Electronic Supplementary Information

Cubane-1,3-dicarboxamides as structural isosteres for isophthalamides in hydrogen bond templated interlocked molecules

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Part 1: Experimental Information

General Procedures

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}. Deionised water was used in all cases. All aqueous solutions are saturated unless otherwise stated.

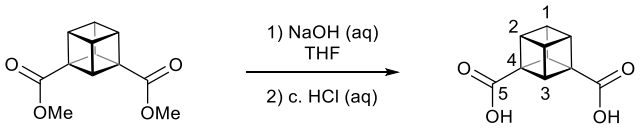
Silica gel with a 60 Å particle size was used as the stationary phase for column chromatography. Analytical TLC was used to monitor the progress of column chromatography, with analytical TLC plates examined under short wavelength (254 nm) UV light or staining with potassium permanganate and phosphomolybdic 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 Bruker or Agilent Technologies FTIR spectrometers. NMR spectra were recorded on Bruker AVANCE III 400 or Bruker Neo 400 spectrometers at 298 K (unless otherwise stated). Mass spectra were recorded on an Agilent 6545 Q-TOF instrument. Melting points were recorded on a Gallenkamp capillary melting point apparatus and are uncorrected.

Dimethylcubane-1,3-dicarboxylate,[1] axle **3**[2], alkyne-azide **6**[3], azide **8**[4], alkyne **9**[5], bis-amine **ESI-4**[6], methyl-pyridinium template **ESI-5**[6], axle **ESI-6**[4] and the all-isophthalamide [2]catenane **ESI-7**[3] were all synthesized according to previously reported procedures.

Experimental Procedures

Procedure for preparation of cubane-1,3-dicarboxylic acid:



To a solution of dimethylcubane-1,3-dicarboxylate (1.24 g, 5.63 mmol) in THF (25 mL) was added dropwise an aqueous solution of NaOH (6.8 mL, 2.5 M) at room temperature. The reaction was stirred at room temperature for 24 hours, then the THF was evaporated under reduced pressure, with the resulting residue being re-suspended in water (30 mL) and extracted with $CHCl_3$ (3 x 10 mL). The aqueous layer was acidified to pH < 1 with conc. HCl (aq), then extracted with EtOAc (5 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure to provide the *title product* (1.08 g, 93%) as a white solid.

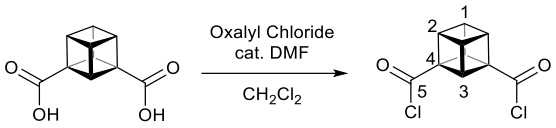
ν_{max}/cm^{-1} (neat): 2989 (C-H), 2832 (C-H), 2704 (C-H), 2598 (C-H), 1671 (C=O).

δ_H (400 MHz, *d*$_6$-DMSO): 12.40 (s, 2H, OH), 4.29-4.26 (m, 2H, H^1), 4.11 (app. septet, 2H, H^2), 3.91 (app. q, 2H, H^3).

δ_C (100 MHz, *d*$_6$-DMSO): 172.1 (C^5), 52.8 (C^4), 50.2 (C^1), 48.9 (C^2), 41.7 (C^3).

m/z (ESI): 215.0313 ($[M + Na]^+$); neutral observed mass: 192.0422, $C_{10}H_8O_4$ requires 192.0423; 191.0350 ($[M - H]^-$); neutral observed mass: 192.0423, $C_{24}H_{22}N_2O_2$ requires 192.0423.

*Procedure for conversion of cubane-1,3-dicarboxylic acid to cubane-1,3-diacyl chloride **1**:*



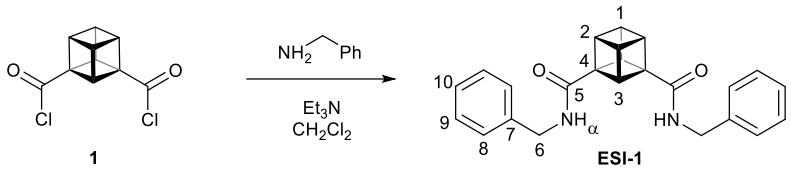
1

Cubane-1,3-dicarboxylic acid was suspended in dry CH_2Cl_2 (5 mL per 1.0 mmol of cubane) and placed under an atmosphere of argon. To this suspension was added oxalyl chloride (6 eq.) and a catalytic amount of DMF. The reaction was stirred at room temperature until the solution become homogenous. After such time, excess volatiles were removed *in vacu*o to afford cubane-1,3-diacyl chloride **1** as an orange oil, which was reacted on immediately in subsequent reactions.

δ_H (400 MHz, $CDCl_3$): 4.84-4.81 (m, 2H, H^1), 4.45 (app. septet, 2H, H^2), 4.11 (app. q, 2H, H^3).

δ_C (100 MHz, $CDCl_3$): 169.6 (C^5), 60.2 (C^4), 53.8 (C^1), 51.6 (C^2), 42.0 (C^3).

Model cubane-1,3-dicarboxamide **ESI-1**



To a solution of benzylamine (61 mg, 0.06 mL, 0.57 mmol) and Et_3N (78 mg, 0.10 mL, 0.78 mmol) in dry CH_2Cl_2 (2 mL) under argon was added a dropwise solution of cubane-1,3-diacyl chloride **1** (59 mg, 0.26 mmol) in dry CH_2Cl_2 (3 mL). The reaction was stirred at room temperature for 1 hour, then the reaction was diluted to 10 mL and washed with 1 M HCl (aq) (1 x 10 mL), $NaHCO_3$ (aq) (1 x 10 mL) and brine (1 x 10 mL). The organic layer dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by silica gel column chromatography (98:2 CH_2Cl_2/CH_3OH) to afford the *title product* (75 mg, 78%) as a colourless solid.

***R*$_f$:** 0.17 [CH_2Cl_2/CH_3OH 98:2].

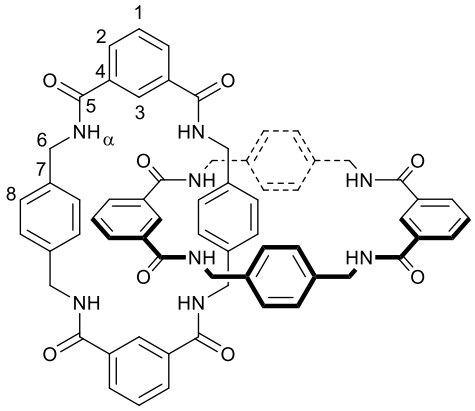
ν_{max}/cm^{-1} (neat): 3255 (N-H), 3065 (C-H), 2991 (C-H), 1623 (C=O), 1237 (C-N).

δ_H (400 MHz, $CDCl_3$): 7.39-7.27 (10H, m, H^8, H^9 & H^{10}), 5.92 (2H, bs, H^{α}), 4.47 (4H, d, *J* = 5.8 Hz, H^6), 4.40-4.37 (2H, m, H^1), 4.22 (2H, app. septet, H^2), 3.97 (2H, app. q, H^3).

δ_C (100 MHz, $CDCl_3$): 170.8 (C^5), 138.0 (C^7), 128.7 (C^9), 127.9 (C^8), 127.6 (C^{10}), 54.7 (C^4), 51.1 (C^1), 49.5 (C^2), 43.3 (C^6), 41.9 (C^3).

m/z (ESI): 371.1756 ([M + H]$^+$); neutral observed mass: 370.1684, $C_{24}H_{22}N_2O_2$ requires 370.1681.

Leigh-style isophthalamide [2]catenane **ESI-2**[7]

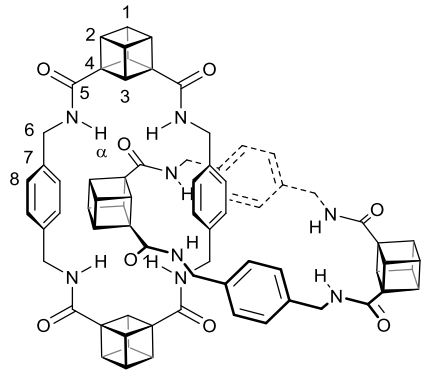


To a vigorously stirring solution of Et_3N (924 mg, 1.26 mL, 9.15 mmol) in dry $CHCl_3$ (30 mL) was added dropwise solutions of isophthaloyl chloride (211 mg, 1.04 mmol) in dry $CHCl_3$ (30 mL) and *p*-xylylenediamine (141 mg, 1.04 mmol) in dry $CHCl_3$ (30 mL) simultaneously by the use of a motorised syringe pump (rate = 0.15 mL/min). After addition, the reaction was stirred under argon at room temperature for 16 hours. The reaction mixture was then filtrated under gravity and washed with 1 M HCl (aq) (2 x 50 mL), 1 M NaOH (aq) (2 x 50 mL) and water (1 x 50 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo* to afford the *title product* (48 mg, 17%) as a colourless solid.

δ_H (400 MHz, d_6-DMSO): 8.50 (8H, bs, H^{α}), 7.97 (4H, s, H^3), 7.80 (8H, d, *J* = 8.0 Hz, H^2), 7.43 (4H, t, *J* = 8.0 Hz, H^1), 6.66 (16H, bs, H^8), 3.93 (16H, bs, H^6).

Data matches literature values.[7]

Leigh-style cubane [2]catenane **2**



To a vigorously stirring solution of Et_3N (924 mg, 1.26 mL, 9.15 mmol) in dry $CHCl_3$ (30 mL) was added dropwise solutions of cubane-1,3-diacyl chloride **1** (200 mg, 1.04 mmol) in dry $CHCl_3$ (30 mL) and *p*-xylylenediamine (141 mg, 1.04 mmol) in dry $CHCl_3$ (30 mL) simultaneously by the use of a motorised syringe pump (rate = 0.15 mL/min). After addition, the reaction was stirred under argon at room temperature for 16 hours. The reaction mixture was then filtrated under gravity and washed with 1 M HCl (aq) (2 x 50 mL), 1 M NaOH (aq) (2 x 50 mL) and water (1 x 50 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by careful silica gel column chromatography (97:3 – 95:5 CH_2Cl_2:CH_3OH) to afford the *title product* (12.5 mg, 4%) as colourless solid.

***R*$_f$:** 0.19 [CH_2Cl_2/CH_3OH 97:3].

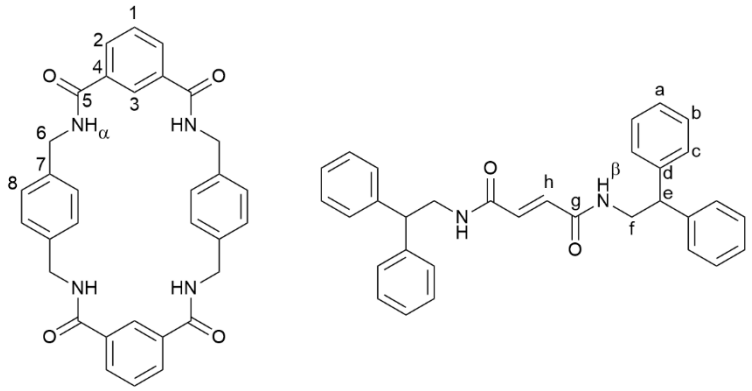
ν_{max}/cm^{-1} (neat): 3295 (N-H), 2480 (C-H), 1623 (C=O), 1528 (C-O), 1438 (C-H).

δ_H (400 MHz, 1:1 $CDCl_3$:CD_3OD): 7.26-7.23 (8H, m, H^8), 7.22 (8H, s, $H^{8'}$), 4.40-4.37 (12H, m, H^1 & H^6), 4.35 (8H, s, $H^{6'}$), 4.32-4.29 (4H, m, $H^{1'}$), 4.25-4.20 (8H, m, H^2), 3.99-3.95 (8H, m, H^3).

δ_C (100 MHz, 1:1 $CDCl_3$:CD_3OD): 172.5 (C^5), 137.4 (C^7), 127.7 ($C^{8'}$), 127.7 (C^8), 54.7 (C^4), 51.4 (C^1), 51.1 ($C^{1'}$), 49.5 (C^2), 42.7 ($C^{6'}$), 42.7 (C^6), 41.9 (C^3).

m/z (ESI): 1169.4918 ($[M + H]^+$); neutral observed mass: 1168.4859, $C_{72}H_{64}N_8O_8$ requires 1168.4847.

Leigh-style isophthalamide [2]rotaxane **ESI-3**[2]

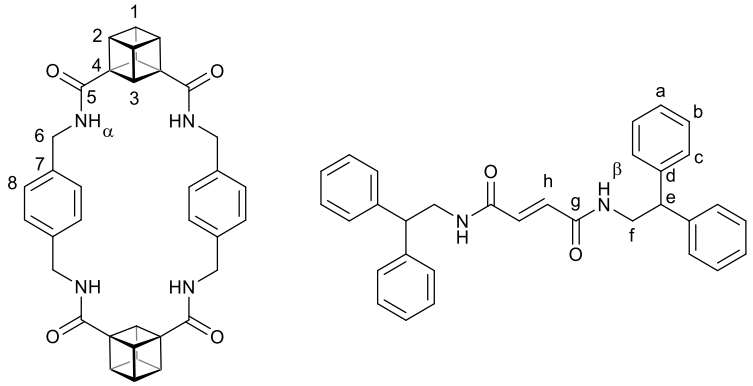


To a vigorously stirring solution of Et_3N (184.8 mg, 0.25 mL, 1.83 mmol) and axle **3** (51.8 mg, 0.109 mmol) in dry $CHCl_3/CH_3CN$ (9:1, 50 mL) was added dropwise solutions of isophthaloyl chloride (88.5 mg, 0.436 mmol) in dry $CHCl_3$ (15 mL) and *p*-xylylenediamine (59.3 mg, 0.436 mmol) in dry $CHCl_3$ (15 mL) simultaneously by the use of a motorised syringe pump (rate = 0.1 mL/min). After addition, the reaction was stirred under argon at room temperature for 16 hours. The reaction mixture was concentrated *in vacuo* and the crude material triturated with CH_2Cl_2 (3 x 1 mL) to afford the *title product* (calculated yield: 82 mg, 75%), contaminated with axle **4**, as a colourless solid.

δ_H (400 MHz, d_6-DMSO): 8.62 (2H, s, H^3), 8.52 (2H, bs, H^β), 8.15 (4H, bs, H^α), 8.09 (8H, d, *J* = 8.0 Hz, H^2), 7.71 (4H, t, *J* = 8.0 Hz, H^1), 7.31-7.14 (20H, m, H^a, H^b & H^c), 6.65 (8H, s, H^8), 5.64 (2H, s, H^h), 4.21 (8H, s, H^6), 4.10 (2H, t, *J* = 7.8 Hz, H^e), 3.66 (4H, t, *J* = 7.8 Hz, H^f).

Data matches literature values.[2]

Leigh-style cubane [2]rotaxane **4**



To a vigorously stirring solution of Et_3N (184 mg, 0.25 mL, 1.83 mmol) and axle **3** (51.8 mg, 0.109 mmol) in dry $CHCl_3/CH_3CN$ (9:1, 50 mL) was added dropwise solutions of cubane-1,3-diacyl chloride **1** (100 mg, 0.436 mmol) in dry $CHCl_3$ (15 mL) and *p*-xylylenediamine (59 mg, 0.436 mmol) in dry $CHCl_3$ (15 mL) simultaneously by the use of a motorised syringe pump (rate = 0.1 mL/min). After addition, the reaction was stirred under argon at room temperature for 16 hours. The reaction mixture was then filtrated under gravity and washed with 1 M HCl (aq) (2 x 40 mL) and water (1 x 40 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by silica gel column chromatography (98.5:1.5-95:5 CH_2Cl_2/CH_3OH) to afford the *title product* (35 mg, 30%) as a colourless solid.

***R*$_f$:** 0.18 [CH_2Cl_2/CH_3OH 98.5:1.5].

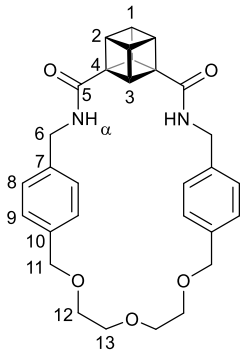
ν_{max}/cm^{-1} (neat): 3240 (N-H), 2987 (C-H), 1621 (C=O), 1528 (C-O), 695 (C-C).

δ_H (400 MHz, *d*$_6$-DMSO): 8.10 (4H, bt, *J* = 5.3 Hz, H^{α}), 8.07 (2H, bt, *J* = 5.4 Hz, H^{β}), 7.38 (8H, d, *J* = 7.4 Hz, H^{c}), 7.32 (8H, app. t, H^{b}), 7.21 (4H, t, *J* = 7.3 Hz, H^{a}), 6.52 (8H, s, H^{8}), 5.03 (2H, s, H^{h}), 4.47 (4H, s, H^{1}), 4.25 (2H, t, *J* = 7.8 Hz, H^{e}), 4.16 (4H, app. septet, H^{2}), 3.99 (8H, d, *J* = 5.3 Hz, H^{6}), 3.93 (4H, app. q, H^{3}), 3.71 (4H, app. t, H^{f}).

δ_C (100 MHz, *d*$_6$-DMSO): 170.9 (C^{5}), 164.7 (C^{g}), 143.2 (C^{d}), 137.4 (C^{7}), 129.6 (C^{h}), 128.9 (C^{b}), 128.3 (C^{c}), 127.9 (C^{8}), 126.9 (C^{a}), 54.5 (C^{4}), 50.8 (C^{1}), 50.1 (C^{e}), 49.2 (C^{2}), 44.2 (C^{f}), 42.5 (C^{6}), 41.6 (C^{3}).

m/z (ESI): 1059.4803 ($[M + H]^+$); neutral observed mass: 1058.4730, $C_{68}H_{62}N_6O_6$ requires 1058.4731.

Evans-style cubane macrocycle **5**



Bis-amine **ESI-4** (300 mg, 0.874 mmol) and methyl-pyridinium template **ESI-5** (334 mg, 0.874 mmol) were dissolved in dry CH_2Cl_2 (25 mL) and placed under an argon atmosphere. To this solution was added Et_3N (220 mg, 0.30 mL, 2.18 mmol), followed immediately by a dropwise solution of cubane-1,3-diacyl chloride **1** (200 mg, 0.874 mmol). The reaction was stirred at room temperature for 2 hours, then the reaction mixture was washed with 1 M HCl (aq) (2 x 20 mL) and brine (1 x 20 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by silica gel column chromatography (99:1-96:4 CH_2Cl_2/CH_3OH) to afford the *title product* (110 mg, 25%) as an off-white solid.

***R*$_f$:** 0.19 [CH_2Cl_2/CH_3OH 98:2].

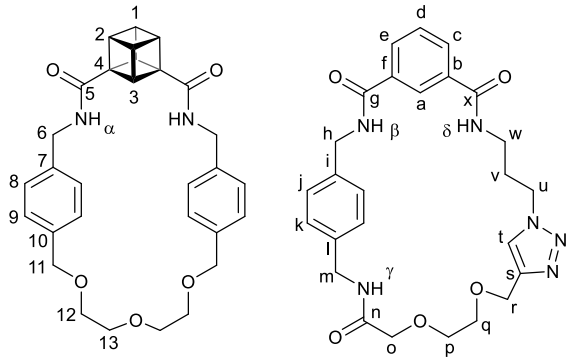
ν_{max}/cm^{-1} (neat): 3326 (N-H), 2853 (C-H), 1627 (C=O), 1528 (C-O), 1088 (C-C).

δ_H (400 MHz, $CDCl_3$): 7.29 (4H, d, *J* = 7.7 Hz, H^9), 7.19 (4H, d, *J* = 7.7 Hz, H^8), 6.08 (2H, bs, H^{α}), 4.56 (4H, s, H^{11}), 4.42 (4H, d, *J* = 5.5 Hz, H^6), 4.36 (2H, bs, H^1), 4.26 (2H, app. septet, H^2), 3.93 (4H, app. q, H^3), 3.74-3.65 (8H, m, H^{12} & H^{13}).

δ_C (100 MHz, $CDCl_3$): 170.9 (C^5), 137.6 (C^{10}), 137.4 (C^7), 128.1 (C^9), 127.6 (C^8), 72.8 (C^{11}), 70.8 ($C^{12 \text{ or } 13}$), 69.6 ($C^{12 \text{ or } 13}$), 54.6 (C^4), 50.9 (C^1), 49.7 (C^2), 43.0 (C^6), 42.0 (C^3).

m/z (ESI): 501.2379 ($[M + H]^+$); neutral observed mass: 500.2307, $C_{30}H_{32}N_2O_5$ requires 500.2311.

Evans-style cubane [2]catenane **7**



To a solution of macrocycle **5** (32.5 mg, 0.065 mmol) and alkyne-azide **6** (32.9 mg, 0.065 mmol) in dry CH_2Cl_2 (10 mL) under argon was added $Cu(CH_3CN)_4BF_4$ (4.7 mg, 0.015 mmol), TBTA (8.0 mg, 0.015 mmol) and DIPEA (8.39 mg, 0.011 mL, 0.065 mmol). The reaction was stirred at room temperature for 16 hours. The reaction mixture was diluted with further CH_2Cl_2 (10 mL) and then the solution washed with 0.02 M EDTA in 1 M NH_3 (aq) (2 x 10 mL) and brine (1 x 10 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was first purified by silica gel column chromatography (98:2-97:3 CH_2Cl_2/CH_3OH) followed by preparative TLC (94.7:5:0.3 CH_2Cl_2/CH_3OH/Acetone) to afford the *title product* (15 mg, 23%) as a colourless glassy solid.

***R*$_f$:** 0.10 [CH_2Cl_2/CH_3OH 98:2].

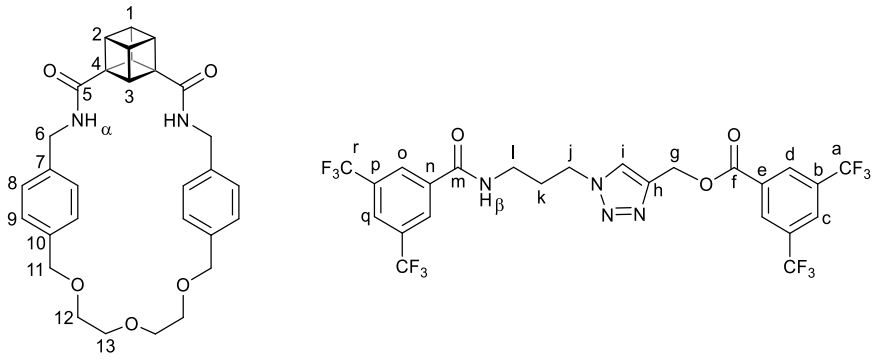
ν_{max}/cm^{-1} (neat): 3302 (N-H), 2868 (C-H), 1638 (C=O), 1526 (C-O), 1071 (C-C).

δ_H (400 MHz, $CDCl_3$): 8.15 (1H, d, *J* = 8.0 Hz, H^c), 7.82 (1H, d, *J* = 8.0 Hz, H^e), 7.64-7.59 (2H, m, H^d & H^t), 7.42 (1H, bs, H$^\delta$), 7.36 (2H, d, *J* = 7.9 Hz, H^k), 7.31 (1H, s, H^a), 7.26 (2H, bs, H$^\alpha$), 7.20 (2H, d, *J* = 7.9 Hz, H^j), 6.87 (1H, bs, H$^\beta$), 6.82 (1H, bt, *J* = 6.0 Hz, H$^\gamma$), 6.77 (4H, d, *J* = 8.0 Hz, H^8), 6.53 (4H, d, *J* = 8.0 Hz, H^9), 4.93 (1H, b app. sextet, H^1), 4.67 (2H, bs, H^r), 4.62 (1H, b app. sextet, H$^{1'}$), 4.55-4.47 (4H, m, H^6 & H^m), 4.41 (2H, bt, *J* = 6.0 Hz, H^u), 4.34 (2H, app. septet, H^2), 4.11-3.93 (12H, m, H$^{6'}$, H^3, H$^{3'}$, H^h, H^{11}, H$^{11'}$ & H^o), 3.72 (4H, s, H$^{p/q}$), 3.21-3.03 (8H, m, H^w & H$^{12/13}$), 2.79-2.71 (2H, m, H$^{12'/13'}$), 2.20 (2H, bs, H^v).

