Synthesis of a [2]catenane by ring closing metathesis of a [2]rotaxane prepared by crown ether active templation

Sean R. Barlow and Nicholas H. Evans*

Department of Chemistry, Lancaster University, Lancaster, LA1 4YB, UK.
n.h.evans@lancaster.ac.uk

Part 1: 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. Petrol refers to the fractions of petroleum that boil between 40°C and 60°C. Deionized 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/or phosphomolybdic acid solutions. Preparatory TLC was carried out on silica gel possessing a fluorescent indicator to allow for examination with short wavelength UV light.

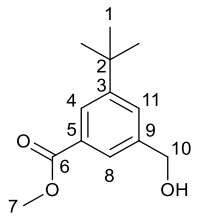
IR spectra were recorded on an Agilent Technologies Cary 630 FTIR spectrometer. NMR spectra were recorded on Bruker AVANCE III 400 or Bruker Neo 400 spectrometers at 298 K (unless otherwise stated). Mass spectra were recorded on Bruker Compact ToF coupled to an Agilent 1260 Infinity LC and Shimadzu LCMS-8040 instruments. Melting points were recorded on a Gallenkamp capillary melting point apparatus and are uncorrected.

Dimethyl 5-*tert*-butylisophthalate,[1] compounds **5**,[2] **7**,[3] **8**,[4] and 24-crown-8 (**24-c-8**)[5] were synthesized by adaptation of previously reported procedures.

In addition, **ESI-3**[6] was synthesized by adaptation of previously reported procedures.

Part 2a: Experimental procedures for main article

Compound 1



A solution of dimethyl 5-*tert*-butylisophthalate (3.5 g, 13.9 mmol) in CH_3OH (150 mL) was cooled to 0 °C under nitrogen. $NaBH_4$ (26.4 g, 699 mmol) was added in 50 mmol portions every 30 minutes until the total amount was added. The reaction was stirred for a further hour then quenched with $NaHCO_3$ (aq). Excess CH_3OH was removed *in vacuo*. The remaining aqueous solution was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by silica gel column chromatography (Petrol:EtOAc 4:1) to afford the *title product* (1.63 g, 53%) as a colourless solid.

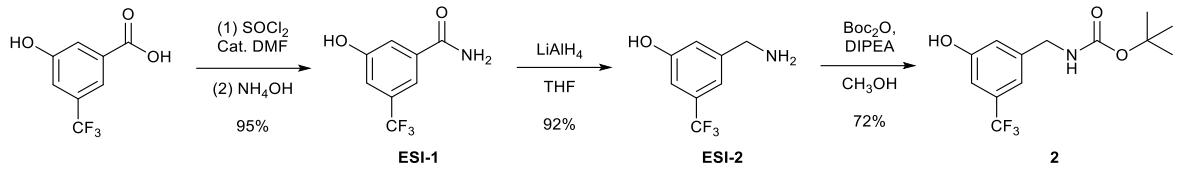
m.p. 111-113 °C.

***R_f*:** 0.36 [EtOAc:Petrol 1:4].

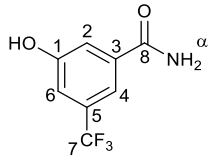
δ_H (400 MHz, $CDCl_3$): 8.02 (1H, s, H^4), 7.87 (1H, s, H^8), 7.62 (1H, s, H^{11}), 4.76 (2H, s, H^{10}), 3.94 (3H, s, H^7), 1.37 (9H, s, H^1).

δ_C (100 MHz, $CDCl_3$): 167.4 (C^6), 152.0 (C^3), 140.9 (C^9), 130.2 (C^5), 128.6 (C^{11}), 125.9 (C^4), 125.3 (C^8), 65.2 (C^{10}), 52.1 (C^7), 34.9 (C^2), 31.3 (C^1).

Synthesis of Compound 2



Compound ESI-1



To a flask containing 3-hydroxy-5-(trifluoromethyl)benzoic acid (500 mg, 2.42 mmol) was added $SOCl_2$ (7 mL) and a catalytic amount of DMF. The flask was connected to a reflux condenser fitted with a $CaCl_2$ drying tube and the reaction was refluxed with stirring for 5 hours. The reaction was cooled to room temperature and excess $SOCl_2$ was then removed by vacuum distillation. The crude material was redissolved in dry THF (7 mL) and cooled to 0 ^oC. Conc. NH_4OH (aq) (2 mL) was then added dropwise. The reaction was allowed to warm to room temperature and stirred for a further 5 hours. Excess THF was then removed *in vacuo*. The crude material was then redissolved in water (10 mL) and stirred for 5 minutes. The resulting precipitate was collected by vacuum filtration and washed with water to afford the *title product* (472 mg, 95%) as an off-white solid.

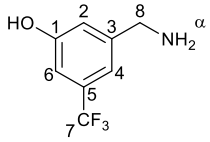
m.p. 187-189 ^oC

δ_H (400 MHz, d_6-DMSO): 10.37 (1H, bs, H^{OH}), 8.12 (1H, bs, H^{α}), 7.64 (1H, s, H^4), 7.54 (1H, s, H^2), 7.52 (1H, bs, $H^{\alpha'}$), 7.19 (1H, s, H^6).

δ_C (100 MHz, d_6-DMSO): 166.9 (C^8), 158.4 (C^1), 137.4 (C^3), 130.6 (q, J = 32 Hz, C^5), 124.3 (q, J = 274 Hz, C^7), 119.0 (C^2), 114.9 (q, J = 4 Hz, C^4), 114.6 (q, J = 4 Hz, C^6).

δ_F (377 MHz, d_6-DMSO): –61.2.

Compound ESI-2



To a flask containing dry THF (20 mL) cooled to 0 °C was added $LiAlH_4$ (739 mg, 19.5 mmol) portion wise. The flask was then placed under an argon atmosphere. To the above solution was added a dropwise solution of **ESI-1** (800 mg, 3.90 mmol) in dry THF (5 mL). The reaction was then heated to reflux with stirring for 6 hours. Upon cooling to room temperature, the excess $LiAlH_4$ was quenched with water (5 mL). The reaction mixture was filtrated through cotton and sand and washed with CH_3OH (10 x 5 mL). The filtrate was concentrated *in vacuo* to afford the *title product* (687 mg, 92%) as an off-white solid.

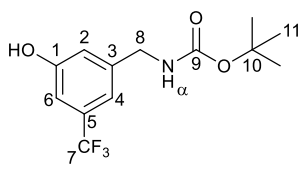
m.p. 167-169 °C.

δ_H (400 MHz, CD_3OD): 6.73 (2H, app s, H^2 & H^6), 6.66 (1H, s, H^4), 3.67 (2H, s, H^8).

δ_C (100 MHz, CD_3OD): 167.8 (C^1), 143.9 (C^3), 130.9 (q, *J* = 32 Hz, C^5), 123.5 (q, *J* = 270 Hz, C^7), 120.8 (C^2), 113.5 (q, *J* = 4 Hz, C^6), 108.3 (q, *J* = 4 Hz, C^4), 45.5 (C^8).

δ_F (377 MHz, CD_3OD): −63.8.

Compound 2



To a solution of **ESI-2** (840 mg, 4.39 mmol) in CH_3OH (25 mL) cooled to 0 °C was added DIPEA (339 mg, 4.58 mL, 26.3 mmol), followed by a solution of Boc_2O (1.00 g, 4.61 mmol) in CH_3OH (5 mL) dropwise. The reaction was stirred at 0 °C for 3 hours, then all volatiles were removed *in vacuo*. The crude material was re-dissolved in $CHCl_3$ (50 mL) and washed with 1M HCl (aq) (2 x 30 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo* to afford the *title product* (923 mg, apparent yield 72%) as an off-colourless crystalline solid. Impurities were detected in NMR spectra but material was deemed to be sufficiently pure to be used without the need for further purification.

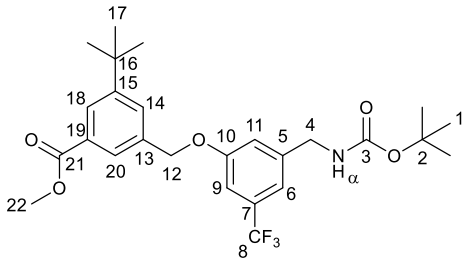
m.p. 139-142 °C (dec).

δ_H (400 MHz, $CDCl_3$): 7.05 (1H, s, H^4), 6.97 (1H, s, H^6), 6.93 (1H, s, H^2), 5.03 (1H, bs, H^α), 4.32 (2H, bd, *J* = 5.6 Hz, H^8), 1.50 (9H, s, H^{11}).

δ_C (100 MHz, $CDCl_3$): 156.6 (C^1), 156.3 (C^9), 141.6 (C^3), 132.2 (q, *J* = 32 Hz, C^5), 123.5 (q, *J* = 271 Hz, C^7), 117.4 (C^2), 115.7 (C^4), 111.6 (C^6), 80.4 (C^{10}), 44.0 (C^8), 28.4 (C^{11}).

δ_F (377 MHz, $CDCl_3$): −62.8.

Compound 3



Methanesulfonyl chloride (843 mg, 0.57 mL, 7.31 mmol) and Et_3N (975 mg, 1.35 mL, 9.74 mmol) were added to a solution of **1** (1.08 g, 4.87 mmol) in dry CH_2Cl_2 (20 mL) under argon cooled to 0 °C. The reaction was stirred for 3 hours then quenched with $NaHCO_3$ (aq) (20 mL). The organic and aqueous layers were separated, and the aqueous layer washed with CH_2Cl_2 (30 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to afford the mesylated alcohol. To a separate flask containing **2** (1.42 g, 4.87 mmol) dissolved in dry CH_3CN (20 mL) was added K_2CO_3 (807 mg, 5.84 mmol). The solution was stirred for 10 minutes then a solution of the mesylated alcohol in dry CH_3CN (5 mL) was added. The reaction was then refluxed with stirring under argon for 16 hours. Upon cooling to room temperature, the reaction mixture was filtrated under gravity and concentrated *in vacuo*. The crude material was purified by silica gel column chromatography (Heptane:EtOAc 3:1) to afford the *title product* (1.58 g, 72%) as a clear gel.

***R_f*:** 0.23 [EtOAc:Heptane 1:3].

IR ν_{max} (neat): 3375 (N-H), 2967 (C-H), 1709 (2 x C=O).

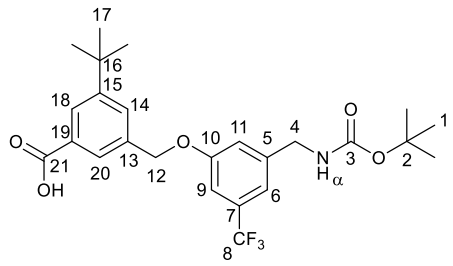
δ_H (400 MHz, $CDCl_3$): 8.09 (1H, app t, H^{18}), 7.95 (1H, app t, H^{20}), 7.66 (1H, app t, H^{14}), 7.17 (1H, s, H^6), 7.15 (1H, s, H^9), 7.13 (1H, s, H^{11}), 5.12 (2H, s, H^{12}), 4.94 (1H, bs, H^{α}), 4.36 (2H, bd, *J* = 5.6 Hz, H^4), 3.95 (3H, s, H^{22}), 1.49 (9H, s, H^1), 1.39 (9H, s, H^{17}).

δ_C (100 MHz, $CDCl_3$): 167.1 (C^{21}), 159.0 (C^{10}), 155.9 (C^3), 152.2 (C^{15}), 141.9 (C^5), 136.1 (C^{13}), 132.1 (q, *J* = 32 Hz, C^7), 130.4 (C^{19}), 129.3 (C^{14}), 126.6 (C^{18}), 126.1 (C^{20}), 123.7 (q, *J* = 278 Hz, C^8), 117.2 (C^{11}), 116.5 (q, *J* = 4 Hz, C^6), 110.5 (q, *J*= 4 Hz, C^9), 79.9 (C^2), 70.2 (C^{12}), 52.2 (C^{22}), 44.2 (C^4), 34.9 (C^{16}), 31.3 (C^{17}), 28.4 (C^1).

δ_F (377 MHz, $CDCl_3$): –62.6.

m/z (ES): 518.2130 ($[M+Na]^+$ $C_{26}H_{32}F_3NNaO_5$ requires 518.2125).

Compound 4



To a solution of Boc-amine-ester **3** (1.55 g, 3.12 mmol) in CH_3OH (15 mL) was added a solution of KOH (2.27 g, 40.6 mmol) in water (0.5 mL). The reaction was stirred for 5 hours then acidified to pH 3 with 1M HCl (aq). Excess CH_3OH was then removed *in vacuo* and the resulting precipitate was collected by vacuum filtration to afford the *title product* (1.15 g, 76%) as a colourless solid.

m.p. 188-190 °C (dec).

IR ν_{max} (neat): 2967 (C-H), 1690 (2 x C=O).

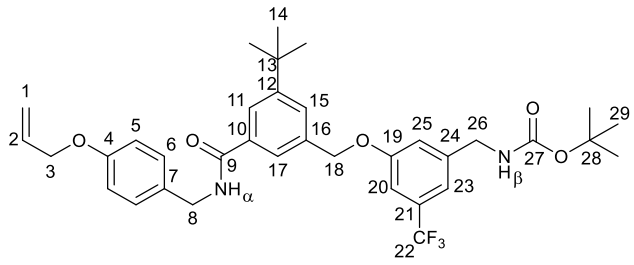
δ_H (400 MHz, $CDCl_3$): 8.15 (1H, s, H^{18}), 8.02 (1H, s, H^{20}), 7.71 (1H, s, H^{14}), 7.18 (1H, s, H^{6}), 7.15 (2H, bs, H^{9} & H^{11}), 5.14 (2H, s, H^{12}), 4.95 (1H, bs, H^{α}), 4.37 (2H, bd, *J* = 5.2 Hz, H^{4}), 1.49 (9H, s, H^{1}), 1.40 (9H, s, H^{17}).

δ_C (100 MHz, $CDCl_3$): 171.3 (C^{21}), 159.1 (C^{10}), 156.0 (C^{3}), 152.3 (C^{15}), 141.9 (C^{5}), 136.3 (C^{13}), 132.1 (q, *J* = 32 Hz, C^{7}), 130.0 (C^{14}), 129.7 (C^{19}), 127.2 (C^{18}), 126.6 (C^{20}), 123.8 (q, *J* = 271 Hz, C^{8}), 117.2 (C^{11}), 116.6 (C^{6}), 110.6 (C^{9}), 79.9 (C^{2}), 70.1 (C^{12}), 44.3 (C^{4}), 34.9 (C^{16}), 31.2 (C^{17}), 28.4 (C^{1}).

δ_F (377 MHz, $CDCl_3$): −62.7.

m/z (ES): 504.1976 ($[M+Na]^+ C_{25}H_{30}F_3NNaO_5$ requires 504.1968).

Compound 6



To a solution of **4** (1.09 g, 2.26 mmol) in dry CH_3CN (20 mL) was added DCC (513 mg, 2.49 mmol) and *N*-hydroxysuccinimide (286 mg, 1.49 mmol). The reaction was then stirred at room temperature under argon for 16 hours. The reaction mixture was filtrated under gravity and concentrated *in vacuo*. The crude material was redissolved in dry CH_2Cl_2 (20 mL) and placed under argon. To the solution was added **5** (406 mg, 2.49 mmol) and Et_3N (272 mg, 0.37 mL, 2.71 mmol). The reaction was then stirred at room temperature for 16 hours. The reaction mixture was then washed with 1M HCl (aq) (2 x 20 mL), $NaHCO_3$ (aq) (2 x 20 mL) and water (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 (Heptane:EtOAc 3:1) to afford the *title product* (941 mg, 67%) as a sticky colourless solid.

***R_f*:** 0.36 [EtOAc:Heptane 1:3].

IR ν_{max} (neat): 3304 (N-H), 2967 (C-H), 1690 (C=O), 1638 (C=O).

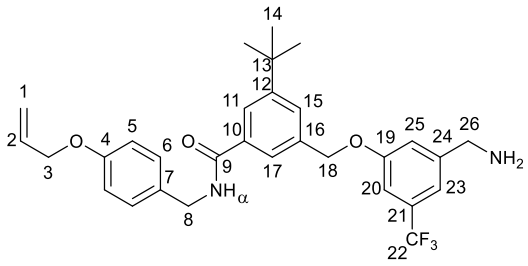
δ_H (400 MHz, $CDCl_3$): 7.87 (1H, app t, H^{11}), 7.62 (1H, bs, H^{17}), 7.59 (1H, bs, H^{15}), 7.31 (2H, d, *J* = 8.5 Hz, H^6), 7.15 (1H, s, H^{23}), 7.12 (2H, bs, H^{20} & H^{25}), 6.92 (2H, d, *J* = 8.5 Hz, H^5), 6.52 (1H, bs, H^{α}), 6.12-6.02 (1H, m, H^2), 5.43 (1H, dq, *J* = 17 Hz, 1.5 Hz, H^1), 5.30 (1H, dq, *J* = 11 Hz, 1.5 Hz, $H^{1'}$), 5.09 (2H, s, H^{18}), 4.98 (1H, bs, H^{β}), 4.62 (2H, d, *J* = 5.6 Hz, H^8), 4.55 (2H, dt, *J* = 5.2 Hz, 1.5 Hz, H^3), 4.33 (2H, bd, *J* = 5.2 Hz, H^{26}), 1.48 (9H, s, H^{29}), 1.37 (9H, s, H^{14}).

δ_C (100 MHz, $CDCl_3$): 167.4 (C^9), 158.9 (C^{19}), 158.1 (C^4), 155.9 (C^{27}), 152.2 (C^{12}), 141.9 (C^{24}), 136.1 (C^{16}), 134.7 (C^{10}), 133.1 (C^2), 132.1 (q, *J* = 32 Hz, C^{21}), 130.5 (C^7), 129.3 (C^6), 127.9 (C^{15}), 124.2 (C^{11}), 123.7 (q, *J* = 278 Hz, C^{22}), 123.1 (C^{17}) 117.7 (C^1), 117.1 (C^{25}), 116.5 (C^{23}), 114.9 (C^5), 110.6 (C^{20}), 79.9 (C^{28}), 70.2 (C^{18}), 68.8 (C^3), 44.2 (C^{26}), 43.6 (C^8), 34.9 (C^{13}), 31.2 (C^{14}), 28.3 (C^{29}).

δ_F (377 MHz, $CDCl_3$): –62.7.

m/z (ES): 649.2879 ($[M+H]^+$ $C_{35}H_{41}F_3N_2NaO_5$ requires 649.2860).

Half Axle HA-1



Boc-amine-alkene **6** (600 mg, 0.95 mmol) was dissolved in dry CH_2Cl_2 (15 mL) under argon and cooled to 0 °C. To the solution was added TFA (1.08 g, 0.73 mL, 9.57 mmol). The reaction was allowed to warm to room temperature and stirred for 4 hours. All volatiles were then removed *in vacuo*. The crude material was redissolved in EtOAc (20 mL) and washed with $NaHCO_3$ (aq) (25 mL). The aqueous was then extracted with EtOAc (2 x 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to afford the *title product* (500 mg, 99%) as a clear gel.

IR ν_{max} (neat): 3285 (N-H), 2957 (C-H), 1634 (C=O).

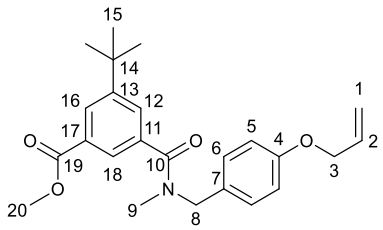
δ_H (400 MHz, $CDCl_3$): 7.85 (1H, app t, H^{11}), 7.64 (1H, s, H^{17}), 7.58 (1H, s, H^{15}), 7.29 (2H, d, *J* = 8.5 Hz, H^6), 7.20 (1H, s, H^{23}), 7.17 (1H, s, H^{25}), 7.11 (1H, s, H^{20}), 6.91 (2H, d, *J* = 8.5 Hz, H^5), 6.58 (1H, bs, H^{α}), 6.11-6.01 (1H, m, H^2), 5.43 (1H, dq, *J* = 17 Hz, 1.5 Hz, H^1), 5.30 (1H, dq, *J* = 17 Hz, 1.5 Hz, $H^{1'}$), 5.10 (2H, s, H^{18}), 4.59 (2H, d, *J* = 5.6 Hz, H^8), 4.54 (2H, dt, *J* = 5.2, 1.5 Hz, H^3), 3.92 (2H, s, H^{26}), 1.36 (9H, s, H^{14}).

δ_C (100 MHz, $CDCl_3$): 167.5 (C^9), 159.0 (C^{19}), 158.1 (C^4), 152.4 (C^{12}), 144.9 (C^{24}), 136.3 (C^{16}), 134.8 (C^{10}), 133.2 (C^2), 132.0 (q, *J* = 32 Hz, C^{21}), 130.5 (C^7), 129.3 (C^6), 127.8 (C^{15}), 124.2 (C^{11}), 123.7 (q, *J* = 278 Hz, C^{22}), 123.1 (C^{17}), 117.8 (C^1), 117.1 (C^{25}), 116.6 (q, *J* = 4 Hz, C^{23}), 115.0 (C^5), 110.3 (q, *J* = 4 Hz, C^{20}), 70.2 (C^{18}), 68.9 (C^3), 45.7 (C^{26}), 43.7 (C^8), 35.0 (C^{13}), 31.2 (C^{14}).

δ_F (377 MHz, $CDCl_3$): −62.6.

m/z (ES): 527.2519 ($[M+H]^+ C_{30}H_{34}F_3N_2O_2$ requires 527.2516).

Compound 9



To a solution of **7** (230 mg, 0.973 mmol) in dry CH_2Cl_2 (5 mL) was added oxalyl chloride (370 mg, 0.25 mL, 2.919 mmol) and a catalytic amount of DMF. The solution was stirred for 2 hours, then all volatiles removed *in vacuo*. The resulting yellow oil was redissolved in dry CH_2Cl_2 (5 mL), placed under argon, and cooled to 0 °C. A solution of **8** (189 mg, 1.07 mmol) and Et_3N (117 mg, 0.16 mL, 1.16 mmol) in dry CH_2Cl_2 (3 mL) was added dropwise. The reaction was then allowed to warm to room temperature and stirred for a further 2 hours. The reaction mixture was washed with 1M HCl (aq) (2 x 10 mL), $NaHCO_3$ (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 purified by silica gel column chromatography (CH_2Cl_2:CH_3OH 99:1) to afford the *title product* (364 mg, 95% as a 1:1 mixture of rotamers determined by ^1H NMR in $CDCl_3$ at RT) as a yellow oil.

***R_f*:** 0.50 [CH_2Cl_2:CH_3OH 99:1].

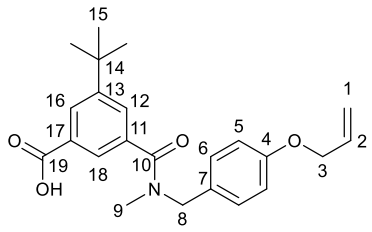
IR ν_{max} (neat): 2952 (C-H), 2864 (C-H), 1720 (C=O), 1628 (C=O).

δ_H (400 MHz, $CDCl_3$): 8.12 (1H, s, H^{16}), 7.99 (0.5H, s, $H^{12\text{ or }18}$), 7.92 (0.5H, s, $H^{12'\text{ or }18'}$), 7.69 (0.5H, s, $H^{12\text{ or }18}$), 7.66 (0.5H, s, $H^{12'\text{ or }18'}$), 7.32 (1H, bd, H^6), 7.08 (1H, bd, $H^{6'}$), 6.93 (2H, bs, H^5), 6.08 (1H, bs, H^2), 5.43 (1H, d, *J* = 17 Hz, H^1), 5.31 (1H, dd, *J* = 11 Hz, 1.5 Hz, $H^{1'}$), 4.71 (1H, s, H^8), 4.56 (2H, s, H^3), 4.43 (1H, s, $H^{8'}$), 3.93 (3H, s, H^{20}), 3.07 (1.5H, s, H^9), 2.87 (1.5H, s, $H^{9'}$), 1.38 (4.5H, s, H^{15}), 1.29 (4.5H, s, $H^{15'}$).

δ_C (100 MHz, $CDCl_3$): 171.7 ($C^{10\text{ or }10'}$), 170.9 ($C^{10\text{ or }10'}$), 166.7 (C^{19}), 158.2 (C^4), 152.1 (C^{13}), 136.2, 133.2 (C^2), 130.1, 129.7 (C^6), 128.7 ($C^{H@7.69\text{ or }H@7.66}$), 128.5 ($C^{H@7.69\text{ or }H@7.66}$), 128.4, 128.0 ($C^{6'}$), 127.8 ($C^{16}$), 125.3 ($C^{H@7.99}$ & $C^{H@7.92}$), 117.8 (C^1), 115.1 ($C^{5\text{ or }5'}$), 115.0 ($C^{5\text{ or }5'}$), 68.9 (C^3), 54.6 ($C^{8'}$), 52.3 (C^{20}), 50.3 (C^8), 36.8 ($C^{9'}$), 35.0 (C^{14}), 33.3 (C^9), 31.2 (C^{15}).

m/z (ES): 418.1993 ($[M+Na]^+$ $C_{24}H_{29}NNaO_4$ requires 418.1989).

Compound 10



To a solution of **9** (1.32 g, 3.33 mmol) in CH_3OH (20 mL) was added a solution KOH (936 mg, 16.6 mmol) in water (2 mL). The reaction was then refluxed with stirring for 3 hours. After cooling to room temperature, the CH_3OH was *in vacuo*. The crude material was redissolved in water (15 mL). The solution was acidified with conc. HCl (aq) and the resulting precipitate was collected by vacuum filtration to afford the *title product* (1.14 g, 90% as a 1:1 mixture of rotamers determined by ^1H NMR in $CDCl_3$ at RT) as an off-white solid.

m.p. 156-158 ^oC.

IR ν_{max} (neat): 2959 (C-H), 2866 (C-H), 1720 (C=O), 1604 (C=O).

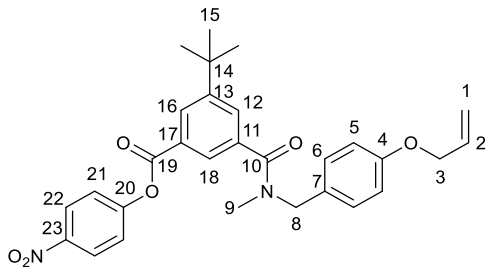
δ_H (400 MHz, $CDCl_3$): 8.19 (1H, s, H^{16}), 8.06 (0.5H, s, $H^{12\text{ or }18}$), 7.99 (0.5H, s, $H^{12'\text{ or }18'}$), 7.76 (0.5H, s, $H^{12\text{ or }18}$), 7.71 (0.5H, s, $H^{12'\text{ or }18'}$), 7.33 (1H, bd, H^6), 7.08 (1H, bd, $H^{6'}$), 6.94 (2H, bs, H^5), 6.08 (1H, bs, H^2), 5.44 (1H, d, J = 17 Hz, H^1), 5.31 (1H, d, J = 11 Hz, $H^{1'}$), 4.73 (1H, s, H^8), 4.57 (2H, s, H^3), 4.44 (1H, s, $H^{8'}$), 3.09 (1.5H, s, H^9), 2.89 (1.5H, s, $H^{9'}$), 1.39 (4.5H, s, H^{15}), 1.30 (4.5H, s, $H^{15'}$).

δ_C (100 MHz, $CDCl_3$): 170.7 (C^{19}), 158.2 (C^4), 152.4 (m, C^{13}), 136.4, 133.2 (m, C^2), 129.7 (b, C^6), 129.4 (b, $C^{H@7.76}$), 129.1 (b, $C^{H@7.71}$), 128.4 (C^{16}), 128.0 ($C^{6'}$), 125.8 ($C^{H@8.06}$ & $C^{H@7.99}$), 117.8 (C^1), 115.2 ($C^{5\text{ or }5'}$), 115.0 ($C^{5\text{ or }5'}$), 68.9 (C^3), 54.7 ($C^{8'}$), 50.4 (C^8), 36.8 ($C^{9'}$), 35.0 (C^{14}), 33.4 (C^9), 31.1 (C^{15}).

Three quaternary resonances (including C^{10}) not observed – attributed to rotamers arising from presence of N-Me group.

m/z (ES): 404.1847 ($[M+Na]^+$ $C_{23}H_{27}NNaO_4$ requires 404.1832).

Half Axle HA-2



To a solution of alkene-carboxylic acid **10** (900 mg, 2.35 mmol) in dry CH_2Cl_2 under argon was added DMAP (115 mg, 0.943 mmol), EDC·HCl (678 mg, 3.53 mmol) and *p*-nitrophenol (492 mg, 3.53 mmol). The reaction was stirred at room temperature for 16 hours. The reaction mixture was then washed with 0.1M HCl (aq) (1 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by silica gel column chromatography (Hexane:EtOAc 3:1) to afford the *title product* (1.01 g, 85% as a 1:1 mixture of rotamers determined by ^{1}H NMR in $CDCl_3$ at RT) as an off-white gel.

***R*$_f$:** 0.35 [EtOAc:Heptane 1:3].

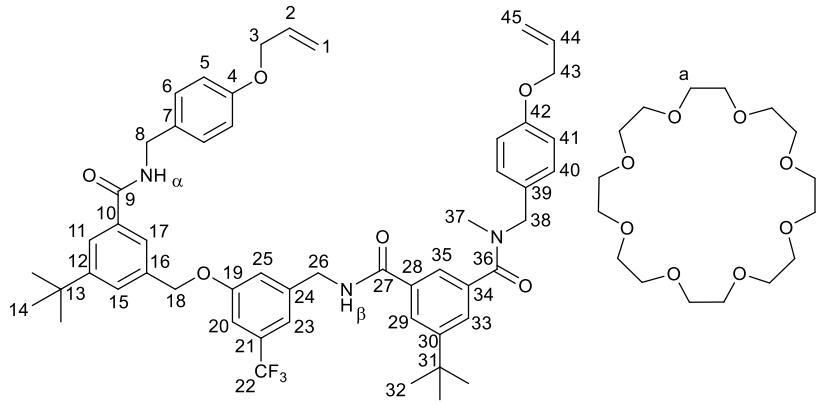
IR ν_{max} (neat): 2961 (C-H), 2862 (C-H), 1740 (C=O), 1630 (C=O).

δ_H (400 MHz, $CDCl_3$): 8.35 (2H, bd, H^{22}), 8.25 (1H, bd, $H^{12\ or\ 18}$), 8.12 (1H, bd, $H^{12\ or\ 18}$), 7.78 (1H, s, H^{16}), 7.49-7.30 (3H, m, H^{21} & H^{6}), 7.11 (1H, bd, $H^{6'}$), 6.94 (2H, bs, H^{5}), 6.07 (1H, bs, H^{2}), 5.43 (1H, d, *J* = 17 Hz, H^{1}), 5.31 (1H, dq, *J* = 11 Hz, 1.5 Hz, $H^{1'}$), 4.73 (1H, s, H^{8}), 4.55 (2H, bs, H^{3}), 4.47 (1H, s, $H^{8'}$), 3.12 (1.5H, s, H^{9}), 2.91 (1.5H, s, $H^{9'}$), 1.42 (4.5H, s, H^{15}), 1.32 (4.5H, s, $H^{15'}$).

δ_C (100 MHz, $CDCl_3$): 171.3 ($C^{10\ or\ 10'}$), 170.5 ($C^{10\ or\ 10'}$), 163.9 (C^{19}), 158.2 (C^{4}), 155.6 (C^{20}), 152.7 (C^{13}), 145.5 (C^{23}), 137.0 (m, $C^{11\ or\ 17}$), 136.7 (m, $C^{11\ or\ 17}$), 133.2 (C^{2}), 129.8 (m, C^{16} & C^{6}), 129.0 (C^{7}), 128.5 (m, $C^{H@8.25}$), 127.8 ($C^{6'}$), 126.0 ($C^{H@8.12}$), 125.3 (C^{22}), 122.6 (m, C^{21}), 117.8 (C^{1}), 115.2 ($C^{5\ or\ 5'}$), 115.0 ($C^{5\ or\ 5'}$), 68.9 (C^{3}), 54.7 ($C^{8'}$), 50.4 (C^{8}), 36.8 ($C^{9'}$), 35.1 (C^{14}), 33.6 (C^{9}), 31.1 (C^{15}).

m/z (ES): 525.2006 ($[M+Na]^+$ $C_{29}H_{30}N_2NaO_6$ requires 525.1996).

[2]Rotaxane R



To a solution of half-axle **HA-1** (448 mg, 0.851 mmol) and 24-crown-8 (**24-c-8**) (300 mg, 0.851 mmol) in dry toluene (1.5 mL) was added Et_3N (852 mg, 1.17 mL, 8.51 mmol) and half-axle **HA-2** (555 mg, 1.10 mmol). The reaction was allowed to stir for 4 days under argon at room temperature. The reaction mixture was then concentrated *in vacuo* to afford a yellow gel. The crude material was purified by silica gel column chromatography (CH_2Cl_2:CH_3OH 99:1-98:2) to afford the *title product* (528 mg, 50% as a ~ 1.3:1 mixture of rotamers by ^1H NMR in $CDCl_3$ at RT) as a foaming colourless solid.

***R_f*:** 0.24 [CH_2Cl_2:CH_3OH 99:1].

m.p. 240-242 °C.

IR ν_{max} (neat): 3362 (N-H), 2950 (C-H), 2871 (C-H), 1634 (3 x C=O).

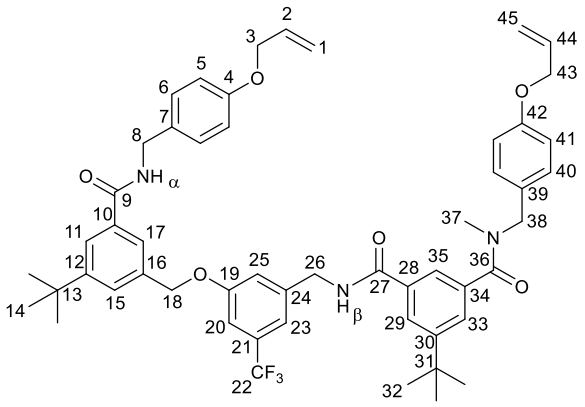
δ_H (400 MHz, $CDCl_3$): 8.05-7.88 (5H, m H^{29}, H^{23}, H^{β}, H^{25} & H^{35}), 7.86 (1H, t, *J* = 1.6 Hz, H^{11}), 7.62 (1H, s, H^{17}), 7.60 (1H, s, H^{15}), 7.49 (1H, bs, H^{33}), 7.30-7.27 (3H, m, H^6 & H^{40}), 7.15 (1H, s, H^{20}), 7.02 (1H, bs, $H^{40'}$), 6.90 (2H, d, *J* = 8.6 Hz, H^5), 6.86 (2H, d, *J* = 8.6 Hz, H^{41}), 6.70 (1H, t, *J* = 5.4 Hz, H^{α}), 6.10-6.01 (2H, m, H^2 & H^{44}), 5.44-5.39 (2H, m, H^1 & H^{45}), 5.32-5.28 (2H, m, $H^{1'}$ & $H^{45'}$), 5.20 (2H, s, H^{18}), 4.89 (2H, s, H^{26}), 4.66 (1.1H, s, $H^{38\ major}$), 4.59 (2H, d, *J* = 5.4 Hz, H^8), 4.55-4.52 (4H, m, H^3 & H^{43}), 4.38 (0.9H, s, $H^{38\ minor}$), 3.39 (16H, bs, H^a), 3.17 (16H, bs, $H^{a'}$), 2.99 (1.3H, s, $H^{37\ minor}$), 2.80 (1.7H, s, $H^{37\ major}$), 1.36-1.27 (18H, m, H^{14} & H^{32}).

δ_C (100 MHz, $CDCl_3$): 171.6 (C^{36}), 167.6 (C^9), 167.1 (C^{27}), 158.1 (C^4), 158.0 (C^{42}), 157.4 (C^{19}), 152.1 (C^{12} & C^{30}), 141.3 (C^{24}), 137.7 (C^{16}), 136.0 (q, *J* = 27 Hz, C^{21}), 134.6, 133.2 (C^2 & C^{44}), 130.6 (C^7), 129.7 (C^{40}), 129.3 (C^6), 128.1 ($C^{40'}$), 127.3 (C^{15}), 126.3 (C^{29}), 125.7 (C^{33}), 124.5 (q, *J* = 271 Hz, C^{22}), 124.0 (C^{11}), 123.6 (C^{23}), 122.8 (C^{17}), 122.0 (C^{25}), 117.8 (C^1 & C^{45}), 115.0 (C^5), 114.8 (C^{41}), 111.4 (C^{20}), 70.3 (C^a), 70.0 (C^{18}), 68.9 (C^3 & C^{43}), 54.6 ($C^{38\ minor}$), 50.2 ($C^{38\ major}$), 45.3 (C^{26}), 43.6 (C^8), 36.7 ($C^{37\ major}$), 35.0 (C^{31}), 34.9 (C^{13}), 32.9 ($C^{37\ minor}$), 31.3 (C^{14} & C^{32}).

δ_F (377 MHz, $CDCl_3$): −62.6.

m/z (ES): 1264.6311 ($[M+Na]^+$ $C_{69}H_{90}F_3N_3NaO_{14}$ requires 1264.6267).

Axle Ax



Axle **Ax** was isolated from the reaction that formed rotaxane **R** upon purification of the crude reaction mixture by silica gel column chromatography as a colourless solid (197 mg, 26% as a 1:1 mixture of rotamers by ^{1}H NMR in $CDCl_3$ at RT).

***R_f*:** 0.68 [CH_2Cl_2:CH_3OH 99:1].

m.p. 221-224 °C.

IR ν_{max} (neat): 3296 (N-H), 2957 (C-H), 1634 (3 x C=O).

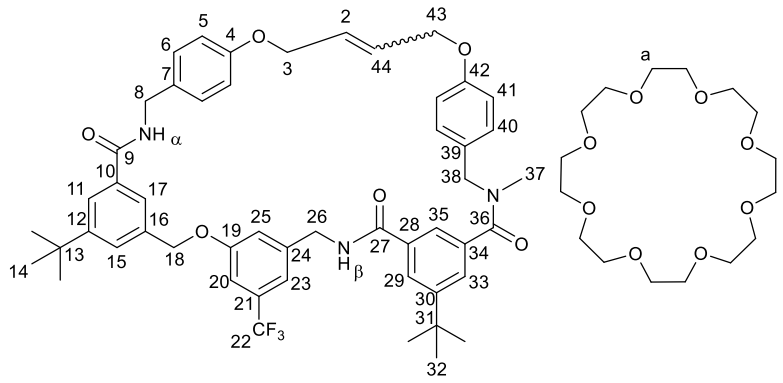
δ_H (400 MHz, $CDCl_3$): 7.94 (1H, t, *J* = 1.6 Hz, H^{29}), 7.87 (1H, s, H^{11}), 7.64 (1H, s, H^{35}), 7.62 (1H, s, H^{17}), 7.56 (2H, bs, H^{15} & H^{33}), 7.30-7.28 (3H, m, H^6 & H^{40}), 7.20-7.12 (4H, m, $H^{20, 23 \& 25}$ & H^{β}), 7.06-7.05 (1H, m, $H^{40'}$), 6.89-6.87 (5H, m, H^{41}, H^5 & H^{α}), 6.10-6.00 (2H, m, H^2 & H^{44}), 5.44-5.39 (2H, m, H^1 & H^{45}), 5.31-5.28 (2H, m, $H^{1'}$ & $H^{45'}$), 5.02 (2H, s, H^{18}), 4.67 (1H, s, H^{38}), 4.59-4.57 (4H, m, H^{26} & H^8), 4.53-4.52 (4H, m, H^3 & H^{43}), 4.40 (1H, s, $H^{38'}$), 3.06 (1.5H, s, H^{37}), 2.83 (1.5H, s, $H^{37'}$), 1.34 (9H, s, H^{14}), 1.32 (4.5H, s H^{32}), 1.21 (4.5H, s, $H^{32'}$).

δ_C (100 MHz, $CDCl_3$): 171.8 ($C^{36 \text{ or } 36'}$), 171.0 ($C^{36 \text{ or } 36'}$), 167.5 (C^9), 167.2 (C^{27}), 159.1 (C^{19}), 158.2 ($C^{4 \text{ or } 42}$), 158.1 ($C^{4 \text{ or } 42}$), 152.4 (C^{12} & C^{30}), 141.1, 136.0 (C^{16}), 134.8, 134.2, 133.2 (C^2 & C^{44}), 133.0, 132.1 (q, *J* = 32 Hz, C^{21}), 130.7 (C^7), 129.7, 129.3 (C^6), 127.9 (C^{15}), 127.7 (C^{40} & $C^{40'}$), 127.1 (m, C^{33}), 126.0 (m, C^{29}), 124.5 (C^{11}), 123.8 (q, *J* = 271 Hz, C^{22}), 123.3 (C^{17}), 122.4 (m, C^{35}), 117.8 ($C^{20 \text{ or } 23 \text{ or } 25}$), 117.7 ($C^1$ & C^{45}), 117.1 ($C^{20 \text{ or } 23 \text{ or } 25}$), 115.2 ($C^{41}$), 114.9 ($C^5$), 111.1 ($C^{20 \text{ or } 23 \text{ or } 25}$), 70.3 ($C^{18}$), 68.9 ($C^3$ & C^{43}), 54.7 ($C^{38'}$), 50.4 (C^{38}), 43.7 ($C^{26 \text{ or } 8}$), 43.6 ($C^{8 \text{ or } 26}$), 36.8 ($C^{37'}$), 35.0 (C^{31}), 34.9 (C^{13}), 33.6 (C^{37}), 31.3 (C^{14}), 31.0 (m, C^{32}).

δ_F (377 MHz, $CDCl_3$): –62.5.

m/z (ES): 912.4201 ($[M+Na]^+$ $C_{53}H_{58}F_3N_3NaO_6$ requires 912.4170).

