Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

The influence of backbone fluorination on the helicity of α/γ-hybrid peptides

Alpesh Patel, Aggie Lawer, Mohan Bhadbhade and Luke Hunter

SUPPORTING INFORMATION

Contents:

1. Synthetic procedures and characterization data

Reagents and instrumentation

All reactions were performed in oven dried glassware under the protection of a nitrogen atmosphere unless otherwise stated. Anhydrous reagents and solvents were prepared according to the following procedures: dry dichloromethane was obtained from a solvent purification system and further dried over 4Å molecular sieves; *N,N′*-dimethylformamide was dried over 4Å molecular sieves; purified water was obtained from a Millipore Milli-Q plus system. All other reagents and solvents were purchased in the highest available quality and used as received. NMR spectra were recorded using a Bruker Avance III 300 MHz, 400 MHz or 600 MHz spectrometer at 300 K unless otherwise stated. A mixing time of 200 ms was employed for ROESY spectra. The Bruker Topspin software was used to process spectra, and the Daisy module of this software package was used to simulate complex spectra in order to obtain accurate coupling constants. Circular Dichroism (CD) spectra were recorded on Applied Photophysics Chirascan™-plus CD spectrometer. Analytical LC–MS was performed using a Shimadzu LCMS–2010 EV(A) instrument equipped with a Grace VisionHT C18 1.5 μm column and a LCQ Deca XP Plus ion trap mass spectrometer on an elution gradient of 5–100% eluent A / eluent B over 10 min with a flow rate of 0.2 mL/min. Preparative reversed phase HPLC was performed using a Shimadzu LC10–AD pump equipped with a SPDM20A PDA detector (254 nm) and Waters Sunfire C18 column (150 mm × 19 nm) on a gradient elution of 1–100% eluent A / eluent B over 40 min with a flow rate of 5 mL/min. 0.1% Formic acid/MilliQ water was used as eluent A and 0.1% formic acid/acetonitrile was used as eluent B for both analytical and preparative HPLC. A Christ Alpha 1–4 LDplus freeze dryer was used to remove residual solvent from the purified peptides. **PRECAUTION:** due to the possibility that small amounts of HF could be formed as a side-product in these experiments, appropriate personal protective equipment was employed (including a tube of calcium gluconate gel kept close at hand).

General procedure A: SPPS resin loading

Solid phase peptide synthesis was conducted manually in a sinter-fitted polypropylene syringe. Wang resin (100–200 mesh) was agitated in DCM for 1 h, then drained and washed with DCM (3 × 2 min) and DMF (5 × 2 min). Fmoc-Aib-OH (10 equiv.) was dissolved in 10:1 mixture of dry DCM/DMF. A solution of DIC (10 equiv.) in dry DCM (minimum) was added and the mixture was stirred at 0 °C for 20 min before being concentrated. The residue was dissolved in DMF (minimum) and added to the pre-swelled Wang resin (with 0.1 equiv. of DMAP) and the syringe was agitated for 2 h. The resin was drained and washed with DMF (3 × 2 min), DCM (3 × 2 min) and DMF (5 × 2 min).

General procedure B: Fmoc deprotection

The resin was agitated with a solution of 10% piperidine in DMF (2 × 3 min) and the solution was collected. The deprotection solutions were combined and diluted 100-fold with 10% piperidine in DMF, and the absorbance of the diluted solution was measured at 301 nm against 10% piperidine in DMF as reference. The resin loading was determined by calculating the concentration of the piperidine-fulvene adduct (ε = 7800 $M^{-1}cm^{-1}$) in the deprotection solution. The resin was subsequently washed with DMF (3 × 2 min), DCM (3 × 2 min) and DMF (5 × 2 min).

General procedure C: Peptide coupling (non-fluorinated amino acids)

A solution was prepared of the appropriate Fmoc-protected amino acid (3 equiv. relative to resin loading) and HBTU (2.9 equiv. relative to resin loading) in minimal DMF. To this solution was added DIPEA (6 equiv. relative to resin loading), and the mixture was immediately added to the resin and agitated for 2 h. The resin was drained and washed with DMF (3 × 2 min), DCM (3 × 2 min) and DMF (5 × 2 min).

General procedure D: Peptide coupling (fluorinated amino acids)*

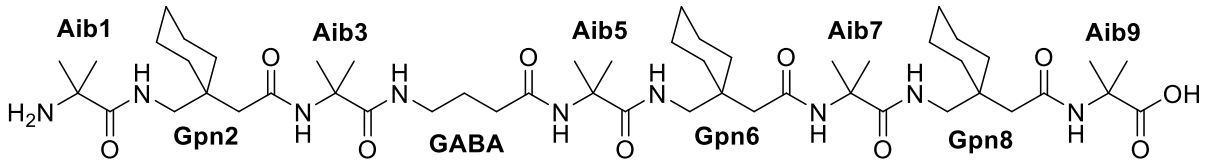
A solution was prepared of the appropriate Fmoc-protected amino acid (1.5 equiv. relative to resin loading), HOBt (1.5 equiv.) and DIC (1.5 equiv.) in minimal DMF. This solution was stirred for 20 min, then added to the resin and agitated overnight. The resin was drained and washed with DMF (3 × 2 min), DCM (3 × 2 min) and DMF (5 × 2 min).

*The coupling of the next amino acid after the fluorinated amino acid was performed twice.

General procedure E: Cleavage of peptide from resin

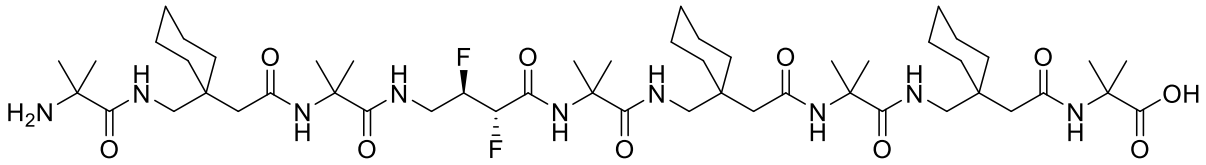
After the last Fmoc deprotection, the resin was washed with DMF (3 × 2 min) and DCM (3 × 2 min) then dried *in vacuo*. The resin was agitated with a solution of 95:2.5:2.5 TFA/TIS/H_2O for 2 h. The resin was drained and washed with TFA (2 × 1 min). The combined cleavage solutions were concentrated *in vacuo*. The residue was dissolved in water (~20 mL per mmol of peptide) and this solution was washed four times with an equal volume of diethyl ether. The aqueous layer was freeze-dried to afford the crude peptide, which was purified by reverse-phase HPLC.

H_2N–Aib–Gpn–Aib–GABA–Aib–Gpn–Aib–Gpn–Aib–OH (6):



The title compound was synthesized according to General procedures A–C,E on 50 mmol scale. The product was obtained as a white solid (36.5 mg, 74%); **^{1}H NMR** (600 MHz, DMSO-d_6) δ 12.1 (br s, 1H, CO_2H), 8.38 (s, 1H, Aib #9 NH), 8.36 (t, J = 5.7 Hz, 1H, Gpn #2 NH), 8.13 (s, 1H, Aib #3 NH), 8.11 (s, 2H, NH_2), 8.09 (s, 1H, Aib #7 NH), 7.89 (s, 1H, Aib #5 NH), 7.64 (t, J = 6.0 Hz, 1H, Gpn #8 NH), 7.63 (t, J = 6.0 Hz, 1H, Gpn #6 NH), 7.52 (t, J = 5.9 Hz, 1H, GABA NH), 3.22 (d, J = 5.7 Hz, 2H, γ–CH_2 Gpn #2), 3.10 (d, J = 6.0 Hz, 2H, γ–CH_2 Gpn #8), 3.07 (d, J = 6.0 Hz, 2H, γ–CH_2 Gpn #6), 3.03 (dt, J = 6.5, 5.9 Hz, 2H, γ–CH_2 GABA), 2.17 (s, 2H, α–CH_2 Gpn #2), 2.08 (t, J = 7.4 Hz, 2H, α–CH_2 GABA), 2.00 (s, 4H, α–CH_2 Gpn #6 & Gpn #8), 1.60 (quint, J = 7.0 Hz, 2H, β–CH_2 GABA), 1.47–1.20 (m, 60H, Aib CH_3 & cyclohexane ring CH_2); **^{13}C{^{1}H} NMR** (150 MHz, DMSO-d_6) δ 175.6, 174.3, 174.25, 173.8, 171.9, 171.6, 171.1, 170.8, 173.0, 170.3, 56.5, 56.1, 56.05, 56.0, 54.7, 40.1, 38.4, 37.6, 37.5, 37.2, 33.8, 33.7, 33.2, 32.9, 25.8, 25.75, 25.31, 25.29, 25.2, 24.9, 23.7, 21.2, 21.1; **HRMS** (ESI, +ve) $C_{51}H_{90}N_9O_{10}^+$ [M+H$^+$] requires m/z 988.6727, found 988.6799.

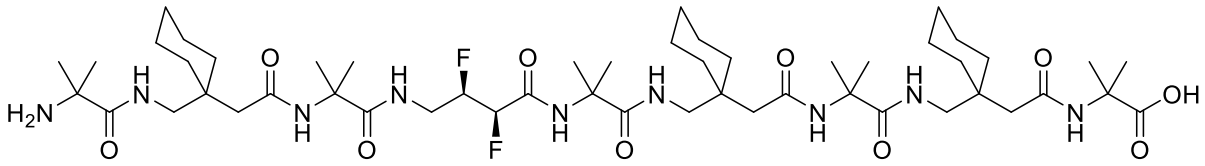
H_2N–Aib–Gpn–Aib–*erythro*-FAA–Aib–Gpn–Aib–Gpn–Aib–OH (7):



The title compound was synthesized according to General Procedures A–E on 27 mmol scale. The product was obtained as a white solid (20.0 mg, 72%); **^{1}H NMR** (600 MHz, DMSO-d_6) δ 12.1 (br s, 1H, CO_2H), 8.38 (t, J = 5.8 Hz, 1H, Gpn #2 NH), 8.33 (s, 1H, Aib #9 NH), 8.25 (s, 1H, Aib #5 NH), 8.18 (s, 1H, Aib #3 NH), 8.16 (s, 1H, Aib #7 NH), 8.10 (br s, 2H, NH_2), 7.90 (t, J = 5.9 Hz, 1H, Gpn #6 NH), 7.76 (t, J = 5.5 Hz, 1H, *erythro*-FAA NH), 7.58 (t, J = 6.4 Hz, 1H, Gpn #8 NH), 5.20 (ddd, J = 47.8 ($^1J_{HF}$), 20.9 ($^2J_{HF}$), 1.6 Hz, 1H, α–H *erythro*-FAA), 4.87 (dddt, J = 47.7 ($^1J_{HF}$), 23.7 ($^2J_{HF}$), 6.0, 1.6 Hz, 1H, β–H *erythro*-FAA), 3.43–3.41 (m, 2H, γ–CH_2 *erythro*-FAA), 3.22 (d, J