δ_C (100 MHz, $CDCl_3$): 171.7 (C^5), 168.7 (C^n), 166.3 (C^x), 165.9 (C^g), 144.7 (C^s), 138.4 (C^i), 137.3 (C^l), 137.2 (C^7), 134.5 (C^{10}), 133.2 (C$^{b/f}$), 132.9 (C$^{b/f}$), 132.2 (C^e), 131.9 (C^c), 129.8 (C^j), 129.4 (C^9), 128.9 (C^k), 128.3 (C^8), 128.2 (C^d), 124.1 (C^a), 122.6 (C^t), 73.9 (C^{11}), 70.6 (C^o), 70.6 (C$^{p/q}$), 70.3 (C$^{12(')/13(')}$), 69.6 (C$^{p/q}$), 68.8 (C$^{12/13}$), 64.8 (C^r), 54.8 (C^4), 52.9 (C$^{1'}$), 51.0 (C^1), 49.1 (C^2), 47.7 (C^u), 44.1 (C^6), 43.9 (C^h), 42.5 (C^m), 42.4 (C^3), 41.4 (C$^{3'}$), 36.8 (C^w), 29.9 (C^v).

m/z (ESI): 1007.4658 ([M + H]$^+$); neutral observed mass: 1006.4588, $C_{56}H_{62}N_8O_{10}$ requires 1006.4589.

Evans-style cubane [2]rotaxane **10**



To a solution of macrocycle **5** (20 mg, 0.040 mmol) and azide **8** (16 mg, 0.047 mmol) in dry CH_2Cl_2 (1 mL) under argon was added alkyne **9** (13 mg, 0.047 mmol), $Cu(CH_3CN)_4BF_4$ (1.4 mg, 0.0046 mmol), TBTA (2.4 mg, 0.0046 mmol) and DIPEA (6.6 mg, 0.009 mL, 0.051 mmol). The reaction was stirred at room temperature for 16 hours. The reaction mixture was diluted with further CH_2Cl_2 (10 mL) and then the solution washed with 0.02 M EDTA in 1 M NH_3 (aq) (2 x 10 mL) and brine (1 x 10 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was first purified by silica gel column chromatography (98:2-95:5 CH_2Cl_2/CH_3OH) followed by preparative TLC (87:3:10 CH_2Cl_2/CH_3OH/acetone) to afford the *title product* (4.5 mg, 10%) as a glassy colourless solid.

***R*$_f$:** 0.21 [CH_2Cl_2/CH_3OH 98:2].

ν_{max}/cm^{-1} (neat): 3321 (N-H), 2868 (C-H), 1625 (C=O), 1507 (C-O), 1079 (C-C).

δ_H (400 MHz, $CDCl_3$): 8.52 (2H, s, H^d), 8.08 (1H, s, H^c), 8.03 (1H, s, H^q), 7.99 (2H, s, H^o), 7.90 (1H, s, H^i), 7.04 (1H, bs, H^β), 6.75 (4H, d, J = 7.8 Hz, H^8), 6.69 (2H, bs, H^α), 6.60 (4H, d, J = 7.8 Hz, H^9), 5.59 (2H, s, H^g), 4.84 (1H, bs, H^1), 4.60-4.52 (3H, m, $H^{1'}$ & H^6), 4.34 (2H, app. septet, H^2), 4.29 (2H, d, J = 9.7 Hz, H^{11}), 4.22 (2H, t, J = 5.9 Hz, H^j), 4.12-4.06 (1H, m, H^3), 4.03-3.92 (5H, m, $H^{3'}$, $H^{11'}$ & $H^{6'}$), 3.82-3.58 (8H, m, H^{12} & H^{13}), 2.85 (2H, app. q, H^l), 1.88 (2H, app. quintet, H^k).

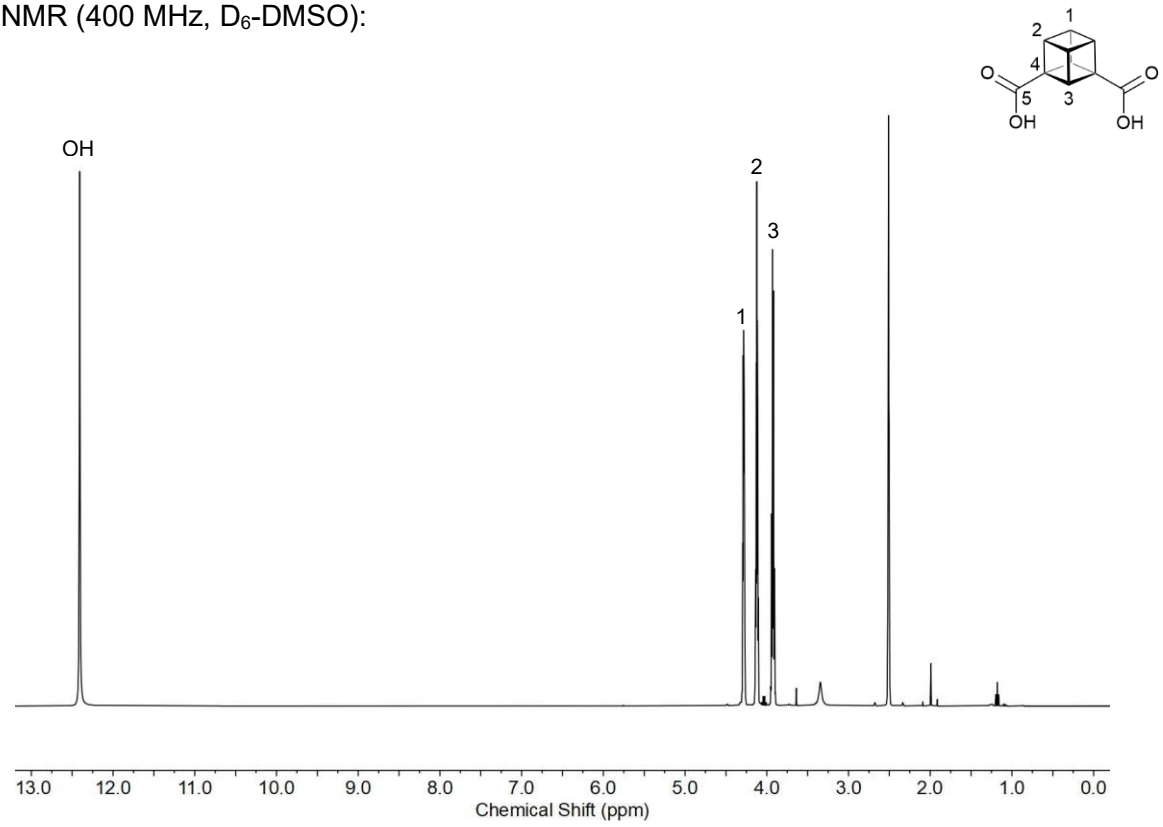
δ_C (100 MHz, $CDCl_3$): 171.4 (C^5), 163.8 (C^f), 163.7 (C^m), 141.6 (C^h), 137.2 (C^7), 135.8 (C^{10}), 134.9 ($C^{n\text{ or }e}$), 132.3 (q, J = 34 Hz, $C^{b\text{ or }p}$), 131.9 ($C^{n\text{ or }e}$), 131.0 (q, J = 34 Hz, $C^{b\text{ or }p}$), 129.8 (C^d), 128.5 (C^o), 128.5 (C^9) 128.1 (C^8), 126.6 (C^c), 125.1 (C^i), 124.1 (C^q), 73.6 (C^{11}), 70.8 ($C^{12\text{ or }13}$), 69.6 ($C^{12\text{ or }13}$), 58.9 (C^g), 54.6 (C^4), 52.4 ($C^{1'}$), 50.3 (C^1), 49.4 (C^2), 47.9 (C^j), 43.8 (C^6), 42.5 (C^3), 41.4 ($C^{3'}$), 37.4 (C^l), 29.7 (C^k).

m/z (ESI): 1137.3414 ($[M + H]^+$); neutral observed mass: 1136.3341, $C_{54}H_{48}F_{12}N_6O_8$ requires 1136.3342.

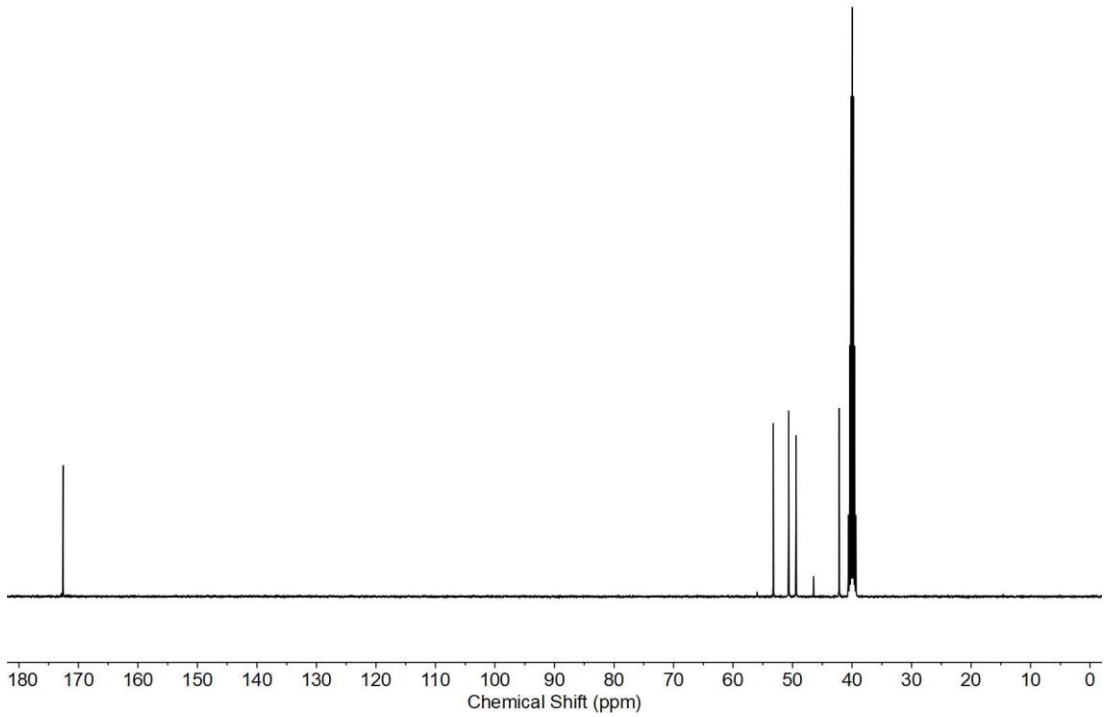
Part 2: Spectra Data

Cubane-1,3-dicarboxylic acid

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

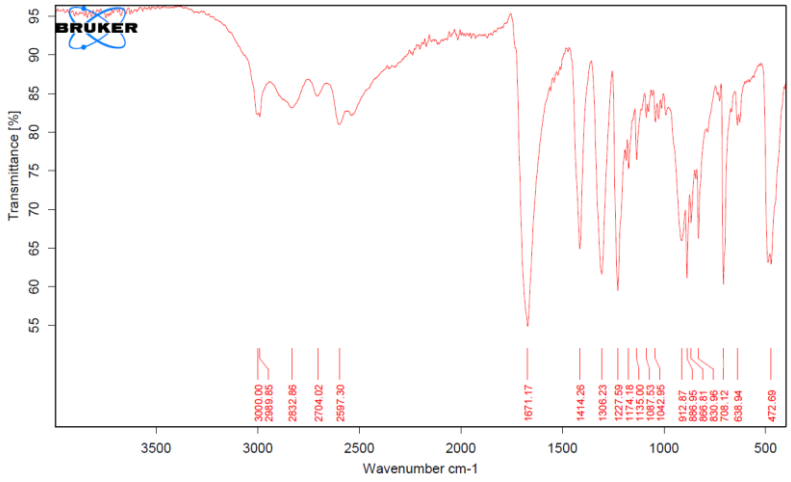


^{13}C NMR (100 MHz, D_6-DMSO):



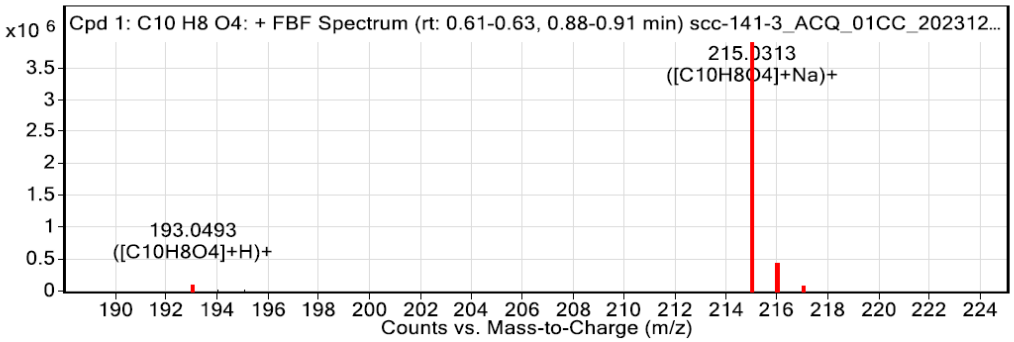
Cubane-1,3-dicarboxylic acid

IR (neat):



HRMS:

Figure: Full range view of Compound spectra and potential adducts.

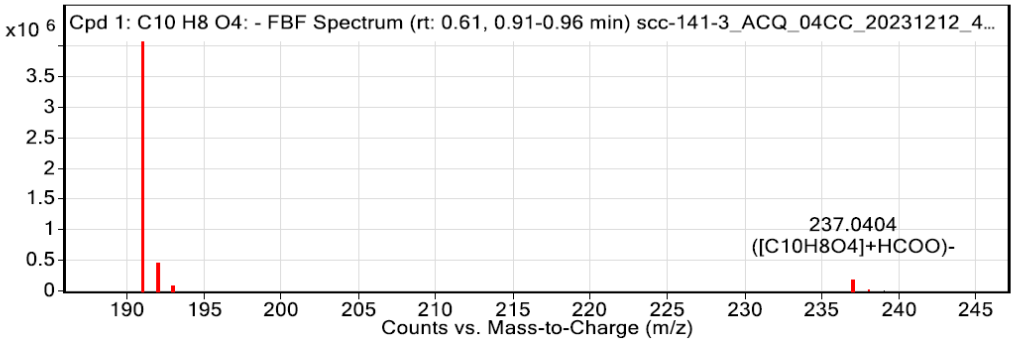


Compound Table

Compound Label	RT (min)	Observed mass (m/z)	Neutral observed mass (Da)	Theoretical mass (Da)	Mass error (ppm)	Isotope match score (%)
Cpd 1: C10 H8 O4	0.75	215.0313	192.0422	192.0423	-0.39	98.43

Mass errors of between -5.00 and 5.00 ppm with isotope match scores above 60% are considered confirmation of molecular formulae

Figure: Full range view of Compound spectra and potential adducts.



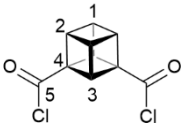
Compound Table

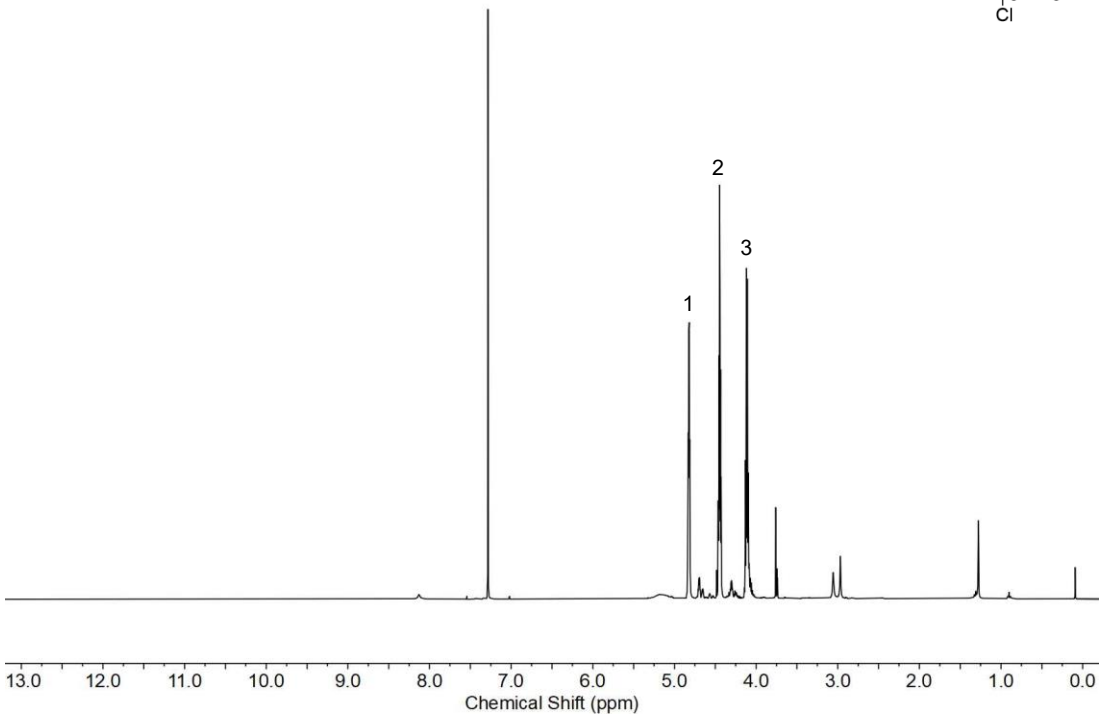
Compound Label	RT (min)	Observed mass (m/z)	Neutral observed mass (Da)	Theoretical mass (Da)	Mass error (ppm)	Isotope match score (%)
Cpd 1: C10 H8 O4	0.76	191.0350	192.0423	192.0423	0.14	99.35

Mass errors of between -5.00 and 5.00 ppm with isotope match scores above 60% are considered confirmation of molecular formulae

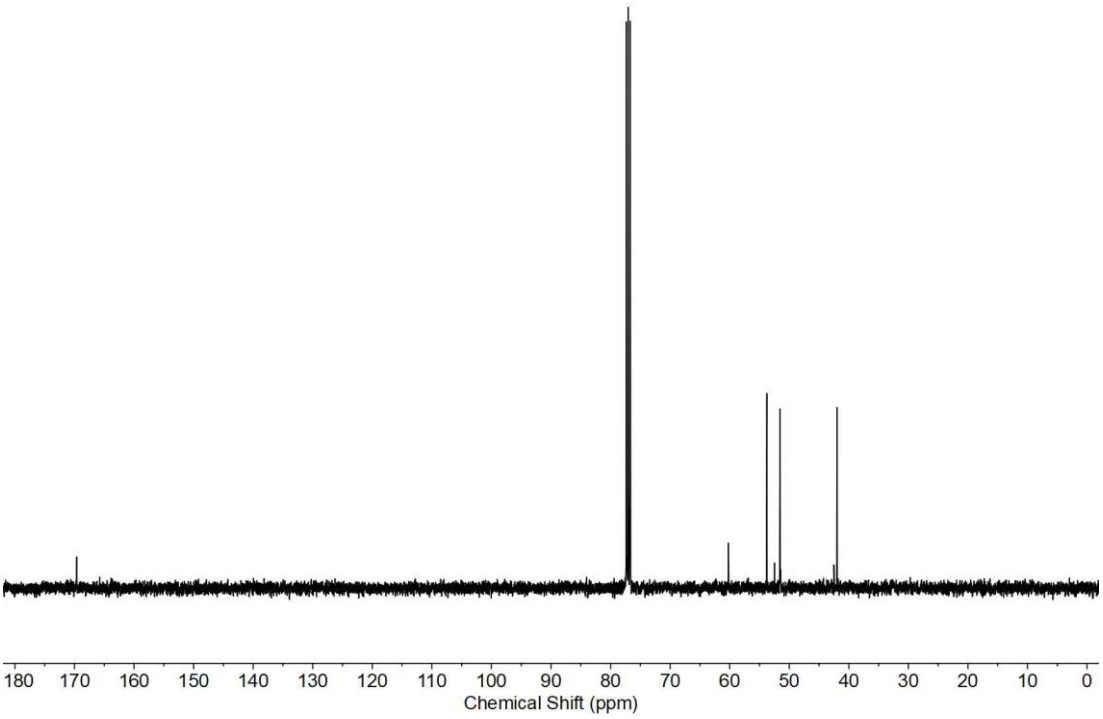
Cubane-1,3-diacyl chloride

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



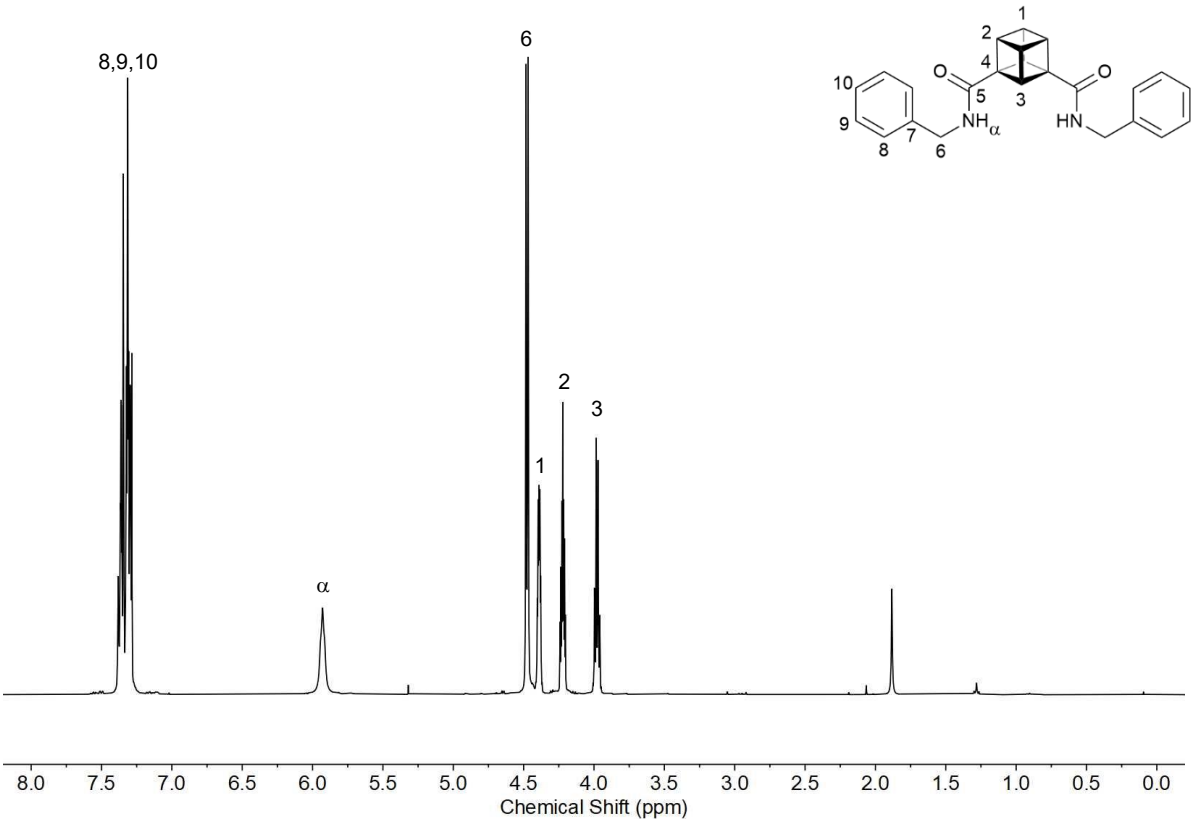


^{13}C NMR (100 MHz, $CDCl_3$):

