Supporting Information

Site selective amide reduction of cyclosporine A opens new structural space for an important cyclic peptide

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General Methods

Unless otherwise stated, all commercially available reagents were used as received. Chloroform was distilled over P_2O_5 and stored over 3Å sieves before use. Trifluorotoluene was distilled from CaH_2 and stored over 4Å molecular sieves before use. Acetonitrile was distilled over CaH_2 before use. Deuterated solvents (Cambridge isotope laboratories) were stored over 3Å sieves before use. All solvents were subjected to 3 freeze-pump-thaw cycles before use. All reactions were performed under an atmosphere of nitrogen unless otherwise stated. Thin layer chromatography (TLC) was performed on SiliCycle Silica Gel 60 F254 plates and was visualized with UV light and $KMnO_4$ stain. NMR spectra were recorded on a Bruker Avance 700 or 600 MHz spectrometer. The residual solvent protons (^1H) or the solvent carbons (^{13}C) were used as internal standards. ^1H NMR data are presented as follows: chemical shift in ppm (δ) downfield from tetramethylsilane (multiplicity, coupling constant, integration). The following abbreviations are used in reporting NMR data: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; dt, doublet of triplets; ddd, doublet of doublet of doublets; m, multiplet. Infrared (IR) spectra were obtained using a Jasco 460 Plus Fourier transform infrared spectrometer. Samples were analyzed with a Q Exactive HF-X (ThermoFisher, Bremen, Germany) mass spectrometer. Samples were introduced via a heated electrospray source (HESI) at a flow rate of 10 µL/min. 100 time domain transients were averaged in the mass spectrum. ESI source conditions were set as: vaporizer temperature 35 °C, sheath gas (nitrogen) 8 arb, auxillary gas (nitrogen) 0 arb, sweep gas (nitrogen) 0 arb, capillary temperature 320 °C, capillary voltage 320 V and funnel Rf level 35 V. The mass range was set to 150-2000 m/z. All measurements were recorded at a resolution setting of 120,000. Solutions were analyzed at 0.1 mg/mL or less based on responsiveness to the ESI mechanism. Xcalibur (ThermoFisher, Breman, Germany) was used to analyze the data. Molecular formula assignments were determined with Molecular Formula Calculator (v 1.2.3). All observed species were singly charged, as verified by unit m/z separation between mass spectral peaks corresponding to the ^{12}C and ^{13}C $^{12}C_{c-1}$ isotope for each elemental composition. The LC method is described in the following table. The column model used was a Waters Acquity UPLC BEH C18 (1.7 µm, 2.1 mm, 50 mm) Absorbances were mmeasured at 210 nm.

Time (min)	**Flow (mL/min)**	**%A**	**%B**
0	0.6	80	20
3.00	0.6	40	60
8.75	0.6	5	95
10.20	0.6	5	95
10.21	0.6	80	20
11.25	0.6	80	20

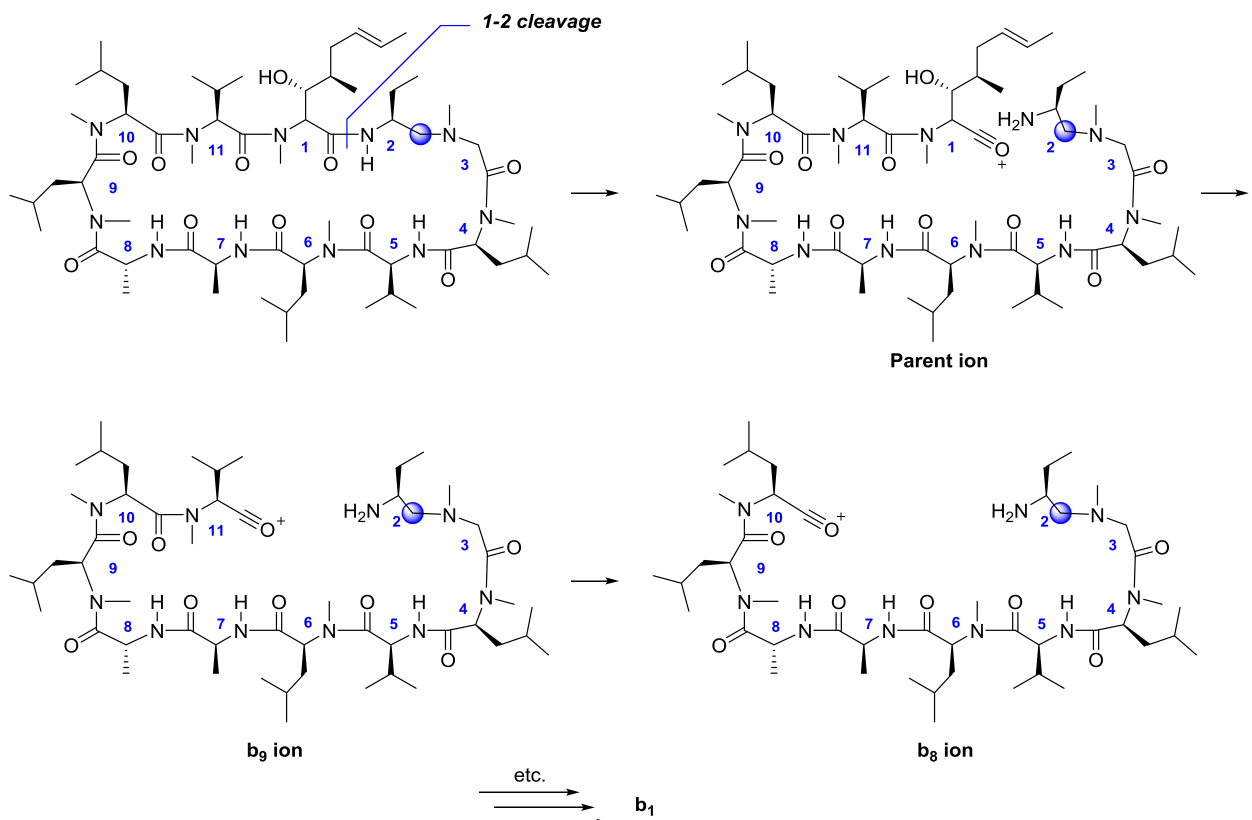
A = H_2O with 1% formic acid
B = ACN with 1% formic acid

MS^2 Analysis

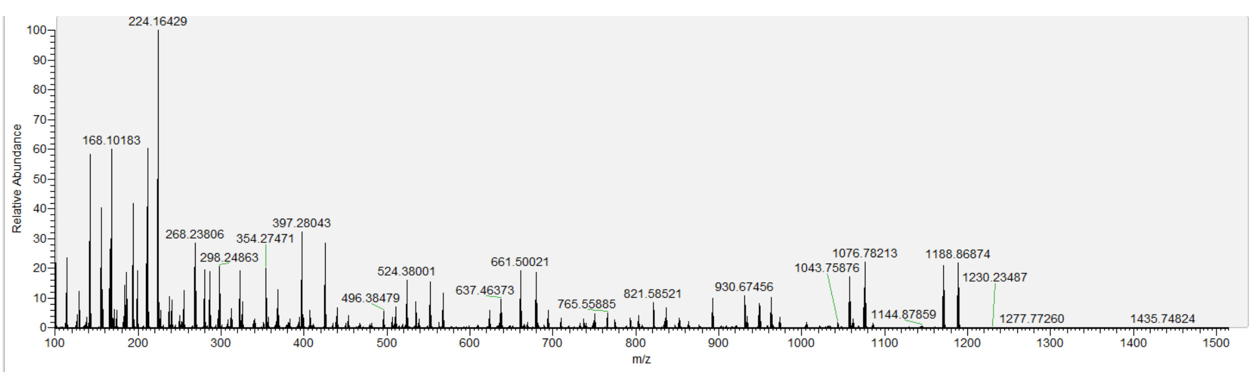
ESI-MS^2 spectra (positive ion mode) were recorded on Q Exactive HF-X (ThermoFisher, Bremen, Germany) mass spectrometer. Samples (0.1 mg/mL) were introduced via a heated electrospray source (HESI) at a flow rate of 10 µL/min. 100 time domain transients were averaged in the mass spectrum. ESI source conditions were set as: vaporizer temperature 35 °C, sheath gas (nitrogen) 8 arb, auxillary gas (nitrogen) 0 arb, sweep gas (nitrogen) 0 arb, capillary temperature 320 °C, capillary voltage 320 V and funnel Rf level 35 V. The mass range was set to 150-2000 m/z. All measurements were recorded at a resolution setting of 120,000. NCE of 25-35. Baselines were adjusted by measuring the six times the standard deviation of baseline signals at five points throughout the mass spectrum. Depending on the sample, most ESI-MS^2 experiments generates >200 fragments which were analyzed as described below.

Prior to MS^2 analysis samples were desilylated by dissolving ~1 mg in MeOH (500 µL) and trifluoroacetic acid (50 µL). After stirring for one hour the sample was concentrated to dryness and redissolved MeOH (Optima, 1 mL)

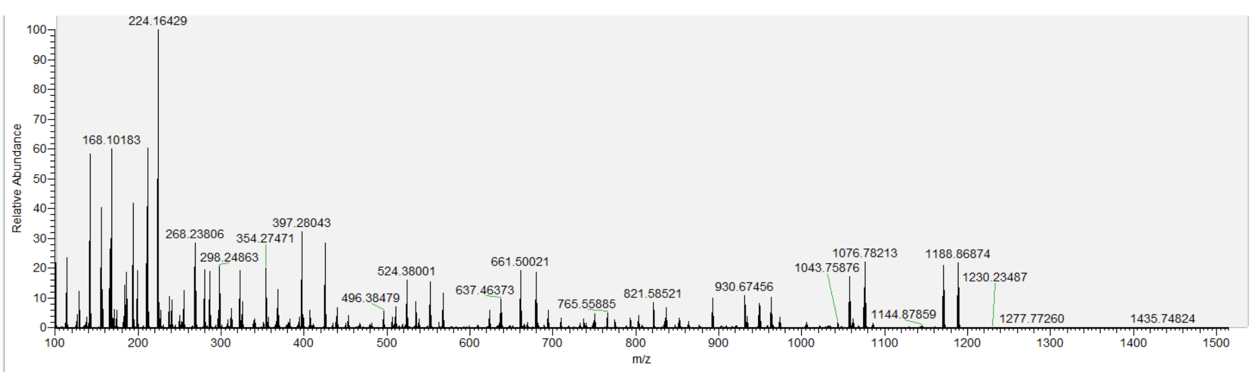
<u>MS^2 fragmentation example</u>



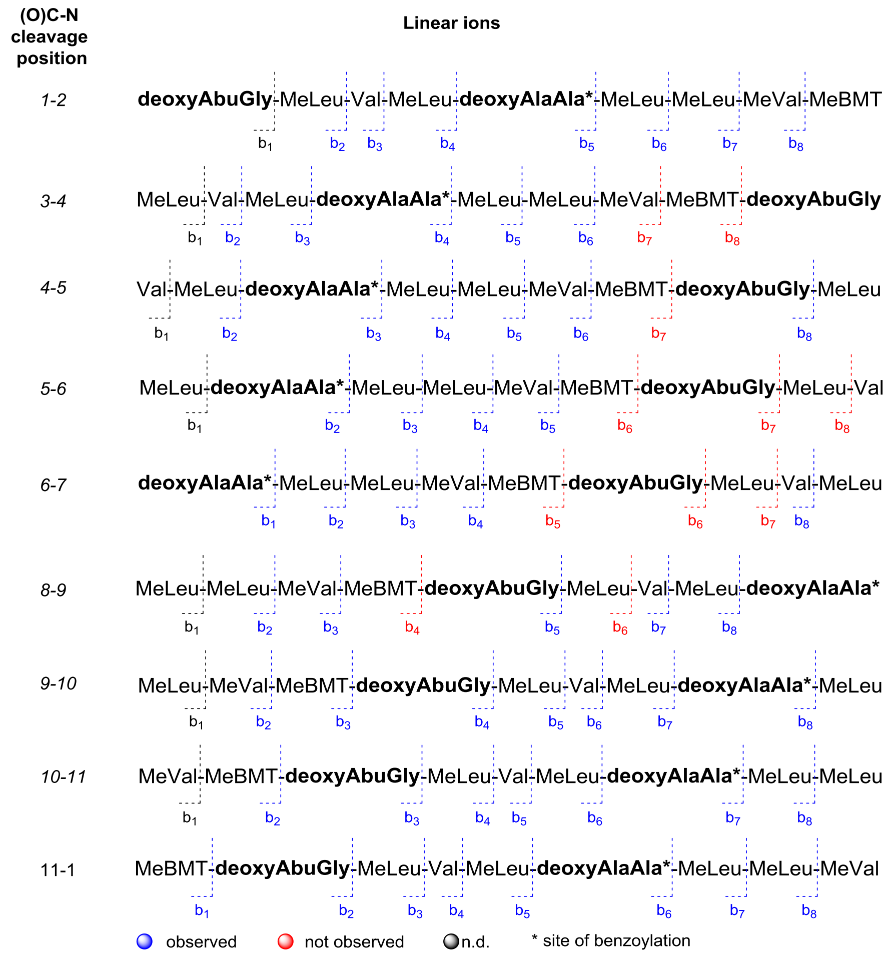
Predicted fragments for reduction at Abu2

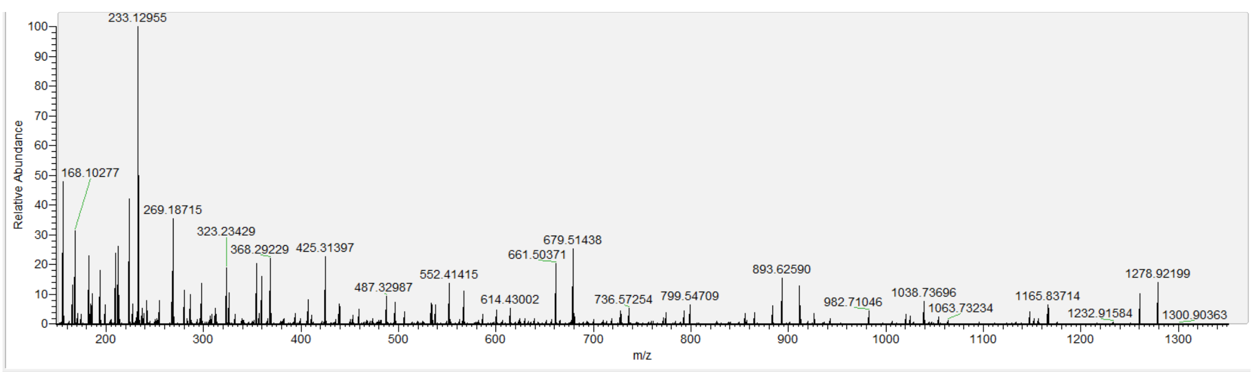


Predicted fragments for reduction at Ala7

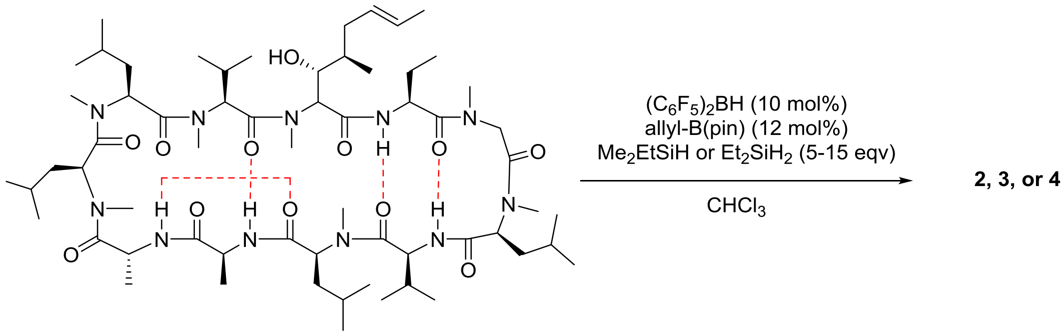


Predicted fragments for reduction at 3d



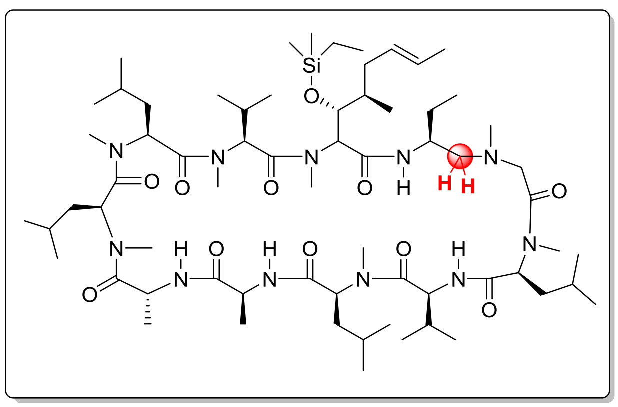


Representative procedure for silane reductions



In a nitrogen filled glovebox, a dram vial containing H–B(C_6F_5)$_2$ (1.7 mg, 0.005 mmol) was diluted with 200 µL $CHCl_3$ before adding allyl-Bpin (1.1 µL, 0.006 mmol). After complete dissolution of the suspension (c.a 5 min), silane (see below) was added and the solution transferred to a separate vial containing the cyclosporine A (0.060 g, 0.05 mmol) dissolved in 200 µL $CHCl_3$. The vial which contained the catalyst/silane mixture was rinsed with an additional 100 µL $CHCl_3$ and transferred to the reaction flask. After capping the vial with a screw top septum lid (PTFE), the vial was allowed to stir outside of the glovebox for 24h. After the allotted time, the solution was concentrated in vacuo before purifying by column chromatography.

(2) – 2Abu$_{deoxy}$-CsA-OSiMe$_2$Et



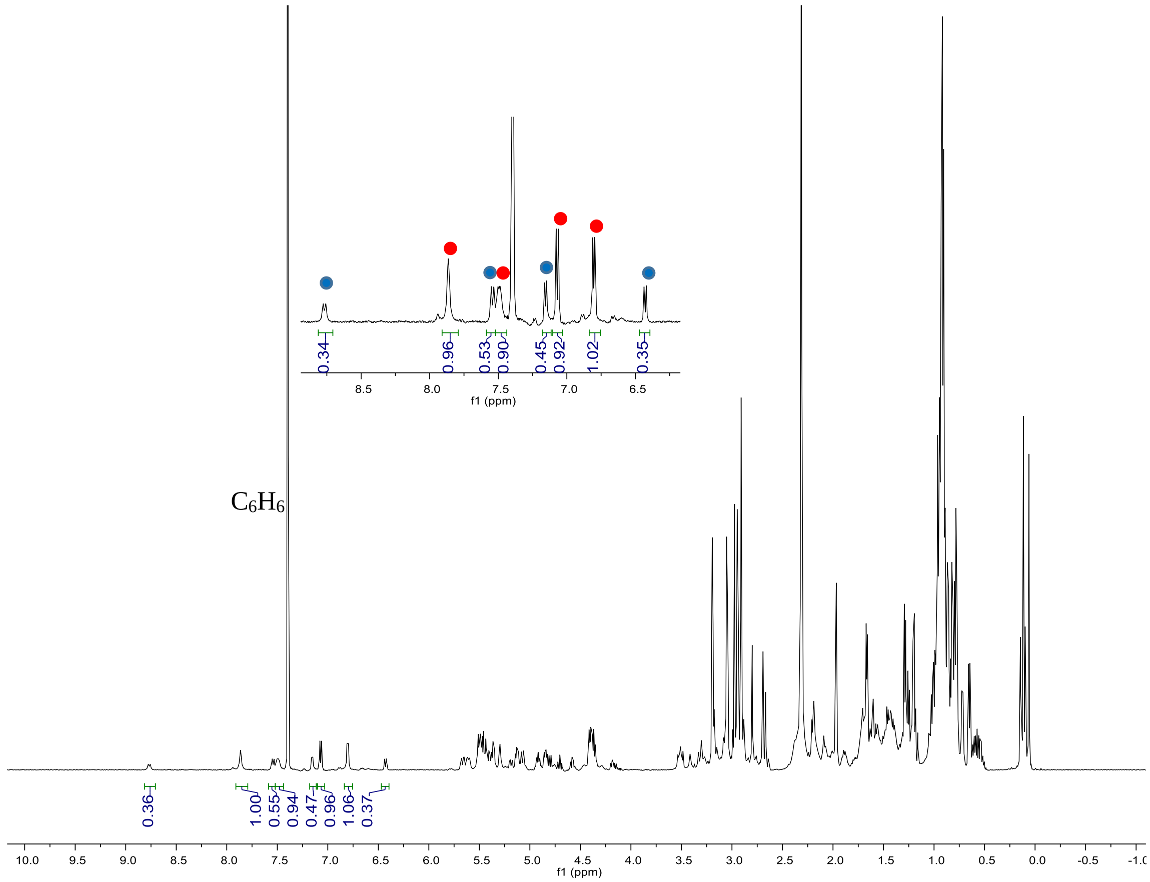
15 eqv. Me_2EtSiH (99 µL), (SiO_2, hexane:acetone 4:1→3:1→2:1→1:1→1:3)

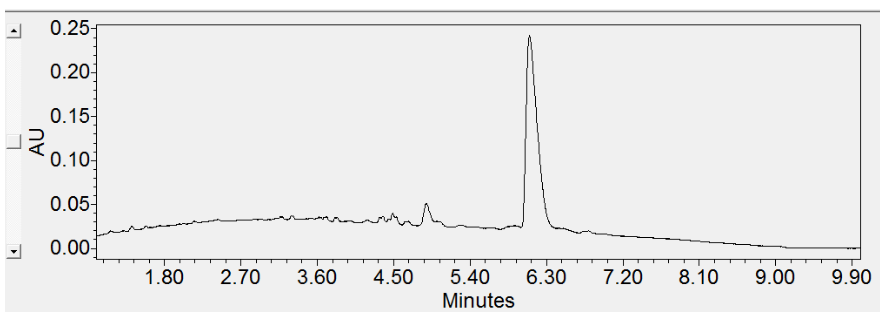
21.7 mg (35 % yield), white solid

HRMS (ESI) calcd for $C_{66}H_{124}N_{11}O_{11}Si$ $(M+H)^+$: 1274.92511. Found: 1274.92441.