= 5.8 Hz, 2H, γ–CH_2 Gpn #2), 3.16 (dd, J = 13.4, 5.9 Hz, 1H, γ–CH_2 Gpn #6), 3.11 (dd, J = 13.4, 5.9 Hz, 1H, γ–CH_2 Gpn #6), 3.10 (d, J = 6.4 Hz, 2H, γ–CH_2 Gpn #8), 2.17 (s, 2H, α–CH_2 Gpn #2), 2.09 (t, J = 7.4 Hz, 2H, α–CH_2 Gpn #6), 2.01 (s, 2H, α–CH_2 Gpn #8), 1.49–1.20 (m, 60H, Aib CH_3 & cyclohexane ring CH_2); **^{13}C{^{1}H} NMR** (150 MHz, DMSO-d_6) δ 175.5, 174.5, 174.0, 173.6, 171.5, 171.2, 170.4, 162.0 (dd, J = 32.0 ($^2J_{CF}$), 7.0 ($^3J_{CF}$) Hz, C=O *erythro*-FAA), 89.9 (dd, J = 178.0 ($^1J_{CF}$), 14.0 ($^2J_{CF}$) Hz, β–C *erythro*-FAA), 89.4 (dd, J = 196.0 ($^1J_{CF}$), 14.0 ($^2J_{CF}$) Hz, α–C *erythro*-FAA), 56.5, 56.2, 56.0, 54.7, 37.6, 37.2, 37.1, 33.8, 33.6, 33.2, 33.1, 25.8, 25.7, 25.3, 25.25, 25.0, 24.9, 24.7, 24.5, 23.6, 21.2, 21.1; **^{19}F NMR** (376 MHz, DMSO-d_6) δ –196.7 (m, 1F, β-CHF), –197.4 (m, 1F, α–CHF); **^{19}F{^{1}H} NMR** (376 MHz, DMSO-d_6) δ –196.7 (d, J = 13.9 Hz, 1F, β–CHF), –197.4 (d, J = 13.9 Hz, 1F, α–CHF); **HRMS** (ESI, +ve) $C_{51}H_{87}F_2N_9NaO_{10}^+$ [M+Na^+] requires m/z 1046.6544, found 1046.6549.

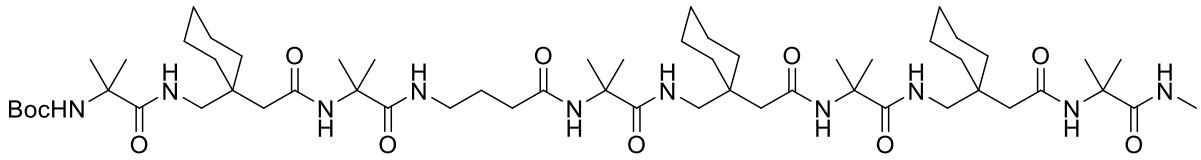
H_2N–Aib–Gpn–Aib–*threo*-FAA–Aib–Gpn–Aib–Gpn–Aib–OH (8):



The title compound was synthesized according to General Procedures A–E on 27 mmol scale. The product was obtained as a white solid (18.9 mg, 68%); **^{1}H NMR** (600 MHz, DMSO-d_6) δ 12.1 (br s, 1H, CO_2H), 8.34 (t, J = 6.2 Hz, 1H, Gpn #2 NH), 8.33 (s, 1H, Aib #9 NH), 8.21 (s, 1H, Aib #3 NH), 8.15 (br s, 1H, Aib #5 NH), 8.13 (s, 1H, Aib #7 NH), 8.10 (br s, 2H, NH_2), 7.90 (t, J = 6.0 Hz, 1H, Gpn #6 NH), 7.81 (t, J = 5.8 Hz, 1H, *threo*-FAA NH), 7.60 (t, J = 6.2 Hz, 1H, Gpn #8 NH), 5.08 (ddd, J = 46.1 ($^1J_{HF}$), 29.6 ($^2J_{HF}$), 1.5 Hz, 1H, α–H *threo*-FAA), 4.94 (dddt, J = 46.1 ($^1J_{HF}$), 27.3 ($^2J_{HF}$), 6.2, 1.5 Hz, 1H, β–H *threo*–FAA), 3.54–3.44 (m, 1H, γ–CH_2 *threo*-FAA), 3.39–3.31 (m, 1H, γ–CH_2 *threo*–FAA), 3.22 (d, J = 6.2 Hz, 2H, γ–CH_2 Gpn #2), 3.13 (d, J = 6.0 Hz, 2H, γ–CH_2 Gpn #6), 3.10 (d, J = 6.2 Hz, 2H, γ–CH_2 Gpn #8), 2.17 (s, 2H, α–CH_2 Gpn #2), 2.08 (t, J = 7.4 Hz, 2H, α–CH_2 Gpn #6), 2.01 (s, 2H, α–CH_2 Gpn #8), 1.48–1.19 (m, 60H, Aib CH_3 & cyclohexane ring CH_2); **^{13}C{^{1}H} NMR** (150 MHz, DMSO-d_6) δ 175.5, 174.4, 174.1, 173.7, 171.5, 171.2, 171.1, 170.4, 165.2 (dd, J = 19.8 ($^2J_{CF}$), 3.4 ($^3J_{CF}$) Hz, C=O *threo*-FAA), 89.4 (dd, J = 178.1 ($^1J_{CF}$), 16.9 ($^2J_{CF}$) Hz, β–C *threo*-FAA), 89.0 (dd, J = 193.5 ($^1J_{CF}$), 20.0 ($^2J_{CF}$) Hz, α–C *threo*-FAA), 56.5, 56.4, 56.2, 55.9, 54.7, 37.6, 37.2, 37.1, 33.7, 33.5, 33.2, 25.75, 25.7, 25.3, 25.27, 25.0, 24.9, 24.7, 24.2, 23.63, 23.61, 21.15, 21.11, 21.07; **^{19}F NMR** (376 MHz, DMSO-d_6) δ –201.8 (m, 1F, β-CHF), –206.5 (m, 1F, α–CHF); **^{19}F{^{1}H} NMR** (376 MHz, DMSO-d_6) δ –201.8 (d, J = 11.9 Hz, 1F, β–CHF),

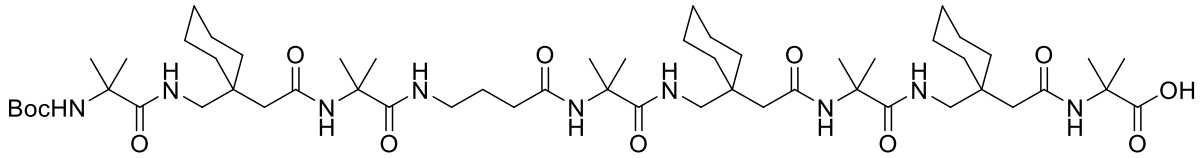
–206.5 (d, J = 11.9 Hz, 1F, α–CHF); **HRMS** (ESI, +ve) $C_{51}H_{87}F_2N_9NaO_{10}^+$ [M+Na^+] requires m/z 1046.6544, found 1046.6540.

BocHN–Aib–Gpn–Aib–GABA–Aib–Gpn–Aib–Gpn–Aib–NHMe (9):



Peptide **10** (10.9 mg, 10 μmol) and HATU (8.4 mg, 11 μmol) were dissolved in dry DMF (0.2 mL) and the resulting solution was stirred for 10 min at room temperature. $MeNH_2$ (2 M in THF; 10 μL, 20 μmol) was injected and the resulting solution was stirred for 20 min before DIPEA (5.3 μL, 30 μmol) was added. The reaction mixture was stirred for 16 h before addition of brine solution (3 mL) to form white precipitates. The mixture was extracted with CH_2Cl_2 (3 × 5 mL) and the combined organic layers were dried (Na_2SO_4). The organic layer was concentrated *in vacuo*, and the residue was subjected to preparative reversed phase HPLC (0%→25% ACN in water with 0.1% TFA over 50 min; retention time 41 min.) to afford the title compound as a white solid (9.1 mg, 83%); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.30 (s, 1H, Aib #7 NH), 8.12 (s, 1H, Aib #9 NH), 7.91 (br s, 1H, GABA NH), 7.88 (br s, 1H, Gpn #6 NH), 7.76 (s, 1H, Aib #5 NH), 7.69 (br s, 1H, N<u>H</u>Me), 7.65 (br s, 1H, Gpn #8 NH), 7.60 (s, 1H, Aib #3 NH), 6.55 (br s, 1H, Gpn #2 NH), 5.21 (s, 1H, Aib #1 NH), 3.41 (br s, 2H, γ–CH_2 GABA), 3.29 (br s, 2H, γ–CH_2 Gpn #6), 3.22 (br s, 2H, γ–CH_2 Gpn #8), 3.15 (br s, 2H, γ–CH_2 Gpn #2), 2.81 (d, J = 4.6 Hz, 3H, NHC<u>H</u>$_3$), 2.27 (t, J = 6.1 Hz, 2H, α–CH_2 GABA), 2.16 (s, 2H, α–CH_2 Gpn #8), 2.14 (s, 4H, α–CH_2 Gpn #2 and #6), 1.91 (quint, J = 5.9 Hz, 2H, β–CH_2 GABA), 1.84–1.23 (m, 69H, Aib CH_3, Boc & cyclohexane ring CH_2); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 176.6, 176.3, 175.9, 175.3, 175.1, 173.0, 171.8, 171.6, 155.2, 81.3, 57.2, 57.0, 56.9, 56.7, 38.1, 37.9, 37.8, 37.0, 34.9, 34.8, 32.6, 29.8, 28.5, 26.5, 26.3, 26.2, 26.1, 25.8, 25.6, 25.5, 25.4, 21.7, 21.6, 21.4; **HRMS** (ESI, +ve) $C_{57}H_{100}N_{10}NaO_{11}^+$ [M+Na^+] requires m/z 1123.7502, found 1123.7505.