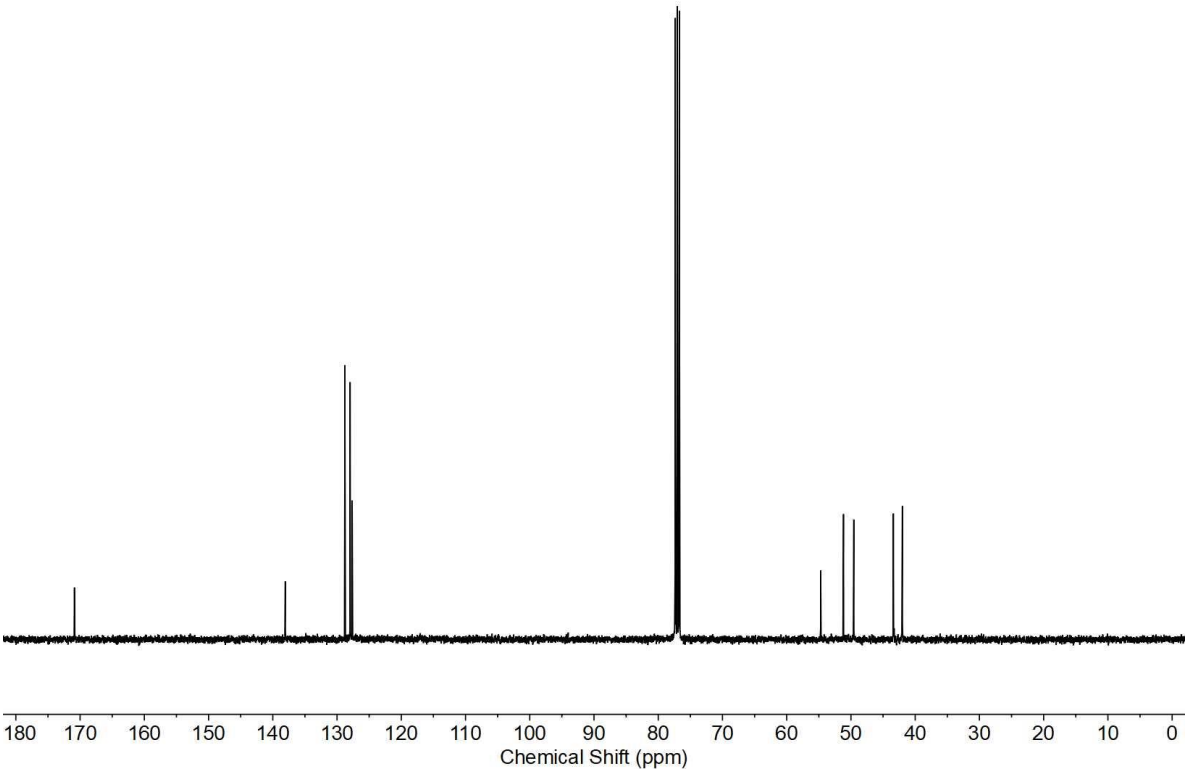


Model cubane-1,3-dicarboxamide **ESI-1**

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

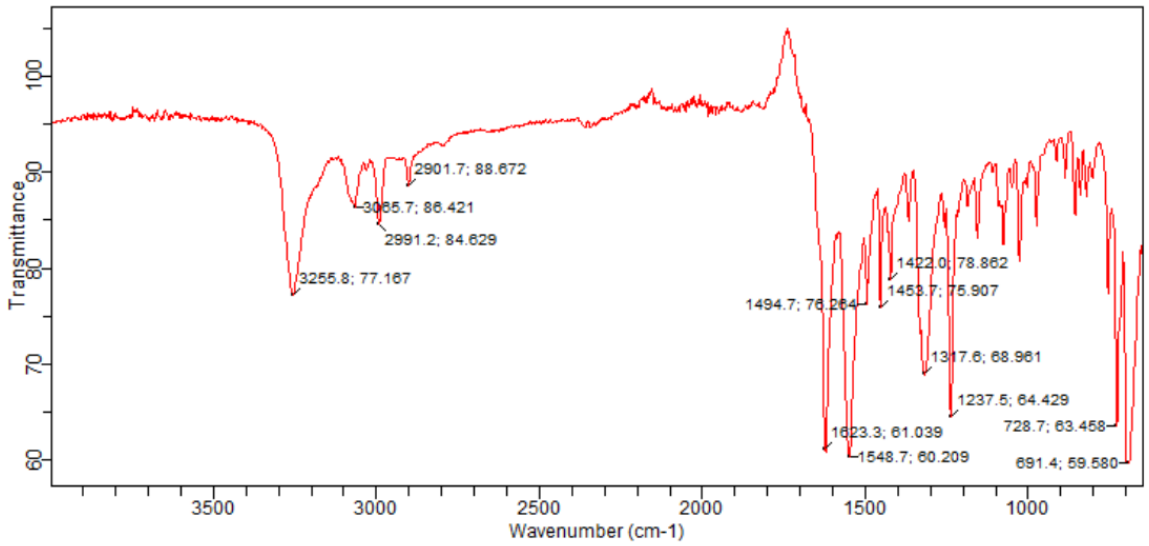


^{13}C NMR (100 MHz, $CDCl_3$):



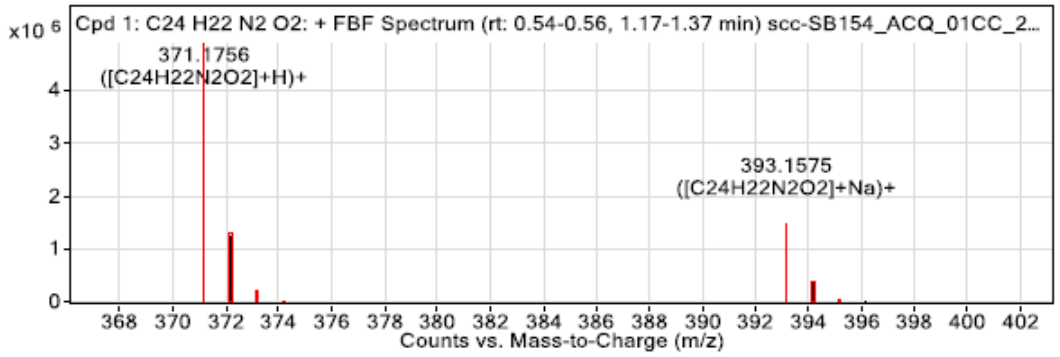
Model cubane-1,3-dicarboxamide **ESI-1**

IR (neat):



HRMS:

Figure: Full range view of Compound spectra and potential adducts.



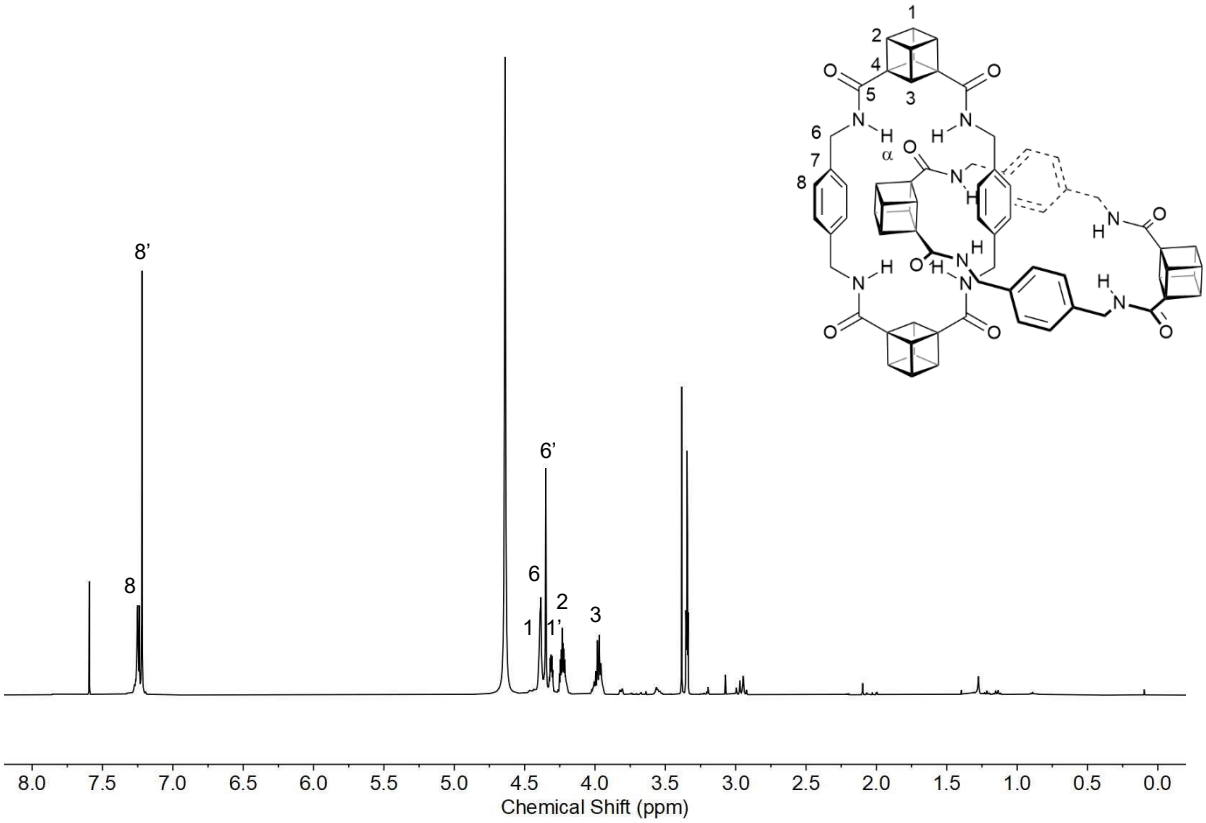
Compound Table

Compound Label	RT (min)	Observed mass (m/z)	Neutral observed mass (Da)	Theoretical mass (Da)	Mass error (ppm)	Isotope match score (%)
Cpd 1: C24 H22 N2 O2	0.78	371.1756	370.1684	370.1681	0.61	99.28

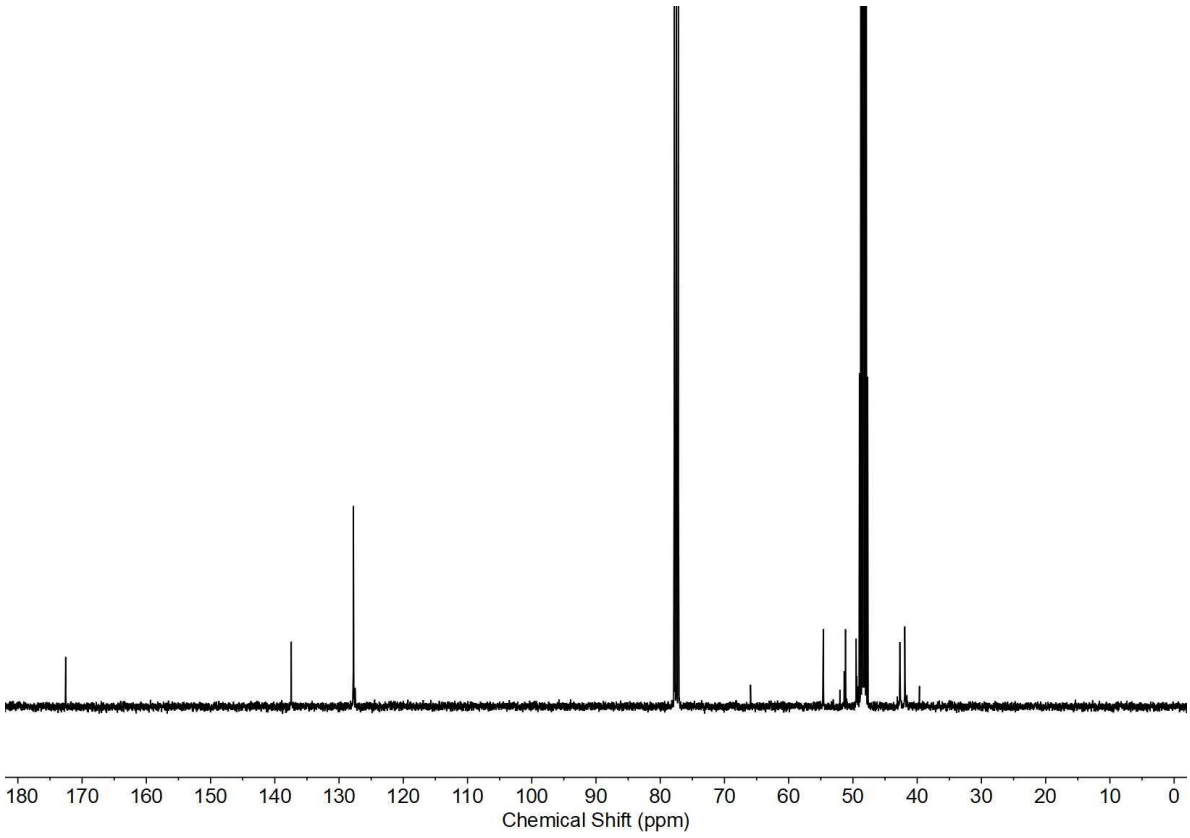
Mass errors of between -5.00 and 5.00 ppm with isotope match scores above 60% are considered confirmation of molecular formulae

Leigh-style cubane [2]catenane **2**

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

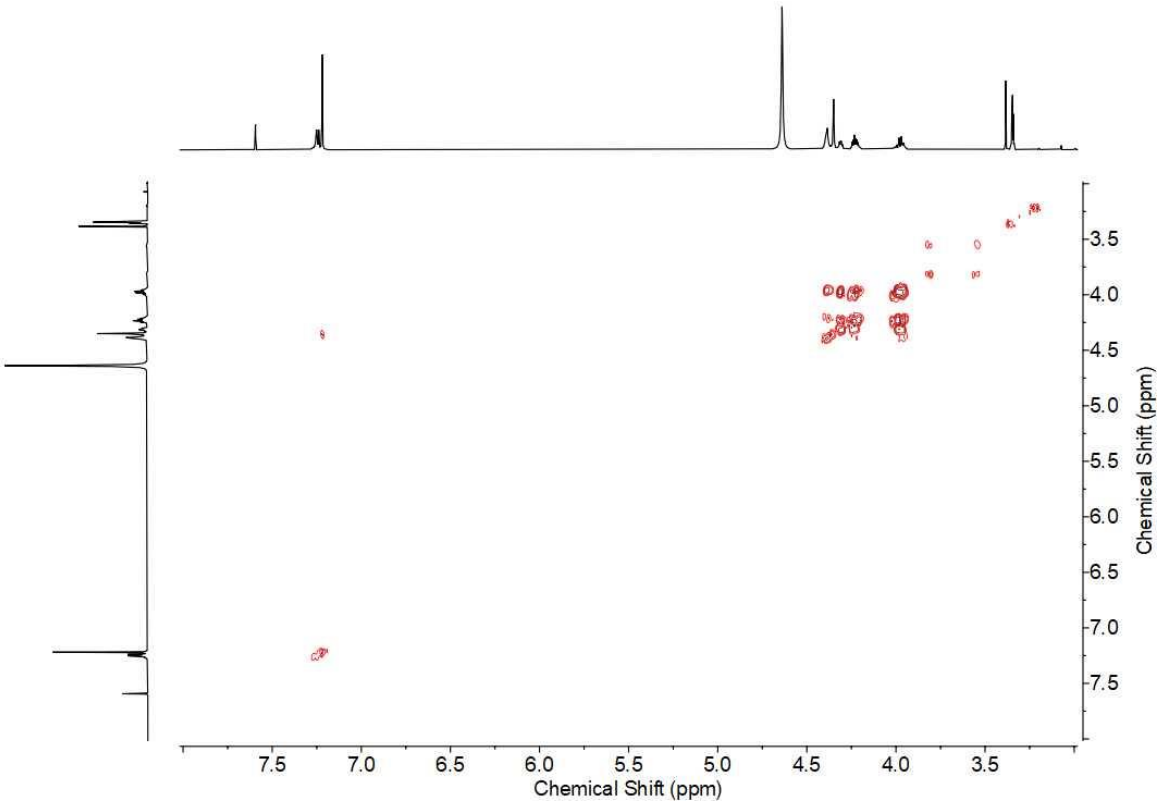


^{13}C NMR (100 MHz, 1:1 $CDCl_3$:CD_3OD):

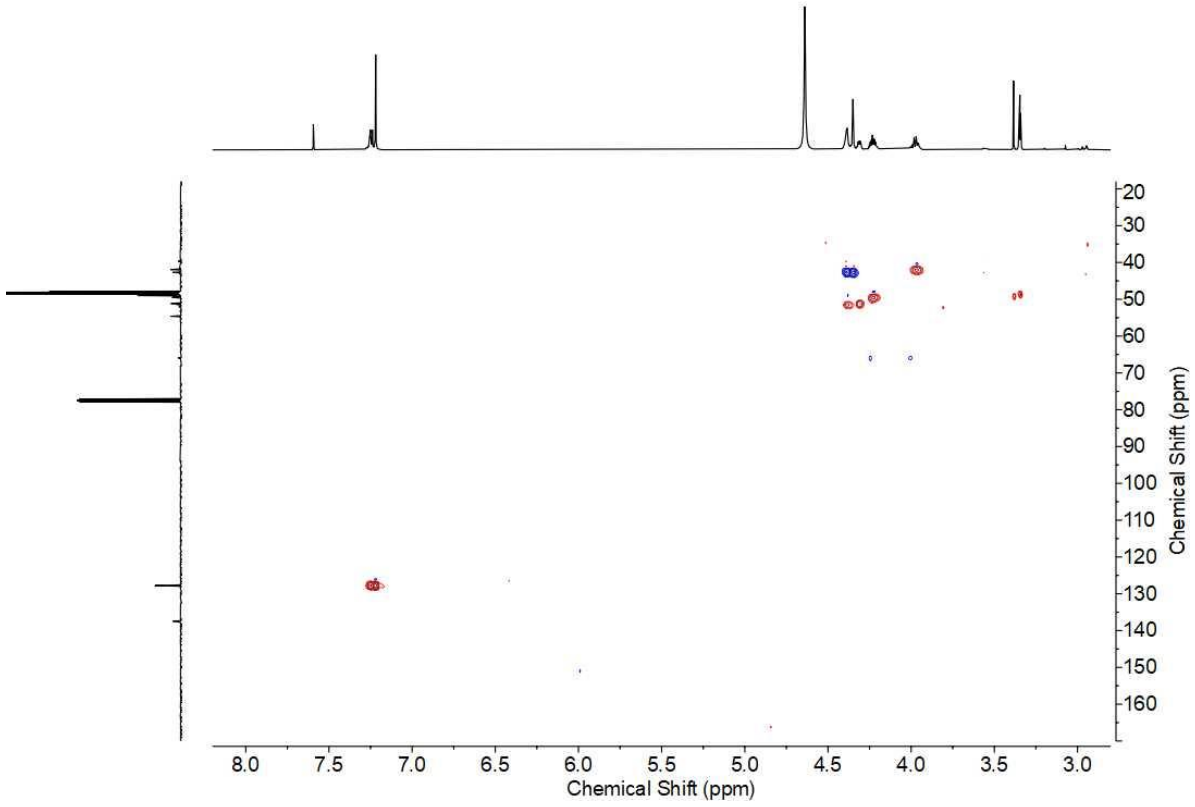


Leigh-style cubane [2]catenane **2**

^{1}H-^{1}H COSY NMR (1:1 $CDCl_3$:CD_3OD):

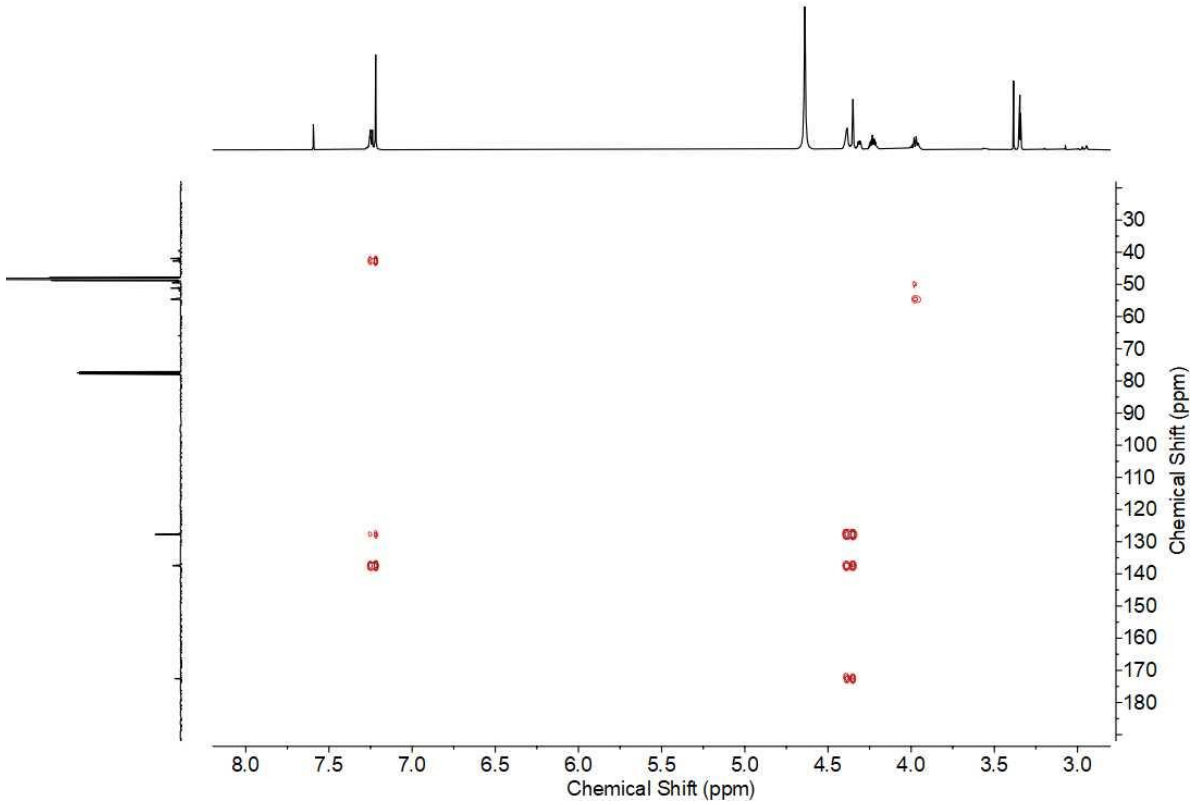


^{1}H-^{13}C HSQC NMR (1:1 $CDCl_3$:CD_3OD):

