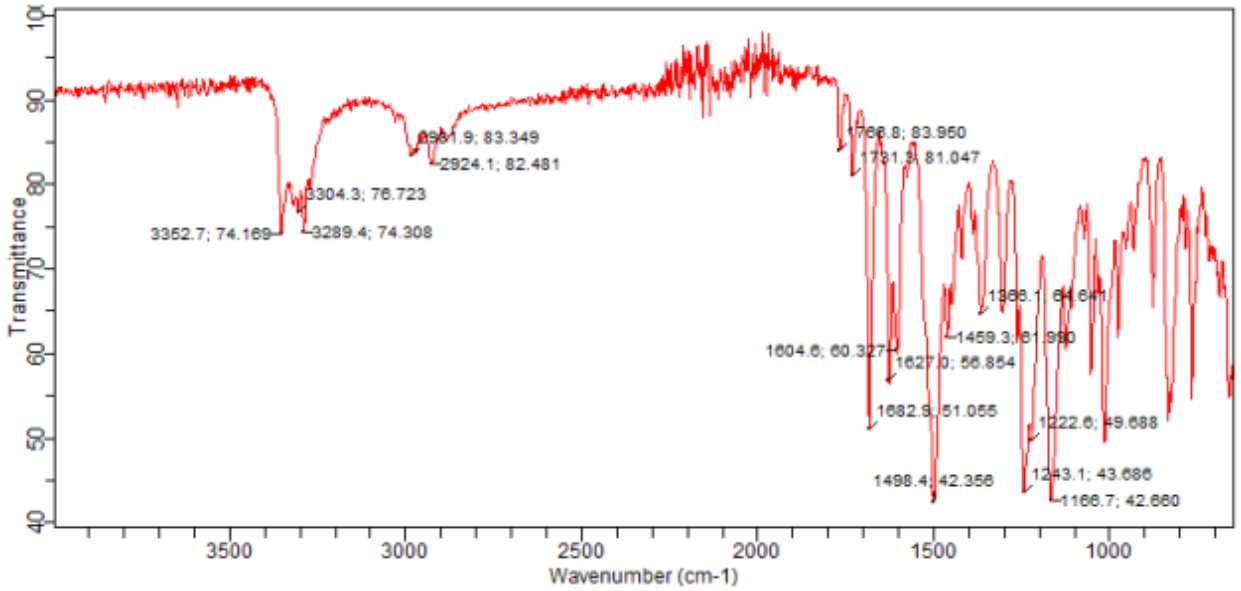
^{1}H NMR: (400 MHz, $CDCl_3$)



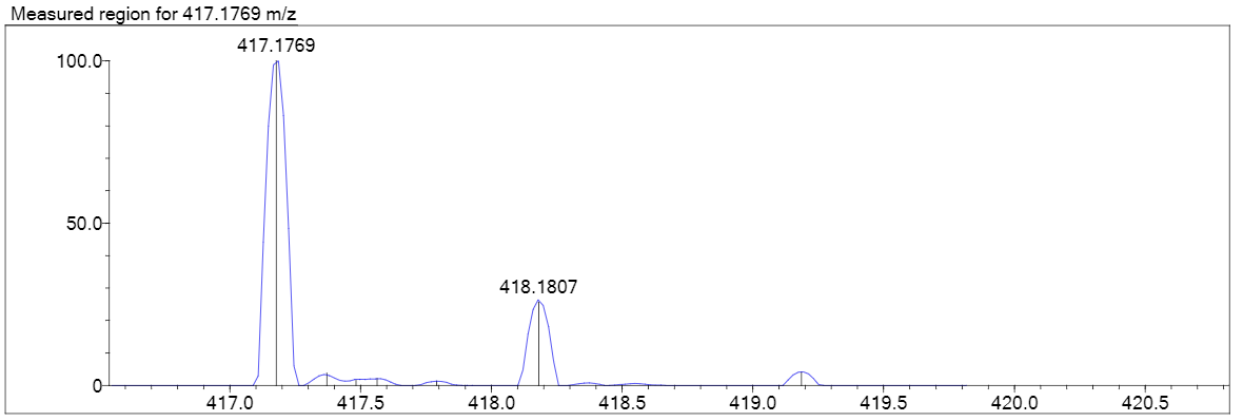
^{13}C NMR: (100 MHz, $CDCl_3$)

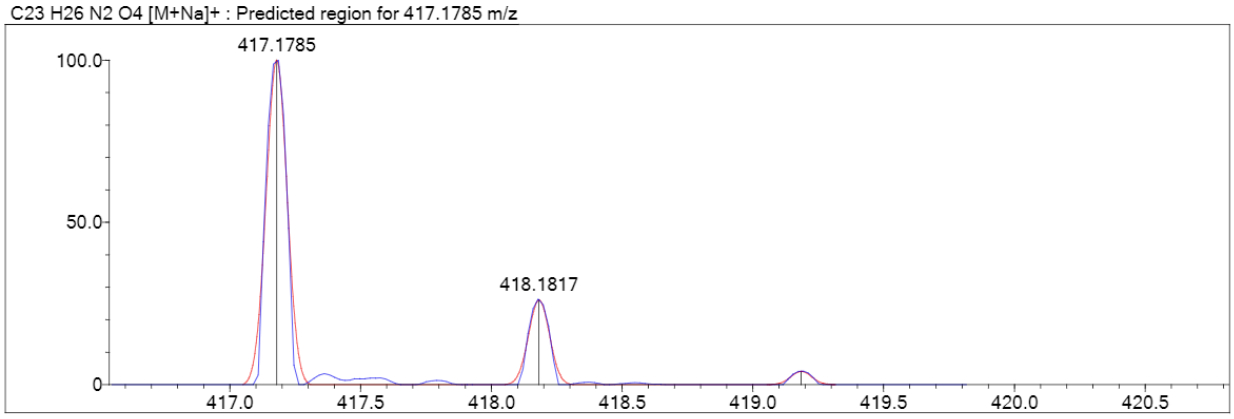


IR Spectrum (neat)



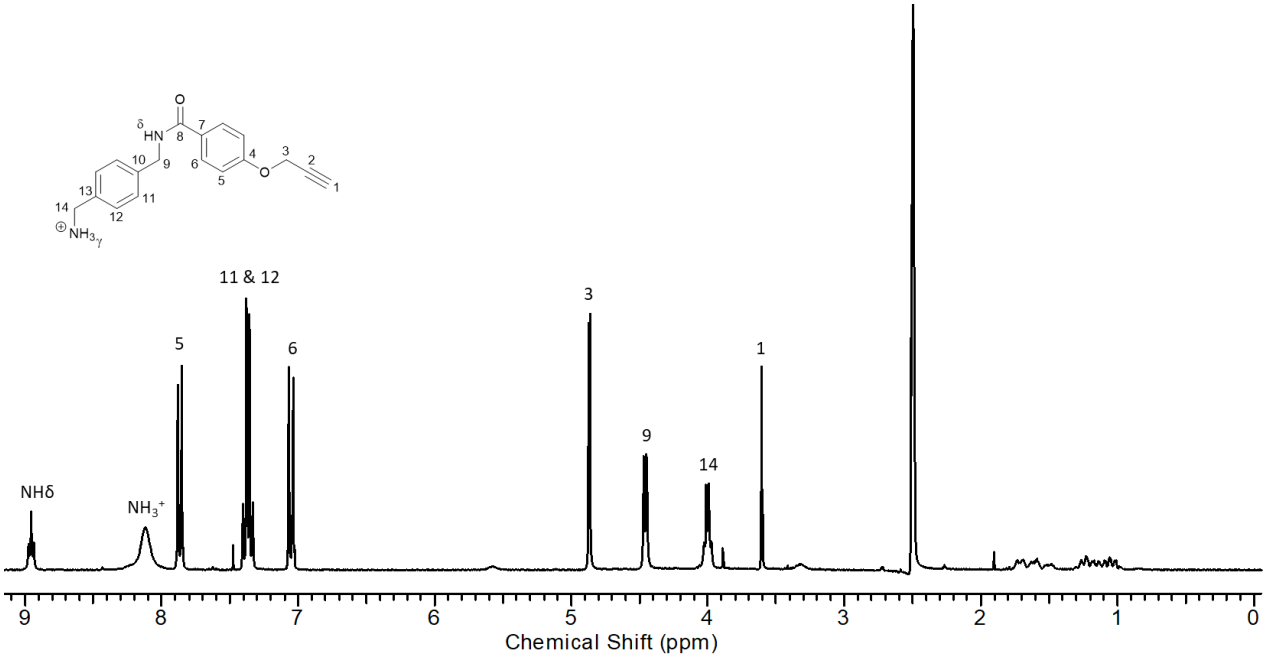
HRMS (ES +ve)





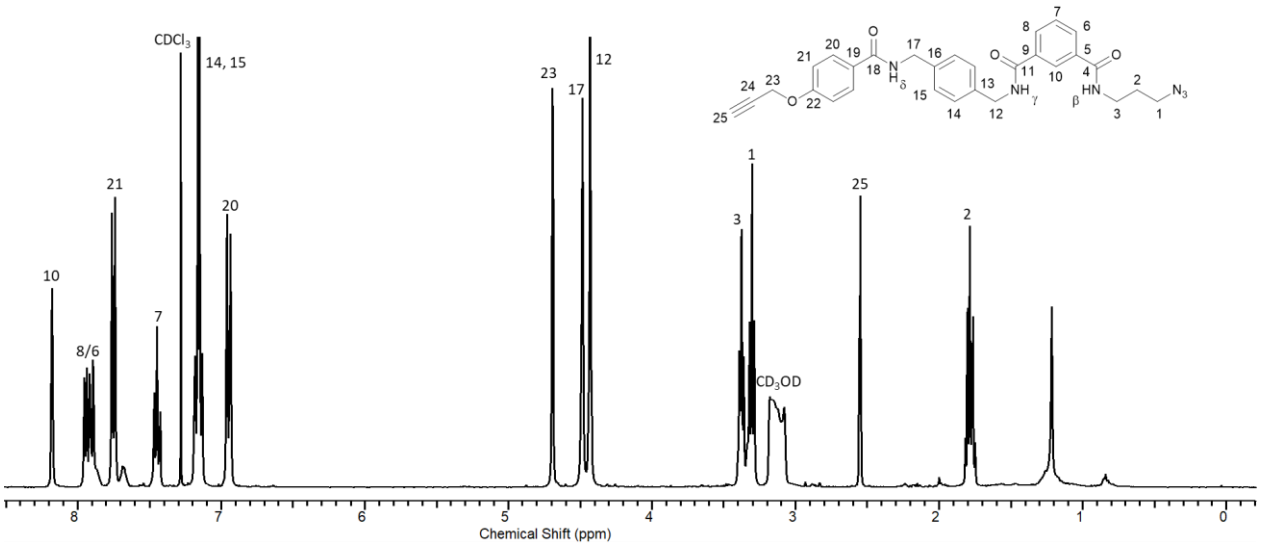
Deprotected amine alkyne salt 8

^{1}H NMR: (300 MHz, D_6-DMSO)

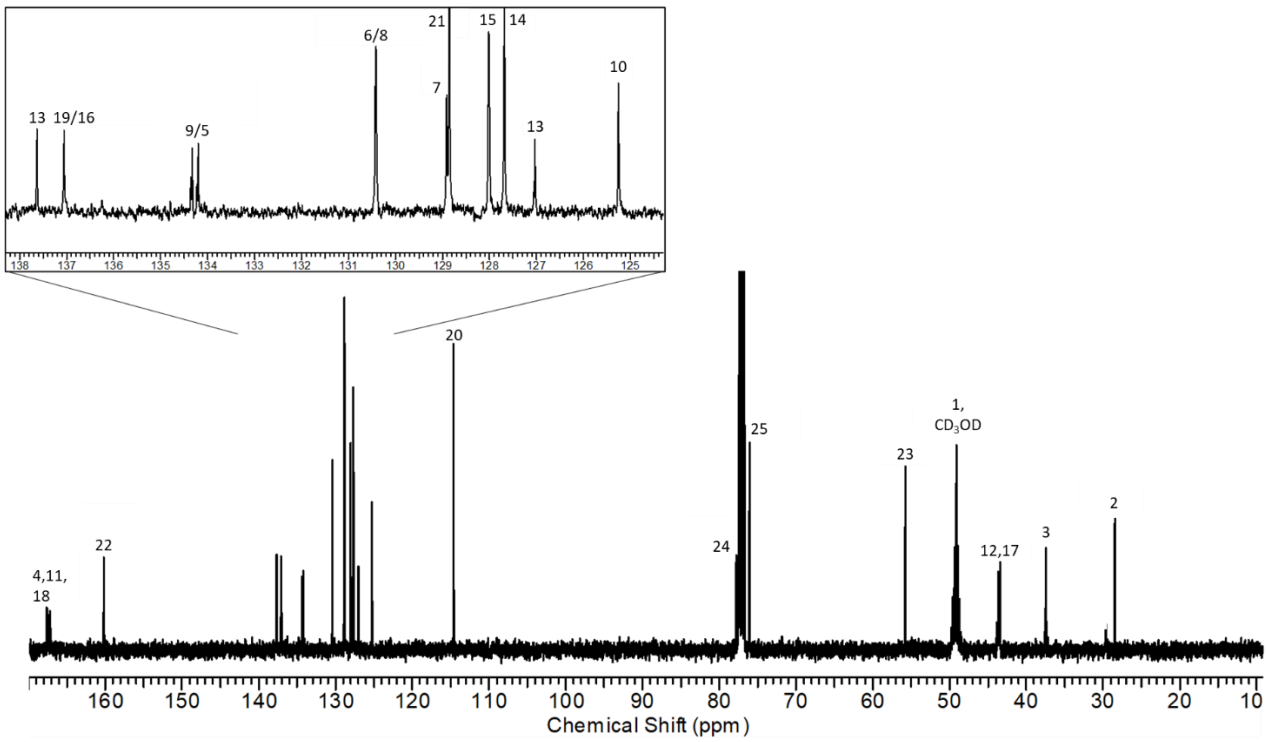


Alkyne-azide 11

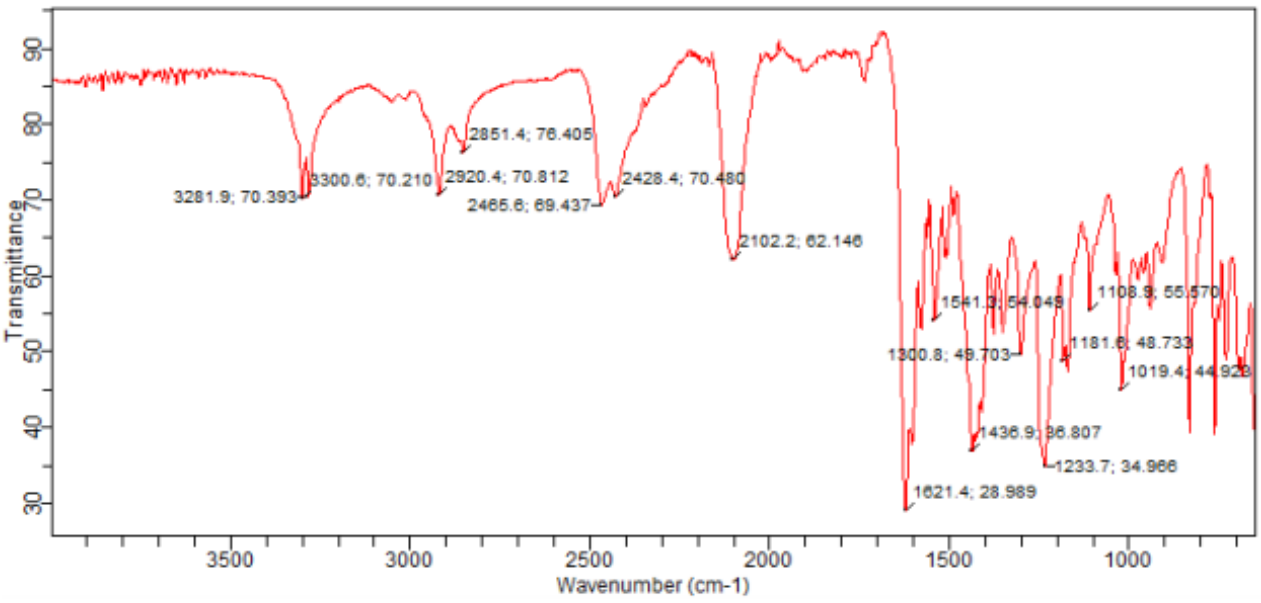
^{1}H NMR: (400 MHz, 9:1 $CDCl_3$/ CD_3OD)



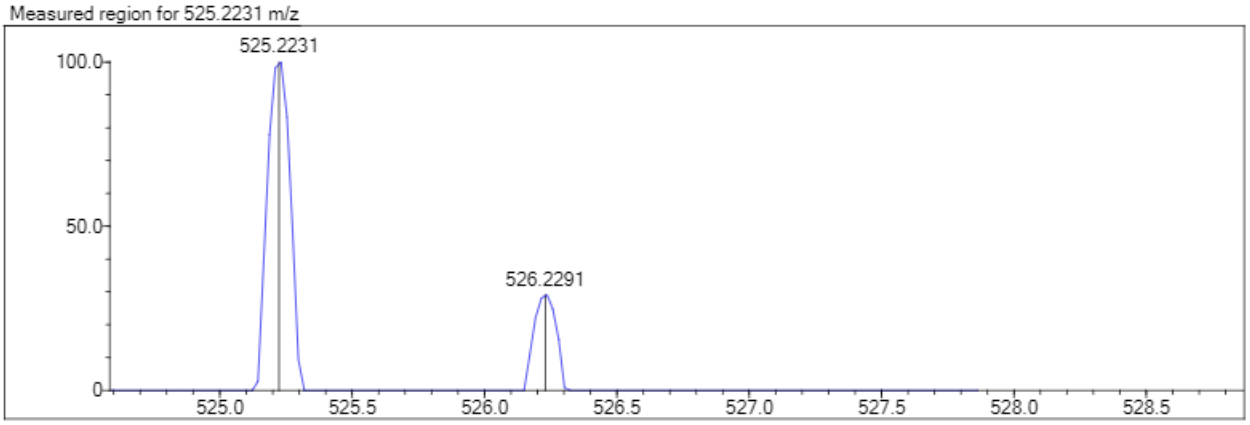
^{13}C NMR: (100 MHz, 9:1 $CDCl_3$/ CD_3OD)

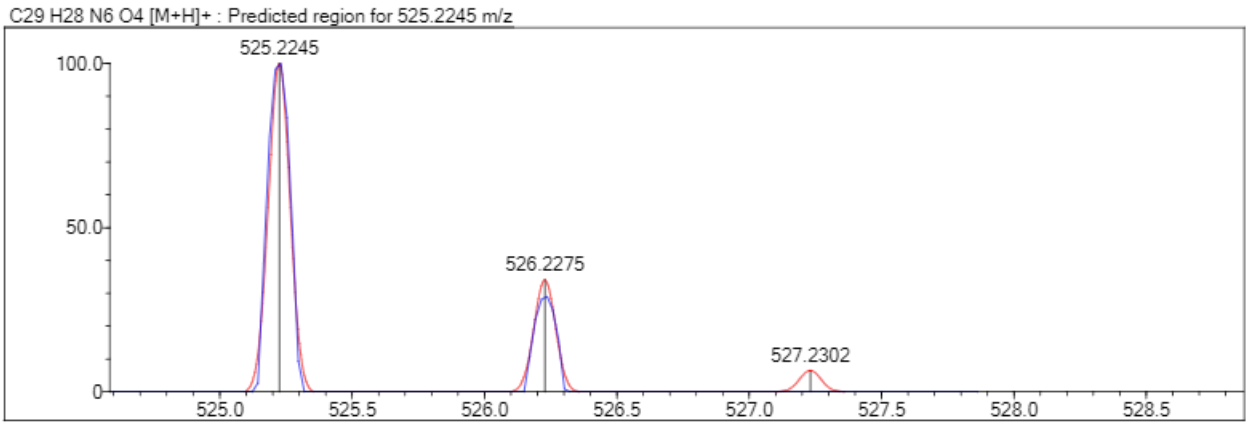


IR Spectrum (neat)



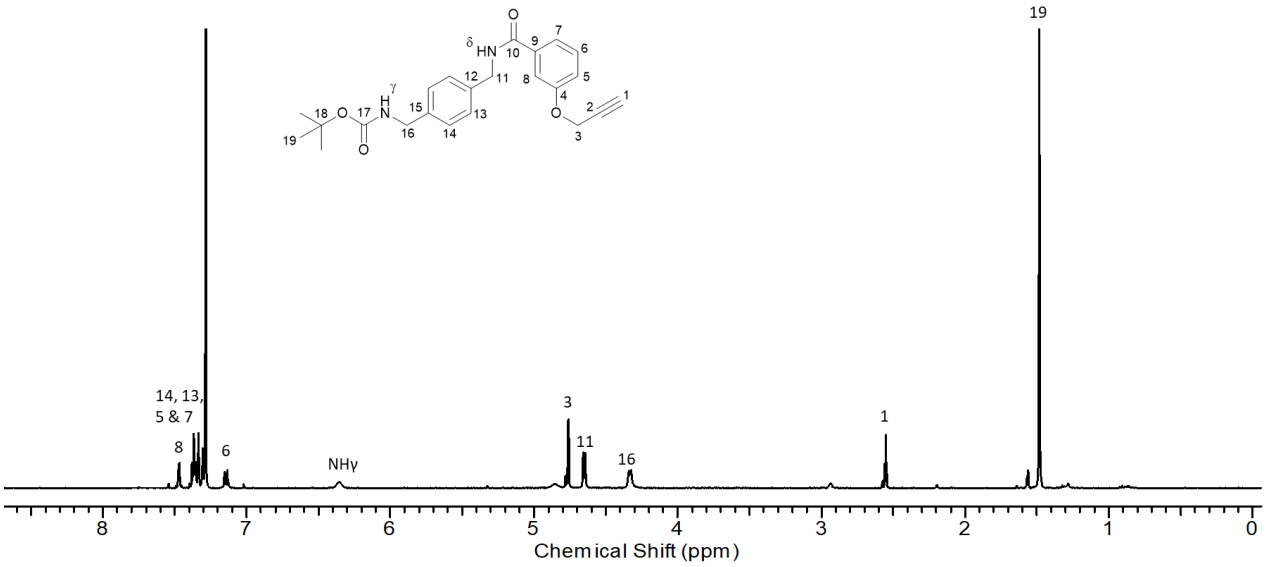
HRMS (ES +ve)



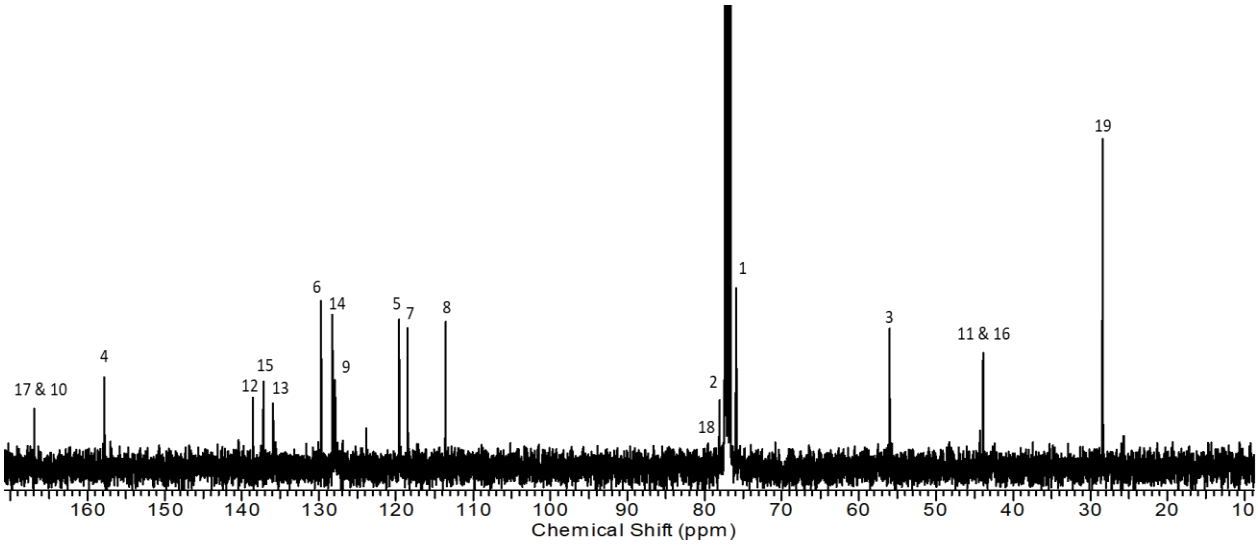


Alkyne 6

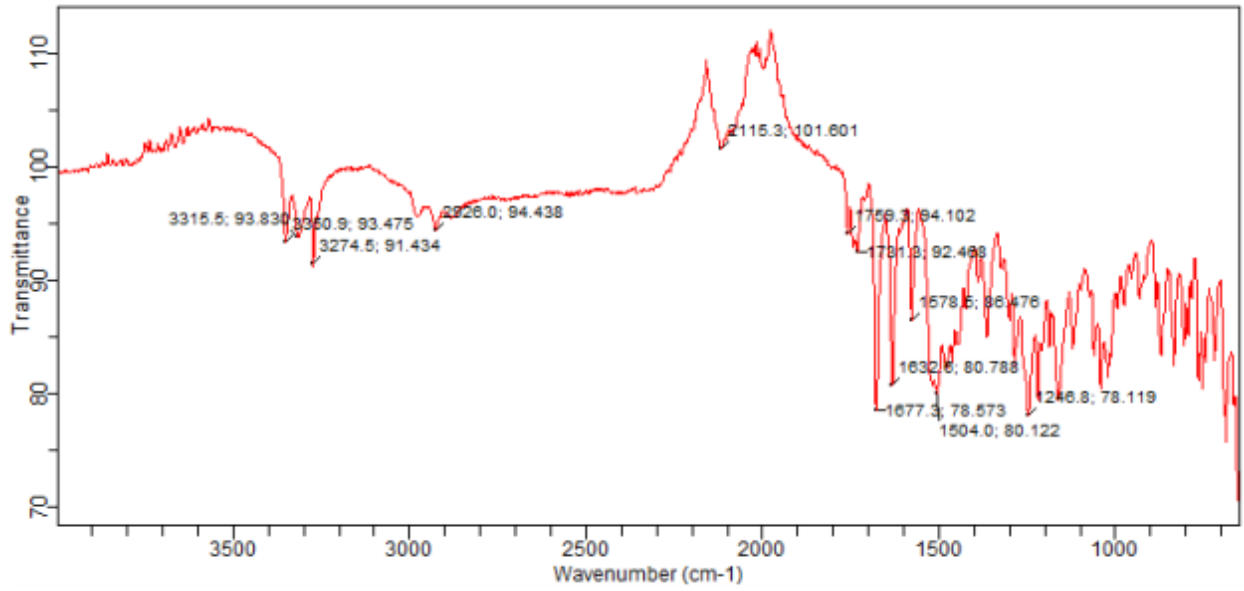
^{1}H NMR: (400 MHz, $CDCl_3$)



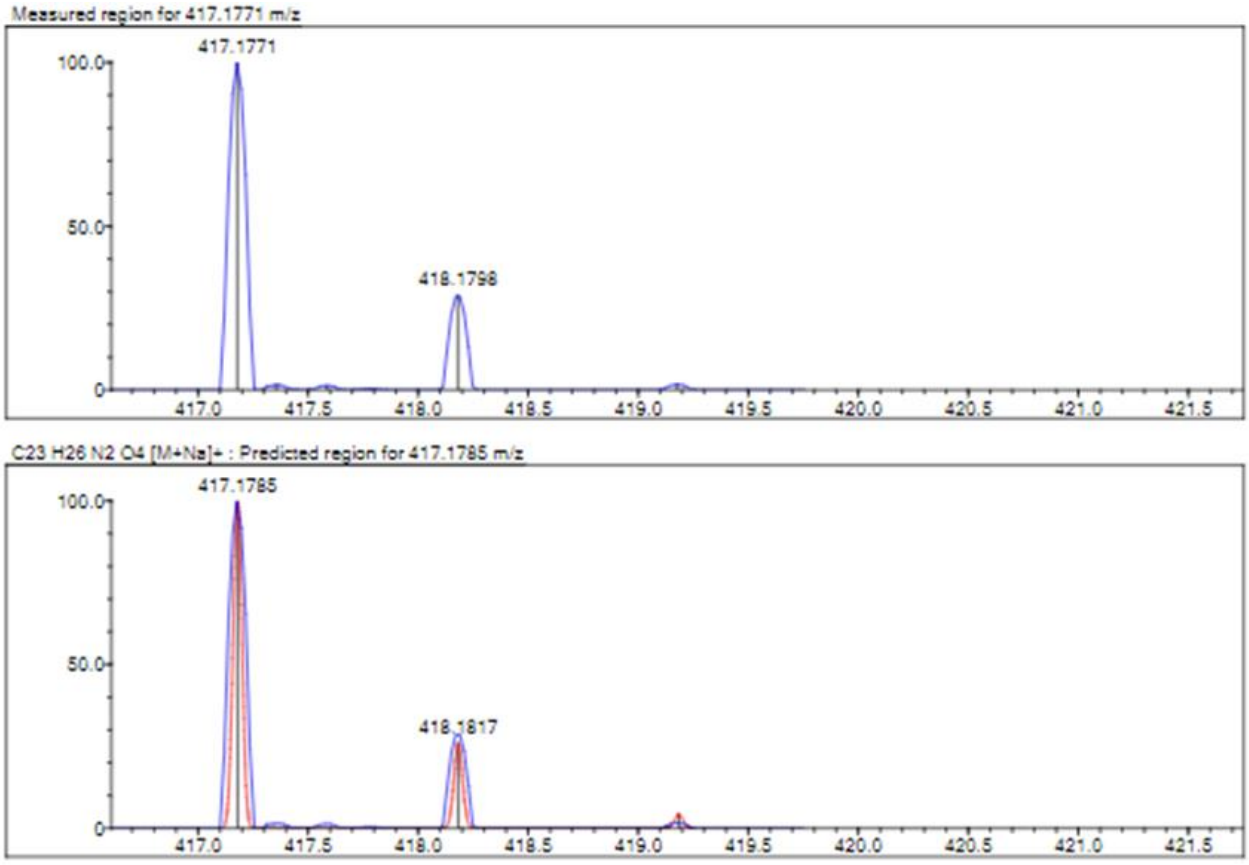
^{13}C NMR: (100 MHz, $CDCl_3$)



IR Spectrum (neat)

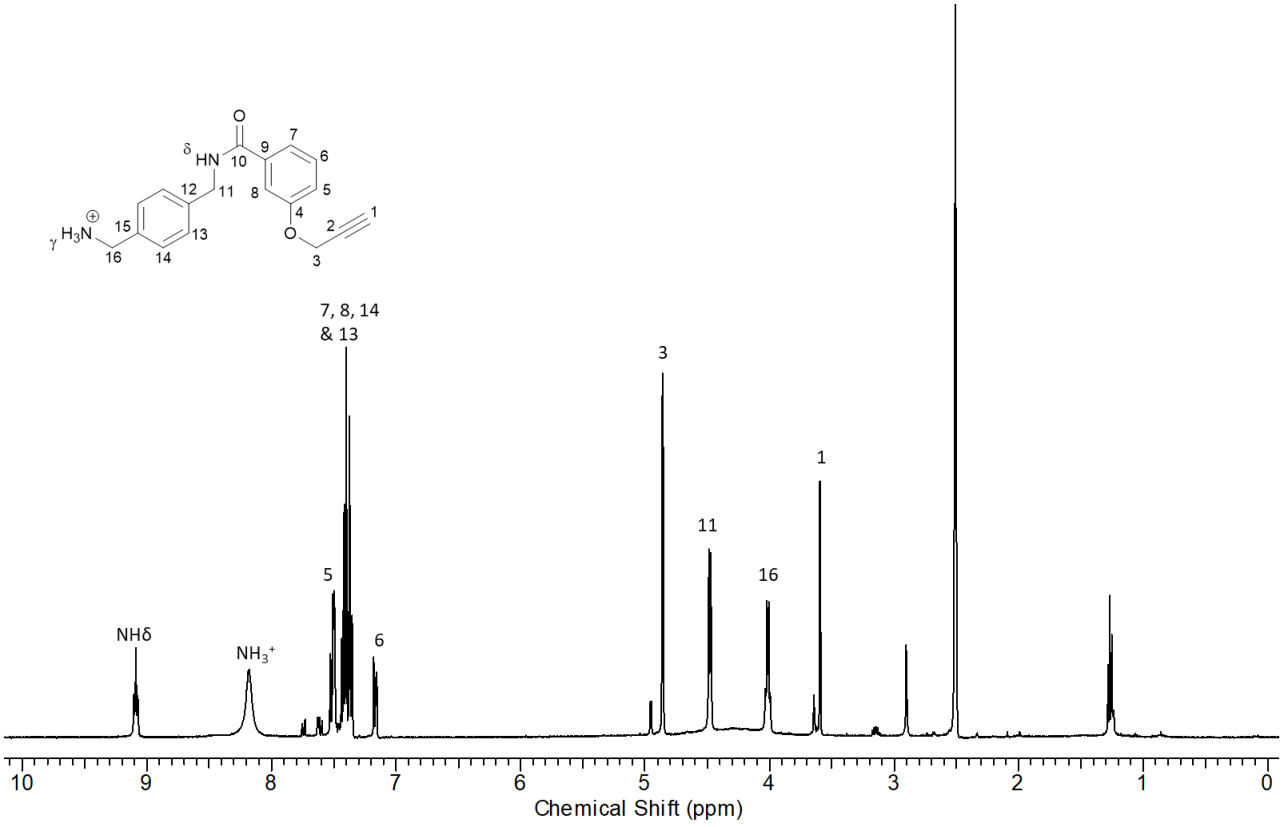


HRMS (ES +ve)



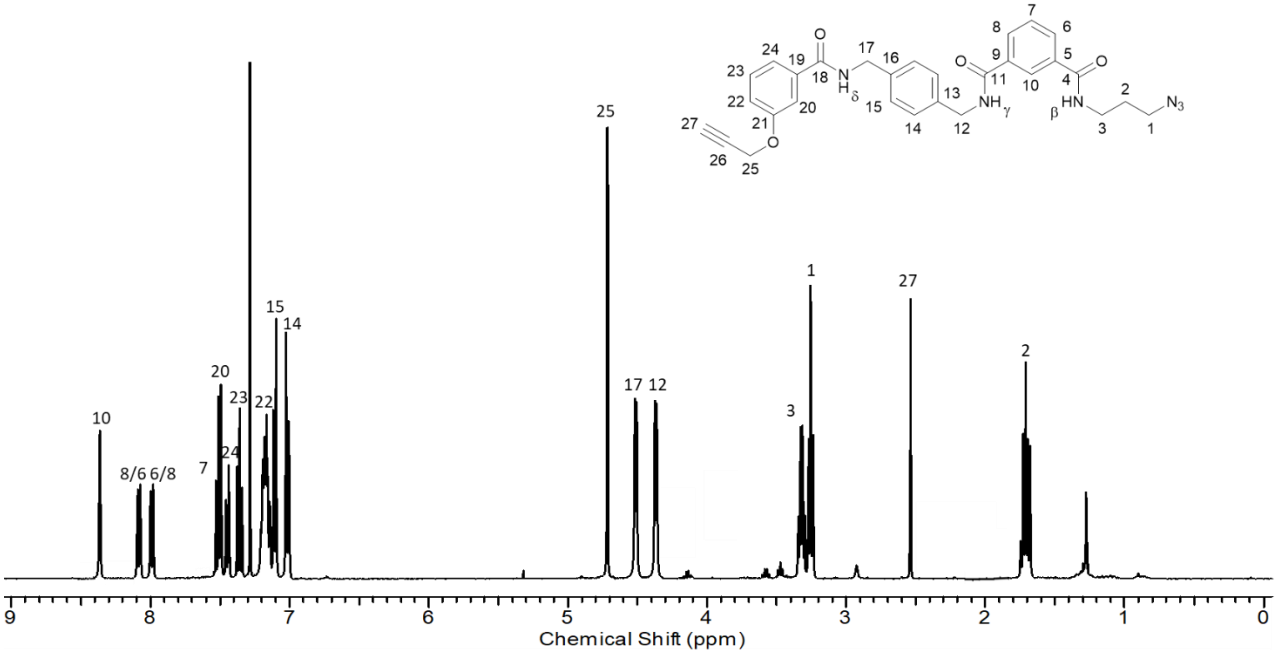
Deprotected amine alkyne salt 9

^{1}H NMR: (400 MHz, D_6-DMSO)

