Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supporting information

Tripeptide based super-organogelators: structure and function

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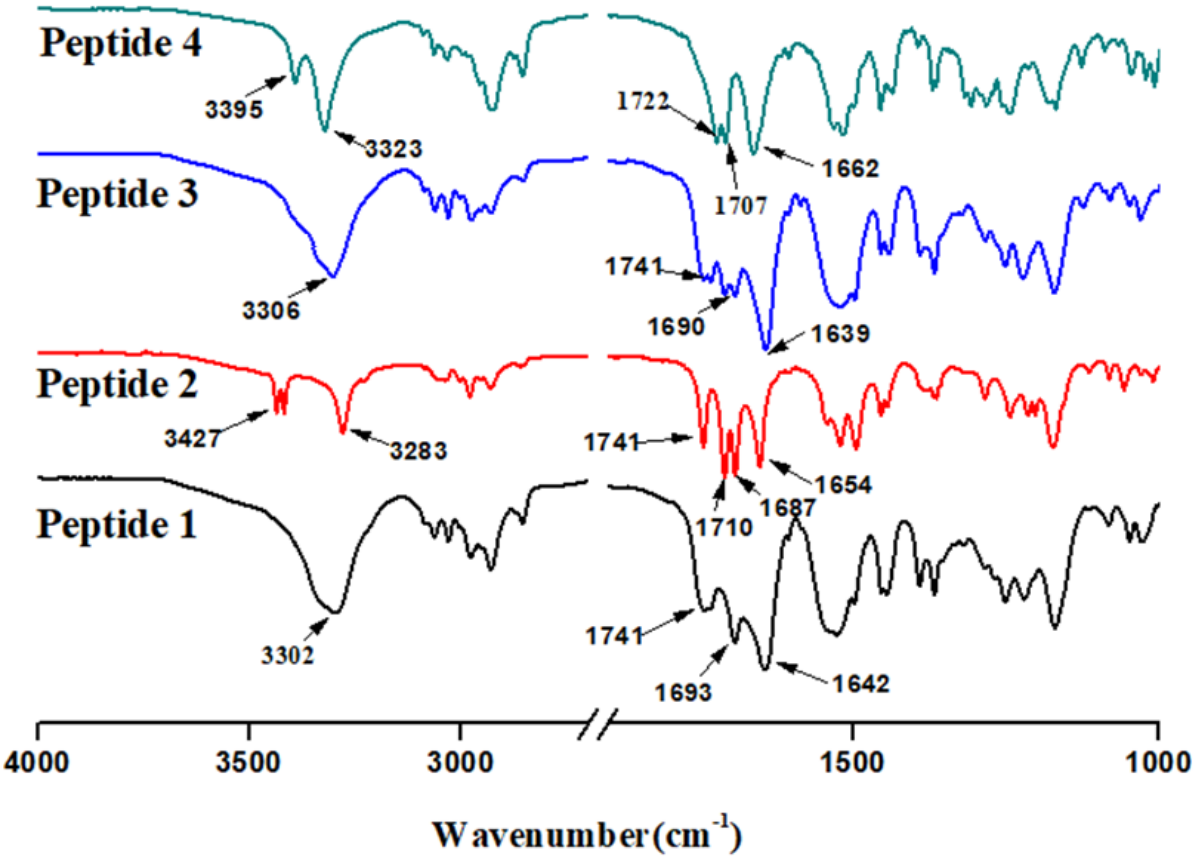
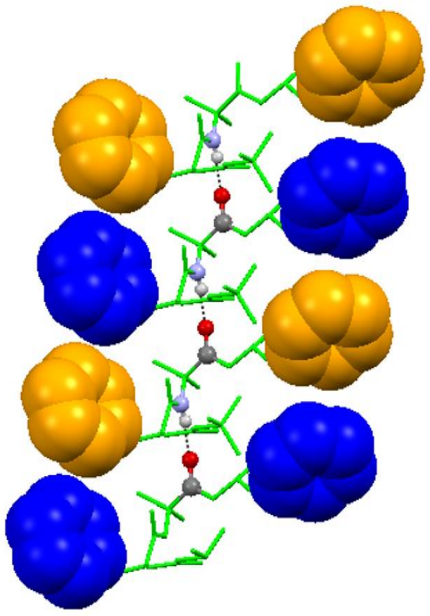
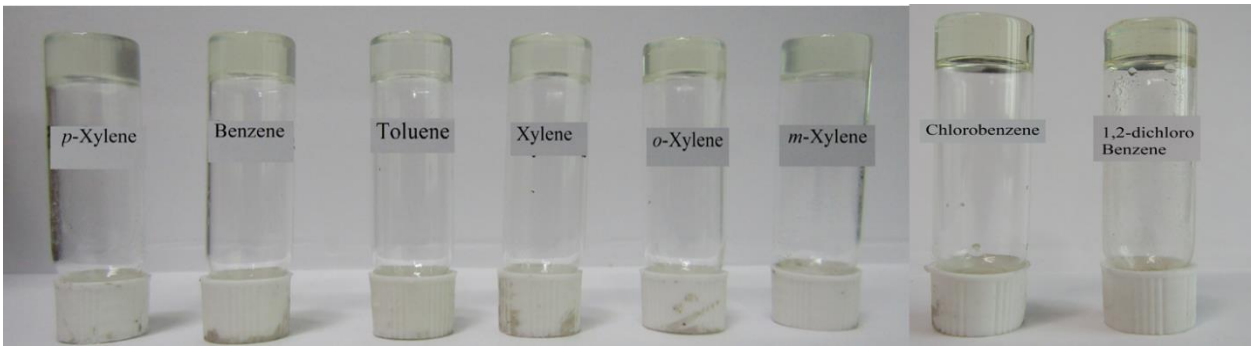


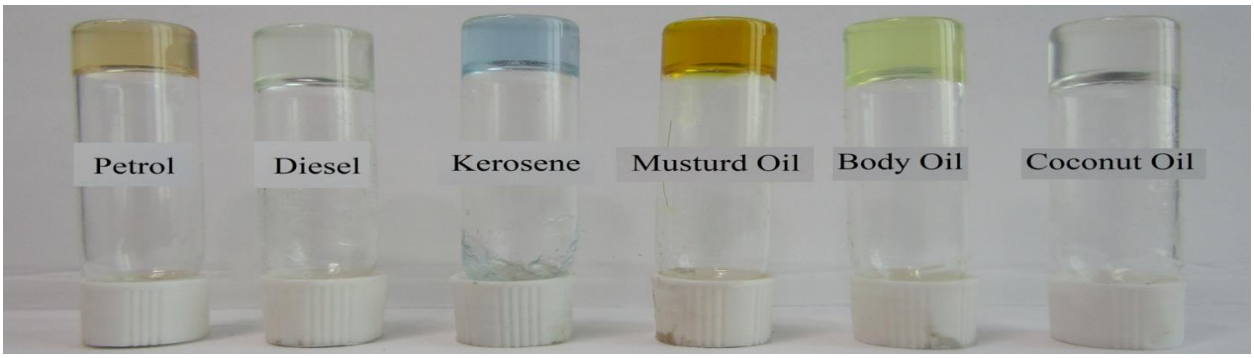
ESI Figure 1: FT-IR spectra of tripeptides **1-4**.



ESI Figure 2: Columnar packing of peptide **2** through intermolecular hydrogen bonding.



ESI Figure 3: The transparent gel of peptide **3** in aromatic solvents.



ESI Figure 4: The transparent gel of peptide **1** in oil.

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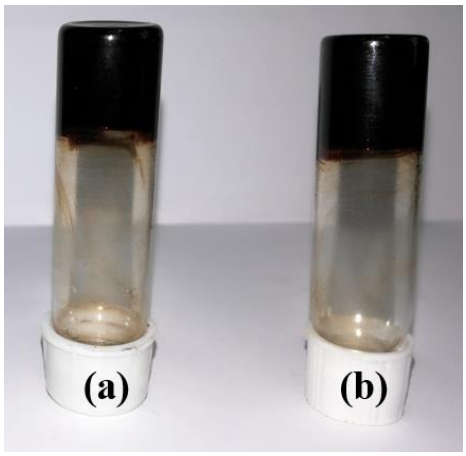
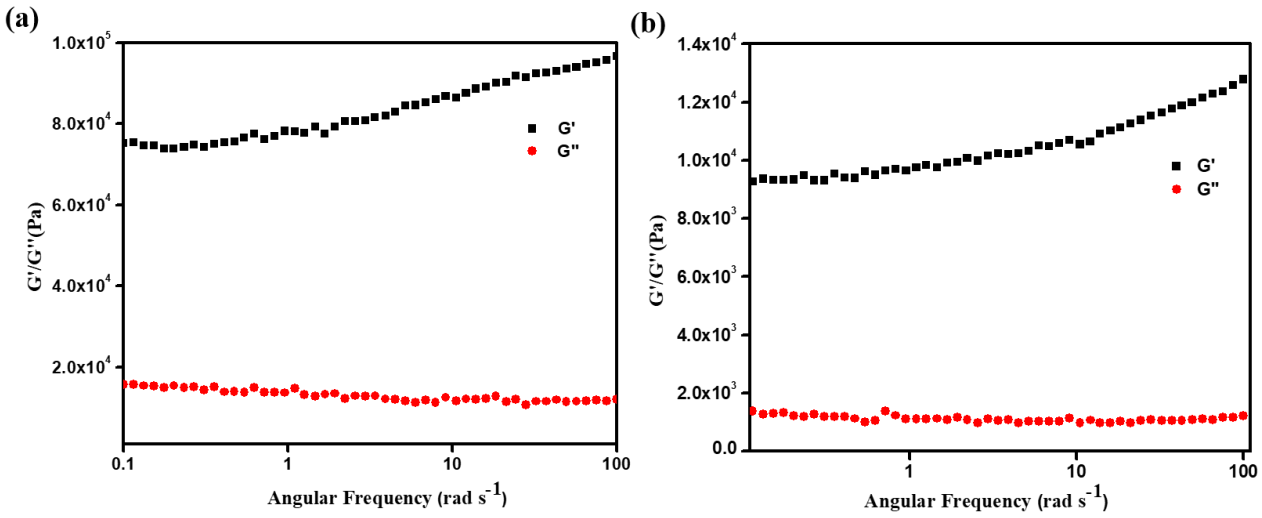
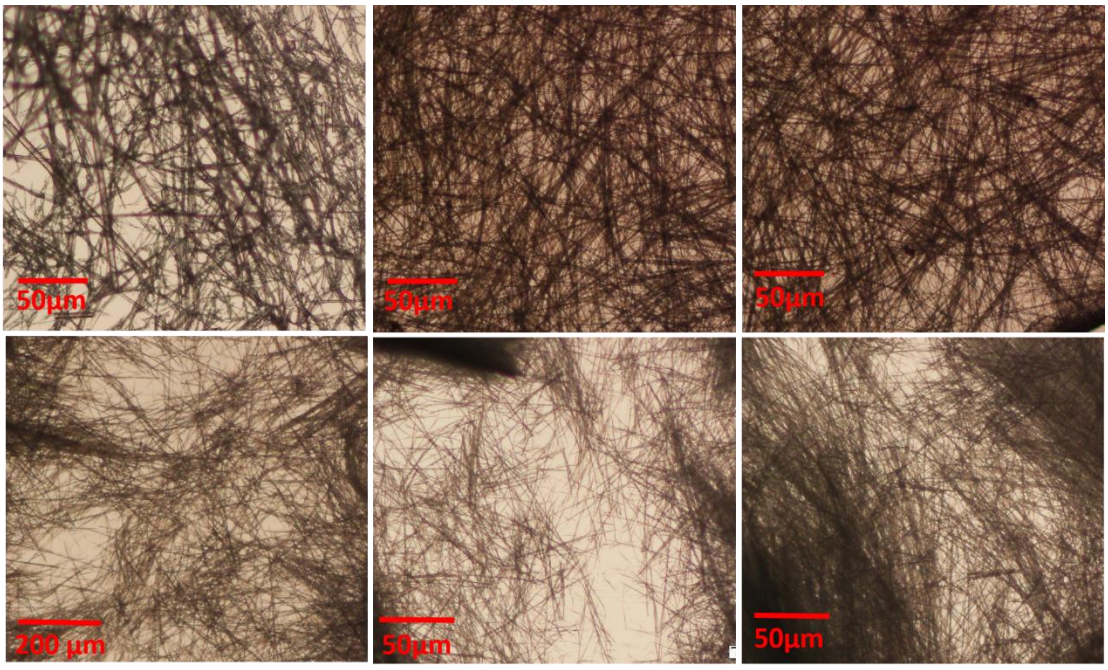


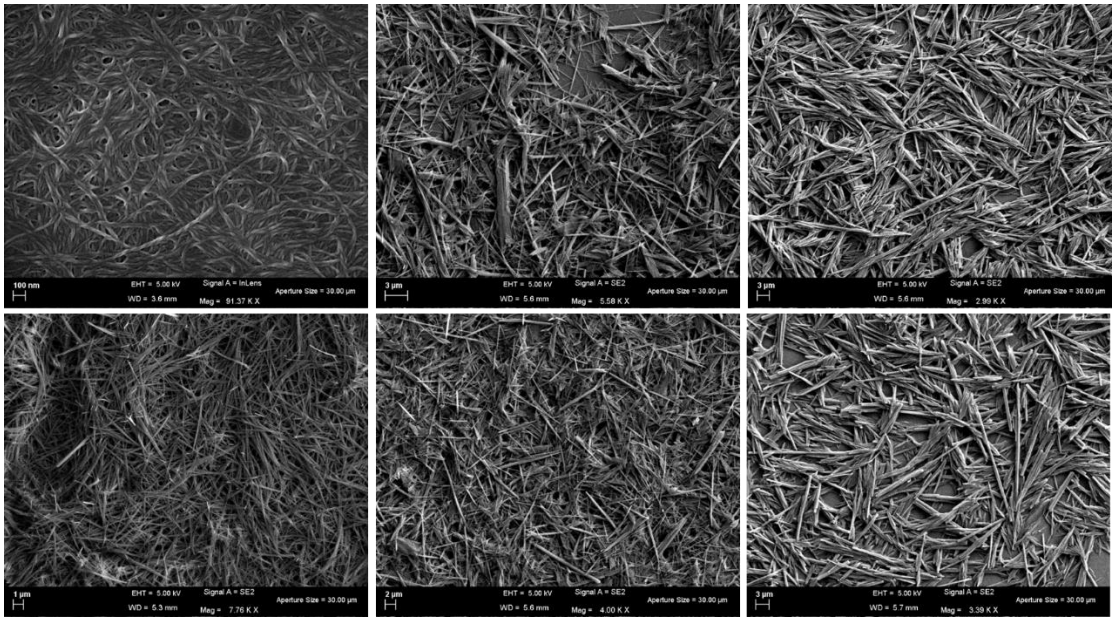
ESI Figure 5: The gelation of (a) peptide **1** (b) peptide **3** in crude oil.



ESI Figure 6: Rheology measurement of the gel from diesel of (a) peptide **1** and (b) peptide **3**. The storage modulus G'' of the gel (1 wt%) was found to be larger than the loss modulus G" indicates an elastic rather than viscous material.



ESI Figure 7: Optical Microscope images of peptide **1** in (a) Xylene (b) 1,2-Dichlorobenzene (c) Toluene (d) m-xylene (e) p-xylene (f) o-Xylene.



ESI Figure 8: FE-SEM images of the xerogel of peptide 3 from different solvent (a) 1,2-dichlorobenzene (b) *m*-Xylene (c) Toluene (d) Xylene (e) *p*-Xylene (f) *o*-Xylene.

ESI Table 1: Important torsional angles for peptide **2**

	Phe	Aib	Phe
ϕ/°	-60.91	60.54	-60.43
ψ/°	149.47	30.57	137.26

ESI Table 2: MGC of peptide **1** and peptide **3** in different solvents

Solvent/Oil	Peptide **1**(in mg/ml)	Peptide **3** (in mg/ml)
Xylene	2.5	2.2
m-Xylene	2.7	2.6
o-Xylene	2.7	2.7
p-Xylene	2.6	2.7
Benzene	3.1	3.0
Toluene	2.8	2.7
1,2-dichlorobenzene	4.5	4.1
Chlorobenzene	6.0	4.8
Petrol	1.6	1.4
Diesel	1.2	1.4
Kerosene	1.7	1.6
Mustard Oil	1.7	1.7
Body Oil	1.9	2.0
Olive Oil	2.1	2.1

ESI Table 3: T_{gel} in ^{o}C of the gel of the peptide 1 and peptide 3

Solvent/Oil	Peptide **1**(T_{gel} in ^{o}C)	Peptide **3** (T_{gel} in ^{o}C)
Xylene	48.3	48.2
m-Xylene	51.0	51.4
o-Xylene	49.5	51.5
p-Xylene	49.4	47.9
Benzene	49.0	48.1
Toluene	48.4	47.8
1,2-dichlorobenzene	48.5	48.9
Chlorobenzene	48.4	49.1
Petrol	74.3	74.2
Diesel	74.7	75.8
Kerosene	74.3	73.5
Mustard Oil	73.2	74.3
Body Oil	75.1	75.9
Olive Oil	74.5	75.0

Experimental

Synthesis of peptide 1:

Boc-Phe-Aib-OMe: This compound is synthesized according to previous report.[S1]

^{1}H NMR (500MHz, $CDCl_3$, δ in ppm): 7.26-7.27 (m, 2H, phenyl ring protons), 7.21-7.22 (m, 2H, phenyl ring protons),7.22-7.20(m, 1H, phenyl ring proton) 6.48 (s, 1H, Aib NH), 5.22-5.19(s, 1H, Phe NH), 4.22 (m, 1H, Phe $C^{\alpha}H$), 3.70 (s, 3H,-OCH3), 2.95-2.90 (m, 2H, Phe $C^{\beta}H$), 1.44 (s, 6H, Aib $C^{\alpha}H$), 1.41 (s, 9H, BOC -CH_3). ^{13}C NMR (125MHz, $CDCl_3$, δ in ppm): 174.17, 170.44, 156.31, 136.86, 129.54, 128.26, 126.95, 80.20, 56.43, 56.40, 52.65, 38.54, 28.32, 24.76; Mass spectral data TOF-MS m/z: $[M+Na]^+$ = 387 with an isotope peak at 388, $[M+K]^+$ = 403 with an isotope peak at 404; $[M\text{-}Boc+Na]^+$ = 287 with an isotope peak at 288; $[M\text{-}Boc+H]^+$ = 265 with an isotope peak at 266; M_{cal} =364;

Boc-Phe-Aib-OH: This compound is synthesized according to previous report**.**[S1]

^{1}H NMR (400 MHz, DMSO-d_6, δ in ppm): 12.39-12.16 (b, 1H, Acid OH), 8.05 (s, 1H, Aib NH), 7.26-7.17 (m, 5H, phenyl ring protons), 6.76 (s, 1H, Phe -NH), 4.20 (m, 1H, Phe $C^{\alpha}H$), 2.96-2.91 (m, 1H,Phe $C^{\beta}H$), 2.74-2.68 (m, 1H,Phe $C^{\beta}H$), 1.36 (s, 6H, Aib $C^{\beta}H$), 1.29 (s, 9H, BOC -CH3). ^{13}C NMR (100MHz, DMSO-d_6, δ in ppm): 175.48, 170.88, 155.10, 138.10, 129.31, 127.94, 126.13, 77.98, 55.36, 54.92, 37.19, 28.14, 24.77; Mass spectral data TOF-MS m/z: $[M+H]^+$ = 351,

$[M+Na]^+$ = 372 with an isotope peak at 373, $[M-Boc+Na]^+$ = 273 with an isotope peak at 274; $[M-Boc+H]^+$ = 251 with an isotope peak at 252; M_{cal} =350;

Boc-Phe-Aib-Phe-OMe (1). 2.1 g (6 mmol) of Boc-Phe-Aib-OH was dissolved in 25 mL DCM in an ice-water bath. H-Phe-OMe was isolated from 2.15 g (10 mmol) of the corresponding salt of methyl ester hydrochloride by neutralization and subsequent extraction with ethyl acetate and the ethyl acetate extract was concentrated to 10 mL. It was then added to the reaction mixture, followed immediately by 1.85 g (9 mmol) dicyclohexylcarbodiimide (DCC) and 1.21 g (9 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 x 50 mL), brine (2 x 50 mL), 1M sodium carbonate (3 x50 mL) and brine (2 x50 mL) and dried over anhydrous sodium sulfate. It was evaporated in a vacuum to yield Boc-Phe-Aib-Phe-OMe. Purification was done by silica gel column (60-120 mesh size) with an ethyl acetate and hexane mixture 1: 4 as the eluent. Yield 1.93 g (3.78 mmol, 63%).