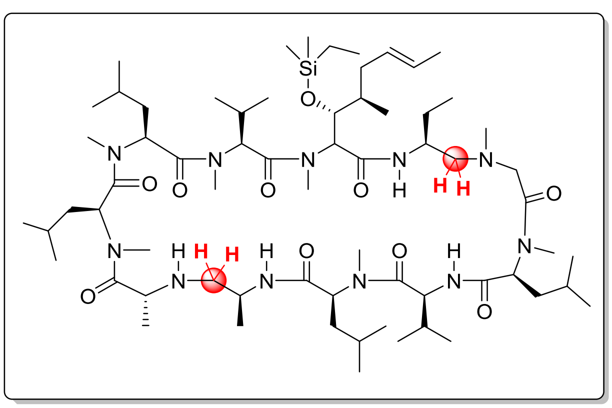
See MS^2 characterization in previous section

In the ^{1}H-NMR spectrum (500 MHz, CD_3CN) below the amide region displays two sets of secondary amide resonances (two conformers), further suggesting the reduction of Abu2 (tertiary amide) over Ala7 (secondary amide)





(2) – 2Abu$_{deoxy}$-7Ala$_{deoxy}$-CsA-OSiMe$_2$Et



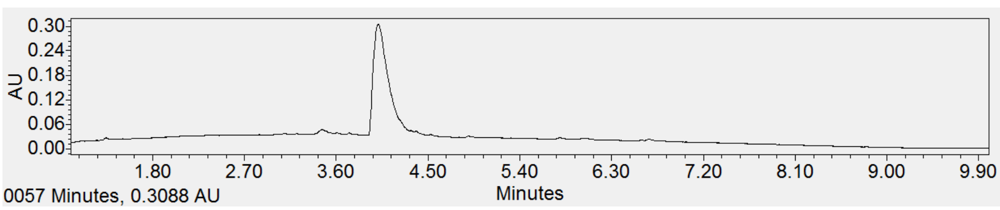
15 eqv. Me_2EtSiH (99 µL), (SiO_2, hexane:acetone 4:1→3:1→2:1→1:1→1:3)

27.2 mg (44 % yield), white solid

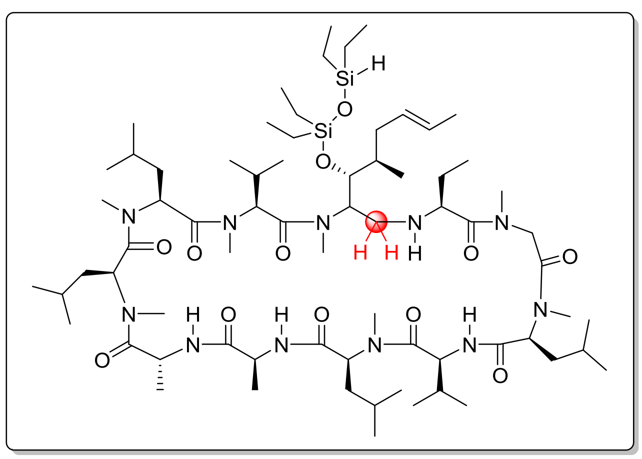
^{1}H NMR (700 MHz, C_6D_6) δ 8.06 (d, *J* = 3.0 Hz, 1H), 7.44 (d, *J* = 9.5 Hz, 1H), 7.10 (d, *J* = 6.3 Hz, 1H), 6.03 (dd, *J* = 9.6, 5.3 Hz, 1H), 5.96 (d, *J* = 2.1 Hz, 1H), 5.92 (dd, *J* = 12.8, 3.1 Hz, 1H), 5.74 (d, *J* = 10.6 Hz, 1H), 5.53 – 5.50 (m, 2H), 5.43 (t, *J* = 7.4 Hz, 1H), 5.22 (dd, *J* = 9.8, 6.5 Hz, 1H), 5.12 (dd, *J* = 9.5, 4.3 Hz, 1H), 4.94 (dd, *J* = 8.7, 2.0 Hz, 1H), 4.15 – 4.07 (m, 1H), 3.79 (m, 1H), 3.57 (s, 3H), 3.51 (s, 3H), 3.11 (q, *J* = 6.9 Hz, 1H), 2.92 (s, 3H), 2.74 – 2.70 (m, 1H), 2.70 (s, 3H), 2.64 (s, 3H), 2.40 (s, 3H), 1.83 (s, 3H), 1.13 – 1.04 (m, 24H), 1.03 – 0.95 (m, 23H), 0.94 – 0.86 (m, 14H), 0.38 (s, 6H).

^{13}C NMR (176 MHz, C_6D_6) δ 176.8, 173.0, 172.5, 171.6, 171.4, 171.3, 171.2, 170.4, 169.8, 130.8, 126.8, 77.7, 60.0, 59.9, 58.89, 58.87, 57.4, 55.2, 54.79, 54.76, 53.8, 53.4, 51.4, 49.9, 46.2, 42.2, 39.9, 38.8, 38.4, 38.3, 36.9, 36.4, 36.2, 34.0, 30.8, 30.5, 30.1, 29.7, 29.1, 26.9, 26.3, 25.5, 25.4, 25.3, 24.8, 24.4, 24.0, 23.6, 22.74, 22.70, 22.5, 22.4, 21.0, 20.0, 19.9, 19.4, 18.9, 18.6, 18.2, 17.2, 15.9, 9.7, 9.7, 7.5, -1.1, -1.6.

HRMS (ESI) calcd for $C_{66}H_{125}N_{11}O_{10}Si$ $(M+H)^+$: 1260.94584. Found: 1260.94598.



<u>(3) – 1MeBmT$_{deoxy}$-CsA-OSi</u>



5 eqv. Et_2SiH_2 (32 µL). (SiO_2, hexane:acetone 4:1→3:1→2:1→1:1→1:3)

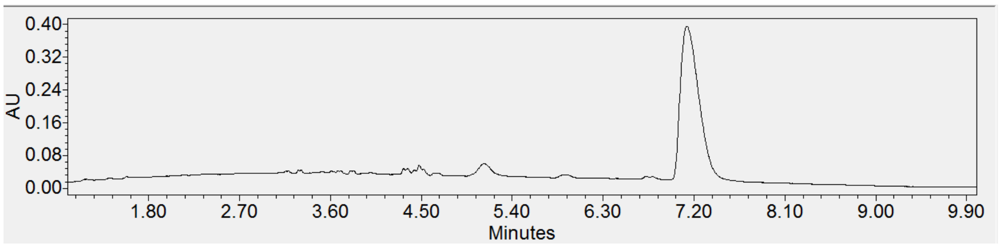
40.3 mg (62 % yield), white solid

^{1}H NMR (600 MHz, C_6D_6) δ 7.64 (d, *J* = 8.9 Hz, 1H), 7.46 (d, *J* = 6.8 Hz, 1H), 7.02 (d, *J* = 7.4 Hz, 1H), 5.88 (dd, *J* = 10.9, 3.7 Hz, 1H), 5.73 – 5.64 (m, 2H), 5.63 – 5.57 (m, 1H), 5.56 – 5.50 (m, 3H), 5.48 (dd, *J* = 10.8, 4.8 Hz, 1H), 4.93 – 4.91 (m, 1H), 4.89 (d, *J* = 6.9 Hz, 1H), 4.86 (d, *J* = 9.0

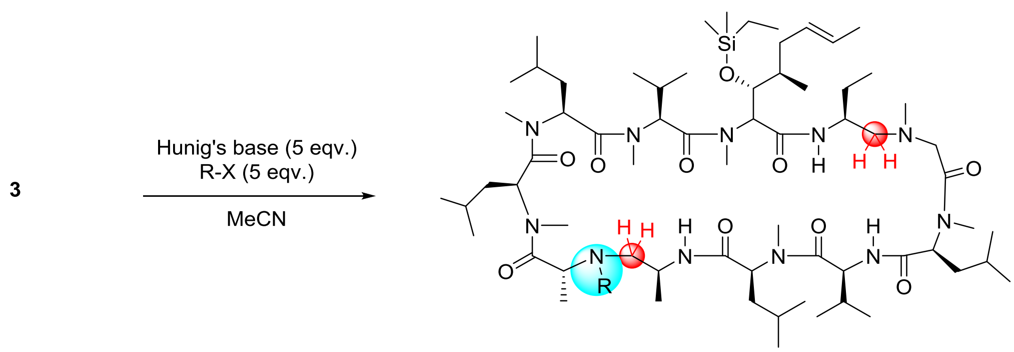
Hz, 1H), 4.74 (dd, J = 7.1 Hz, 1H), 4.17 (d, J = 14.4 Hz, 1H), 4.02 (dd, J = 7.9, 4.1 Hz, 1H), 3.47 (s, 3H), 3.15 (s, 4H), 2.99 (s, 3H), 2.97 (s, 3H), 2.96 (s, 4H), 2.79 (s, 3H), 2.52 (s, 3H), 1.77 – 1.73 (m, 6H), 1.64 – 1.57 (m, 2H), 1.50 – 1.42 (m, 1H), 1.32 (d, J = 6.6 Hz, 3H), 1.28 – 1.16 (m, 16H), 1.11 – 1.02 (m, 15H), 0.99 – 0.94 (m, 9H), 0.91 (dd, J = 11.9, 6.5 Hz, 9H), 0.83 (q, J = 7.4, 6.6 Hz, 7H), 0.77 – 0.72 (m, 7H).

^{13}C NMR (151 MHz, C_6D_6) δ 178.4, 173.9, 173.1, 172.6, 171.7, 171.5, 170.6, 170.4, 169.7, 169.2, 130.8, 126.8, 79.2, 59.6, 58.1, 57.6, 55.0, 54.9, 54.2, 53.9, 50.3, 50.2, 48.7, 48.4, 45.2, 42.2, 39.7, 38.3, 37.9, 37.4, 36.4, 36.3, 31.6, 30.9, 30.3, 30.2, 30.0, 29.7, 28.4, 28.0, 25.6, 25.32, 25.28, 25.0, 24.6, 23.8, 23.64, 23.59, 23.11, 23.05, 22.1, 21.8, 19.7, 19.52, 19.45, 19.2, 18.4, 18.1, 16.7, 15.6, 10.6, 7.54, 7.50, 7.48, 7.41, 7.1, 6.98, 6.96, 6.90, 5.9.

HRMS (ESI) calcd for $C_{70}H_{134}N_{11}O_{11}Si_2$ $(M+H)^+$: 1376.97520. Found: 1376.97457.

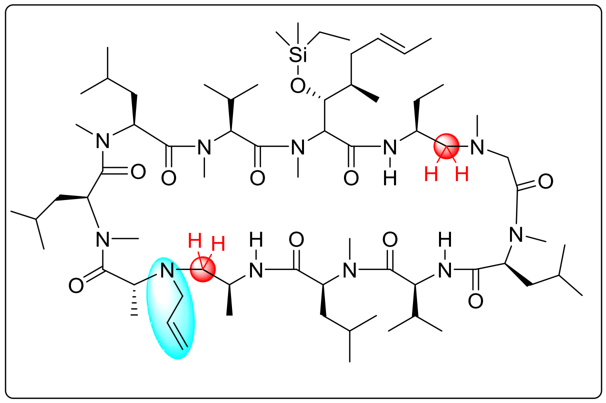


Representative alkylation procedure



A dram vial containing **3**, (0.020 mg, 0.0015 mmol) was sealed with a PTFE lined septum cap after exchanging the atmosphere with nitrogen (x3) MeCN (0.5 mL) was added. Hunig's base was then added followed by the alkylating agent (see below). After 24 hours, the solution was diluted with EtOAc and washed with saturated $NaHCO_{3(aq)}$ (x2), and brine (x1) before drying over Na_2SO_4. After concentrating *in vacuo*, the residue was then purified by column chromatography.

(3a) – 2Abu$_{deoxy}$-7Ala$_{deoxy}$allyl-CsA-OSiMe$_2$Et



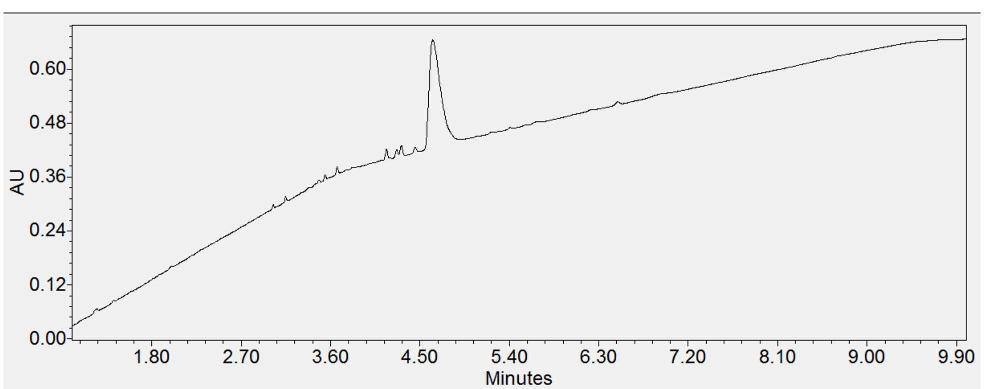
Allyl bromide (7 µL). (SiO_2, hexane:acetone 4:1→3:1→2:1→1:1→1:3)

10.2 mg (47% yield), white solid

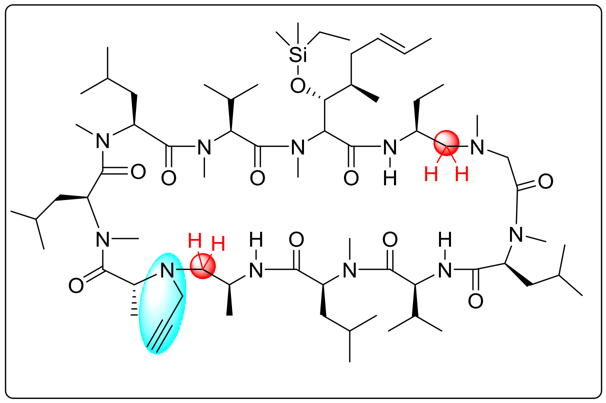
^{1}H NMR (600 MHz, C_6D_6) δ 8.30 (d, *J* = 4.3 Hz, 1H), 8.11 (d, *J* = 2.9 Hz, 1H), 7.60 (d, *J* = 9.5 Hz, 1H), 6.11 (dd, *J* = 9.8, 4.9 Hz, 1H), 5.99 (d, *J* = 1.9 Hz, 1H), 5.81 (dd, *J* = 12.8, 2.5 Hz, 1H), 5.78 (d, *J* = 10.6 Hz, 1H), 5.68 – 5.60 (m, 1H), 5.55 (t, *J* = 7.8 Hz, 1H), 5.53 – 5.49 (m, 2H), 5.17 (m, 2H), 5.03 – 4.93 (m, 3H), 3.97 – 3.90 (m, 1H), 3.81 (m, 1H), 3.53 (s, 3H), 3.51 (s, 3H), 3.39 (d, *J* = 6.7 Hz, 1H), 3.06 – 2.94 (m, 2H), 2.93 (s, 3H), 2.88 (s, 3H), 2.80 (d, *J* = 16.7 Hz, 1H), 2.65 (s, 3H), 2.49 (s, 3H), 2.43 (t, *J* = 12.3 Hz, 1H), 2.32 – 2.24 (m, 1H), 2.13 (tt, *J* = 6.9, 3.5 Hz, 1H), 2.09 – 2.00 (m, 1H), 1.82 (s, 4H), 1.22 – 1.12 (m, 15H), 1.12 – 1.06 (m, 11H), 1.06 – 1.00 (m, 12H), 1.00 – 0.89 (m, 30H), 0.40 (s, 3H), 0.39 (s, 3H).

^{13}C NMR (151 MHz, C_6D_6) δ 175.1, 172.9, 172.2, 171.6, 171.30, 171.27, 171.01, 170.96, 169.9, 134.8, 130.8, 126.7, 117.8, 77.7, 60.1, 59.9, 58.8, 57.4, 57.0, 54.7, 54.0, 53.3, 52.1, 49.9, 45.2, 42.2, 39.9, 38.6, 38.4, 38.3, 37.2, 36.91, 36.88, 36.6, 33.8, 30.7, 30.5, 30.2, 30.08, 30.06, 29.4, 26.8, 26.4, 25.5, 25.3, 25.2, 25.1, 24.8, 24.6, 24.2, 23.6, 23.0, 22.62, 22.57, 22.3, 20.8, 20.0, 19.8, 18.7, 18.3, 18.2, 17.1, 16.0, 14.4, 9.8, 9.7, 7.5, -1.1, -1.6.

HRMS (ESI) calcd for $C_{69}H_{130}N_{11}O_{10}Si$ $(M+H)^+$: 1300.97714. Found: 1300.97754.



<u>(3b) – 2Abu$_{deoxy}$-7Ala$_{deoxy}$propargyl-CsA-OSiMe$_2$Et</u>



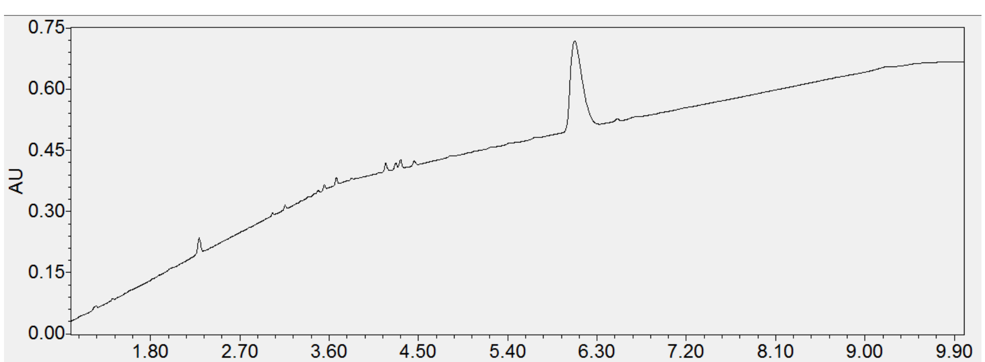
Propargyl bromide, 80% solution in toluene (9 μL). (SiO_2, hexane:acetone 4:1→3:1→2:1→1:1→1:3)

10.7 mg (50% yield), white solid

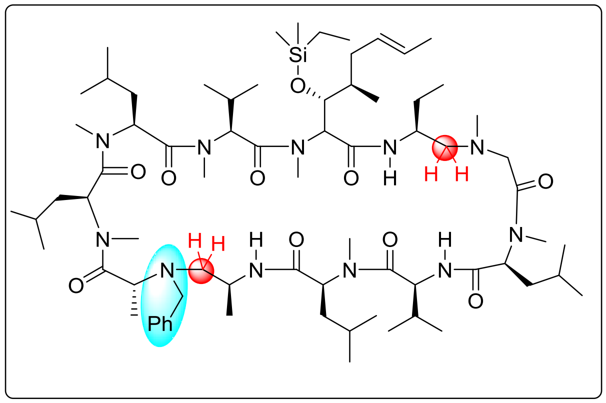
^{1}H NMR (600 MHz, C_6D_6) δ 8.11 (s, 1H), 8.04 (s, 1H), 7.55 (d, J = 9.4 Hz, 1H), 6.14 (t, J = 7.5 Hz, 1H), 5.98 (s, 1H), 5.81 (d, J = 12.1 Hz, 1H), 5.76 (d, J = 10.6 Hz, 1H), 5.55 – 5.48 (m, 3H), 5.21 – 5.14 (m, 2H), 4.95 (d, J = 8.8 Hz, 1H), 3.84 – 3.75 (m, 2H), 3.60 (d, J = 6.6 Hz, 1H), 3.54 (s, 3H), 3.51 (d, J = 1.9 Hz, 3H), 3.25 (d, J = 18.4 Hz, 1H), 3.15 (d, J = 18.6 Hz, 1H), 2.90 (d, J = 1.9 Hz, 3H), 2.83 (d, J = 2.0 Hz, 3H), 2.80 (d, J = 9.0 Hz, 1H), 2.65 (d, J = 1.9 Hz, 3H), 2.53 (d, J = 1.9 Hz, 3H), 2.41 (d, J = 12.3 Hz, 1H), 2.33 – 2.23 (m, 1H), 2.14 – 2.05 (m, 2H), 2.06 – 1.99 (m, 2H), 1.82 (s, 3H), 1.65 (s, 3H), 1.59 (d, J = 7.6 Hz, 3H), 1.22 – 1.11 (m, 17H), 1.11 – 1.01 (m, 17H), 1.01 – 0.86 (m, 39H), 0.39 (s, 6H).

^{13}C NMR (151 MHz, C_6D_6) δ 174.1, 172.6, 172.0, 171.1, 171.0, 170.9, 170.8, 170.4, 169.5, 130.5, 126.3, 78.1, 77.3, 72.7, 59.7, 59.5, 58.5, 58.4, 58.1, 57.4, 57.1, 54.2, 53.6, 53.0, 51.6, 49.6, 43.8, 41.8, 39.6, 38.2, 38.05, 37.98, 36.5, 36.3, 36.2, 33.6, 30.2, 30.1, 29.9, 29.6, 29.5, 29.0, 26.5, 26.1, 25.2, 25.0, 24.8, 24.3, 24.2, 23.9, 23.2, 22.6, 22.2, 22.1, 21.6, 20.3, 19.6, 19.5, 18.3, 17.89, 17.86, 16.5, 15.9, 15.6, 9.4, 9.3, 7.1, -1.4, -2.0.

HRMS (ESI) calcd for $C_{69}H_{128}N_{11}O_{10}Si$ $(M+H)^+$: 1298.96149. Found: 1298.96132.



