ESI

A new peptide motif in the formation of supramolecular double helices

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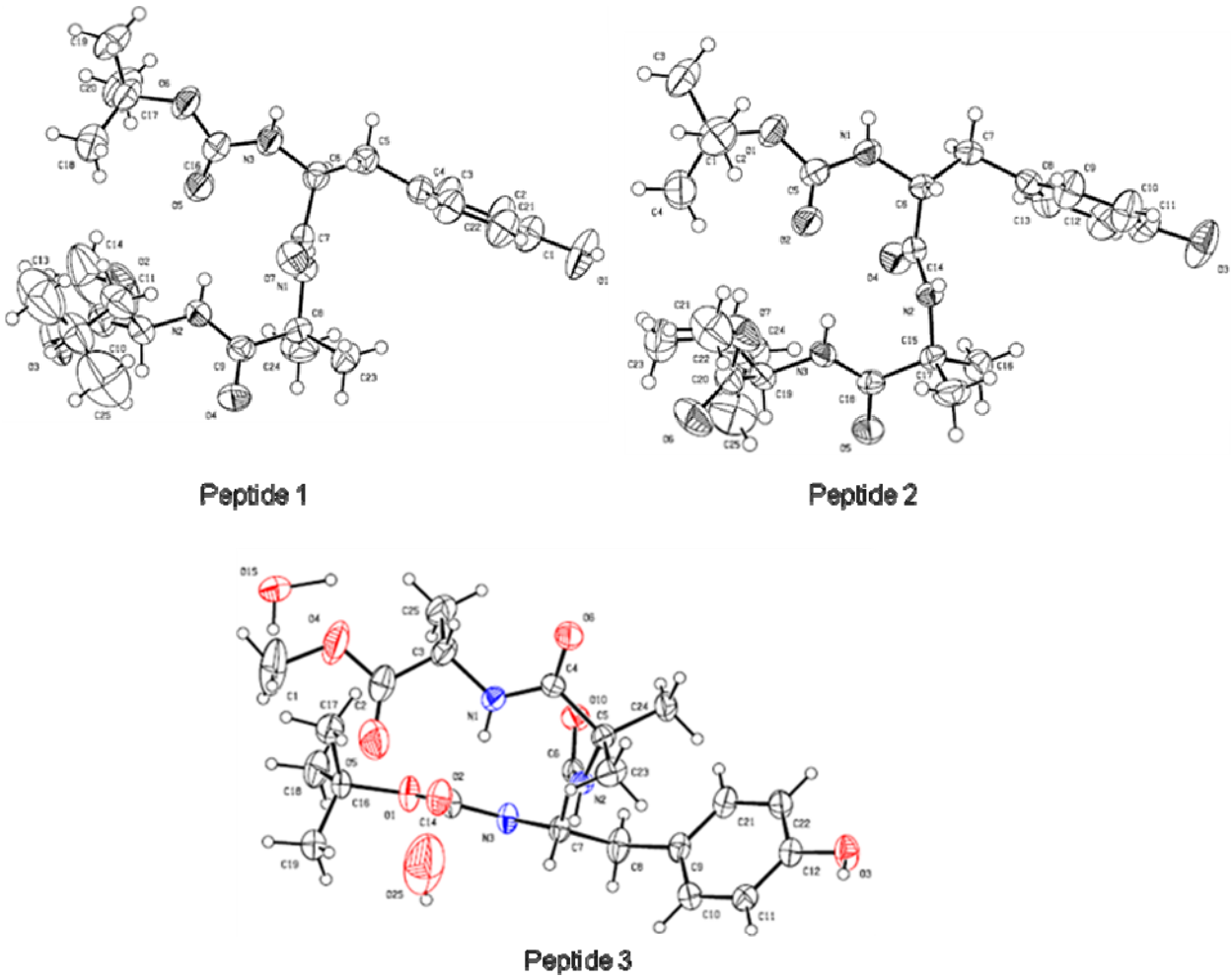
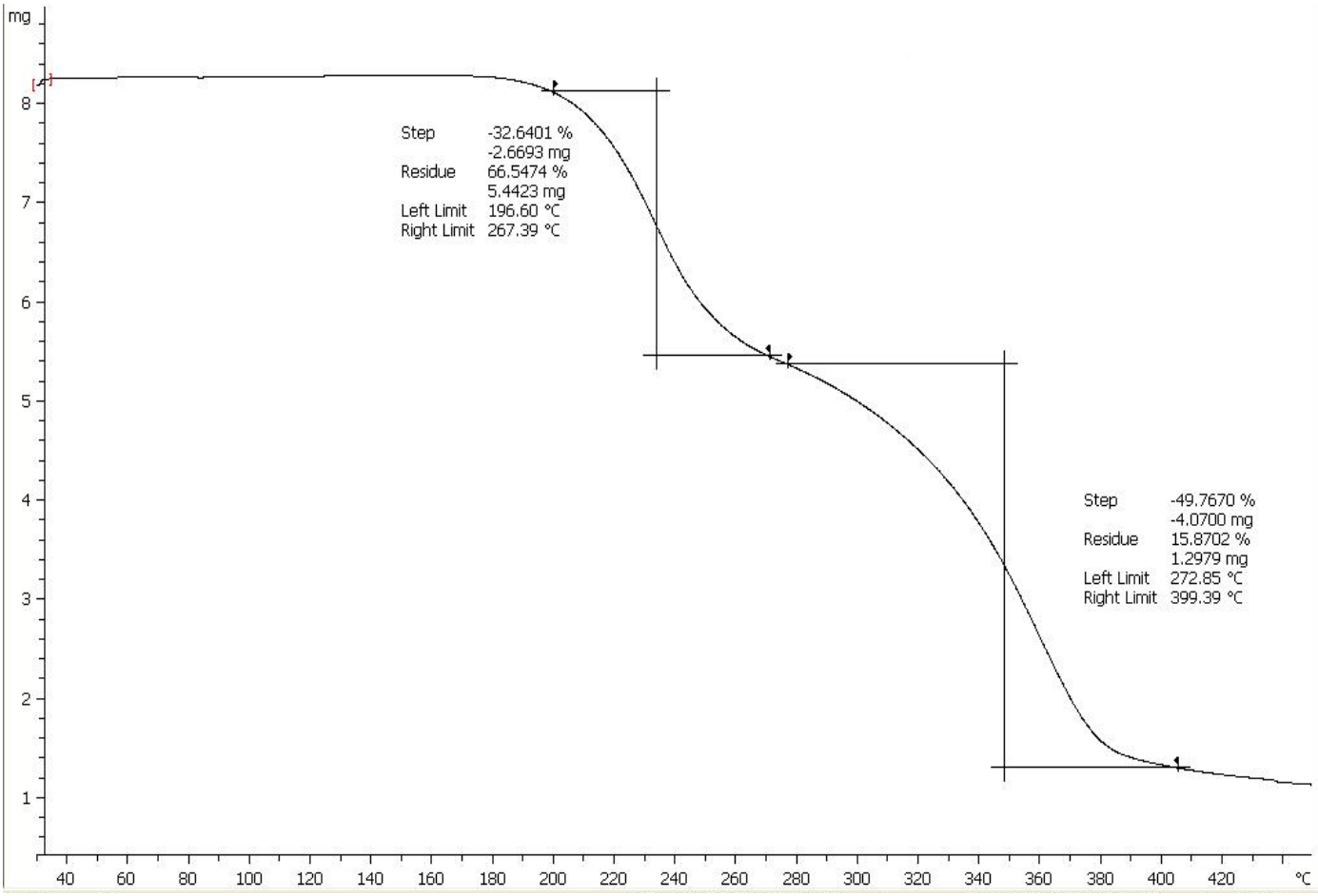
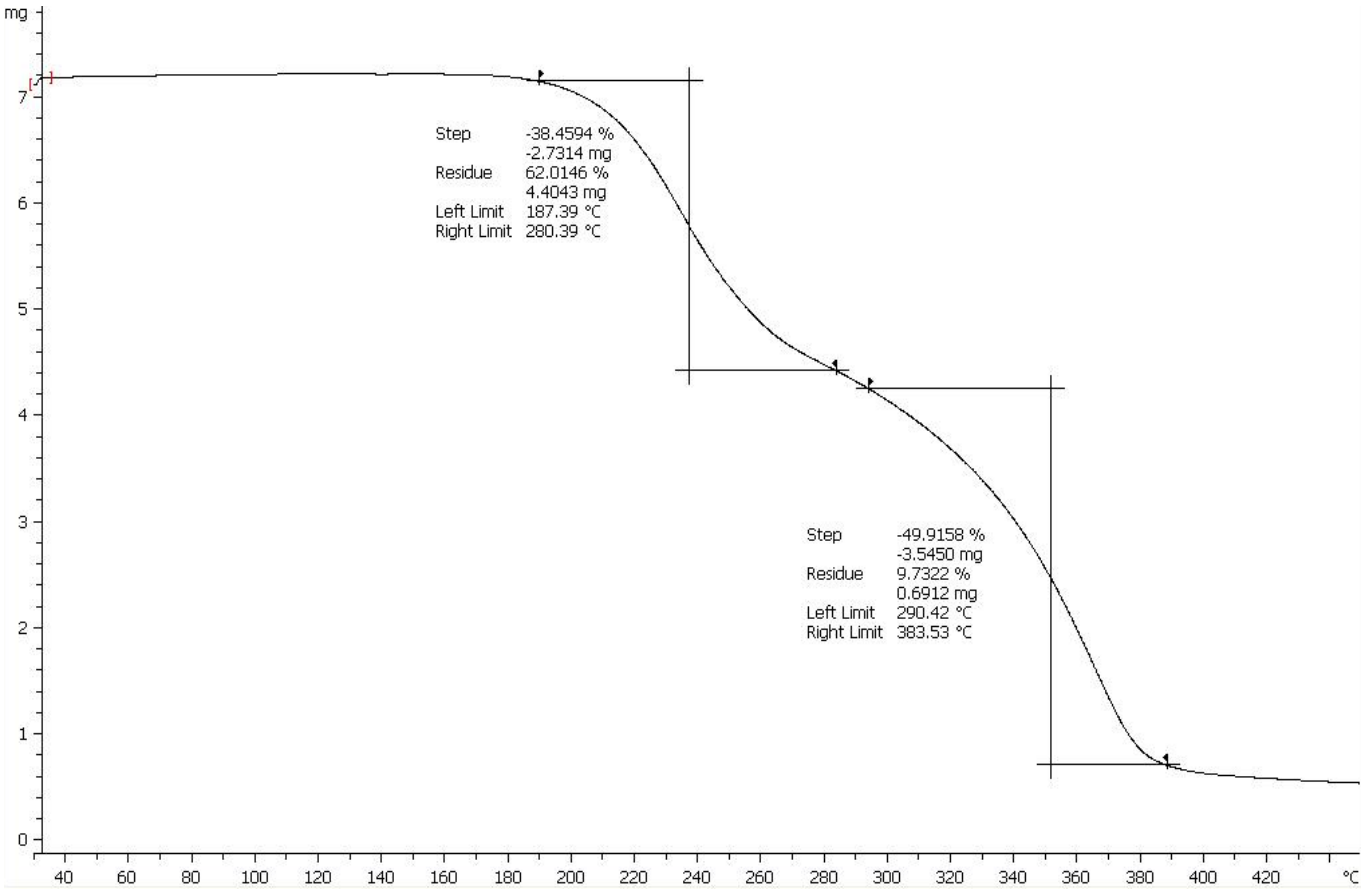


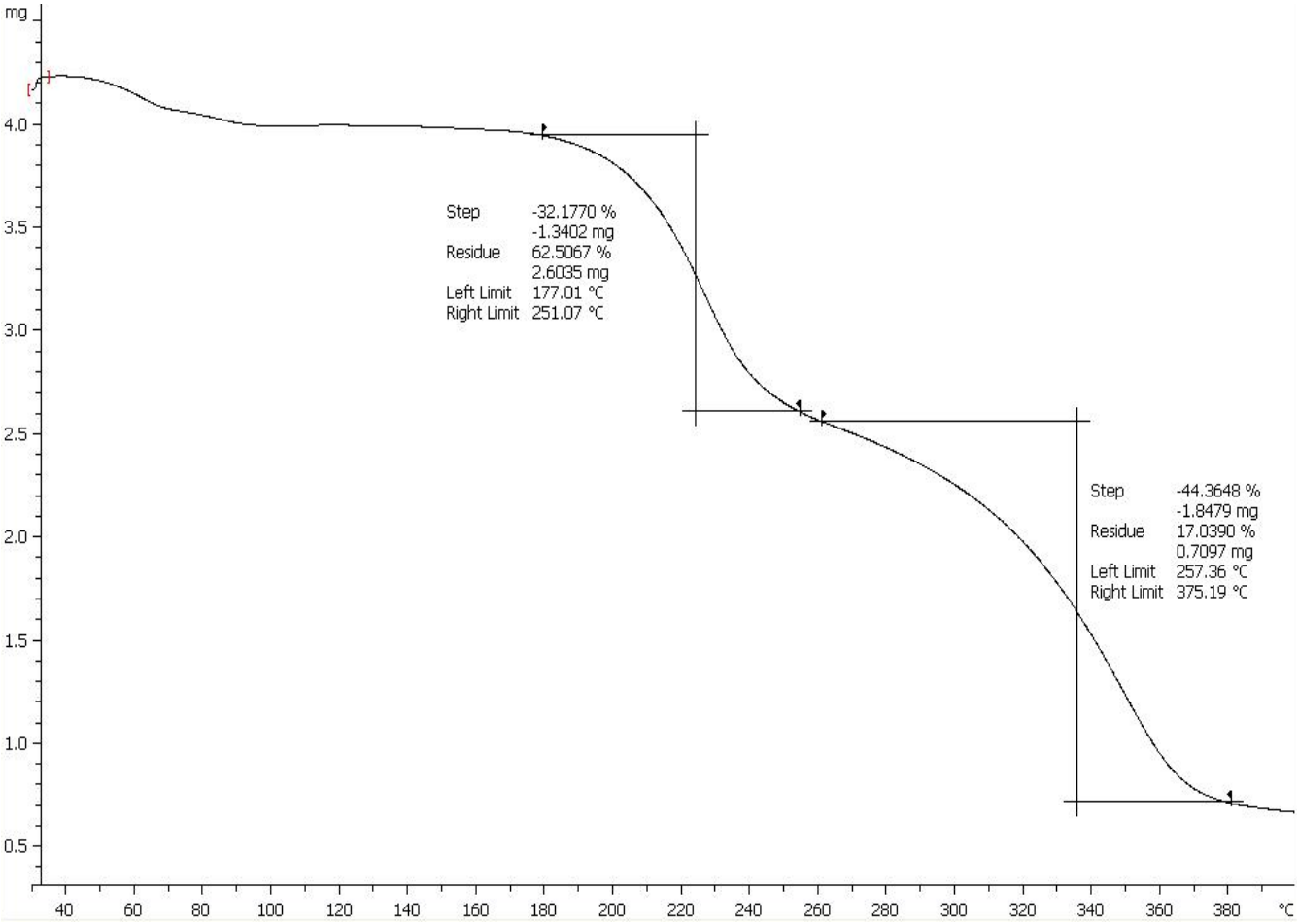
ESI Figure S1: ORTEP diagram of peptide **1**, **2** and **3** with the atomic numbering scheme. Ellipsoids at 30% probability



