Electronic Supplementary Material (ESI) for ChemComm.

Engineering polypeptide folding through *trans* double bonds: Transformation of miniature β-meanders to hybrid helices

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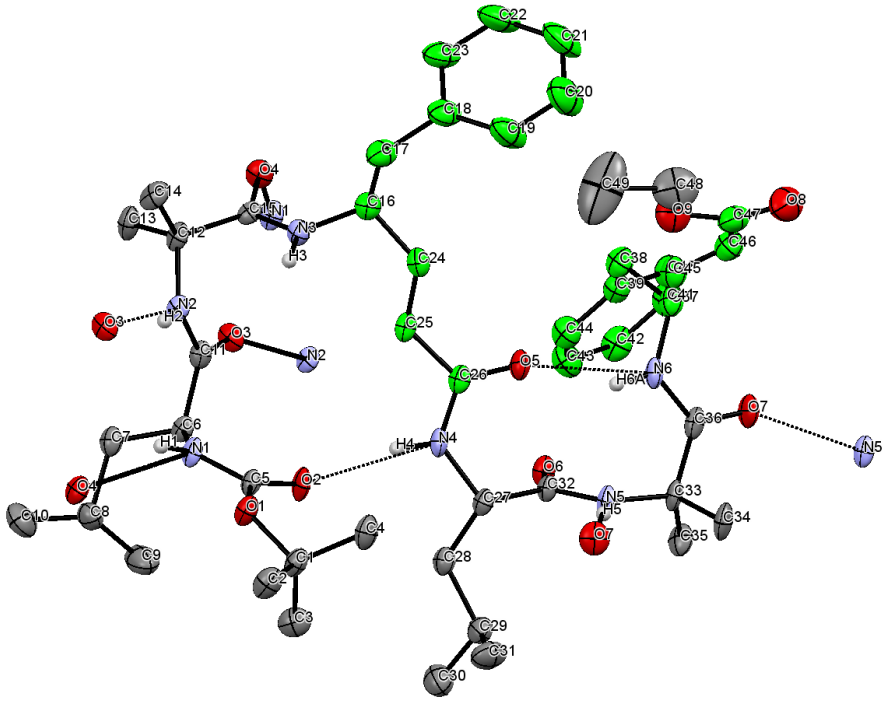
List of Contents

1. ORTEP diagrams of peptides

Peptide P1:

A)



B)

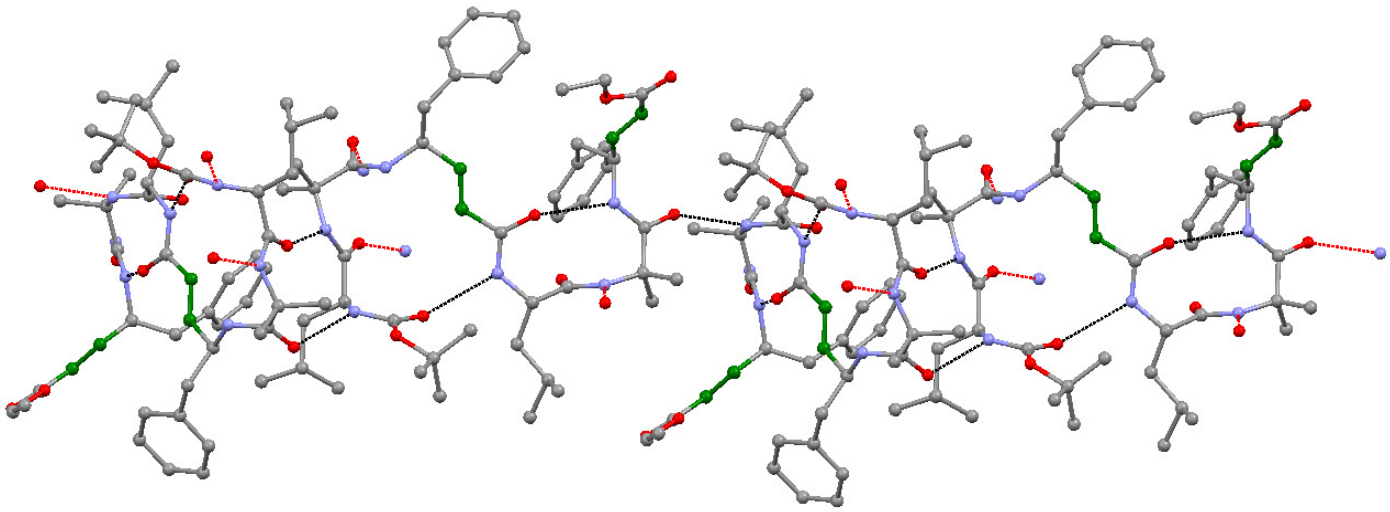


Figure S1: A) ORTEP diagram of hybrid peptide Boc-(LUdγF)$_2$-OEt (**P1**) containing*α, β*-unsaturated *γ*-phenylalanine residues (represented by green color atoms) where ellipsoids are drawn to 70% probability. Hydrogen bonds are represented in dotted lines. Only polar H-atoms were shown for clarity. (CCDC number 1063358). B) View of Crystal packing for**P1**along b-axis.

Peptide P3:

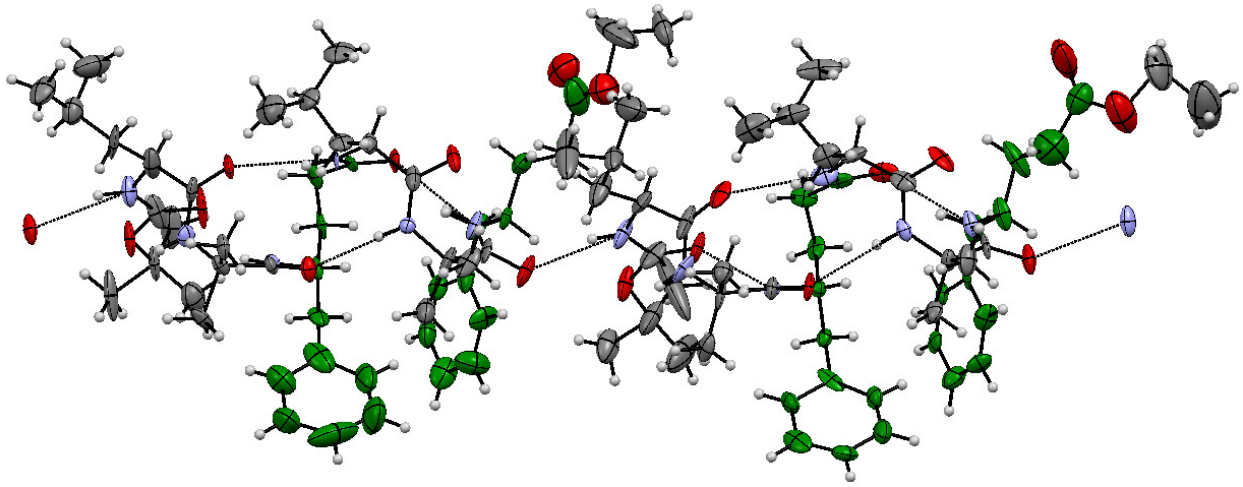


Figure S2: ORTEP diagram of hybrid peptide Boc-(LUγF)$_2$-OEt(**P3**)containing γ^4-phenylalanine residues (represented by green color atoms) where ellipsoids are drawn to 70% probability. Two molecules of **P3** present in an asymmetric unit.Hydrogen bonds are represented in dotted lines. Only polar H-atoms were shown for clarity. (CCDC number 1060827).

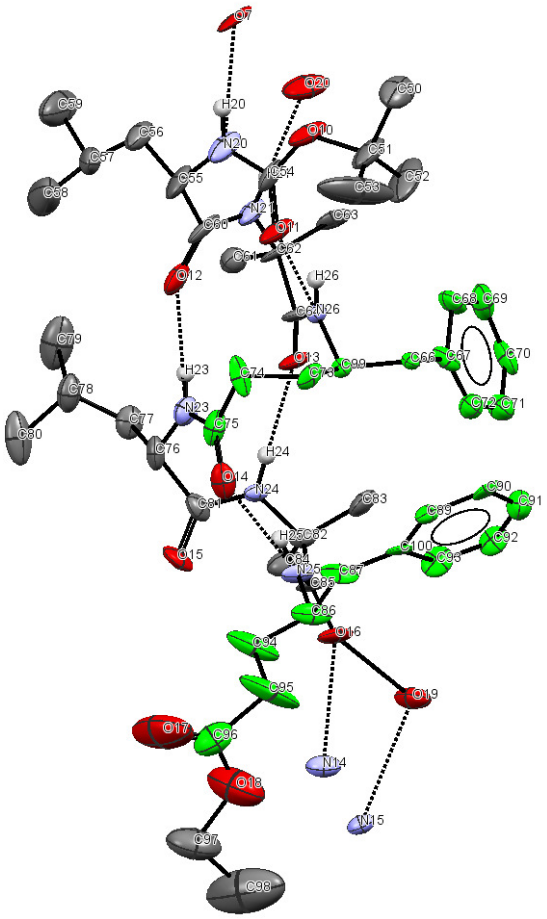


Figure S3: ORTEP diagram of peptide Boc-(LUγF)$_2$-OEt(**P3**)(showing one molecule) where ellipsoids are drawn to 70% probability. Hydrogen bonds are represented in dotted lines. Only polar H-atoms were shown for clarity.

Peptide P4:

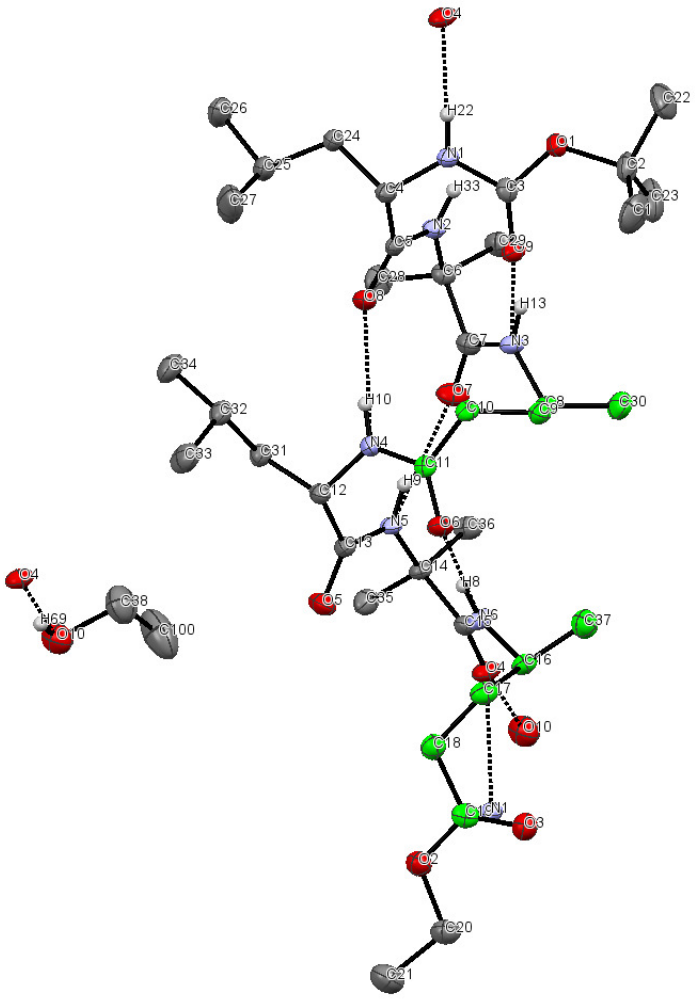


Figure S4: ORTEP diagram of peptide Boc-(LUγA)$_2$-OEt(**P4**)containing γ^4-alanine residues (represented by green color atoms) where ellipsoids are drawn to 69% probability. One ethanol solvent molecule present in the asymmetric unit. Hydrogen bonds are represented in dotted lines. Only polar H-atoms are shown for clarity. (CCDC number 1060826).

2. H-bond Parameters

Table S1: Peptide P1 [Boc-LUdγFLUdγF-OEt]

i) Intramolecular H-bond parameters

Donor (D)	Acceptor (A)	D….A (Å)	DH….A (Å)	∠NH….O (deg)
N4	O2	2.944	2.235	139.70
N6	O5	2.853	2.055	153.98

ii) Intermolecular H-bond parameters

Donor (D)	Acceptor (A)	D….A (Å)	DH….A (Å)	∠NH….O (deg)
N1	O4[§]	2.931	2.160	148.05
N2	O3[§]	3.063	2.238	160.90
N5	O7[†]	2.934	2.075	176.72
O3	N2[‡]	3.063	2.238	160.90
O4	N1[‡]	2.931	2.160	148.05
O7	N5[*]	2.934	2.075	176.72

Symmetry transformations used to generate equivalent atoms:

§ 1.5-x, 1/2+y, 2-z;† 1.5-x, 1/2+y, 1-z; ‡ 1.5-x, 1/2+y, 2-z;* 1.5-x, 1/2+y, 1-z

Table S2: Peptide P3[Boc-LUγFLUγF-OEt]

i) Intramolecular H-bond parameters for two molecules A and B in the asymmetric unit

Acceptor (A)	Donor (D)	D….A (Å)	DH….A (Å)	∠NH….O (deg)
O2 (A)	N19 (A)	3.08	2.35	142.8
O3 (A)	N16 (A)	2.95	2.12	163.5
O4 (A)	N18 (A)	2.99	2.14	169.5
O5 (A)	N17 (A)	2.84	2.04	153
O11 (B)	N26 (B)	2.99	2.25	143.9
O12 (B)	N23 (B)	2.92	2.07	164.8
O13 (B)	N24(B)	3.04	2.20	165
O14 (B)	N25 (B)	2.84	2.03	157.4

ii) Intermolecular H-bond parameters for two molecules A and B in the asymmetric unit

Donor (D)	Acceptor (A)	D….A (Å)	DH….A (Å)	∠NH….O (deg)
Molecule A				
N14	O16[*]	2.90	2.153	161
N15	O19[*]	3.00	2.068	169
O00B	O21[#]	2.70	-	-
O8[†]	O21[#]	2.97	-	-
O7	O20	2.84	-	-
O7	N20 (B)	2.87	2.04	161
Molecule B				
N20	O7 (A)	2.87	2.04	161
N21	O20	2.99	2.14	167
O16	O19	2.84	-	-
N14 (A)[‡]	O16	2.90	2.07	161

Symmetry transformations used to generate equivalent atoms:

[*]x, y, -1+z; [#] -1+x, y, z; [†] 1+x, y, z; [‡] x, y, 1+z

Table S3: Peptide P4 [Boc-LUγALUγA-OEt]

i) Intramolecular Hydrogen bond parameters

Acceptor (A)	Donor (D)	D….A (Å)	DH….A (Å)	∠NH….O (deg)
O9	N3	2.92	2.162	146.95
O8	N4	2.94	2.0841	171.6
O7	N5	2.93	2.102	160.68
O6	N6	3.00	2.209	153.93

ii) Intermolecular Hydrogen bond parameters

Acceptor (A)	Donor (D)	D….A (Å)	DH….A (Å)	∠NH….O (deg)
N1	O4 [*]	2.80	1.95	168
O4	N1 [†]	2.80	1.95	168
O4 [‡]	O10 [#]	2.88	2.14	165

Symmetry transformations used to generate equivalent atoms:

[*] 1+x, 1+y, 1+z; [†] -1+x, -1+y, -1+z; [#] x, -1+y, z; [‡] x, 1+y, z

3. Torsion angles of hybrid peptides

Table S4: Torsion angles of peptides **P1, P4** and **P6.**

Pept.	Resd.	ϕ	θ_1	θ_2	ψ	ω
P1	Leu1	-95	-	-	-46	-163
	Aib2	-60	-	-	-45	-174
	dγF3	-129	18	-178	178	-178
	Leu4	-48	-	-	128	177
	Aib5	68	-	-	11	173
	dγF6	-122	118	-178	-10	-
P4	Leu1	-53	-	-	-40±2	-175±2
	Aib2	-57	-	-	-34	-174
	γF3	-127±1	52	61	-114	-175±1
	Leu4	-55±2	-	-	-39	178
	Aib5	-59	-	-	-25	-173±1
	γF6	-104	172±4	176/-161	98±15	-
P6	Leu1	-46	-	-	-41	-177
	Aib2	-54	-	-	-37	-173
	γA3	-132	55	59	-122	-169
	Leu4	-62	-	-	-37	-178
	Aib5	-67	-	-	-12	-177
	γA6	-121	74	82	172	-

4. Crystallographic Information

Crystal structure analysis of Boc-L-U-dγF-L-U-dγF-OEt (P1): Crystals of peptide were grown by slow evaporation from a solution of methanol/toluene (1:1). A single crystal (0.21 × 0.08 × 0.1 mm) was mounted on loop with a small amount of the paraffin oil. The X-ray data were collected at 100K temperature on a Bruker APEX(II) DUO CCD diffractometer using Mo K_α radiation (λ = 0.71073 Å), ω-scans (2θ = 52.52), for a total of 14074 independent reflections. Space group C2, a = 35.352(11), b = 10.430(3), c = 17.876(5), β = 107.549(5), V = 6285 (3) Å^3, Monoclinic C, Z = 4 for chemical formula $C_{49}H_{72}N_6O_9$ (C_7H_8), with one molecule in asymmetric unit; ρcalcd = 1.037 gcm^{-3}, μ = 0.070 mm^{-1}, F(000) = 2120, R_{int} = 0.0506. The structure was obtained by direct methods using SHELXS-97.[1] The final R value was 0.0542 (wR2 = 0.1280) 14074 observed reflections ($F_0 \geq 4\sigma(|F_0|)$) and 589 variables, S = 0.832. The largest difference peak and hole were 0.228 and -0.256 eÅ^3, respectively.

There is some partially occupied solvent molecule also present in the asymmetric unit. A significant amount of time was invested in identifying and refining the disordered molecule. Option SQUEEZE of program PLATON[2] was used to correct the diffraction data for diffuse scattering effects and to identify the solvent molecule. PLATON calculated the upper limit of volume that can be occupied by the solvent to be 1740 Å ^{3}, or 27.7% of the unit cell volume. The program calculated 118 electrons in the unit cell for the diffuse species. No data are given for the diffusely scattering species. Outputs of SQUEEZE report are appended in cif file **P1**.