^{1}H NMR (400MHz, $CDCl_3$, δ in ppm): 7.31-7.25 (t, 4H, phenyl ring protons), 7.26-7.22 (t, 2H, phenyl ring protons), 7.21-7.19 (d, 2H, phenyl ring proton), 7.12-7.10 (d, 2H, phenyl ring proton); 6.85 (s, 1H, NH), 6.17 (s,1H ,NH), 5.08 (s, 1H, NH), 4.82-4.78 (q, 1H, Phe $C^{\alpha}H$), 4.24-4.18 (q, 1H, Phe $C^{\alpha}H$), 3.69 (s, 3H, -OCH3), 3.17-3.10 (m, 1H, Phe $C^{\beta}H$), 3.10-3.02 (q, 2H, Phe $C^{\beta}H$), 3.00-2.94 (q, 1H, Phe $C^{\beta}H$), 1.41 (s, 9H, BOC -CH_3), 1.36 (s, 3H, Aib $C^{\alpha}H$), 1.32 (s, 3H, Aib $C^{\alpha}H$),. ^{13}C NMR (100MHz, $CDCl_3$, δ in ppm): 173.50, 171.88, 170.56, 155.50, 136.72, 135.99, 129.33, 129.26, 128.71, 128.43, 126.98, 80.29, 57.10, 56.32, 53.39, 52.2, 38.17, 37.70, 28.22, 25.18, 24.53. Mass spectral data TOF-MS m/z: $[M+Na]^+$ = 534 with an isotope peak at 535, $[M+K]^+$ = 550 with an isotope peak at 551;M_{cal} =511;

Synthesis of peptide 2:

Boc-Phe-Ala-OMe: This compound is synthesized according to previous report**.**[S2]

^{1}H NMR (400MHz, $CDCl_3$, δ in ppm): 7.29-7.26 (m, 2H, phenyl ring protons), 7.23-7.18 (m, 2H, phenyl ring protons), 6.42 (s, 1H, Ala NH), 4.98(s, 1H, Phe NH), 4.53-4.46 (m, 1H, Phe $C^{\alpha}H$), 4.38-4.31 (m, 1H, Ala $C^{\alpha}H$), 3.69 (s, 3H,-OCH3), 3.09-3.00 (m, 2H, Phe $C^{\beta}H$), 1.39 (s, 9H, BOC -CH_3), 1.33-1.31 (d, J=6.81, 3H, Ala -CH_3). ^{13}C NMR (100MHz, $CDCl_3$, δ in ppm): 173.05, 170.93, 154.92, 136.72, 129.59, 128.86, 127.18, 79.16, 55.87, 52.63, 48.32, 38.55, 28.46, 18.58;

Mass spectral data TOF-MS m/z: $[M+Na]^+$ = 372 with an isotope peak at 373, $[M+K]^+$ = 388 with an isotope peak at 389, $[M\text{-}Boc+Na]^+$ = 273 with an isotope peak at 274; $[M\text{-}Boc+H]^+$ = 251; M_{cal} =350;

Boc-Phe-Ala-OH. To 2.80 g (8 mmol) of Boc-Phe-Ala-OMe, 25 mL MeOH and 2(M) 15 mL NaOH were added and the progress of saponification was monitored by thin layer chromatography (TLC). The reaction mixture was stirred. After10 h, methanol was removed under vacuum; the residue was dissolved in 50 mL of water and washed with diethyl ether (2 X 50mL). Then the pH of the aqueous layer was adjusted to 2 using 1M HCl and it was extracted with ethyl acetate (3 X 50 mL). The extracts were pooled, dried over anhydrous sodium sulfate, and evaporated under vacuum to obtained compound as a waxy solid. Yield: 2.46 g (7.30 mmol, 91.20%).

^{1}H NMR (400 MHz, DMSO-d_6, δ in ppm): 12.66-12.50 (br, 1H, Acid OH), 8.23 (s, 1H, Ala-NH), 7.31-7.27 (m, 3H, phenyl ring protons), 7.23-7.20 (m, 2H, phenyl ring protons), 6.88 (s, 1H, Phe-NH), 4.26-4.4.22 (m, 2H, Phe C$^{\alpha}$H and Ala C$^{\alpha}$H), 3.02-2.98 (m, 1H,Phe C$^{\beta}$H), 2.75-2.69 (m, 1H,Phe C$^{\beta}$H), 1.31 (s, 9H, BOC -CH3), 1.24 (s, 3H, Ala CH_3). ^{13}C NMR (100MHz, DMS0-d_6, δ in ppm): 174.14, 171.66, 155.29, 138.29, 129.28, 128.02, 126.18, 78.00, 55.52, 47.54, 37.44, 28.17, 17.28;

Boc-Phe-Ala-Phe-OMe (2). 2.01 g (6 mmol) of Boc-Phe-Ala-OH was dissolved in 25 mL DCM in an ice-water bath. H-Phe-OMe was isolated from 2.15 g (10 mmol) of the corresponding salt of methyl ester hydrochloride by neutralization and subsequent extraction with ethyl acetate and the ethyl acetate extract was concentrated to 10 mL. It was then added to the reaction mixture, followed immediately by 1.85 g (9 mmol) dicyclohexylcarbodiimide (DCC) and 1.21 g (9 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 x 50 mL), brine (2 x 50 mL), 1M sodium carbonate (3 x50 mL) and brine (2 x50 mL) and dried over anhydrous sodium sulfate. It was evaporated in a vacuum to yield Boc-Phe-Ala-Phe- OMe. Purification was done by silica gel column (60-120 mesh size) with an ethyl acetate and hexane mixture 1: 4 as the eluent. Yield 1.88 g (3.8 mmol, 63%).

^{1}H NMR (400MHz, $CDCl_3$, δ in ppm): 7.28-7.24 (t, 4H, phenyl ring protons), 7.22-7.18 (t, 2H, phenyl ring protons), 7.16-7.12 (d, 2H, phenyl ring proton), 7.10-7.07 (d, 2H, phenyl ring proton), 6.84-6.80 (d, 1H, NH), 6.7(s,1H, NH), 5.16-5.12 (s, 1H, NH), 4.81-4.75 (q, 1H, Phe $C^{\alpha}H$), 4.5-4.42(q, 1H, Phe $C^{\alpha}H$), 4.4-4.3 (m,1H, Ala $C^{\alpha}H$) , 3.67 (s, 3H,-OCH3), 3.08-3.03 (m, 2H, Phe $C^{\beta}H$), 3.04-2.94 (m, 2H, Phe $C^{\beta}H$), 1.38 (s, 9H, BOC -CH_3), 1.26-1.24 (d,3H, Ala CH_3). ^{13}C NMR (100MHz, $CDCl_3$, δ in ppm): 171.65, 171.45, 171.08, 155.40, 136.48, 135.75, 129.31, 129.15, 128.52, 127.07, 126.83, 80.09, 55.42, 53.39, 52.24, 48.74, 38.17, 37.77, 28.17, 18.28. Mass spectral data TOF-MS m/z: $[M+Na]^+$ = 520 with an isotope peak at 521, $[M+K]^+$ = 536 ,M_{cal} =497.

Synthesis of peptide 3:

Boc-Phe-PG-OMe: 2.65 g (10 mmol) of Boc-Phe-OH was dissolved in 25 mL DCM in an ice-water bath. H-PG-OMe was isolated from 3.01 g (15 mmol) of the corresponding methyl ester hydrochloride by neutralization and subsequent extraction with ethyl acetate and the ethyl acetate extract was concentrated to 10 mL. It was then added to the reaction mixture, followed immediately by 2.47 g (12 mmol) N, N'-dicyclohexylcarbodiimide (DCC) and 1.62 g (12 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 X 50 mL), brine (2x50 mL), 1M sodium carbonate (3 X 50 mL) and brine (2 X 50 mL) and dried over anhydrous sodium sulfate. It was evaporated in a vacuum to yield Boc-Phe-PG-OMe as a white solid.

^{1}H NMR (400MHz, $CDCl_3$, δ in ppm): 7.30-7.26 (t, 4H, phenyl ring protons), 7.26-7.24 (t, 2H, phenyl ring protons), 7.23-7.21 (d, 2H, phenyl ring proton), 7.16-7.12 (d, 2H, phenyl ring proton), 7.01 (s, 1H, NH proton), 5.49-5.47 (s, 1H, NH proton), 5.05 (m, 1H, Phe $C^{\alpha}H$), 4.43 (b, 1H, Phe $C^{\alpha}H$), 3.65 (s, 3H,-OCH3), 3.08-3.00 (m, 2H, Phe $C^{\beta}H$), 1.37 (s, 9H, BOC -CH_3). ^{13}C NMR (100MHz, $CDCl_3$, δ in ppm):170.65, 170.60, 155.29, 136.39, 136.10, 129.30, 128.80, 128.41, 127.14, 126.81, 80.16, 56.38, 55.40, 52.68, 28.15 ; Mass spectral data TOF-MS m/z: $[M+Na]^+$ = 435 with an isotope peak at 436, $[M-Boc+Na]^+$ = 335 with an isotope peak at 336; $[M-Boc+H]^+$ = 313 ;$[2M+Na]^+$ =847 with an isotope peak at 848. M_{cal} =412;

Boc-Phe-PG-OH. To 2.88 g (7mmol) of Boc-Phe-PG-OMe, 25 mL MeOH and 2(M) 15 mL NaOH were added and the progress of saponification was monitored by thin layer chromatography (TLC). The reaction mixture was stirred. After10 h, methanol was removed under vacuum; the

residue was dissolved in 50 mL of water and washed with diethyl ether (2 X 50mL). Then the pH of the aqueous layer was adjusted to 2 using 1M HCl and it was extracted with ethyl acetate (3 X 50 mL). The extracts were pooled, dried over anhydrous sodium sulfate, and evaporated under vacuum to obtained compound as a waxy solid.

^{1}H NMR (400MHz, $CDCl_3$, δ in ppm): 12.9(b,1H –COOH proton): 8.66-8.56 (d, 1H, NH proton), 7.46-7.42 (d, 1H, phenyl ring protons), 7.42-7.38 (d, 1H, phenyl ring protons), 7.38-7.35 (d, 2H, phenyl ring proton), 7.35-7.30 (m, 2H, phenyl ring proton), 7.29-7.27 (d, 1H, phenyl ring proton) ,7.27-7.23 (d, 2H, phenyl ring proton), 7.21-7.15 (m, 1H, phenyl ring proton), 7.01-6.93 (d, 1H, NH proton), 5.39-5.34 (t, 1H, Phe $C^{\alpha}H$), 4.38-4.28 (m, 1H, Phe $C^{\alpha}H$), 3.05-2.9 (m, 1H, Phe $C^{\beta}H$), 2.78-2.64 (m, 1H, Phe $C^{\beta}H$), 1.3 (s, 9H, BOC -CH_3).^{13}C NMR (100MHz, $CDCl_3$, δ in ppm):171.80 171.60, 155.22, 138.17, 137.05, 129.26, 128.53, 127.99, 127.56,127.26, 126.19, 78.08, 56.24, 55.47, 28.13 ; Mass spectral data TOF-MS m/z: $[M+Na]^+$ = 421 with an isotope peak at 422,; $[M-Boc+Na]^+$ = 321 with an isotope peak at 322; $[M-Boc+H]^+$ = 299; M_{cal} =398;

Boc-Phe-PG-Phe-OMe (3). 2.388 g (6 mmol) of Boc-Phe-PG-OH was dissolved in 25 mL DCM in an ice-water bath. H-Phe-OMe was isolated from 2.15 g (10 mmol) of the corresponding salt of methyl ester hydrochloride by neutralization and subsequent extraction with ethyl acetate and the ethyl acetate extract was concentrated to 10 mL. It was then added to the reaction mixture, followed immediately by 1.85 g (9 mmol) dicyclohexylcarbodiimide (DCC) and 1.21 g (9 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 x 50 mL), brine (2 x 50 mL), 1M sodium carbonate (3 x50 mL) and brine (2 x50 mL) and dried over anhydrous sodium sulfate. It was evaporated in a vacuum to yield Boc-Phe(1)-PG(2)-Phe(3)- OMe. Purification was done by silica gel column (60-120 mesh size) with an ethyl acetate and hexane mixture 1: 3 as the eluent.

^{1}H NMR (400MHz, $CDCl_3$, δ in ppm): 7.34-7.27 (5H, phenyl ring protons), 7.25-7.17 (5H, phenyl ring protons), 7.16-7.08 (4H, phenyl ring proton), 7.05-7.03 (d, 2H, NH), 7.02-7.00 (2H, phenyl ring protons), 6.63-6.61 (d, 1H, NH), 6.05 (s, 1H, PG $C^{\alpha}H$)5.32-5.28 (m, 1H, Phe $C^{\alpha}H$), 4.79-4.73 (m, 1H, Phe $C^{\alpha}H$), 3.63 (s, 3H,-OCH3), 3.17-3.13 (m, 1H, Phe $C^{\beta}H$), 3.08-3.02 (m, 2H, Phe $C^{\beta}H$), 2.98-2.94 (m, 1H, Phe $C^{\beta}H$), 1.39 (s, 9H, BOC -CH_3),. ^{13}C NMR (100MHz, $CDCl_3$, δ in

ppm): 171.84, 171.78, 171.33, 155.85, 136.94, 136.13, 129.78, 129.65, 129.53, 129.23, 128.99, 128.76, 128.59, 127.76, 127.61, 127.53, 127.28, 127.25, 127.12, 80.49, 57.36, 57.01, 54.09, 53.60, 38.05, 38.16, 28.66. Mass spectral data TOF-MS m/z: $[M+Na]^+$ = 582 with an isotope peak at 583, $[M+K]^+$ = 598 with an isotope peak at 599; $[M+ Na]^+$= 1141 with an isotopic peak at 1142;M_{cal} =559.

Synthesis of peptide 4:

Boc-Phe-AC-OMe: 2.65 g (10 mmol) of Boc-Phe-OH was dissolved in 25 mL DCM in an ice-water bath. H-AC-OMe was isolated from 2.89 g (15 mmol) of the corresponding methyl ester hydrochloride by neutralization and subsequent extraction with ethyl acetate and the ethyl acetate extract was concentrated to 10 mL. It was then added to the reaction mixture, followed immediately by 2.47 g (12 mmol) N,N'-dicyclohexylcarbodiimide (DCC) and 1.62 g (12 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 X 50 mL), brine (2x50 mL), 1M sodium carbonate (3 X 50 mL) and brine (2 X 50 mL) and dried over anhydrous sodium sulfate. It was evaporated in a vacuum to yield Boc-Phe-AC-OMe as a white solid. Yield: 2.55 g (6.3 mmol, 63%).

^{1}H NMR (400MHz, $CDCl_3$, δ in ppm): 7.3-7.22 (m, 5H, phenyl ring protons), 6.3 (s, 1H, NH proton), 5.2-5.16 (d, 1H, NH proton), 4.40-4.30 (m, 1H, Phe $C^{\alpha}H$), 3.67 (s, 3H, -OCH3), 3.08-3.02 (m, 2H, Phe $C^{\beta}H$), 1.94-1.88 (m,2H,cyclohexane ring), 1.79-1.71 (m, 2H, cyclohexane ring), 1.58-1.48 (m, 4H, cyclohexane ring), 1.41 (s, 9H, BOC -CH_3), 1.24-1.18 (m, 2H, cyclohexane ring). ^{13}C NMR (100MHz, $CDCl_3$, δ in ppm): 174.20, 170.46, 156, 136.86, 129.35, 128.55, 126.80, 80.20, 58.69, 55.50, 52.16, 37.61, 32.20, 31.93, 29.62, 28.18, 24.91, 21.14, 21.03. Mass spectral data TOF-MS m/z: $[M+Na]^+$ = 427 with an isotope peak at 428, $[M-Boc+Na]^+$ = 327 with an isotope peak at 305; $[M-Boc+H]^+$ = 251; M_{cal} =404;

Boc-Phe-Ac-OH. To 2.43 g (6 mmol) of Boc-Phe-AC-OMe, 25 mL MeOH and 2(M) 10 mL NaOH were added and the progress of saponification was monitored by thin layer chromatography (TLC). The reaction mixture was stirred. After10 h, methanol was removed under vacuum; the residue was dissolved in 50 mL of water and washed with diethyl ether (2 X 50mL). Then the pH of the aqueous layer was adjusted to 2 using 1M HCl and it was extracted with ethyl acetate (3 X

50 mL). The extracts were pooled, dried over anhydrous sodium sulfate, and evaporated under vacuum to obtained compound as a waxy solid.

^{1}H NMR (400MHz, DMSO-*d*$_6$, δ in ppm): 12.4-11.6 (b, 1H, COOH Proton), 7.78 (s, 1H, NH proton) , 7.39-7.28 (m, 4H, phenyl ring protons), 7.20-7.14 (t, 1H, phenyl ring protons), 6.86-6.82 (d, 1H, NH proton), 4.25-4.19 (m, 1H, Phe C$^{\alpha}$H), 2.96-2.90 (m, 1H, Phe C$^{\beta}$H), 2.76-2.70 (m, 1H, Phe C$^{\beta}$H), 1.68-1.58 (m,2H,cyclohexane ring), 1.52-1.4 (m, 4H, cyclohexane ring), 1.28 (s, 9H, BOC -CH_3), 1.24-1.21 (m, 4H, cyclohexane ring). ^{13}C NMR (100MHz DMSO-*d*$_6$, δ in ppm): 175.39, 171.29, 155.11, 138.15, 129.23, 127.95, 126.11, 77.94, 57.63, 55.53, 37.39, 31.75, 31.30, 28.08, 27.82, 24.94, 20.89. Mass spectral data TOF-MS m/z: $[M+Na]^+$ = 413 with an isotope peak at 414, , $[M-Boc+Na]^+$ = 313 with an isotope peak at 314; $[M-Boc+H]^+$ = 291; M_{cal} =390;

Boc-Phe-AC-Phe-OMe (4). 2.01 g (6 mmol) of Boc-Phe-Ala-OH was dissolved in 25 mL DCM in an ice-water bath. H-Phe-OMe was isolated from 2.15 g (10 mmol) of the corresponding salt of methyl ester hydrochloride by neutralization and subsequent extraction with ethyl acetate and the ethyl acetate extract was concentrated to 10 mL. It was then added to the reaction mixture, followed immediately by 1.85 g (9 mmol) dicyclohexylcarbodiimide (DCC) and 1.21 g (9 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 x 50 mL), brine (2 x 50 mL), 1M sodium carbonate (3 x50 mL) and brine (2 x50 mL) and dried over anhydrous sodium sulfate. It was evaporated in a vacuum to yield Boc-Phe-AC-Phe-OMe. Purification was done by silica gel column (60-120 mesh size) with an ethyl acetate and hexane mixture 1: 5 as the eluent. Yield 1.82 g (3.3mmol, 55%).