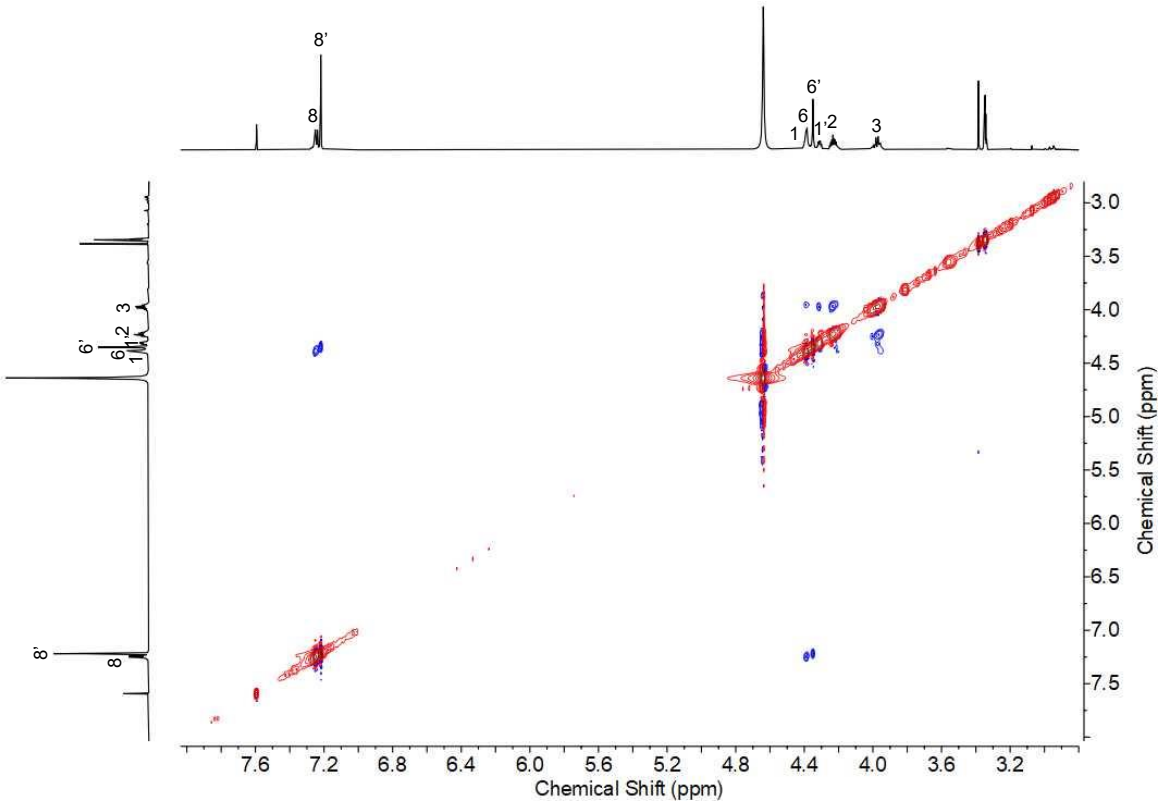


Leigh-style cubane [2]catenane **2**

^{1}H-^{13}C HMBC NMR (1:1 $CDCl_3$:CD_3OD):

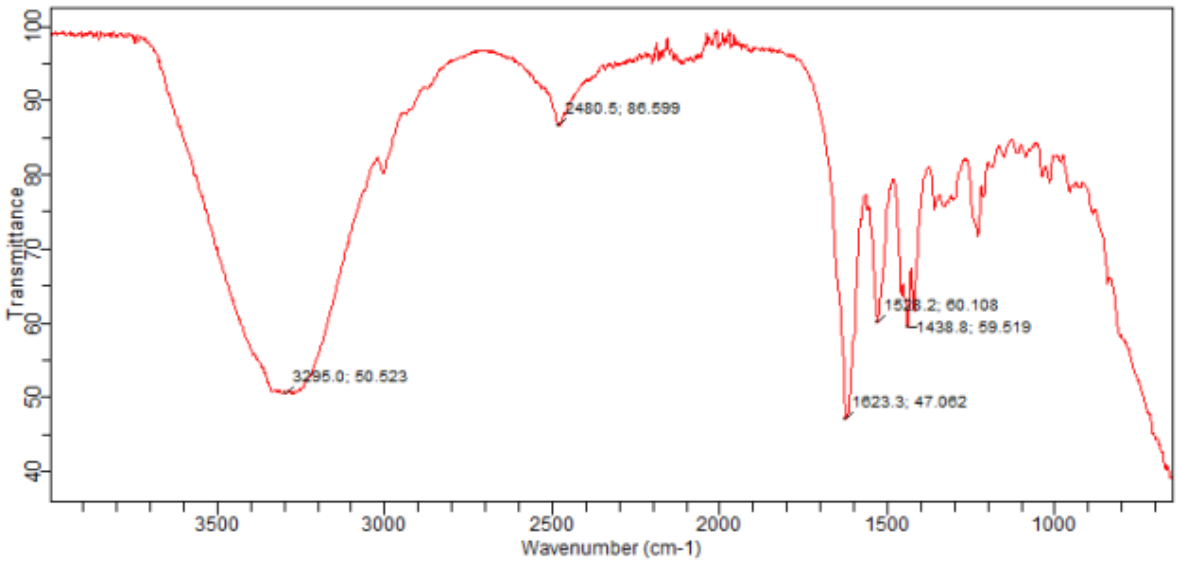


^{1}H-^{1}H ROESY NMR (1:1 $CDCl_3$:CD_3OD):



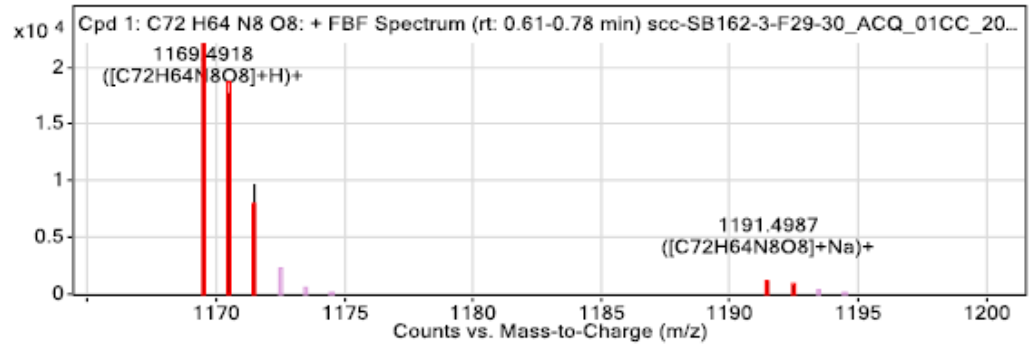
Leigh-style cubane [2]catenane **2**

IR (neat):



HRMS:

Figure: Full range view of Compound spectra and potential adducts.



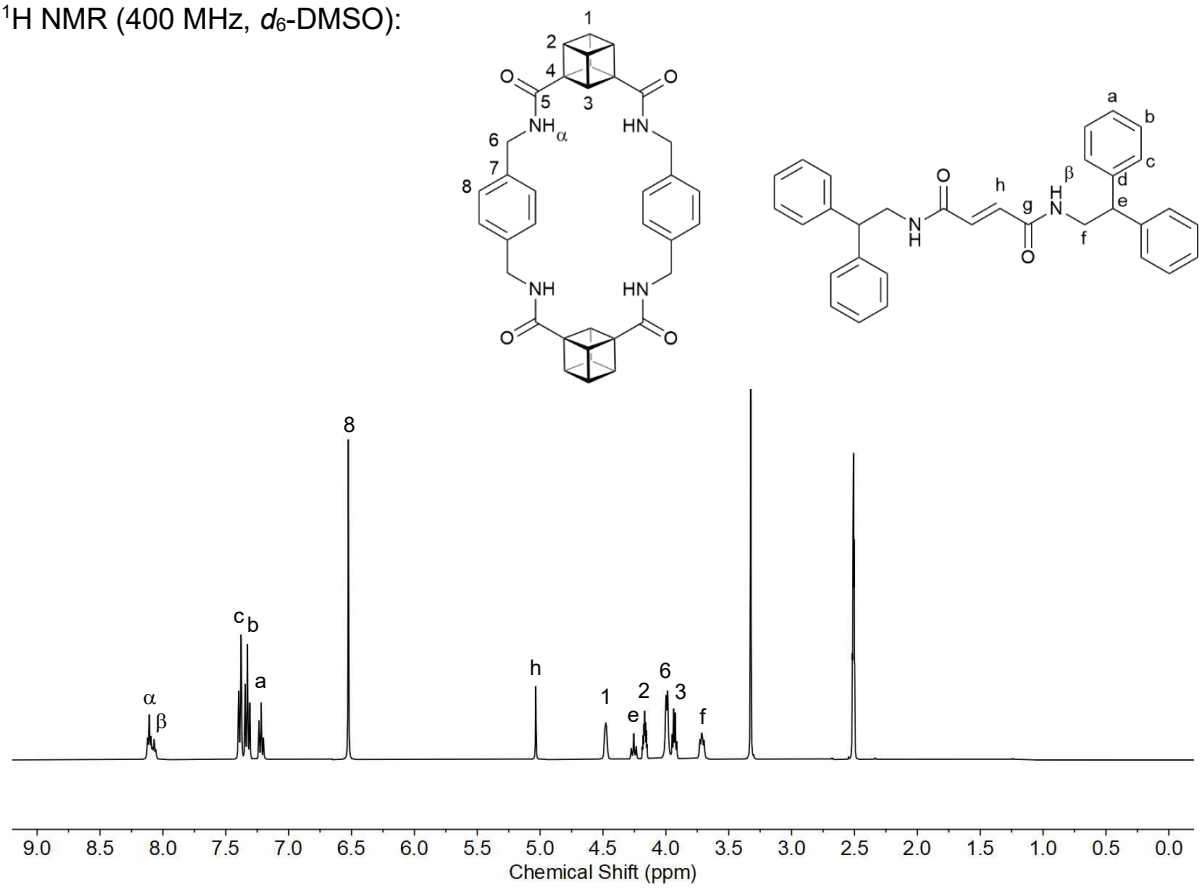
Compound Table

Compound Label	RT (min)	Observed mass (m/z)	Neutral observed mass (Da)	Theoretical mass (Da)	Mass error (ppm)	Isotope match score (%)
Cpd 1: C72 H64 N8 O8	0.68	1169.4918	1168.4859	1168.4847	0.99	74.16

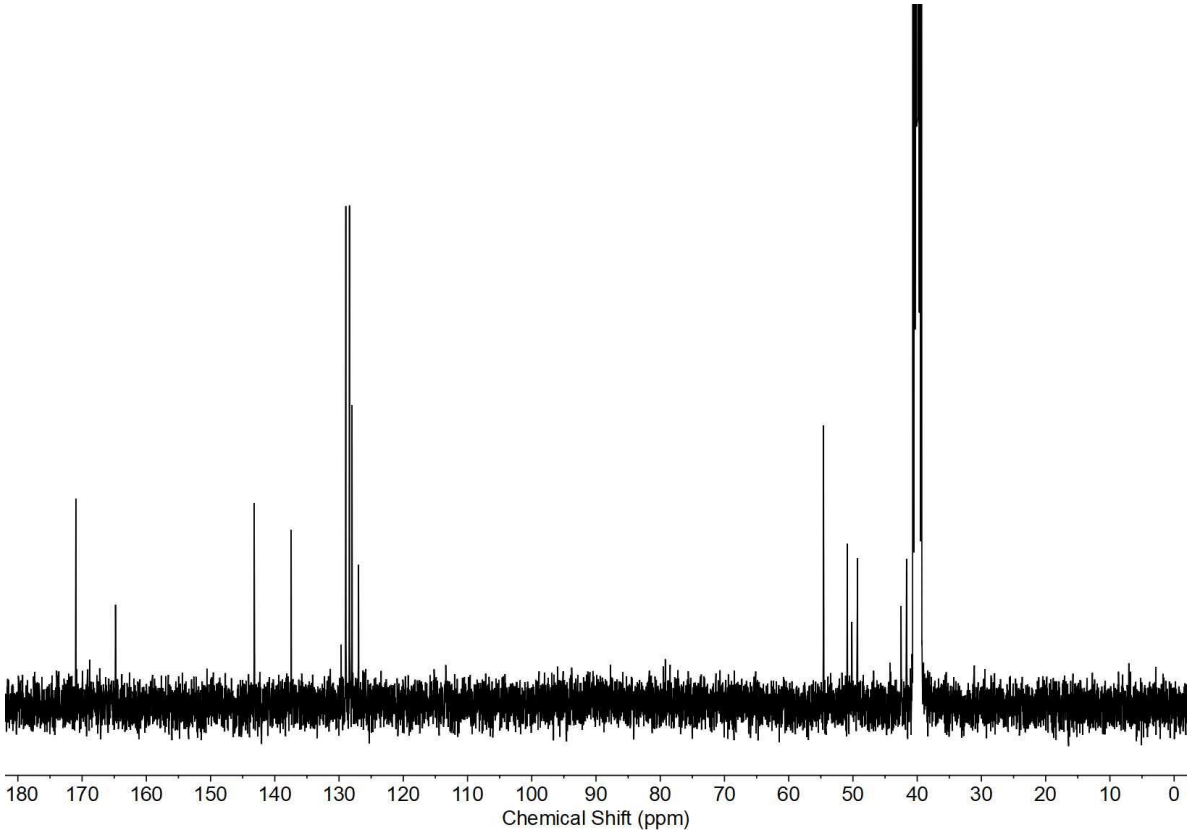
Mass errors of between -5.00 and 5.00 ppm with isotope match scores above 60% are considered confirmation of molecular formulae

Leigh-style cubane [2]rotaxane **4**

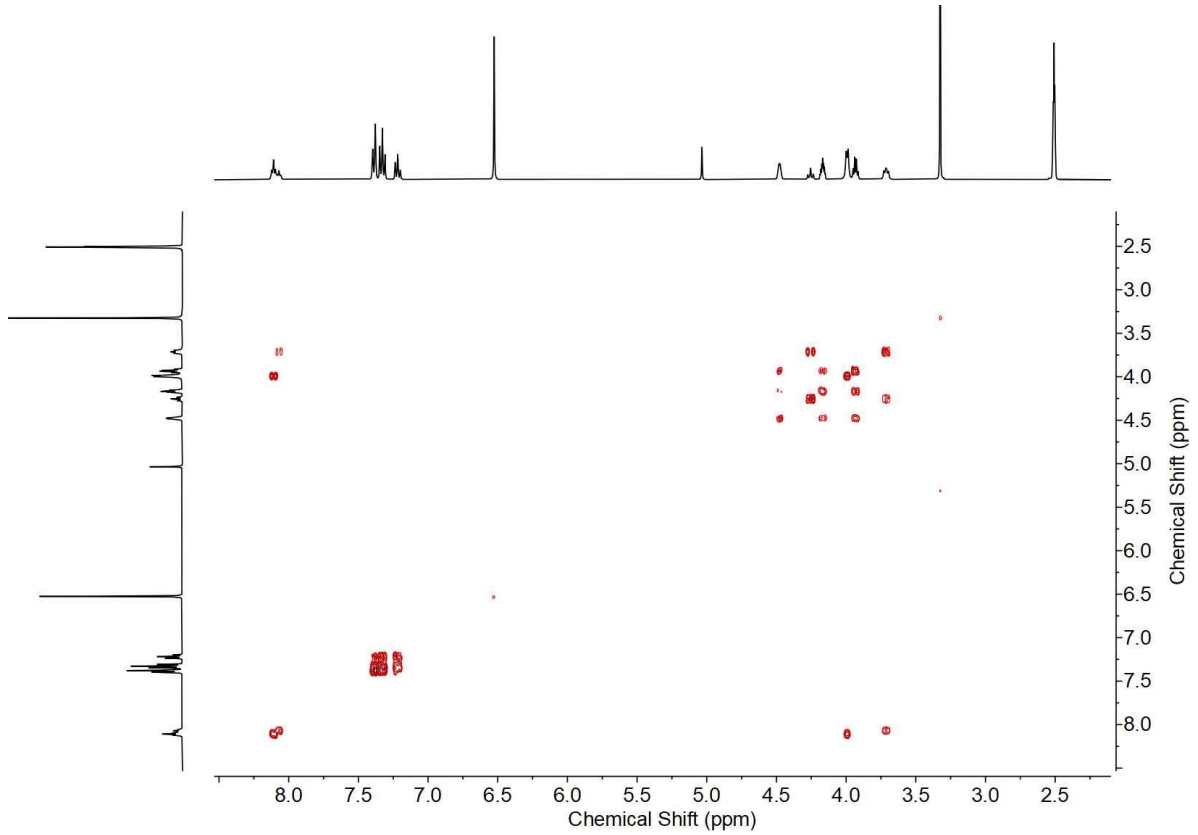
^{1}H NMR (400 MHz, d_6-DMSO):



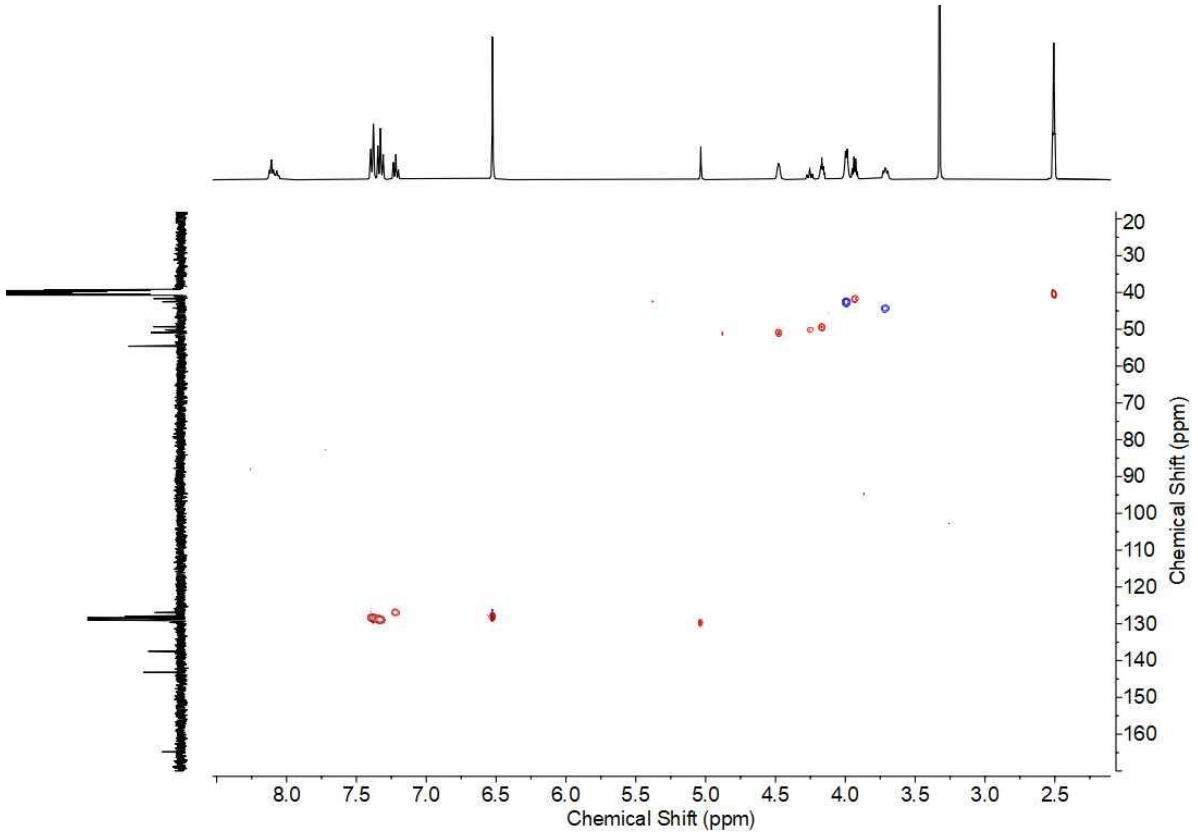
^{13}C NMR (100 MHz, d_6-DMSO):



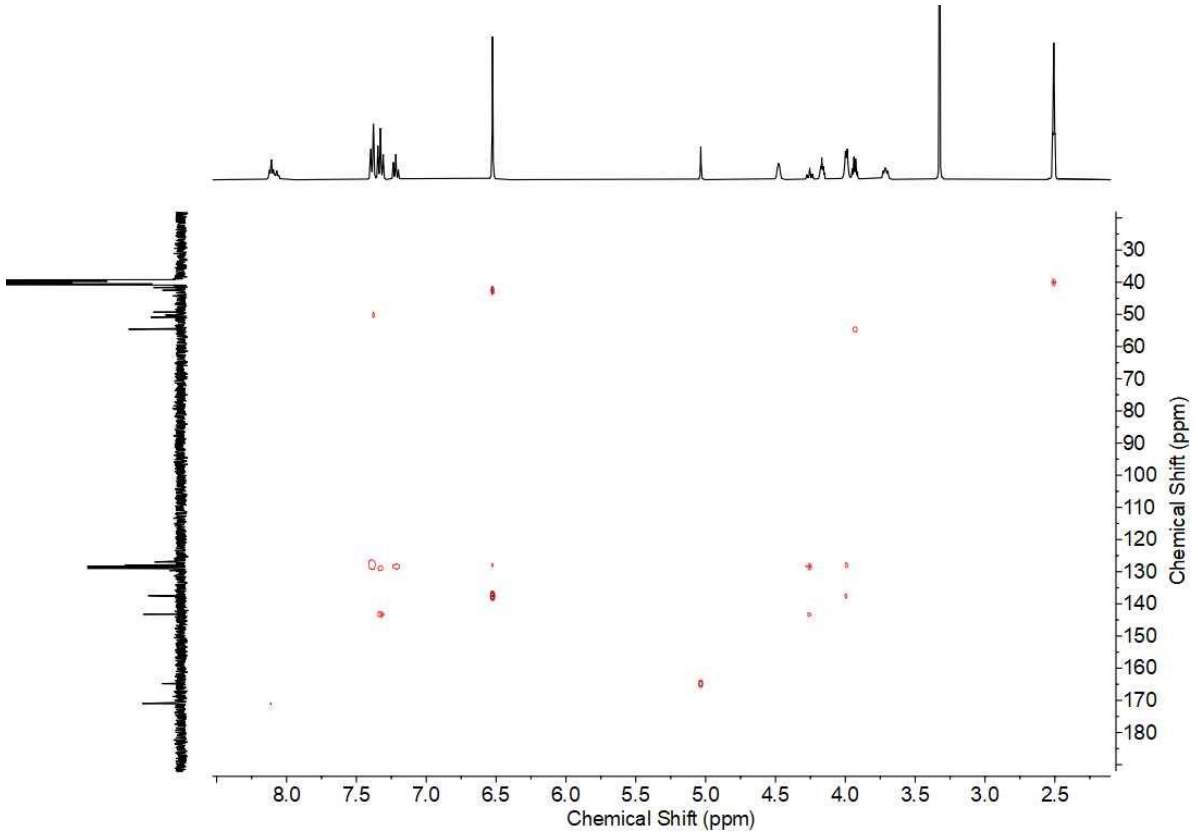
^{1}H-^{1}H COSY NMR (d_6-DMSO):