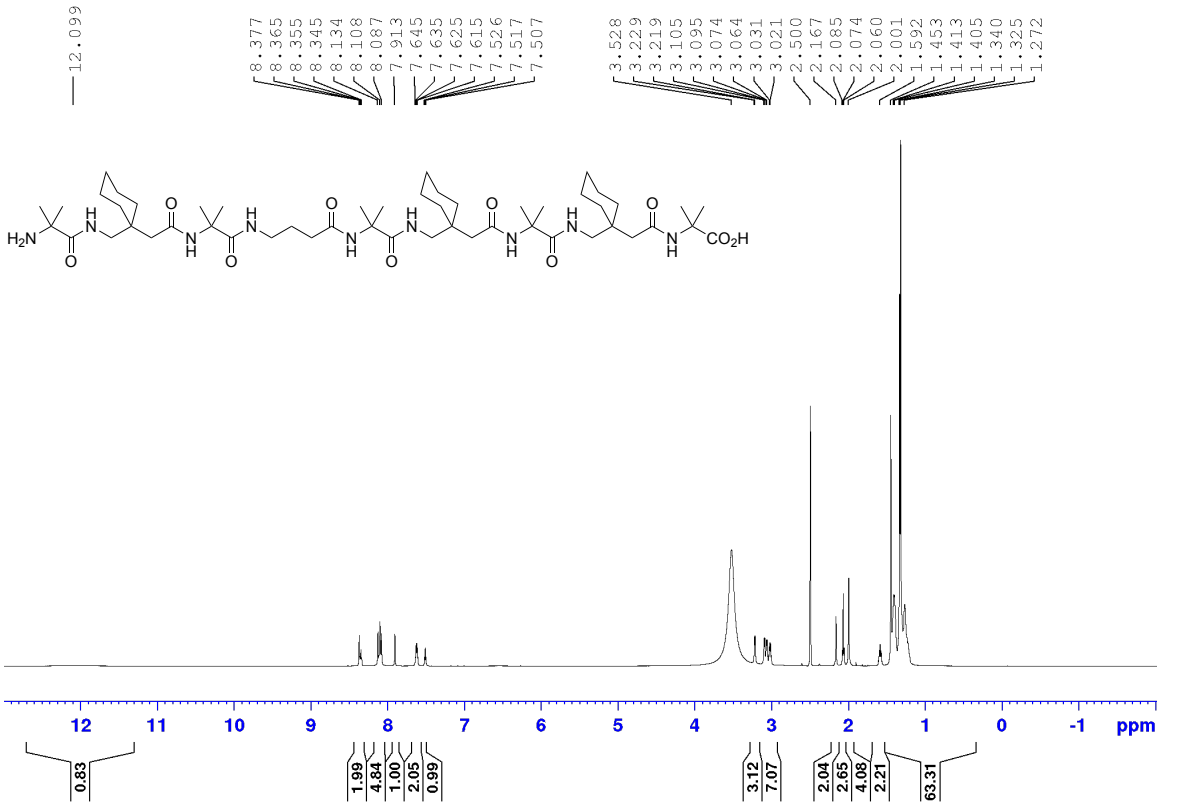
BocHN–Aib–Gpn–Aib–GABA–Aib–Gpn–Aib–Gpn–Aib–OH (10):



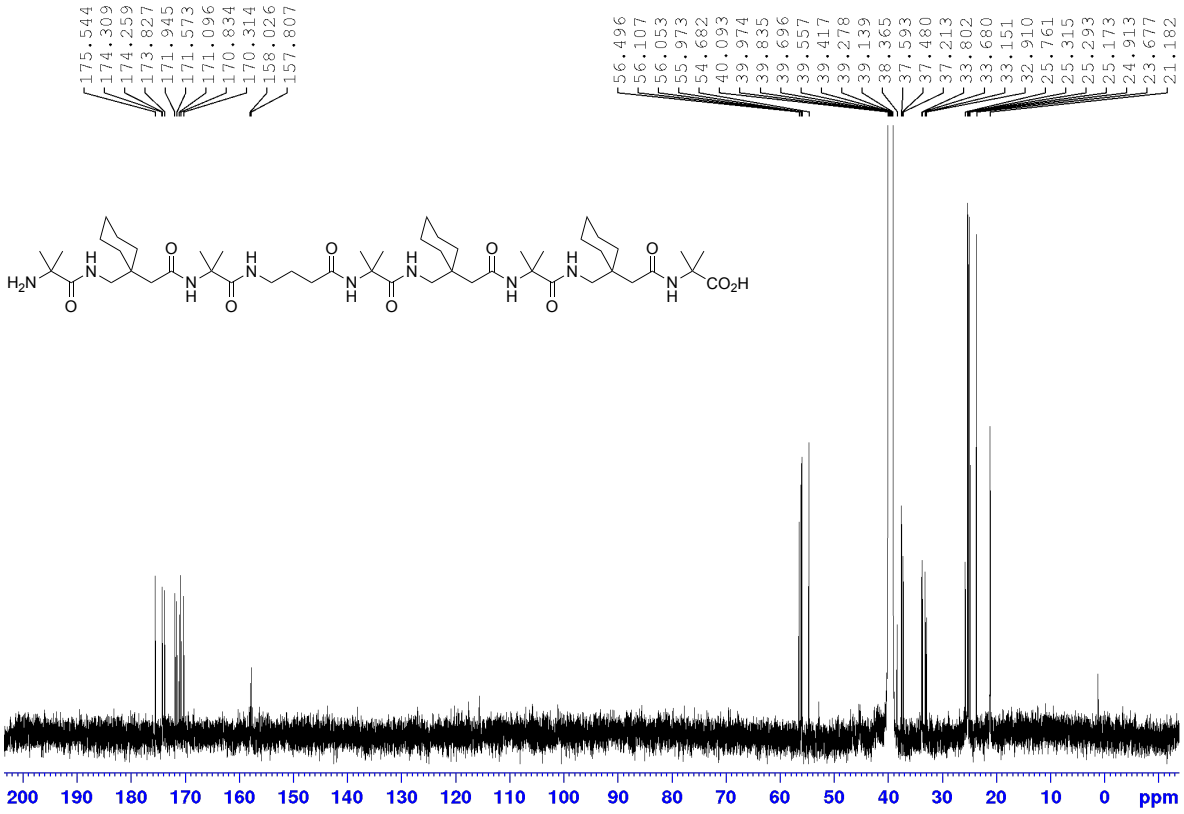
To a stirred solution of peptide **6** (35 mg, 35.5 μmol) and NaOH (3.5 mg, 88.7 μmol) in THF/water (1:1, 1.5 mL) under N_2 at 0 °C was added $(Boc)_2O$ (9.3 mg, 42.6 μmol) and the solution was allowed to warm at room temperature. The mixture was stirred for 16 h at room temperature before addition of ice-cooled HCl solution (0.1 M) to get pH 6 (~1 mL). Then the mixture was extracted with CH_2Cl_2 (3 × 5 mL) and the combined organic layers were dried (Na_2SO_4). The organic layer was concentrated *in vacuo*, and the residue was subjected to preparative reversed phase HPLC (0%→25% ACN in water with 0.1% TFA over 50 min; retention time 40 min.) to afford the title compound as a white solid (35.5 mg, 92%); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.77 (s, 1H, Aib #9 NH), 8.22 (s, 1H, Aib #7 NH), 7.92 (t, J = 6.1 Hz, 1H, Gpn #8 NH), 7.86 (t, J = 6.2 Hz, 1H, GABA NH), 7.85 (t, J = 6.2 Hz, 1H, Gpn #6 NH), 7.75 (s, 1H, Aib #5 NH), 7.55 (s, 1H, Aib #3 NH), 6.46 (t, J = 6.1 Hz, 1H, Gpn #2 NH), 4.98 (s, 1H, Aib #1 NH), 3.41 (br s, 2H, γ–CH_2 GABA), 3.29 (br s, 2H, γ–CH_2 Gpn #6), 3.22 (br s, 2H, γ–CH_2 Gpn #8), 3.15 (br s, 2H, γ–CH_2 Gpn #2), 2.27 (t, J = 5.8 Hz, 2H, α–CH_2 GABA), 2.21 (s, 2H, α–CH_2 Gpn #8), 2.14 (s, 2H, α–CH_2 Gpn #2), 2.12 (s, 2H, α–CH_2 Gpn #6), 1.91 (quint, J = 5.8 Hz, 2H, β–CH_2 GABA), 1.66–1.40 (m, 69H, Aib CH_3, Boc & cyclohexane ring CH_2); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 176.9, 175.8, 175.4, 175.2, 174.9, 174.1, 173.0, 171.8, 171.5, 155.1, 81.5, 58.0, 57.2, 57.0, 56.9, 56.7, 38.3, 38.1, 37.9, 37.0, 34.9, 34.8, 32.6, 29.9, 28.5, 27.6, 26.2, 26.1, 25.8, 25.6, 25.4, 25.0, 21.6, 21.4; **HRMS** (ESI, +ve) $C_{56}H_{97}N_9NaO_{12}^+$ [M+Na$^+$] requires m/z 1110.7257, found 1110.7249.

2. NMR spectra

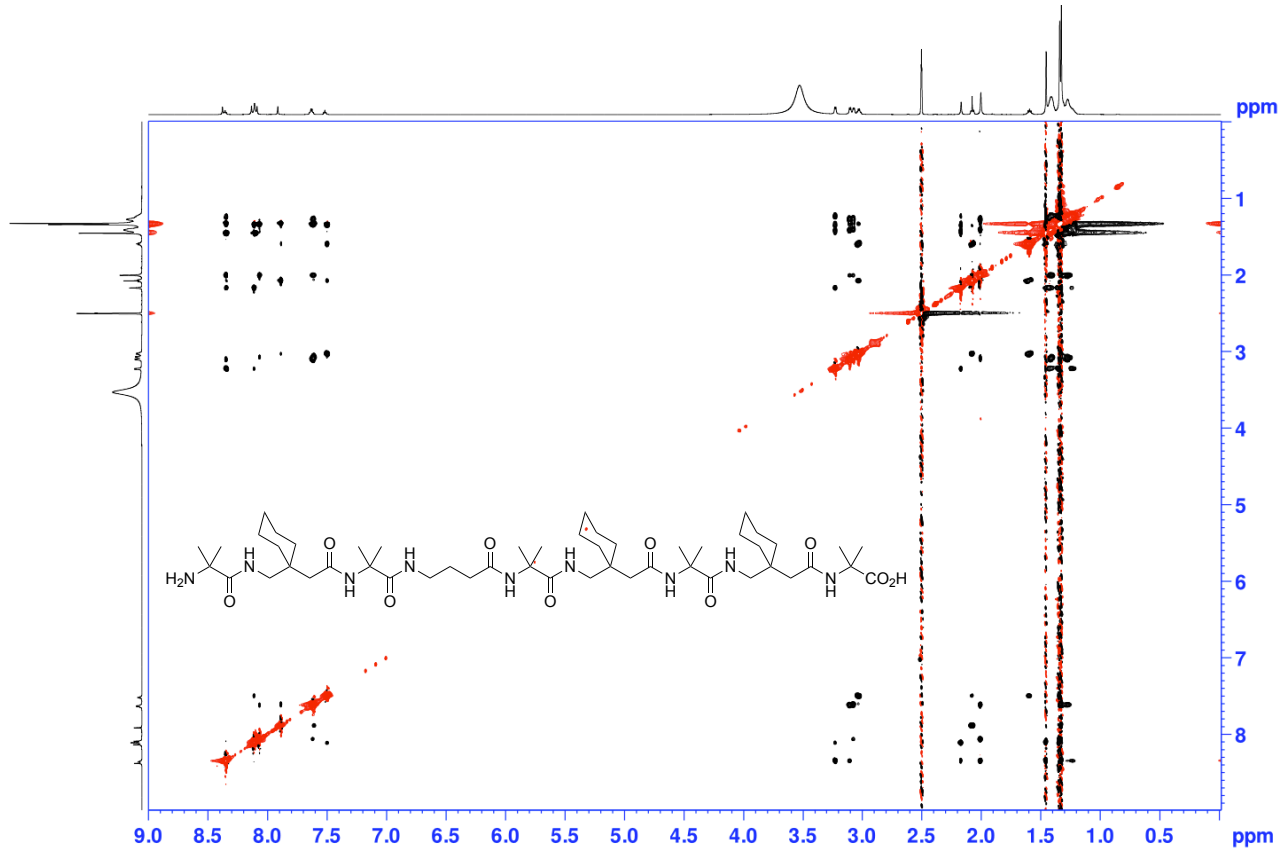
^{1}H NMR (600 MHz, DMSO-d$_6$) of **6**