Crystal structure analysis of Boc-L-U-γF-L-U-γF-OEt (P3): Crystals of peptide were grown by slow evaporation from a solution of methanol. A single crystal (0.12 × 0.09 × 0.1 mm) was mounted on loop with a small amount of the paraffin oil. The X-ray data were collected at 100K temperature on a Bruker APEX(II) DUO CCD diffractometer using Mo K_α radiation (λ = 0.71073 Å), ω-scans (2θ = 56.7), for a total of 90866 independent reflections. Space group P 21, a = 9.286 (3), b = 20.892 (7), c = 27.661 (9), β = 98.639(6), V = 5305 (3) Å^3, Monoclinic C, Z = 2 for chemical formula C_{49} H_{76} N_6 O_9(CH_4 O, 3 O), with two molecule in asymmetric unit; ρcalcd = 1.168 gcm^{-3}, μ = 0.082 mm^{-1}, F(000) = 1936, R_{int} = 0.1470. The structure was obtained

by direct methods using SHELXS-97.[1] The final R value was 0.1509 (wR2 = 0.3727) 26002 observed reflections ($F_0 \geq 4\sigma(|F_0|)$) and 1224 variables, S = 1.642.

There are partially occupied solvent molecules along with peptide molecules.Option SQUEEZE of program PLATON[2] was used to correct the diffraction data for diffuse scattering effects and to identify the solvent molecule. PLATON calculated the upper limit of volume that can be occupied by the solvent to be 470 Å ^{3}, or 8.8% of the unit cell volume. Outputs of SQUEEZE report are appended in CIF file **P4**.This structure contains ethyl ester groups. Even though this structure was collected at 100K the thermal parameters for one of the ethyl ester group was very high. This was attempted to be modeled as disorder but this was not successful. The conclusion is that this group is not well defined and thus was refined isotropically.

Crystal structure analysis of Boc-L-U-γA-L-U-γA-OEt (P4): Crystals of peptide were grown by slow evaporation from a solution of ethanol. A single crystal (0.15 × 0.04 × 0.07 mm) was mounted on loop with a small amount of the paraffin oil. The X-ray data were collected at 100K temperature on a Bruker APEX(II) DUO CCD diffractometer using Mo K_α radiation (λ = 0.71073 Å), ω-scans (2θ = 56.9), for a total of 7174 independent reflections. Space group P1, a = 9.7972 (4), b = 10.4809 (5), c = 12.3285 (6), β = 102.4740 (10), V = 1132 (9) Å^3, Triclinic, Z = 1 for chemical formula C_{37} H_{68} N_6 O_9 (C_2 H_6 O), with one molecule in asymmetric unit; ρcalcd = 1.129 gcm^{-3}, μ = 0.081 mm^{-1}, F (000) = 419, R_{int} = 0.0401. The structure was obtained by direct methods using SHELXS-97.[1] The final R value was 0.035 (wR2 = 0.1052) 7363 observed reflections ($F_0 \geq 4\sigma$ ($|F_0|$)) and 514 variables, S = 0.908.

5. General experimental details

All amino acids, triphenylphosphine, TFA, Ethyl bromoacetate, DCC, HOBt and LAH were commercially available. DCM, DMF, ethyl acetate and petether(60-80 ^{o}C) have used after distillation. THF was dried over sodium and distilled immediately prior to use. Column chromatography was performed on silica gel (120-200 mesh). Final peptides were purified on reverse phase HPLC (C18 column, MeOH/H_2O 60:40-95:5 as gradient with flow rate 1.00 mL/min). ^{1}H spectra were recorded on 500 MHz (or ^{13}C on 125 MHz) and 400 MHz (or ^{13}C on 100 MHz) using residual solvents as internal standards ($CDCl_3$ δ_H 7.26 *ppm*, δ_C77.3 *ppm*). Chemical shifts (δ) reported in *ppm* and coupling constants (*J*) reported in Hz.

NMR spectroscopy: All NMR studies were carried out by using a Bruker AVANCE^{III}-500 MHz spectrometer. Resonance assignments were obtained by TOCSY and ROESY analysis. All two-dimensional data were collected in phase-sensitive mode, by using the time-proportional phase incrementation (TPPI) method. Sets of 1024 and 512 data points were used in the t_2 and t_1 dimensions, respectively. For TOCSY and ROESY analysis, 32 and 72 transients were collected, respectively. A spectral width of 6007 Hz was used in both dimensions. A spin-lock time of 256 ms was used to obtain ROESY spectra. Zero-filling was carried out to finally yield a data set of 2 K × 1 K. A shifted square-sine-bell window was used before processing.

Circular dichroism (CD) spectroscopy:CD analysis was performed using cylindrical, jacketed quartz cell (1 mm path length). Spectra were recorded with a spectral resolution of 0.05 nm, band width 1 nm at a scan speed of 50nm/min and a response time 1 sec. All the spectra were corrected for water solvent and are typically averaged over 3 scans.

6. 2D NMR data of Peptides P1 and P2

Table S5: List of NOE's observed in ROESY spectrum of **P1**

Residue	H-atom	Residue	H-atom	NOE observed
Leu (1)	α CH	Aib (2)	NH	Strong
Leu (1)	NH	Aib (2)	NH	Strong
Leu (1)	NH	Leu (1)	αCH	Medium
Leu (1)	NH	Leu (1)	β CH	Strong
Leu (1)	NH	Leu (1)	γ CH	Strong
Leu (1)	NH	Leu (1)	δ CH	Strong
Leu (1)	α CH	Aib (2)	$(CH_3)_2$	Strong
Aib (2)	NH	dγF (3)	NH	Strong
Aib (2)	NH	Aib (2)	$(CH_3)_2$	Strong
dγF (3)	NH	Aib (2)	$(CH_3)_2$	Medium
dγF (3)	αCH	Leu (4)	NH	Strong
dγF (3)	NH	dγF (3)	ω CH_2	Strong
dγF (3)	β CH	dγF (3)	ω CH_2	Strong
dγF (3)	γ CH	dγF (3)	Aromatic	Strong
dγF (3)	αCH	dγF (3)	γ CH	Weak
Leu (4)	NH	Leu (4)	β CH	Medium
Leu (4)	NH	Leu (4)	γ CH	Weak
Aib (5)	NH	Leu (4)	β CH	Weak
Aib (5)	NH	Leu (4)	αCH	Strong
Aib (5)	NH	dγF (6)	NH	Strong
Aib (5)	NH	Aib (5)	$(CH_3)_2$	Strong
dγF (6)	NH	Aib (5)	$(CH_3)_2$	Medium
dγF (6)	NH	dγF (6)	ω CH_2	Strong
dγF (6)	NH	dγF (6)	αCH	Strong
dγF (6)	αCH	dγF (6)	ω CH_2	Weak
dγF (6)	αCH	dγF (6)	γCH	Weak
dγF (6)	αCH	Aib (5)	$(CH_3)_2$	Weak
dγF (6)	β CH	dγF (6)	ω CH_2	Strong

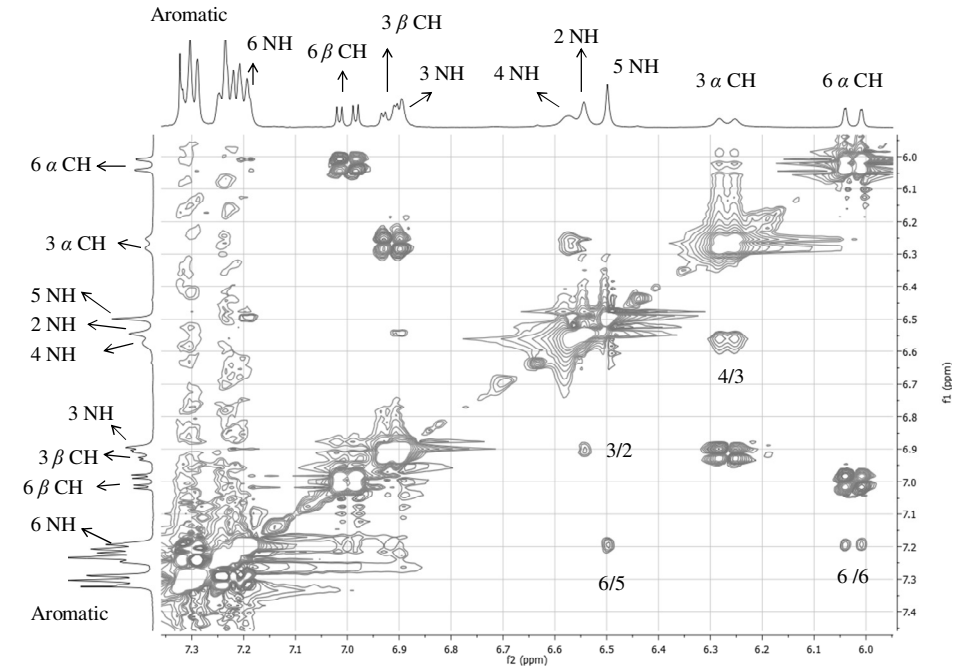


Figure S5: Partial ROESY spectrum of Peptide **P1**.

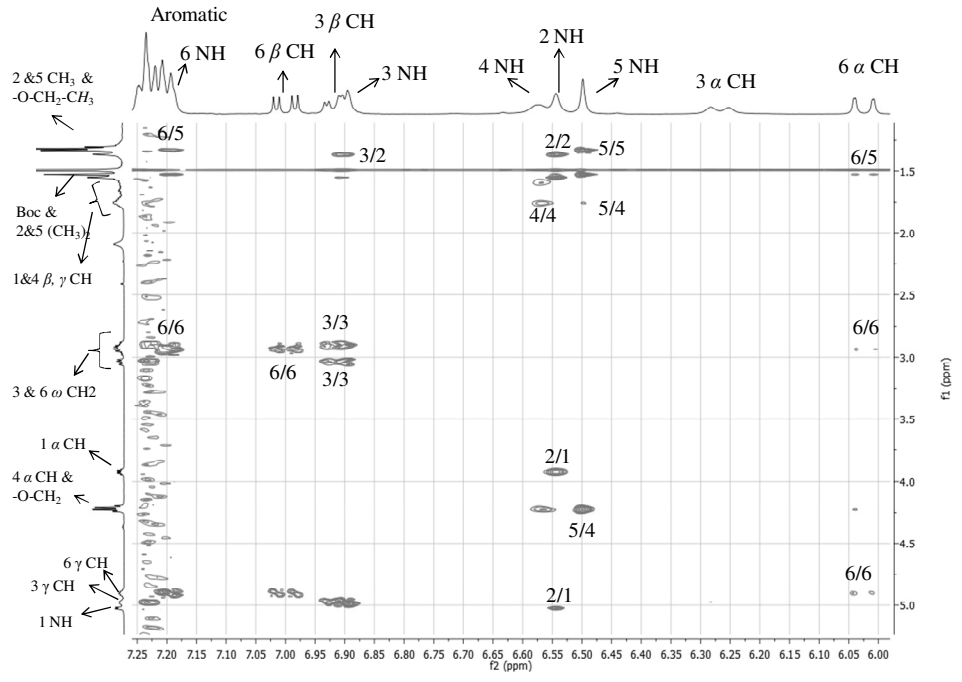


Figure S6: Partial ROESY spectrum of Peptide **P1**.

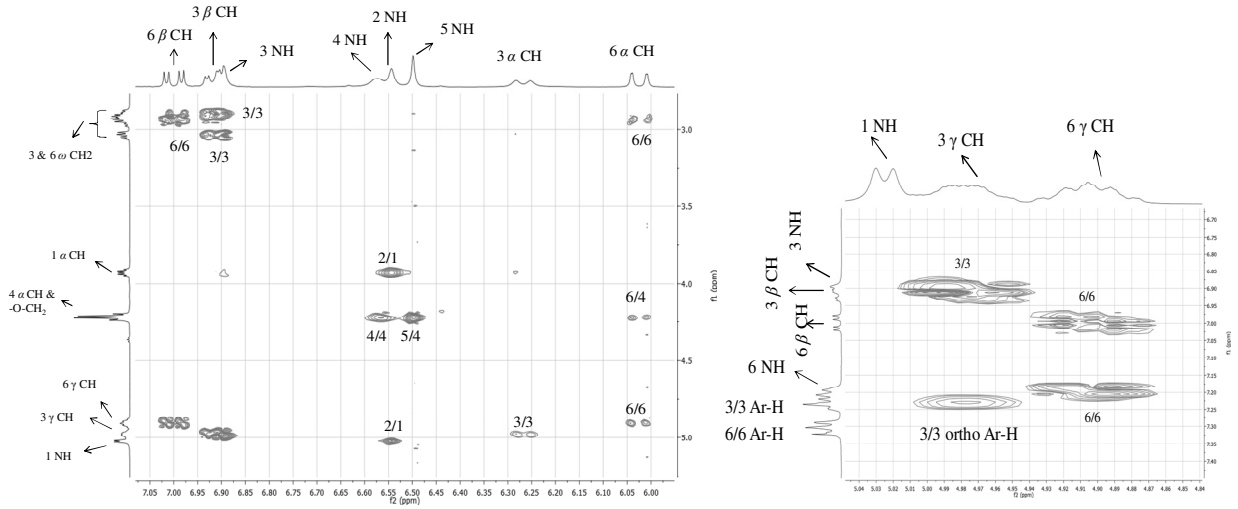


Figure S7: Partial ROESY spectrum of Peptide **P1**.

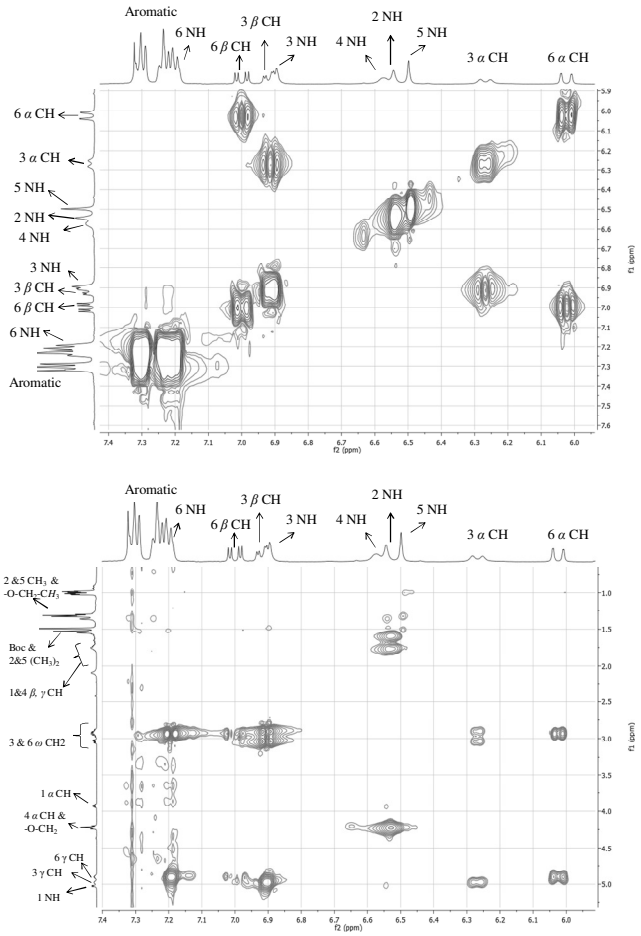


Figure S8: Partial ROESY spectrum of Peptide **P1**.

Table S6: List of NOE's observed in ROESY spectrum of **P2**

Residue	H-atom	Residue	H-atom	NOE observed
Leu (1)	NH	Aib (2)	NH	Strong
Leu (1)	α CH	Aib (2)	NH	Strong
Leu (1)	NH	Aib (2)	$(CH_3)_2$	Medium
Leu (1)	NH	Leu (1)	β CH	Strong
Leu (1)	NH	Leu (1)	γ CH	Weak
Aib(2)	NH	dγA (3)	NH	Weak
Aib(2)	NH	Aib (2)	$(CH_3)_2$	Strong
Aib(2)	$(CH_3)_2$	dγA (3)	NH	Strong
Aib(2)	$(CH_3)_2$	dγA (3)	α CH	Weak
Aib(2)	$(CH_3)_2$	dγA (3)	γ CH	Weak
dγA (3)	NH	dγA (3)	CH_3	Strong
dγA (3)	β CH	dγA (3)	CH_3	Strong
dγA (3)	β CH	dγA (6)	CH_3	Strong
dγA (3)	α CH	Leu (4)	NH	Strong
dγA (3)	α CH	dγA (3)	NH	Strong
dγA (3)	α CH	dγA (3)	CH_3	Medium
Leu (4)	NH	Leu (4)	β CH	Medium
Leu (4)	NH	Leu (4)	γ CH	Medium
Leu (4)	α CH	Aib (5)	NH	Strong
Leu (4)	α CH	Leu (4)	δ CH	Strong
Aib (5)	NH	dγA (6)	NH	Medium
Aib (5)	NH	Aib (5)	$(CH_3)_2$	Strong
Aib (5)	$(CH_3)_2$	dγA (6)	NH	Strong
Aib (5)	$(CH_3)_2$	dγA (6)	α CH	Weak
Aib (5)	$(CH_3)_2$	dγA (6)	γ CH	Strong
dγA (6)	α CH	dγA (6)	NH	medium
dgA (6)	α CH	dgA (6)	CH_3	Weak
dgA (6)	NH	dgA (6)	CH_3	Strong
dgA (6)	β CH	dgA (6)	CH_3	Strong

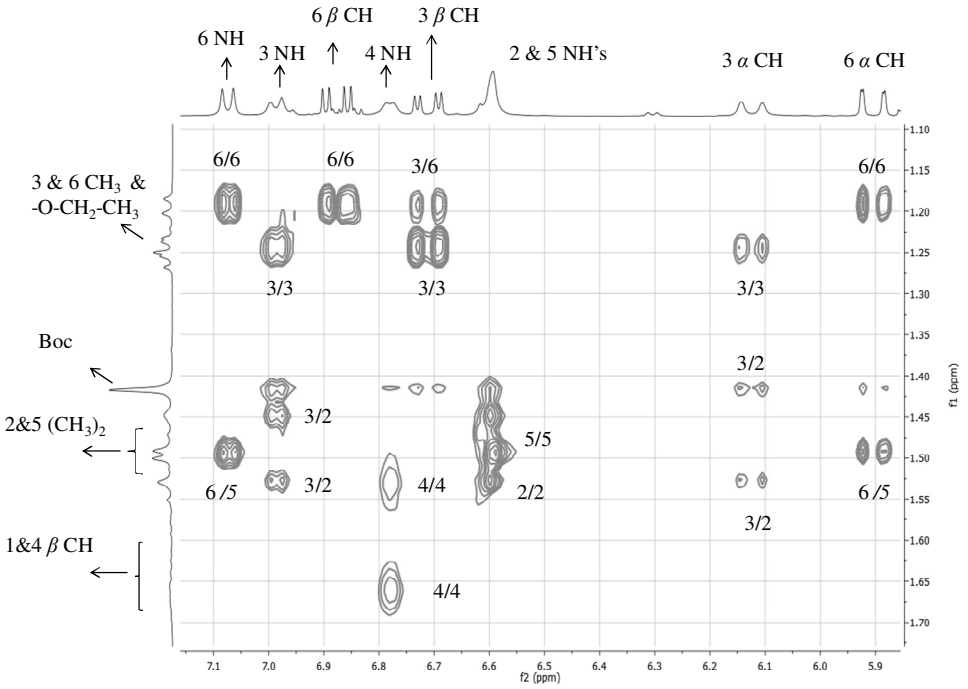


Figure S9: Partial ROESY spectrum of Peptide **P2**.