(3c) – 2Abu<u>deoxy</u>-7Ala<u>deoxy</u>benzyl-CsA-OSiMe2Et



Benzyl bromide (18 µL). (SiO_2, hexane:acetone 4:1→3:1→2:1→1:1→1:3)

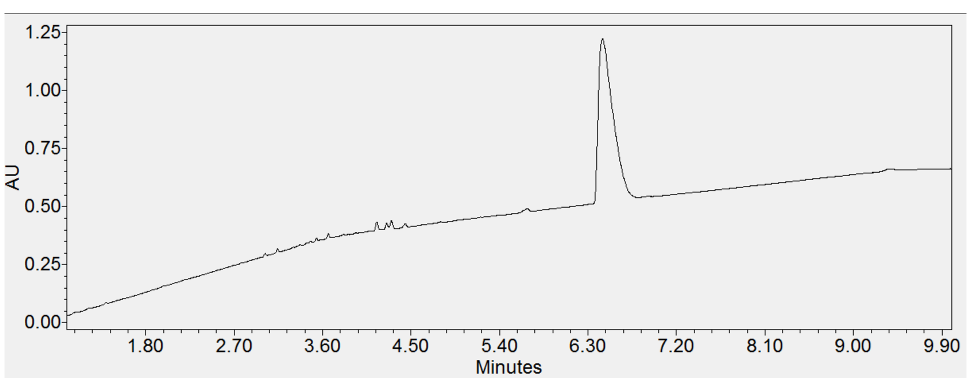
18.4 mg (43% yield), white solid

^{1}H NMR (600 MHz, C_6D_6) δ 8.45 (s, 1H), 8.10 (s, 1H), 7.58 (d, *J* = 9.4 Hz, 1H), 7.34 (d, *J* = 7.5 Hz, 2H), 7.25 (t, *J* = 7.5 Hz, 2H), 6.06 (dd, *J* = 9.4, 5.1 Hz, 1H), 5.98 (s, 1H), 5.84 (dd, *J* = 12.7, 2.9 Hz, 1H), 5.78 (d, *J* = 10.6 Hz, 1H), 5.60 (t, *J* = 7.8 Hz, 1H), 5.57 – 5.43 (m, 2H), 5.28 – 5.11 (m, 2H), 4.96 (dd, *J* = 8.8, 1.9 Hz, 1H), 3.89 – 3.72 (m, 2H), 3.52 (s, 3H), 3.49 (s, 3H), 3.39 – 3.33 (m, 1H), 3.30 (q, *J* = 6.4 Hz, 1H), 2.91 (s, 6H), 2.79 (d, *J* = 16.7 Hz, 1H), 2.65 (s, 3H), 2.62 (d, *J* = 17.0 Hz, 1H), 2.42 (t, *J* = 12.2 Hz, 1H), 2.34 (s, 3H), 2.30 – 2.22 (m, 1H), 2.18 – 2.10 (m, 1H), 1.82 (s, 3H), 1.19 – 1.01 (m, 30H), 1.02 – 0.70 (m, 27H), 0.40 (s, 3H), 0.40 (s, 3H).

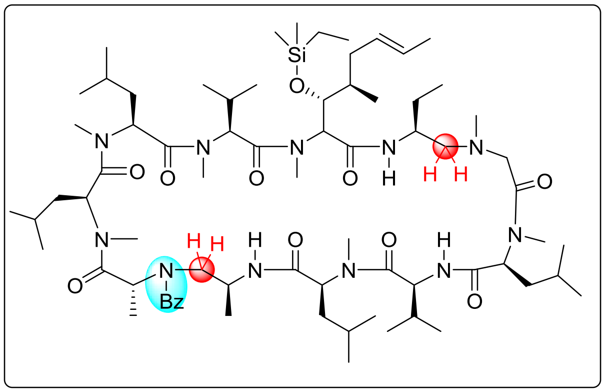
^{13}C NMR (151 MHz, C_6D_6) δ 174.5, 172.5, 171.9, 171.0, 170.92, 170.89, 170.81, 170.4, 169.5, 140.8, 130.5, 129.5, 127.0, 126.4, 77.4, 59.7, 59.5, 58.5, 57.0, 56.5, 54.5, 53.7, 53.1, 51.6, 49.5, 45.4, 41.9, 39.5, 38.3, 38.1, 38.0, 37.3, 36.5, 36.2, 33.3, 32.0, 30.5, 30.1, 29.9, 29.8, 29.7, 29.5, 29.0, 26.5, 26.0, 25.1, 25.0, 25.0, 24.7, 24.4, 24.2, 23.7, 23.4, 23.3, 22.8, 22.7, 22.5, 22.3, 20.5, 19.6, 19.3, 18.3, 17.9, 17.8, 17.0, 15.6, 9.4, 9.3, 7.2, -1.4, -2.0.

One aryl resonance missing in ^{1}H spectrum

HRMS (ESI) calcd for $C_{73}H_{132}N_{11}O_{10}Si$ $(M+H)^+$: 1350.99279. Found: 1350.99317.



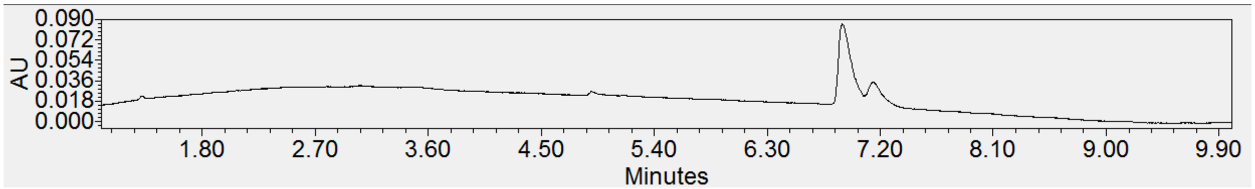
(3d) – 2Abu$_{deoxy}$-7Ala$_{deoxy}$benzoyl-CsA-OSiMe$_2$Et



Benzoyl chloride(9 µL). (SiO_2, hexane:acetone 4:1→3:1→2:1→1:1→1:3)

15.5 mg (66% yield), white solid

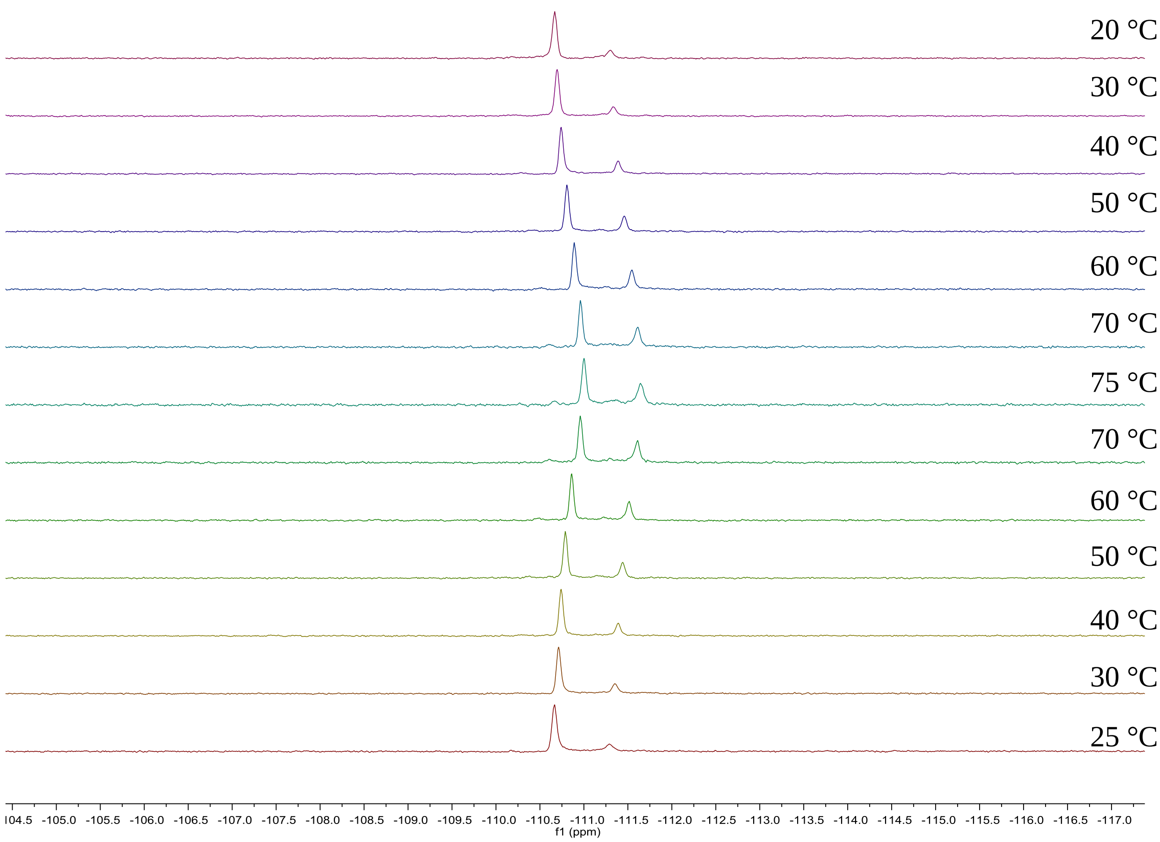
HRMS (ESI) calcd for $C_{73}H_{130}N_{11}O_{11}Si$ $(M+H)^+$: 1364.97206. Found: 1364.97217.



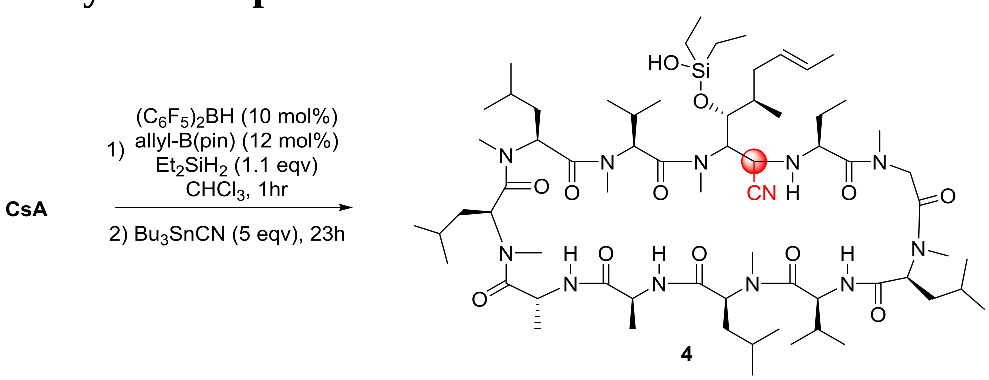
3d's NMR spectrum was complex due to multiple conformers. LCMS analysis indicates two major species with the same m/z. MS^2 analysis (see previous section) shows good agreement with the assigned structure.

The analogous 4-fluoro benzoyl analog was synthesized to examine the number of potential isomers by NMR. The ^{19}F-spectrum acquired in MeOH or iPrOH indicate that 2 major and one minor conformer exist. Variable temperature NMR studies indicated that the two conformers were not in fast exchange even at temperatures of 75 °C, although the relative population of each conformer was dependent on temperature and reversible. (See NMR spectra below)

^{19}F NMR (470 MHz) of **3d**'s 4-Fluoroanalog in *i*PrOH.



Reductive cyanation procedure



In a nitrogen filled glovebox, a dram vial containing H–B(C_6F_5)$_2$ (1.7 mg, 0.005 mmol) was diluted with 200 µL $CHCl_3$ before adding allyl-Bpin (1.1 µL, 0.006 mmol). After complete dissolution of the suspension (c.a 5 min), silane (see below) was added and the solution transferred to a separate vial containing the cyclosporine A (0.060 g, 0.05 mmol) dissolved in 200 µL $CHCl_3$. The vial which contained the catalyst/silane mixture was rinsed with an additional 100 µL $CHCl_3$ and transferred to the reaction flask. After capping the vial with a screw top septum lid (PTFE), the vial was allowed to stir inside of the glovebox for 1h. Tributyltin cyanide was then added (0.080 g, 0.25 mmol) and the flask recapped before stirring outside of the glovebox for 24h. After the allotted time, the solution was concentrated under a stream of nitrogen gas before purifying by column chromatography.

(SiO_2, hexane:acetone 4:1→3:1→2:1→1:1→1:3)

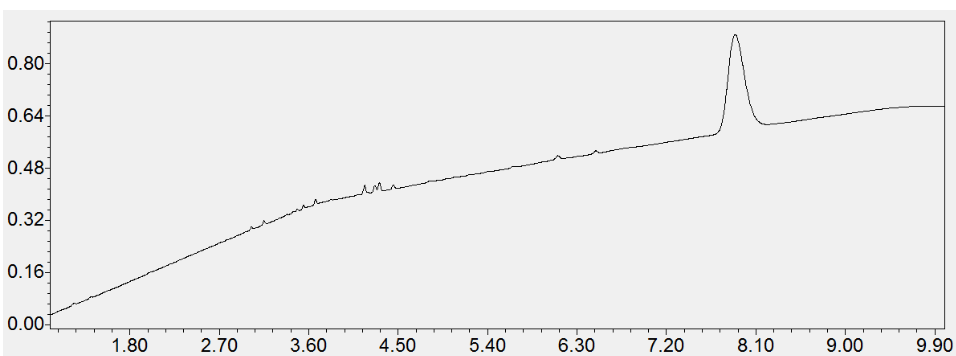
28.0 mg (43% yield), white solid

^{1}H NMR (600 MHz, C_6D_6) δ 8.33 (d, *J* = 7.0 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 9.3 Hz, 1H), 5.89 (dd, *J* = 11.1, 3.6 Hz, 1H), 5.75 – 5.72 (m, 2H), 5.53 (ddd, *J* = 15.9, 11.3, 4.3 Hz, 3H), 5.51 – 5.44 (m, 1H), 5.40 (t, *J* = 6.9 Hz, 1H), 5.32 – 5.27 (m, 1H), 5.14 (dd, *J* = 9.3, 7.7 Hz, 1H), 5.05 (d, *J* = 11.0 Hz, 1H), 4.84 – 4.79 (m, 1H), 4.67 (d, *J* = 7.1 Hz, 1H), 4.45 (t, *J* = 3.1 Hz, 1H), 4.36 (dd, *J* = 8.3, 3.2 Hz, 1H), 3.97 – 3.91 (m, 1H), 3.81 (d, *J* = 14.3 Hz, 1H), 3.73 (s, 3H), 3.06 (s, 3H), 3.05 (s, 3H), 3.04 (s, 3H), 2.97 (s, 3H), 2.84 (s, 3H), 2.42 (s, 3H), 2.37 – 2.28 (m, 3H), 1.99 (dtt, *J* = 9.8, 6.4, 3.4 Hz, 1H), 1.88 (dt, *J* = 13.6, 10.1 Hz, 1H), 1.81 (dd, *J* = 6.4, 1.6 Hz, 3H), 1.69 – 1.60 (m, 3H), 1.59 (d, *J* = 7.2 Hz, 3H), 1.28 – 1.20 (m, 15H), 1.16 (dd, *J* = 13.7, 6.6 Hz, 7H), 1.09 (dd, *J* = 7.1, 5.5 Hz, 6H), 1.05 (d, *J* = 6.5 Hz, 3H), 1.03 – 0.97 (m, 9H), 0.92 (dt, *J* = 8.1, 5.0 Hz, 11H), 0.82 (d, *J* = 5.8 Hz, 4H), 0.75 (t, *J* = 7.4 Hz, 4H), 0.72 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (151 MHz, C_6D_6) δ 176.4, 174.9, 174.5, 172.7, 171.8, 171.6, 171.5, 171.0, 170.4, 169.5, 130.7, 126.9, 120.4, 76.4, 60.7, 59.5, 57.7, 56.1, 55.7, 55.3, 54.4, 54.3, 50.3, 48.6, 48.2, 45.0, 41.0, 39.9, 38.5, 37.2, 36.6, 36.5, 35.1, 33.9, 31.9, 31.3, 30.84, 30.81, 30.1, 30.0, 29.5, 26.8, 25.19, 25.18, 25.0, 24.8, 24.7, 24.4, 23.94, 23.92, 23.71, 23.66, 22.2, 22.1, 21.9, 20.8, 19.2, 19.1, 18.4, 18.2, 17.6, 15.5, 10.2, 7.8, 7.7, 7.2, 5.6.

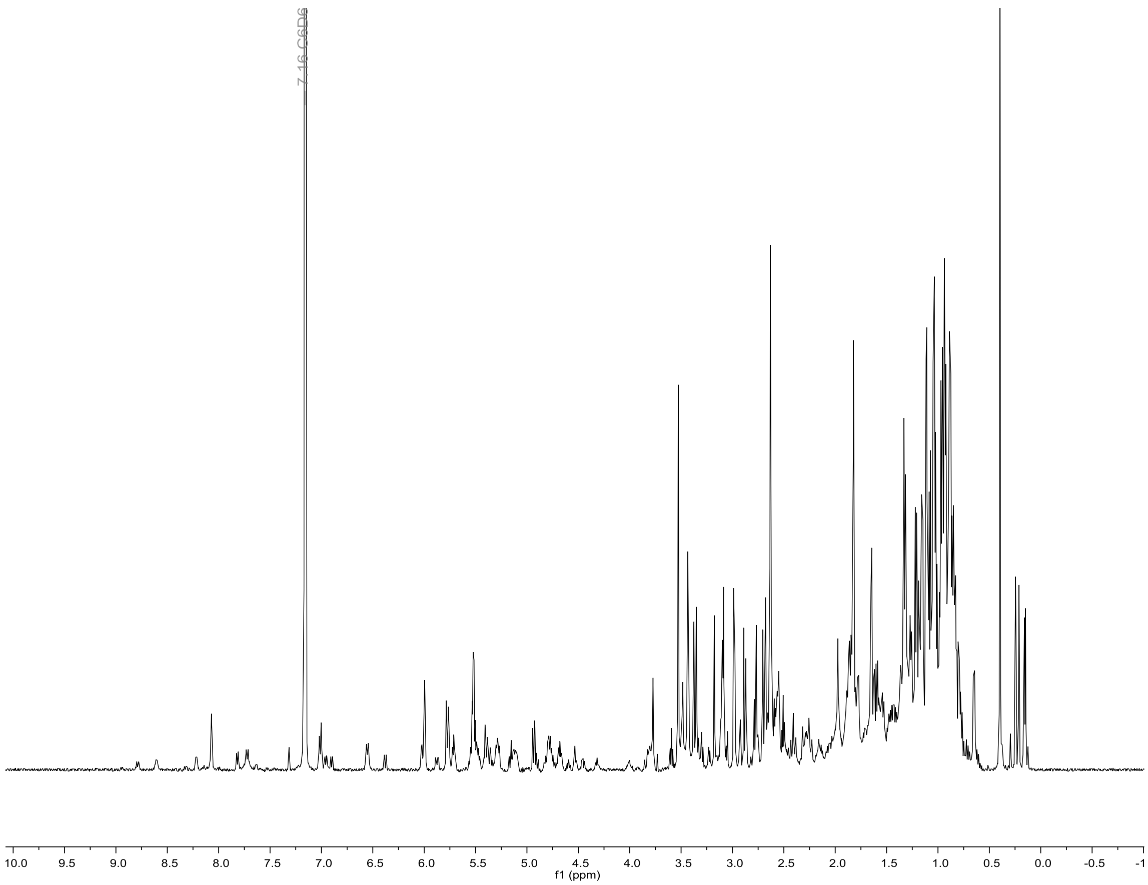
HRMS (ESI) calcd for $C_{67}H_{123}N_{12}O_{12}Si$ $(M+H)^+$: 1315.91527. Found: 1315.91559.