[2]Catenane C



SRB Synthesis: A flask containing rotaxane **R** (150 mg, 0.120 mmol) in dry CH_2Cl_2 (100 mL) was placed under nitrogen and degassed for 30 minutes. Grubbs I catalyst (19.8 mg, 0.024 mmol) was added, and the reaction stirred for 16 hours at room temperature under dark conditions. The reaction mixture was then concentrated *in vacuo* to afford a brown oil. The crude material was purified by silica gel column chromatography (CH_2Cl_2:CH_3OH 98.5:1.5-96:4) to afford two fractions containing predominantly *title product* (one fraction > 99:1 **C**:**R**), as a 2:1 mixture of rotamers and 1:1 of olefin isomers, as a foaming off-white solid.

NHE Synthesis: A flask containing rotaxane **R** (50 mg, 0.040 mmol) in dry CH_2Cl_2 (33 mL) was placed under nitrogen and degassed for 30 minutes. Grubbs' I catalyst (6.6 mg, 0.008 mmol) was added, and the reaction stirred for 16 hours at room temperature under dark conditions. The reaction mixture was then concentrated *in vacuo* to afford a brown oil. The crude material was purified by silica gel column chromatography (CH_2Cl_2:EtOAc:CH_3OH 90:8:2-90:6:4) then silica prep TLC (CH_2Cl_2:CH_3OH 98:2 then EtOAc) to afford pure *title product* (42 mg, 86%).

*NB: Based on earlier work by SRB, we believe it is entirely possible to use the simpler CH_2Cl_2 / CH_3OH solvent mixture as eluent for the preliminary column (to remove decomposed Grubbs I catalyst), prior to successfully separating the small amounts of [2]rotaxane **R** from [2]catenane **C** using prep TLC as described above.*

***R_f*:** 0.38 [CH_2Cl_2:CH_3OH 99:1].

m.p. 251-253 °C.

IR ν_{max} (neat): 2871 (C-H), 1632 (3 x C=O).

For simplicity, only major rotamer peaks recorded for ^1H and ^{13}C NMR (apart for 37 and a').

δ_H (400 MHz, $CDCl_3$): 8.10 (1H, s, H^{29}), 8.07 (1H, s, H^{23}), 8.02 (1H, s, H^{11}), 7.97 (1H, s, H^{β}), 7.92 (1H, s, H^{25}) 7.89 (1H, s, H^{35}), 7.61-7.45 (3H, m, H^{17}, H^{15} & H^{33}), 7.32 (2H, d, *J* = 8.3 Hz, H^6), 7.24 (2H, d, *J* = 8.3 Hz, H^{40}), 7.14 (1H, s, H^{20}), 6.92 (2H, d, *J* = 8.3 Hz, H^5), 6.76 (2H, d, *J* = 8.3 Hz, H^{41}), 6.60 (1H, bs, H^{α}), 6.00-5.95 (2H, m, H^2 & H^{44}), 5.10 (2H, s, H^{18}), 4.84-4.44 (10H, m, H^{26}, $H^{3 \text{ or } 43}$, H^{38}, H^8, $H^{3 \text{ or } 43}$), 3.37 (16H, bs, H^a), 3.18 (16H, s, $H^{a' \text{ major}}$), 3.07 (16H, m, $H^{a' \text{ minor}}$) 2.99 (1H, s, $H^{37 \text{ minor}}$) 2.79 (2H, s, $H^{37 \text{ major}}$), 1.34 (18H, app s, H^{14} & H^{32}).

δ_C (100 MHz, $CDCl_3$): 171.6 (C^{36}), 167.4 (C^{9}), 167.0 (C^{27}), 157.8 (C^{42}), 157.6 (C^{4}), 157.3 (C^{19}), 152.3 ($C^{12\ or\ 30}$), 151.5 ($C^{12\ or\ 30}$), 141.3 (C^{24}), 137.2 (C^{16}), 136.0, 135.8, 134.5, 130.5, 129.8 (C^{40}), 129.7 (C^{6}), 129.5, 128.3 (C^{2} & C^{44}), 128.0, 127.8 ($C^{15\ or\ 33}$), 126.4 (C^{29}), 125.6 ($C^{15\ or\ 33}$), 125.0 (C^{11}), 124.6 (q, *J* = 271 Hz, C^{22}), 123.7 (m, C^{23}), 123.3 (C^{35}), 122.1 (C^{17}), 121.7 (C^{25}), 115.2 (C^{5}), 114.4 (C^{41}), 111.5 (m, C^{20}), 70.3 ($C^{a(')\ major}$ & C^{18}), 70.1 ($C^{a(')\ minor}$), 67.6 ($C^{3\ or\ 43}$), 67.3 ($C^{3\ or\ 43}$), 50.2 (C^{38}), 45.3 (C^{26}), 43.6 (C^{8}), 36.9 ($C^{37\ major}$), 35.0 ($C^{13\ or\ 31}$), 34.9 ($C^{13\ or\ 31}$), 33.0 ($C^{37\ minor}$), 31.3 (C^{14} & C^{32}).

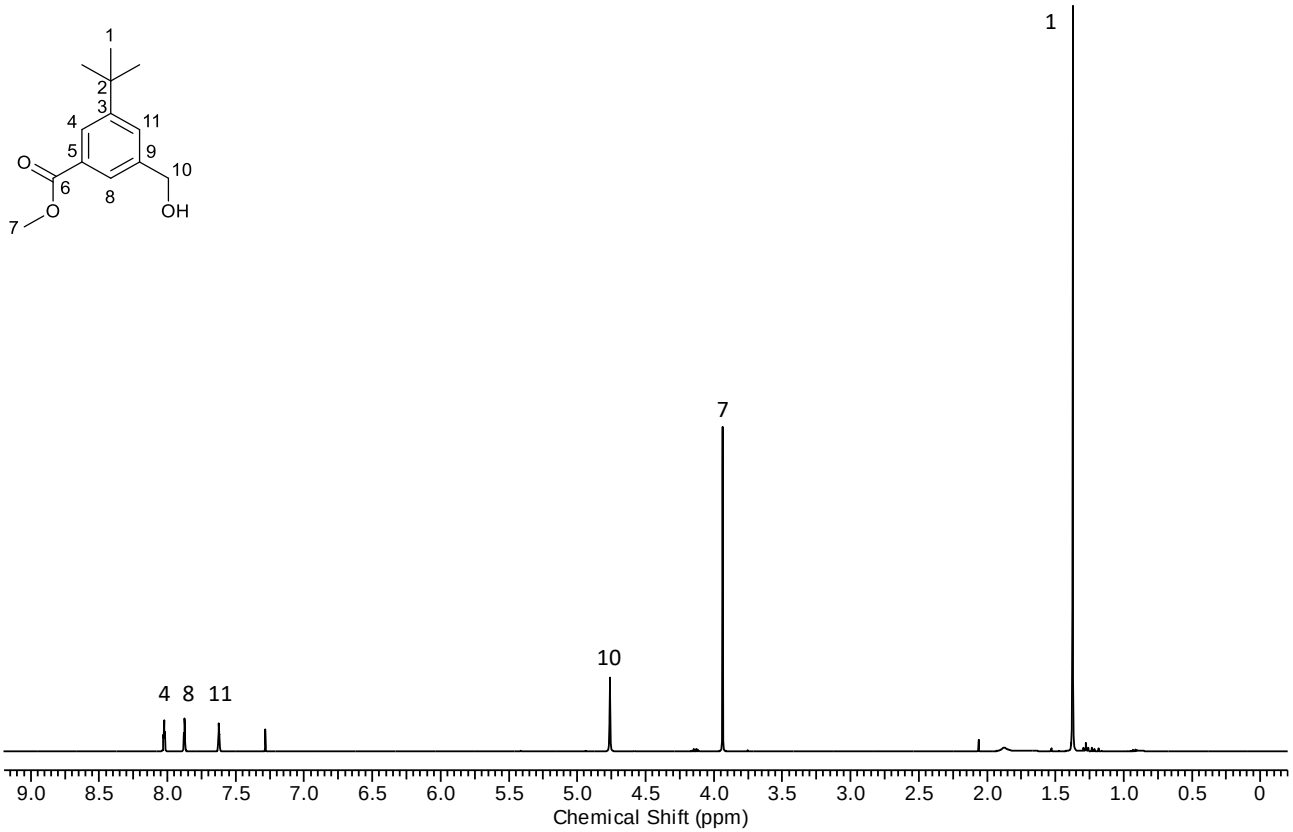
δ_F (377 MHz, $CDCl_3$): –62.2 (singlet, major), –62.3 (singlet, minor).

m/z (ES): 1236.5997 ($[M+Na]^+$ $C_{67}H_{86}F_3N_3NaO_{14}$ requires 1236.5954).

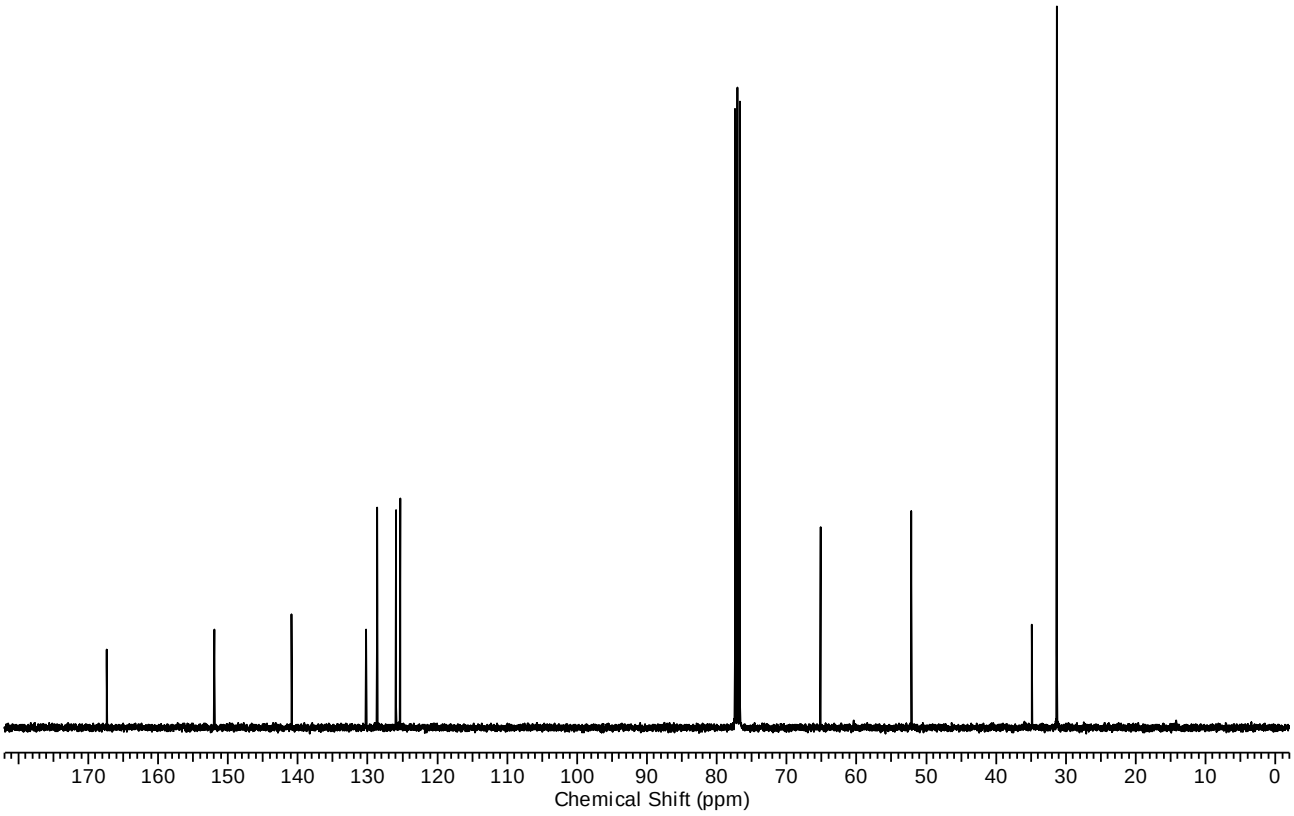
Part 2b: Spectral data for main article

Compound 1

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

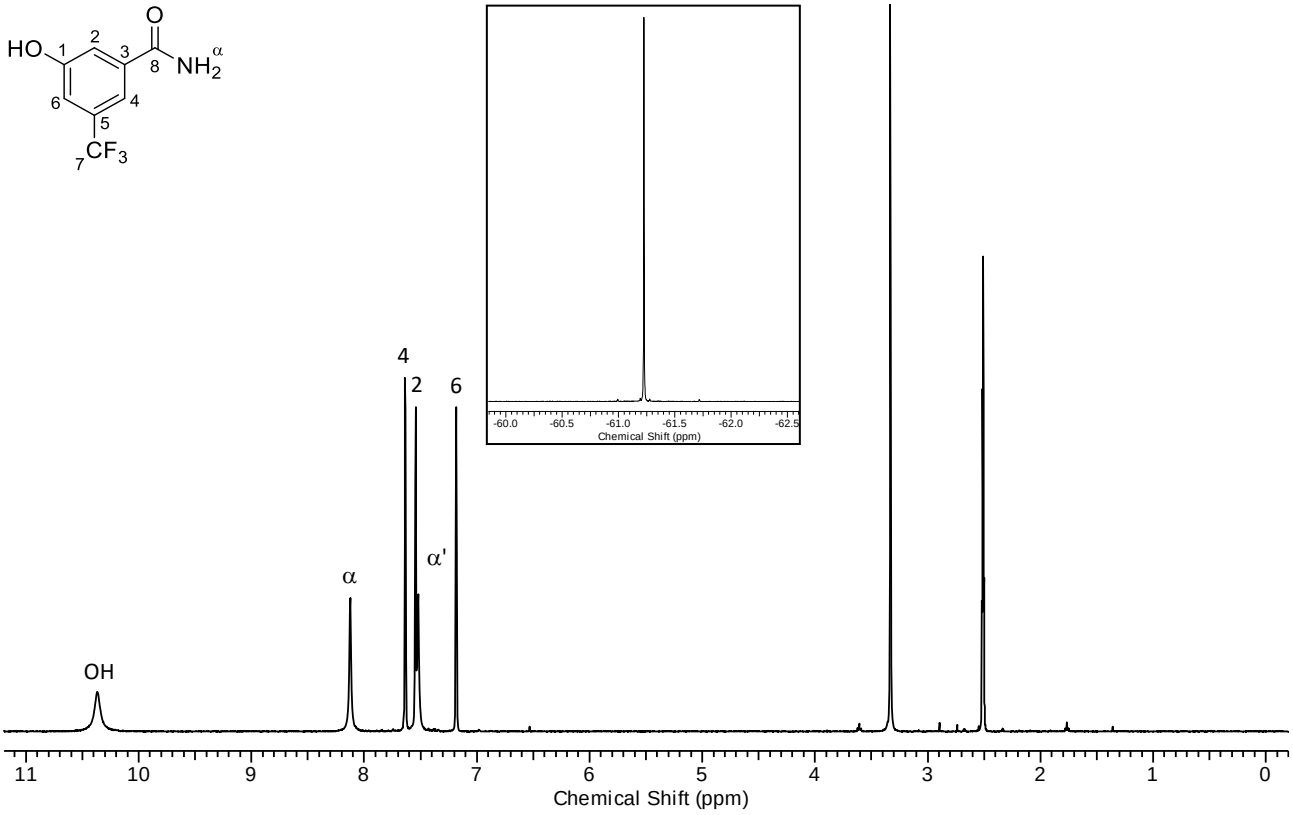


^{13}C NMR ($CDCl_3$, 100 MHz)

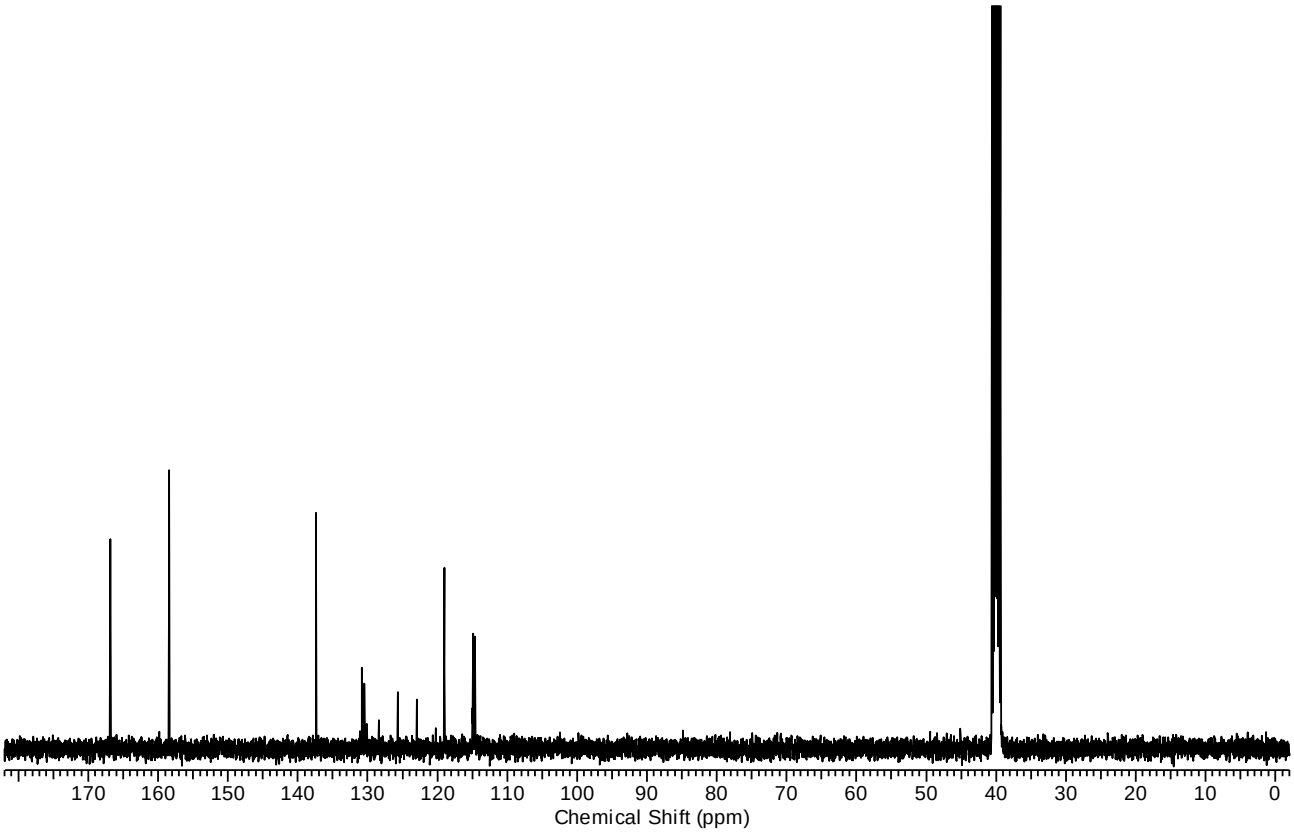


Compound ESI-1

^{1}H NMR (d_6-DMSO, 400 MHz) *Inset:* ^{19}F NMR (d_6-DMSO, 377 MHz)

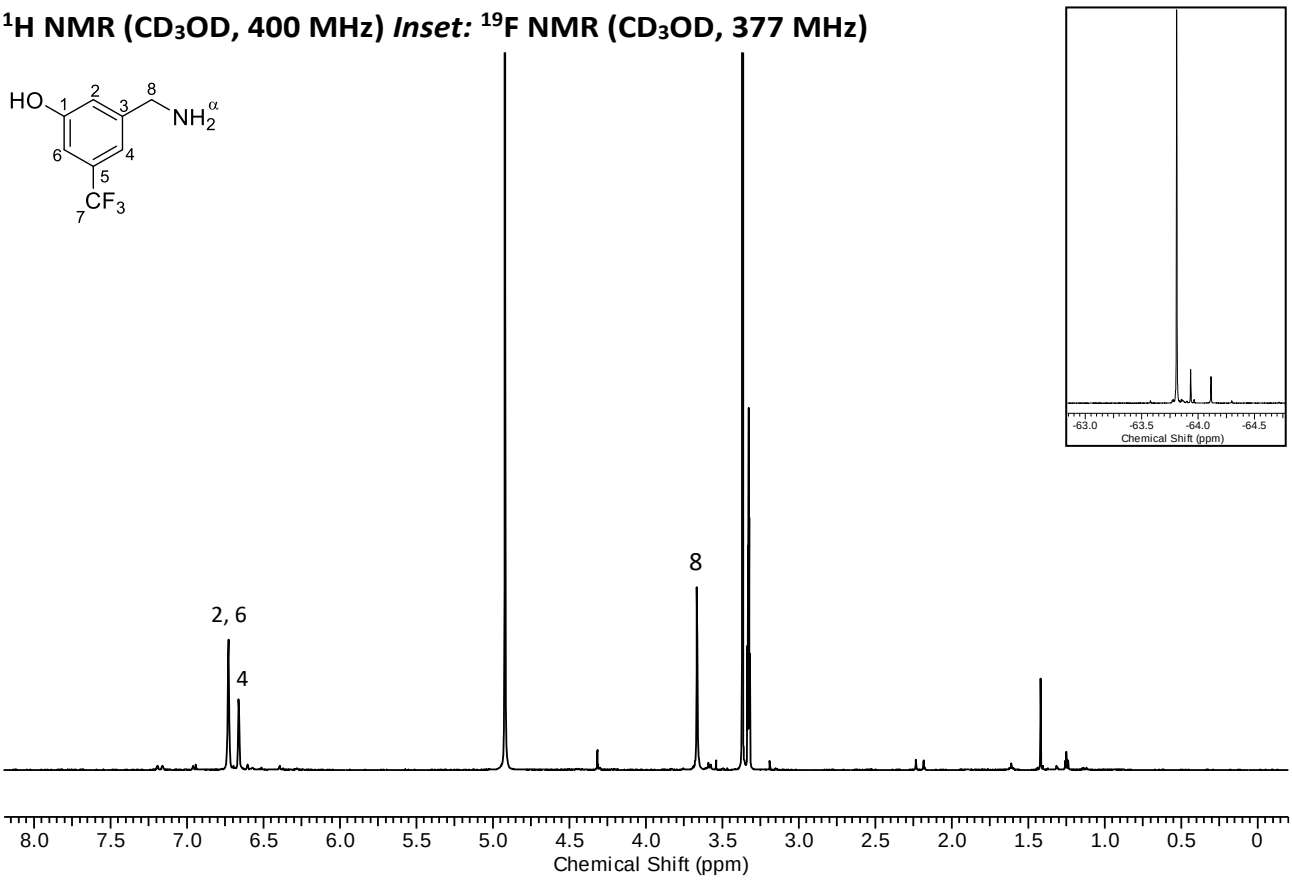


^{13}C NMR (d_6-DMSO, 100 MHz)

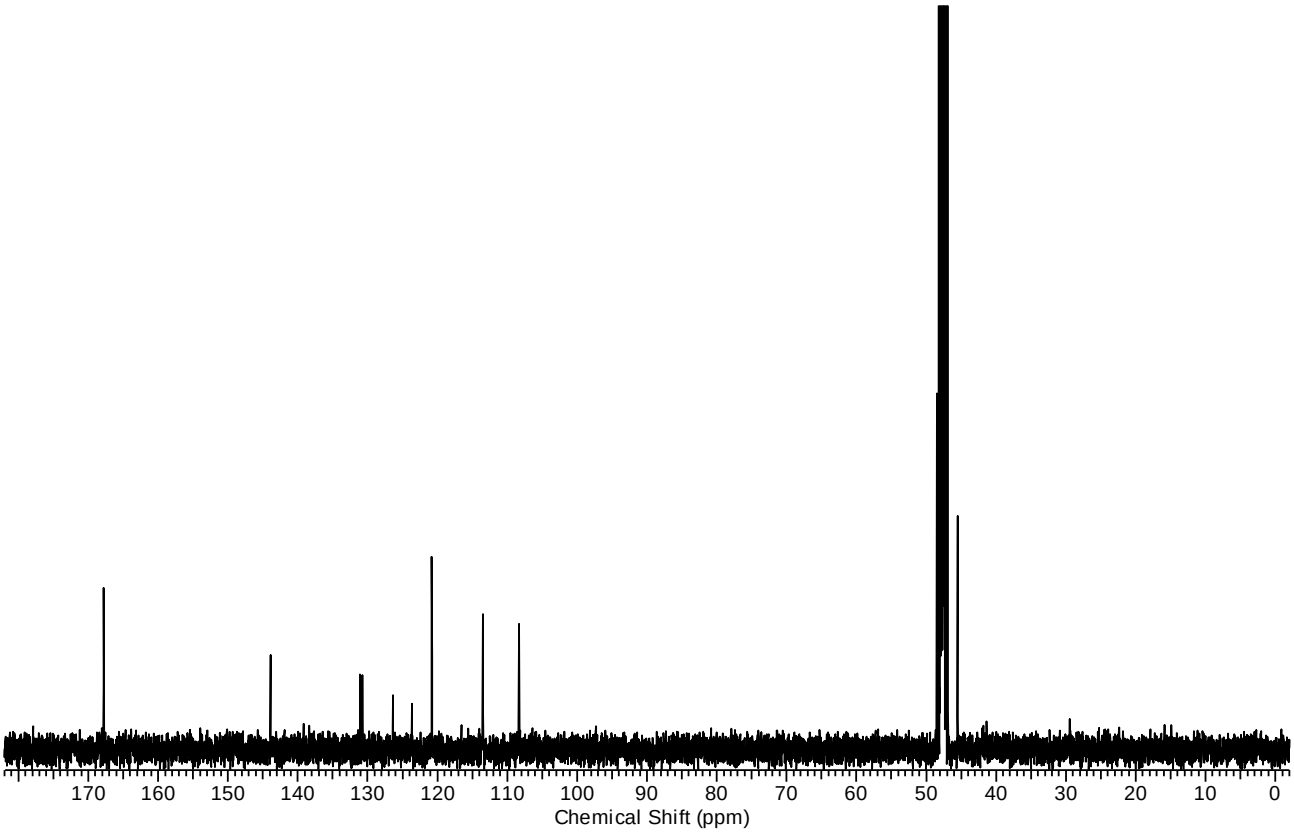


Compound ESI-2

^{1}H NMR (CD_3OD, 400 MHz) *Inset:* ^{19}F NMR (CD_3OD, 377 MHz)

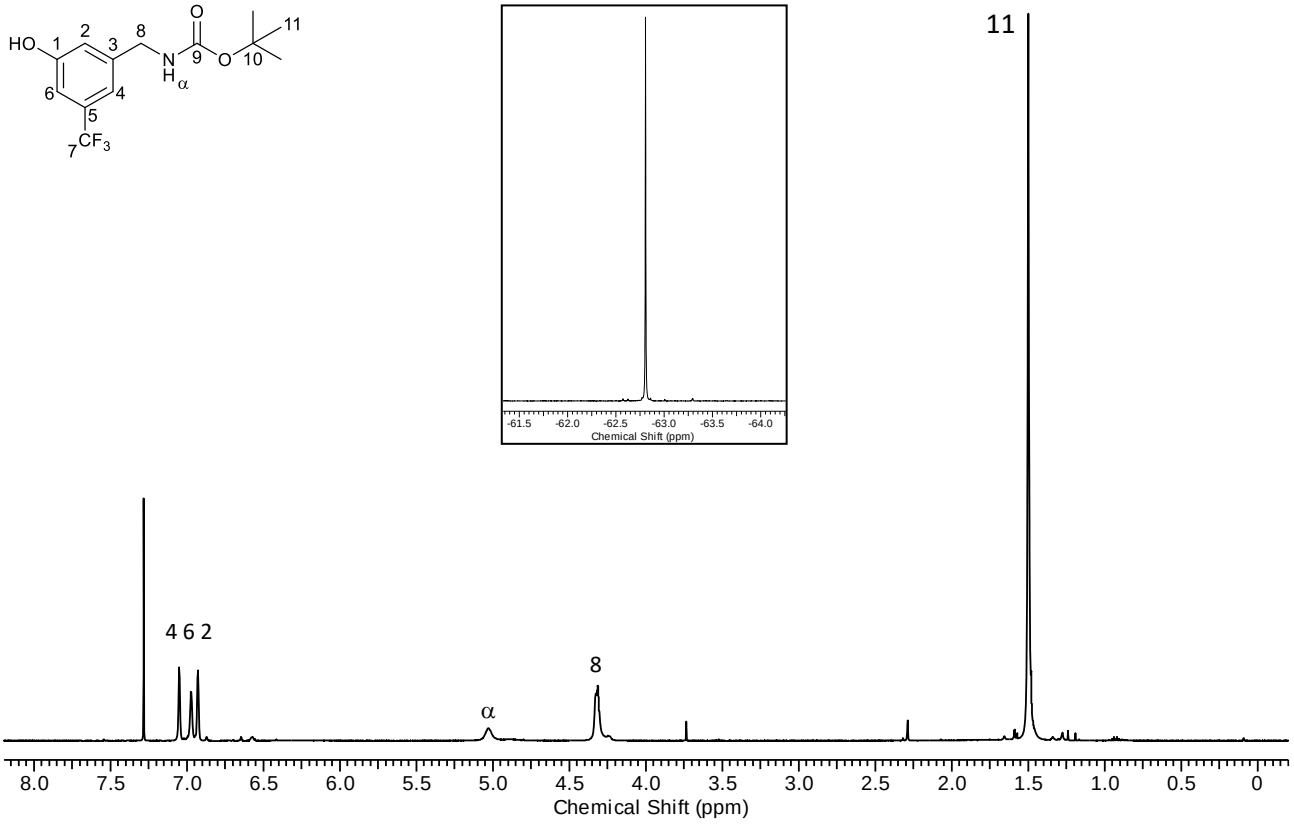


^{13}C NMR (CD_3OD, 100 MHz)

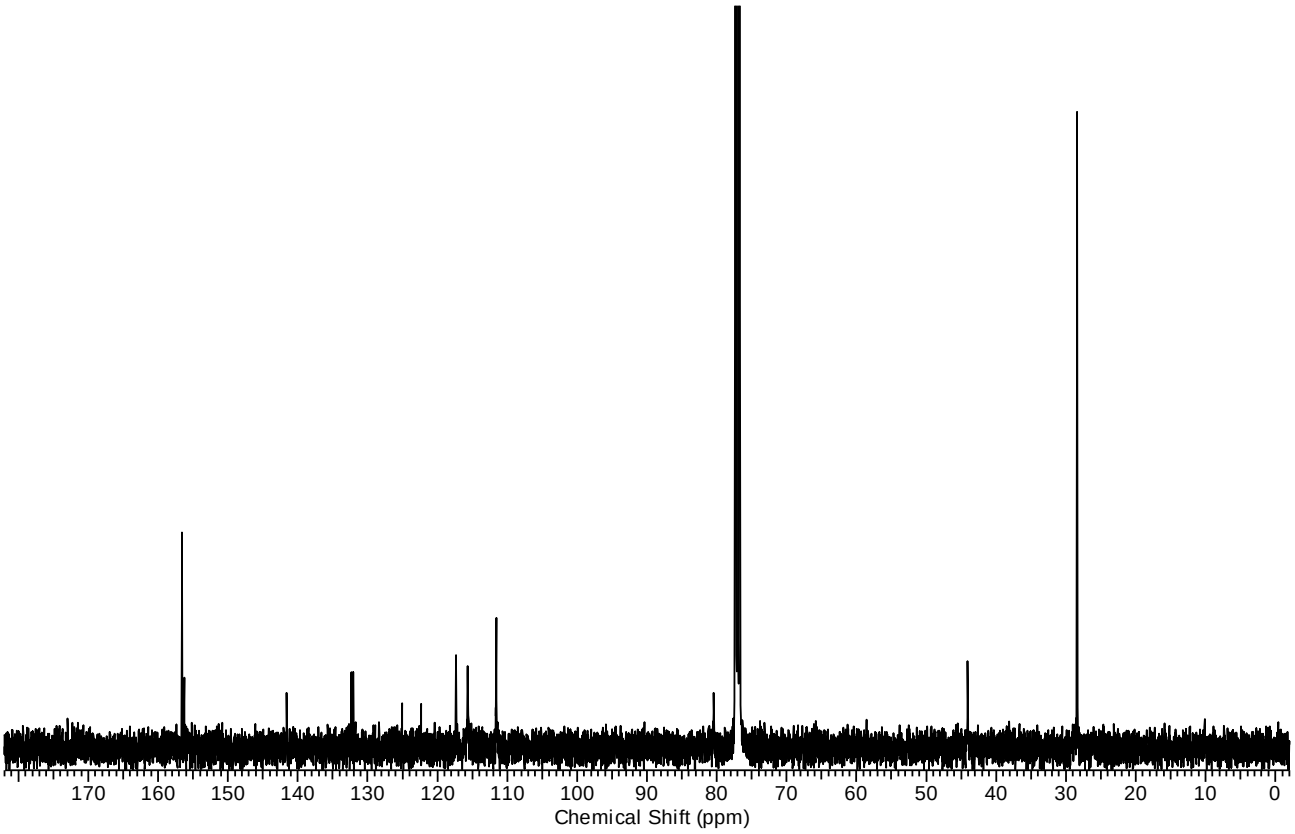


Compound 2

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

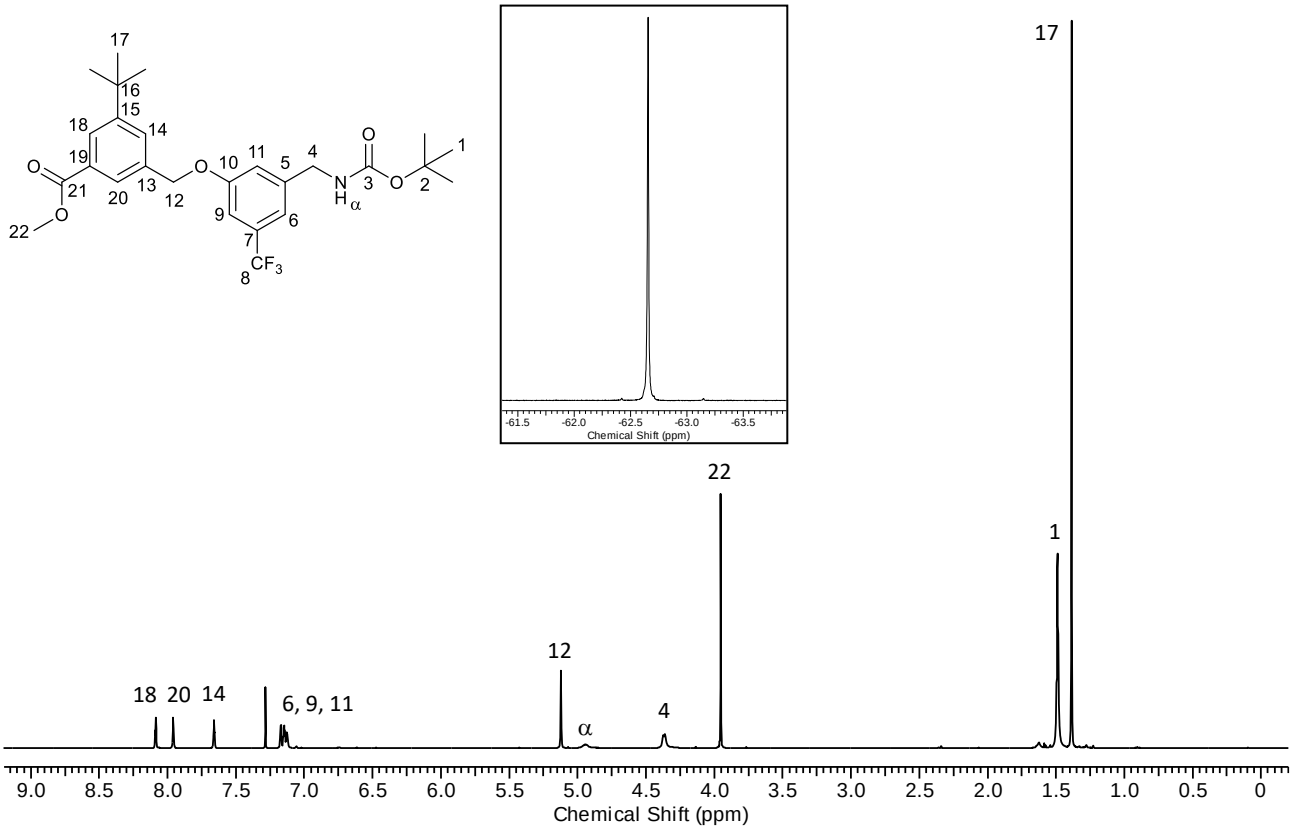


^{13}C NMR ($CDCl_3$, 100 MHz)

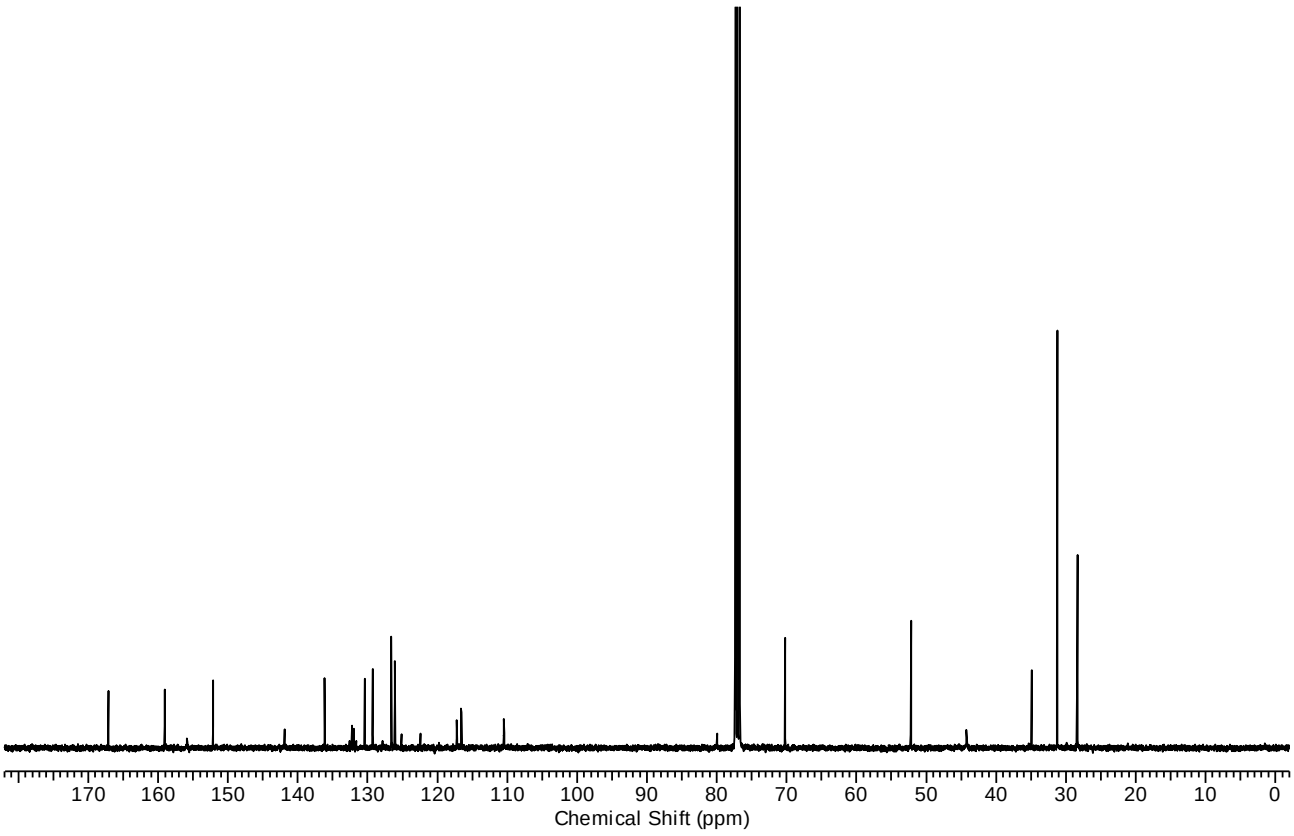


Compound 3

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

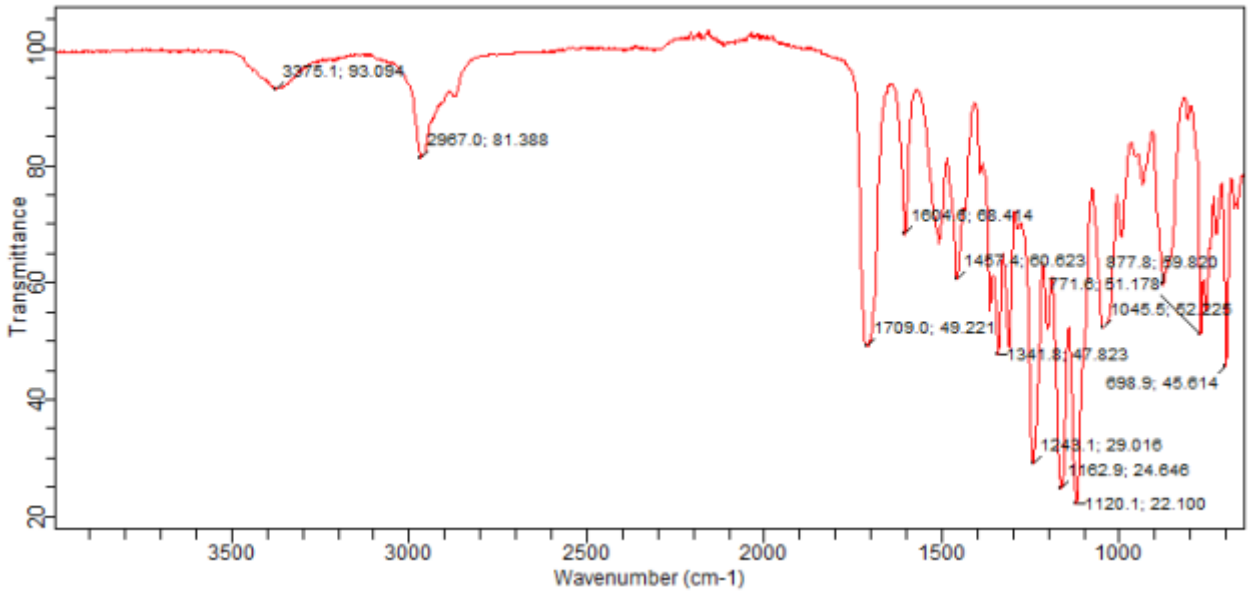


^{13}C NMR ($CDCl_3$, 100 MHz)