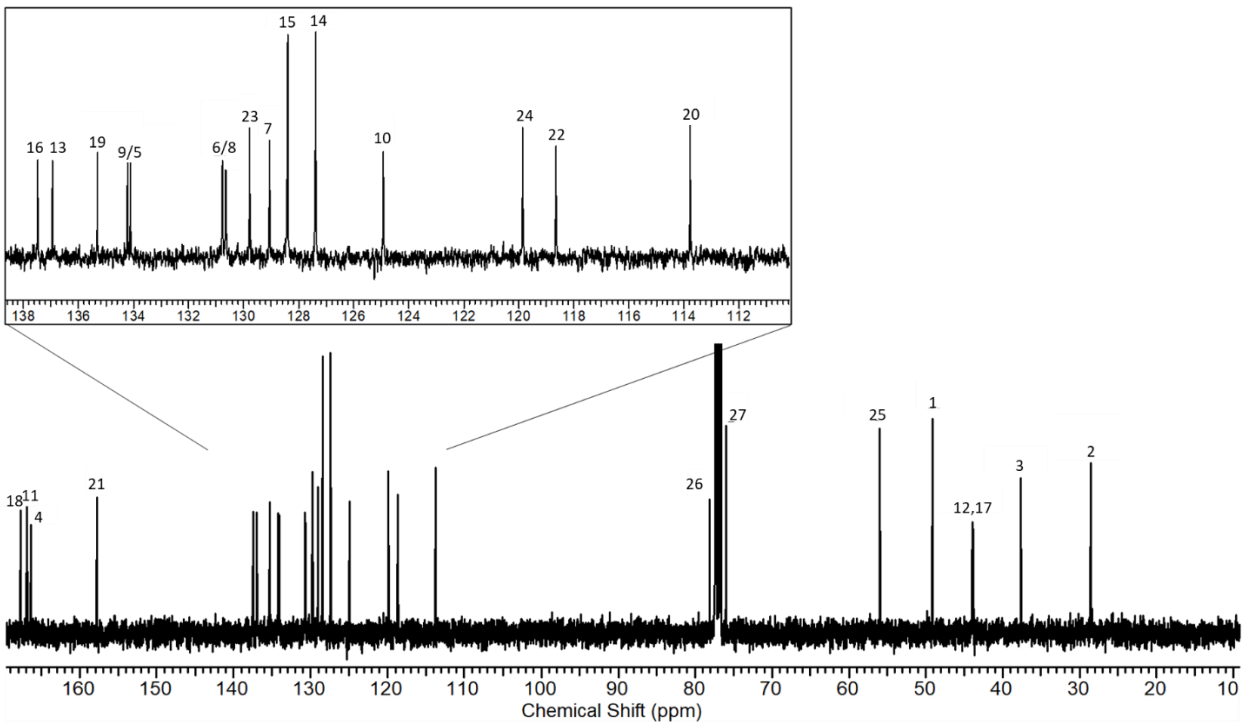


Alkyne-Azide 12

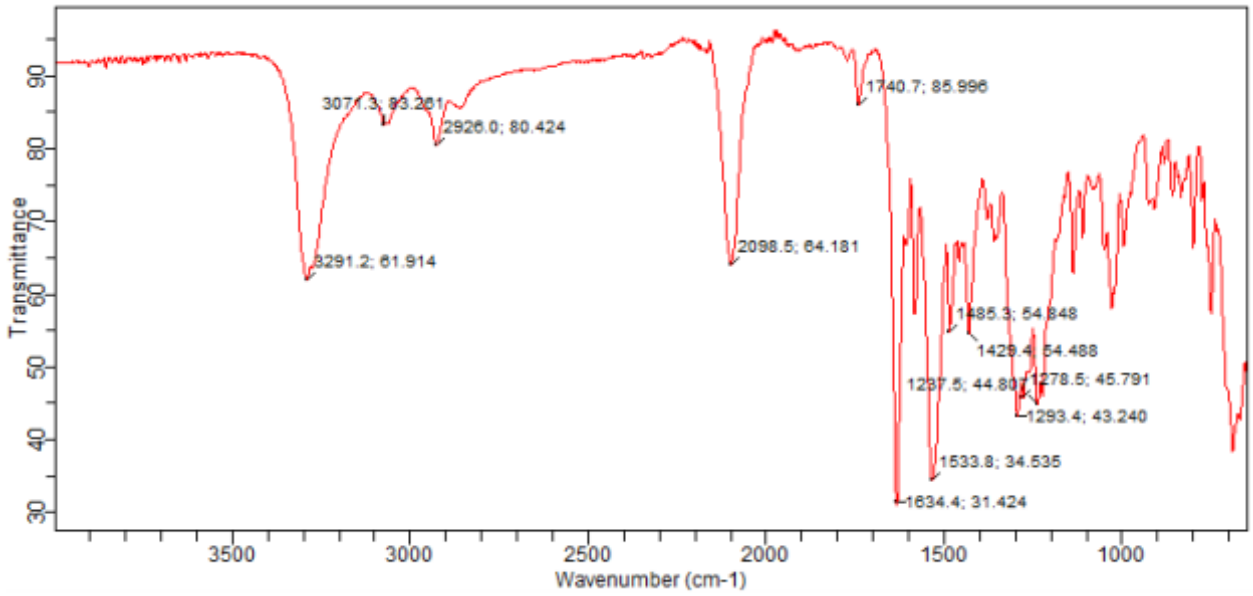
^{1}H NMR: (400 MHz, $CDCl_3$)



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



IR Spectrum (neat)



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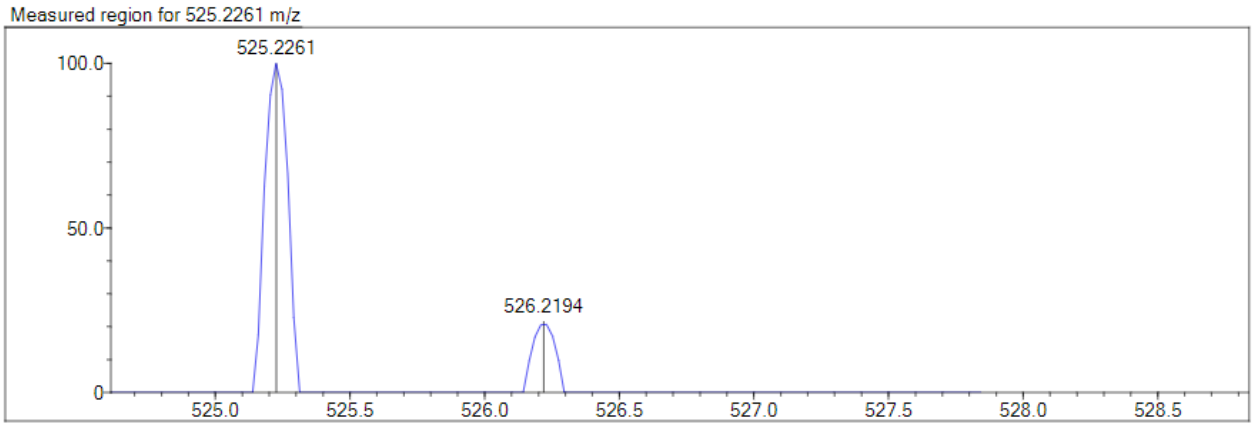
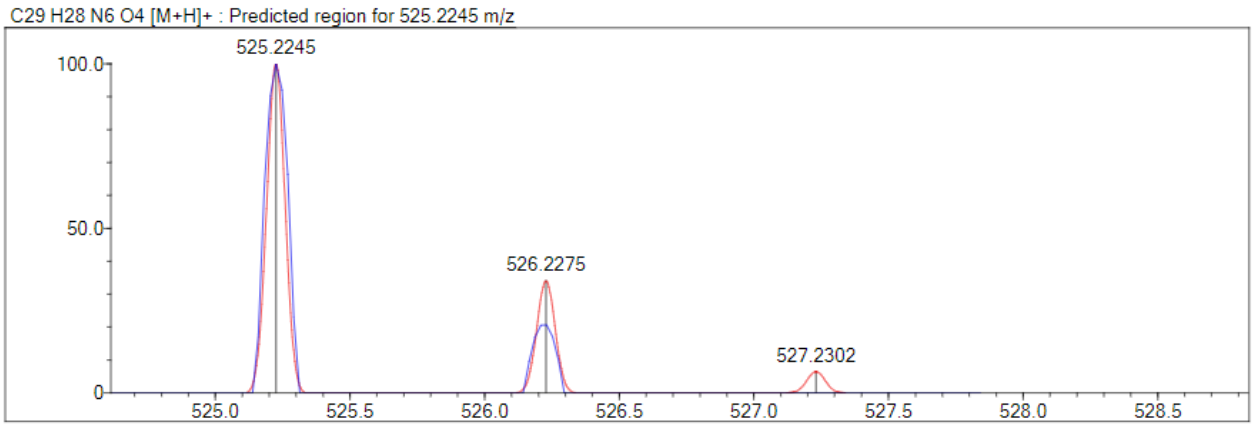
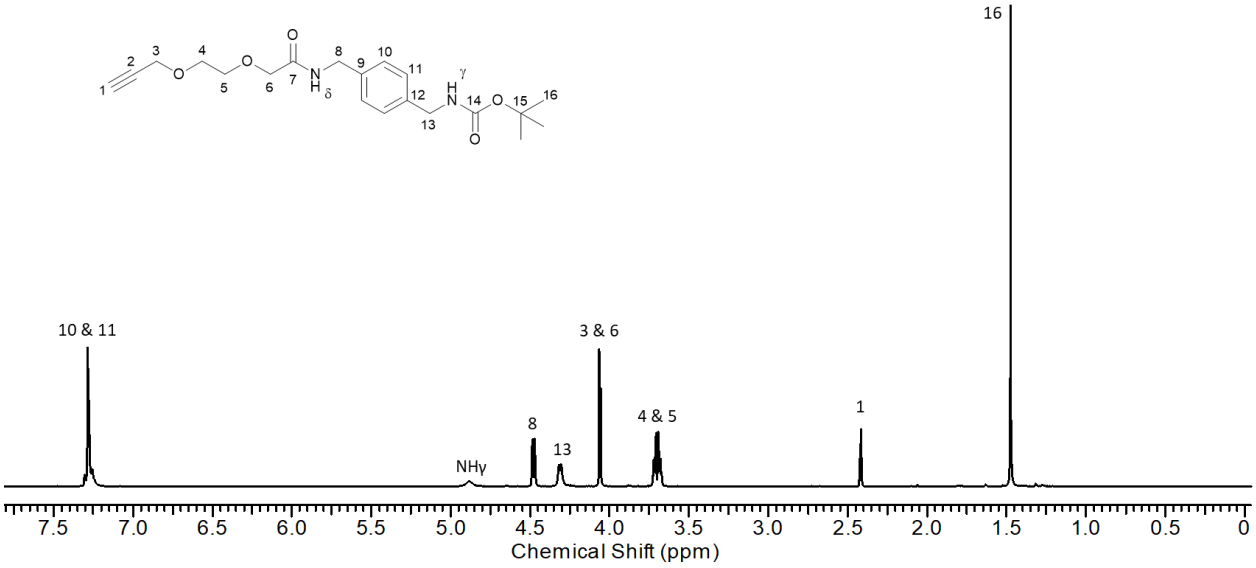


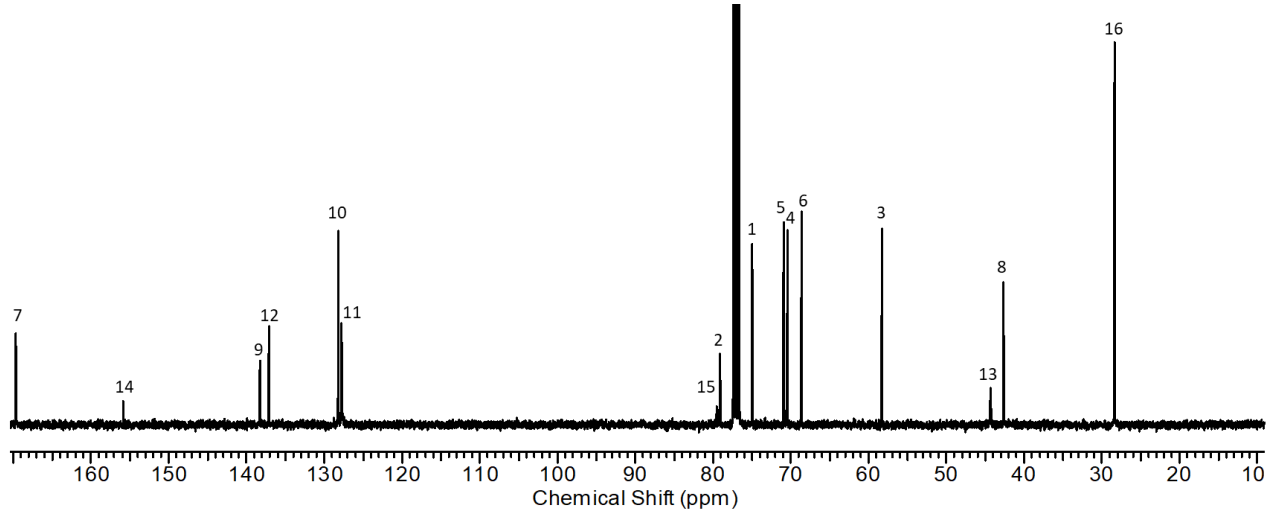


Alkyne 7

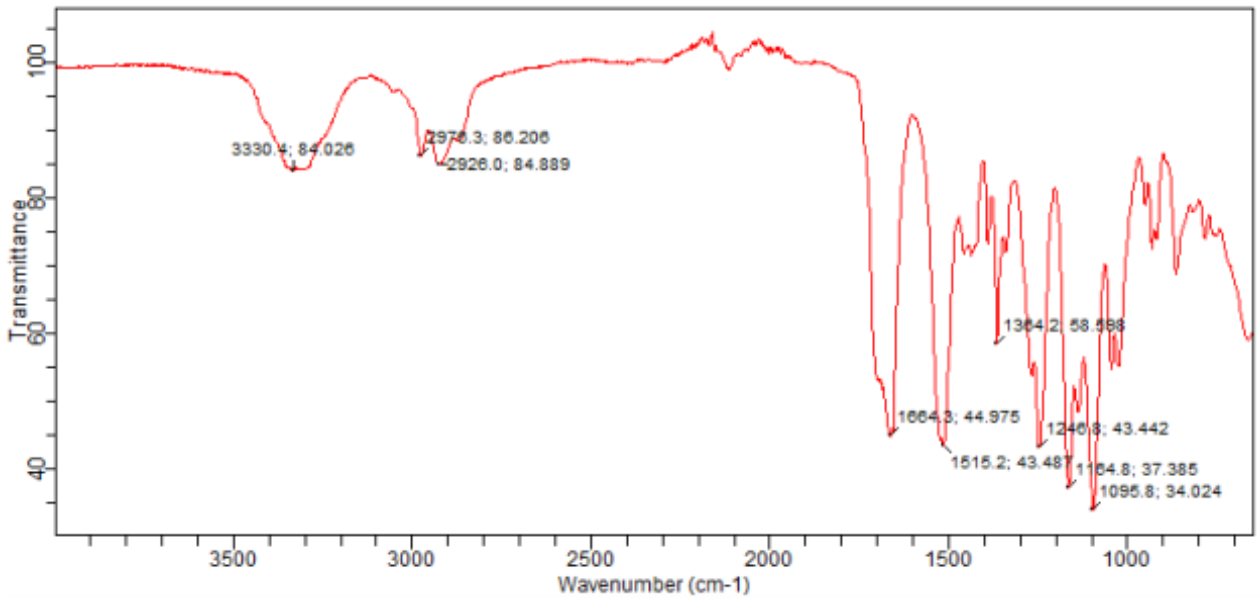
^{1}H NMR: (400 MHz, $CDCl_3$)



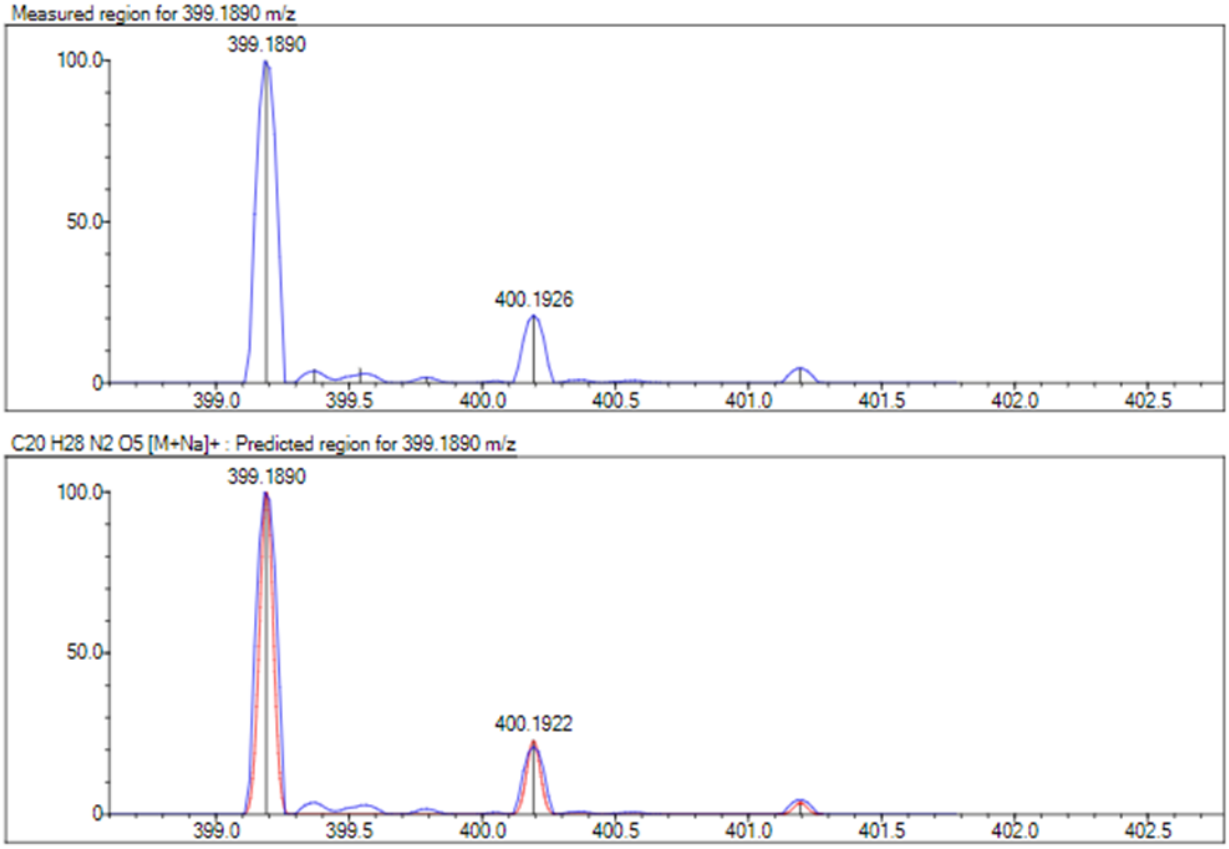
^{13}C NMR: (100 MHz, $CDCl_3$)



IR Spectrum (neat)

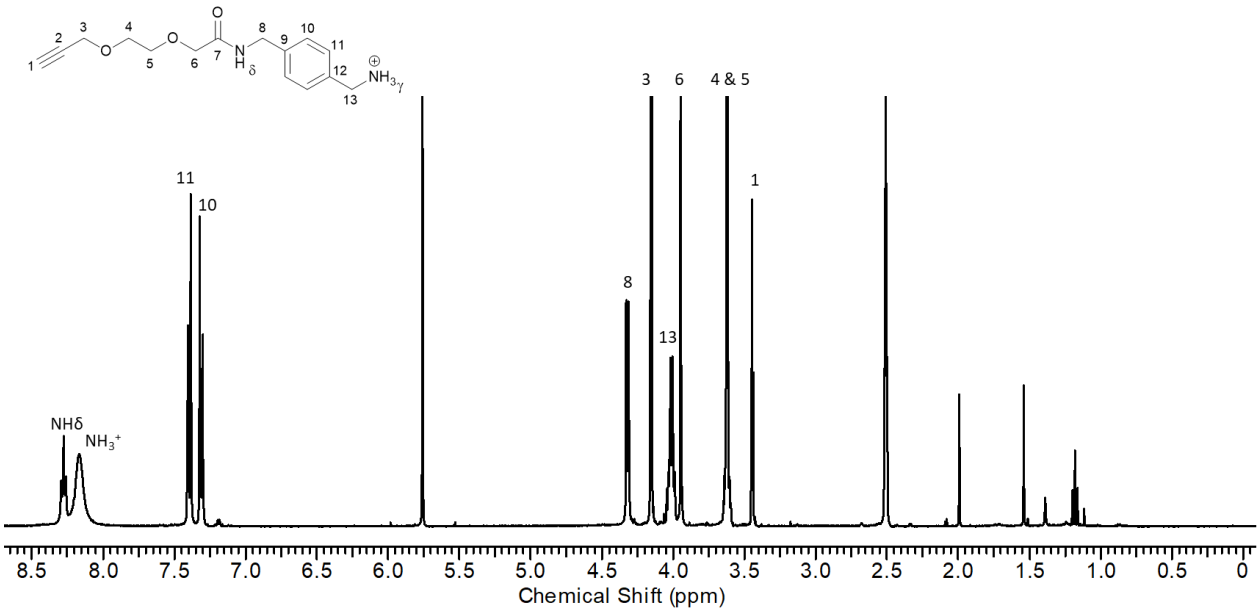


HRMS (ES +ve)



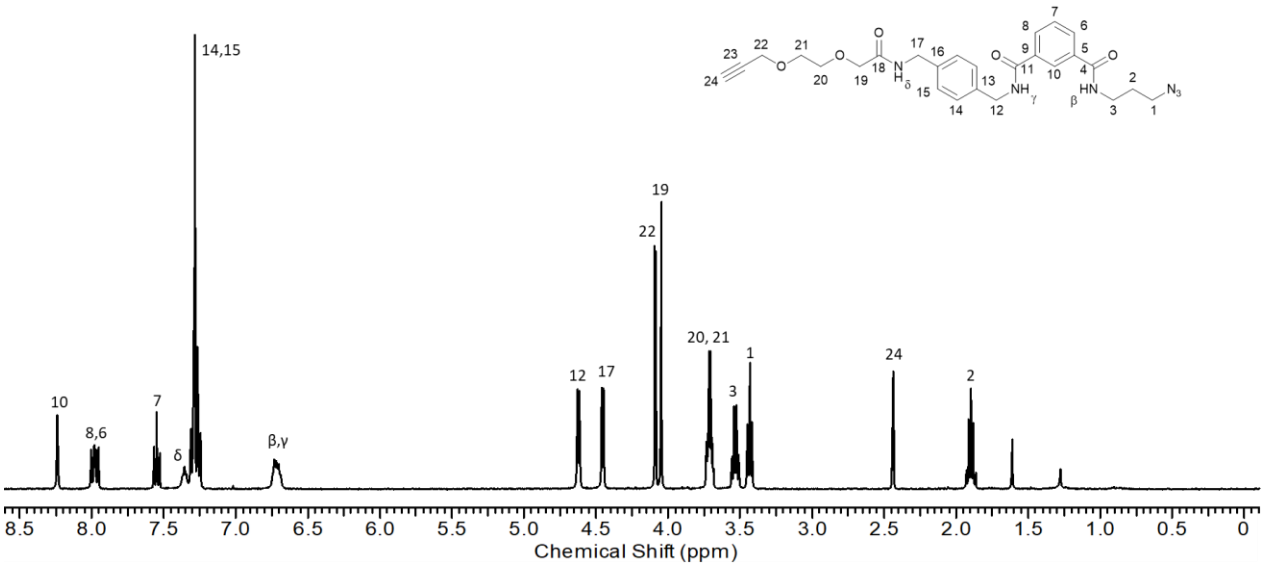
Deprotected amine alkyne salt 10

^{1}H NMR: (400 MHz, D_6-DMSO)

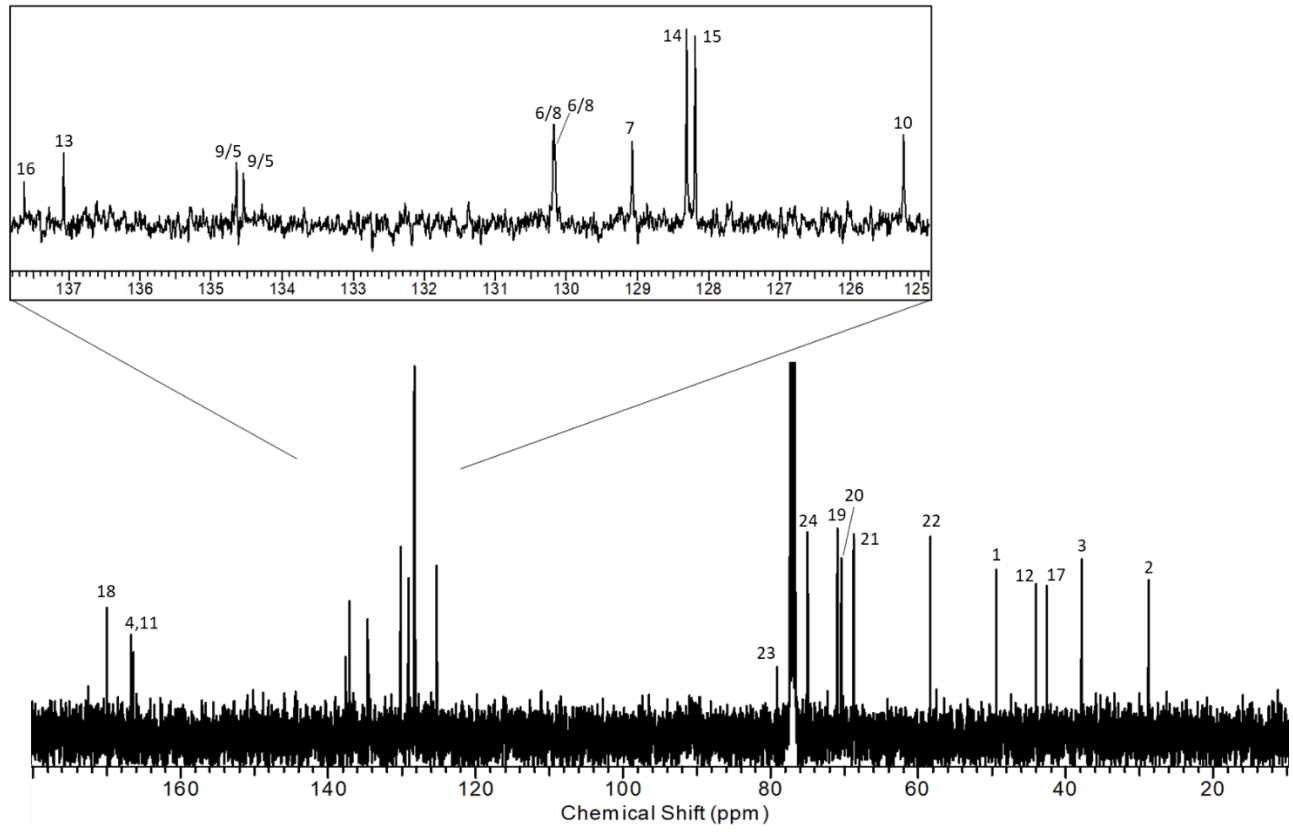


Alkyne-azide 13

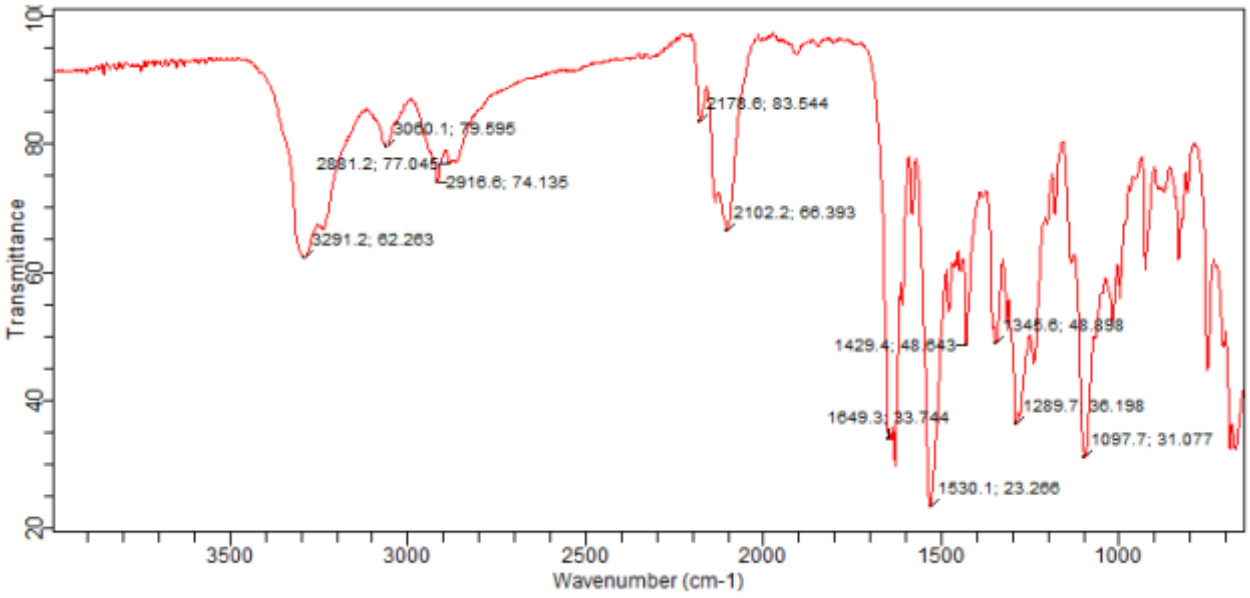
^{1}H NMR: (400 MHz, $CDCl_3$)



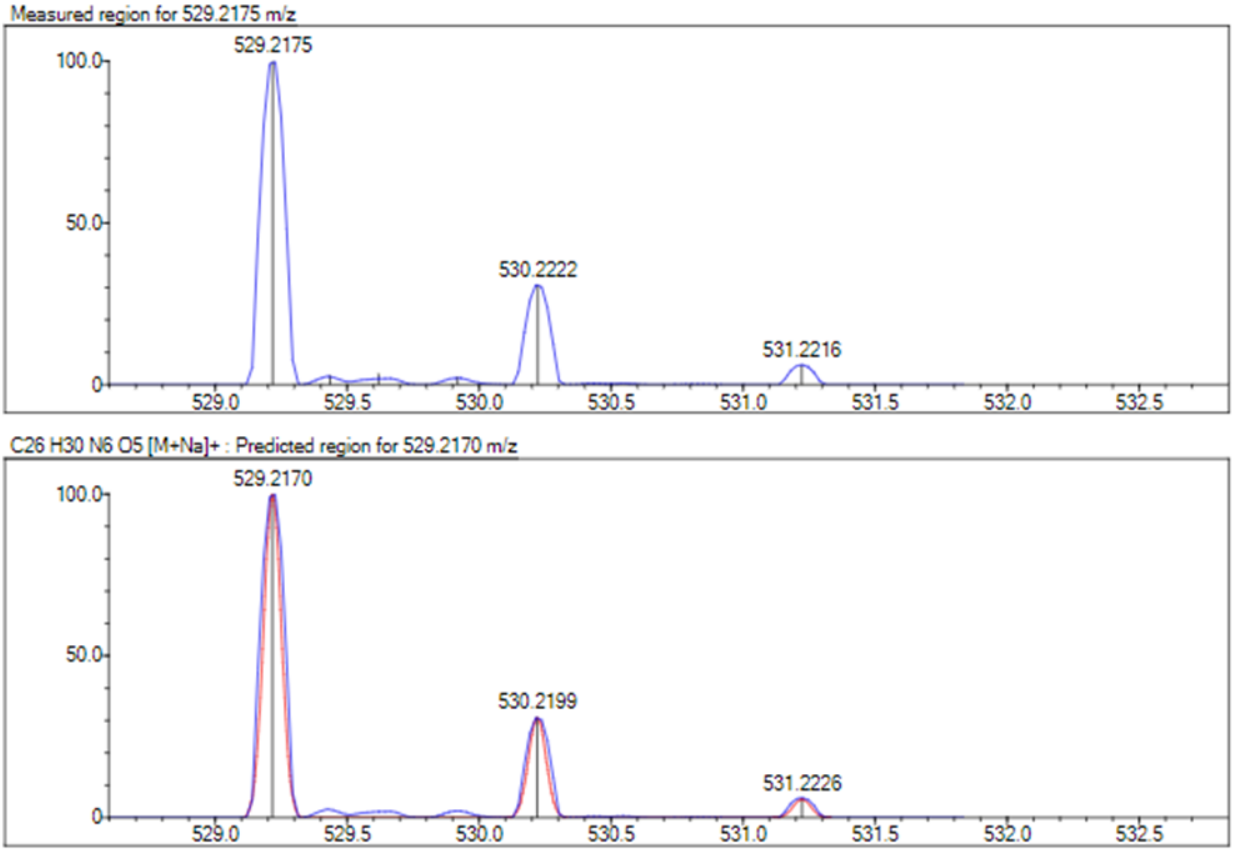
^{13}C NMR: (100 MHz, $CDCl_3$)



IR Spectrum (neat)

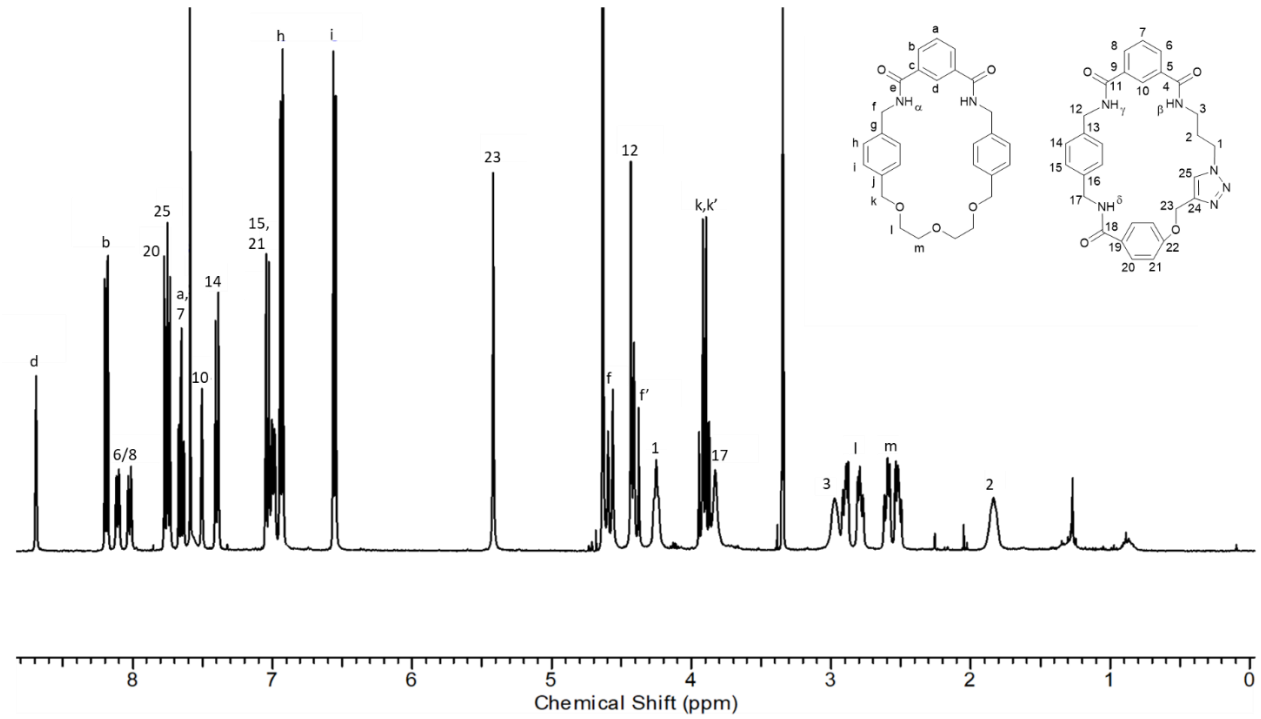


HRMS (ES +ve)

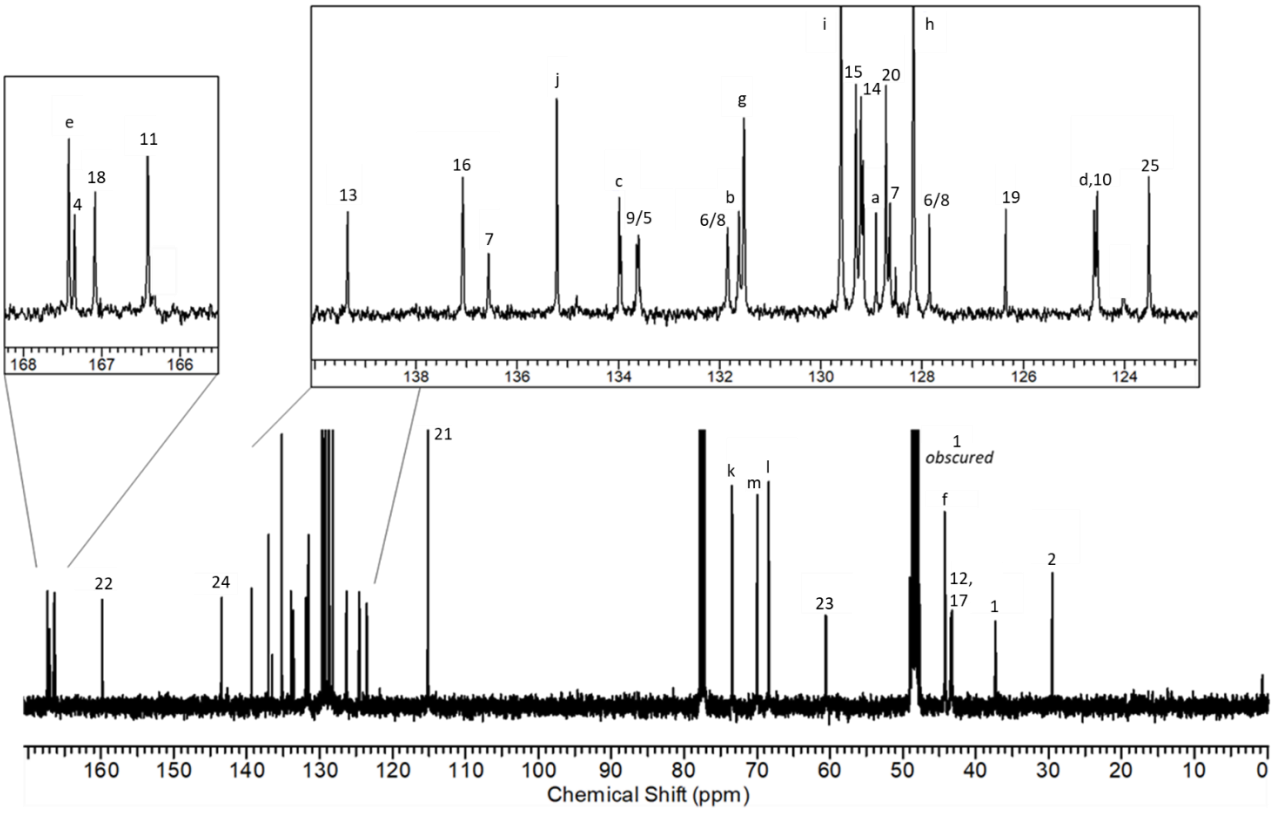


Catenane 15

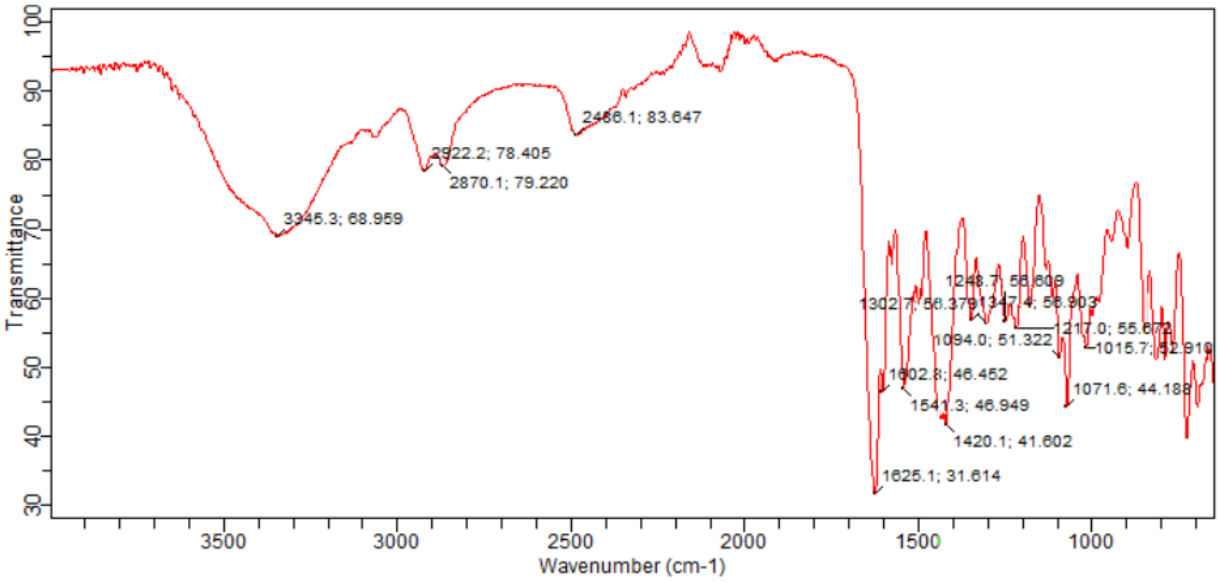
^{1}H NMR: (400 MHz, 50:50 $CDCl_3/CD_3OD$)