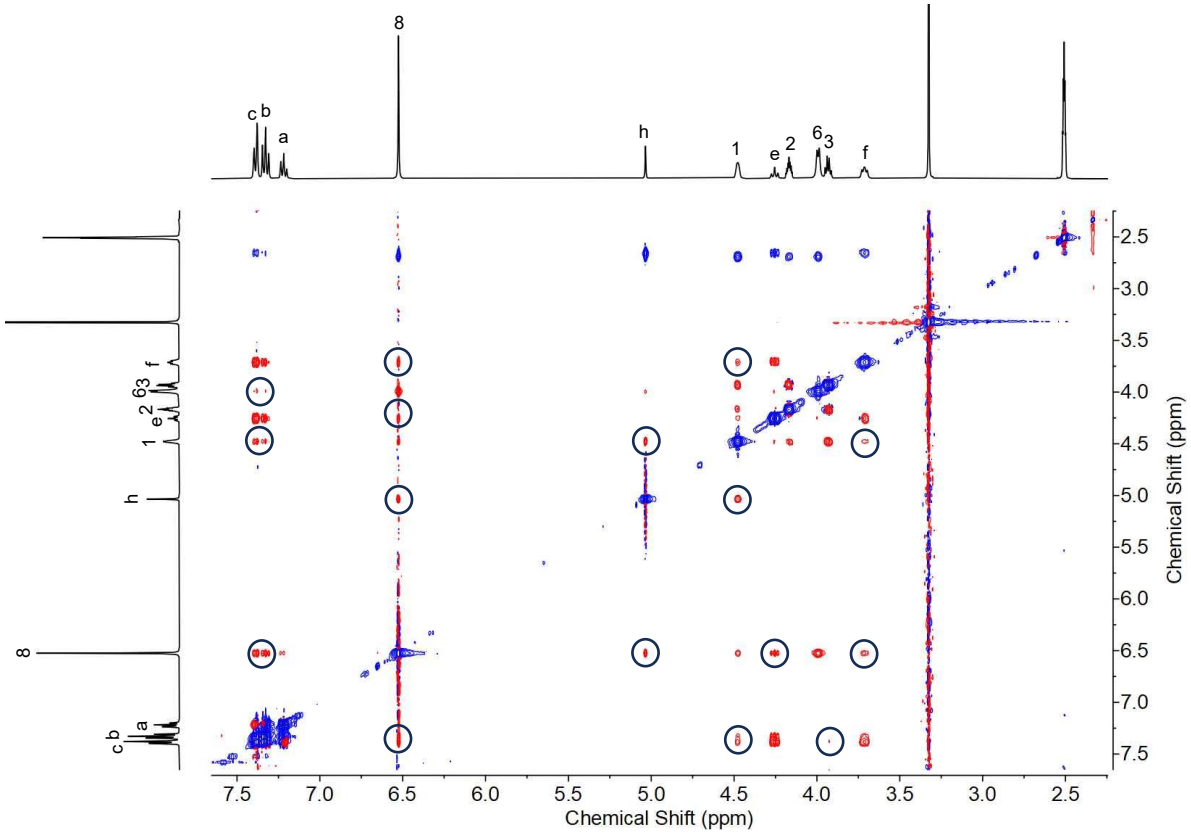
^{1}H-^{13}C HSQC NMR (d_6-DMSO):



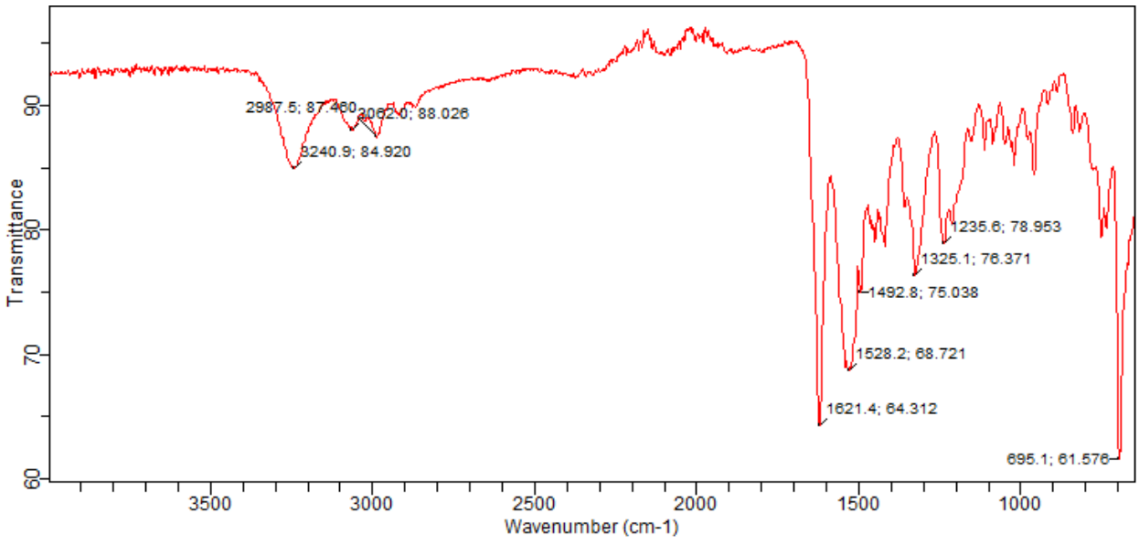
^{1}H-^{13}C HMBC NMR (d_6-DMSO):



^{1}H-^{1}H ROESY NMR (d_6-DMSO): *Intercomponent couplings circled*

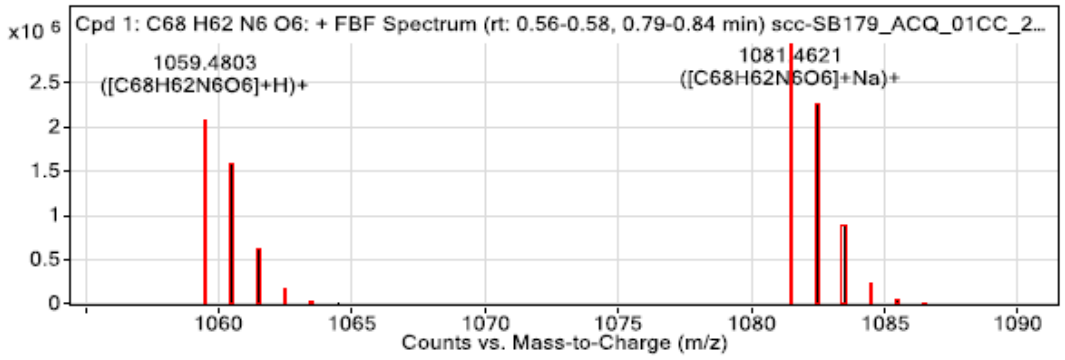


IR (neat):



HRMS:

Figure: Full range view of Compound spectra and potential adducts.



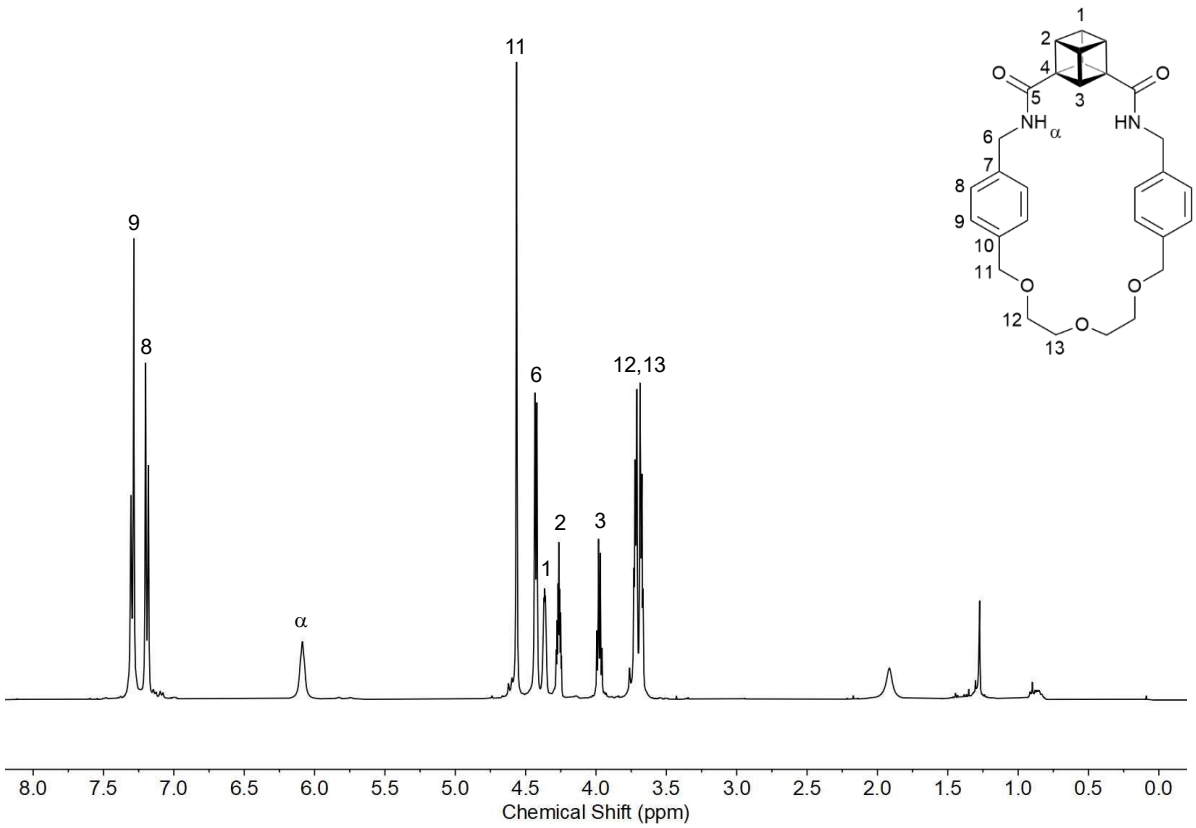
Compound Table

Compound Label	RT (min)	Observed mass (m/z)	Neutral observed mass (Da)	Theoretical mass (Da)	Mass error (ppm)	Isotope match score (%)
Cpd 1: C68 H62 N6 O6	0.69	1059.4803	1058.4730	1058.4731	-0.06	99.88

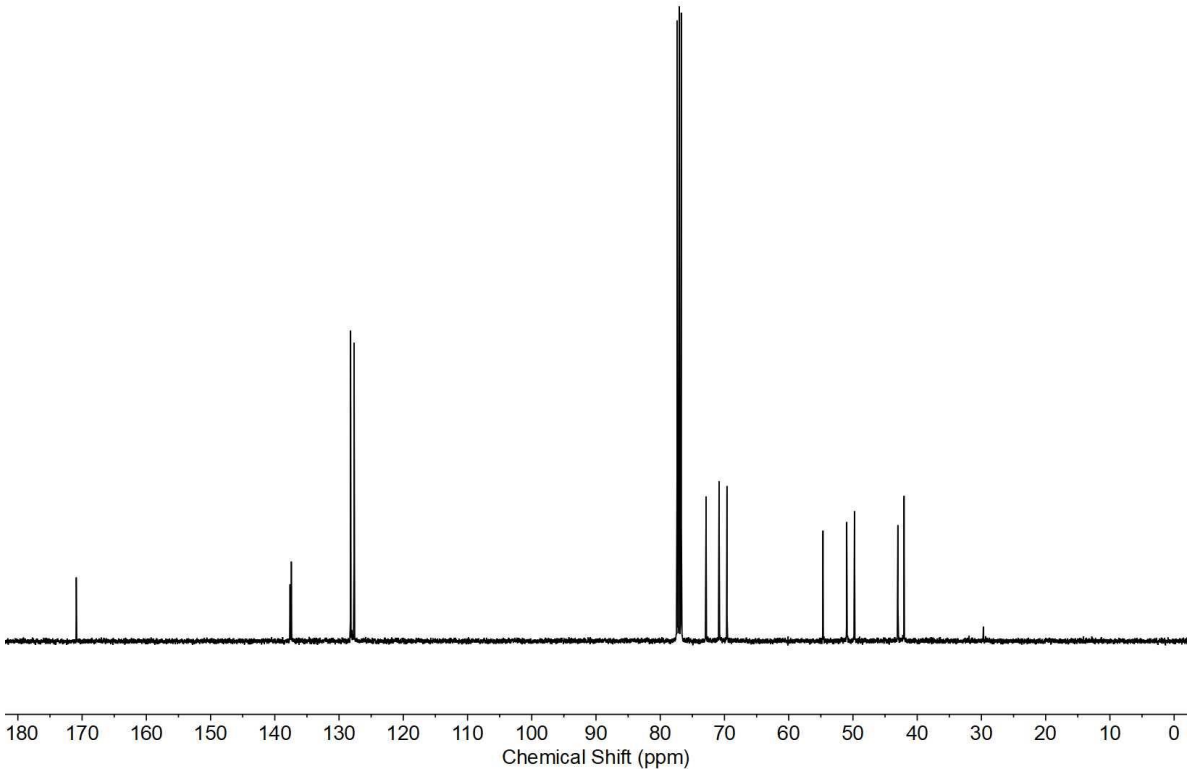
Mass errors of between -5.00 and 5.00 ppm with isotope match scores above 60% are considered confirmation of molecular formulae

Evans-style cubane macrocycle **5**

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

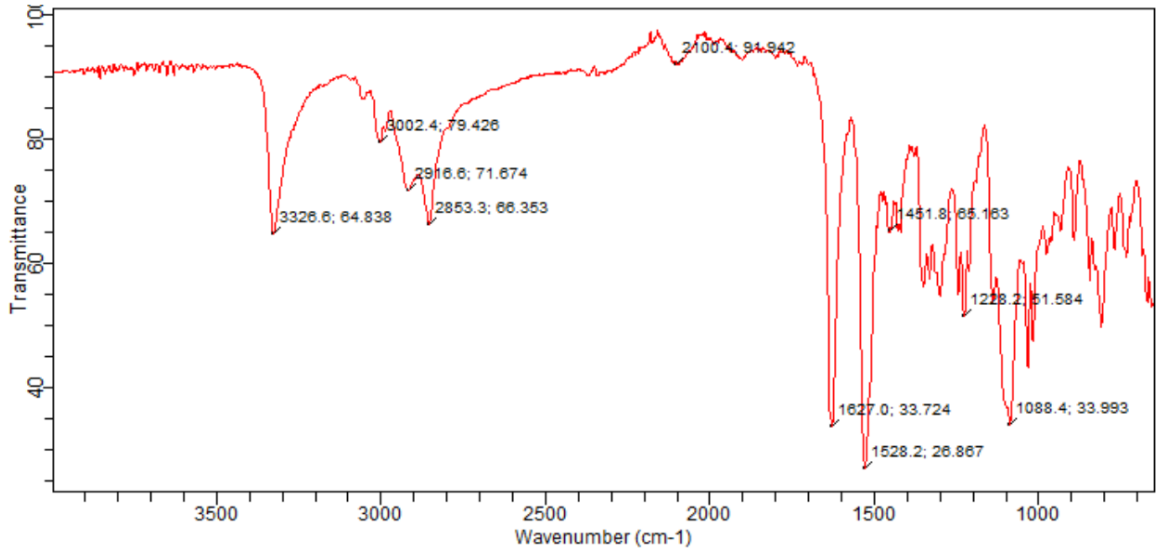


^{13}C NMR (100 MHz, $CDCl_3$):



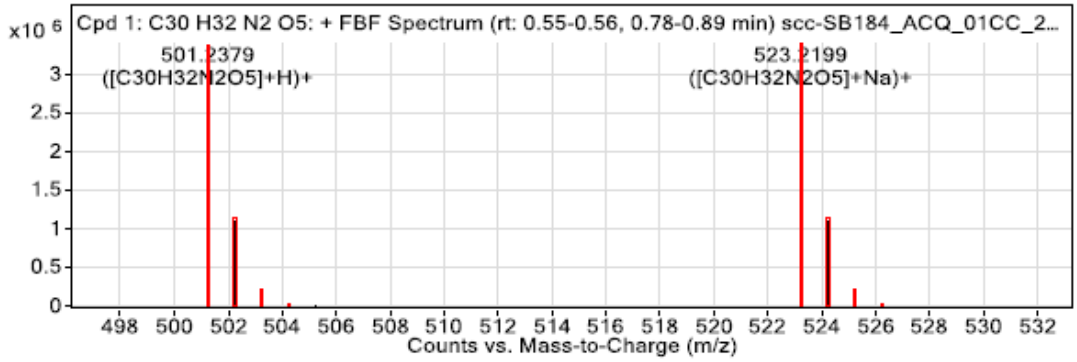
Evans-style cubane macrocycle **5**

IR (neat):



HRMS:

Figure: Full range view of Compound spectra and potential adducts.



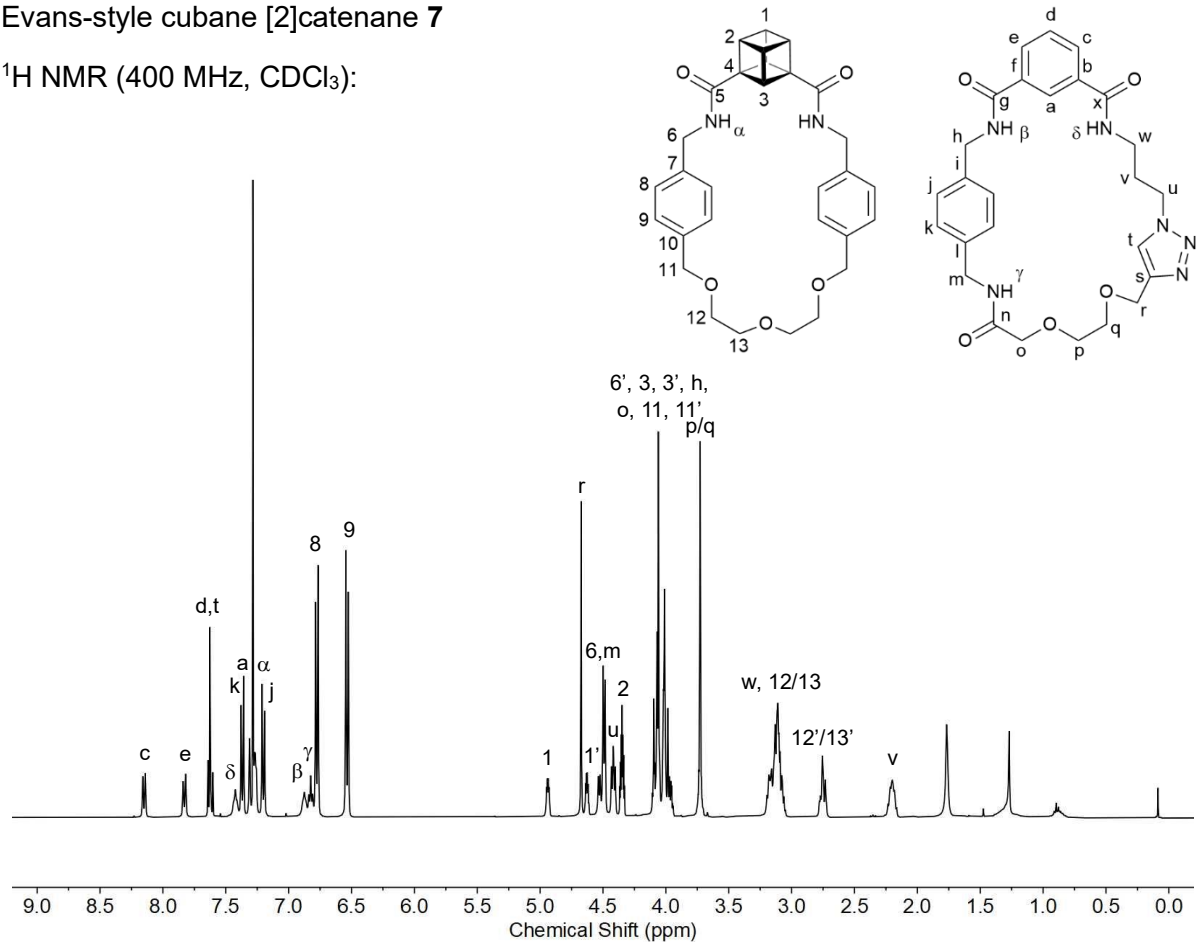
Compound Table

Compound Label	RT (min)	Observed mass (m/z)	Neutral observed mass (Da)	Theoretical mass (Da)	Mass error (ppm)	Isotope match score (%)
Cpd 1: C30 H32 N2 O5	0.67	501.2379	500.2307	500.2311	-0.83	99.51

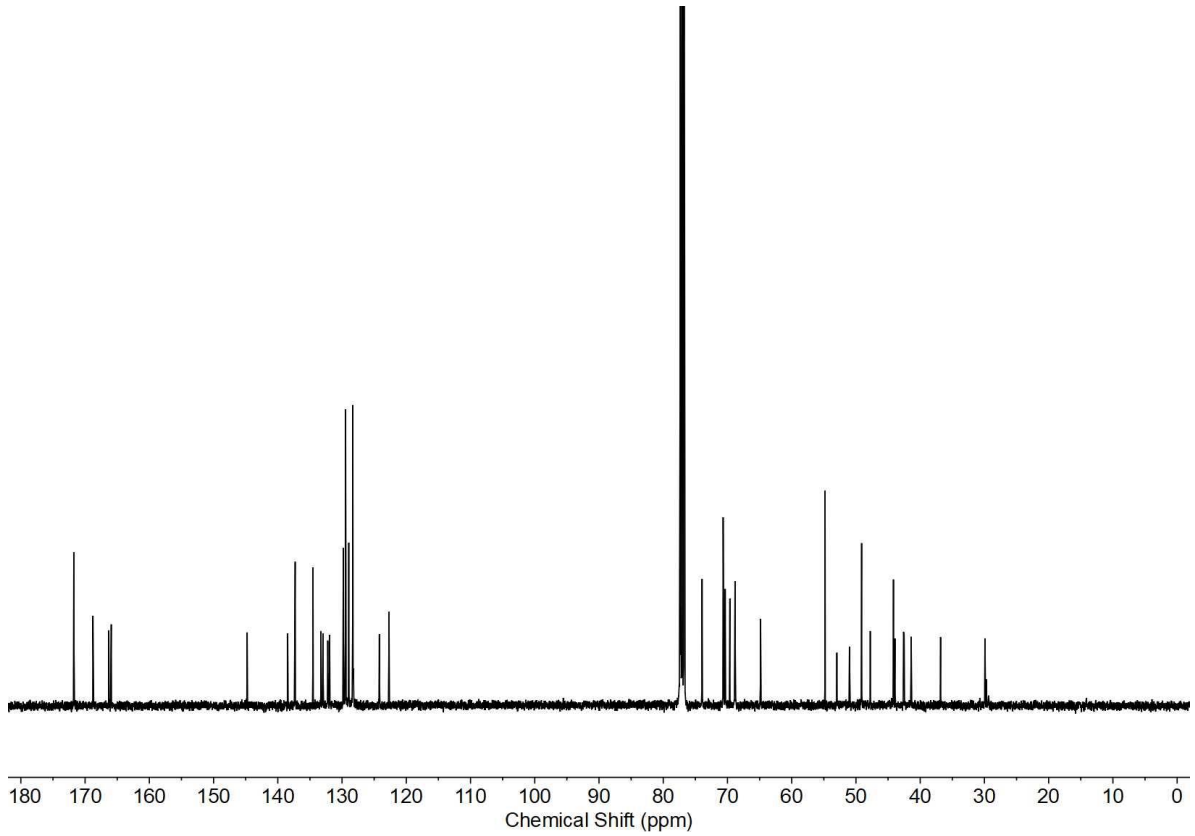
Mass errors of between -5.00 and 5.00 ppm with isotope match scores above 60% are considered confirmation of molecular formulae

Evans-style cubane [2]catenane **7**

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

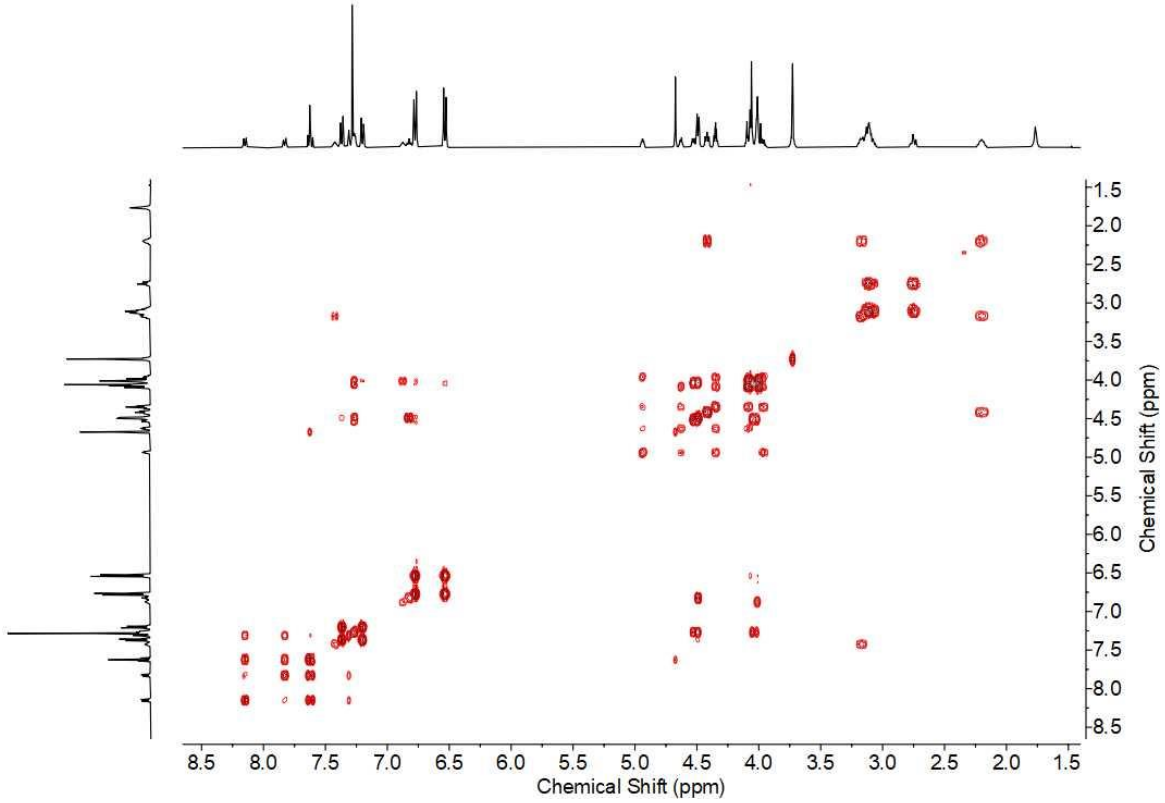


^{13}C NMR (100 MHz, $CDCl_3$):