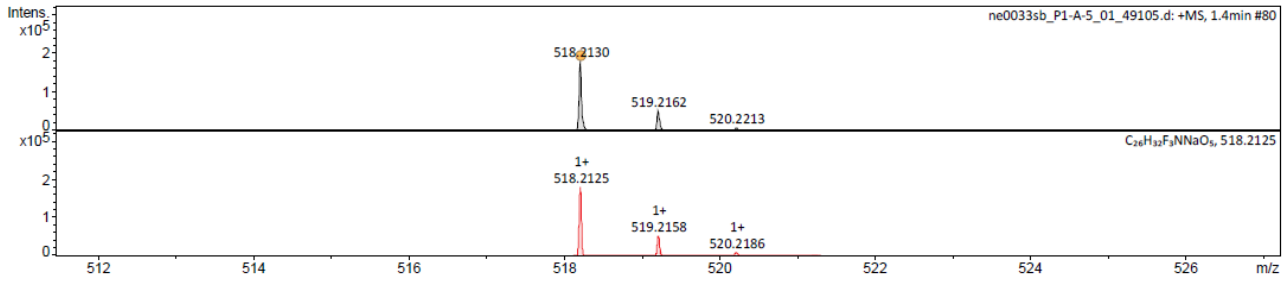


Compound 3

IR (neat)



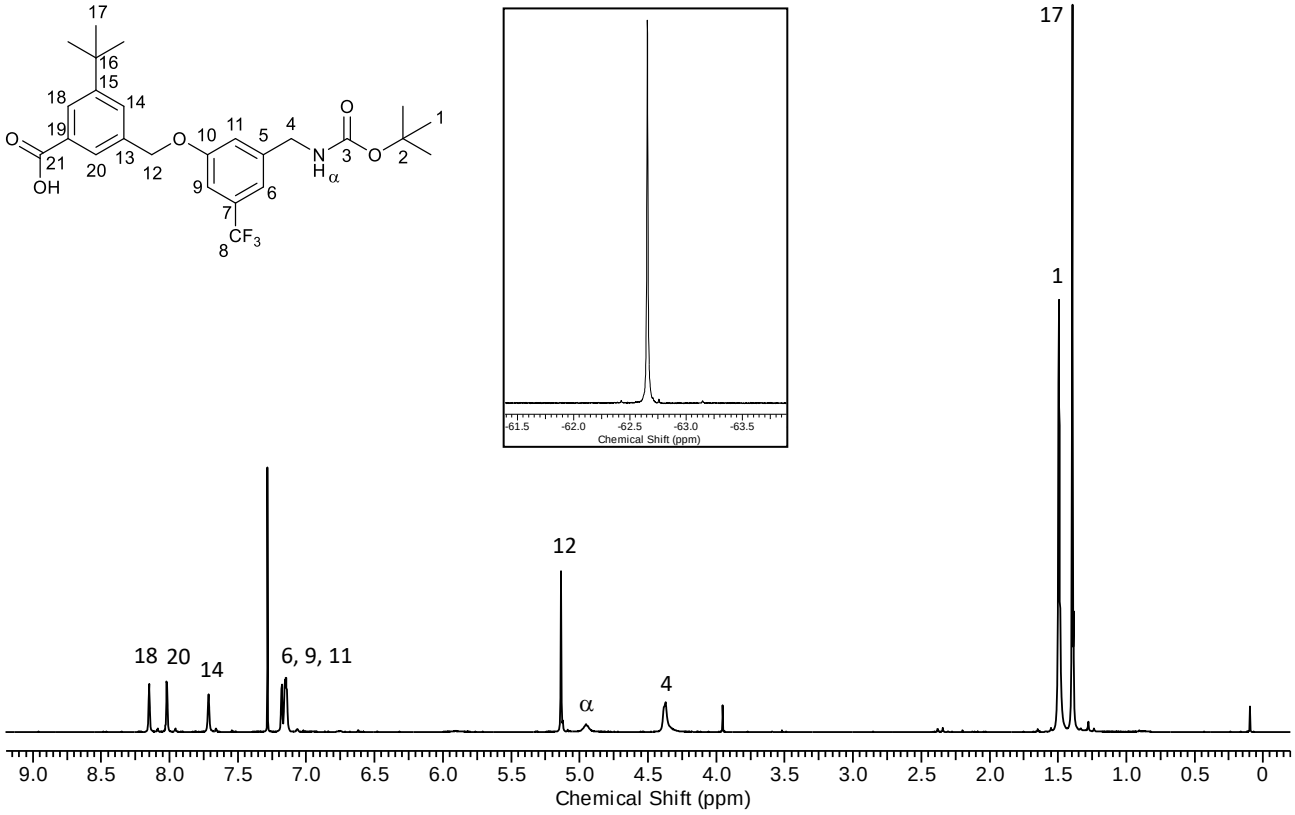
MS (ES +ve)



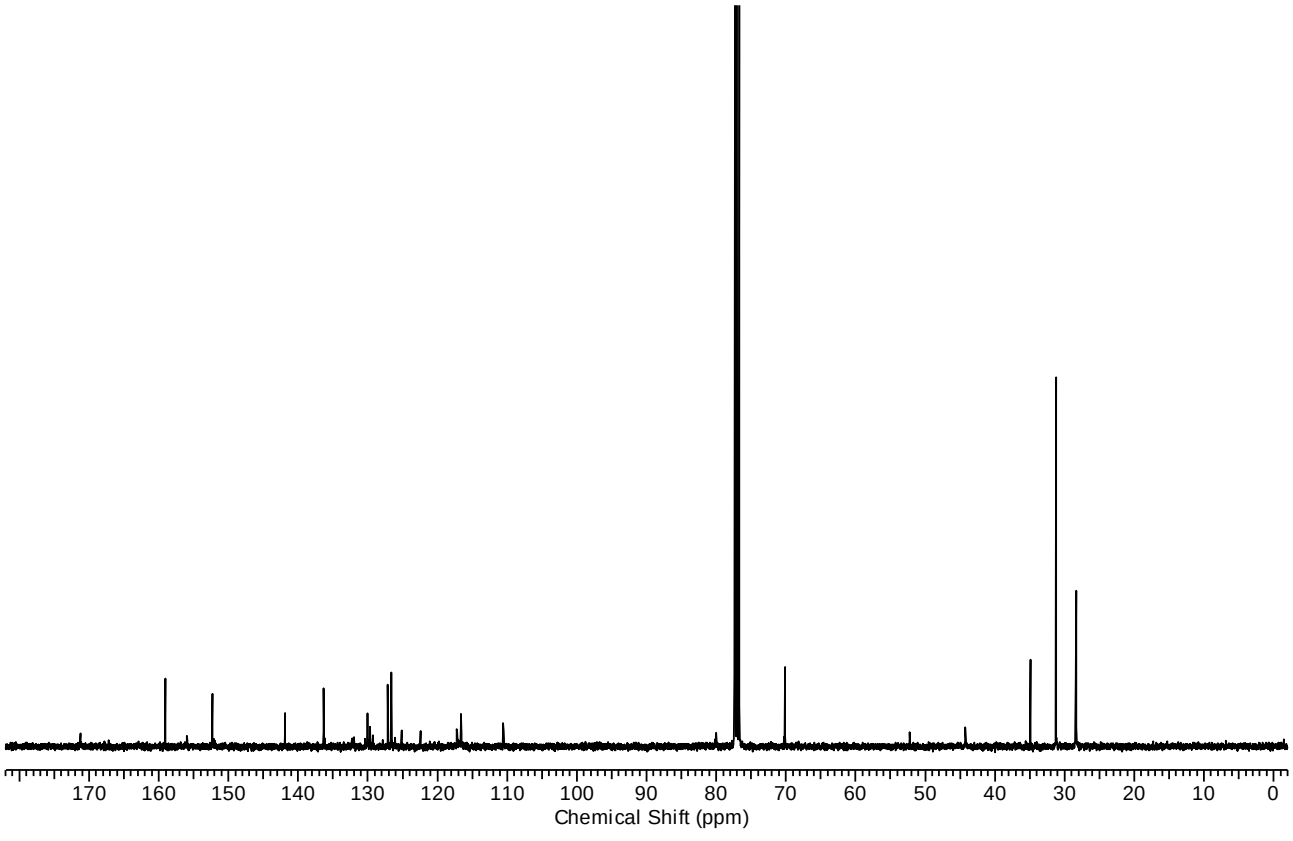
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
518.2130	1	C26H32F3NNaO5	518.2125	-1.0	-0.5	4.9	-1.8

Compound 4

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

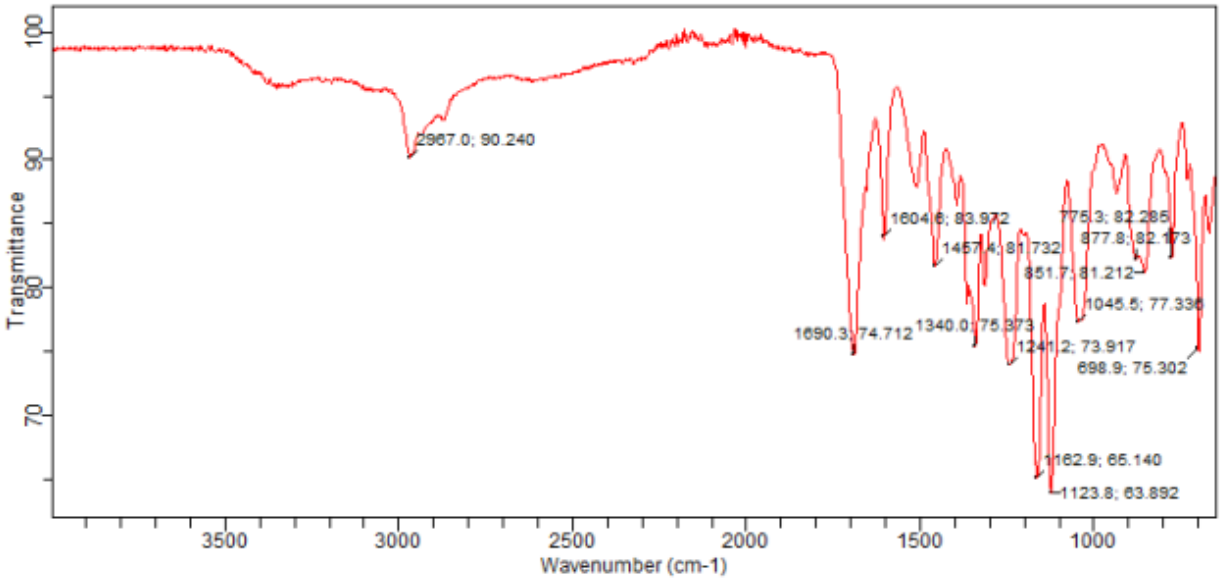


^{13}C NMR ($CDCl_3$, 100 MHz)

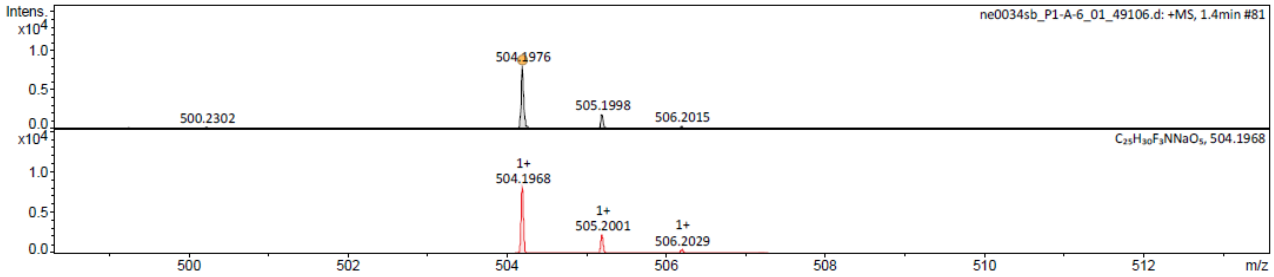


Compound 4

IR (neat)



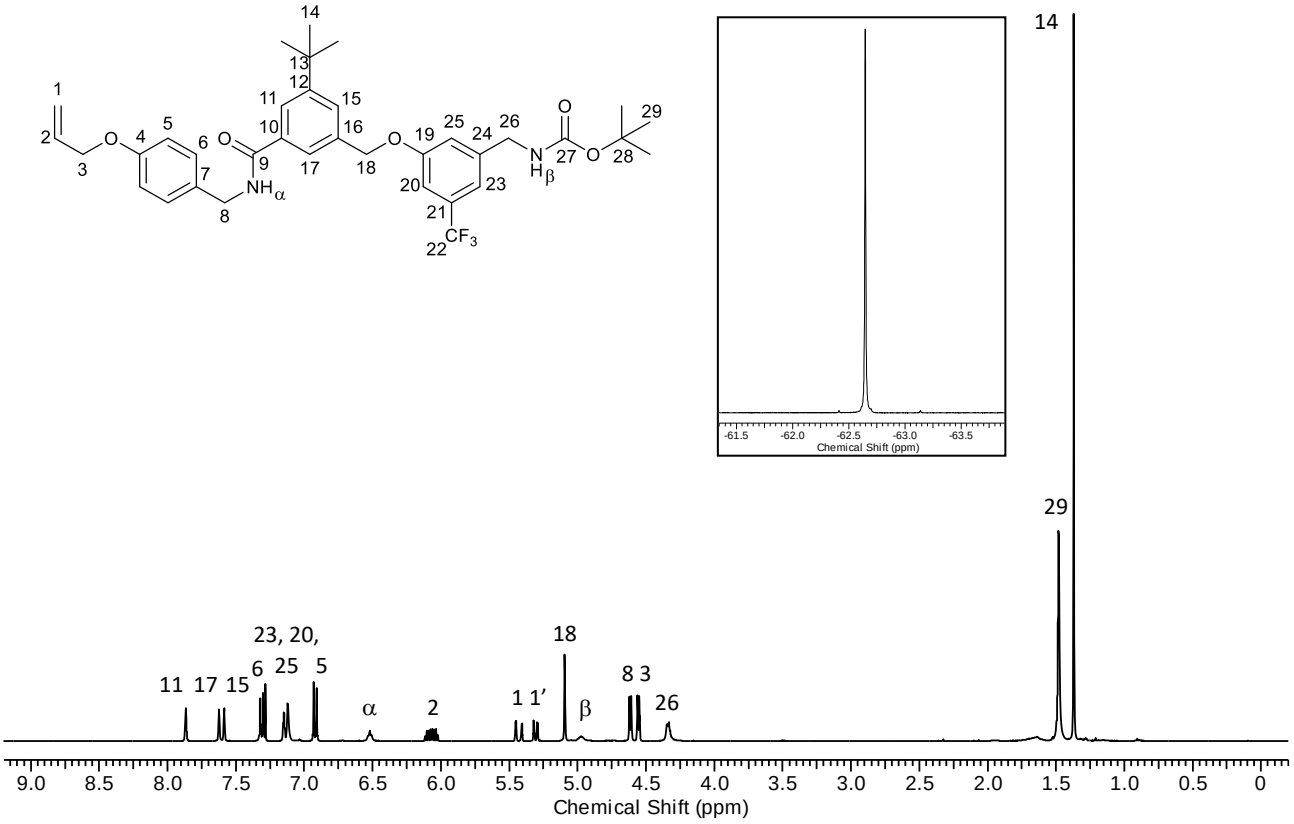
MS (ES +ve)



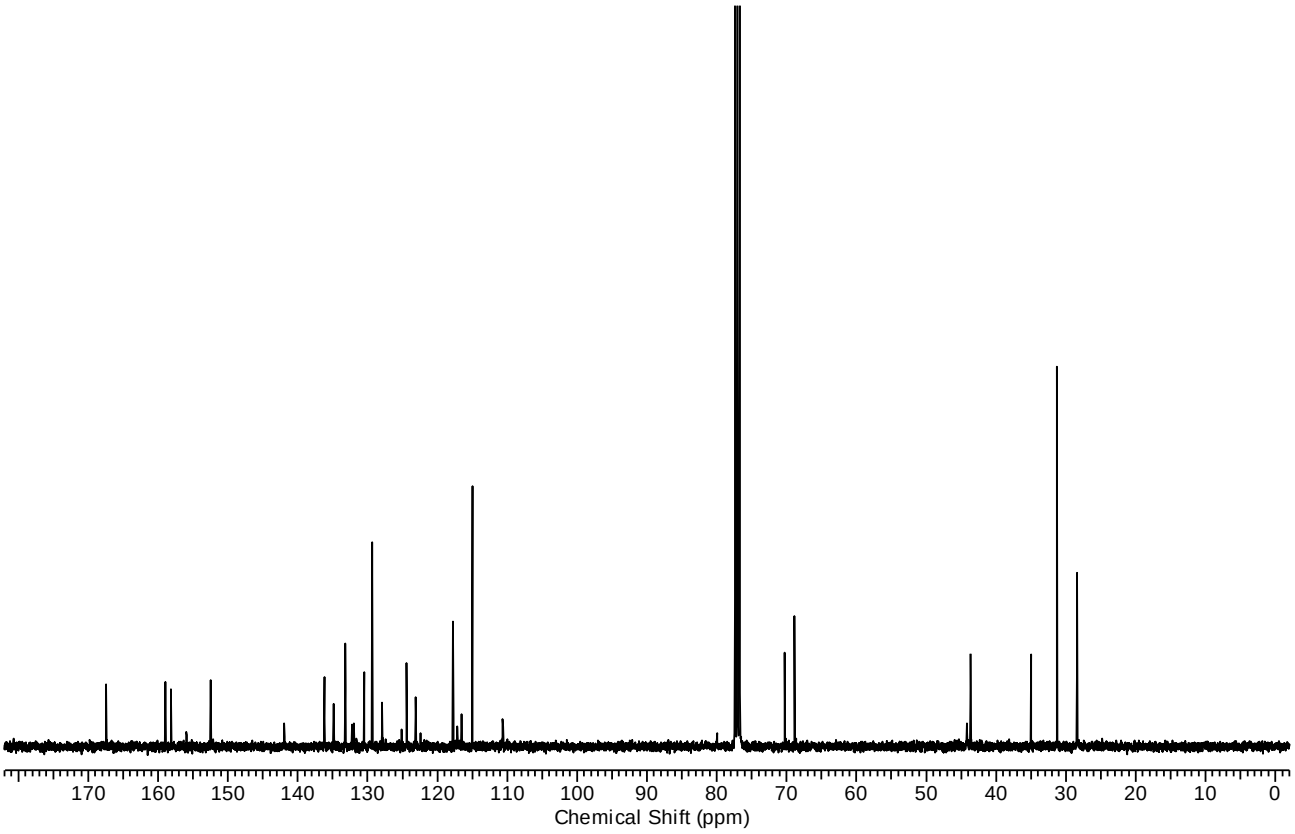
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
504.1976	1	C25H30F3NNaO5	504.1968	-1.5	-0.8	23.7	-0.0

Compound 6

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

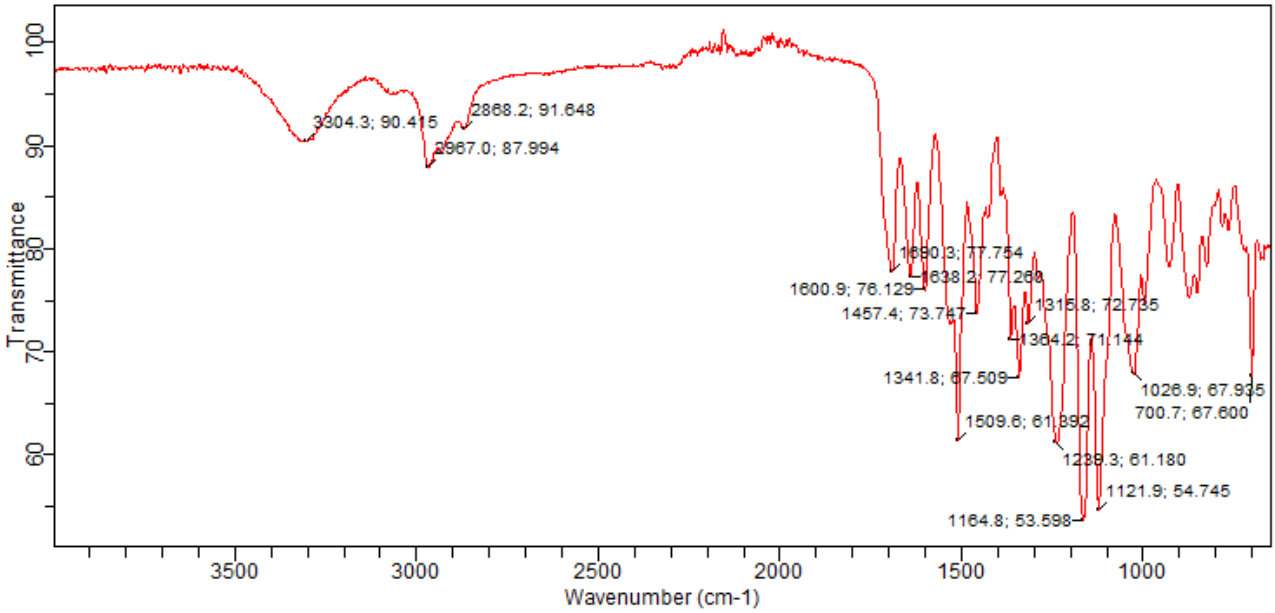


^{13}C NMR ($CDCl_3$, 100 MHz)

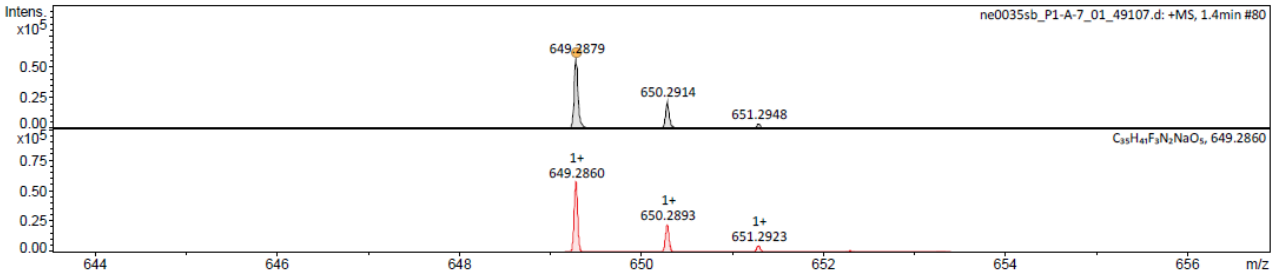


Compound 6

IR (neat)



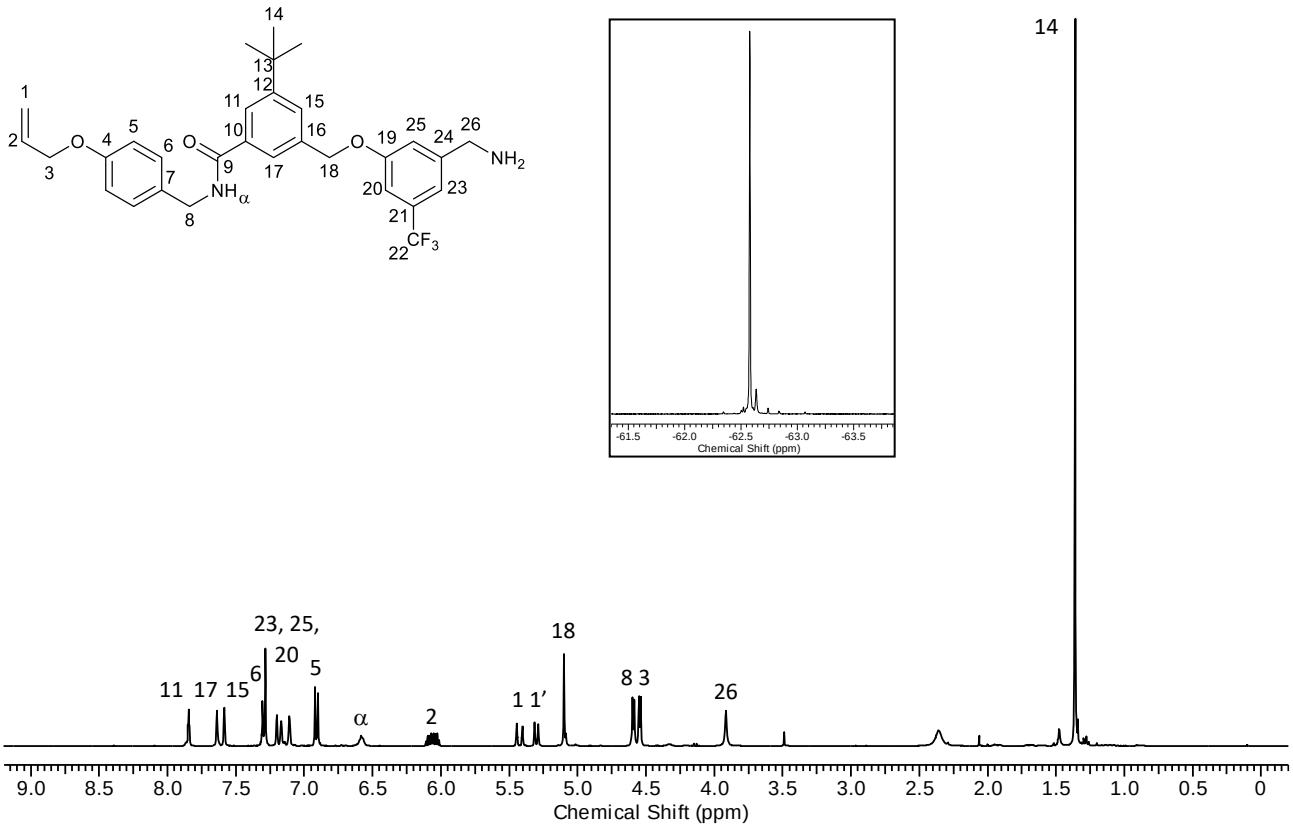
MS (ES +ve)



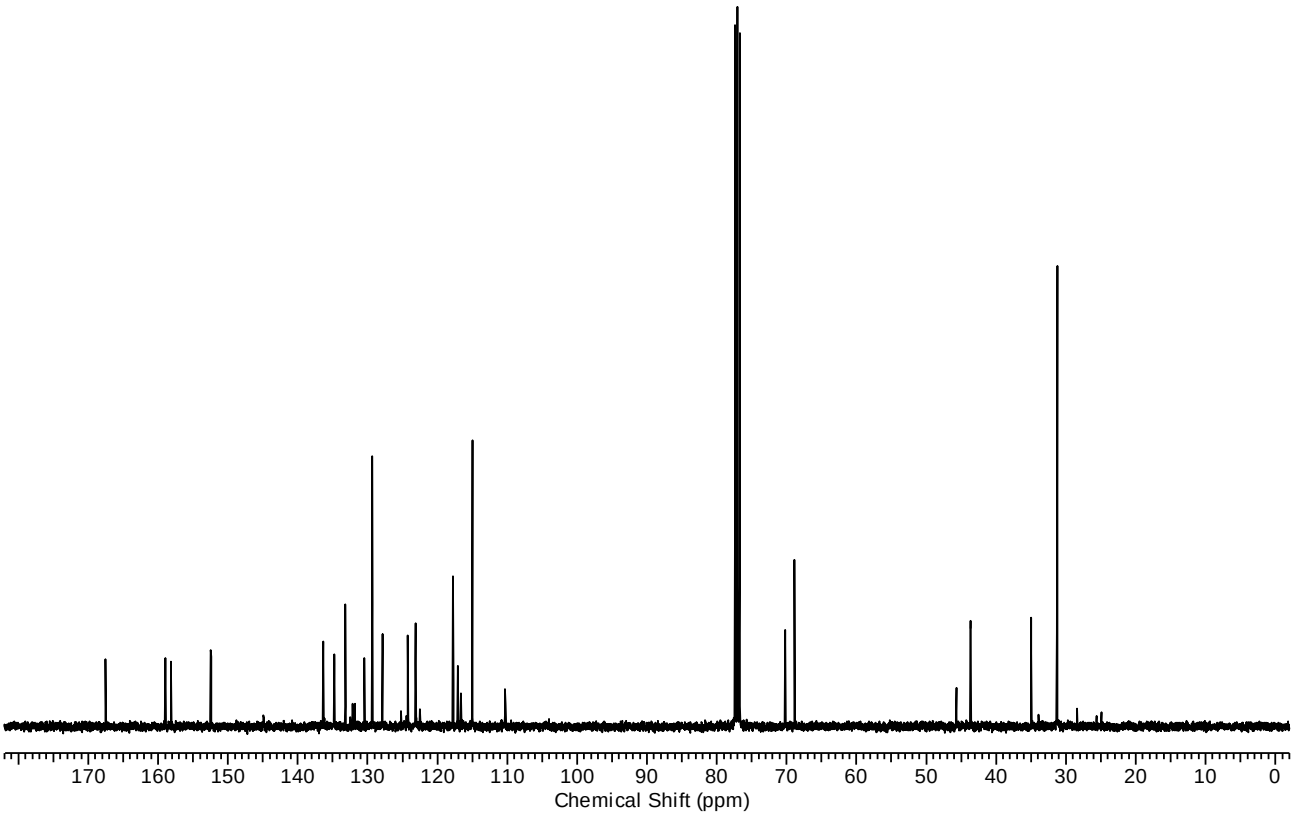
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
627.3046	1	C35H42F3N2O5	627.3040	-0.9	-0.6	41.4	-3.0
649.2879	1	C35H41F3N2NaO5	649.2860	-2.9	-1.9	6.2	-3.6

Half Axle HA-1

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

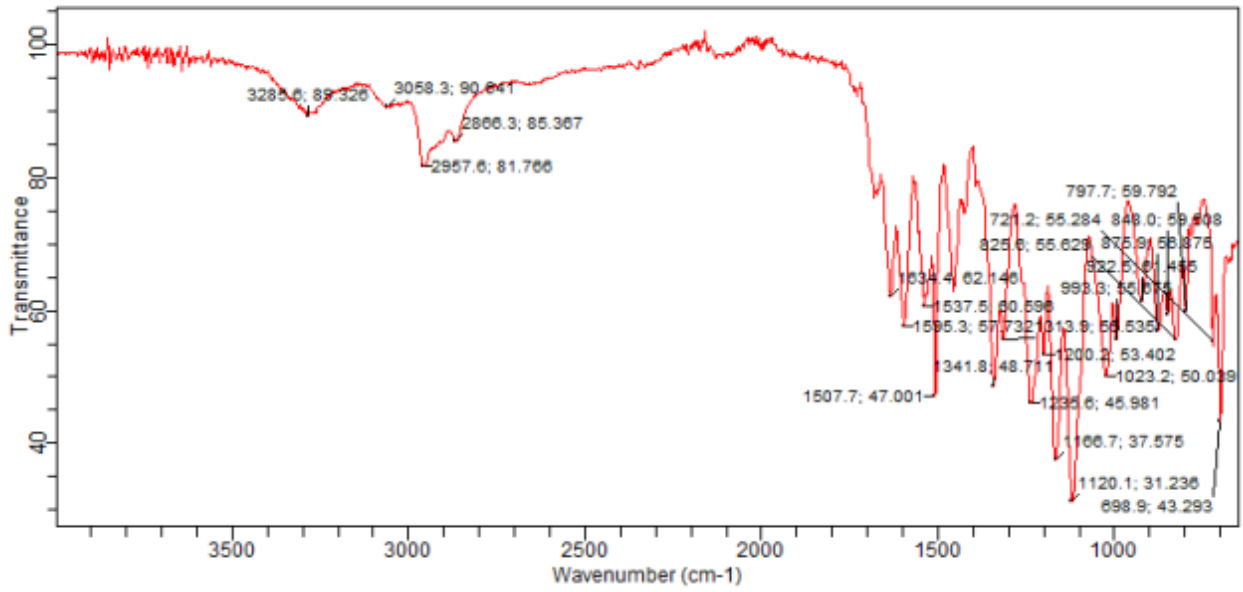


^{13}C NMR ($CDCl_3$, 100 MHz)

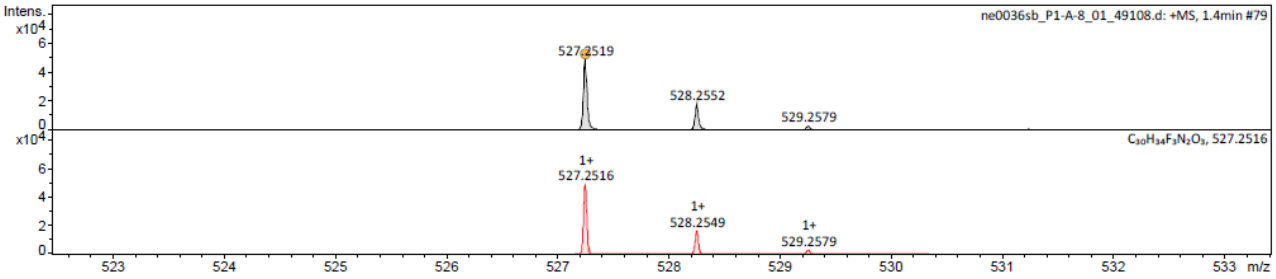


Half Axle HA-1

IR (neat)



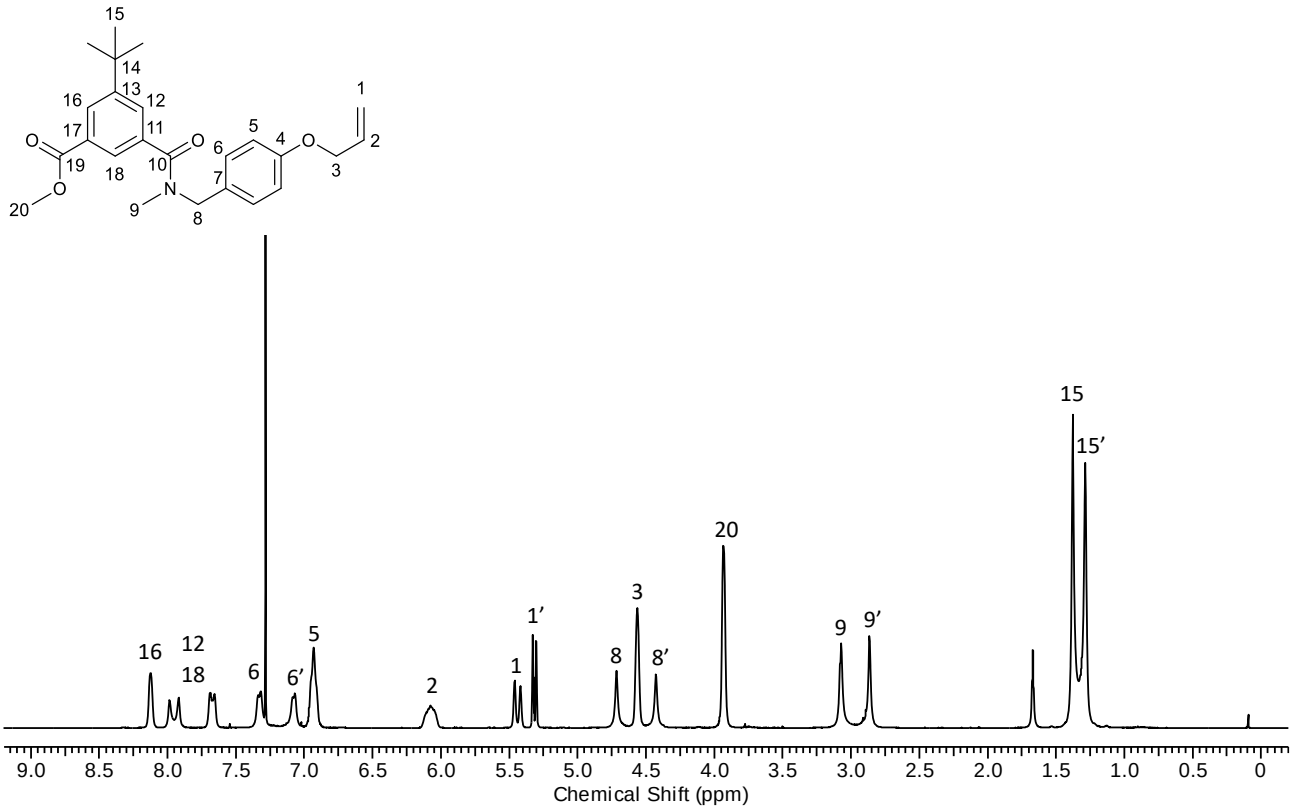
MS (ES +ve)



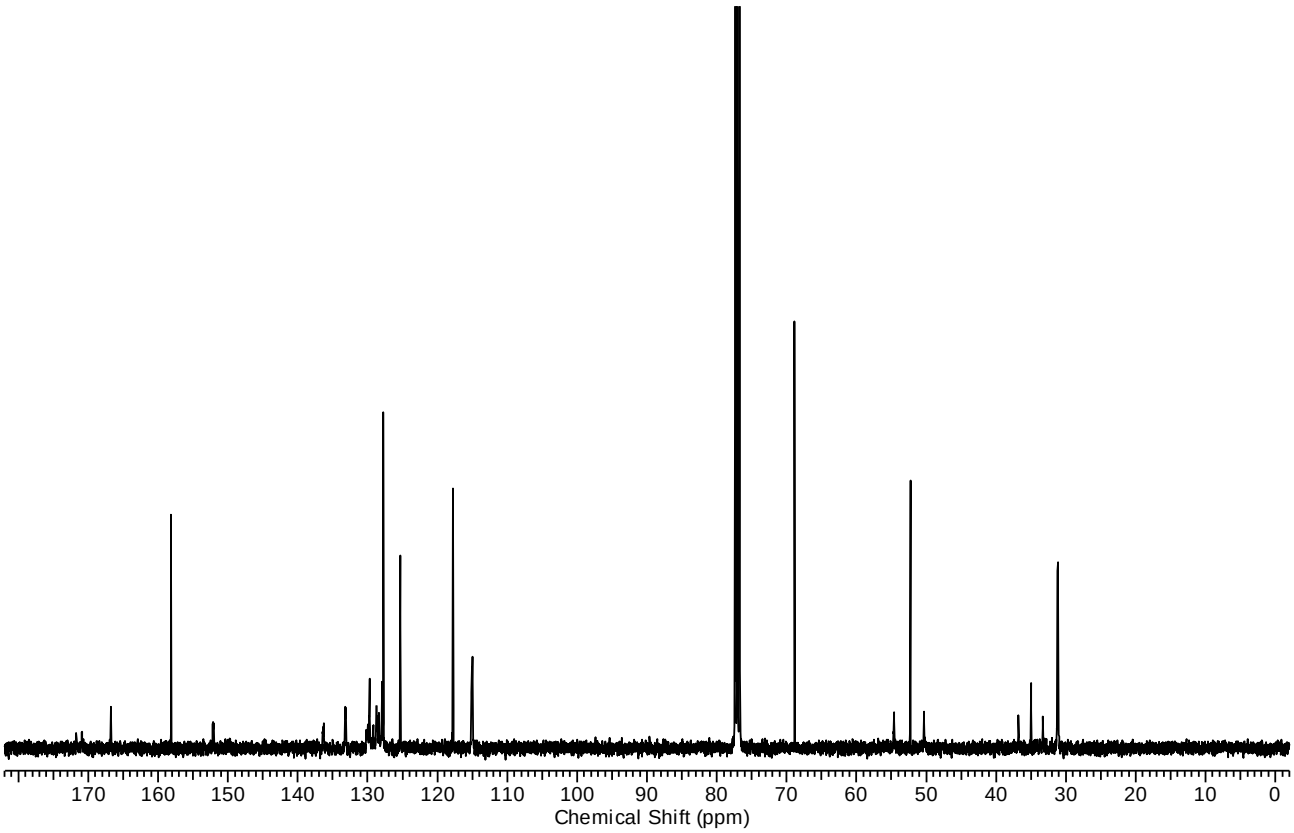
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
527.2519	1	C30H34F3N2O3	527.2516	-0.6	-0.3	16.0	0.1

Compound 9

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

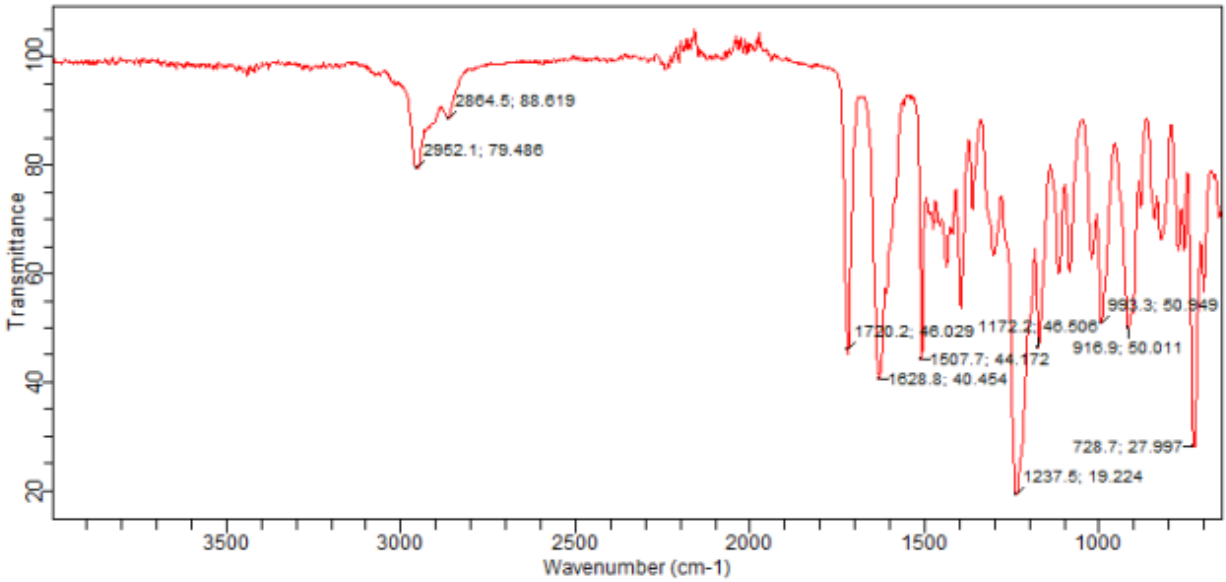


^{13}C NMR ($CDCl_3$, 100 MHz)