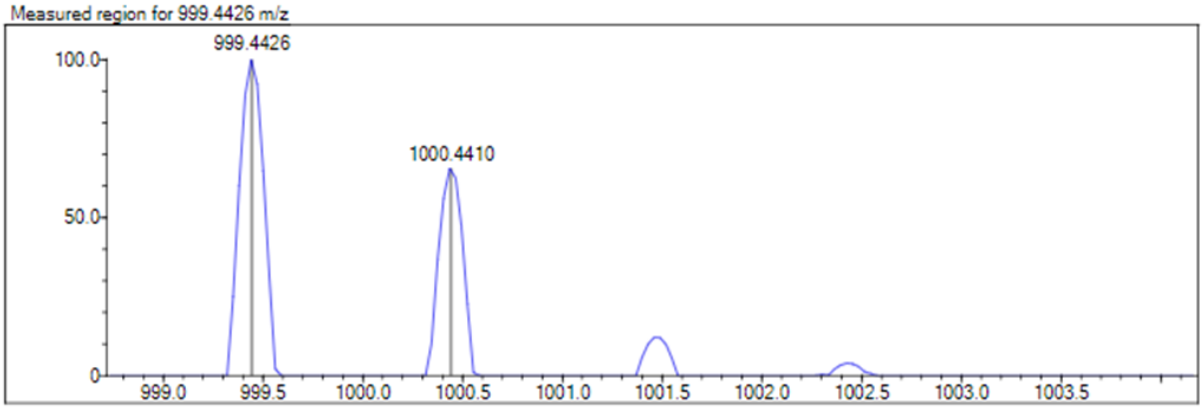
^{13}C NMR: (100 MHz, 50:50 $CDCl_3/CD_3OD$)

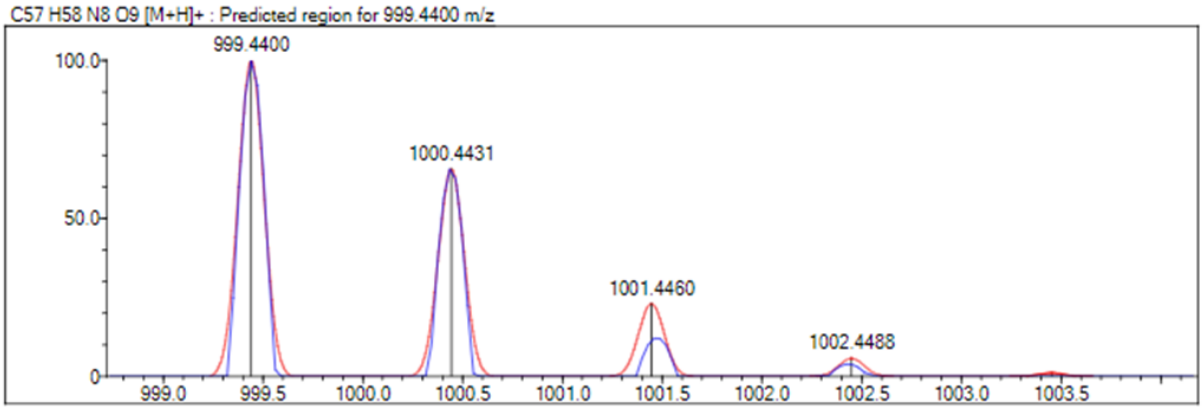


IR Spectrum (neat)



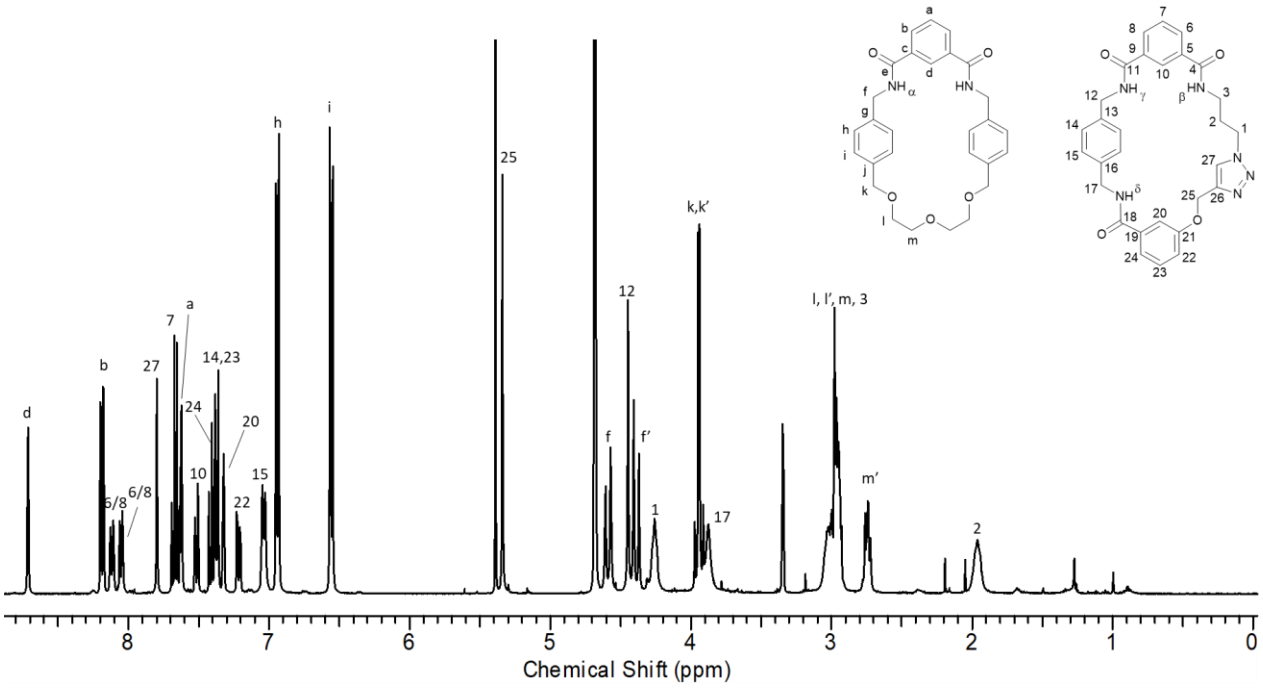
HRMS (ES +ve)





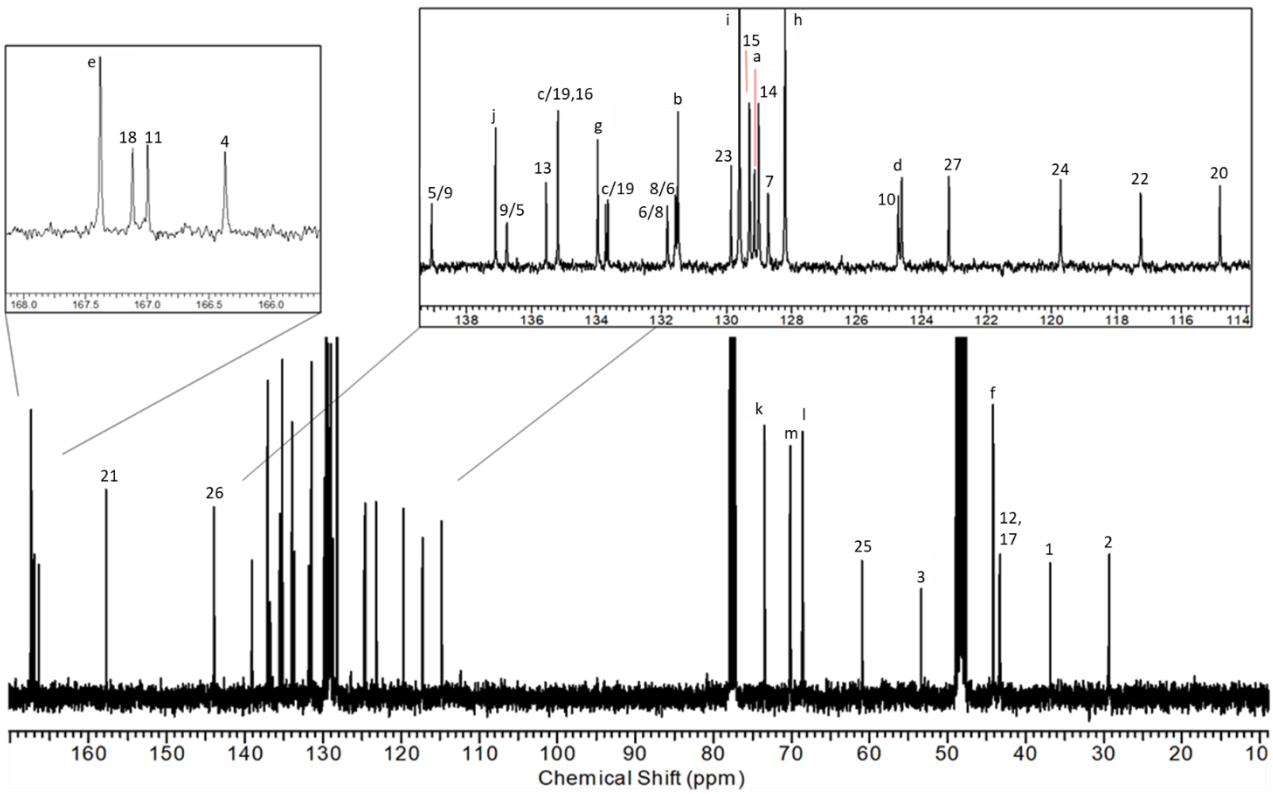
Catenane 16

^{1}H NMR: (400 MHz, 50:50 $CDCl_3/CD_3OD$)

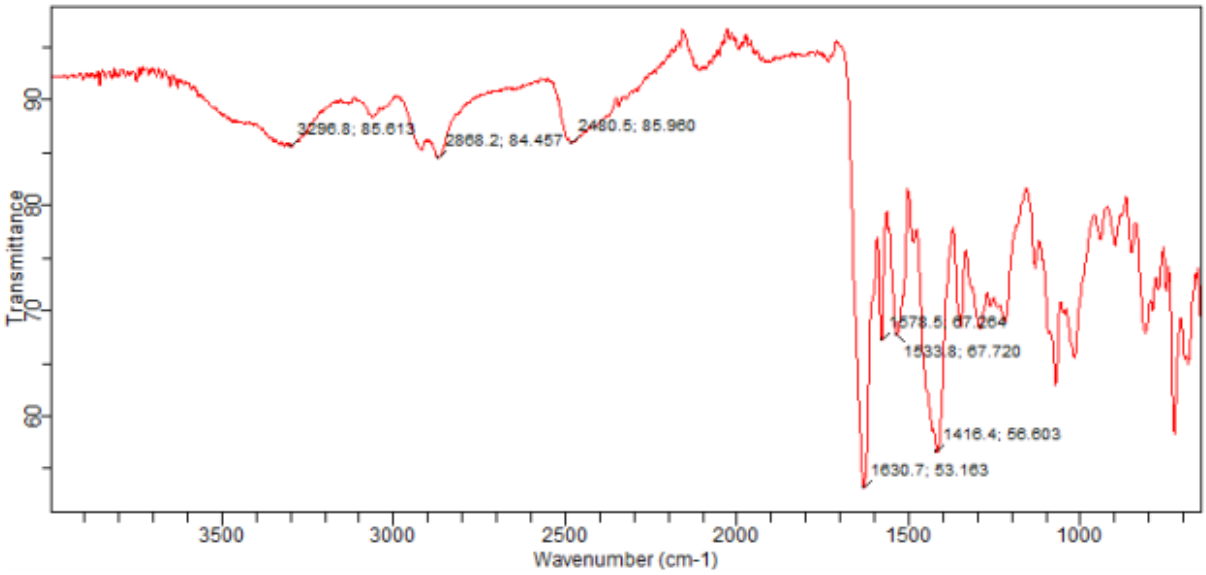


NB: Despite drying, residual CH_2Cl_2 (1 eq) from purification remains in sample.

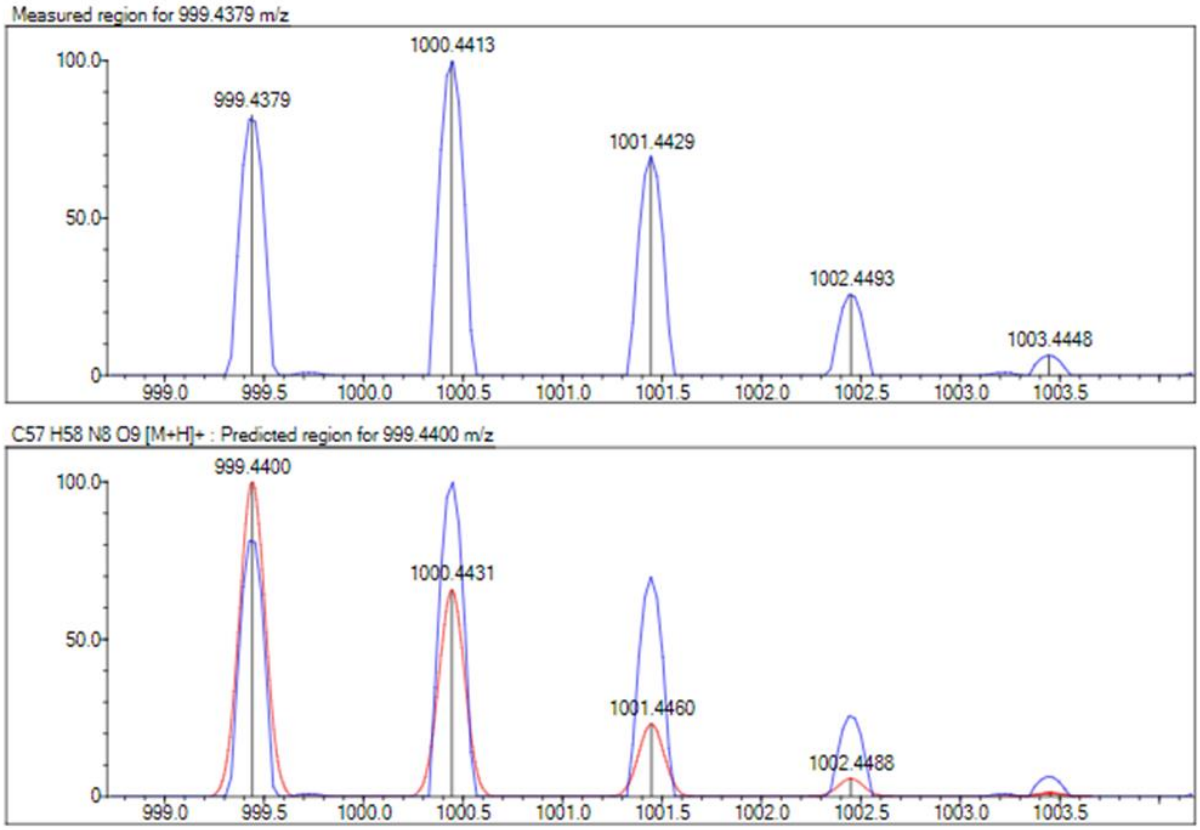
^{13}C NMR: (100 MHz, 50:50 $CDCl_3/CD_3OD$)



IR Spectrum (neat)



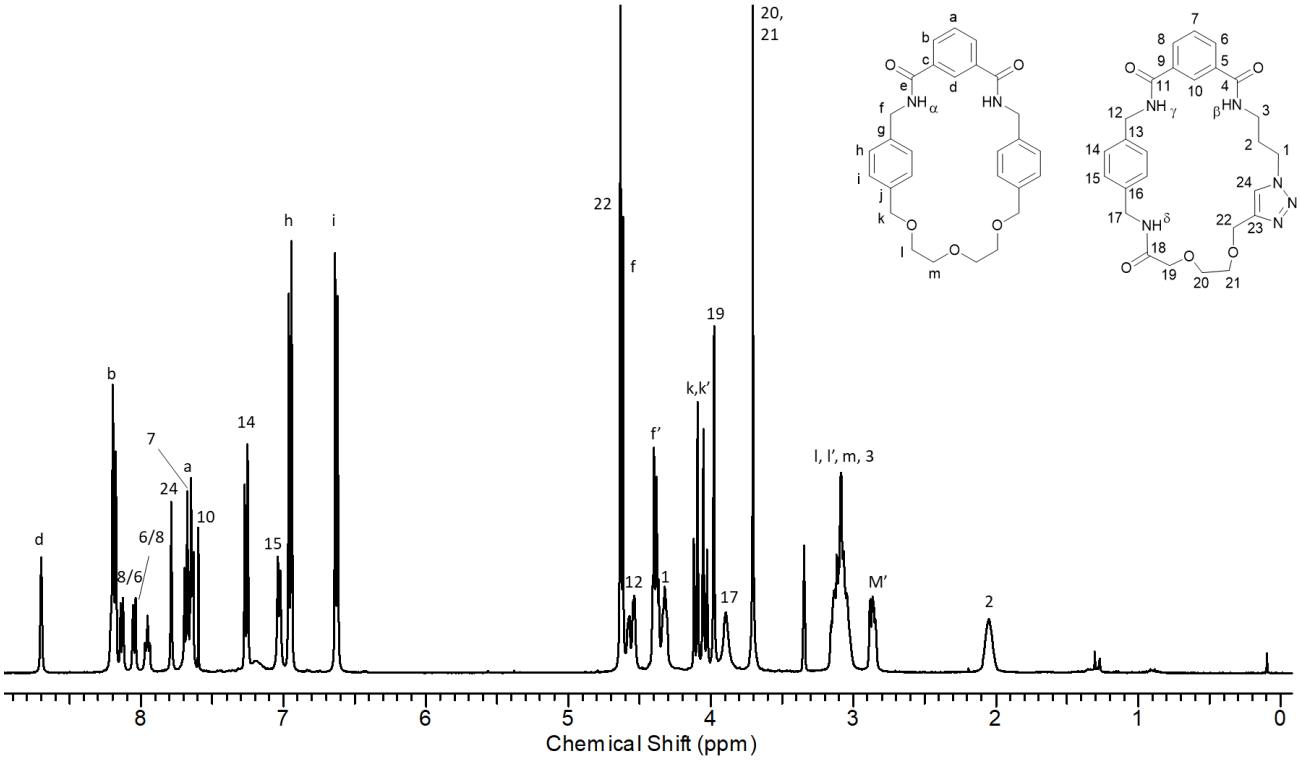
HRMS (ES +ve)



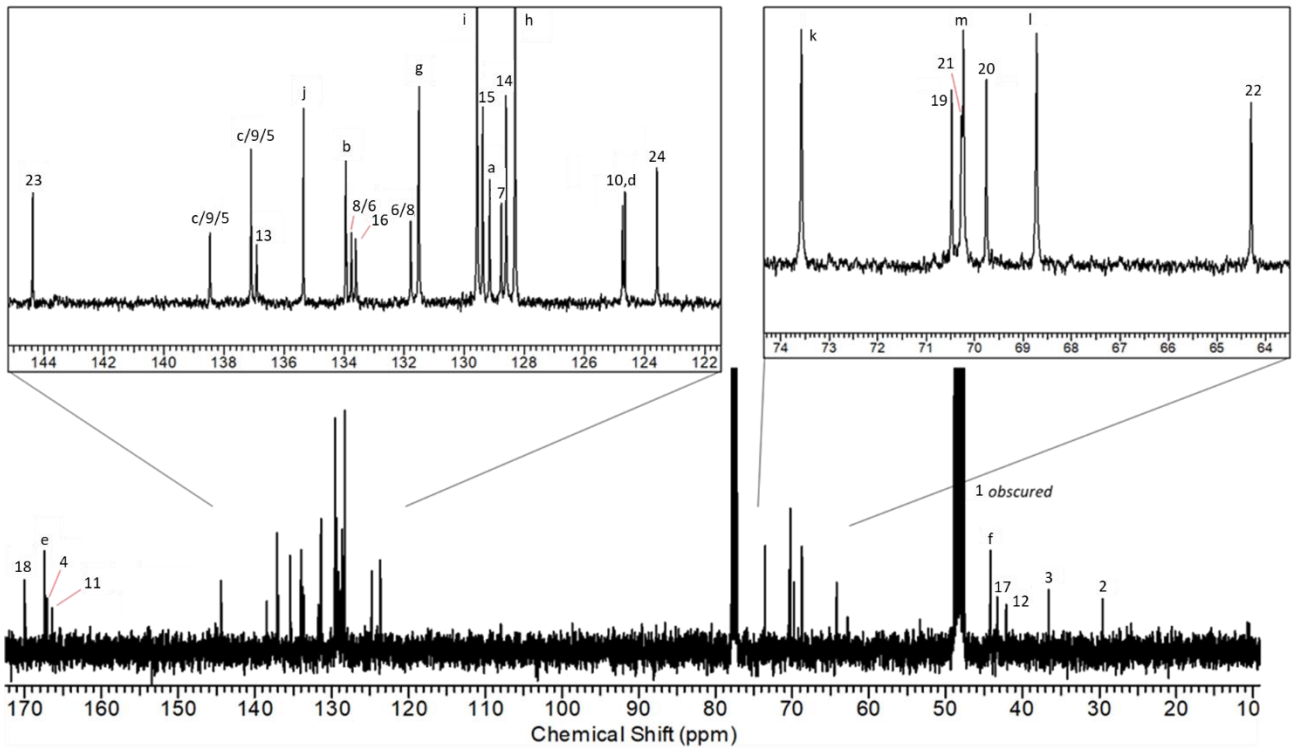
NB: Evidence of some H/D exchange (samples exposed to $CDCl_3$/CD_3OD).

Catenane 17

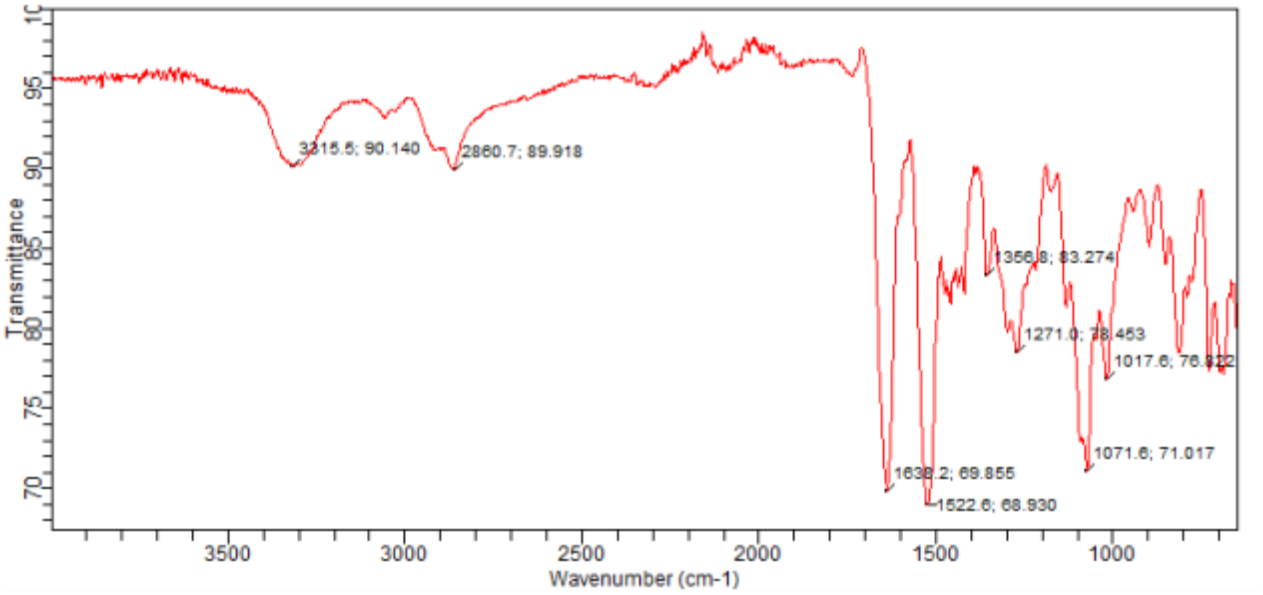
^{1}H NMR: (400 MHz, 50:50 $CDCl_3/CD_3OD$)



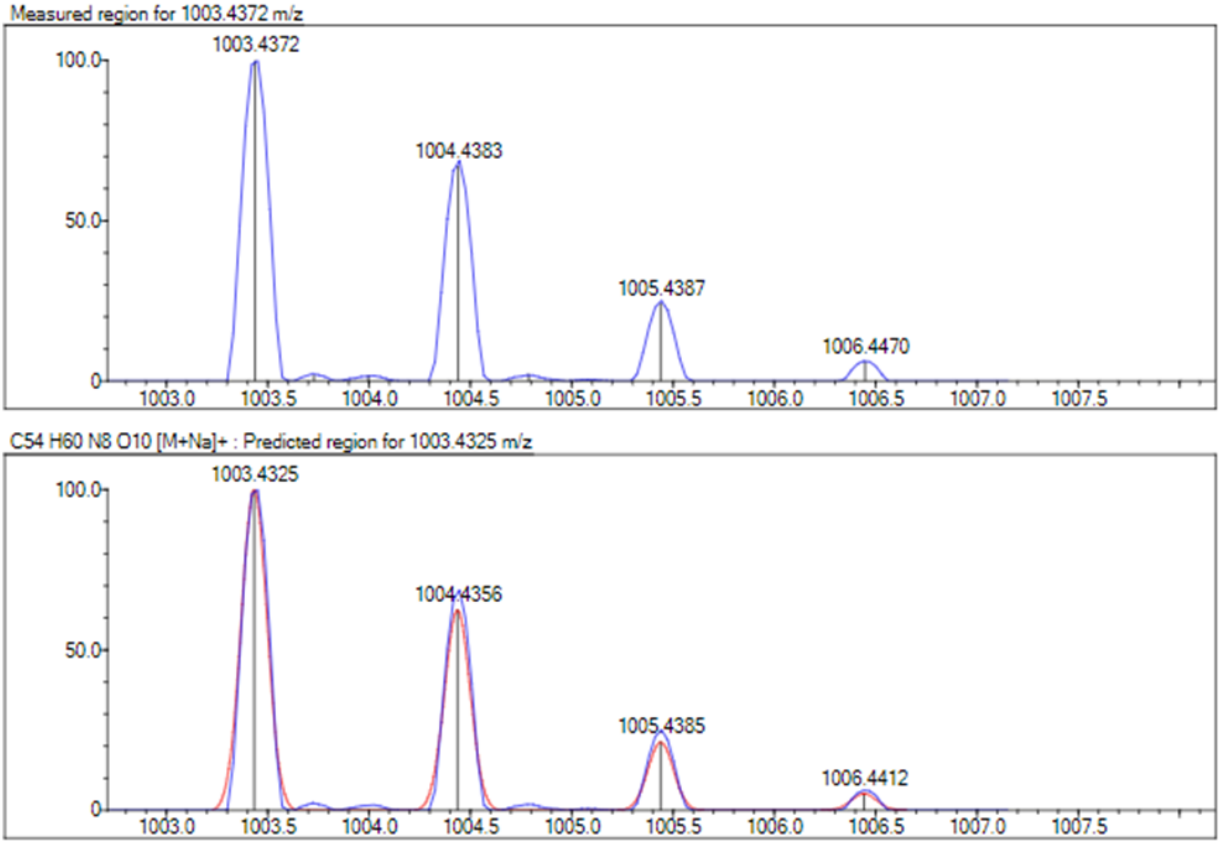
^{13}C NMR: (100 MHz, 50:50 $CDCl_3/CD_3OD$)



IR Spectrum (neat)

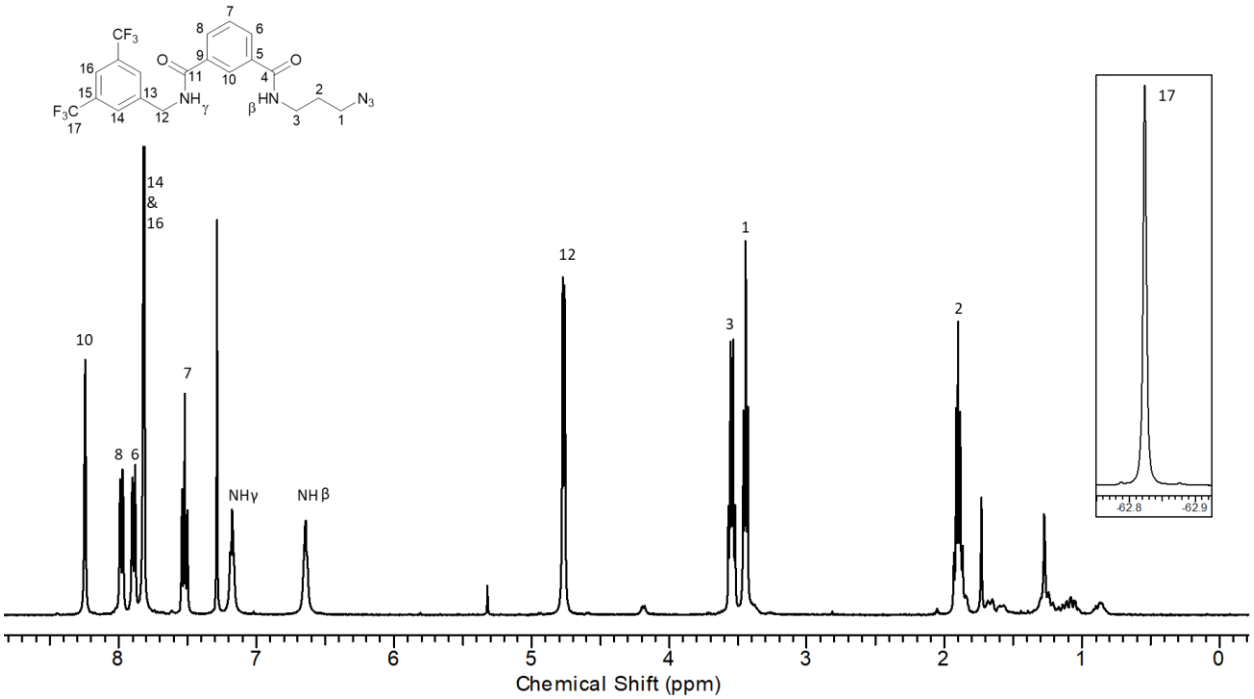


HRMS (ES +ve)

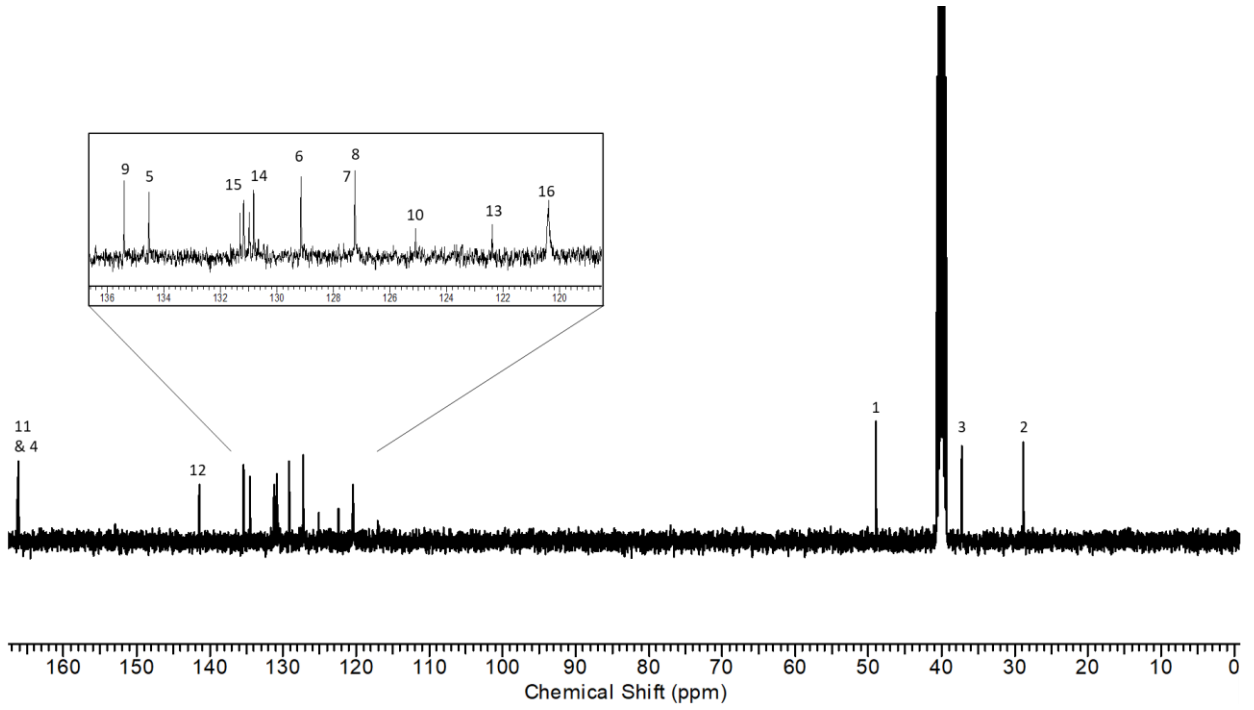


Azide 18

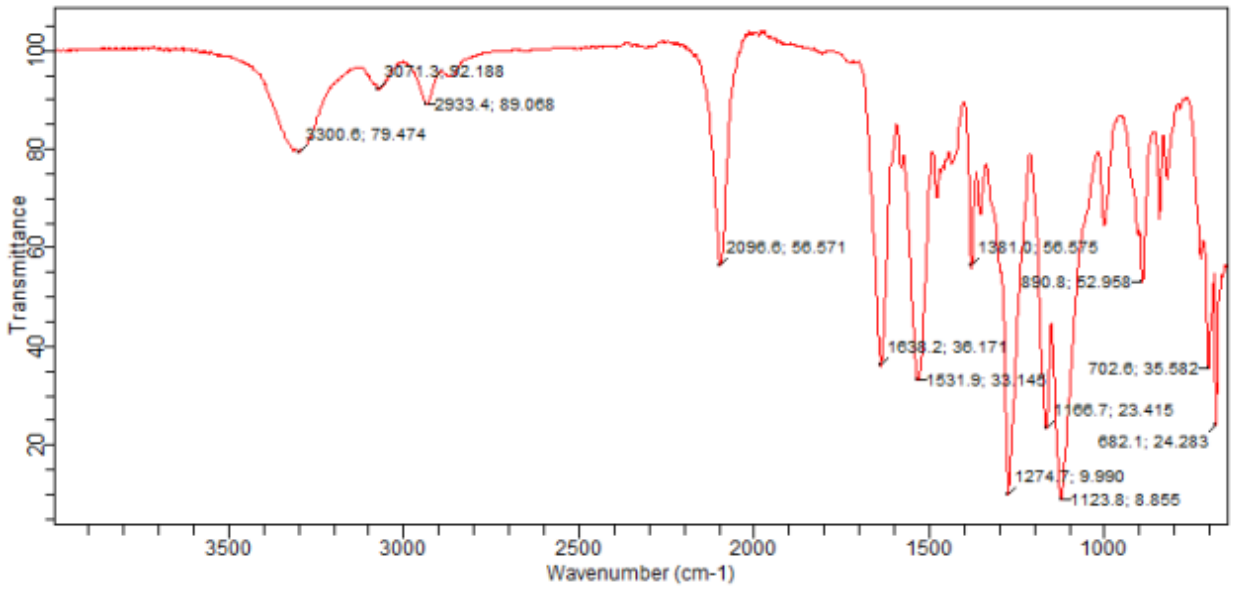
^{1}H NMR: (400 MHz, $CDCl_3$) with ^{19}F NMR insert (377 MHz)