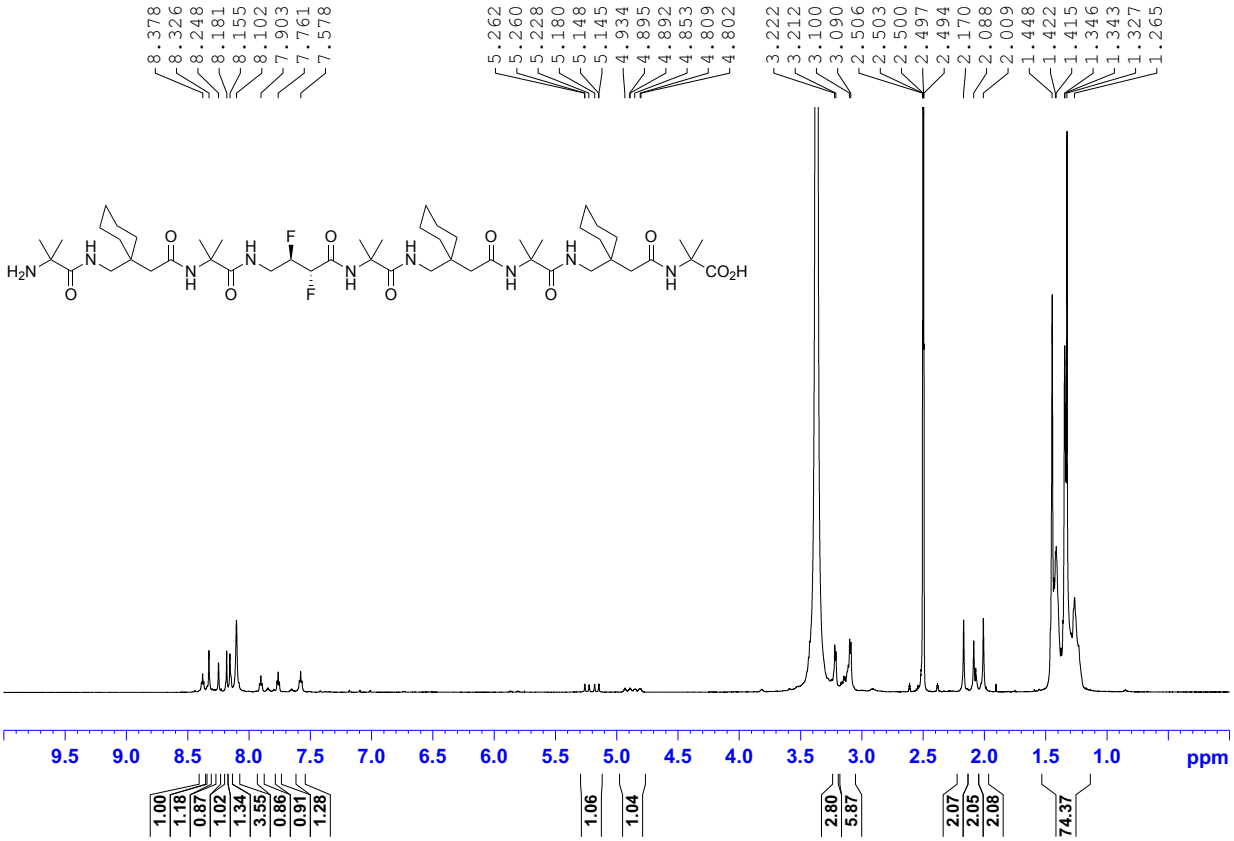
^{13}C{^{1}H} NMR (150 MHz, DMSO-d$_6$) of **6**



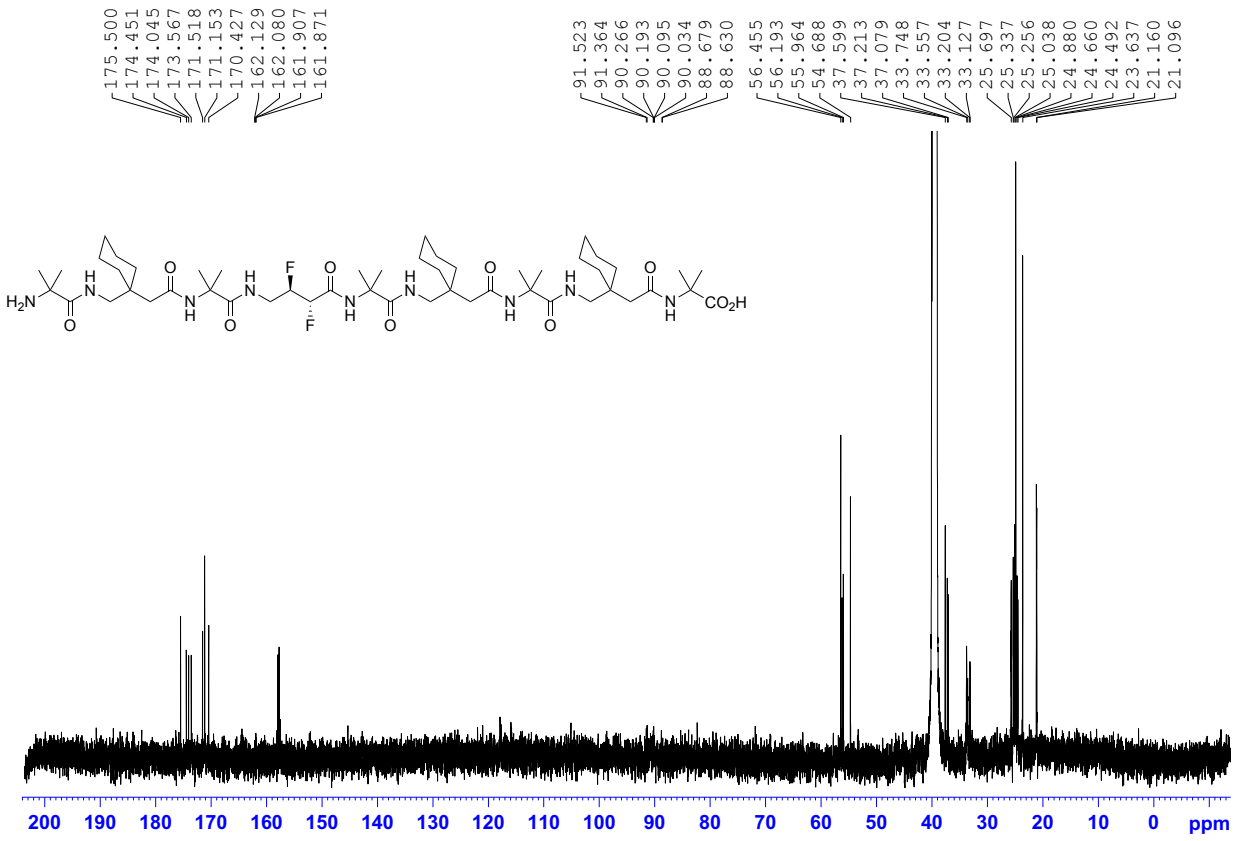
^{1}H-^{1}H ROESY NMR (600 MHz, DMSO-d$_6$) of **6**



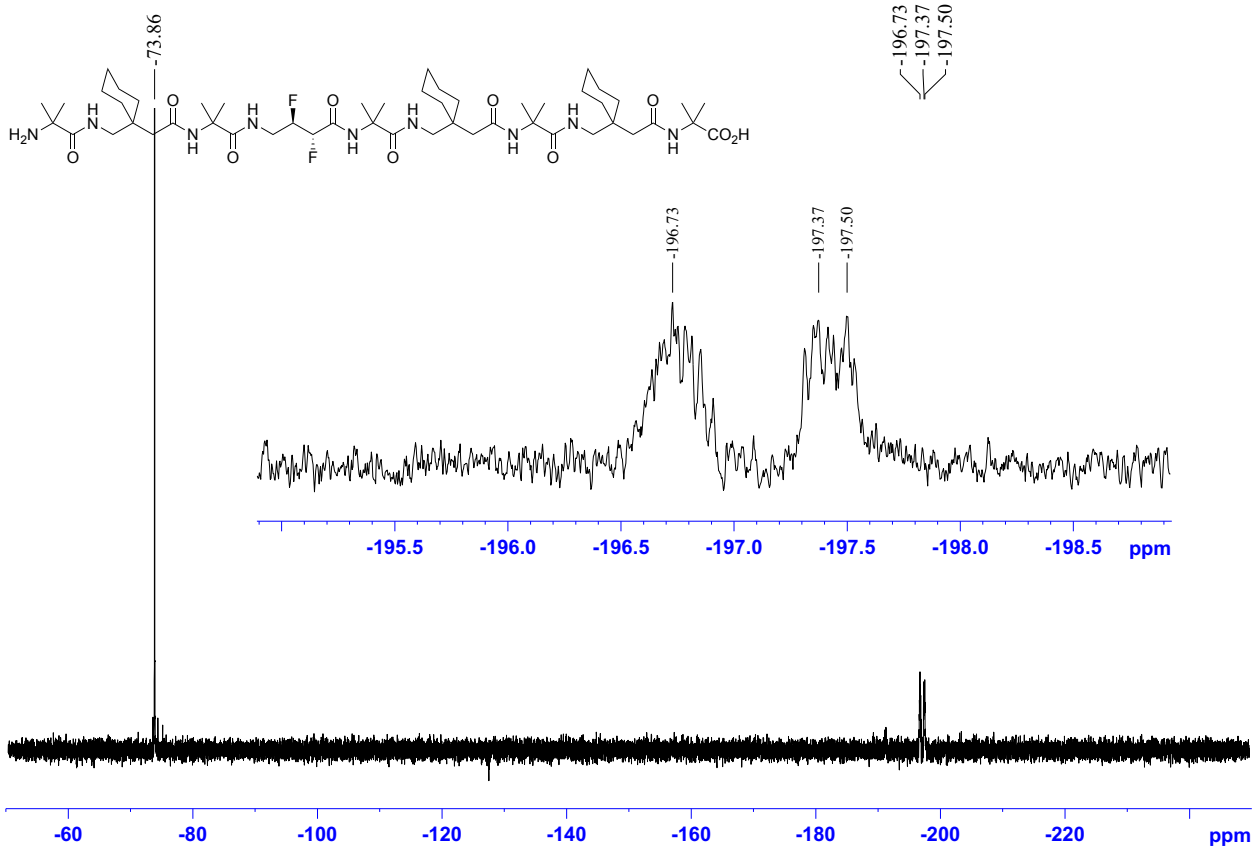
^{1}H NMR (600 MHz, DMSO-d$_6$) of **7**