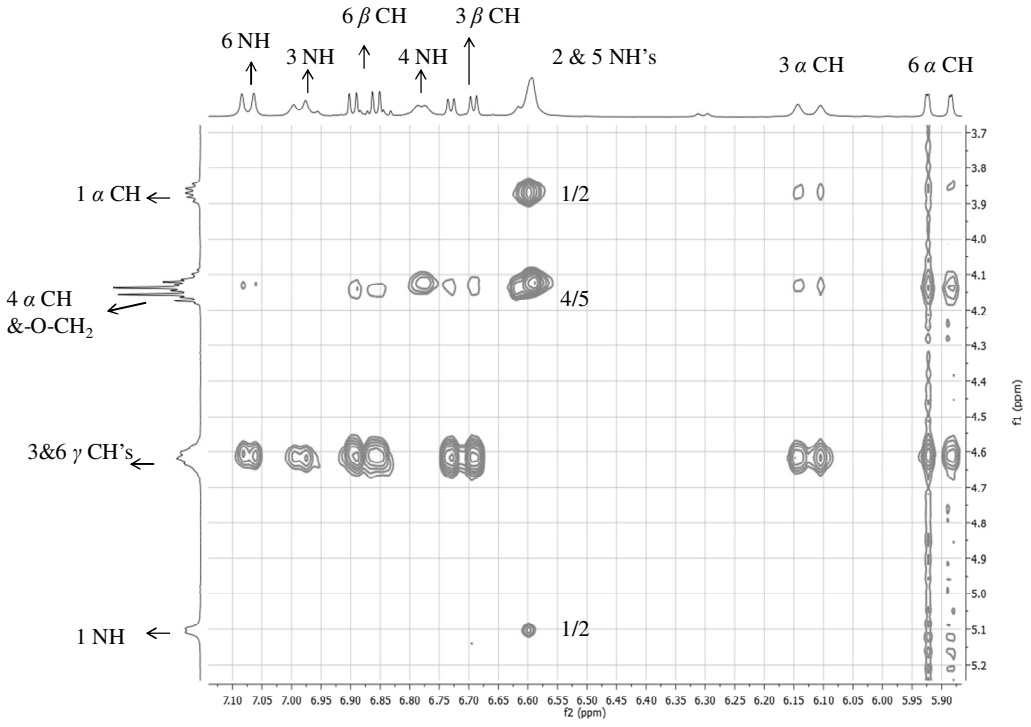


Figure S10: Partial ROESY spectrum of Peptide **P2**.

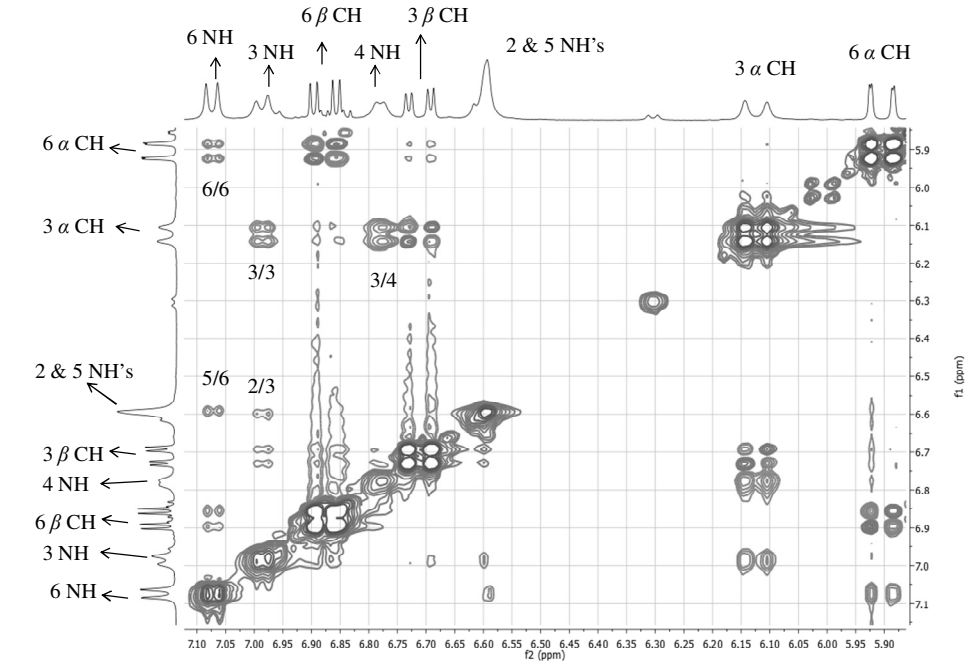


Figure S11: Partial TOCSY spectrum of Peptide **P2**.

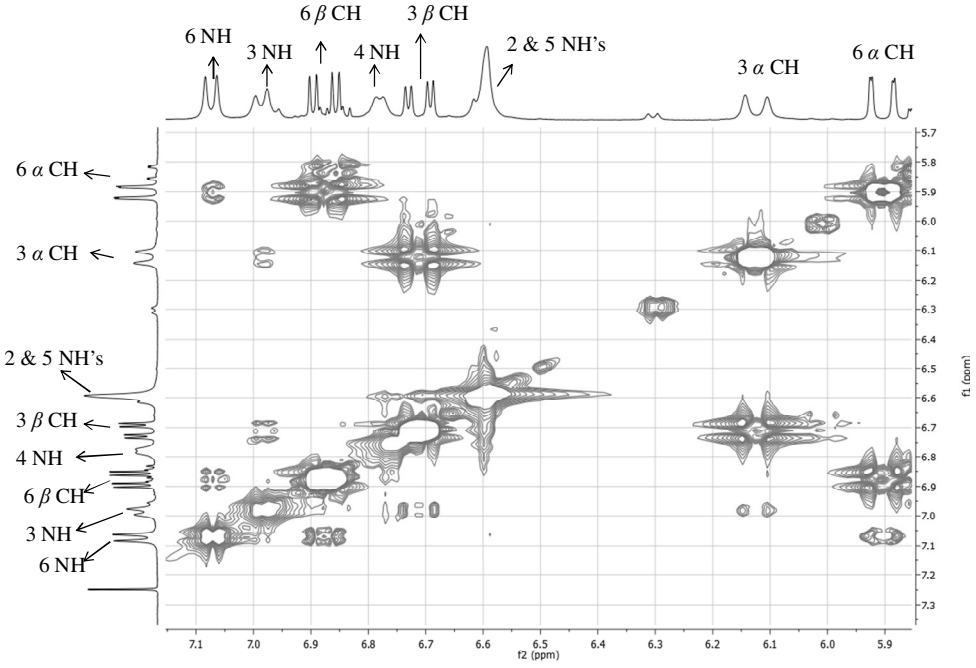


Figure S12: Partial TOCSY spectrum of Peptide **P2**.

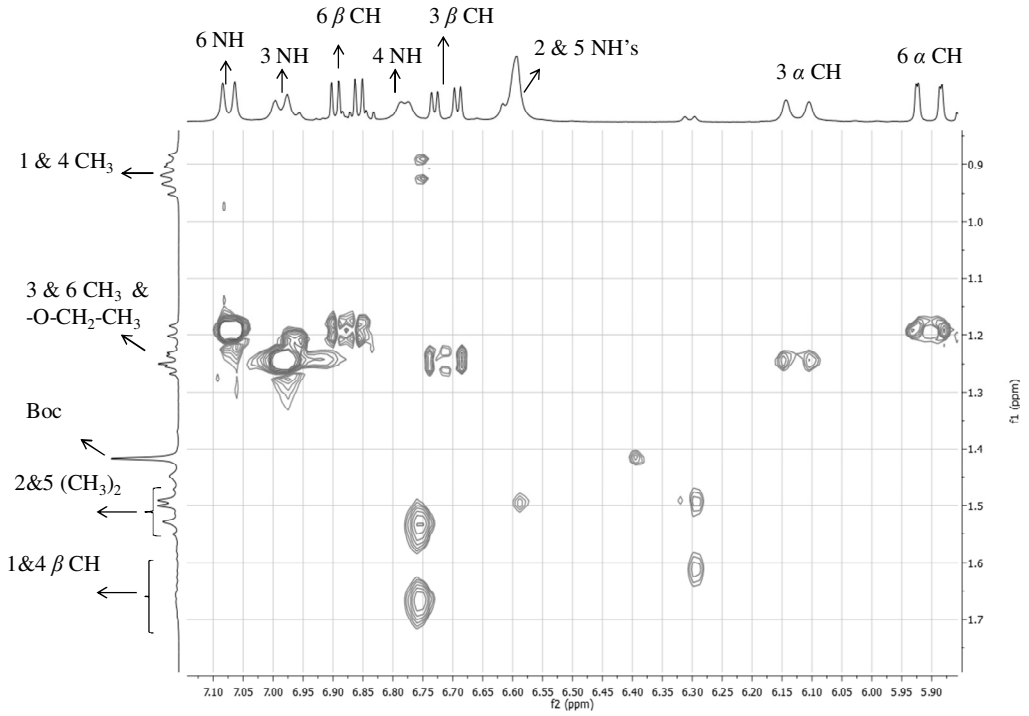


Figure S13: Partial TOCSY spectrum of Peptide **P2**.

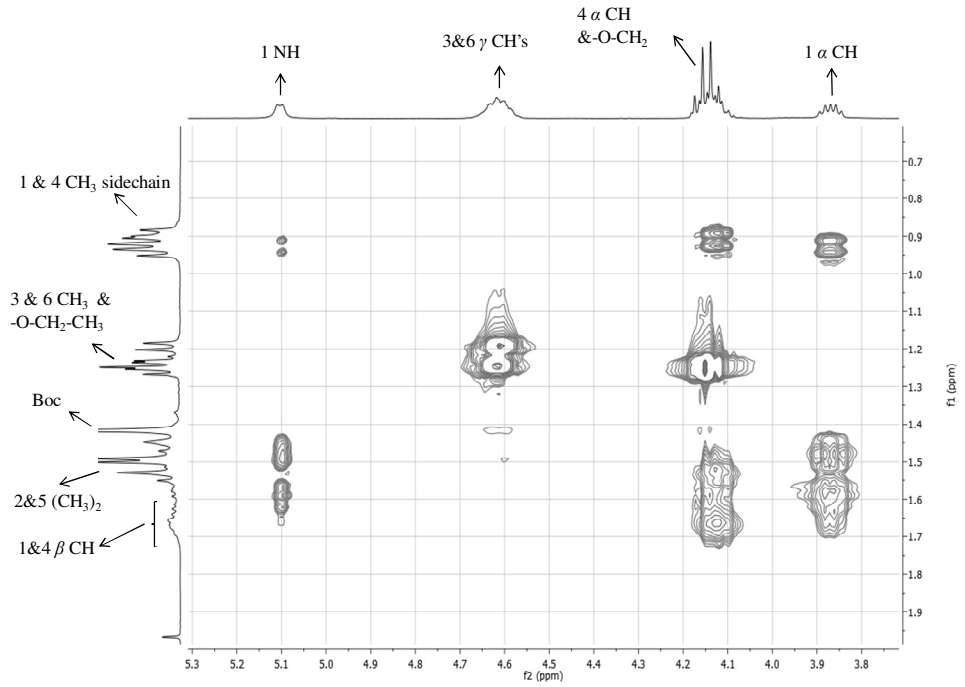


Figure S14: Partial TOCSY spectrum of Peptide **P2**.

iii)

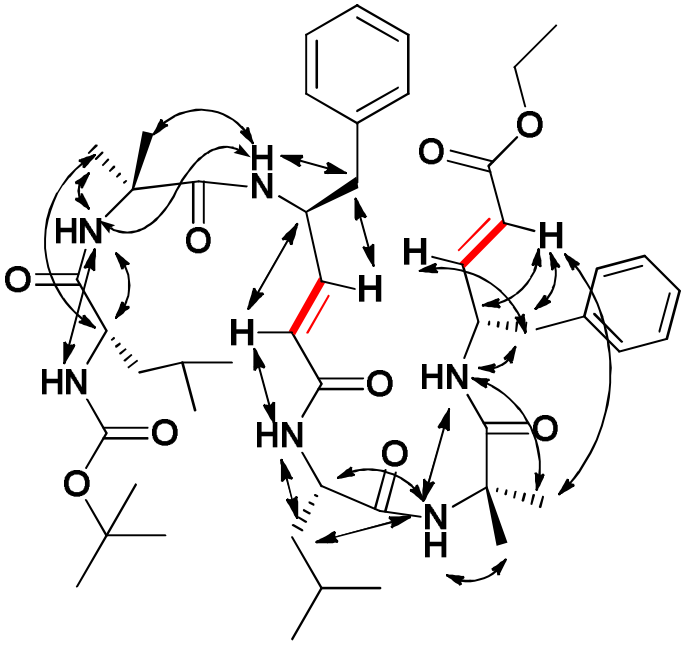


Figure S15: A) Observed NOEs of the peptide **P1** in the ROESY are schematically represented by double headed arrows.

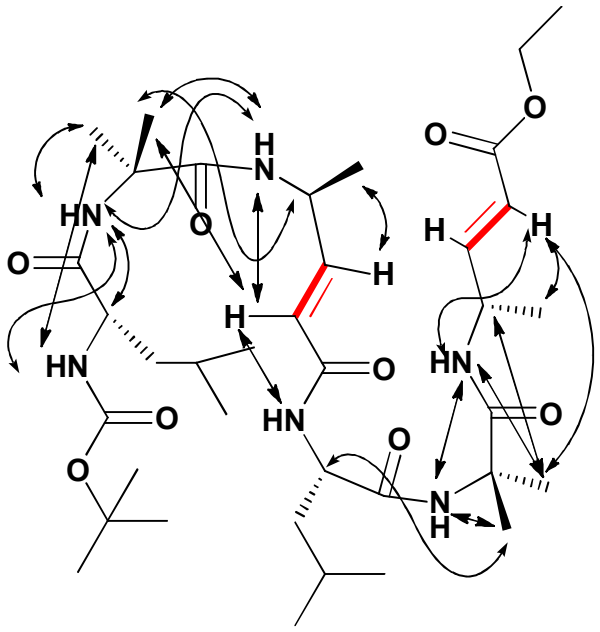
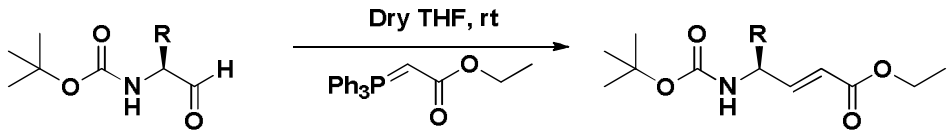


Figure S15: B) Observed NOEs of the peptide **P2** in the ROESY are schematically represented by double headed arrows.

Molecular Dynamics (MD): Model building and molecular dynamics simulation of **P1** and **P2** was carried out using Insight II (97.0) / Discover program on a Silicon Graphics Octane workstation. The cvff force field with default parameters was used throughout the simulations. Minimization's were done first with steepest decent, followed by conjugate gradient methods for a maximum of 1000 iterations each or RMS deviation of 0.001 kcal/mol, whichever was earlier. The energy-minimized structures were then subjected to MD simulations. A number of inter atomic distance constraints obtained from NMR data were used as restraints in the minimization as well as MD runs. For MD runs, a temperature of 300 K was used. The molecules were initially equilibrated for 50 ps and subsequently subjected to a 1 ns dynamics with a step size of 1 fs, sampling the trajectory at equal intervals of 10 ps. In trajectory 50 samples were generated and the best structures were again energy minimized with above protocol and superimposed these structures.

7. Synthesis and Characterization of Boc-dγF-OEt, Boc-dγA-OEt and Peptides P1-P4

Synthesis of Boc-dγX-OEt:[3] *N*-Boc-Amino aldehyde (10 mmol) was dissolved in 30 mL of dry THF followed by Wittig ylide (11 mmol) was added at RT. Reaction mixture was stirred for about 5 hrs at RT. Completion of the reaction was monitored by TLC. After completion, solvent was evaporated and the crude product was purified by column chromatography using EtOAc/pet ether to get (88%) of pure product.



(S,E)-ethyl 4-((tert-butoxycarbonyl)amino)-5-phenylpent-2-enoate:[3] White powder solid;Yield 88%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.14 (m, 5H), 6.89 (dd, *J*=16 Hz, *J*=4 Hz, 1H), 5.84 (dd, *J*=16 Hz, *J*=2 Hz, 1H), 4.59 (b, 1H), 4.16 (q, *J*=7 Hz, 2H), 2.88 (m, 2H), 1.37 (s, 9H), 1.25 (t, *J*=7.1 Hz, 3H); ^{13}CNMR (100 MHz, $CDCl_3$) δ166.3, 155.2, 147.6, 136.4, 129.4, 128.6, 126.9,

121.1, 79.9, 60.5, 52.3, 40.9, 28.3, 14.2; MALDI TOF/TOF *m/z* calculated value for $C_{18}H_{25}NO_4$ [M+Na^+] 342.1676 and observed 342.1657.

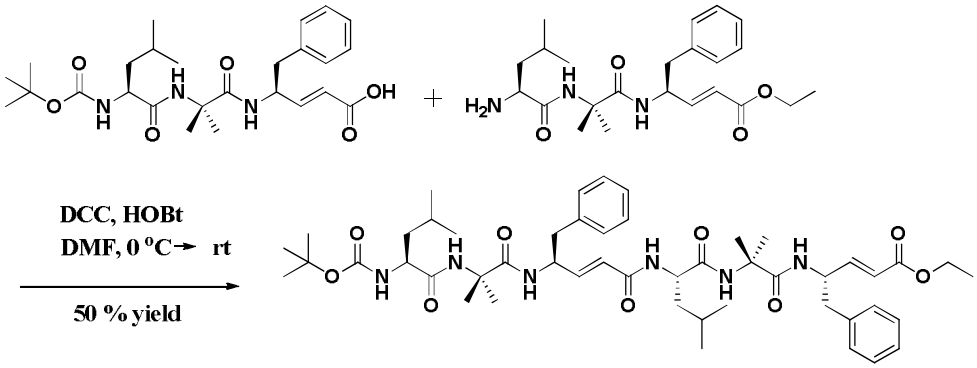
(S,E)-ethyl 4-((tert-butoxycarbonyl)amino)pent-2-enoate:[3]Colourless Oil; Yield 93%; ^{1}H NMR(400 MHz, CDCl3)δ 6.87-6.82 (dd, J = 16 Hz, J = 4 Hz, 1H), 5.89-5.85 (d, J = 16 Hz, 1H), 4.5 (br, 1H), 4.38 (br, 1H), 4.19-4.14(q, *J*= 8 Hz, 2H), 1.43 (s, 9H), 1.26-1.24 (m, 6H); ^{13}C NMR(100 MHz, CDCl3) 166.4, 154.9, 120.2, 79.8, 60.5, 47.0, 28.4, 20.4, 14.3;MALDI.TOF/TOF*m/z* Calculated value for $C_{12}H_{21}NO_4$[M+Na]$^+$ 266.1368 and Observed266.1365.