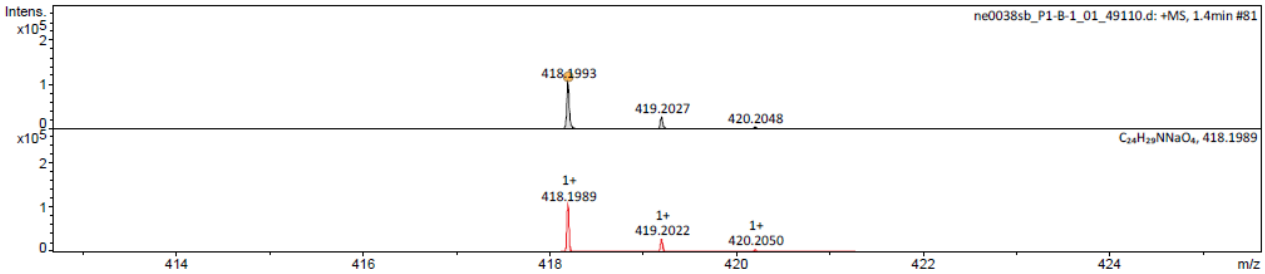


Compound 9

IR (neat)



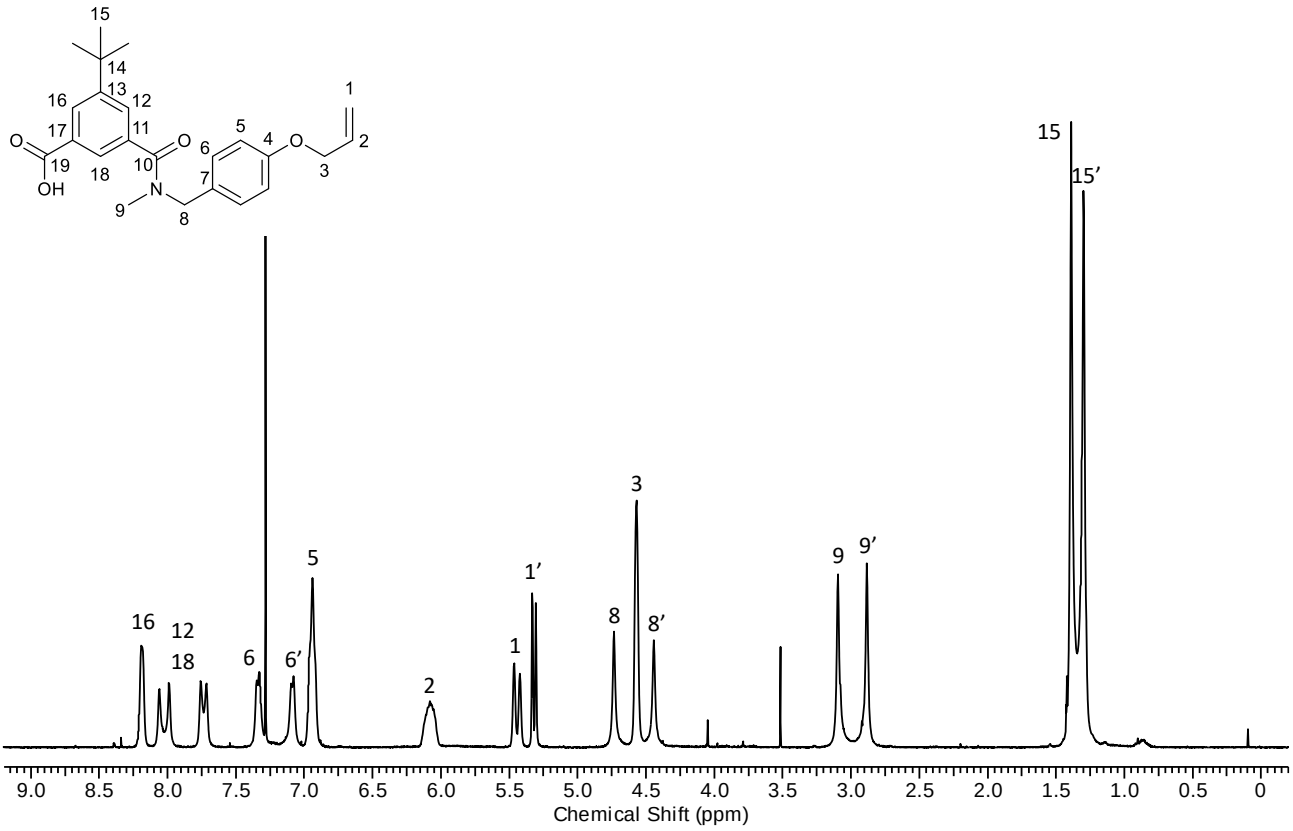
MS (ES +ve)



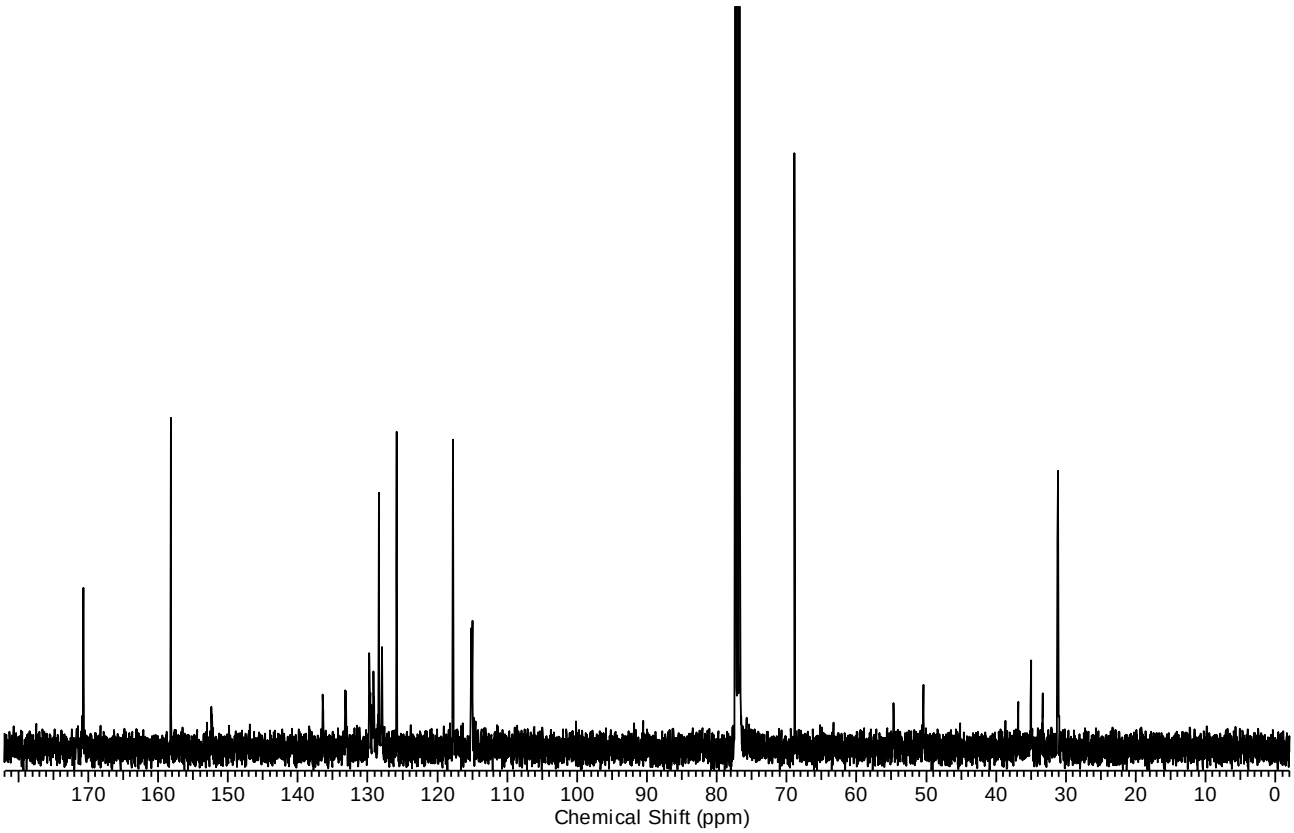
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
396.2172	1	C24H30NO4	396.2169	-0.6	-0.2	21.3	-0.3
418.1993	1	C24H29NNaO4	418.1989	-0.9	-0.4	7.4	-0.7

Compound 10

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

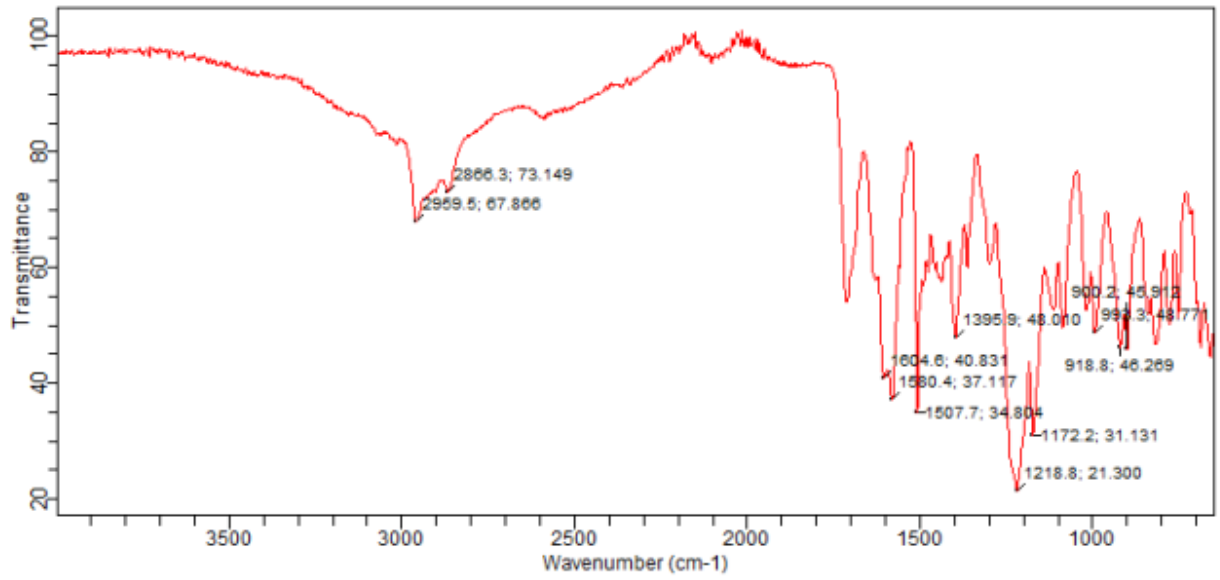


^{13}C NMR ($CDCl_3$, 100 MHz)

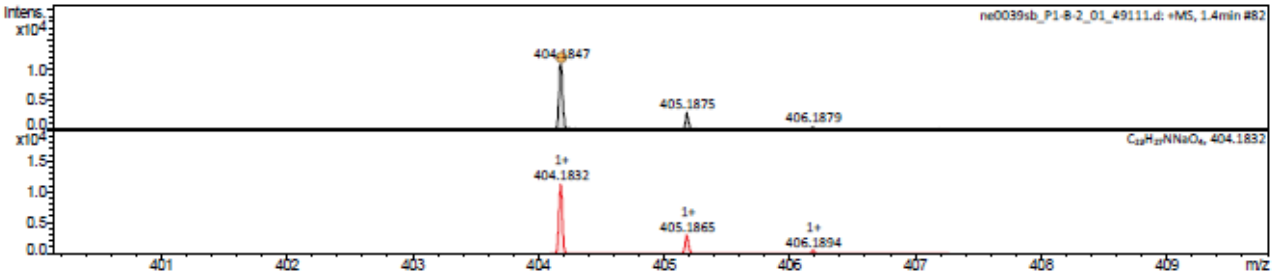


Compound 10

IR (neat)



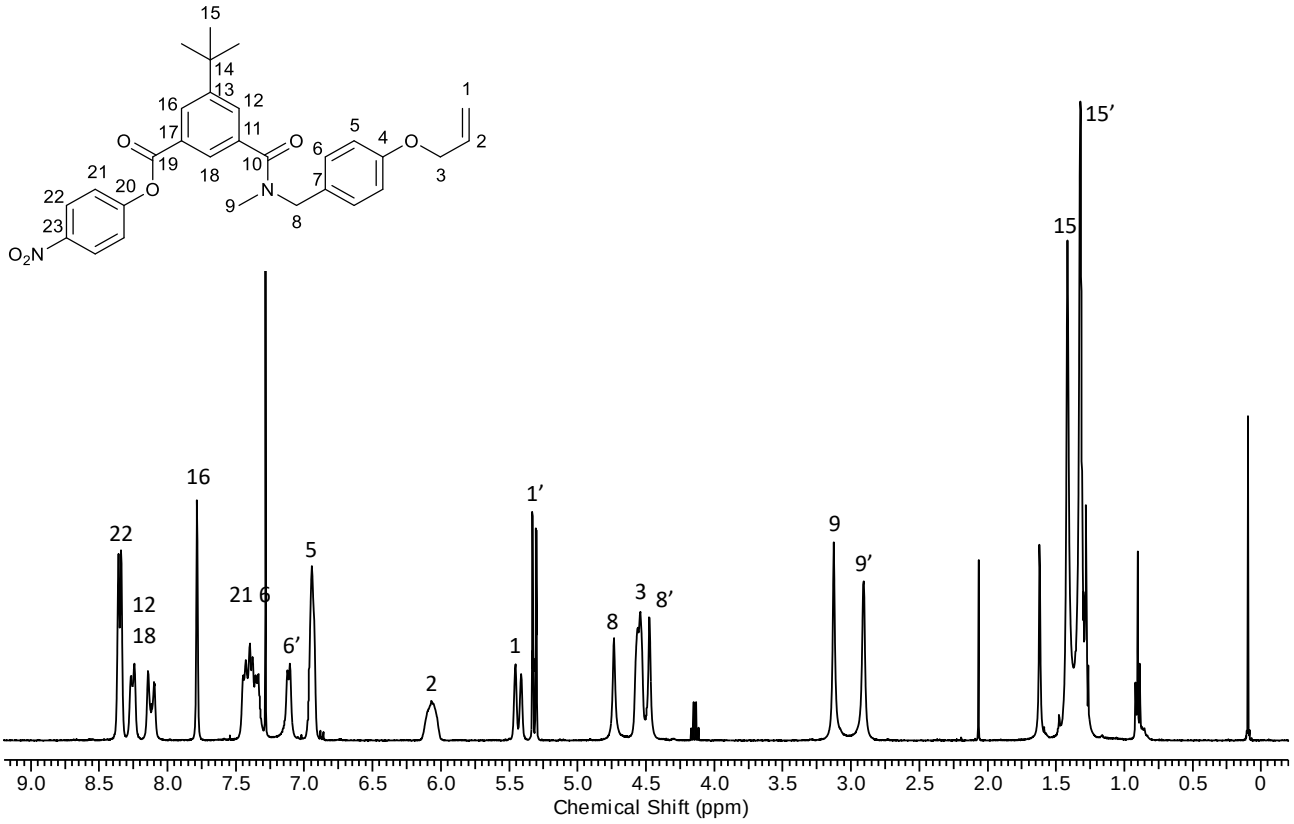
MS (ES +ve)



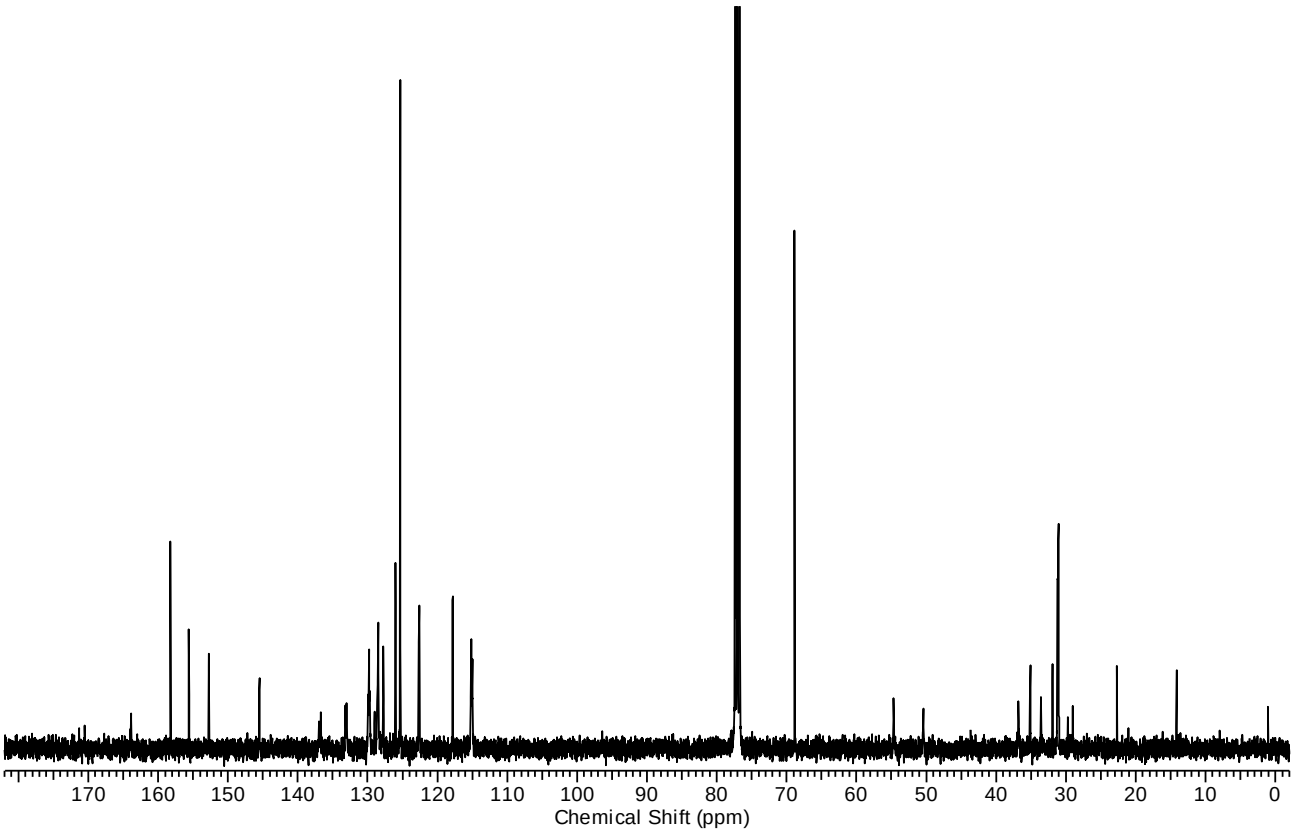
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
382.2042	1	C23H28NO4	382.2013	-7.7	-3.0	29.3	-3.0
404.1847	1	C23H27NNaO4	404.1832	-3.6	-1.4	6.5	-1.8

Half Axle HA-2

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

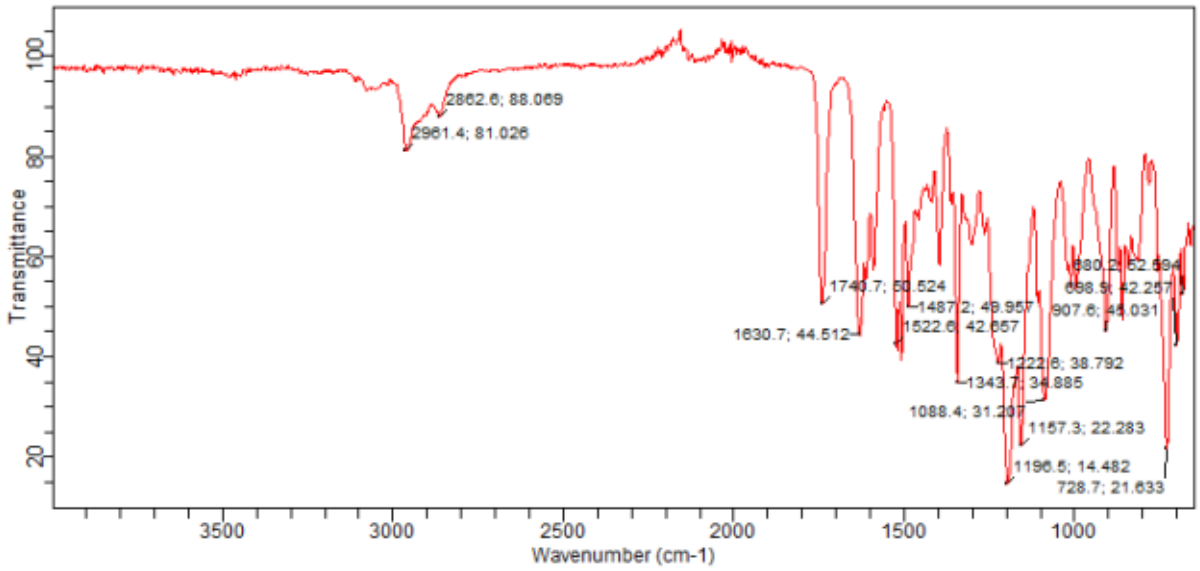


^{13}C NMR ($CDCl_3$, 100 MHz)

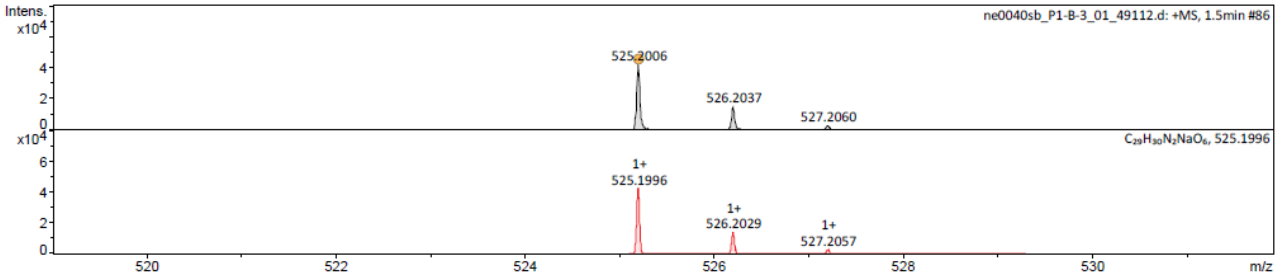


Half Axle HA-2

IR (neat)



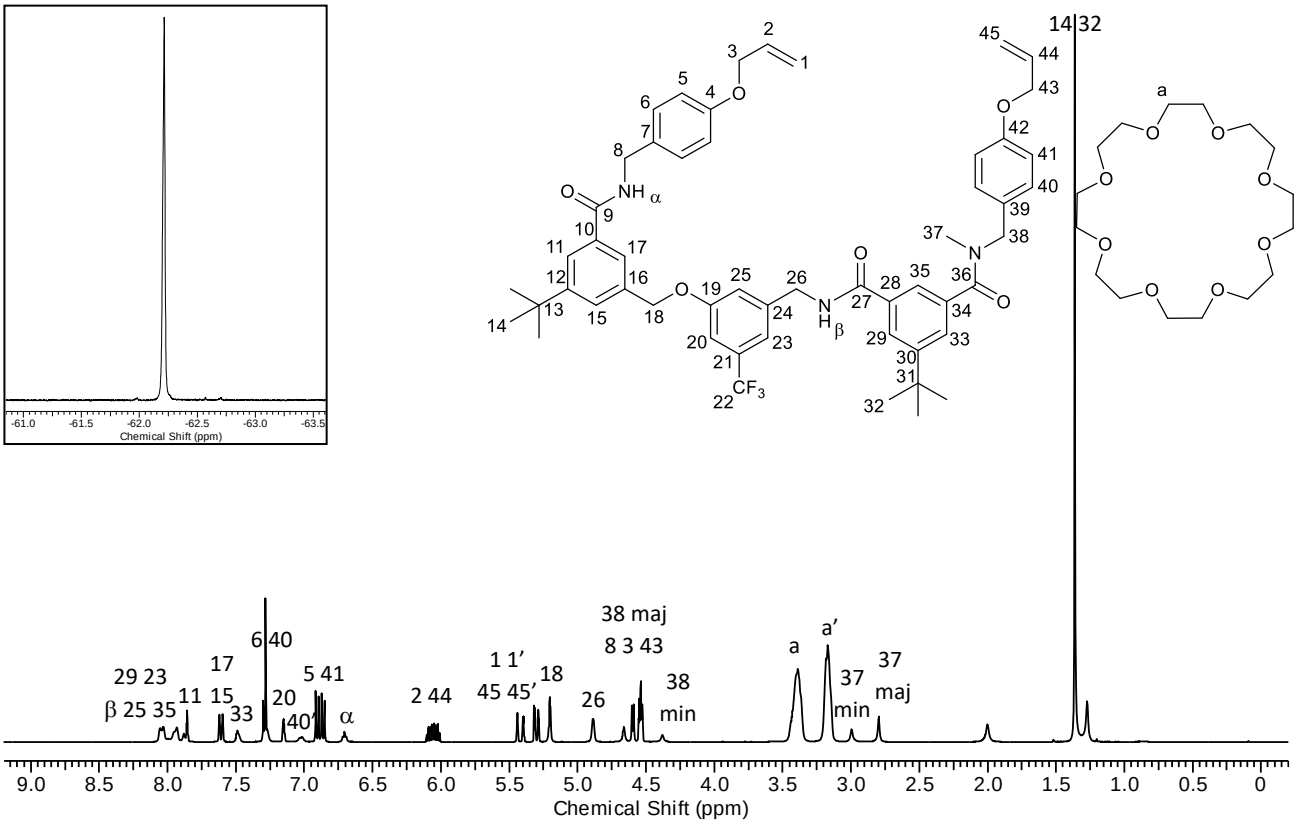
MS (ES +ve)



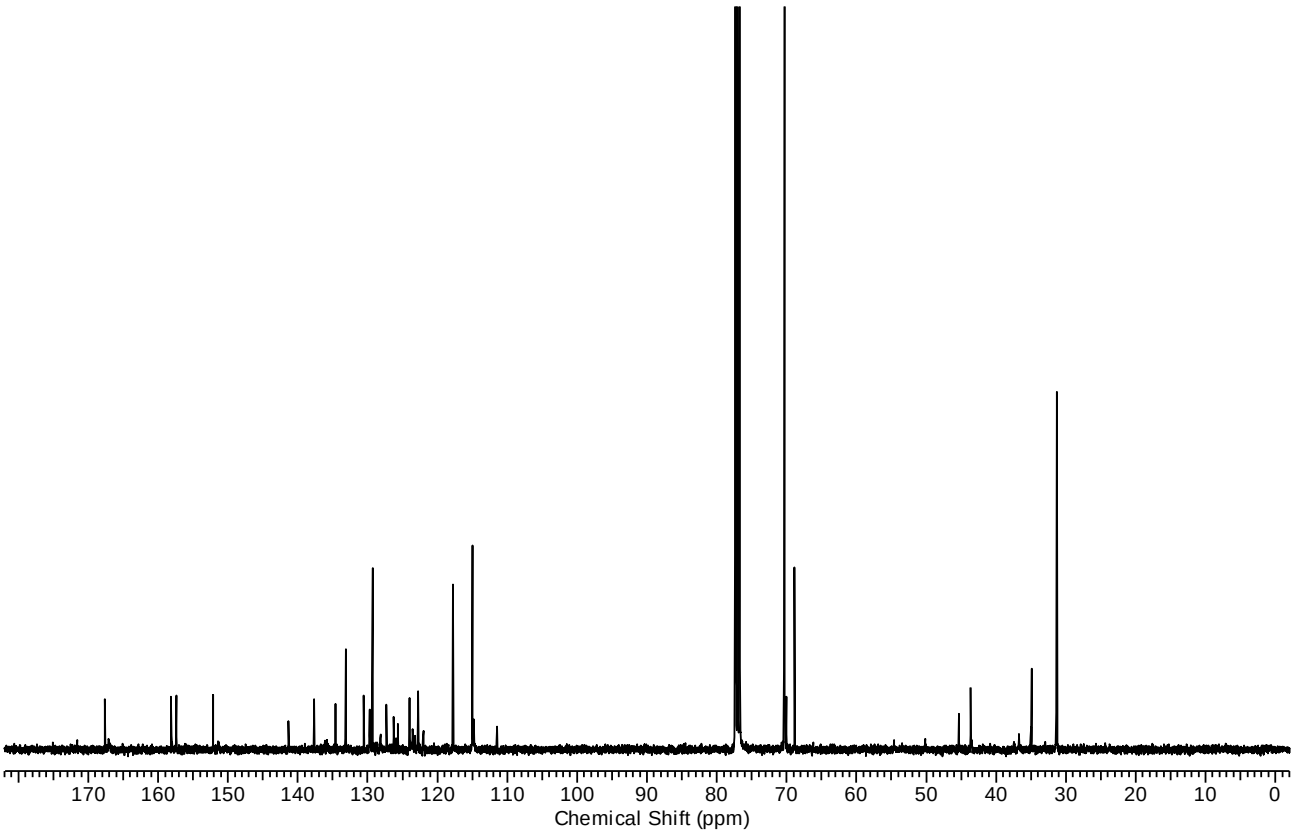
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
503.2175	1	C29H31N2O6	503.2177	0.3	0.2	4.9	-1.0
525.2006	1	C29H30N2NaO6	525.1996	-1.8	-1.0	10.4	-3.6

[2]Rotaxane R

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

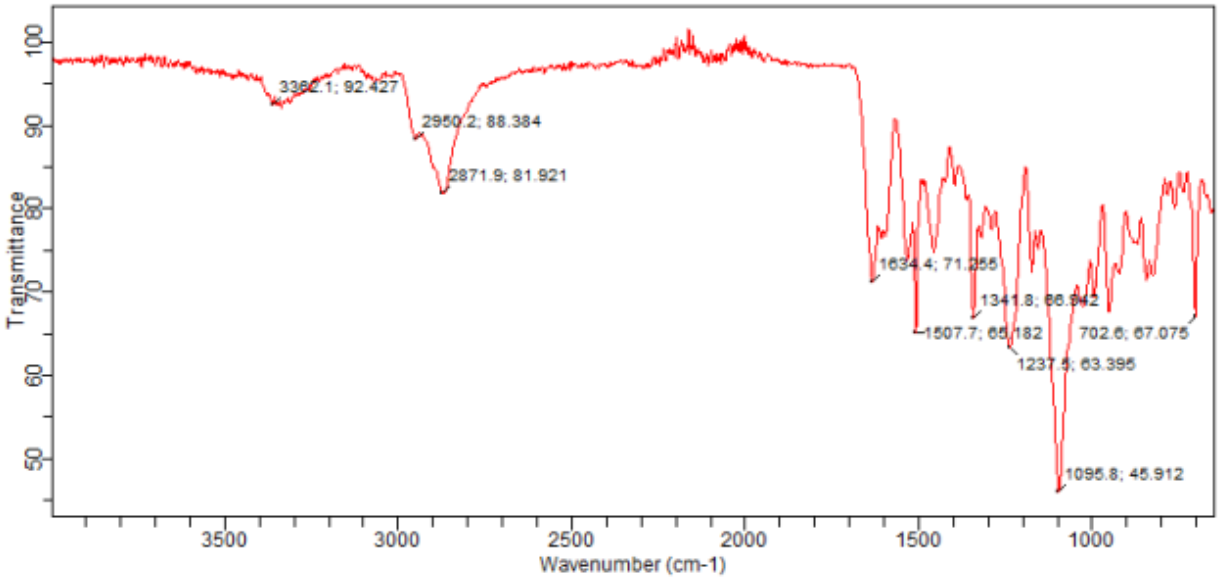


^{13}C NMR ($CDCl_3$, 100 MHz)

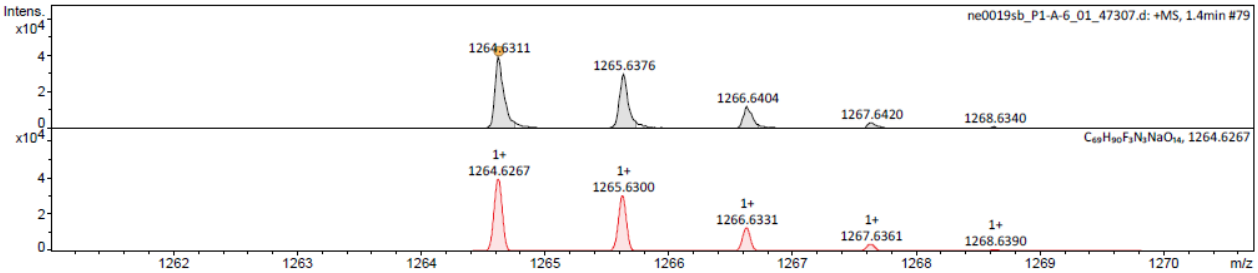


[2]Rotaxane R

IR (neat)



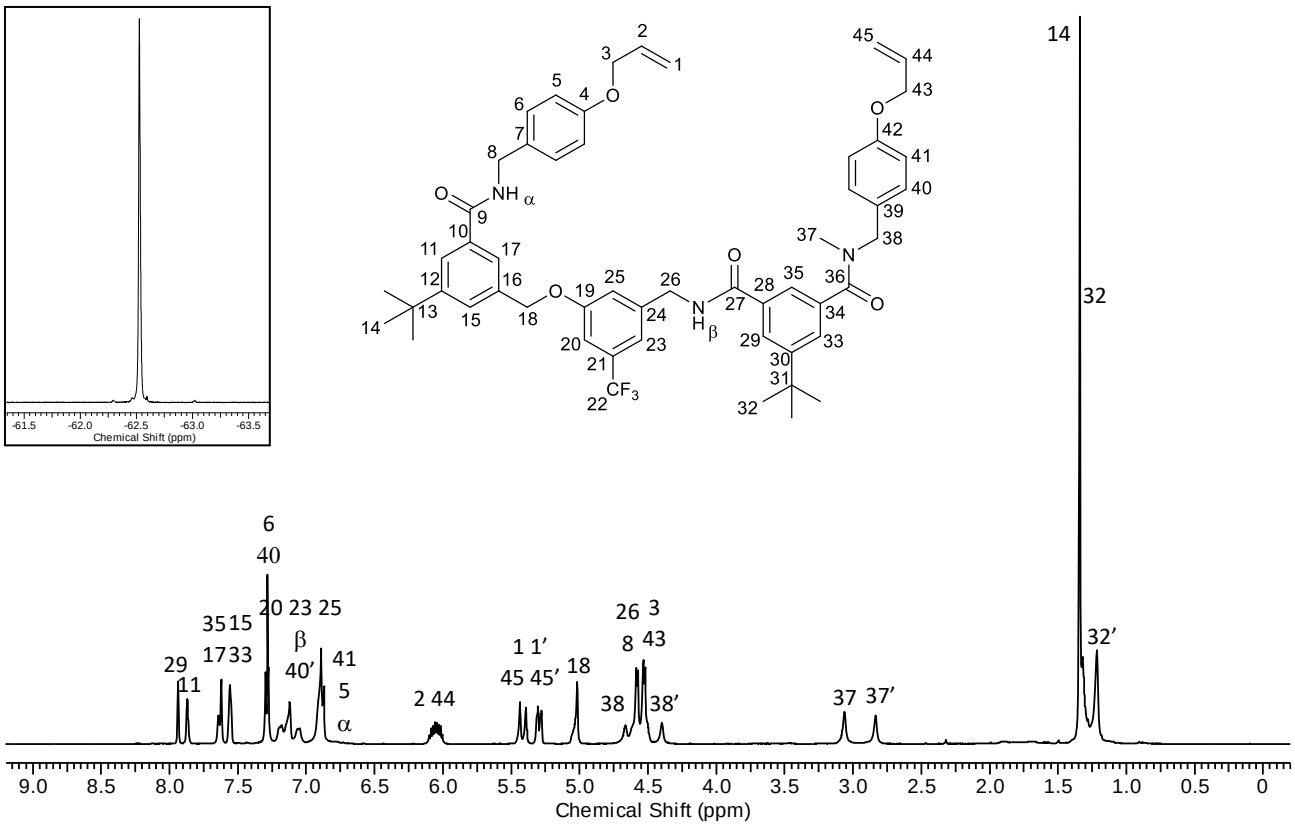
MS (ES +ve)



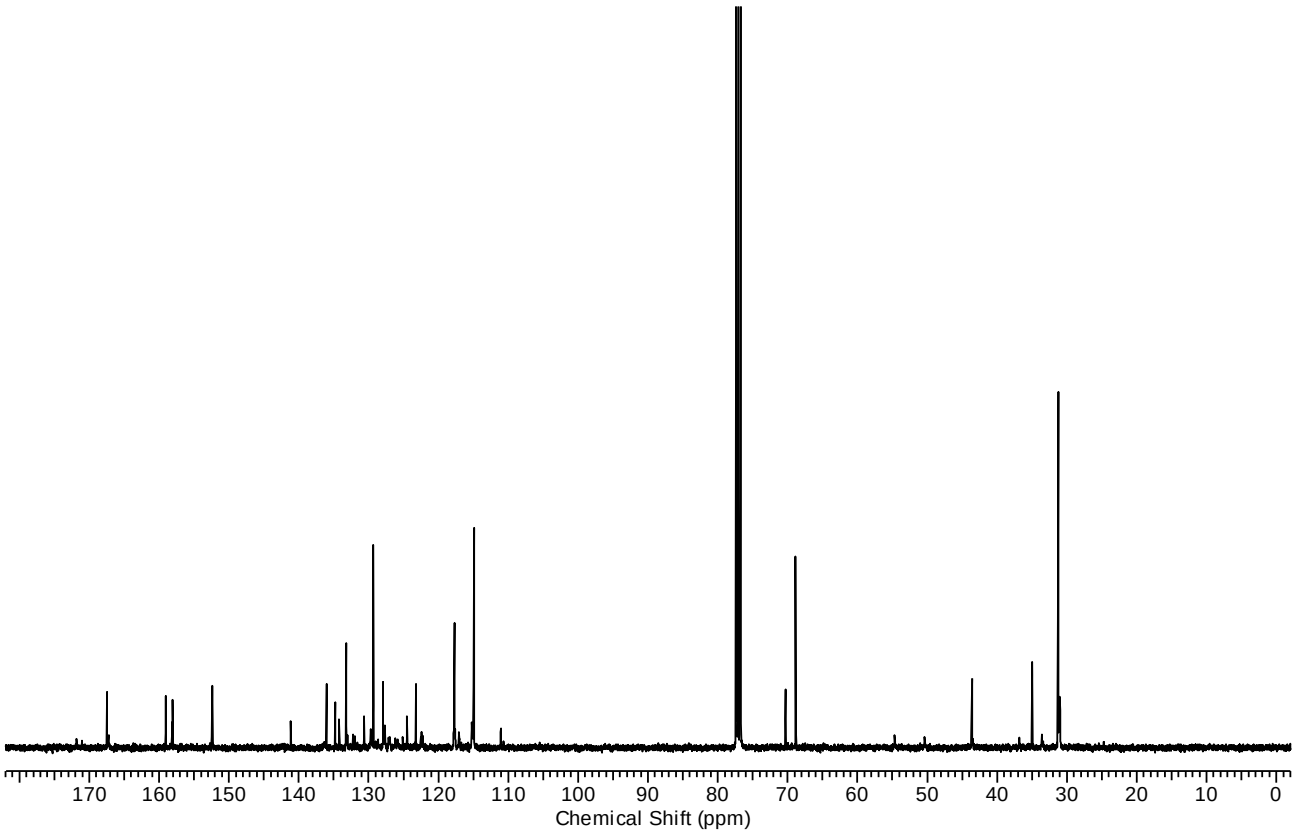
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
1242.6509	1	C69H91F3N3O14	1242.6448	-5.0	-6.2	63.0	-4.5
1264.6311	1	C69H90F3N3NaO14	1264.6267	-3.5	-4.4	13.2	-3.8

Axle Ax

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

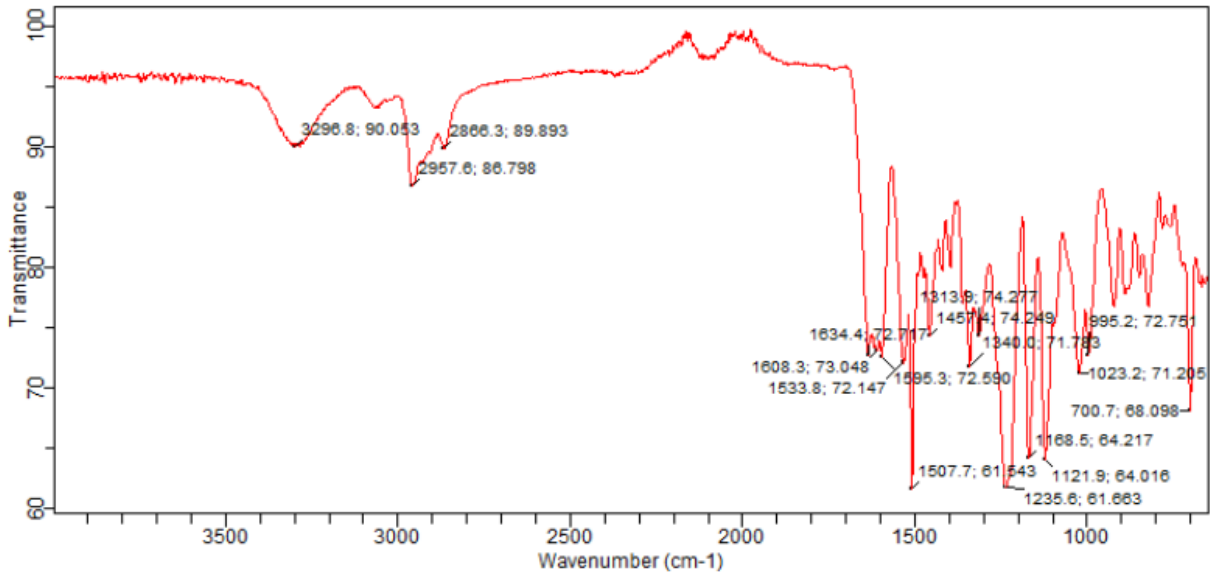


^{13}C NMR ($CDCl_3$, 100 MHz)