ESI Figure S2: TGA of BOC-Tyr-Aib-Leu-OMe (1). From this graph, the compound exhibits no decomposition, phase transitions, or mass loss up to 196^0C and this temperature is higher than its melting point (164^0C)**.**



ESI Figure S3: TGA of BOC-Tyr-Aib-Ileu-OMe (2). From this graph, the compound exhibits no decomposition, phase transitions or mass loss up to 187^0C and this temperature is higher than its melting point (137^0C)**.**



ESI Figure S4: TGA of BOC-Tyr-Aib-Ala-OMe (3). From this graph, the compound exhibits no decomposition, phase transitions or mass loss up to 177^0C and this temperature is higher than its melting point(158^0C)**.**

ESI Table 1. Hydrogen bonding parameters of peptide **1.**

D-H….A	H….A(Å)	D…A(Å)	D-H…A (°)
O1—H1···O4a	1.91	2.72	170.00
N1--H1···· O4d	2.00	2.84	167.00
N2--H2···O5	2.23	3.03	156.00
N3—H3···O3f	2.22	3.02	157.00

Symmetry equivalent

a = 2-x,1/2+y,1/2-z
d = -1/2+x,1/2-y,-z
f = 3/2-x,-y,1/2+z

ESI Table 2. Hydrogen bonding parameters of peptide **2.**

D-H….A	H….A(Å)	D…A(Å)	D-H…A (°)
O3—H16····O4f	1.90	2.68	160.00
N1--H10···· O6b	2.19	3.00	158.00
N2—H19····O5a	2.05	2.88	162.00
N3—H26····O2	2.35	3.14	155.00

Symmetry equivalent

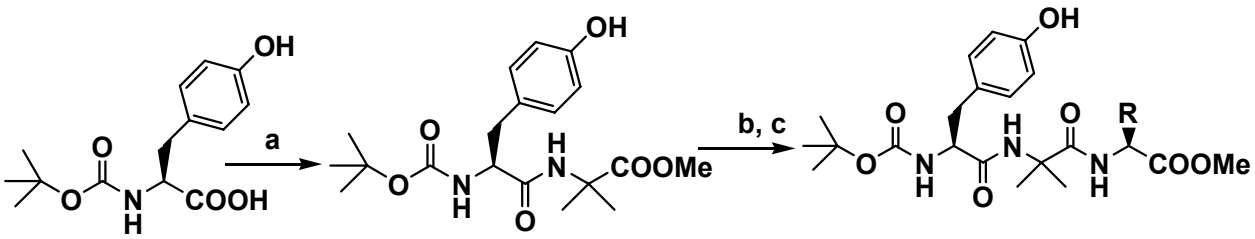
a = -1/2+x,1/2-y,-z
b =2-x,-1/2+y,1/2-z
f = 3/2-x,1-y,1/2+z

ESI Table 3. Hydrogen bonding parameters of peptide **3.**

D-H….A	H….A(Å)	D…A(Å)	D-H…A (°)
O3—H3B···O1Sa	1.92	2.72	164.00
O1S—H81···O6o	1.89	2.73	168.00
O1S—H83···O2Sg	1.58	2.75	164.00
N1--H1··· O2	2.57	3.30	144.00
N2—H2···O1Sg	2.17	3.02	172.00
N3—H3···O10f	2.17	2.99	162.00

Symmetry equivalent

a = -1+x,y,z
g = 1-x,y,1-z
o = 1-x,-1+y,1-z
f = 1/2-x,1/2+y,1-z



Peptide 1, R = $CH_2CH(CH_3)_2$

Peptide 2, R = $CH(CH_3)CH_2CH_3$

Peptide 3, R = CH_3

Figure S1: Schematic presentation of synthesis of tripeptide **1**. Reagents and conditions: (a) DMF, H-Aib-OMe, DCC, HOBt, 0°C, 90% yield; (b) MeOH, 2M NaOH, 85% yield; (c) DMF, H-Leu-OMe(1)/ H-Ileu-OMe(2)/ H-Ala-OMe(3), DCC, HOBt, 0°C, 80% yield.

Experimental

General Methods and Materials. All L-amino acids (L-tyrosine, L-alanine, L-leucine, L-isoleucine and α-amino isobutyric acid) were purchased from Sigma chemicals. HOBt (1-hydroxybenzotriazole) and DCC dicyclohexylcarbodiimide) were purchased from SRL.

Synthesis. The peptides were synthesized by conventional solution-phase methodology by using a racemization free fragment condensation strategy. The Boc group was used for N-terminal protection and the C-terminus was protected as a methyl ester. Couplings were mediated by dicyclohexylcarbodiimide/1- hydroxybenzotriazole (DCC/HOBt). Deprotection of the methyl ester was performed using the saponification method. All the intermediates were characterized by 500 MHz and 400MHz ^{1}H NMR and mass spectrometry. The final compound was fully characterized by 500 MHz and 400MHz ^{1}H NMR spectroscopy, ^{13}C NMR spectroscopy (125 MHz, 100MHz), mass spectrometry, and IR spectroscopy. The peptide **1, 2** and **3** were characterized by X-ray crystallography.

(a) Boc-Tyr-OH (4). A solution of L-tyrosine (3.62 g, 20 mmol) in a mixture of dioxane (40 mL), water (20 mL) and 1M NaOH (20 mL) was stirred and cooled in an ice-water bath. Di-tert-butylpyrocarbonate (4.8 g, 22 mmol) was added and stirring was continued at room temperature for 6 h. Then the solution was concentrated under vacuum to about 20-30mL, cooled in an ice-water bath, covered with a layer of ethyl acetate (about 50 mL) and acidified with a dilute solution of $KHSO_4$ to pH 2-3 (Congo red). The aqueous phase was extracted with ethyl acetate and this operation was done repeatedly. The ethyl acetate extracts were pooled, washed with water and dried over anhydrous Na_2SO_4 and evaporated under vacuum. The pure material was obtained as a waxy solid.

Yield 4.87 g (17.31 mmol, 86.56%).

^{1}H NMR (500MHz, DMSO-d^{6}, δ in ppm): 12.75 (br, 1H, -COOH); 9.21 (s, 1H, Tyr –OH); 7.02-7.00 (d, 2H, J=10Hz, Tyr phenyl ring protons); 6.65-6.63 (d, 2H, J=10Hz, Tyr phenyl ring protons); 4.04 (m,1H, Tyr C^{α} H); 3.93-3.91 (d, 1H, J= 10Hz, Tyr NH); 2.88 (m, 2H, Tyr C^{β} H); 1.42 (s, 9H, BOC CH_3). ^{13}C NMR (125 MHz,DMSO-d^{6}): δ 173.74, 155.78, 129.96, 127.98, 114.87,77.97, 55.50, 35.61, 28.13.

Anal. Calcd for $C_{14}H_{19}NO_5$ (281): C, 59.78; H, 6.81; N, 4.98.

Found: C, 59.81; H, 6.79; N, 4.99.

(b) Boc-Tyr-Aib-OMe (5). 4.5 g (16 mmol) of Boc-Tyr-OH was dissolved in 25 mL DCM in an ice-water bath. H-Aib-OMe was isolated from 4.91 g (32 mmol) of the corresponding methyl ester hydrochloride by neutralization, subsequent extraction with ethyl acetate and ethyl acetate extract was concentrated to 10 mL. It was then added to the reaction mixture, followed immediately by 3.3 g (16 mmol) dicyclohexylcarbodiimide (DCC) and 2.45 g (16 mmol) of HOBt. The reaction mixture was allowed to come to room temperature and stirred for 48 h. DCM was evaporated and the residue was dissolved in ethyl acetate (60 mL) and dicyclohexylurea (DCU) was filtered off. The organic layer was washed with 2M HCl (3 × 50 mL), brine (2 × 50 mL), 1M sodium carbonate (3 × 50 mL) and brine (2 × 50 mL) and dried over anhydrous sodium sulfate; and evaporated in a vacuum to yield Boc-Tyr-Aib-OMe as a white solid.

Yield 4.56 g (11.98 mmol, 74.87%).

Mp.122-128˚C.

^{1}H NMR (500MHz, $CDCl_3$, δ in ppm): 7.03-7.02 (d, 2H, J= 5Hz, Tyr phenyl ring protons); 6.75-6.74 (d, 2H, J=5Hz, Tyr phenyl ring protons);6.30 (s, 1H, Aib NH); 5.22-5.21 (d, 1H, J= 5Hz, Tyr NH); 4.22 (m,1H, Tyr C^{α} H); 3.70 (s, 3H, -OCH_3); 2.95-2.90 (m, 2H, Tyr C^{β} H); 1.44 (s, 6H, Aib C^{β} H); 1.41 (s, 9H, BOC CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.17, 170.74, 155.66, 130.58, 127.97, 115.56, 56.45, 53.45, 37.58, 29.70, 24.74.

HRMS *m*/*z* 403.10 [M + Na]+; *M*calcd: 380.44. FTIR (KBr): 3329, 3063, 2982, 2932 , 2852, 1682, 1595,1519. Anal. Calcd for $C_{19}H_{28}N_2O_6$ (380): C, 59.98; H, 7.42; N, 7.36.

Found: C, 60.01; H, 7.38; N, 7.38.

(c) Boc-Tyr(1)-Aib(2)-OH (6). To 4.4 g (11.56 mmol) of Boc-Tyr-Aib-OMe, 25 mL MeOH and 2M 15 mL NaOH were added and the progress of saponification was monitored by thin layer chromatography (TLC). The reaction mixture was stirred. After 10 h, methanol was removed under vacuum; the residue was dissolved in 50 mL of water, and washed with diethyl ether (2 × 50 mL). Then the pH of the aqueous layer was adjusted to 2 using 1M HCl and it was extracted with ethyl acetate (3 × 50 mL). The extracts were pooled, dried over anhydrous sodium sulfate, and evaporated under vacuum to obtained compound as a white solid.

Yield 3.8 g (10.38 mmol, 89.7%).

^{1}H NMR (500MHz, DMSO-d_6, δ in ppm): 12.75 (br, 1H, -COOH); 9.14 (s, 1H, Tyr –OH); 8.02 (s, 1H, Aib NH); 7.03-7.01 (d, 2H, J= 10Hz, Tyr phenyl ring protons); 6.66-6.65 (d, 1H, J= 5Hz, Tyr NH); 6.63- 6.61(d, 2H, J=10Hz, Tyr phenyl ring protons); 4.01 (m,1H, Tyr C^{α} H); 2.78-2.81 (m, 2H, Tyr C^{β} H); 1.34 (s, 3H, Aib C^{β} H); 1.32 (s, 3H, Aib C^{β} H); 1.30 (s, 9H, BOC CH_3). ^{13}C NMR (125 MHz, DMSO-d_6): δ 175.43, 170.95, 155.64, 130.14, 128.02, 114.69, 77.91, 55.61, 54.82, 28.10, 24.70. HRMS *m*/*z* 405.66 [M + K]+; *M*calcd :366.41.

Anal. Calcd for $C_{18}H_{26}N_2O_6$ (366): C, 59.00; H, 7.15; N, 7.65.

Found: C, 58.98; H, 7.18; N, 7.63.

(d) Boc-Tyr-Aib-Leu-OMe (1). 1.1 g (3 mmol) Boc-Tyr-Aib-OH was dissolved in 10 mL DMF in an ice-water bath. H-Leu-OMe 1.08 g (6 mmol) was isolated from corresponding methyl ester hydrochloride by neutralization, subsequent extraction with ethyl acetate and concentrated to 7 mL. Then it was added to the reaction mixture, followed immediately by 0.618 g (3 mmol) dicyclohexylcarbodiimide (DCC) and 0.459 g (3 mmol) HOBt. The reaction mixture was allowed to come to room temperature and stirred for 72 h. The residue was taken in 30 mL ethyl acetate and dicyclohexylurea (DCU) was filtered off. The organic layer was washed with 2 M HCL (3 × 50 mL), brine (2 × 50 mL), then 1 M sodium carbonate (3 × 30 mL) and brine (2 × 30 mL) and dried over anhydrous sodium sulfate and evaporated under vacuum to yield the tripeptide **1** as a white solid. Purification was done by silica gel column (100-200 mesh size) and ethyl acetate and hexane 1:2 as eluent.

Yield 1.20g (2.43 mmol, 81 %).

Mp. 164-165˚C.

^{1}H NMR (500MHz, CDCl3, δ in ppm): 8.16 (s, 1H, Tyr –OH); 7.21-7.19 (d, 1H, J=10Hz,Tyr NH); 6.97-6.95 (d, 2H, J = 10Hz, Tyr phenyl ring proton); 6.77-6.76 (d, 2H, J = 5Hz, Tyr phenyl ring protons); 6.43 (s, 1H,, Aib NH); 5.30-5.29 (d, 1H, J = 5Hz, Leu NH); 4.51-4.49 (m,1H, Tyr C^{α} H); 4.07-4.06 (m,1H, Leu C^{α} H); 3.68 (s, 3H, -OCH_3); 2.93-2.92 (m, 2H, Tyr C^{β} H); 1.64(m,1H,Leu C^{γ}H);1.60-1.59 (d,2H,J=5 Hz, Leu C^{β} H); 1.44 (s, 3H, Aib CH_3); 1.41 (s, 9H, Boc CH_3); 1.22 (s, 3H, Aib CH_3),0.91-0.83(m, 6H, Leu C^{δ}H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.13, 173.38, 155.40, 130.46, 127.83, 115.73, 80.53, 57.54, 56.55, 52.15, 51.01, 40.69, 36.72, 28.14, 25.84, 24.55, 22.71.

$[\alpha]_D^{27.8}$ -10.640 (c 1.00, $CHCl_3$). Mass Spectral data $[M + Na]^+$ = 516.12 with an isotope peak at 517.12; $[M + K]^+$ = 532.10 with an isotope peak at 533.10; M_{calcd} = 493. FTIR(KBr): 3350, 3268, 3082, 2961, 2872, 1721, 1701, 1673, 1645, 1617, 1595, 1536, 1520,1455,1384,1367cm^{-1}.

Anal. Calcd for $C_{25}H_{39}N_3O_7$ (493): C, 60.11; H, 7.78; N, 8.76.

Found: C, 60.09; H, 7.80; N, 8.73.

(e) Boc-Tyr-Aib-Ile-OMe (2). 1.1 g (3 mmol) Boc-Tyr-Aib-OH was dissolved in 10 mL DMF in an ice-water bath. H-Ile-OMe 1.08 g (6 mmol) was isolated from corresponding methyl ester hydrochloride by neutralization, subsequent extraction with ethyl acetate and concentrated to 7 mL. Then it was added to the reaction mixture, followed immediately by 0.618 g (3 mmol) dicyclohexylcarbodiimide (DCC) and 0.459 g (3 mmol) HOBt. The reaction mixture was allowed to come to room temperature and stirred for 72 h. The residue was taken in 30 mL ethyl acetate and dicyclohexylurea (DCU) was filtered off. The organic layer was washed with 2 M HCL (3 × 50 mL), brine (2 × 50 mL), then 1 M sodium carbonate (3 × 30 mL) and brine (2 × 30 mL) and dried over anhydrous sodium sulfate and evaporated under vacuum to yield the tripeptide **2** as a white solid. Purification was done by silica gel column (100-200 mesh size) and ethyl acetate and hexane 1:2 as eluent.