*Procedure for the synthesis of Boc-L-U-dγX-L-U-dγX-OEt:*Tripeptide and hexapeptide were prepared by conventional solution-phase fragment condensation strategy. Deprotections were performed with trifloroacetic acid and saponification for *N*- and *C*-termini respectively. Couplings were carried out using dicyclohexcarbodimide (DCC) and 1-hydroxybenzotriazole (HOBt). Tripeptide was synthesised using 1+2 condensation strategy involving Boc-Leu-OH and NH_2-U-dgF-OEt. Hexapeptide was synthesized by 3+3 condensation strategy involving Boc-L-U-dgX-COOH and NH_2-L-U-dgX-OEt. All peptides were purified by RP-HPLC using MeOH/H_2O system.

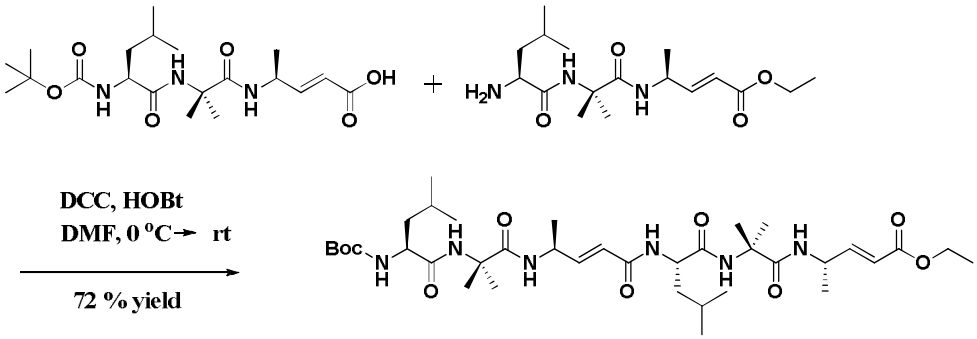
*Boc-LUdγF-OEt:*White solid; yield 88%;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (bs, 1H), 7.29-7.17 (m, 5H), 7.06 (d, *J*=7.8 Hz, 1H), 6.92 (dd, *J* = 15.8 Hz, *J* = 4.8 Hz, 1H), 6.47 (bs, 1H) 5.90 (d, *J* = 15.57 Hz, 1H), 4.90 (m, 2H), 4.16(q, 2H, *J* = 8 Hz), 2.91 (m, 2H) , 1.65 (m, 2H), 1.50-1.40 (m, 16H), 1.26 (t, *J*= 7.1, 3H), 0.94(m, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 173.53, 172.38, 147.05, 136.92, 129.35, 128.56, 126.83, 121.21, 80.82, 60.44, 57.54, 54.05, 53.53, 51.26, 40.62, 40.17, 34.03, 28.35, 25.61, 25.46, 25.03, 24.86, 23.03, 21.92, 14.33;HR-MS*m/z* calculated for $C_{28}H_{43}N_3O_6$ [M+Na] $^+$ 540.3050, observed 540.3057.

Boc-LUdγA-OEt:^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8 Hz, 1H), 6.88 (dd, *J* = 16 Hz, *J* = 4 Hz, 1H), 6.48 (s, 1H), 5.92 (d, *J* = 16 Hz, 1H), 4.99 (bs, 1H), 4.65 (m, 1H), 4.16 (q, *J* = 8 Hz, 2H), 3.90 (m, 1H), 1.65 (m, 2H), 1.52 (s, 3H), 1.51 (s, 3H), 1.42 (s, 9H), 1.26 (m, 6H), 0.93 (m, 6H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 173.5, 172.2, 166.7, 156.3, 149.1, 120.4, 80.8, 60.5, 57.5, 54.4, 46.1, 40.3, 28.4, 25.8, 24.9, 23.0, 22.0, 20.0, 14.4; HR-MS *m/z* value calculated for $C_{22}H_{39}N_3O_6$ [M+Na^+] 464.2736, observed 464.2740.

Boc-L-U-dγF-L-U-dγF-OEt (***P1***)*:* White color solid; Yield 50%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12-7.02 (m, 11H), 6.66 (dd, *J*=15.6 Hz, *J*=5 Hz, 1H), 6.77 (m, 2H), 6.43 (b, 1H), 6.40 (s, 1H), 6.35 (s, 1H), 6.13 (d, *J*=15 Hz, 1H), 5.88 (dd, *J*=16 Hz, *J*=1 Hz, 1H), 4.88 (d, *J*=5 Hz, 1H), 4.83 (m, 1H), 4.76 (m, 1H), 4.07 (m, 2H), 3.78 (m, 1H), 2.91-2.73 (m, 4H), 1.66-1.42 (m, 6H), 1.40-1.16 (m, 25H), 0.86 (m, 12H);HR-MS*m/z* calculated value for $C_{49}H_{72}N_6O_9$ [M+Na$^+$] 911.5253, observed 912.5266.



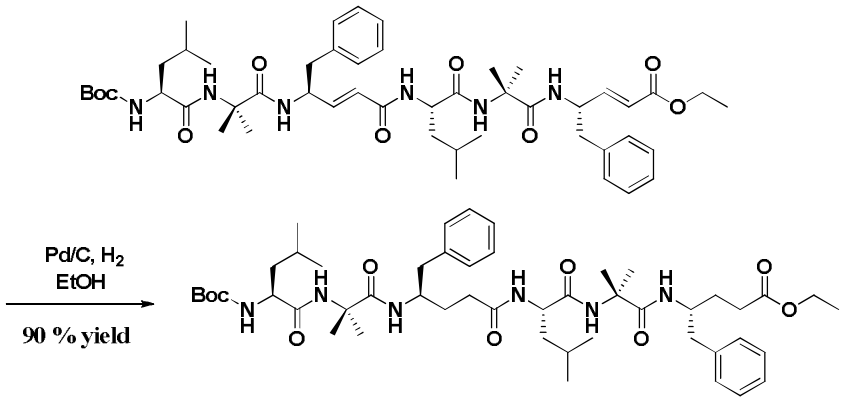
Boc-L-U-dγA-L-U-dγA-OEt (***P2***)*:* White color solid; Yield 72%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8 Hz, 1H), 7.01 (d, *J* = 8 Hz, 1H), 6.93 (d, *J* = 4 Hz, 1H), 6.89 (d, *J* = 4 Hz, 1H), 6.80 (d, *J* = 4 Hz, 1H), 6.76 (d, *J* = 4 Hz, 1H), 6.72 (d, *J* = 8 Hz, 1H), 6.58 (s, 1H), 6.57 (s, 1H), 6.14 (d, *J* = 16 Hz, 1H), 5.93 (d, *J* = 16 Hz, 1H), 5.08 (d, *J* = 4 Hz, 1H), 4.70-4.60 (m, 2H), 4.20-4.12 (m, 4H), 3.92-3.87 (m, 1H), 1.74-1.47 (m, 22H), 1.44 (s, 9H), 1.29-1.21 (m, 11H), 0.98-0.91 (m, 15H); HR-MS*m/z*calculated value for $C_{37}H_{64}N_6O_9$ [M+Na$^+$] 759.4632, observed 759.4623.



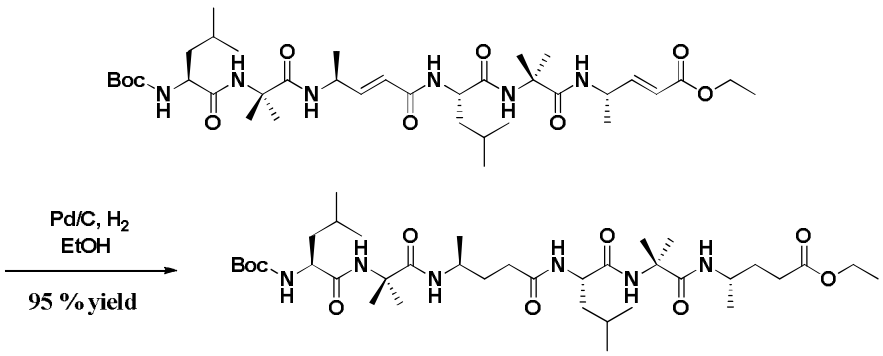
Transformation of β-miniature peptides into their saturated analogs of 10/12-helices through catalytic hydrogenation:Boc-L-U-dγX-L-U-dγX-OEt (0.10 mmol, 100

mg) was dissolved in EtOH (4 mL), and was treated with 20 mg of 20% Pd/C. The hydrogen gas was supplied through balloon. The reaction mixture was stirred under hydrogen atmosphere for about 5 h. The completion of the reaction was monitored by MALDI-TOF/TOF and RP-HPLC. After the completion of reaction, the reaction mixture was diluted with EtOH (10 mL) and it was filtered through sintered funnel using celite bed and celite bed was washed with EtOH (3 × 15 mL). The filtrate was evaporated under *vacuum* to get white crystalline pure product.

*Boc-L-U-γF-L-U-γF-OEt (**P3**):* White color solid; Yield 90%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (bs, 1H), 7.62 (bs, 1H), 7.40 (d, *J* = 15 Hz), 7.29-7.10 (m, 11H), 6.92-6.90 (m, 2H), 6.74-6.63 (m, 2H), 5.53 (bs, 1H), 4.36-4.27 (m, 1H), 4.12-4.04 (m, 3H), 3.89-3.80 (m, 2H), 2.96-2.64 (m, 4H), 2.53-2.35 (m, 5H), 2.23-2.17 (m, 3H), 1.94-1.85 (m, 3H), 1.72-1.67 (m, 2H), 1.57 (s, 3H), 1.49 (s, 9H), 1.42 (s, 3H), 1.30 (s, 3H), 1.22 (t, *J* = 5 Hz, 3H), 1.02 (s, 3H), 0.98-0.88 (m, 12H); HR-MS*m/z* calculated value for $C_{49}H_{76}N_6O_9$ [M+Na$^+$] 915.5571, observed 915.5574.



*Boc-L-U-γA-L-U-γA-OEt (**P4**):* White color solid; Yield 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ8.03 (s, 1H), 7.15 (s, 1H), 7.08 (s, 1H), 6.83 (d, *J* = 10 Hz, 1H), 6.63 (s, 1H), 5.10 (d, *J* = 5 Hz, 1H), 4.13-4.06 (m, 2H), 4.03-3.86 (m, 5H), 2.55-2.34 (m, 4H), 2.16-2.13 (m, 1H), 2.03-1.97 (m, 1H), 1.86-1.73 (m, 10H), 1.60 (s, 3H), 1.53 (s, 3H), 1.48 (s, 9H), 1.44 (s, 3H), 1.37 (s, 3H), 1.23 (t, *J* = 5 Hz), 1.14 (d, *J* = 5 Hz, 3H), 1.04 (d, *J* = 5 Hz, 3H), 1.00-0.90 (m, 14H); HR-MS *m/z* calculated value for $C_{37}H_{68}N_6O_9$ [M+Na$^+$] 763.4945, observed 763.4940.



9. CD spectra of peptides

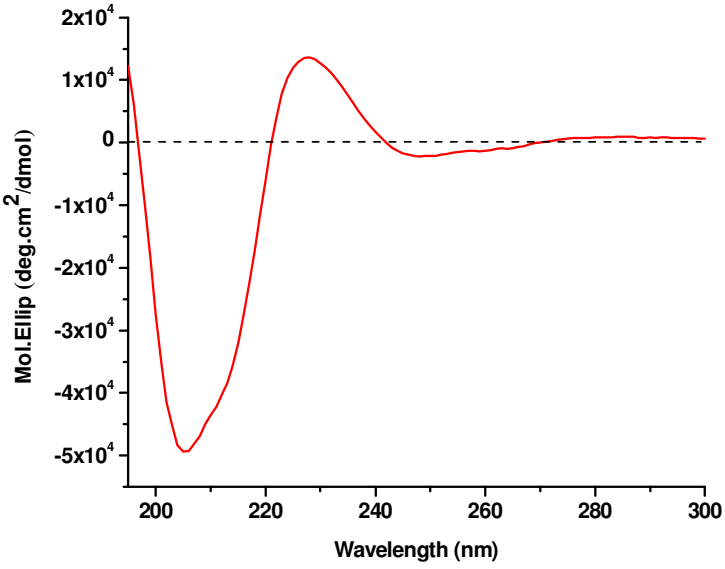


Figure S16: CD spectrum of peptide **P1** in methanol (*c* 0.2 mM).

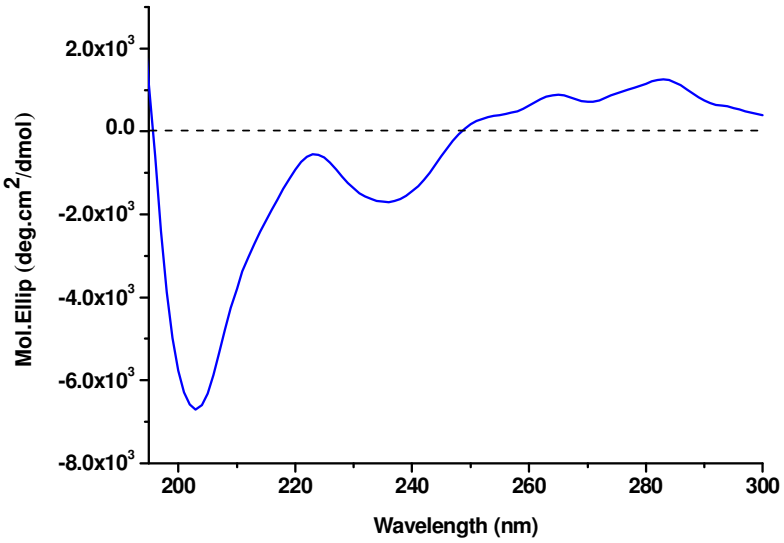


Figure S17: CD spectrum of peptide **P2** in methanol (*c* 0.2 mM).

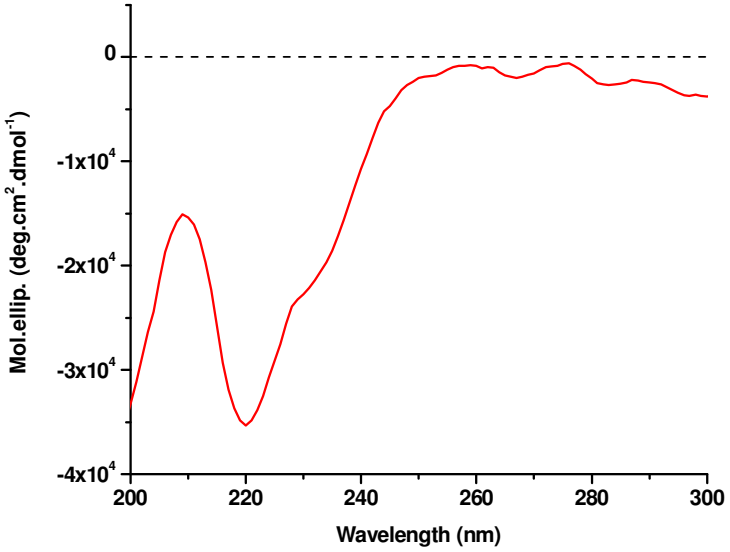


Figure S18: CD spectrum of peptide **P3** in methanol (*c* 0.2 mM).

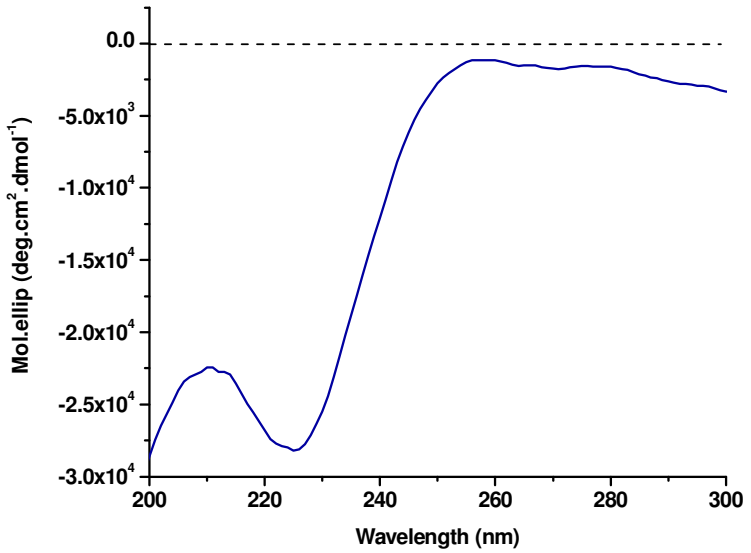


Figure S19: CD spectrum of peptide **P4** in methanol (*c* 0.2 mM).

10. HPLC traces of peptides

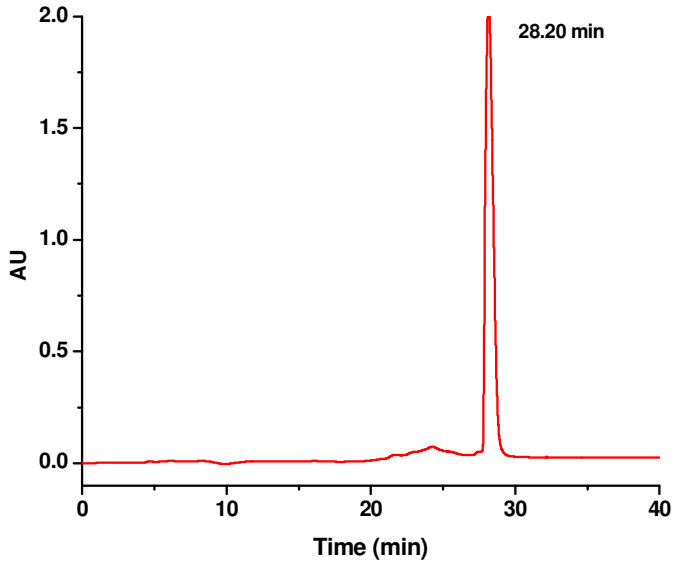


Figure S20: HPLC trace of peptide **P1**.