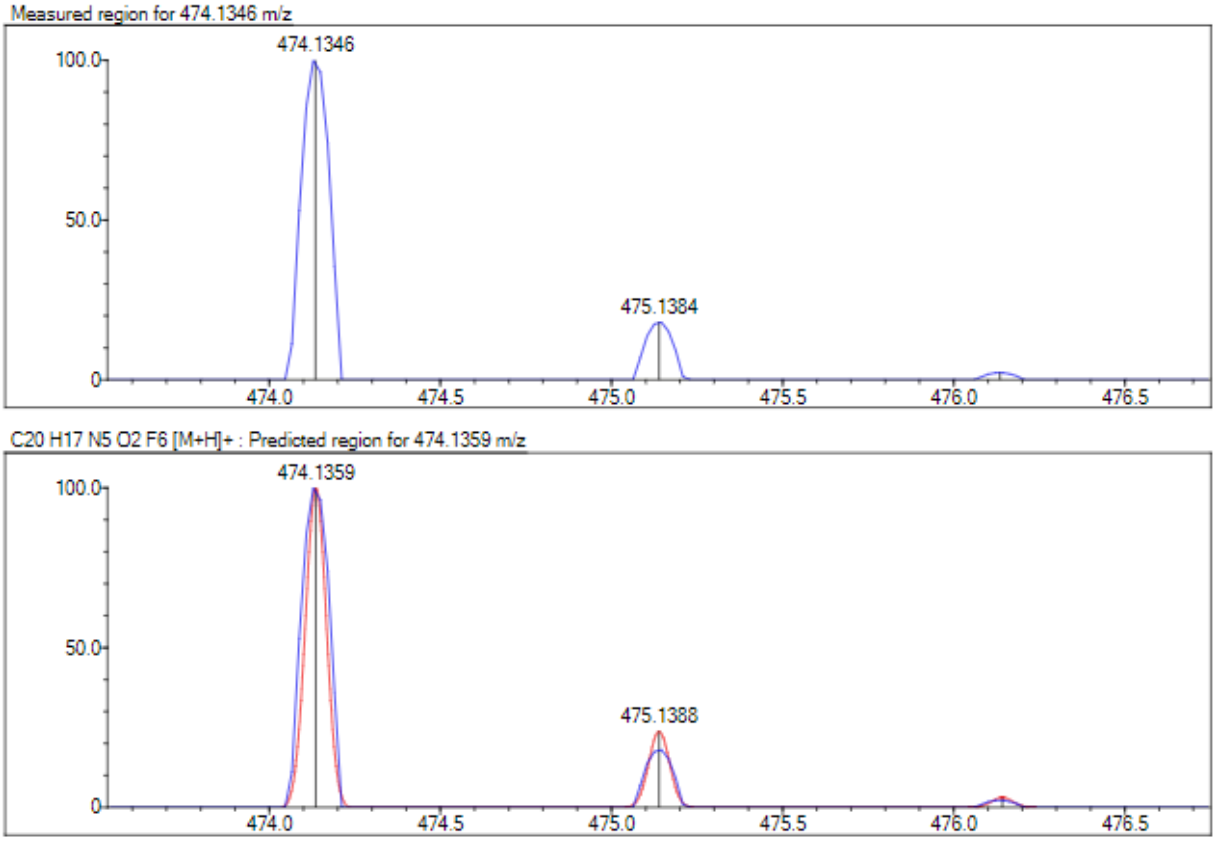
^{13}C NMR: (100 MHz, D_6-DMSO)



IR Spectrum (neat)

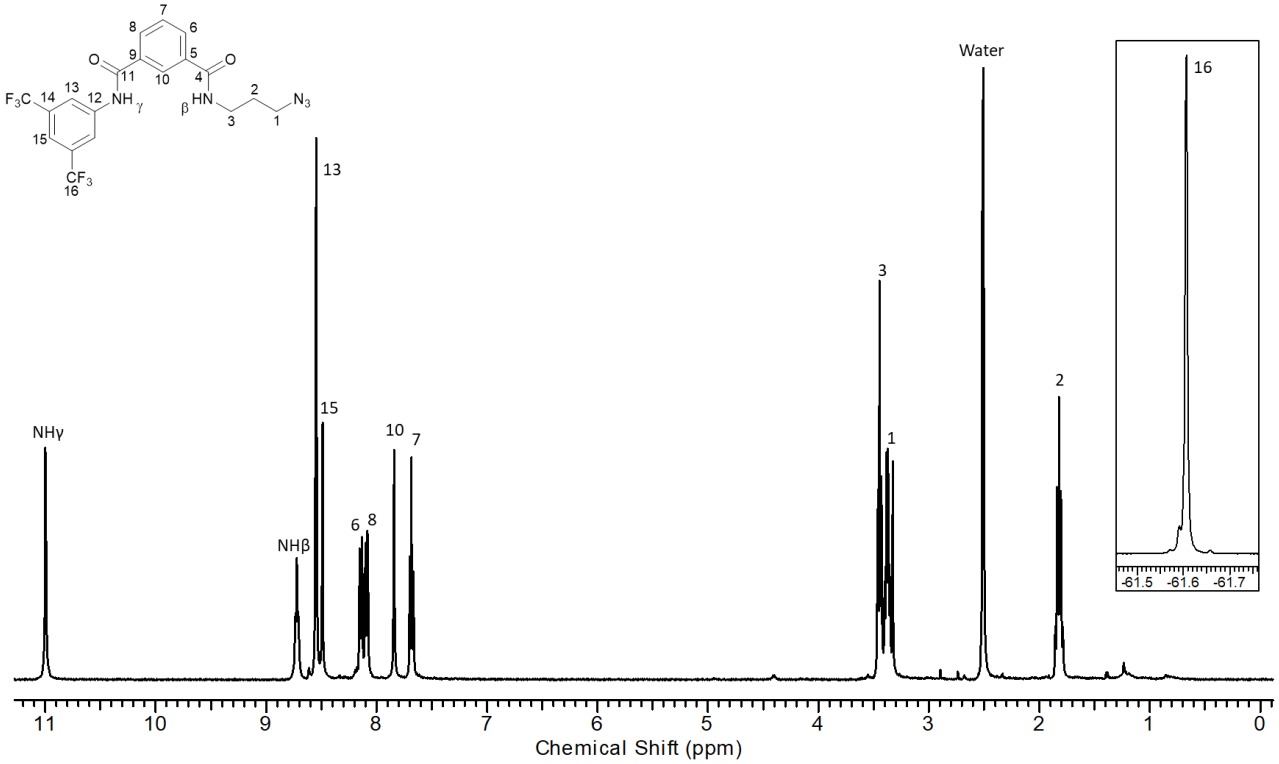


HRMS (ES +ve)

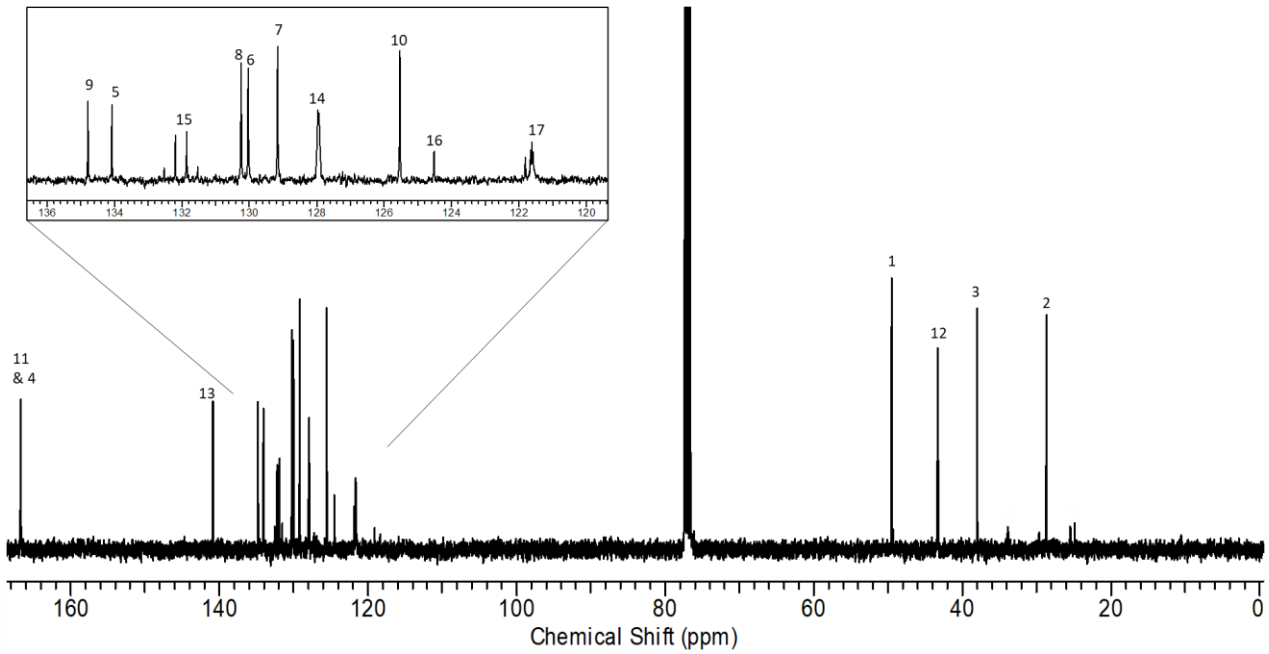


Azide 19

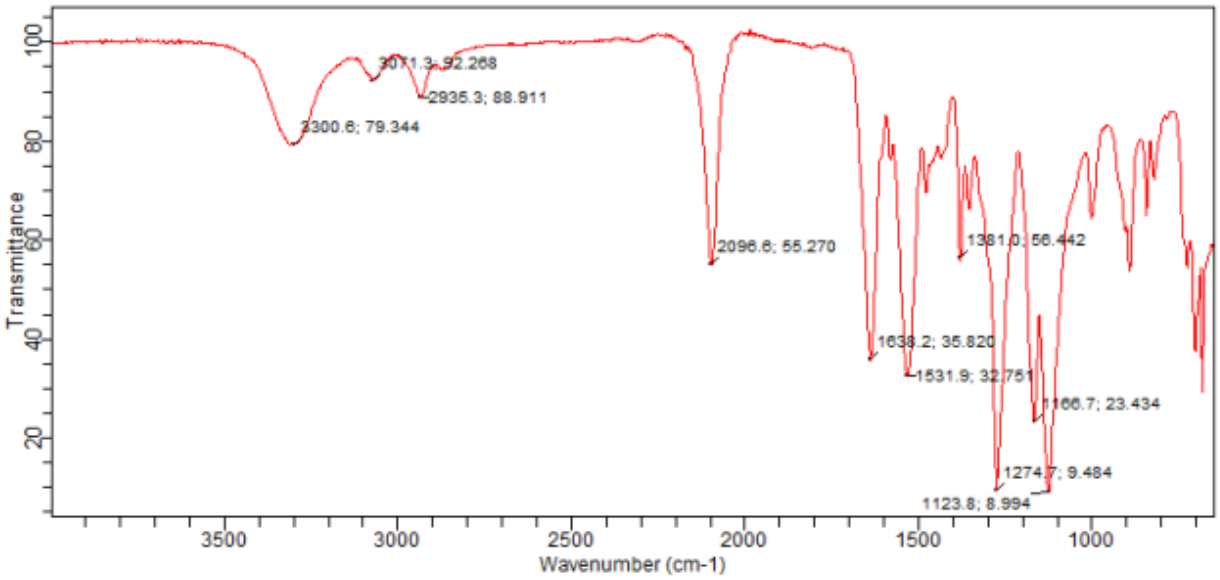
^{1}H NMR: (400 MHz, D_6-DMSO) with ^{19}F NMR insert (377 MHz)



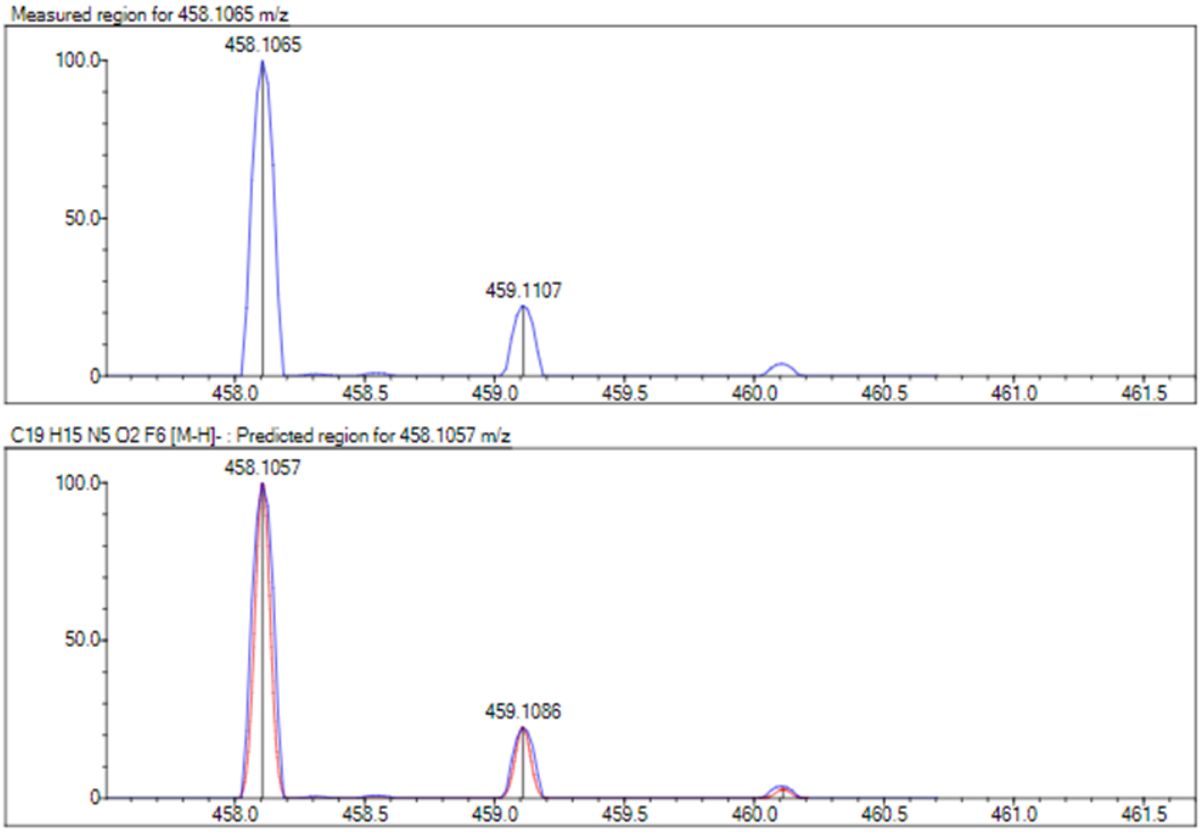
^{13}C NMR: (100 MHz, D_6-DMSO)



IR Spectrum (neat)

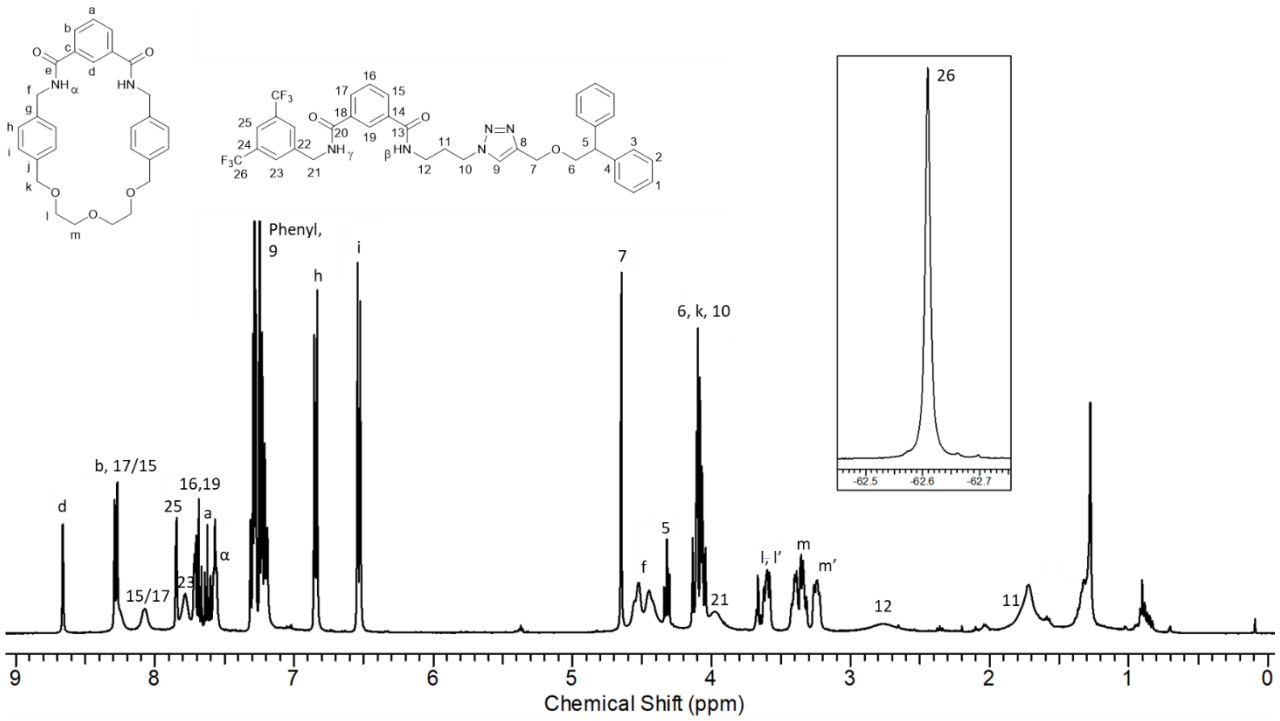


HRMS (ES +ve)

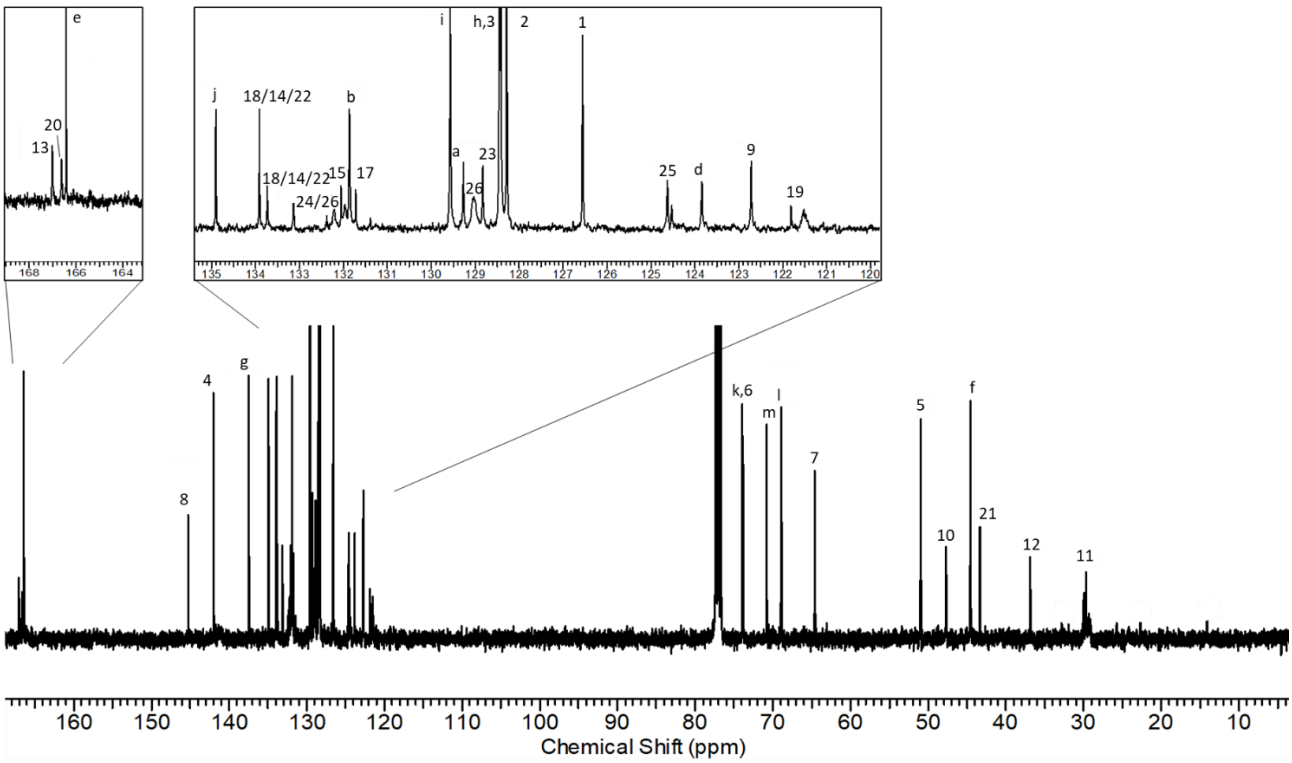


Rotaxane 21

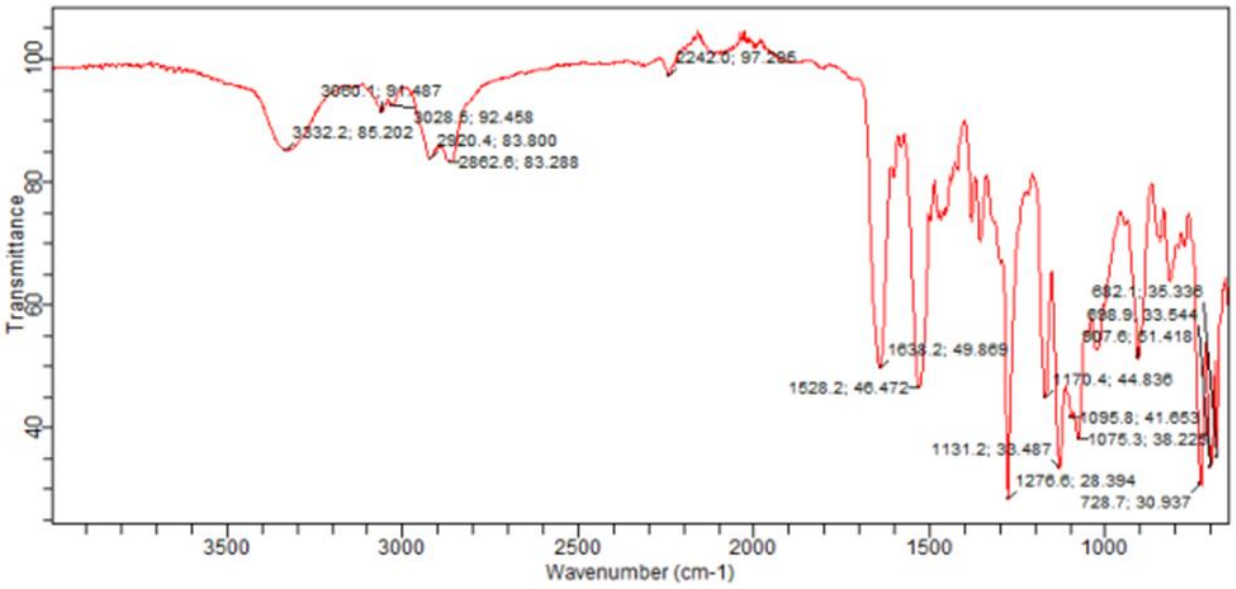
^{1}H NMR: (400 MHz, $CDCl_3$) with ^{19}F NMR insert (377 MHz)



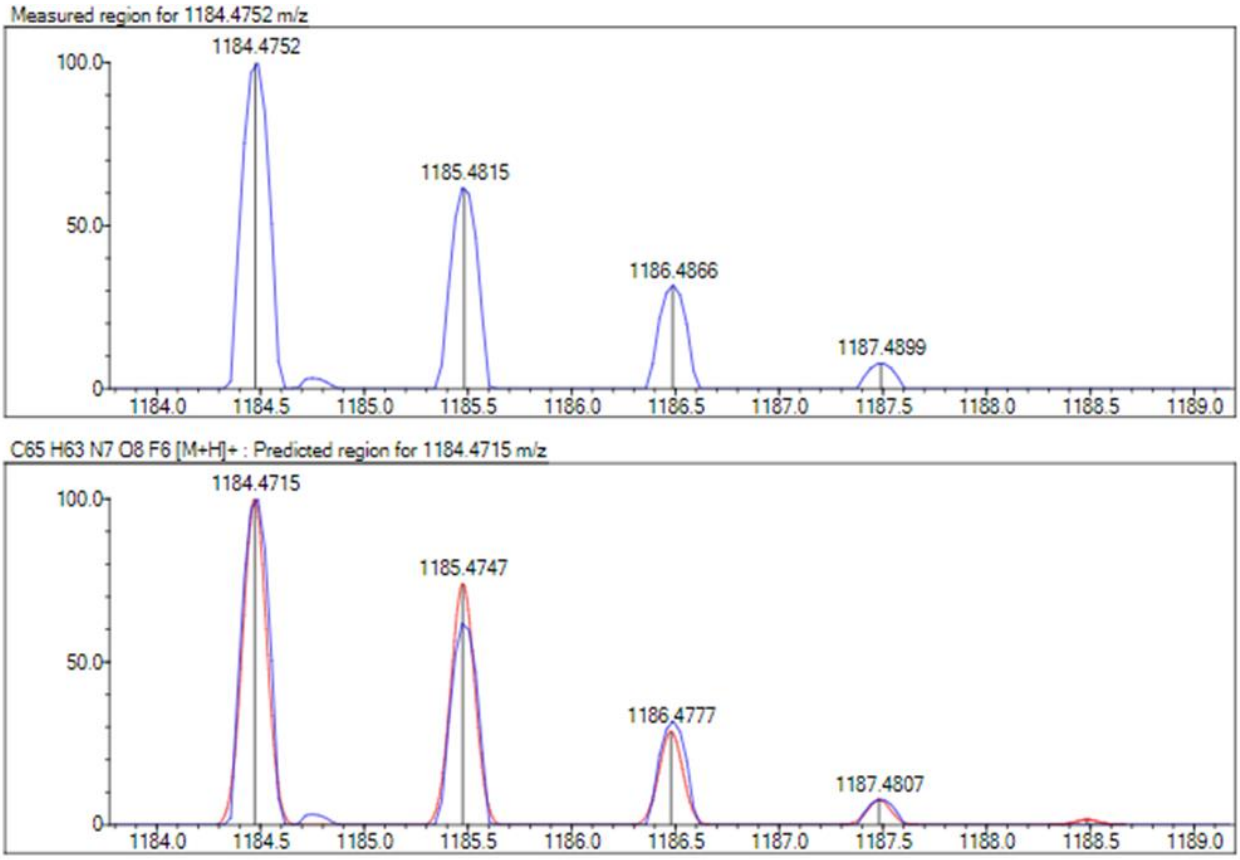
^{13}C NMR: (100 MHz, $CDCl_3$)



IR Spectrum (neat)

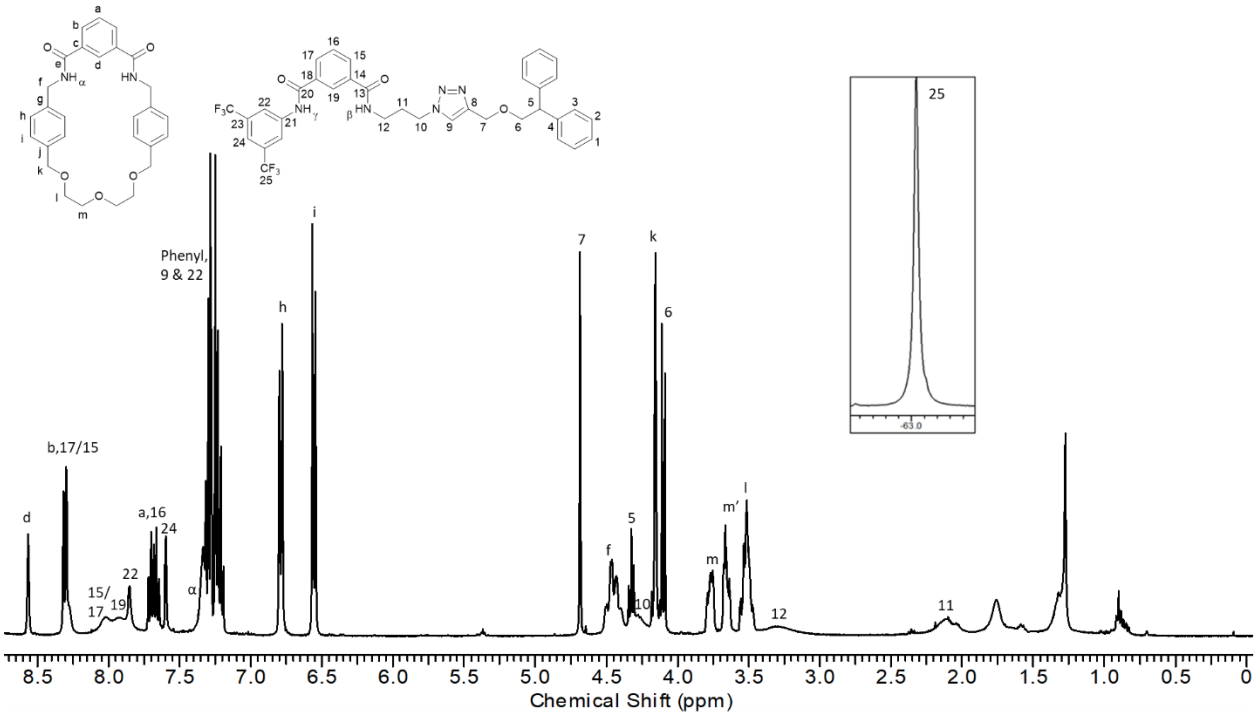


HRMS (ES +ve)

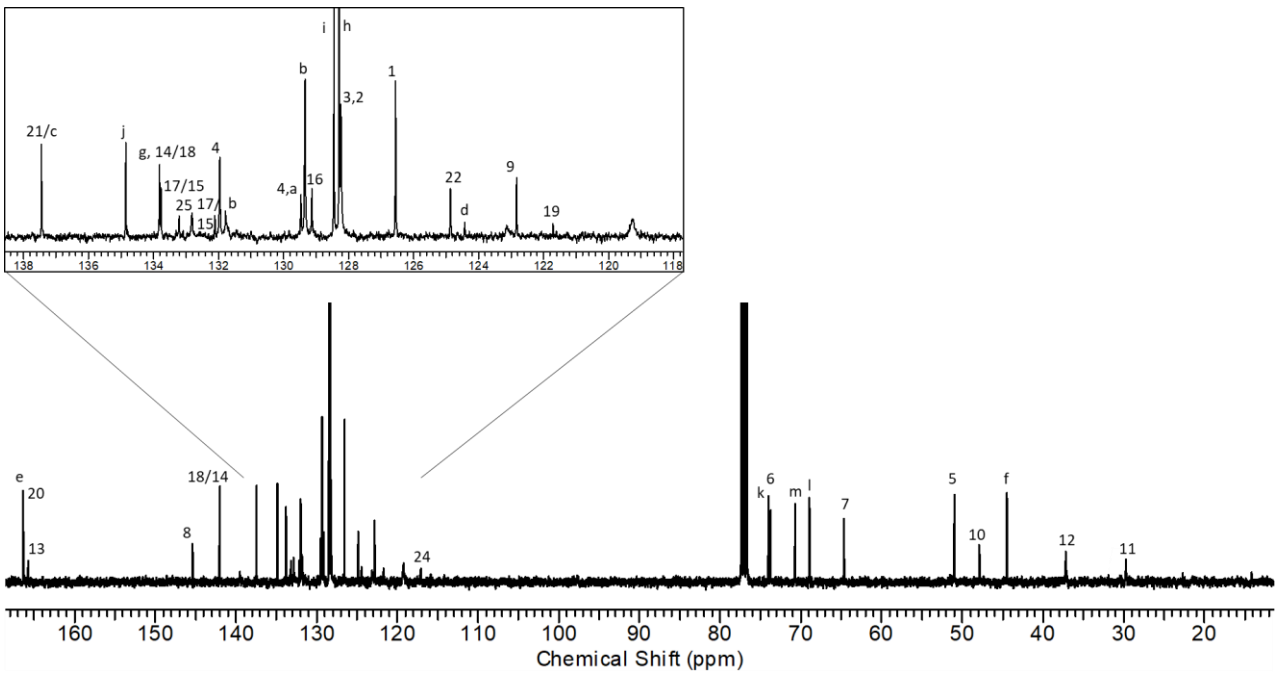


Rotaxane 23

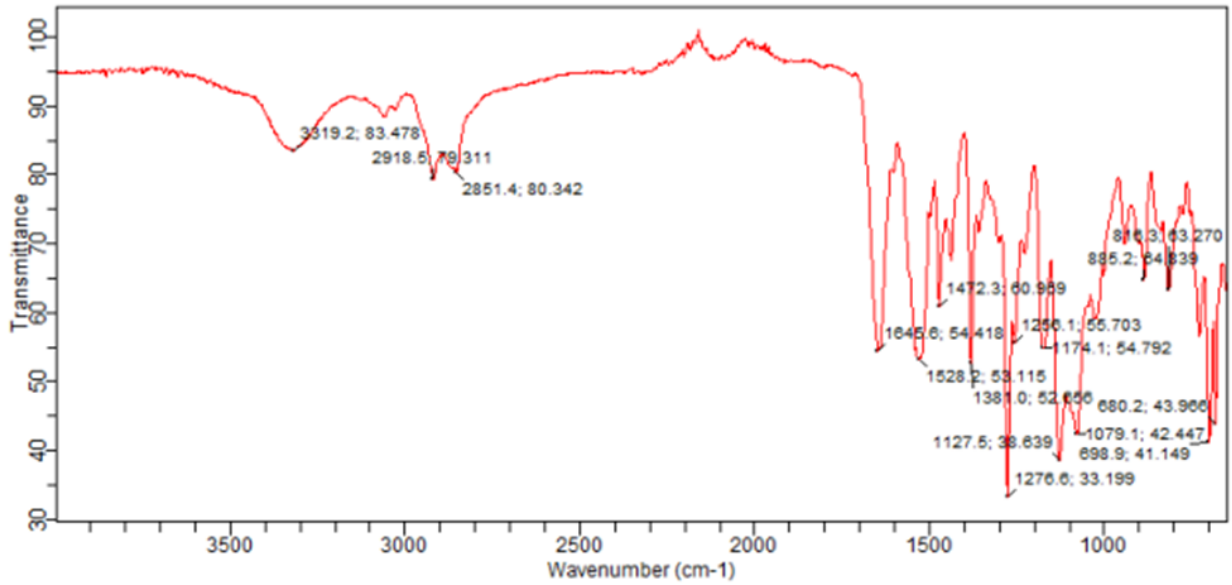
^{1}H NMR: (400 MHz, $CDCl_3$) with ^{19}F NMR insert (377 MHz)



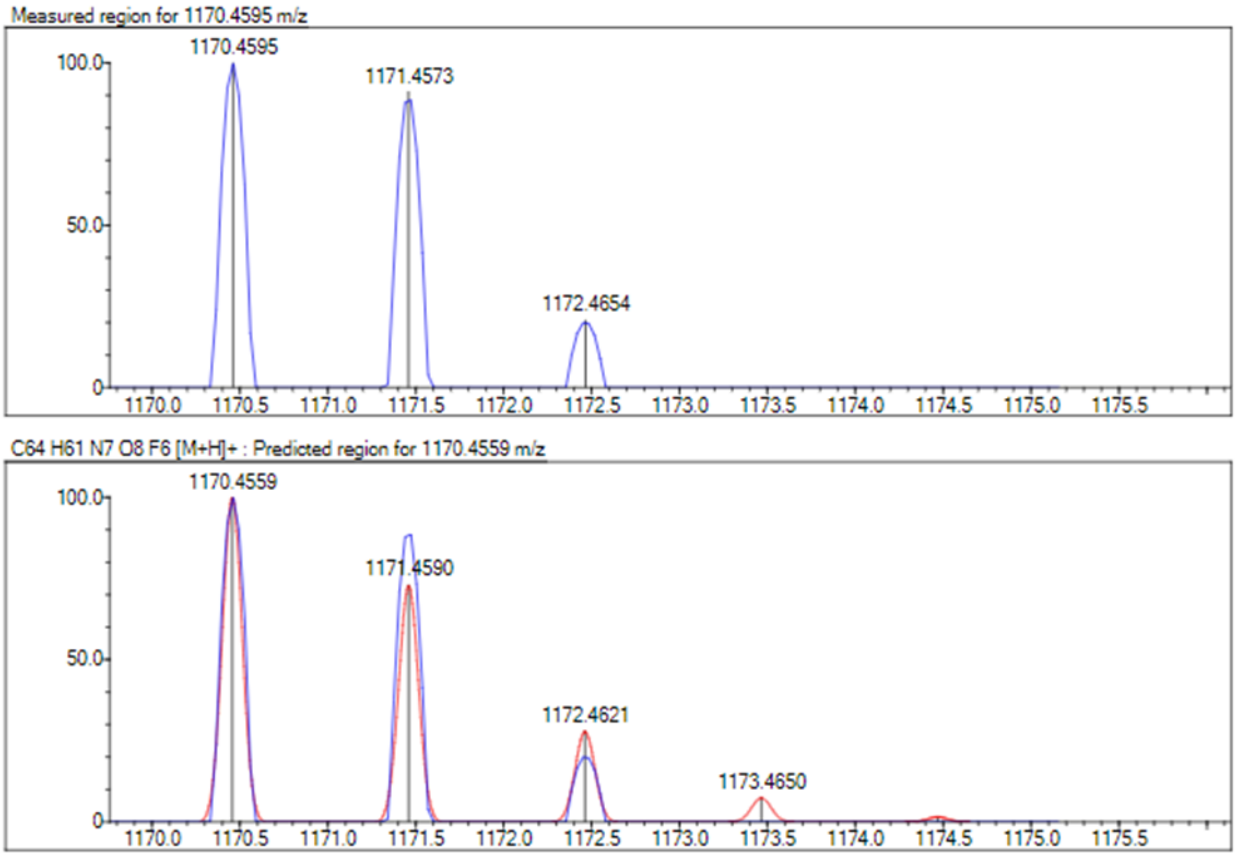
^{13}C NMR: (100 MHz, $CDCl_3$)