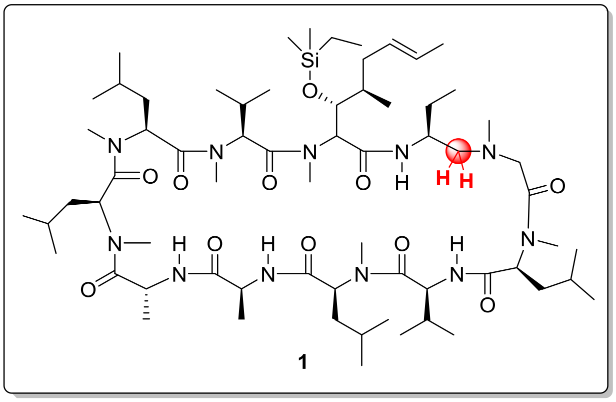
IR (thin film, cm^{-1}) 3317, 2958, 2240, 1682, 1668, 1659, 1651, 1644, 1633



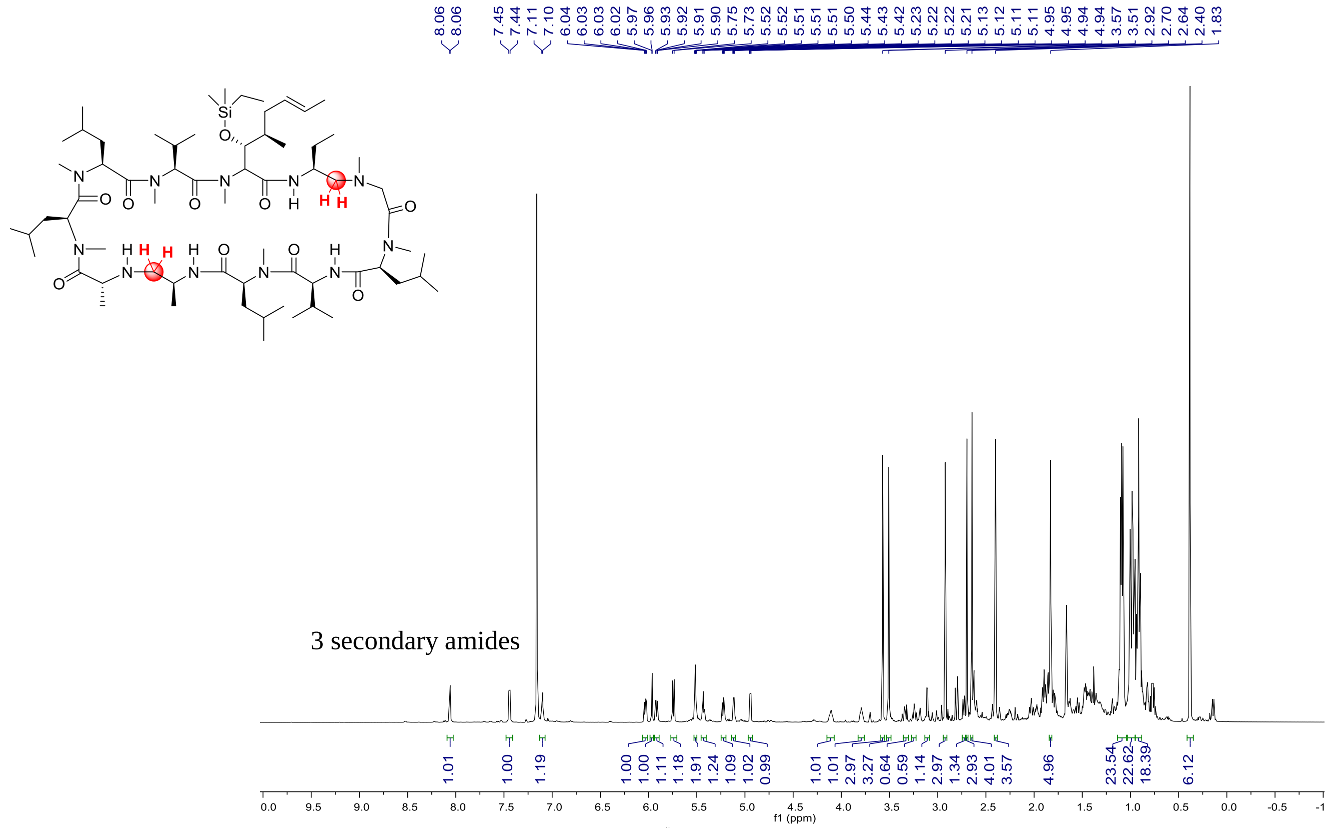
NMR spectra

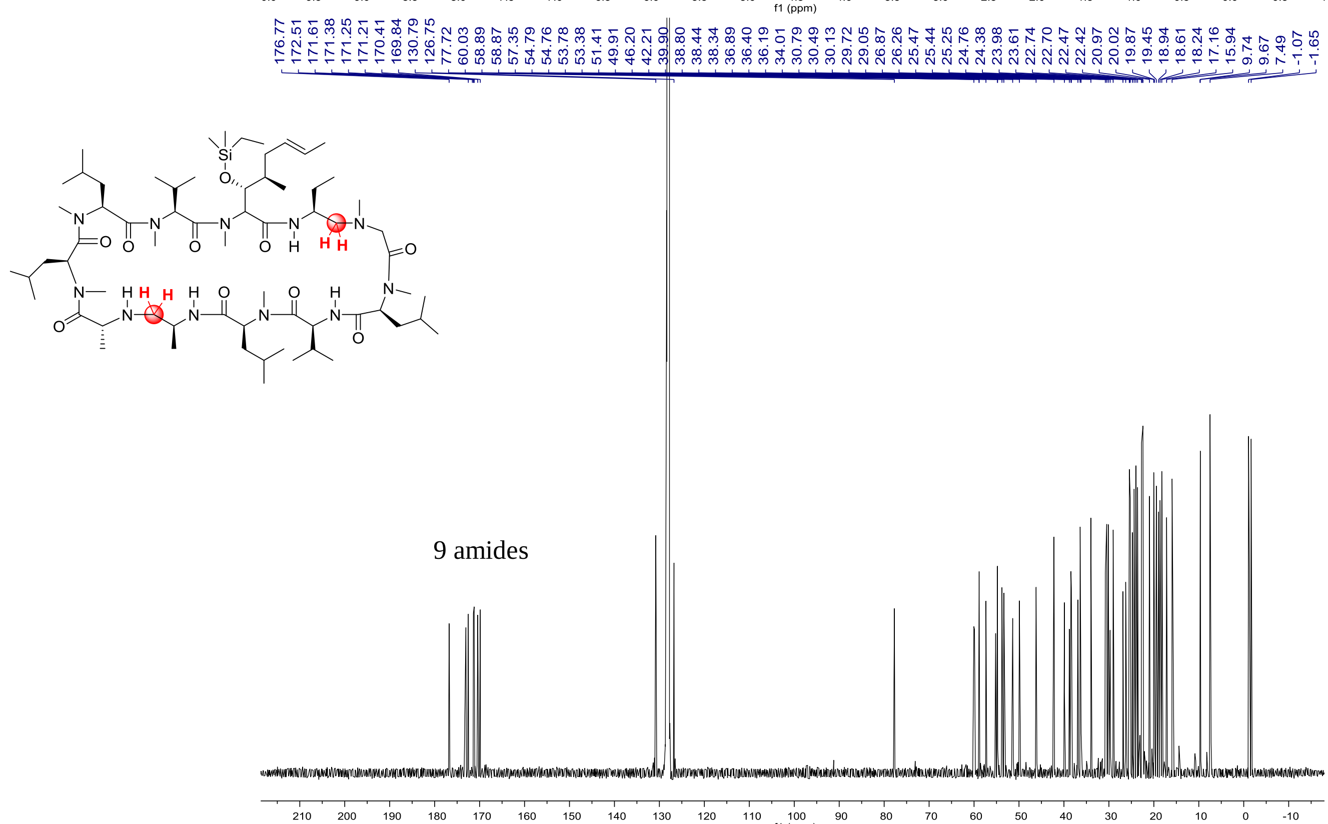
^{1}H (600 MHz) NMR of **1** in C_6D_6 at 25 °C