^{1}H NMR (400MHz, $CDCl_3$, δ in ppm): 7.29-7.25 (t, 4H, phenyl ring protons), 7.22-7.18 (t, 4H, phenyl ring protons), 7.15-7.11 (d, 2H, phenyl ring proton), 6.93 (s, 1H, NH), 4.96 (s,1H, NH), 4.81-4.75 (q, 1H, Phe C$^{\alpha}$H), 4.28-4.22 (q, 1H, Phe C$^{\alpha}$H), 3.67 (s, 3H,-OCH_3), 3.18-3.10 (m, 1H, Phe C$^{\beta}$H), 3.08-3.00 (m, 3H, Phe C$^{\beta}$H), 1.58 (s, 4H, cyclohexane ring), 1.39 (s, 9H, BOC -CH_3), 1.23(s,6H, cyclohexane ring). ^{13}C NMR (100MHz, $CDCl_3$, δ in ppm): 174.15, 172.52, 171.69. 156.11, 137.30, 136.72, 129.8, 129.25, 128.84, 127.43, 127.32, 80.91, 60.61, 56.65, 53.92, 52.57, 38.29, 32.30, 32.20, 30.11, 28.65, 25.38, 21.50, 21.44 .Mass spectral data TOF-MS m/z: $[M+Na]^+$ = 574 with an isotope peak at 575, M_{cal} =551

Synthesis of Peptide 5-7:

We have synthesized peptide 5, peptide 6 and peptide 7 by following the above procedure and characterized by ^{1}H NMR, ^{13}C NMR spectroscopy and Mass spectrometry.

Boc-Leu-Ala-Leu-OMe (5):

^{1}H NMR (400MHz, $CDCl_3$, δ in ppm): 7.14-7.10 (1H, d, NH Proton); 7.09-7.04 (1H, d, NH Proton); 5.25-5.20 (1H, d, NH Proton); 4.59-4.48 (2H, m, Leu $C^{\alpha}H$); 4.17-4.11 (1H, m, Ala $C^{\alpha}H$); 3.67 (3H, S, OMe); 1.61-1.56 (2H, m, Leu $C^{\beta}H$); 1.55-1.50 (2H, m, Leu $C^{\beta}H$); 1.48-1.43 (2H, m, Leu $C^{\gamma}H$); 1.38 (9H, s, Boc CH_3); 1.31-1.29 (3H, d, Ala CH_3); 0.94-0.90 (12H, m, Leu CH_3). ^{13}C NMR (100MHz, $CDCl_3$, δ in ppm): 173.57, 173.17, 172.45, 156.13, 80.32, 53.39, 52.64, 51.17, 49.02, 41.94, 41.50, 28.69, 25.12, 23.39, 23.17, 22.19, 18.43

Boc-Val-Ala-Val-OMe (6):

^{1}H NMR (400MHz, $CDCl_3$, δ in ppm): 7.24-7.20 (1H, d, NH Proton); 7.15-7.11 (1H, d, NH Proton); 5.45-5.41 (1H, d, NH Proton); 4.66-4.62 (1H, m, Ala $C^{\alpha}H$); 4.47-4.43 (1H, m, Val $C^{\alpha}H$); 4.02-3.96 43 (1H, m, Val $C^{\alpha}H$); 3.67 (3H, S, OMe); 2.13-2.01 (2H, m, Val $C^{\beta}H$); 1.37 (9H, s, Boc CH_3); 1.32-1.28 (3H, d, Ala CH_3); 0.9-0.88 (12H, m, Val CH_3). ^{13}C NMR (100MHz, $CDCl_3$, δ in ppm): 172.74, 172.60, 172.17, 156.33, 80.01, 60.06, 57.73, 52.46, 49.15, 31.57, 31.42, 28.66, 19.66, 19.30, 18.70, 18.18.

Boc-Ala-Ala-Ala-OMe (7):

^{1}H NMR (400MHz, $CDCl_3$, δ in ppm): 6.90-6.84 (1H, d, NH Proton); 6.84-6.78 (1H,d, NH proton); 5.12-5.06 (1H, d, NH Proton); 4.57-4.47 (2H, m, Ala $C^{\alpha}H$); 4.21-4.11 (1H, m, Ala $C^{\alpha}H$); 3.73 (3H, S, OMe); 1.43 (9H, s, Boc CH_3); 1.41-1.38 (3H, d, Ala CH_3); 1.37-1.34 (6H, d, Ala CH_3). ^{13}C NMR (100MHz, $CDCl_3$, δ in ppm): 173.58, 173.13, 172.17, 156, 80.68, 52.91, 50.5, 49.22, 48.57, 28.75, 18.90, 18.74, 18.51

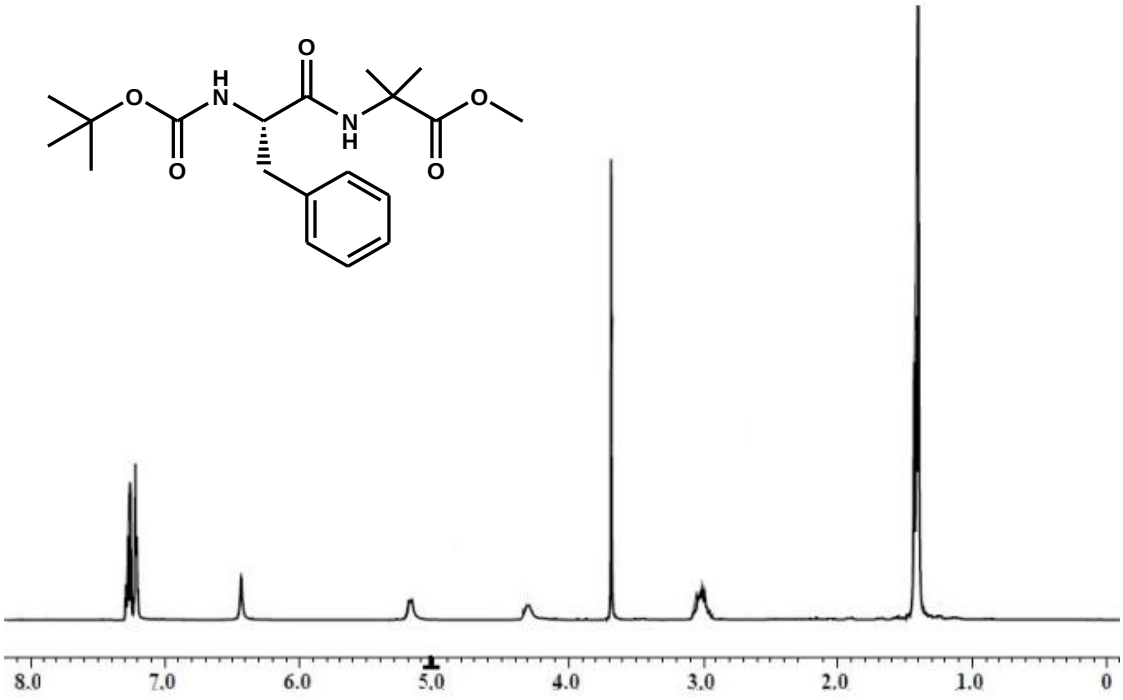


Figure S1: ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of Boc-Phe-Aib-OMe.

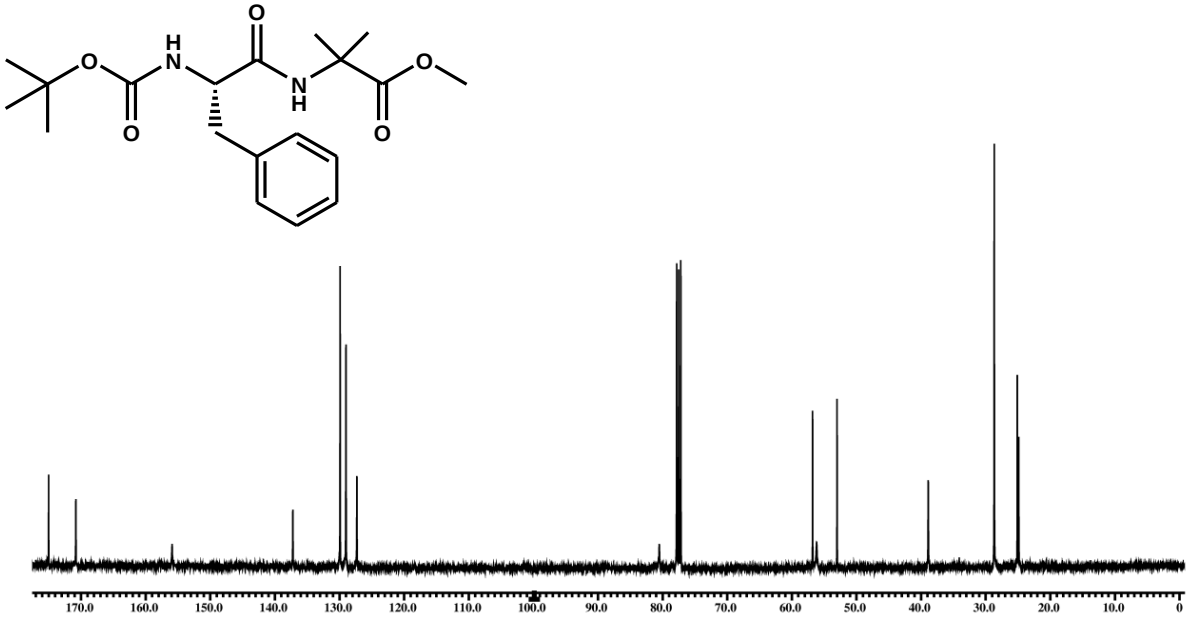


Figure S2: ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of Boc-Phe-Aib-OMe.

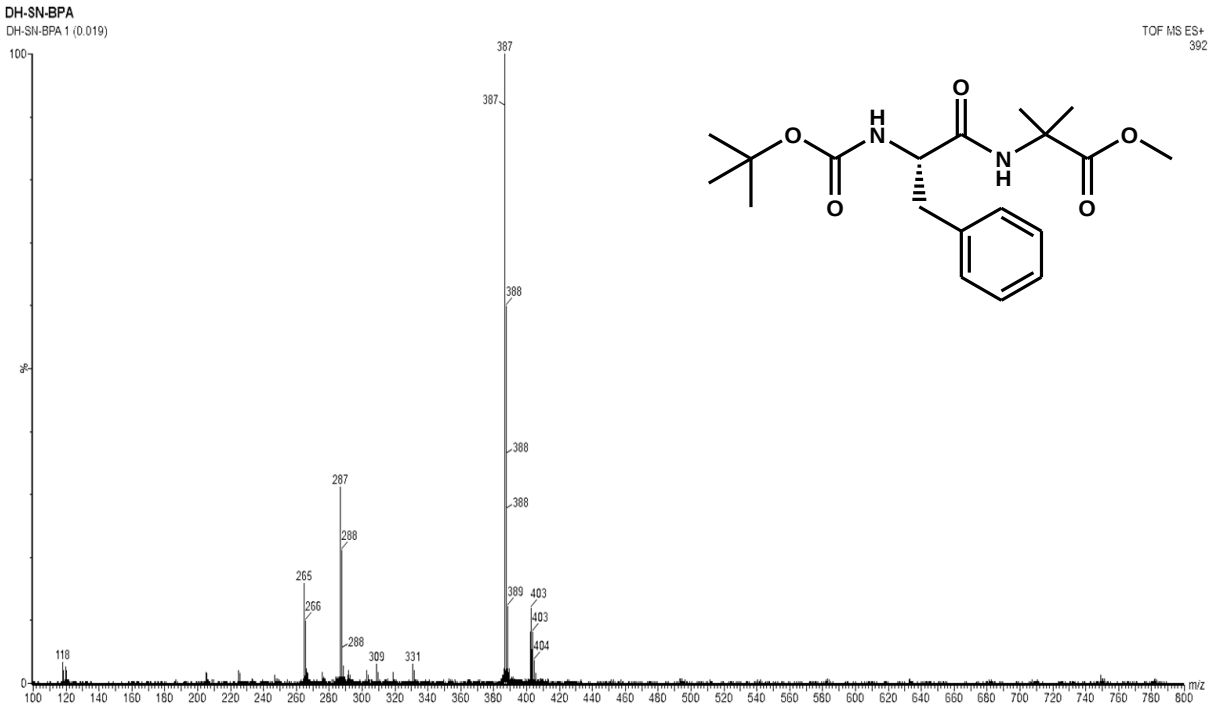


Figure S3: Mass spectrum of Boc-Phe-Aib-OMe

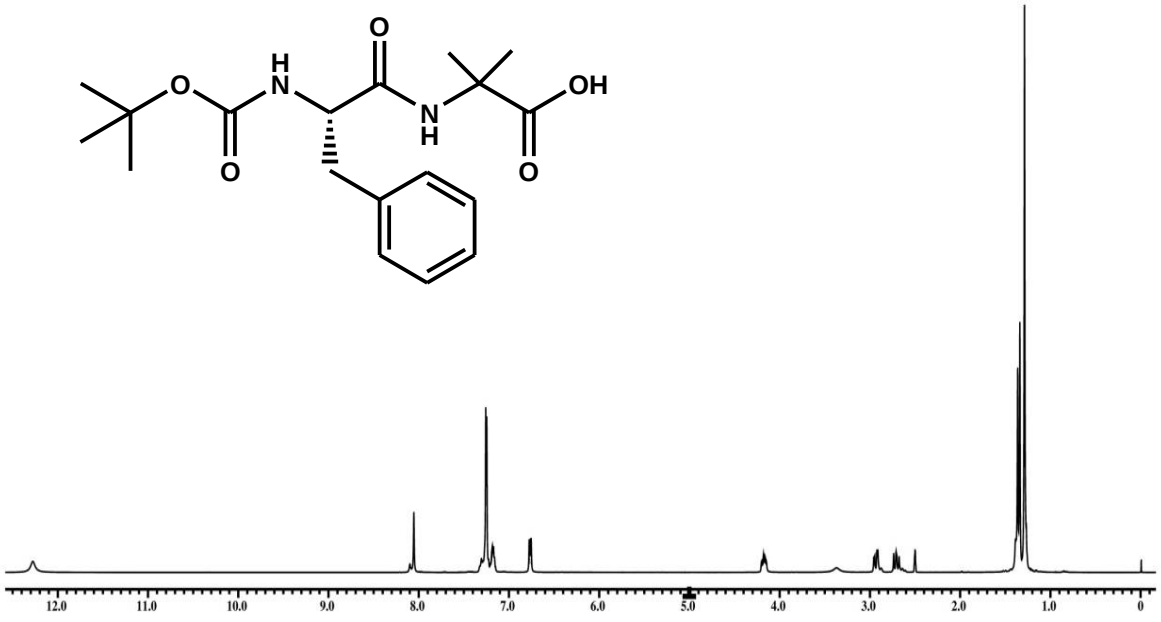


Figure S4: ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of Boc-Phe-Aib-OH.

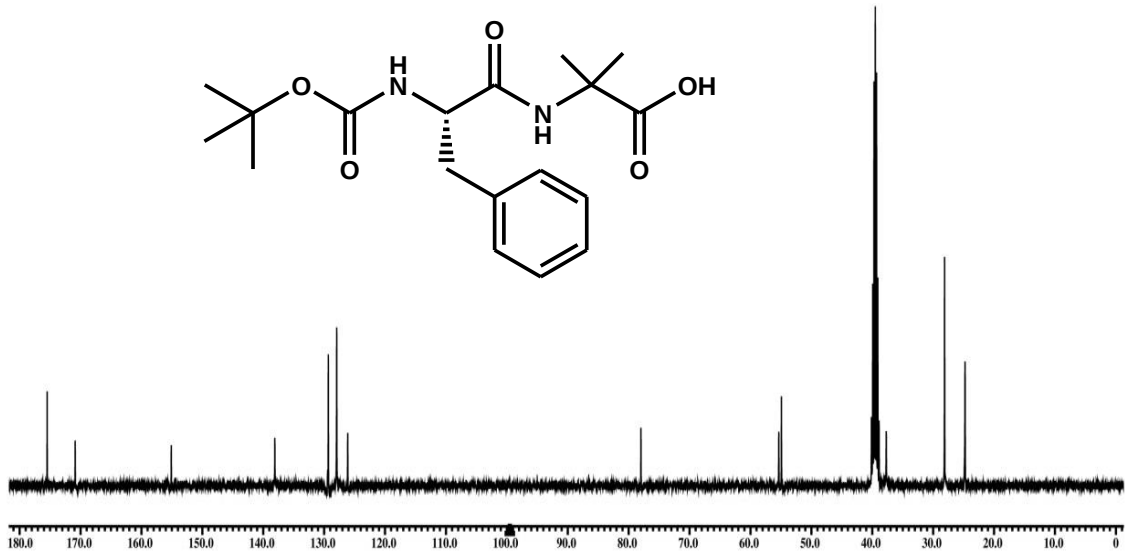


Figure S5: ^{13}C NMR (100MHz, DMSO-d_6) spectrum of Boc-Phe-Aib-OH.

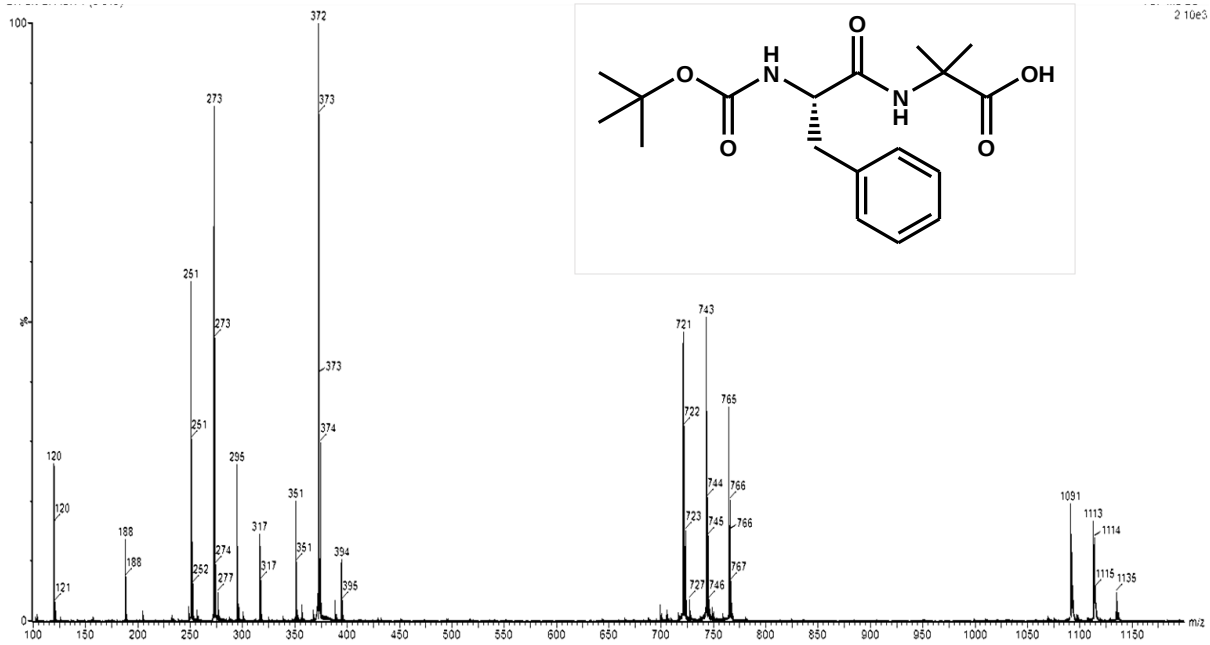


Figure S6: Mass spectrum of Boc-Phe-Aib-OH.