IR Spectrum (neat)

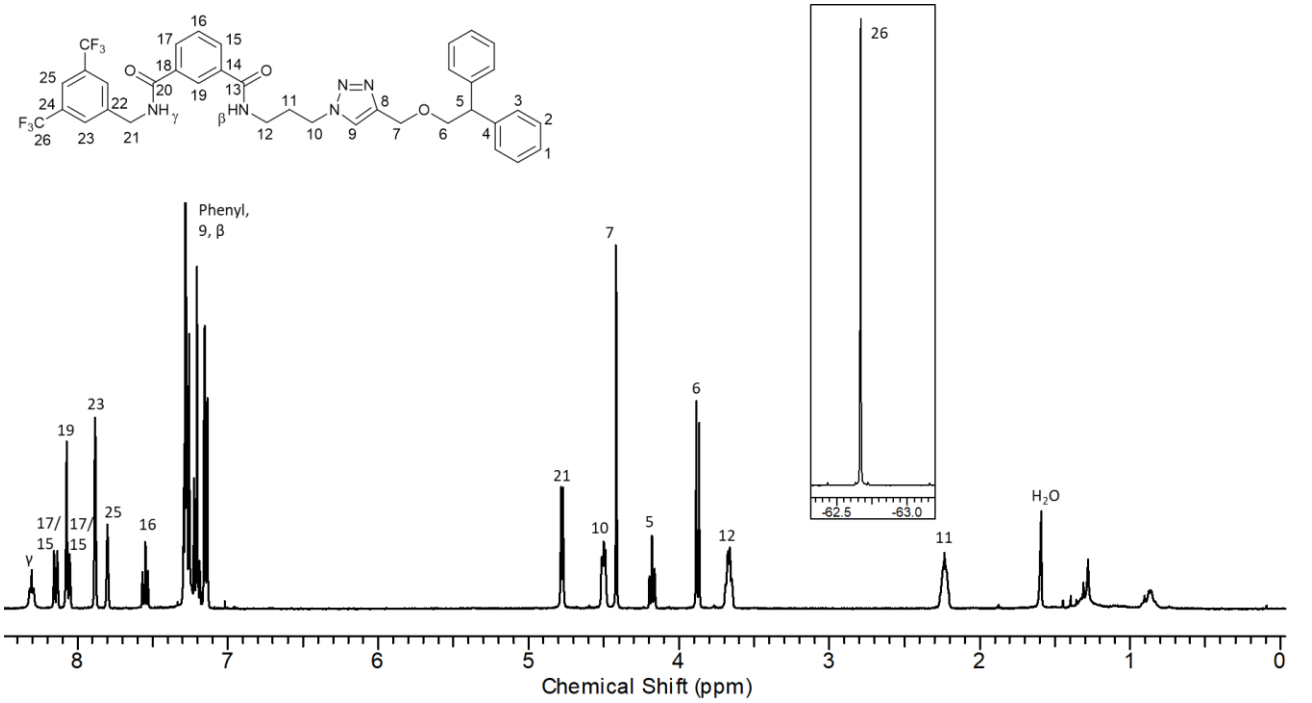


HRMS (ES +ve)

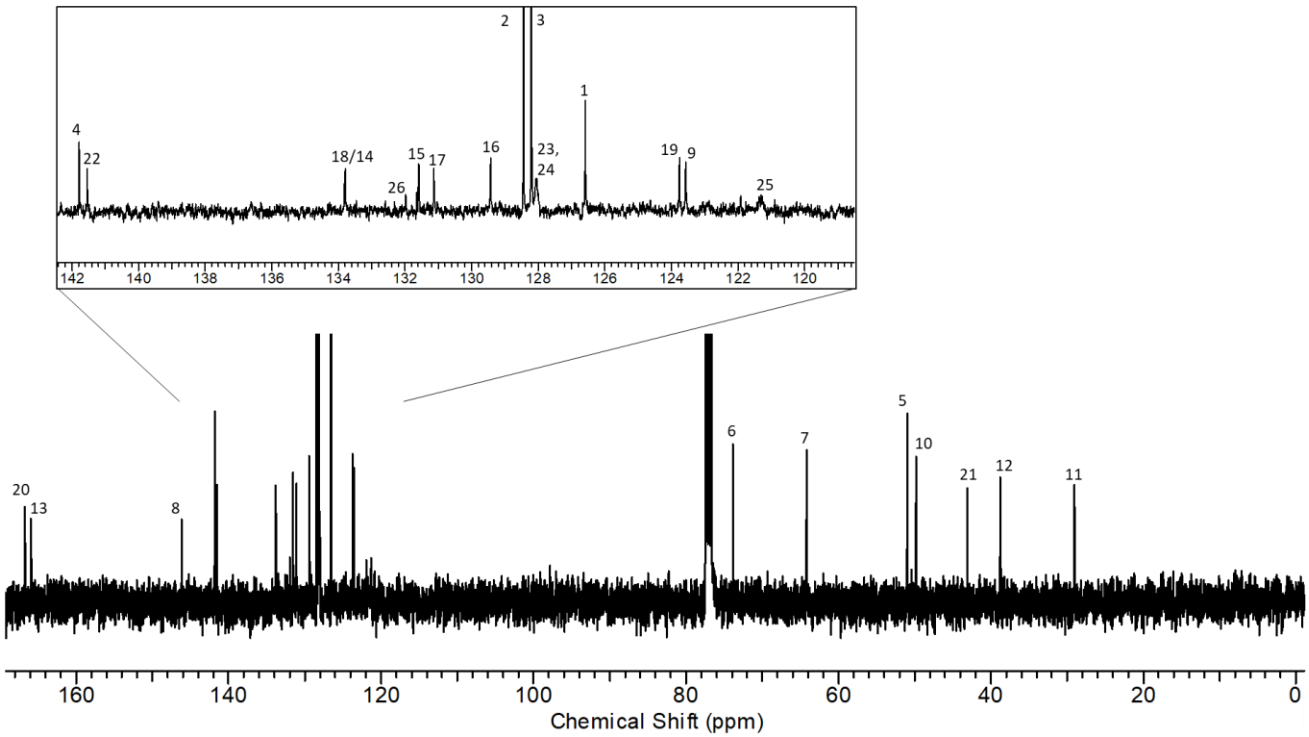


Axle 22

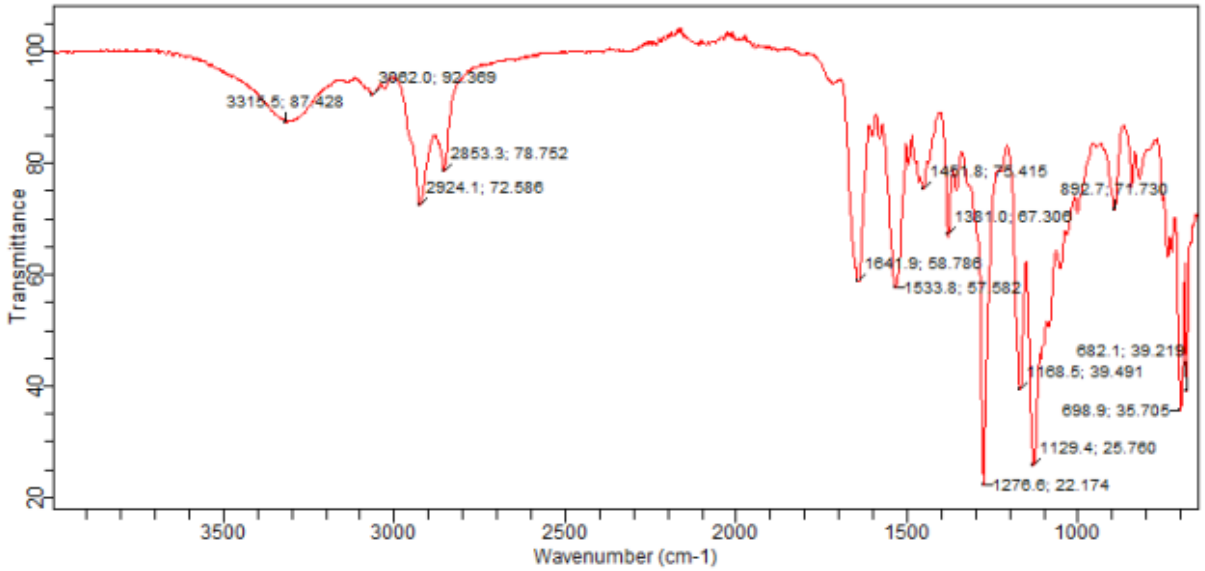
^{1}H NMR: (400 MHz, $CDCl_3$) with ^{19}F NMR insert (377 MHz)



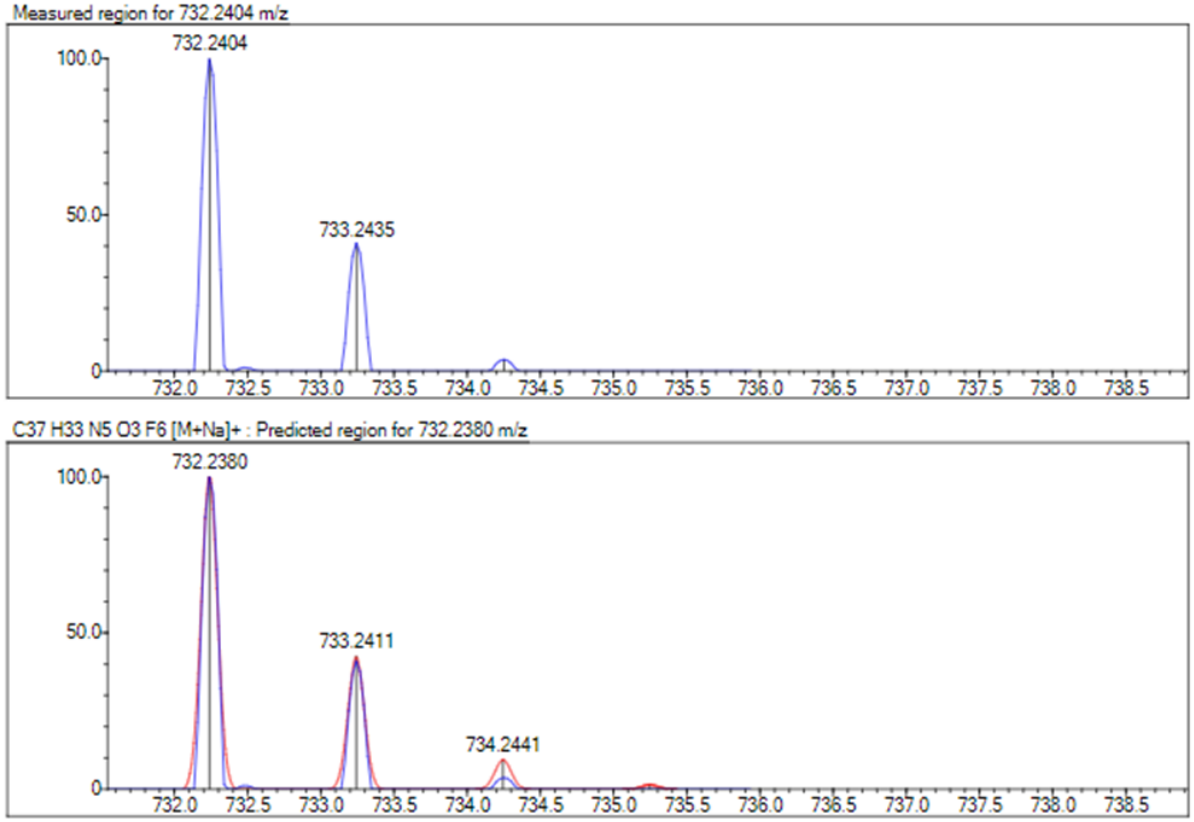
^{13}C NMR: (100 MHz, $CDCl_3$)



IR Spectrum (neat)

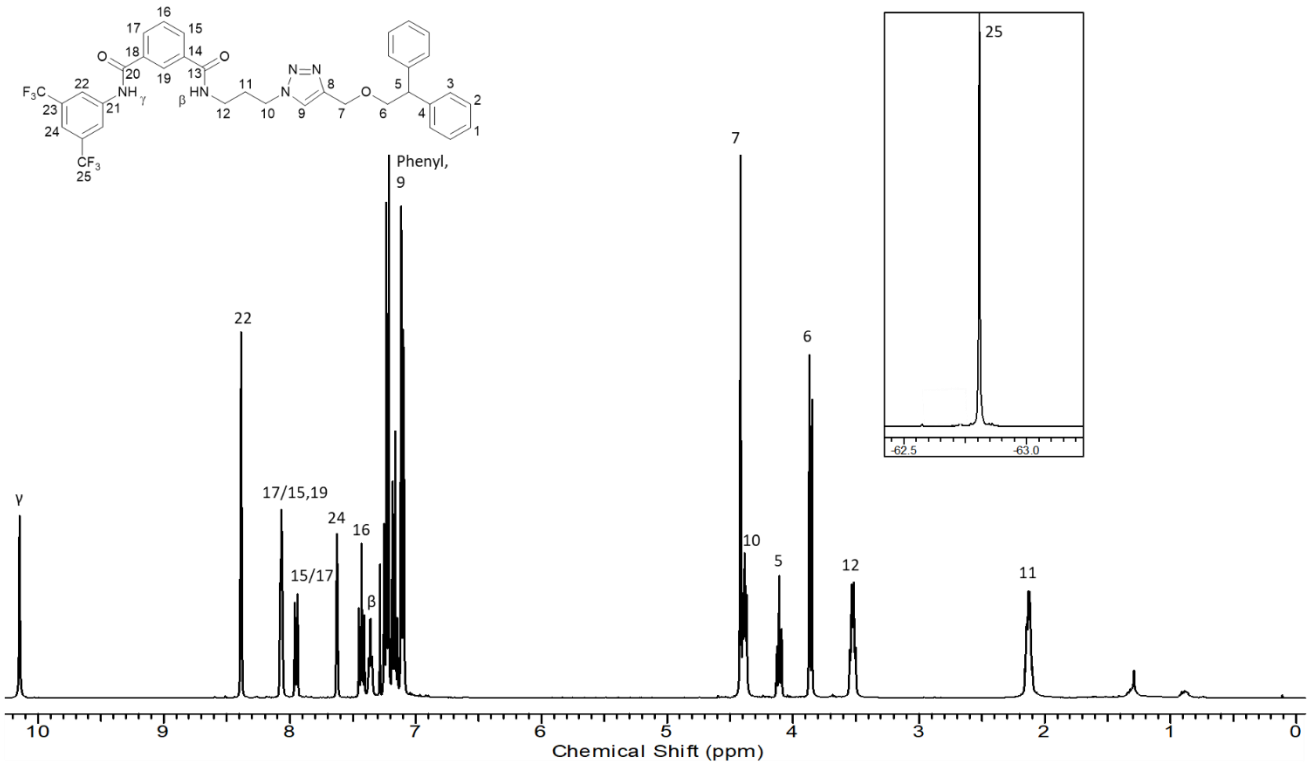


HRMS (ES +ve)

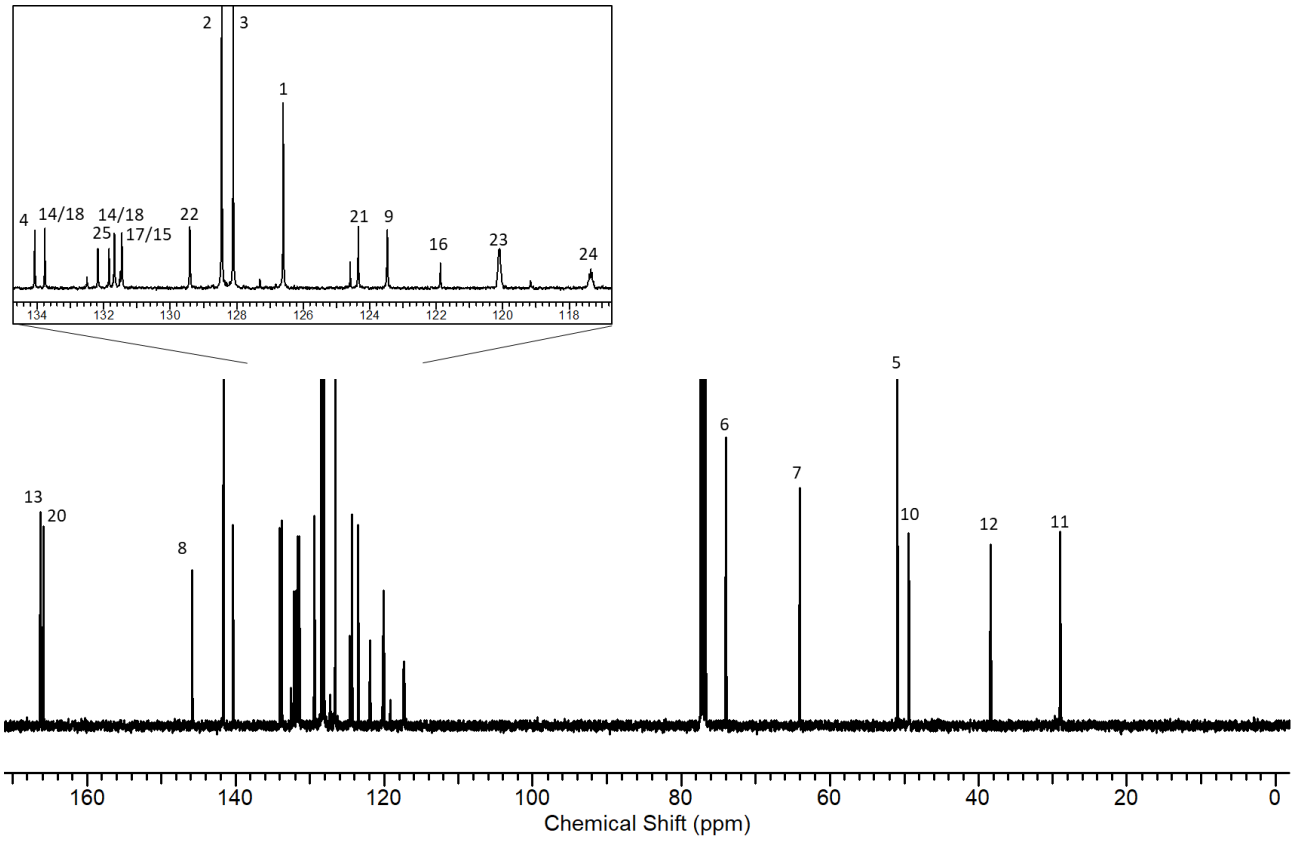


Axle 24

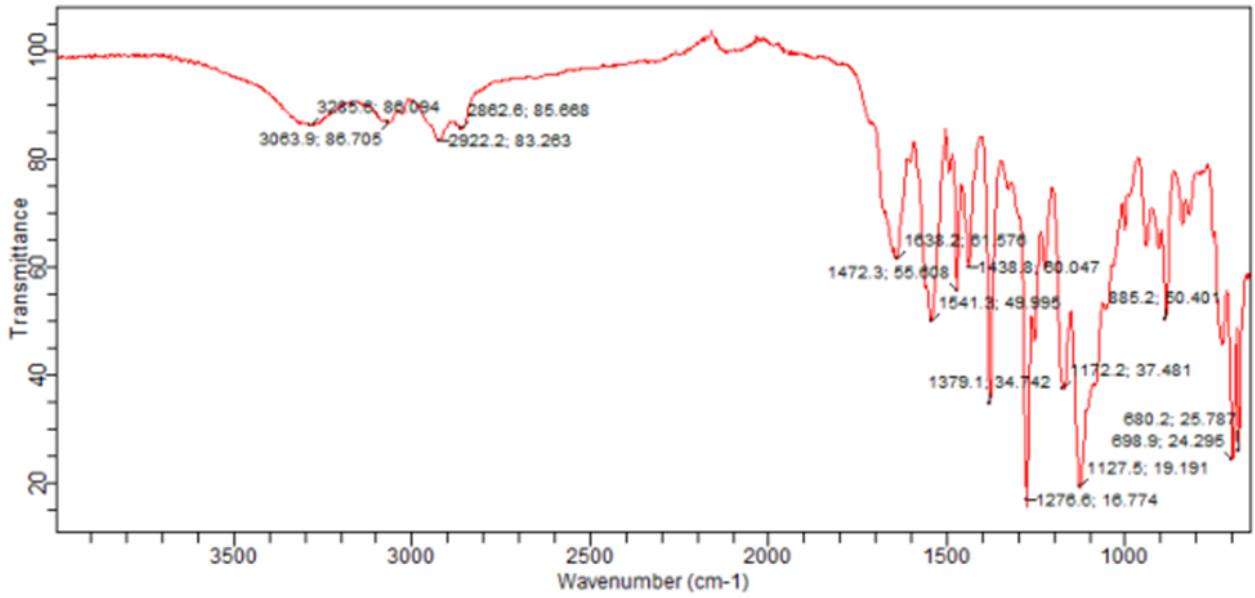
^{1}H NMR: (400 MHz, $CDCl_3$) with ^{19}F NMR insert (377 MHz)



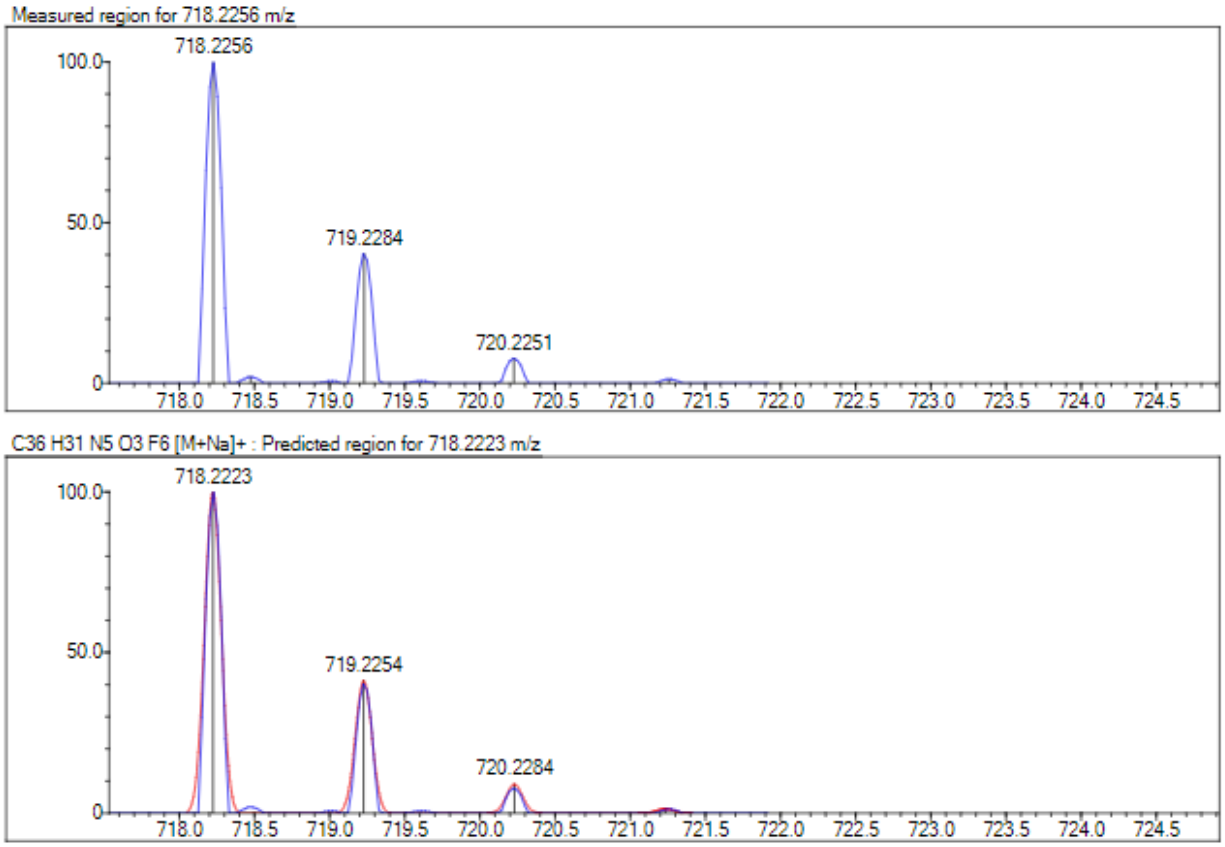
^{13}C NMR: (100 MHz, $CDCl_3$)



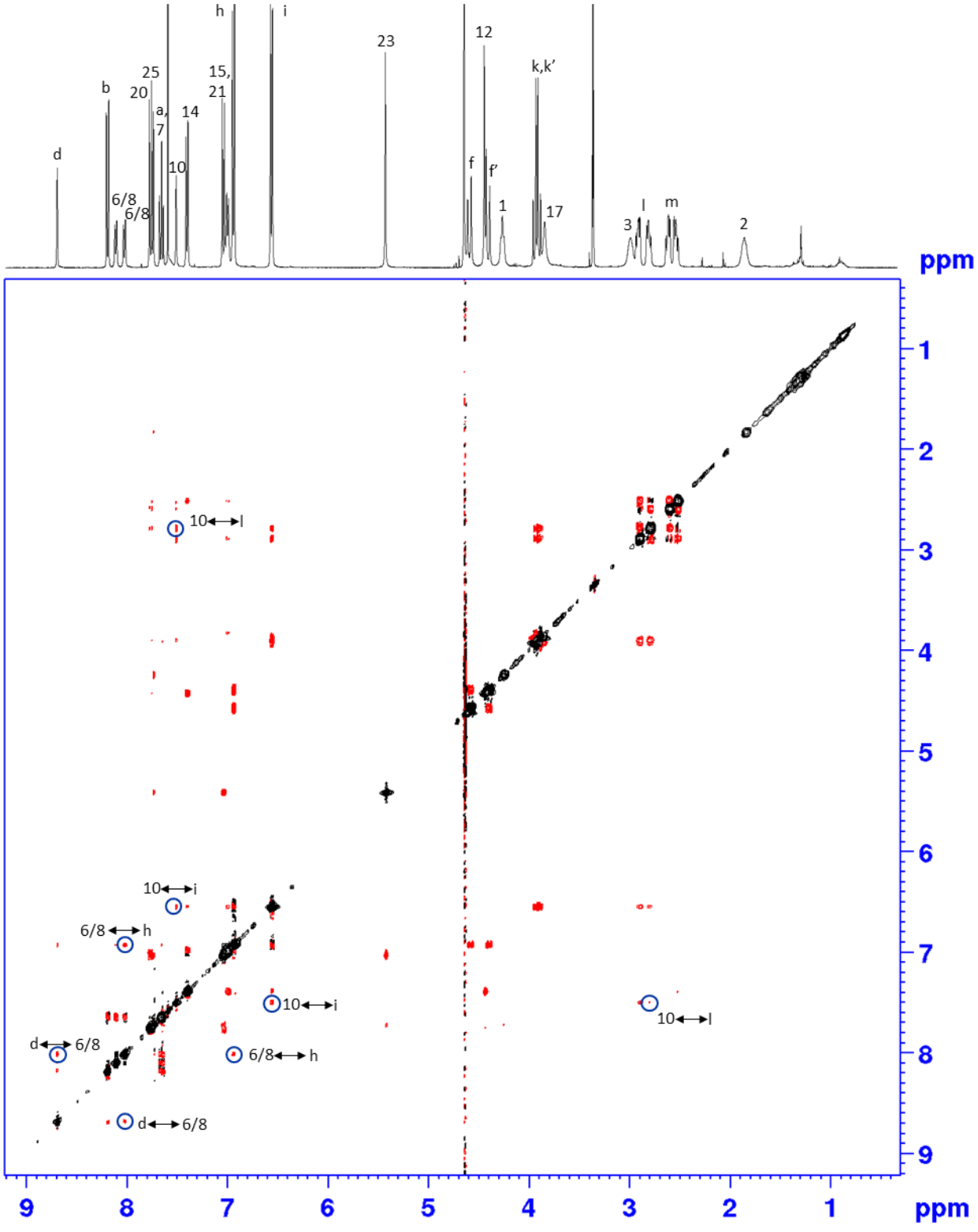
IR Spectrum (neat)



HRMS (ES +ve)

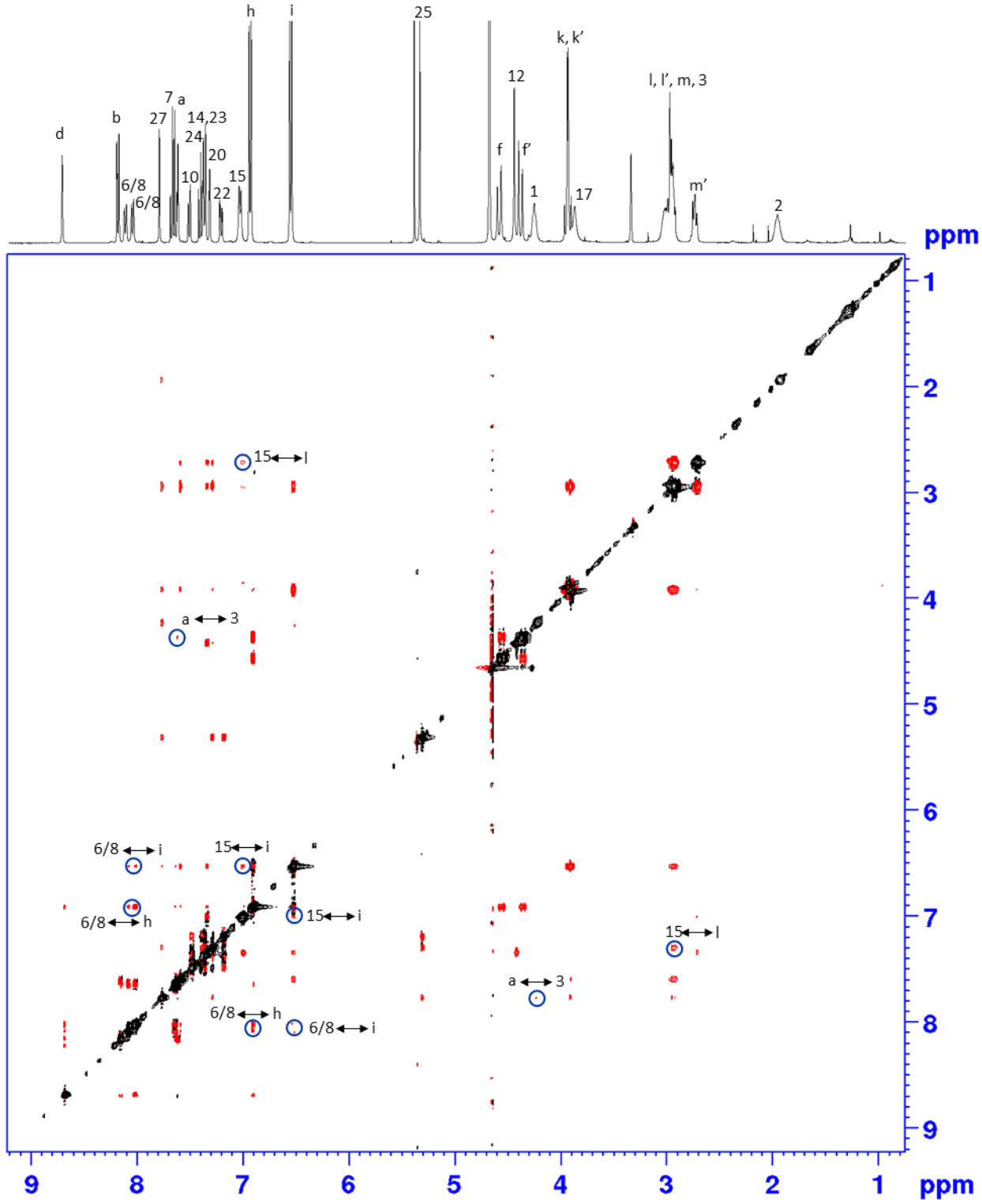


^{1}H-^{1}H ROESY Spectra
Catenane 15



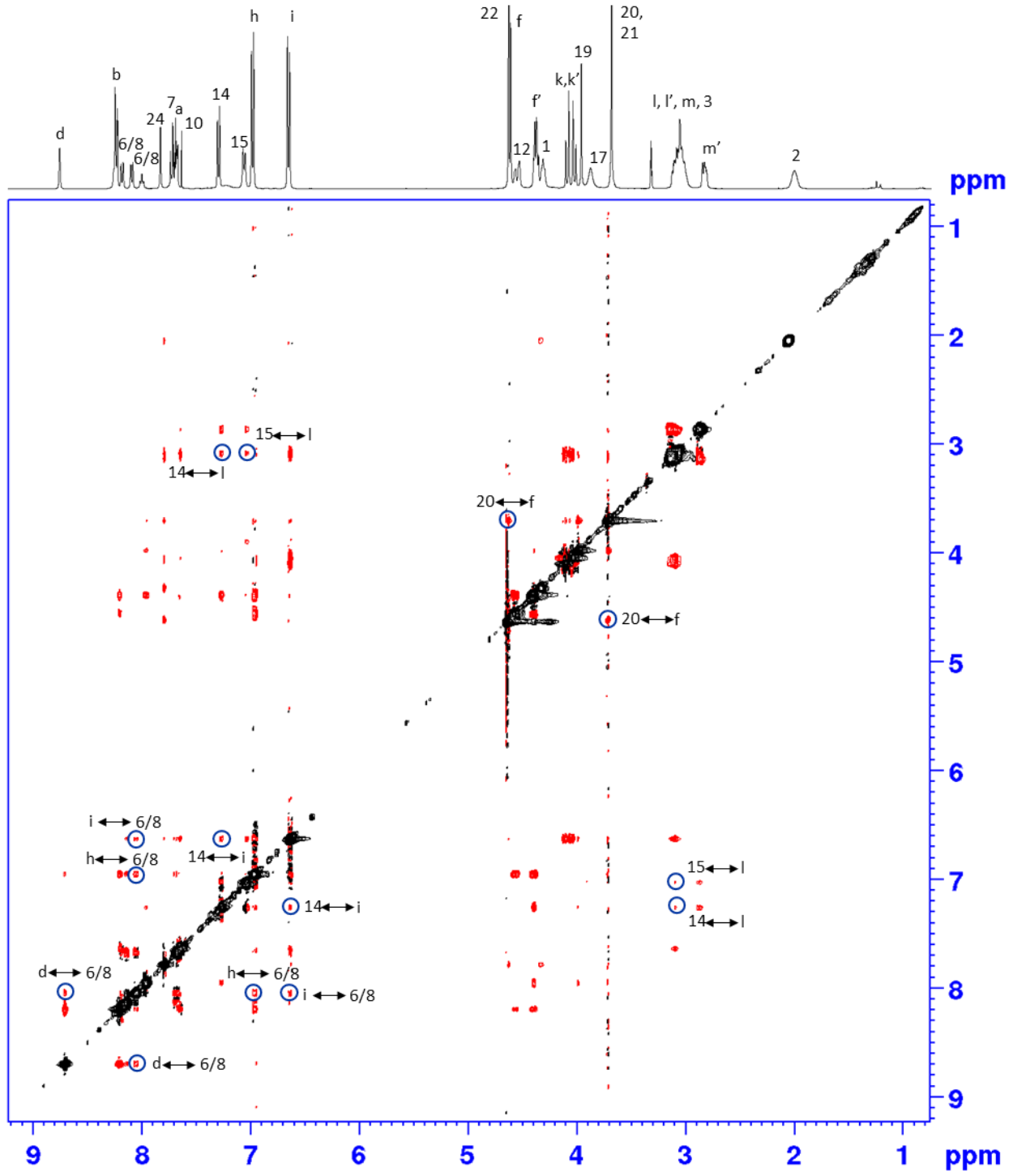
^{1}H–^{1}H ROESY NMR spectrum of catenane **15** (50:50 $CDCl_3$:CD_3OD, 400 MHz, 298 K). Inter-component through-space cross-peaks are circled.

Catenane 16

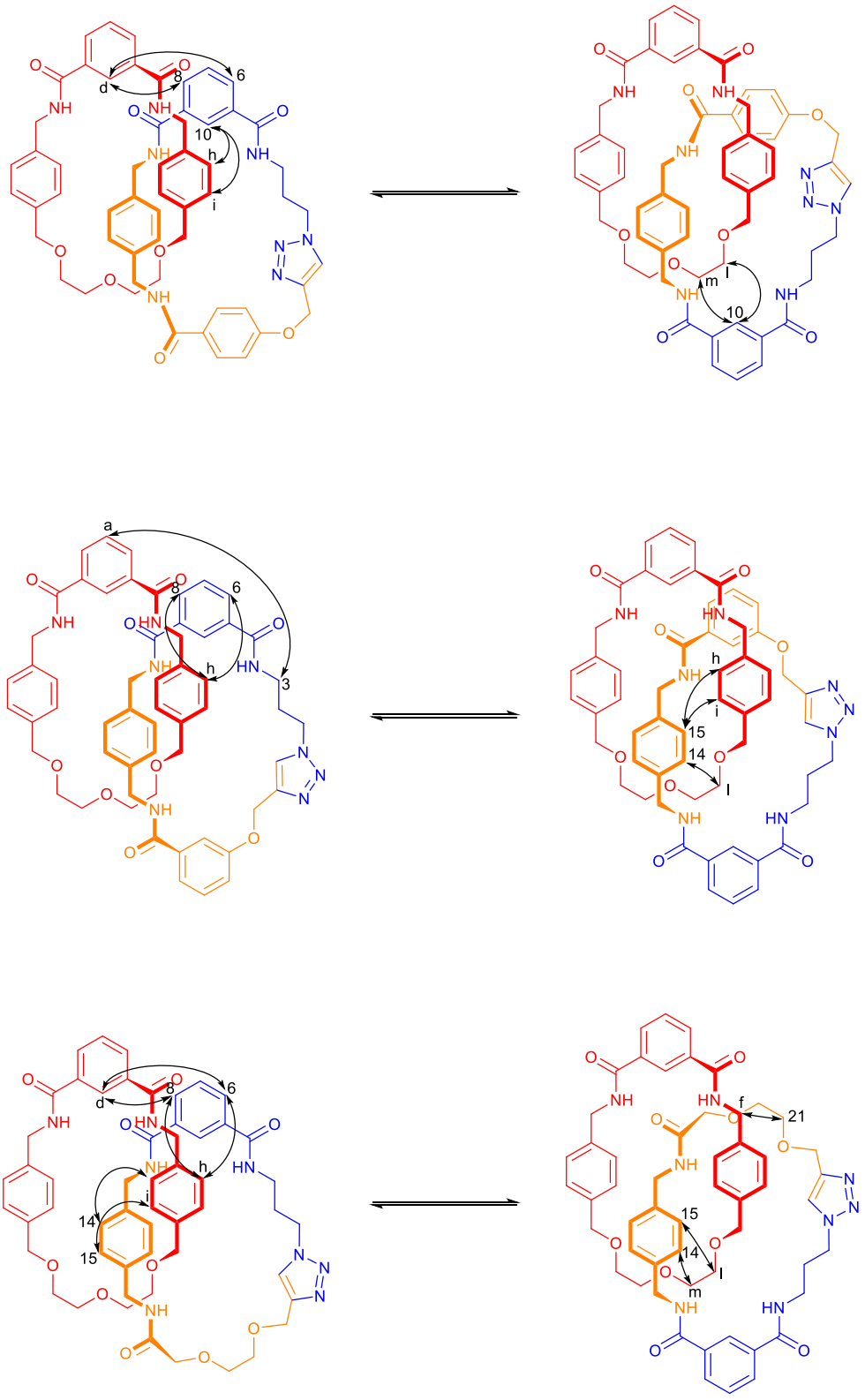


^{1}H–^{1}H ROESY NMR spectrum of catenane **16** (50:50 $CDCl_3$:CD_3OD, 400 MHz, 298 K). Inter-component through-space cross-peaks are circled.