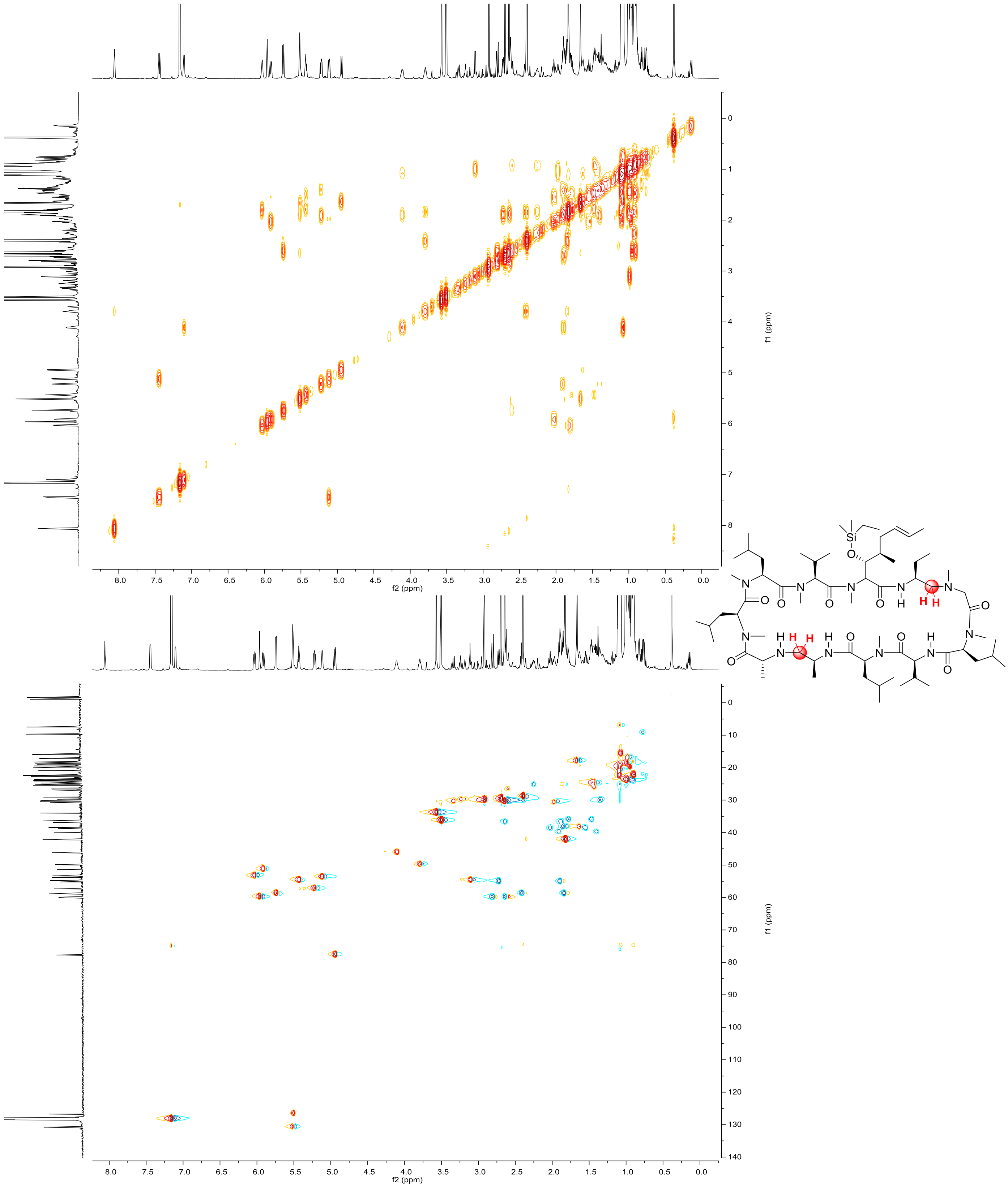


^{1}H (700 MHz) and $^{13}C\{H\}$ (157 MHz) NMR of **2** in C_6D_6 at 25 °C

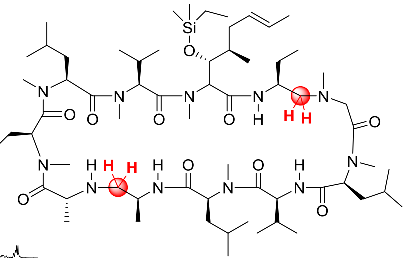


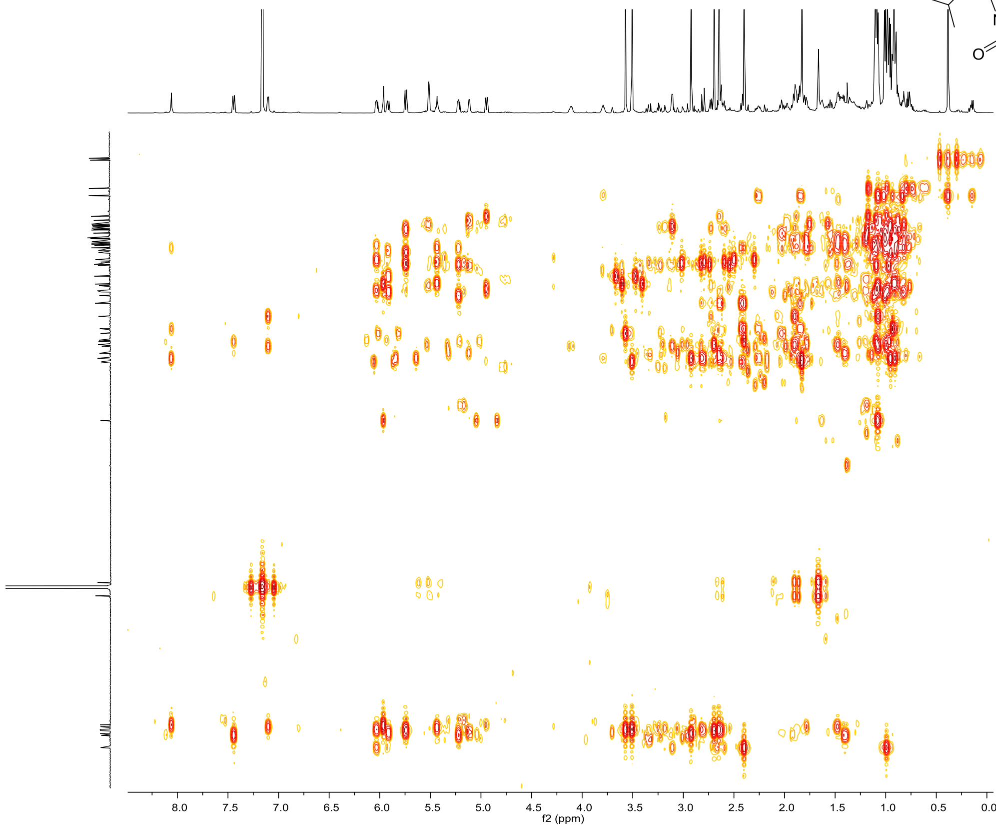


COSY and HSQC of **2** in C_6D_6 at 25 °C

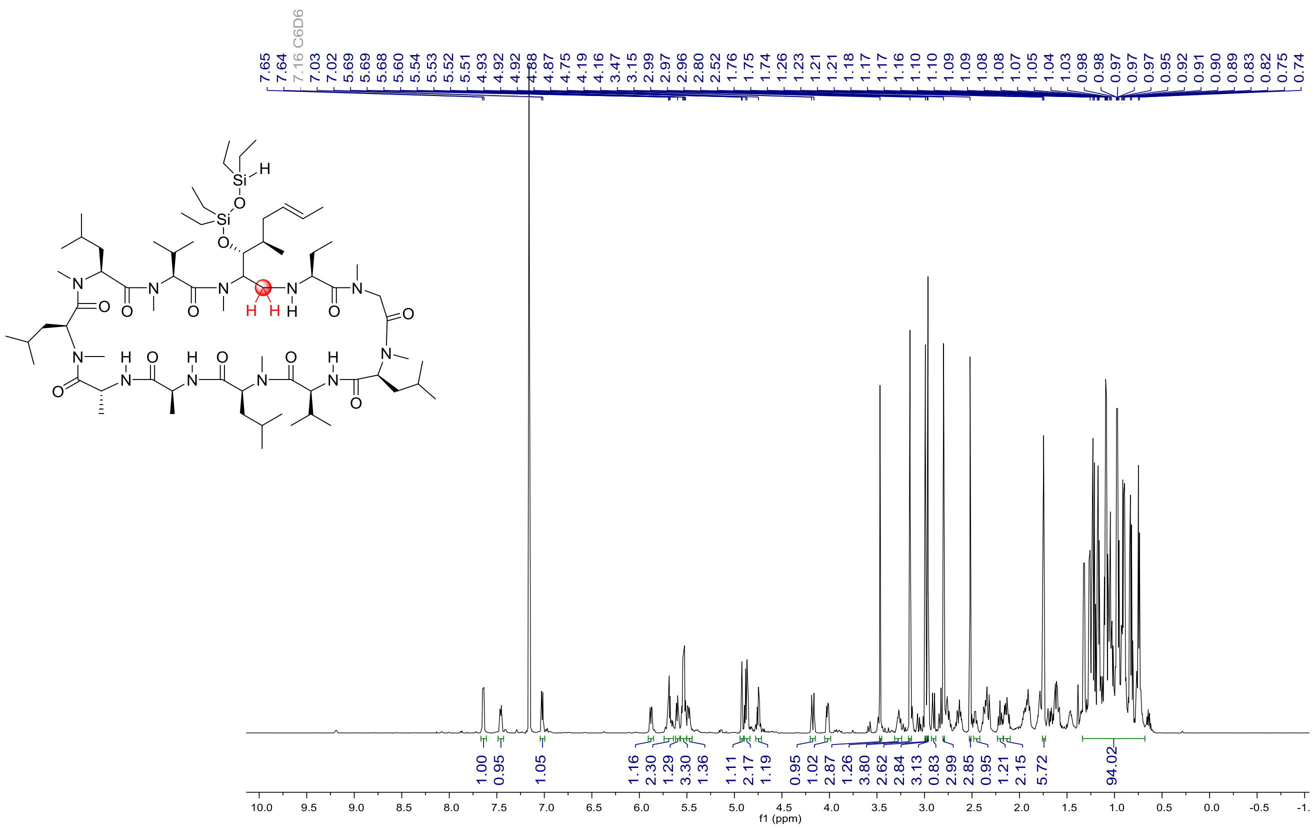


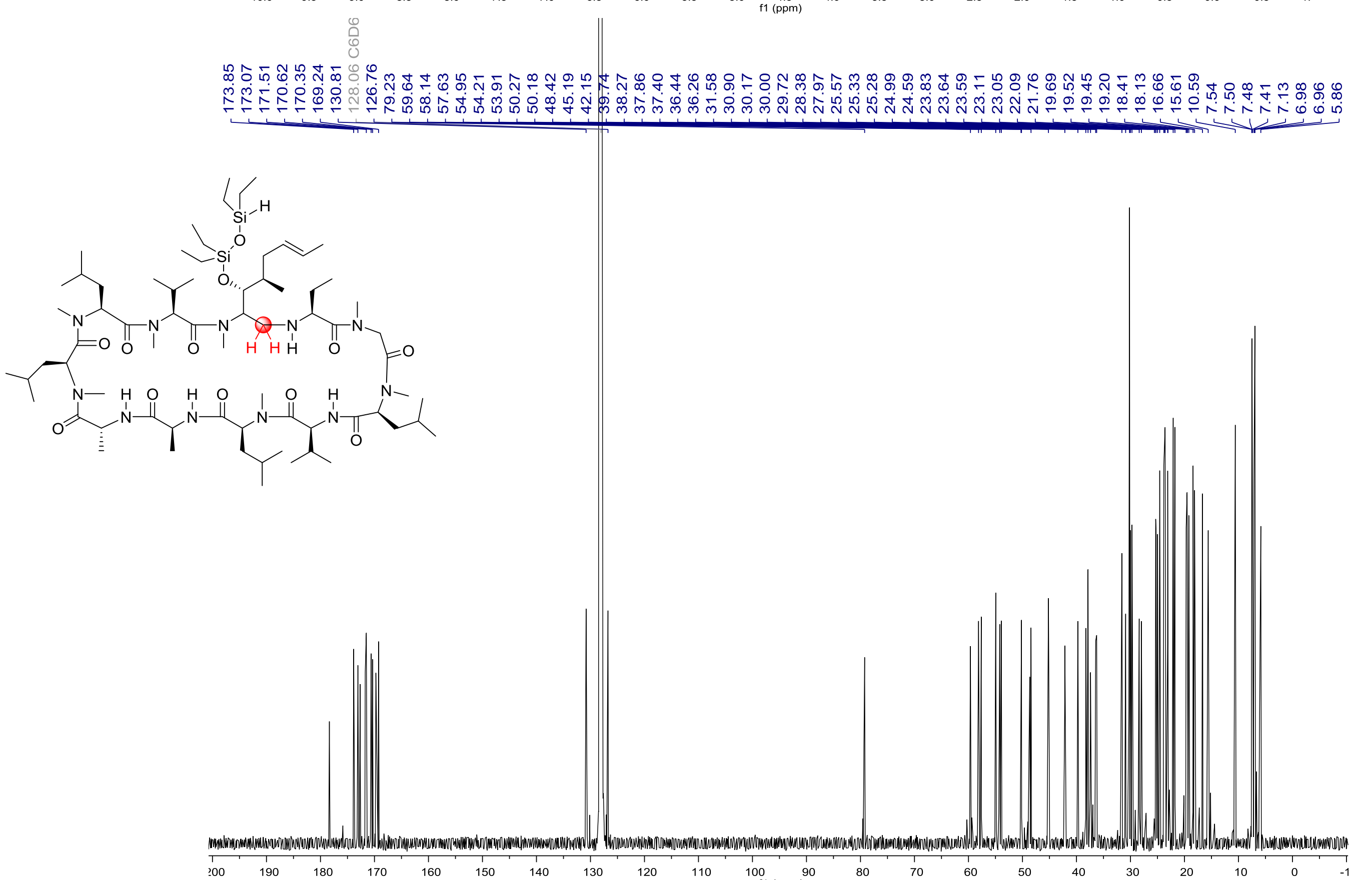
HMBC of **2** in C_6D_6 at 25 °C



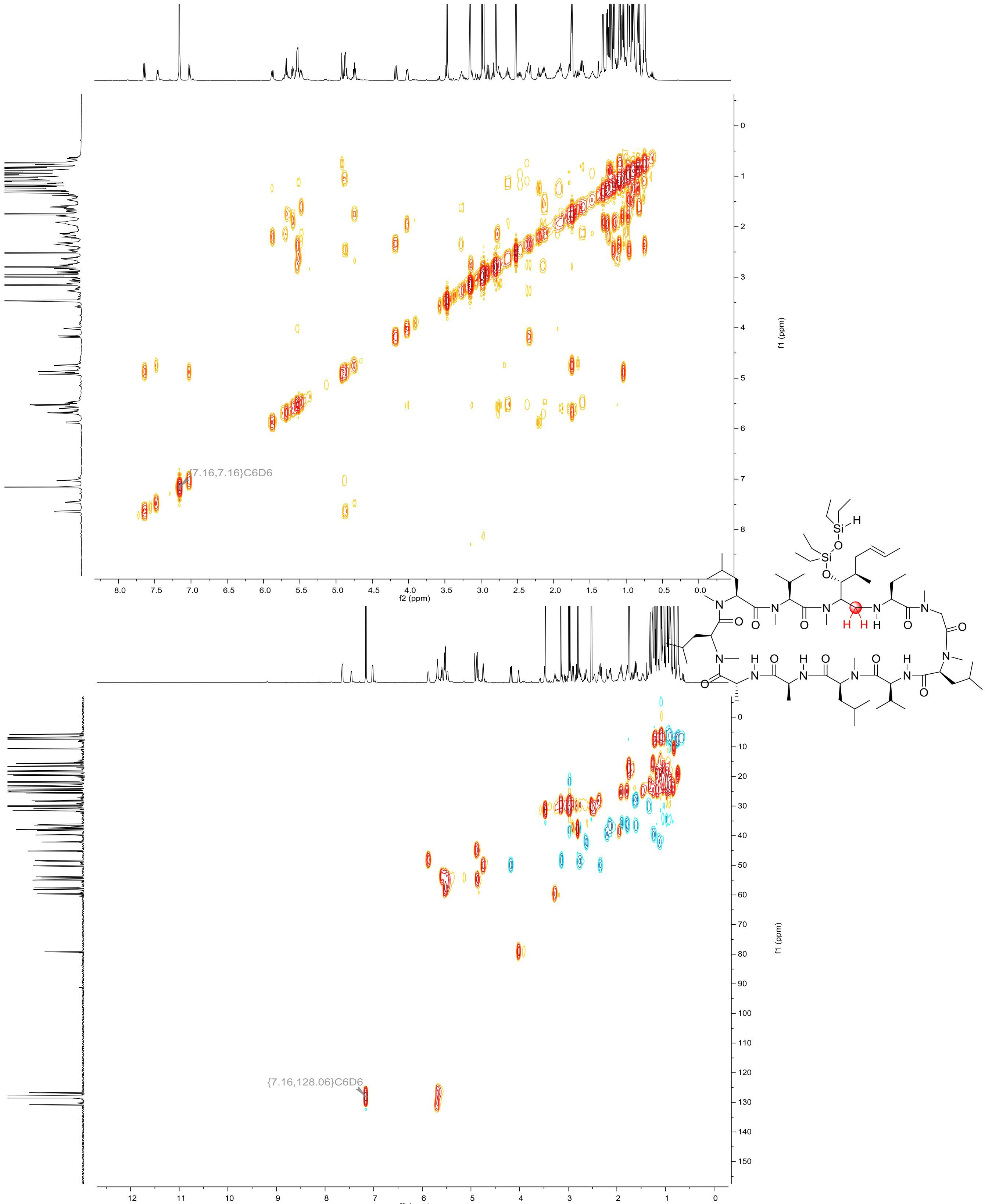


^{1}H (600 MHz) and $^{13}C\{H\}$ (151 MHz) NMR of **3** in C_6D_6 at 25 °C

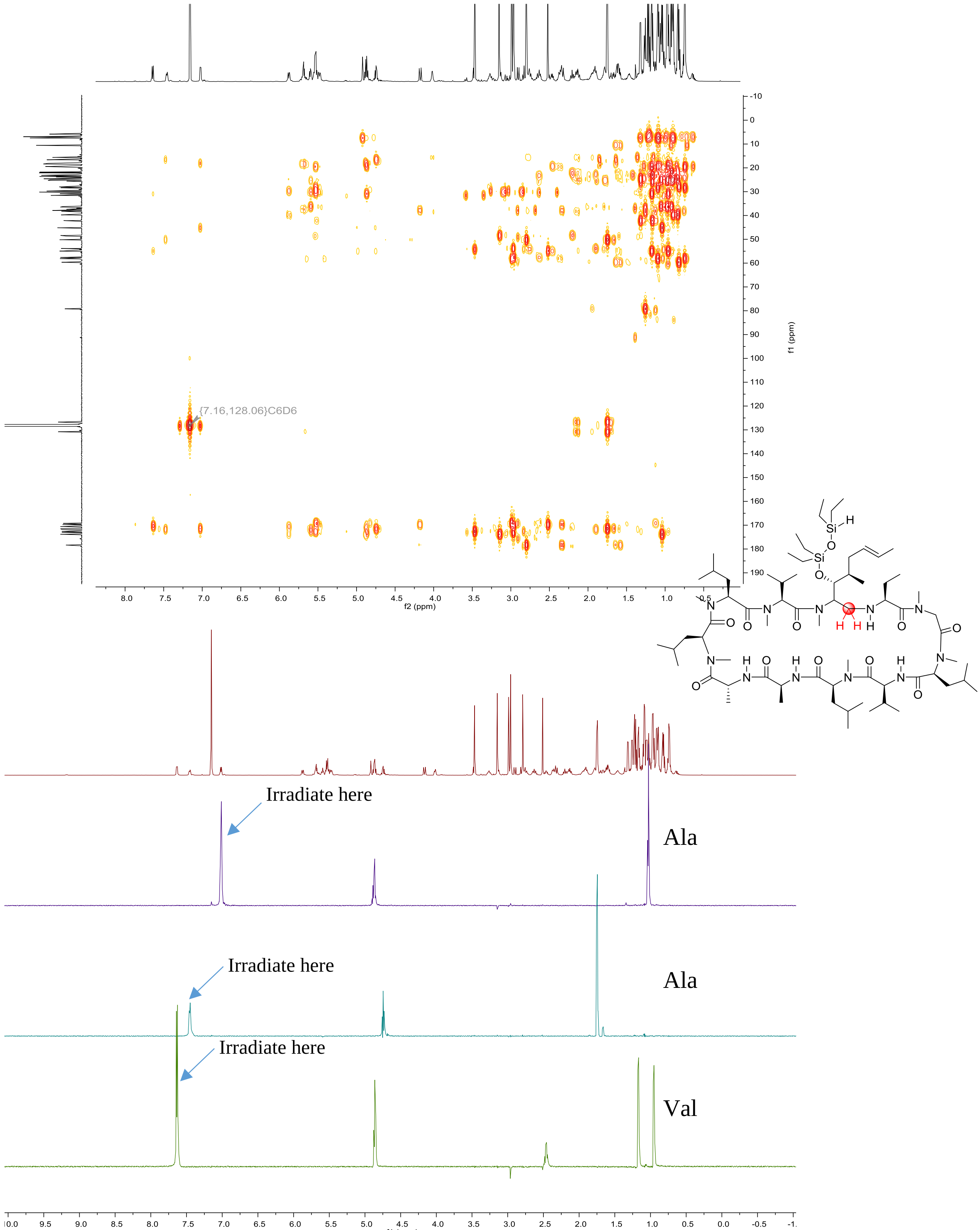




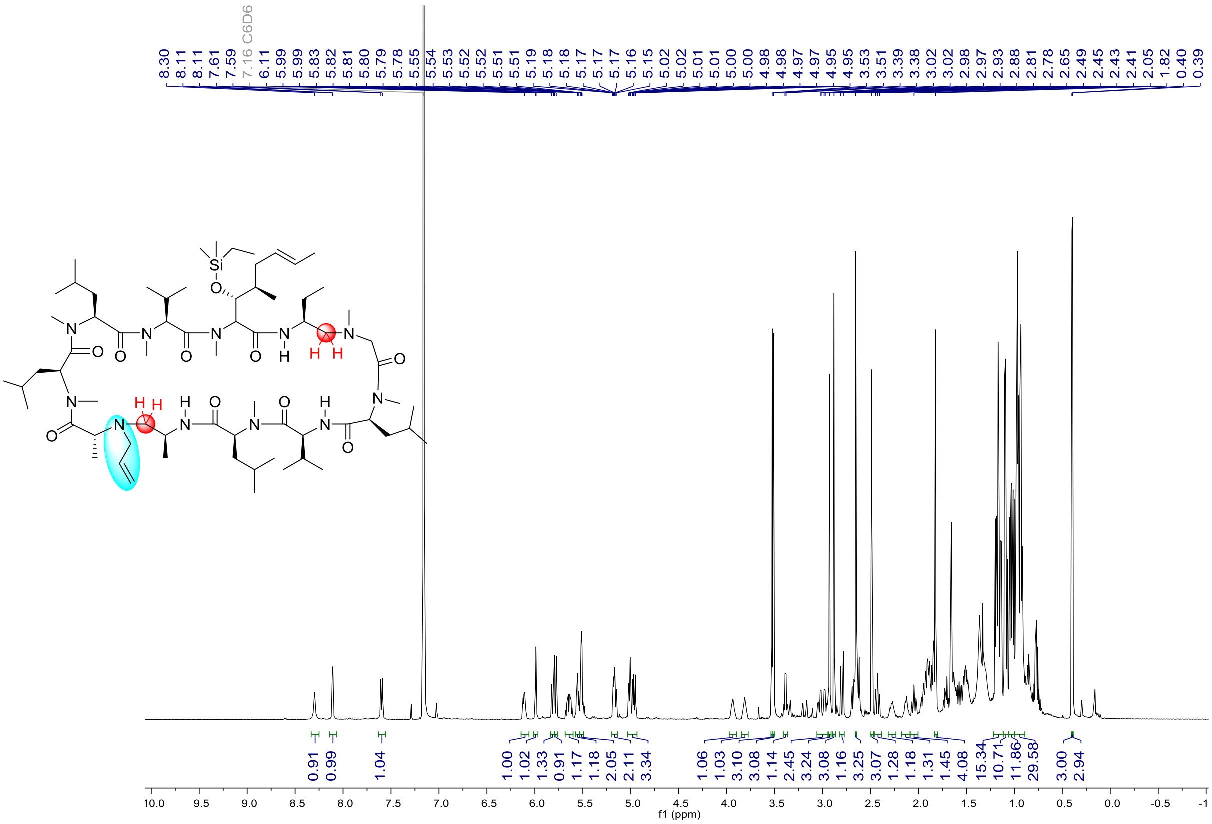
COSY and HSQC of **3** in C_6D_6 at 25 °C

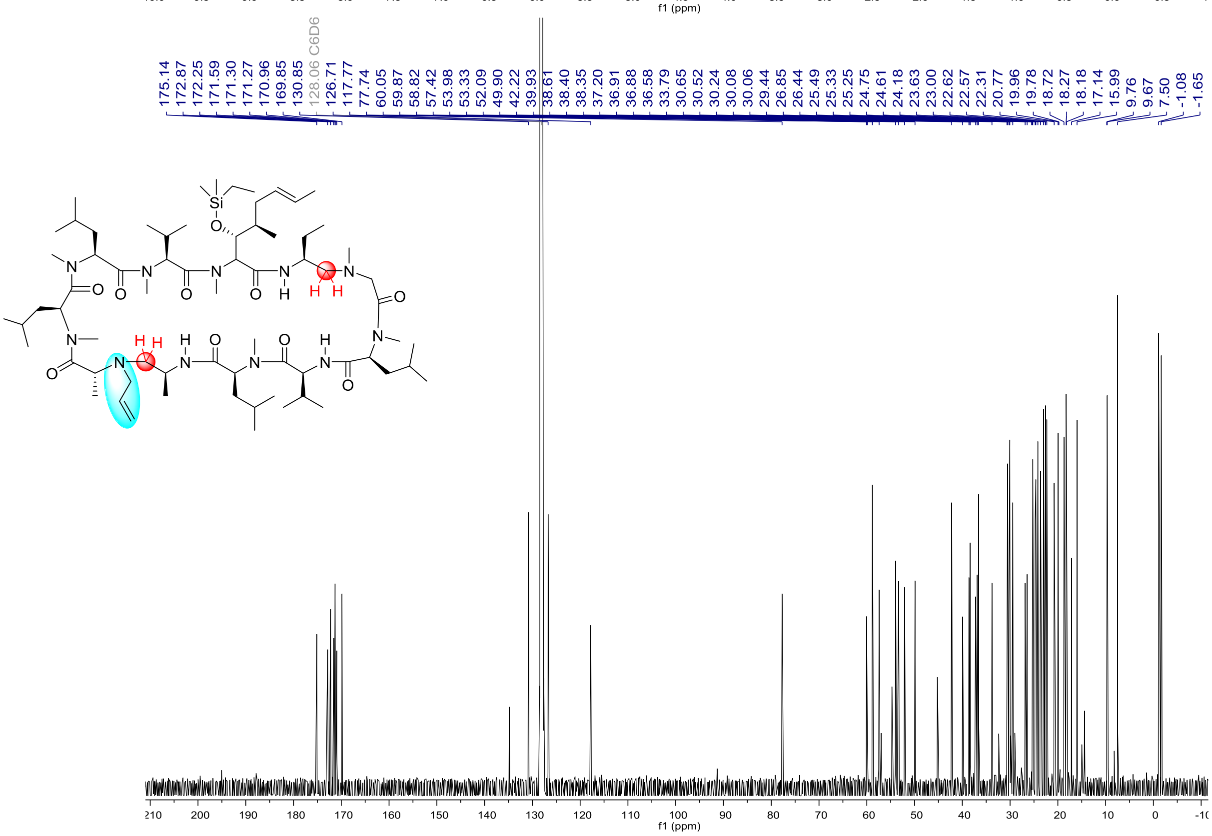


HMBC and 1D-TOCSY of **3** in C_6D_6 at 25 °C

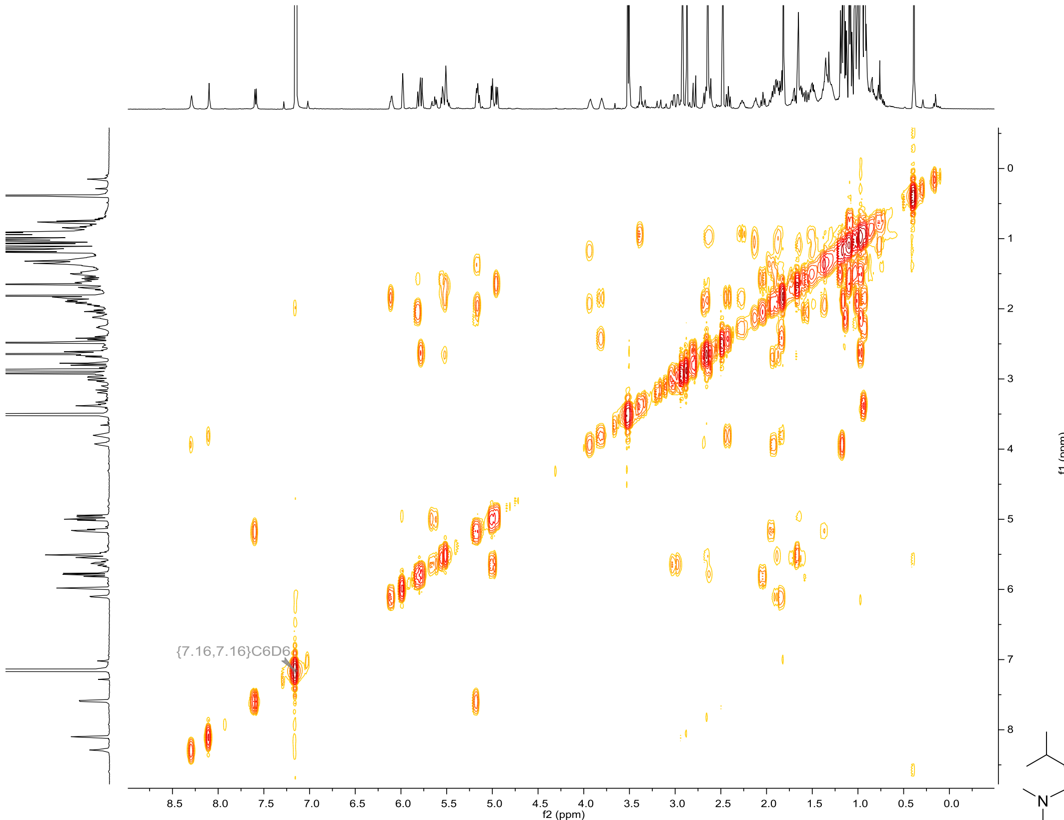


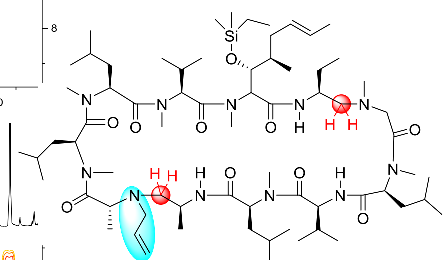
^{1}H (600 MHz) and $^{13}C\{H\}$ (151 MHz) NMR of **3a** in C_6D_6 at 25 °C

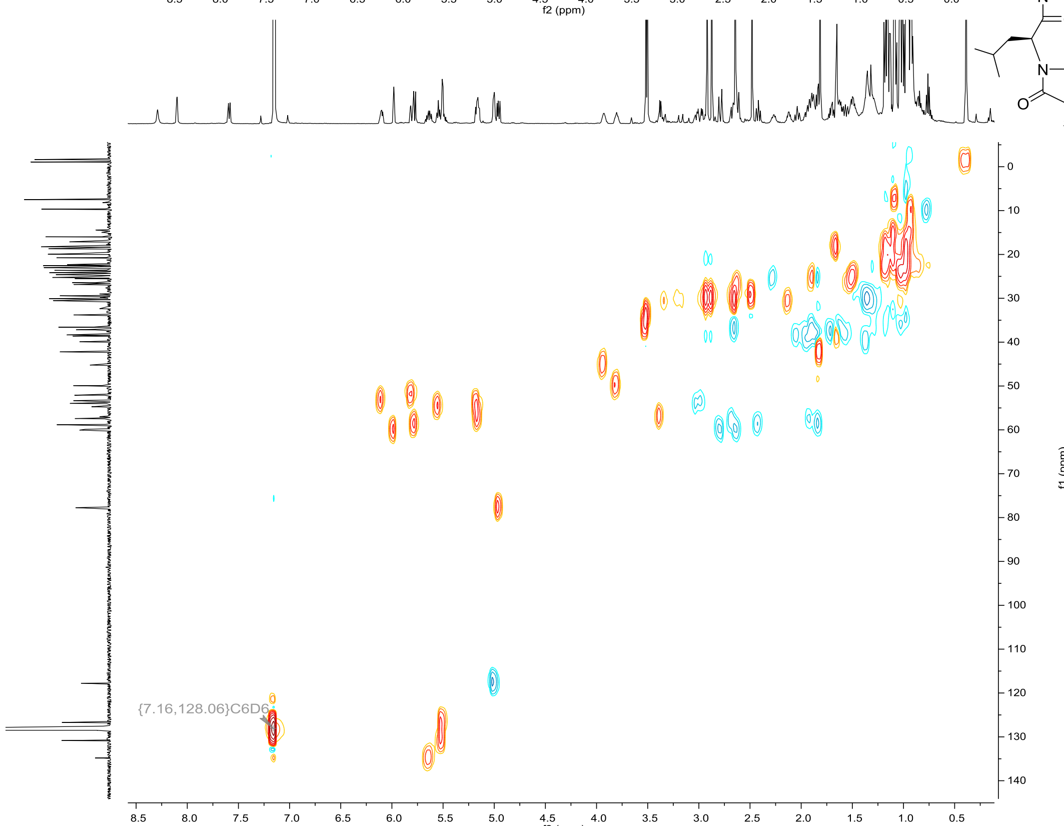




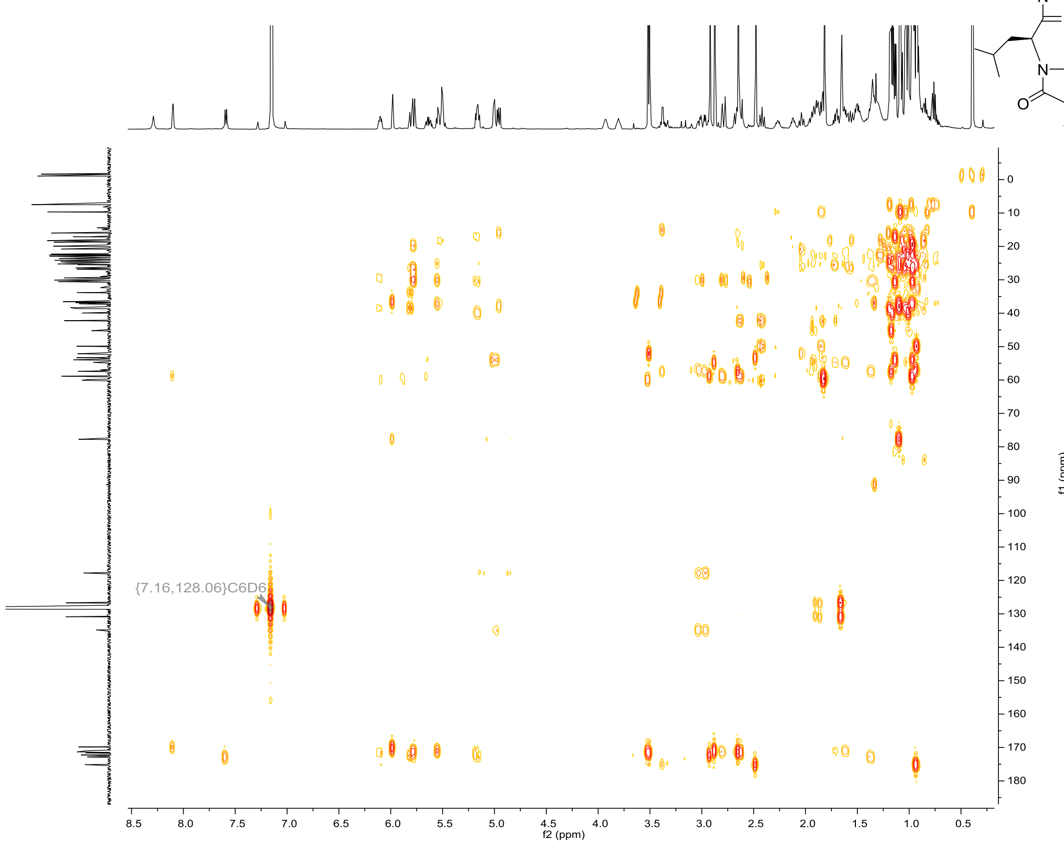
COSY and HSQC of **3a** in C_6D_6 at 25 °C