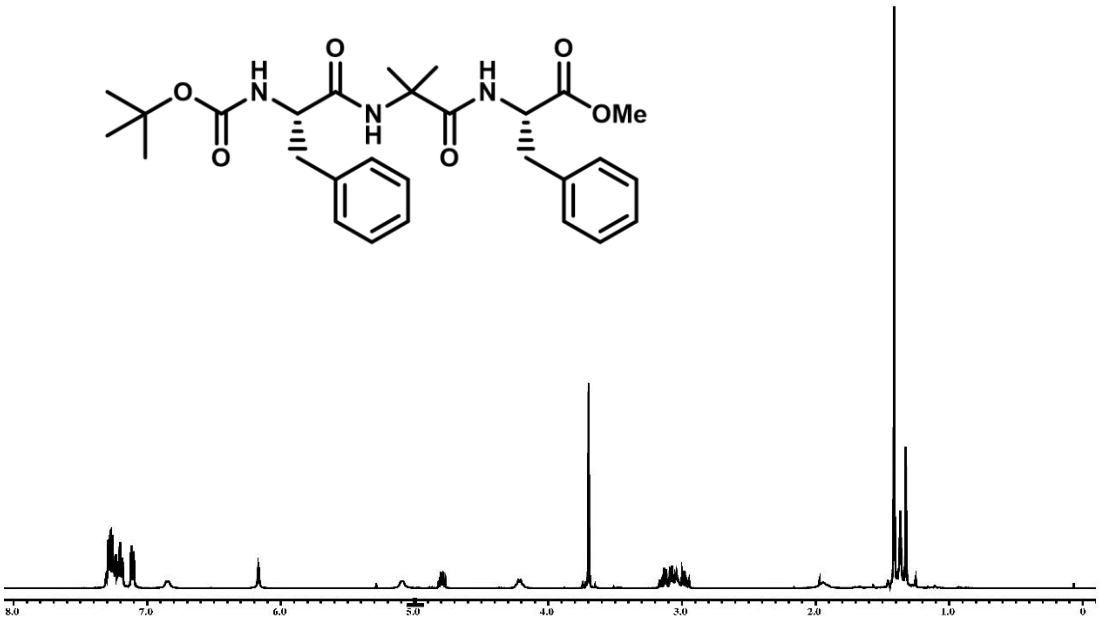


Figure S7: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Boc-Phe-Aib-Phe-OMe.

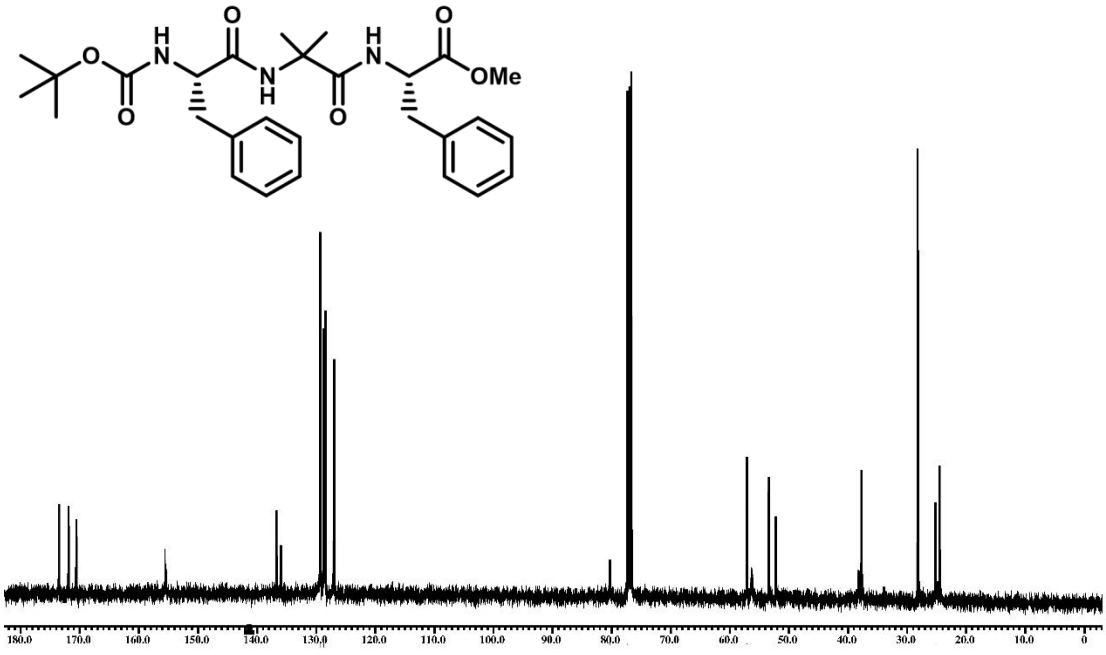


Figure S8: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of Boc-Phe-Aib-Phe-OMe.

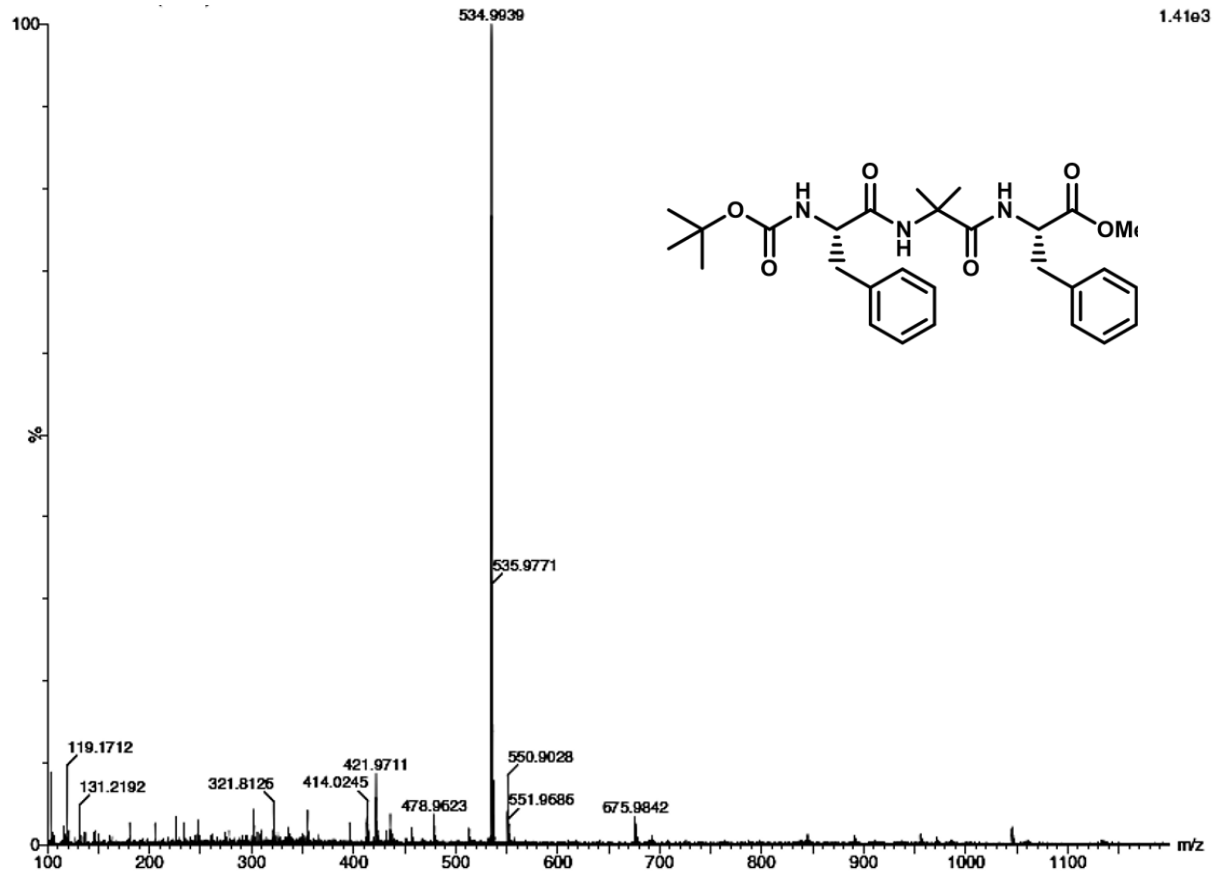


Figure S9: Mass spectrum of Boc-Phe-Aib-Phe-OMe**.**

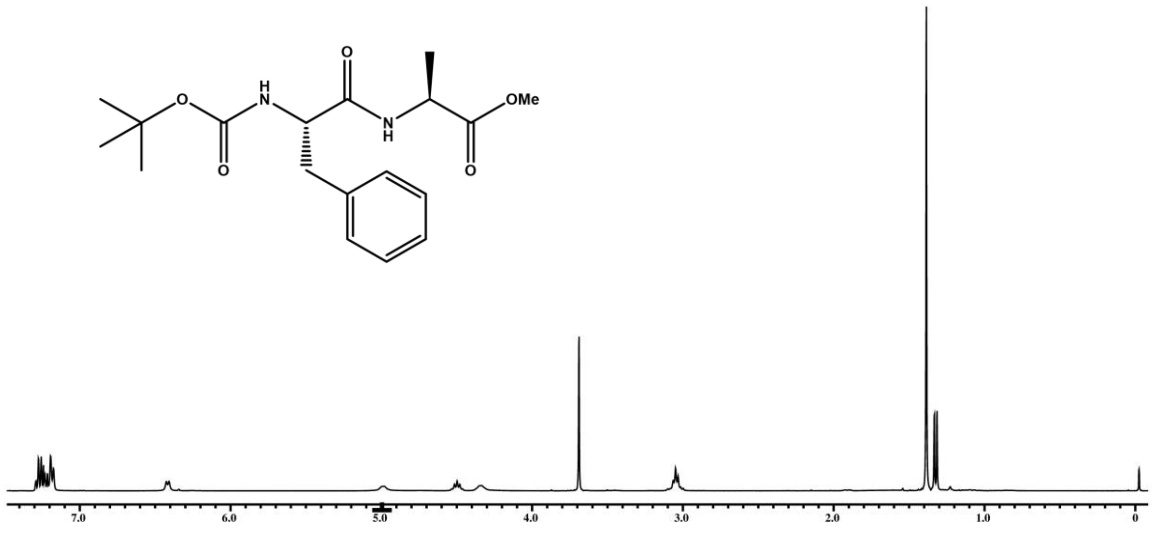


Figure S10: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Boc-Phe-Ala-OMe.

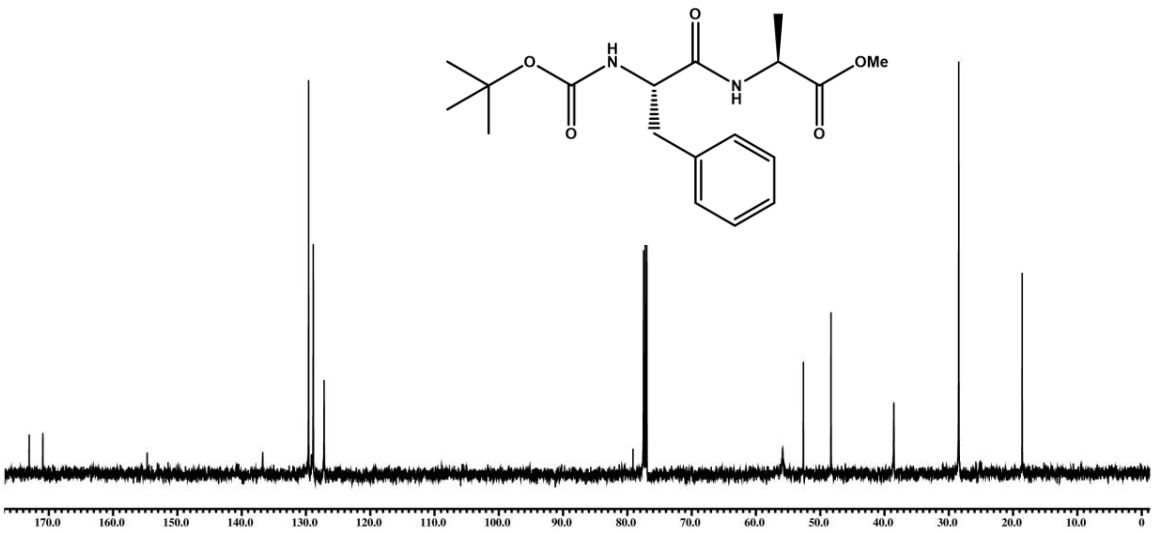


Figure S11: ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of Boc-Phe-Ala-OMe.

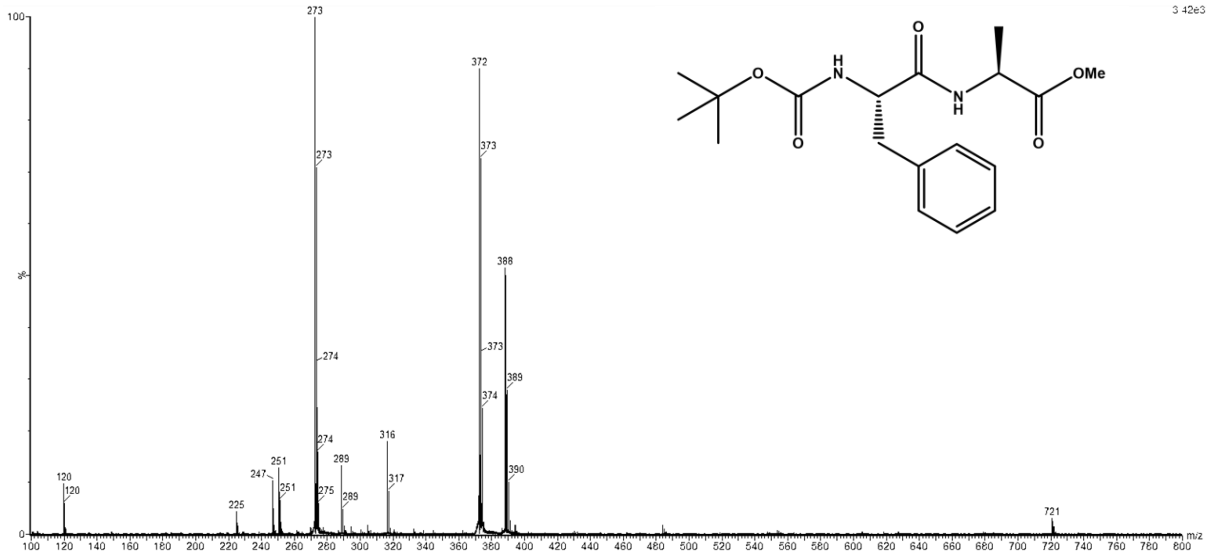


Figure S12: Mass spectrum of Boc-Phe-Ala-OMe.

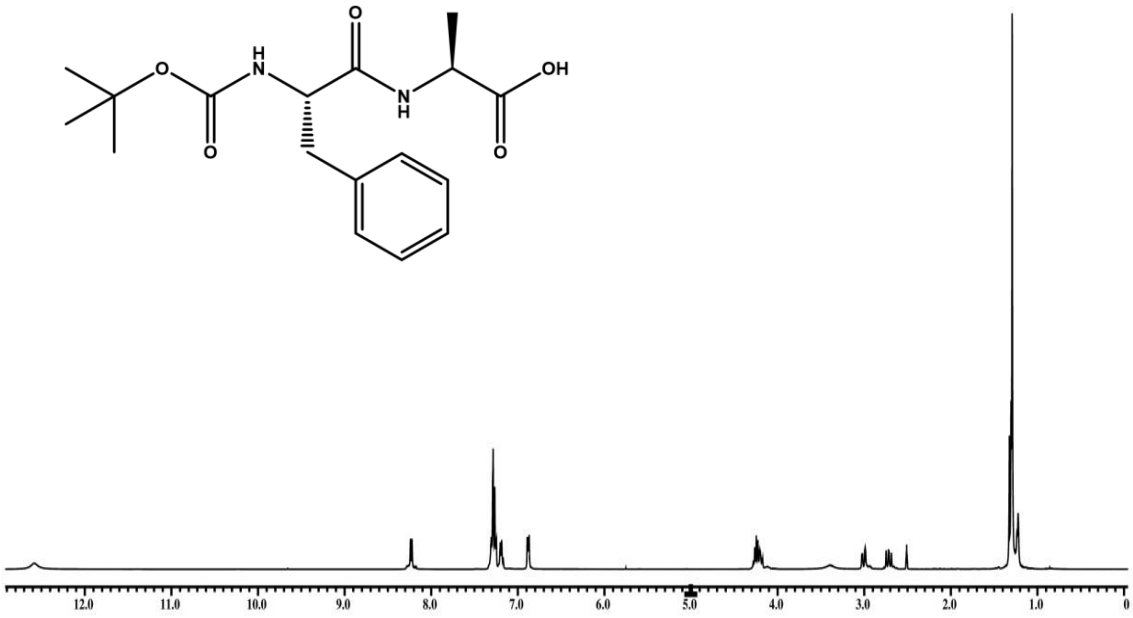


Figure S13: ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of Boc-Phe-Ala-OH.

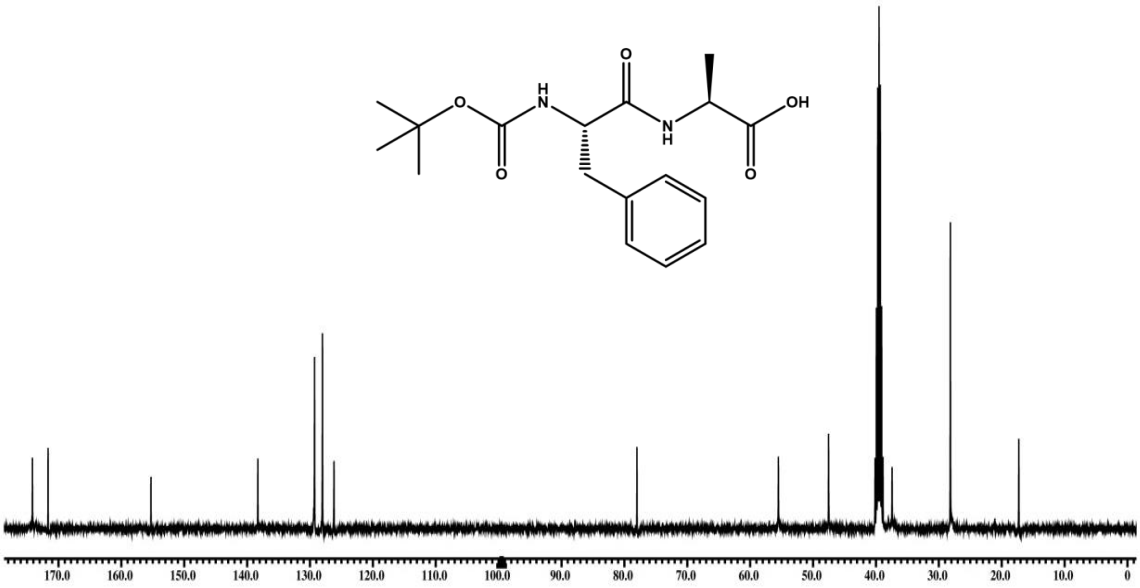


Figure S14: ^{13}C NMR (100MHz, DMSO-d_6) spectrum of Boc-Phe-Ala-OH.

