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Supporting Information

Amide Neighbouring-Group Effects in Peptides: Phenylalanine as Relay Amino Acid in Long-Distance Electron Transfer

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Supporting Information

Contents

1. Supplementary figures and tables

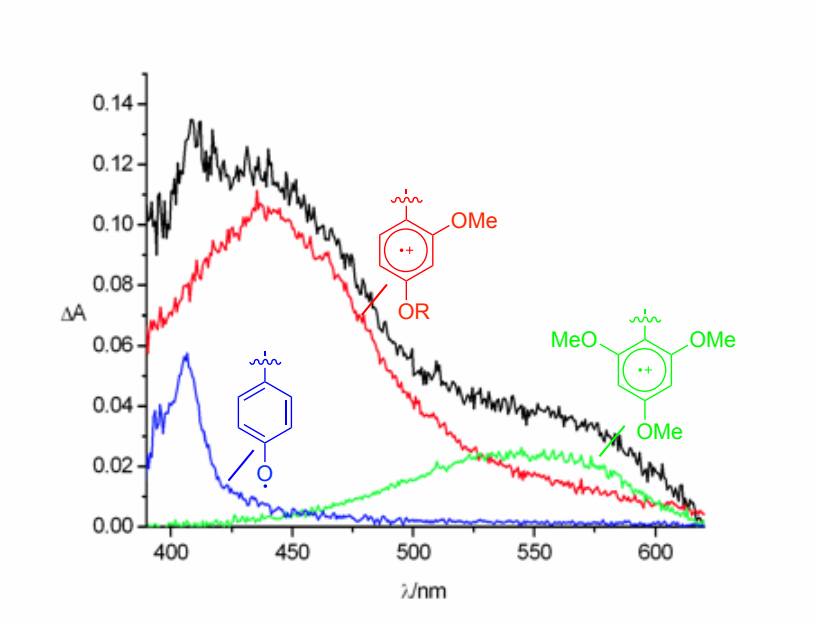


Figure S1. UV/Vis spectrum (black) 40 ns after the laser flash of a nonapeptide with 2,4,6-trimethoxybenzene as functional group at the central amino acid. Subtraction by red line (electron acceptor) leads to blue and green lines (oxidized electron donor and relay amino acid, respectively). Data taken from: M. Cordes, A. Köttgen, C. Jasper, O. Jacques, H. Boudebous, B. Giese, *Angew. Chem.* **2008**, *120*, 3511-3513; *Angew. Chem. Int. Ed*. **2008**, *47*, 3461-3663.

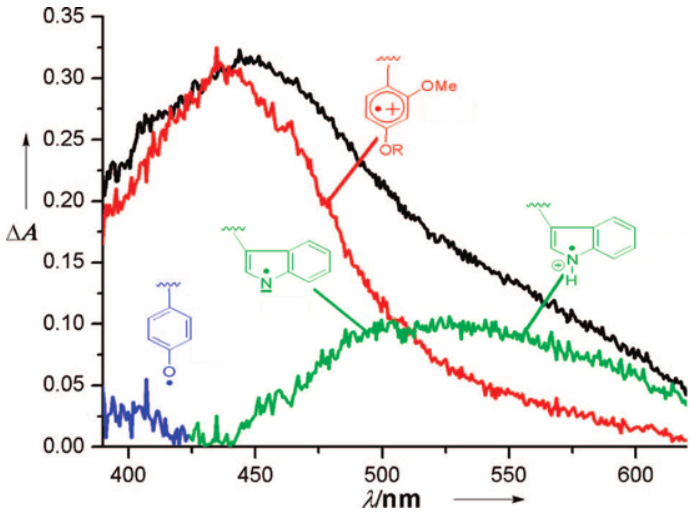


Figure S2. UV/Vis spectrum (black) 40 ns after the laser flash of **1b**. Subtraction by red line (electron acceptor) leads to blue and green lines (oxidized electron donor and relay amino acid, respectively). Data taken from: B. Giese, M. Wang, J. Gao, M. Stoltz, M. Gruber, *J. Org. Chem.* **2009**, *74*, 3621-3625.

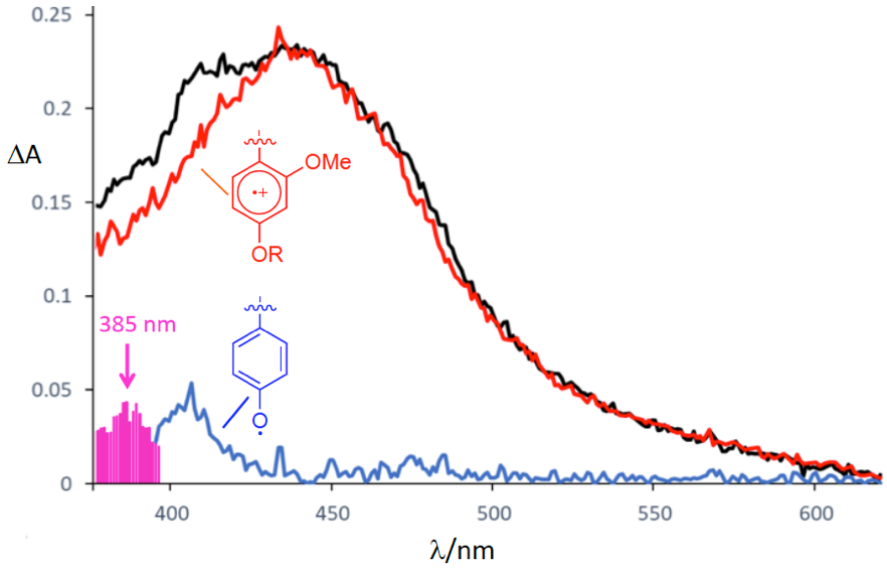


Figure S3. UV/Vis spectrum (black) 40 ns after the laser flash of **1c** (Met as central amino acid). Subtraction by red line (electron acceptor) leads to blue (oxidized electron donor) and pink lines. The pink absorption corresponds well to the absorption of a thioether radical cation, which is stabilized by a neighbouring pyrrolidine amide (ref. [13] in the paper).

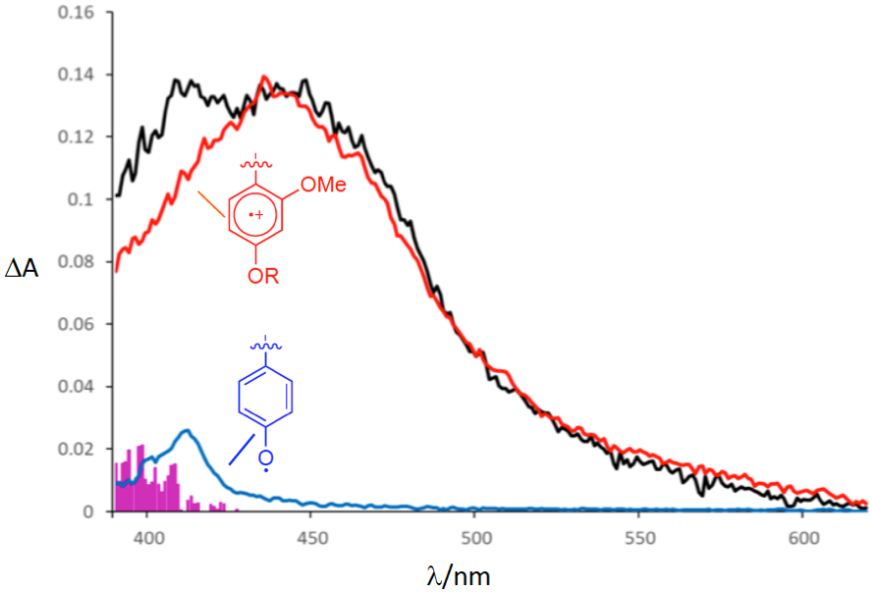


Figure S4. UV/Vis spectrum 40 ns after the laser flash of **1d** (Phe as central amino acid). Subtraction by red line (electron acceptor) leads to blue (oxidized electron donor) and pink lines. The pink absorption is blue-shifted compared to the toluene radical cation (ref. [17] in the paper) and could indicate the Phe radical cation **4d**, which is stabilized by a neighbouring amide.

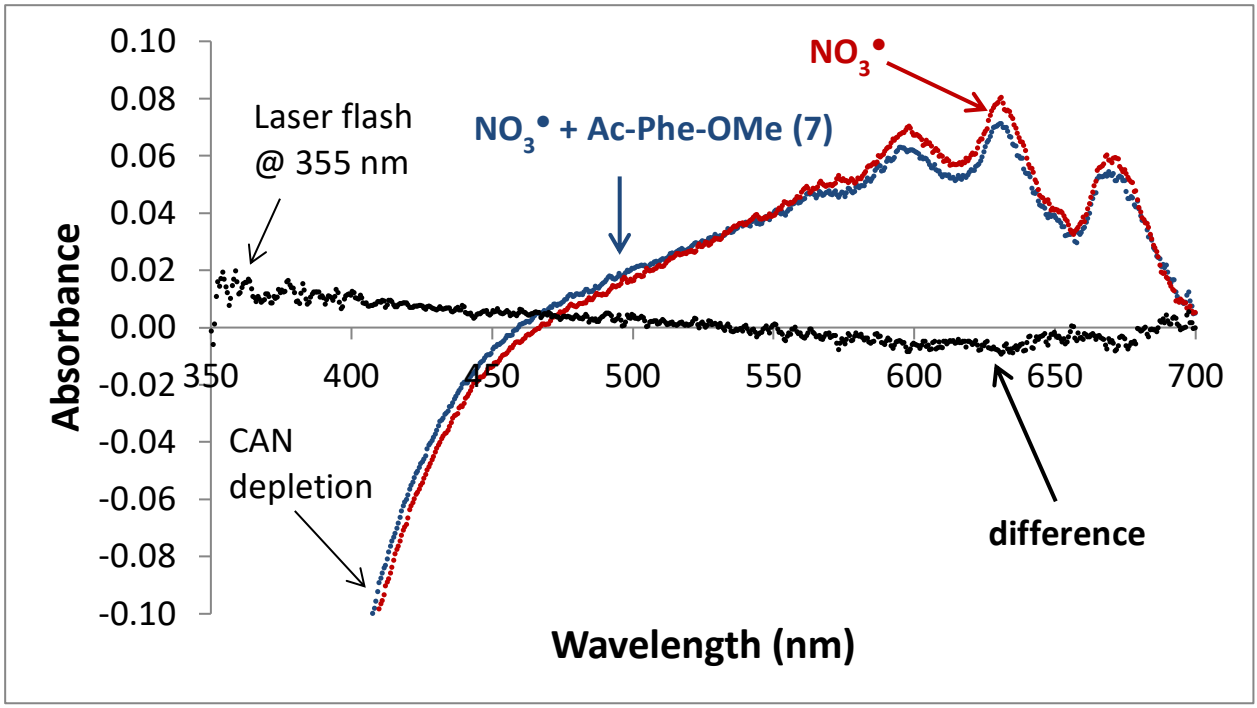


Figure S5a. UV/Vis spectra 180 ns after the laser flash of a 0.3 mM CAN solution in the absence (*red line*) and presence of 10 mM Ac-Phe-OMe (**7**) (*blue line*). Black line: *blue line* and *red line* difference. Spectra taken at 60 ns, 240 ns and 1400 ns after the laser flash showed a similiar behaviour. It was shown in a separate experiment that the decay of the absorption at 500 nm has the same kinetic behaviour as that of the $NO_3^{\bullet}$ absorption at 630 nm. Because of the strong CAN depletion possible transient formation below 480 nm cannot be detected.

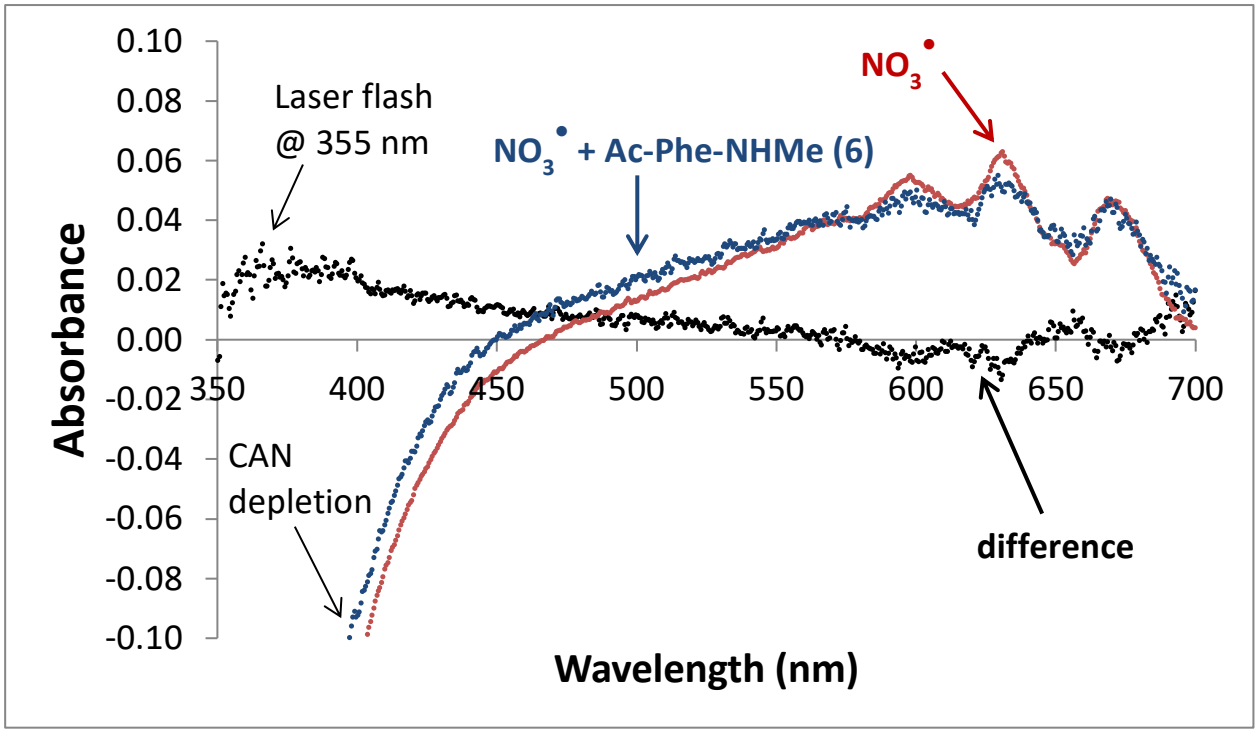
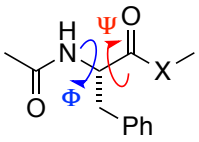


Figure S5b. UV/Vis spectra 180 ns after the laser flash of a 0.3 mM CAN solution in the absence (*red line*) and presence of 10 mM Ac-Phe-NHMe (**6**) (*blue line*). Black line: *blue line* and *red line* difference. Spectra taken at 60 ns, 240 ns and 1400 ns showed a similiar behaviour. The decay of the absorption at 500 nm shows the same kinetics as that of the $NO_3^{\bullet}$ absorption at 630 nm. Because of the strong CAN depletion possible transient formation below 480 nm cannot be detected.

Table S1. Calculated peptide backbone dihedral angles for structures shown in Schemes 2 and 4 (M062X/6-31G*).



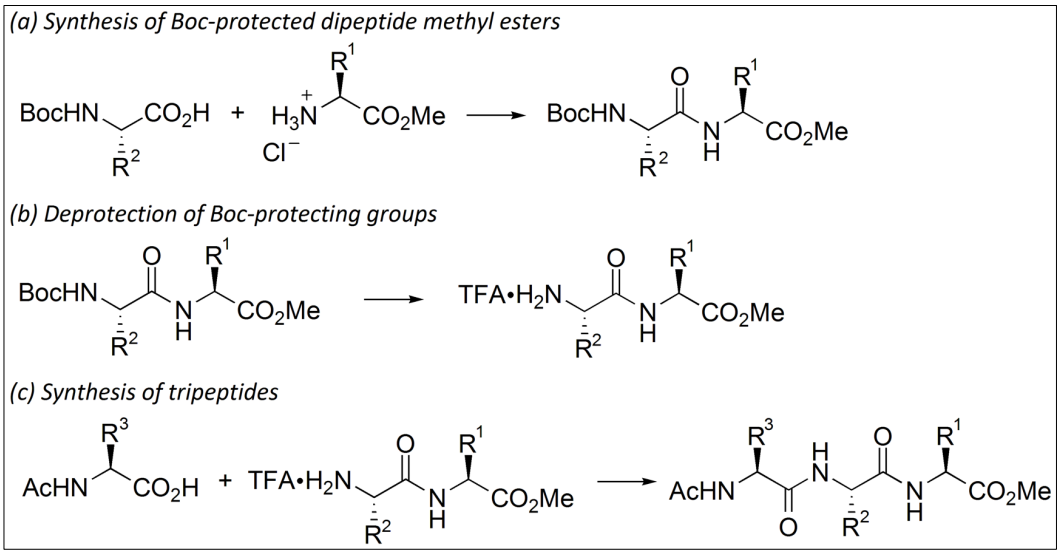
6: X = NH
7: X = O

Compound	Φ = C(O)C$^{\alpha}$NC(O)	Ψ = NC(O)C$^{\alpha}$N	Ψ = OC(O)C$^{\alpha}$N
6	-164.9°	168.3°	
6$^{\bullet+}$	-164.9°	168.3°	
6a$^{\bullet+}$	60.9°	31.7°	
6b$^{\bullet+}$	56.6°	45.7°	
6c$^{\bullet+}$	145.4°	-168.8°	
7	-164.2°		175.7°
7$^{\bullet+}$	-164.2°		175.7°
7a$^{\bullet+}$	50.4°		38.4°
7b$^{\bullet+}$	-176.6°		177.5°
7c$^{\bullet+}$	144.9°		-169.6°

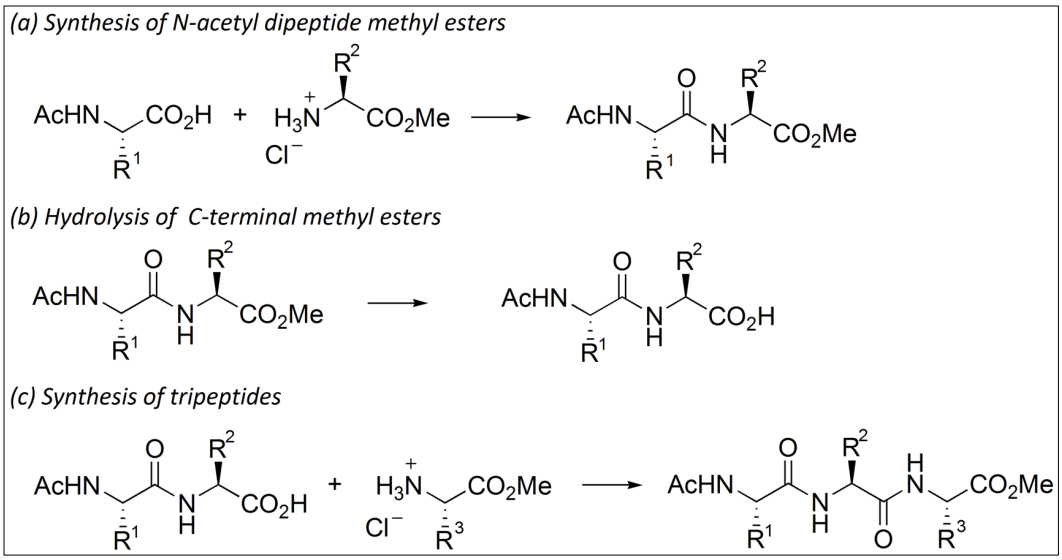
2. Peptide synthesis

The *N*-acetyl amino acid methyl esters were prepared by *N*-acetylation of the amino acids, followed by methylation of the *C*-termini. Dipeptides were obtained by coupling the *N*-protected and *C*-protected amino acids.

Tripeptides were synthesised sequentially either from (i) the *C*-terminus (starting with the *C*-protected methyl ester hydrochloride salt) via *N*-Boc-protected intermediates (**Procedure A,** scheme S1), or (ii) the *N*-terminus (starting with the *N*-acetyl amino acid) via *N*-acetyl dipeptides (**Procedure B**, Scheme S2). Compounds for which no spectroscopic details are provided, were obtained commercially (Sigma Aldrich, AK Scientific).



Scheme S1. Sequential synthesis of tripeptides from the *C*-terminus (Procedure A).



Scheme S2. Sequential synthesis of tripeptides from the *N*-terminus (Procedure B).

^{1}H and ^{13}C spectra were recorded on either an Agilent MR 400 MHz NMR spectrometer or an Agilent DD2 500 MHz NMR spectrometer, in either deuterated dimethylsulfoxide (DMSO-d_6), deuterated acetonitrile (Acetonitrile-d_3) or deuterated methanol (Methanol-d_4). Chemical

shifts are reported in ppm (δ) using respective residual solvents as reference (DMSO: δ = 2.50 ppm for ^{1}H NMR, δ = 39.52 ppm for ^{13}C NMR; Acetonitrile: δ = 1.94 ppm for ^{1}H NMR, δ = 118.26 ppm for ^{13}C NMR; and Methanol: δ = 3.31 ppm for ^{1}H NMR, δ = 49.00 ppm for ^{13}C NMR).

High Resolution Mass Spectrometry (HRMS) was conducted by ionising the samples using ESI into a Thermo Scientific Exactive Plus Orbitrap mass spectrometer.

The crude products were purified by silica column chromatography with approximately 30 g of dry silica per 1 g of crude product mixture. The eluting solvent consisted of a mixture of petroleum ether and ethyl acetate or dichloromethane and methanol. Purity was assessed by analytical reversed-phase HPLC on an Alltech Hypersil BDS-C18 5 µm 150 x 4.6 mm (Gradient: 100% water buffered with 0.1% TFA to 100% acetonitrile buffered with 0.1% TFA over 25 minutes, 4%/min, flow rate: 1 mL/min).

2.1. General procedure for the *N*-acetylation of the amino acids

Amino acid (53.4 mmol) was suspended in 5% aq. $NaHCO_3$ (150 mL) and cooled to 0 ^{o}C. Acetic anhydride (6.1 mL, 64.5 mmol, 1.2 eq.) was added dropwise over a period of 1 hour. The mixture was stirred at room temperature for 2-4 hours and the reaction was monitored by TLC (9:1 ethanol/1 M acetic acid, ninhydrin stain) until consumption of the starting material was observed. The mixture was then acidified to pH 2-3 with 6 M HCl and cooled overnight. The resulting precipitate was filtered off, washed with cold water (2 x 10 mL) and dried to give the *N*-acetylated amino acid as a white solid.

2.2. General procedure for the esterification of the amino acids

Amino acid (78.8 mmol) was suspended in methanol (250 mL) and cooled at 0 ^{o}C. Thionyl chloride (10 mL, 138 mmol, 1.7 eq.) was added dropwise. The mixture was stirred overnight at room temperature and the reaction was monitored by TLC (9:1 ethanol/1 M acetic acid, ninhydrin stain) until consumption of the starting material was observed. The solvent was removed under reduced pressure to give the amino acid as the methyl ester hydrochloride salt.

2.3. General procedure for the esterification of the *N*-acetylated amino acids

Amino acid (12.0 mmol) was suspended in methanol (11 mL) and cooled to 0 ^{o}C. Thionyl chloride (1.0 mL, 13.8 mmol, 1.2 eq.) was added dropwise. The mixture was stirred for 4 hours and the reaction was monitored by TLC (ethyl acetate, PMA or Hanessian's stain) until consumption of starting material was observed. The solvent was removed under reduced pressure and water (20 mL) was added. The crude product was extracted with dichloromethane (3 x 15 mL). The combined organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure to give the *N*- and *C*- protected amino acids as white crystals.

2.4. General procedure for the peptide coupling

The *N*-protected amino acid (10.0 mmol), amino acid methyl ester salt (10.1 mmol) and (2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU) (3.75 g, 9.9 mmol) were suspended in anhydrous DMF (15 mL) and cooled to 0 ^{o}C. Triethylamine (4.2 mL, 30.0 mmol) was added dropwise and the mixture was stirred overnight at room temperature. The reaction was monitored by TLC (ethyl acetate, PMA or ninhydrin stain) until consumption of starting material was observed. The mixture was then partitioned between 1 M HCl (100 mL) and ethyl acetate (100 mL). The aqueous phase was extracted with ethyl acetate (2 x 100 mL), and the combined extracts were washed with 5% aq. $NaHCO_3$ (100 mL) and brine (100 mL). The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure to give a sticky oil or a white solid. The residue was purified by silica column chromatography or by recrystallisation from ethyl acetate.