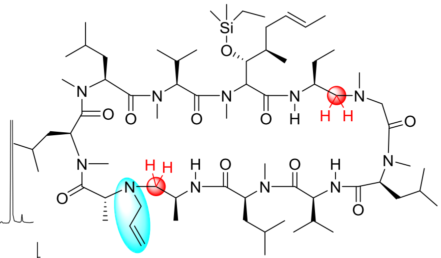




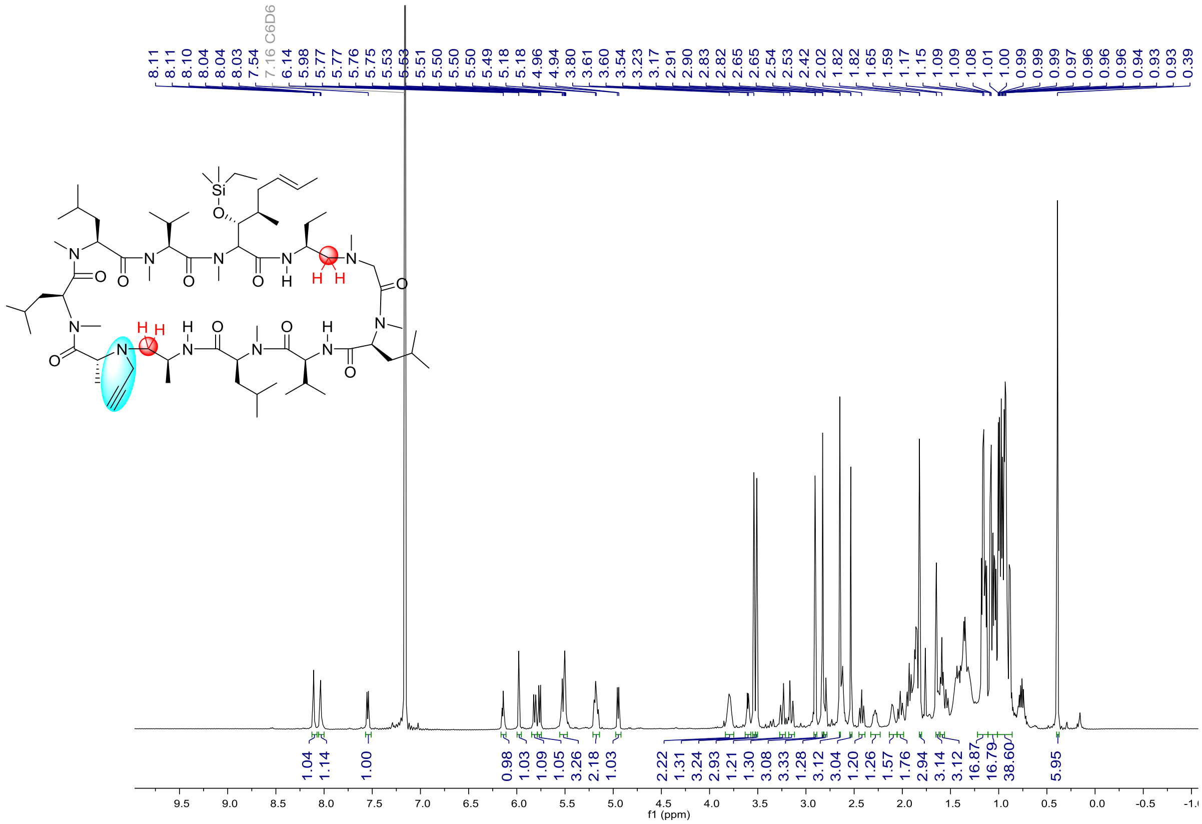


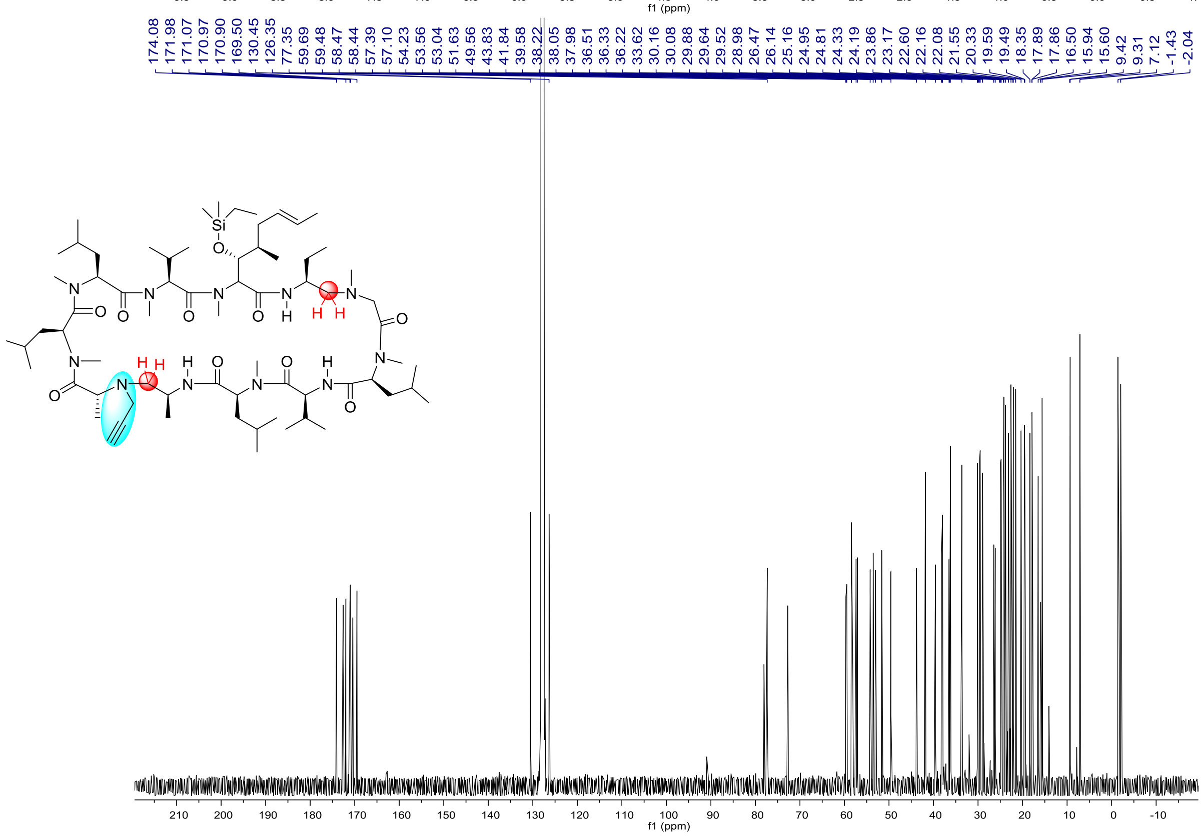
HMBC of **3a** in C_6D_6 at 25 °C



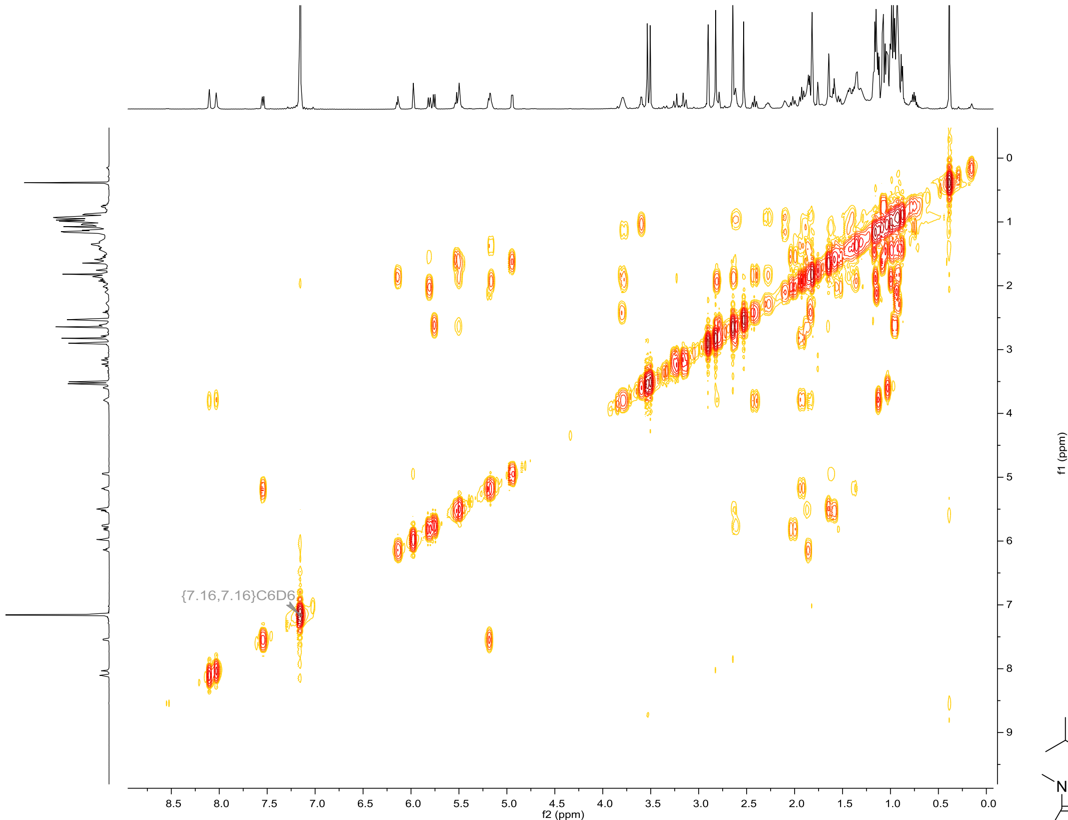


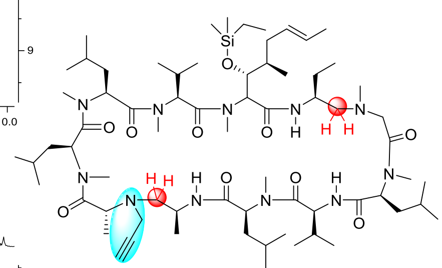
[1]H (600 MHz) and [13]C{H} (151 MHz) NMR of **3b** in C_6D_6 at 25 °C

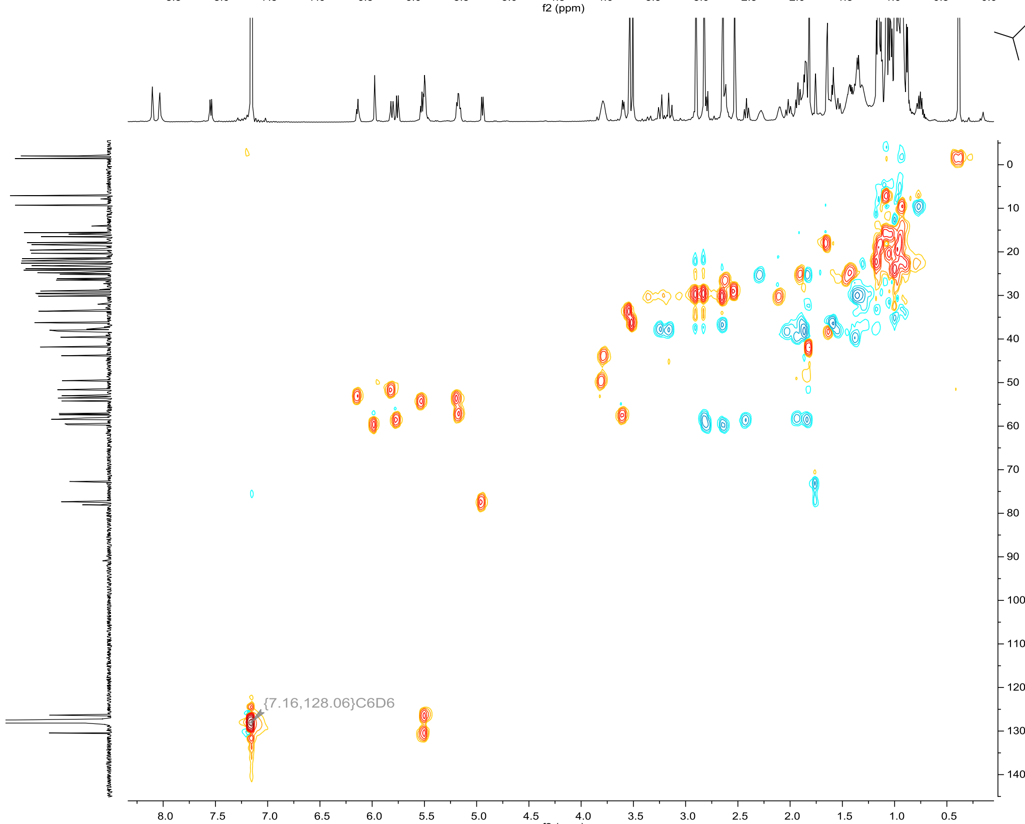




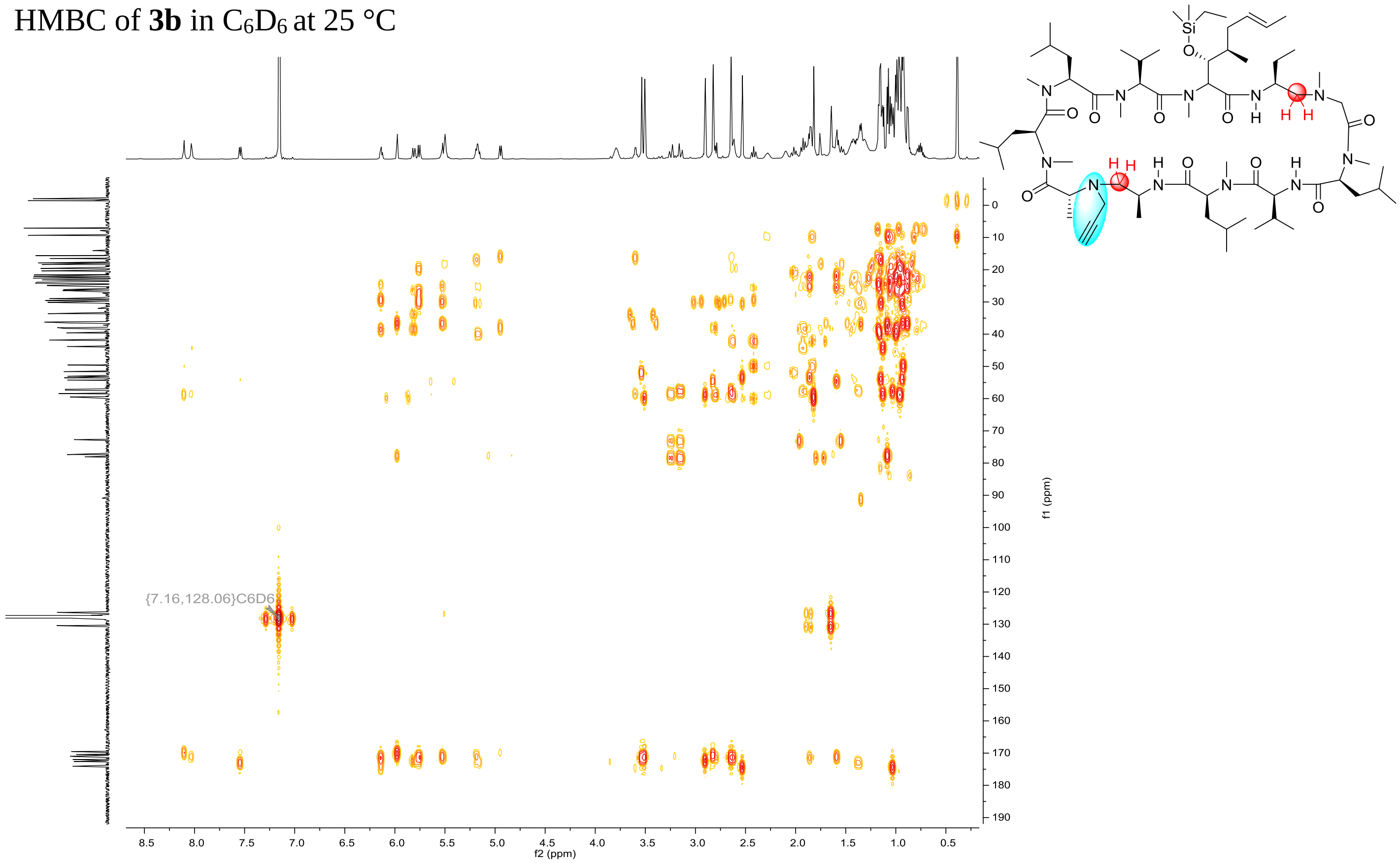
COSY and HSQC of **3b** in C_6D_6 at 25 °C