Yield 1.23g (2.53 mmol, 83 %).

Mp. 137-139˚C.

^{1}H NMR (400MHz, $CDCl_3$, δ in ppm): 8.16 (s, 1H, Tyr –OH); 7.08-7.07 (d, 1H,J=4Hz, Tyr –NH); 7.06-7.04 (d, 2H, J=8 Hz,Tyr phenyl ring proton); 6.78-6.76 (d, 2H, J = 8Hz, Tyr phenyl ring proton); 6.29 (s, 1H, Aib NH); 5.12-5.10 (d, 1H, J = 8Hz, Ile NH); 4.53-4.51 (m, 1H, Tyr C^{α} H ,); 4.21-4.18(m,1H, Ile C^{α} H); 3.75 (s, 3H, -OCH_3); 3.00-2.91 (m, 2H, Tyr C^{β} H); 1.91-1.89 (m, 1H, Ile C^{β} H); 1.50 (s, 3H, Aib CH_3); 1.42(s, 9H, BOC, CH_3); 1.39 (s, 3H, Aib CH_3,);1.29(d,

3H, Ile $C^{\gamma}H$); 1.25(m, 1H, Ile $C^{\gamma}H$); 0.94-0.87(t, 3H, $Ile^{\delta}H$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.13, 172.38, 155.40, 130.68, 129.03, 115.39, 80.04, 58.80, 56.95, 51.65, 38.37, 36.80, 27.90,26.60, 25.49, 15.13,11.30. $[\alpha]_D^{27.8}$ 6.66 (c 1.0, $CHCl_3$). Mass Spectral data $[M + Na]^+$ = 516.06 with an isotope peak at 517.06; $[M + K]^+$ = 532.05 with an isotope peak at 533.06; M_{calcd} = 493. FTIR (KBr): 3344, 3268, 3230, 3081, 2976, 2881,2823, 1727, 1703, 1673, 1651, 1615, 1593, 1537, 1454, 1384. cm^{-1}.

Anal. Calcd for $C_{25}H_{39}N_3O_7$ (493): C, 60.11; H, 7.78; N, 8.76.

Found: C, 60.14; H, 7.75; N, 8.73.

(d) Boc-Tyr-Aib-Ala-OMe (3). 1.1 g (3 mmol) Boc-Tyr-Aib-OH was dissolved in 10 mL DMF in an ice-water bath. H-Ala-OMe 0.834 g (6 mmol) was isolated from corresponding methyl ester hydrochloride by neutralization, subsequent extraction with ethyl acetate and concentrated to 7 mL. Then it was added to the reaction mixture, followed immediately by 0.618g (3mmol) dicyclohexylcarbodiimide (DCC) and 0.459 g (3 mmol) HOBt. The reaction mixture was allowed to come to room temperature and stirred for 72 h. The residue was taken in 30 mL ethyl acetate and dicyclohexylurea (DCU) was filtered off. The organic layer was washed with 2 M HCL (3 × 50 mL), brine (2 × 50 mL), then 1 M sodium carbonate (3 × 30 mL) and brine (2 × 30 mL) and dried over anhydrous sodium sulfate and evaporated under vacuum to yield the tripeptide **3** as a white solid. Purification was done by silica gel column (100-200 mesh size) and ethyl acetate and hexane 1:2 as eluent.

Yield 1.21g (2.65mmol, 88.59 %).

Mp. 158-159˚C.

^1H NMR (400MHz, $CDCl_3$, δ in ppm): 7.73 (s, 1H, Tyr –OH); 7.06-7.04 (d, 1H, J=8 Hz,Tyr –NH); 6.96-6.94 (d, 2H, J=8 Hz,Tyr phenyl ring proton); 6.79-6.77 (d, 2H, J = 8Hz, Tyr phenyl

ring proton); 6.35 (s, 1H, Aib NH); 5.03-5.01 (d, 1H, J = 8Hz, Ala NH); 4.54-4.50 (m,1H, Tyr C^{α} H); 4.14-4.09 (m,1H, Ala C^{α} H); 3.77 (s, 3H, -OCH_3); 2.99-2.97 (m, 2H, Tyr C^{β} H); 1.50(s,3H,Aib CH_3);1.46(s,3H,Aib CH_3); 1.41 (s, 9H, BOC CH_3); 1.25 (m, 3H, Ala C^{β} H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.13, 171.38, 155.40, 129.83,115.72, 80.60,57.14, 56.80, 55.35,51.60, 48.41, 37.02, 28.88, 17.75. $[\alpha]_D^{27.8}$ 1.5 (c 1.00, $CHCl_3$). Mass Spectral data $[M + Na]^+$ = 474.05 with an isotope peak at 475.10; $[M + K]^+$ = 490.10; M_{calcd} = 451. FTIR (KBr): 3369, 3345, 3303, 2974, 2929, 2851, 1755, 1744, 1739, 1678, 1645, 1594, 1519, 1455 cm^{-1}.

Anal. Calcd for $C_{22}H_{33}N_3O_7$ (451.51): C, 60.11; H, 7.78; N, 8.76.

Found: C, 60.07; H, 7.73; N, 8.80.

NMR experiments. All NMR studies were carried out on a Brüker AVANCE 500 MHz ,and JNM-ECS400MHz spectrometer at 298 K. Compounds concentrations were in the range 1–10 mmol in $CDCl_3$ and $(CD_3)_2SO$.

FTIR spectroscopy. All reported solid-state FTIR spectra were obtained with a Perkin Elmer Spectrum RX1 spectrophotometer with the KBr disk technique.

Mass spectrometry. Mass spectra were recorded on a Q-Tof Micro YA263 high-resolution (Waters Corporation) mass spectrometer by positive-mode electrospray ionization.

Polarimeter. Rudolph Research analytical instrument. Model Autopol IV Polarimeter was used.

WAXS. Crystals of peptides **1**, **2** and **3** were grounded to a powder and examined. Experiments were carried out by using an X-ray diffractometer (Bruker D8 Advance) with a parallel beam optics attachment. The instrument was operated at a 35 kV voltage and 30 mA current using Ni-filtered CuK_{α} radiation and was calibrated with a standard silicon sample. Samples were scanned from 5^o to 50^o (2θ) at the step scan mode (step size 0.03°, preset time 2 s) and the diffraction patterns were recorded using a scintillation scan detector.

N_2 Gas Adsorption Experiment. Nitrogen adsorption/desorption isotherms were obtained using a Quantachrome Autosorb Automated Gas Sorption System at 77 K. Before the analysis the samples were degassed at 40^o C for 4 h. The N_2 gas adsorption /desorption isotherms (77K) of the tri-peptide(**1**) was shown in Fig-1 and was close to the type III adsorption isotherm . From the N_2 gas adsorption at low P/P_0, the following pore size distribution of the sample using the NLDFT method. The pore size distribution curve of tri-peptide exhibits one peak at 6.50 nm. From the Brunauer-Emmett-Teller (BET) equation,the BET surface areas were calculated as 9.809 m^2g^{-1}. This analysis was done for compound **2** and **3** also, compound **2** gives the same result (Figure S4 and S5, Table 5) as compound **1**, but compound **3** do not show satisfactory result. This is consistant with the size of helix hollow obtained from X-ray crystallography.

Table-4

Property	**Peptide (1)**
Surface area	9.809 m^2 /gm
Pore volume	0.0213 cc/gm
Pore size	6.50 nm
Isotherm type	III
Max Amount of gas Ads.	18.31 cc/gm

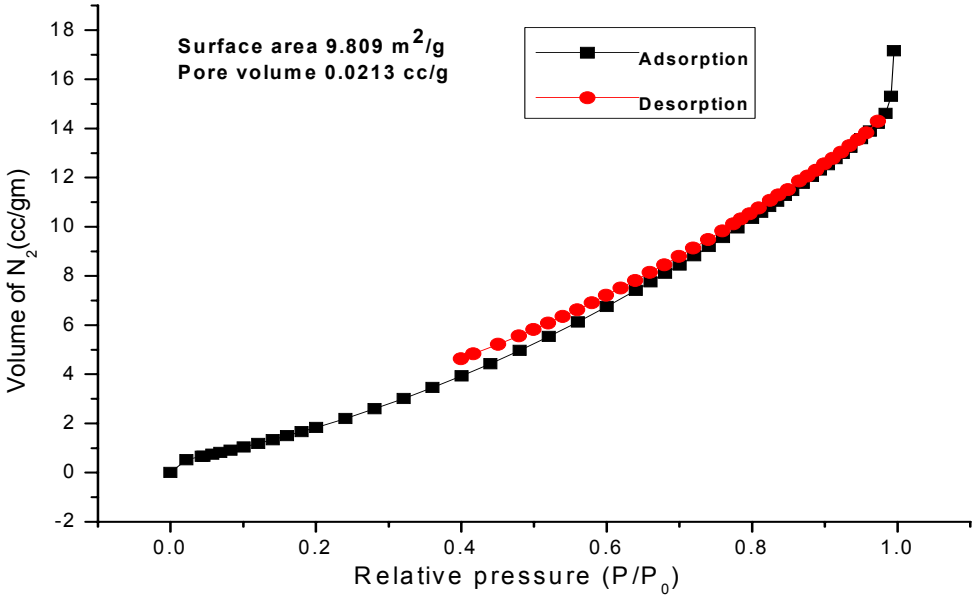


Figure S2: Type-III N_2 gas adsorption isotherm of peptide **1**.

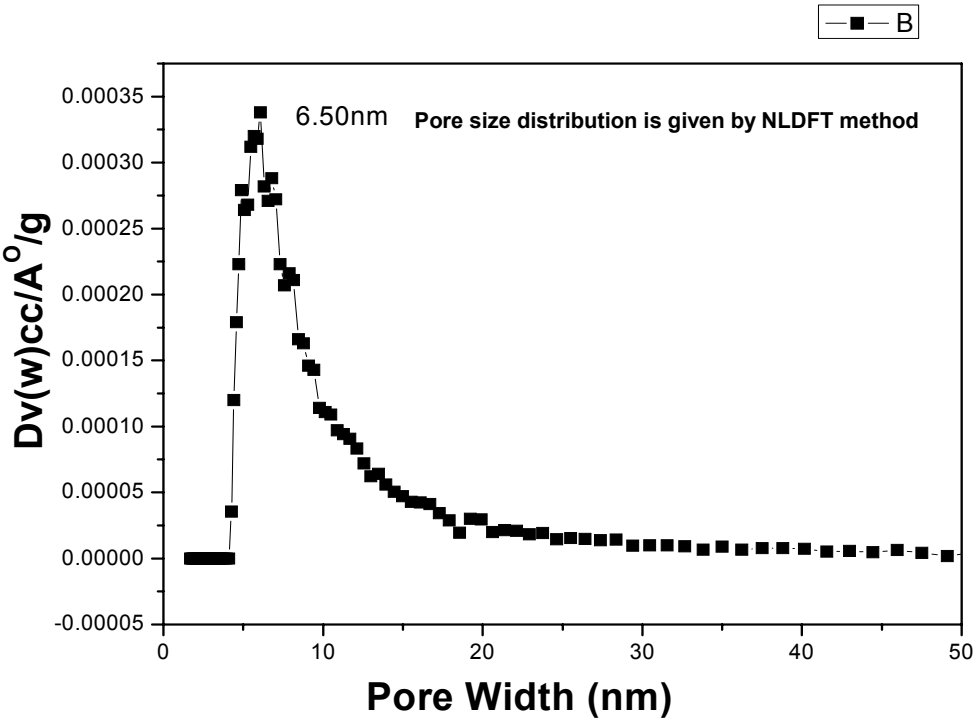


Figure S3: Pore size distribution curve of peptide **1.**

Table 5: Peptide **2**.

Surface area	8.68 m^2 /gm
Pore volume	0.0193 cc/gm
Pore size(diameter)	6.04 nm
Isotherm type	III
Max Amount of gas Ads.	13.99 cc/gm

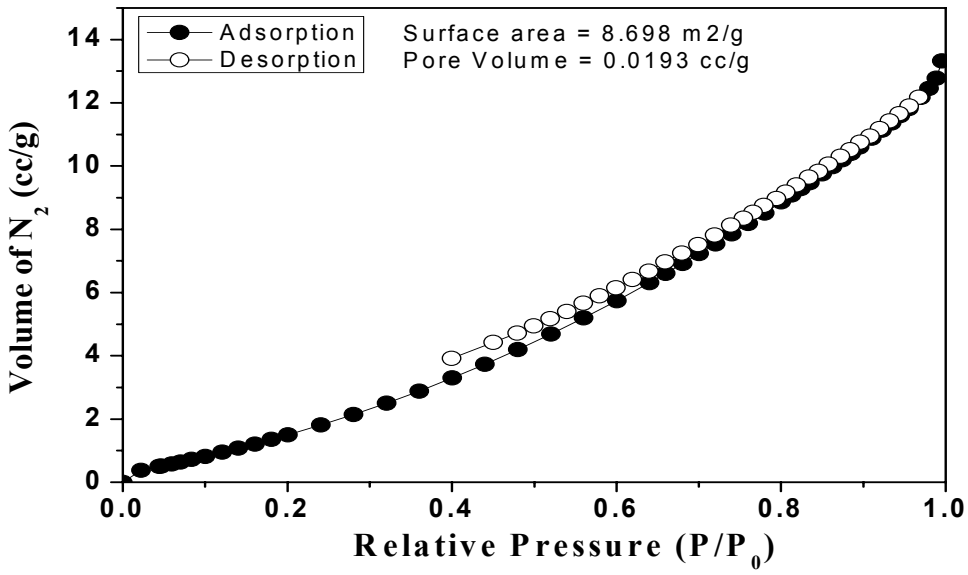


Figure S4: Type-III N_2 gas adsorption isotherm of peptide **2**.