2.5. General procedure for the *N*-Boc deprotection

The *N*-Boc protected peptide methyl ester (10.0 mmol) was dissolved in dichloromethane (8 mL) and cooled to 0 ^{o}C. Trifluoroacetic acid (8 mL, 104.5 mmol) was added dropwise. The mixture was stirred overnight and the reaction was monitored by TLC (ethyl acetate, ninhydrin stain) until consumption of the starting material was observed. The solvent was removed under reduced pressure, followed by azeotroping with toluene to remove residual trifluoroacetic acid, to give a white or yellow solid. The crude material was obtained as the trifluoroacetate salt and used without further purification.

2.6. General procedure for the hydrolysis of *C*-terminal methyl esters

The *N*-acetyl protected peptide methyl ester (1.82 mmol) was dissolved in tetrahydrofuran (28 mL) and cooled to 0 ^{o}C. A solution of lithium hydroxide (0.60 g, 25.2 mmol) in water (28 mL) was cooled to 0 ^{o}C and then added to the first solution. After stirring overnight, a solution of 3 M HCl (10 mL) was added, followed by an addition of brine (20 mL). The mixture was then extracted with ethyl acetate (4 x 20 mL), and the combined organic extracts were washed with brine (50 mL). The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the product as a white solid.

2.7. Preparation of *N*-acetyl-L-phenylalanine amide (Ac-Phe-NH_2 (14))

L-Phenylalanine methyl ester hydrochloride (2.40 g, 11.1 mmol) was dissolved in 28% aqueous ammonia solution (25 mL). After stirring overnight, the mixture was concentrated under reduced pressure to give a white-off solid. The solid was dissolved in acetonitrile (5 mL) and acetic anhydride (1 mL, 10.6 mmol) was added dropwise. The mixture was stirred for 1 day at room temperature and filtered off to give the product as a white solid.

2.8. Preparation of *N*-acetyl-L-phenylalanine methyl amide (Ac-Phe-NHMe (6))

N-Methyl morpholine (1.2 mL, 10.9 mmol) was added to a solution of *N*-acetyl-L-phenylalanine (2.10 g, 10.1 mmol) in dimethylformamide (7 mL) and tetrahydrofuran (7 mL) at -10 ^{o}C. Trimethylacetyl (pivaloyl) chloride (1.25 mL, 10.2 mmol) was added dropwise. After 10 minutes, a solution of methylamine hydrochloride (3.36 g, 49.8 mmol) and triethylamine (7.0 mL, 50.2 mmol) in water (7 mL) was added. The resulting mixture was stirred for 1.5 hours and the solvent was removed under reduced pressure. The residue was dissolved in chloroform (30 mL) and washed with water (2 x 30 mL). The organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure to give a white solid. The crude product was purified by silica column chromatography to give the pure product.

2.9. Preparation of *N*-acetyl-L-phenylalanine *t*-butyl amide (Ac-Phe-NH*t*Bu (13))

N-acetyl-L-phenylalanine (3.50 g, 16.9 mmol) and *p*-nitrophenol (2.37 g, 17.1 mmol) were dissolved in dichloromethane (20 mL). *N*,*N'*-Dicyclohexylcarbodiimide/DCC (3.48 g, 16.9 mmol) was added in portions. The resulting mixture was heated at 40 ^{o}C for 8 hours and filtered through a bed of celite. The filter cake was washed with dichloromethane and the filtrate was concentrated under reduced pressure. The yellow solid was dissolved in dichloromethane (150 mL) and *t*-butylamine (2.0 mL, 18.8 mmol) was added dropwise. The resulting mixture was heated at 40 ^{o}C for 16 hours and filtered through a bed of celite. The filtrate was concentrated under reduced pressure and the crude material was recrystallised from hot ethanol to give a colourless crystal.

3. Spectroscopic details for the synthesised compounds

3.1. *N*-Acetyl-L-phenylalanine methyl ester (Ac-Phe-OMe (7))

(a) *N*-Acetyl-L-phenylalanine: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.65 (s, 1H), 8.18 (d, *J* = 8.1 Hz, 1H), 7.31 – 7.25 (m, 2H), 7.24 – 7.17 (m, 3H), 4.40 (ddd, *J* = 9.6, 8.1, 4.9 Hz, 1H), 3.03 (dd, *J* = 13.8, 4.9 Hz, 1H), 2.83 (dd, *J* = 13.8, 9.6 Hz, 1H), 1.77 ppm (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 173.15, 169.19, 137.71, 129.03, 128.16, 126.38, 53.48, 36.77, 22.33 ppm. HRMS (ESI) *m/z* calcd. for $[C_{11}H_{14}NO_3]^+$: 208.0978 $[M+H]^+$, found 208.0975, HRMS (ESI) *m/z* calcd. for $[C_{22}H_{27}N_2O_6]^+$: 415.1869 $[2M+H]^+$, found 415.1893.

(b) *N*-Acetyl-L-phenylalanine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.33 (d, *J* = 7.8 Hz, 1H), 7.33 – 7.23 (m, 2H), 7.26 – 7.16 (m, 3H), 4.44 (ddd, *J* = 9.1, 7.7, 5.6 Hz, 1H), 3.59 (s, 3H), 3.00 (dd, *J* = 13.8, 5.6 Hz, 1H), 2.87 (dd, *J* = 13.7, 9.3 Hz, 1H), 1.79 ppm (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.19, 169.29, 137.25, 128.99, 128.23, 126.52, 53.60, 51.79, 36.72, 22.23 ppm. HRMS (ESI) *m/z* calcd. for $[C_{12}H_{16}NO_3]^+$: 222.1130 $[M+H]^+$, found 222.1137, HRMS (ESI) *m/z* calcd. for $[C_{12}H_{15}NO_3Na]^+$: 375.2495 $[M+Na]^+$, found 375.2517.

3.2. *N*-acetyl-L-phenylalanine amide (Ac-Phe-NH_2 (14))

(a) L-Phenylalanine methyl ester hydrochloride: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.74 (s, 3H), 7.38 – 7.28 (m, 2H), 7.32 – 7.20 (m, 3H), 4.23 (dd, *J* = 7.4, 5.9 Hz, 1H), 3.65 (s, 3H), 3.21 (dd, *J* = 14.0, 5.7 Hz, 1H), 3.10 ppm (dd, *J* = 14.0, 7.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.34, 134.69, 129.38, 128.57, 127.24, 53.22, 52.53, 35.83 ppm. HRMS (ESI) *m/z* calcd. for $[C_{10}H_{14}NO_2]^+$: 180.1019 $[M-Cl]^+$, found 180.1010.

(b) *N*-Acetyl-L-phenylalanine amide: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.01 (d, *J* = 8.5 Hz, 1H), 7.42 (s, 1H), 7.29 – 7.21 (m, 4H), 7.22 – 7.13 (m, 1H), 7.01 (s, 1H), 4.41 (td, *J* = 9.2, 4.7 Hz, 1H), 2.98 (dd, *J* = 13.7, 4.7 Hz, 1H), 2.72 (dd, *J* = 13.7, 9.7 Hz, 1H), 1.75 ppm (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 173.24, 168.97, 138.22, 129.07, 127.99, 126.15, 53.78, 37.65, 22.50 ppm. HRMS (ESI) *m/z* calcd. for $[C_{11}H_{15}N_2O_2]^+$: 207.1134 $[M+H]^+$, found 207.1130, HRMS (ESI) *m/z* calcd. for $[C_{11}H_{14}N_2O_4Na]^+$: 229.0953 $[M+Na]^+$, found 229.0949.

3.3. *N*-Acetyl-L-phenylalanine methyl amide (Ac-Phe-NHMe (6))

(a) *N*-Acetyl-L-phenylalanine: see section 2.1(a)

(b) *N*-Acetyl-L-phenylalanyl methyl amide: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (d, *J* = 8.5 Hz, 1H), 7.88 (q, *J* = 4.6 Hz, 1H), 7.30 – 7.21 (m, 2H), 7.24 – 7.13, (m, 3H), 4.40 (ddd, *J* = 9.5, 8.4, 5.0 Hz, 1H), 2.95 (dd, *J* = 13.7, 5.0 Hz, 1H), 2.72 (dd, *J* = 13.7, 9.6 Hz, 1H), 2.56 (d, *J* = 4.5 Hz, 3H), 1.75 ppm (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.58, 169.00, 138.16, 129.03, 128.02, 126.19, 54.07, 37.78, 25.52, 22.50 ppm. HRMS (ESI) *m/z* calcd. for $[C_{12}H_{17}N_2O_2]^+$: 221.1290 $[M+H]^+$, found 221.1283, HRMS (ESI) *m/z* calcd. for $[C_{24}H_{33}N_4O_4]^+$: 441.2502 $[2M+H]^+$, found 441.2495.

3.4. *N*-Acetyl-L-phenylalanine *t*-butyl amide (Ac-Phe-NH*t*Bu (13))

(a) *N*-Acetyl-L-phenylalanine: see section 2.1(a)

(b) *N*-Acetyl-L-phenylalanyl *t*-butyl amide: ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.96 (d, *J* = 8.4 Hz, 1H), 7.49 (s, 1H), 7.29 – 7.18 (m, 4H), 7.22 – 7.13, (m, 1H), 4.46 (td, *J* = 8.7, 6.1 Hz, 1H), 2.85 (dd, *J* = 13.5, 5.7 Hz, 1H), 2.72 (dd, *J* = 13.5, 8.9 Hz, 1H), 1.75 (s, 3H), 1.19 ppm (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.47, 168.77, 137.90, 129.25, 127.86, 126.10, 54.07, 50.02, 38.33, 28.38, 22.48 ppm. HRMS (ESI) *m/z* calcd. for $[C_{15}H_{23}N_2O_2]^+$: 263.1760 $[M+H]^+$, found 263.1752, HRMS (ESI) *m/z* calcd. for $[C_{15}H_{22}N_2O_2K]^+$: 301.1318 $[M+K]^+$, found 301.1310.

3.5. *N*-Acetyl-L-leucyl-L-phenylalanine methyl ester (Ac-Leu-Phe-OMe (15))

(a) L-Phenylalanine methyl ester hydrochloride: see section 2.2(a)

(b) *N*-Acetyl-L-leucine: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.46 (s, 1H), 8.07 (d, *J* = 7.9 Hz, 1H), 4.19 (ddd, *J* = 9.1, 8.1, 6.0 Hz, 1H), 1.83 (s, 3H), 1.69 – 1.54 (m, 1H), 1.48 ppm (ddd, *J* = 8.5, 5.5, 3.0 Hz, 2H), 0.89 (d, *J* = 6.5 Hz, 3H), 0.84 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 174.26, 169.24, 50.18, 40.00, 24.32, 22.84, 22.33, 21.30 ppm. HRMS (ESI) *m/z* calcd. for $[C_8H_{16}NO_3]^+$: 174.1130 $[M+H]^+$, found 174.1133, HRMS (ESI) *m/z* calcd. for $[C_{16}H_{31}N_2O_6]^+$: 347.2182 $[2M+H]^+$, found 347.2182.

(c) *N*-Acetyl-leucyl-L-phenylalanine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.30 (d, *J* = 7.4 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.29 – 7.24 (m, 2H), 7.24 – 7.18 (m, 3H), 4.48 – 4.40 (m, 1H), 4.32 (td, *J* = 8.7, 6.0 Hz, 1H), 3.56 (s, 3H), 3.02 (dd, *J* = 13.9, 5.9 Hz, 1H), 2.94 (dd, *J* = 13.9, 8.6 Hz, 1H), 1.80 (s, 3H), 1.61 – 1.49 (m, 1H), 1.44 – 1.28 (m, 2H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.82 ppm (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.30, 171.79, 168.90, 137.12, 129.04, 128.19, 126.50, 53.45, 51.75, 50.51, 40.85, 36.43, 24.09, 22.93, 22.44, 21.71 ppm. HRMS (ESI) *m/z* calcd. for $[C_{18}H_{27}N_2O_4]^+$: 335.1965 $[M+H]^+$, found 335.1976, HRMS (ESI) *m/z* calcd. for $[C_{18}H_{26}N_2O_4Na]^+$: 357.1785 $[M+Na]^+$, found 357.1790.

3.6. *N*-Acetyl-L-phenylalanyl-L-leucine methyl ester (Ac-Phe-Leu-OMe (16))

(a) L-Leucine methyl ester hydrochloride: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.73 (s, 3H), 3.90 (t, *J* = 7.0, 1H), 3.73 (s, 3H), 1.81 – 1.72 (m, 1H), 1.72 – 1.58 (m, 2H), 0.88 ppm (d, *J* = 6.4 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.25, 52.69, 50.47, 39.11, 23.71, 22.16, 21.97 ppm. HRMS (ESI) *m/z* calcd. for $[C_7H_{16}NO_2]^+$: 146.1181 $[M-Cl]^+$, found 146.1182.

(b) *N*-Acetyl-L-phenylalanine: see section 2.1(a)

(c) *N*-Acetyl-phenylalanyl-L-leucine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.37 (d, *J* = 7.7 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.26 (d, *J* = 4.4 Hz, 4H), 7.19 (p, *J* = 4.5 Hz, 1H), 4.54 (ddd, *J* = 10.1, 8.5, 4.3 Hz, 1H), 4.29 (ddd, *J* = 9.6, 7.7, 5.3 Hz, 1H), 3.61 (s, 3H), 2.99 (dd, *J* = 13.9, 4.3 Hz, 1H), 2.71 (dd, *J* = 13.9, 10.0 Hz, 1H), 1.74 (s, 3H), 1.68 – 1.57 (m, 1H), 1.60 – 1.44 (m, 2H), 0.90 (d, *J* = 6.4 Hz, 3H), 0.84 ppm (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.78, 171.68, 169.00, 137.95, 129.12, 127.97, 126.19, 53.55, 51.83, 50.28, 39.68, 37.56, 24.18,

22.74, 22.42, 21.31 ppm. HRMS (ESI) *m/z* calcd. for $[C_{18}H_{27}N_2O_4]^+$: 335.1965 $[M+H]^+$, found 335.1975, HRMS (ESI) *m/z* calcd. for $[C_{18}H_{26}N_2O_4Na]^+$: 357.1785 $[M+Na]^+$, found 357.1784.

3.7. *N*-Acetyl-L-valyl-L-phenylalanine methyl ester (Ac-Val-Phe-OMe (17))

(a) L-Phenylalanine methyl ester hydrochloride: see section 2.2(a)

(b) *N*-Acetyl-valyl-L-phenylalanine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.39 (d, *J* = 7.3 Hz, 1H), 7.79 (d, *J* = 9.0 Hz, 1H), 7.31 – 7.22 (m, 2H), 7.25 – 7.15 (m, 3H), 4.45 (dt, *J* = 8.5, 6.5 Hz, 1H), 4.18 (dd, *J* = 9.1, 7.0 Hz, 1H), 3.55 (s, 3H), 3.01 (dd, *J* = 13.9, 6.1 Hz, 1H), 2.93 (dd, *J* = 13.9, 8.8 Hz, 1H), 1.91 (hept, *J* = 7.0 Hz, 1H), 1.83 (s, 3H), 0.82 (d, *J* = 7.0 Hz, 3H), 0.79 ppm (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.79, 171.32, 169.04, 137.12, 129.02, 128.19, 126.52, 57.18, 53.53, 51.68, 36.50, 30.56, 22.44, 19.06, 18.08 ppm. HRMS (ESI) *m/z* calcd. for $[C_{17}H_{25}N_2O_4]^+$: 321.1814 $[M+H]^+$, found 321.1814, HRMS (ESI) *m/z* calcd. for $[C_{17}H_{24}N_2O_4Na]^+$: 343.1633 $[M+Na]^+$, found 343.1638.

3.8. *N*-Acetyl-L-phenylalanyl-L-valine methyl ester (Ac-Phe-Val-OMe (18))

(a) L-Valine methyl ester hydrochloride: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.66 (s, 3H), 3.83 (d, *J* = 4.7, 1H), 3.74 (s, 3H), 2.19 (heptd, *J* = 6.9, 4.5 Hz, 1H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.93 ppm (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.20, 57.23, 52.23, 29.31, 18.44, 17.56 ppm. HRMS (ESI) *m/z* calcd. for $[C_6H_{14}NO_2]^+$: 132.1019 $[M-Cl]^+$, found 132.1021.

(b) *N*-Acetyl-L-phenylalanine: see section 2.1(a)

(c) *N*-Acetyl-phenylalanyl-L-valine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.24 (d, *J* = 8.1 Hz, 1H), 8.07 (d, *J* = 8.3 Hz, 1H), 7.28 – 7.24 (m, 4H), 7.24 – 7.13 (m, 1H), 4.62 (ddd, *J* = 10.0, 8.4, 4.4 Hz, 1H), 4.17 (dd, *J* = 8.1, 6.3 Hz, 1H), 3.62 (s, 3H), 2.96 (dd, *J* = 13.9, 4.4 Hz, 1H), 2.71 (dd, *J* = 13.9, 10.1 Hz, 1H), 2.04 (h, *J* = 6.8 Hz, 1H), 1.74 (s, 3H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.87 ppm (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.87, 171.81, 169.08, 137.91, 129.15, 127.95, 126.18, 57.42, 53.50, 51.68, 37.47, 29.88, 22.40, 18.92, 18.25 ppm. HRMS (ESI) *m/z* calcd. for $[C_{17}H_{25}N_2O_4]^+$: 321.1814 $[M+H]^+$, found 321.1809, HRMS (ESI) *m/z* calcd. for $[C_{17}H_{25}N_2O_4Na]^+$: 343.1633 $[M+Na]^+$, found 343.1628.

3.9. *N*-Acetyl-L-leucyl-L-leucyl-L-phenylalanine methyl ester (Ac-Leu-Leu-Phe-OMe (19))

This tripeptide was synthesised from the *C*-terminus according to **Procedure A**, Scheme S1.

(a) L-Phenylalanine methyl ester hydrochloride: see section 2.5(a)

(b) *N*-Boc-L-leucyl-L-phenylalanine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.12 (d, *J* = 7.7 Hz, 1H), 7.30 – 7.22 (m, 2H), 7.22 – 7.18 (m, 3H), 6.80 (d, *J* = 8.5 Hz, 1H), 4.48 (td, *J* = 8.2, 5.7 Hz, 1H), 3.96 (td, *J* = 9.0, 5.7 Hz, 1H), 3.57 (s, 3H), 3.02 (dd, *J* = 13.8, 5.8 Hz, 1H), 2.94 (dd, *J* = 13.9, 8.7 Hz, 1H), 1.61 – 1.44 (m, 1H), 1.37 (s, 9H), 1.31 (d, *J* = 7.5 Hz, 2H), 0.85 (d, *J* = 6.6 Hz, 3H), 0.81 ppm (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.54, 171.83, 155.10,

137.04, 129.07, 128.17, 126.48, 77.97, 53.25, 52.62, 51.79, 40.78, 36.61, 28.17, 24.12, 22.84, 21.62 ppm. HRMS (ESI) *m/z* calcd. for $[C_{21}H_{33}N_2O_5]^+$: 393.2384 $[M+H]^+$, found 393.2383, HRMS (ESI) *m/z* calcd. for $[C_{21}H_{32}N_2O_5Na]^+$: 415.2204 $[M+Na]^+$, found 415.2203.

(c) L-Leucyl-L-phenylalanine methyl ester trifluoroacetate: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.96 (d, *J* = 7.3 Hz, 1H), 8.14 (s, 3H), 7.35 – 7.26 (m, 2H), 7.28 – 7.19 (m, 3H), 4.61 – 4.49 (m, 1H), 3.77 (dd, *J* = 8.5, 5.3 Hz, 1H), 3.60 (s, 3H), 3.07 (dd, *J* = 14.0, 5.9 Hz, 1H), 2.99 (dd, *J* = 14.0, 8.6 Hz, 1H), 1.73 – 1.58 (m, 1H), 1.53 (dd, *J* = 7.7, 5.9 Hz, 2H), 0.90 (d, *J* = 5.1 Hz, 3H), 0.88 ppm (d, *J* = 4.7 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.30, 169.35, 136.83, 129.02, 128.37, 126.72, 53.88, 52.00, 50.58, 40.22, 36.32, 23.36, 22.76, 21.71 ppm. HRMS (ESI) *m/z* calcd. for $[C_{16}H_{25}N_2O_3]^+$: 293.1865 $[M-CF_3CO_2]^+$, found 293.1860.

(d) *N*-Acetyl-L-leucine: see section 2.5(b)

(e) *N*-Acetyl-L-leucyl-L-leucyl-L-phenylalanine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.21 (d, *J* = 7.4 Hz, 1H), 7.95 (d, *J* = 8.1 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.27 (dd, *J* = 8.0, 6.1 Hz, 2H), 7.20 (td, *J* = 6.6, 1.7 Hz, 3H), 4.46 (td, *J* = 8.2, 6.1 Hz, 1H), 4.28 (dq, *J* = 15.0, 7.8 Hz, 2H), 3.56 (s, 3H), 3.01 (dd, *J* = 13.9, 6.0 Hz, 1H), 2.94 (dd, *J* = 14.0, 8.5 Hz, 1H), 1.82 (s, 3H), 1.55 (dh, *J* = 13.5, 6.8 Hz, 2H), 1.38 (q, *J* = 7.1 Hz, 4H), 0.86 (d, *J* = 6.6 Hz, 6H), 0.82 ppm (dd, *J* = 6.6, 3.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.96, 171.85, 171.69, 169.12, 137.02, 128.97, 128.20, 126.50, 53.38, 51.75, 50.91, 50.63, 40.86, 40.71, 36.49, 24.15, 24.03, 23.04, 22.93, 22.48, 21.72, 21.59 ppm. HRMS (ESI) *m/z* calcd. for $[C_{24}H_{38}N_3O_5]^+$: 448.2812 $[M+H]^+$, found 448.2809, HRMS (ESI) *m/z* calcd. for $[C_{24}H_{37}N_3O_5K]^+$: 486.2370 $[M+K]^+$, found 486.2366.

3.10. *N*-Acetyl-L-leucyl-L-phenylalanyl-L-leucine methyl ester (Ac-Leu-Phe-Leu-OMe (20))

This tripeptide was synthesised from the *N*-terminus according to **Procedure B**, Scheme S2.

(a) *N*-Acetyl-L-leucyl-L-phenylalanine methyl ester: see section 2.5

(b) *N*-Acetyl-L-leucyl-L-phenylalanine: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.66 (s, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.90 (d, *J* = 8.5 Hz, 1H), 7.30 – 7.21 (m, 2H), 7.24 – 7.15 (m, 3H), 4.40 (td, *J* = 8.2, 5.3 Hz, 1H), 4.31 (td, *J* = 8.8, 5.9 Hz, 1H), 3.04 (dd, *J* = 13.9, 5.2 Hz, 1H), 2.91 (dd, *J* = 13.9, 8.8 Hz, 1H), 1.80 (s, 3H), 1.55 (dp, *J* = 13.4, 6.7 Hz, 1H), 1.43 – 1.30 (m, 2H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.82 ppm (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.73, 172.13, 168.93, 137.49, 129.12, 128.12, 126.38, 53.27, 50.61, 40.82, 36.51, 24.09, 23.02, 22.46, 21.66 ppm. HRMS (ESI) *m/z* calcd. for $[C_{17}H_{25}N_2O_4]^+$: 321.1814 $[M+H]^+$, found 321.1811, HRMS (ESI) *m/z* calcd. for $[C_{17}H_{24}N_2O_4Na]^+$: 343.1634 $[M+Na]^+$, found 343.1630.