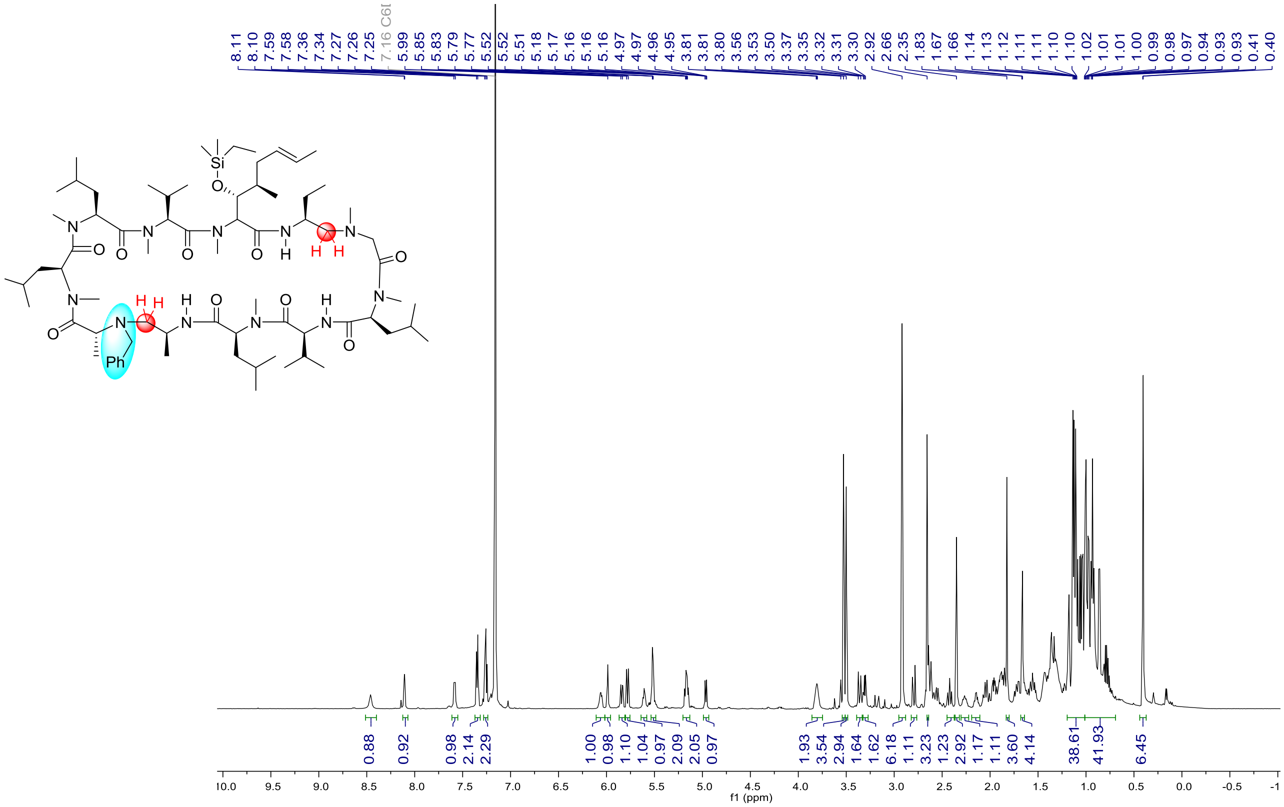


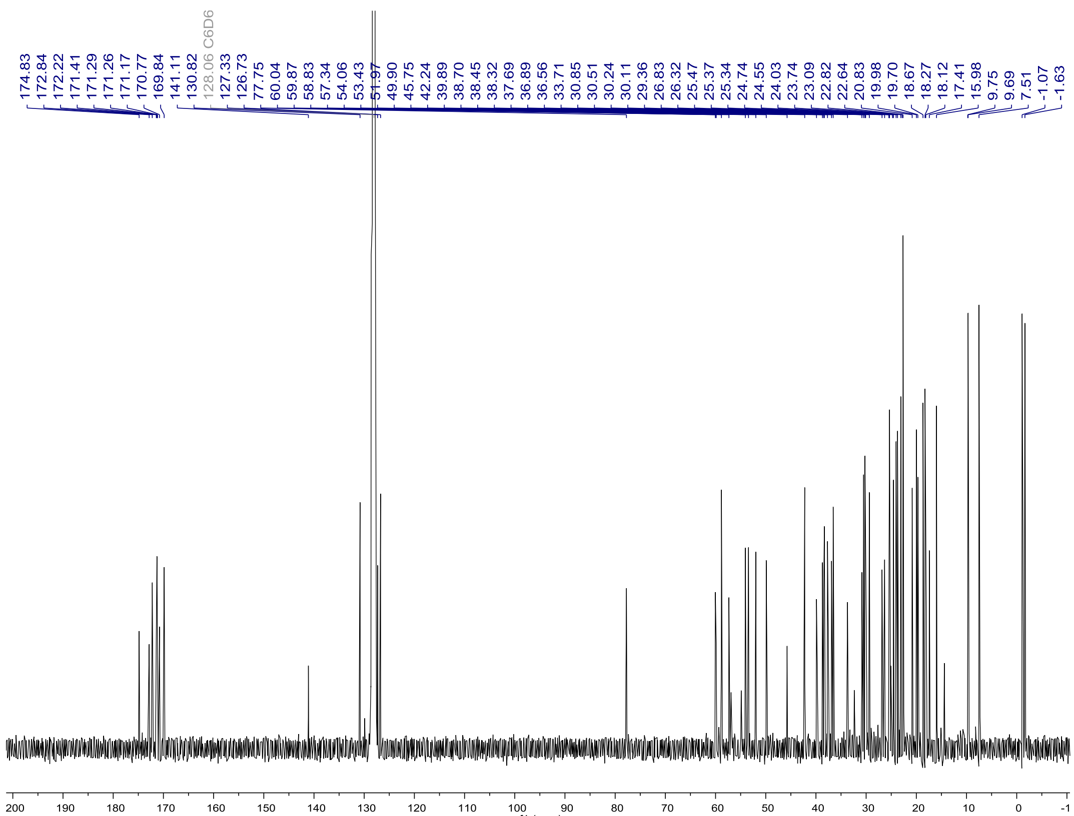


HMBC of **3b** in C_6D_6 at 25 °C

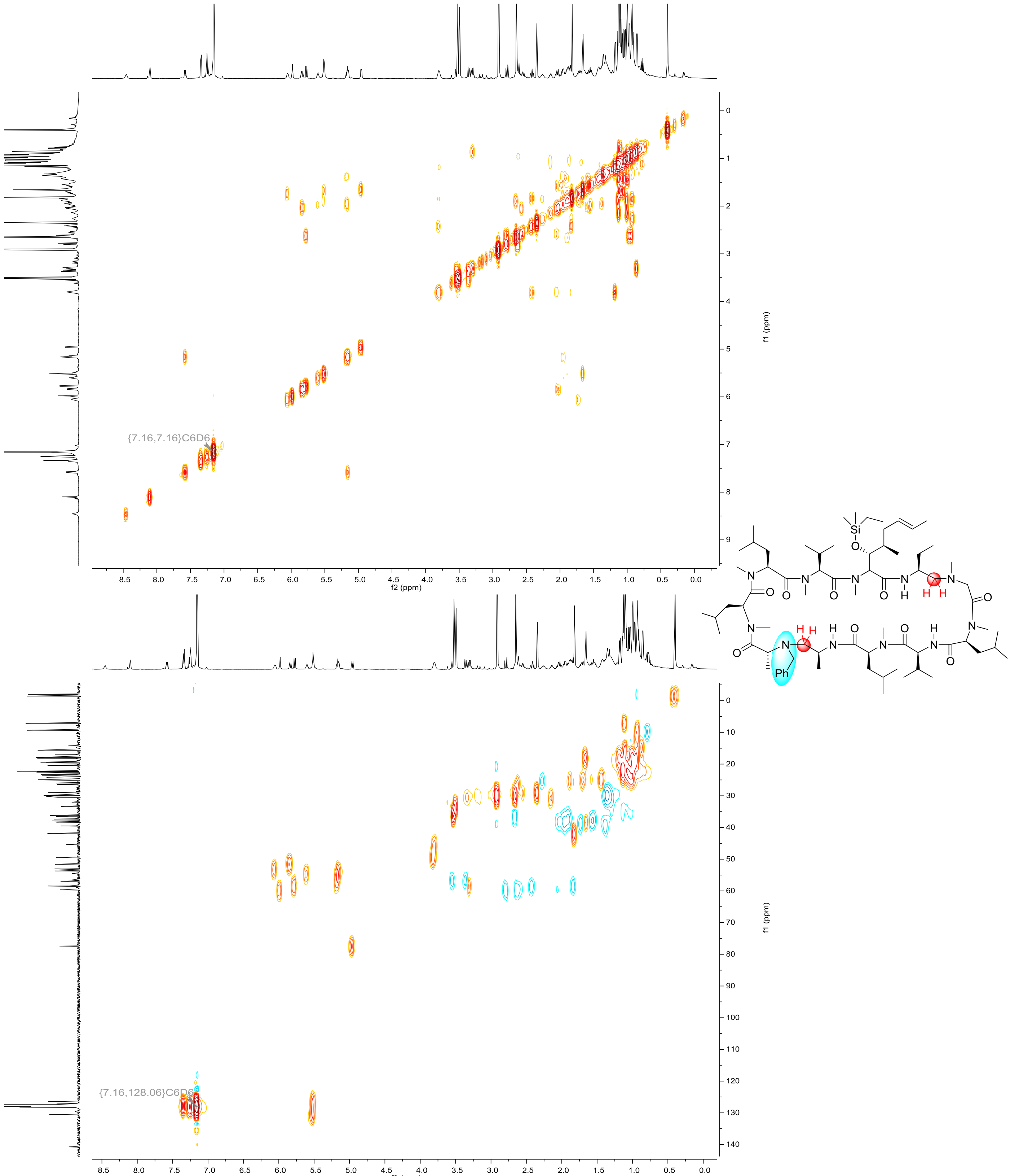


[1]H (600 MHz) and [13]C{H} (151 MHz) NMR of **3c** in C_6D_6 at 25 °C

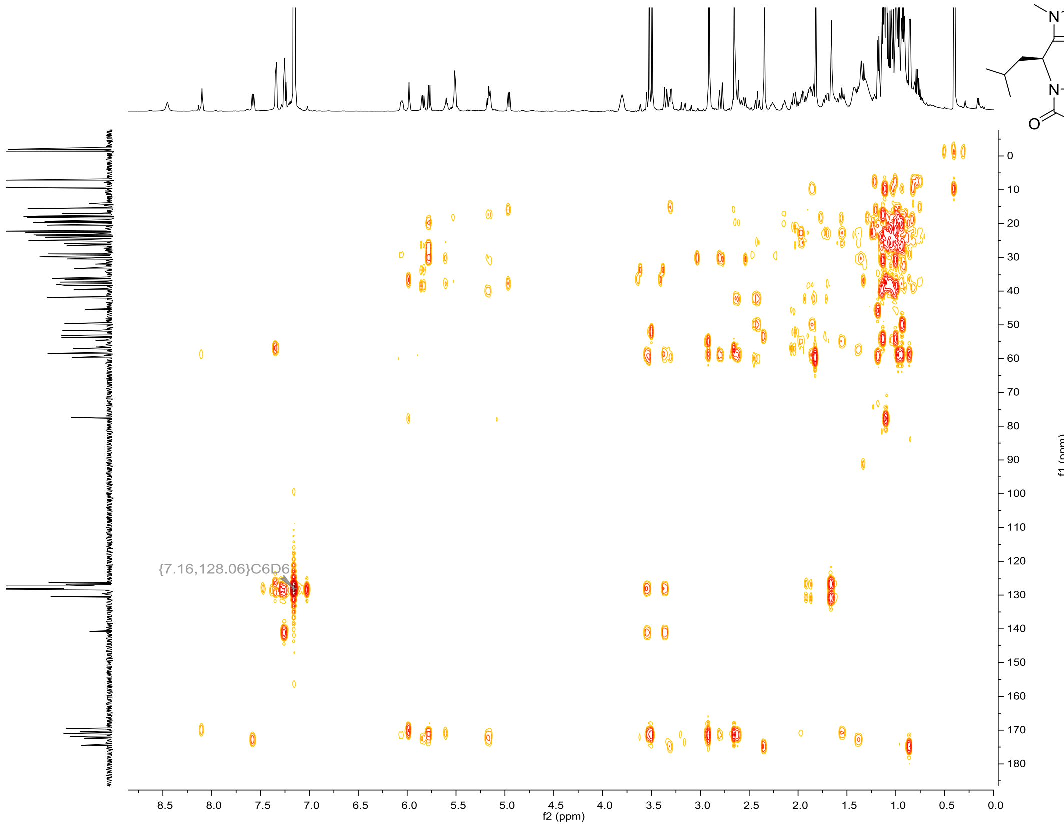


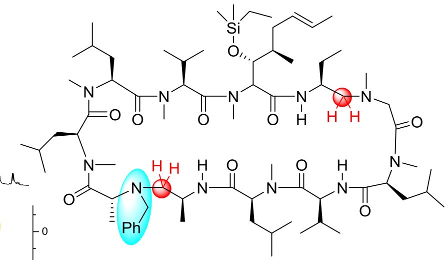


COSY and HSQC of **3c** in C_6D_6 at 25 °C

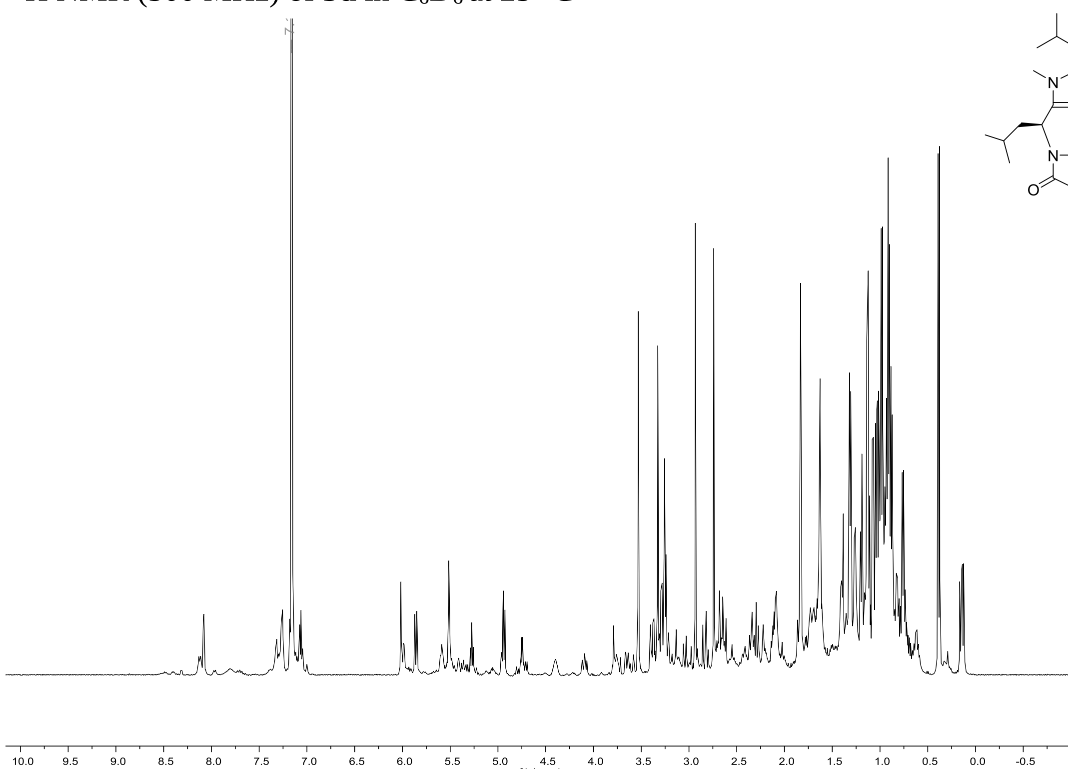


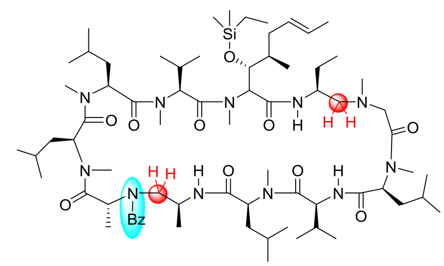
HMBC of **3c** in C_6D_6 at 25 °C



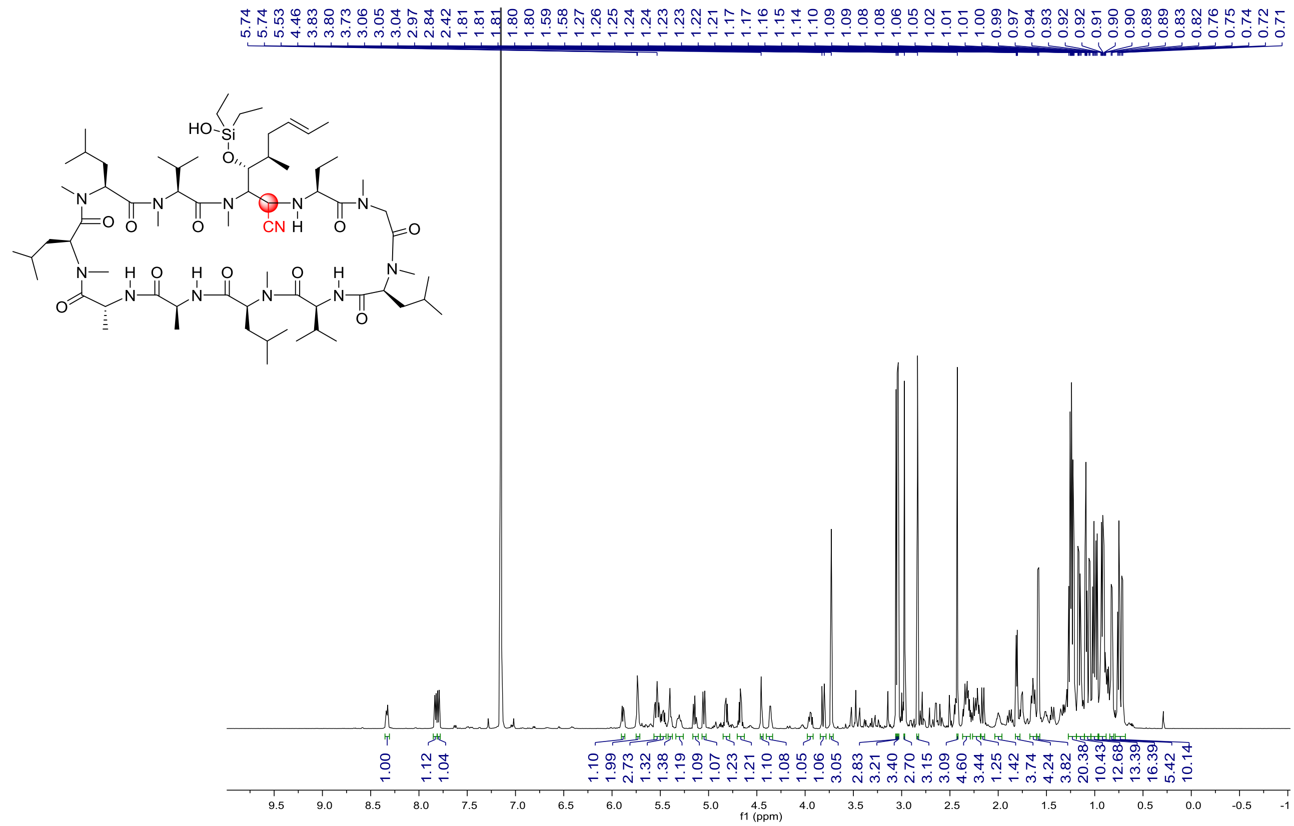


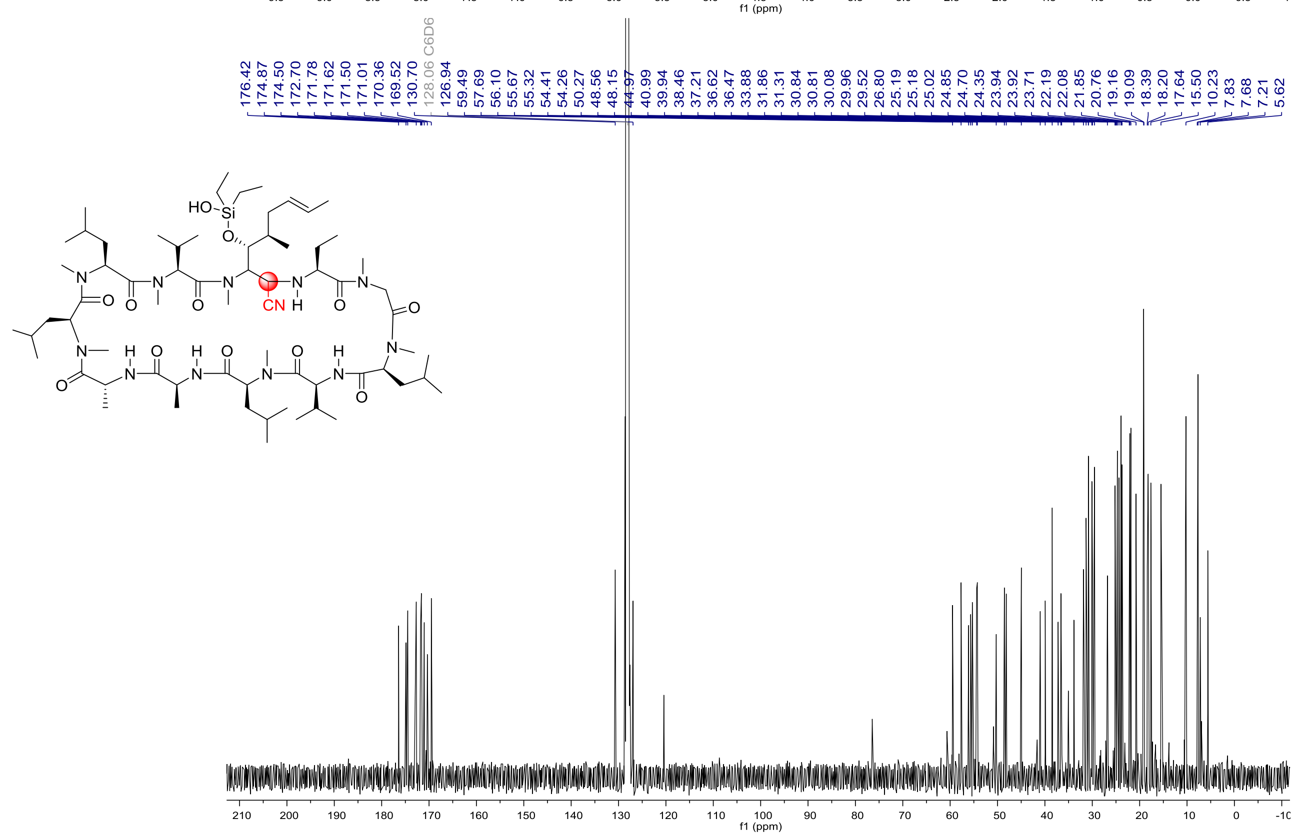
^{1}H NMR (500 MHz) of **3d** in C_6D_6 at 25 °C



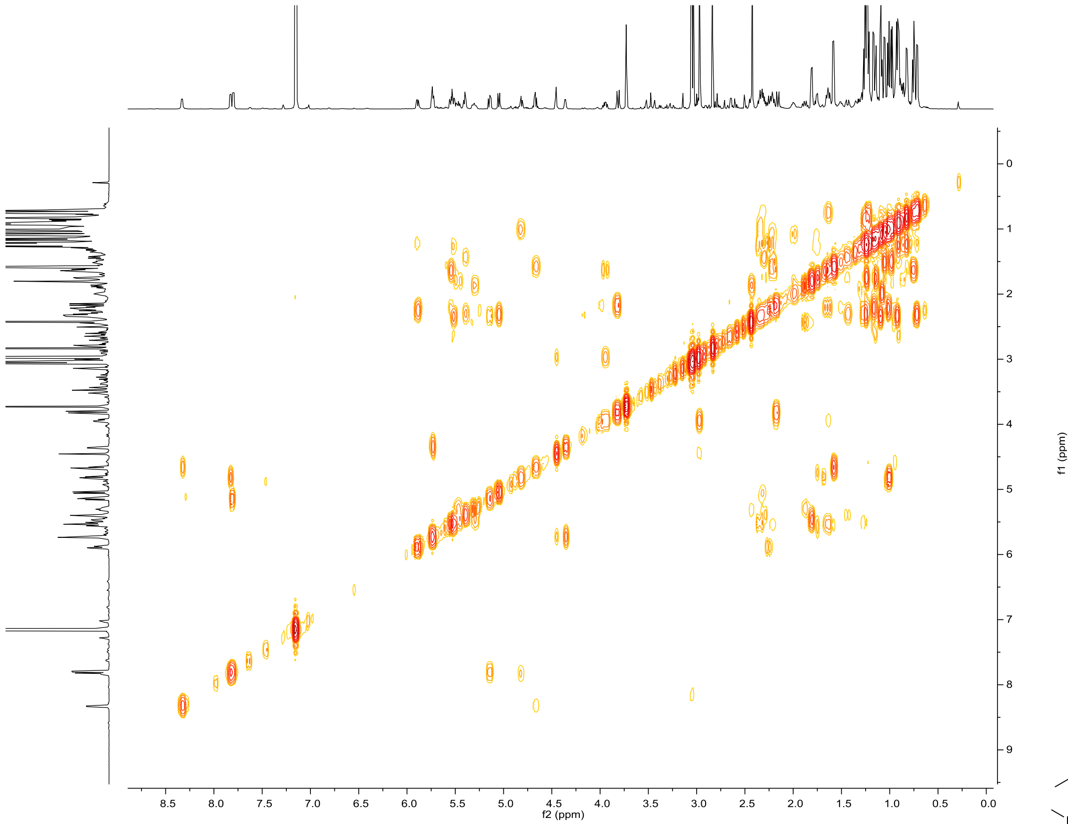


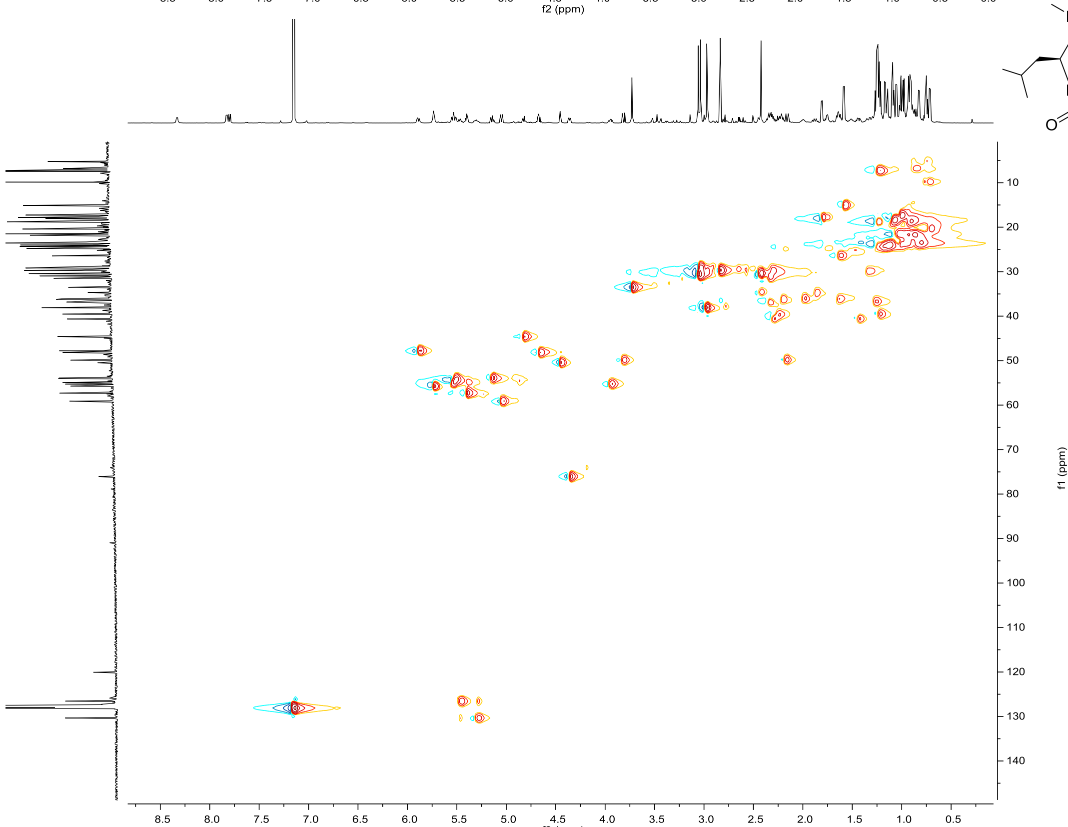
[1]H (600 MHz) and [13]C{H} (151 MHz) NMR of **5** in C_6D_6 at 25 °C