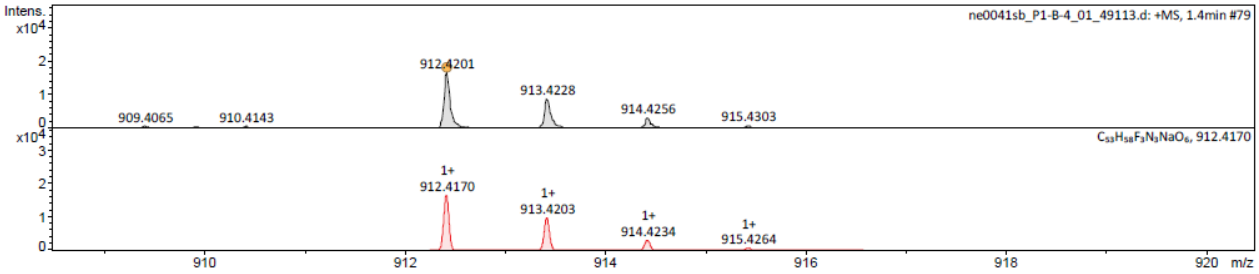


Axle Ax

IR (neat)



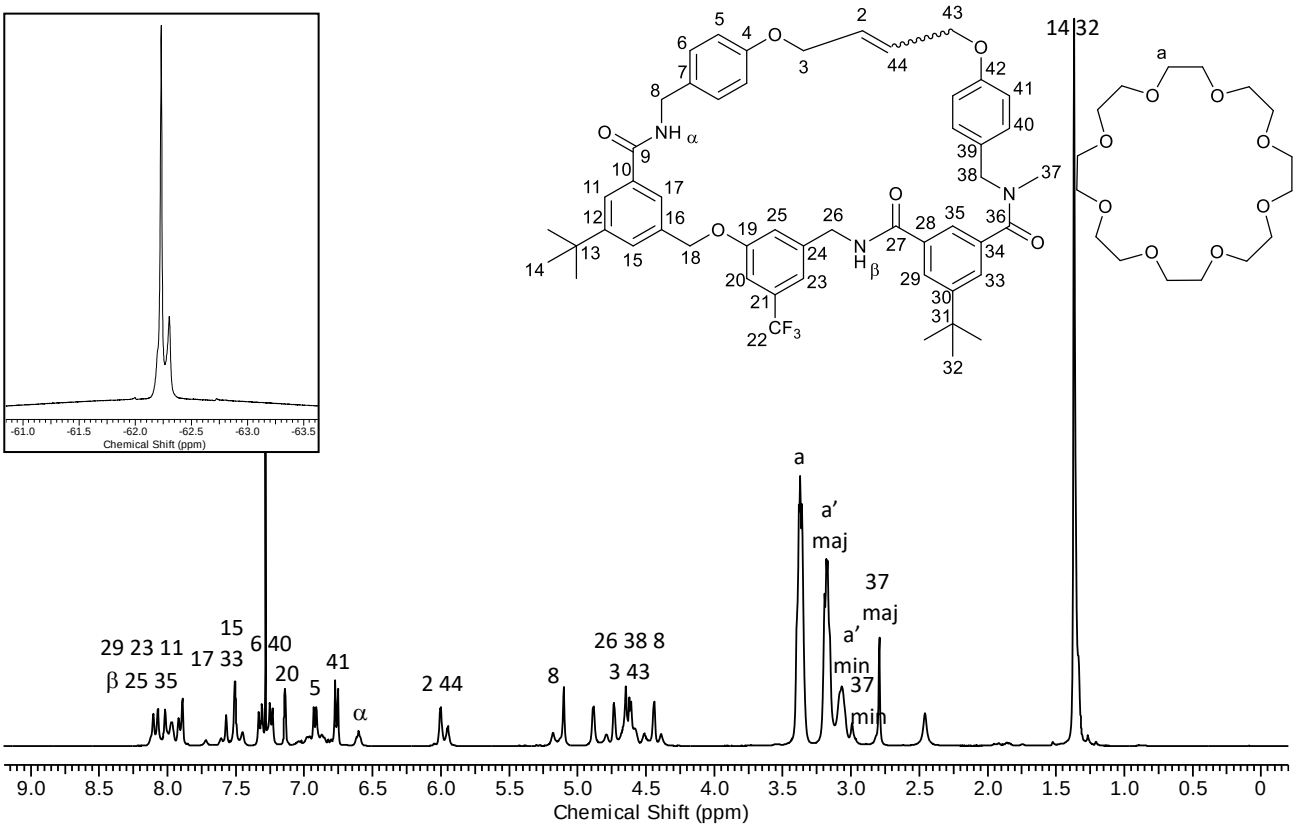
MS (ES +ve)



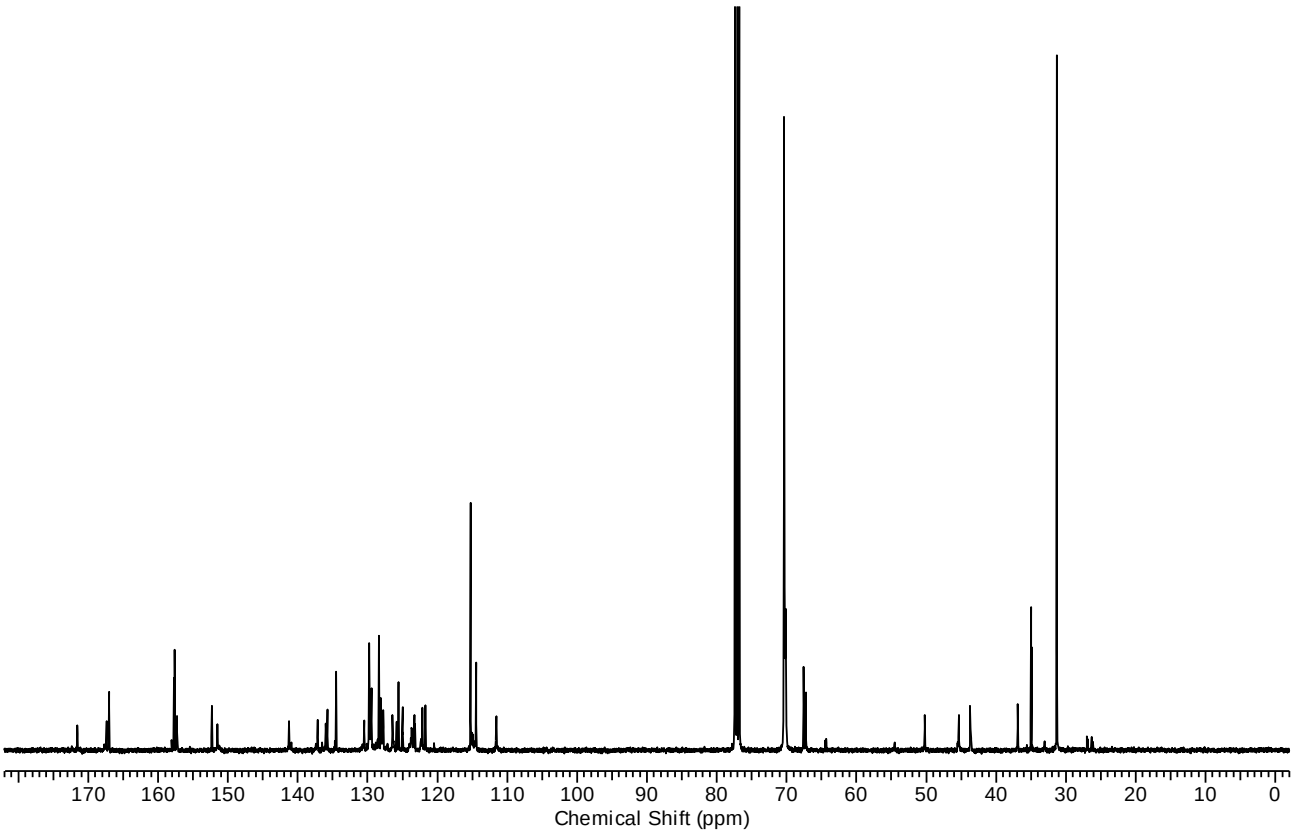
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
912.4201	1	C53H58F3N3NaO6	912.4170	-3.4	-3.1	38.5	-3.2

[2]Catenane C

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

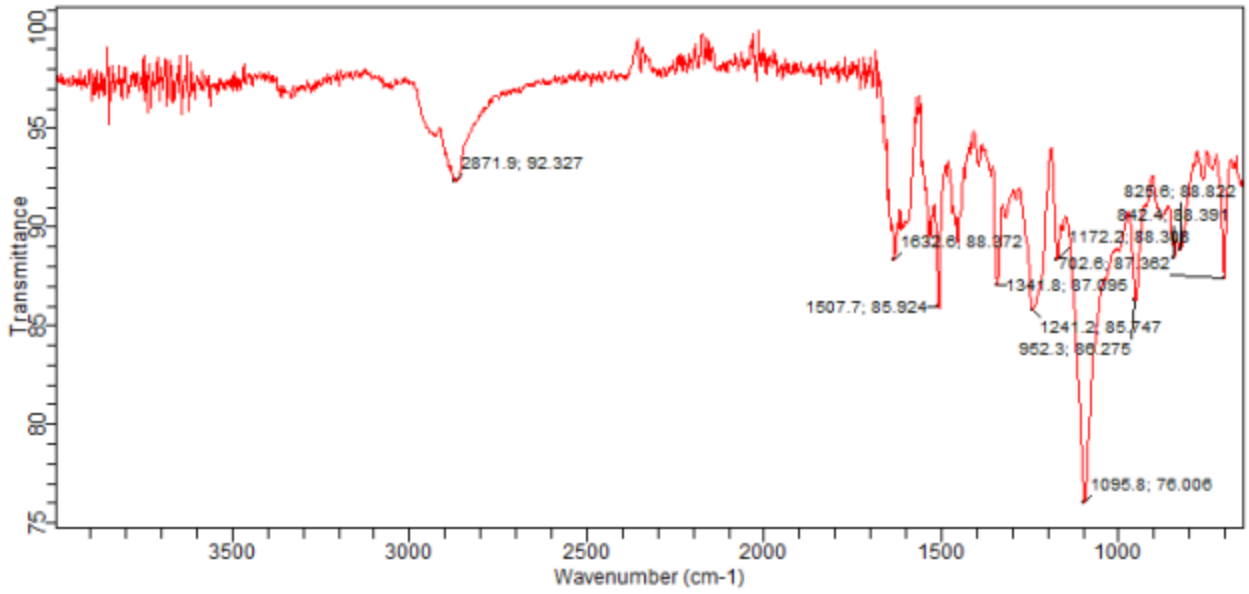


^{13}C NMR ($CDCl_3$, 100 MHz)

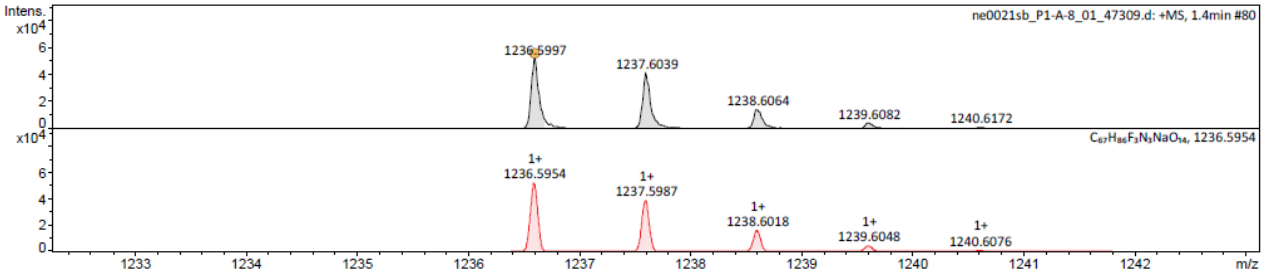


[2]Catenane C

IR (neat)



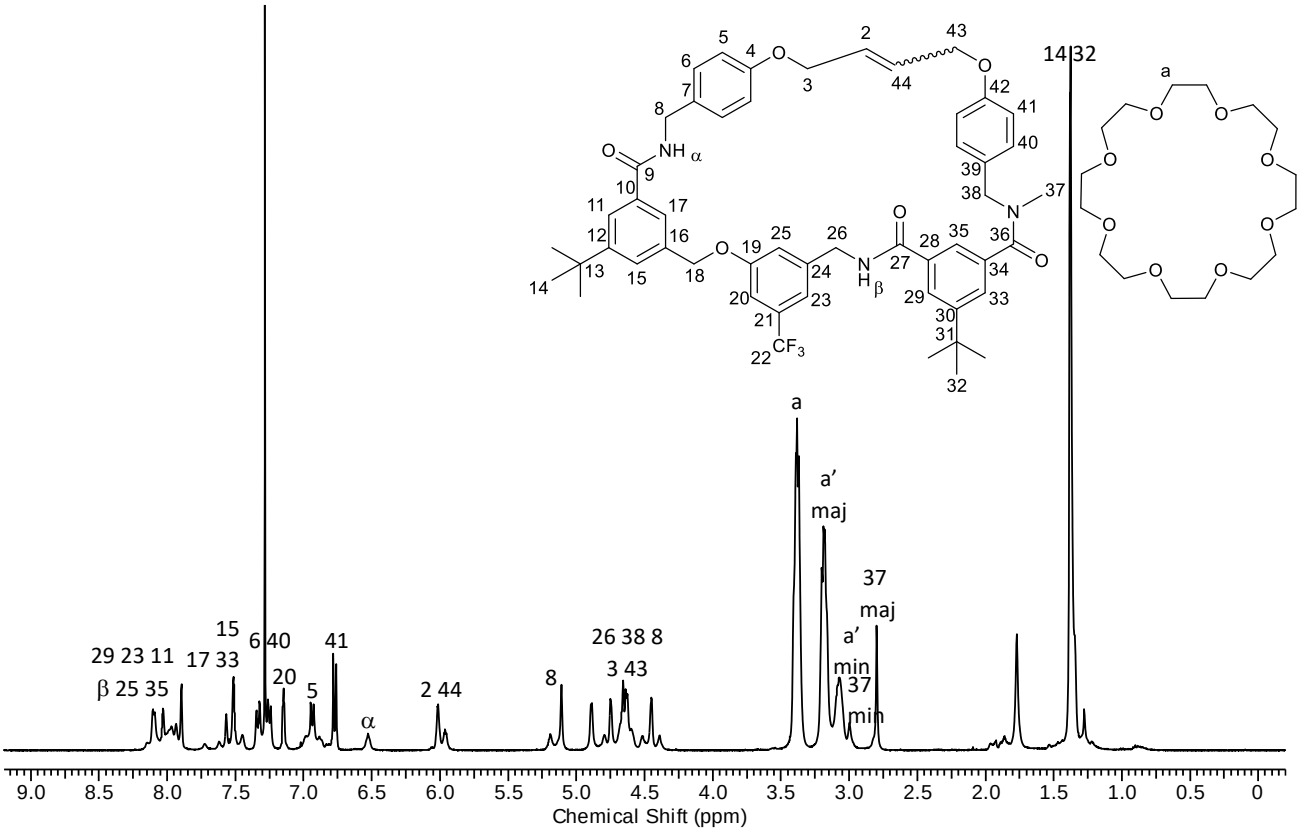
MS (ES +ve)



Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
1214.6211	1	C67H87F3N3O14	1214.6135	-6.3	-7.7	104.2	-3.9
1236.5997	1	C67H86F3N3NaO14	1236.5954	-3.5	-4.3	24.2	-4.1

[2]Catenane C

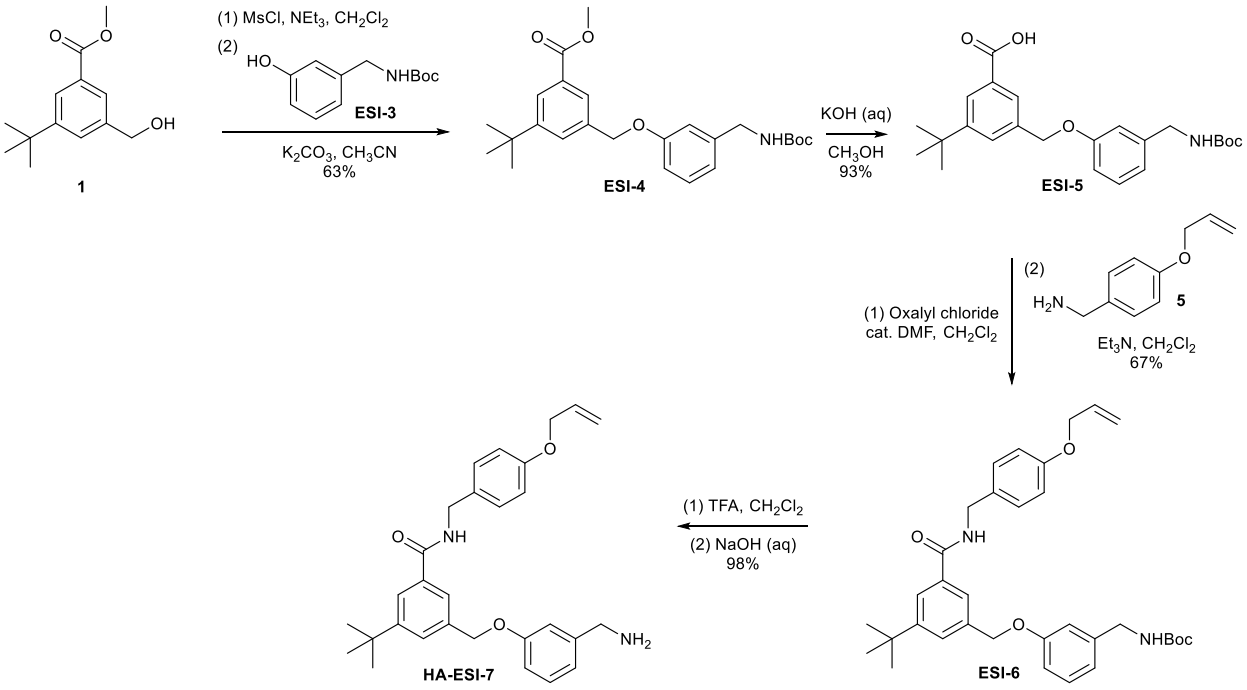
^{1}H NMR ($CDCl_3$, 400 MHz) *from NHE repeat of synthesis*

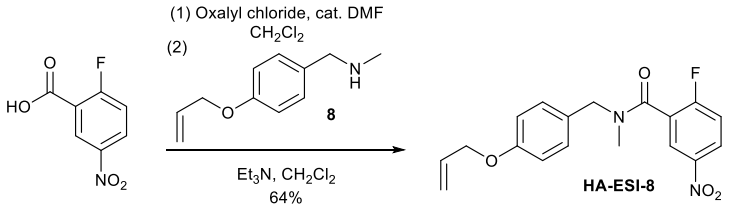


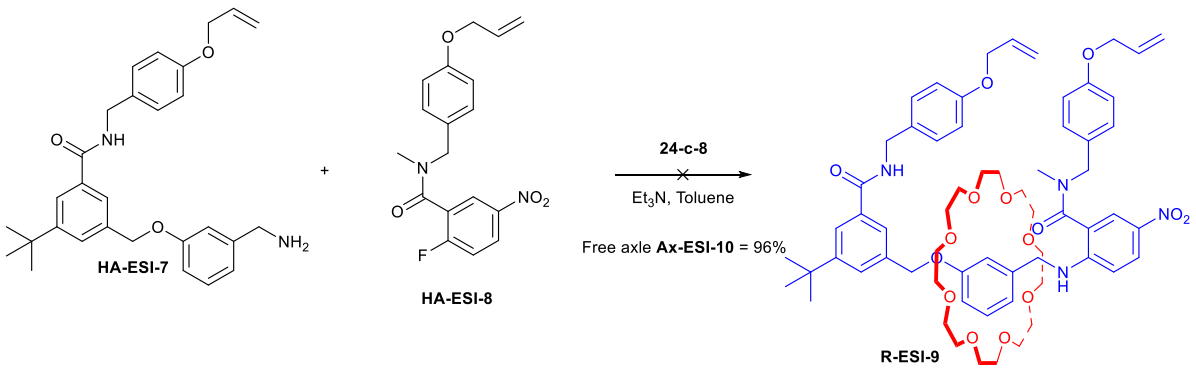
Part 3a: Preliminary experimental investigations (Design 1)

DESIGN 1:

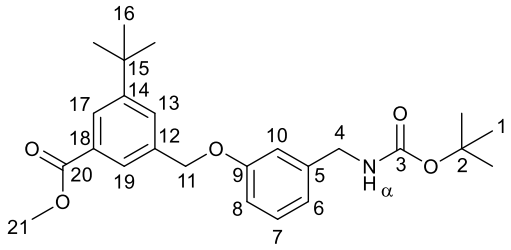
The first route investigated intended to make use of the nucleophilic aromatic substitution variant of CEATS:







Compound ESI-4



Methanesulfonyl chloride (384mg, 0.26 mL, 3.37 mmol) and Et_3N (451 mg, 0.62 mL, 4.50 mmol) were added to a solution of **1** (500 mg, 2.25 mmol) in dry CH_2Cl_2 (10 mL) under argon cooled to 0 °C. The reaction was stirred for 3 hours then quenched with $NaHCO_3$ (aq) (15 mL). The organic and aqueous layers were separated, and the aqueous layer washed with CH_2Cl_2 (20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to afford the mesylated alcohol. To a separate flask containing **ESI-3** (502 mg, 2.25 mmol) dissolved in dry CH_3CN (15 mL) was added K_2CO_3 (373 mg, 2.70 mmol). The solution was stirred for 10 minutes then a solution of the mesylated alcohol in dry CH_3CN (5 mL) was added. The reaction was then refluxed with stirring under argon for 16 hours. Upon cooling to room temperature, the reaction mixture was filtrated under gravity and concentrated *in vacuo*. The crude material was purified by silica gel column chromatography (Heptane:EtOAc 85:15) to afford the *title product* (604 mg, 63%) as a clear gel.

***R_f*:** 0.20 [EtOAc:Heptane 15:85].

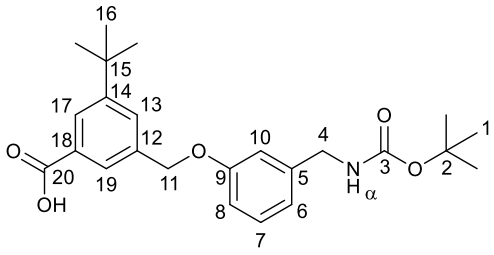
IR ν_{max} (neat): 3339 (N-H), 2927 (C-H), 1718 (C=O), 1684 (C=O).

δ_H (400 MHz, $CDCl_3$): 8.07 (1H, app t, H^{17}), 7.96 (1H, app t, H^{19}), 7.67 (1H, app t, H^{13}), 7.28 (1H, app t, H^{7}), 6.96 (1H, s, H^{10}), 6.93-6.90 (2H, m, H^{6} & H^{8}), 5.09 (2H, s, H^{11}), 4.85 (1H, bs, H^{α}), 4.32 (2H, d, *J* = 5.2 Hz, H^{4}), 3.95 (3H, s, H^{21}), 1.49 (9H, s, H^{1}), 1.38 (9H, s, H^{16}).

δ_C (100 MHz, $CDCl_3$): 167.2 (C^{20}), 159.0 (C^{9}), 155.9 (C^{3}), 152.0 (C^{14}), 140.7 (C^{5}), 136.9 (C^{12}), 130.3 (C^{18}), 129.7 (C^{7}), 129.2 (C^{13}), 126.4 (C^{17}), 126.0 (C^{19}), 120.2 (C^{6}), 114.0 (C^{10}), 113.6 (C^{8}), 79.6 (C^{2}), 69.9 (C^{11}), 52.1 (C^{21}), 44.6 (C^{4}), 34.9 (C^{15}), 31.3 (C^{16}), 28.4 (C^{1}).

m/z (ES): 428.10 ($[M+H]^+$ $C_{25}H_{34}NO_5$ requires 428.24).

Compound ESI-5



To a solution of **ESI-4** (578 mg, 1.35 mmol) in CH_3OH (5 mL) was added a solution of KOH (757 mg, 13.5 mmol) in water (0.5 mL). The reaction was stirred for 5 hours then acidified to pH 3 with 1M HCl (aq). Excess CH_3OH was then removed *in vacuo* and the resulting precipitate was collected by vacuum filtration to afford the *title product* (519 mg, 93%) as a sticky colourless solid.

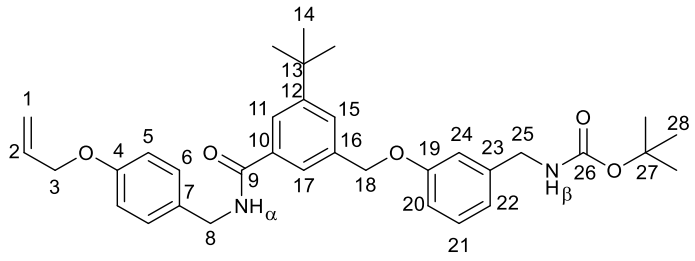
IR ν_{max} (neat): 2965 (C-H), 2870 (C-H), 1686 (2 x C=O).

δ_H (400 MHz, $CDCl_3$): 8.14 (1H, s, H^{17}), 8.03 (1H, s, H^{19}), 7.72 (1H, s, H^{13}), 7.28 (1H, app t, H^7), 6.98 (1H, s, H^{10}), 6.93-6.91 (2H, m, H^6 & H^8), 5.11 (2H, s, H^{11}), 4.90 (1H, bs, H^{α}), 4.33 (2H, d, *J* = 5.2 Hz, H^4), 1.49 (9H, s, H^1), 1.39 (9H, s, H^{16}).

δ_C (100 MHz, $CDCl_3$): 171.6 (C^{20}), 159.0 (C^9), 156.0 (C^3), 152.1 (C^{14}), 140.6 (C^5), 137.1 (C^{12}), 130.0 (C^{13}), 129.7 (C^7), 129.6 (C^{18}), 126.9 (C^{17}), 126.6 (C^{19}), 120.2 (C^6), 114.1 (C^{10}), 113.7 (C^8), 79.6 (C^2), 69.8 (C^{11}), 44.6 (C^4), 34.9 (C^{15}), 31.3 (C^{16}), 28.4 (C^1).

m/z (ES): 414.10 ($[M+H]^+$ $C_{24}H_{32}NO_5$ requires 414.23).

Compound ESI-6



To a solution of Boc-amine-carboxylic acid **ESI-5** (468 mg, 1.13 mmol) in dry CH_3CN (15 mL) was added DCC (256 mg, 1.24 mmol) and *N*-hydroxysuccinimide (143 mg, 1.24 mmol). The reaction was then stirred at room temperature under argon for 16 hours. The reaction mixture was filtrated under gravity and concentrated *in vacuo* to afford a colourless solid. The crude material was redissolved in dry CH_2Cl_2 (15 mL) and placed under argon. To the solution was added **5** (203 mg, 1.24 mmol) and Et_3N (136 mg, 0.19 mL, 1.35 mmol). The reaction was then stirred at room temperature for 16 hours. The reaction mixture was then washed with 1M HCl (aq) (2 x 15 mL), $NaHCO_3$ (aq) (2 x 15 mL) and water (1 x 15 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by silica gel column chromatography (Heptane:EtOAc 7:3) to afford the *title product* (424 mg, 67%) as a colourless solid.

***R_f*:** 0.26 [EtOAc:Heptane 3:7].

m.p. 210-212 °C.

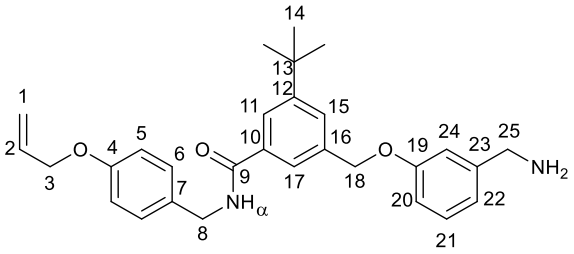
IR: ν_{max} (neat): 3358 (N-H), 3270 (N-H), 2965 (C-H), 1684 (C=O).

δ_H (400 MHz, $CDCl_3$): 7.86 (1H, app t, H^{11}), 7.61 (1H, bs, H^{17}), 7.59 (1H, bs, H^{15}), 7.31 (2H, d, *J* = 8.5 Hz, H^6), 7.26 (1H, app t, H^{21}), 6.97-6.86 (5H, m, H^{24}, H^5, H^{22} & H^{20}), 6.47 (1H, bs, H^{α}), 6.12-6.02 (1H, m, H^2), 5.43 (1H, dq, *J* = 17 Hz, 1.5 Hz, H^1), 5.30 (1H, dq, *J* = 11 Hz, 1.5 Hz, $H^{1'}$), 5.07 (2H, s, H^{18}), 4.86 (1H, bs, H^{β}), 4.61 (2H, d, *J* = 5.6 Hz, H^8), 4.55 (2H, dt, *J* = 5.2 Hz, 1.5 Hz, H^3), 4.30 (2H, bd, *J* = 5.2 Hz, H^{25}), 1.48 (9H, s, H^{28}), 1.37 (9H, s, H^{14}).

δ_C (100 MHz, $CDCl_3$): 167.5 (C^9), 158.9 (C^{19}), 158.1 (C^4), 155.9 (C^{26}), 152.3 (C^{12}), 140.7 (C^{23}), 137.0 (C^{16}), 134.8 (C^{10}), 133.2 (C^2), 130.5 (C^7), 129.7 (C^{21}), 129.3 (C^6), 127.9 (C^{15}), 124.2 (C^{11}), 123.0 (C^{17}), 120.1 (C^{22}), 117.7 (C^1), 115.0 (C^5), 113.9 (C^{24}), 113.8 (C^{20}), 79.6 (C^{27}), 69.9 (C^{18}), 68.9 (C^3), 44.6 (C^{25}), 43.6 (C^8), 35.0 (C^{13}), 31.3 (C^{14}), 28.4 (C^{28}).

m/z (ES): 559.15 ($[M+H]^+$ $C_{34}H_{43}N_2O_5$ requires 559.32).

Half Axle HA-ESI-7



ESI-6 (417 mg, 0.74 mmol) was dissolved in dry CH_2Cl_2 (15 mL) under argon and cooled to 0 °C. To this solution was added TFA (849 mg, 0.57 mL, 7.46 mmol). The reaction was allowed to warm to room temperature and stirred for 4 hours. All volatiles were then removed *in vacuo*. The crude material was redissolved in EtOAc (10 mL) and washed with $NaHCO_3$ (aq) (20 mL). The aqueous was then extracted with EtOAc (2 x 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to afford the *title product* (400 mg, 98%) as a clear gel.

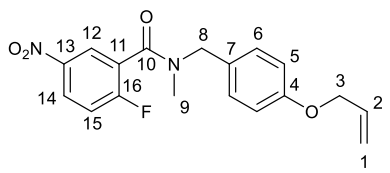
IR: ν_{max} (neat): 3281 (N-H), 2959 (C-H), 2866 (C-H), 1636 (C=O).

δ_H (400 MHz, $CDCl_3$): 7.84 (1H, t, *J* = 1.7 Hz, H^{11}), 7.63 (1H, bs, H^{17}), 7.58 (1H, bs, H^{15}), 7.31-7.28 (2H, m, H^6), 7.25 (1H, app t, H^{21}), 6.98 (1H, bs, H^{24}), 6.92-6.89 (3H, m, H^5 & H^{22}) 6.87 (1H, dd, *J* = 8.0 Hz, 2.0 Hz, H^{20}), 6.60 (1H, t, *J* = 5.5 Hz, H^{α}), 6.11-6.01 (1H, m, H^2), 5.42 (1H, dq, *J* = 17 Hz, 1.5 Hz, H^1), 5.30 (1H, dq, *J* = 11 Hz, 1.5 Hz, $H^{1'}$), 5.06 (2H, s, H^{18}), 4.59 (H, d, *J* = Hz, H^8) 4.54 (H, dt, *J* = 5.3 Hz, 1.5 Hz, H^3), 3.85 (2H, s, H^{25}), 1.35 (9H, s, H^{14}).

δ_C (100 MHz, $CDCl_3$): 167.6 (C^9), 158.9 (C^{19}), 158.1 (C^4), 152.3 (C^{12}), 143.3 (C^{23}), 137.1 (C^{16}), 134.7 (C^{10}), 133.2 (C^2), 130.5 (C^7), 129.7 (C^{21}), 129.3 (C^6), 127.8 (C^{15}), 124.1 (C^{11}), 123.0 (C^{17}), 120.1 (C^{22}), 117.7 (C^1), 115.0 (C^5), 113.9 (C^{24}), 113.5 (C^{20}), 69.9 (C^{18}), 68.9 (C^3), 45.9 (C^{25}), 43.6 (C^8), 34.9 (C^{13}), 31.3 (C^{14}).

m/z (ES): 461.10 ($[M+H]^+$ $C_{29}D_2H_{33}N_2O_3$ requires 461.28).

Half Axle HA-ESI-8



To a solution of 2-fluoro-5-nitrobenzoic acid (1.57 g, 8.50 mmol) in dry CH_2Cl_2 (20 mL) was added oxalyl chloride (3.22 g, 2.18 mL, 25.5 mmol) and a catalytic amount of DMF. The solution was stirred for 2 hours, then all volatiles removed *in vacuo*. The resulting yellow oil was redissolved in dry CH_2Cl_2 (20 mL), placed under argon, and cooled to 0 °C. A solution of **8** (1.56 g, 8.80 mmol) and Et_3N (1.85 g, 2.56 mL, 18.4 mmol) in dry CH_2Cl_2 (30 mL) was added dropwise. The reaction was then allowed to warm to room temperature and stirred for a further 2 hours. The reaction mixture was washed with 1M HCl (aq) (2 x 20 mL), $NaHCO_3$ (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 (CH_2Cl_2:CH_3OH 99.5:0.5) to afford the *title product* (1.87 g, 64%, as a ≈3:2 mixture of rotamers determined by ^1H NMR in $CDCl_3$ at RT) as a yellow oil.

***R_f*:** 0.38 [CH_2Cl_2:CH_3OH 99.5:0.5].

IR ν_{max} (neat): 2931 (C-H), 1638 (C=O).

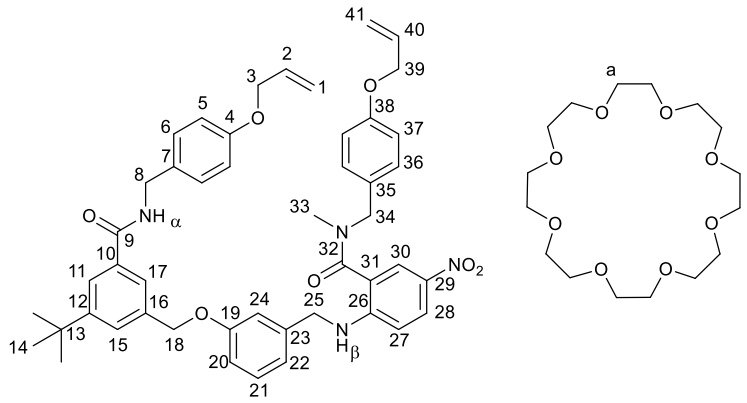
δ_H (400 MHz, $CDCl_3$): 8.37-8.27 (2H, m, H^{12} both & H^{14} both), 7.32-7.28 (2.2H, m, H^{15} both & H^6 major), 7.05 (0.8H, d, *J* = 8.7 Hz, H^6 minor), 6.94 (1.2H, d, *J* = 8.7 Hz, H^5 major), 6.90 (0.8H, d, *J* = 8.7 Hz, H^5 minor), 6.12-6.00 (1H, m, H^2 both), 5.43 (0.6H, dq, *J* = 17 Hz, 1.6 Hz, H^1 major), 5.41 (0.4H, dq, *J* = 17 Hz, 1.6 Hz, H^1 minor), 5.33-5.27 (1H, m, $H^{1'}$ both), 4.72 (1.2H, s, H^8 major), 4.56 (1.2H, dt, *J* = 5.2, 1.5 Hz, H^3 major), 4.53 (0.8H, dt, *J* = 5.2, 1.5 Hz, H^3 minor), 4.36 (0.8H, s, H^8 minor), 3.05 (1.2H, s, H^9 minor), 2.83 (1.8H, d, *J* = 1.2 Hz, H^9 major).

δ_C (100 MHz, $CDCl_3$): 164.3 (C^{10} minor), 164.2 (C^{10} major), 161.6 (d, *J* = 257 Hz, C^{16} minor), 161.5 (d, *J* = 257 Hz, C^{16} major), 158.5 (C^4 minor), 158.3 (C^4 major), 144.5 (d, *J* = 3 Hz, C^{13} major), 144.4 (d, *J* = 3 Hz, C^{13} minor), 133.2 (C^2 major), 133.0 (C^2 minor), 129.5 (C^6 major), 128.4 (C^6 minor), 128.2 (C^7 major), 127.3 (C^7, minor), 126.8 (d, *J* = 10 Hz, C^{14} major), 126.7 (d, *J* = 10 Hz, C^{14} minor), 126.1 (d, *J* = 21 Hz, C^{11} major), 126.0 (d, *J* = 21 Hz, C^{11} minor), 125.4 (d, *J* = 6 Hz, C^{12} major), 125.2 (d, *J* = 6 Hz, C^{12} minor), 117.8 (C^1 minor), 117.7 (C^1 major), 117.3 (d, *J* = 24 Hz, C^{15} minor), 117.1 (d, *J* = 24 Hz, C^{15} major), 115.2 (C^5 minor), 115.0 (C^5 major), 68.9 (C^3), 54.2 (C^8 minor), 50.2 (C^8 major), 35.6 (d, *J* = 3 Hz, C^9 major), 32.8 (C^9 minor).

δ_F (377 MHz, $CDCl_3$): −104.2 (minor), −104.7 (major).

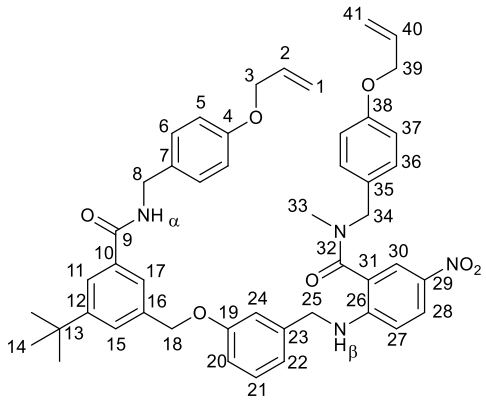
m/z (ES): 344.95 ($[M+H]^+$ $C_{18}H_{18}FN_2O_4$ requires 345.13).

[2]Rotaxane R-ESI-9



In an attempted synthesis of rotaxane **R-ESI-9**, to a solution of half-axle **HA-ESI-7** (62 mg, 0.135 mmol) and 24-crown-8 (**24-c-8**) (47 mg, 0.135 mmol) in dry toluene (0.25 mL) was added Et_3N (118 mg, 0.18 mL, 1.35 mmol) and half-axle **HA-ESI-8** (69 mg, 0.202 mmol). The reaction was stirred for 4 days under argon at room temperature. The reaction mixture was then concentrated *in vacuo* to afford a yellow oil. The crude material was purified by silica gel column chromatography (CH_2Cl_2:CH_3OH 99:1) to afford the corresponding free axle **Ax-ESI-10** and unreacted starting material.

Axle Ax-ESI-10



Axle **Ax-ESI-10** was isolated from the reaction to form rotaxane **R-ESI-9** upon purification of the crude reaction mixture by silica gel column chromatography (CH_2Cl_2:CH_3OH 99:1) as a yellow glassy solid (101 mg, 96%).

***R_f*:** 0.61 [CH_2Cl_2:CH_3OH 98:2].

IR ν_{max} (neat): 3334 (N-H), 2957 (C-H), 2864 (C-H), 1623 (2 x C=O).

δ_H (400 MHz, $CDCl_3$): 8.11-8.07 (2H, m, H^{30} & H^{28}), 7.85 (1H, s, H^{11}), 7.63 (1H, s, H^{17}), 7.56 (1H, s, H^{15}), 7.32-7.28 (3H, m, H^{21} & H^{6}), 7.17 (2H, bs, H^{36}), 6.95-6.88 (7H, m, H^{24}, H^{22}, H^{20}, H^{5} & H^{37}), 6.69 (1H, bs, H^{β}), 6.62 (2H, m, H^{27} & H^{α}), 6.11-5.99 (2H, m, H^{2} & H^{40}), 5.45-5.39 (2H, m, H^{1} & H^{41}), 5.32-5.28 (2H, m, $H^{1'}$ & $H^{41'}$), 5.04 (2H, s, H^{18}) 4.63 (2H, bs, H^{34}), 4.59 (2H, d, *J* = 5.6 Hz, H^{8}), 4.54 (2H, dt, *J* = 5.2 Hz, 1.5 Hz, $H^{3 \text{ or } 39}$), 4.51 (2H, bd, *J* = 5.4 Hz, $H^{3 \text{ or } 39}$), 4.44 (2H, s, H^{25}), 2.99 (3H, s, H^{33}), 1.34 (9H, s, H^{14}).