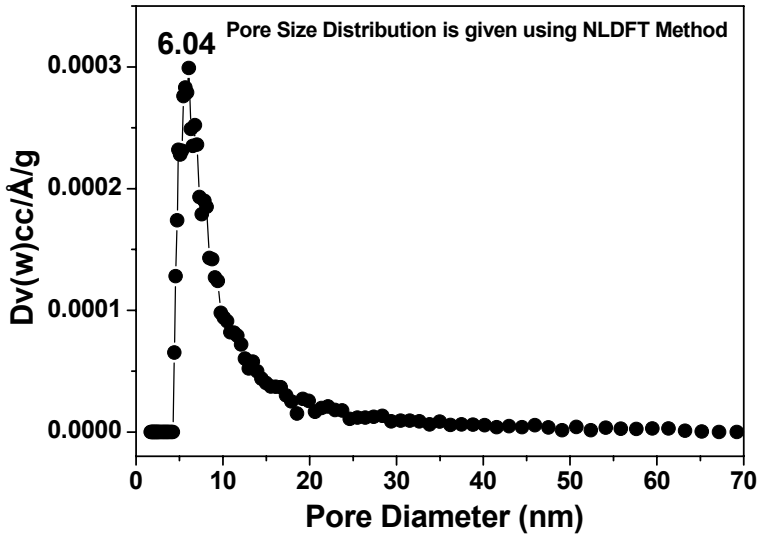


Figure S5: Pore size distribution curve of peptide **2.**

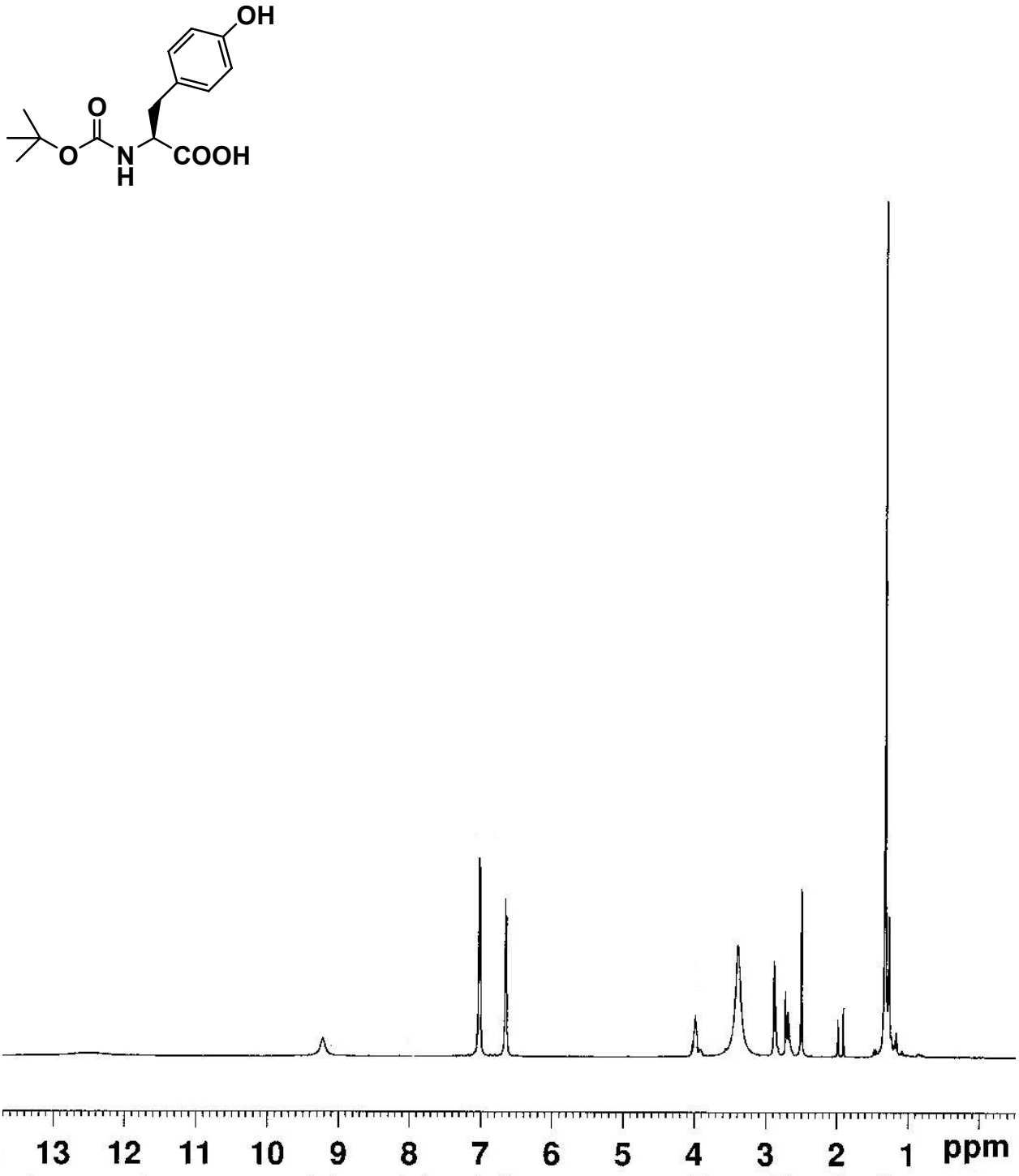


Figure S6: ^{1}H NMR (500 MHz, DMSO-d^{6}) spectra of Boc-Tyr-OH

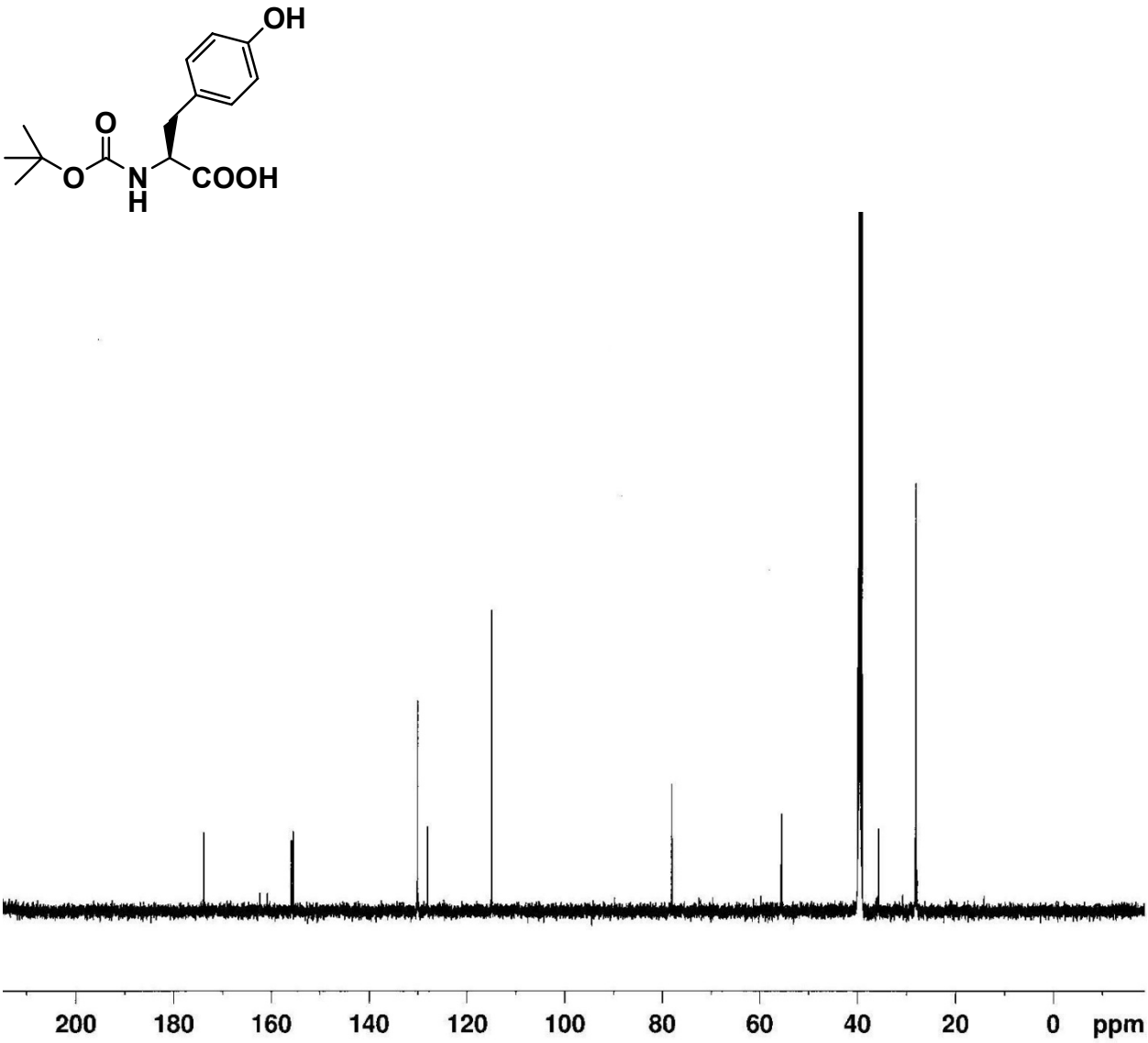


Figure S7: ^{13}C NMR (125 MHz, DMSO-d^6) spectra of Boc-Tyr-OH.

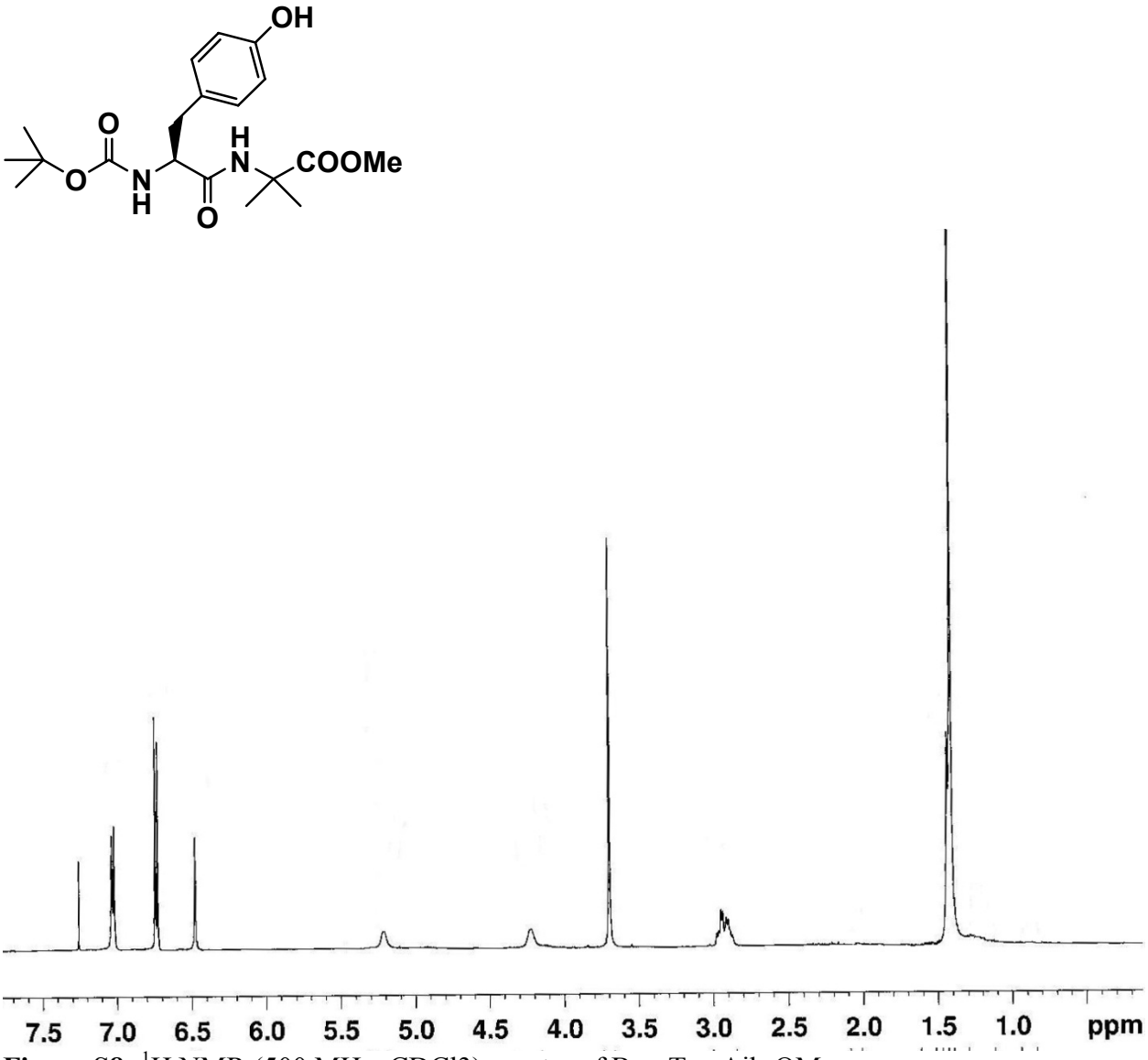


Figure S8: ^{1}H NMR (500 MHz, CDCl3) spectra of Boc-Tyr-Aib-OMe

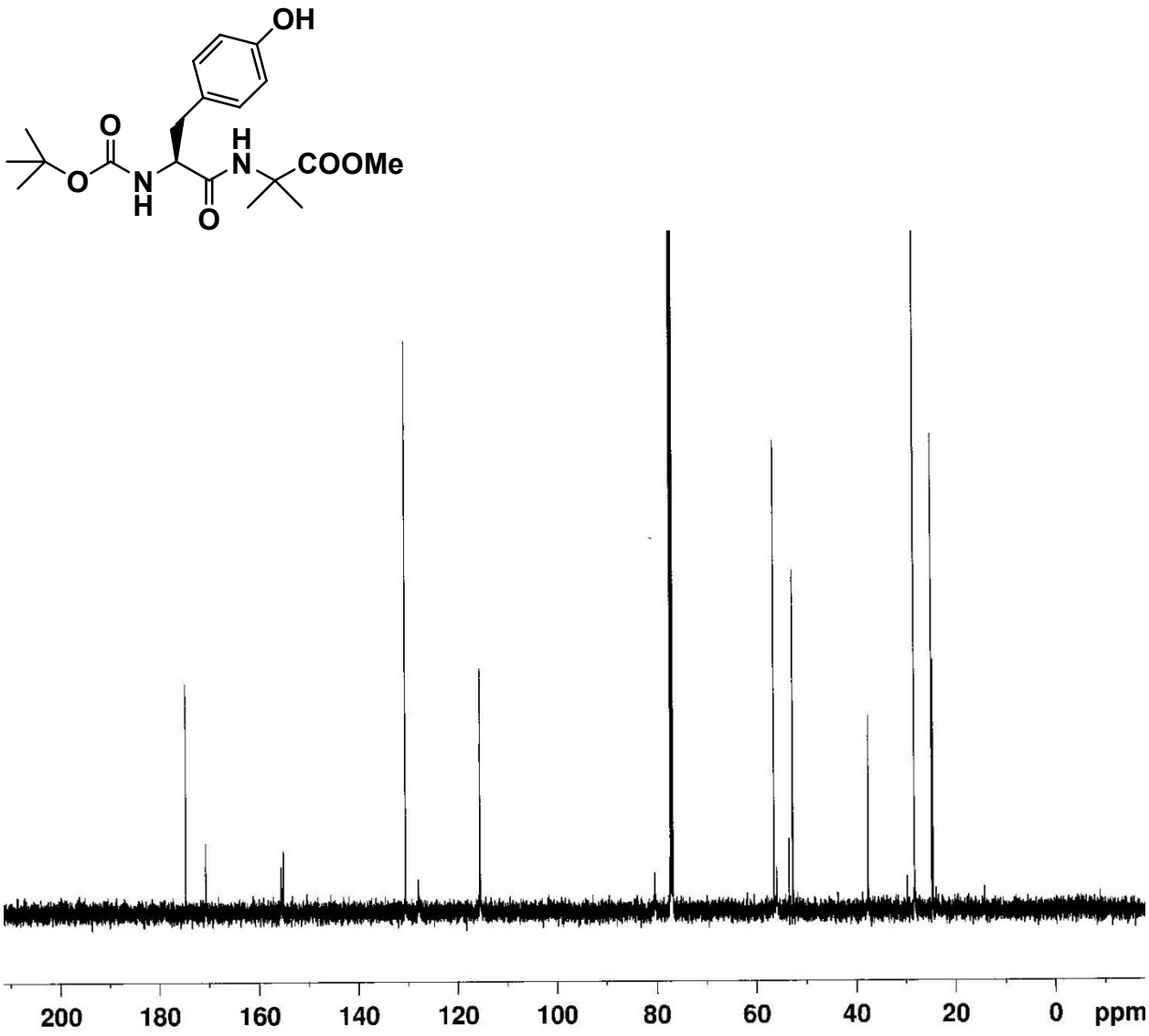


Figure S9: ^{13}C NMR (125 MHz, CDCl3) spectra of Boc-Tyr-Aib-OMe.