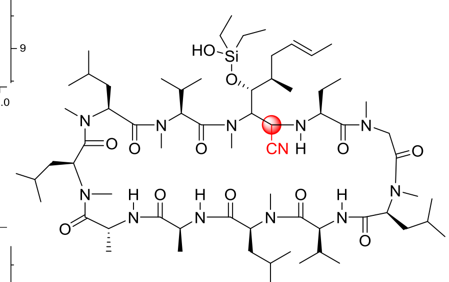




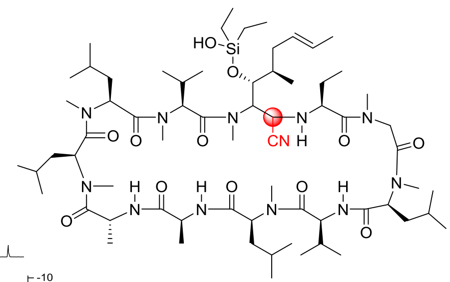
COSY and HSQC NMR of **5** in C_6D_6 at 25 °C

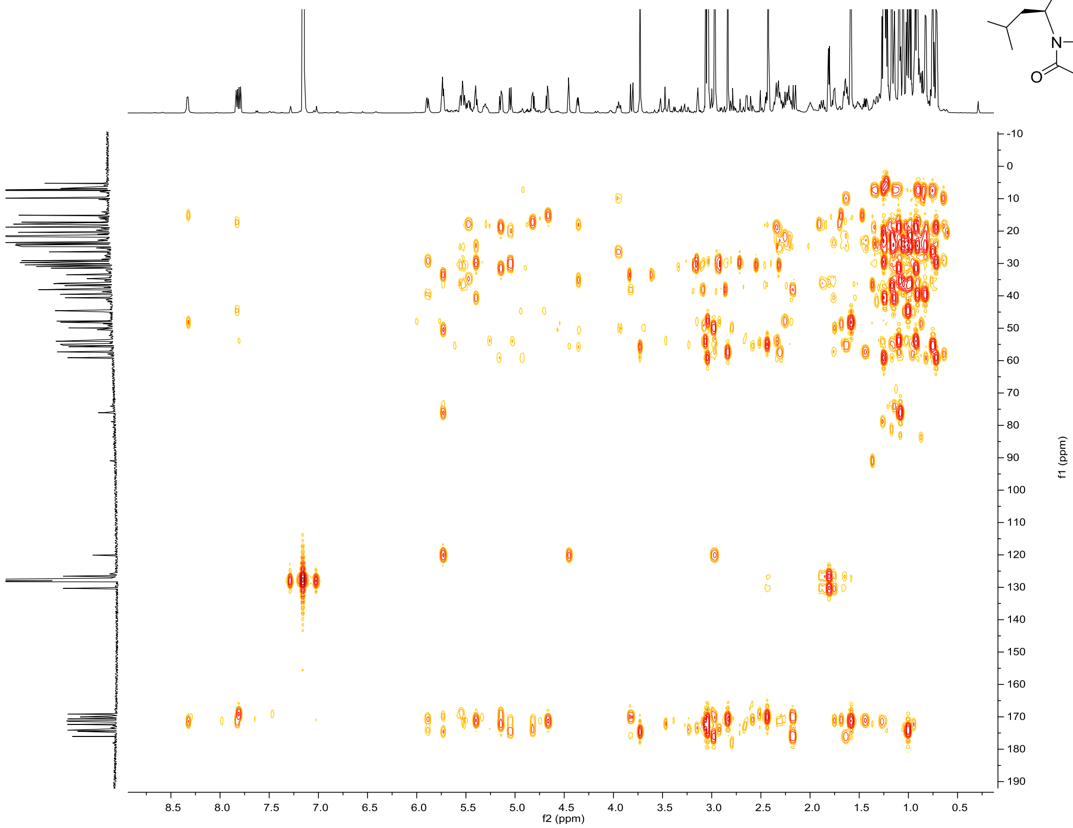






HMBC of **5** in C_6D_6 at 25 °C





MS^2 peak lists

Observed ions for 1-OH

m/z	Intensity	Relative
1189.87183	13695330	10.2
1188.86972	22706180	50.52
1188.86877	23341270	17.38
1171.86133	13183650	9.82
1170.85885	21243790	47.26
1170.85815	23225390	17.3
1085.76982	1641238.5	3.65
1085.76917	1882172.3	1.4
1077.7832	8671761	6.46
1076.78198	23319406	17.37
1076.78097	14719960	32.75
1075.78573	12745071	28.36
1075.78467	14419864	10.74
1062.77148	1700087.1	1.27
1061.76968	2843990.3	6.33
1061.76868	3243125	2.42
1058.77698	9595828	7.15
1057.77501	15910833	35.4
1057.77393	18080698	13.47
1043.75949	1810769.6	4.03
1043.75842	2188972	1.63
1005.74352	1686728.4	3.75
1005.74292	2064188.6	1.54
974.68268	1738723.9	1.29
973.68067	3106184	6.91
973.67987	3860002	2.87
964.69879	4875033	3.63
963.69663	8677061	19.31
963.69574	10762784	8.02
950.68359	2080918.1	1.55
949.68323	7680364.5	5.72
949.68112	3694479.5	8.22
948.68544	6931748	15.42
948.68469	8524024	6.35
934.66935	3134253	6.97
934.6684	3854505.8	2.87
931.677	4956370.5	3.69
930.67495	9077565	20.2
930.67419	11965571	8.91
893.66217	3848824	2.87
892.65923	7994814	17.79
892.65839	9863546	7.35
863.63257	1666319.8	3.71
863.63202	2152206	1.6
853.62585	2442069.8	1.82
852.62785	2597481.5	5.78
852.62714	3699706.3	2.76
837.59894	2636937.8	1.96
836.59612	5156522	11.47
836.59558	7386873	5.5
834.61732	1597815.8	3.55
834.61694	2250508.5	1.68
822.58575	3864690	2.88
821.58545	6258856.5	13.93
821.58478	8615165	6.42
803.57481	2896090	6.44
803.57416	4165573	3.1
793.59387	1992960.5	1.48
792.59525	2440190.5	5.43
792.59485	3200622.3	2.38
774.58469	1955403	4.35
774.5838	2684932.5	2
765.55893	3447872.5	7.67
765.55853	4884022	3.64
751.55072	1748672.3	1.3
750.54955	3275158.8	7.29
750.54901	4824993.5	3.59
748.53137	1650908.5	1.23
740.53827	1660862	1.24
736.53263	2036913.5	4.53
736.5321	3081420.5	2.29
709.49649	1998618.1	4.45
709.49591	3310923	2.47
695.48871	1660447.6	1.24
694.48608	3828772.3	8.52
694.48566	6254752	4.66
681.50763	1646277.3	1.23
680.51025	8119519	6.05
680.50647	2892698.8	6.44

679.51137	11591917	25.79	440.32295	3305455.8	7.35
679.5108	17930716	13.35	440.32227	7522032	5.6
669.5011	1689872.1	1.26	439.32773	1998692.6	4.45
662.5033	5314113.5	3.96	439.32742	4577722	3.41
661.50041	12156435	27.05	435.33246	1727800.5	1.29
661.50006	19116668	14.24	426.31522	4712205.5	3.51
638.46155	4872717.5	3.63	425.34747	2585726	5.75
638.45949	2095752.5	4.66	425.34711	5851186.5	4.36
637.46416	6040486.5	13.44	425.31201	14200438	31.59
637.46387	9762297	7.27	425.31171	32652852	24.32
635.44818	1561570.9	1.16	407.33791	2932608.3	6.52
623.44871	3535721.5	7.87	407.33759	6838865.5	5.09
623.44824	6120070	4.56	399.33283	1656521.3	3.69
568.42474	2665172.5	1.98	399.33252	3819042	2.84
567.42247	6419633	14.28	398.28406	4839480	3.6
567.42175	12222716	9.1	397.28077	15852816	35.27
567.38639	1943201.6	4.32	397.28043	37723320	28.1
567.38525	3582971.5	2.67	394.26985	1687971.9	3.76
562.39557	2073255.1	1.54	394.26956	3976669	2.96
553.41211	4166740.8	3.1	383.26474	3411317.5	2.54
552.4115	8940201	19.89	381.32199	2097974.3	1.56
552.41125	16653552	12.4	369.2858	2241165.3	4.99
538.39602	1627323.6	3.62	369.28427	4734764.5	3.53
538.39569	3180049.8	2.37	368.29067	6055347.5	13.47
535.40387	1917616.9	1.43	368.29034	14455517	10.77
534.40104	4960781	11.04	366.27469	2746583	2.05
534.4007	9684131	7.21	366.23846	2040572.4	1.52
525.38324	3356141	2.5	357.28582	1610001.5	3.58
524.3804	9036276	20.1	357.28561	3999060.8	2.98
524.38	17684222	13.17	355.27826	2876584.8	2.14
510.36491	3687872.3	8.21	354.27497	9705597	21.59
510.36444	7644322.5	5.69	354.27469	24432240	18.2
506.36997	1959456.8	4.36	352.25912	1619992.9	1.21
506.36948	3898945.8	2.9	350.27979	2167155.8	1.61
496.38512	2920800.5	6.5	341.25366	2002068.8	1.49
496.38474	6052968.5	4.51	340.25916	3694905	2.75
496.34956	2684641	5.97	339.27505	2810791	2.09
496.34915	5701796.5	4.25	326.24372	3922059.5	8.73
481.37411	1775537.9	1.32	326.2435	10014745	7.46
467.3587	1548724.4	1.15	324.23605	2636737.8	1.96
453.34322	2130315	4.74	323.23284	8810326	19.6
453.3429	4545848.5	3.39	323.2326	23814576	17.74
450.30688	1849651	1.38	313.25937	3438031.3	2.56

312.22799	3006681	6.69
312.22781	7652110.5	5.7
308.23291	3115980.8	2.32
299.25214	2228060.8	1.66
299.24371	2873287.8	2.14
298.24877	9379162	20.87
298.24857	25163482	18.74
298.21254	3671760	8.17
298.21231	9776687	7.28
297.21709	2750543.8	6.12
297.21695	7147997	5.32
287.25201	1609699.1	1.2
287.24406	1935432.8	4.31
287.2438	5034137.5	3.75
286.24877	8398680	18.69
286.24863	22105368	16.46
281.24142	2385964.5	1.78
280.23831	8692181	19.34
280.23807	23272260	17.33
270.21719	3282060	2.44
270.18113	5441283.5	12.11
270.18103	14851423	11.06
269.24133	3084332.8	2.3
269.18591	5384679.5	11.98
269.1857	15147603	11.28
268.23827	12406901	27.6
268.2381	35180232	26.2
255.20668	5414767.5	12.05
255.20647	15755250	11.73
253.19077	2299667	1.71
252.20683	2642153.5	1.97
250.22777	1896932.1	4.22
250.22758	5428987.5	4.04
241.19103	4157959.5	9.25
241.19086	11825330	8.81
239.17514	2995315.3	2.23
237.19595	14246427	10.61
227.17517	7428008.5	5.53
225.16756	10637802	7.92
224.16426	134266848	100
213.13113	4903086.5	3.65
213.12325	6492317	4.84
212.12793	76550632	57.01

211.15199	3713153.5	2.77
210.14873	53783880	40.06
209.20116	3389433.3	2.52
199.14403	25339008	18.87
195.14909	3509189	2.61
195.12077	3716517.3	2.77
194.11749	57121516	42.54
186.15999	25468458	18.97
185.12839	1582474.8	1.18
184.14371	1730538.9	1.29
184.13313	19754144	14.71
182.11748	5695772	4.24
174.15996	8319207.5	6.2
171.14899	8375172.5	6.24
169.10503	4248700.5	3.16
168.1492	2883788.8	2.15
168.10173	81324712	60.57
167.12579	2127492.8	1.58
166.12254	37599856	28
157.10503	2503075.3	1.86
156.14917	5827506	4.34
156.13812	18190694	13.55
156.10184	55448296	41.3
155.11772	2697389.8	2.01
143.11768	6493618	4.84
143.08942	3288592	2.45
142.08609	78846176	58.72
141.10204	4124918.8	3.07
140.14317	1634775.5	1.22
138.12758	4991110	3.72
136.11192	1587813.6	1.18
128.10696	17705752	13.19
126.05491	6820436.5	5.08
125.09598	2076448.5	1.55
114.09148	32932776	24.53
113.10747	4666722.5	3.48
107.08561	1597010.8	1.19
100.11236	29952714	22.31
100.0396	16069140	11.97

Observed ions for 3d

m/z	Intensity	Relative
1278.92199	36042376	14.01
1260.91095	26170330	10.17
1232.91584	2173574.5	0.85
1175.82175	1549508.9	0.6
1166.83261	14144423	5.5
1165.83714	16962372	6.59
1156.88473	4501804	1.75
1151.82201	4784671.5	1.86
1147.82661	11280128	4.39
1133.81122	2036090.1	0.79
1128.88944	1313084.8	0.51
1095.7952	1892703.9	0.74
1063.73234	3496134	1.36
1053.7482	6435564.5	2.5
1046.7997	1769398.5	0.69
1044.79537	2204449.3	0.86
1039.73255	3170827	1.23
1038.73696	19921036	7.74
1028.78898	1599682.4	0.62
1024.7215	7024794	2.73
1020.72653	8706051	3.38
1006.71061	2917682.5	1.13
982.71046	11516644	4.48
942.67897	5129964	1.99
936.63192	2017359.1	0.78
926.64764	9318923	3.62
919.69913	2401769.8	0.93
912.63177	3843225.3	1.49
911.63662	33018848	12.84
901.68853	1524128.9	0.59
893.6259	39699168	15.43
883.64141	16494973	6.41
867.64644	1359099.3	0.53
865.63086	9780654	3.8
857.62555	3607781.8	1.4
855.6099	9143639	3.55
849.65684	1534627.6	0.6
840.59902	1568167.5	0.61
838.58331	1495974.5	0.58
827.61475	1474755	0.57
826.58311	2375614.3	0.92
807.60986	1477502.8	0.57
799.54709	16921142	6.58
792.59882	11436330	4.45
789.59929	2021956.5	0.79
784.57208	2034838.1	0.79
784.53646	2628321.8	1.02
781.53757	1407484.3	0.55
774.58833	9815040	3.82
771.55207	5898258.5	2.29
770.55692	1372590.1	0.53
765.53003	1360210.4	0.53
761.60432	2307096.8	0.9
759.55224	2554424.5	0.99
756.5413	1863858.6	0.72
744.5412	1567640.3	0.61
736.57254	13762228	5.35
728.50991	8410490	3.27
727.51458	11363994	4.42
718.5619	4959782.5	1.93
713.4989	2892849.5	1.12
710.49913	3554552.5	1.38
709.50383	1969636.1	0.77
700.51478	4364468.5	1.7
694.52538	2049719.5	0.8
693.5301	2846846.3	1.11
689.49878	2204502.8	0.86
680.50965	9352445	3.64
679.51438	65363940	25.41
677.51027	3208250.8	1.25
674.49908	1373167.4	0.53
665.53502	3624719.5	1.41
665.49881	2375871	0.92
661.50371	54302328	21.11
657.47233	2589120.8	1.01
657.43619	4126350.8	1.6
651.51946	3002262.8	1.17
643.45665	1580716.1	0.61
639.42536	4584070	1.78

635.52433	1621995.5	0.63
633.50878	2548038.3	0.99
629.44101	5106268.5	1.99
624.48314	5099516	1.98
623.48793	3115839.3	1.21
620.4769	2140657.8	0.83
615.46162	1308885	0.51
614.43002	14319477	5.57
606.47247	3441845.5	1.34
600.41432	12329323	4.79
598.39858	1778101	0.69
594.4612	1494630.6	0.58
586.39867	8934034	3.47
582.40371	3060132.3	1.19
579.46153	1713507.4	0.67
568.38795	1851132	0.72
567.42504	29336054	11.41
566.42983	4647957	1.81
562.39855	3791029.8	1.47
558.40355	1339721.5	0.52
558.36722	1351806.5	0.53
553.44588	4347834.5	1.69
553.40955	2243898.8	0.87
552.44999	2235011	0.87
552.41415	36107528	14.04
549.40339	2575747.3	1
548.41929	1413981.9	0.55
538.43487	16656781	6.48
538.3986	3320382	1.29
535.39883	3662182	1.42
534.40363	16791110	6.53
533.40835	18393080	7.15
525.34585	1561441.6	0.61
524.41927	2938699.8	1.14
524.38287	2039247.9	0.79
520.42435	2164860.3	0.84
519.39268	2379841.3	0.93
514.39853	1903519.4	0.74
506.37234	10814657	4.2
497.37182	2411458.3	0.94
496.38784	18935338	7.36
495.39248	2871748.5	1.12
488.31393	2003878.8	0.78
487.32987	24673034	9.59
482.37211	3522737.8	1.37
481.37693	3191988.5	1.24
479.36117	3439143.8	1.34
478.37718	1796834.8	0.7
473.31423	4969465.5	1.93
471.2986	2726764.3	1.06
468.39282	2533615.8	0.99
467.36124	3351813.5	1.3
464.36157	1822601.1	0.71
459.29841	13156615	5.11
453.34541	7931707	3.08
451.32983	1315722.9	0.51
450.30926	4250317	1.65
440.32495	14882123	5.79
439.32969	17302032	6.73
435.33473	4189545	1.63
430.27181	1383237.8	0.54
426.34559	2336473.8	0.91
425.35021	55531148	21.59
425.31397	58224312	22.64
424.31866	3359813	1.31
421.319	2980815	1.16
420.32373	1433114.4	0.56
412.32987	1684423.1	0.65
411.33466	7694958	2.99
407.33968	21834822	8.49
406.30809	4643661.5	1.81
399.33459	4638689	1.8
398.24544	2171883.8	0.84
394.27167	9504305	3.7
393.32399	1530357.4	0.59
392.29231	2196639	0.85
391.27193	1427232	0.55
382.30797	4692308	1.82
381.32392	2354187	0.92
380.29231	1932807.4	0.75
379.27186	2557538.8	0.99
369.28754	9271605	3.6
368.29229	56892088	22.12
366.27663	4961194	1.93
360.2296	41999840	16.33
357.28743	9774528	3.8

354.2765	53199936	20.68	239.17651	9415311	3.66
352.26087	3111638.3	1.21	237.19725	13776984	5.36
350.28159	2363139.3	0.92	237.1609	1351855.3	0.53
346.2139	1836554.3	0.71	234.11357	3390369.8	1.32
342.219	1481834.1	0.58	233.12955	257217648	100
341.2925	1421190.6	0.55	232.13436	10868739	4.23
341.25612	3461918.8	1.35	230.22382	2268999.8	0.88
340.26091	3596330.8	1.4	228.20814	1323252	0.51
339.27691	5157122.5	2	227.1765	17744724	6.9
332.23457	8337806	3.24	227.1401	1387034.6	0.54
326.24513	26993092	10.49	225.19719	1846918.1	0.72
325.21356	1585657.9	0.62	224.1656	108055808	42.01
323.23429	49910900	19.4	214.15605	4292270.5	1.67
314.1876	1557202.9	0.61	213.16077	1974869.3	0.77
313.26105	8307657	3.23	213.12441	24741676	9.62
312.22944	14091608	5.48	212.12916	67364336	26.19
308.23457	8252762	3.21	211.18154	1351807.9	0.53
307.20294	6734531	2.62	210.14991	61123912	23.76
306.21893	3237233.5	1.26	209.20229	2776956	1.08
303.17161	1799520.3	0.7	205.13459	4268897.5	1.66
301.2611	1905022.1	0.74	204.13934	3350208.5	1.3
299.24543	2531666.3	0.98	199.1815	2704218.3	1.05
298.25021	35150556	13.67	199.14512	17004688	6.61
298.21385	10456267	4.07	195.1502	3232632.3	1.26
297.21861	9449814	3.67	194.11858	46971668	18.26
293.22356	4313496.5	1.68	186.16104	26426420	10.27
287.2454	3080058.8	1.2	185.1658	6214432.5	2.42
286.25013	26306776	10.23	185.12939	1445667	0.56
283.20285	4496704.5	1.75	184.14537	1606767.8	0.62
280.23962	29240616	11.37	184.13416	17283358	6.72
280.20325	2306638.5	0.9	182.11854	60560112	23.54
279.208	1345934.1	0.52	174.16099	8776369	3.41
270.2188	6373204	2.48	171.15001	9088278	3.53
269.18715	91232896	35.47	168.17547	3262220	1.27
268.23954	38233076	14.86	168.15032	3035683.8	1.18
255.20785	20319702	7.9	168.10277	80679944	31.37
253.1922	3770298.8	1.47	166.12351	34106360	13.26
252.20819	4749032.5	1.85	162.09211	2320499.3	0.9
250.22892	4473590.5	1.74	157.1707	6908930	2.69
245.19836	2922027.3	1.14	156.15027	6596958.5	2.56
242.22381	3686906	1.43	156.13906	15622533	6.07
241.19217	20708710	8.05	156.10272	122613400	47.67
239.21289	1728971.4	0.67	155.11859	3793366.8	1.47

154.08695	1982302.6	0.77