δ_C (100 MHz, $CDCl_3$): 169.3 (C^{32}), 167.5 (C^{9}), 159.2 (C^{19}), 158.3 ($C^{4 \text{ or } 38}$), 158.1 ($C^{4 \text{ or } 38}$), 152.3 (C^{12}), 151.9 (C^{26}), 138.9 (C^{23}), 136.9 (C^{16}), 136.7, 134.8, 133.2 ($C^{2 \text{ or } 40}$), 133.1 ($C^{2 \text{ or } 40}$), 130.6, 130.1, 129.3 (C^{6}), 129.0 (b, C^{36}), 128.2, 127.8 (C^{15}), 127.4 (C^{28}), 124.8 (C^{30}), 124.2 (C^{11}), 123.1 (C^{17}), 119.7 (C^{22}), 117.8 ($C^{1(')\text{ or } 41(')}$), 117.7 ($C^{1(')\text{ or } 41(')}$), 115.2 ($C^{5 \text{ or } 37}$), 115.0 ($C^{5 \text{ or } 37}$), 114.0 ($C^{20}$), 113.6 ($C^{24}$), 110.9 ($C^{27}$), 69.9 ($C^{18}$), 68.9 ($C^{3}$ & C^{39}), 47.3 (C^{25}), 43.6 (C^{8}), 34.9 (C^{13}), 31.3 (C^{14}).

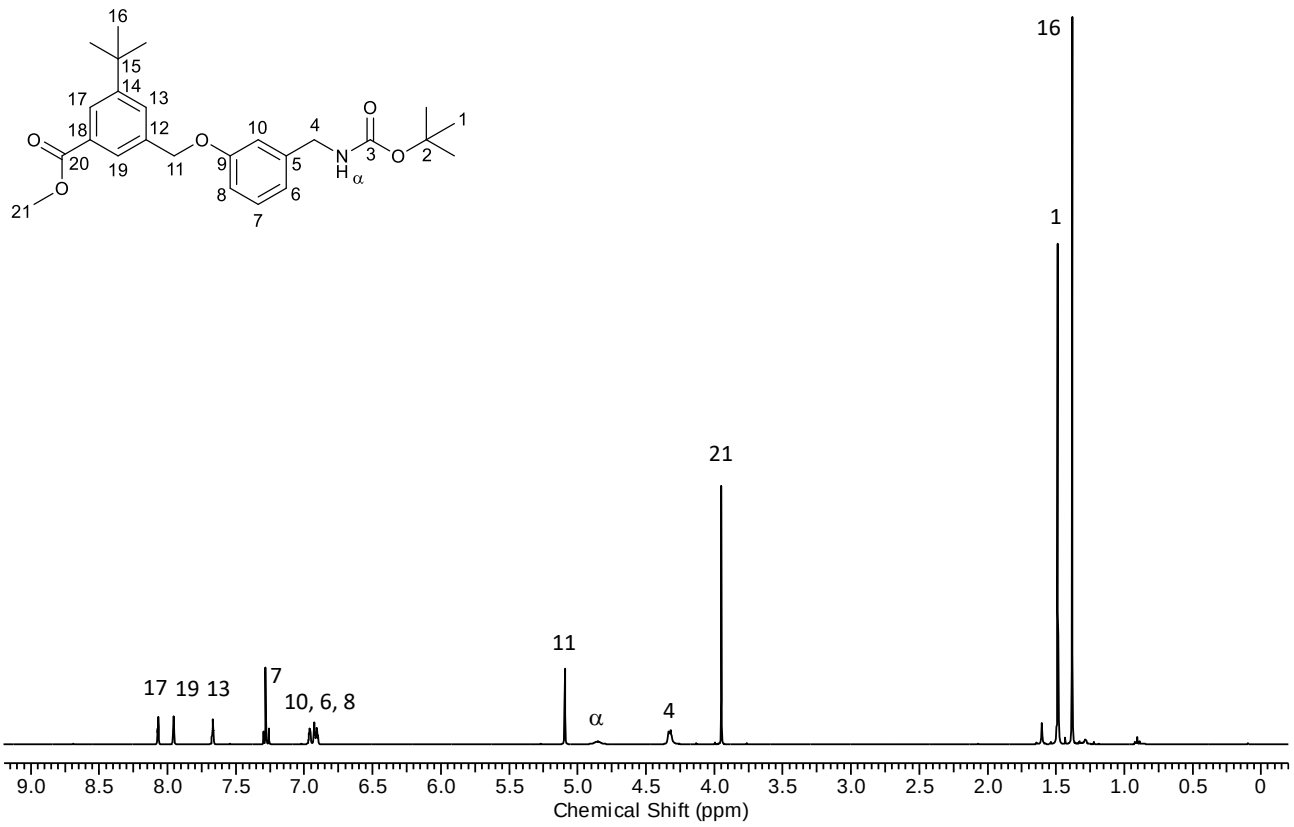
Resonances C^{33} and C^{34} not observed.

m/z (ES): 805.3606 ($[M+Na]^+$ $C_{47}H_{50}N_4NaO_7$ requires 805.3572).

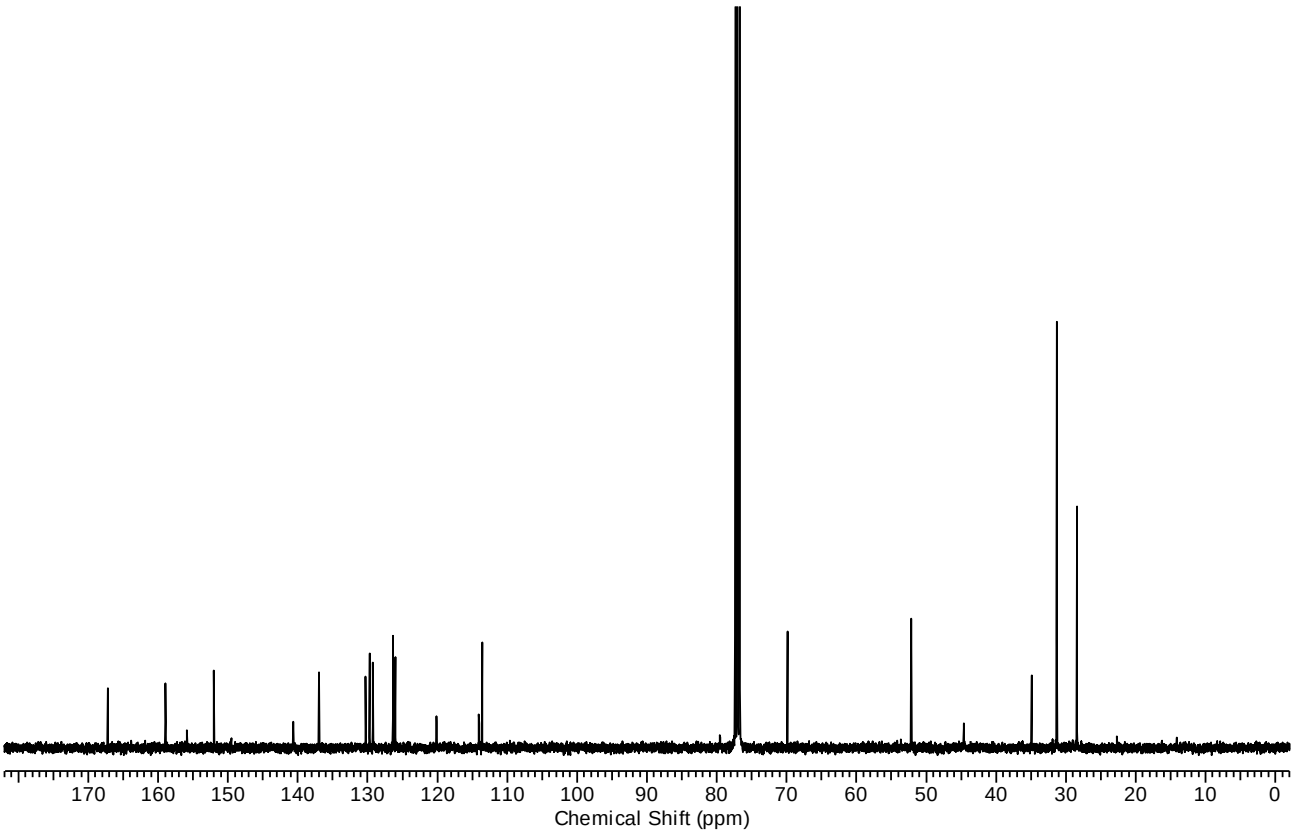
Part 3b: Spectral data for preliminary experimental investigations (Design 1)

Compound ESI-4

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

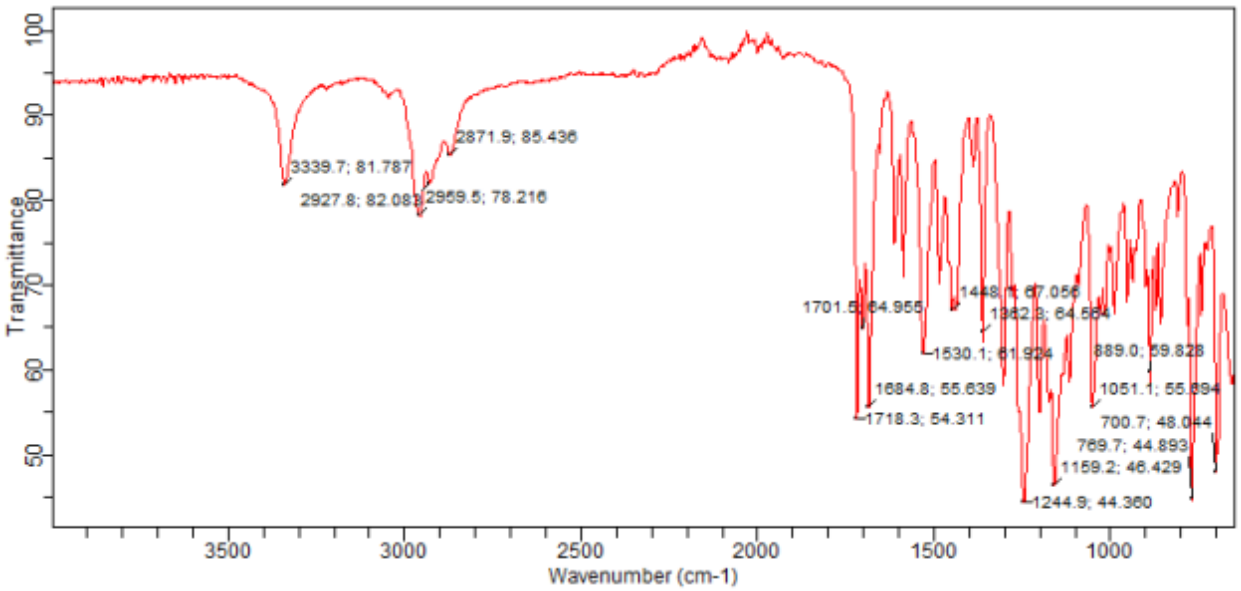


^{13}C NMR ($CDCl_3$, 100 MHz)

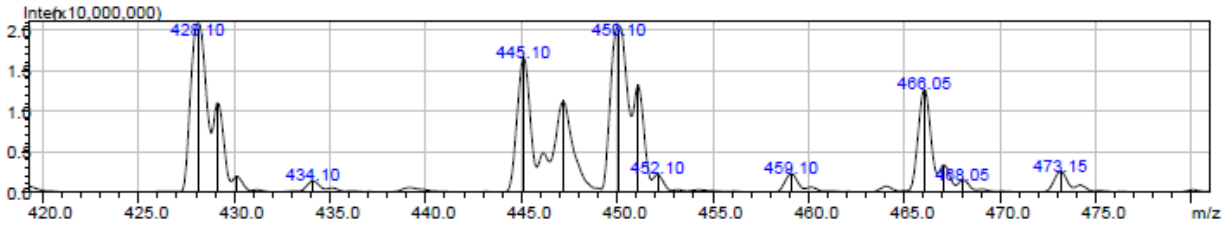


Compound ESI-4

IR (neat)

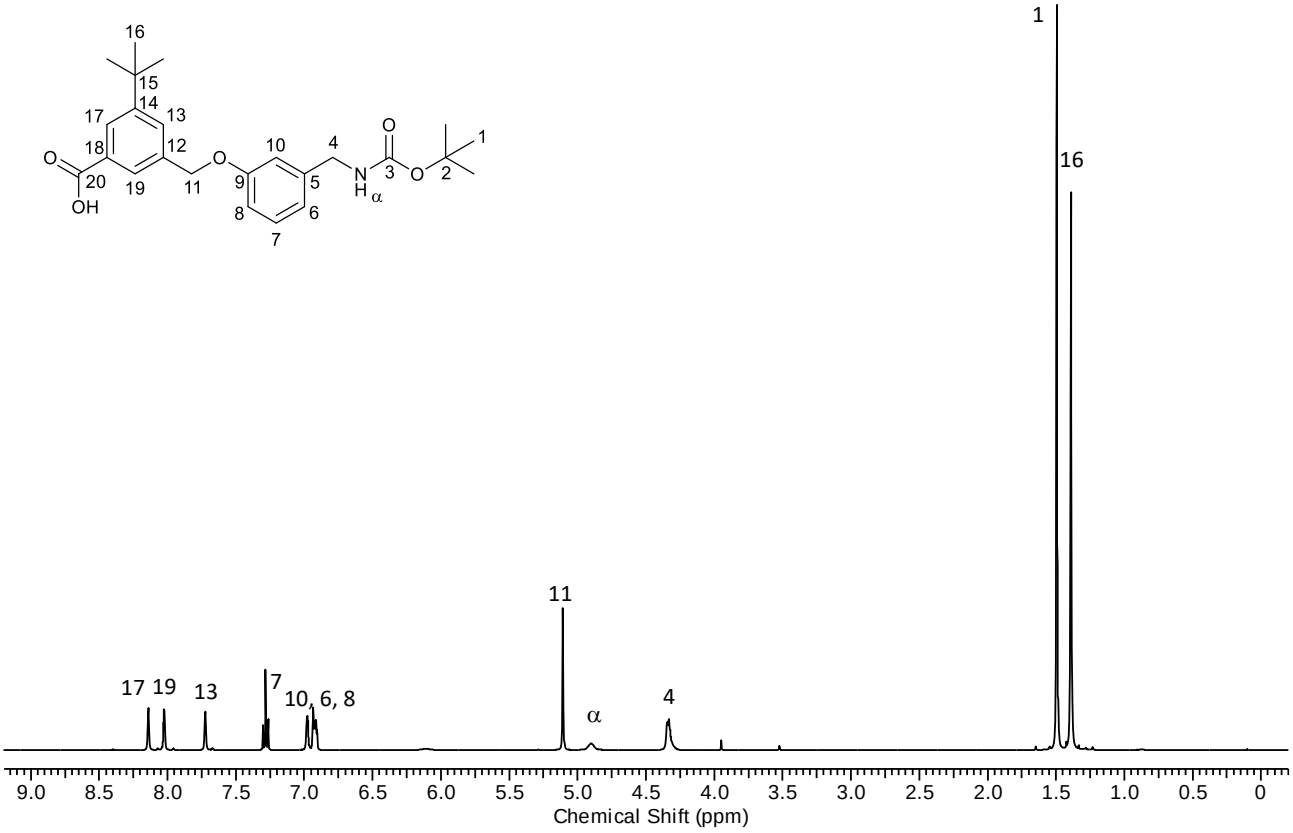


MS (ES +ve)

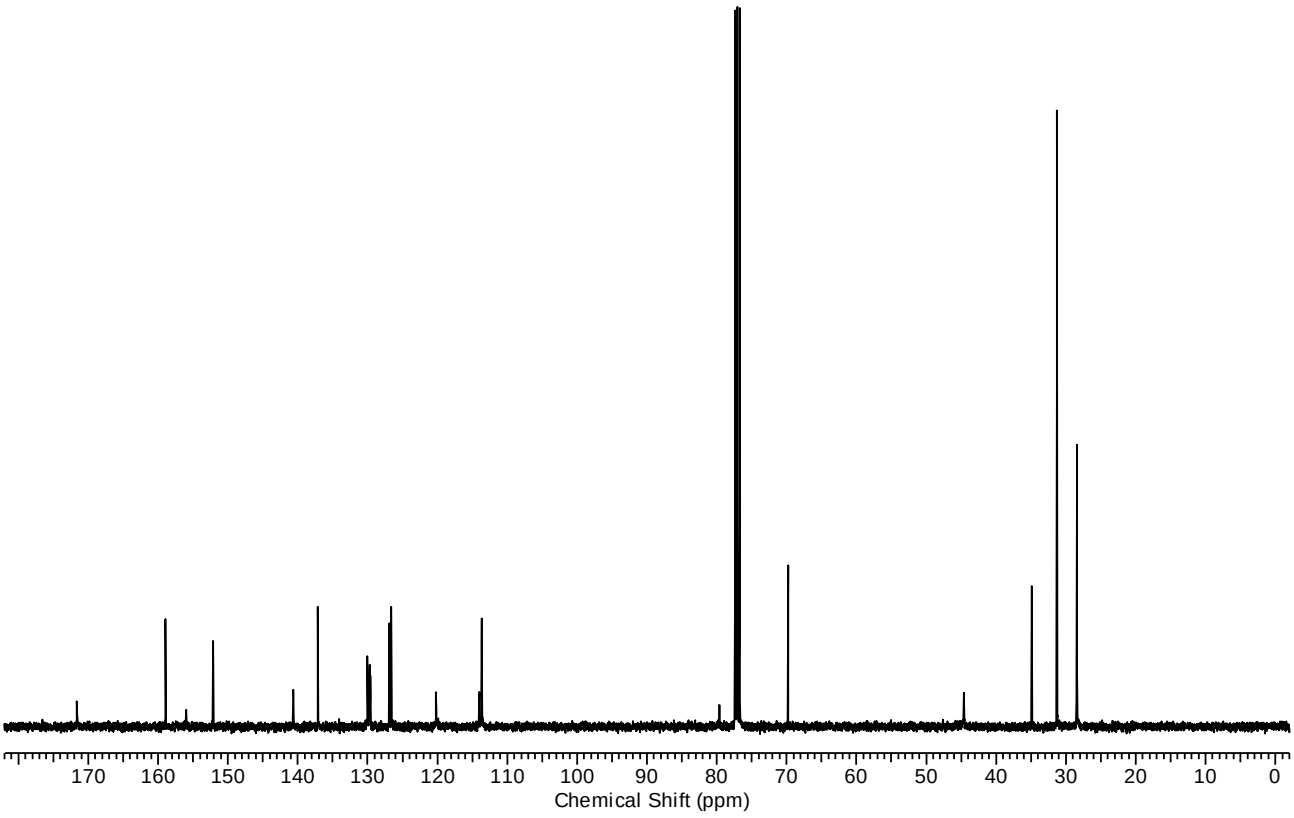


Compound ESI-5

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

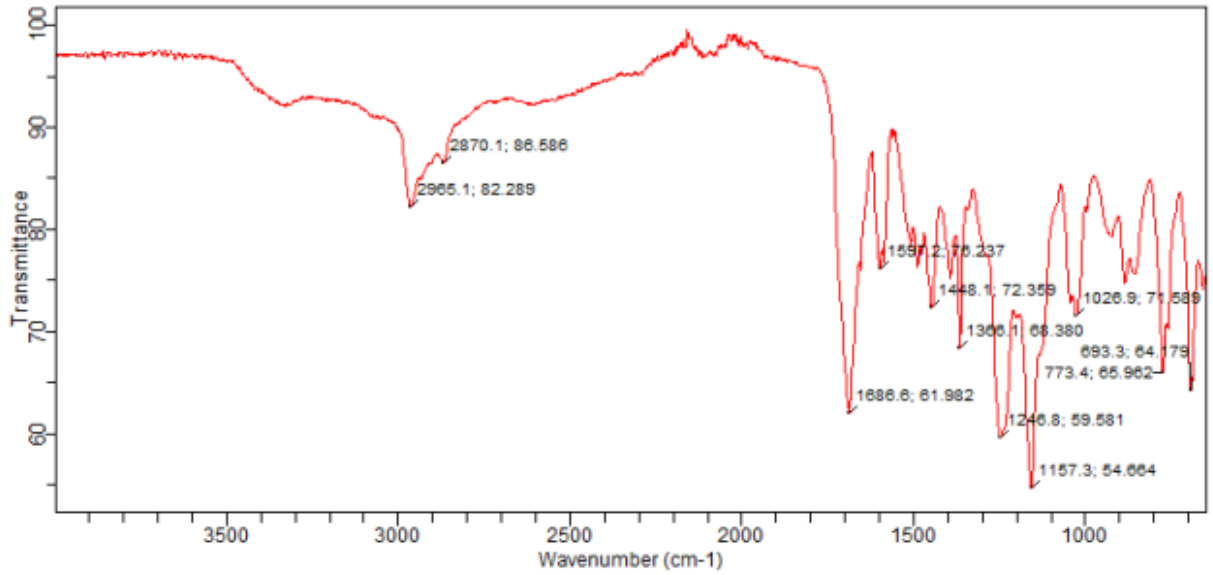


^{13}C NMR ($CDCl_3$, 100 MHz)

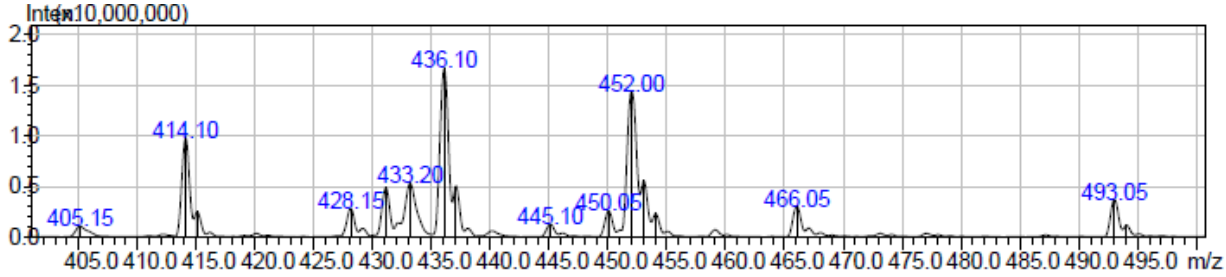


Compound ESI-5

IR (neat)

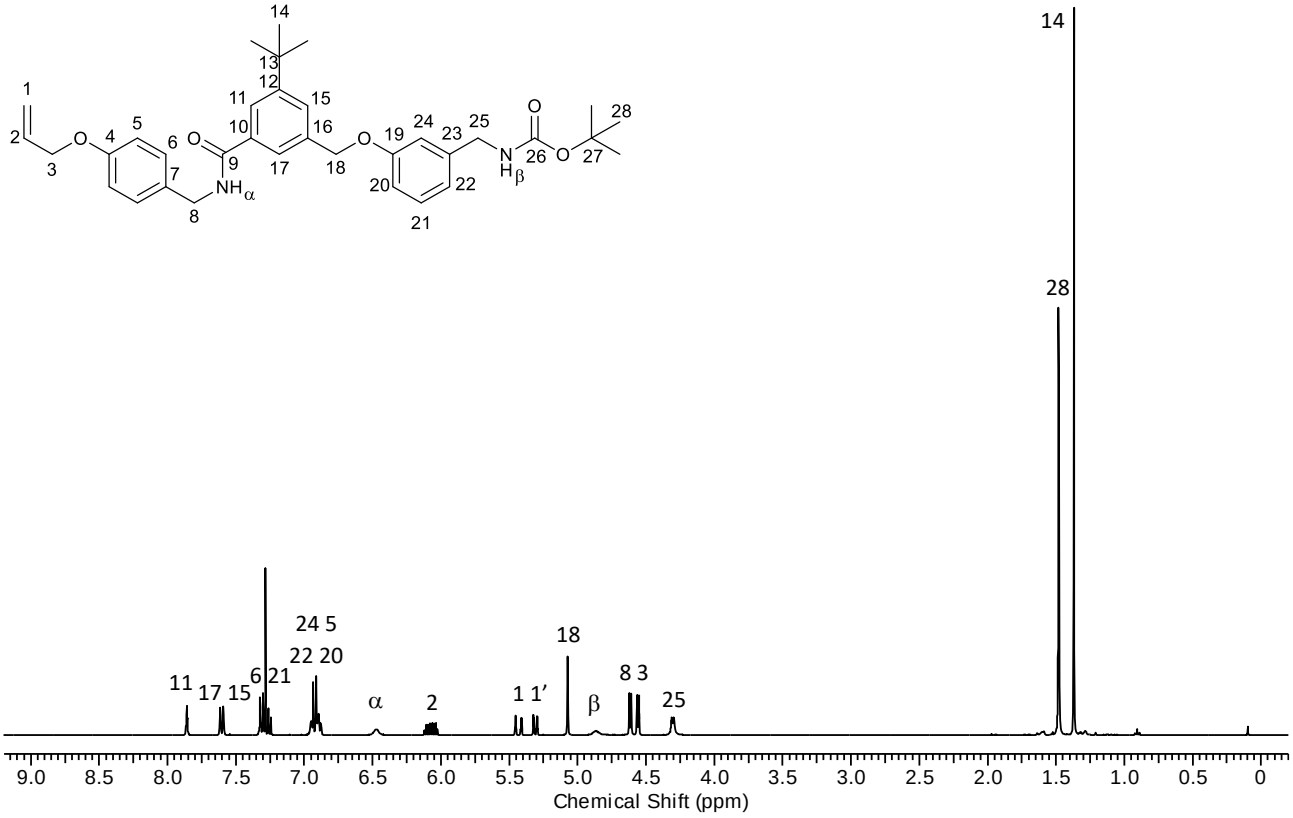


MS (ES +ve)

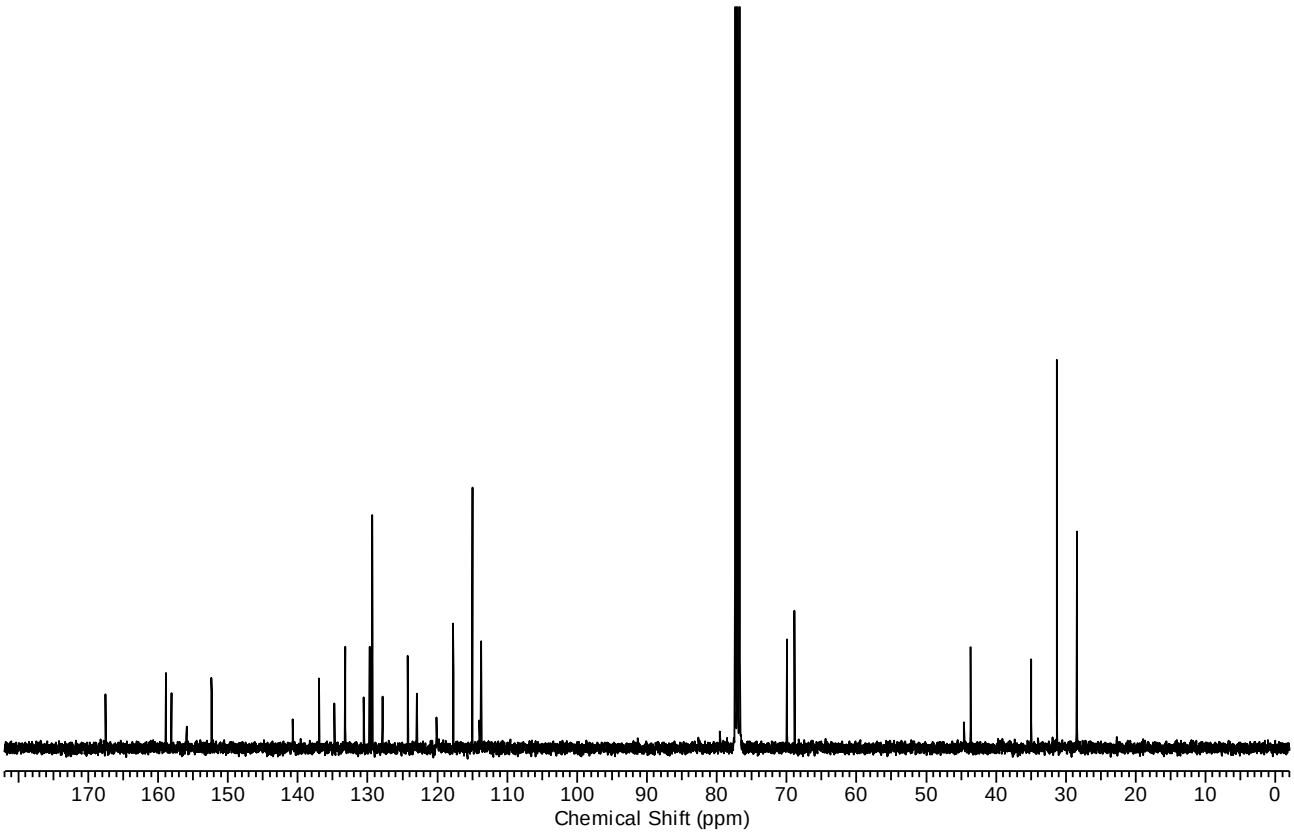


Compound ESI-6

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

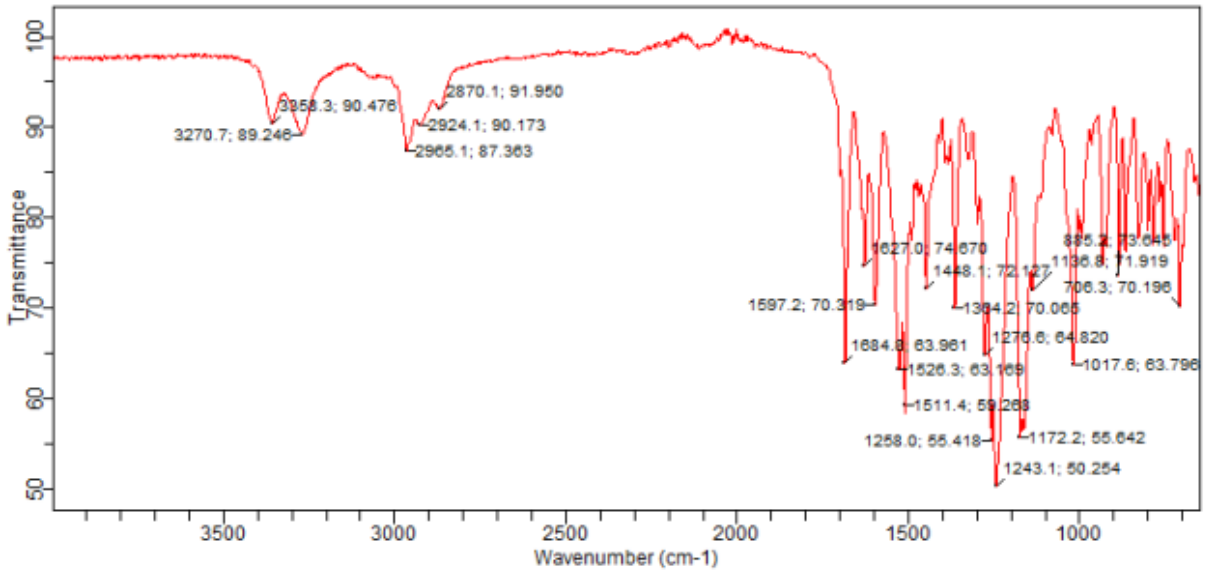


^{13}C NMR ($CDCl_3$, 100 MHz)

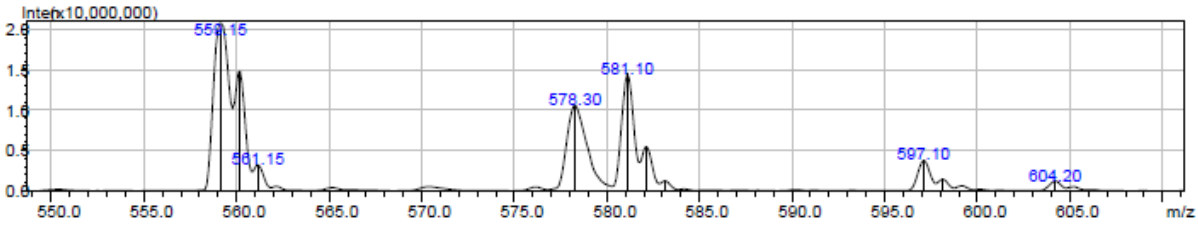


Compound ESI-6

IR (neat)

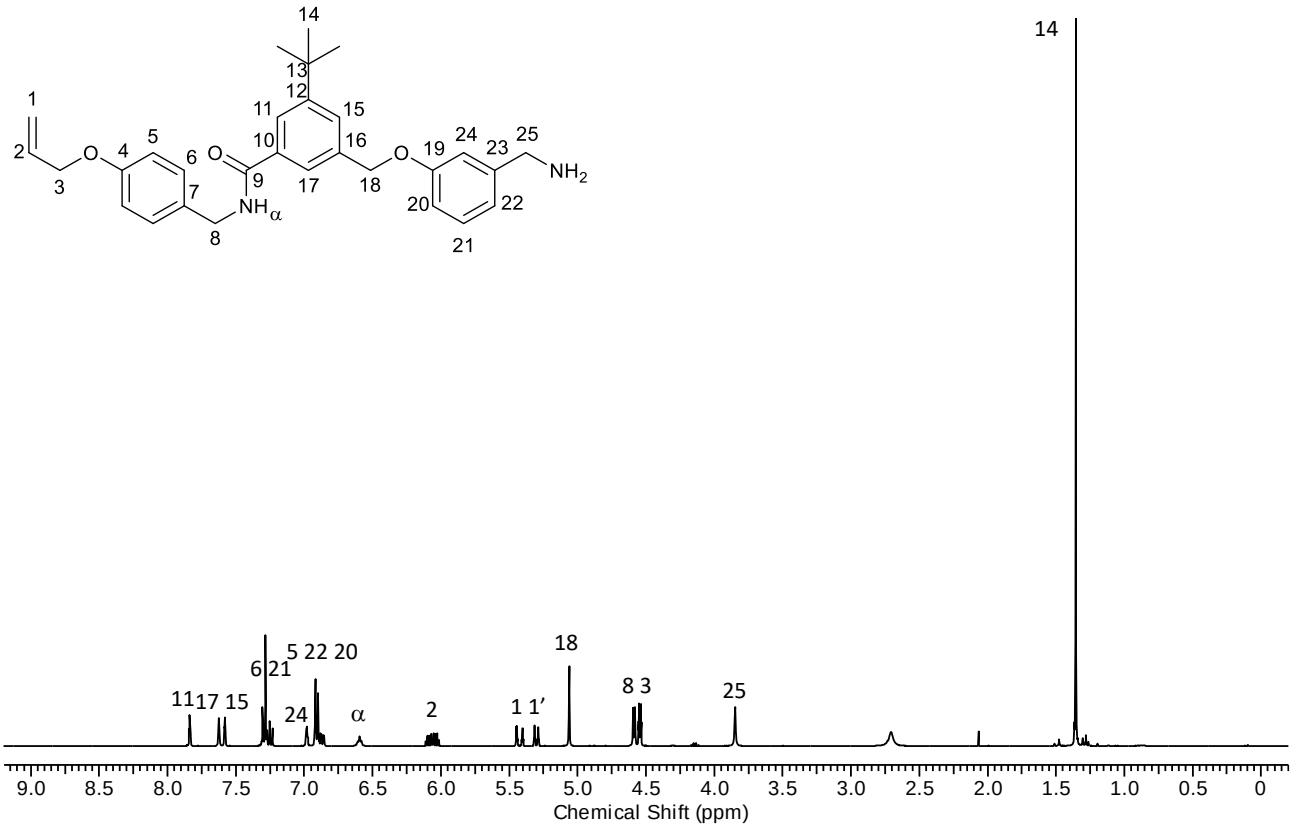


MS (ES +ve)

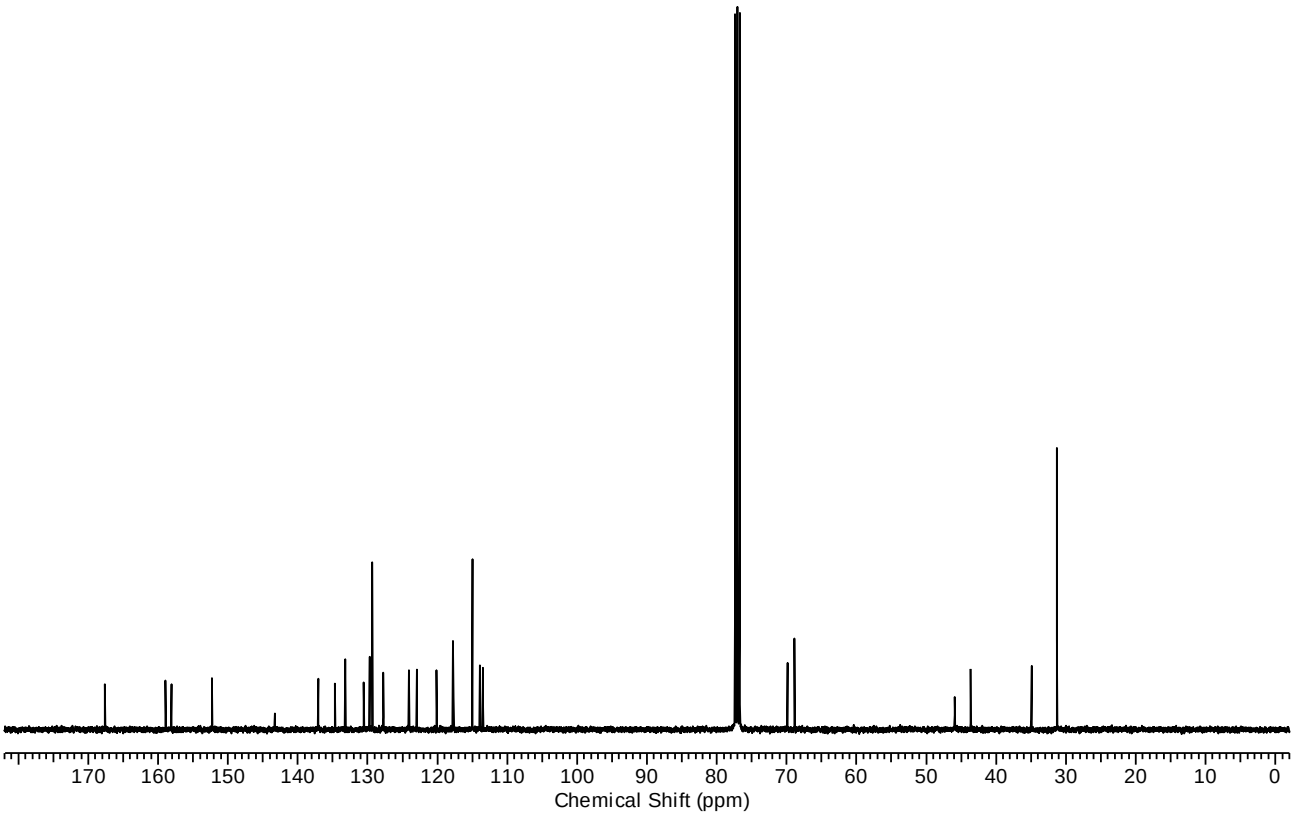


Half Axle HA-ESI-7

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

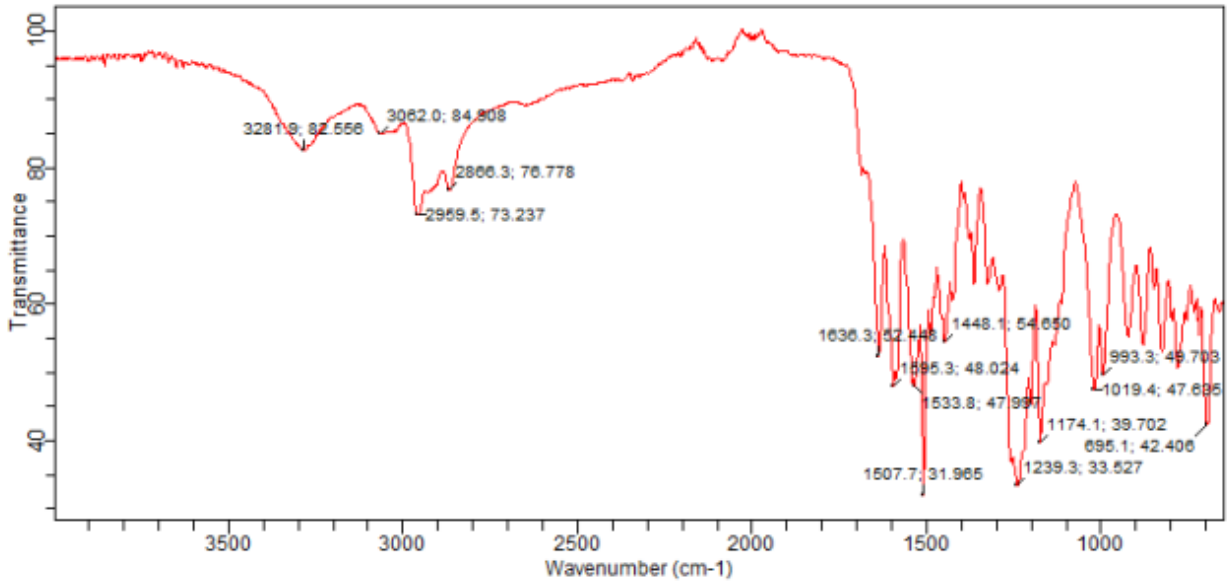


^{13}C NMR ($CDCl_3$, 100 MHz)

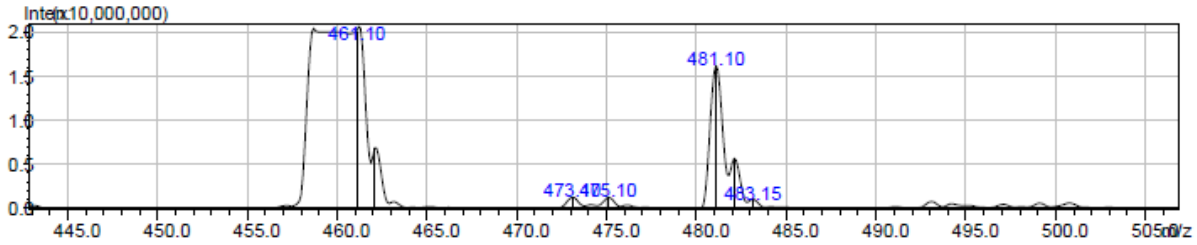


Half Axle HA-ESI-7

IR (neat)