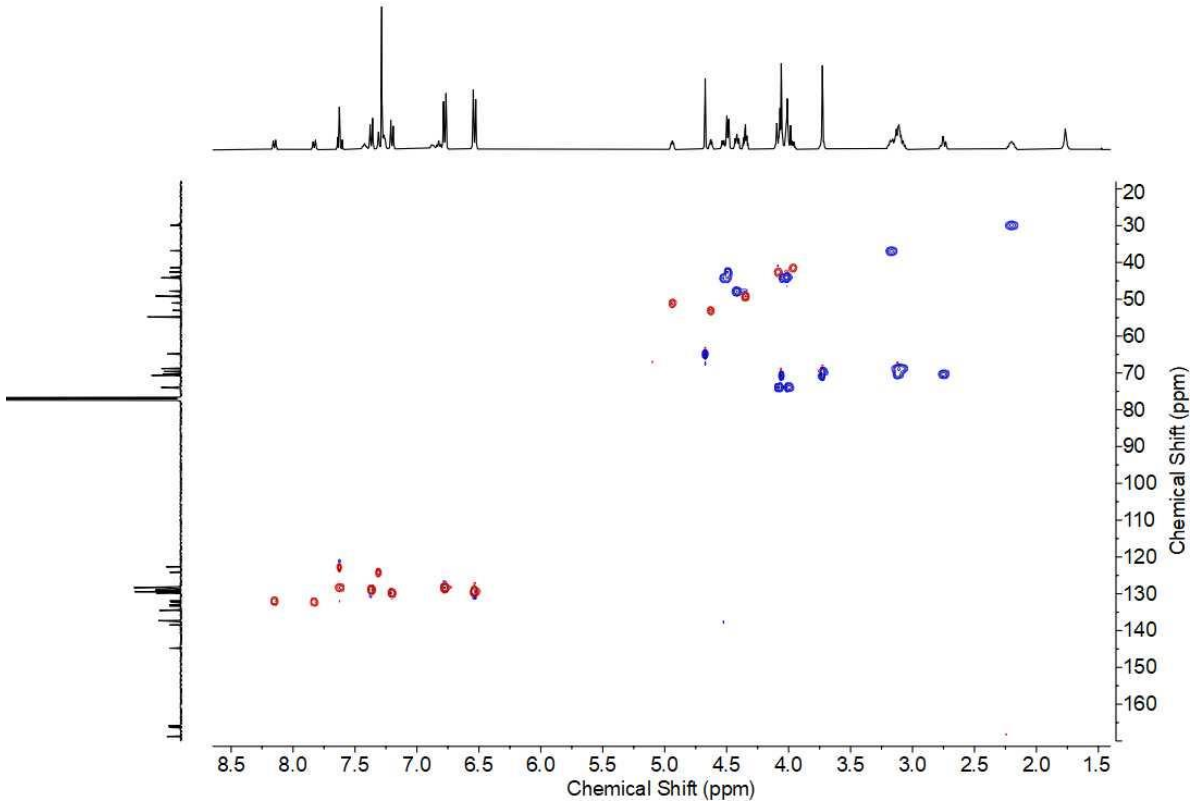


Evans-style cubane [2]catenane **7**

^{1}H-^{1}H COSY NMR ($CDCl_3$):

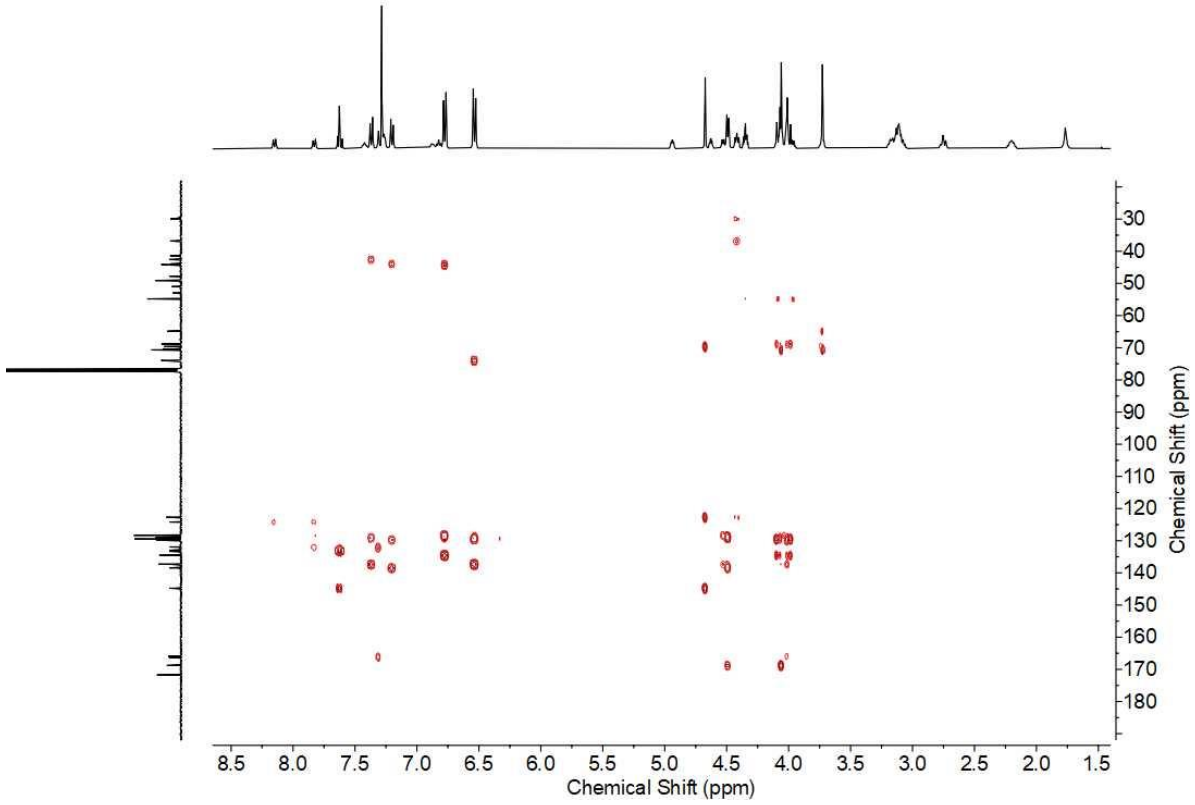


^{1}H-^{13}C HSQC NMR ($CDCl_3$):

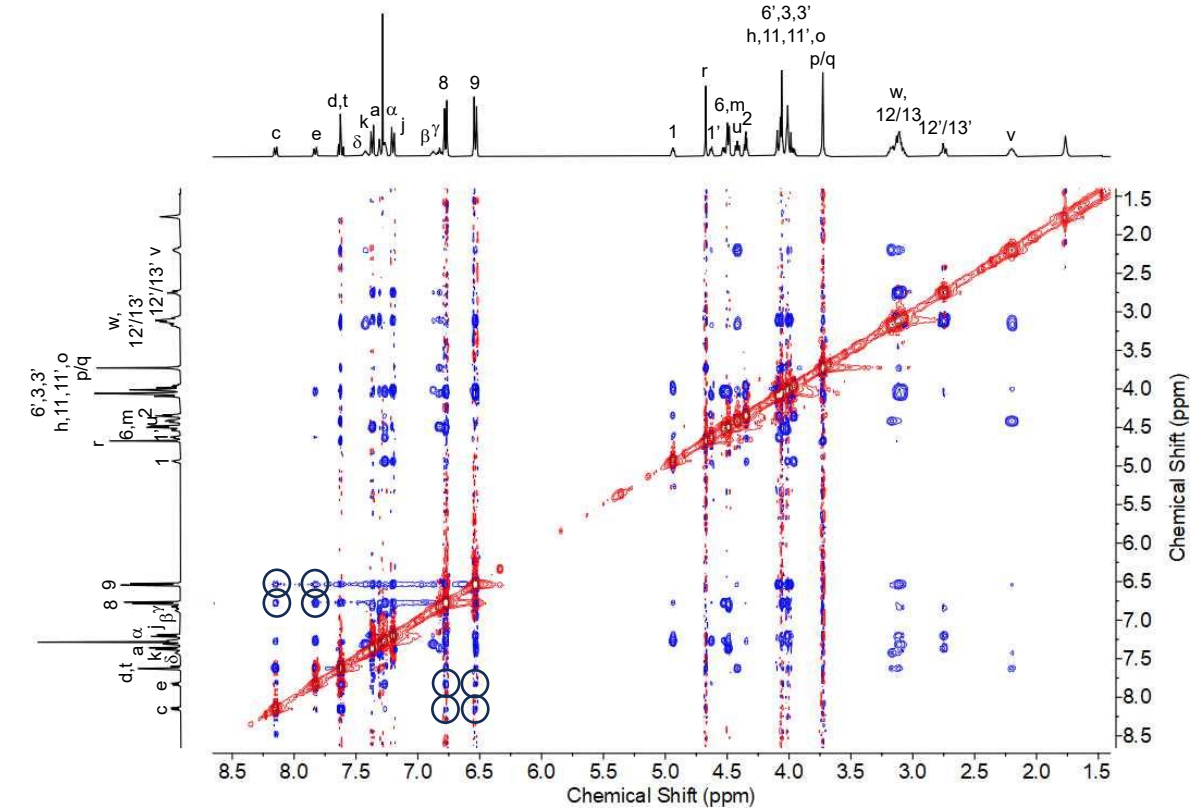


Evans-style cubane [2]catenane **7**

^{1}H-^{13}C HMBC NMR ($CDCl_3$):

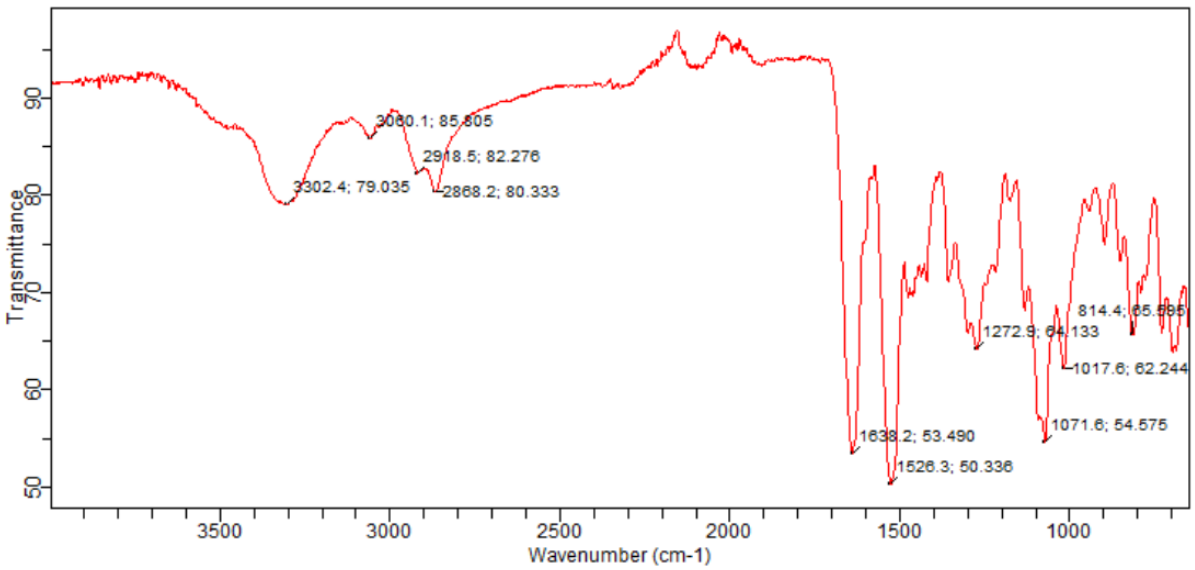


^{1}H-^{1}H ROESY NMR ($CDCl_3$): *Intercomponent couplings circled*



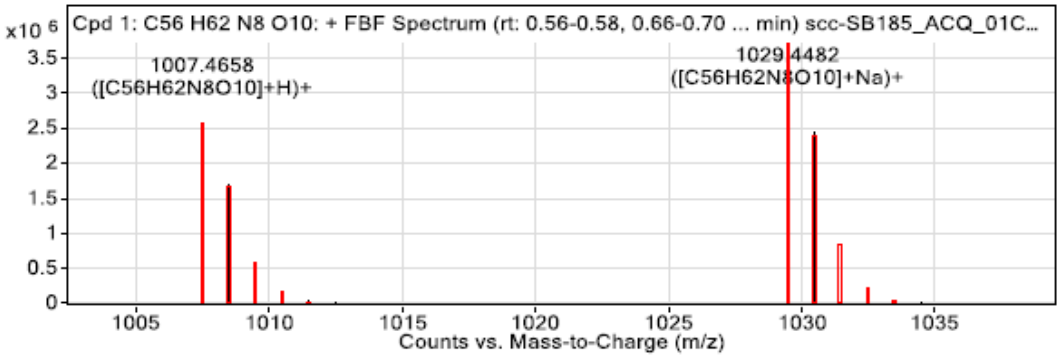
Evans-style cubane [2]catenane **7**

IR (neat):



HRMS:

Figure: Full range view of Compound spectra and potential adducts.



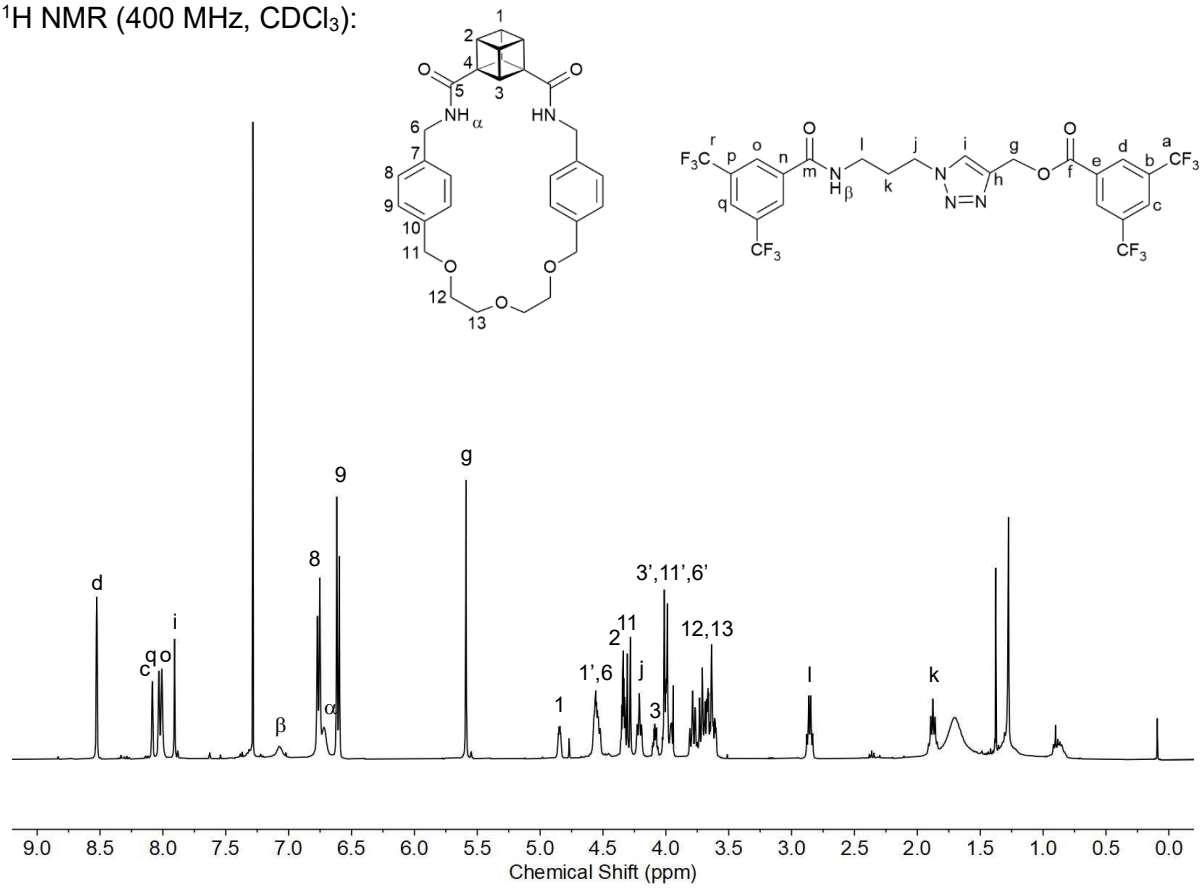
Compound Table

Compound Label	RT (min)	Observed mass (m/z)	Neutral observed mass (Da)	Theoretical mass (Da)	Mass error (ppm)	Isotope match score (%)
Cpd 1: C56 H62 N8 O10	0.78	1007.4658	1006.4588	1006.4589	-0.06	99.70

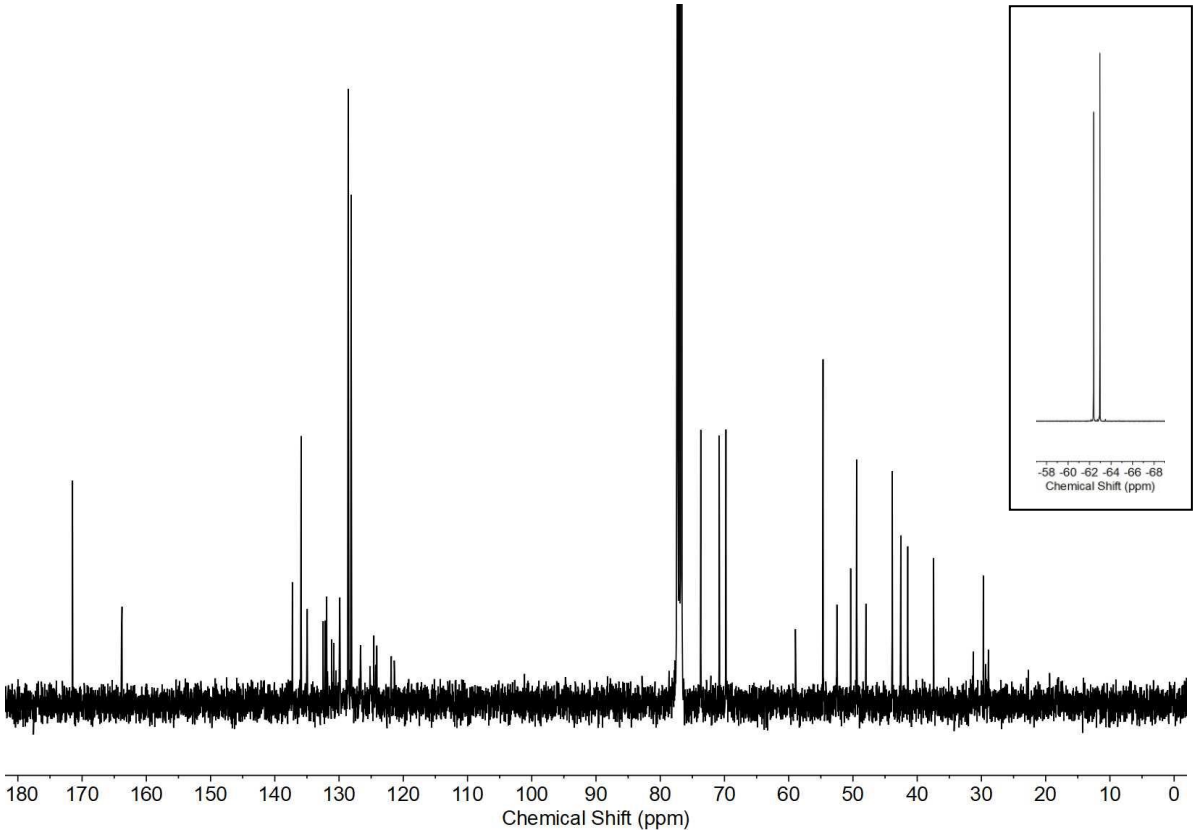
Mass errors of between -5.00 and 5.00 ppm with isotope match scores above 60% are considered confirmation of molecular formulae

Evans-style cubane [2]rotaxane **10**

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

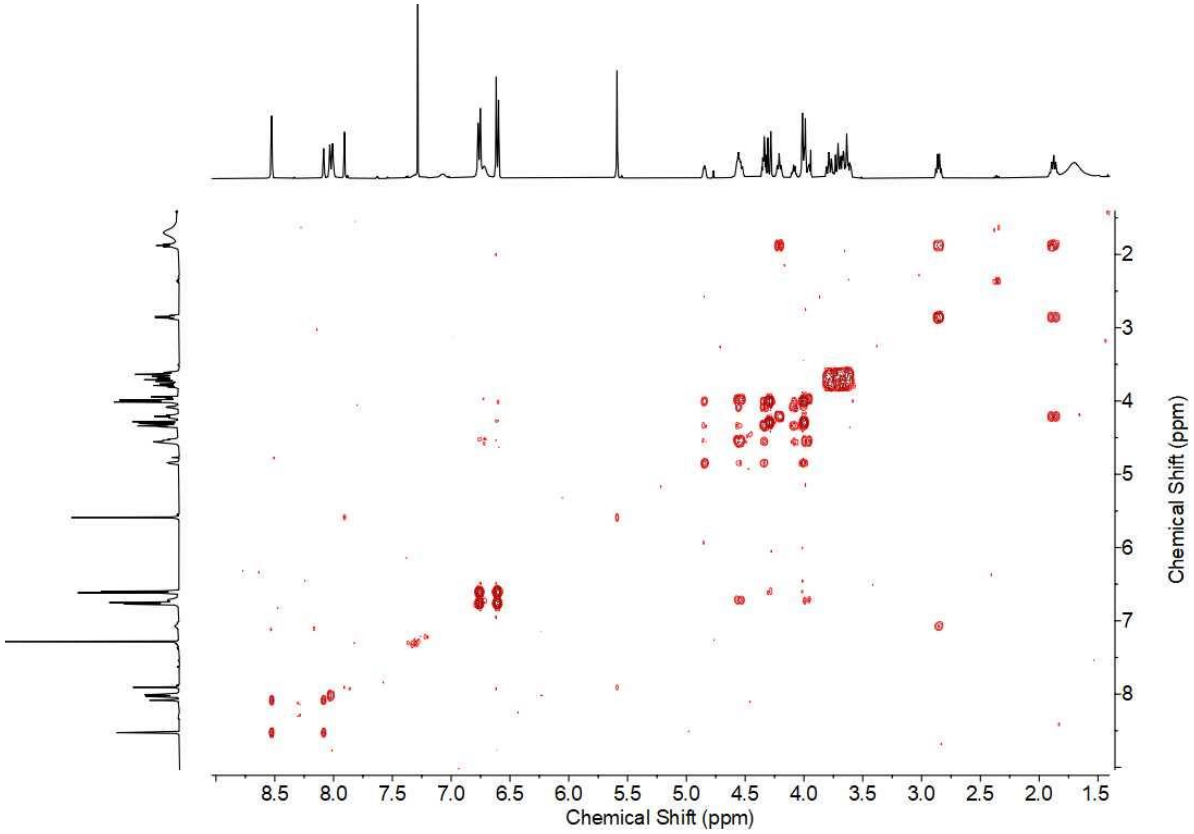


^{13}C NMR (100 MHz, $CDCl_3$); *Inset:* ^{19}F NMR (377 MHz, $CDCl_3$):