Catenane 17

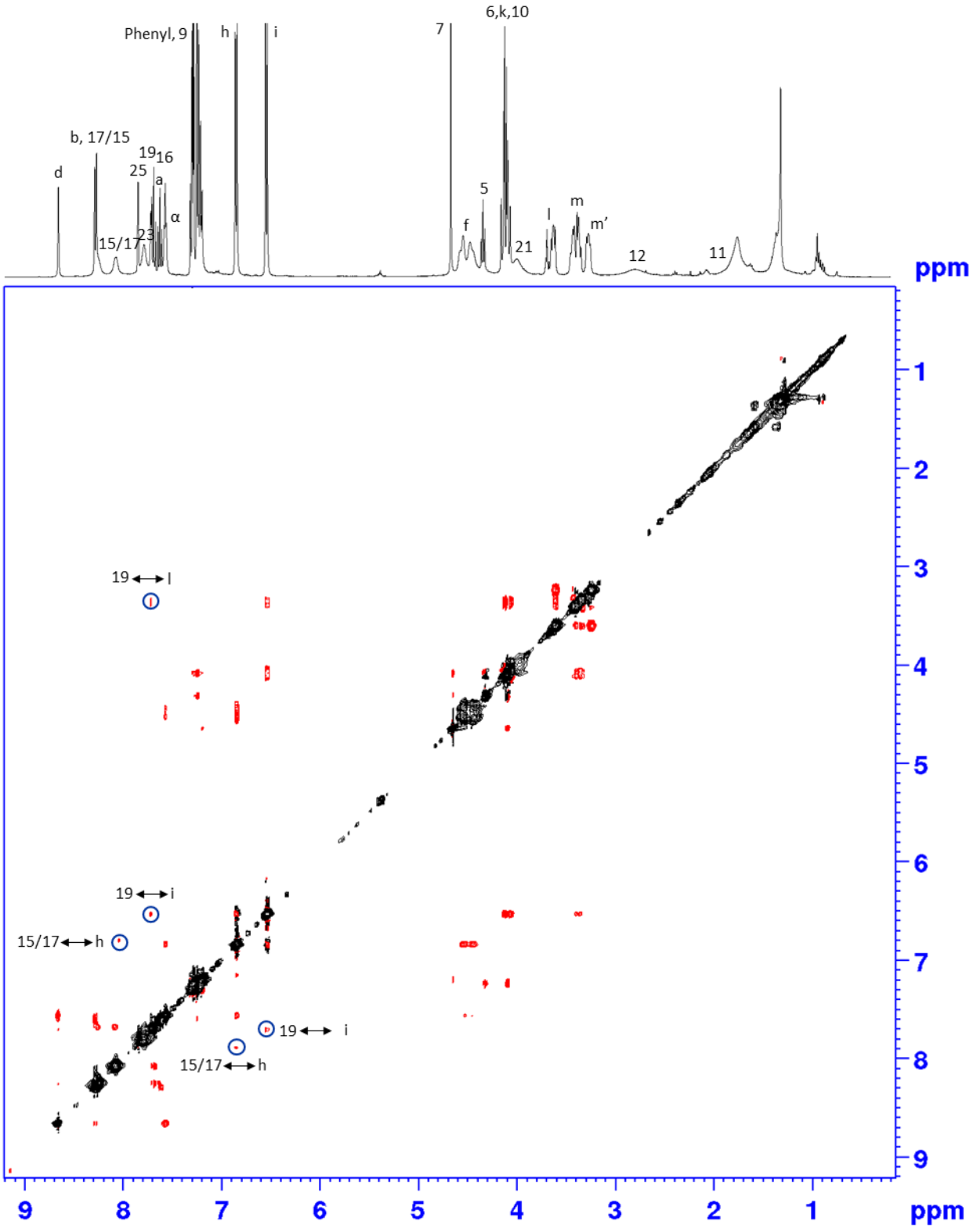


^{1}H–^{1}H ROESY NMR spectrum of catenane **17** (50:50 $CDCl_3$:CD_3OD, 400 MHz, 298 K). Inter-component through-space cross-peaks are circled.



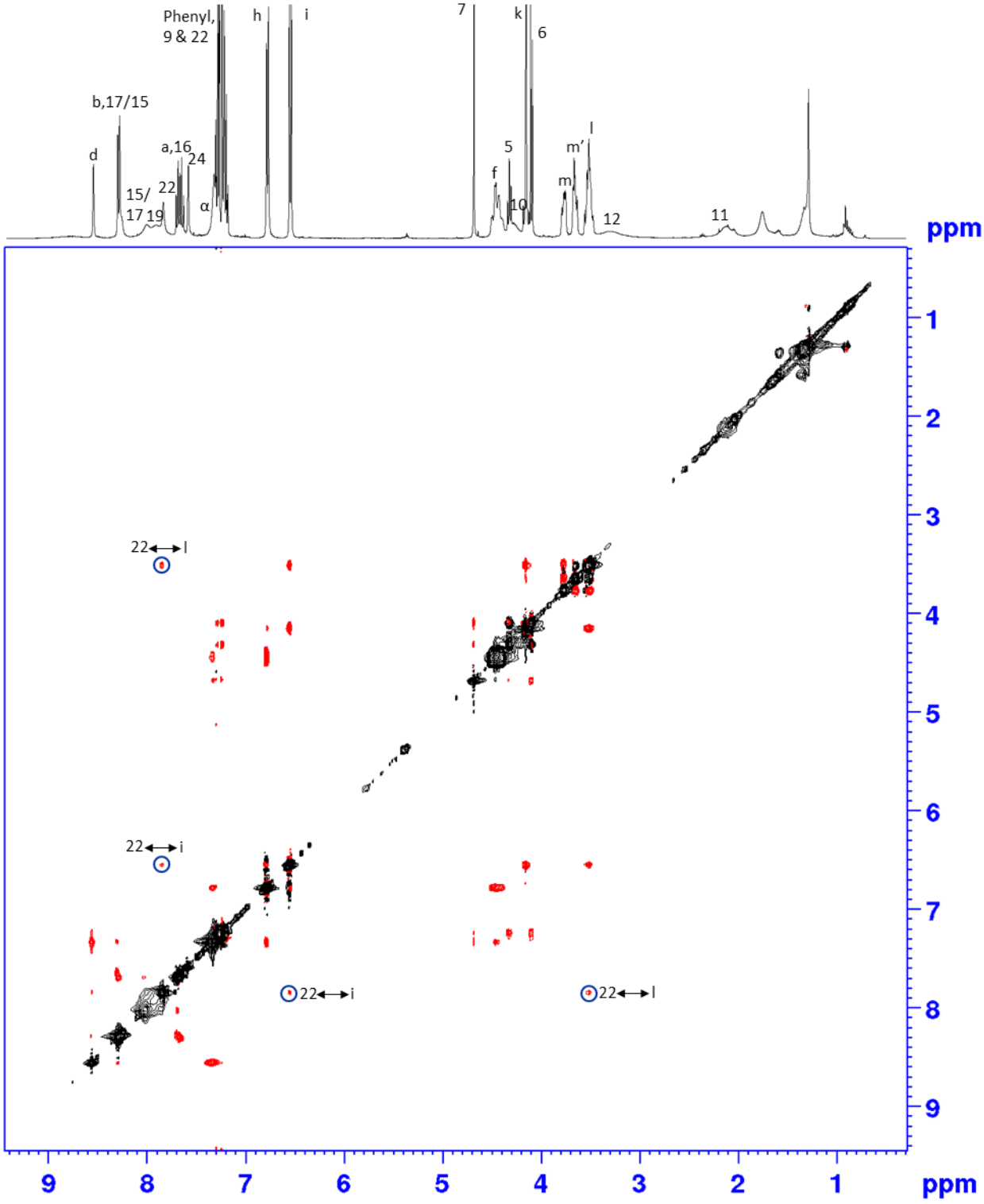
Plausible co-conformations of catenanes **15-17**
with inter-component ROESY NMR interactions highlighted.

Rotaxane 21

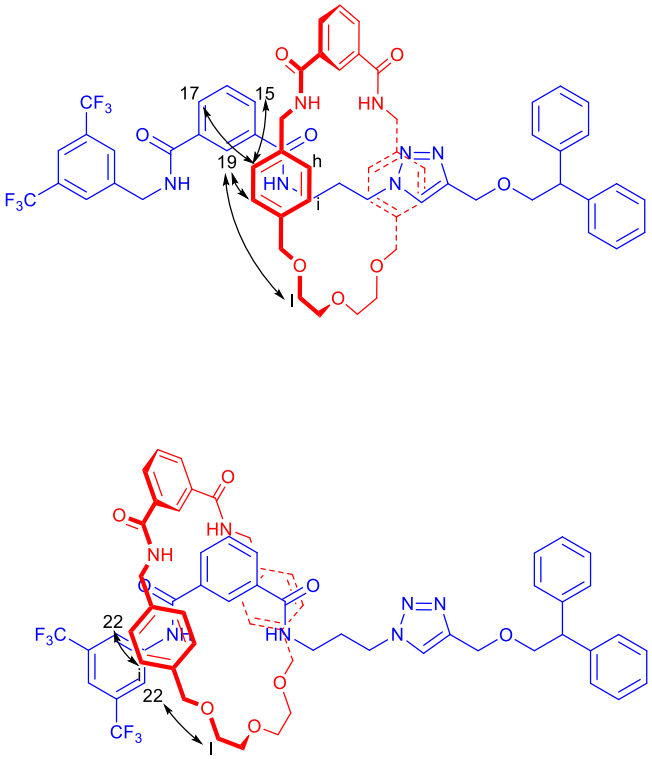


^{1}H–^{1}H ROESY NMR spectrum of rotaxane **21** ($CDCl_3$, 400 MHz, 298 K).
Inter-component through-space cross-peaks are circled.

Rotaxane 23

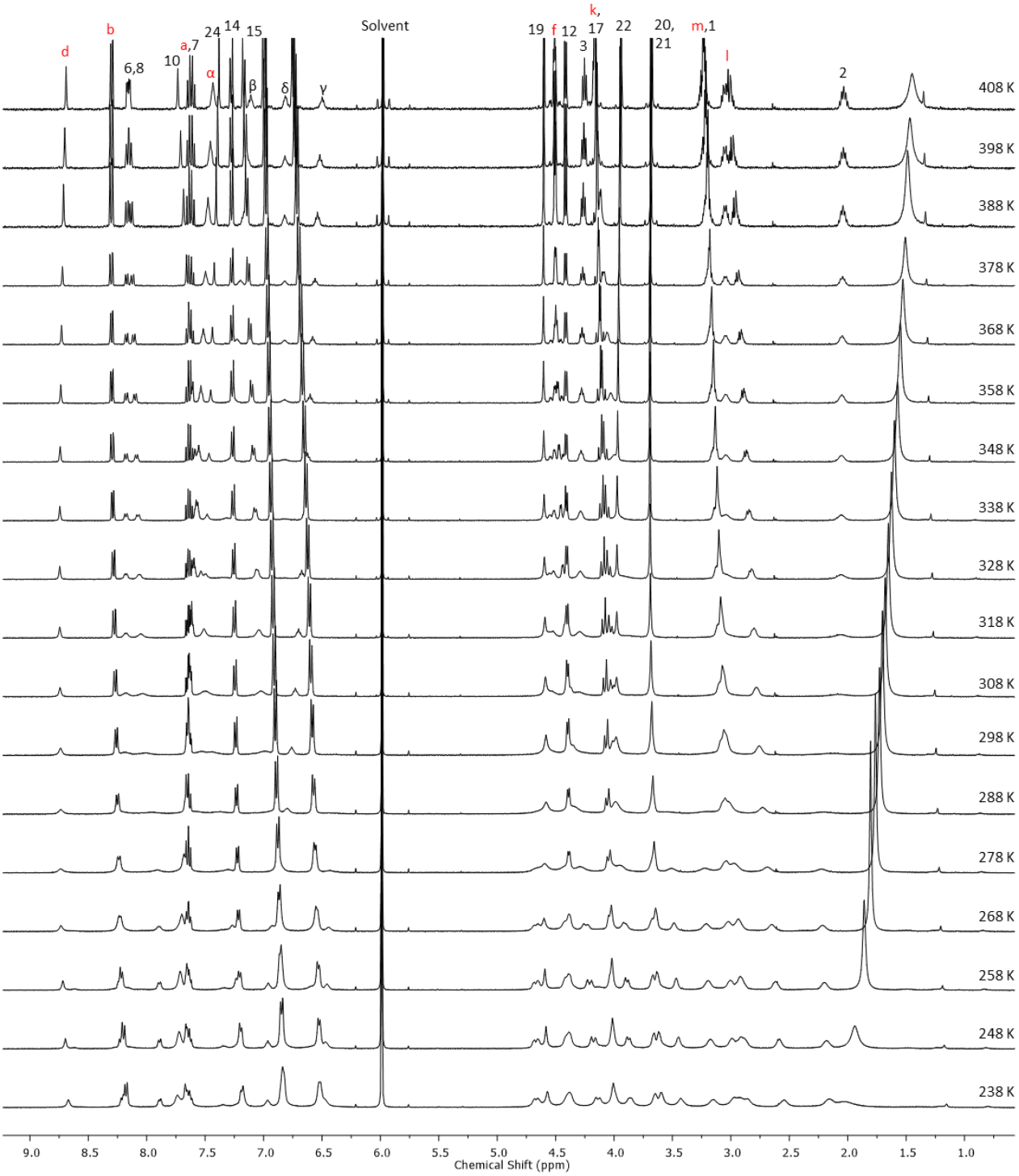


^{1}H–^{1}H ROESY NMR spectrum of rotaxane **23** ($CDCl_3$, 400 MHz, 298 K).
Inter-component through-space cross-peaks are circled.



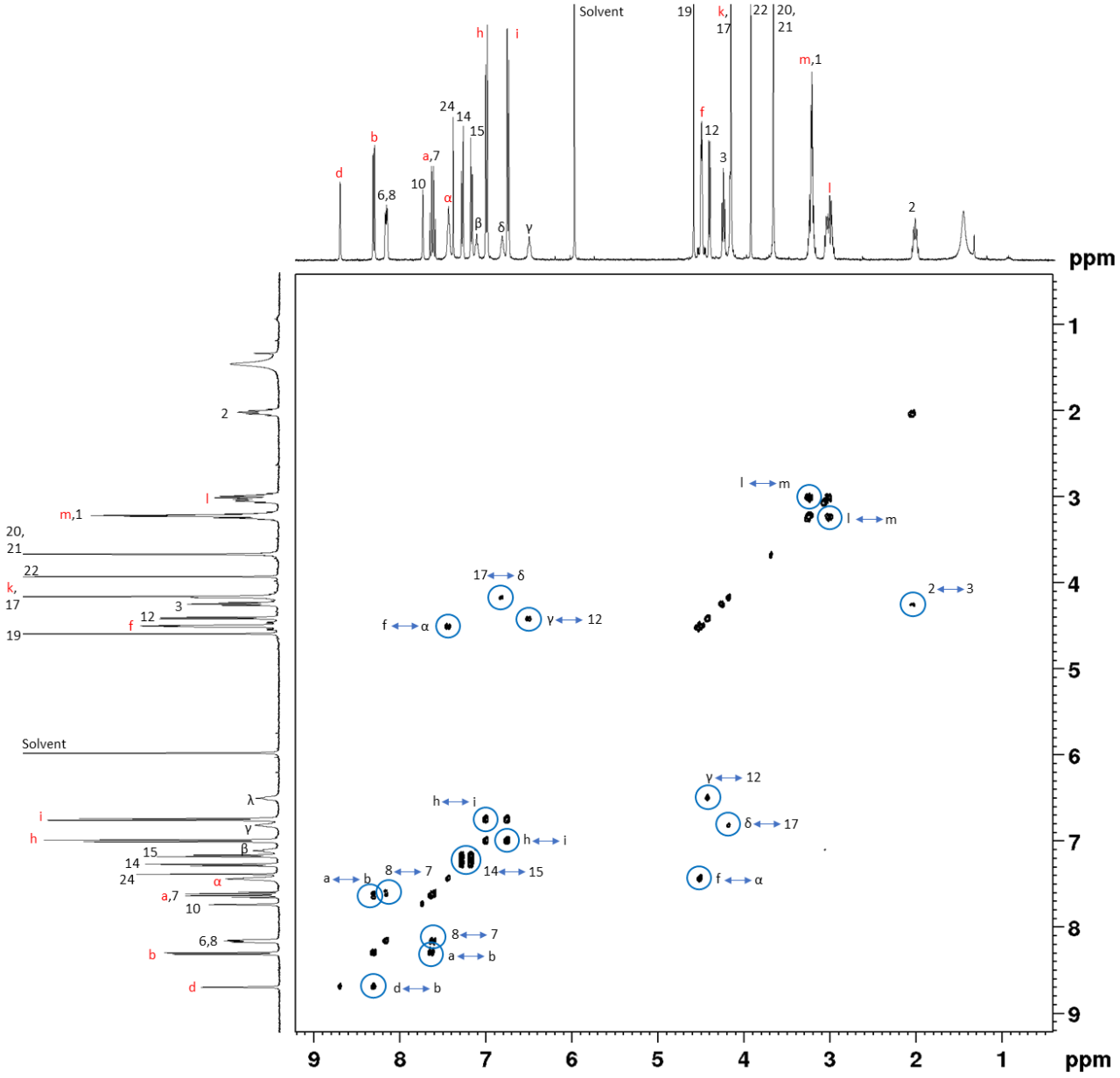
Plausible conformations of rotaxanes **21** and **23**
with inter-component ROESY NMR interactions highlighted.

VT ^{1}H NMR Stacked Spectra
Catenane 17



^{1}H NMR spectra of catenane **17** recorded at *T* = 238 K to 408 K in $C_2D_2Cl_4$ (400 MHz).

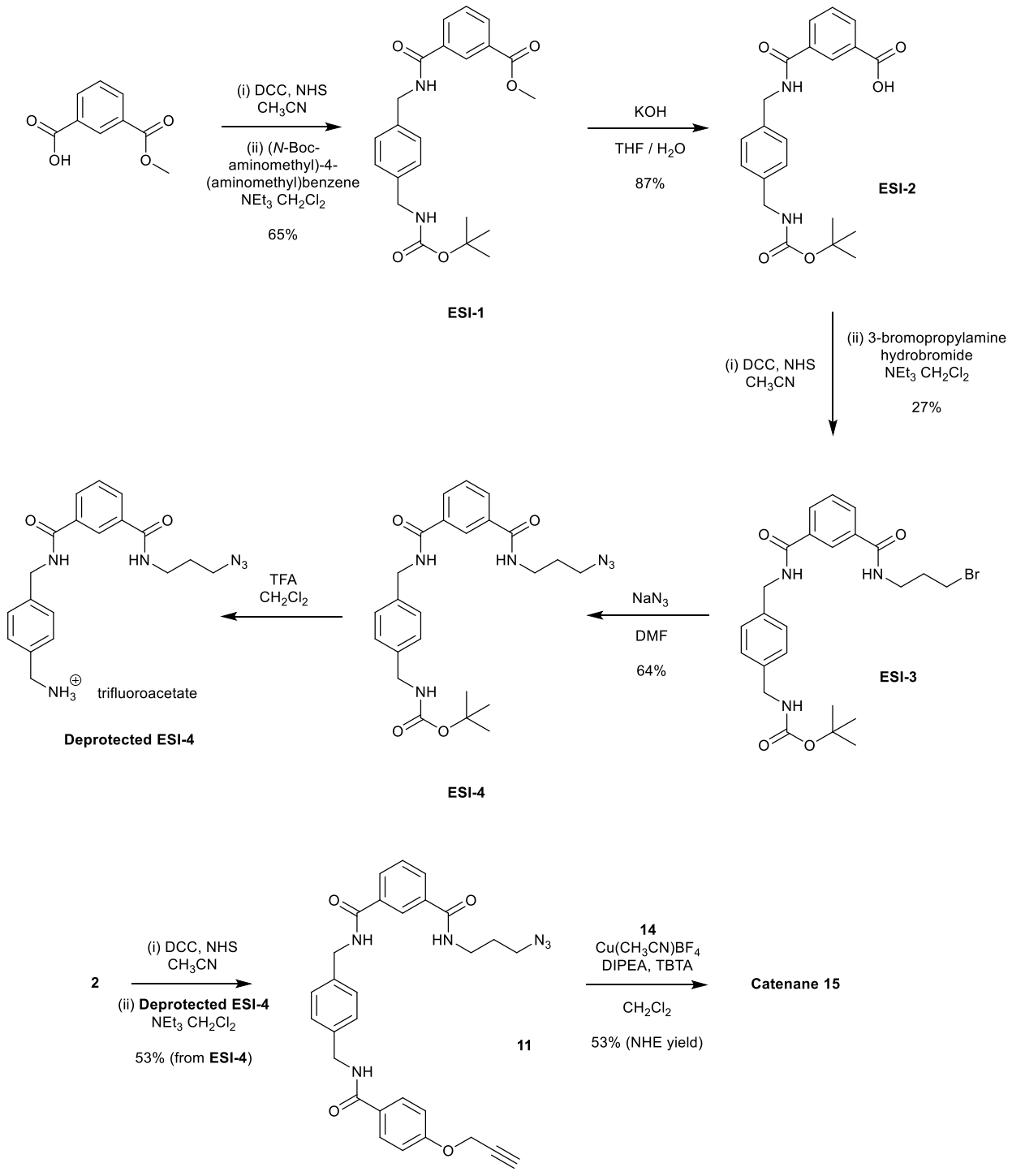
Catenane 17



^{1}H-^{1}H COSY NMR spectrum of catenane **17** ($C_2D_2Cl_4$, 408 K, 400 MHz) used to aid with 1D ^{1}H NMR proton assignment.

Part 3: Alternative Synthesis of Catenane 15

Reaction Scheme



Supplementary Scheme 3: *Alternative synthesis of catenane* ***15****.*

Experimental Procedures

Boc-ester ESI-1

To a suspension of mono-methyl isophthalate (381 mg, 2.12 mmol) in dry CH_3CN (20 mL), DCC (480 mg, 2.33 mmol) and *N*-hydroxysuccinimide (292 mg, 2.54 mmol) were added. The reaction mixture was stirred under an Ar (g) atmosphere for 20 h. The urea precipitate was filtered off and the solvent of the filtrate removed *in vacuo*. The residue was dissolved in dry CH_2Cl_2 (15 mL) and added to a suspension of 1-(*N*-Boc-aminomethyl)-4-(aminomethyl)benzene (500 mg, 2.12 mmol) and NEt_3 (368 μL, 268 mg, 2.64 mmol) in dry CH_2Cl_2 (20 mL). The reaction mixture was stirred under an Ar (g) atmosphere for 20 h. The mixture was diluted with CH_2Cl_2, and then washed with 1M HCl (aq) (2 × 25 mL), sat. $NaHCO_3$ (2 × 25 mL) and H_2O (1 × 25 mL), then the organic layer dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude material was purified by silica gel chromatography (CH_2Cl_2/CH_3OH 99.5:0.5 to 98:2) to yield the pure product as a white solid (568 mg, 65%).

R_f 0.22 (CH_2Cl_2/CH_3OH 98:2)

Mp 140-142 °C

υ_{max}/cm^{-1} (neat) 3340, 3290 (multiple N–H), 3020, 2980, 2850 (multiple C–H), 1720, 1680, 1630 (3 × C=O), 1520, 1300, 1250, 1150, 1080, 1050.

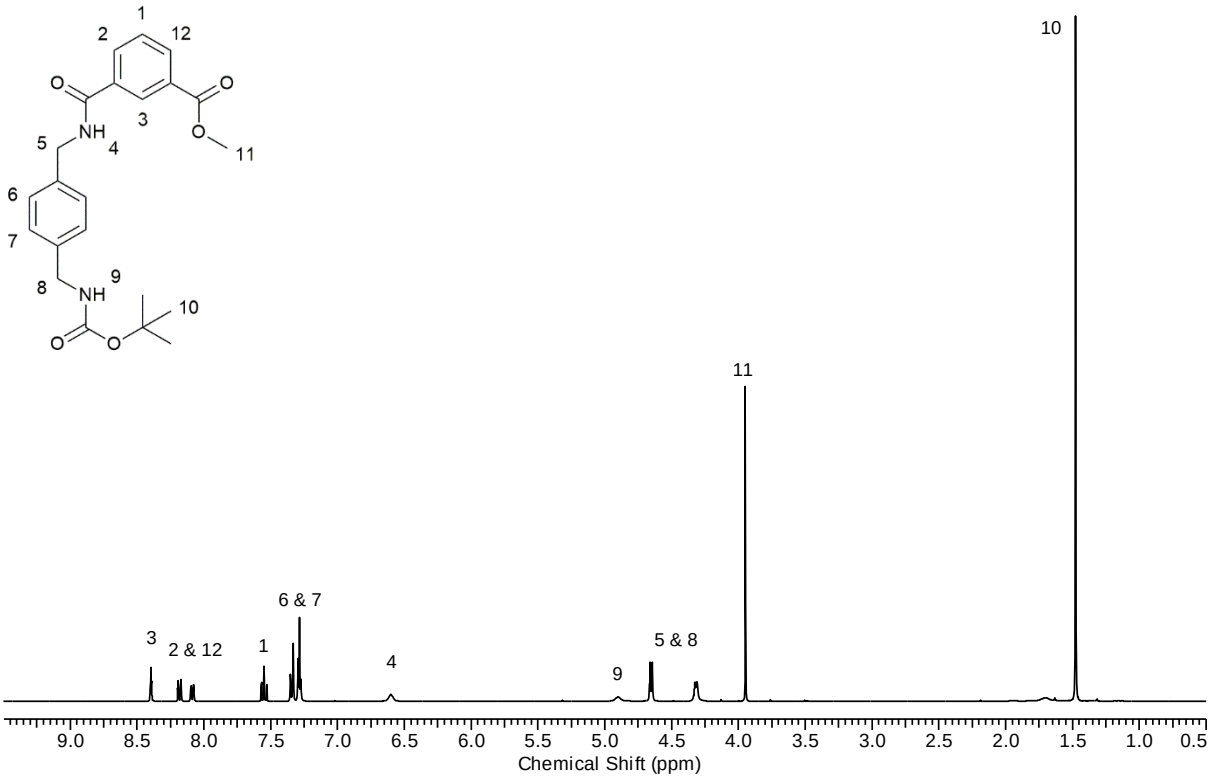
δH(400 MHz; $CDCl_3$) 8.38 (1H, t, ^4J = 1.5 Hz, 2-iso *H*), 8.17 (1H, dt, ^3J = 7.8 Hz ^4J = 1.5 Hz, 4- or 6-iso *H*), 8.07 (1H, dt, ^3J = 7.8 Hz ^4J = 1.5 Hz, 4- or 6-iso *H*), 7.54 (1H, t, ^3J = 7.8 Hz, 5-iso *H*), 7.26-7.34 (4H, m, Ar*H*), 6.59 (1H, br s, iso N*H*), 4.89 (1H, br s, Boc N*H*), 4.64 (2H, d, ^3J = 5.6 Hz, CH_2), 4.30 (2H, d, ^3J = 5.6 Hz, CH_2), 3.93 (3H, s, OCH_3), 1.46 (9H, s, C(CH_3)$_3$).

δC(100 MHz; $CDCl_3$) 166.3, 166.2, 155.9 (3 × *C*=O), 138.6, 137.0, 134.6, 132.5, 131.9, 130.5, 128.9, 128.3, 127.9, 127.5 (10 × Ar*C*), 79.6 (O*C*(CH_3)$_3$), 52.4 (O*C*H_3), 44.3, 43.9 (2 × N*C*H_2), 28.4 (OC(*C*H_3)$_3$).

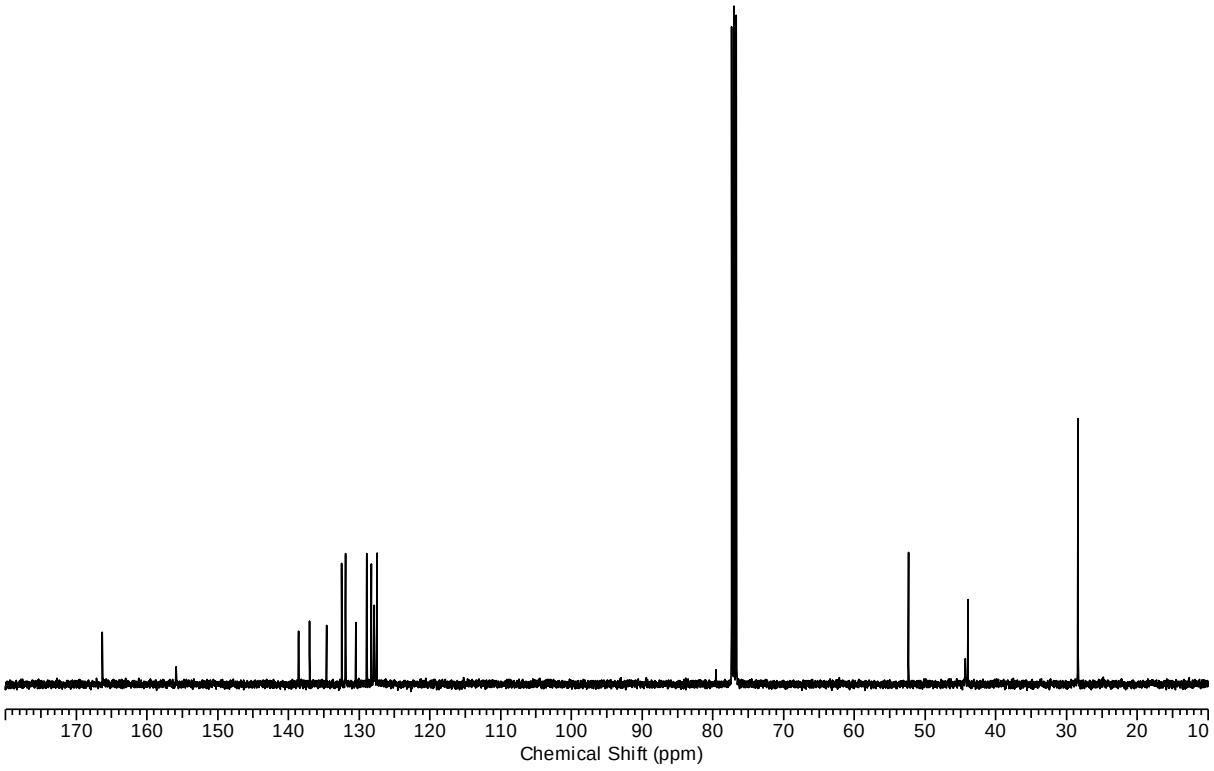
***m/z* (ES)** 421.1731 ($[M + Na]^+$ $C_{22}H_{26}N_2NaO_5$ requires 421.1734).

Boc-ester ESI-1

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

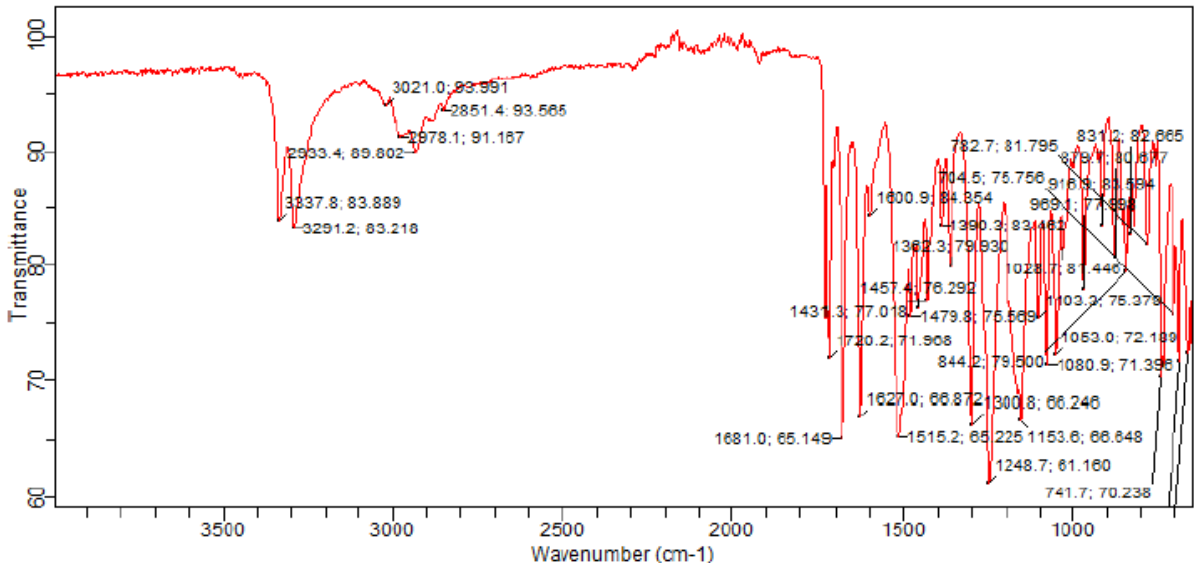


^{13}C NMR ($CDCl_3$, 100 MHz)

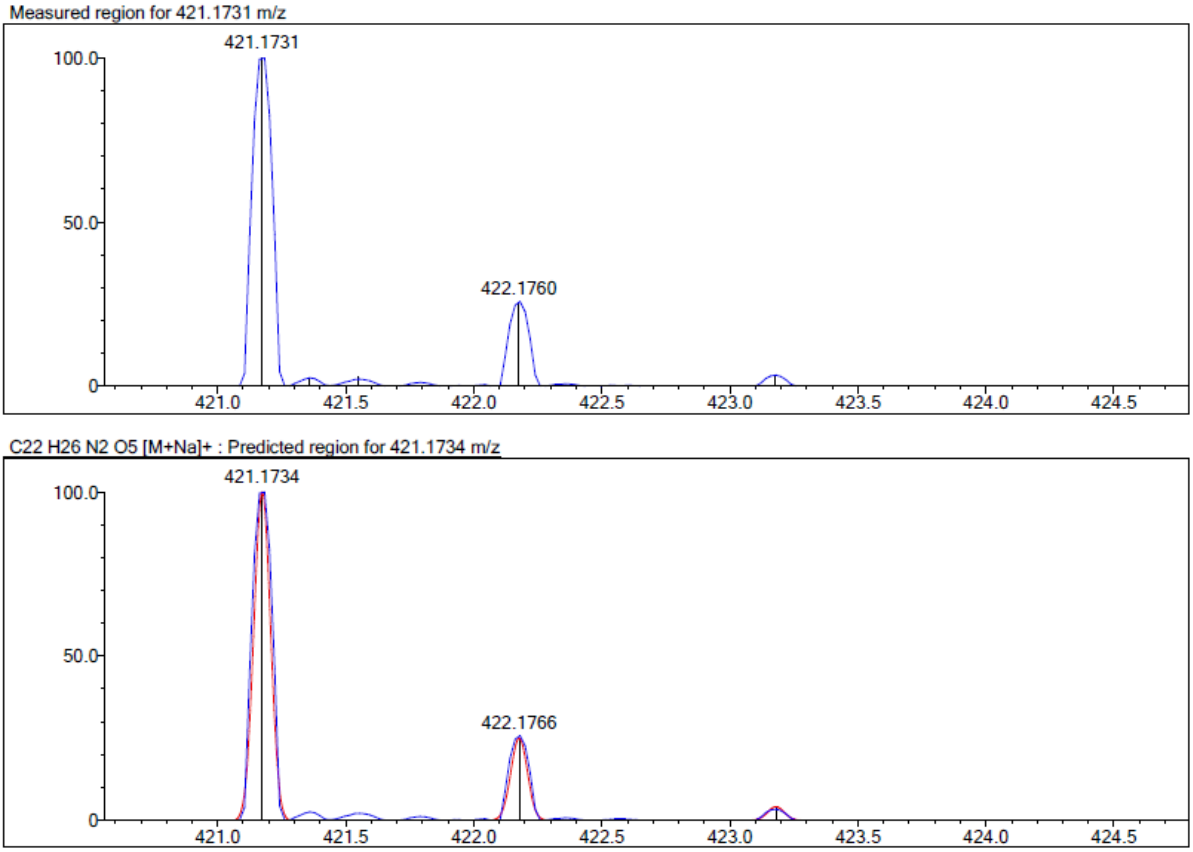


Boc-ester ESI-1

IR (neat)



Mass Spectrum (ES +ve)



Boc-acid ESI-2

KOH (68 mg, 1.2 mmol) in H_2O (1 mL) was added to a solution of **ESI-1** (400 mg, 1.00 mmol) in THF (10 mL), and the reaction mixture was stirred for 22 h. THF was removed *in vacuo*, and then the residue was diluted with H_2O and then 10% citric acid (aq) was added generating a white precipitate. This solid was collected by vacuum filtration, washed with CH_2Cl_2 and H_2O, and then dried to yield the pure product as a white solid (336 mg, 87%).