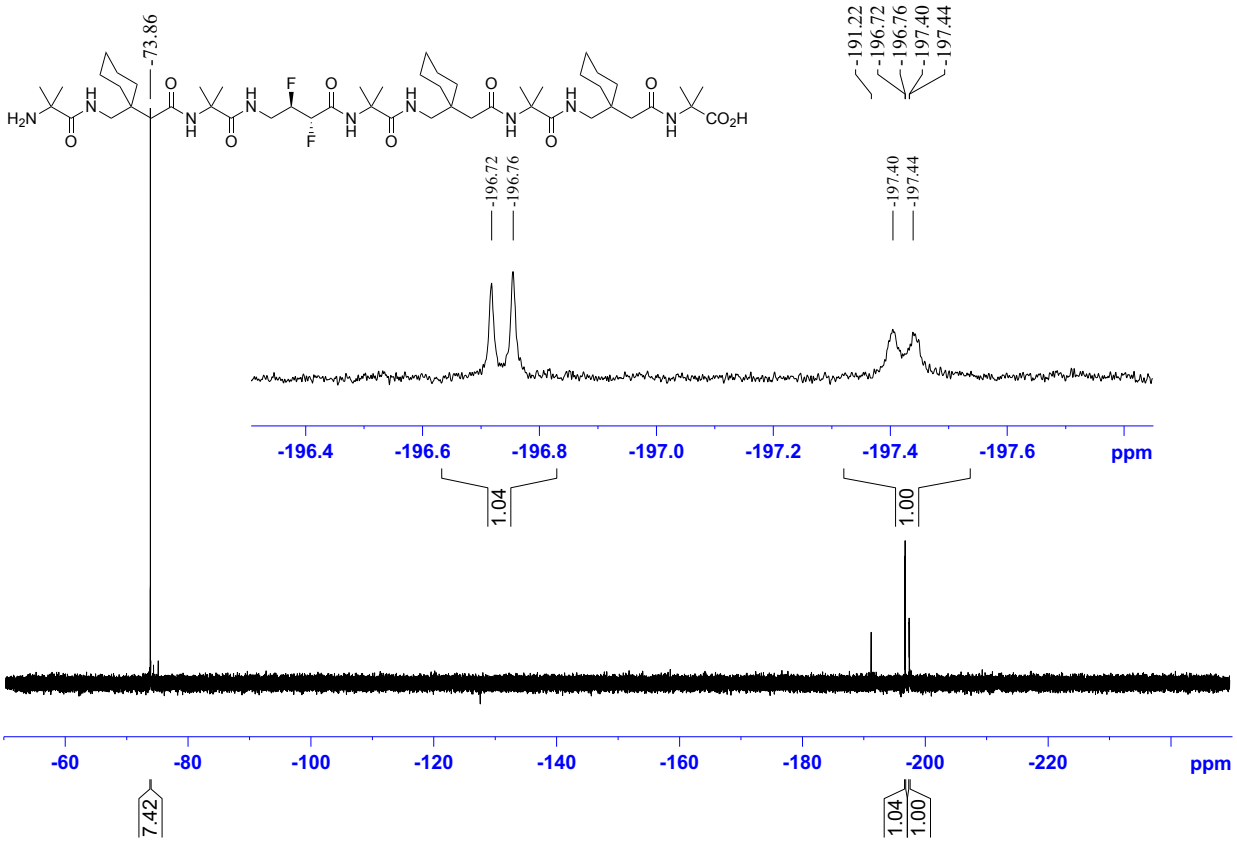
$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) of **7**



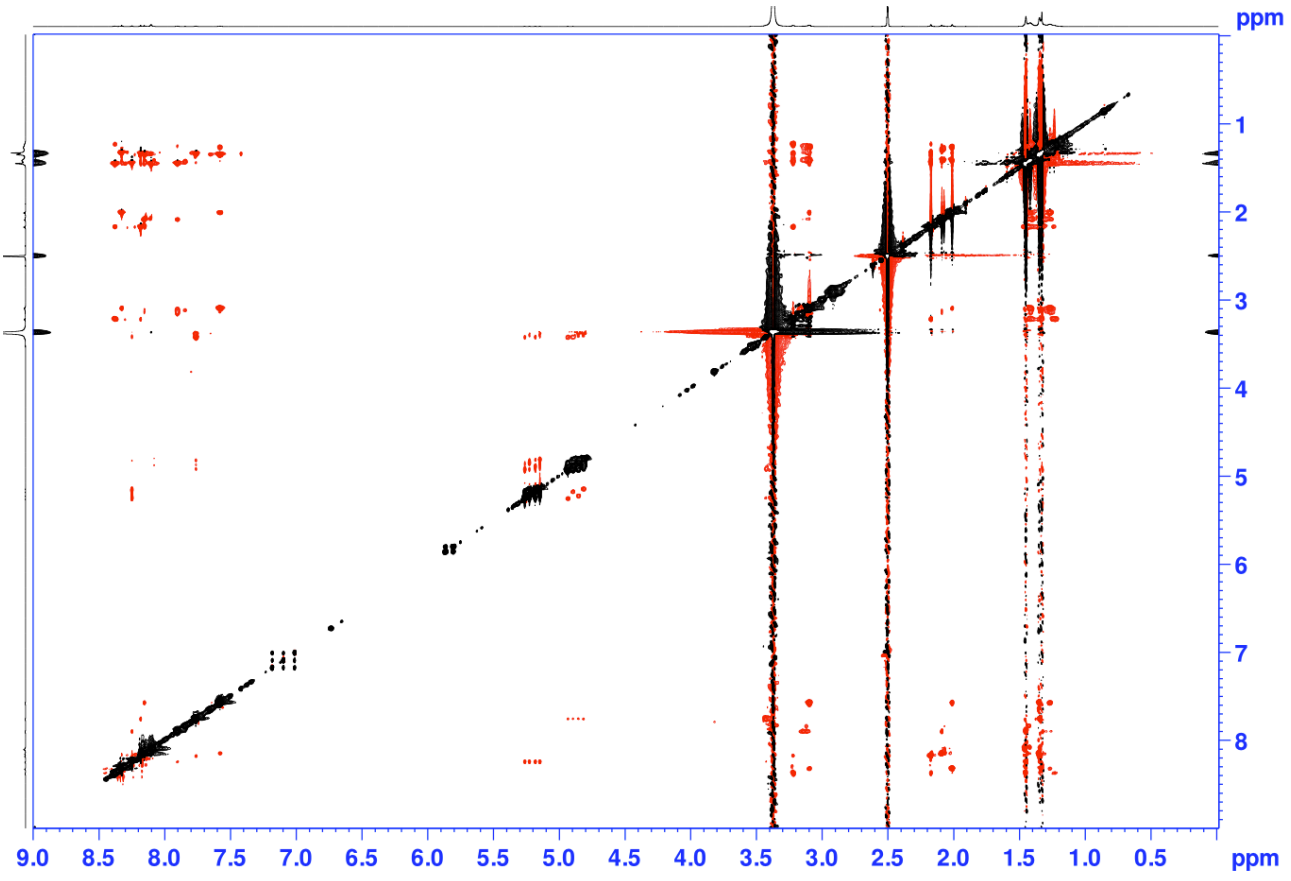
^{19}F NMR (376 MHz, DMSO-d_6) of **7**



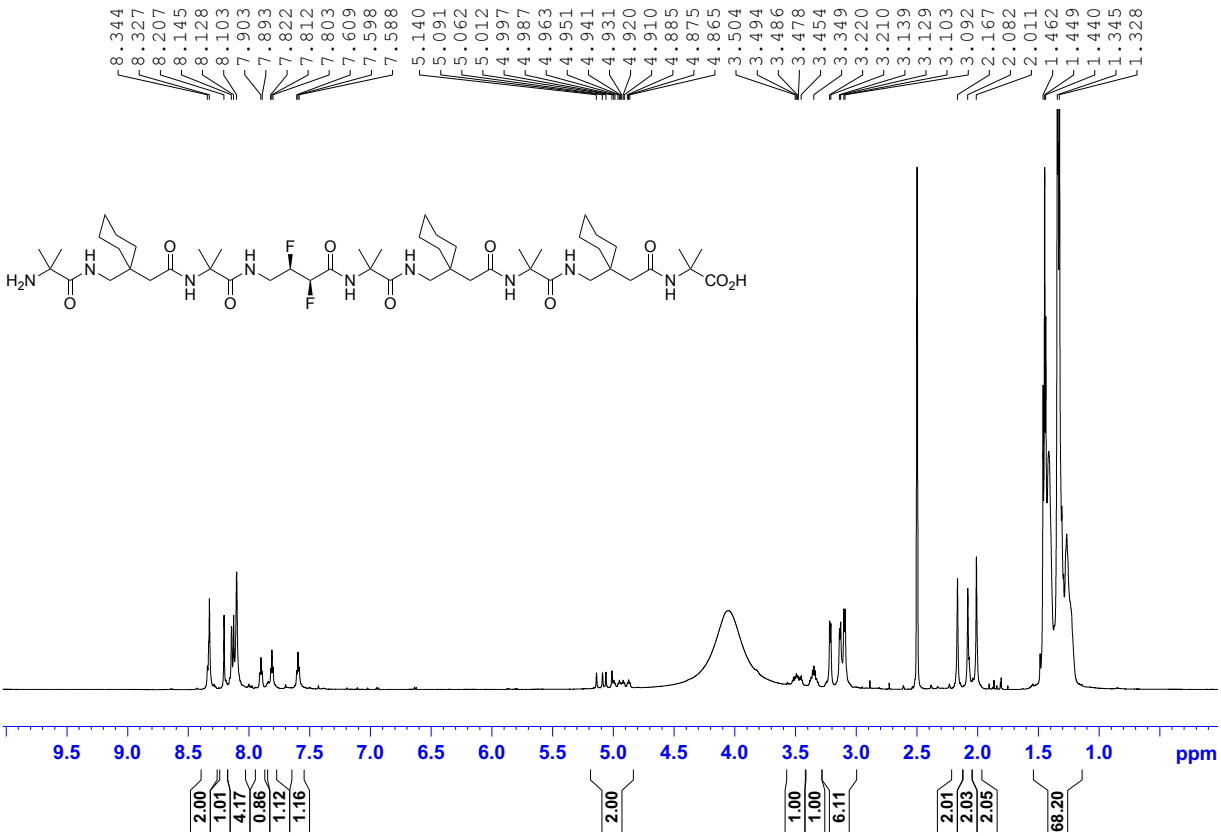
$^{19}F\{^{1}H\}$ NMR (376 MHz, DMSO-d_6) of **7**