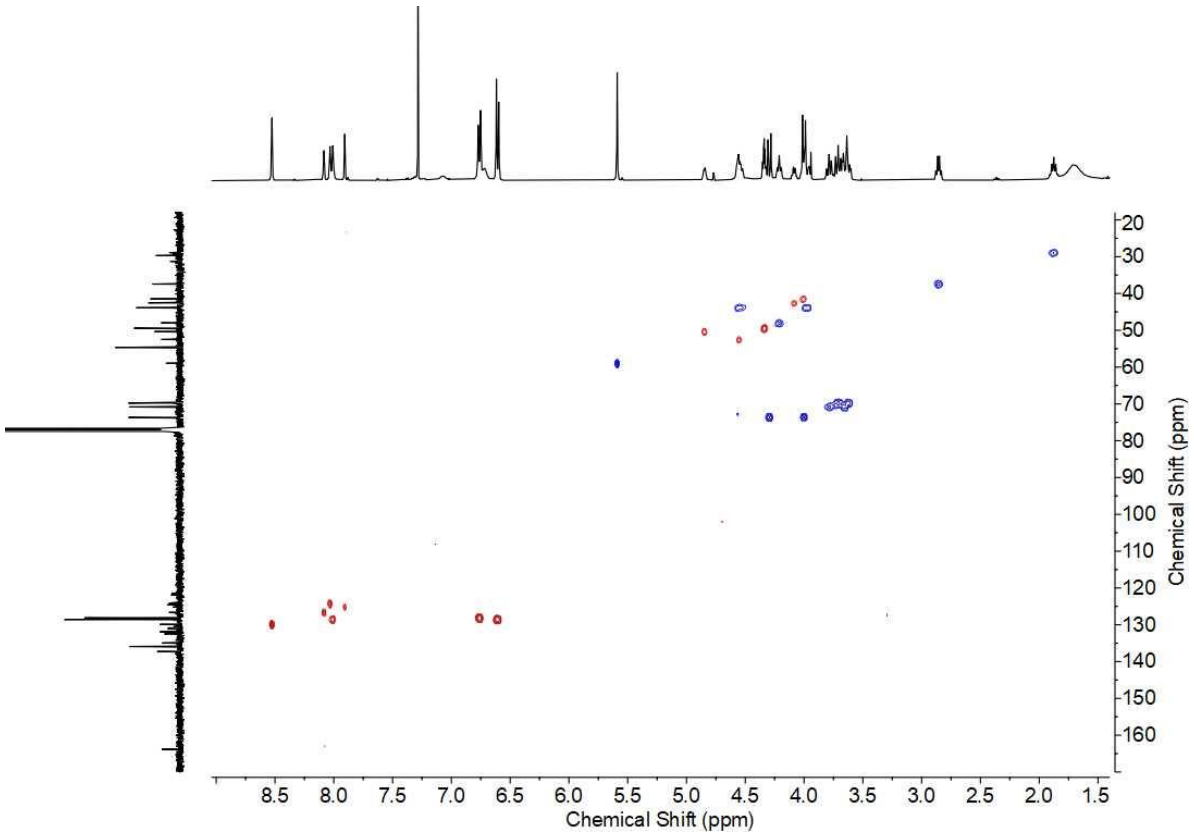


Evans-style cubane [2]rotaxane **10**

^{1}H-^{1}H COSY NMR ($CDCl_3$):

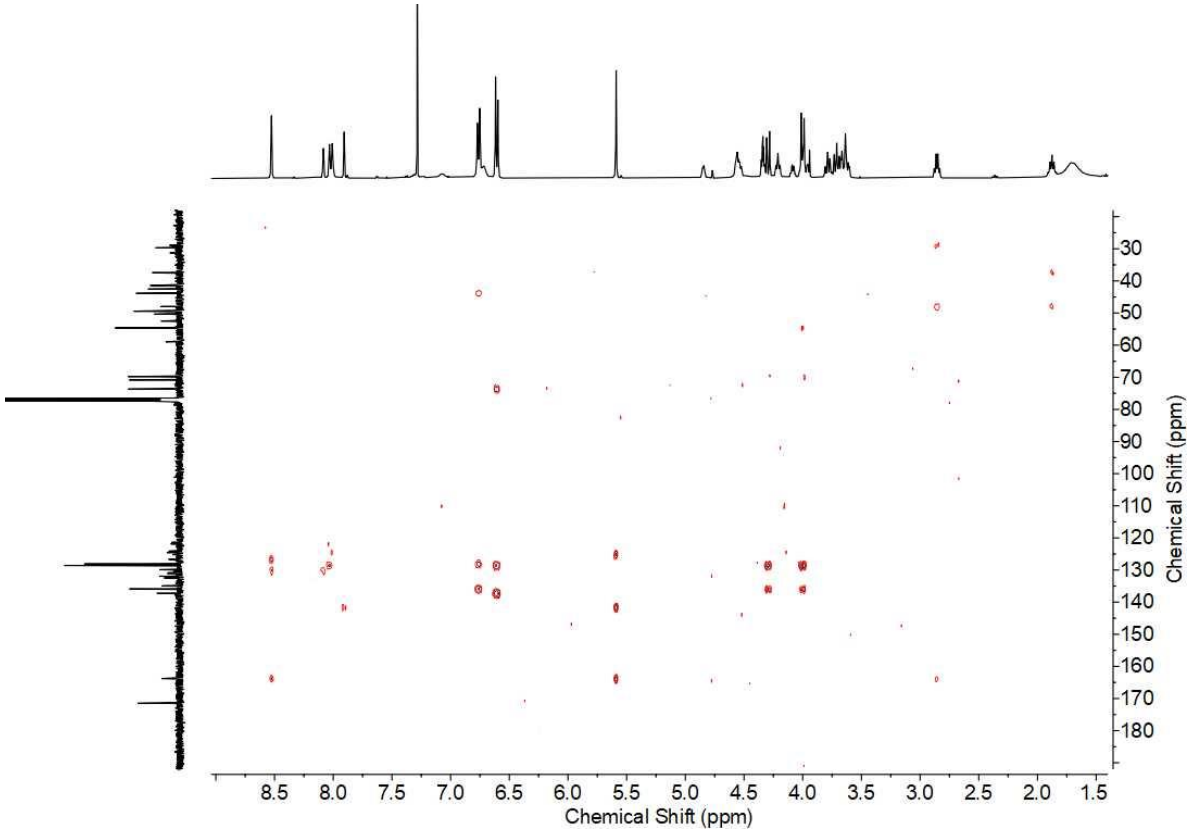


^{1}H-^{13}C HSQC NMR ($CDCl_3$):

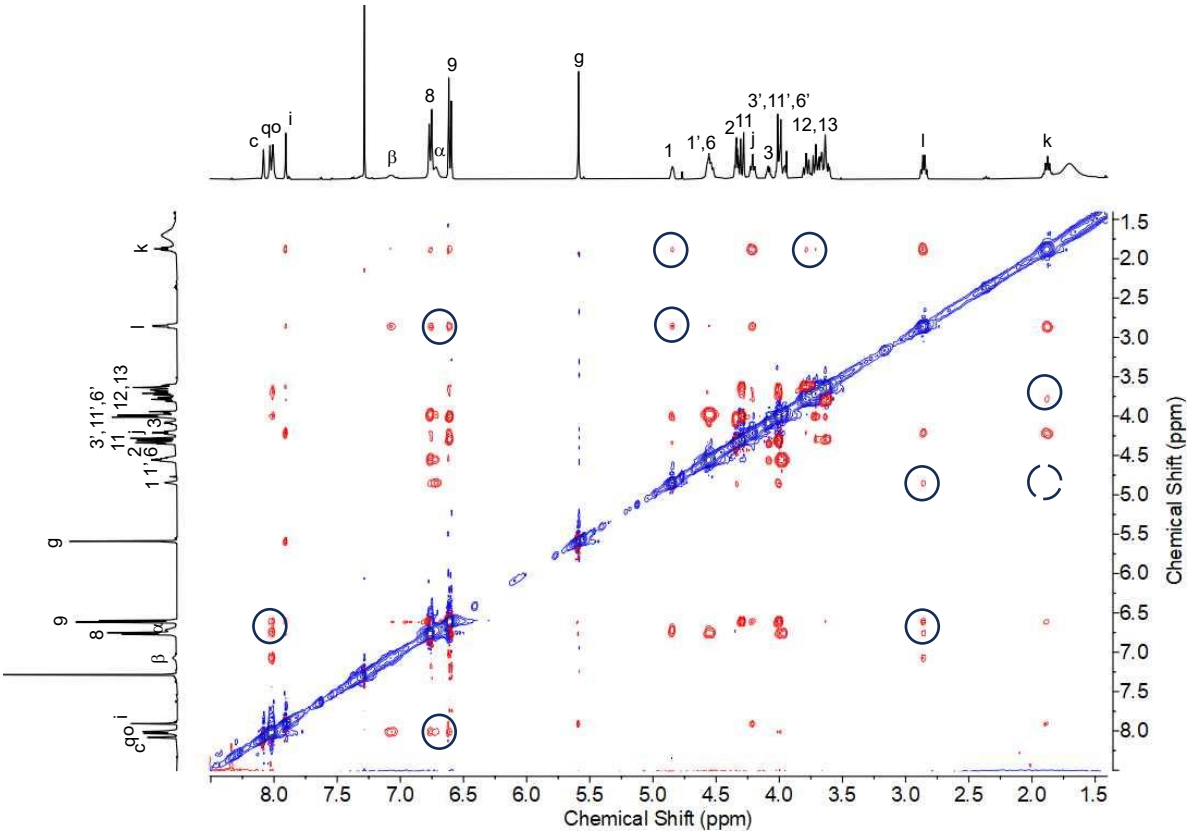


Evans-style cubane [2]rotaxane **10**

^{1}H-^{13}C HMBC NMR ($CDCl_3$):

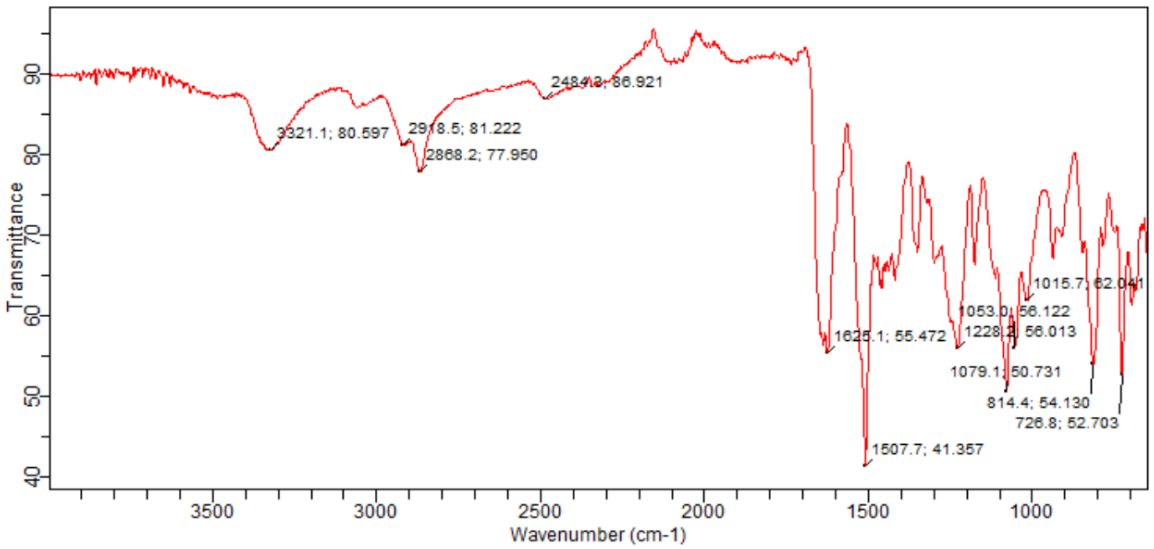


^{1}H-^{1}H ROESY NMR ($CDCl_3$): *Intercomponent couplings circled*



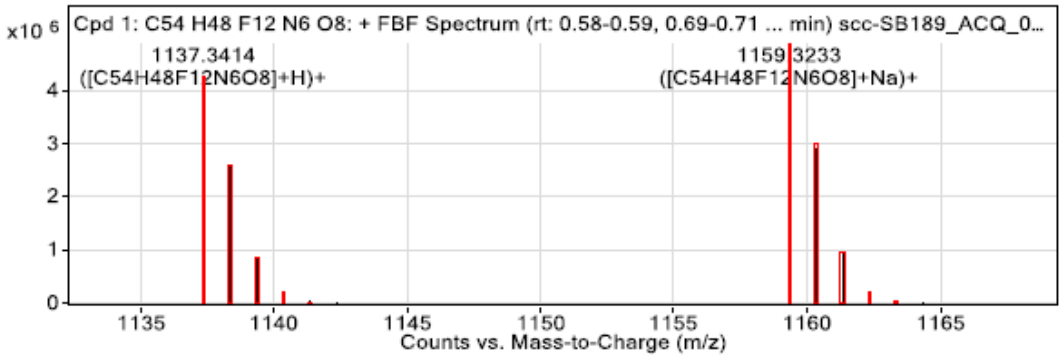
Evans-style cubane [2]rotaxane **10**

IR (neat):



HRMS:

Figure: Full range view of Compound spectra and potential adducts.



Compound Table

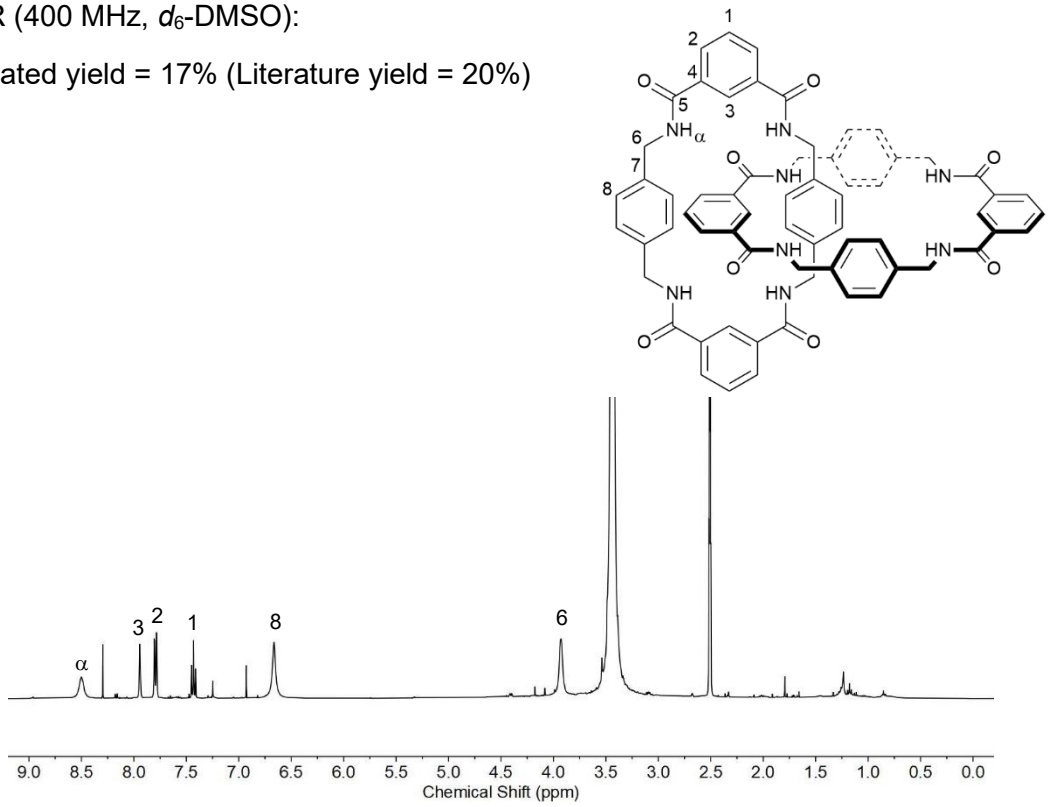
Compound Label	RT (min)	Observed mass (m/z)	Neutral observed mass (Da)	Theoretical mass (Da)	Mass error (ppm)	Isotope match score (%)
Cpd 1: C54 H48 F12 N6 O8	0.80	1137.3414	1136.3341	1136.3342	-0.06	99.81

Mass errors of between -5.00 and 5.00 ppm with isotope match scores above 60% are considered confirmation of molecular formulae

Leigh-style isophthalamide [2]catenane **ESI-2**[7]

^{1}H NMR (400 MHz, d_6-DMSO):

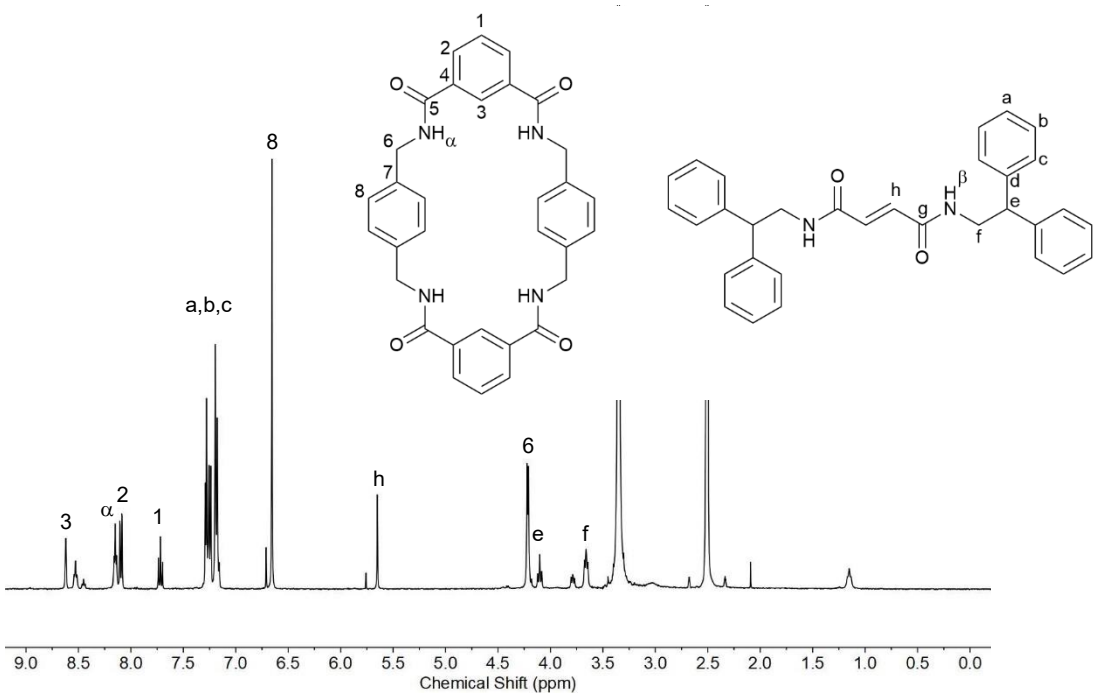
Our isolated yield = 17% (Literature yield = 20%)



Leigh-style isophthalamide [2]rotaxane **ESI-3**[2]

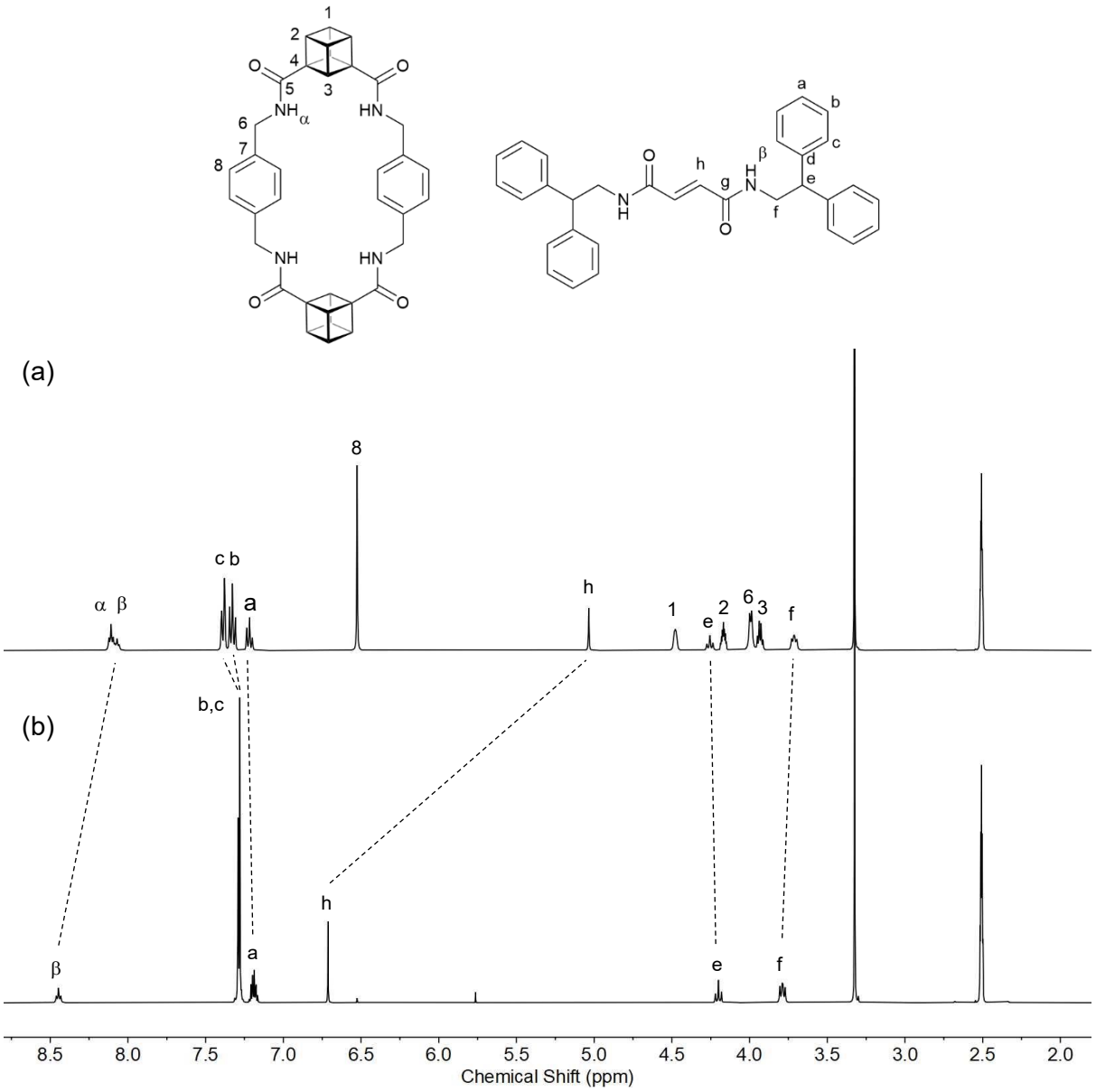
^{1}H NMR (400 MHz, d_6-DMSO):