(c) L-Leucine methyl ester hydrochloride: see section 2.6(a)

(d) *N*-Acetyl-L-leucyl-L-phenylalanyl-L-leucine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.18 (d, *J* = 7.6 Hz, 1H), 7.93 (dd, *J* = 8.3, 5.0 Hz, 2H), 7.29 – 7.11 (m, 5H), 4.51 (td, *J* = 8.9, 4.9 Hz, 1H), 4.29 (td, *J* = 9.1, 5.2 Hz, 1H), 4.19 (q, *J* = 7.6 Hz, 1H), 3.60 (s, 3H), 3.03 (dd, *J* = 14.1,

4.8 Hz, 1H), 2.80 (dd, *J* = 13.9, 9.3 Hz, 1H), 1.80 (s, 3H), 1.67 – 1.52 (m, 2H), 1.54 – 1.42 (m, 2H), 1.30 (t, *J* = 7.3 Hz, 2H), 0.89 (d, *J* = 6.3 Hz, 3H), 0.83 (d, *J* = 6.4 Hz, 6H), 0.79 ppm (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.65, 171.87, 171.01, 169.21, 137.67, 129.15, 127.95, 126.17, 53.31, 51.82, 51.09, 50.23, 40.65, 39.66, 37.05, 24.05, 24.04, 22.90, 22.81, 22.44, 21.67, 21.22 ppm. HRMS (ESI) *m/z* calcd. for $[C_{24}H_{38}N_3O_5]^+$: 448.2812 $[M+H]^+$, found 448.2809, HRMS (ESI) *m/z* calcd. for $[C_{24}H_{37}N_3O_5Na]^+$: 470.2631 $[M+Na]^+$, found 470.2628.

3.11. *N*-Acetyl-L-phenylalanyl-L-leucyl-L-leucine methyl ester (Ac-Phe-Leu-Leu-OMe (21))

This tripeptide was synthesised from the *N*-terminus according to **Procedure B**, Scheme S2.

(a) *N*-Acetyl-L-phenylalanyl-L-leucine methyl ester: see section 2.6

(b) *N*-Acetyl-L-phenylalanyl-L-leucine: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.55 (s, 1H), 8.23 (d, *J* = 7.9 Hz, 1H), 8.04 (d, *J* = 8.5 Hz, 1H), 7.29 – 7.20 (m, 4H), 7.22 – 7.14 (m, 1H), 4.54 (ddd, *J* = 10.2, 8.6, 4.0 Hz, 1H), 4.22 (ddd, *J* = 9.2, 7.8, 5.6 Hz, 1H), 3.00 (dd, *J* = 14.0, 4.0 Hz, 1H), 2.70 (dd, *J* = 13.8, 10.2 Hz, 1H), 1.73 (s, 3H), 1.70 – 1.56 (m, 1H), 1.56 – 1.49 (m, 2H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.85 ppm (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, Acetonitrile-d_3) δ 174.80, 172.43, 171.81, 137.84, 129.83, 128.85, 127.14, 54.92, 51.44, 40.55, 37.88, 25.02, 22.74, 22.33, 21.29 ppm. HRMS (ESI) *m/z* calcd. for $[C_{17}H_{25}N_2O_4]^+$: 321.1814 $[M+H]^+$, found 321.1810, HRMS (ESI) *m/z* calcd. for $[C_{17}H_{24}N_2O_4Na]^+$: 343.1634 $[M+Na]^+$, found 343.1630.

(c) L-Leucine methyl ester hydrochloride: see section 2.6(a)

(d) *N*-Acetyl-L-phenylalanyl-L-leucyl-L-leucine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.20 (d, *J* = 7.7 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 4.3 Hz, 4H), 7.20 – 7.15 (m, 1H), 4.51 (td, *J* = 9.8, 4.2 Hz, 1H), 4.39 – 4.23 (m, 2H), 3.60 (s, 3H), 2.97 (dd, *J* = 13.9, 4.1 Hz, 1H), 2.70 (dd, *J* = 13.9, 9.9 Hz, 1H), 1.74 (s, 3H), 1.68 – 1.52 (m, 3H), 1.54 – 1.41 (m, 3H), 0.90 (dd, *J* = 6.3, 1.6 Hz, 6H), 0.85 ppm (dd, *J* = 8.5, 6.4 Hz, 6H). ^{13}C NMR (101 MHz, Acetonitrile-d_3) δ 173.89, 173.01, 172.04, 171.47, 138.37, 130.22, 129.29, 127.57, 55.87, 52.58, 52.35, 51.69, 41.48, 40.95, 38.07, 25.43, 25.29, 23.34, 23.17, 22.96, 21.82, 21.67 ppm. HRMS (ESI) *m/z* calcd. for $[C_{24}H_{38}N_3O_5]^+$: 448.2812 $[M+H]^+$, found 448.2809, HRMS (ESI) *m/z* calcd. for $[C_{24}H_{37}N_3O_5Na]^+$: 470.2631 $[M+Na]^+$, found 470.2629.

3.12. *N*-Acetyl-L-valyl-L-valyl-L-phenylalanine methyl ester (Ac-Val-Val-Phe-OMe (22))

This tripeptide was synthesised from the *C*-terminus according to **Procedure A**, Scheme S1.

(a) L-Phenylalanine methyl ester hydrochloride: see section 2.2(a)

(b) *N*-Boc-L-valyl-L-phenylalanine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.25 (d, *J* = 7.6 Hz, 1H), 7.30 – 7.22 (m, 2H), 7.25 – 7.15 (m, 3H), 6.56 (d, *J* = 9.1 Hz, 1H), 4.49 (ddd, *J* = 9.4, 7.7, 5.8 Hz, 1H), 3.78 (dd, *J* = 9.0, 7.3 Hz, 1H), 3.57 (s, 3H), 3.02 (dd, *J* = 13.9, 5.7 Hz, 1H), 2.92

(dd, *J* = 13.9, 8.9 Hz, 1H), 1.93 – 1.77 (m, 1H), 1.37 (s, 9H), 0.77 (d, *J* = 6.6 Hz, 3H), 0.76 ppm (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.83, 171.44, 155.24, 137.07, 129.02, 128.19, 126.51, 77.99, 59.50, 53.37, 51.74, 36.65, 30.50, 28.17, 19.02, 18.11 ppm. HRMS (ESI) *m/z* calcd. for $[C_{20}H_{31}N_2O_5]^+$: 379.2233 $[M+H]^+$, found 379.2222, HRMS (ESI) *m/z* calcd. for $[C_{20}H_{30}N_2O_5Na]^+$: 401.2052 $[M+Na]^+$, found 401.2052.

(c) L-Valyl-L-phenylalanine methyl ester trifluoroacetate: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.90 (d, *J* = 7.1 Hz, 1H), 8.10 (s, 3H), 7.35 – 7.26 (m, 2H), 7.28 – 7.19 (m, 3H), 4.55 (dt, *J* = 7.4, 6.0 Hz, 1H), 3.65 (d, *J* = 5.1 Hz, 1H), 3.59 (s, 3H), 3.07 (dd, *J* = 14.0, 5.9 Hz, 1H), 2.98 (dd, *J* = 14.0, 8.5 Hz, 1H), 2.18 – 2.04 (m, 1H), 0.95 (d, *J* = 6.9 Hz, 3H) 0.91 ppm (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.34, 168.22, 136.77, 129.03, 128.36, 126.73, 57.01, 53.90, 51.94, 36.38, 29.87, 18.25, 17.10 ppm. HRMS (ESI) *m/z* calcd. for $[C_{15}H_{23}N_2O_3]^+$: 279.1709 $[M-CF_3CO_2]^+$, found 279.1719.

(d) *N*-Acetyl-L-valyl-L-valyl-L-phenylalanine methyl ester: ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.34 (d, *J* = 7.4 Hz, 1H), 7.87 (d, *J* = 8.8 Hz, 1H), 7.66 (d, *J* = 9.0 Hz, 1H), 7.25 (t, *J* = 7.4 Hz, 2H), 7.20 (d, *J* = 7.2 Hz, 3H), 4.49 (ddd, *J* = 8.7, 7.2, 5.7 Hz, 1H), 4.16 (dd, *J* = 8.9, 6.9 Hz, 2H), 3.55 (s, 3H), 3.02 (dd, *J* = 14.0, 5.8 Hz, 1H), 2.92 (dd, *J* = 14.0, 8.9 Hz, 1H), 1.90 (dt, *J* = 13.8, 6.9 Hz, 2H), 1.85 (s, 3H), 0.80 (d, *J* = 7.7 Hz, 6H), 0.77 ppm (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.70, 170.91, 169.15, 137.01, 128.86, 128.19, 126.49, 57.72, 57.21, 53.29, 51.70, 36.49, 30.75, 30.18, 22.46, 19.20, 19.00, 18.21, 18.07 ppm. HRMS (ESI) *m/z* calcd. for $[C_{22}H_{34}N_3O_5]^+$: 420.2499 $[M+H]^+$, found 420.2496, HRMS (ESI) *m/z* calcd. for $[C_{22}H_{33}N_3O_5Na]^+$: 442.2318 $[M+Na]^+$, found 442.2314.

3.13. *N*-Acetyl-L-valyl-L-phenylalanyl-L-valine methyl ester (Ac-Val-Phe-Val-OMe (23))

This tripeptide was synthesised from the *C*-terminus according to **Procedure A**, Scheme S1.

(a) L-Valine methyl ester hydrochloride: see section 2.8(a)

(b) *N*-Boc-L-phenylalanyl-L-valine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.08 (d, *J* = 8.3 Hz, 1H), 7.30 – 7.24 (m, 4H), 7.23 – 7.15 (m, 1H), 6.93 (d, *J* = 8.6 Hz, 1H), 4.25 (ddd, *J* = 23.0, 9.3, 5.2 Hz, 2H), 3.63 (s, 3H), 2.94 (dd, *J* = 13.9, 4.3 Hz, 1H), 2.73 (dd, *J* = 13.8, 10.4 Hz, 1H), 2.05 (h, *J* = 6.7 Hz, 1H), 1.30 (s, 9H), 0.89 ppm (dd, *J* = 9.0, 6.8 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.09, 171.86, 155.21, 138.06, 129.19, 127.95, 126.14, 78.01, 57.23, 55.44, 51.71, 37.21, 30.11, 28.10, 18.88, 18.12 ppm. HRMS (ESI) *m/z* calcd. for $[C_{20}H_{31}N_2O_5]^+$: 379.2233 $[M+H]^+$, found 379.2228, HRMS (ESI) *m/z* calcd. for $[C_{20}H_{30}N_2O_5Na]^+$: 401.2052 $[M+Na]^+$, found 401.2048.

(c) L-Phenylalanyl-L-valine methyl ester trifluoroacetate: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.73 (d, *J* = 8.1 Hz, 1H), 8.25 (s, 3H), 7.32 (dd, *J* = 7.8, 6.1 Hz, 2H), 7.32 – 7.21 (m, 3H), 4.21 (dd, *J* = 8.1, 6.3 Hz, 1H), 4.16 (t, *J* = 6.8 Hz, 1H), 3.63 (s, 3H), 3.08 (dd, *J* = 14.0, 6.1 Hz, 1H), 2.97 (dd, *J* = 14.0, 7.4 Hz, 1H), 2.11 – 1.97 (m, 1H), 0.90 ppm (t, *J* = 7.0 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-

d_6) δ 171.18, 168.32, 134.73, 129.51, 128.47, 127.13, 57.64, 53.09, 51.87, 36.96, 30.06, 18.84, 18.18 ppm. HRMS (ESI) *m/z* calcd. for $[C_{15}H_{23}N_2O_3]^+$: 279.1709 $[M\text{-}CF_3CO_2]^+$, found 279.1703, HRMS (ESI) *m/z* calcd. for $[C_{30}H_{45}N_4O_6]^+$: 557.3339 $[2M\text{-}C_4HO_4F_6]^+$, found 557.3332.

(d) *N*-Acetyl-L-valyl-L-phenylalanyl-L-valine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.13 (d, *J* = 7.7 Hz, 1H), 8.09 (d, *J* = 8.1 Hz, 1H), 7.85 (d, *J* = 8.7 Hz, 1H), 7.29 – 7.18 (m, 4H), 7.22 – 7.13 (m, 1H), 4.60 (ddd, *J* = 9.7, 8.1, 4.7 Hz, 1H), 4.16 (dd, *J* = 8.1, 6.4 Hz, 1H), 4.09 (dd, *J* = 8.9, 7.0 Hz, 1H), 3.60 (s, 3H), 2.99 (dd, *J* = 14.0, 4.7 Hz, 1H), 2.80 (dd, *J* = 13.9, 9.7 Hz, 1H), 2.04 (hept, *J* = 6.9 Hz, 1H), 1.94 – 1.84 (m, 1H), 1.83 (s, 3H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.86 (d, *J* = 7.0 Hz, 3H), 0.74 (d, *J* = 2.7 Hz, 3H), 0.72 ppm (d, *J* = 2.7 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.65, 171.35, 170.93, 169.14, 137.69, 129.16, 127.94, 126.18, 57.75, 57.43, 53.59, 51.65, 37.31, 30.34, 29.91, 22.47, 19.12, 18.88, 18.18, 18.09 ppm. HRMS (ESI) *m/z* calcd. for $[C_{22}H_{34}N_3O_5]^+$: 420.2499 $[M+H]^+$, found 420.2496, HRMS (ESI) *m/z* calcd. for $[C_{22}H_{33}N_3O_5Na]^+$: 442.2318 $[M+Na]^+$, found 442.2315.

3.14. *N*-Acetyl-L-phenylalanyl-L-valyl-L-valine methyl ester (Ac-Phe-Val-Val-OMe (24))

This tripeptide was synthesised from the *C*-terminus according to **Procedure A**, Scheme S1.

(a) L-Valine methyl ester hydrochloride: see section 2.8(a)

(b) *N*-Boc-L-valyl-L-valine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.97 (d, *J* = 7.9 Hz, 1H), 6.69 (d, *J* = 9.1 Hz, 1H), 4.18 (dd, *J* = 8.0, 6.2 Hz, 1H), 3.86 (dd, *J* = 9.2, 7.0 Hz, 1H), 3.61 (s, 3H), 2.04 (hept, *J* = 6.8 Hz, 1H), 1.91 (hept, *J* = 6.8 Hz, 1H), 1.38 (s, 9H), 0.91 – 0.80 ppm (m, 12H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.83, 171.78, 155.36, 77.96, 59.49, 57.24, 51.58, 30.32, 29.86, 28.15, 19.12, 18.86, 18.21, 18.17 ppm. HRMS (ESI) *m/z* calcd. for $[C_{16}H_{31}N_2O_5]^+$: 331.2233 $[M+H]^+$, found 331.2227, HRMS (ESI) *m/z* calcd. for $[C_{16}H_{30}N_2O_5Na]^+$: 353.2052 $[M+Na]^+$, found 353.2046.

(c) L-Valyl-L-valine methyl ester trifluoroacetate: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.61 (d, *J* = 7.4 Hz, 1H), 8.14 (d, *J* = 4.4 Hz, 3H), 4.20 (dd, *J* = 7.4, 5.9 Hz, 1H), 3.73 (t, *J* = 4.8 Hz, 1H), 3.64 (s, 3H), 2.17 – 2.00 (m, 2H), 1.00 – 0.88 ppm (m, 12H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.36, 168.35, 57.77, 56.99, 51.77, 29.94, 29.67, 18.84, 18.20, 18.15, 17.45 ppm. HRMS (ESI) *m/z* calcd. for $[C_{11}H_{23}N_2O_3]^+$: 231.1709 $[M\text{-}CF_3CO_2]^+$, found 231.1706, HRMS (ESI) *m/z* calcd. for $[C_{22}H_{45}N_4O_6]^+$: 461.3339 $[2M\text{-}C_4HO_4F_6]^+$, found 461.3338.

(d) *N*-Acetyl-L-phenylalanine: see section 2.1(a)

(e) *N*-Acetyl-L-phenylalanyl-L-valyl-L-valine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.18 (d, *J* = 7.7 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.95 (d, *J* = 8.9 Hz, 1H), 7.27 – 7.19 (m, 4H), 7.21 – 7.12 (m, 1H), 4.56 (ddd, *J* = 10.1, 8.5, 4.2 Hz, 1H), 4.28 (dd, *J* = 8.9, 6.9 Hz, 1H), 4.14 (dd, *J* = 7.5, 6.4 Hz, 1H), 3.60 (s, 3H), 2.98 (dd, *J* = 13.9, 4.2 Hz, 1H), 2.72 (dd, *J* = 14.0, 9.9 Hz, 1H), 2.11 – 1.99 (m, 1H), 2.03 – 1.91 (m, 1H), 1.74 (s, 3H), 0.89 (dd, *J* = 9.5, 5.5 Hz, 6H), 0.85 ppm (dd, *J*

= 7.3, 5.6 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.76, 171.30, 171.26, 169.15, 138.07, 129.17, 127.96, 126.16, 57.54, 57.33, 53.88, 51.57, 37.32, 30.79, 29.66, 22.43, 19.08, 18.91, 18.30, 18.13 ppm. HRMS (ESI) *m/z* calcd. for $[C_{22}H_{34}N_3O_5]^+$: 420.2499 $[M+H]^+$, found 420.2494, HRMS (ESI) *m/z* calcd. for $[C_{22}H_{33}N_3O_5Na]^+$: 442.2318 $[M+Na]^+$, found 442.2313.

3.15. *N*-Acetyl-L-phenylalanyl-L-leucyl-L-phenylalanine methyl ester (Ac-Phe-Leu-Phe-OMe (25))

This tripeptide was synthesised from the *C*-terminus according to **Procedure A**, Scheme S1.

(a) L-Leucyl-L-phenylalanine methyl ester trifluoroacetate: see section 2.9(a) – (c)

(b) *N*-Acetyl-L-phenylalanine: see section 2.1(a)

(c) *N*-Acetyl-L-phenylalanyl-L-leucyl-L-phenylalanine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.29 (d, *J* = 7.4 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.99 (d, *J* = 8.3 Hz, 1H), 7.31 – 7.13 (m, 10H), 4.54 – 4.42 (m, 2H), 4.43 (td, *J* = 8.3, 6.4 Hz, 1H), 3.56 (s, 3H), 3.03 (dd, *J* = 13.9, 6.0 Hz, 1H), 3.00 – 2.88 (m, 2H), 2.67 (dd, *J* = 13.9, 10.2 Hz, 1H), 1.73 (s, 3H), 1.61 – 1.48 (m, 1H), 1.47 – 1.34 (m, 2H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.83 ppm (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.94, 171.72, 171.11, 169.10, 138.04, 137.05, 129.09, 129.00, 128.22, 127.95, 126.50, 126.14, 53.74, 53.43, 51.77, 50.75, 40.99, 37.42, 36.48, 24.03, 22.94, 22.43, 21.78 ppm. HRMS (ESI) *m/z* calcd. for $[C_{27}H_{36}N_3O_5]^+$: 482.2655 $[M+H]^+$, found 482.2656, HRMS (ESI) *m/z* calcd. for $[C_{27}H_{35}N_3O_5Na]^+$: 504.2474 $[M+Na]^+$, found 504.2469.

3.16. *N*-Acetyl-L-phenylalanyl-L-phenylalanyl-L-leucine methyl ester (Ac-Phe-Phe-Leu-OMe (26))

This tripeptide was synthesised from the *N*-terminus according to **Procedure B**, Scheme S2.

(a) L-Phenylalanine methyl ester hydrochloride: see section 2.5(a)

(b) *N*-Acetyl-L-phenylalanine: see section 2.1(a)

(c) *N*-Acetyl-L-phenylalanyl-L-phenylalanine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.44 (d, *J* = 7.5 Hz, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 7.30 – 7.16 (m, 10H), 4.57 – 4.51 (m, 1H), 4.51 – 4.45 (m, 1H), 3.58 (s, 3H), 3.04 (dd, *J* = 13.8, 5.9 Hz, 1H), 2.95 (dd, *J* = 13.0, 5.3 Hz, 1H), 2.94 (dd, *J* = 14.5, 7.7 Hz, 1H), 2.67 (dd, *J* = 13.9, 10.0 Hz, 1H), 1.71 ppm (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.71, 171.54, 168.92, 137.89, 137.02, 129.10, 129.06, 128.24, 127.96, 126.55, 126.18, 53.57, 53.45, 51.82, 37.49, 36.55, 22.39 ppm. HRMS (ESI) *m/z* calcd. for $[C_{21}H_{25}N_2O_4]^+$: 369.1814 $[M+H]^+$, found 369.1804, HRMS (ESI) *m/z* calcd. for $[C_{21}H_{24}N_2O_4Na]^+$: 391.1634 $[M+Na]^+$, found 391.1604.

(d) *N*-Acetyl-L-phenylalanyl-L-phenylalanine: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.77 (s, 1H), 8.29 (d, *J* = 7.8 Hz, 1H), 8.10 (d, *J* = 8.6 Hz, 1H), 7.32 – 7.16 (m, 9H), 7.20 – 7.12 (m, 1H), 4.51 (ddd, *J* = 10.1, 8.5, 4.2 Hz, 1H), 4.44 (td, *J* = 8.4, 5.1 Hz, 1H), 3.08 (dd, *J* = 13.9, 5.1 Hz, 1H), 2.97 (dd, *J* = 10.0, 4.0 Hz, 1H), 2.92 (d, *J* = 14.4 Hz, 1H), 2.67 (dd, *J* = 13.9, 10.2 Hz, 1H), 1.71 ppm (s,

3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.68, 171.46, 168.95, 138.03, 137.47, 129.17, 129.14, 128.16, 127.94, 126.43, 126.14, 53.66, 53.48, 37.44, 36.58, 22.42 ppm. HRMS (ESI) *m/z* calcd. for $[C_{20}H_{23}N_2O_4]^+$: 355.1658 $[M+H]^+$, found 355.1654, HRMS (ESI) *m/z* calcd. for $[C_{20}H_{22}N_2O_4Na]^+$: 377.1477 $[M+Na]^+$, found 377.1474.

(e) L-Leucine methyl ester hydrochloride: see section 2.6(a)

(f) *N*-Acetyl-L-phenylalanyl-L-phenylalanyl-L-leucine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.30 (d, *J* = 7.7 Hz, 1H), 8.09 (d, *J* = 8.2 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 7.31 – 7.23 (m, 4H), 7.25 – 7.11 (m, 6H), 4.54 (td, *J* = 8.8, 4.7 Hz, 1H), 4.45 (ddd, *J* = 9.9, 8.2, 4.2 Hz, 1H), 4.31 (ddd, *J* = 9.7, 7.7, 5.1 Hz, 1H), 3.61 (s, 3H), 3.04 (dd, *J* = 14.0, 4.7 Hz, 1H), 2.91 (dd, *J* = 13.9, 4.2 Hz, 1H), 2.81 (dd, *J* = 13.9, 9.2 Hz, 1H), 2.64 (dd, *J* = 13.9, 9.9 Hz, 1H), 1.71 (s, 3H), 1.69 – 1.42 (m, 3H), 0.90 (d, *J* = 6.4 Hz, 3H), 0.85 ppm (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, Acetonitrile-d_3) δ 173.53, 172.16, 171.87, 171.68, 137.27, 137.12, 129.63, 129.39, 128.63, 128.61, 126.95, 126.93, 55.09, 54.21, 52.36, 51.15, 39.97, 37.41, 37.24, 24.58, 22.38, 21.96, 21.02 ppm. HRMS (ESI) *m/z* calcd. for $[C_{27}H_{36}N_3O_5]^+$: 482.2655 $[M+H]^+$, found 482.2655, HRMS (ESI) *m/z* calcd. for $[C_{27}H_{35}N_3O_5Na]^+$: 504.2474 $[M+Na]^+$, found 504.2472.

3.17. *N*-Acetyl-L-phenylalanyl-L-phenylalanyl-L-valine methyl ester (Ac-Phe-Phe-Val-OMe (27))

This tripeptide was synthesised from the *C*-terminus according to **Procedure A**, Scheme S1.