Mp 206 °C (dec. – decarboxylation)

υ_{max}/cm^{-1} (neat) 3340, 3300 (multiple N–H), 2980, 2930, 2890 (multiple C–H), 1680, 1630 (2 × C=O observed, third coincident), 1510, 1250, 1170.

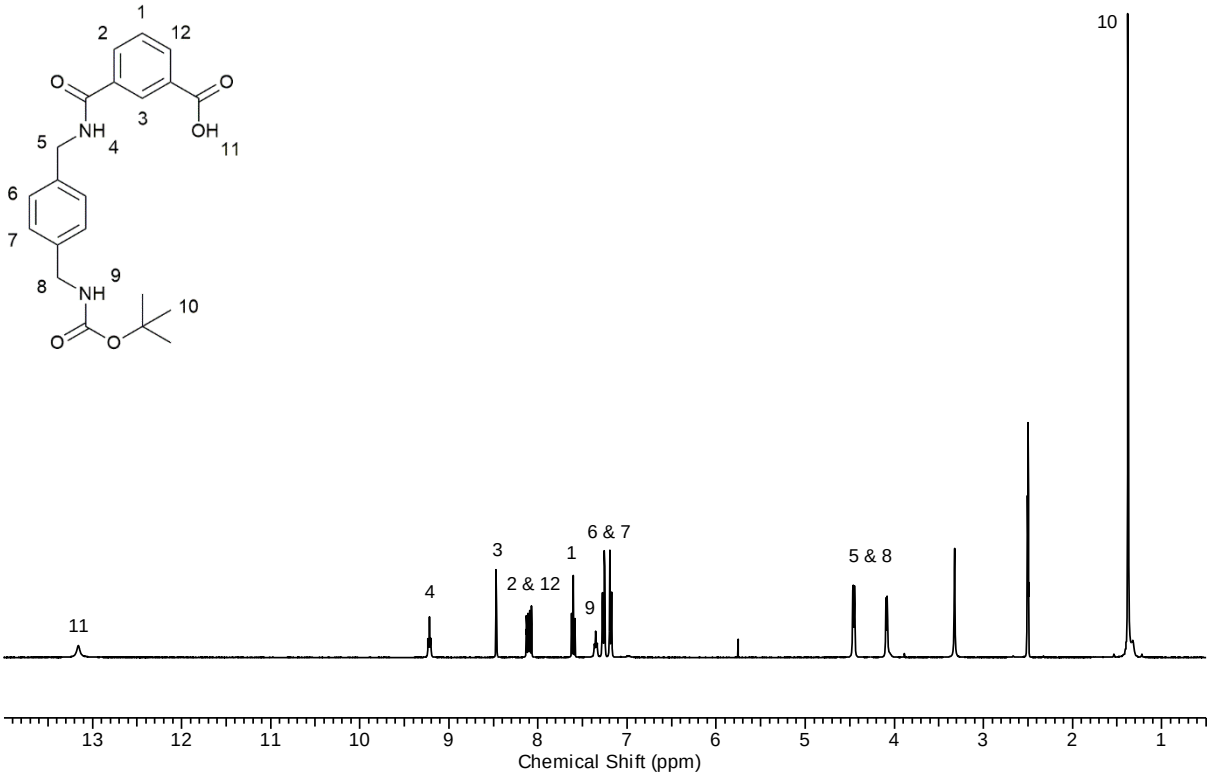
δH(400 MHz; D$_6$-DMSO) 13.16 (1H, br s, COO*H*), 9.22 (1H, t, ^3J = 5.9 Hz, iso N*H*), 8.47 (1H, t, ^4J = 1.6 Hz, 2-iso *H*), 8.12 (1H, dt, ^3J = 7.9 Hz ^4J = 1.4 Hz, 4- or 6-iso *H*), 8.07 (1H, dt, ^3J = 7.9 Hz ^4J = 1.4 Hz, 4- or 6-iso *H*), 7.60 (1H, t, ^3J = 7.8 Hz, 5-iso *H*), 7.35 (1H, t, ^3J = 6.2 Hz, Boc N*H*), 7.17-7.27 (4H, m, Ar*H*), 4.45 (2H, d, ^3J = 6.0 Hz, CH_2), 4.09 (2H, d, ^3J = 6.0 Hz, CH_2), 1.38 (9H, s, C(CH_3)$_3$).

δC(100 MHz; D$_6$-DMSO) 166.9, 165.3, 155.7 (3 × *C*=O), 138.7, 137.9, 134.7, 131.8, 131.6, 131.0, 128.8, 128.1, 127.2, 126.9 (10 × Ar*C*), 77.7 (O*C*(CH$_3$)$_3$), 43.1, 42.5 (2 × N*C*H$_2$), 28.2 (OC(*C*H$_3$)$_3$).

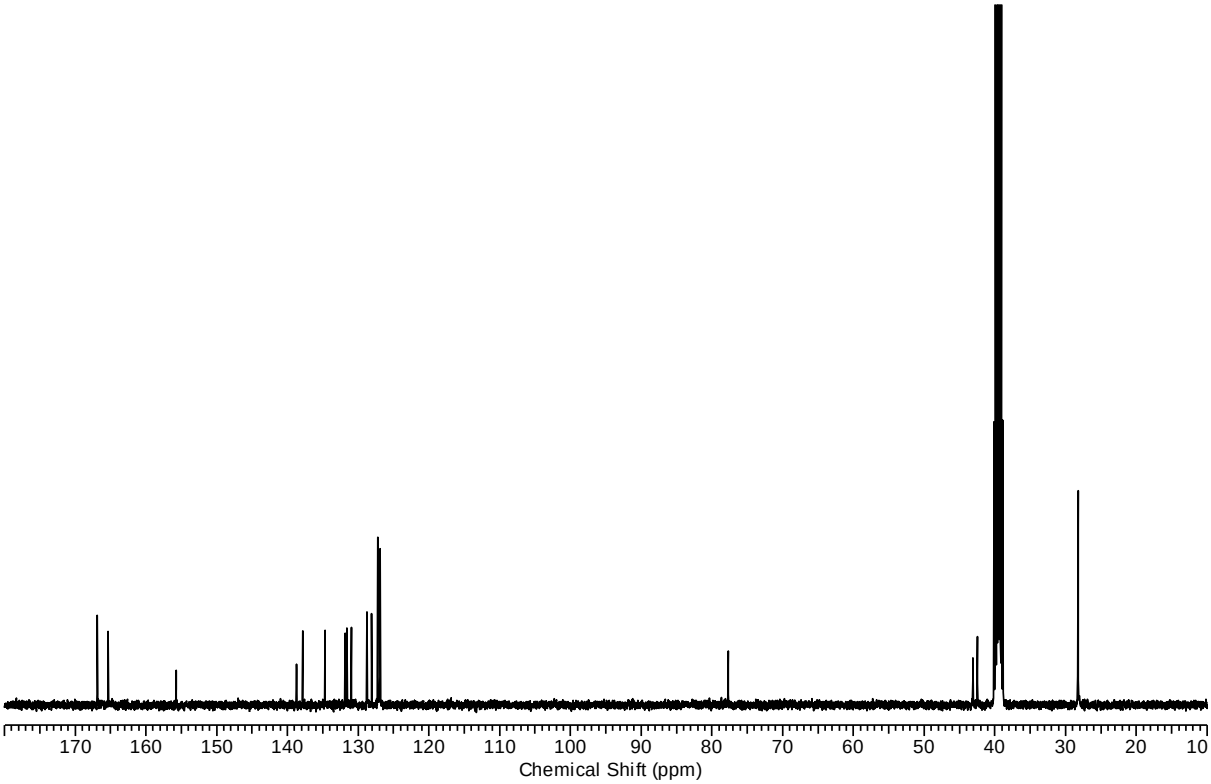
***m/z* (ES)** 407.1568 ([M + Na]$^+$ $C_{21}H_{24}N_2NaO_5$ requires 407.1577).

Boc-acid ESI-2

^{1}H NMR (D_6-DMSO, 400 MHz)

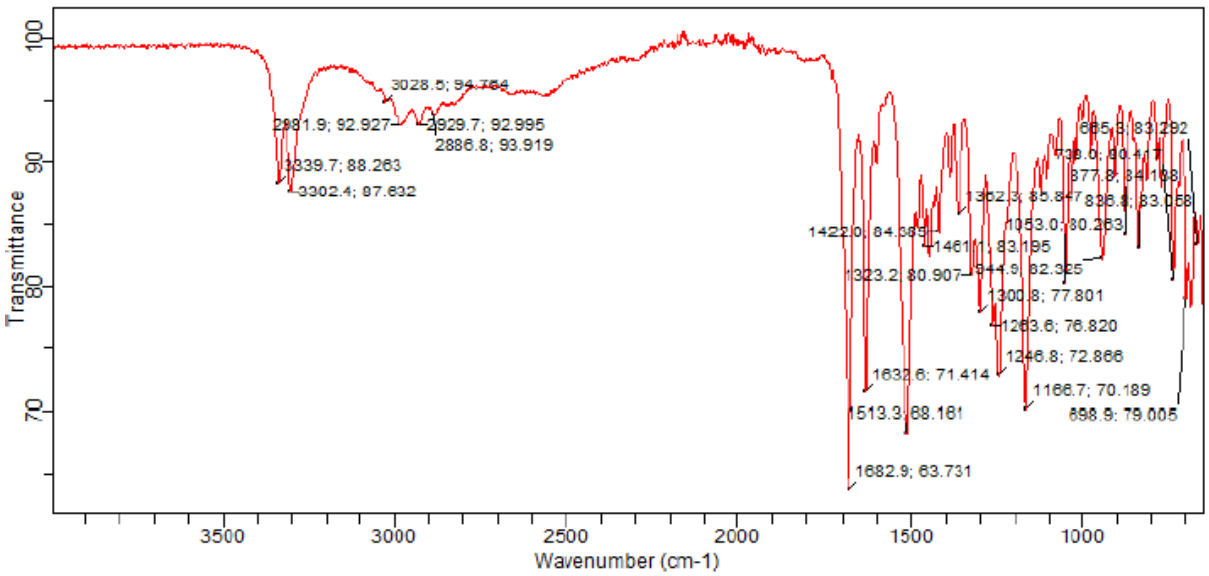


^{13}C NMR (D_6-DMSO, 100 MHz)

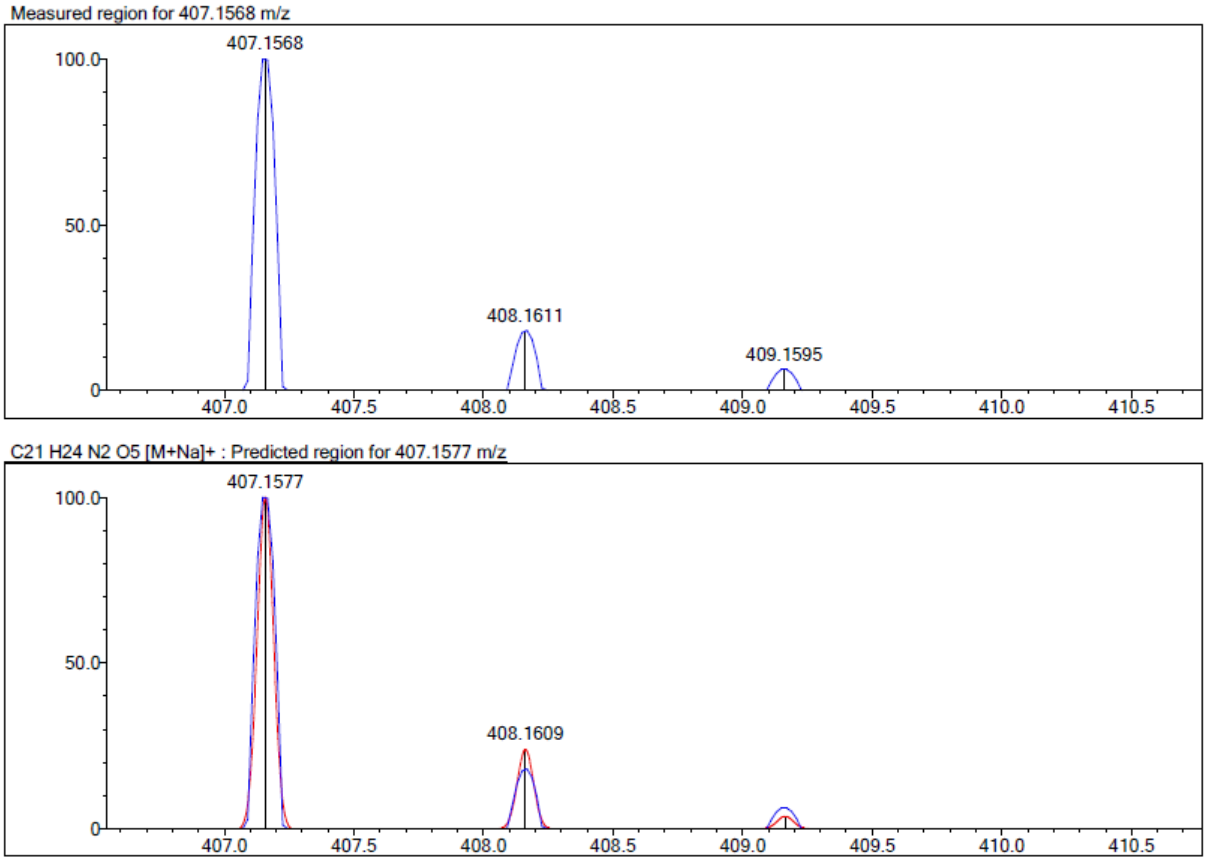


Boc-acid ESI-2

IR (neat)



Mass Spectrum (ES +ve)



Boc-bromo ESI-3

To a suspension of **ESI-2** (320 mg, 0.832 mmol) in dry CH_3CN (50 mL), DCC (189 mg, 0.916 mmol) and *N*-hydroxysuccinimide (115 mg, 0.999 mmol) were added. The reaction mixture was stirred under an Ar (g) atmosphere for 16 h. The urea precipitate was filtered off and the solvent of the filtrate removed *in vacuo*. The residue was dissolved in dry CH_2Cl_2 (15 mL) and added to a solution 3-bromopropyl amine hydrobromide (182 mg, 0.832 mmol) and NEt_3 (261 μL, 190 mg, 1.87 mmol) in dry CH_2Cl_2 (15 mL). The reaction mixture was stirred under an Ar (g) atmosphere for 20 h. The reaction mixture was then washed with 1M HCl (aq) (2 × 30 mL), sat $NaHCO_3$ (2 × 30 mL) and H_2O (1 × 30 mL), then the organic layer dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude material was purified by silica gel chromatography (CH_2Cl_2/CH_3OH 98:2 to 97:3) to yield the pure product as a white solid (113 mg, 27%).

***R*f** 0.39 (CH_2Cl_2/CH_3OH 96:4)

Mp 113-116 °C (phase transition)

υ_{max}/cm^{-1} (neat) 3340, 3270 (multiple N–H), 2990, 2930, 2880 (multiple C–H), 1680, 1630 (2 × C=O observed, third coincident), 1510, 1240, 1160.

δH(400 MHz; $CDCl_3$) 8.22 (1H, s, 2-iso *H*), 7.94-7.99 (2H, app t, 4- & 6-iso *H*), 7.52 (1H, t, ^3J = 7.8 Hz, 5-iso *H*), 7.19-7.27 (4H, m, Ar*H*), 6.72-6.77 (2H, m, 2 × iso N*H*), 4.97 (1H, br s, Boc N*H*), 4.58 (2H, d, ^3J = 5.7 Hz, CH_2), 4.27 (2H, d, ^3J = 5.7 Hz, CH_2), 3.54-3.59 (2H, app quart, NHCH_2CH$_2$CH$_2$Br), 3.45 (2H, t, ^3J = 6.4 Hz, NHCH$_2$CH$_2$CH_2Br), 2.13-2.20 (2H, app quint, NHCH$_2$CH_2CH$_2$Br), 1.46 (9H, s, C(CH_3)$_3$).

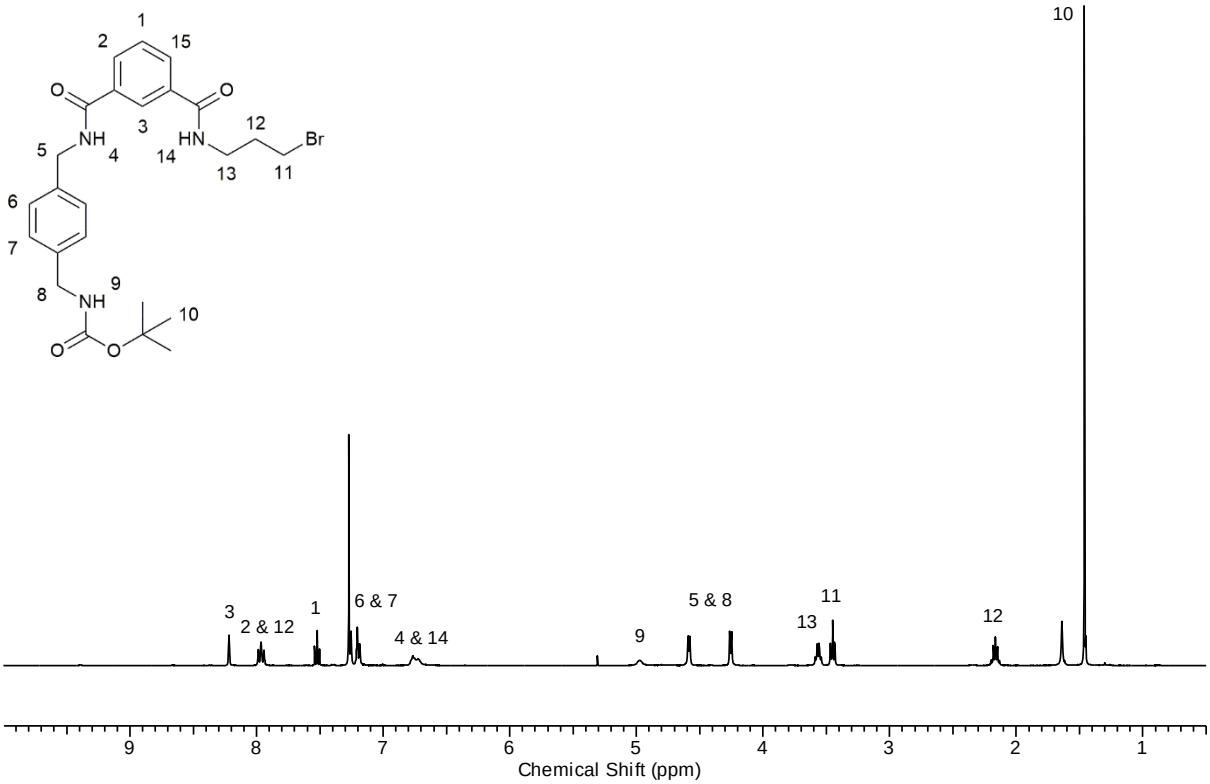
δC(100 MHz; $CDCl_3$) 166.8, 166.4 (2 × *C*=O observed, 1 missing), 138.5, 136.9, 134.5, 134.5 (sic), 130.2, 129.1, 128.2, 127.7, 125.2 (9 × Ar*C*, 2 environments coincident), 79.7 (O*C*(CH$_3$)$_3$), 44.3, 44.0, 38.8 (3 × NH*C*H$_2$), 32.1 (*C*H$_2$CH$_2$Br), 30.8 (CH$_2$*C*H$_2$Br), 28.4 (OC(*C*H$_3$)$_3$).

***m/z* (ES)** 526.1308 ([M + Na]$^+$ $BrC_{24}H_{30}N_3NaO_4$ requires 526.1312).

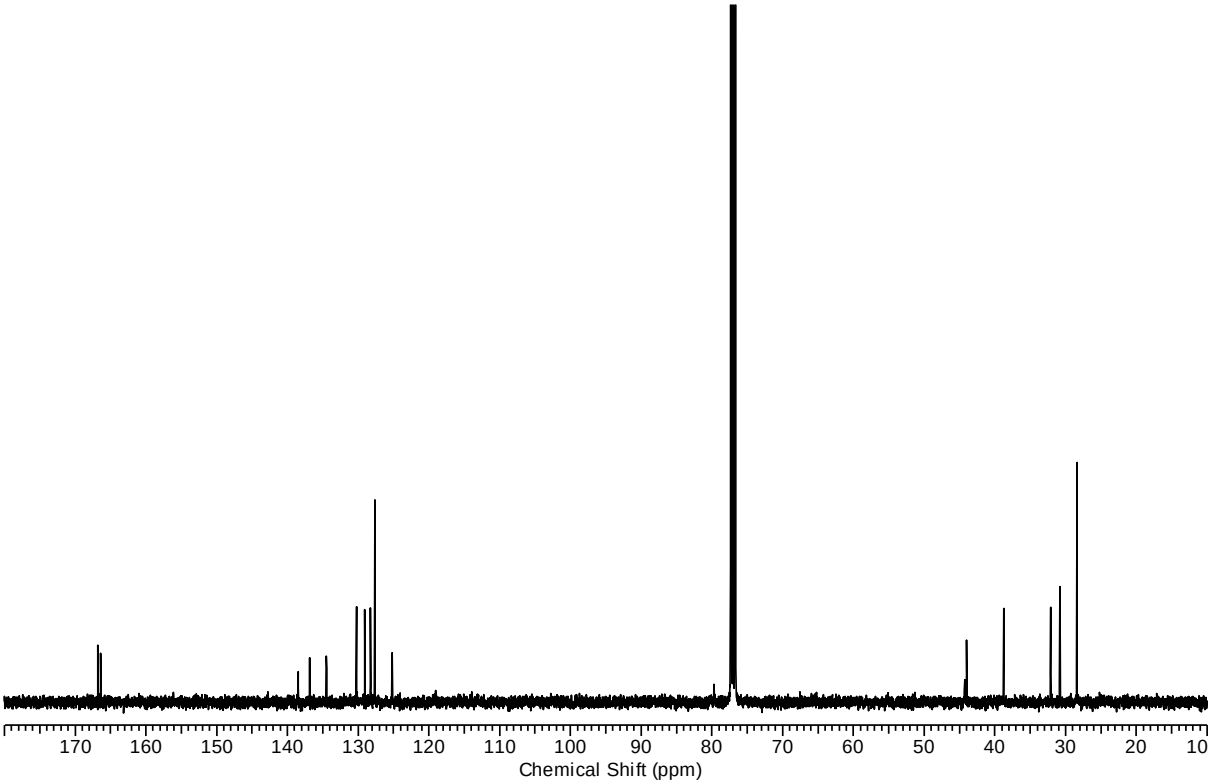
NB: Compound gels in fresh (i.e. anhydrous) $CDCl_3$.

Boc-bromo ESI-3

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

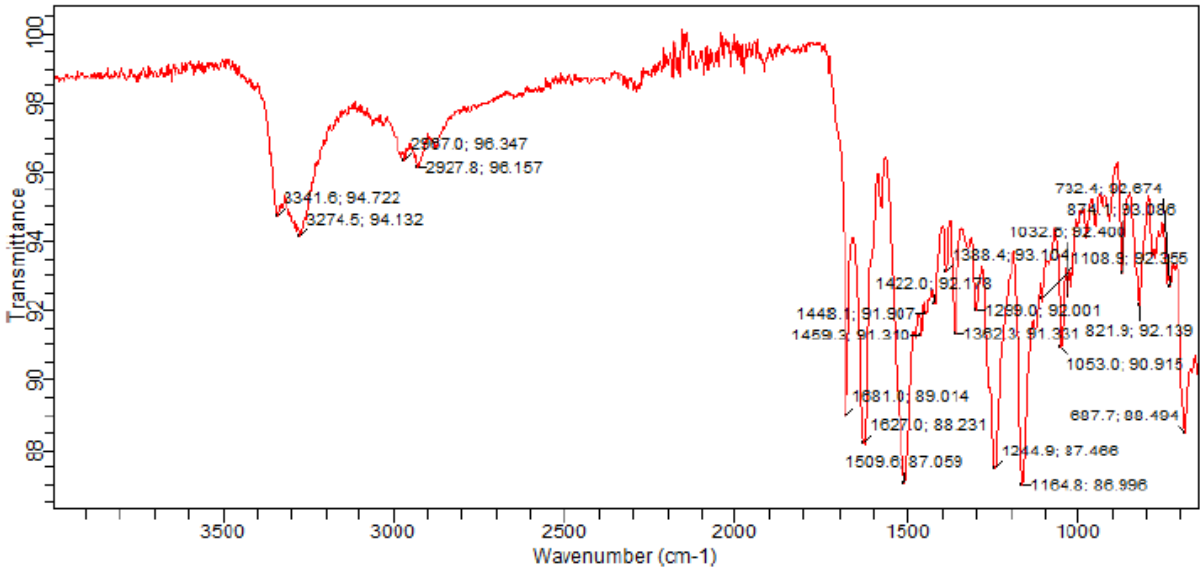


^{13}C NMR ($CDCl_3$, 100 MHz)

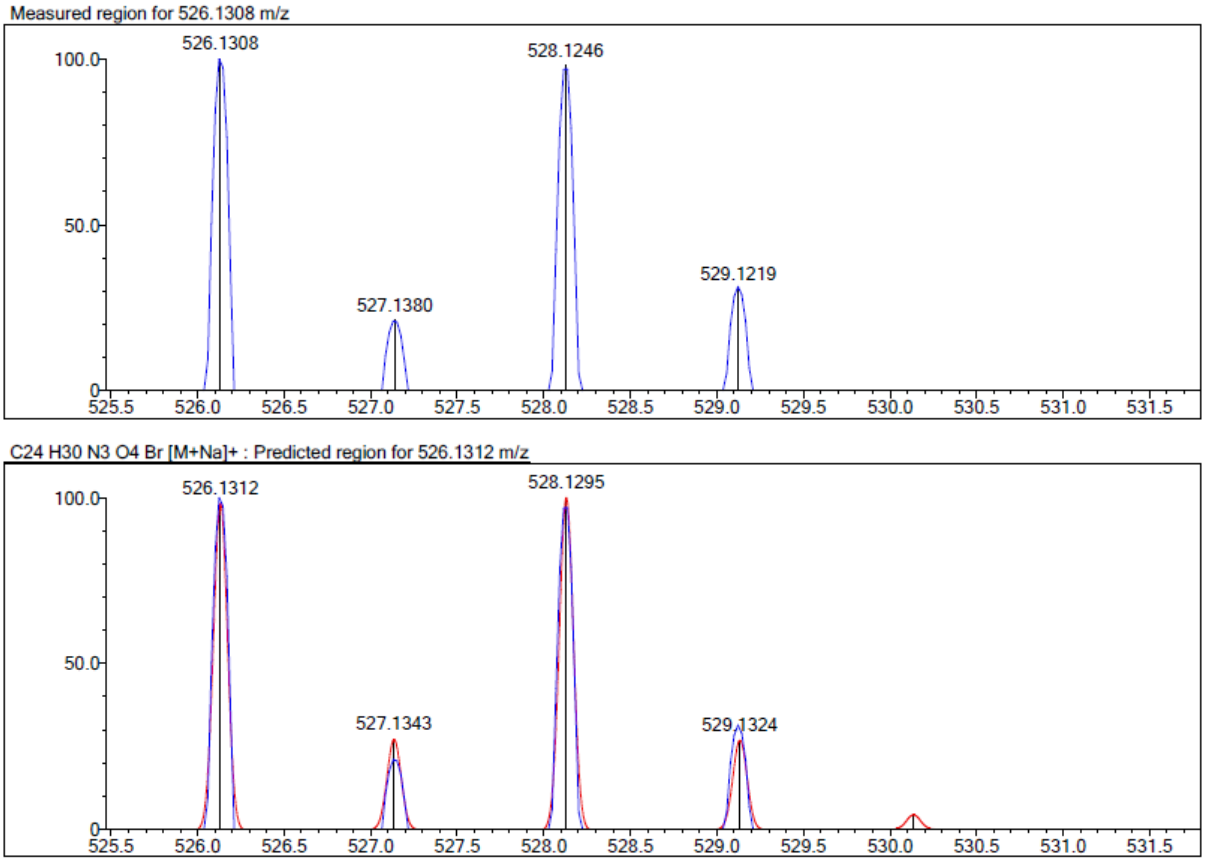


Boc-bromo ESI-3

IR (neat)



Mass Spectrum (ES +ve)



Boc-azide ESI-4

NaN_3 (66 mg, 1.01 mmol) was added to a solution of **ESI-3** (102 mg, 0.202 mmol) in dry DMF (5 mL), and the reaction mixture was heated to 80 °C under an Ar (g) atmosphere for 16 h. After cooling to RT, H_2O (30 mL) was added, and the aqueous layer extracted with EtOAc (4 × 20 mL). The combined organic layers were washed with H_2O (3 × 20 mL), then dried (Na_2SO_4) and the solvent remove *in vacuo* to yield the product as a white solid (60 mg, 64%).

***R*f** 0.39 (CH_2Cl_2/CH_3OH 96:4)

Mp 120 °C (phase transition)

υ_{max}/cm^{-1} (neat) 3350, 3280 (multiple N–H), 2980, 2930, 2870 (multiple C–H), 2090 (N=N=N), 1680, 1630 (2 × C=O observed, third coincident), 1510, 1240, 1160.

δH(400 MHz; $CDCl_3$) 8.22 (1H, s, 2-iso *H*), 7.93-7.99 (2H, m, 4- & 6-iso *H*), 7.52 (1H, t, ^3J = 7.8 Hz, 5-iso *H*), 7.18-7.26 (4H, m, Ar*H*), 6.78-6.81 (2H, m, 2 × iso N*H*), 4.99 (1H, br s, Boc N*H*), 4.57 (2H, d, ^3J = 5.4 Hz, CH_2), 4.25 (2H, d, ^3J = 5.4 Hz, CH_2), 3.47-3.51 (2H, app quart, NHCH_2CH$_2$CH$_2$N$_3$), 3.39 (2H, t, ^3J = 6.4 Hz, NHCH$_2$CH$_2$CH_2N$_3$), 1.83-1.90 (2H, app quint, NHCH$_2$CH_2CH$_2$N$_3$), 1.46 (9H, s, C(CH_3)$_3$).

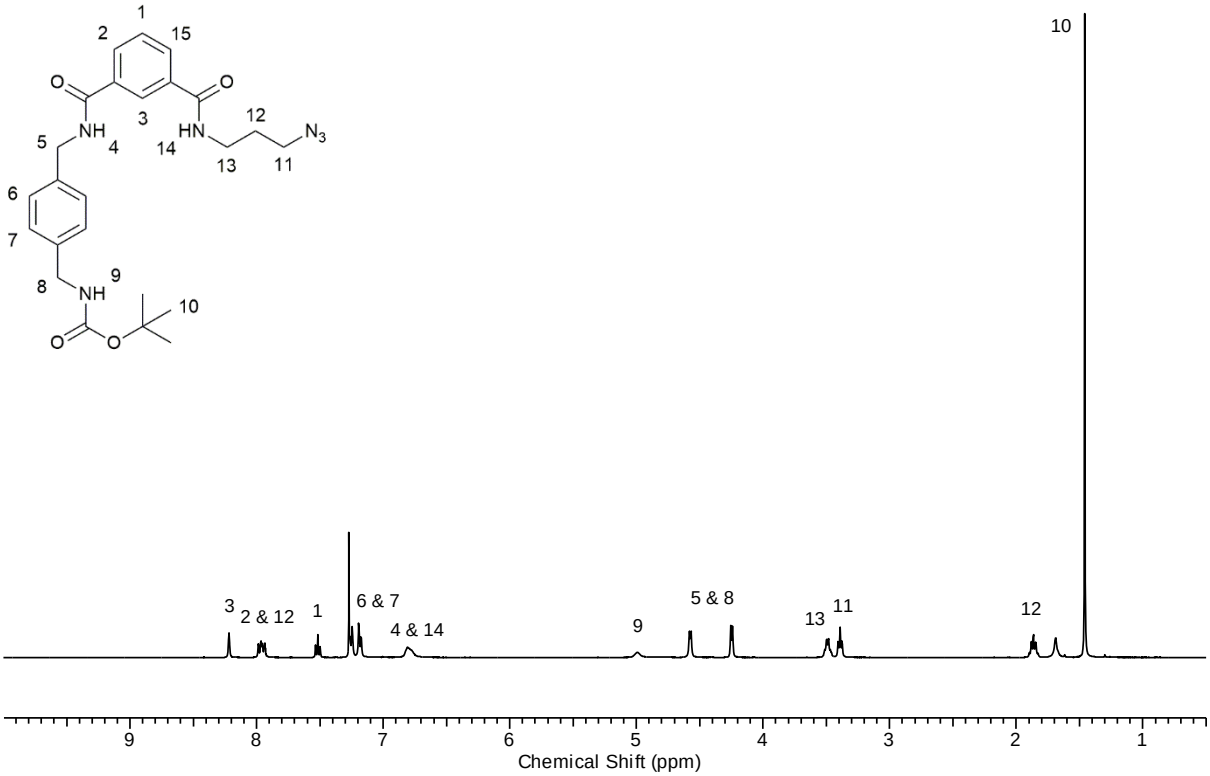
δC(100 MHz; $CDCl_3$) 166.7, 166.4, 156.1 (3 × *C*=O), 138.5, 136.9, 134.6, 134.4, 130.2, 129.0, 128.2, 127.6, 125.2 (9 × Ar*C*, 2 environments coincident), 79.7 (O*C*(CH$_3$)$_3$), 49.4 (CH$_2$*C*H$_2$N$_3$), 44.3, 44.0, 37.8 (3 × NH*C*H$_2$), 28.7 (*C*H$_2$CH$_2$N$_3$), 28.4 (OC(*C*H$_3$)$_3$).

***m/z* (ES)** 489.2238 ([M + Na]$^+$ $C_{24}H_{30}N_6NaO_4$ requires 489.2221).

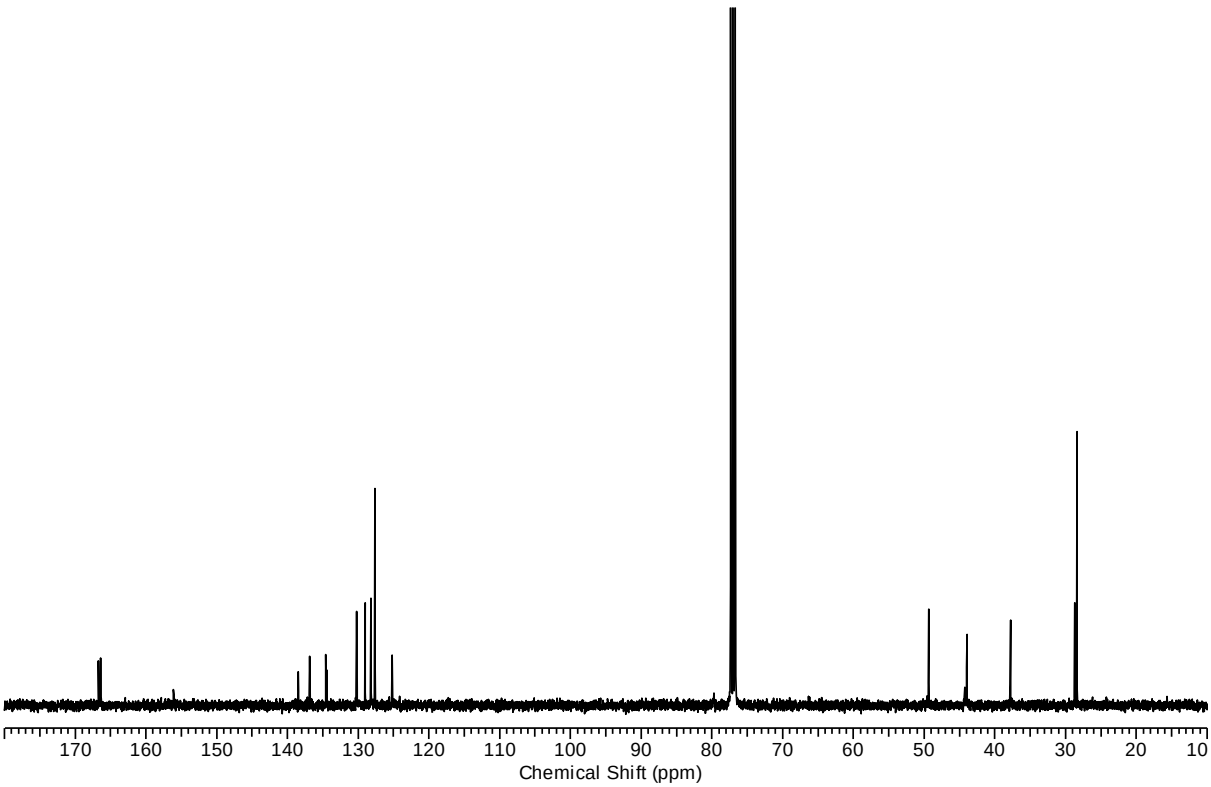
NB: Compound gels in fresh (i.e. anhydrous) $CDCl_3$.