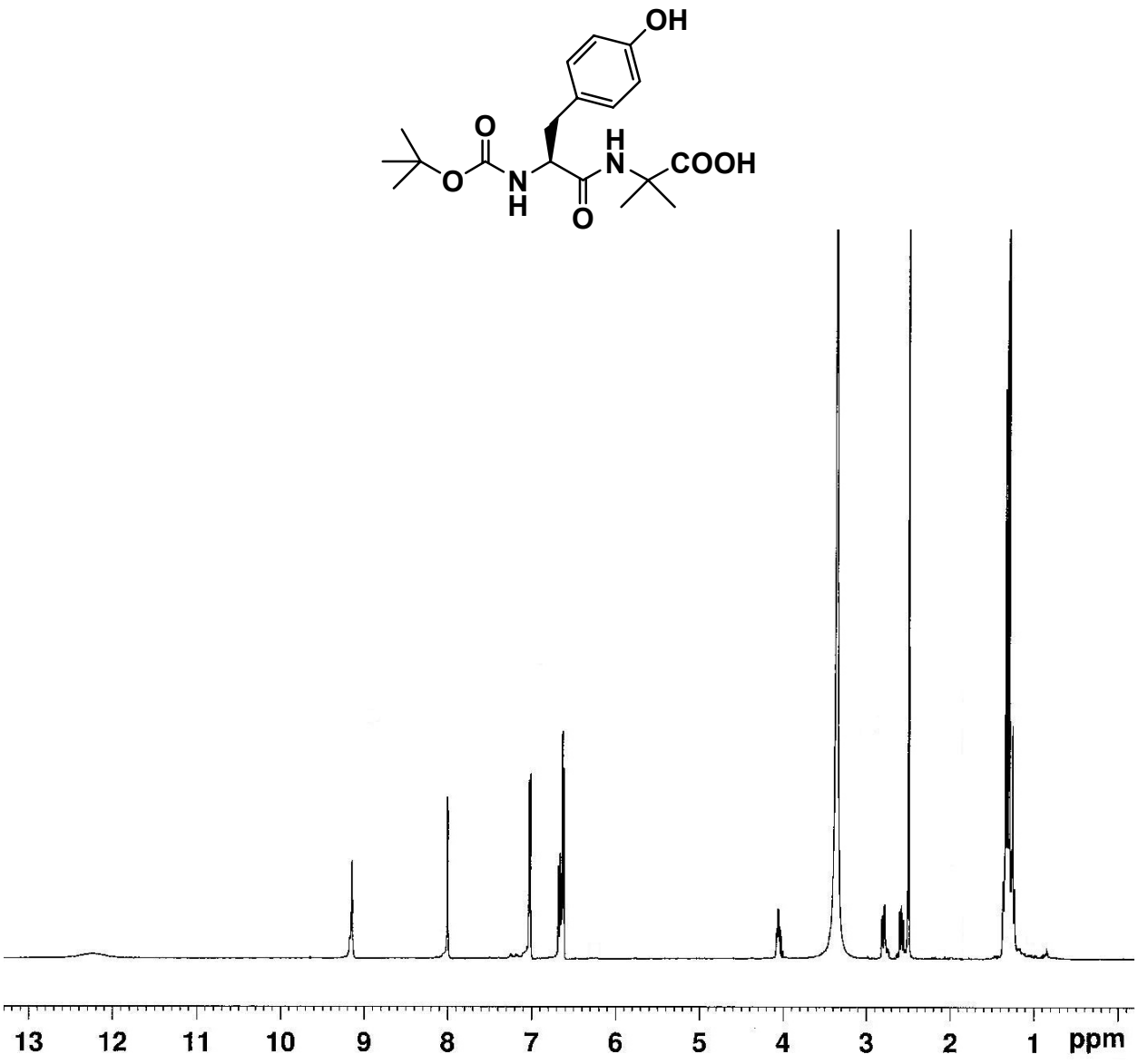


Figure S10: ^{1}H NMR (500 MHz, DMSO-d_6) spectra of Boc-Tyr-Aib-OH

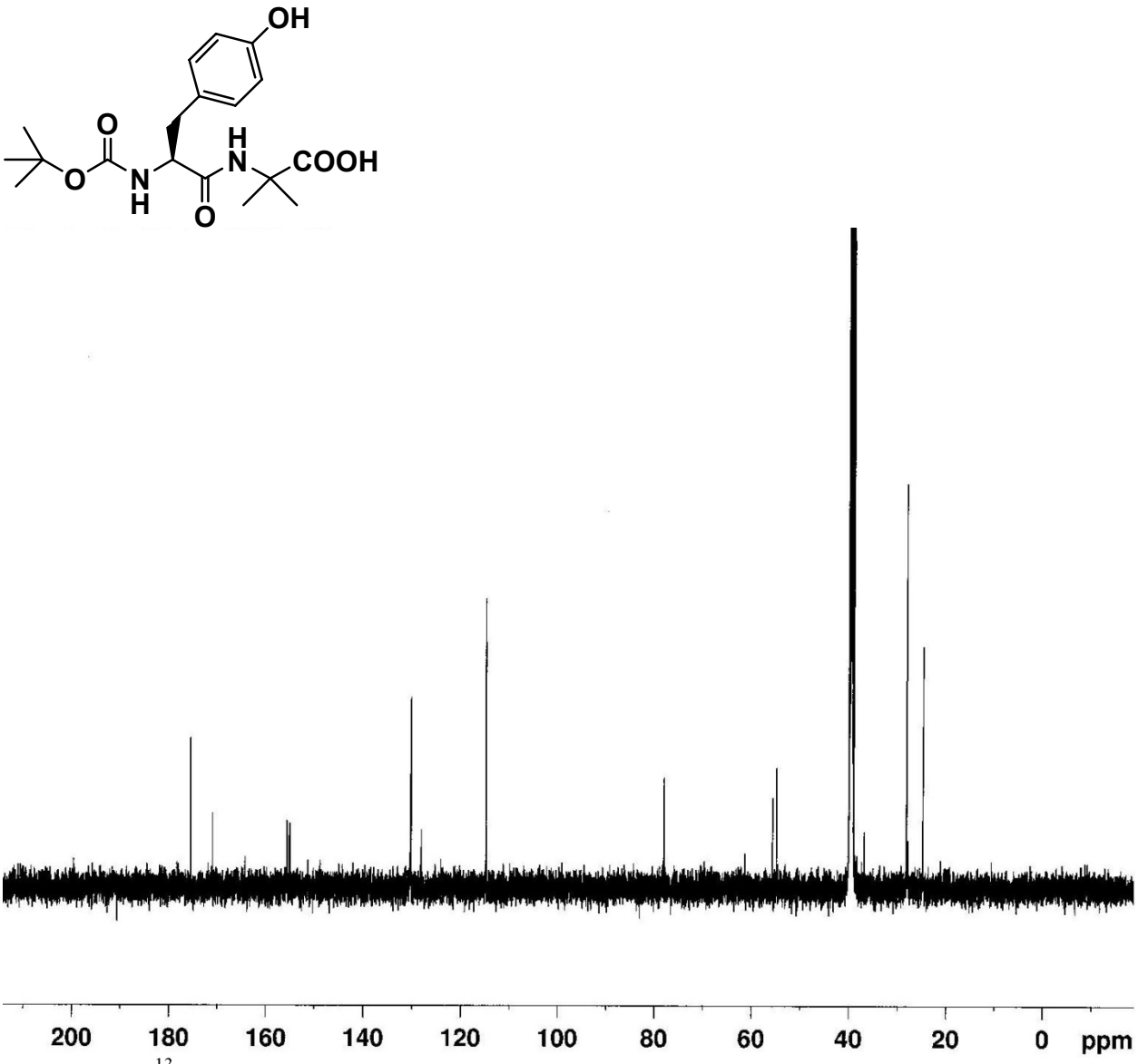


Figure S11: ^{13}C NMR (125 MHz, DMSO-d_6) spectra of Boc-Tyr-Aib-OH

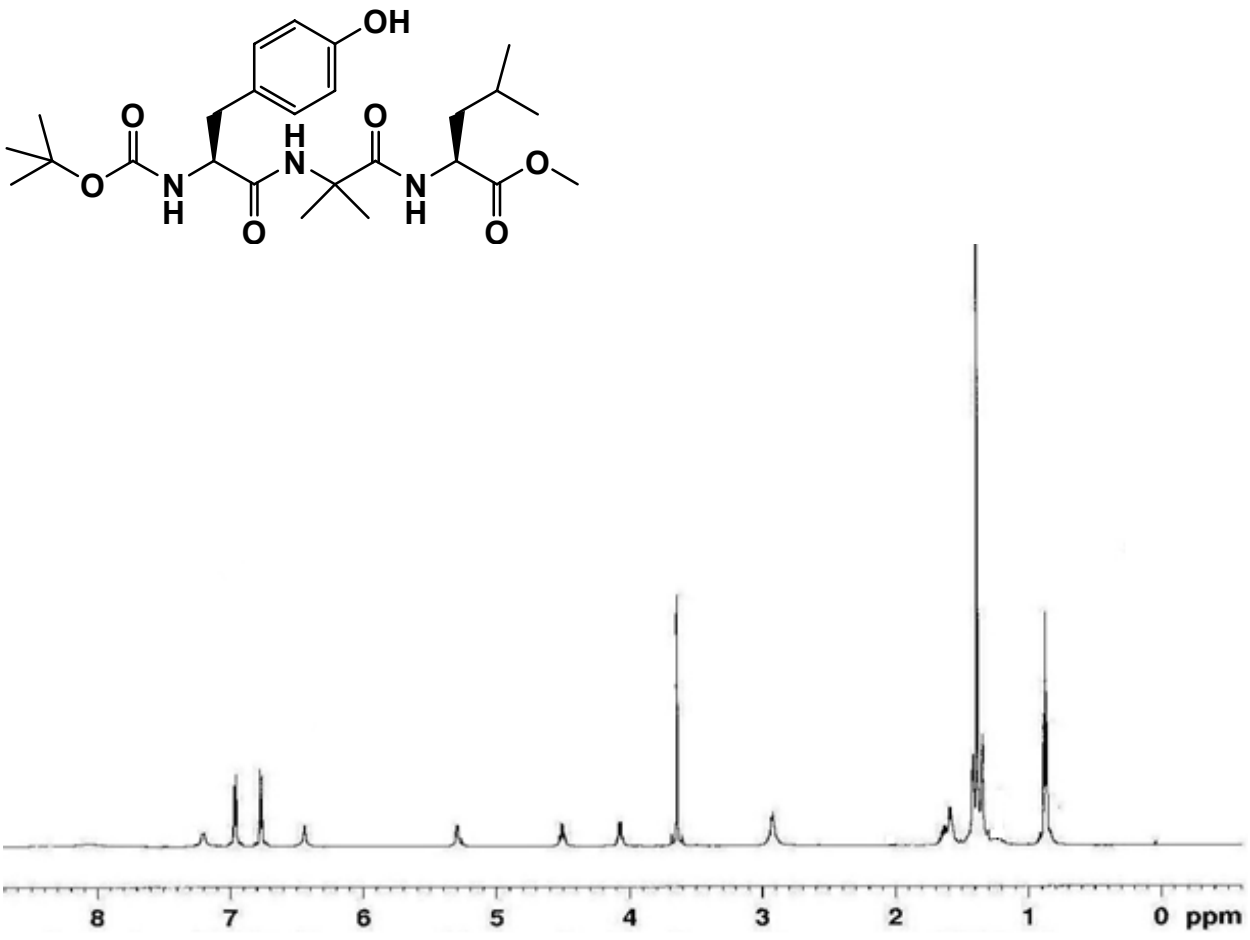


Figure S12: ^{1}H NMR (500 MHz, CDCl3) spectra of Boc-Tyr-Aib-Leu-OMe **(1)**

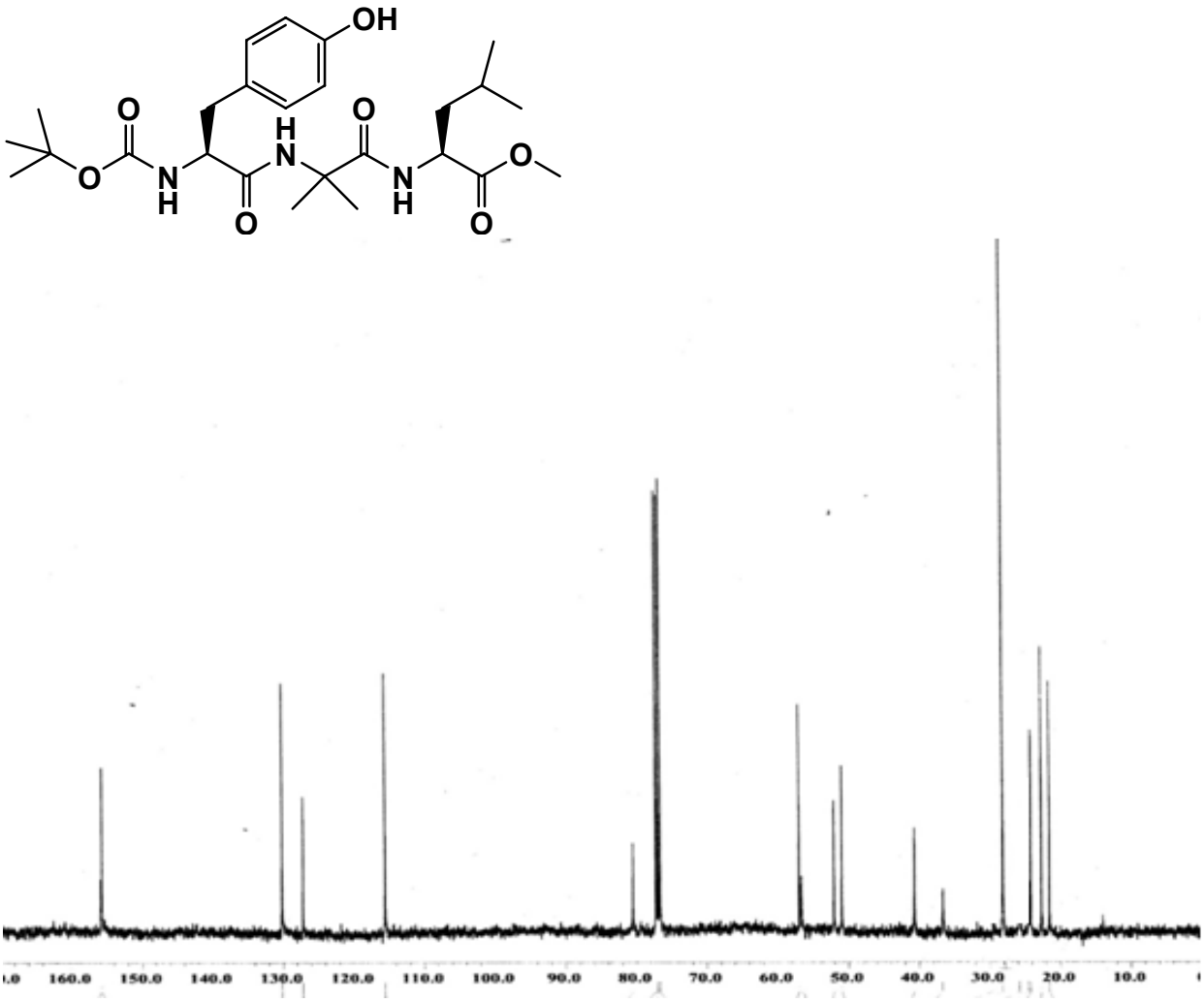
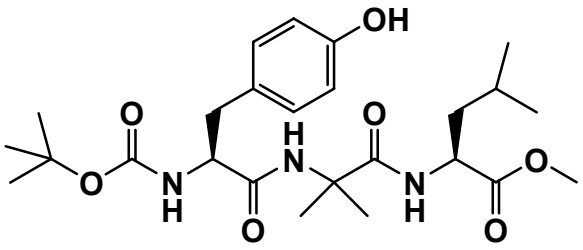