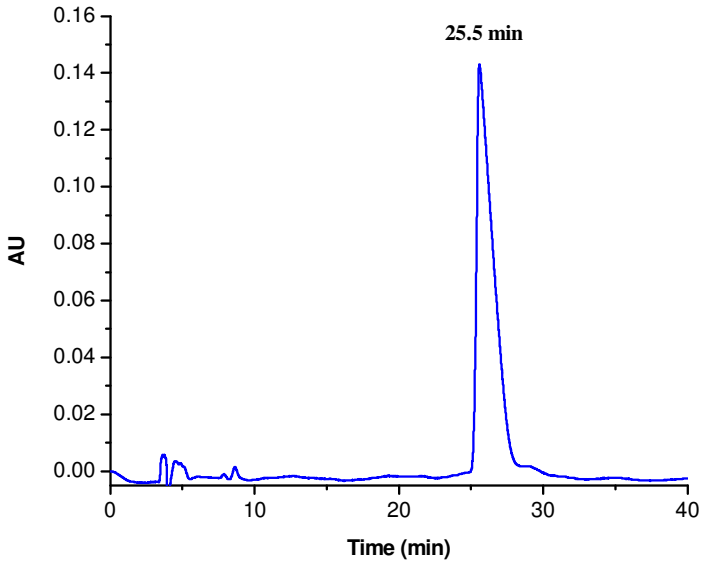


Figure S21: HPLC trace of peptide **P2**.

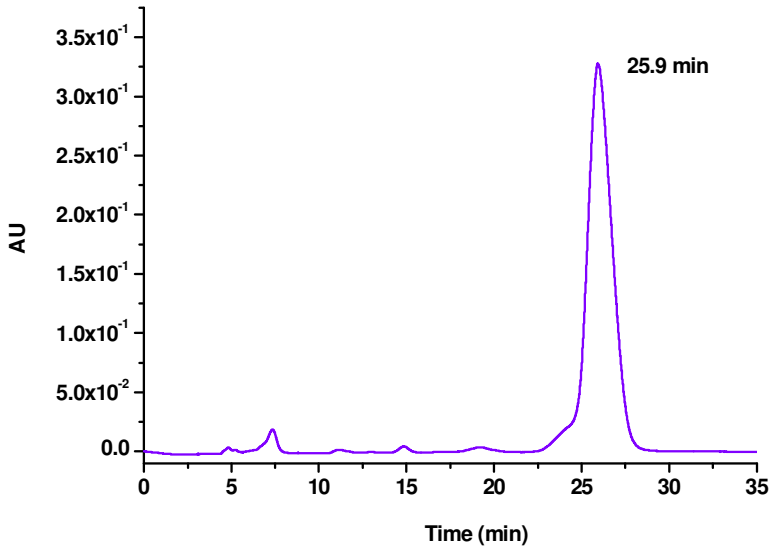


Figure S22:HPLC trace of peptide **P3**.

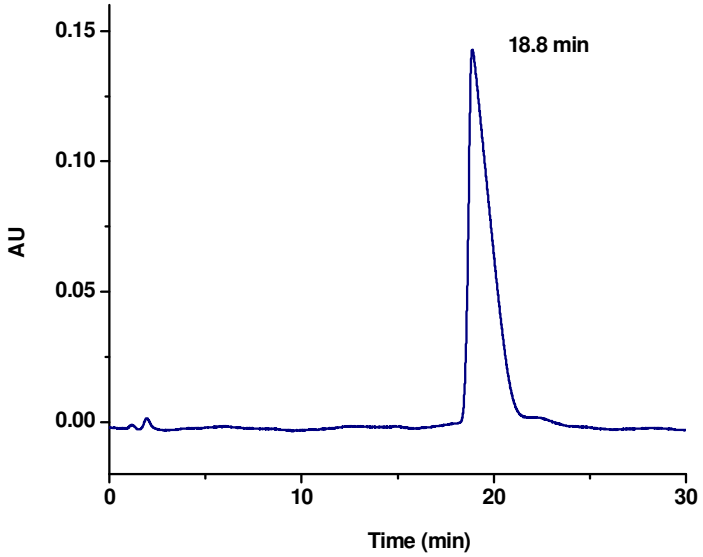


Figure S23: HPLC trace of peptide **P4**.

11. Variable Temperature Study of Beta-meanders

Peptide P1:

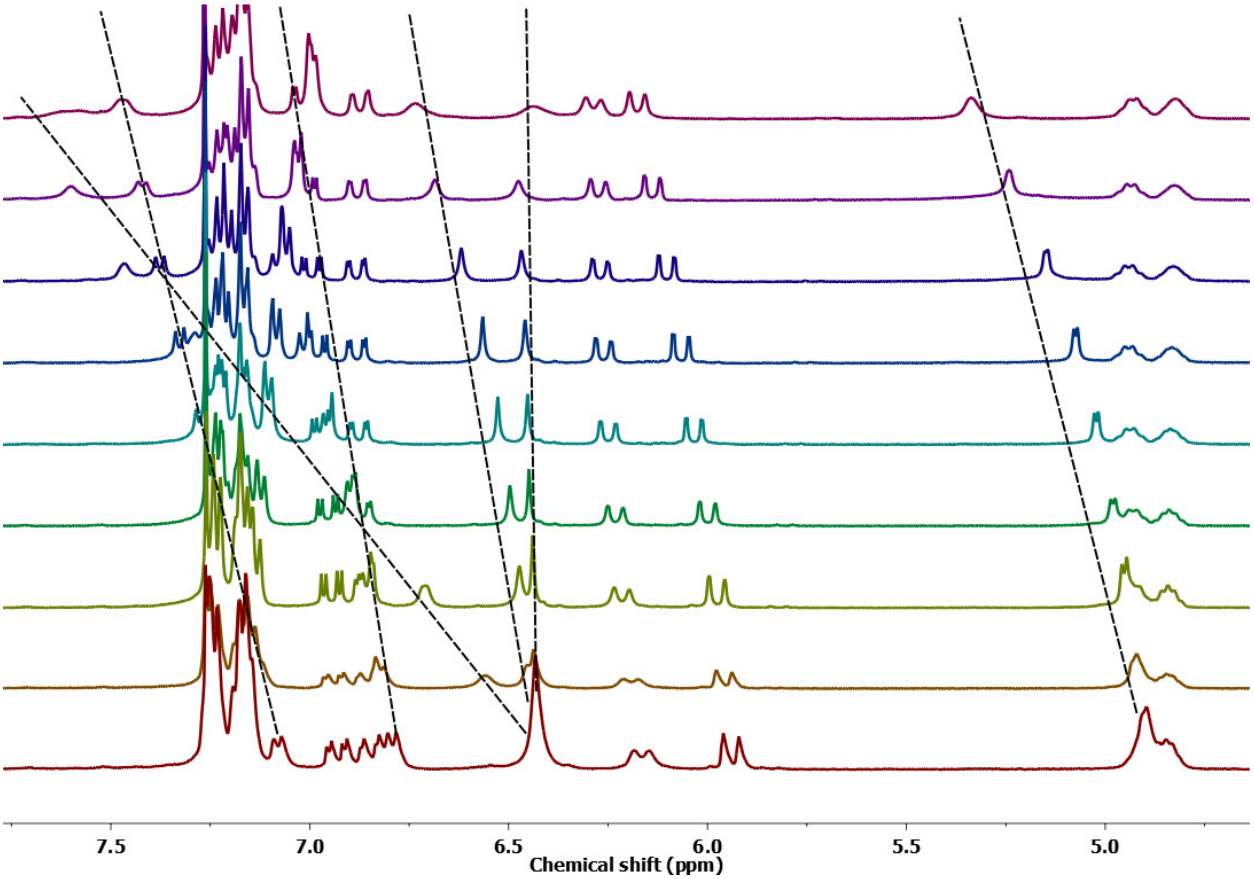


Figure S24: Temperature dependent ^{1}H NMR spectra of amide NH region of **P1**.

Table S7: Chemical shifts of amide NHs of peptide **P1**

Temperature (0 °C)	Leu1	Aib2	dγF3	Leu4	Aib5	dγF6
-40	5.34	6.73	6.99	7.59	6.44	7.47
-30	5.24	6.69	7.03	7.60	6.48	7.42
-20	5.15	6.62	7.06	7.47	6.47	7.38
-10	5.08	6.57	7.02	7.29	6.46	7.33
0	5.03	6.53	6.95	n.d	6.45	n.d

10	4.98	6.50	6.90	n.d	6.45	n.d
20	4.96	6.47	6.85	6.71	6.44	n.d
30	4.93	6.46	6.82	6.56	6.44	n.d
40	4.89	6.43	6.78	6.43	6.43	7.08
dδ/dT (ppb K^{-1})	**-5.4 (± 0.49)**	**-3.8 (± 0.29)**	**-3.4 (± 0.56)**	**-16.0 (± 0.99)**	**-0.4 (± 0.17)**	**-4.9 (± 0.75)**

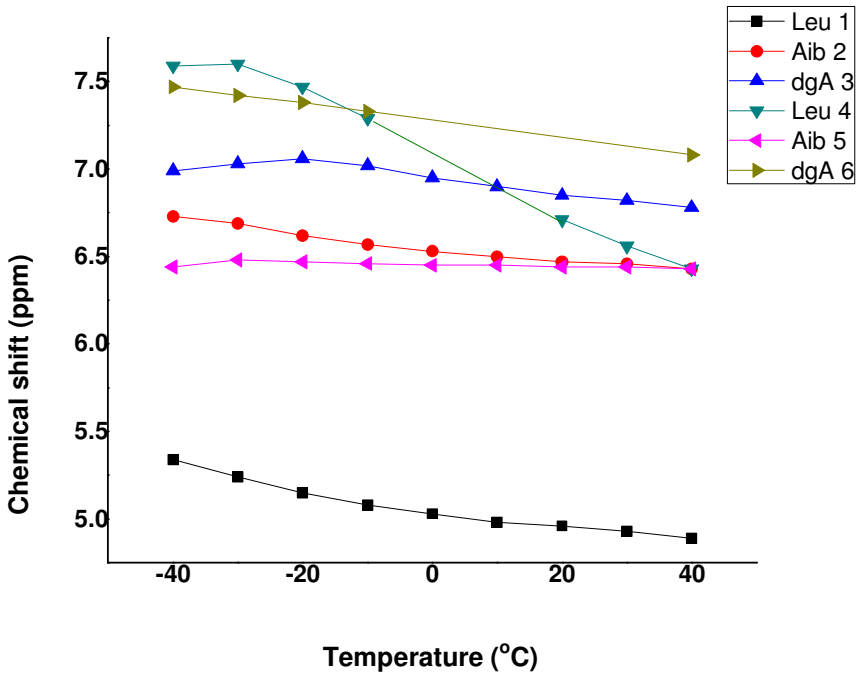


Figure S25: Plot of amides chemical shift and the temperature. The slope dδ/dt for all NHs is given in the Table **S5**.

Peptide P2:

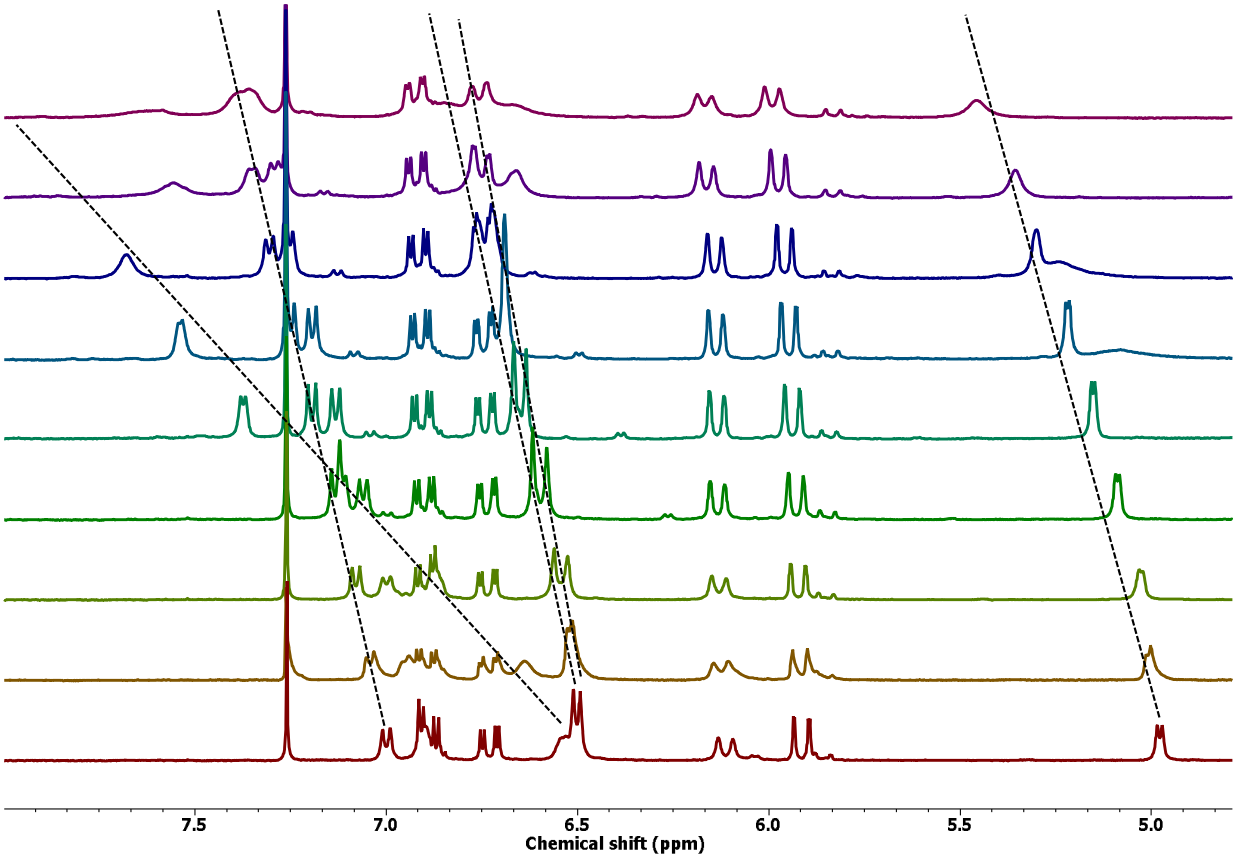


Figure S26: Temperature dependent ^{1}H NMR spectra of amide NH region of **P3**

Table S8: Chemical shifts of amide NHs of peptide **P3**

Temperature (0 °C)	Leu1	Aib2	dγA3	Leu4	Aib5	dγA6
-40	5.46	6.68	7.36	7.58	6.84	7.36
-30	5.36	6.66	7.29	7.55	6.67	7.35
-20	5.31	6.71	7.25	7.68	6.75	7.30
-10	5.22	6.69	7.19	7.54	6.69	7.25
0	5.15	6.63	7.13	7.38	6.67	7.19
10	5.09	6.58	7.06	7.11	6.62	7.13

20	5.02	6.53	7.00	6.86	6.56	7.08
30	5.00	6.51	6.95	6.64	6.53	7.04
40	4.98	6.49	6.89	6.54	6.51	7.00
dδ/dT (ppb K^{-1})	**-6.2 (±0.4)**	**-2.8 (±0.46)**	**-5.9 (±0.09)**	**-14.9 (±2.0)**	**-3.7 (±0.5)**	**-4.9 (±0.18)**

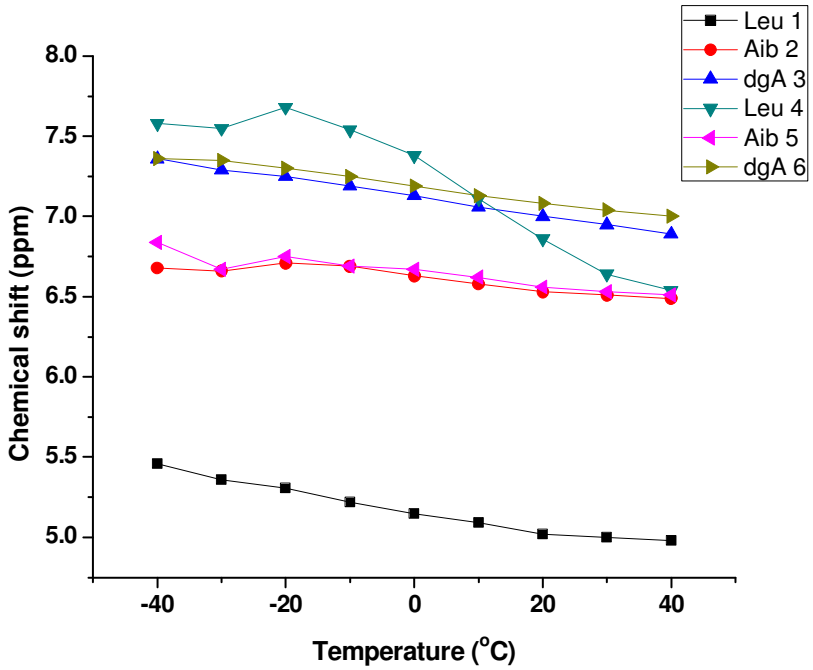


Figure S27: Plot of amides chemical shift and the temperature. The slope dδ/dt for all NHs is given in the Table **S7**.