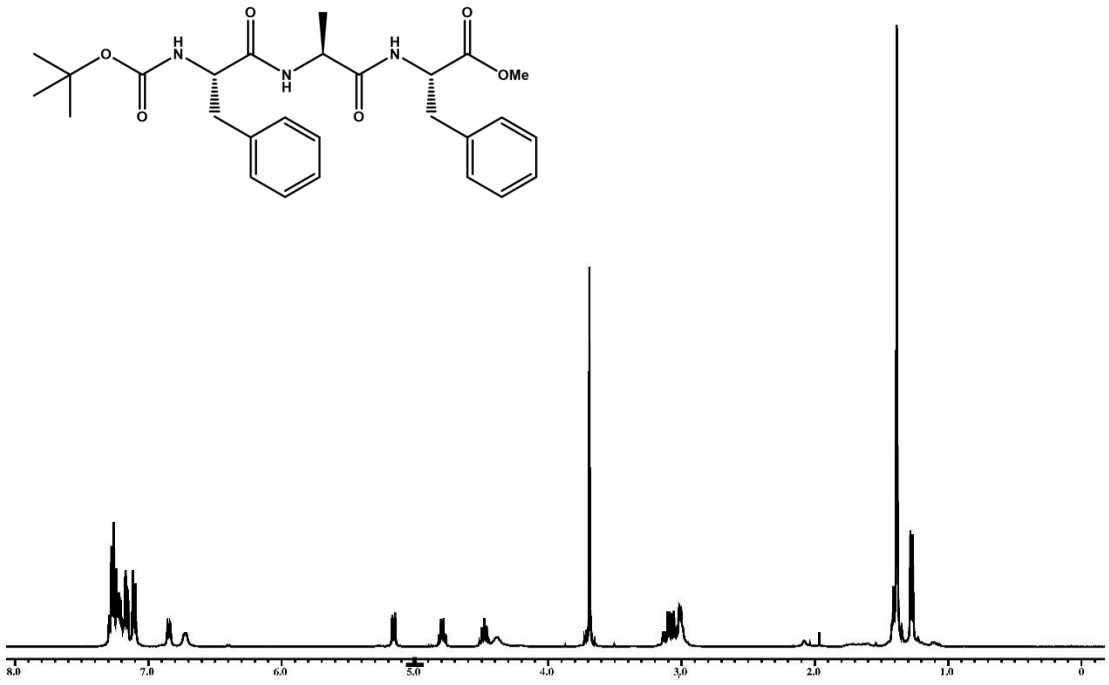


Figure S15: ^{1}H NMR (400MHz, $CDCl_3$) spectrum of Boc-Phe-Ala-Phe-OMe.

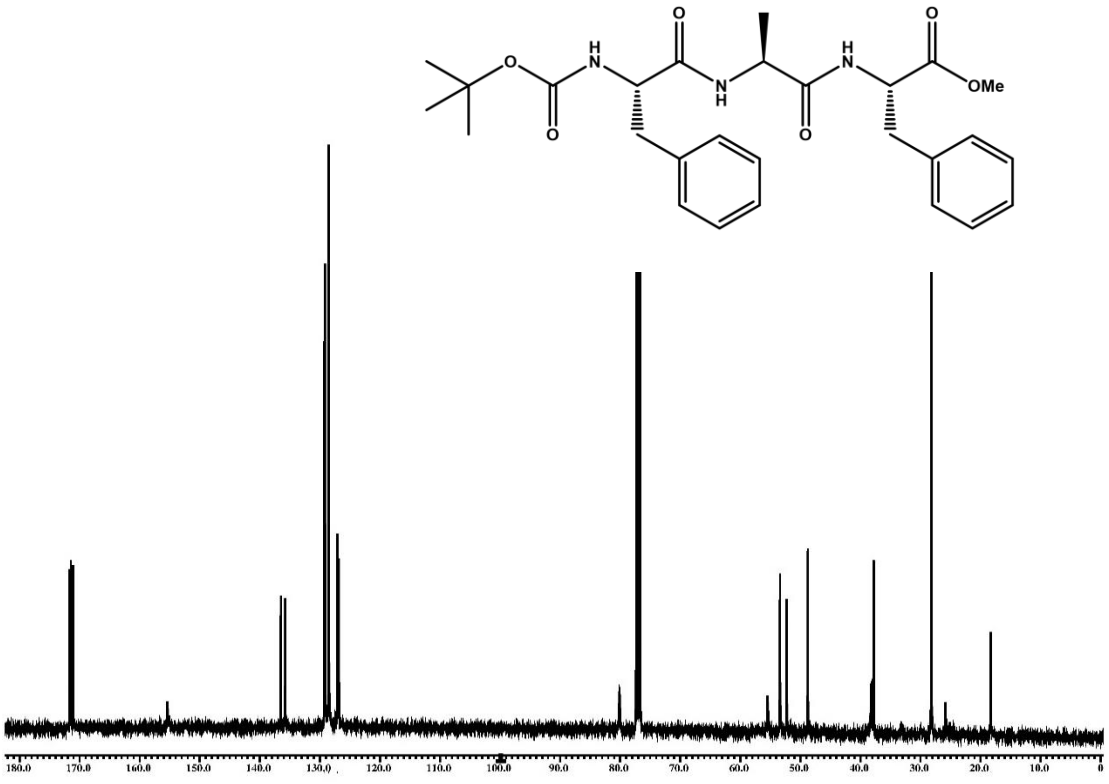


Figure S16: ^{13}C NMR (100MHz, $CDCl_3$) spectrum of Boc-Phe-Ala-Phe-OMe.

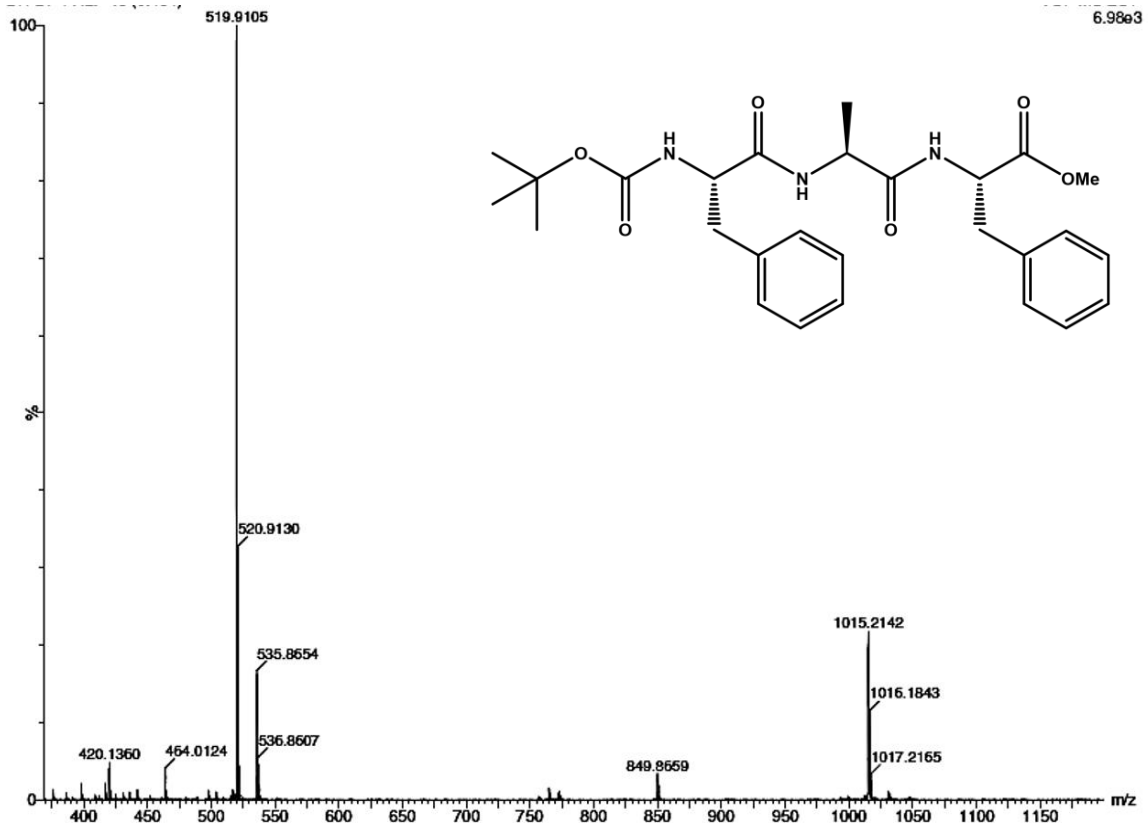


Figure S17: Mass Spectrum of Boc-Phe-Ala-Phe-OMe.

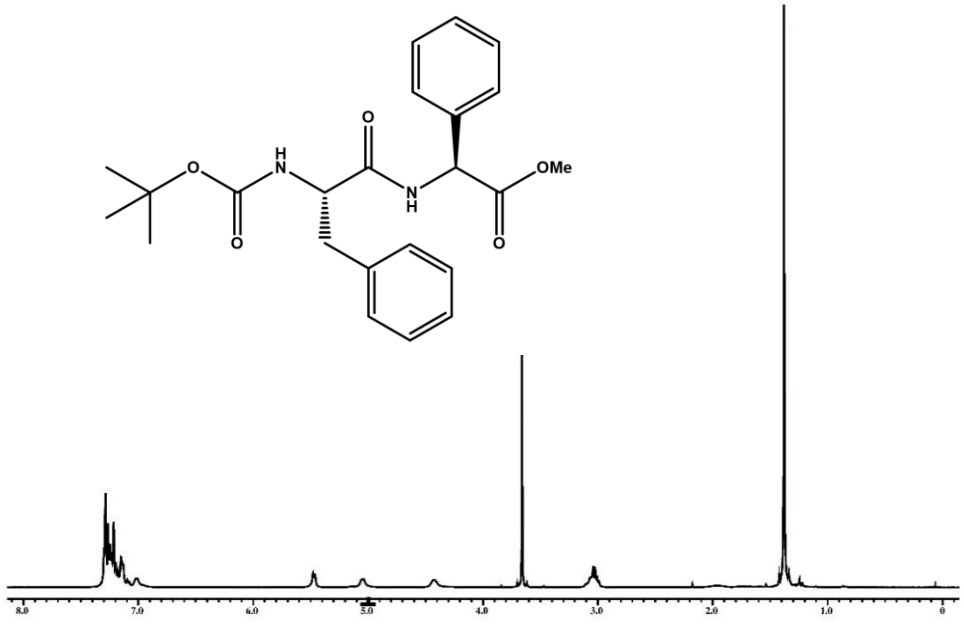


Figure S18: ^{1}H NMR (400MHz, $CDCl_3$) spectrum of Boc-Phe-PG-OMe.

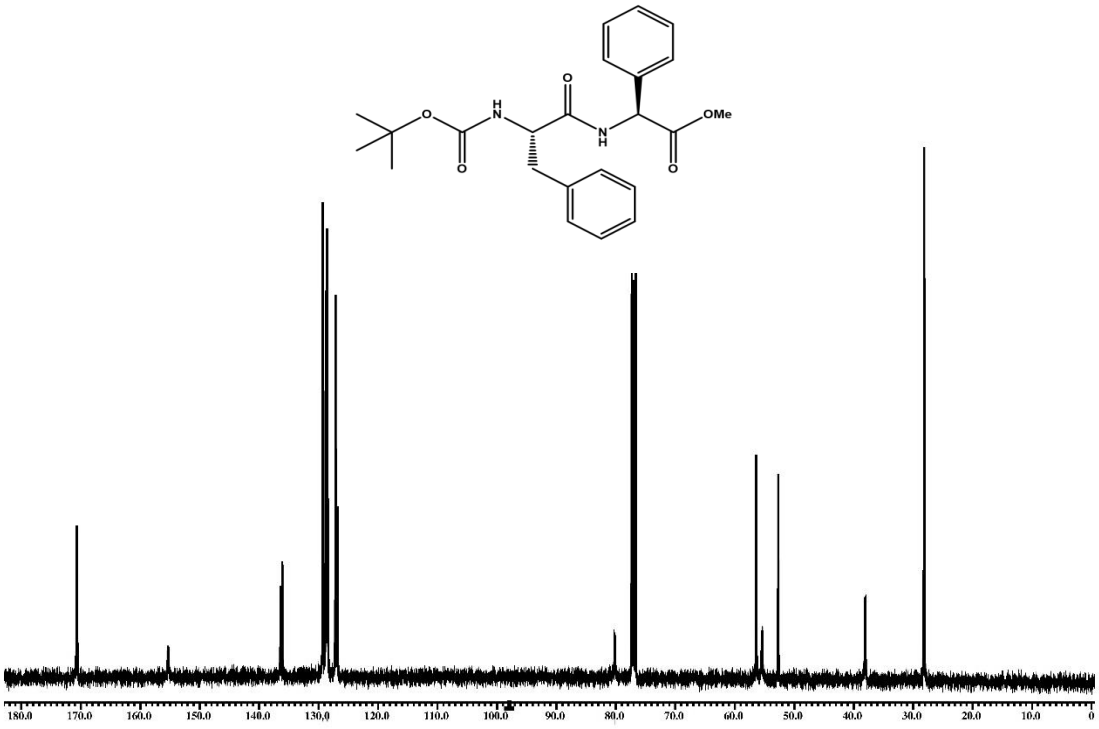


Figure S19: ^{13}C NMR (100MHz, $CDCl_3$) spectrum of Boc-Phe-PG-OMe.

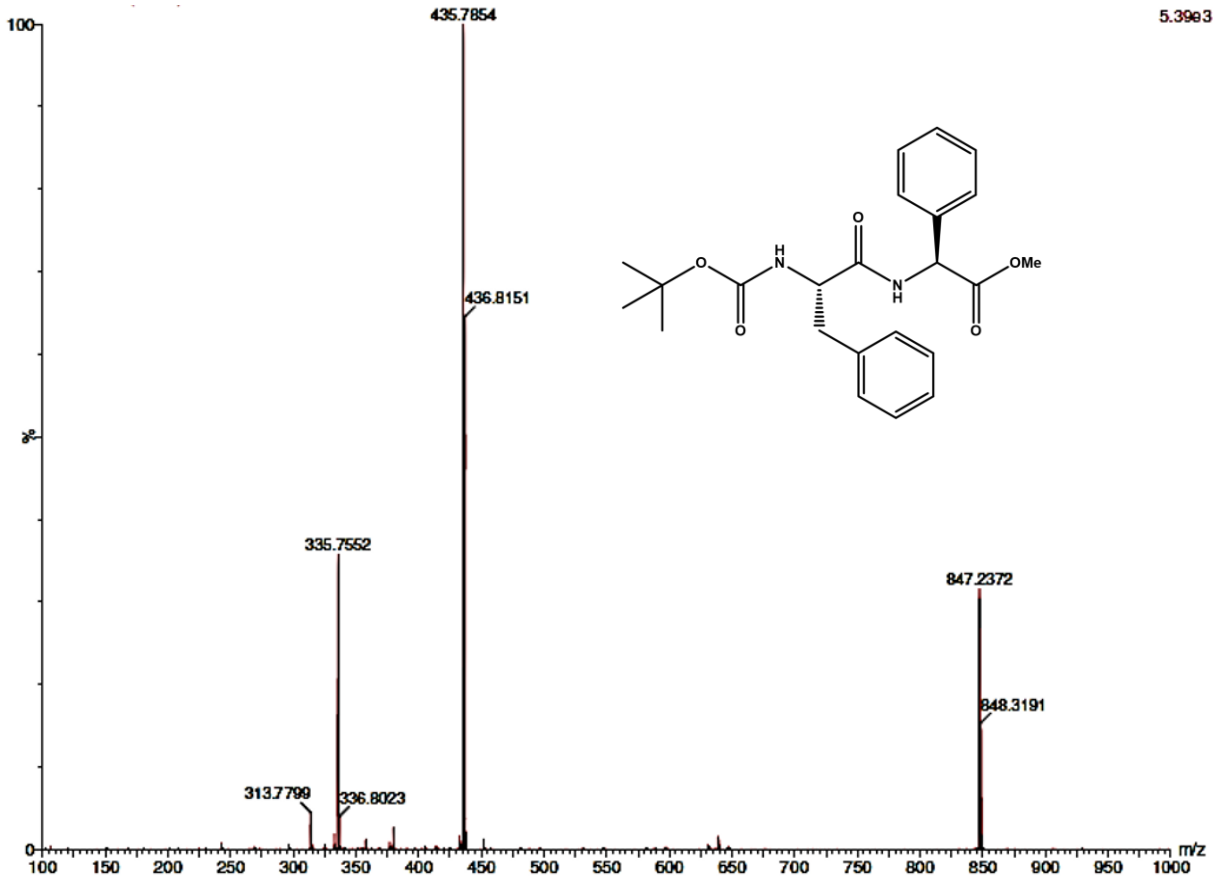


Figure S20: Mass spectrum of Boc-Phe-PG-OMe.

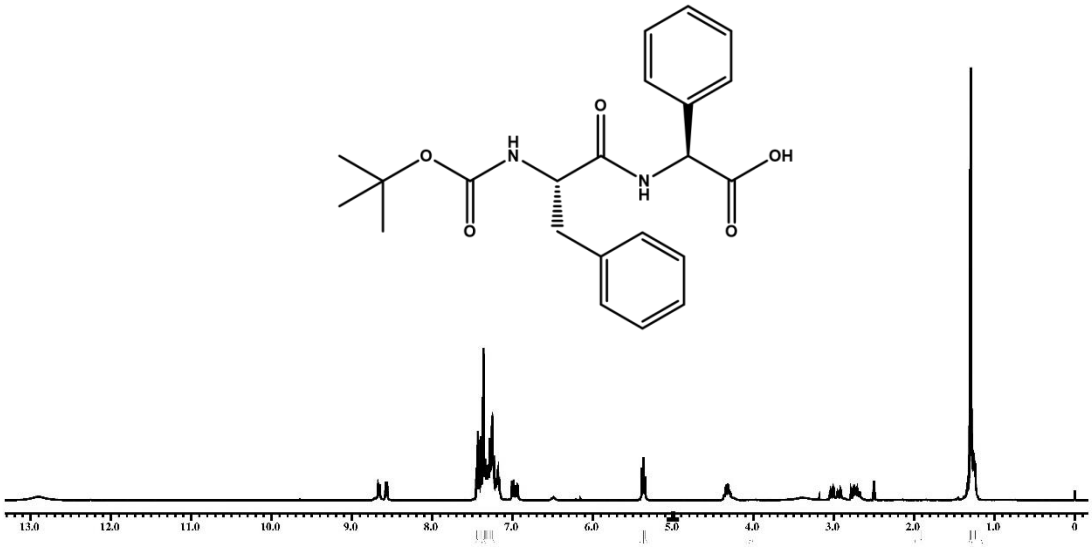


Figure S21: ^{1}H NMR (400MHz, DMSO-d_6) spectrum of Boc-Phe-PG-OH.

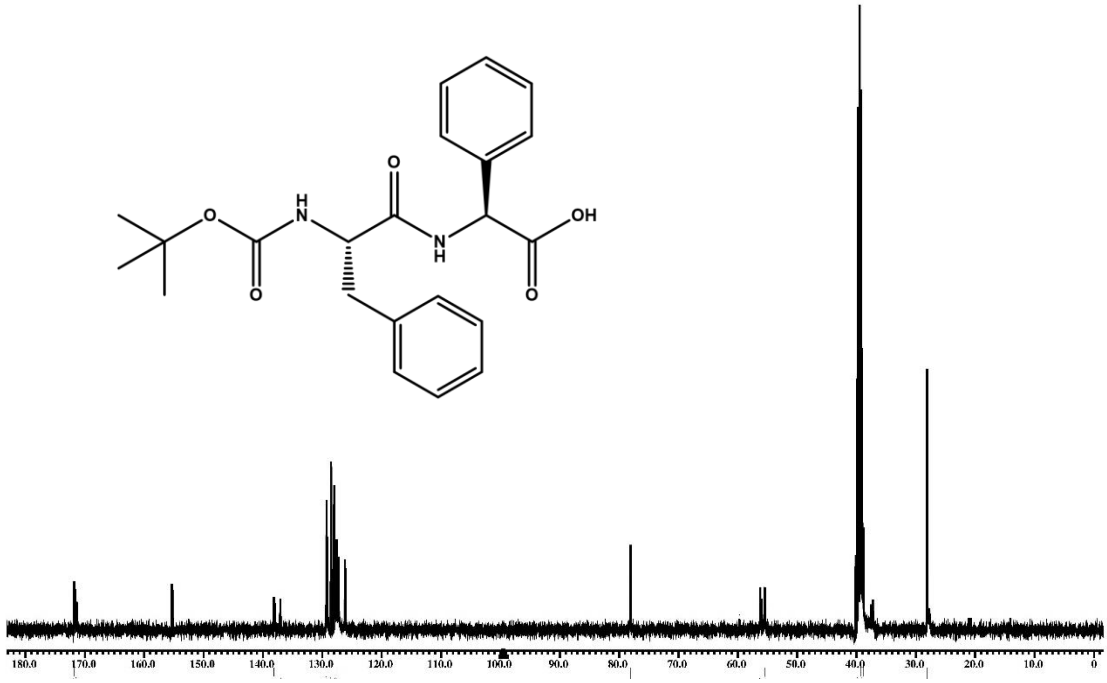


Figure S22: ^{13}C NMR (100MHz, DMSO-d_6) spectrum of Boc-Phe-PG-OH.