(a) L-Phenylalanyl-L-valine methyl ester trifluoroacetate: see section 2.13(a) – (c)

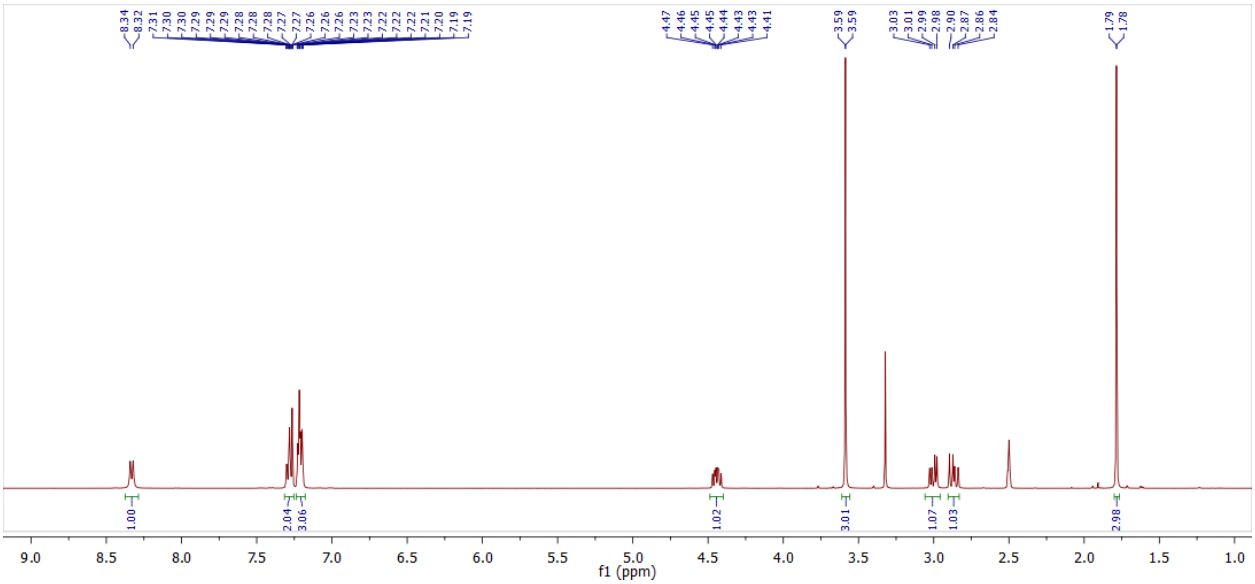
(b) *N*-Acetyl-L-phenylalanine: see section 2.1(a)

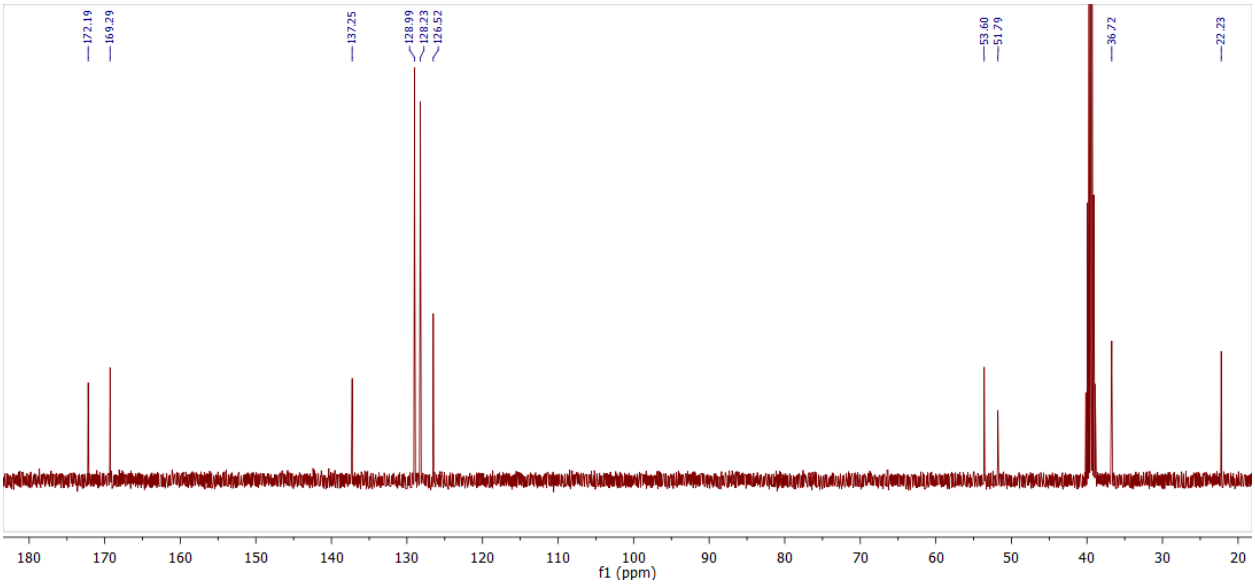
(c) *N*-Acetyl-L-phenylalanyl-L-phenylalanyl-L-valine methyl ester: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.20 (d, *J* = 8.1 Hz, 1H), 8.10 (d, *J* = 8.1 Hz, 1H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.28 – 7.24 (m, 4H), 7.25 – 7.11 (m, 6H), 4.62 (td, *J* = 8.8, 4.8 Hz, 1H), 4.46 (td, *J* = 9.2, 4.1 Hz, 1H), 4.19 (dd, *J* = 8.3, 6.2 Hz, 1H), 3.63 (s, 3H), 3.02 (dd, *J* = 14.0, 4.7 Hz, 1H), 2.92 (dd, *J* = 13.9, 4.2 Hz, 1H), 2.82 (dd, *J* = 14.0, 9.2 Hz, 1H), 2.64 (dd, *J* = 13.9, 9.9 Hz, 1H), 2.04 (h, *J* = 6.7 Hz, 1H), 1.70 (s, 3H), 0.89 ppm (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (101 MHz, Methanol-d_4) δ 173.29, 173.28, 173.16, 173.04, 138.43, 138.10, 130.45, 130.18, 129.39, 129.38, 127.73, 127.69, 59.28, 55.89, 55.63, 52.49, 38.89, 38.62, 31.91, 22.36, 19.44, 18.62 ppm. HRMS (ESI) *m/z* calcd. for $[C_{26}H_{34}N_3O_5]^+$: 468.2499 $[M+H]^+$, found 482.2655, HRMS (ESI) *m/z* calcd. for $[C_{26}H_{33}N_3O_5Na]^+$: 490.2318 $[M+Na]^+$, found 490.2305.

4. Spectra of substrates used in the laser flash photolysis study

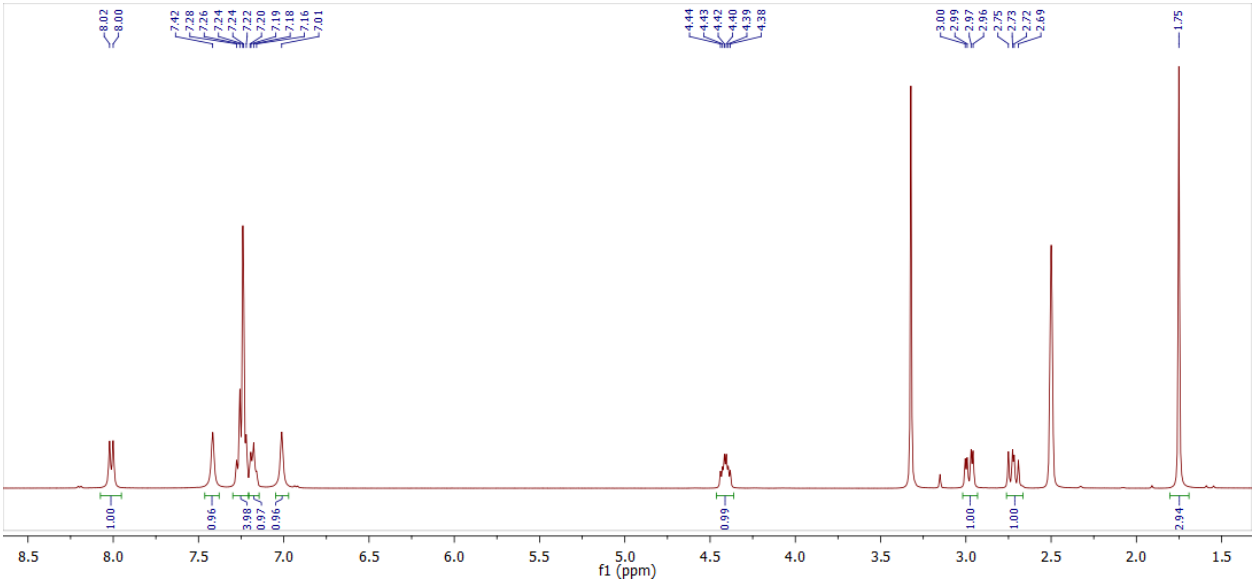
4.1. ^{1}H NMR and ^{13}C NMR spectra

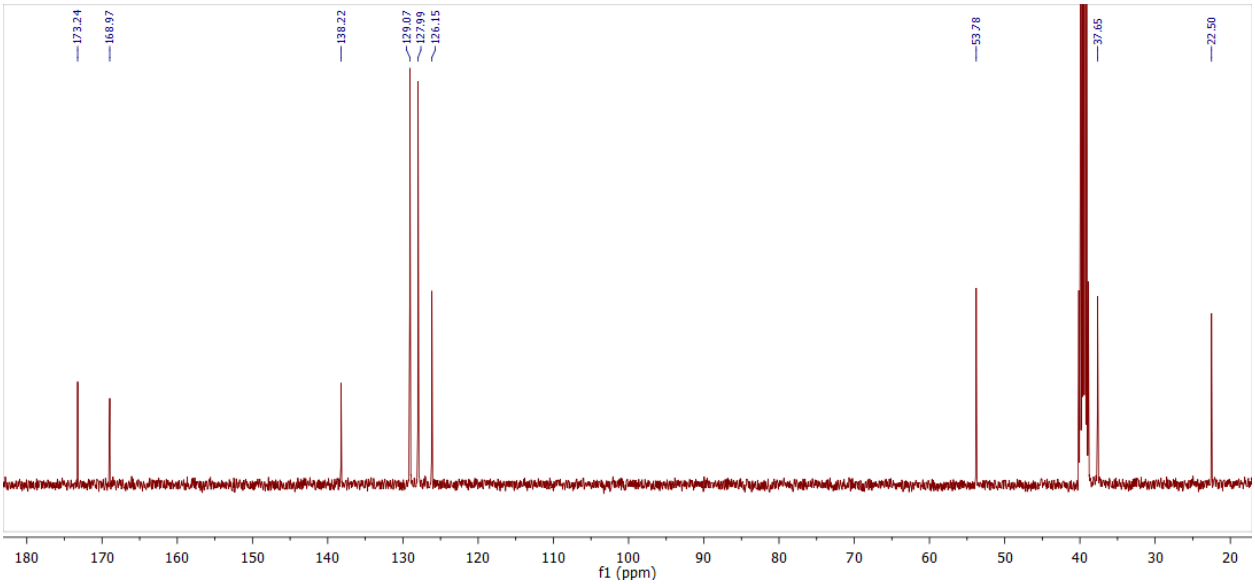
4.1.1. *N*-Acetyl-L-phenylalanine methyl ester (Ac-Phe-OMe (7))



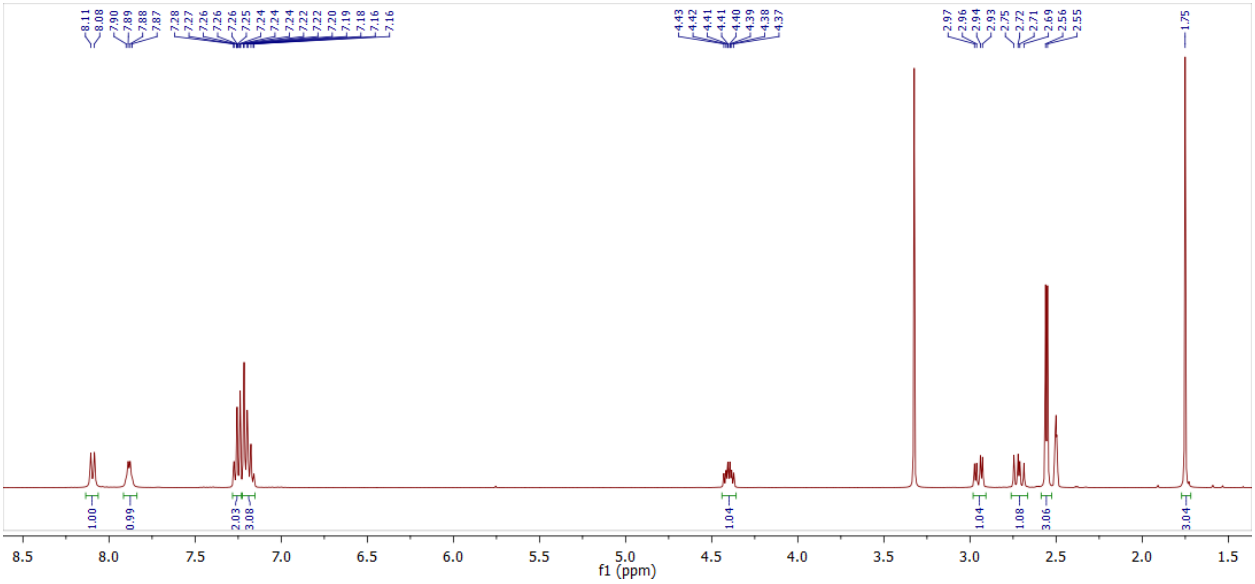


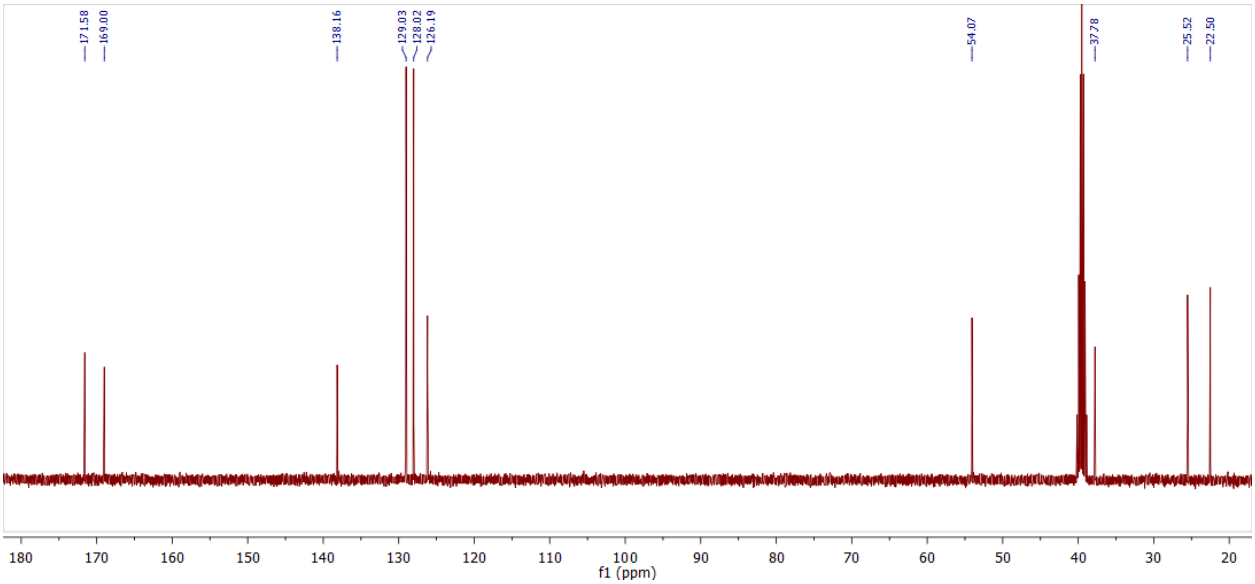
4.1.2. *N*-Acetyl-L-phenylalanine amide (Ac-Phe-NH_2 (14))



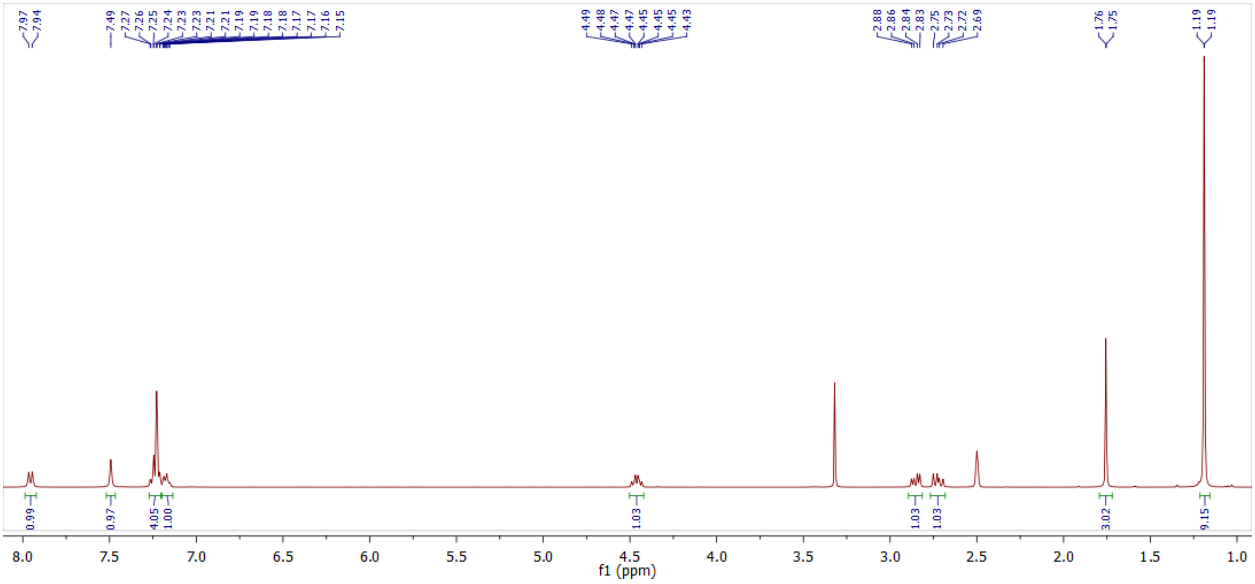


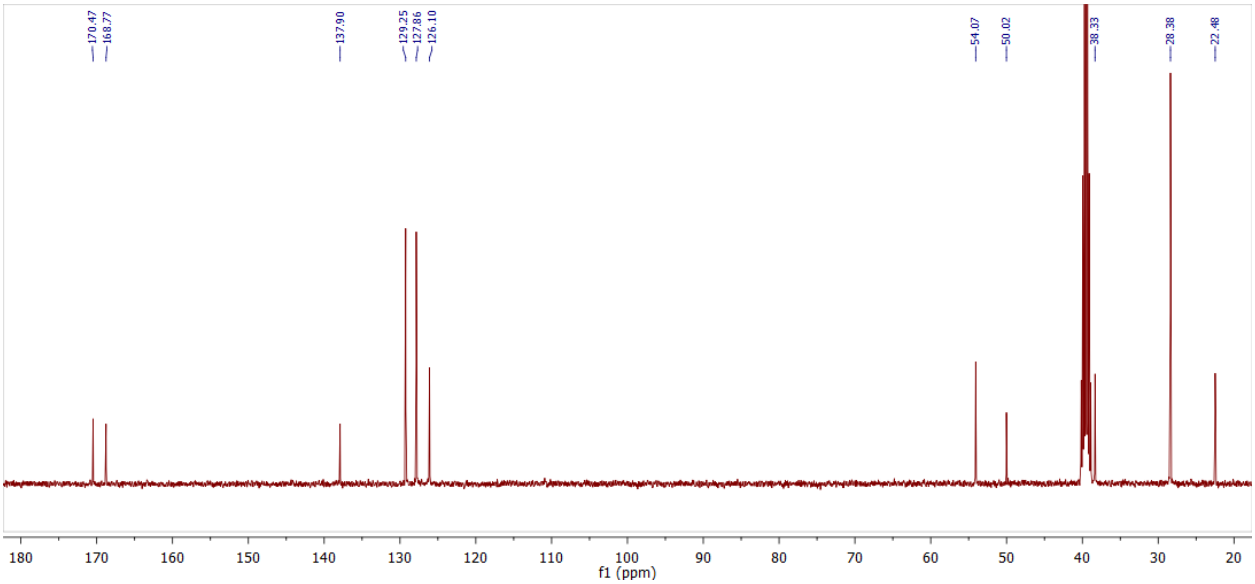
4.1.3. *N*-Acetyl-L-phenylalanine methyl amide (Ac-Phe-NHMe (6))



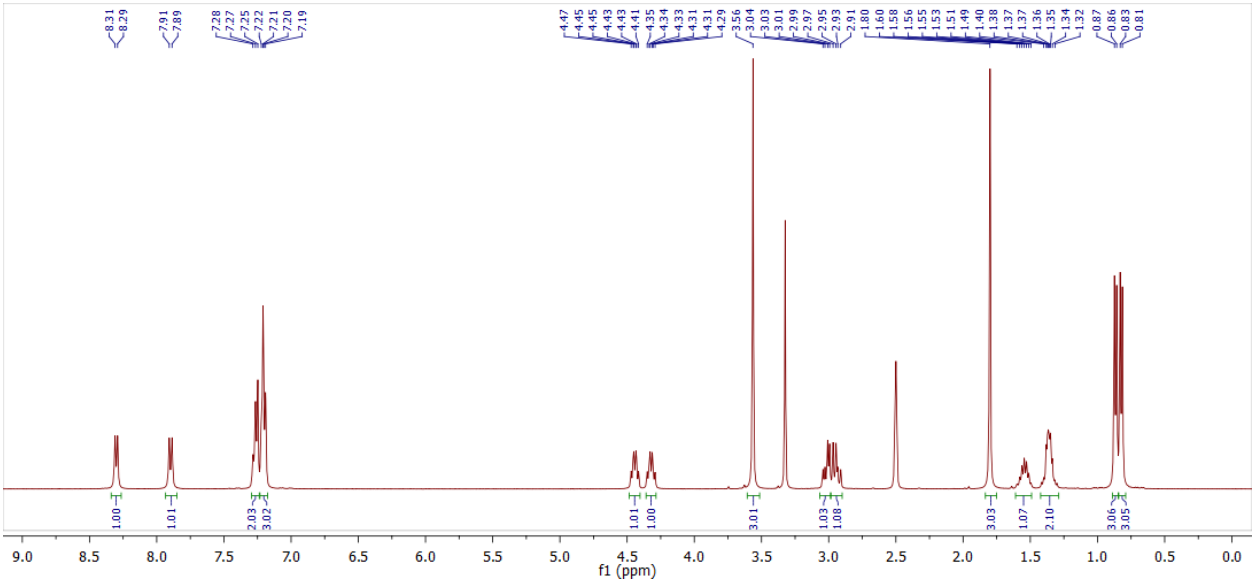


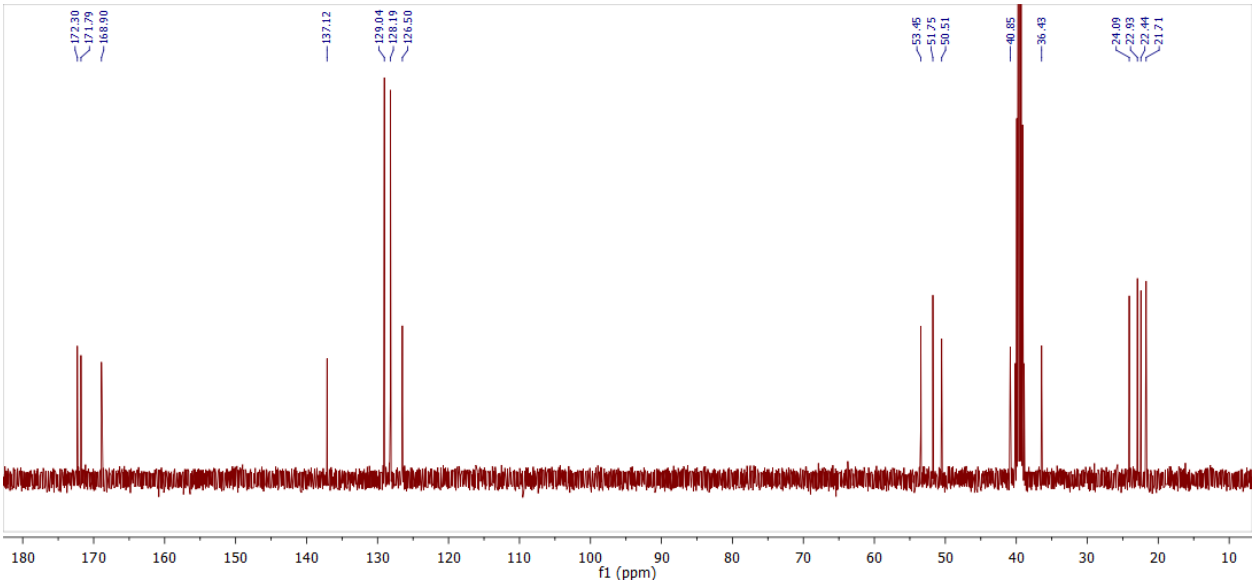
4.1.4. *N*-Acetyl-L-phenylalanine *t*-butyl amide (Ac-Phe-NH*t*Bu (13))