Figure S13: ^{13}C NMR (100 MHz, CDCl3) spectra of Boc-Tyr-Aib-Leu-OMe **(1)**



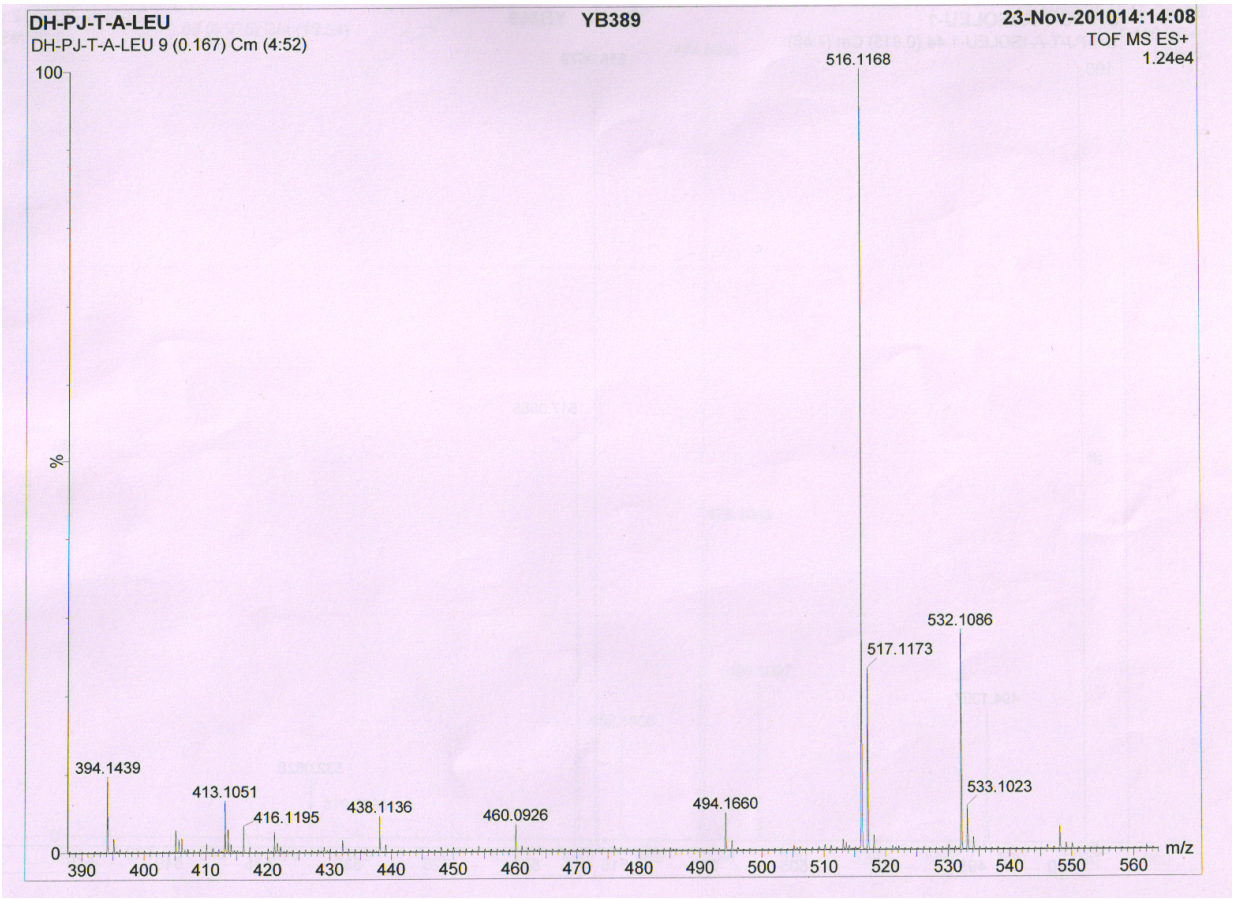


Figure S14: Mass spectra of Boc-Tyr-Aib-Leu-OMe **(1)**

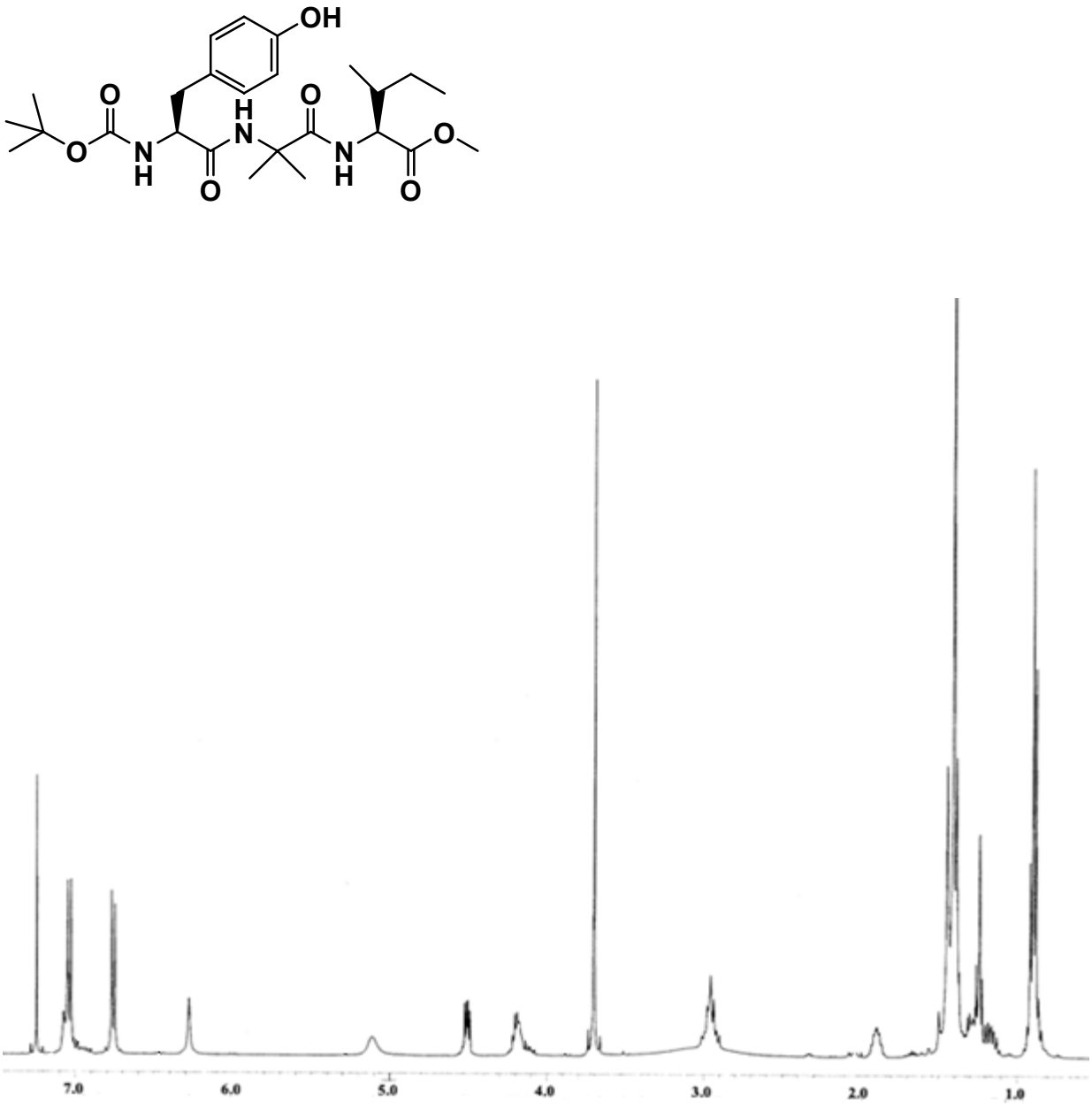
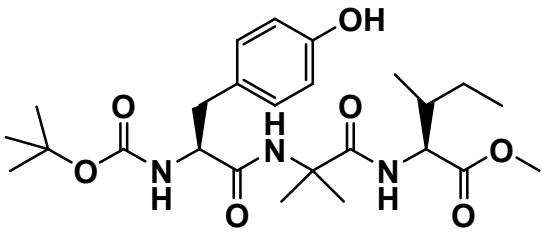


Figure S15: ^{1}H NMR (400 MHz, CDCl3) spectra of Boc-Tyr-Aib-Ileu-OMe **(2)**



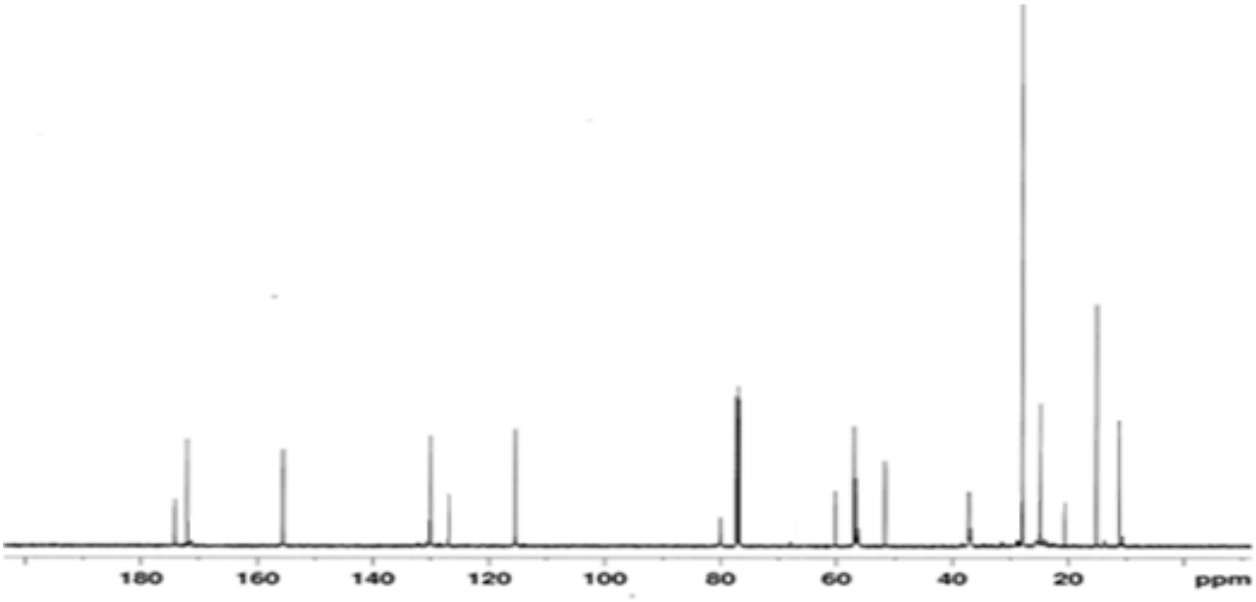
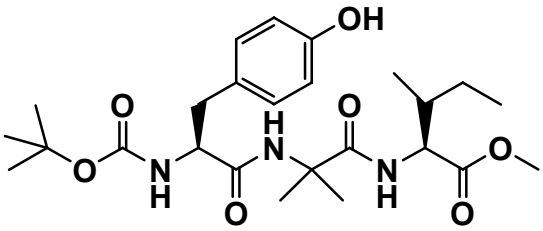


Figure S16: ^{13}C NMR (125 MHz, CDCl3) spectra of Boc-Tyr-Aib-Ileu-OMe (2)