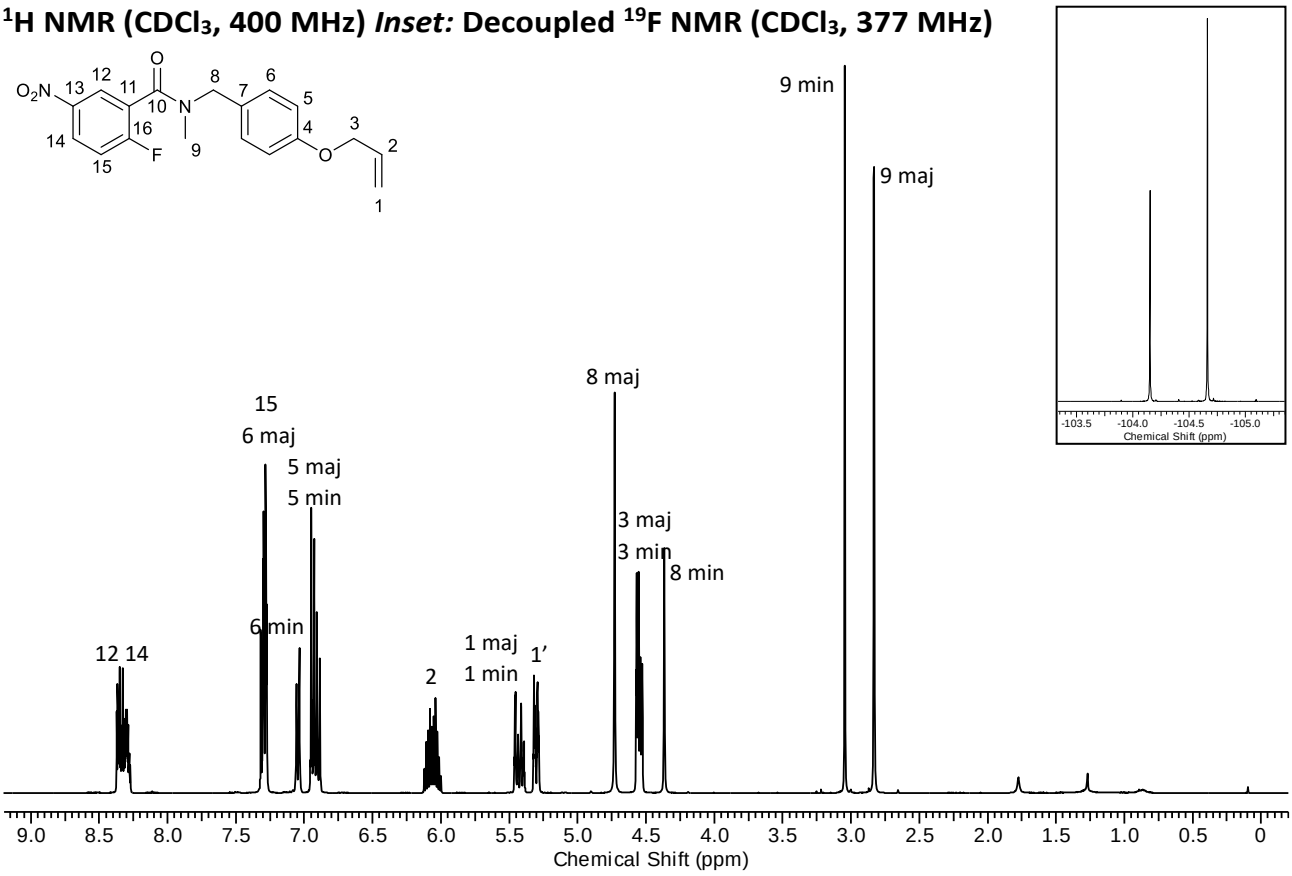


MS (ES +ve)

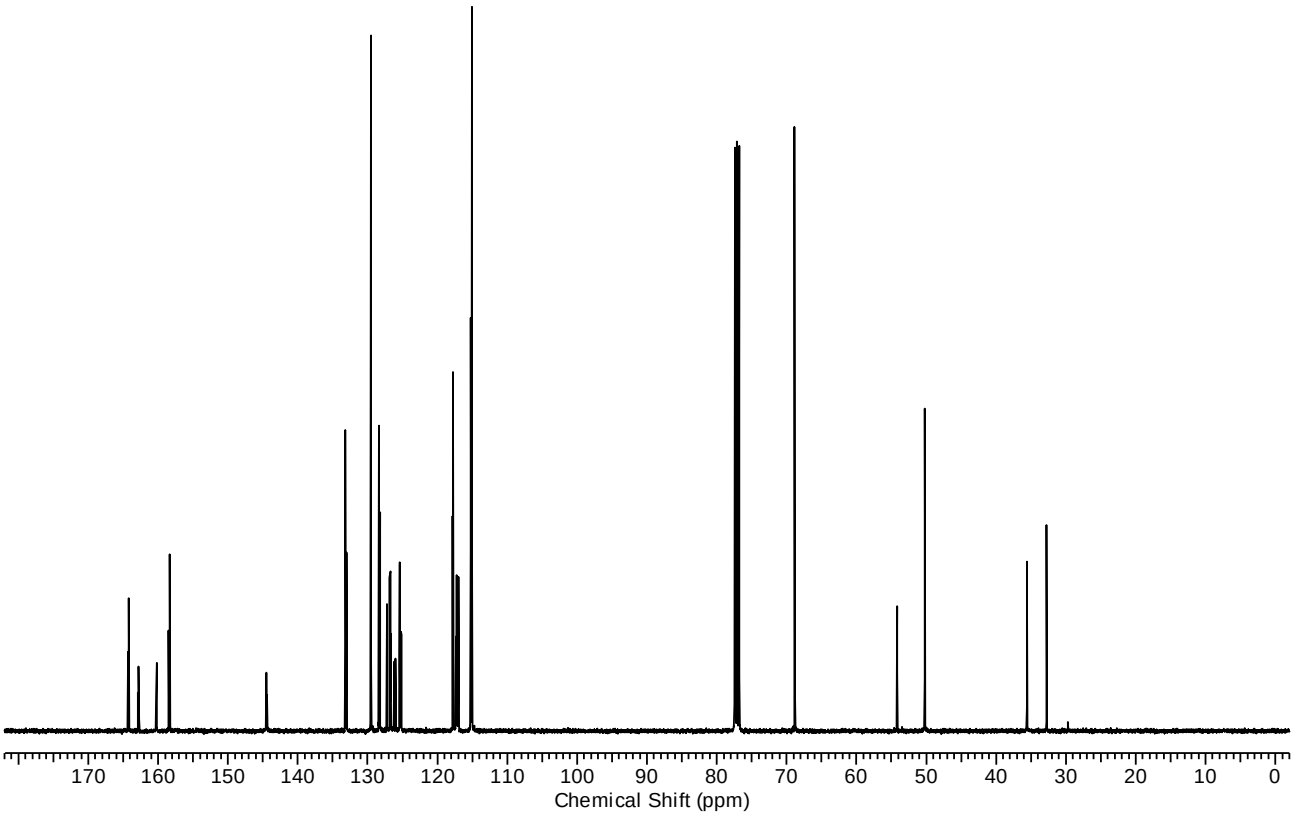


Half Axle HA-ESI-8

^{1}H NMR ($CDCl_3$, 400 MHz) *Inset:* Decoupled ^{19}F NMR ($CDCl_3$, 377 MHz)

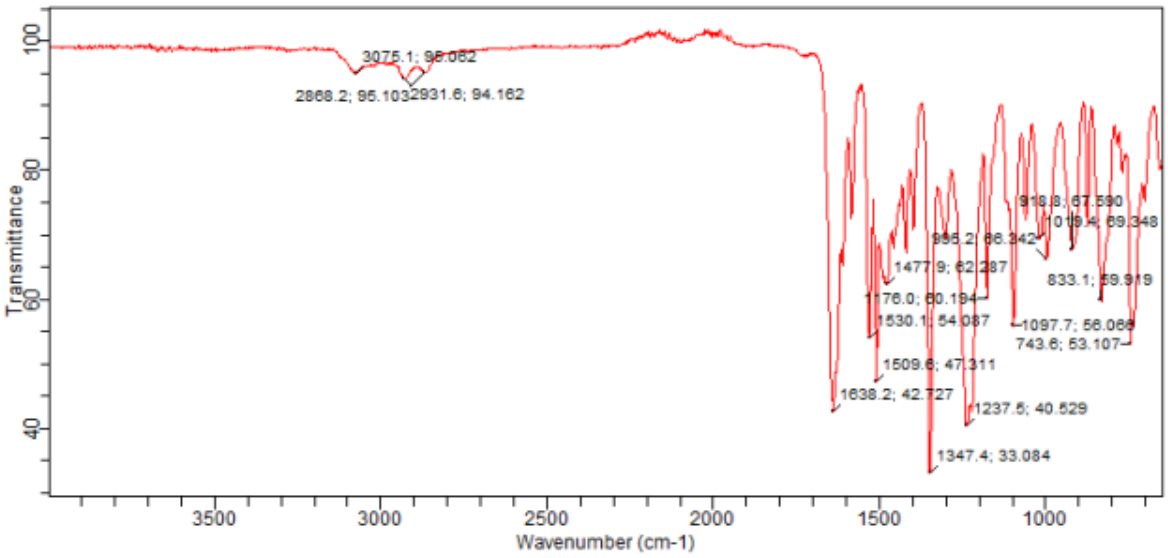


^{13}C NMR ($CDCl_3$, 100 MHz)

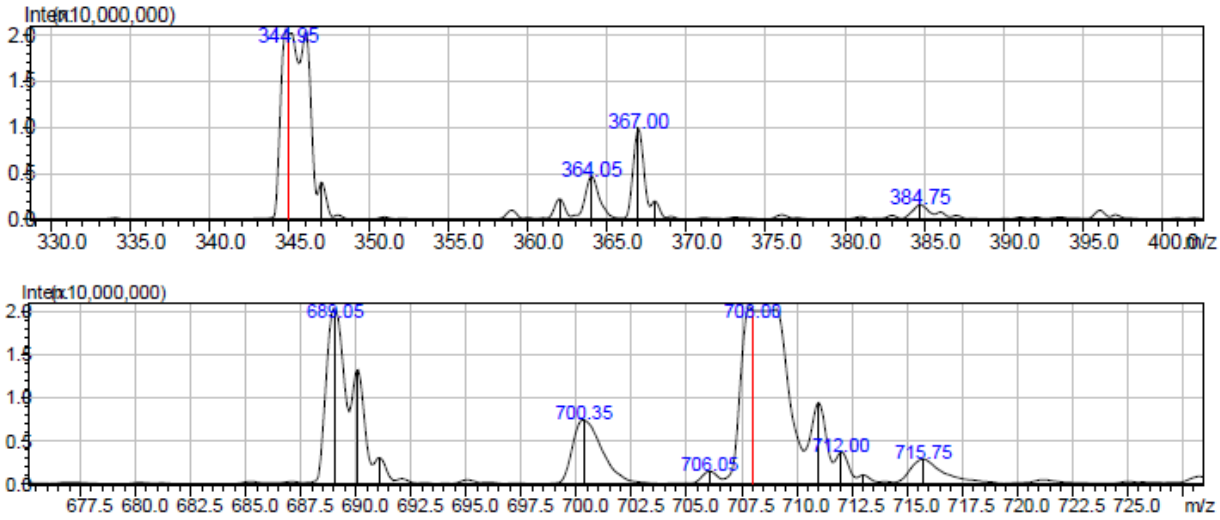


Half Axle HA-ESI-8

IR (neat)

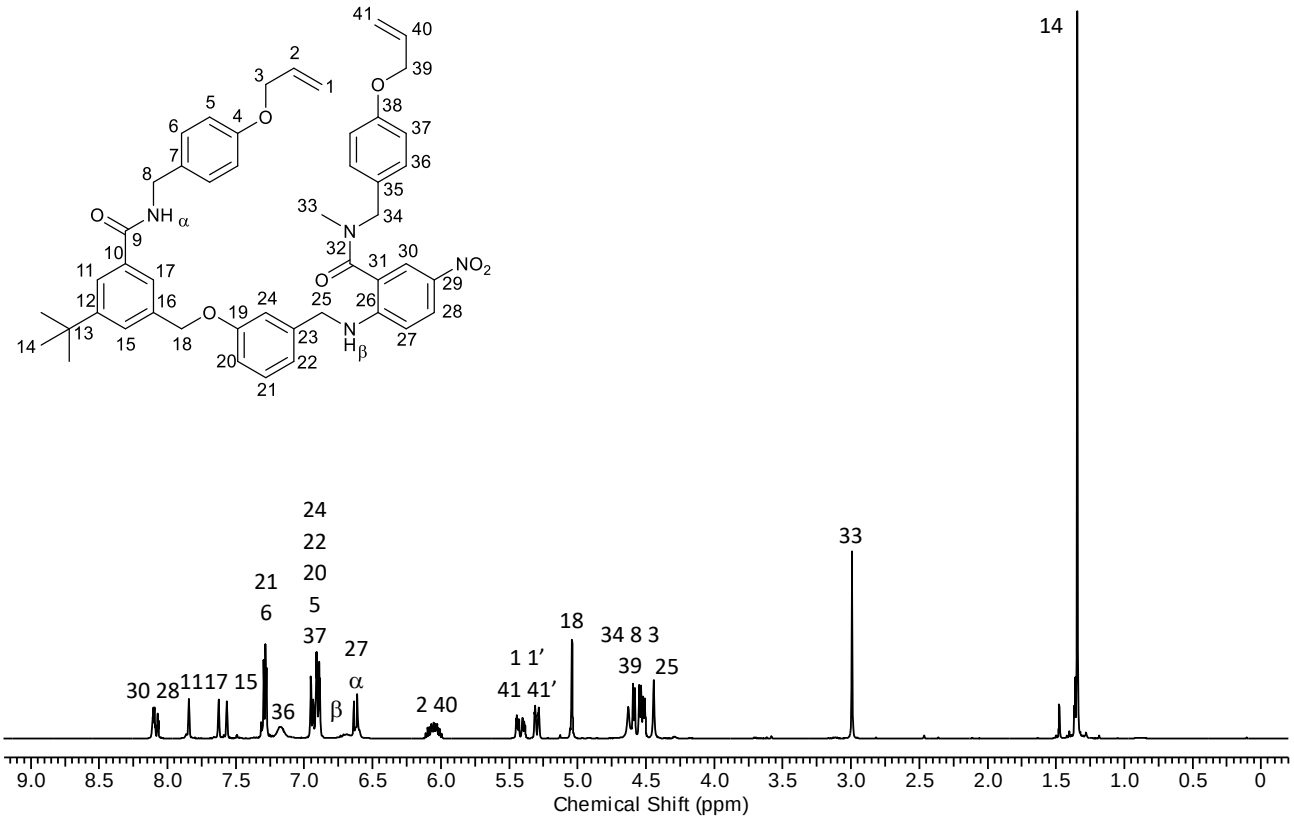


MS (ES +ve)

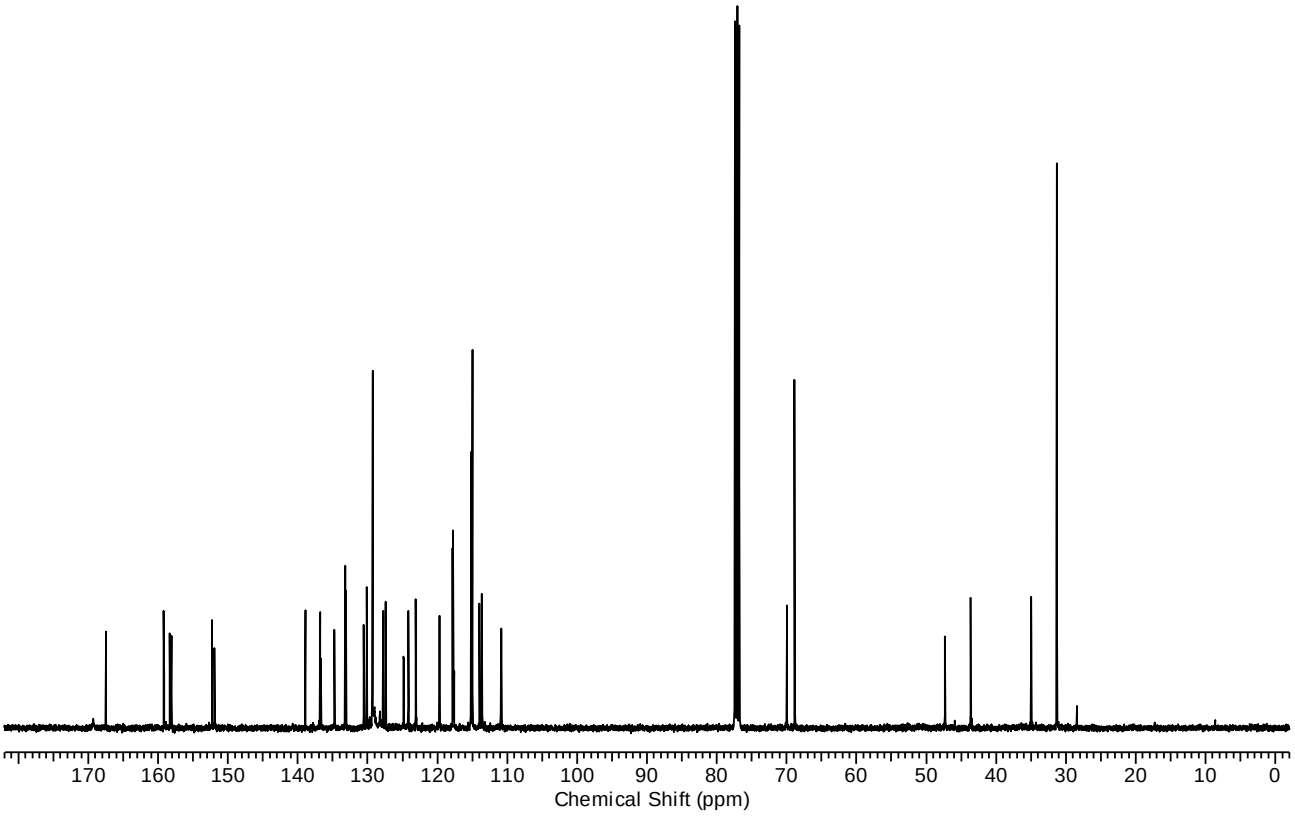


Axle Ax-ESI-10

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

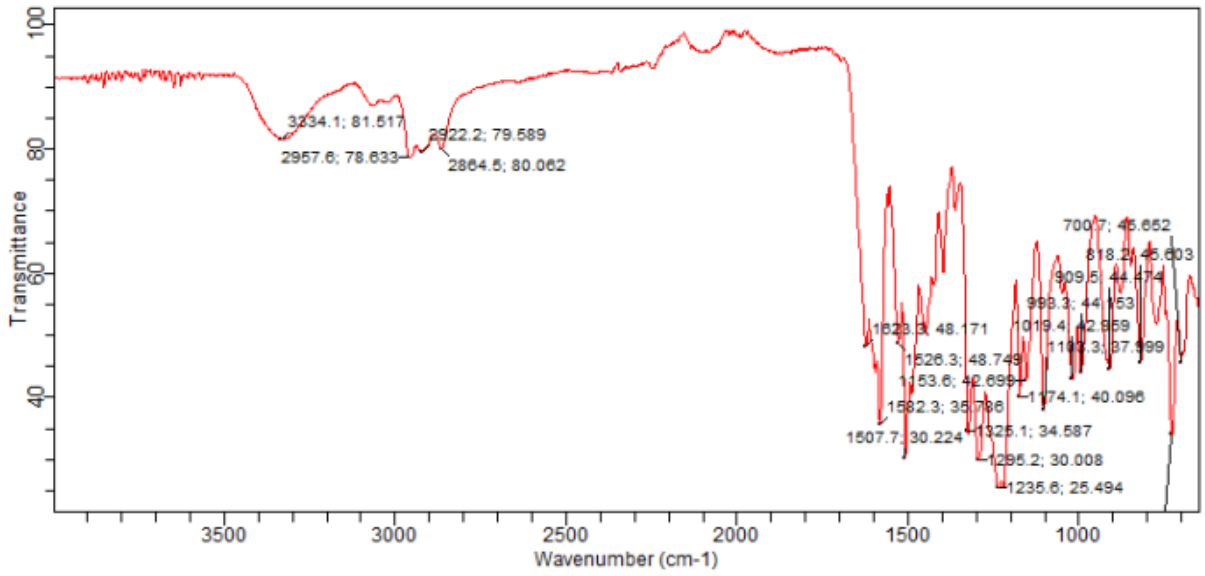


^{13}C NMR ($CDCl_3$, 100 MHz)

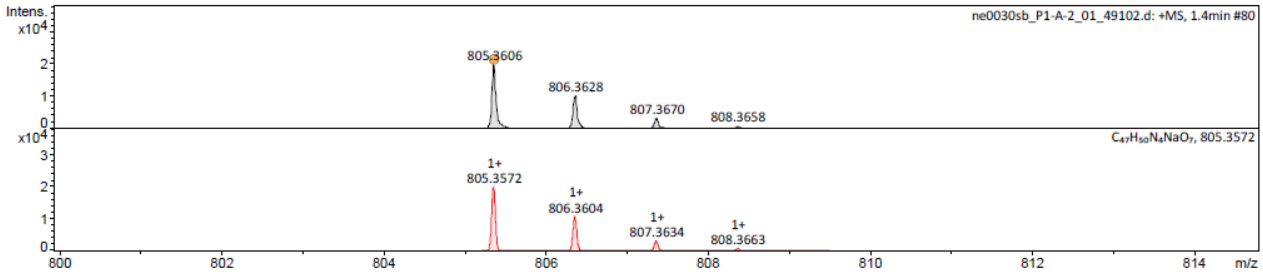


Axle Ax-ESI-10

IR (neat)



MS (ES +ve)

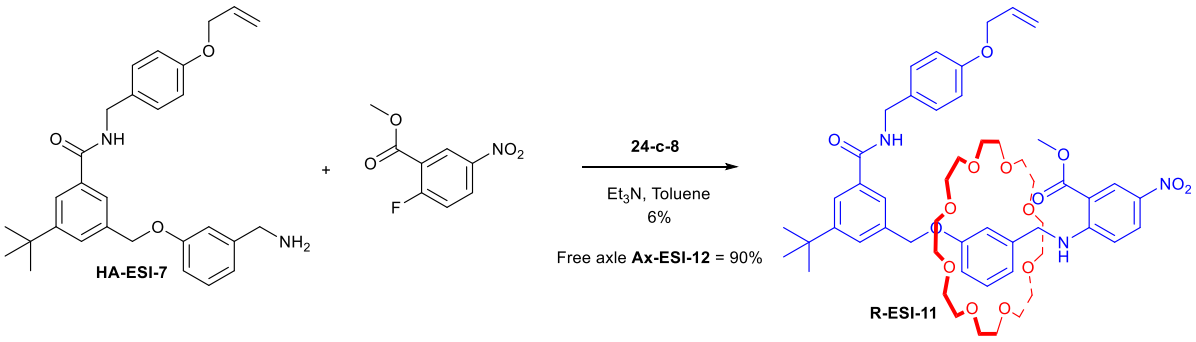


Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
783.3763	1	C47H51N4O7	783.3752	-1.3	-1.1	55.7	-2.9
805.3606	1	C47H50N4NaO7	805.3572	-4.2	-3.4	10.9	-3.2

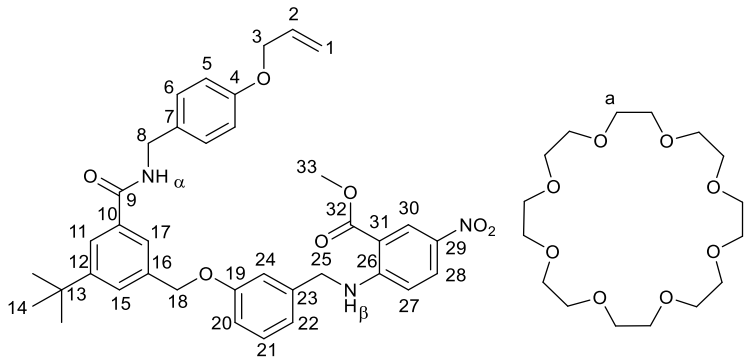
Part 4a: Preliminary experimental investigations (Design 1 - Model)

DESIGN 1 MODEL:

To confirm that the allyl arm of **HA-ESI-8** was not preventing rotaxane formation (through steric clash with **24-c-8**), a simplified model system was investigated. Rotaxane was now formed, but in only very low yield, implying that the presence of the allyl arm on **HA-ESI-8** was not significantly detrimental.



Model [2]Rotaxane R-ESI-11



To a solution of half-axle **HA-ESI-7** (30 mg, 0.065 mmol) and 24-crown-8 (**24-c-8**) (23 mg, 0.065 mmol) in dry toluene (0.15 mL) was added Et_3N (66 mg, 0.1 mL, 0.654 mmol) and 2-fluoro-5-nitro-methylbenzoate (20 mg, 0.0982 mmol). The reaction was stirred for 3 days under argon at room temperature. The reaction mixture was then concentrated *in vacuo* to afford a yellow oil. The crude material was purified by silica gel column chromatography (CH_2Cl_2:CH_3OH 99:1) to afford the *title product* (3.8 mg, 6%) as a yellow oil.

***R*$_f$:** 0.41 [CH_2Cl_2:CH_3OH 99:1].

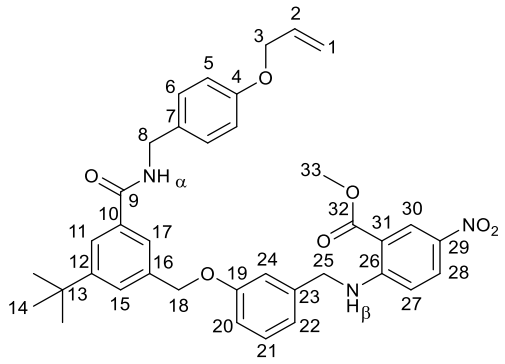
IR ν_{max} (neat): 3337 (N-H), 2868 (C-H), 1690 (C=O), 1650 (C=O).

δ_H (400 MHz, $CDCl_3$): 9.04 (1H, bt, *J* = 5.7 Hz, H^{β}), 8.88 (1H, d, *J* = 2.8 Hz, H^{30}), 8.31 (1H, s, H^{17}), 8.14-8.08 (3H, m, H^{28}, H^{α} & H^{11}), 7.91 (1H, s, H^{15}), 7.31-7.27 (3H, m, H^{21} & H^{6}), 7.25 (1H, bs, H^{24}), 7.18 (1H, d, *J* = 8.0 Hz, H^{20}), 6.88 (1H, d, *J* = 8.0 Hz, H^{22}), 6.85 (2H, d, *J* = 8.8 Hz, H^{5}), 6.70 (1H, d, *J* = 9.8 Hz, H^{27}), 6.10-6.00 (1H, m, H^{2}), 5.46 (2H, s, H^{18}), 5.40 (1H, dq, *J* = 17 Hz, 1.6 Hz, H^{1}), 5.28 (1H, dq, *J* = 11 Hz, 1.5 Hz, $H^{1'}$), 4.58-4.50 (6H, m, H^{8}, H^{25} & H^{3}), 3.92 (3H, s, H^{33}), 3.40-3.31 (16H, m, H^{a}), 3.26-3.18 (16H, m, $H^{a'}$), 1.38 (9H, s, H^{14}).

δ_C (100 MHz, $CDCl_3$): 167.7 (C^{9} & C^{32}), 160.6 (C^{19}), 157.7 (C^{4}), 154.7 (C^{26}), 150.3 (C^{12}), 137.9 (C^{16}), 137.8 (C^{23}), 136.0, 133.3 (C^{2}), 132.7, 131.8 (C^{7}), 131.5 (C^{15}), 129.6 (C^{28}), 129.5 (C^{21}), 129.4 (C^{6}), 129.0 (C^{30}), 126.4 (C^{17}), 124.4 (C^{11}), 118.1 (C^{22}), 117.6 (C^{1}), 114.8 (C^{20}), 114.7 (C^{24}), 114.6 (C^{5}), 111.7 (C^{27}), 109.3, 70.2 (C^{a}), 69.8 (C^{18}), 68.8 (C^{3}), 52.1 (C^{33}), 47.4 (C^{25}), 43.2 (C^{8}), 34.9 (C^{13}), 31.5 (C^{14}).

m/z (ES): 1012.4779 ($[M+Na]^+$ $C_{25}H_{33}NO_5Na$ requires 1012.4777).

Model Axle Ax-ESI-12



Axle **Ax-ESI-12** was isolated from the reaction to form rotaxane **R-ESI-11** upon purification of the crude reaction mixture by silica gel column chromatography as a yellow glassy solid (37 mg, 90%).

***R*$_f$:** 0.62 [CH_2Cl_2:CH_3OH 99:1].

IR ν_{max} (neat): 3326 (N-H), 2953 (C-H), 2864 (C-H), 1690 (C=O), 1640 (C=O).

δ_H (400 MHz, $CDCl_3$): 9.00 (1H, bt, *J* = 5.8 Hz, H^{β}), 8.88 (1H, d, *J* = 2.7 Hz, H^{30}), 8.14 (1H, dd, *J* = 9.4 Hz, 2.7 Hz, H^{28}), 7.83 (1H, t, *J* = 1.7 Hz, H^{11}), 7.64 (1H, bs, H^{17}), 7.57 (1H, bs, H^{15}), 7.33-7.28 (3H, m, H^{21} & H^{6}), 6.96-6.89 (5H, m, H^{20}, H^{22}, H^{24} & H^{5}), 6.64 (1H, d, *J* = 9.4 Hz, H^{27}), 6.50 (1H, bt, *J* = 5.5 Hz, H^{α}), 6.11-6.02 (1H, m, H^{2}), 5.43 (1H, dq, *J* = 17 Hz, 1.6 Hz, H^{1}), 5.30 (1H, qd, *J* = 11 Hz, 1.5 Hz, $H^{1'}$), 5.06 (2H, s, H^{18}), 4.60 (2H, d, *J* = 5.5 Hz, H^{8}), 4.55 (2H, dt, *J* = 5.2 Hz, 1.5 Hz, H^{3}), 4.52 (2H, d, *J* = 5.8 Hz, H^{25}), 3.94 (3H, s, H^{33}), 1.35 (9H, s, H^{14}).

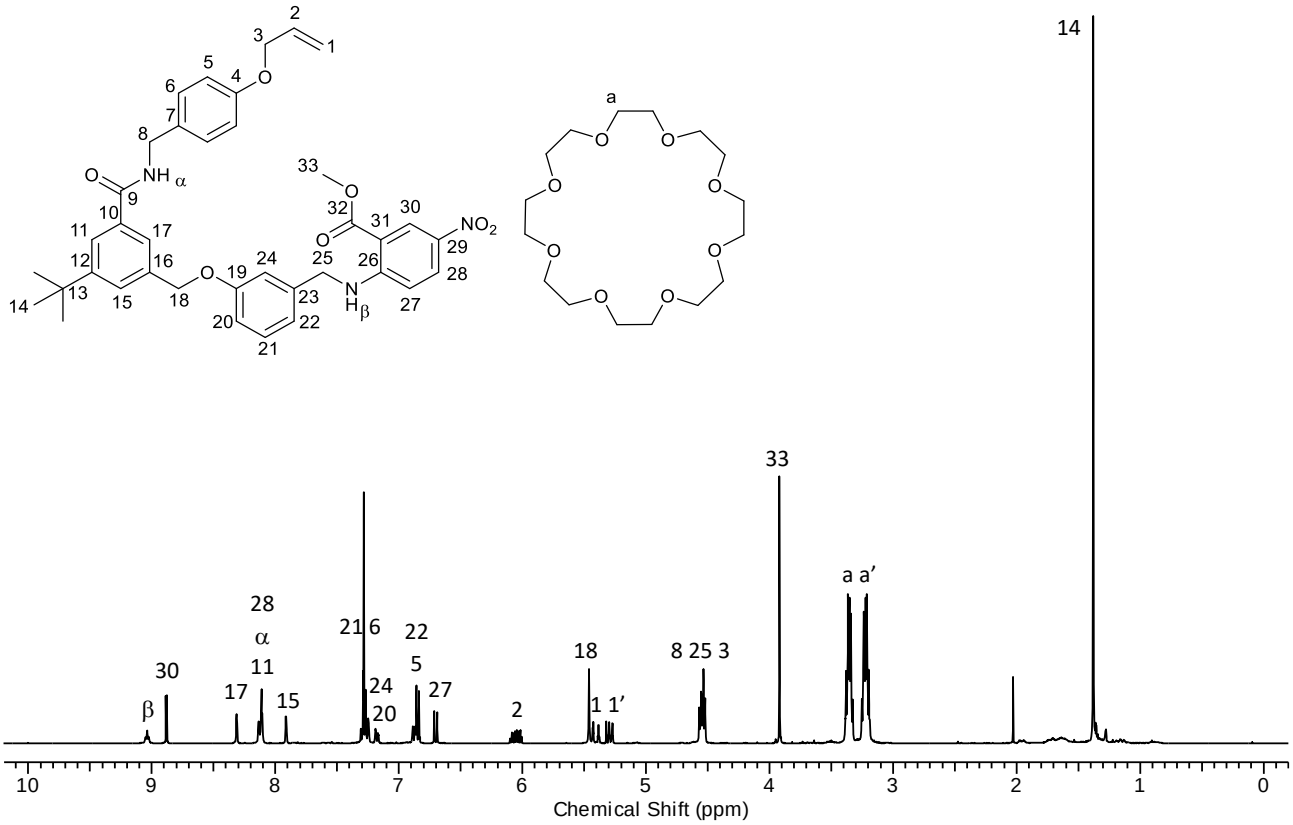
δ_C (100 MHz, $CDCl_3$): 167.9 (C^{32}), 167.4 (C^{9}), 159.1 (C^{19}), 158.1 (C^{4}), 154.5 (C^{26}), 152.3 (C^{12}), 138.6 (C^{23}), 136.8 (C^{16}), 136.3, 134.7, 133.2 (C^{2}), 130.5 (C^{7}), 130.2 (C^{21}) 129.8 (C^{28}), 129.3 (C^{6}), 129.0 (C^{30}), 127.8 (C^{15}), 124.0 (C^{11}), 123.1 (C^{17}), 119.7 ($C^{20 \text{ or } 22 \text{ or } 24}$), 117.7 ($C^{1}$), 115.0 ($C^{5}$), 113.8 ($C^{20 \text{ or } 22 \text{ or } 24}$), 113.7 ($C^{20 \text{ or } 22 \text{ or } 24}$), 111.4 ($C^{27}$), 109.3, 70.0 ($C^{18}$), 68.9 ($C^{3}$), 52.2 ($C^{33}$), 47.0 ($C^{25}$), 43.7 ($C^{8}$), 34.9 ($C^{13}$), 31.3 ($C^{14}$).

m/z (ES): 660.2855 ($[M+Na]^+$ $C_{37}H_{39}N_3NaO_7$ requires 660.2680).

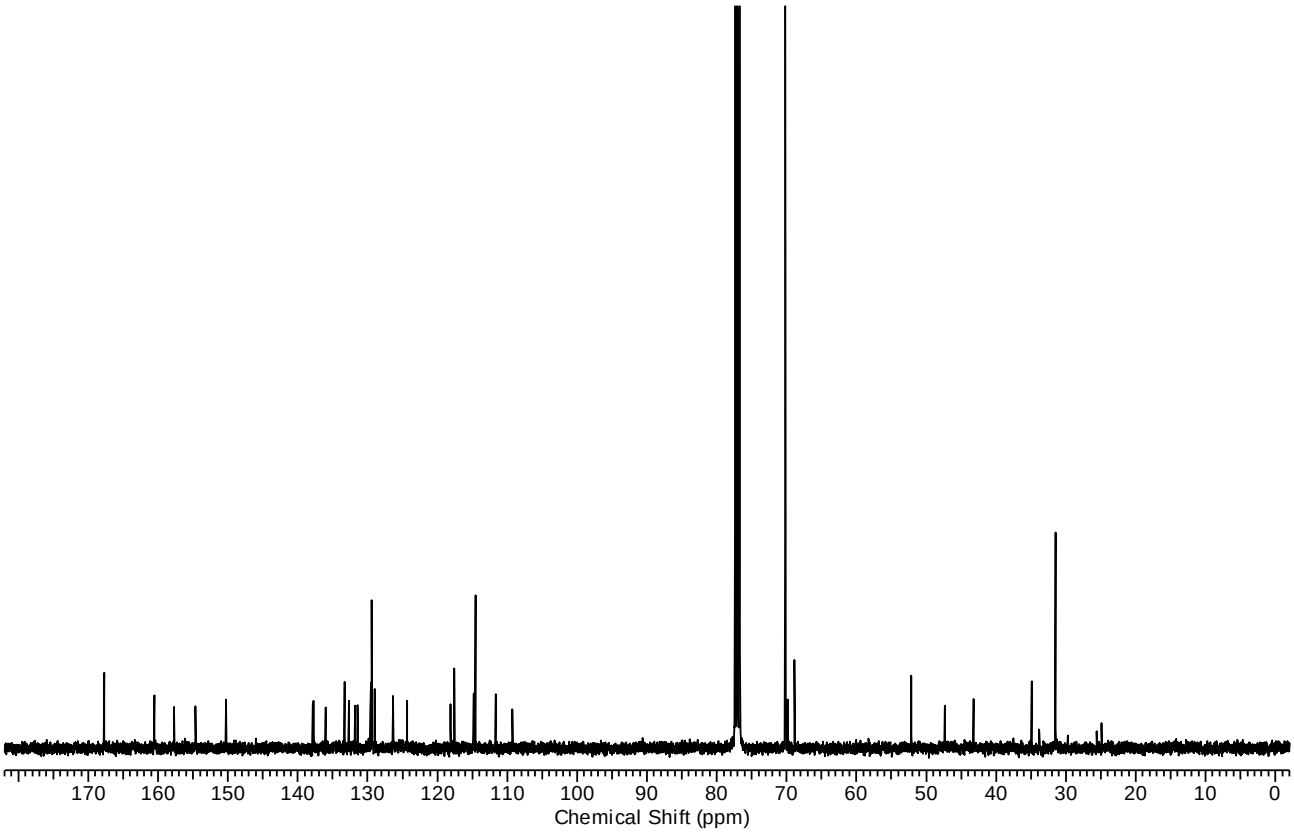
Part 4b: Spectral data for preliminary experimental investigations (Design 1 - Model)

Model [2]Rotaxane R-ESI-11

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

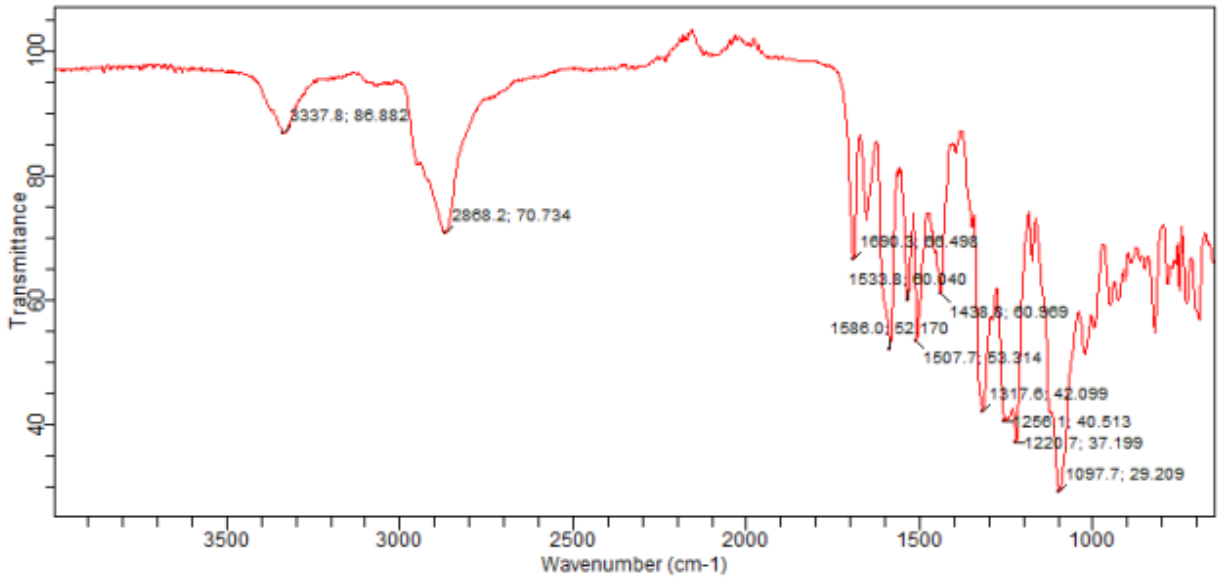


^{13}C NMR ($CDCl_3$, 100 MHz)

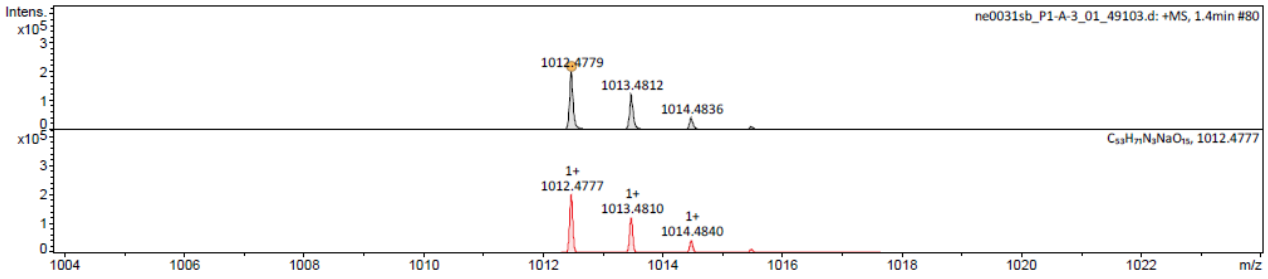


Model [2]Rotaxane R-ESI-11

IR (neat)