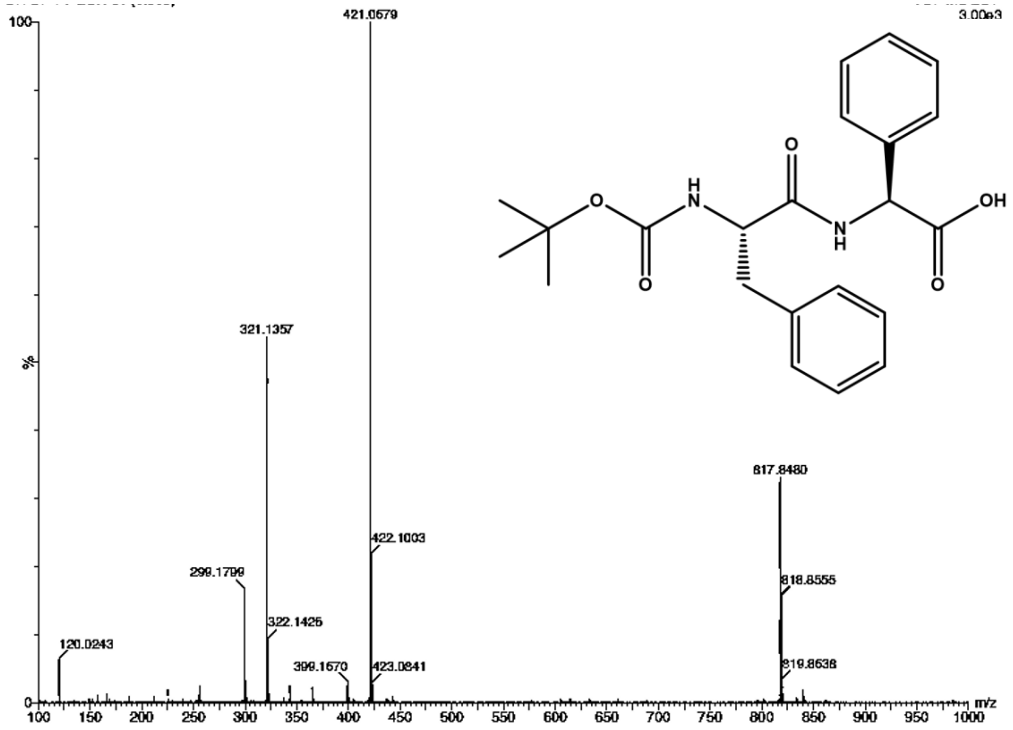


Figure S23: Mass Spectrum of Boc-Phe-PG-OH.

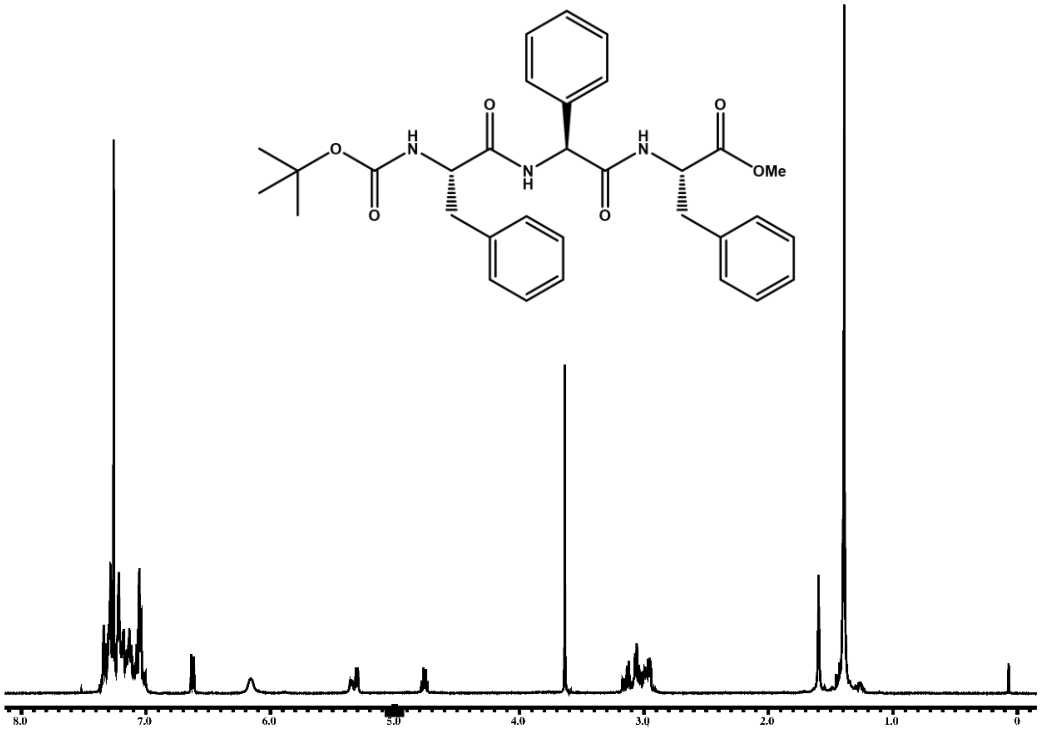


Figure S24: ^{1}H NMR (400MHz, $CDCl_3$) spectrum of Boc-Phe-PG-Phe-OMe.

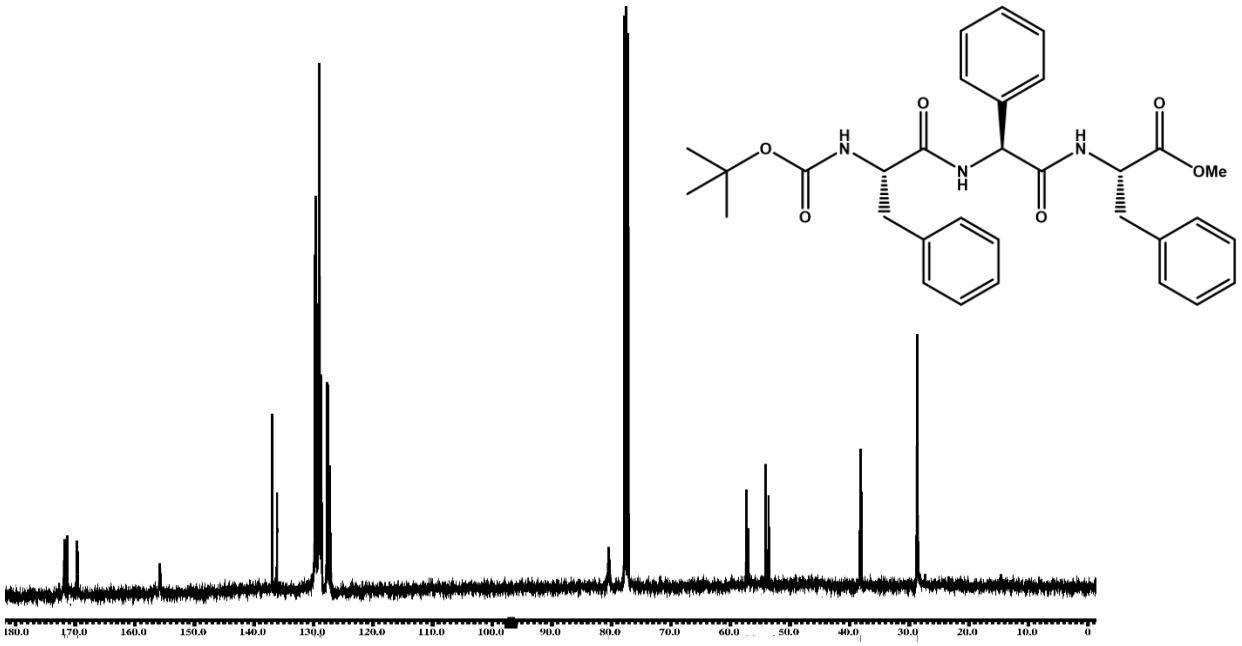


Figure S25: ^{13}C NMR (100MHz, $CDCl_3$) spectrum of Boc-Phe-PG-Phe-OMe.

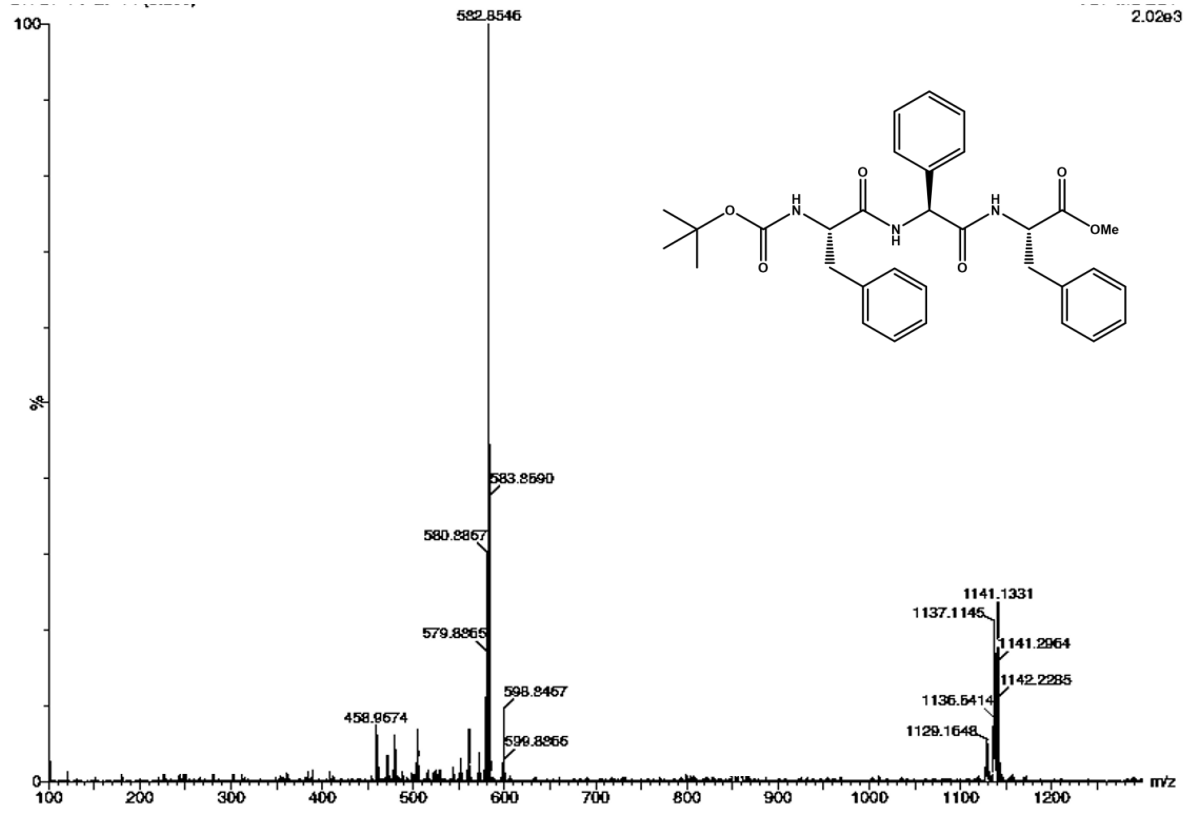


Figure S26: Mass spectrum of Boc-Phe-PG-Phe-OMe.

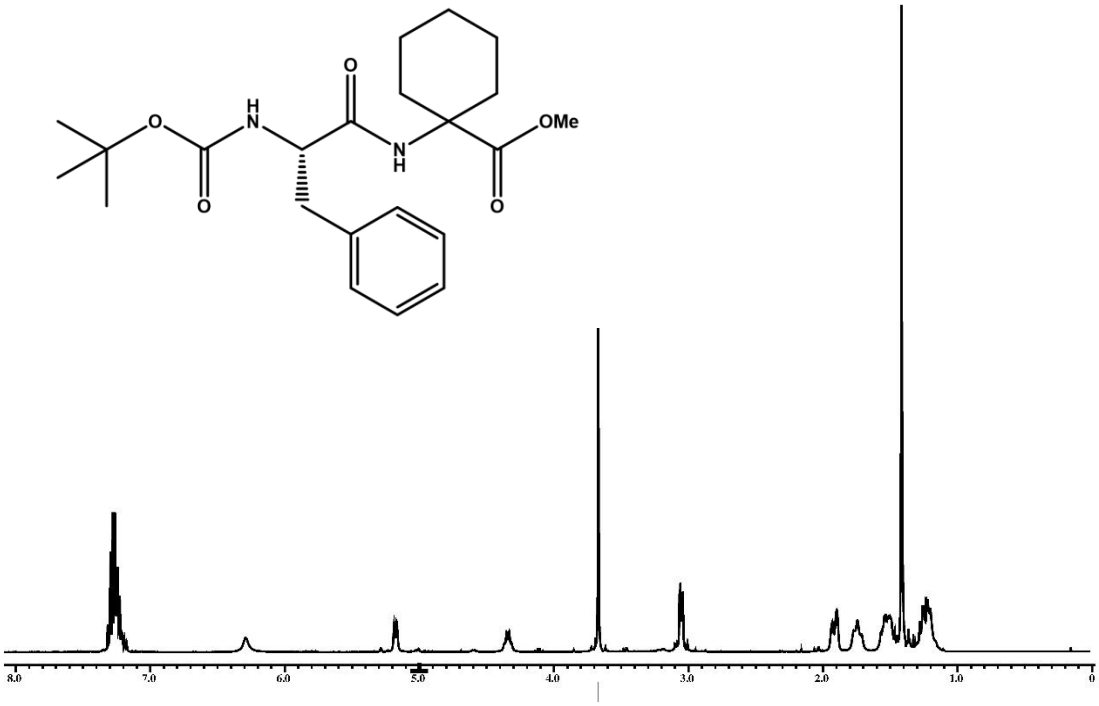


Figure S27: ^{1}H NMR (400MHz, $CDCl_3$) spectrum of Boc-Phe-AC-OMe.

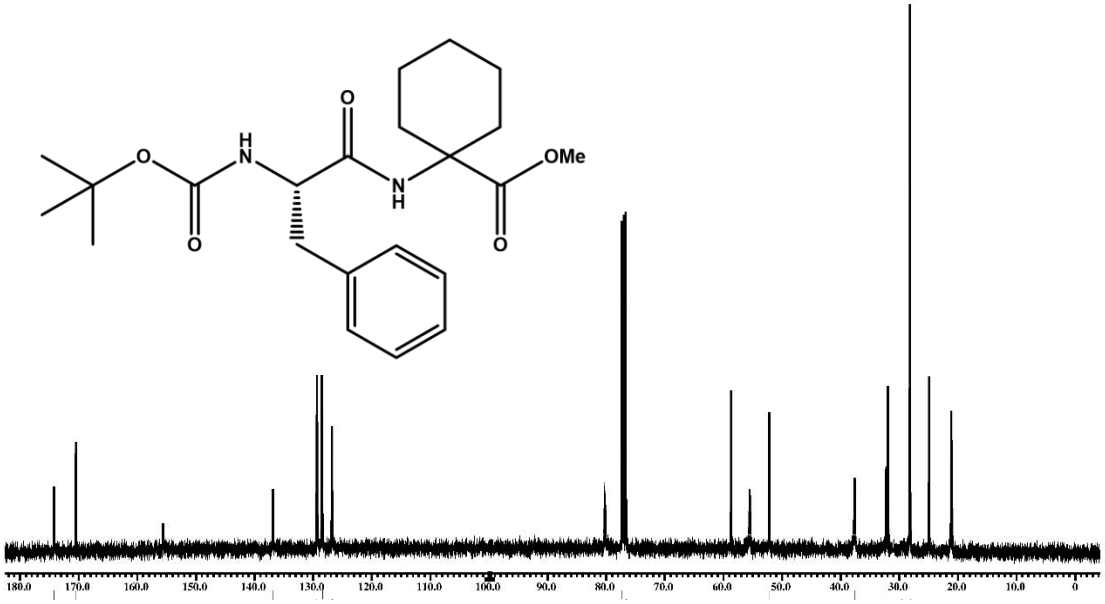


Figure S28: ^{13}C NMR (100MHz, $CDCl_3$) spectrum of Boc-Phe-AC-OMe.

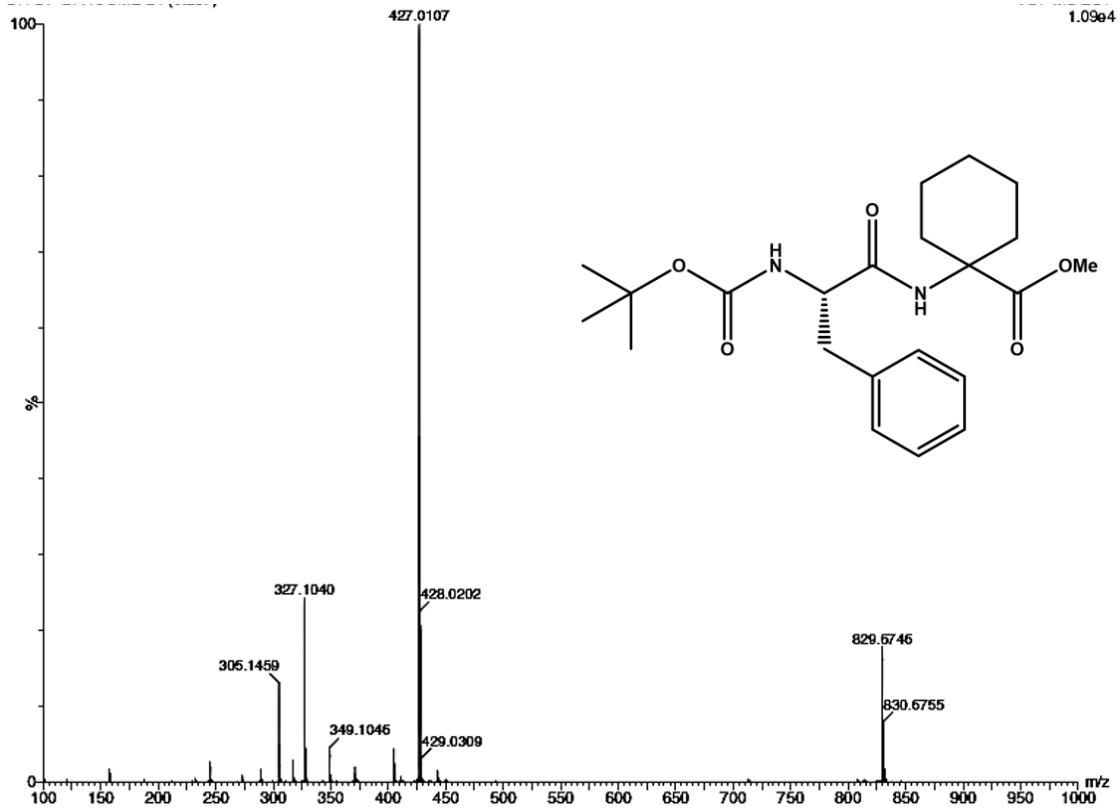


Figure S29: Mass spectrum of Boc-Phe-AC-OMe

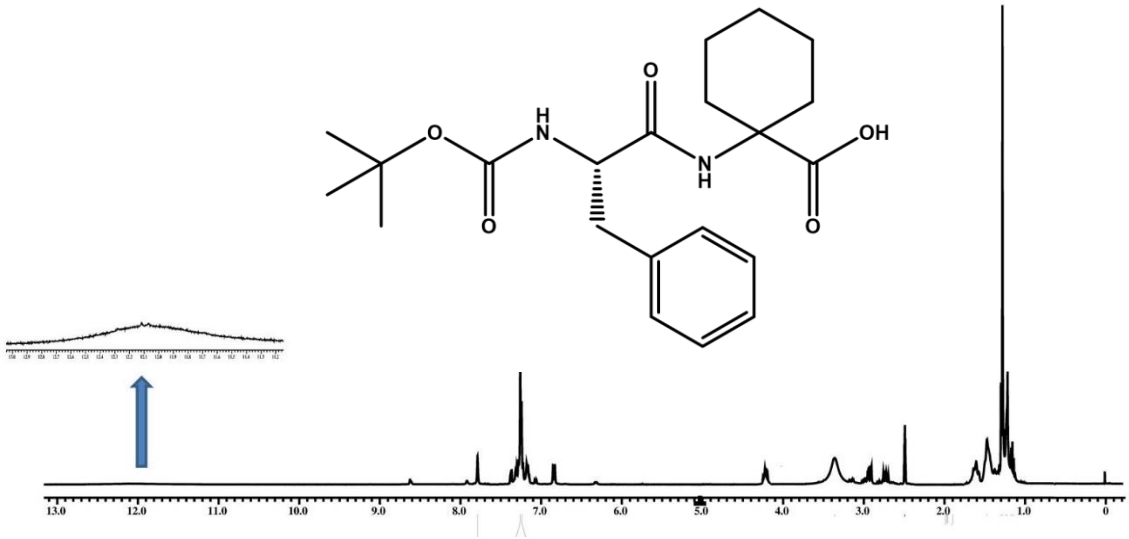


Figure S30: ^{1}H NMR (400MHz, DMSO-d_6) spectrum of Boc-Phe-AC-OH.