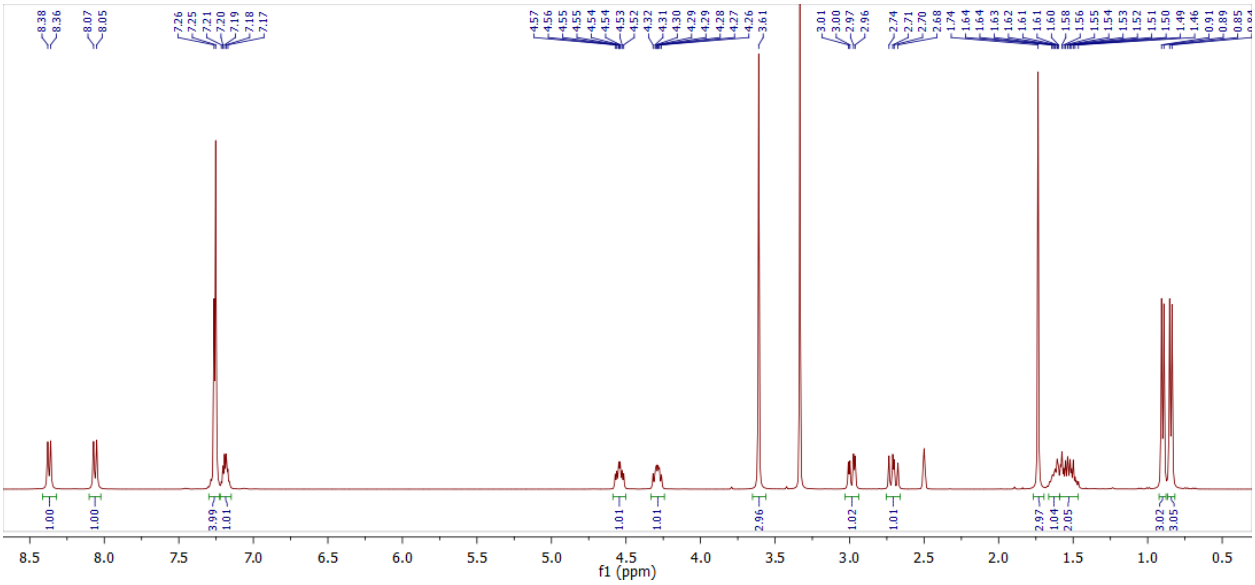


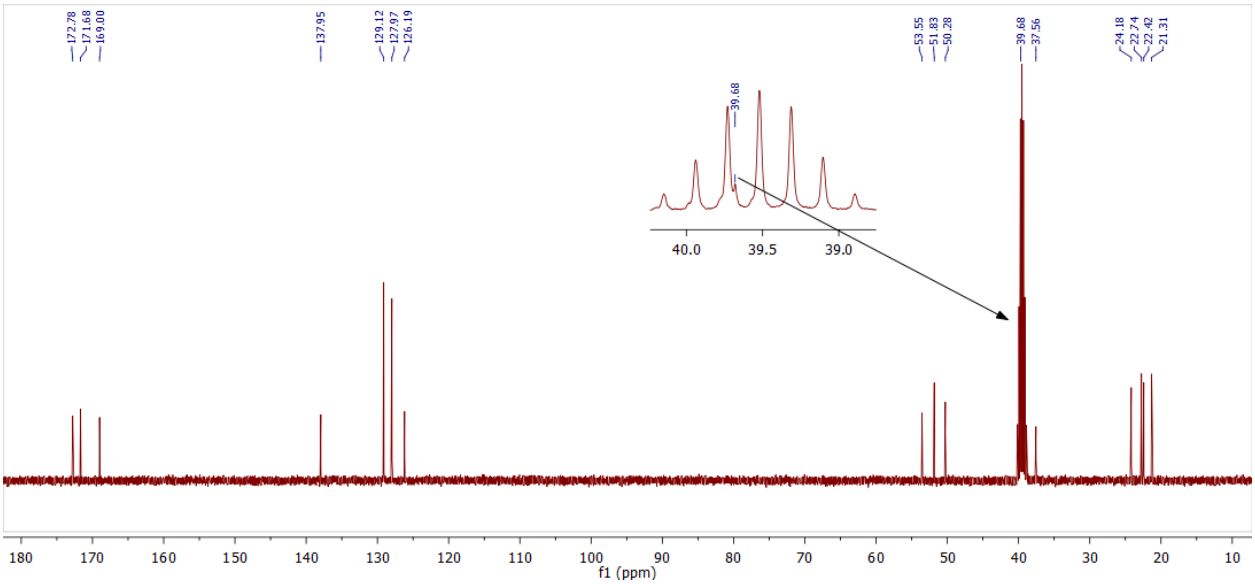
4.1.5. *N*-Acetyl-L-leucyl-L-phenylalanine methyl ester (Ac-Leu-Phe-OMe (15))



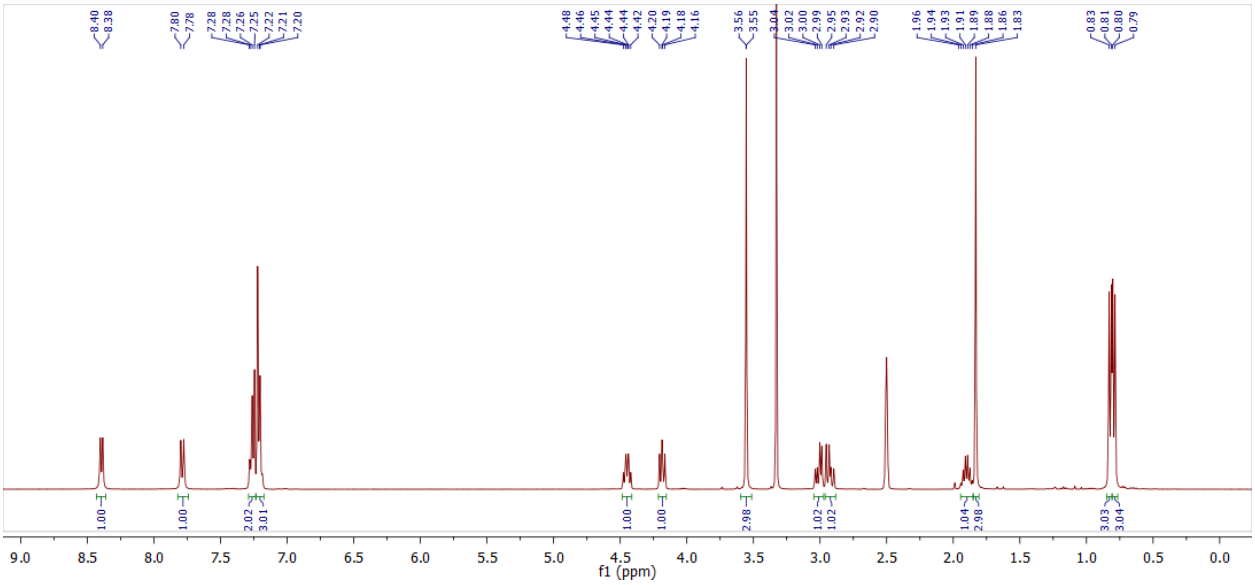


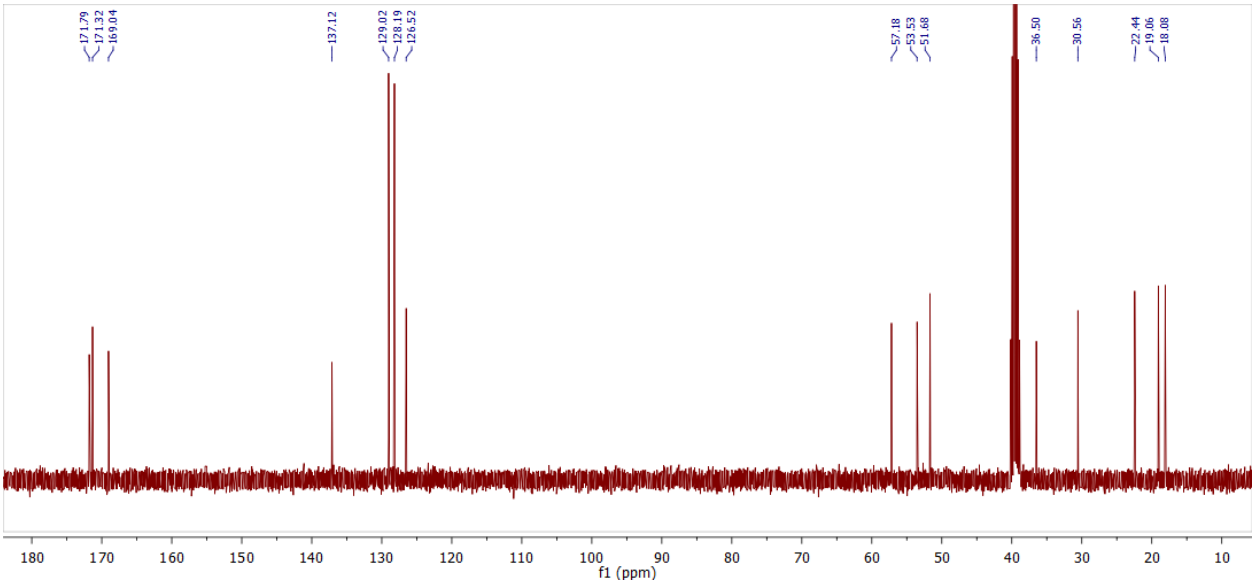
4.1.6. *N*-Acetyl-L-phenylalanyl-L-leucine methyl ester (Ac-Phe-Leu-OMe (16))



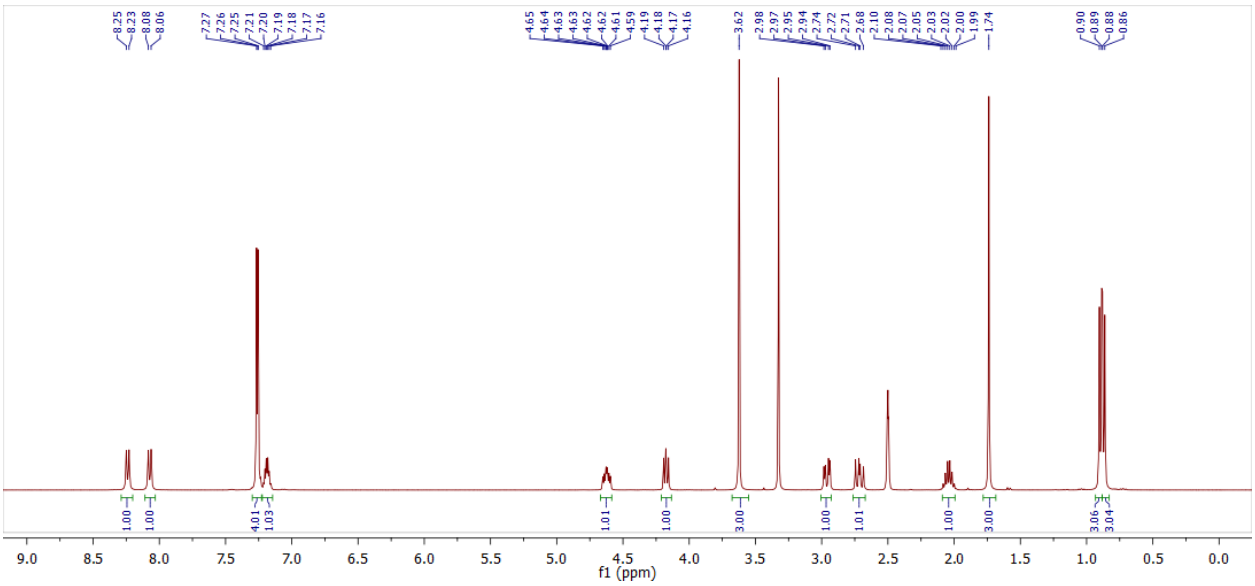


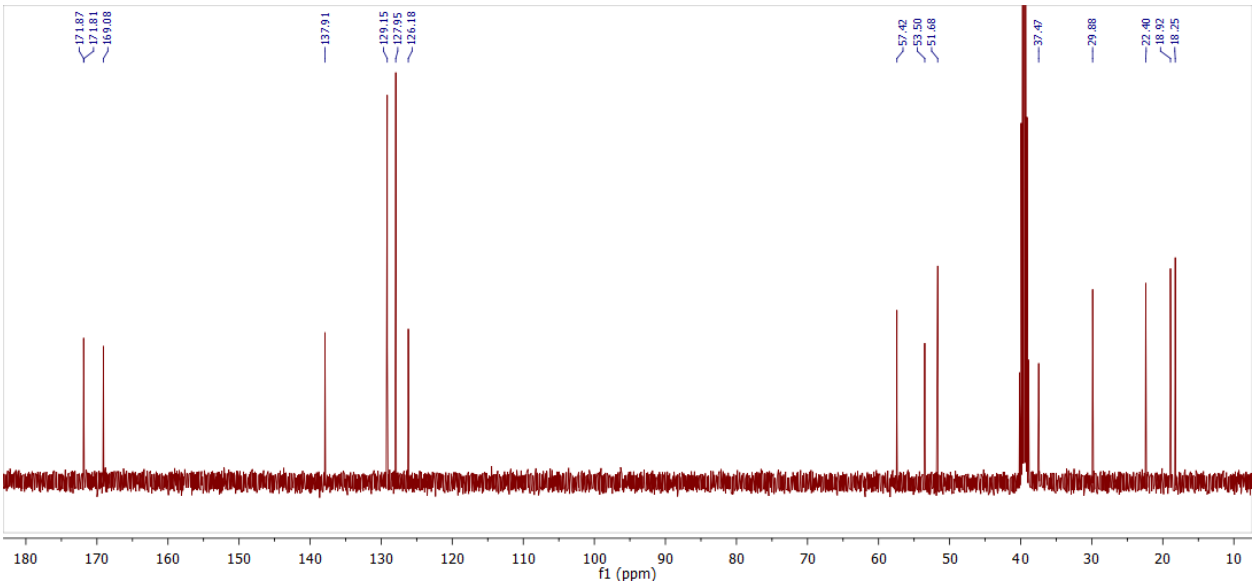
4.1.7. *N*-Acetyl-L-valyl-L-phenylalanine methyl ester (Ac-Val-Phe-OMe (17))



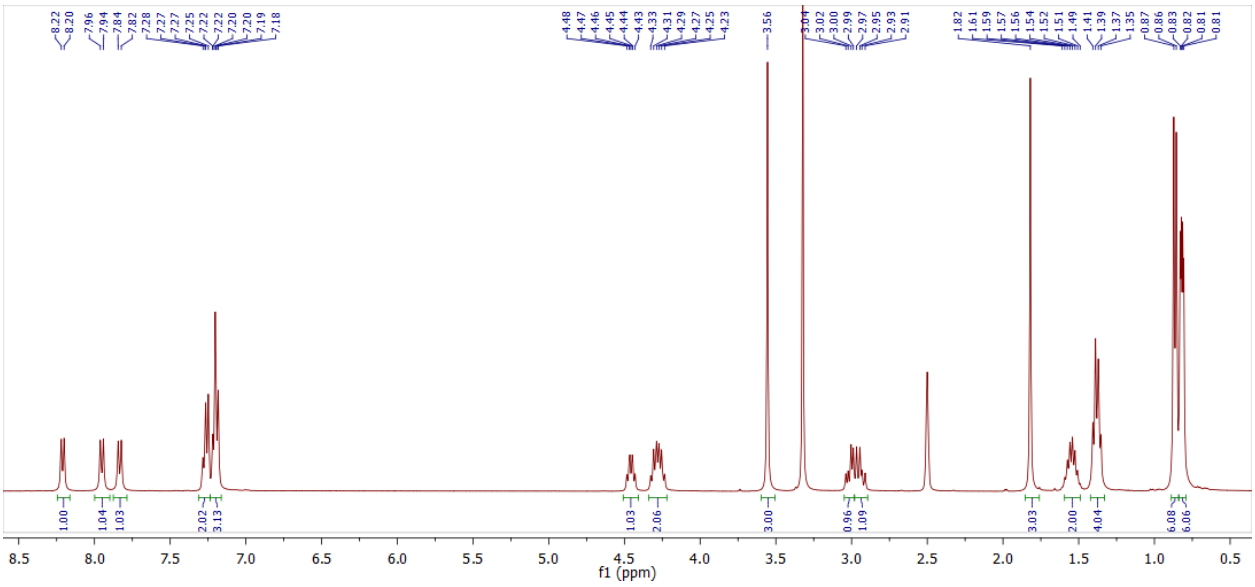


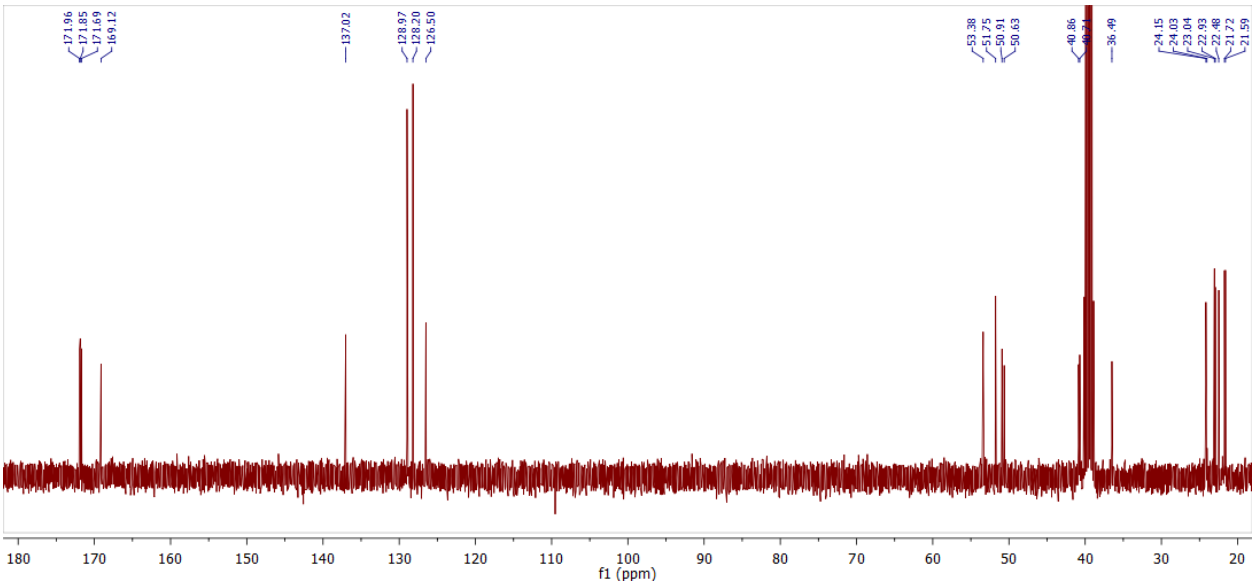
4.1.8. *N*-Acetyl-L-phenylalanyl-L-valine methyl ester (Ac-Phe-Val-OMe (18))



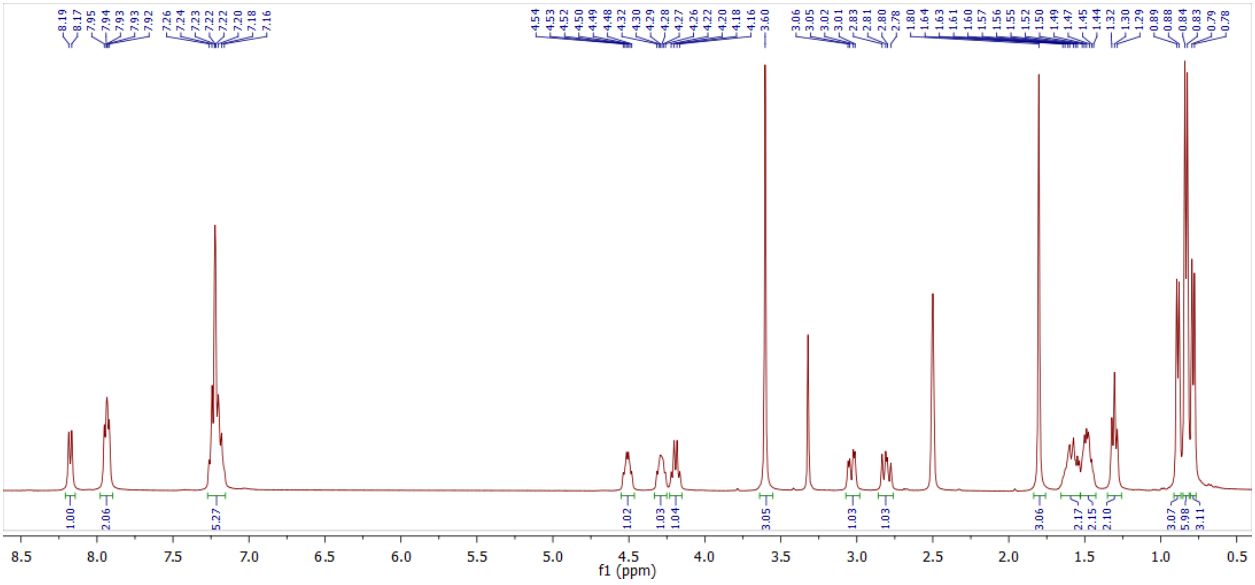


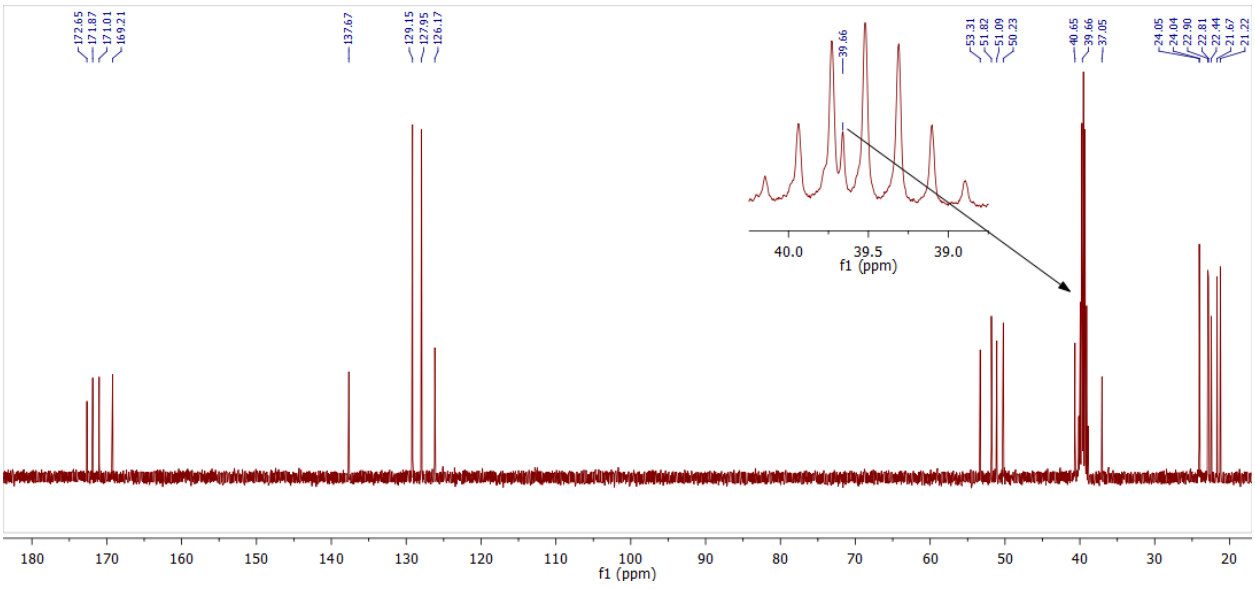
4.1.9. *N*-Acetyl-L-leucyl-L-leucyl-L-phenylalanine methyl ester (Ac-Leu-Leu-Phe-OMe (19))