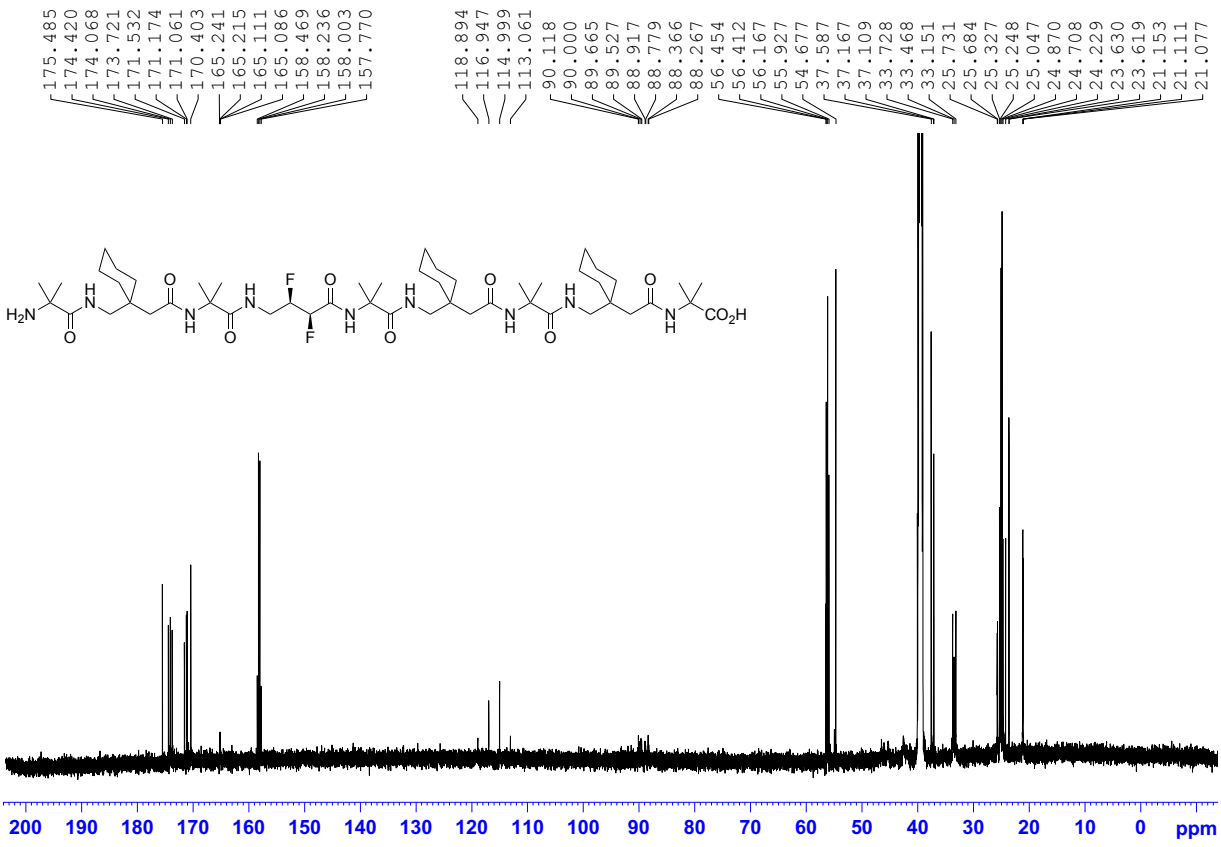
^{1}H-^{1}H ROESY NMR (600 MHz, DMSO-d_6) of **7**



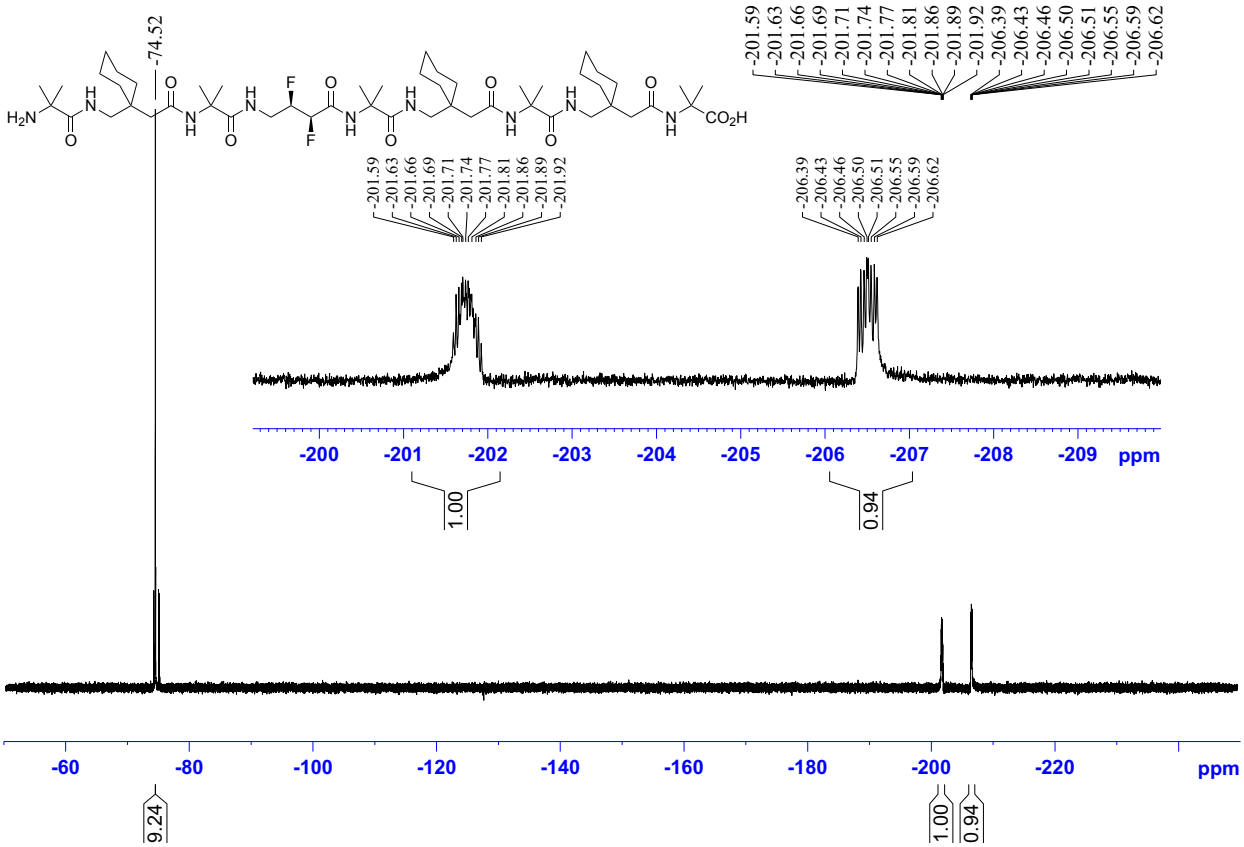
^{1}H NMR (600 MHz, DMSO-d_6) of **8**



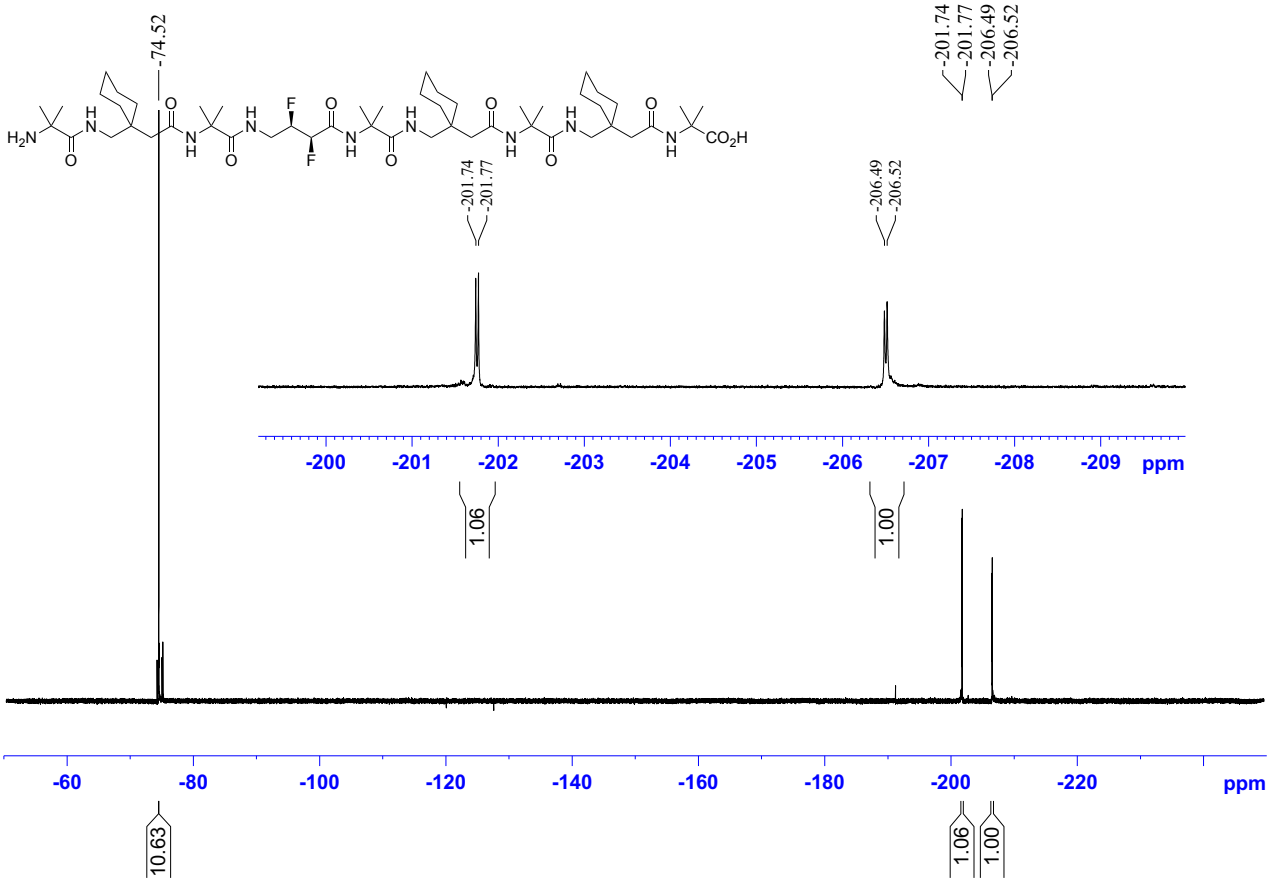
^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) of **8**



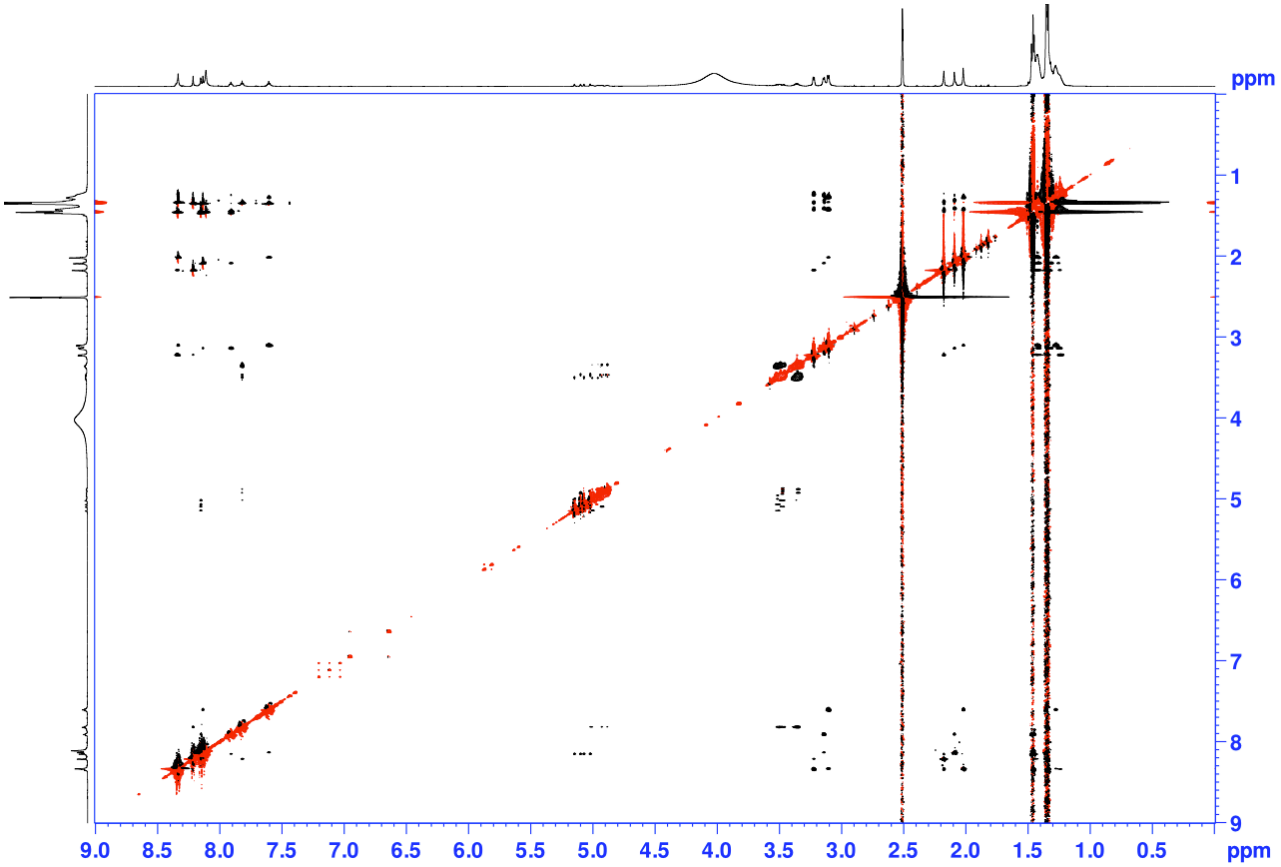
^{19}F NMR (376 MHz, DMSO-d$_6$) of **8**