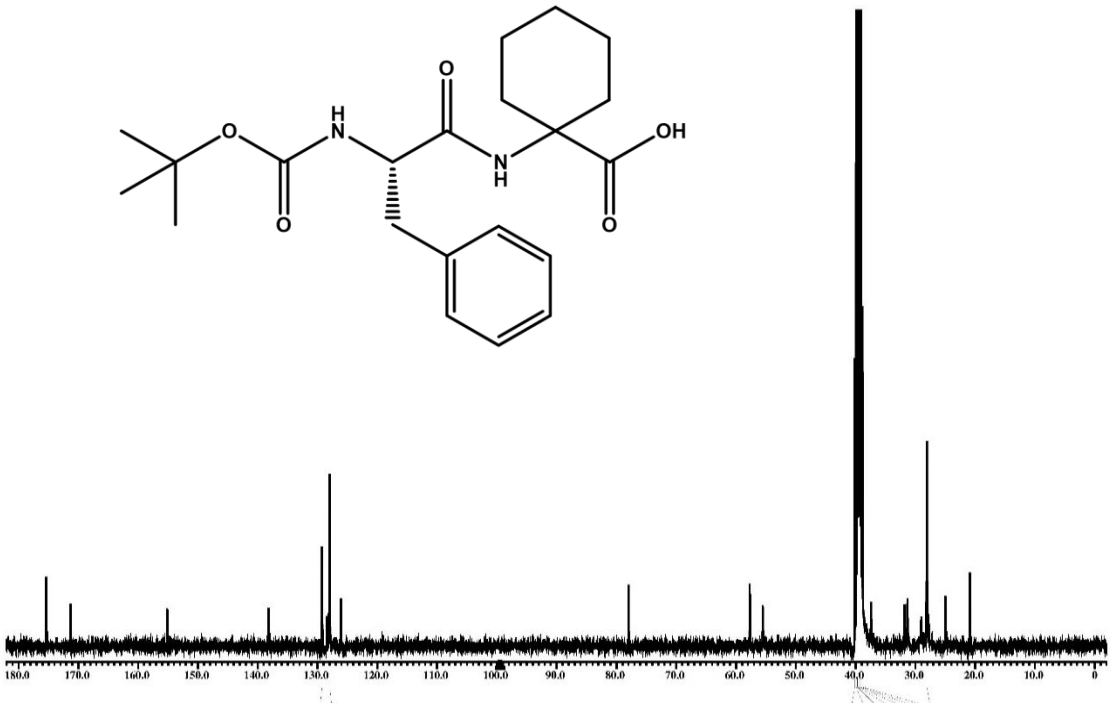


Figure S31: ^{13}C NMR (100MHz, DMSO-d_6) spectrum of Boc-Phe-AC-OH.

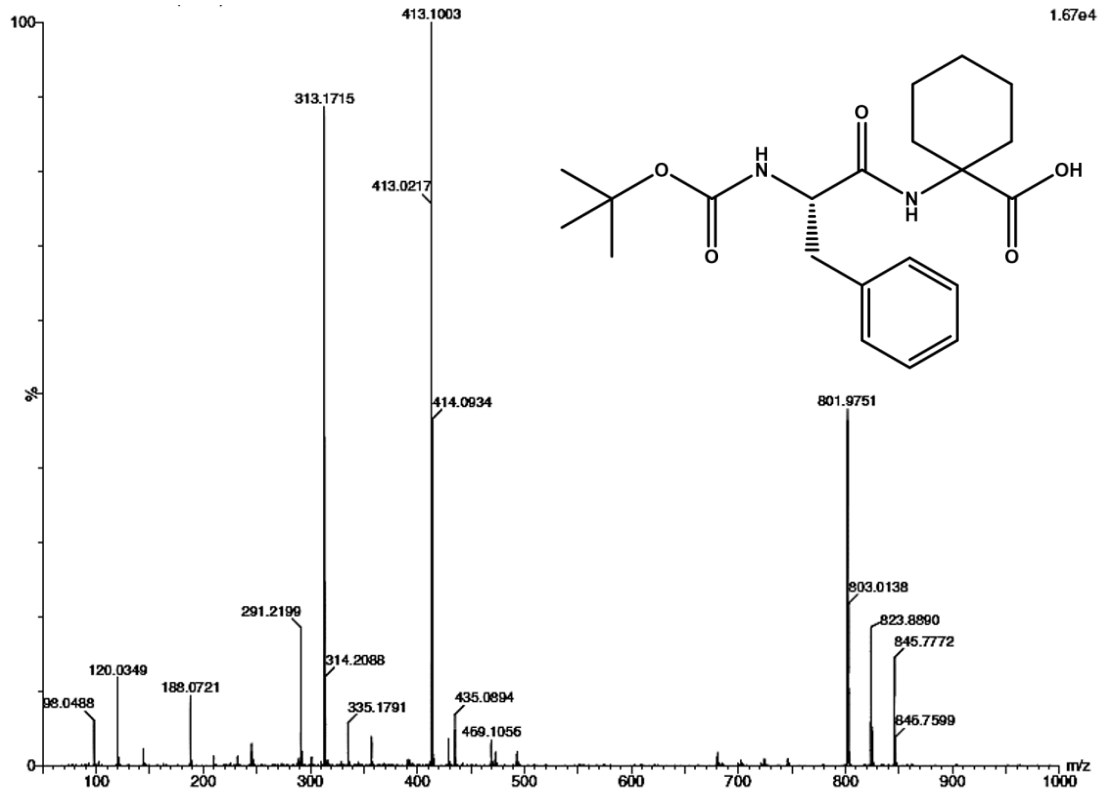


Figure S32: Mass spectrum of Boc-Phe-AC-OH

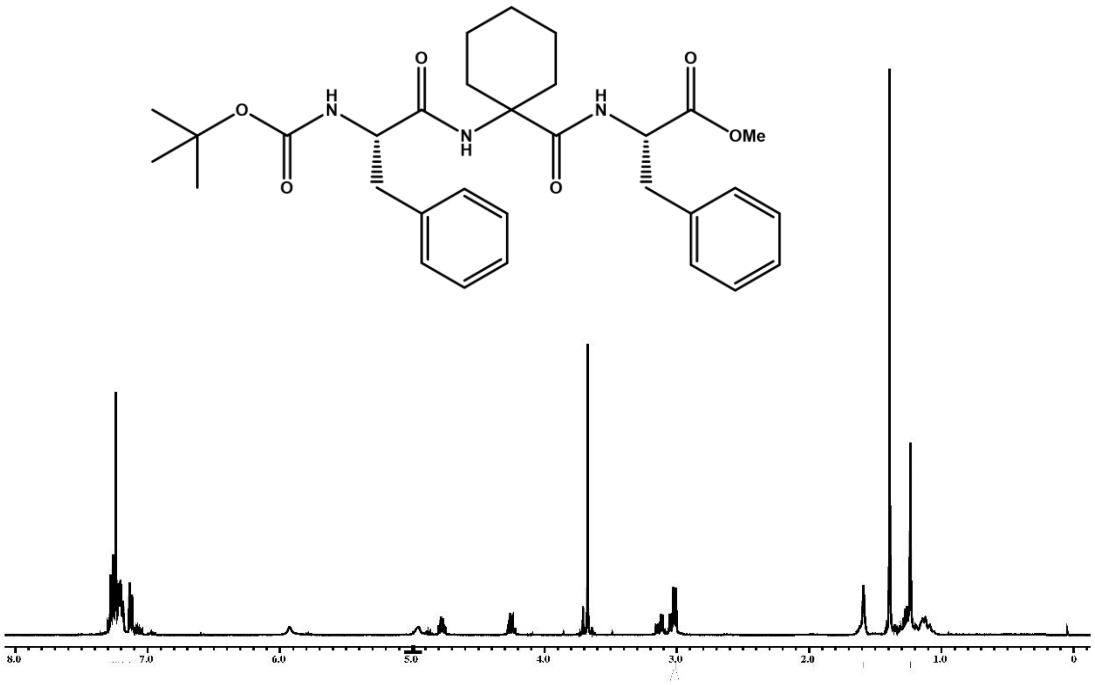


Figure S33: ^{1}H NMR (400MHz, $CDCl_3$) spectrum of Boc-Phe-AC-Phe-OMe.

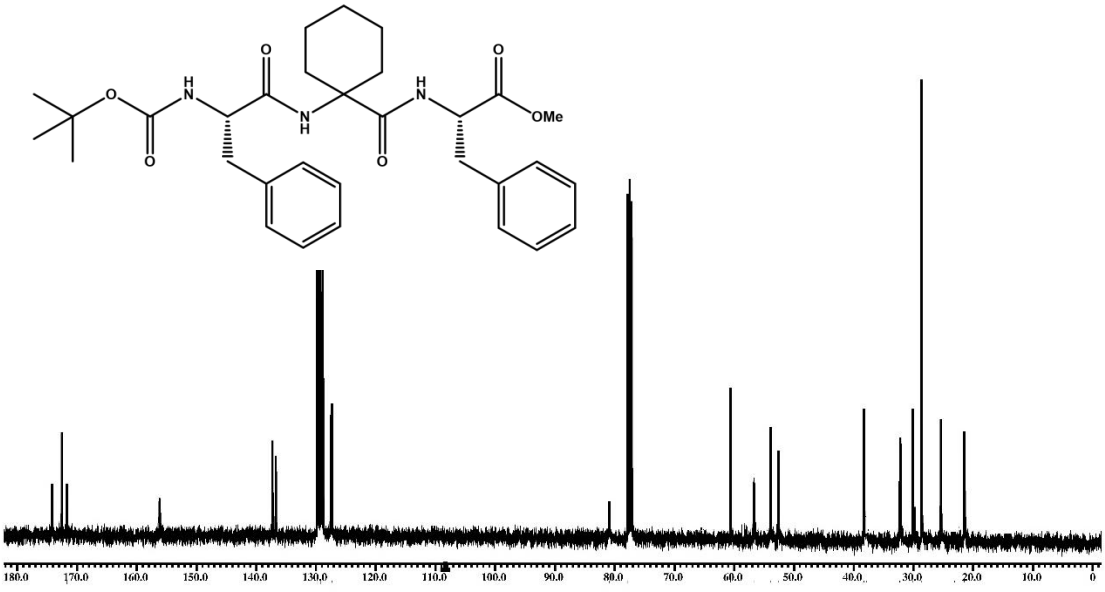


Figure S34: ^{13}C NMR (100MHz, $CDCl_3$) spectrum of Boc-Phe-AC-Phe-OMe.

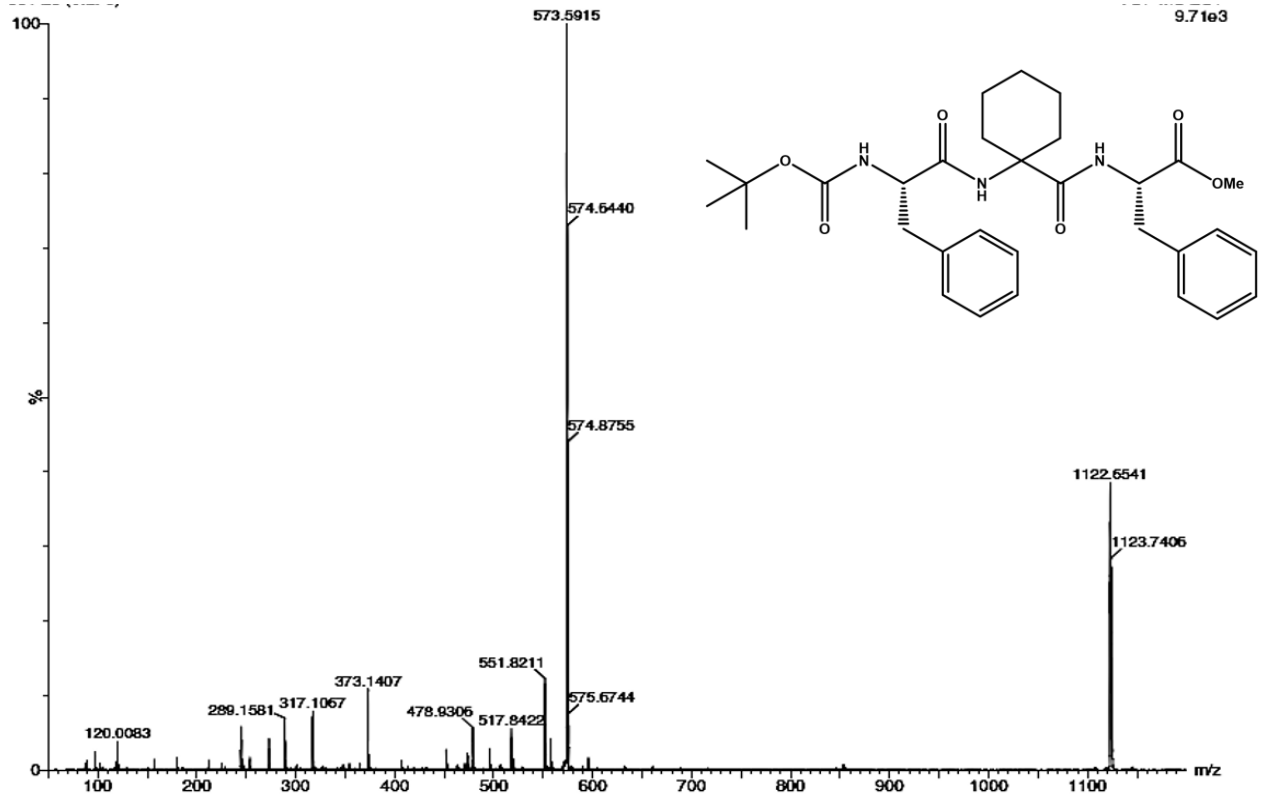


Figure S35: Mass spectrum of Boc-Phe-AC-Phe-OMe.

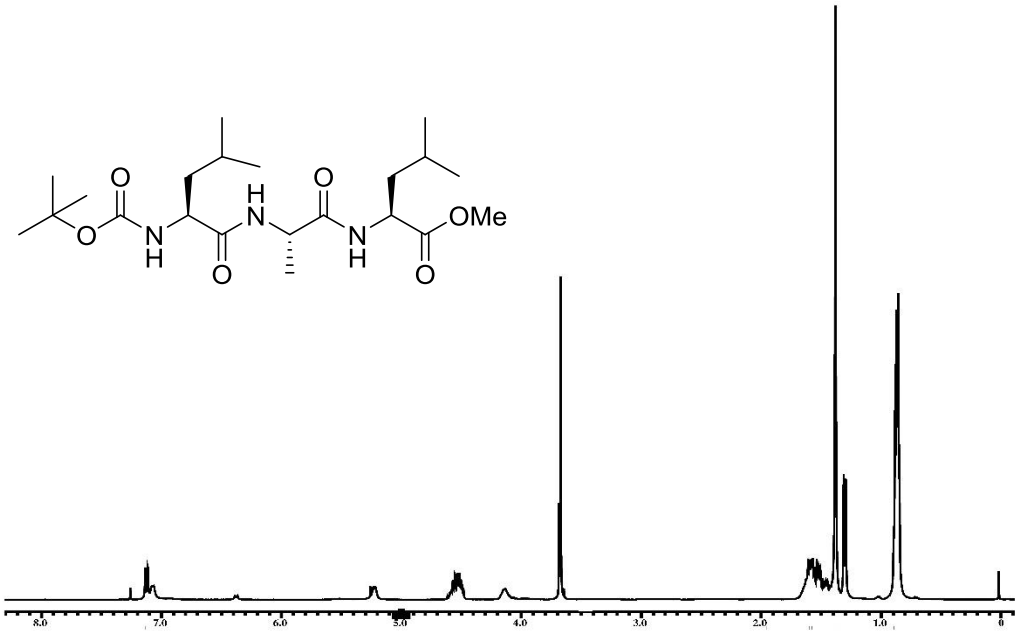


Figure S36: ^{1}H NMR (400MHz, $CDCl_3$) spectrum of Boc-Leu-Ala- Leu-OMe.

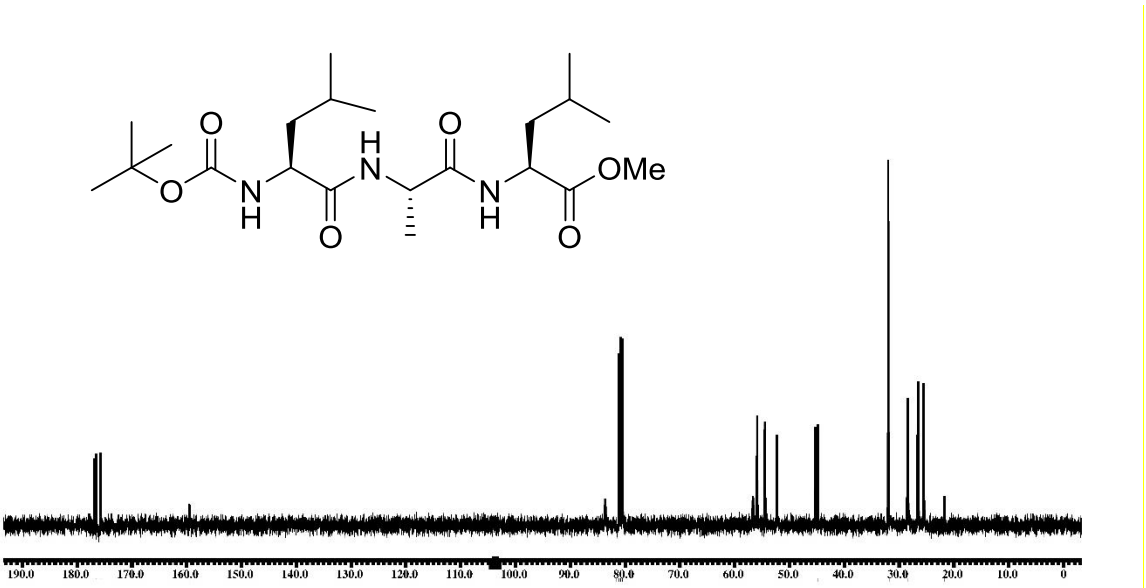


Figure S37: ^{13}C NMR (100MHz, $CDCl_3$) spectrum of Boc-Leu-Ala- Leu-OMe.