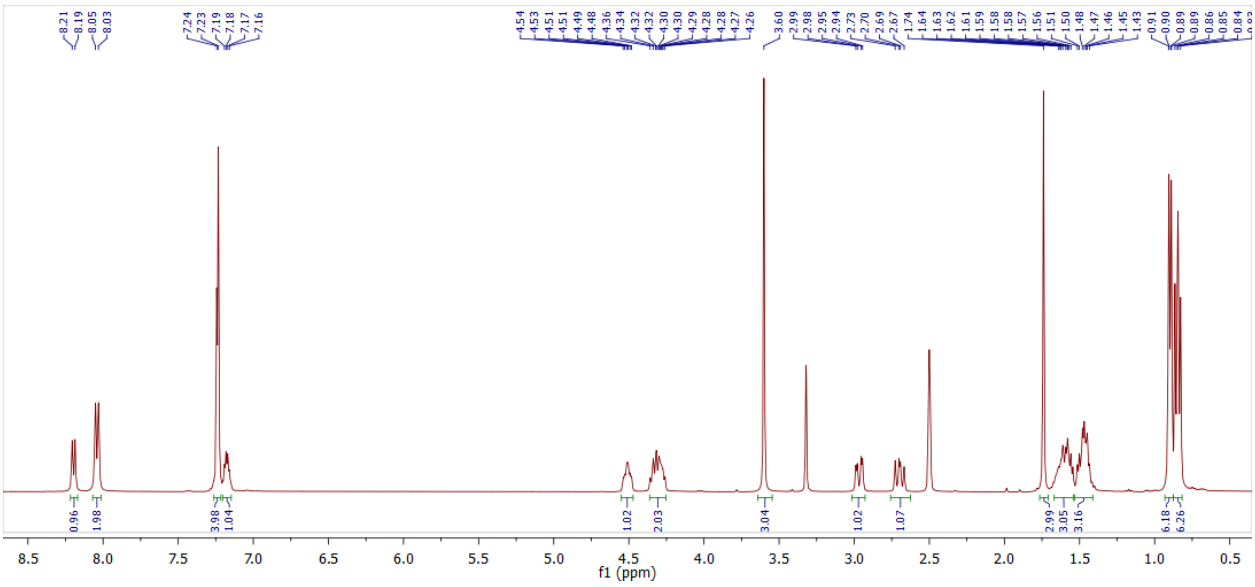


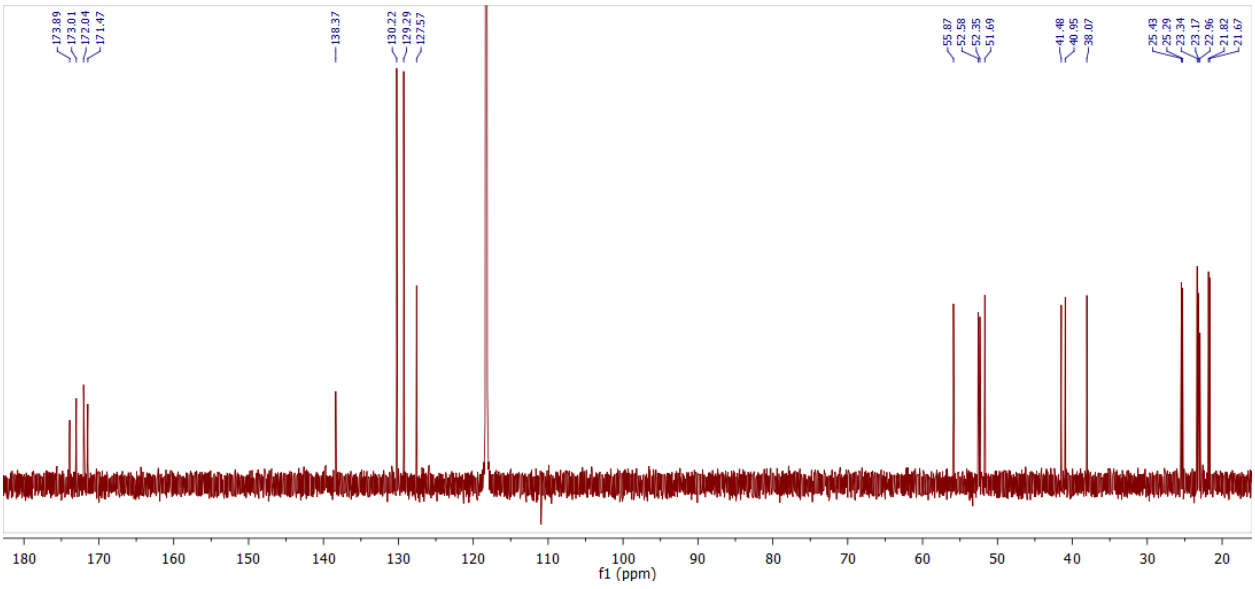
4.1.10. *N*-Acetyl-L-leucyl-L-phenylalanyl-L-leucine methyl ester (Ac-Leu-Phe-Leu-OMe (20))



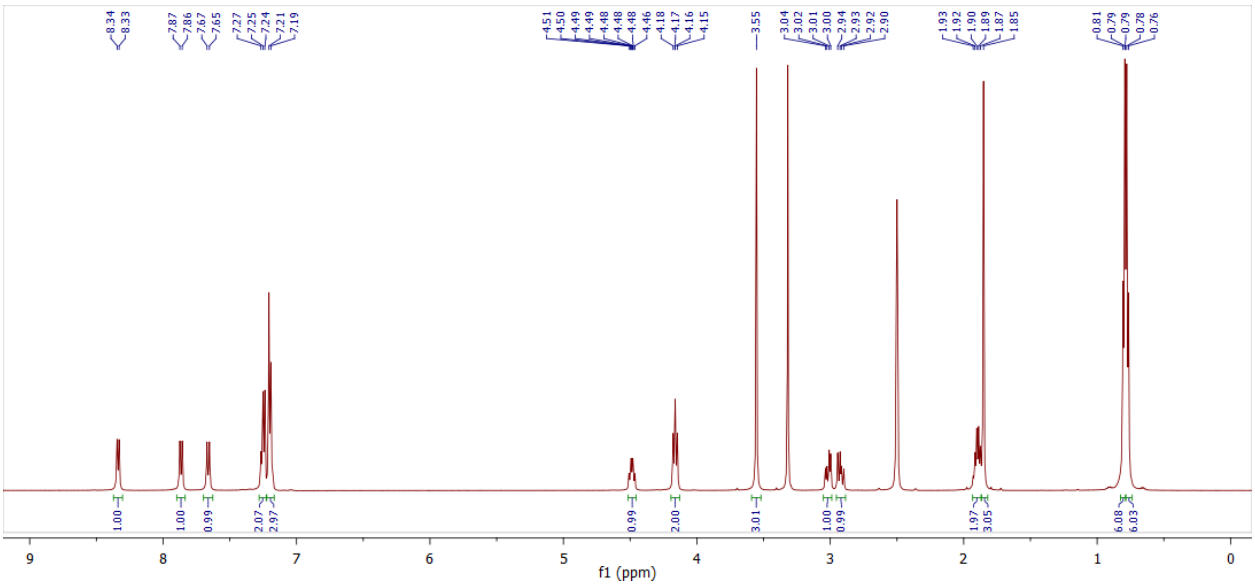


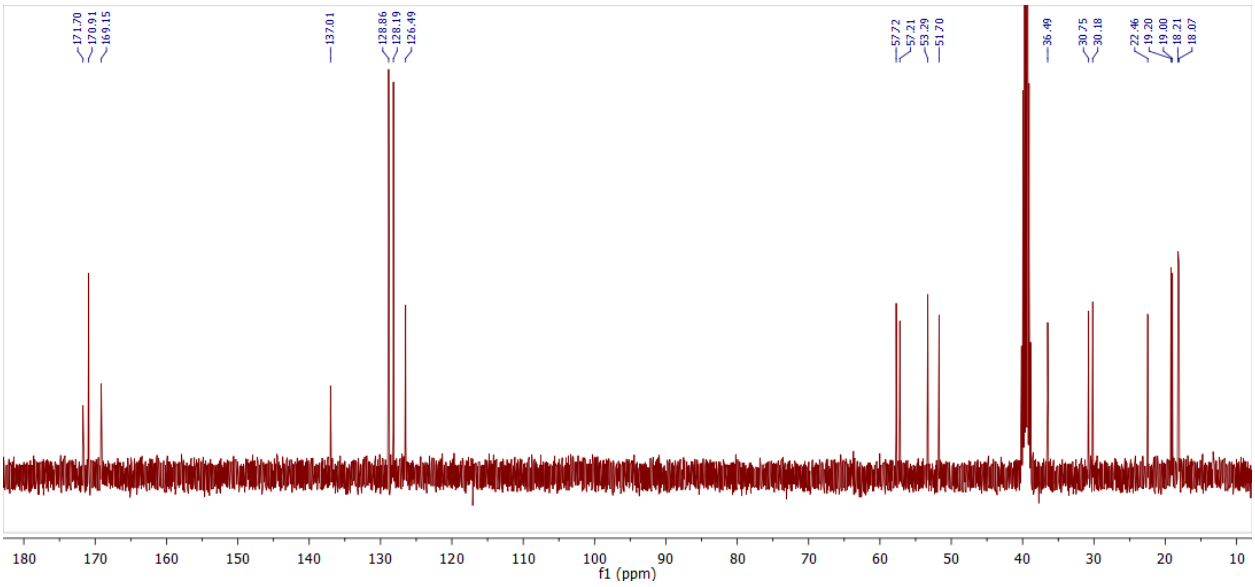
4.1.11. *N*-Acetyl-L-phenylalanyl-L-leucyl-L-leucine methyl ester (Ac-Phe-Leu-Leu-OMe (21))



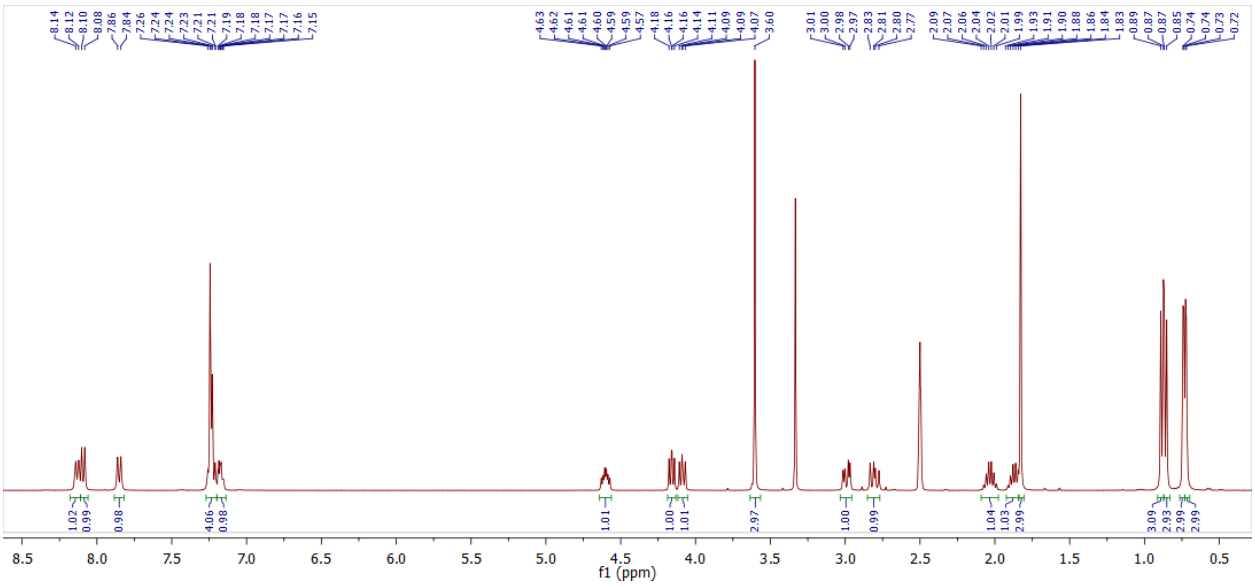


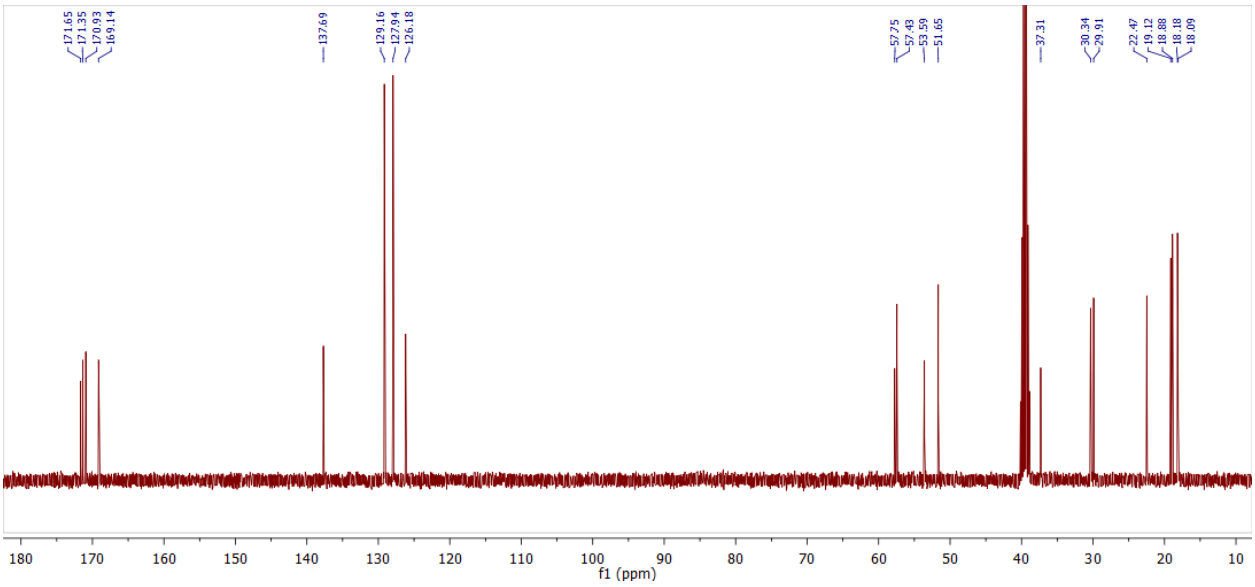
4.1.12. *N*-Acetyl-L-valyl-L-valyl-L-phenylalanine methyl ester (Ac-Val-Val-Phe-OMe (22))



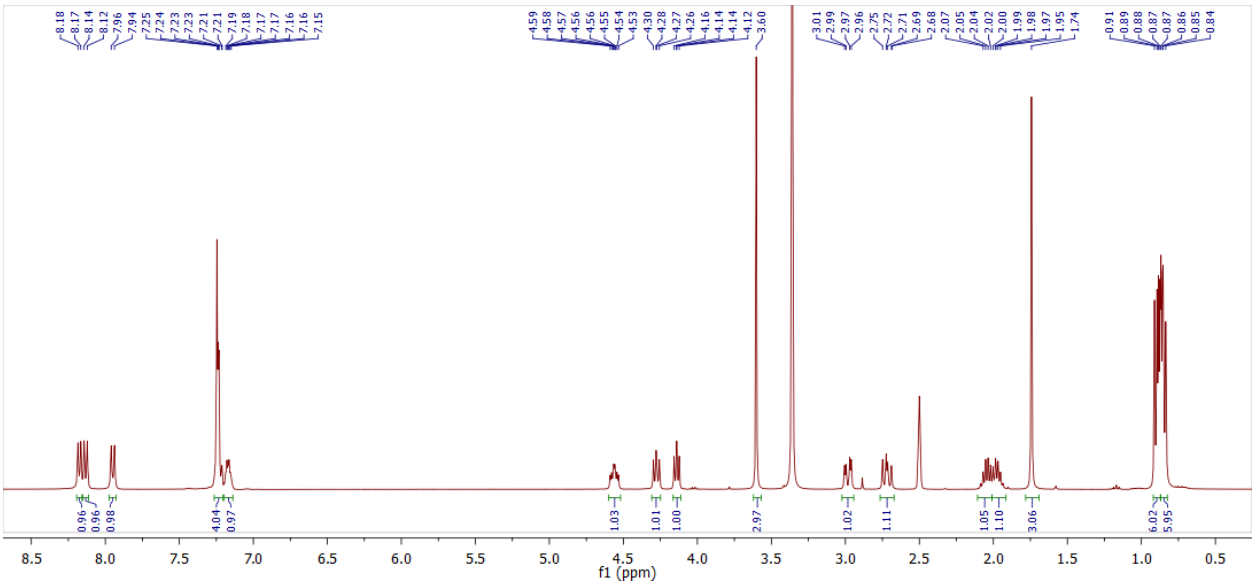


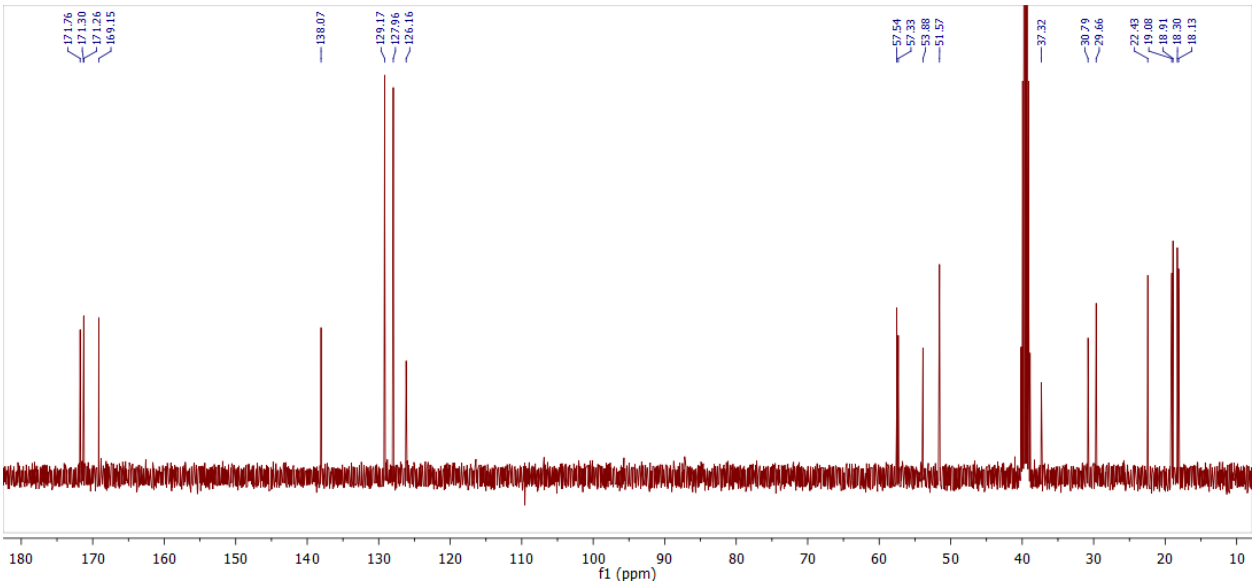
4.1.13. *N*-Acetyl-L-valyl-L-phenylalanyl-L-valine methyl ester (Ac-Val-Phe-Val-OMe (23))



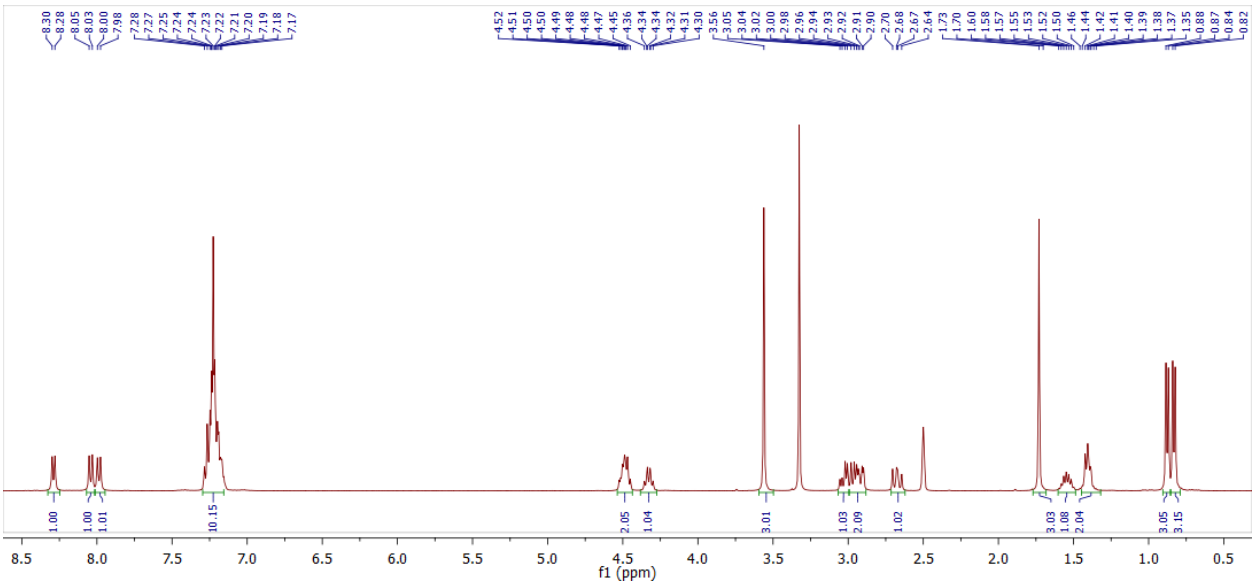


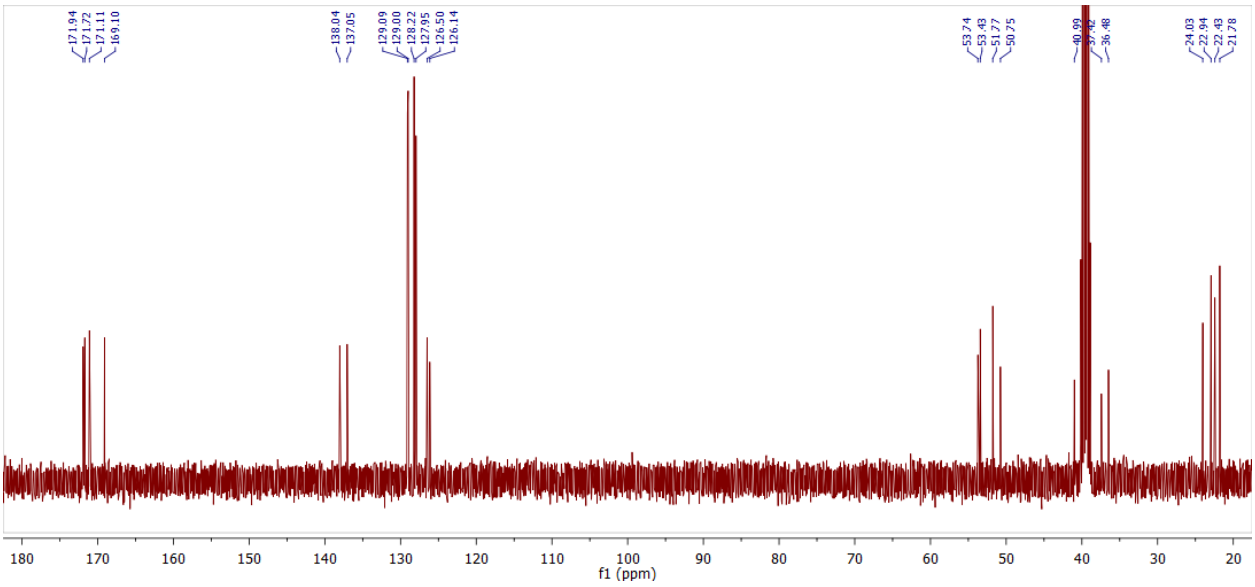
4.1.14. *N*-Acetyl-L-phenylalanyl-L-valyl-L-valine methyl ester (Ac-Phe-Val-Val-OMe (24))