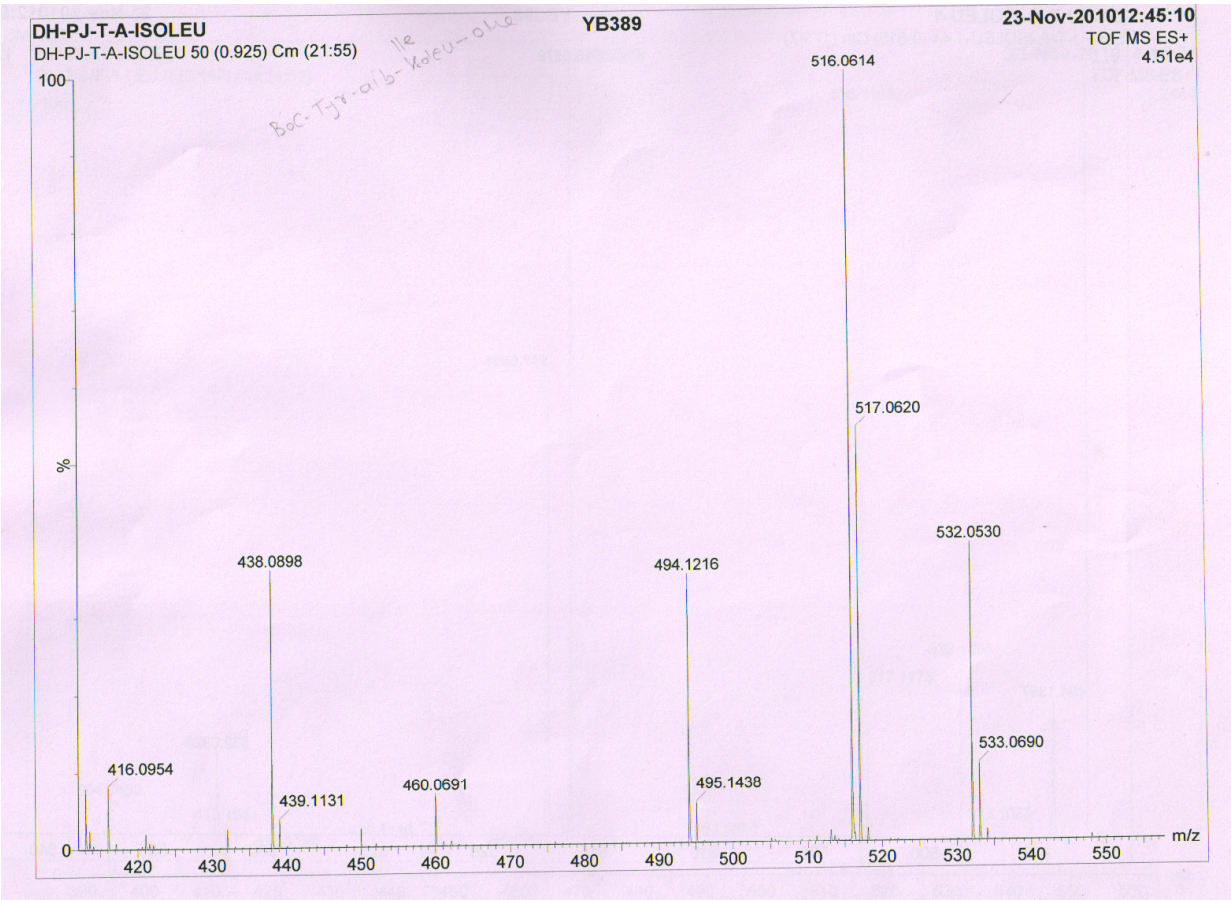
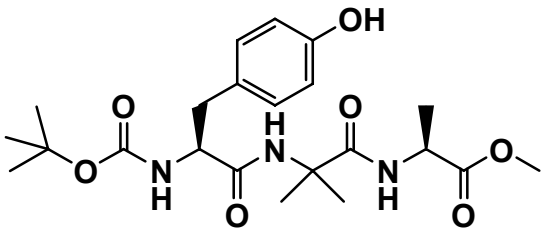


Figure S17: Mass spectra of Boc-Tyr-Aib-Ileu-OMe (2)



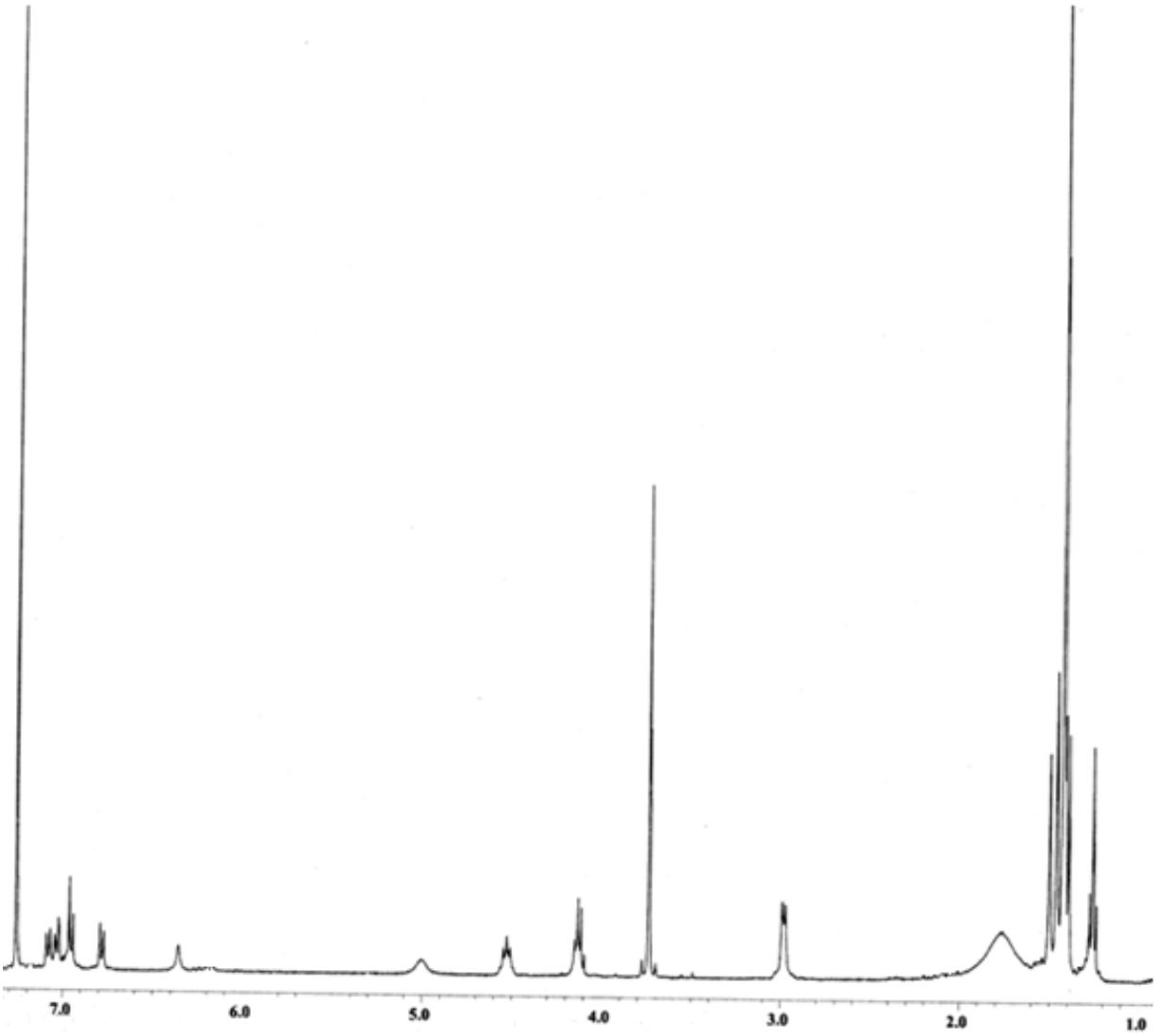


Figure S18: ^{1}H NMR (400 MHz, CDCl3) spectra of Boc-Tyr-Aib-Ala-OMe (3)

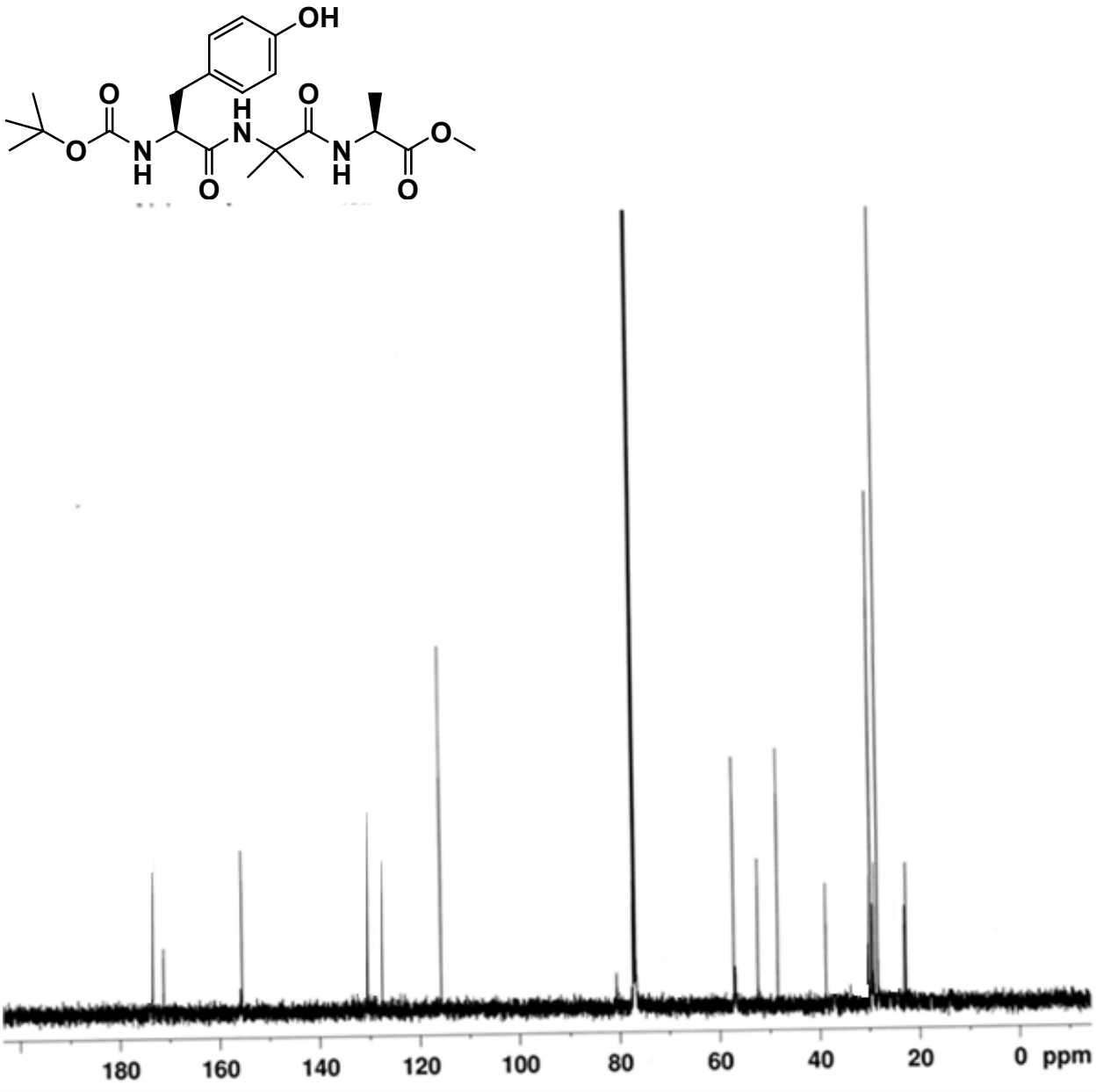
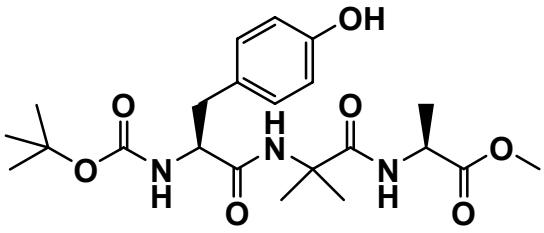


Figure S19: ^{13}C NMR (125 MHz, CDCl3) spectra of Boc-Tyr-Aib-Ala-OMe (3)



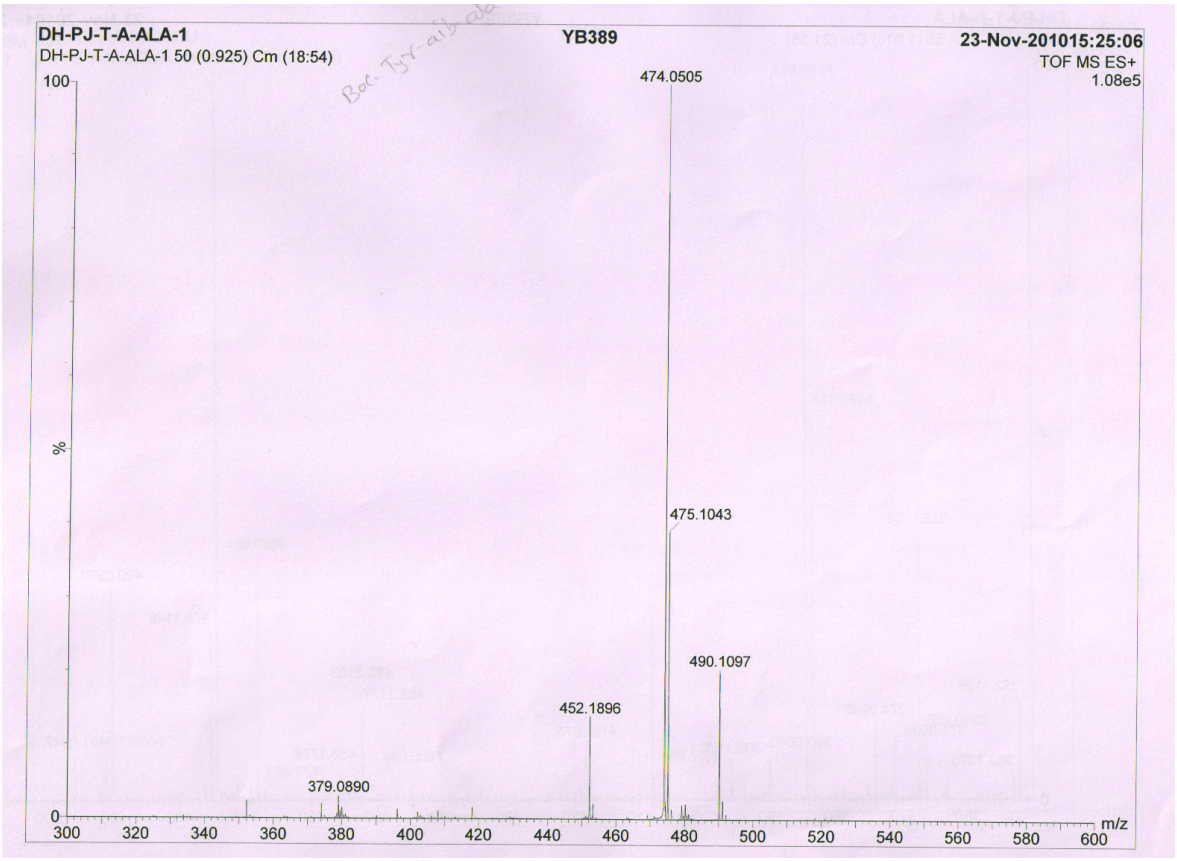


Figure S20: Mass spectra of Boc-Tyr-Aib-Ala-OMe (3)