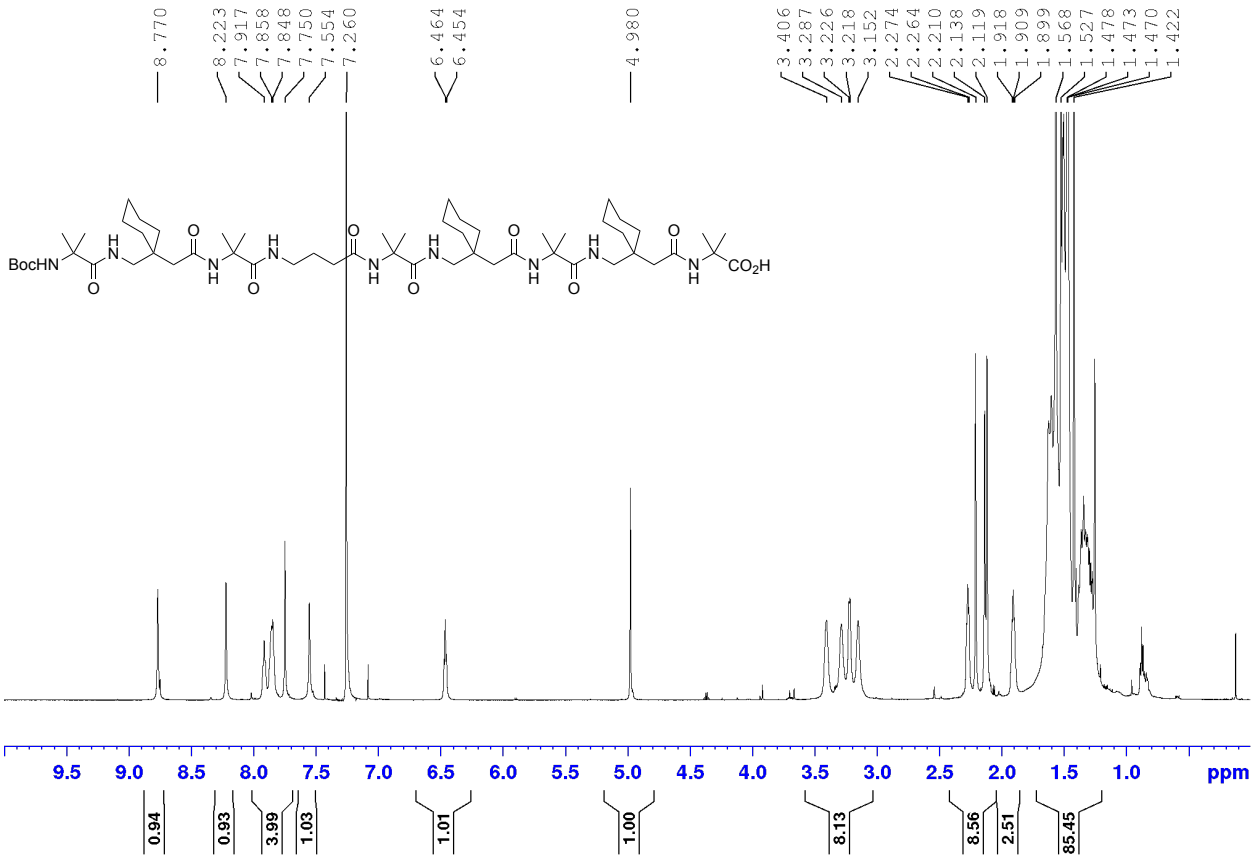
^{19}F{^{1}H} NMR (376 MHz, DMSO-d$_6$) of **8**



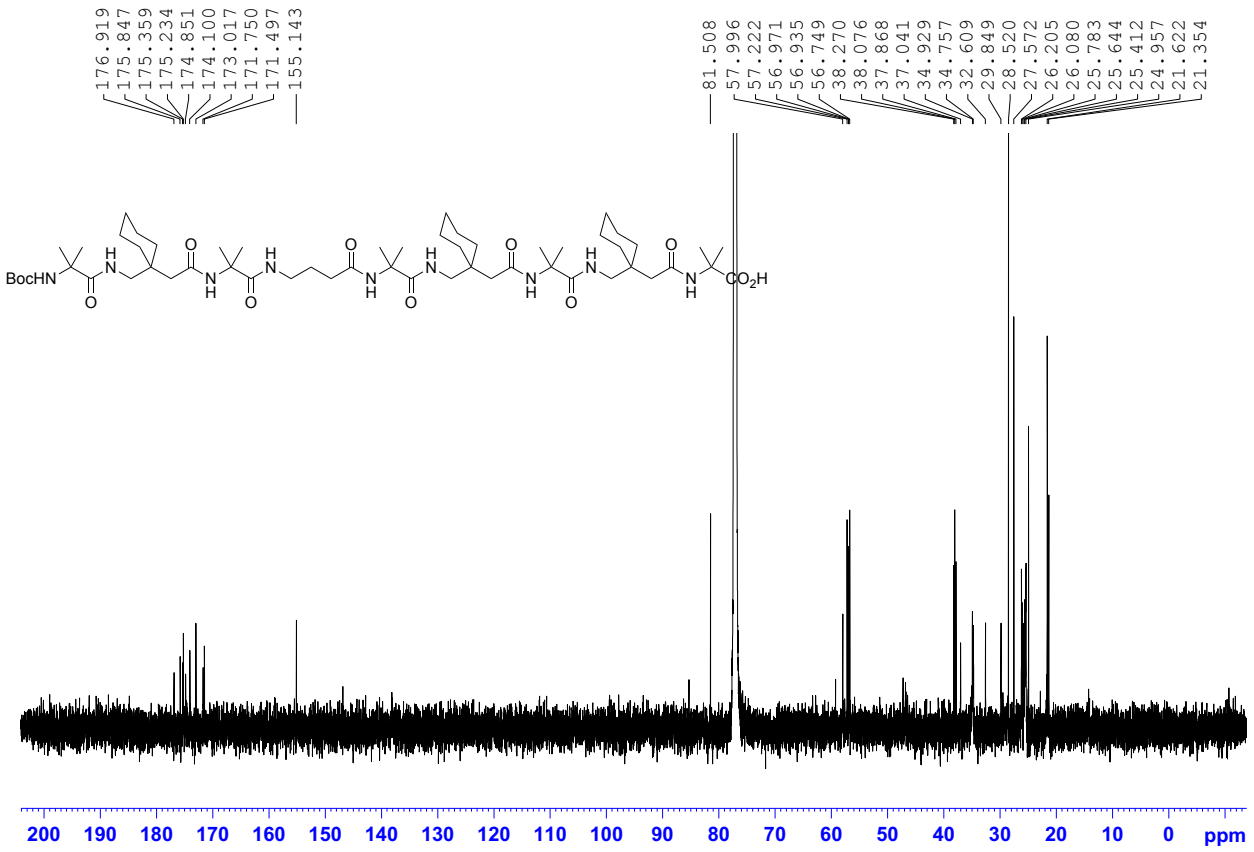
^{1}H-^{1}H ROESY NMR (600 MHz, DMSO-d_6) of **8**