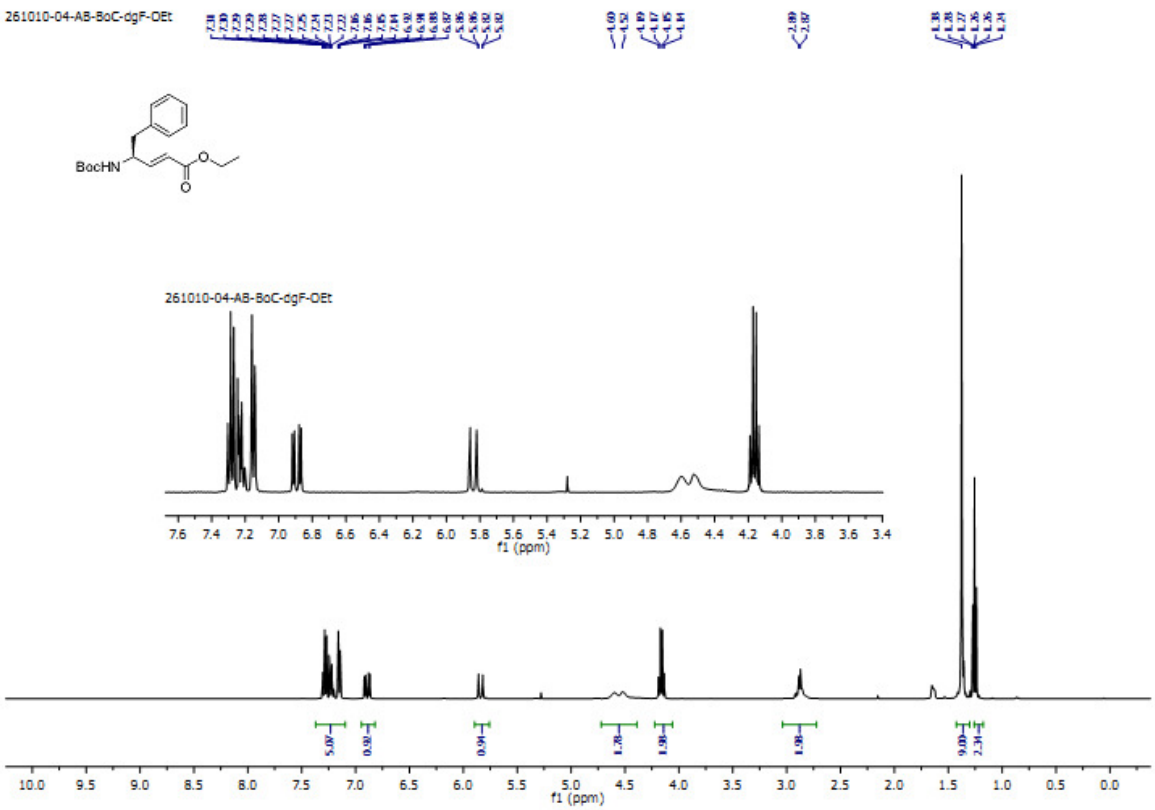
12. References:

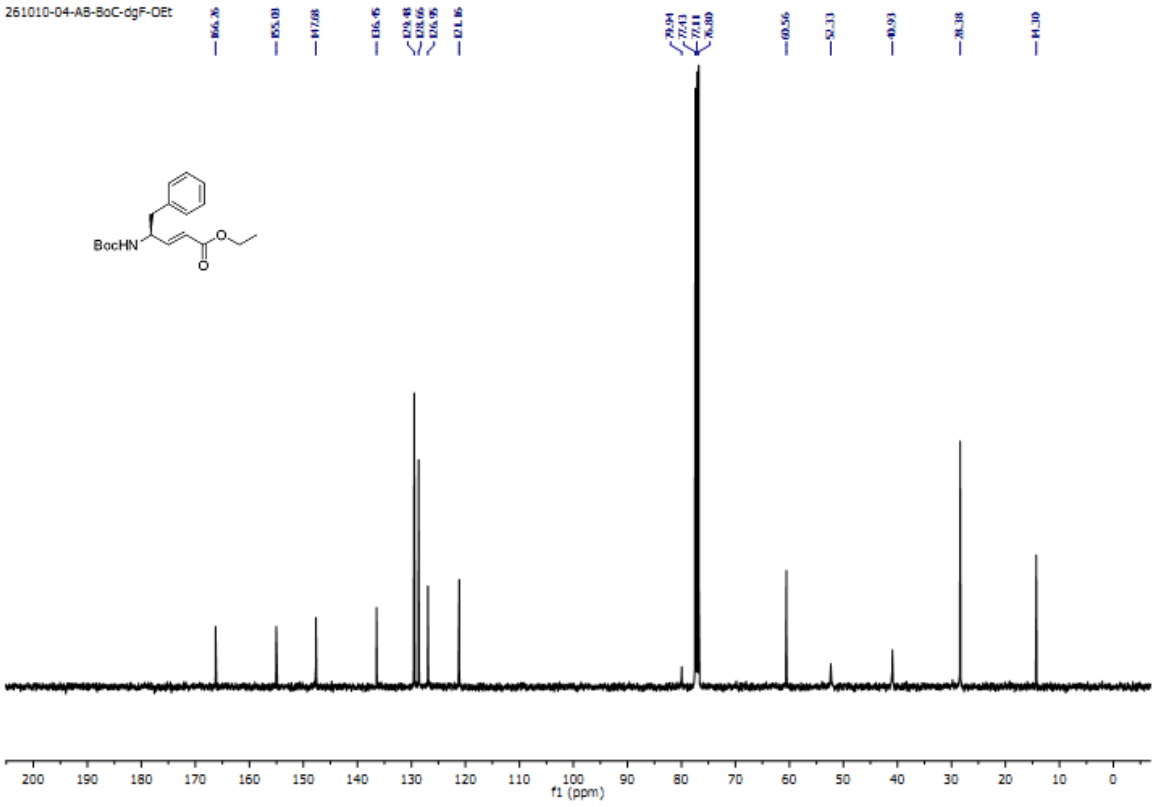
1. (*a*) SHELXS-97: G. M. Sheldrick, *Acta Crystallogr. Sect A*, 1990, **46**, 467;(*b*) G. M. Sheldrick, SHELXL-97, Universität G□ttingen (Germany) 1997.

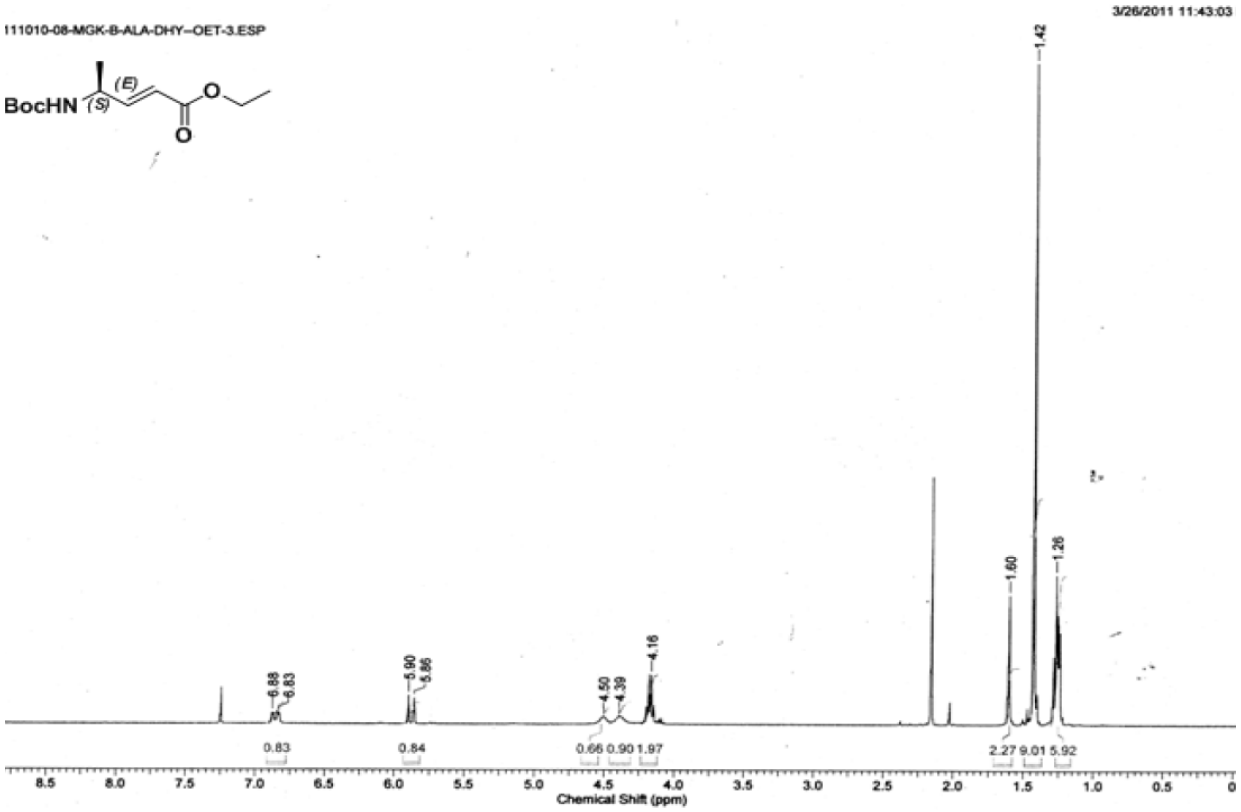
2. Spek, A. L. (1990) *Acta. Cryst*., A46, C34.

3. (*a*) S. M. Mali, A.Bandyopadhyay, S. V. Jadhav, M. GaneshKumar and H. N. Gopi,*Org. Biomol. Chem.*, 2011, **9**, 6566;(*b*) A. Bandyopadhyay and H. N. Gopi, *Org. Lett.*, 2012, **14**, 2770.

13. ^{1}H NMR and MALDI-TOF/TOF spectra of compounds



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(S)
O
O
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1.60
1.26
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6.83
5.90
5.86
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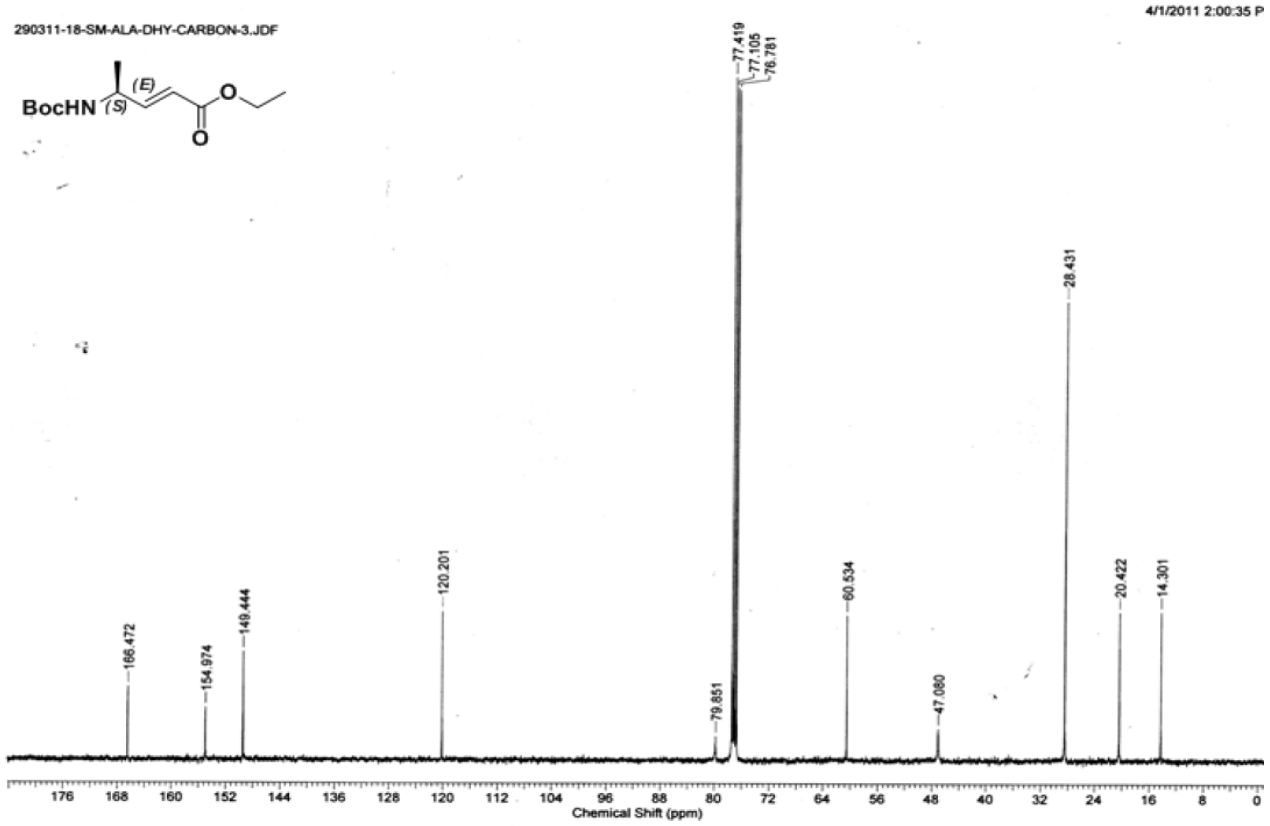
4.16
0.83
0.84
0.66
0.90
1.97
2.27
9.01
5.92
Chemical Shift (ppm)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(S)
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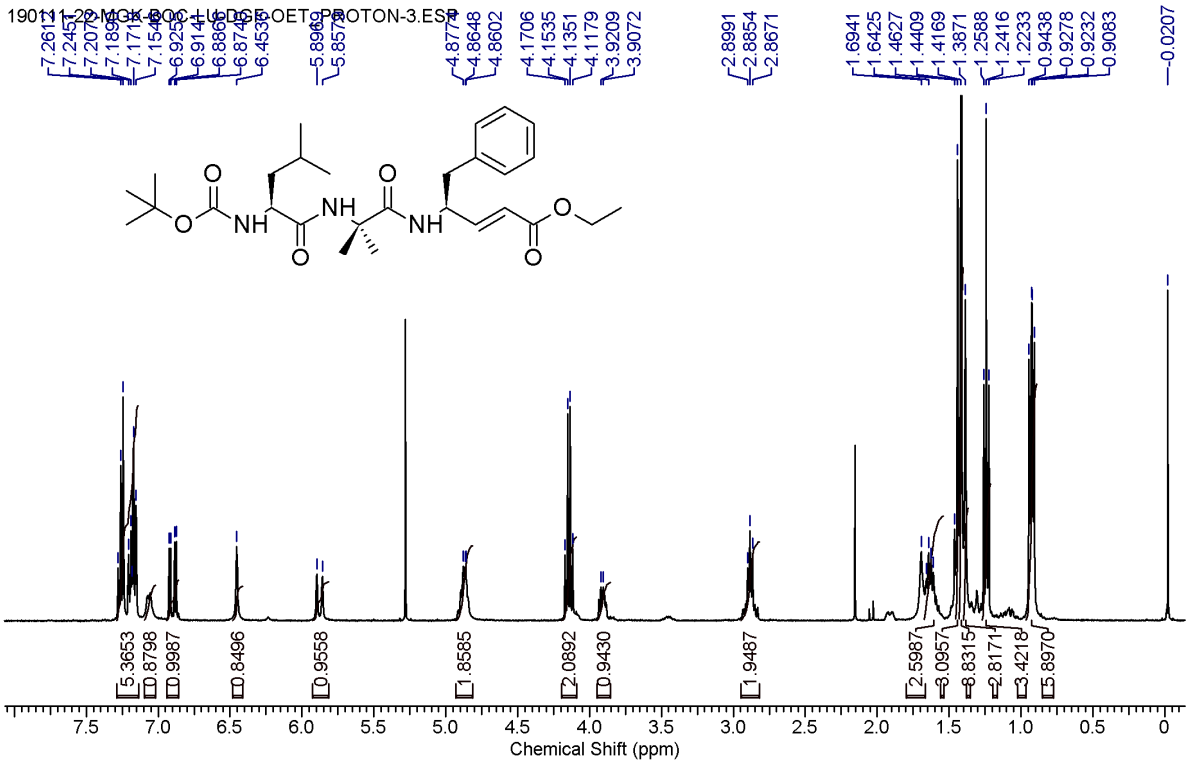
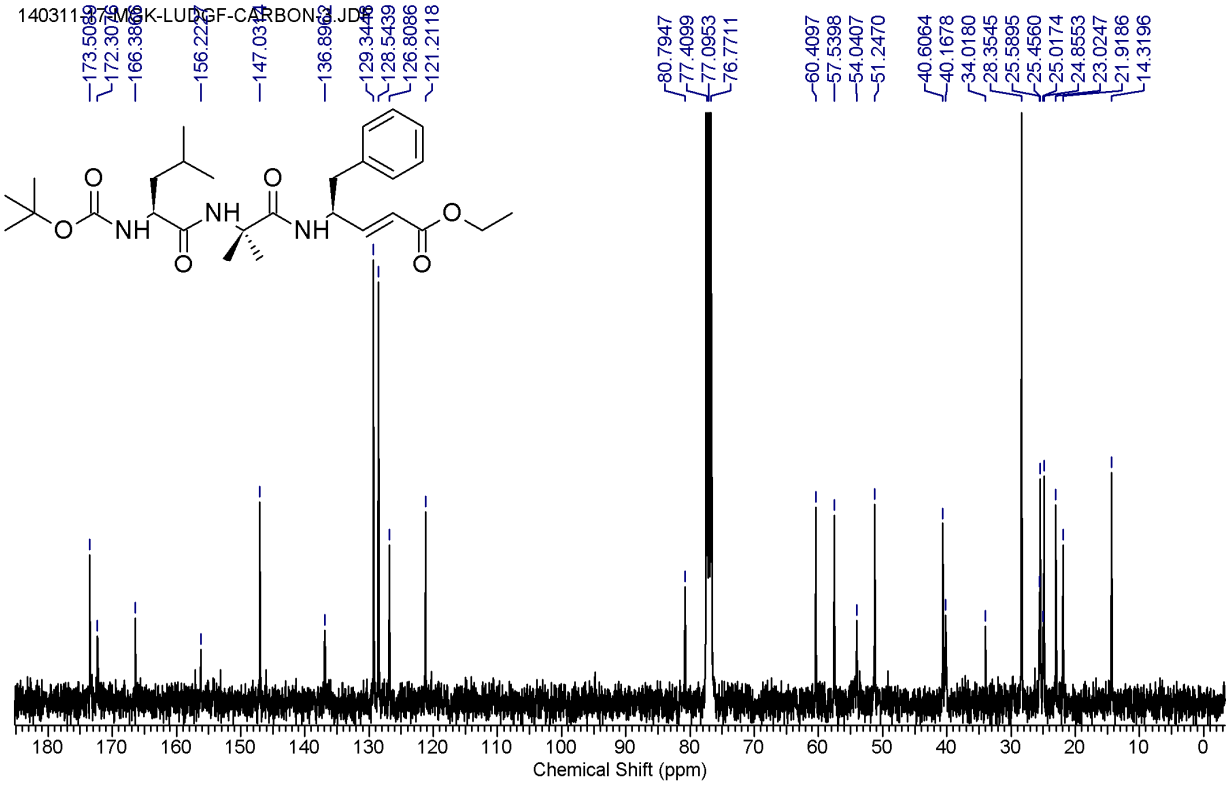
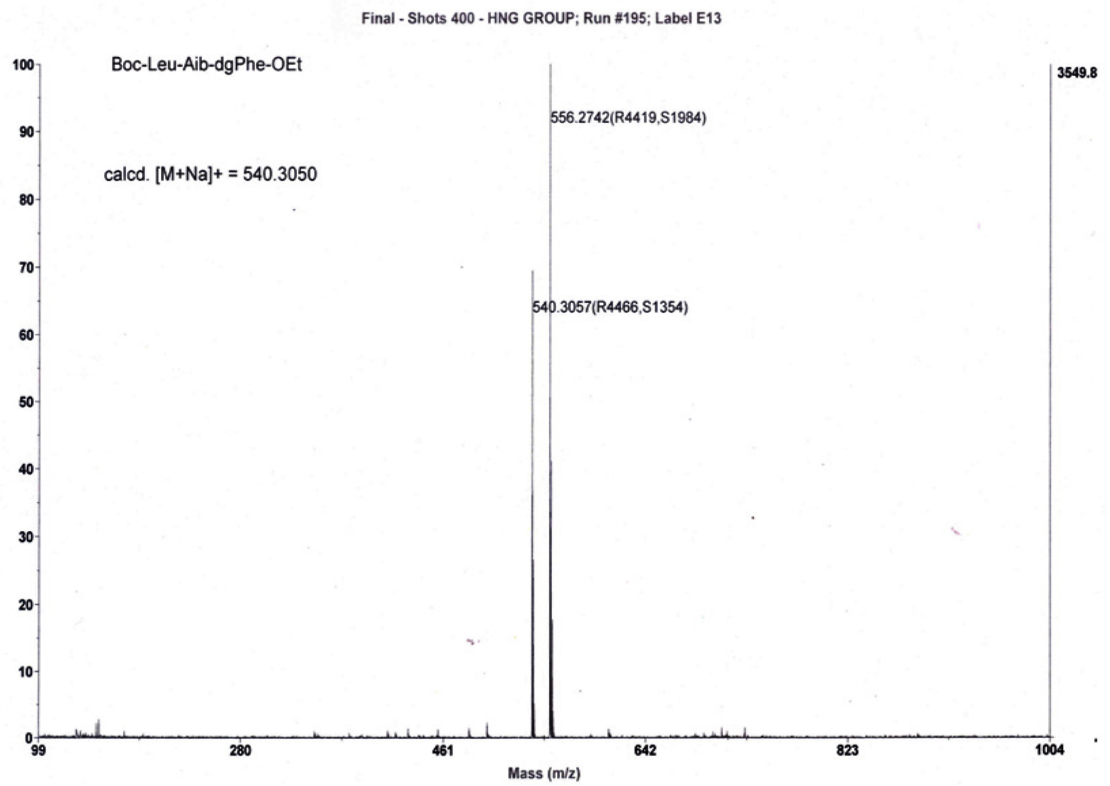
Chemical Shift (ppm)