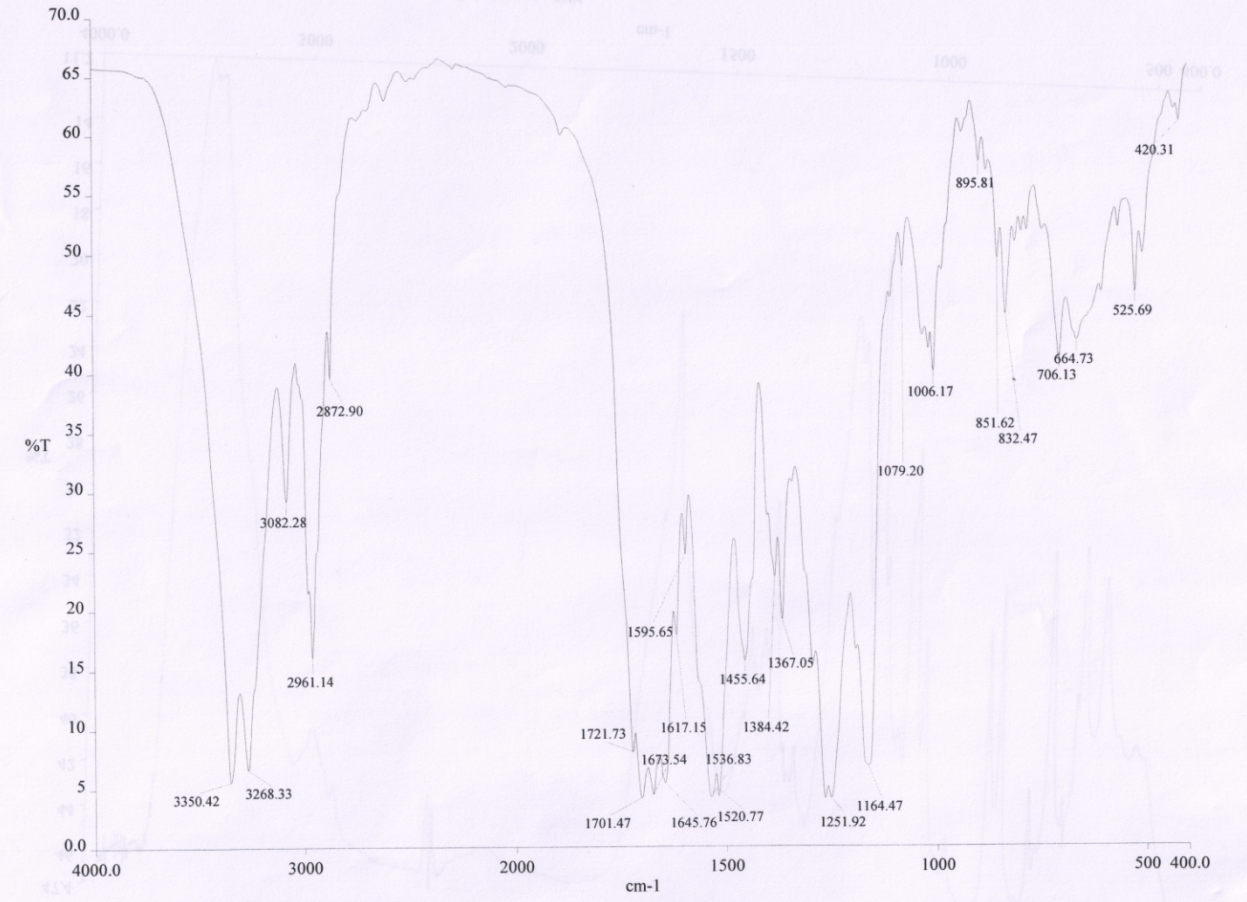


Fig-S21: FTIR spectra of BOC-Tyr-Aib-Leu-OMe(1) in solid state

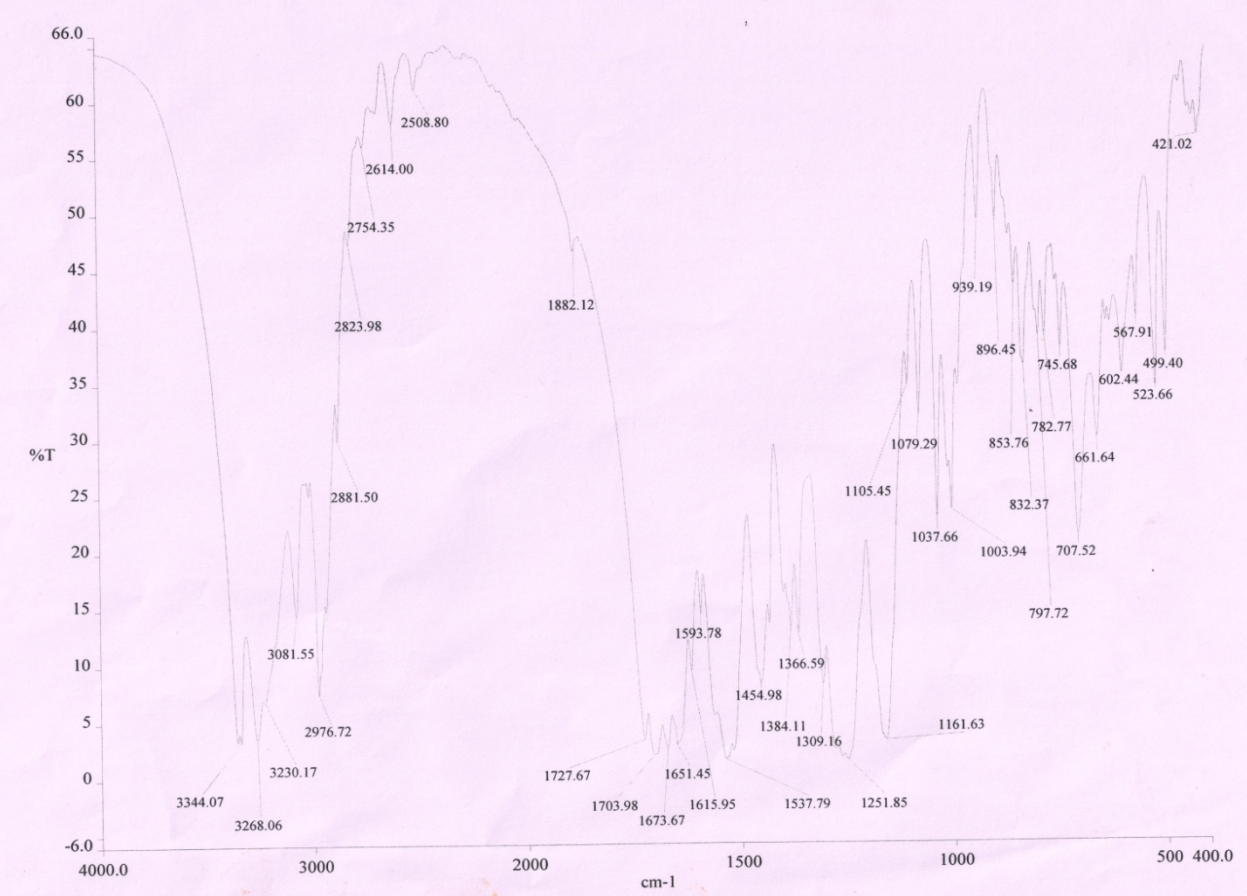


Fig-S22 : FTIR spectra of BOC-Tyr-Aib-Ileu-OMe (2) in solid state

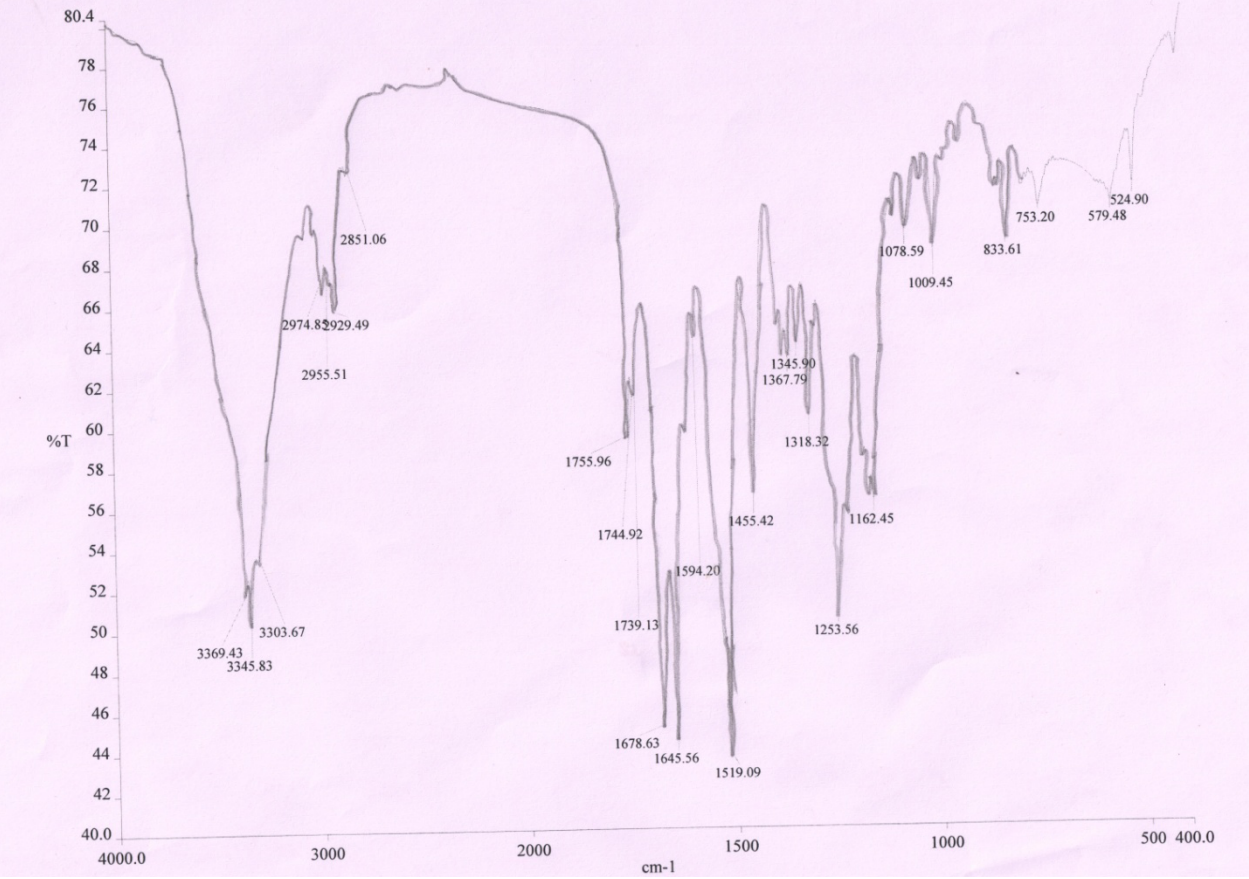


Fig-S23 : FTIR spectra of BOC-Tyr-Aib-Ala-OMe (3) in solid state

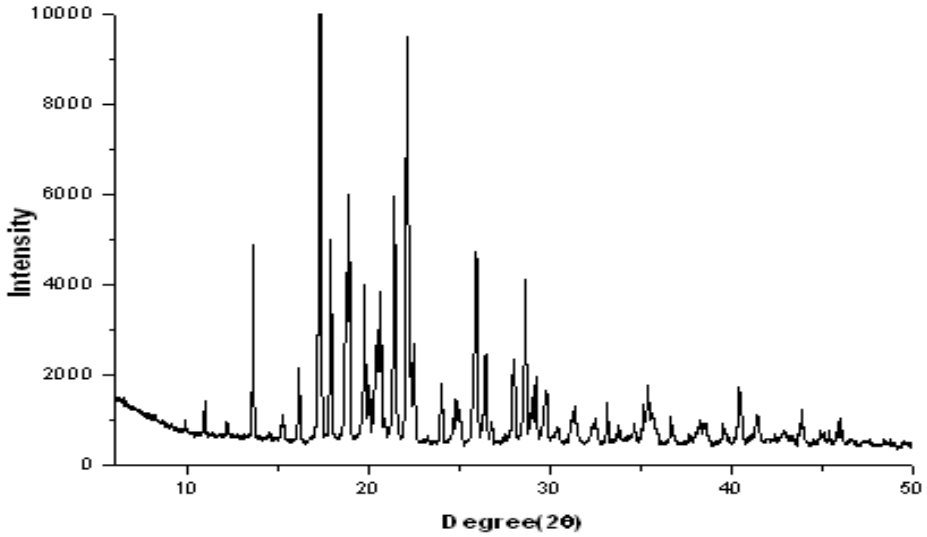


Fig-S24 : WAXS spectra of BOC-Tyr-Aib-Leu-OMe (1).

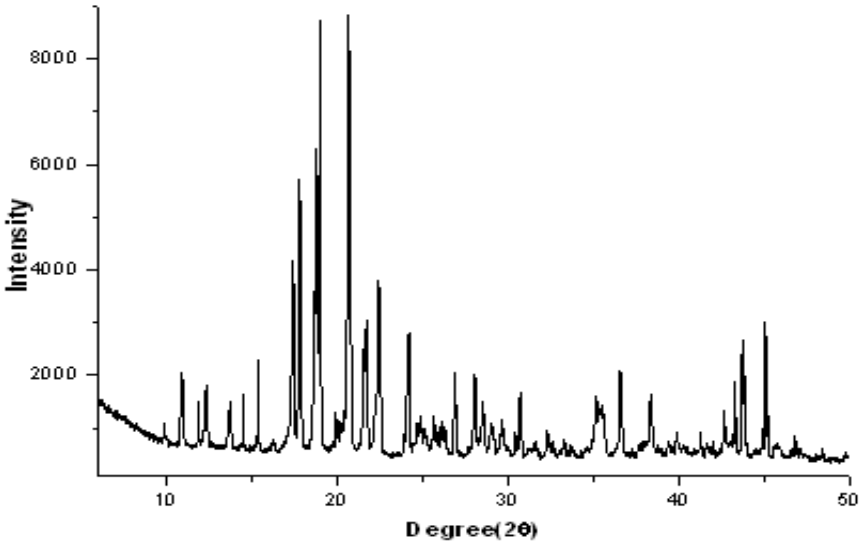


Fig-S25 : WAXS spectra of BOC-Tyr-Aib-Ile-OMe (2).

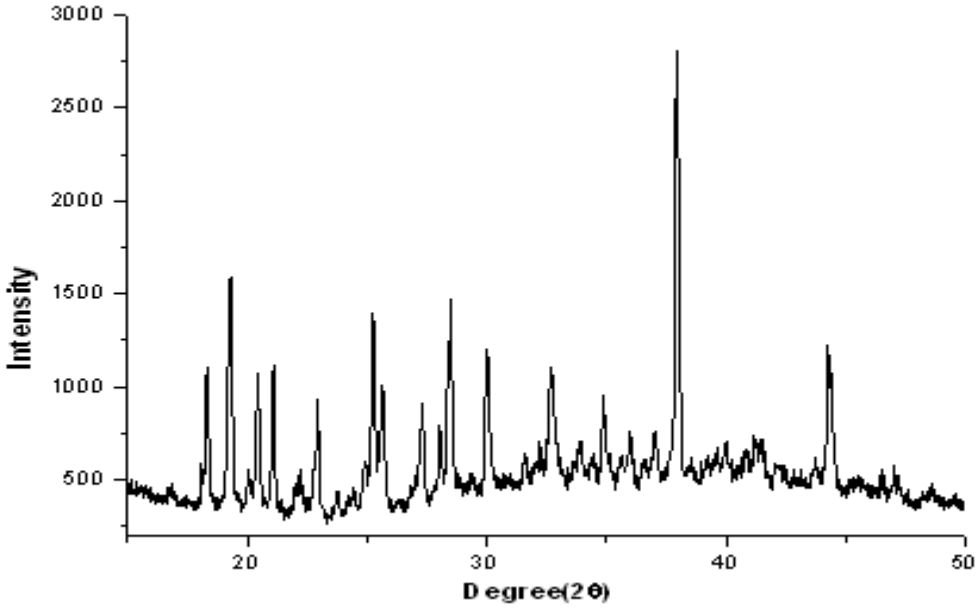


Fig-S26 : WAXS spectra of BOC-Tyr-Aib-Ala-OMe (3).