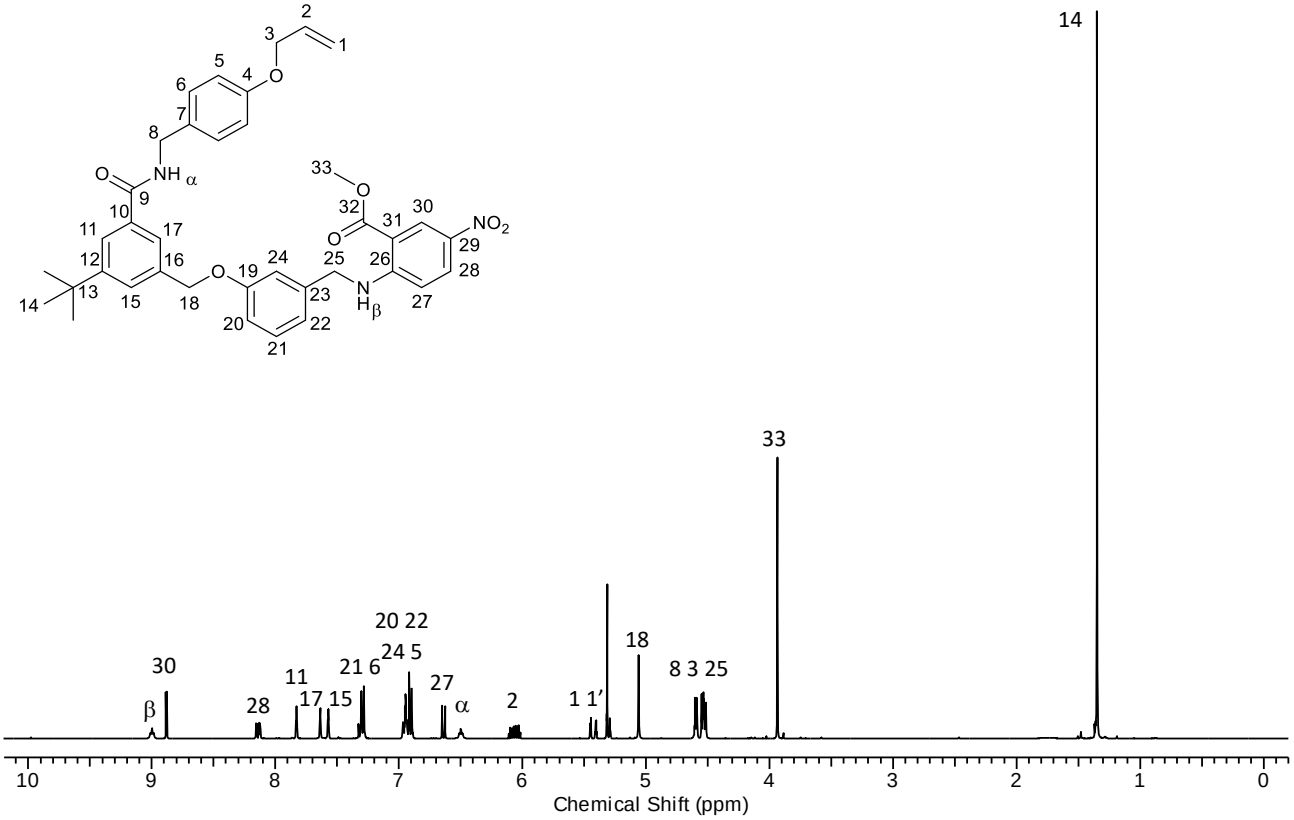
MS (ES +ve)



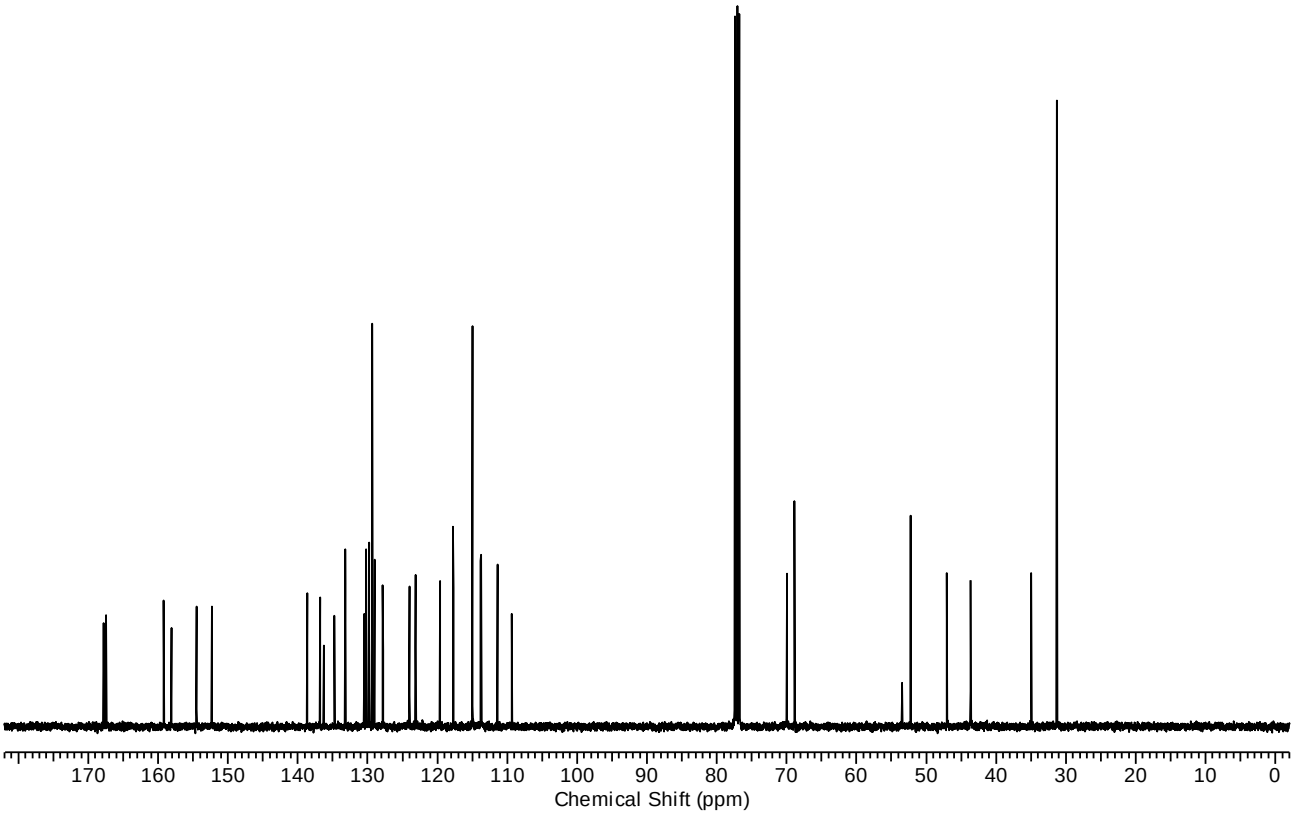
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
1012.4779	1	C53H71N3NaO15	1012.4777	-0.2	-0.2	7.8	-0.4

Model Axle Ax-ESI-12

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

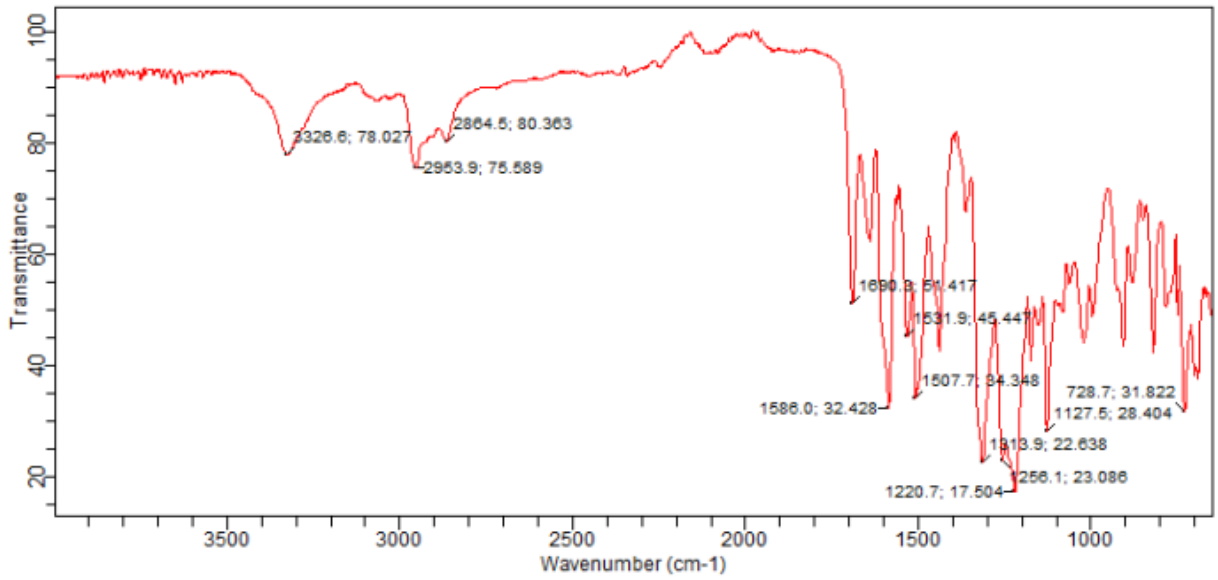


^{13}C NMR ($CDCl_3$, 100 MHz)

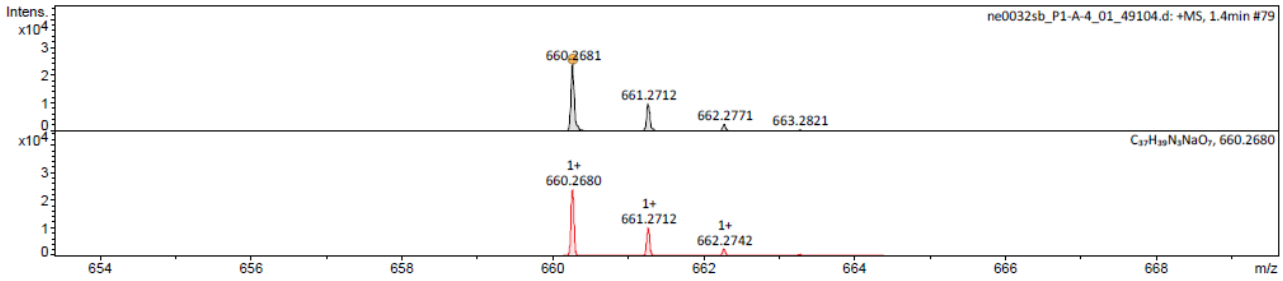


Model Axle R-ESI-12

IR (neat)



MS (ES +ve)

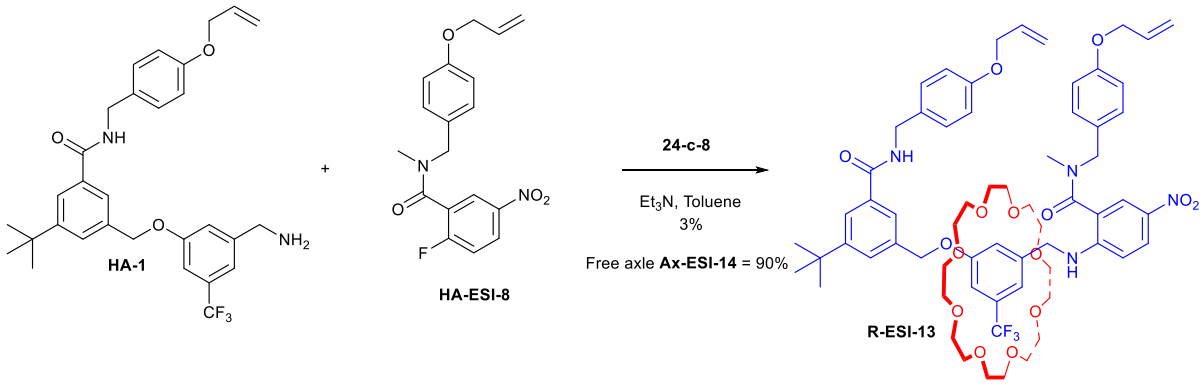


Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
638.2855	1	C37H40N3O7	638.2861	0.9	0.6	69.0	1.0
660.2681	1	C37H39N3NaO7	660.2680	-0.1	-0.1	7.0	-2.1

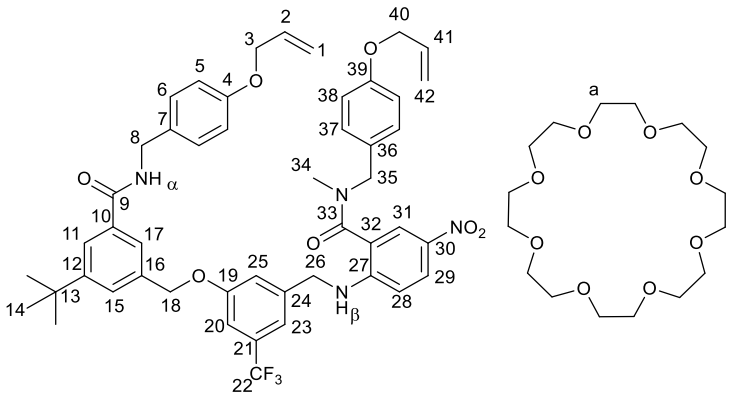
Part 5a: Preliminary experimental investigations (Design 2)

DESIGN 2:

Considering axle formation was the dominant reaction pathway in the above preliminary experimental investigations, it was hypothesized that the nucleophilicity of the benzyl amine needed to be reduced to allow for rotaxane formation. An electron withdrawing trifluoromethyl group was therefore included. However, only very low yield of rotaxane formation was observed. At this point, the decision was made to switch to the amide formation variant of CEATS as described in the main article.



[2]Rotaxane R-ESI-13



To a solution of half-axle **HA-1** (81 mg, 0.155 mmol) and 24-crown-8 (**24-c-8**) (50 mg, 0.141 mmol) in dry toluene (0.4 mL) was added Et_3N (142 mg, 0.20 mL, 1.41 mmol) and half-axle **HA-ESI-8** (72 mg, 0.211 mmol). The reaction was stirred for 4 days under argon at room temperature. The reaction mixture was then concentrated *in vacuo* to afford a yellow oil. The crude material was purified by silica gel column chromatography (CH_2Cl_2:CH_3OH 99.25:0.75-99:1) to afford the *title product* (5.9 mg, 3%) as a yellow oil.

***R_f*:** 0.42 [CH_2Cl_2:CH_3OH 99:1].

IR ν_{max} (neat): 3337 (N-H), 2873 (C-H), 1634 (C=O).

δ_H (400 MHz, $CDCl_3$): 8.14 (1H, dd, *J* = 9.5 Hz, 2.5 Hz, H^{29}), 8.09-8.08 (2H, m, inc H^{25}), 8.01 (1H, bs), 7.85 (1H, t, *J* = 1.6 Hz, H^{11}), 7.66 (1H, s, H^{17}), 7.60 (1H, s, H^{15}), 7.30 (2H, d, *J* = 8.4 Hz, H^{6}), 7.17 (1H, bs, H^{20}), 7.08 (1H, d, *J* = 9.5 Hz, H^{28}), 6.91 (4H, app d, H^{5} & H^{38}), 6.59 (1H, bs, H^{α}), 6.13-6.01 (2H, m, H^{2} & H^{41}), 5.46-5.39 (2H, m, H^{1} & H^{42}), 5.33-5.28 (2H, m, $H^{1'}$ & $H^{42'}$), 5.23 (2H, s, H^{18}), 4.76 (2H, bs, H^{26}), 4.60 (2H, d, *J* = 5.6 Hz, H^{8}), 4.57-4.53 (6H, m H^{35}, H^{3} & H^{40}), 3.45-3.41 (16H, m, H^{a}), 3.23-3.19 (16H, s, $H^{a'}$), 2.85 (3H, bs, H^{34}), 1.38 (9H, s, H^{14}).

Resonance H^{37} broadened into baseline.

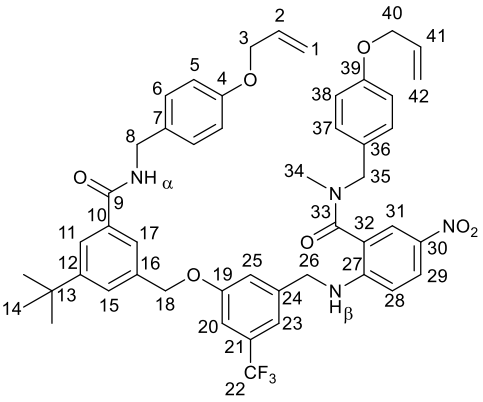
δ_C (100 MHz, $CDCl_3$): 167.5 (C^{9}), 158.2 (C^{4}), 157.3 (C^{19}), 152.2 (C^{12}), 150.9, 137.7 (C^{16}), 134.6, 133.2 ($C^{2 \text{ or } 41}$), 133.1 ($C^{2 \text{ or } 41}$), 130.5, 129.4, 129.3 (C^{6}), 127.3 (C^{15}), 126.8 (C^{29}), 125.6, 124.1, 123.9 (C^{11}), 123.0, 122.7 (C^{17}), 117.8 (C^{1} & C^{42}), 115.0 (b, C^{5} & C^{38}), 111.8 (C^{28}) 111.4 (C^{20}), 70.6 (C^{a}), 70.0 (C^{18}), 68.9 ($C^{3 \text{ or } 40}$), 68.9 ($C^{3 \text{ or } 40}$), 48.3 (C^{26}), 43.6 (C^{8}), 34.9 (C^{13}), 31.3 (C^{14}).

Not all resonances observed in particular C^{34} & C^{35}.

δ_F (377 MHz, $CDCl_3$): −62.1.

m/z (ES): 1225.5606 ($[M+Na]^+$ $C_{64}H_{81}F_3N_4NaO_{15}$ requires 1225.5543).

Axle Ax-ESI-14



Axle **Ax-ESI-14** was isolated from the reaction that formed rotaxane **R-ESI-13** upon purification of the crude reaction mixture by silica gel column chromatography as a yellow glassy solid (118 mg, 90%).

***R*$_f$:** 0.64 [CH_2Cl_2:CH_3OH 99:1].

IR ν_{max} (neat): 3330 (N-H), 2959 (C-H), 2868 (C-H), 1600 (2 x C=O).

δ_H (400 MHz, $CDCl_3$): 8.11 (1H, m, H^{31}), 8.09-8.07 (1H, m, H^{29}), 7.85 (1H, t, *J* = 1.7 Hz, H^{11}), 7.64 (1H, bs, H^{17}), 7.55 (1H, bs, H^{15}), 7.28 (2H, d, *J* = 8.7 Hz, H^{6}), 7.20-7.17 (4H, m, H^{23}, H^{20} & H^{37}), 7.12 (1H, bs, H^{25}), 6.91-6.89 (4H, m, $H^{38?}$ & $H^{5?}$), 6.80 (1H, bs, H^{β}), 6.64 (1H, t, *J* = 5.5 Hz, H^{α}), 6.58 (1H, d, *J* = 9.3 Hz, H^{28}), 6.11-5.99 (2H, m, H^{2} & H^{41}), 5.45-5.38 (2H, m, H^{1} & H^{42}), 5.32-5.28 (2H, m, $H^{1'}$ & $H^{42'}$), 5.07 (2H, s, H^{18}), 4.64 (2H, bs, H^{35}), 4.58 (2H, d, *J* = 5.5 Hz, H^{8}), 4.55-4.51 (4H, m, H^{3} & H^{40}), 4.49 (2H, bs, H^{26}), 3.00 (3H, s, H^{34}), 1.34 (9H, s, H^{14}).

δ_C (100 MHz, $CDCl_3$): 169.2 (b, C^{33}), 167.4 (C^{9}), 159.4 (C^{19}), 158.4 (C^{39}), 158.1 (C^{4}), 152.4 (C^{12}), 151.7, 140.2, 137.0, 136.0 (C^{16}), 134.9, 133.2 ($C^{2 \text{ or } 41}$), 133.1 ($C^{2 \text{ or } 41}$), 132.5 (q, *J* = 33 Hz, C^{21}), 130.5 (C^{7}), 129.3 (C^{6}), 129.0 (b, C^{37}), 127.9 (C^{15}), 127.5 (C^{29}), 124.9 (C^{31}), 124.4 (C^{11}), 123.7 (q, *J* = 271 Hz, C^{22}), 123.3 (C^{17}), 117.8 ($C^{1 \text{ or } 42}$), 117.7 ($C^{1 \text{ or } 42}$), 116.8 (C^{25}), 116.2 (m, C^{23}), 115.2 ($C^{5 \text{ or } 38}$), 115.0 ($C^{5 \text{ or } 38}$), 111.0 (m, C^{20}), 110.9 (C^{28}), 70.3 (C^{18}), 68.9 (C^{3} & C^{40}), 47.0 (C^{26}), 43.6 (C^{8}), 34.9 (C^{13}), 31.2 (C^{14}).

Two quaternary resonances plus C^{34} & C^{35} not observed.

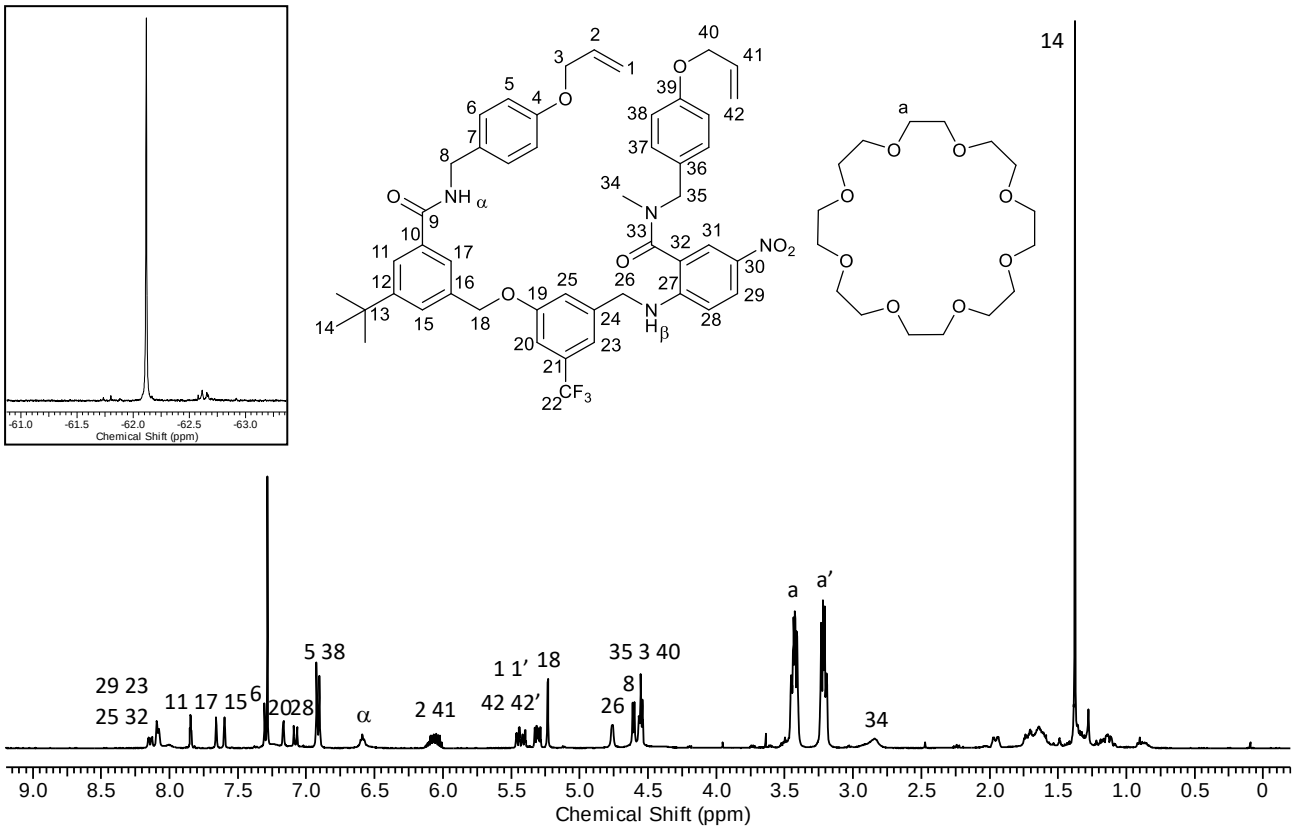
δ_F (377 MHz, $CDCl_3$): –62.6.

m/z (ES): 873.3479 ($[M+Na]^+$ $C_{64}H_{81}F_3N_4NaO_{15}$ requires 873.3446).

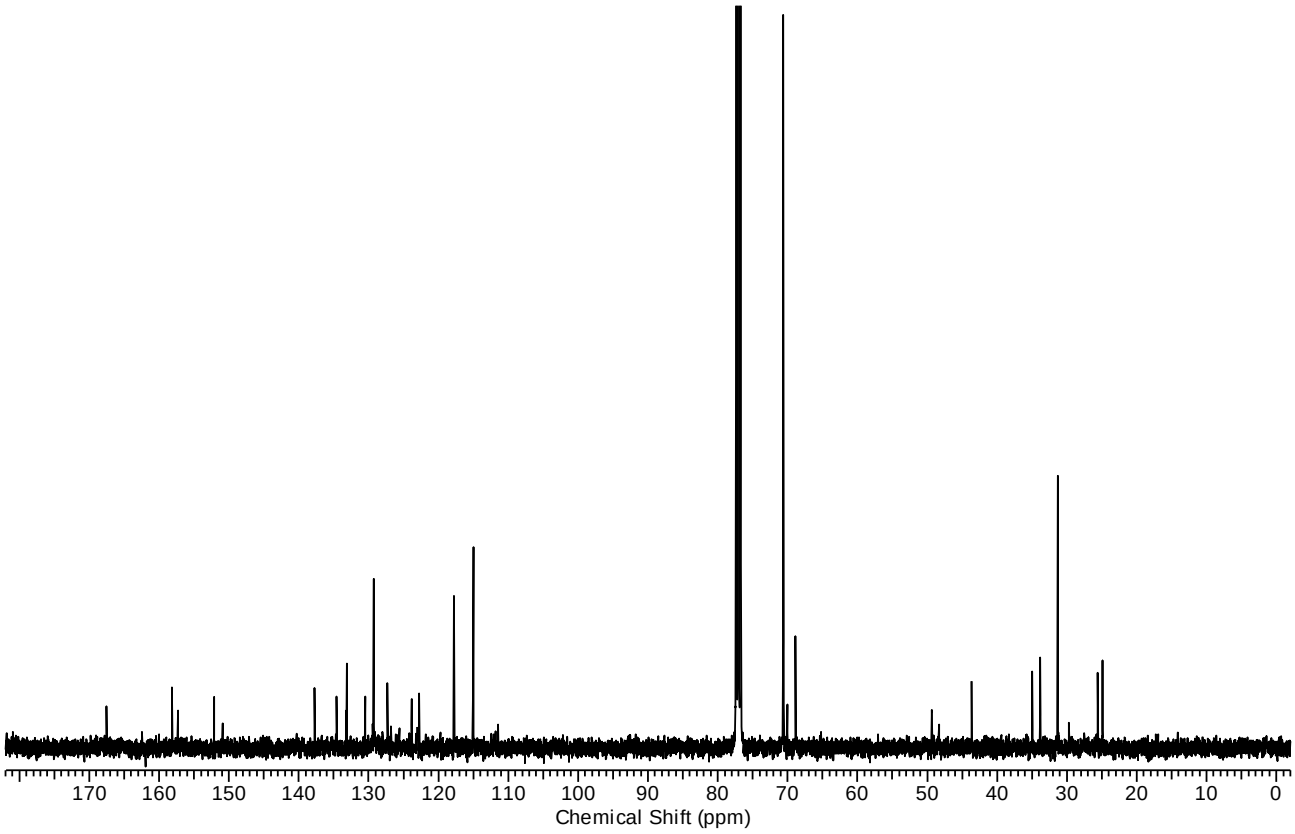
Part 5b: Spectral data for preliminary experimental investigations (Design 2)

[2]Rotaxane R-ESI-13

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

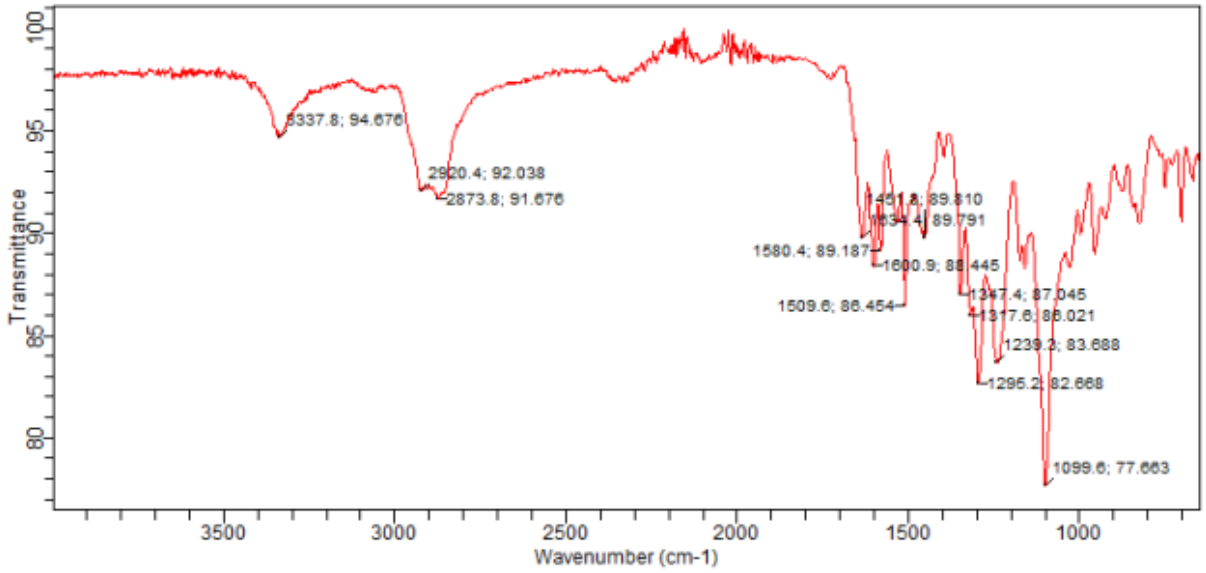


^{13}C NMR ($CDCl_3$, 100 MHz)

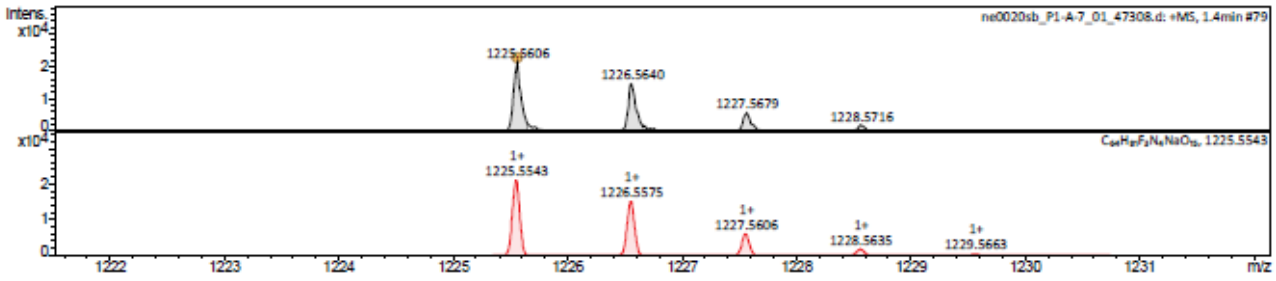


[2]Rotaxane R-ESI-13

IR (neat)



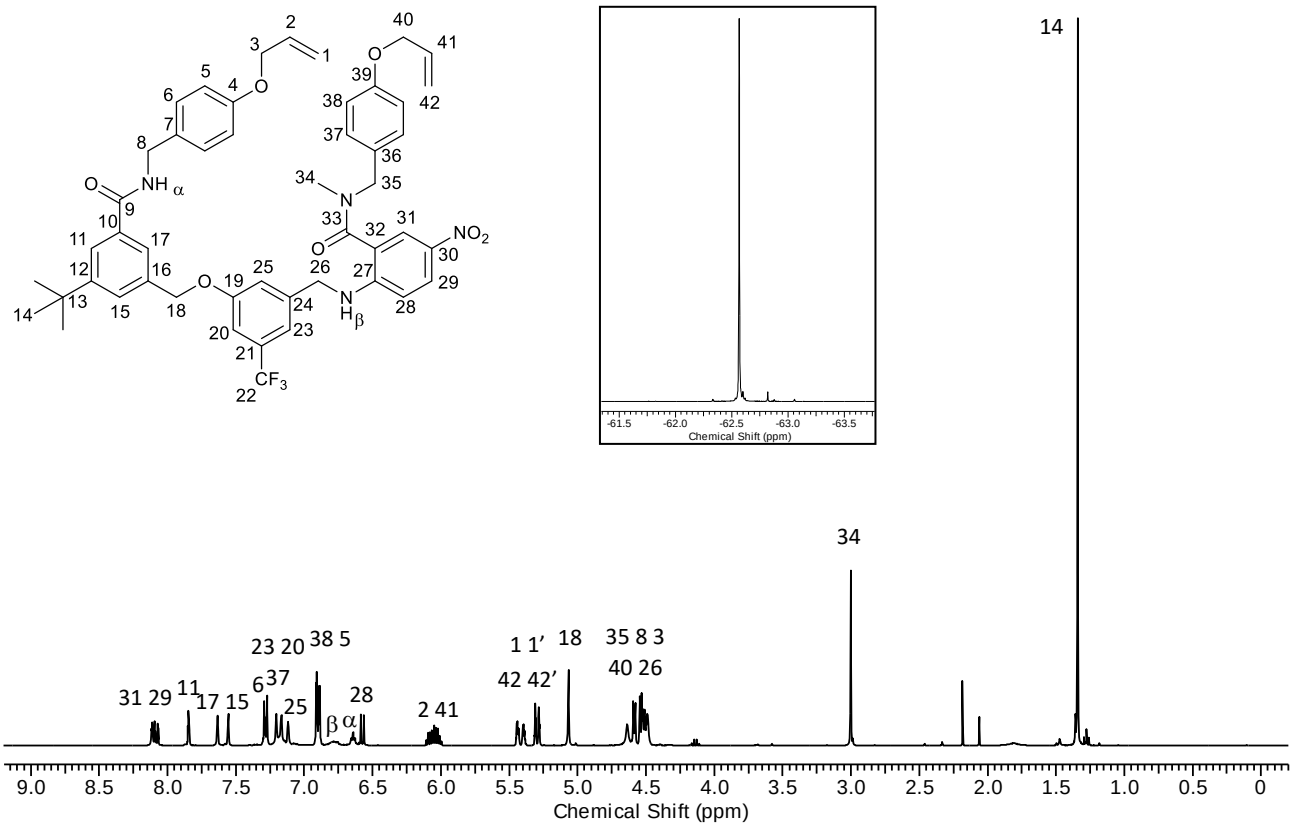
MS (ES +ve)



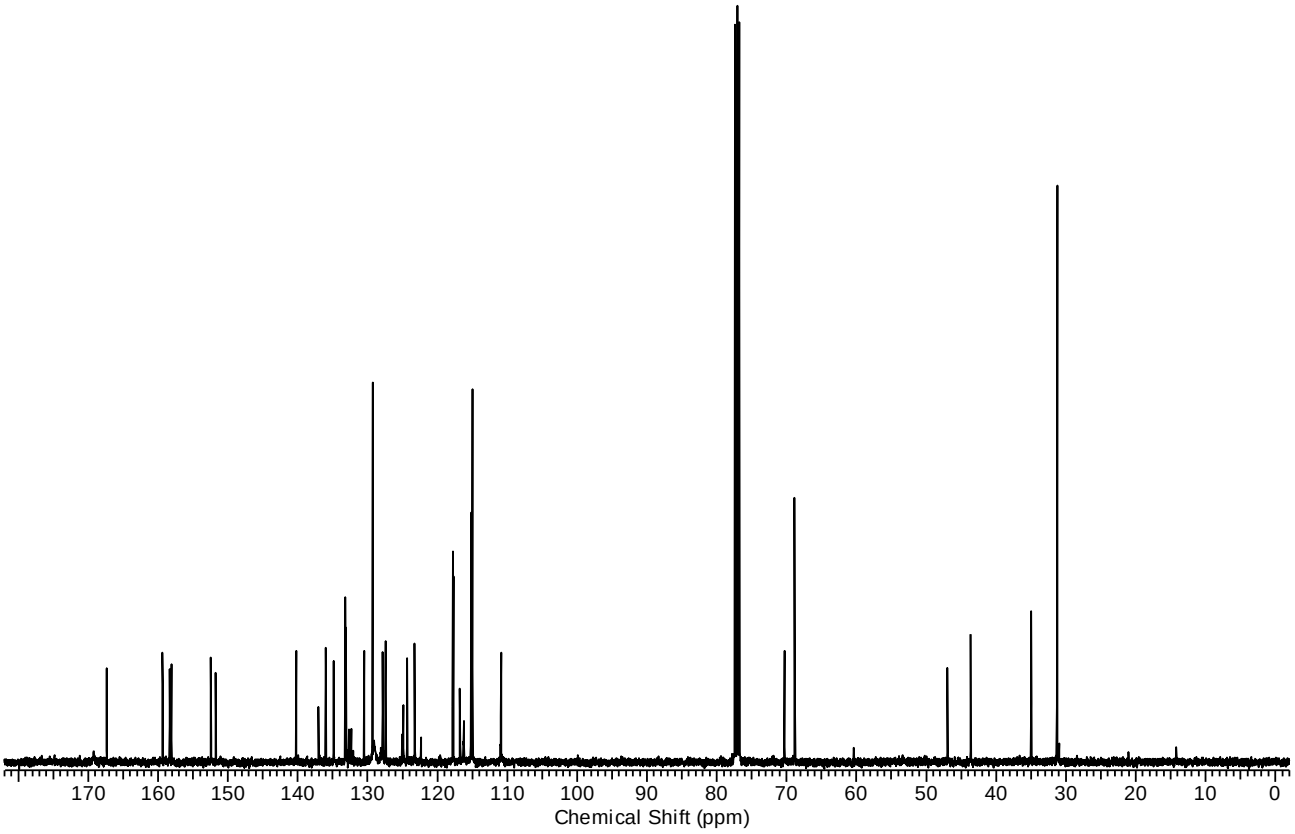
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
1203.5725	1	C64H82F3N4O15	1203.5723	-0.1	-0.1	221.3	0.8
1225.5606	1	C64H81F3N4NaO15	1225.5543	-5.2	-6.3	11.1	-4.7

Axle Ax-ESI-14

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

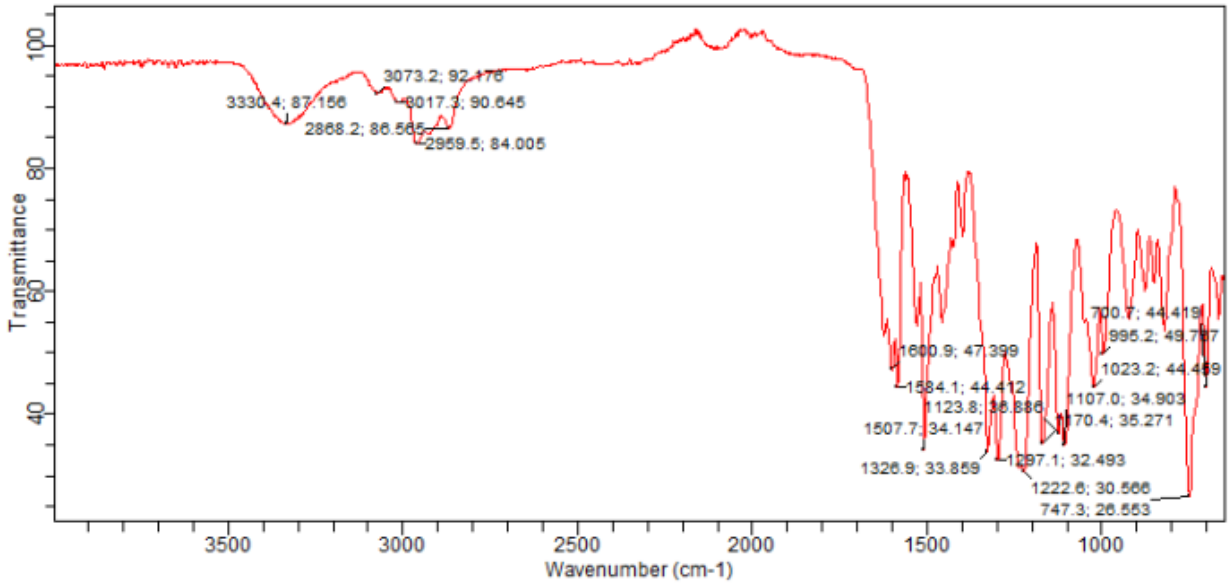


^{13}C NMR ($CDCl_3$, 100 MHz)

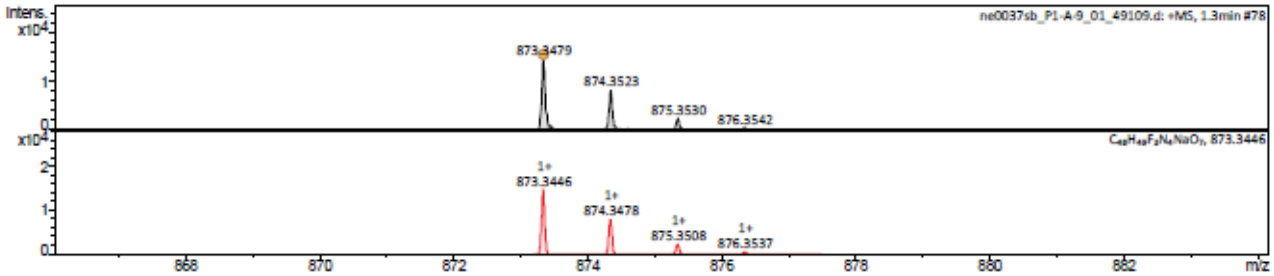


Axle Ax-ESI-14

IR (neat)



MS (ES +ve)



Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
873.3479	1	C48H49F3N4NaO7	873.3446	-3.9	-3.4	15.4	-3.5

Part 6: References

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