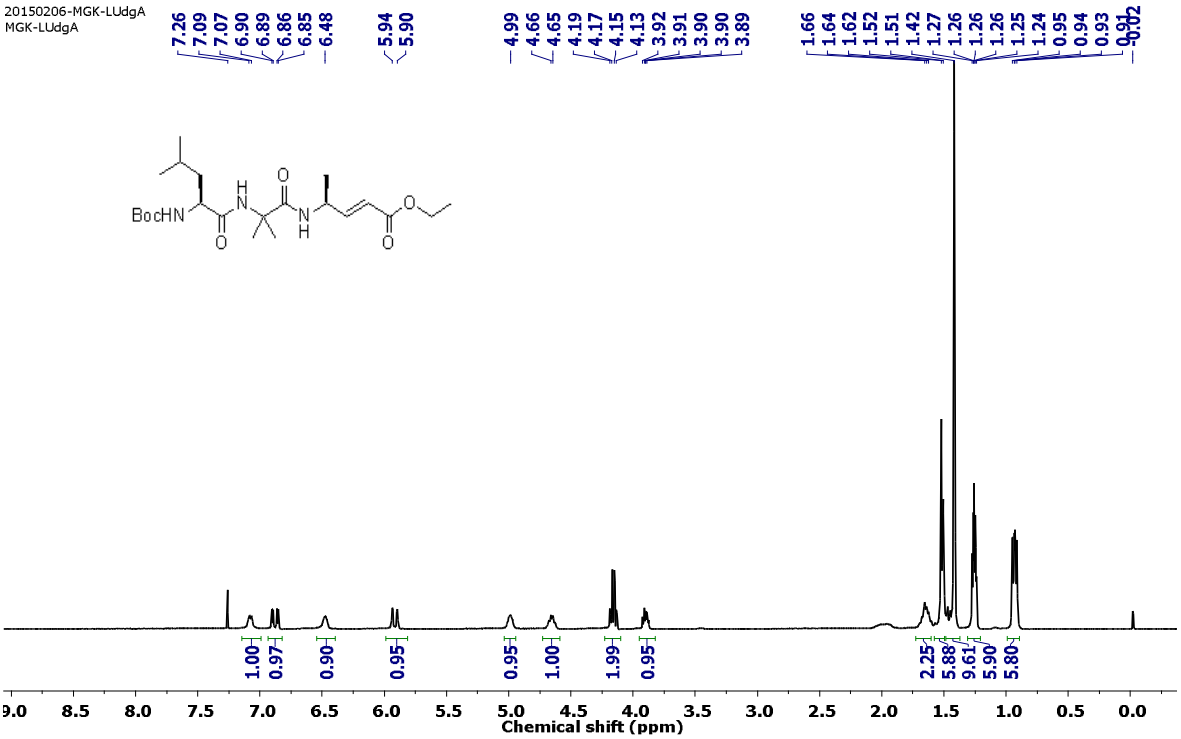
Boc-LUdγF-OEt

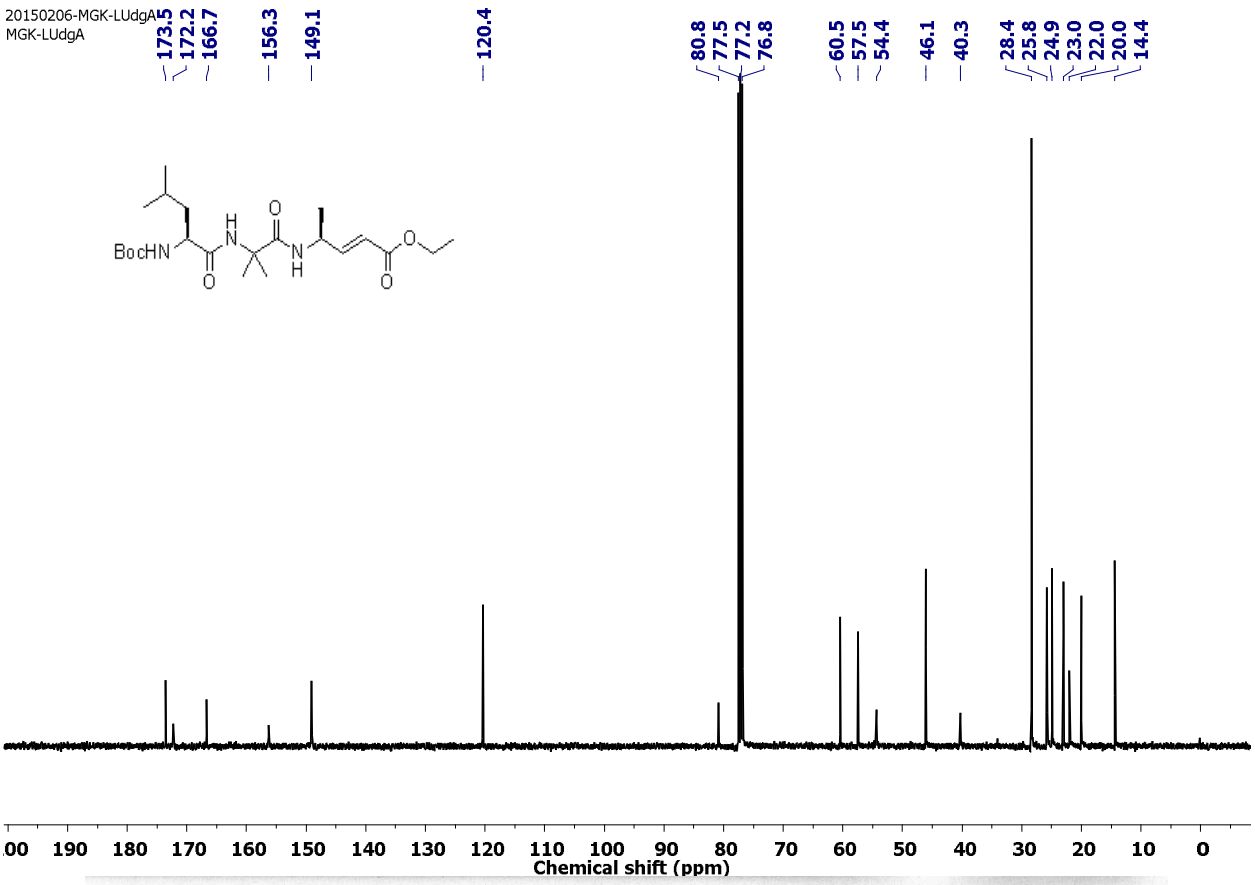


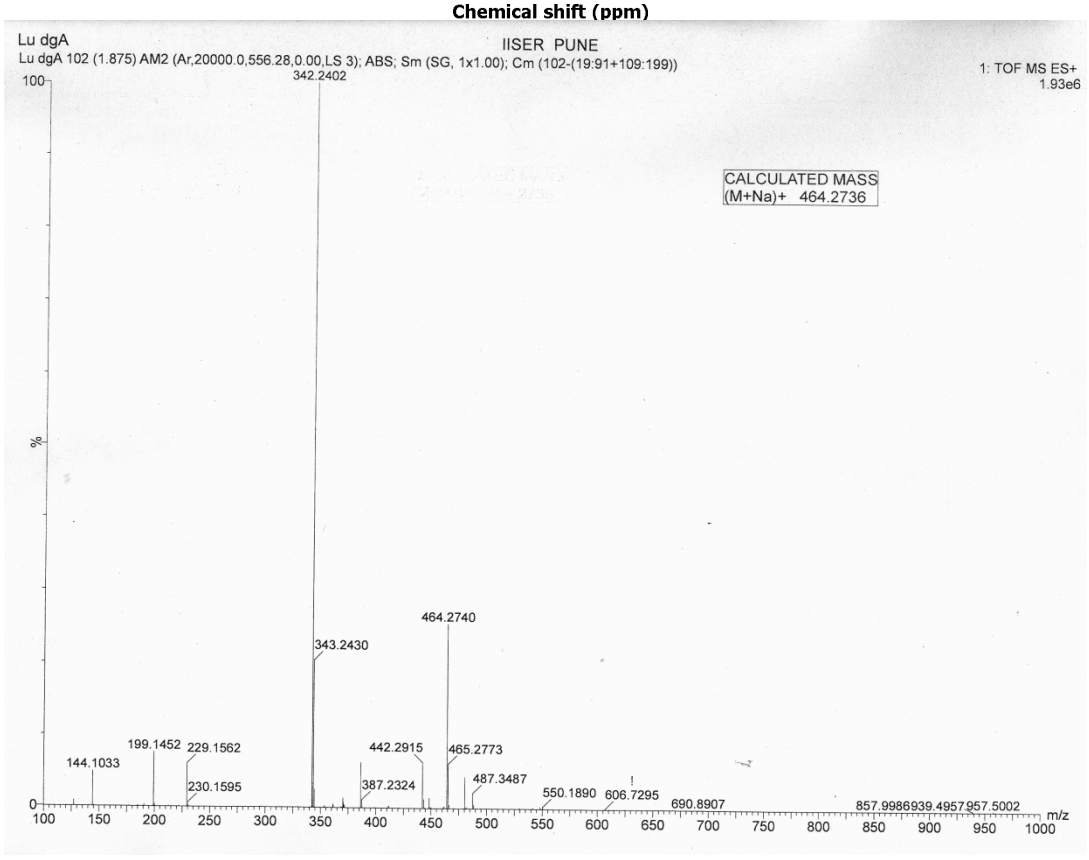




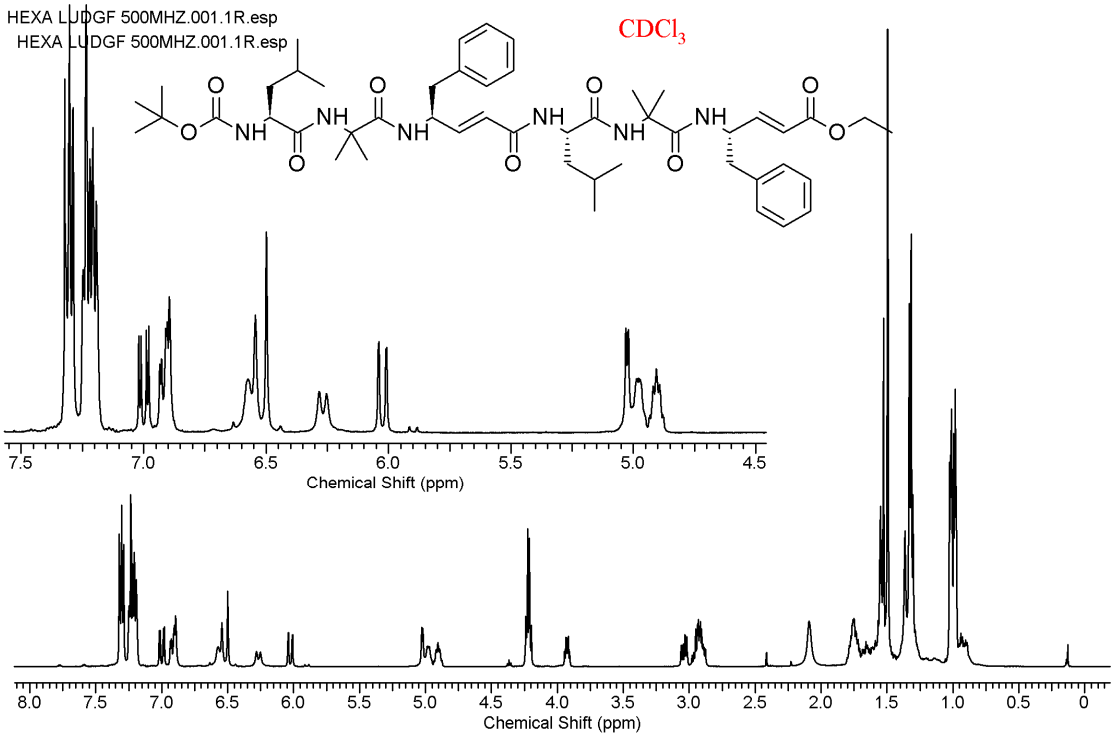
Boc-LUdγA-OEt

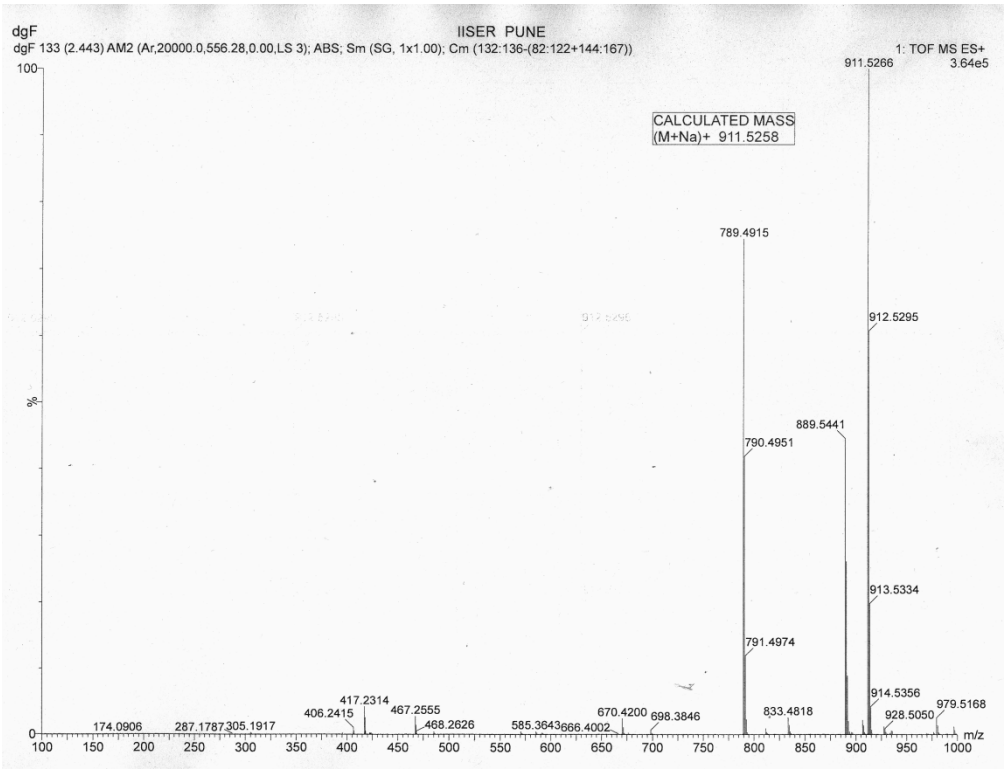



20150206-MGK-LUdgA
MGK-LUdgA
173.5
172.2
166.7
156.3
149.1
120.4
80.8
77.5
77.2
76.8
60.5
57.5
54.4
46.1
40.3
28.4
25.8
24.9
23.0
22.0
20.0
14.4
BocHN
Chemical shift (ppm)

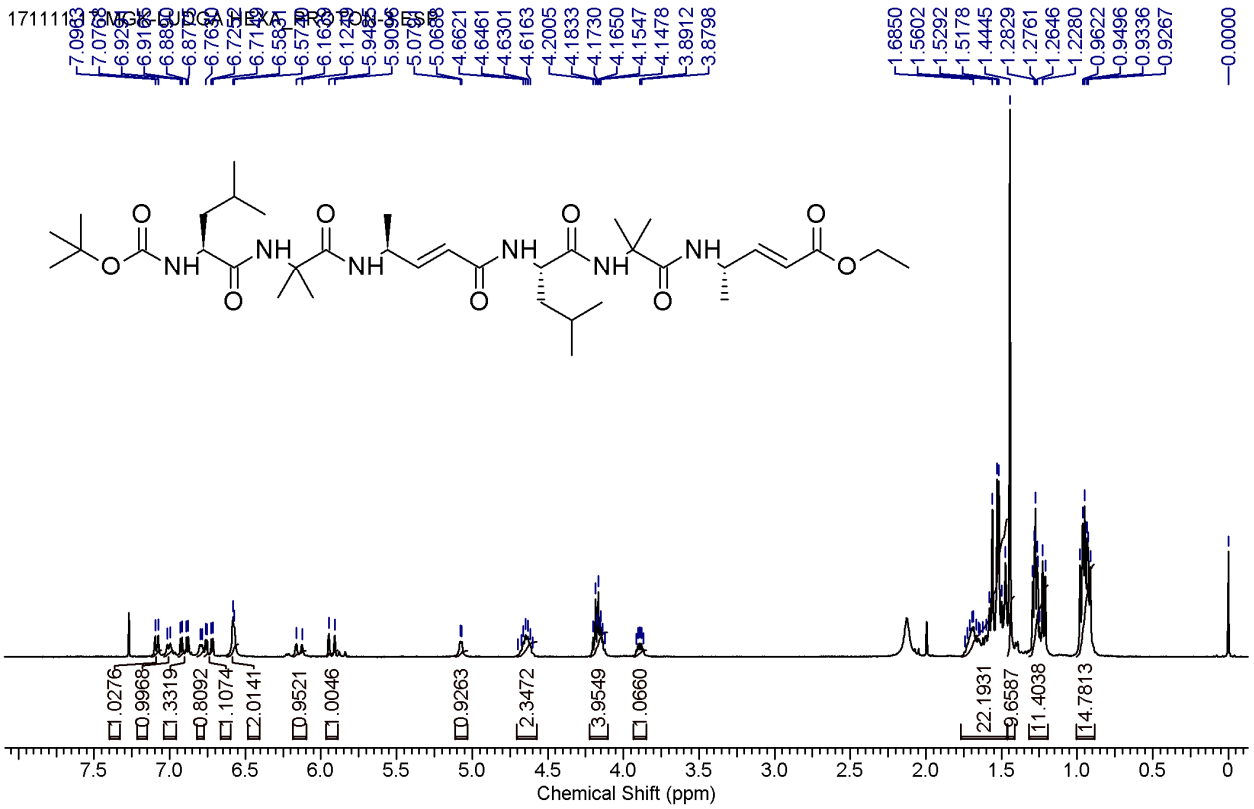

Lu dgA
IISER PUNE
Lu dgA 102 (1.875) AM2 (Ar,20000.0,556.28,0.00,LS 3); ABS; Sm (SG, 1x1.00); Cm (102-(19:91+109:199))
1: TOF MS ES+
1.93e6
CALCULATED MASS
(M+Na)+ 464.2736
342.2402
464.2740
343.2430
199.1452
229.1562
144.1033
230.1595
442.2915
465.2773
387.2324
487.3487
550.1890
606.7295
690.8907
857.9986939.4957957.5002
m/z