10% of axle **3** remains. Our isolated yield = 75% (Literature yield = 97%)



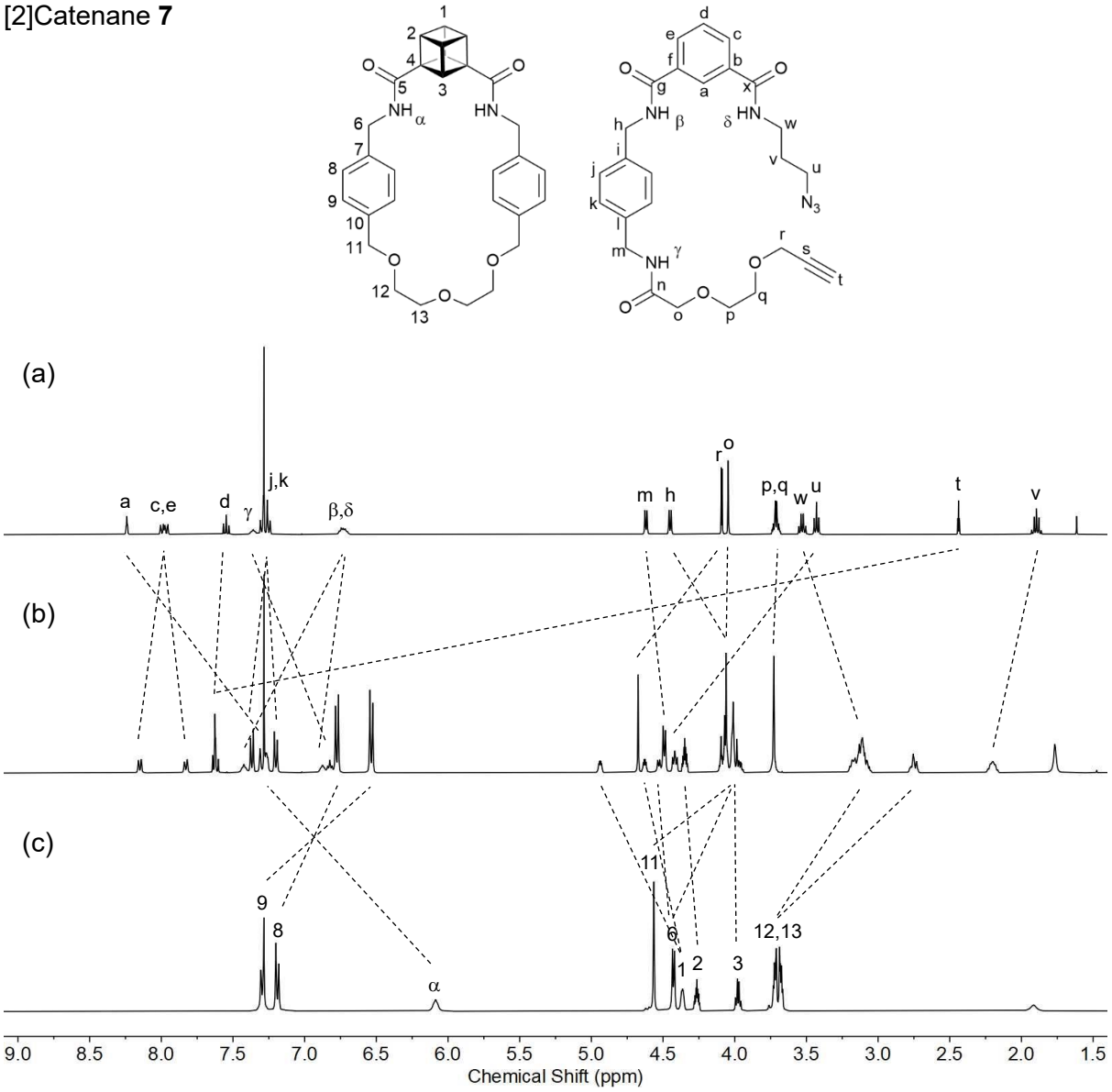
Comparison Spectra of Interlocked Molecules

[2]Rotaxane **4**



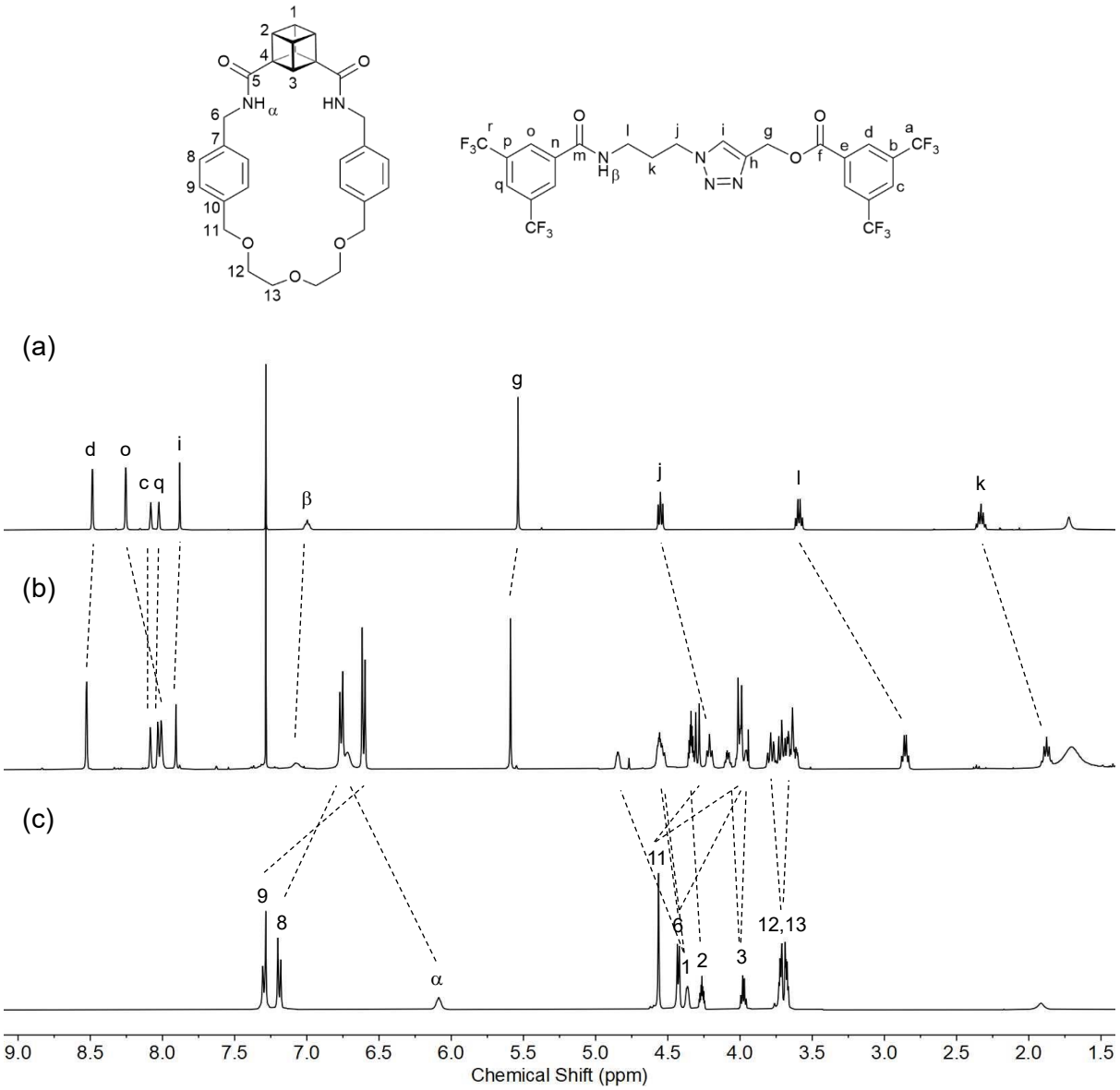
^{1}H NMR spectra of (a) [2]rotaxane **4**, (b) axle **3** (d_6-DMSO, 400 MHz, 298 K).

[2]Catenane **7**



^{1}H NMR spectra of (a) alkyne-azide **6**, (b) [2]catenane **7**, (c) macrocycle **5** ($CDCl_3$, 400 MHz, 298 K).

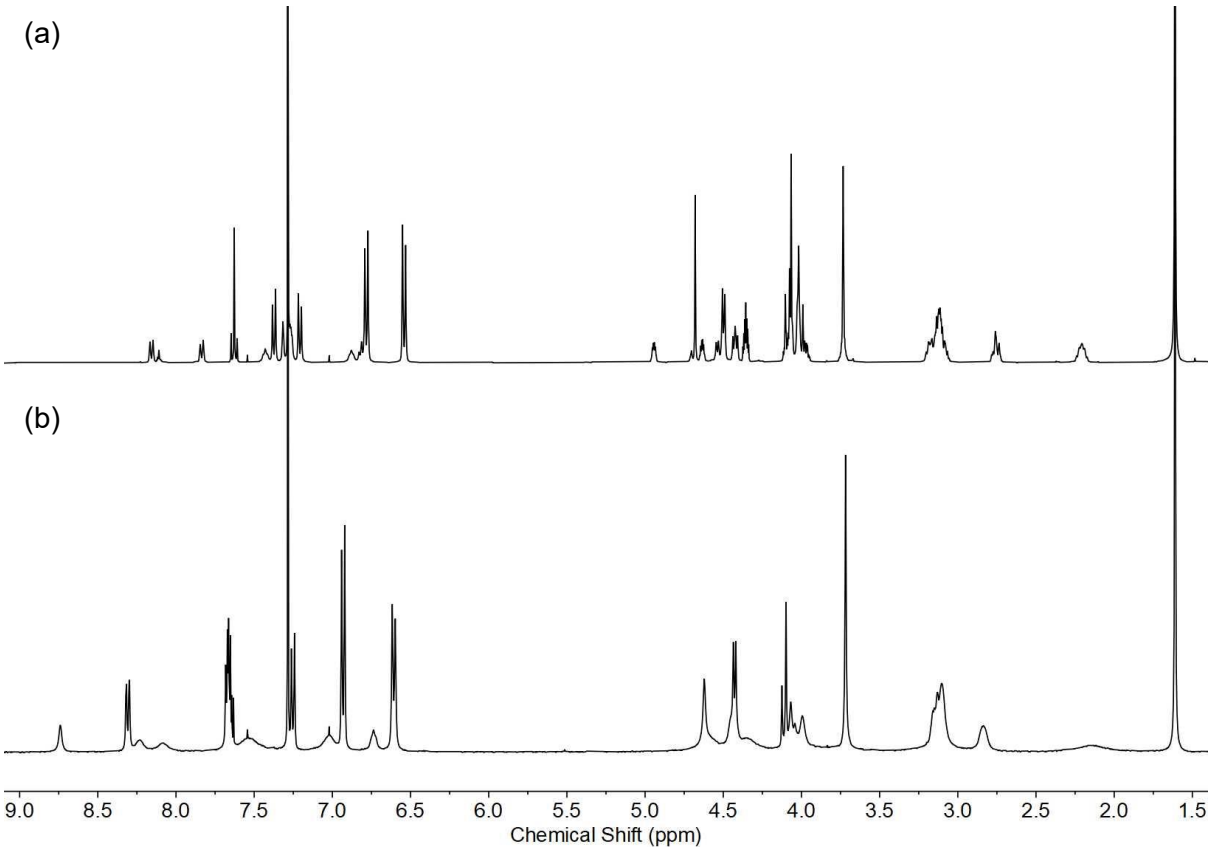
[2]Rotaxane **10**



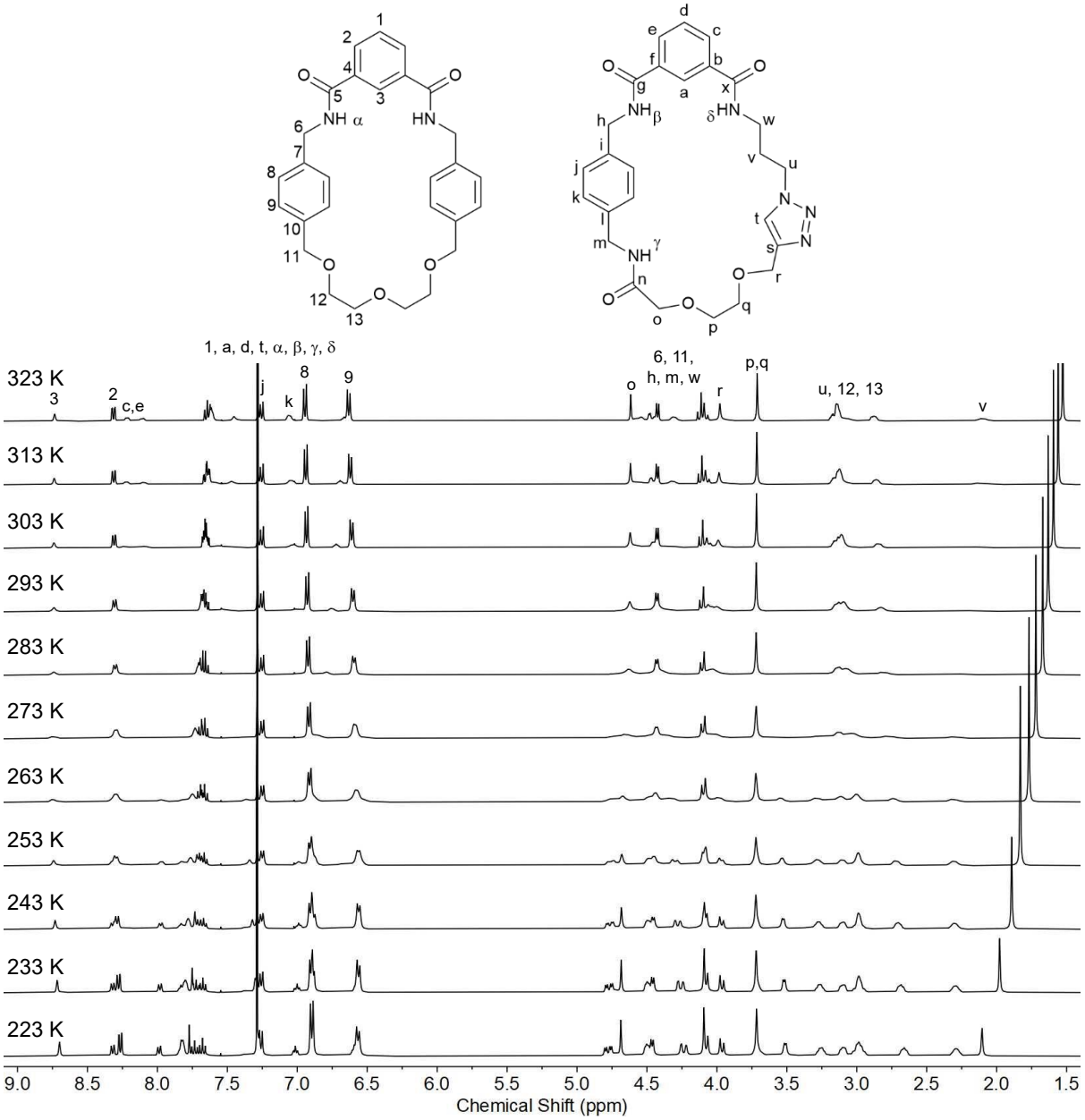
^{1}H NMR spectra of (a) axle **ESI-6**, (b) [2]rotaxane **10**, (c) macrocycle **5** ($CDCl_3$, 400 MHz, 298 K).

Comparison of Cubane [2]Catenane 7 and its all-Isophthalamide analogue ESI-7

*NMR of (a) Cubane [2]Catenane **7** vs (b) all-Isophthalamide analogue **ESI-7** ($CDCl_3$, 298 K)*



*VT NMR of all-isophthalamide analogue **ESI-7***

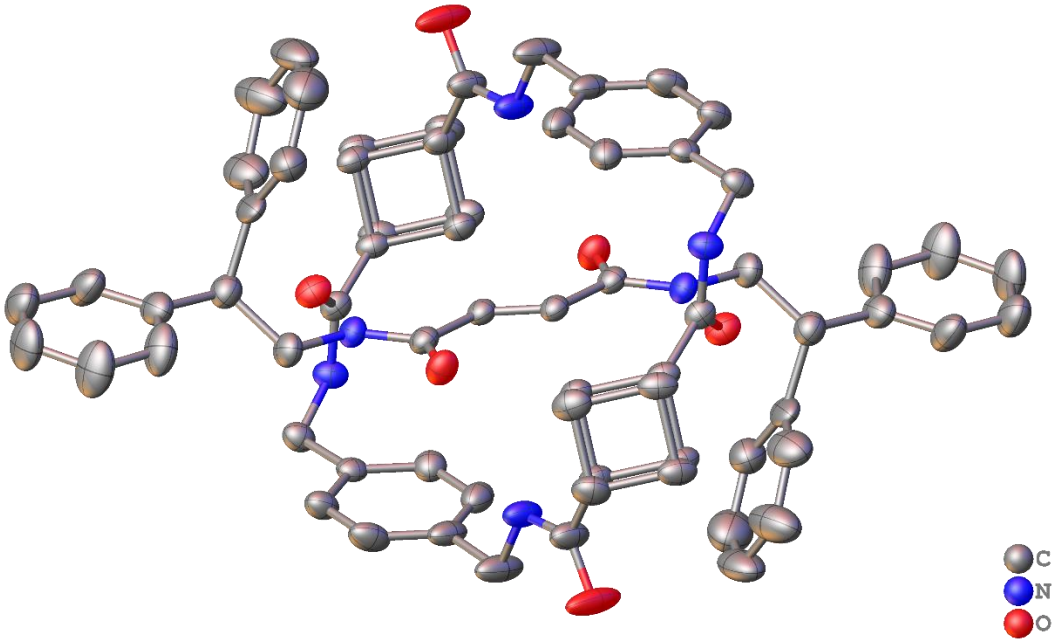


^{1}H NMR spectra of all-isophthalamide [2]catenane **ESI-7** ($CDCl_3$, 400 MHz).

Part 3: Crystallographic Data

Leigh-style cubane [2]rotaxane **4**

Crystals of [2]rotaxane **4** were grown by slow evaporation of a 1:1 chloroform:methanol solution. A suitable crystal was selected and studied using an Agilent SuperNova AtlasS2 diffractometer. Using Olex2[8] the structure was solved with the ShelXT[9] structure solution program using Direct Methods and refined with the ShelXL[10] refinement package using Least Squares minimisation.



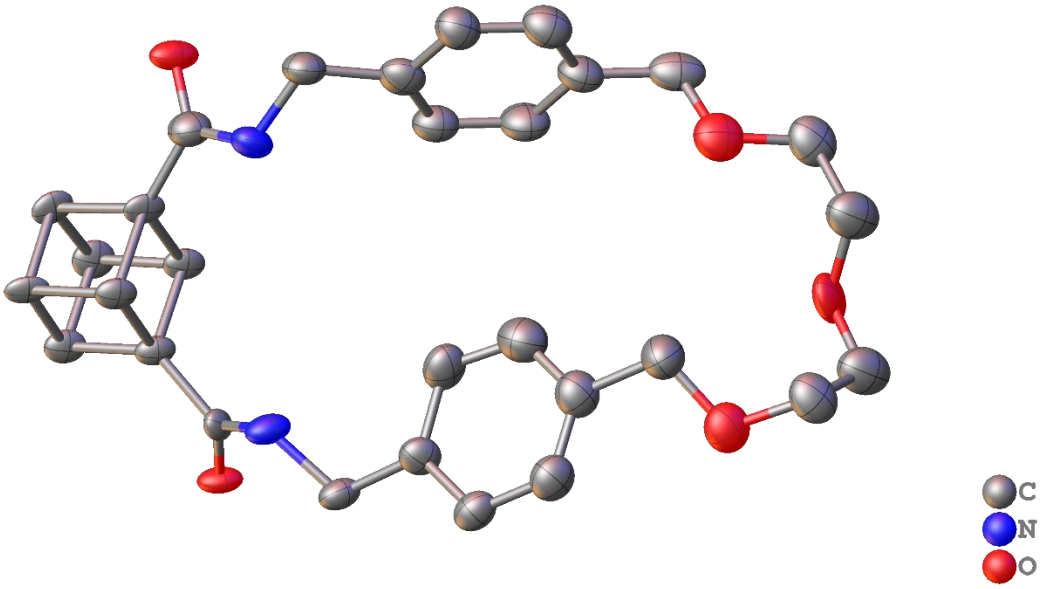
Solid-state molecular structure of [2]rotaxane **4**. Thermal ellipsoids are displayed at 50% probability, with hydrogen atoms and solvent molecules omitted for clarity.

Crystal data and structural refinement for [2]rotaxane **4**:

CCDC Number	2335982
Empirical formula	$C_{71}H_{65}Cl_9N_6O_6$
Formula weight	1417.34
Temperature/K	100.00(10)
Crystal system	orthorhombic
Space group	Pccn
a/Å	22.1773(3)
b/Å	20.9754(3)
c/Å	15.2190(2)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	7079.54(17)
Z	4
ρ_{calc}g/cm^3	1.330
μ/mm^{-1}	3.698
F(000)	2936.0
Crystal size/mm^3	0.12 × 0.09 × 0.05
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.974 to 152.522
Index ranges	-25 ≤ h ≤ 27, -26 ≤ k ≤ 22, -18 ≤ l ≤ 12
Reflections collected	30112
Independent reflections	7251 [R_{int} = 0.0381, R_{sigma} = 0.0218]
Data/restraints/parameters	7251/73/419
Goodness-of-fit on F^2	1.075
Final R indexes [I>=2σ (I)]	R_1 = 0.0821, wR_2 = 0.2500
Final R indexes [all data]	R_1 = 0.0902, wR_2 = 0.2599
Largest diff. peak/hole / e Å^{-3}	0.783/-0.373

Macrocycle **5**

Crystals of macrocycle **5** were grown by slow evaporation of a chloroform solution. A suitable crystal was selected and studied using an Agilent SuperNova AtlasS2 diffractometer. Using Olex2[8] the structure was solved with the ShelXT[9] structure solution program using Intrinsic Phasing and refined with the ShelXL[10] refinement package using Least Squares minimisation. The twin law was found using CrysAlisPro,[11] the twin is comprised of 2 components rotated by 179.97 degrees around [1.00 -0.00 -0.00] (reciprocal) or [0.90 -0.01 0.44] (direct).



Solid-state molecular structure of macrocycle **5**. Thermal ellipsoids are displayed at 50% probability, with hydrogen atoms and solvent molecules omitted for clarity.

Crystal data and structural refinement for macrocycle **5**:

CCDC Number	2335981
Empirical formula	$C_{30}H_{36}N_2O_7$
Formula weight	536.61
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	Cc
a/Å	52.946(3)
b/Å	10.4697(6)
c/Å	9.7763(5)
α/°	90
β/°	95.237(5)
γ/°	90
Volume/Å^3	5296.7(5)
Z	8
ρ_{calc}g/cm^3	1.321
μ/mm^{-1}	0.770
F(000)	2288.0
Crystal size/mm^3	0.11 × 0.09 × 0.04
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.61 to 151.786
Index ranges	-65 ≤ h ≤ 65, -13 ≤ k ≤ 13, -11 ≤ l ≤ 11
Reflections collected	9678
Independent reflections	9678 [R_{sigma} = 0.0322]
Data/restraints/parameters	9678/918/695
Goodness-of-fit on F^2	1.529
Final R indexes [I>=2σ (I)]	R_1 = 0.1099, wR_2 = 0.3276
Final R indexes [all data]	R_1 = 0.1239, wR_2 = 0.3505
Largest diff. peak/hole / e Å^{-3}	0.59/-0.51
Flack parameter	0.4(5)

Part 4: References

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11) CrysAlisPRO, Oxford Diffraction/Agilent Technologies UK Ltd, Yarnton, England.