Boc-azide ESI-4

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

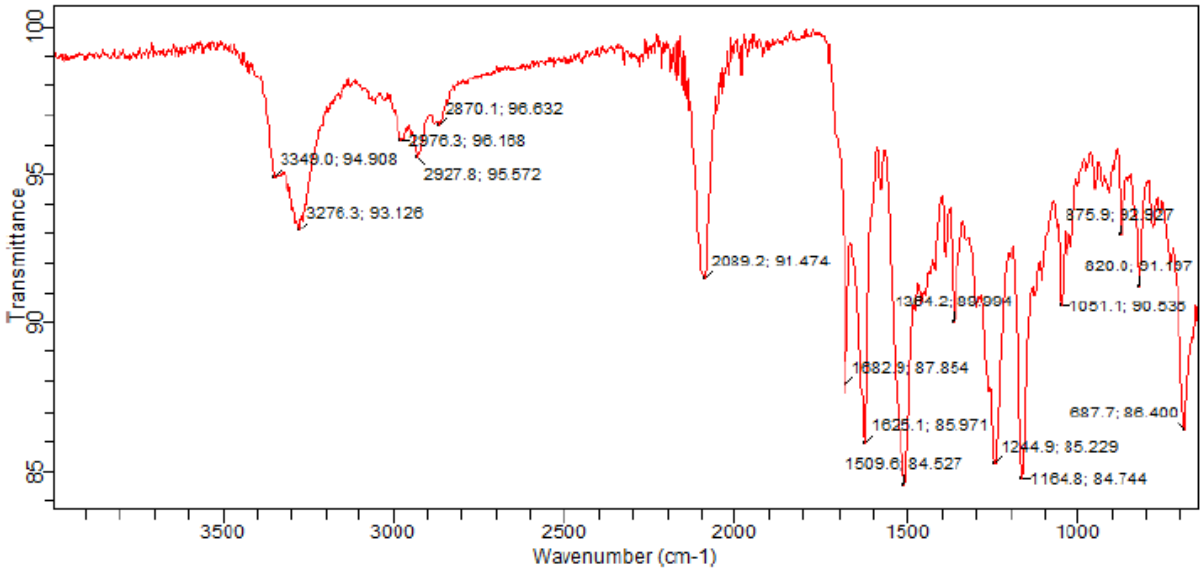


^{13}C NMR ($CDCl_3$, 100 MHz)

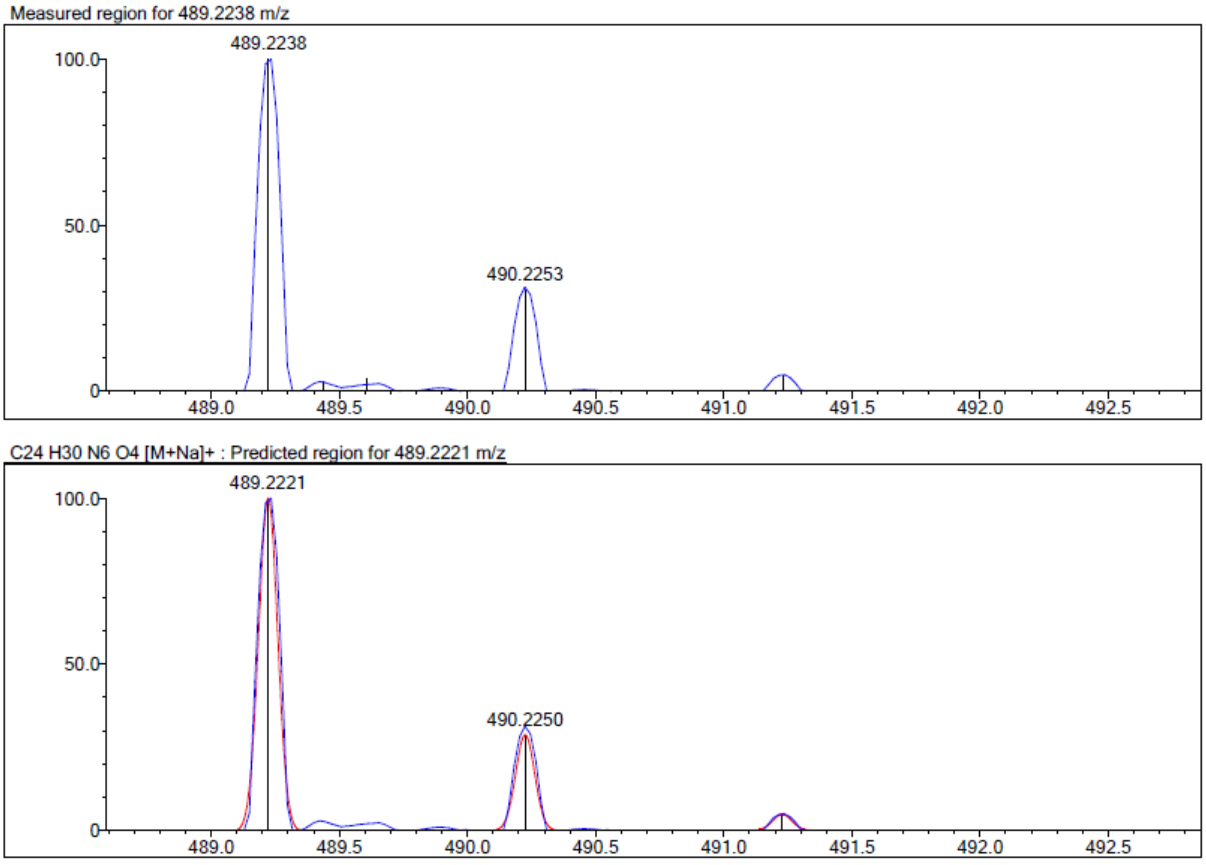


Boc-azide ESI-4

IR (neat)



Mass Spectrum (ES +ve)



Alkyne-azide 11

Boc-azide **ESI-4** (51 mg, 0.11 mmol) was dissolved in CH_2Cl_2 (2 mL) and cooled to 0 °C. TFA (0.5 mL) was added, and the reaction stirred for 2 h, allowing to warm to RT. Solvent and excess TFA were removed *in vacuo* to leave the unprotected amine salt that was taken on assuming quantitative formation.

To a suspension of **2** (19 mg, 0.11 mmol) in dry CH_3CN (2.5 mL), DCC (25 mg, 0.12 mmol) and *N*-hydroxysuccinimide (15 mg, 0.13 mmol) were added. The reaction mixture was stirred under an Ar (g) atmosphere for 16 h. The urea precipitate was filtered off and the solvent of the filtrate removed *in vacuo*. The residue was suspended in dry CH_2Cl_2 (2.5 mL), and a solution of the amine salt prepared above and NEt_3 (150 μL, 109 mg, 1.08 mmol) in dry CH_2Cl_2 (2.5 mL) was added. The reaction mixture was stirred under an Ar (g) atmosphere for 72 h. The reaction mixture was diluted to 10 mL then washed with 1M HCl (aq) (2 × 10 mL), sat $NaHCO_3$ (2 × 10 mL) and H_2O (1 × 10 mL), then the organic layer dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude material was purified by silica gel chromatography (EtOAc/Petrol 40-60 2:1 to 3:1) to yield the pure product as a white solid (30 mg, 52%).

***R*f** 0.21 (EtOAc/Petrol 40-60 3:1)

Mp 196 °C (phase transition)

υ_{max}/cm^{-1} (neat) 3280 (N–H), 3060, 2920, 2870 (multiple C–H), 2100 (N=N=N), 1630, 1600 (2 × C=O observed, third coincident), 1540, 1500, 1300, 1250, 1180, 1020.

δH(400 MHz; 1:1 $CDCl_3$/CD_3OD) 8.21 (1H, t, ^4J = 1.6 Hz, 2-iso *H*), 7.92-7.97 (2H, m, 4- & 6-iso *H*), 7.77-7.81 (2H, m, Ar*H*), 7.51 (1H, t, ^3J = 7.8 Hz, 5-iso *H*), 7.29 (4H, s, Ar*H*), 6.97-7.01 (2H, m, Ar*H*), 4.73 (2H, d, ^4J = 2.3 Hz, CH_2CCH), 4.55 (2H, s, CH_2), 4.52 (2H, s, CH_2), 3.45 (2H, t, ^3J = 6.8 Hz, NHCH_2CH$_2$CH$_2$N$_3$), 3.38 (2H, t, ^3J = 6.8 Hz, NHCH$_2$CH$_2$CH_2N$_3$), 2.72 (1H, t, ^4J = 2.3 Hz, alkynyl *H*), 1.83-1.90 (2H, app quint, NHCH$_2$CH_2CH$_2$N$_3$).

δC(100 MHz; 1:1 $CDCl_3$/CD_3OD) 168.9, 168.9 (sic), 168.6 (3 × *C*=O observed), 161.0, 138.7, 138.1, 135.4, 135.3, 131.0, 129.7, 129.5, 128.5, 128.4, 127.9, 126.5, 115.3, 138.5, 136.9, 134.5, 134.5 (sic), 130.2, 129.1, 128.2, 127.7, 125.2 (13 × Ar*C*, 2 environments coincident), 78.5 (CH$_2$*C*CH), 76.8 (CH$_2$C*C*H), 56.4 (*C*H$_2$CCH), 44.2, 44.0 (2 × NH*C*H$_2$), 38.1 (NH*C*H$_2$CH$_2$CH$_2$N$_3$), 29.3 (*C*H$_2$CH$_2$N$_3$).

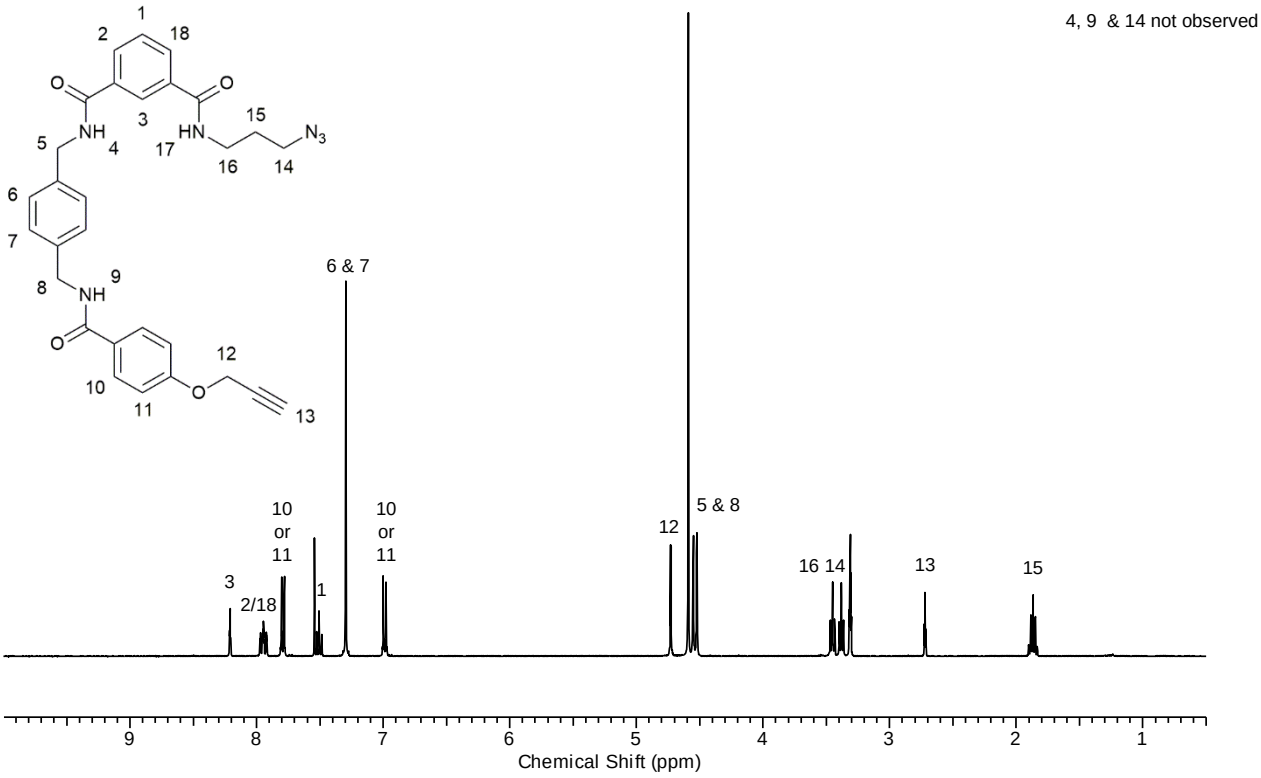
NHCH$_2$CH$_2$*C*H$_2$N$_3$ obscured by methanol solvent peak

***m/z* (ES)** 547.2067 ([M + Na]$^+$ $C_{29}H_{28}N_6NaO_4$ requires 547.2064).

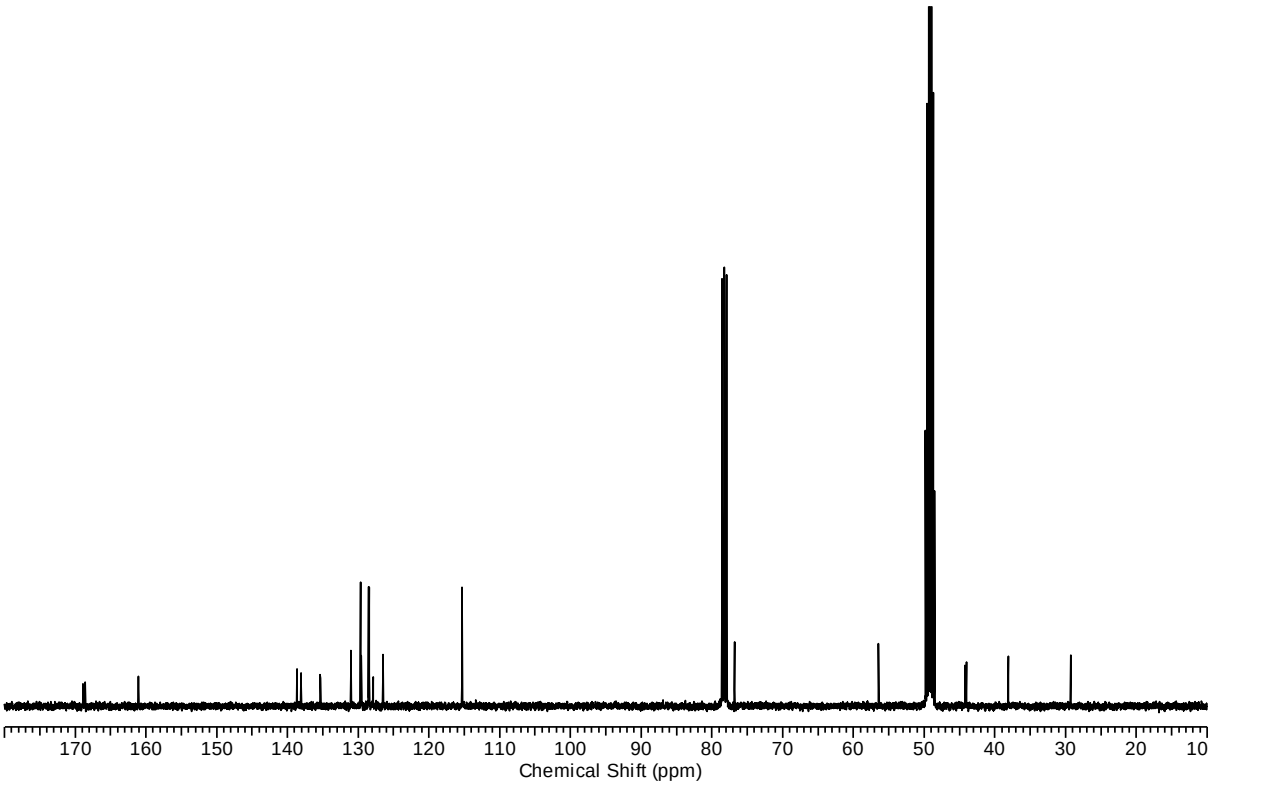
NB: Atoms labelled as on chemical structure on next page.

Alkyne-azide 11

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

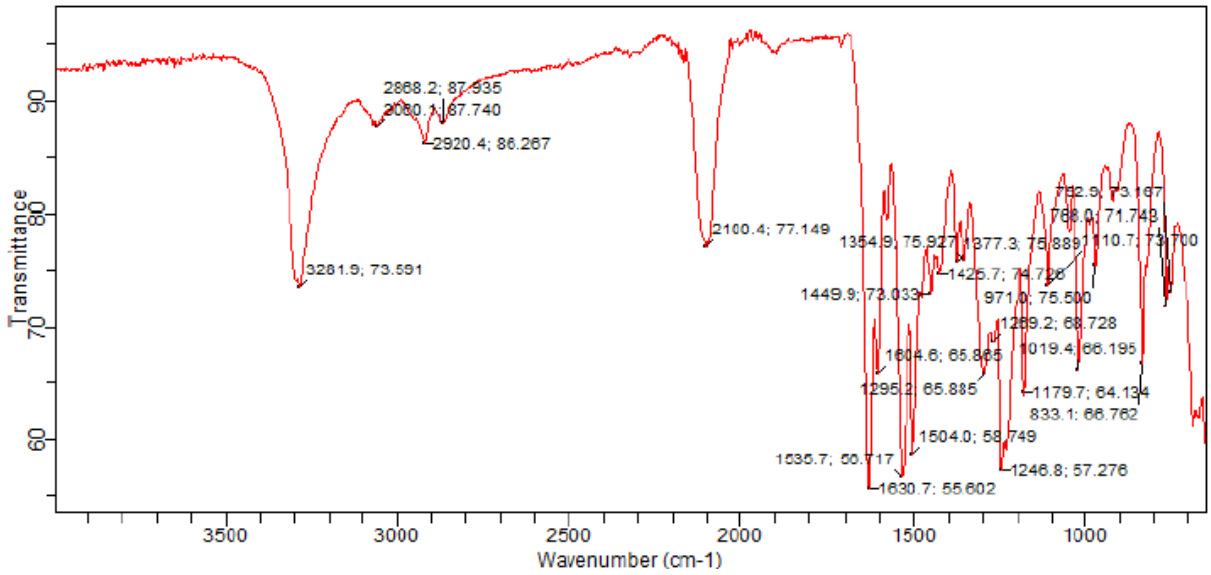


^{13}C NMR (1:1 $CDCl_3$/CD_3OD, 100 MHz)

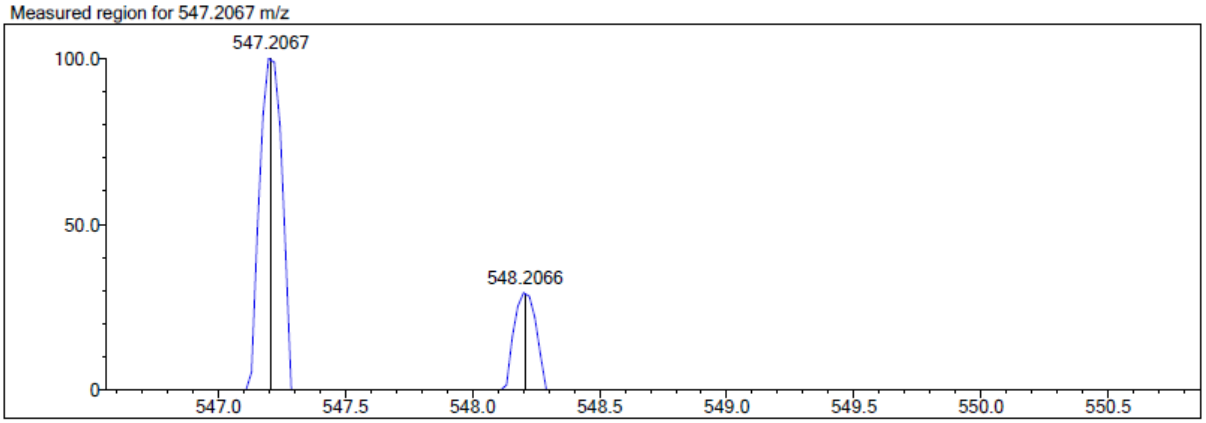


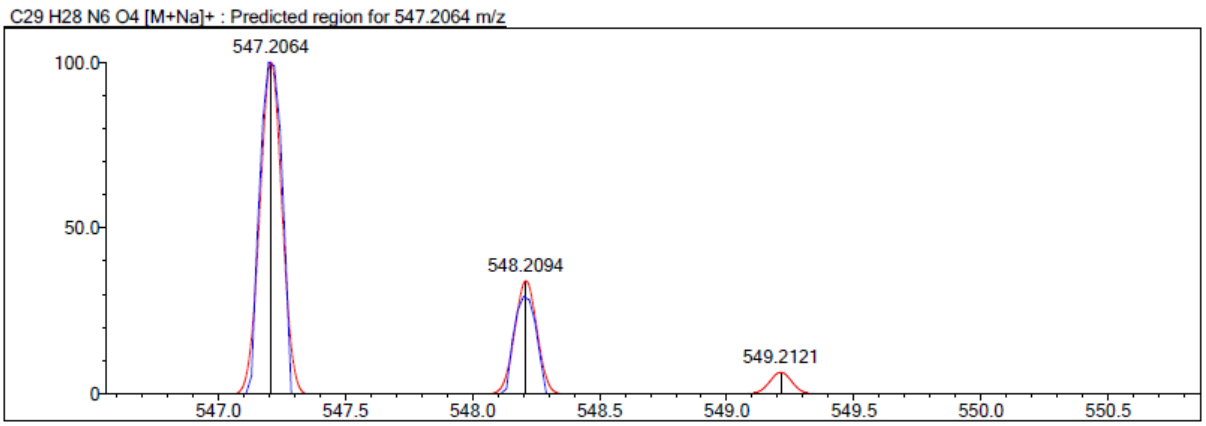
Alkyne-azide 11

IR (neat)



Mass Spectrum (ES +ve)





Catenane 15

Macrocycle **14** (24 mg, 0.051 mmol) and alkyne-azide **11** (27 mg, 0.051 mmol) were dissolved in dry CH_2Cl_2 (20 mL) and stirred under an Ar (g) atmosphere until dissolved. Then $Cu(CH_3CN)_4BF_4$ (3.2 mg, 0.010 mmol), TBTA (5.5 mg, 0.010 mmol) and DIPEA (10 μL, 7.3 mg, 0.057 mmol) were added. The reaction mixture was stirred for 15 h, and then the solvent removed *in vacuo*. The crude material was submitted to silica gel chromatography (CH_2Cl_2/CH_3OH 99:1 to 96:4). To remove DIPEA (salt), a CH_2Cl_2 solution washed with 1M HCl (aq), sat. $NaHCO_3$ (aq) and H_2O, dried ($MgSO_4$), and solvent removed *in vacuo*, to yield pure product as a white solid film (27 mg, 53%).

***R*f** 0.24 (CH_2Cl_2/CH_3OH 96:4)

Mp >166 °C (phase transition)

υ_{max}/cm^{-1} (neat) 3310 (N–H), 3050, 2920, 2870 (multiple C–H), 1630, 1600 (2 × C=O observed, multiple coincident), 1530, 1500, 1290, 1220, 1180, 1070, 1020.

δH(400 MHz; 1:1 $CDCl_3$/CD_3OD) 8.66 (1H, br s, H^{c}), 8.14-8.17 (2H, m, $H^{b\ \&\ b'}$), 8.07 (1H, d, ^3J = 7.8 Hz, $H^{2\ or\ 18}$), 7.98 (1H, d, ^3J = 7.8 Hz, $H^{2\ or\ 18}$), 7.73 (2H, d, ^3J = 8.9 Hz, H^{10}), 7.69 (1H, s, H^{13}), 7.59-7.64 (2H, m, H^{a} & H^{1}), 7.47 (1H, s, H^{3}), 7.36 (2H, d, ^3J = 7.9 Hz, $H^{6\ or\ 7}$), 7.00 (2H, d, ^3J = 8.9 Hz, H^{11}), 6.95 (2H, d, ^3J = 7.9 Hz, $H^{6\ or\ 7}$), 6.90 (4H, d, ^3J = 7.9 Hz, H^{f}), 6.52 (4H, d, ^3J = 7.9 Hz, H^{g}), 5.38 (2H, s, H^{12}), 4.54 (2H, d, ^2J = 14 Hz, H^{e}), 4.39 (2H, s, $H^{5\ or\ 8}$), 4.36 (2H, d, ^2J = 14 Hz, $H^{e'}$), 4.21 (2H, br s, H^{14}), 3.83-3.91 (4H, m, H^{h}), 3.79 (2H, br s, $H^{5\ or\ 8}$), 2.94 (2H, br s, H^{16}), 2.73-2.88 (4H, m, H^{i}), 2.46-2.58 (4H, m, H^{j}), 1.80 (2H, br s, H^{15}).

δC(100 MHz; 1:1 $CDCl_3$/CD_3OD) 168.1, 167.8, 167.2, 167.7 (4 × *C*=O observed), 160.6, 144.3, 140.1, 137.8, 137.3, 136.0, 134.7, 134.4, 134.3, 132.6, 132.4, 132.3, 130.4, 130.1, 130.0, 130.0 (sic), 129.5, 129.4, 129.0, 127.1, 125.4, 125.3, 124.3, 115.9 (24 × Ar*C* & triazole *C*), 78.5 (CH_2*C*CH)??, 74.2 (sym macro O*C*H_2O) ,70.8, 69.2 (2 × sym macro O*C*H_2*C*H_2O), 61.3 (*C*H_2CCH), 45.0 (sym macro NH*C*H_2), 44.2, 44.0 (2 × NH*C*H_2), 38.1 (NH*C*$H_2$$CH_2$$CH_2$$N_3$), 30.3 (*C*$H_2$$CH_2$$N_3$).

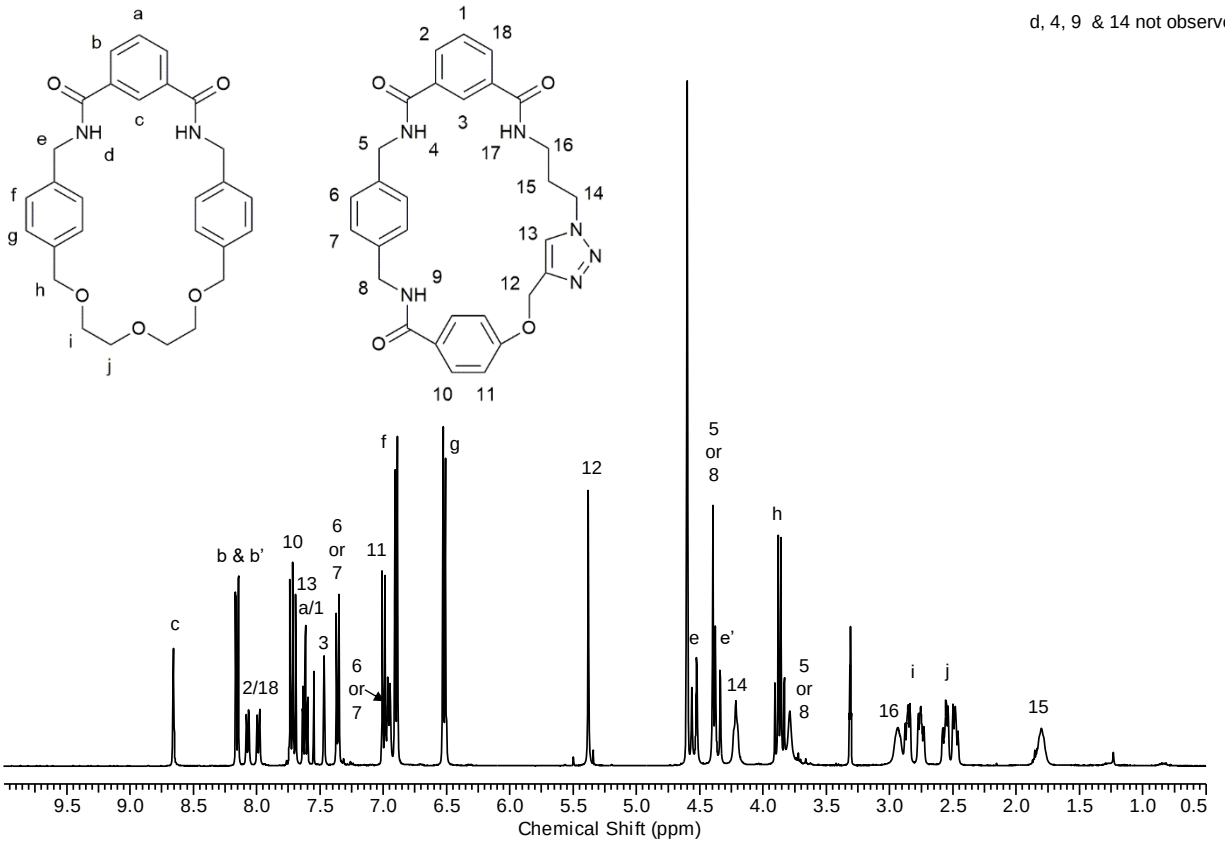
NH$CH_2$$CH_2$*C*$H_2$$N_3$ obscured by methanol solvent peak

***m/z* (ES)** 999.4371 ($[M + H]^+$ $C_{57}H_{59}N_8O_9$ requires 999.4400) & 1021.4216 ($[M + Na]^+$ $C_{57}H_{58}N_8NaO_9$ requires 1021.4219).

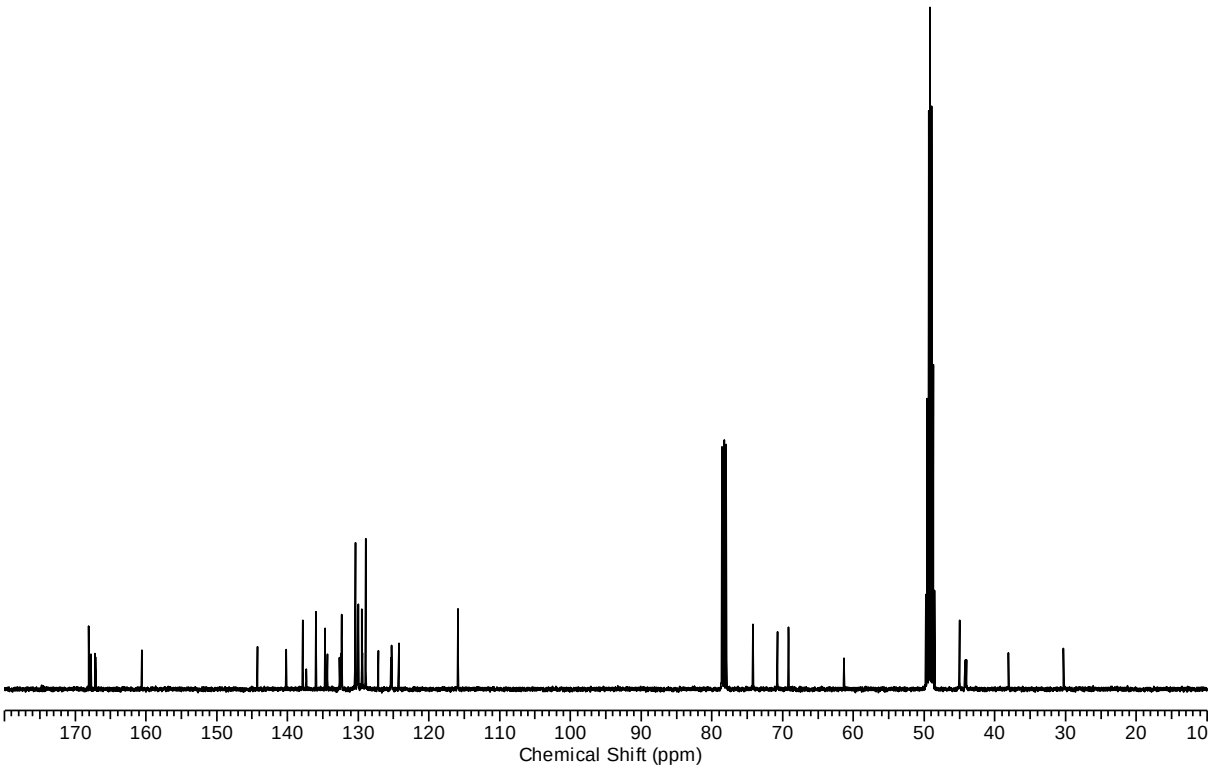
NB: Atoms labelled as on chemical structure on next page.

Catenane 15

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

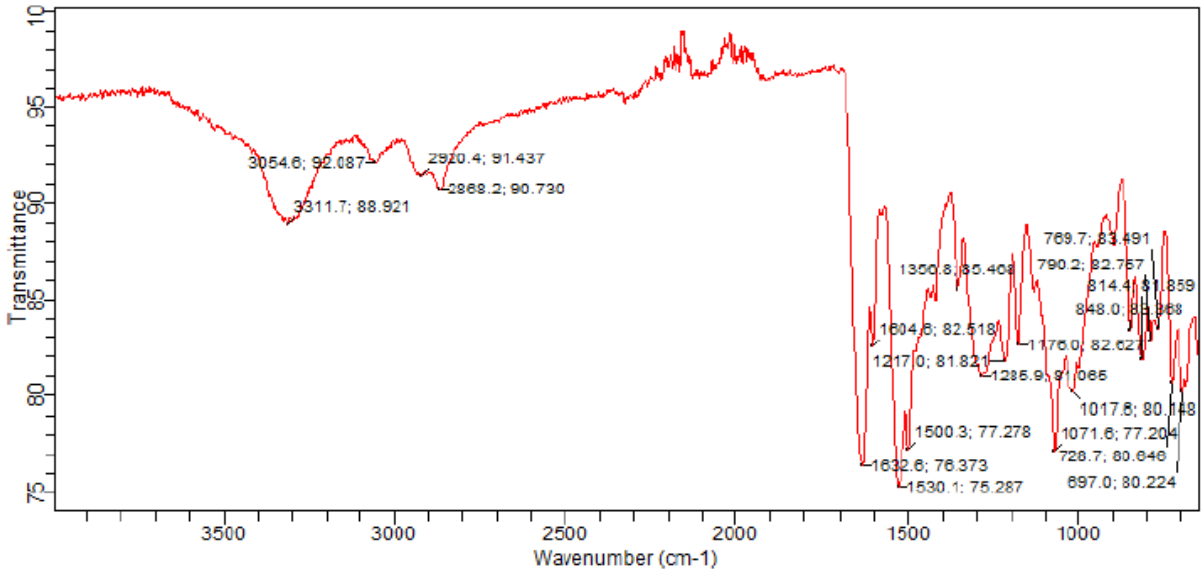


^{13}C NMR (1:1 $CDCl_3$/CD_3OD, 100 MHz)



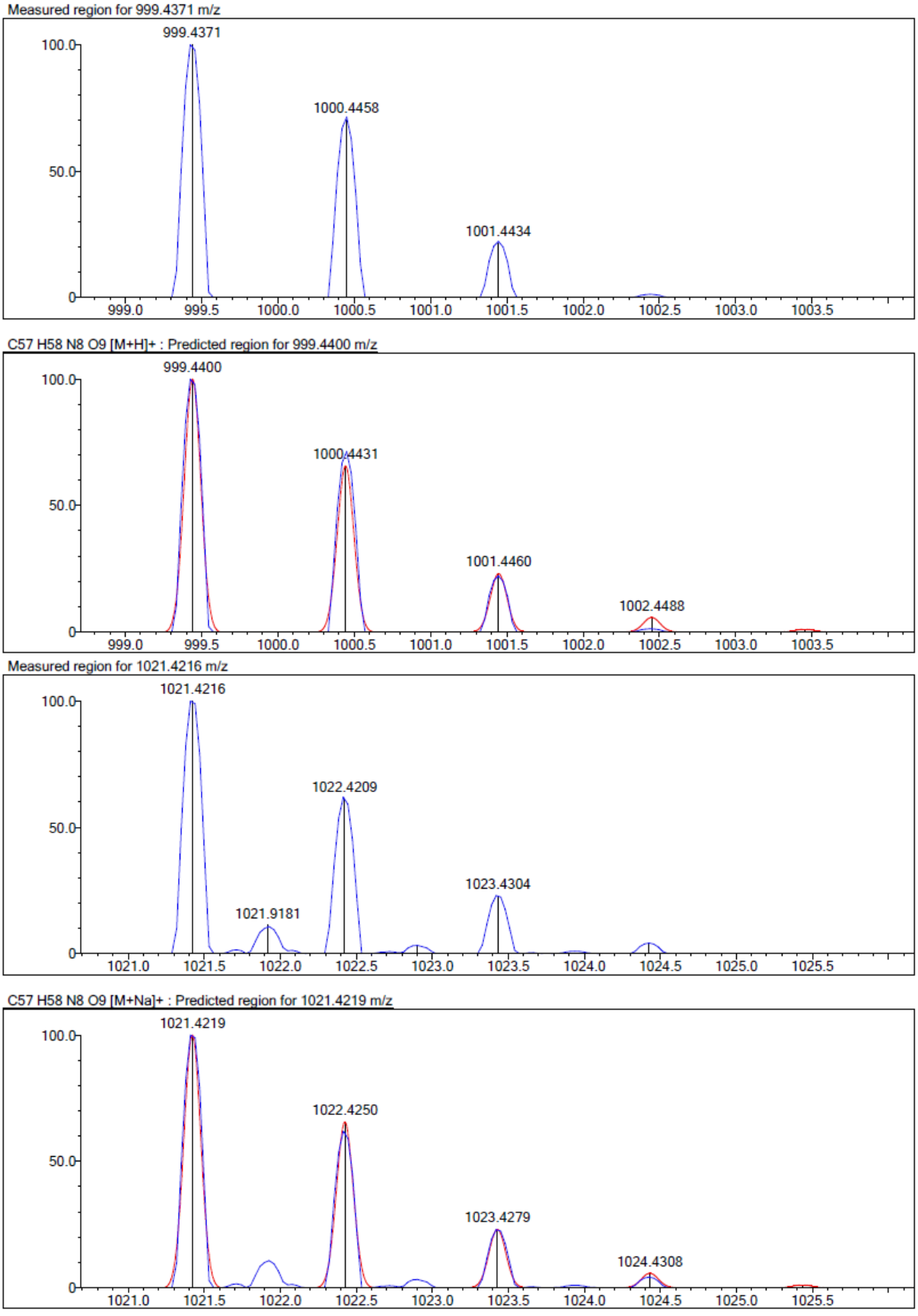
Catenane 15

IR (neat)



Catenane 15

Mass Spectrum (ES +ve)



References

(1) M. J. Langton, L. C. Duckworth and P. D. Beer, *Chem. Commun.*, 2013, **49**, 8608-8610.

(2) N. H. Evans, C. E. Gell and M. J. G. Peach, *Org. Biomol. Chem.*, 2016, **14**, 792-7981.