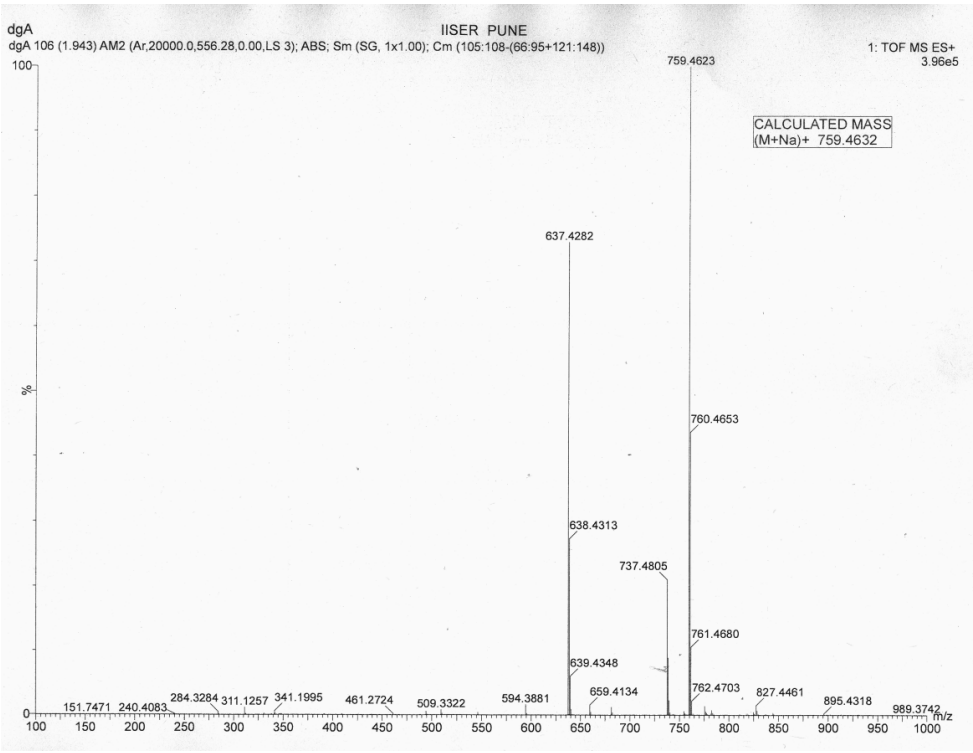
Peptide P1


HEXA LUDGF 500MHZ.001.1R.esp
HEXA LUDGF 500MHZ.001.1R.esp
CDCl3
Chemical Shift (ppm)
Chemical Shift (ppm)


dgF
IISER PUNE
dgF 133 (2.443) AM2 (Ar,20000.0,556.28,0.00,LS 3); ABS; Sm (SG, 1x1.00); Cm (132:136-(82:122+144:167))
1: TOF MS ES+
3.64e5
CALCULATED MASS
(M+Na)+ 911.5258
911.5266
789.4915
912.5295
889.5441
790.4951
913.5334
791.4974
914.5356
979.5168
928.5050
833.4818
698.3846
670.4200
666.4002
585.3643
468.2626
467.2555
417.2314
406.2415
305.1917
287.1787
174.0906
%
m/z

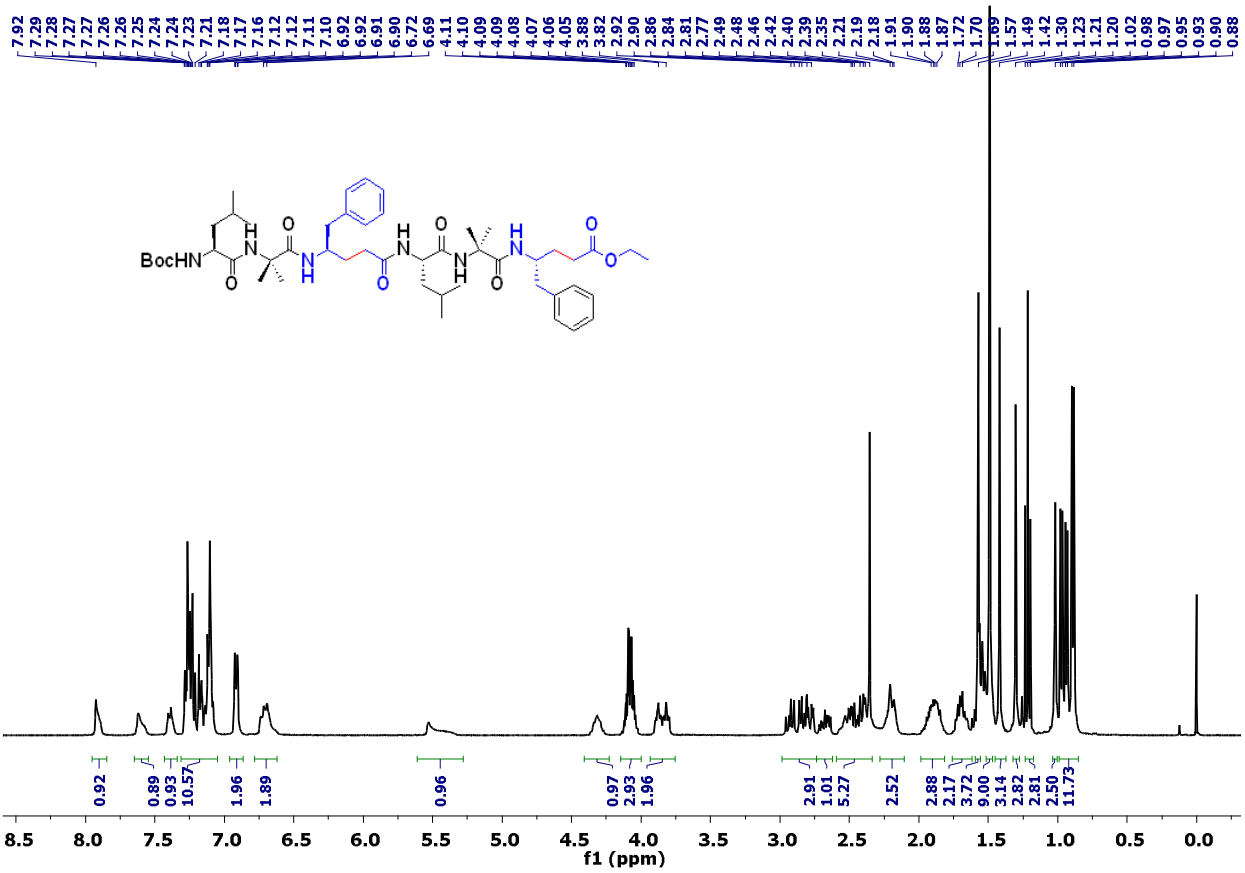
Peptide P2

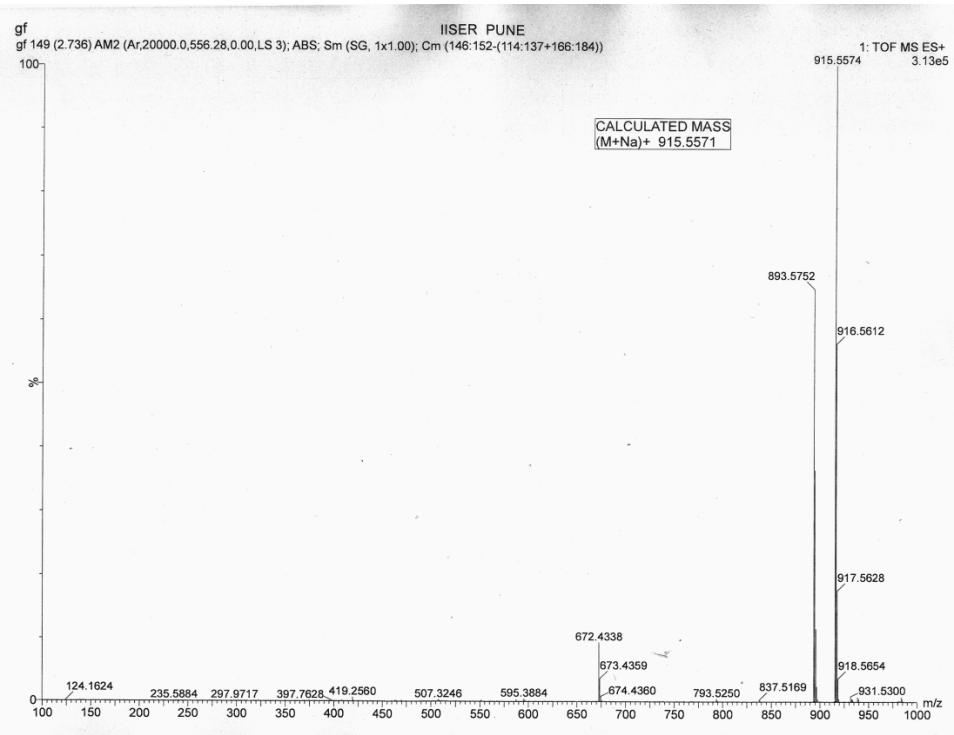

7.0963
7.0763
6.9263
6.9163
6.8863
6.8763
6.7663
6.7263
6.7163
6.5863
6.5763
6.1663
6.1263
5.9463
5.9063
5.0763
5.0663
4.6621
4.6461
4.6301
4.6163
4.2005
4.1833
4.1730
4.1650
4.1547
4.1478
3.8912
3.8798
1.6850
1.5602
1.5292
1.5178
1.4445
1.2829
1.2761
1.2646
1.2280
0.9622
0.9496
0.9336
0.9267
0.0000
0.0276
0.9968
0.3319
0.8092
1.1074
2.0141
0.9521
1.0046
0.9263
2.3472
3.9549
1.0660
22.1931
9.6587
11.4038
14.7813
Chemical Shift (ppm)


dgA
IISER PUNE
dgA 106 (1.943) AM2 (Ar,20000.0,556.28,0.00,LS 3); ABS; Sm (SG, 1x1.00); Cm (105:108-(66:95+121:148))
1: TOF MS ES+
3.96e5
CALCULATED MASS
(M+Na)+ 759.4632
759.4623
637.4282
760.4653
638.4313
737.4805
761.4680
639.4348
762.4703
659.4134
827.4461
895.4318
989.3742
151.7471
240.4083
284.3284
311.1257
341.1995
461.2724
509.3322
594.3881
%
m/z

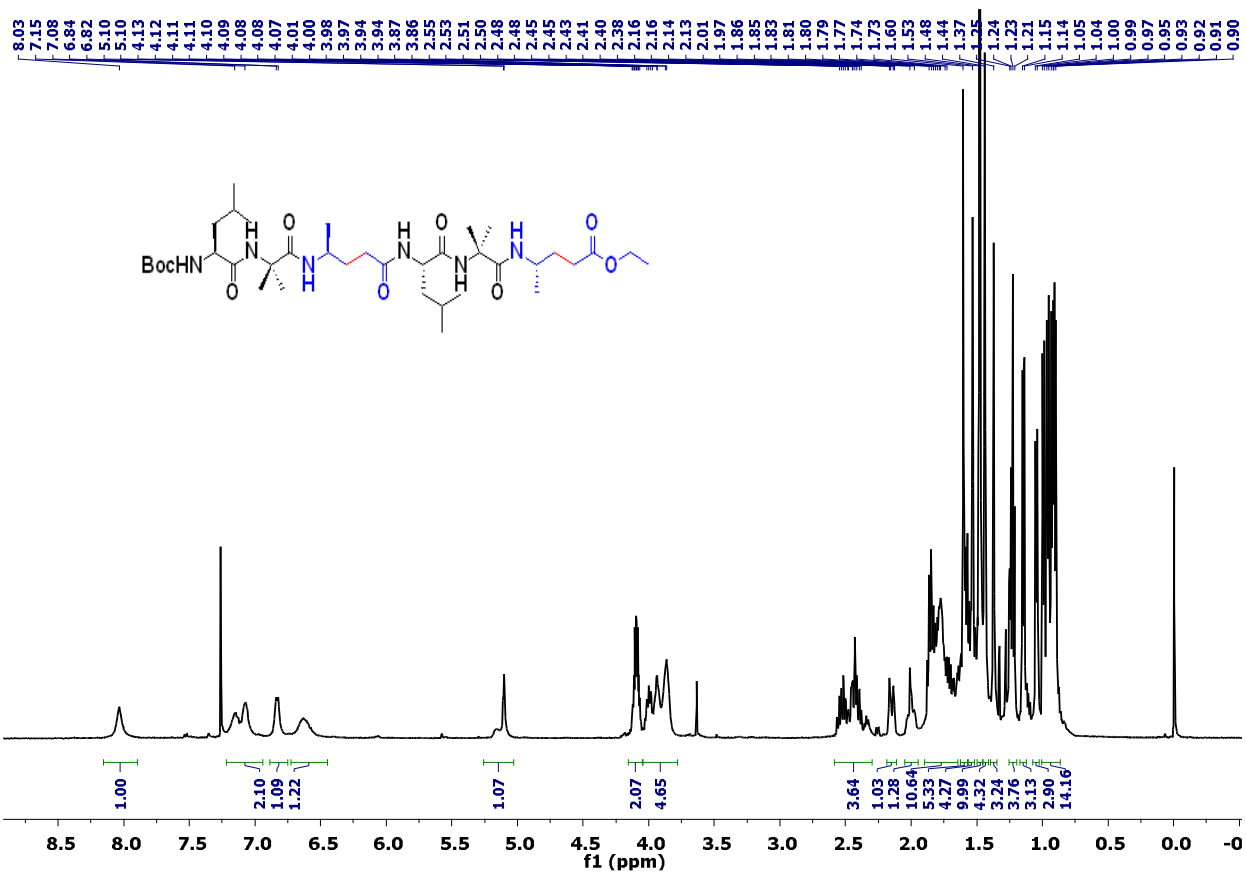
Peptide

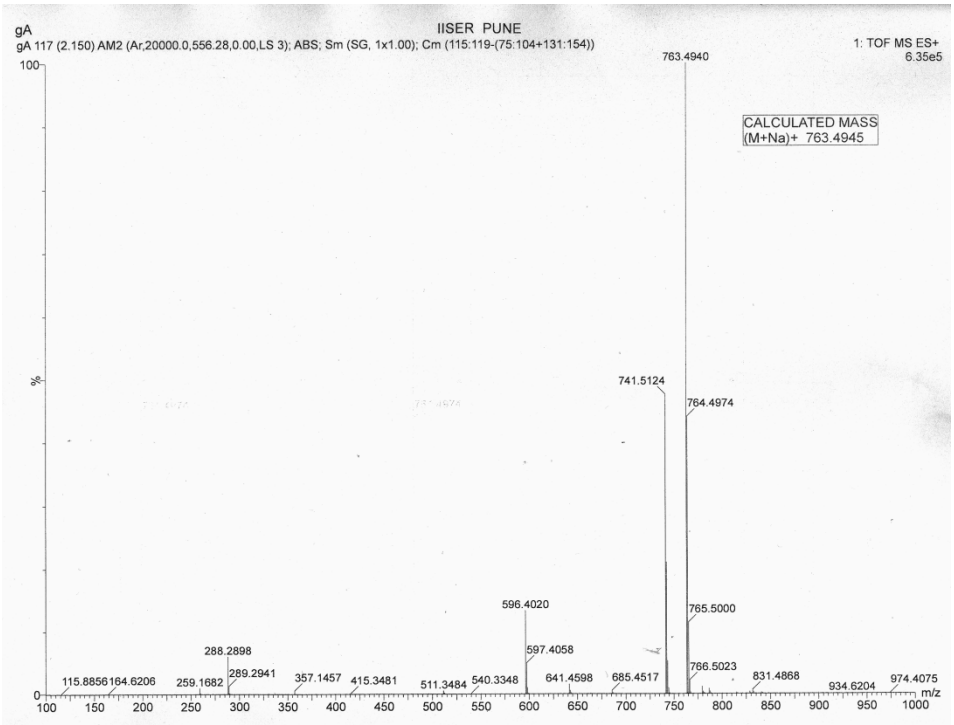
P3


7.92 7.29 7.28 7.27 7.27 7.26 7.26 7.25 7.24 7.24 7.23 7.21 7.18 7.17 7.16 7.12 7.12 7.11 7.10 6.92 6.92 6.91 6.90 6.72 6.69 4.11 4.10 4.09 4.09 4.08 4.07 4.06 4.05 3.88 3.82 2.92 2.90 2.86 2.84 2.81 2.77 2.49 2.48 2.46 2.42 2.40 2.39 2.35 2.21 2.19 2.18 1.91 1.90 1.88 1.87 1.72 1.70 1.69 1.57 1.49 1.42 1.30 1.23 1.21 1.20 1.02 0.98 0.97 0.95 0.93 0.90 0.88
BocHN
0.92 0.89 0.93 10.57 1.96 1.89 0.96 0.97 2.93 1.96 2.91 1.01 5.27 2.52 2.88 2.17 3.72 9.00 3.14 2.82 2.81 2.50 11.73
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


gf
IISER PUNE
gf 149 (2.736) AM2 (Ar,20000.0,556.28,0.00,LS 3); ABS; Sm (SG, 1x1.00); Cm (146:152-(114:137+166:184))
1: TOF MS ES+
3.13e5
CALCULATED MASS
(M+Na)+ 915.5571
915.5574
893.5752
916.5612
917.5628
672.4338
673.4359
674.4360
918.5654
124.1624
235.5884
297.9717
397.7628
419.2560
507.3246
595.3884
793.5250
837.5169
931.5300
m/z

Peptide P4


BocHN
f1 (ppm)


gA
IISER PUNE
gA 117 (2.150) AM2 (Ar,20000.0,556.28,0.00,LS 3); ABS; Sm (SG, 1x1.00); Cm (115:119-(75:104+131:154))
1: TOF MS ES+
6.35e5
100
%
0
763.4940
CALCULATED MASS
(M+Na)+ 763.4945
741.5124
764.4974
596.4020
765.5000
597.4058
288.2898
289.2941
766.5023
115.8856
164.6206
259.1682
357.1457
415.3481
511.3484
540.3348
641.4598
685.4517
831.4868
934.6204
974.4075
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
850
900
950
1000
m/z