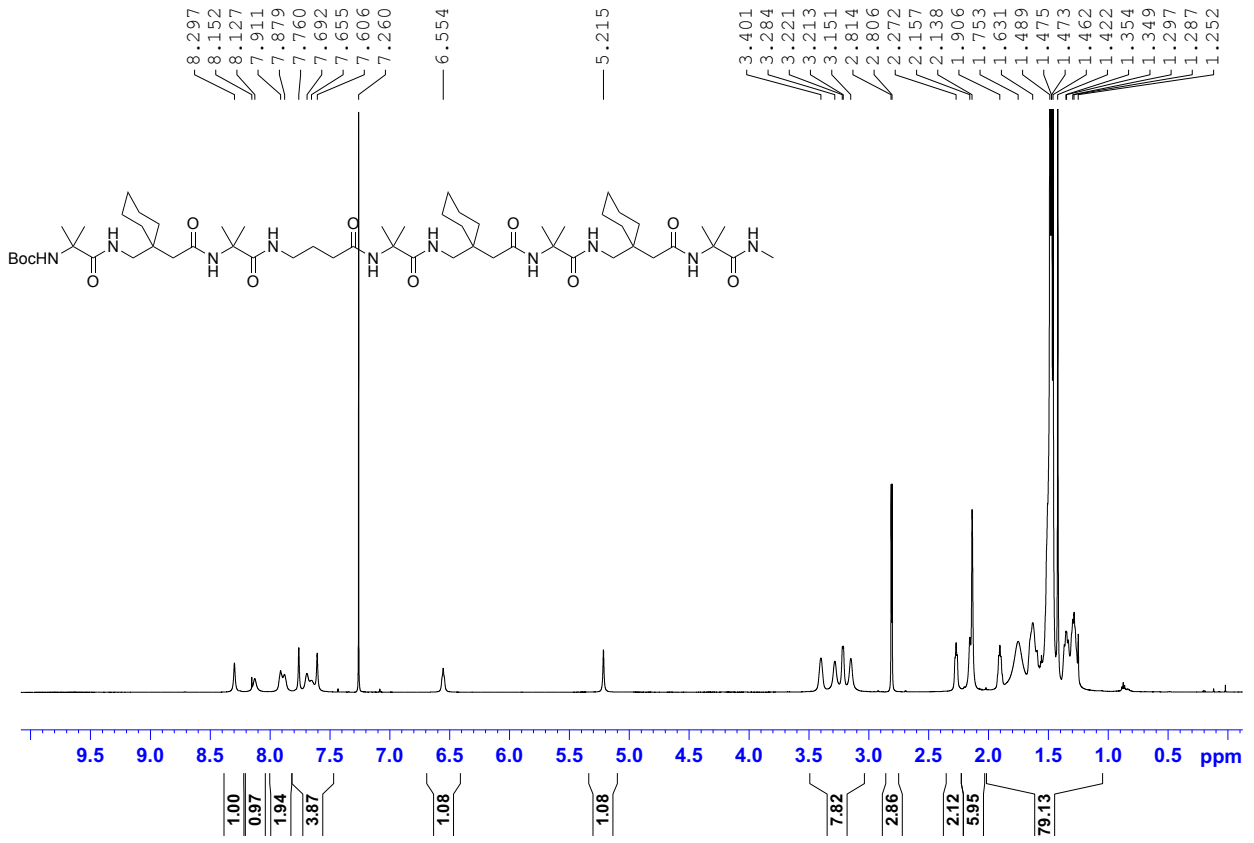
^{1}H NMR (600 MHz, $CDCl_3$) of **9**



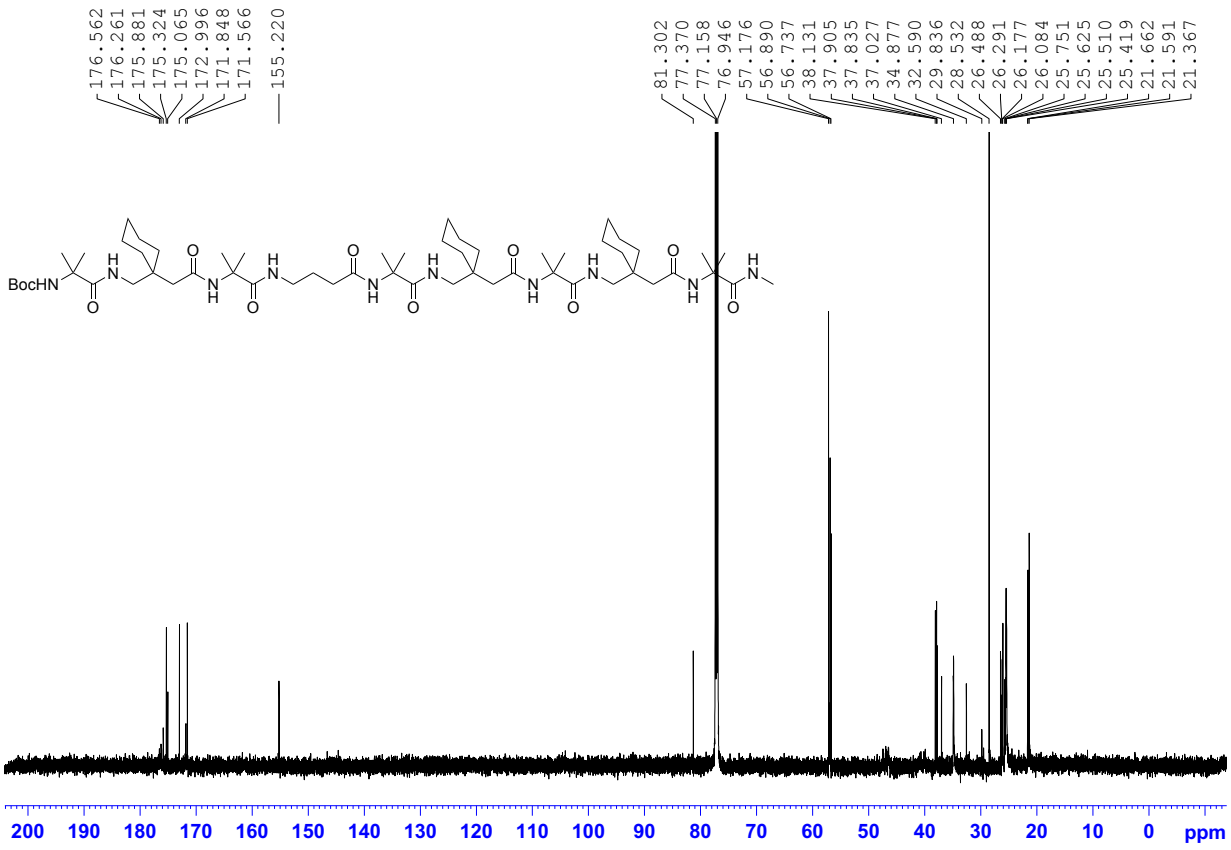
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) of **9**



^{1}H NMR (600 MHz, $CDCl_3$) of **10**



$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) of **10**



3. Crystallographic information

Colourless plate-like crystals of peptides **9**–**10** were selected under a polarizing microscope (Leica M165Z) and picked up on a MicroMount (MiTeGen, USA) consisting of a thin polymer tip with a wicking aperture. X-ray diffraction measurements were carried out on a Bruker APEX-II CCD diffractometer at 152 K using IμS Incoatec Microfocus Source with Mo-Kα radiation (λ = 0.710723 Å). The single crystals, mounted on the goniometer using a cryo loop for intensity measurements, were coated with immersion oil type NVH and then quickly transferred to the cold nitrogen stream generated by an Oxford Cryostream 700 series. Symmetry related absorption corrections using the program SADABS[1] were applied, and the data were corrected for Lorentz and polarisation effects using Bruker APEX3 software.[1] The structures were solved by program SHELXT[2] (with intrinsic phasing) and the full-matrix least-square refinements were carried out using SHELXL-2018[3] through Olex2[4] suit of software. The non-hydrogen atoms were refined anisotropically. A summary of crystallographic data for peptides **9**–**10** is provided overleaf.

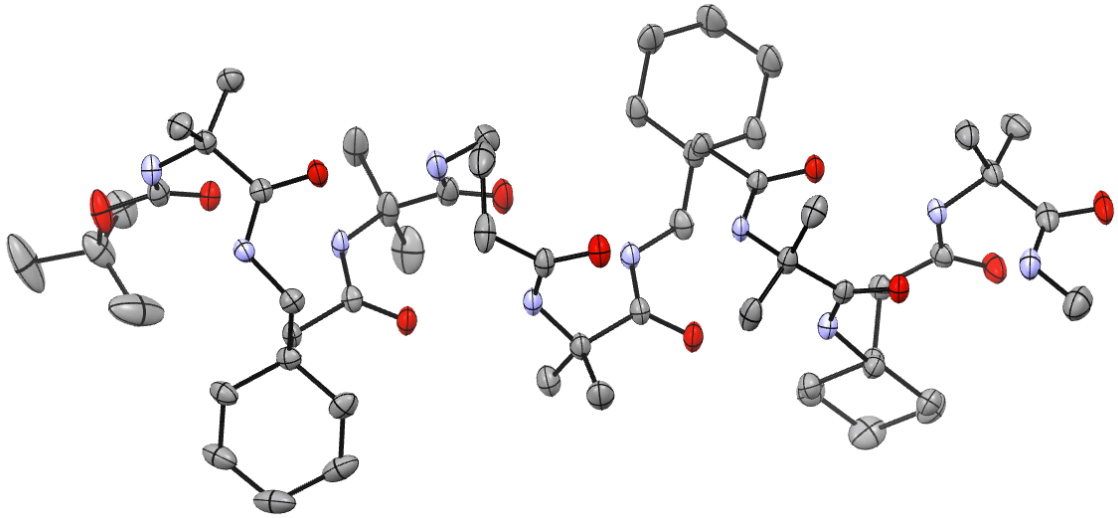
1. Bruker (2016). APEX3, SAINT and SADABS. Bruker AXS Inc., Madison, Wisconsin, USA.

2. Sheldrick, G. M. (2015). Acta Cryst. A71, 3–8.

3. Sheldrick, G. M. (2015). Acta Cryst. C71, 3–8.

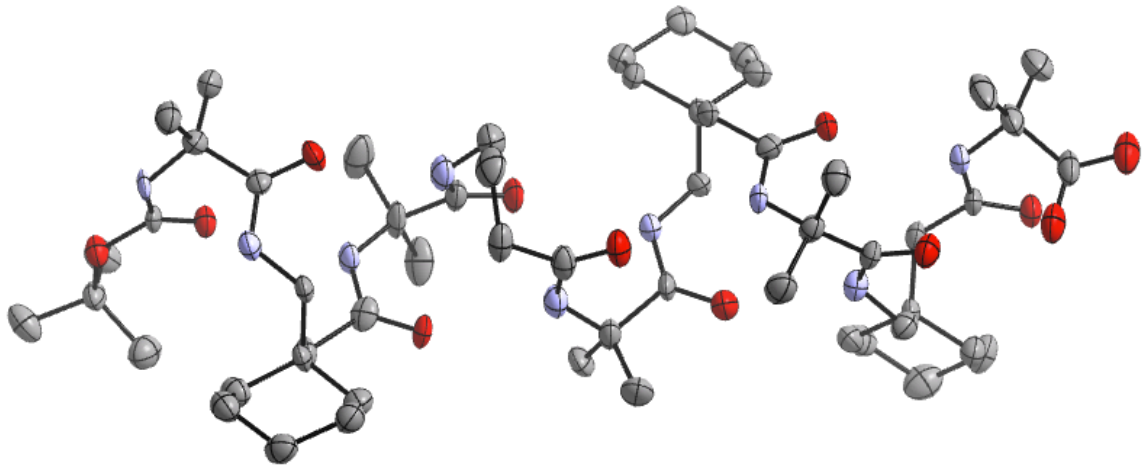
4. Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. (2009) *J. Appl. Crystallogr.* 42 (2), 339-341.

Peptide **9**



Crystal data	
Chemical formula	$1.5(CH_2Cl_2)\cdot C_{57}H_{100}N_{10}O_{11}$
M_r	1228.85
Crystal system, space group	Monoclinic, *P*21/*n*
Temperature (K)	155
a, *b*, *c* (Å)	18.8607 (6), 10.4771 (3), 36.3667 (11)
β (°)	90.447 (2)
V (Å^3)	7186.0 (4)
Z	4
Radiation type	Mo *K*α
μ (mm^{-1})	0.19
Crystal size (mm)	0.26 × 0.20 × 0.09
Data collection	
Diffractometer	Bruker APEXII
Absorption correction	Multi-scan (SADABS)
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	56738, 14103, 10025
R_{int}	0.050
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.617
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.093, 0.304, 1.05
No. of reflections	14103
No. of parameters	771
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	2.74, −1.57

Peptide **10**



Crystal data	
Chemical formula	$C_{56}H_{97}N_9O_{12}$
M_r	1088.42
Crystal system, space group	Tetragonal, $P4_3$
Temperature (K)	152
a, c (Å)	17.7179 (7), 81.727 (3)
V (Å^3)	25656 (2)
Z	16
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.08
Crystal size (mm)	0.08×0.16 ×0.32
Data collection	
Diffractometer	Bruker ApexII
Absorption correction	Multi-scan (SADABS)
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	47584, 30683, 18677
R_{int}	0.069
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.614
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.060, 0.164, 0.91
No. of reflections	30683
No. of parameters	2813
No. of restraints	45
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.25, −0.21
Absolute structure	Flack x determined using 3924 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).
Absolute structure parameter	−0.2 (10)