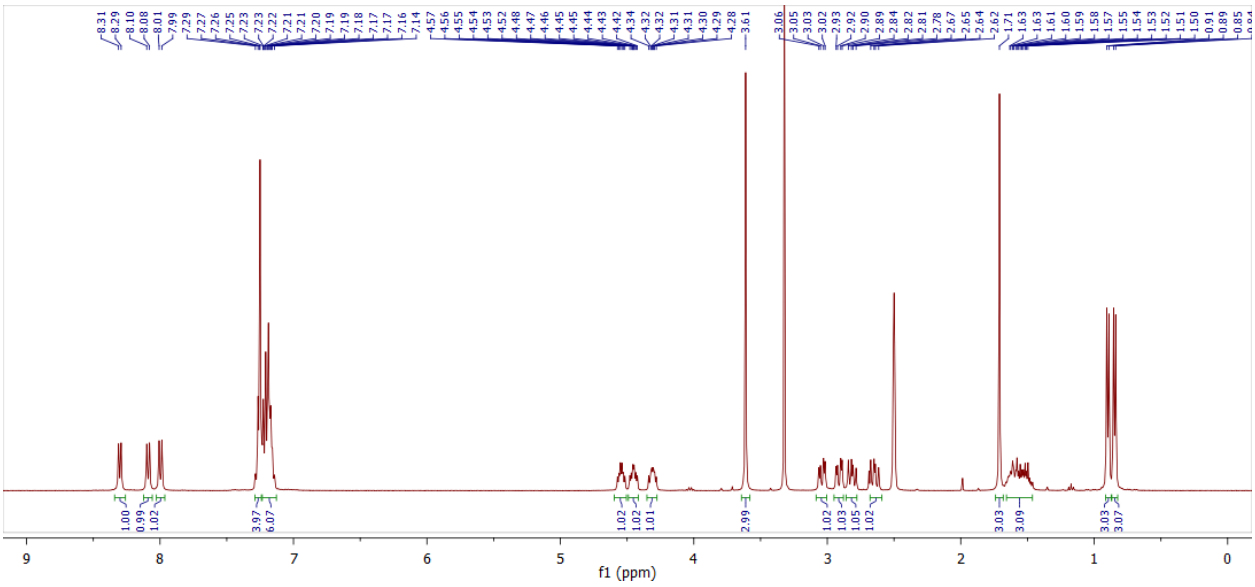


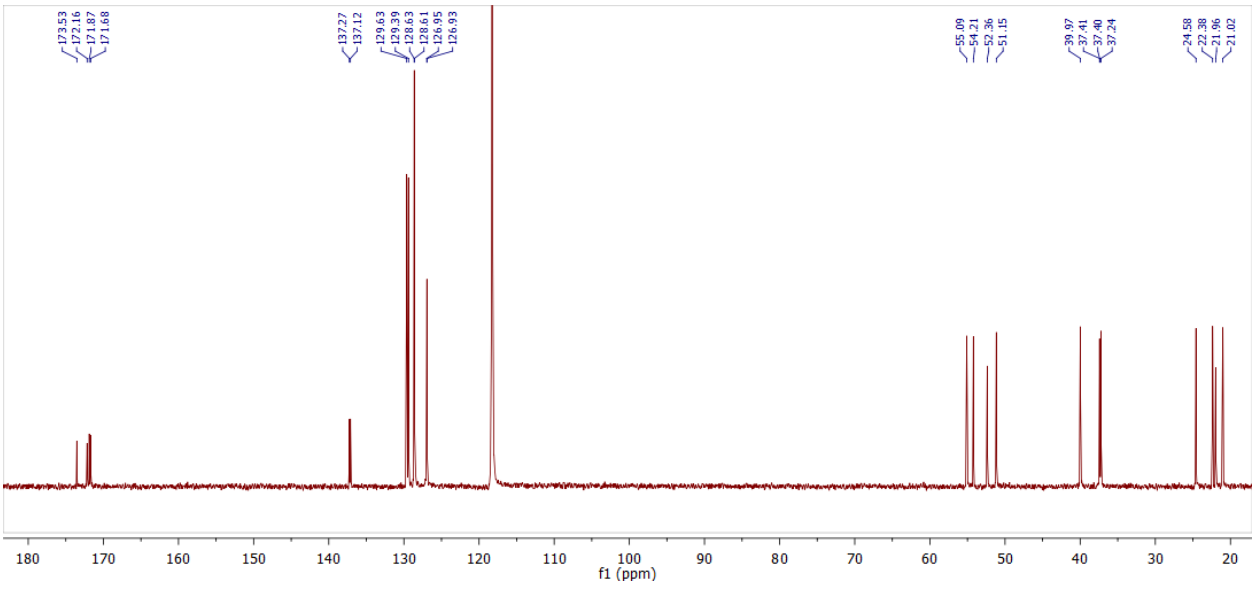
4.1.15. *N*-Acetyl-L-phenylalanyl-L-leucyl-L-phenylalanine methyl ester (Ac-Phe-Leu-Phe-OMe (25))



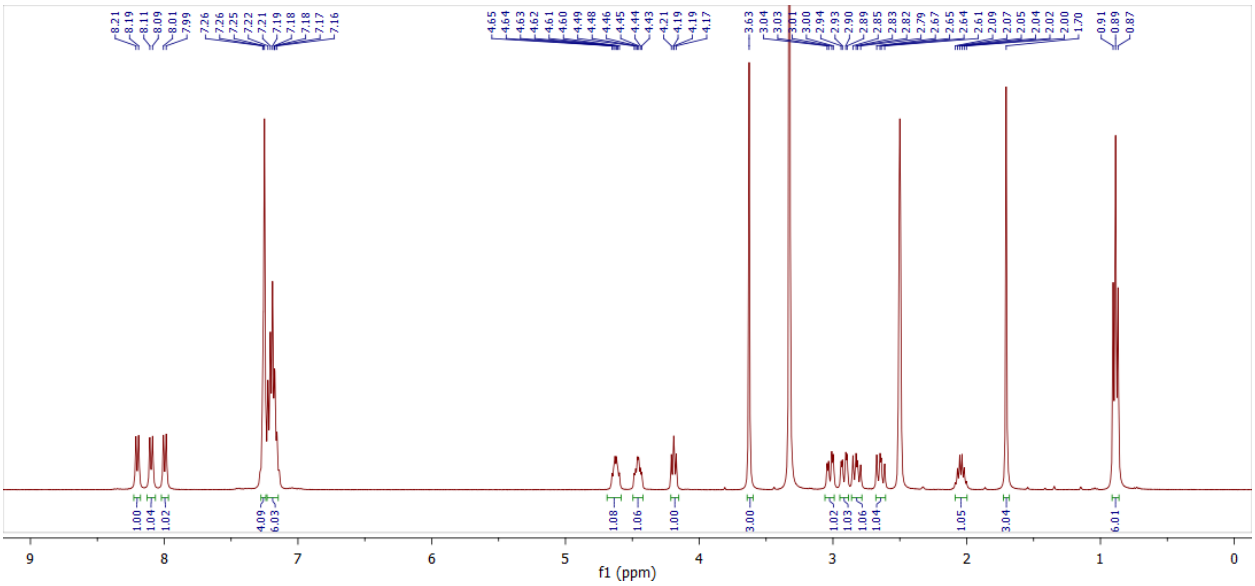


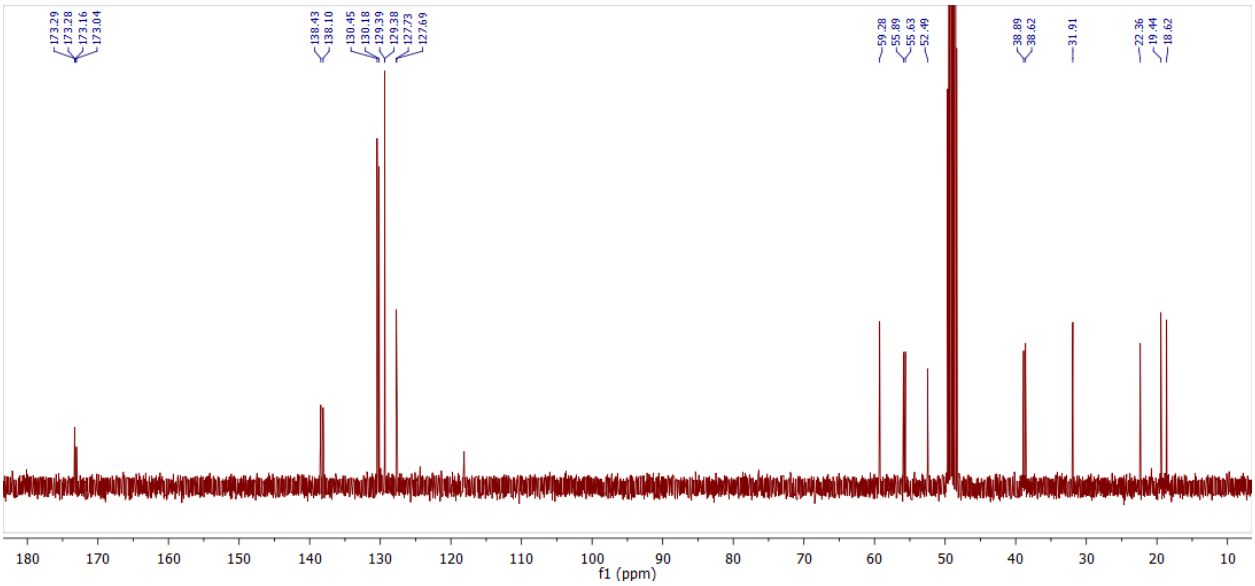
4.1.16. *N*-Acetyl-L-phenylalanyl-L-phenylalanyl-L-leucine methyl ester (Ac-Phe-Phe-Leu-OMe (26))





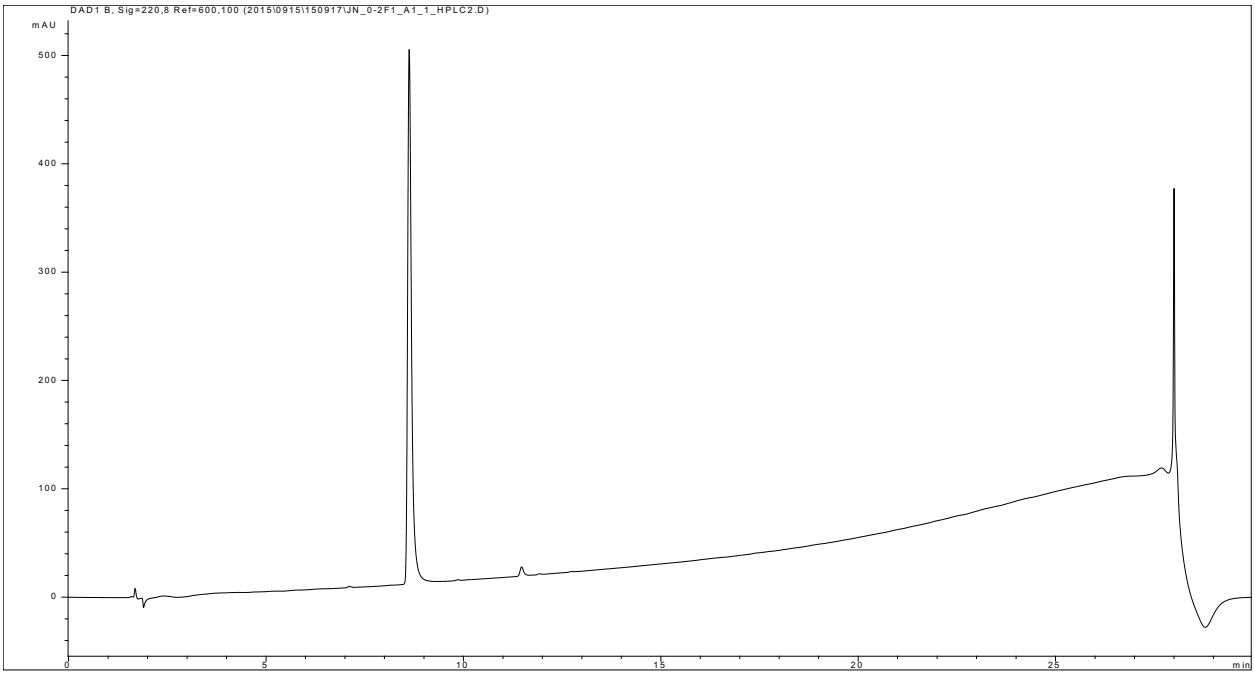
4.1.17. *N*-Acetyl-L-phenylalanyl-L-phenylalanyl-L-valine methyl ester (Ac-Phe-Phe-Val-OMe (27))



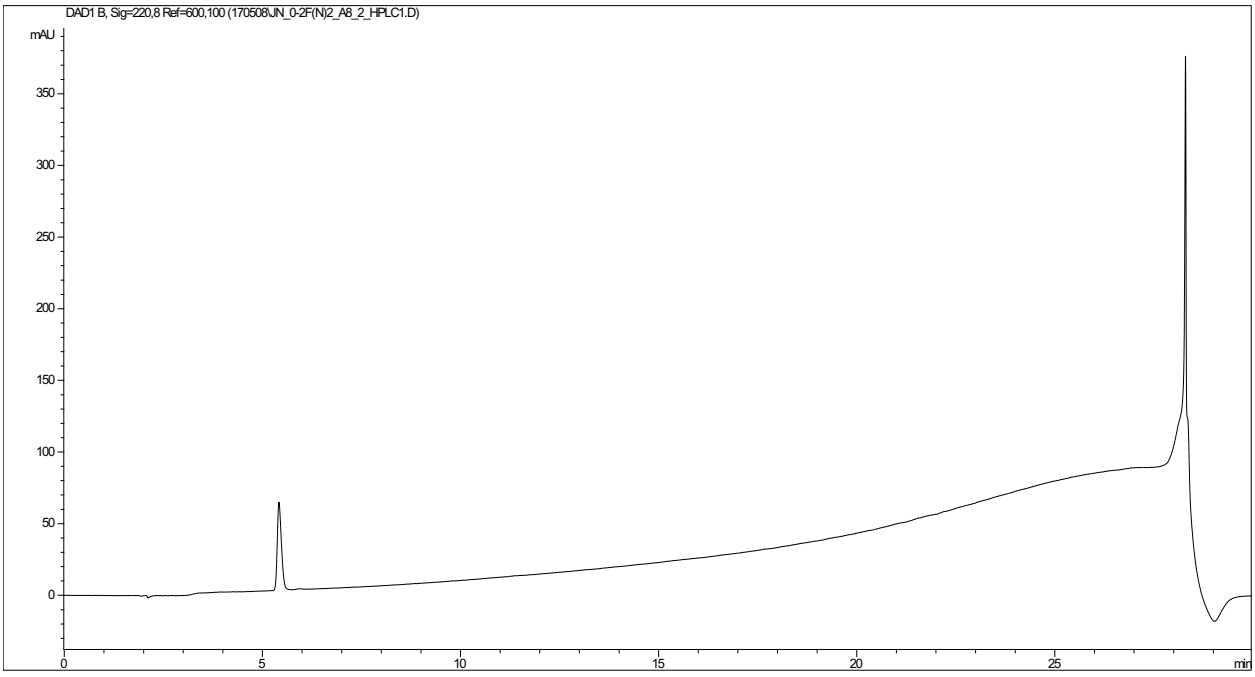


4.2. HPLC spectra

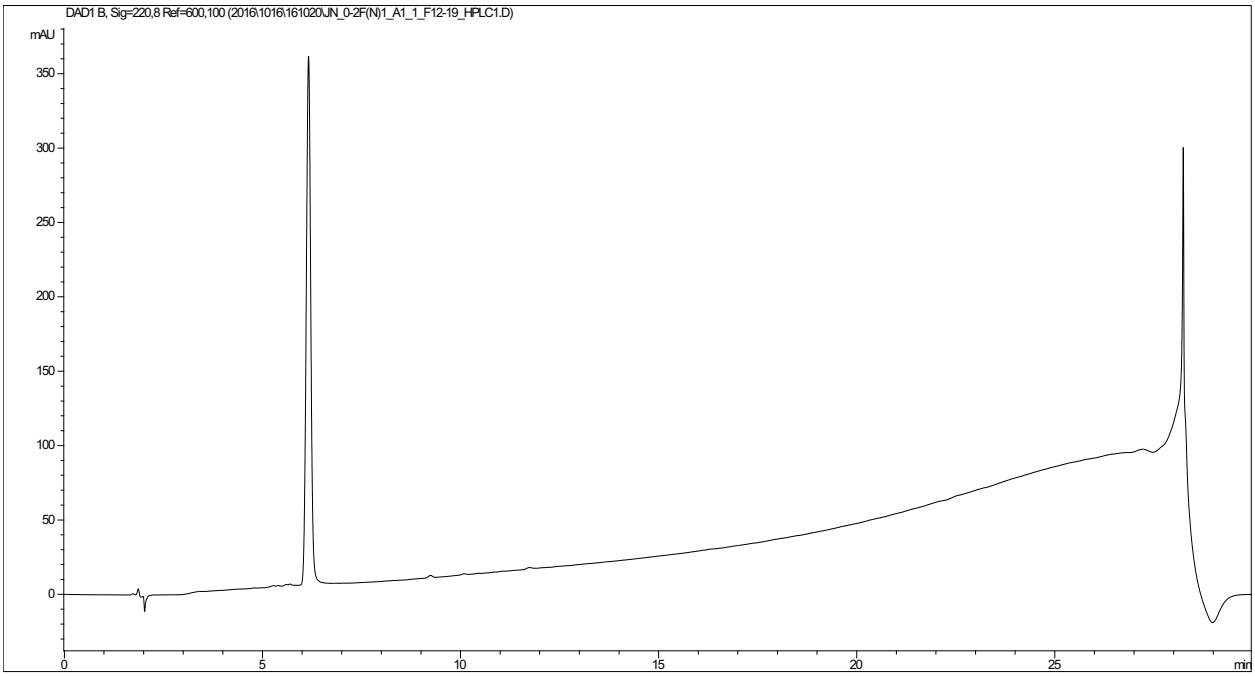
4.2.1. *N*-Acetyl-L-phenylalanine methyl ester (Ac-Phe-OMe (7))



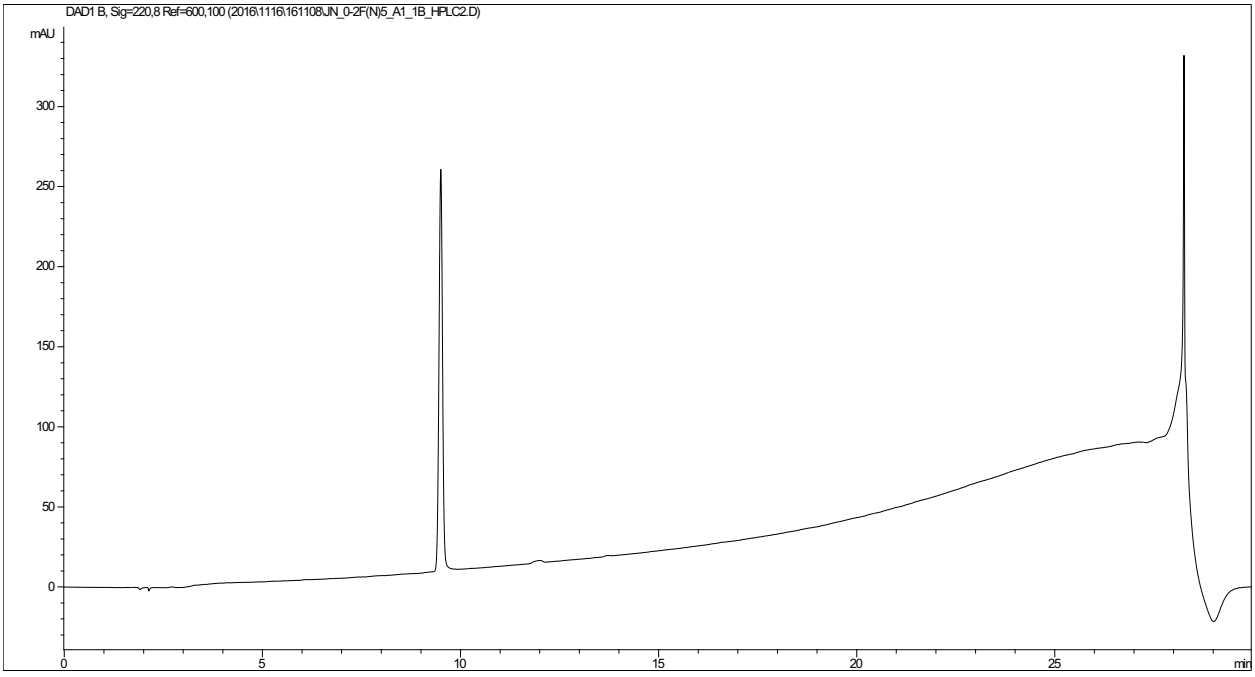
4.2.2. *N*-Acetyl-L-phenylalanine amide (Ac-Phe-NH_2 (14))



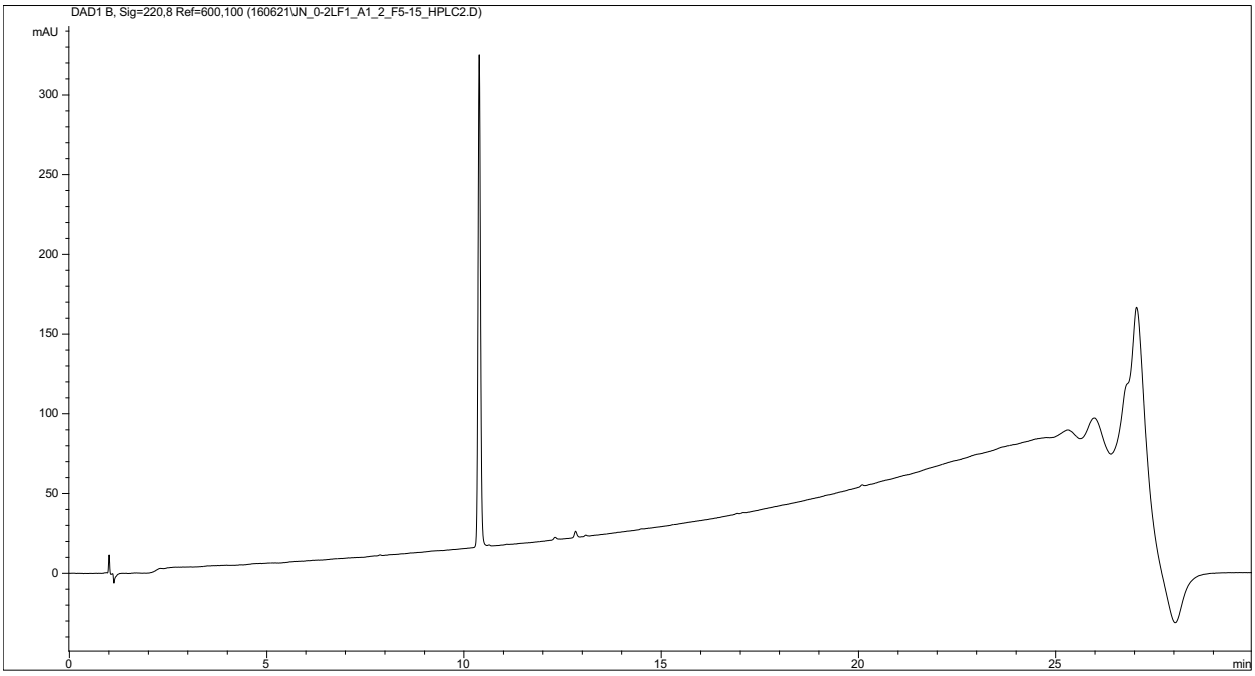
4.2.3. *N*-Acetyl-L-phenylalanine methyl amide (Ac-Phe-NHMe (6))



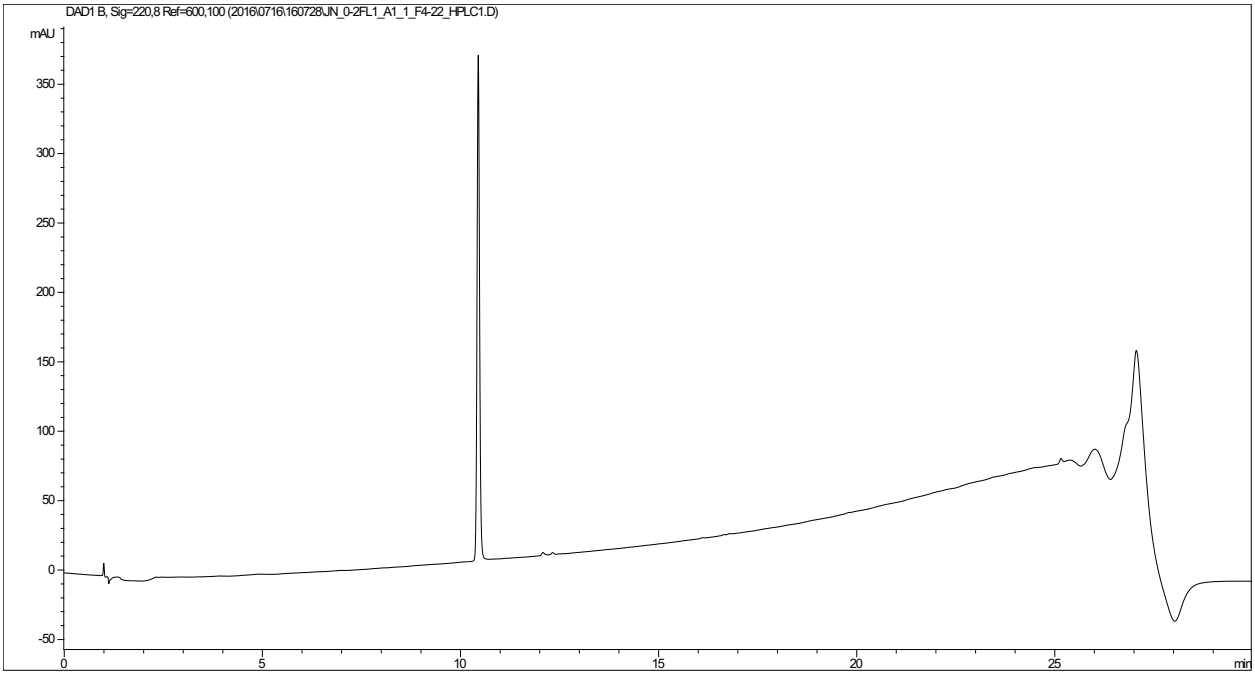
4.2.4. *N*-Acetyl-L-phenylalanine *t*-butyl amide (Ac-Phe-NH*t*Bu (13))