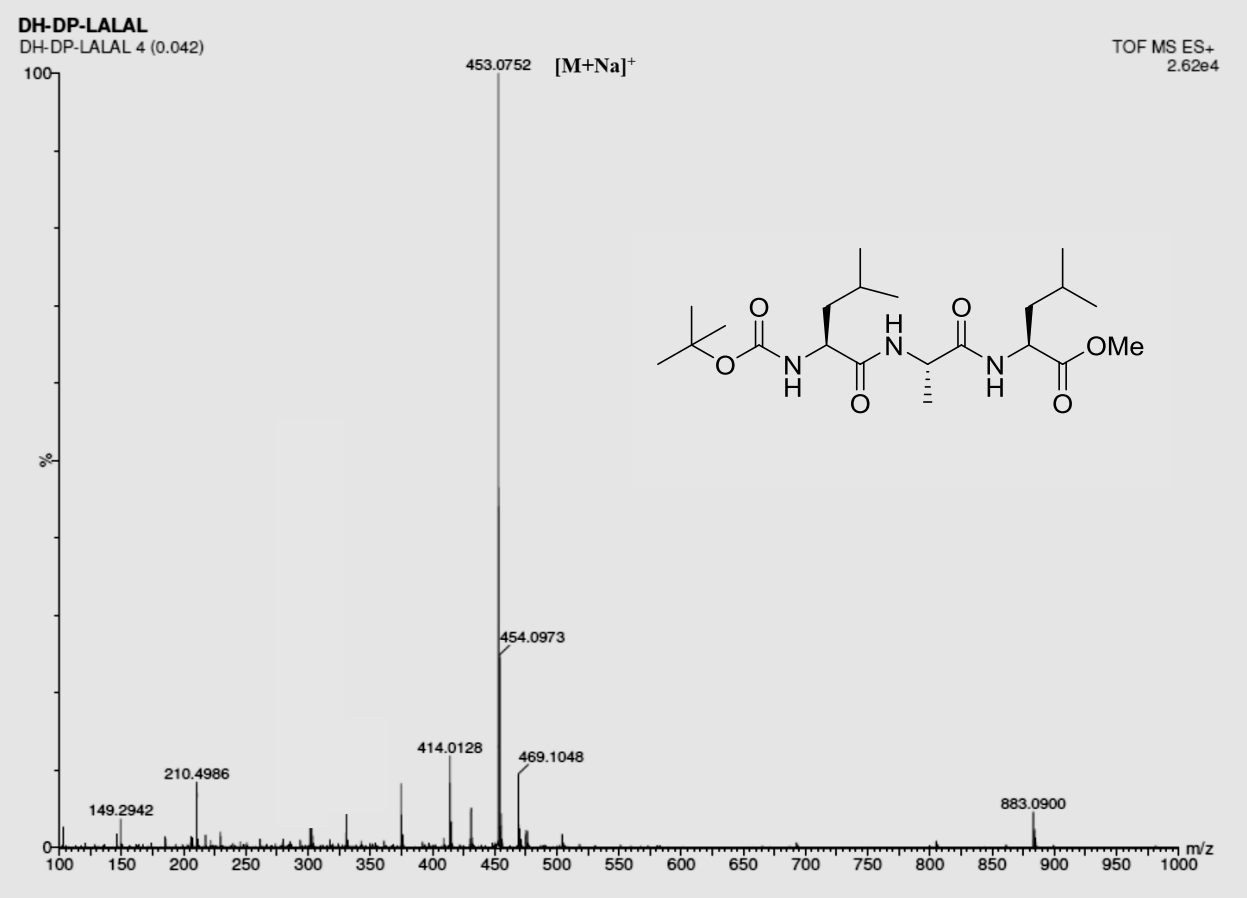


Figure S38: Mass spectrum of Boc-Leu-Ala- Leu-OMe.

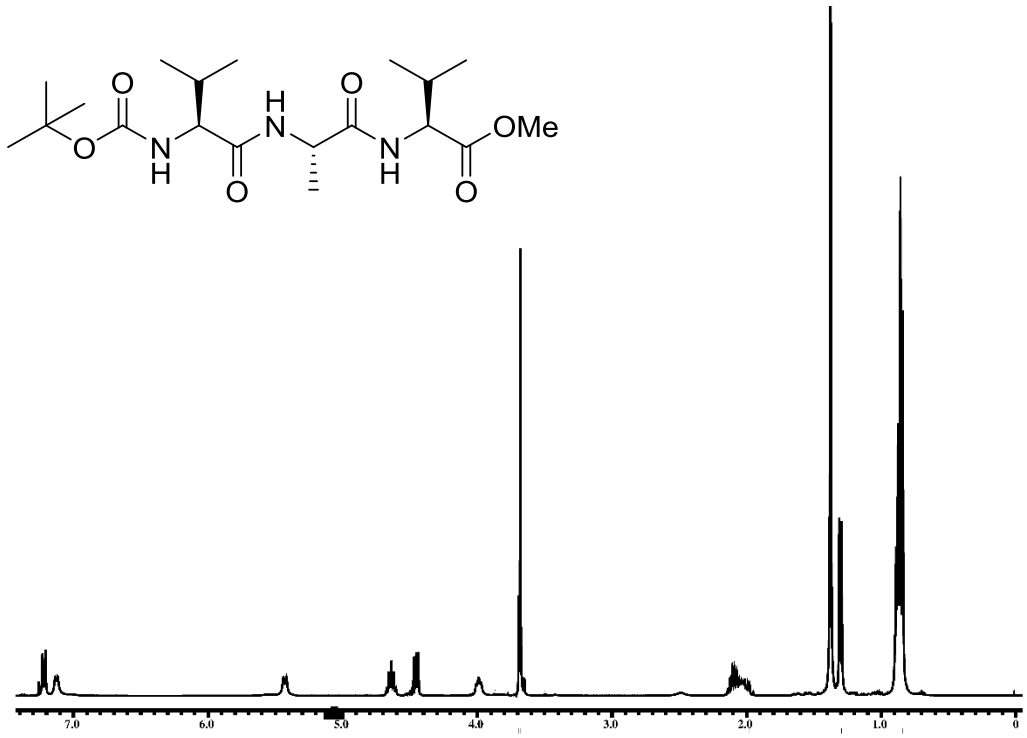


Figure S39: ^{1}H NMR (400MHz, $CDCl_3$) spectrum of Boc-Val-Ala- Val-OMe.

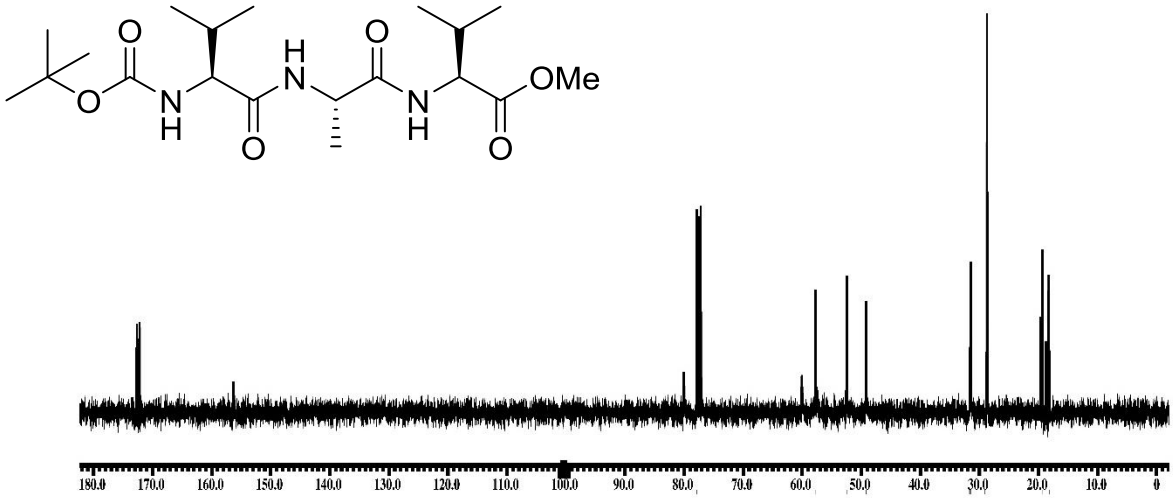


Figure S40: ^{13}C NMR (100MHz, $CDCl_3$) spectrum of Boc-Val-Ala-Val-OMe.

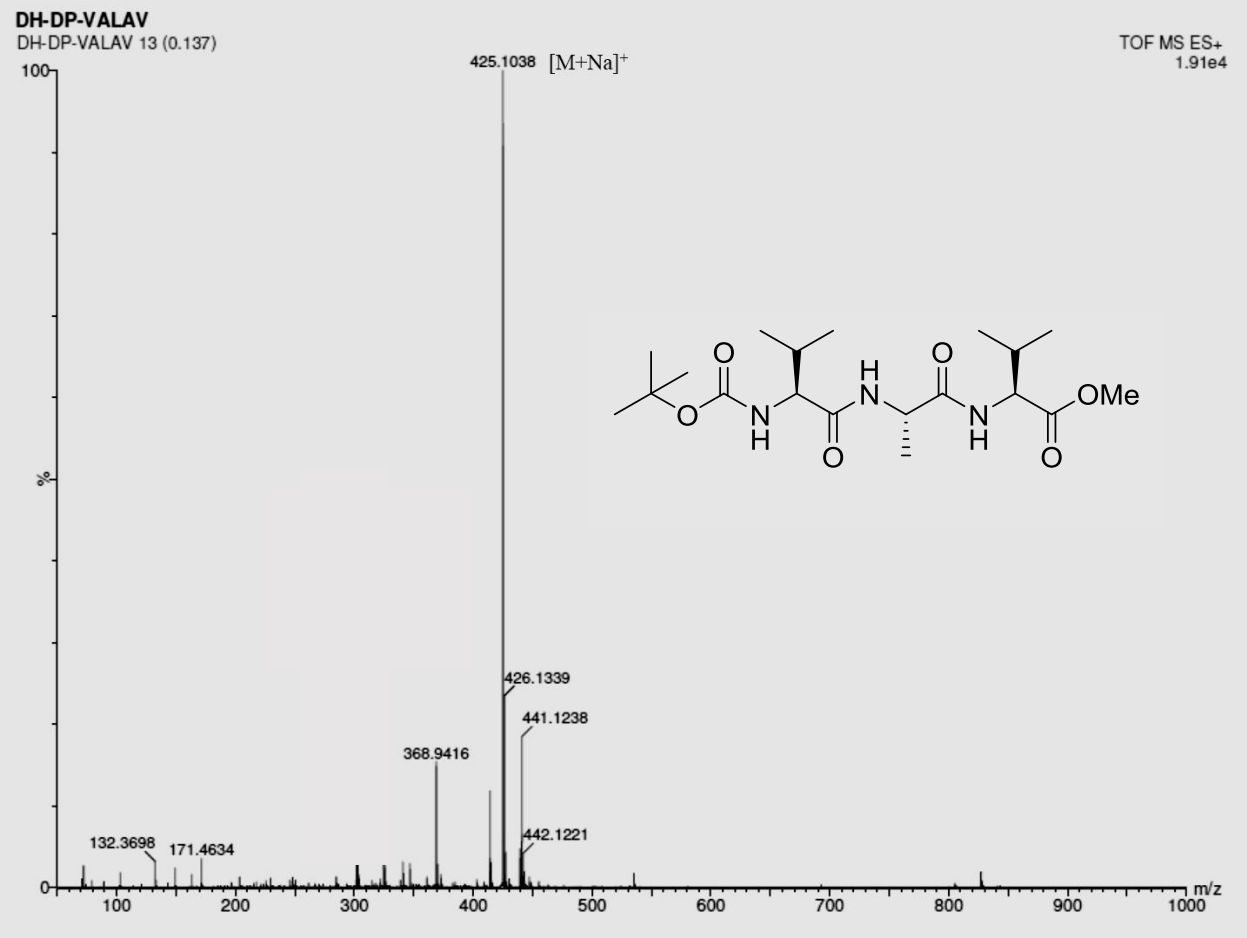


Figure S41: Mass spectrum of Boc-Val-Ala- Val-OMe.

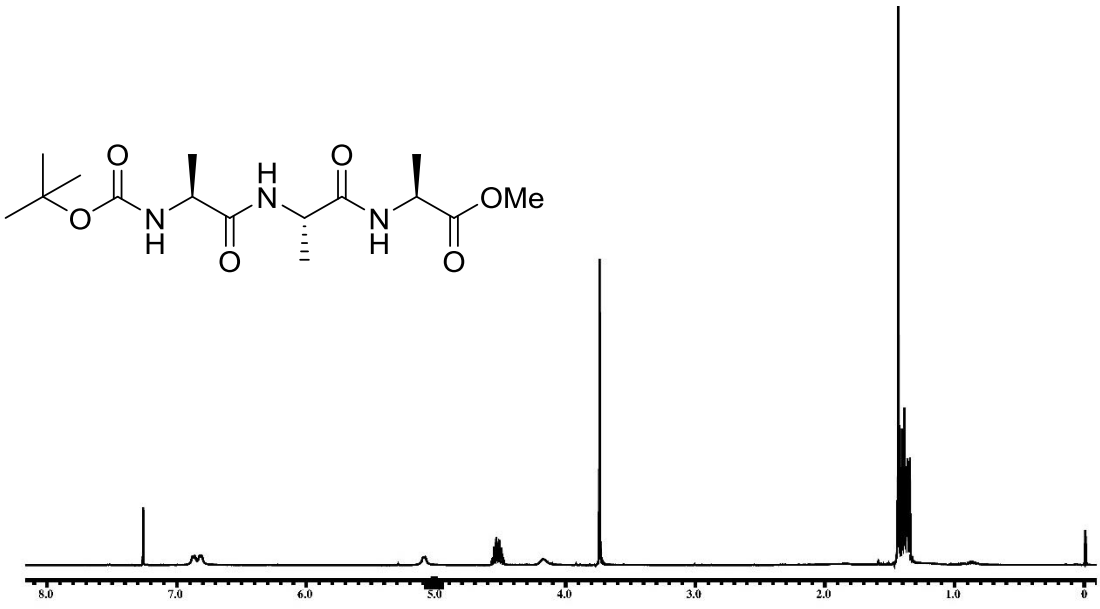


Figure S42: ^{1}H NMR (400MHz, $CDCl_3$) spectrum of Boc-Ala-Ala- Ala-OMe.

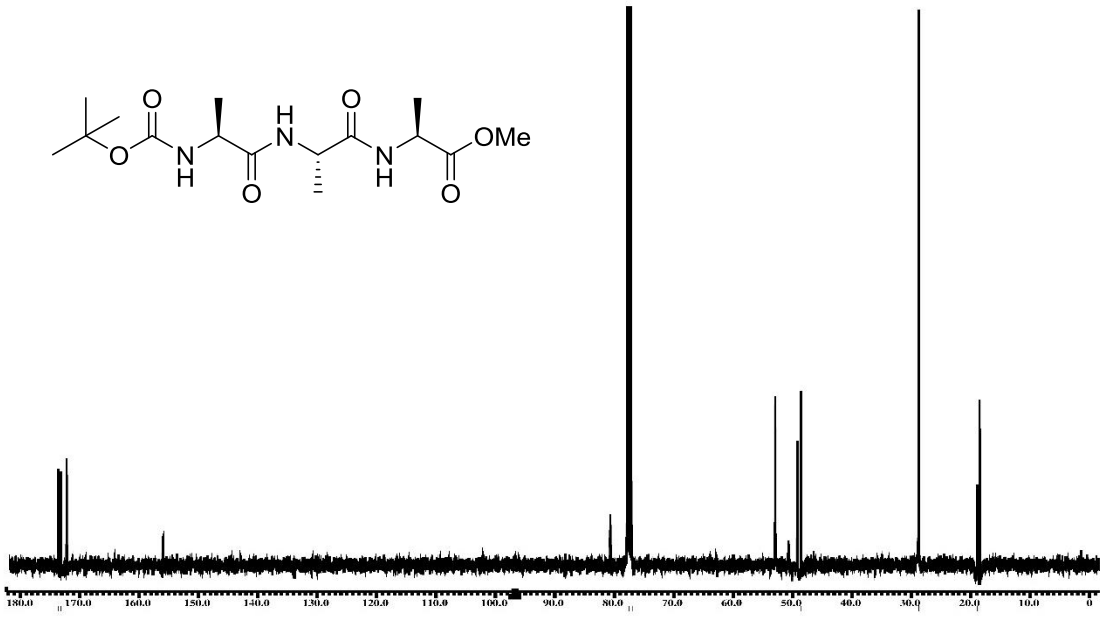


Figure S43: ^{13}C NMR (100MHz, $CDCl_3$) spectrum of Boc-Ala-Ala- Ala-OMe.

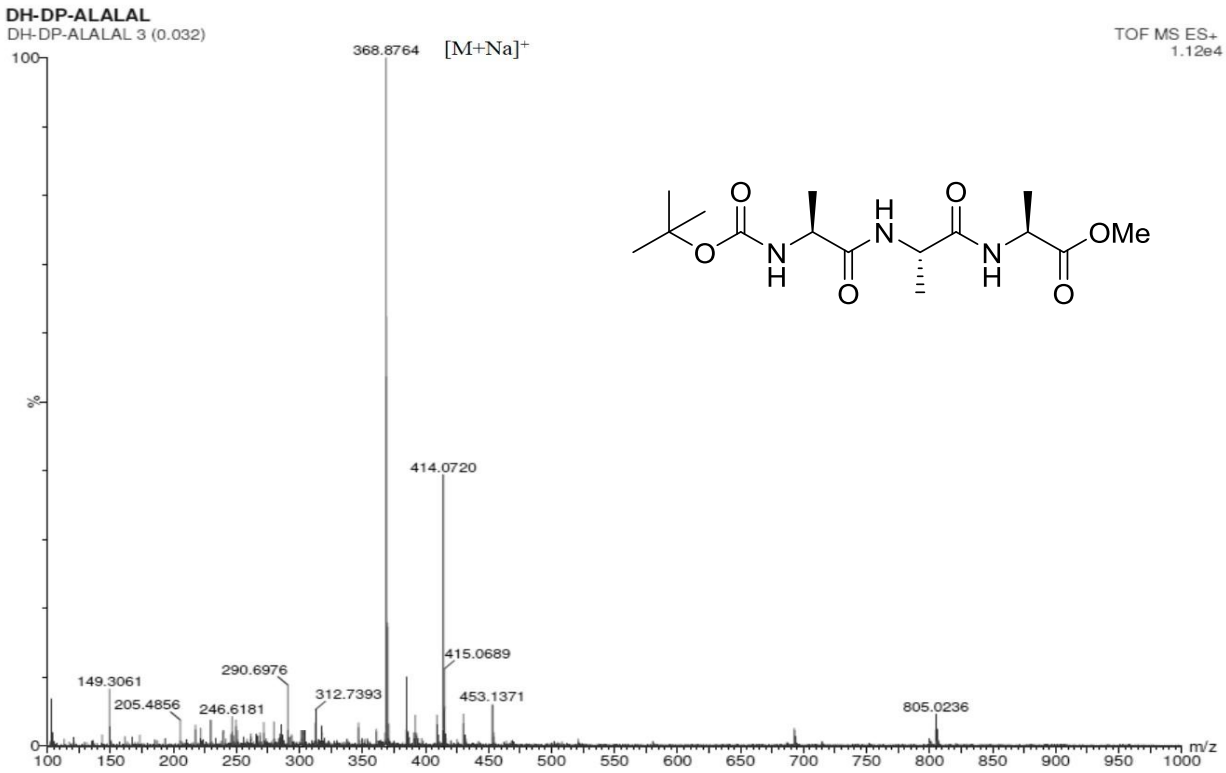


Figure S44: Mass spectrum of Boc-Ala-Ala-Ala-OMe.

Reference:

S1. A. Dutt, R. Frohlich and A. Pramanik, *Org. Biomol. Chem*., 2005, **3**, 661−665.

S2. T. Pospišil, L. F. Hamzić, L. B. Ahmed, M. Lovrić, S. Gajović and L. Frkanec, *Biomater. Sci*., 2016, **4**, 1412-1416.