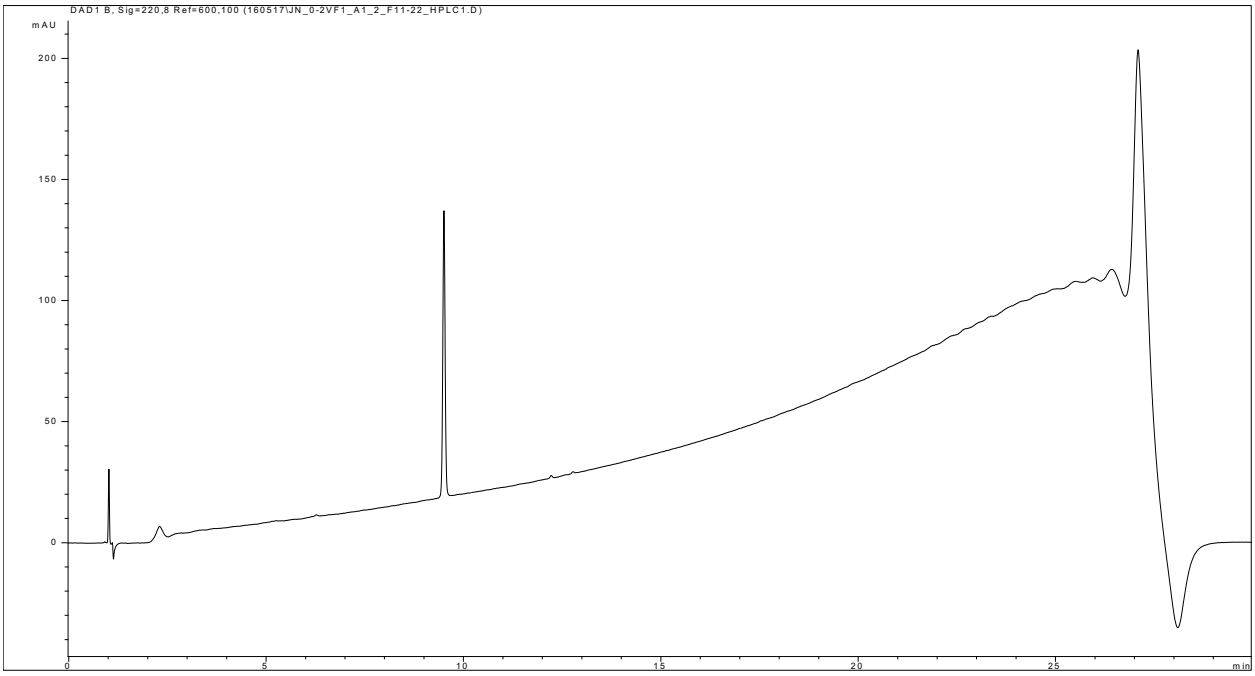
4.2.5. *N*-Acetyl-L-leucyl-L-phenylalanine methyl ester (Ac-Leu-Phe-OMe (15))



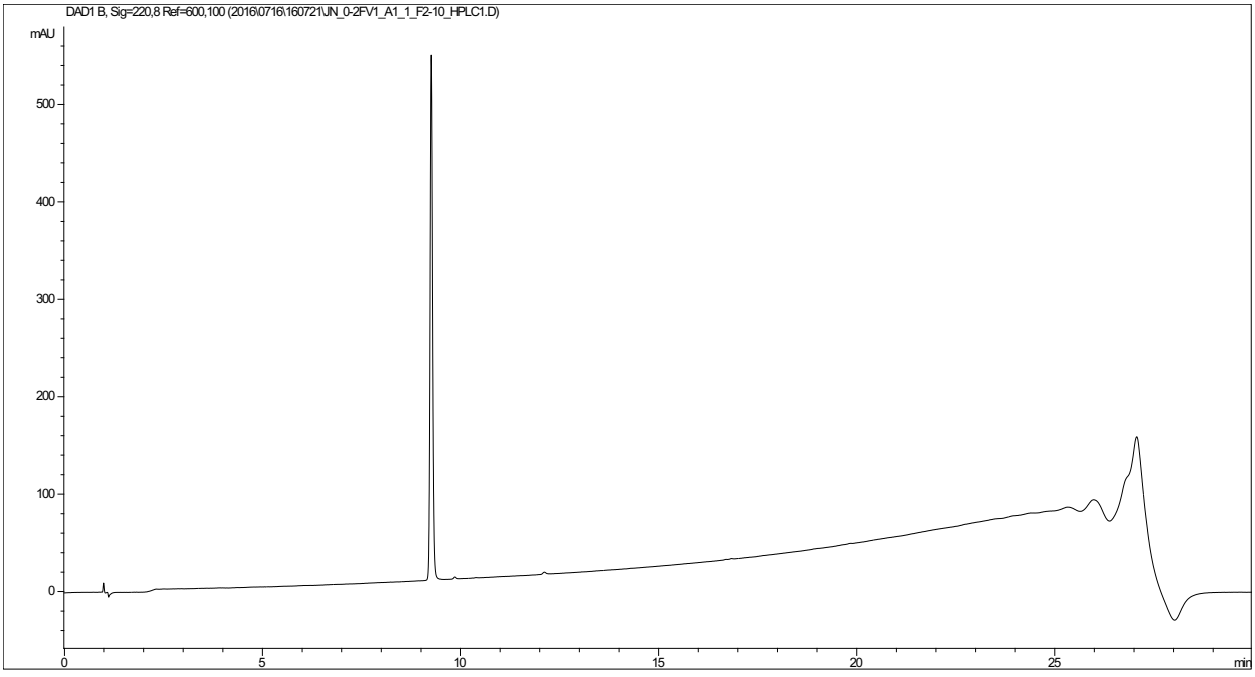
4.2.6. *N*-Acetyl-L-phenylalanyl-L-leucine methyl ester (Ac-Phe-Leu-OMe (16))



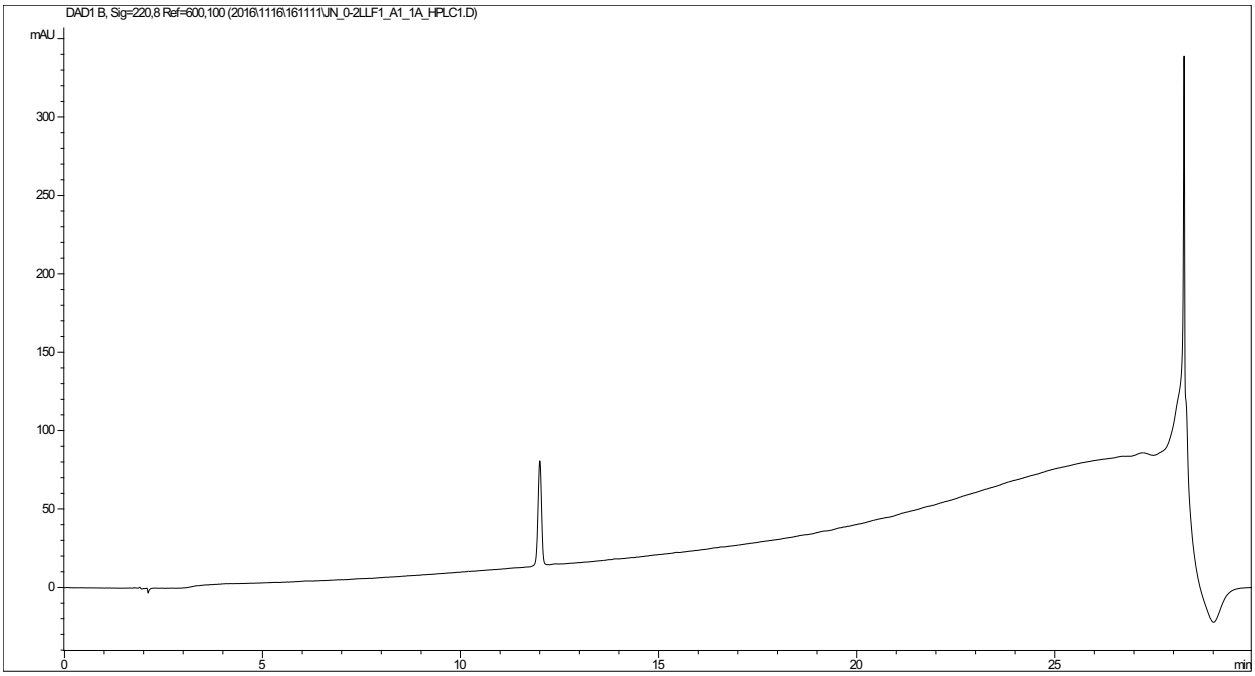
4.2.7. *N*-Acetyl-L-valyl-L-phenylalanine methyl ester (Ac-Val-Phe-OMe (17))



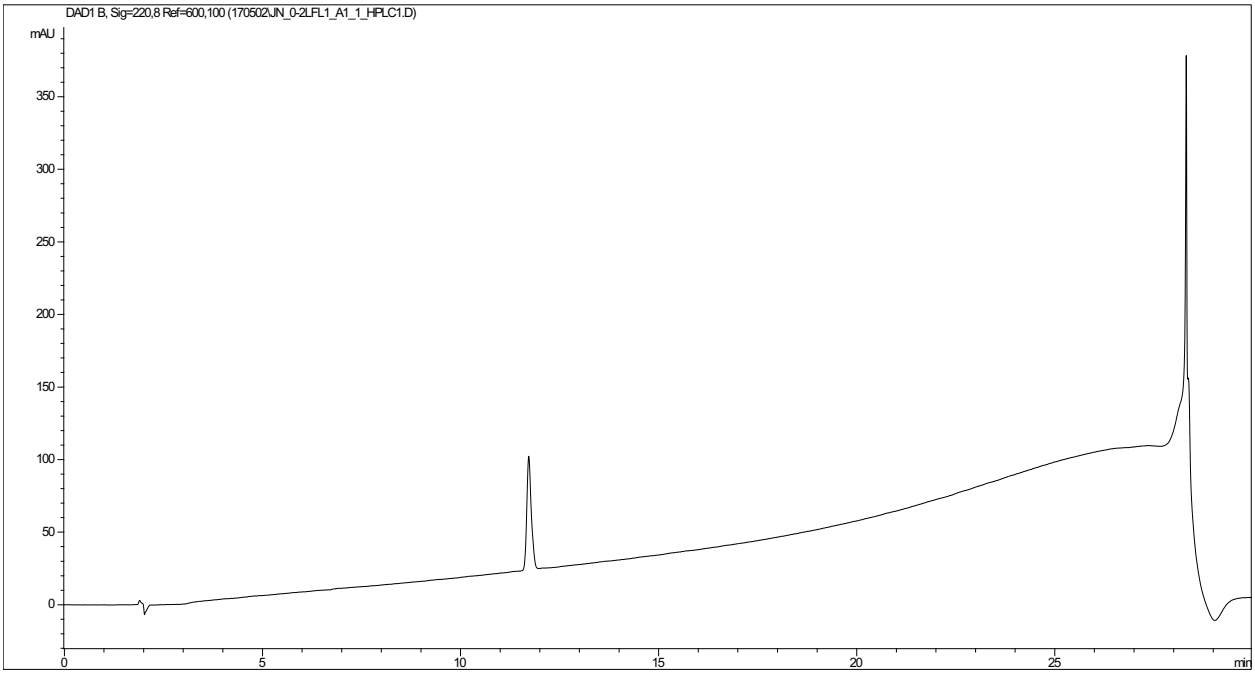
4.2.8. *N*-Acetyl-L-phenylalanyl-L-valine methyl ester (Ac-Phe-Val-OMe (18))



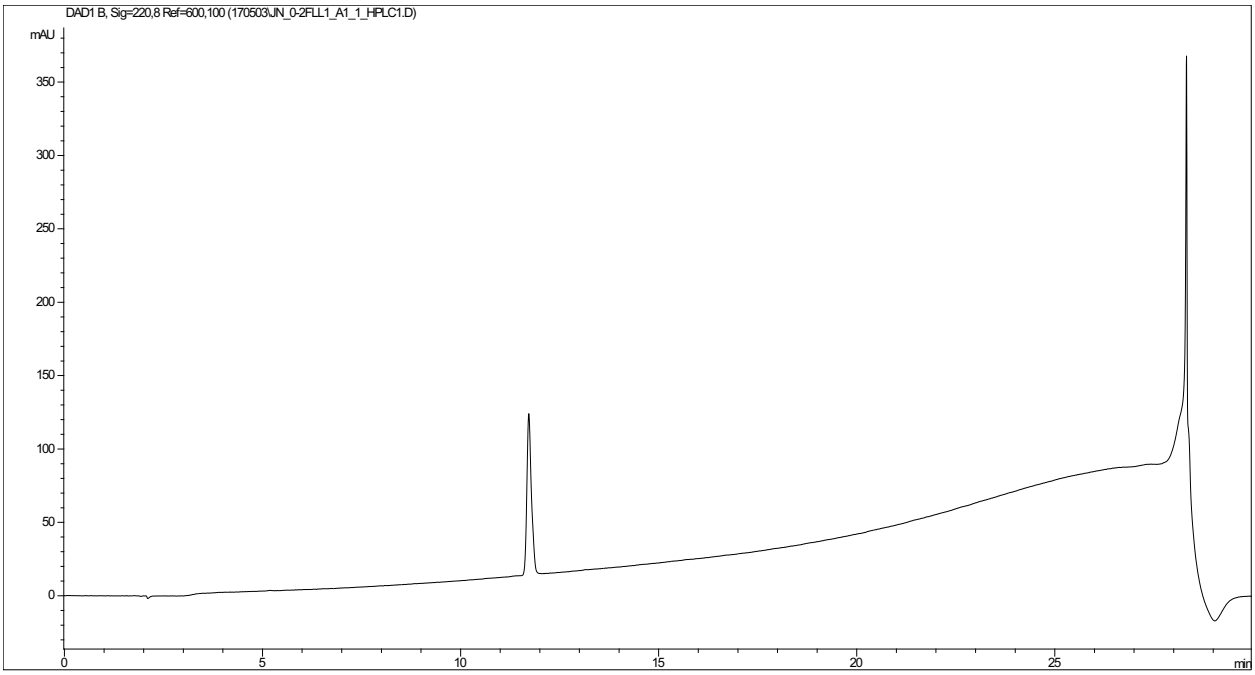
4.2.9. *N*-Acetyl-L-leucyl-L-leucyl-L-phenylalanine methyl ester (Ac-Leu-Leu-Phe-OMe (19))



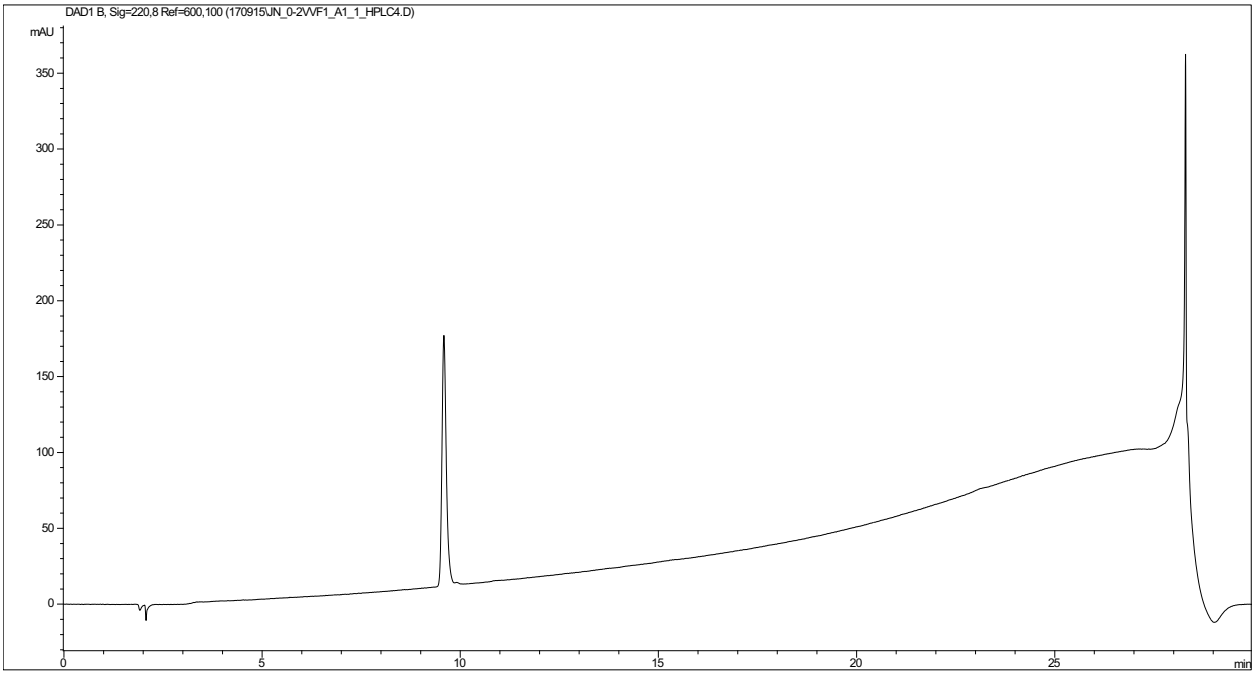
4.2.10. *N*-Acetyl-L-leucyl-L-phenylalanyl-L-leucine methyl ester (Ac-Leu-Phe-Leu-OMe (20))



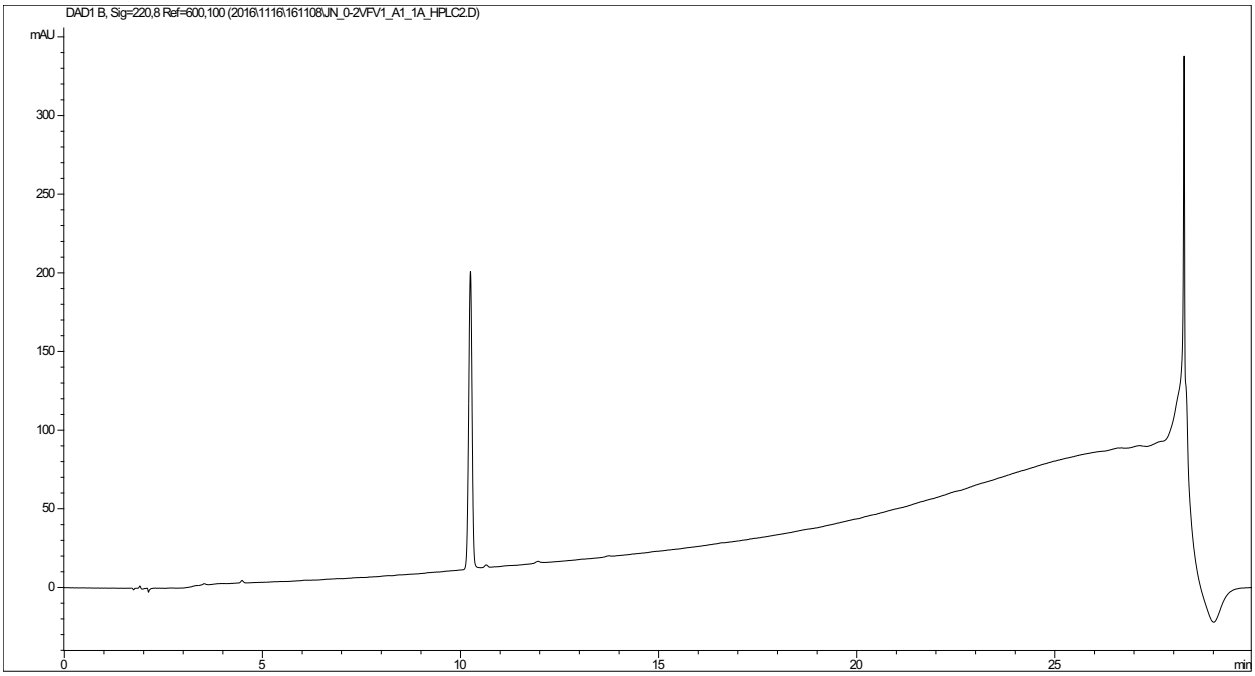
4.2.11. *N*-Acetyl-L-phenylalanyl-L-leucyl-L-leucine methyl ester (Ac-Phe-Leu-Leu-OMe (21))



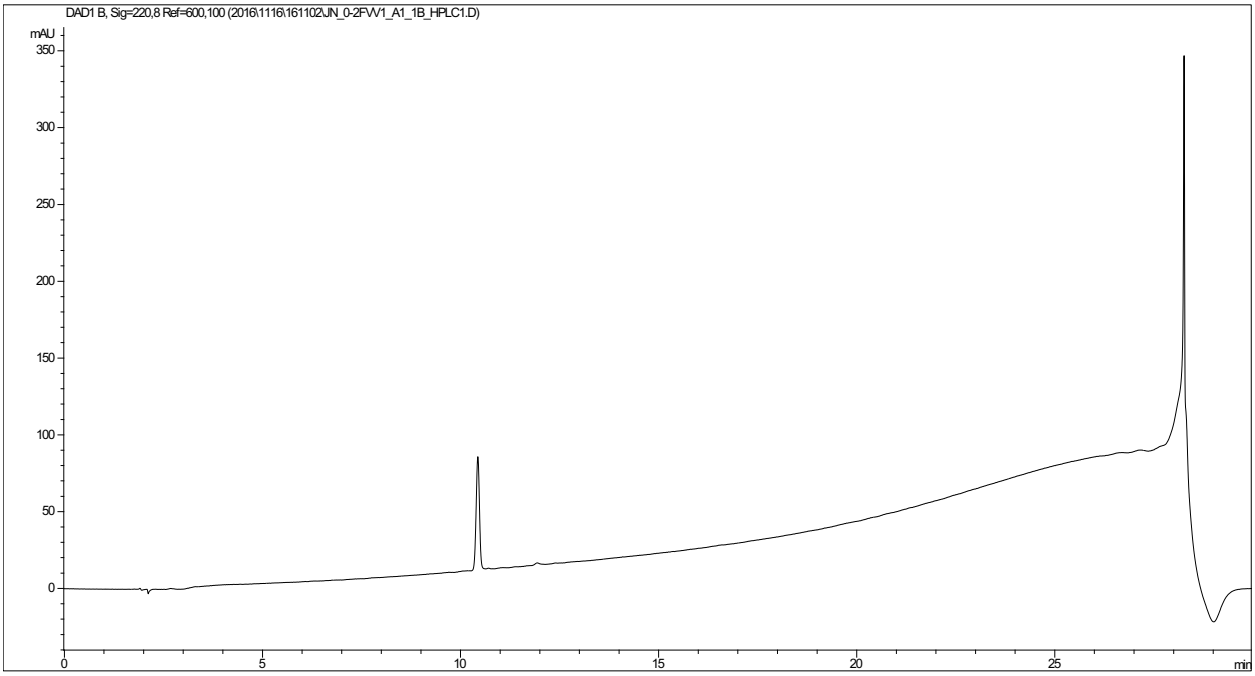
4.2.12. *N*-Acetyl-L-valyl-L-valyl-L-phenylalanine methyl ester (Ac-Val-Val-Phe-OMe (22))



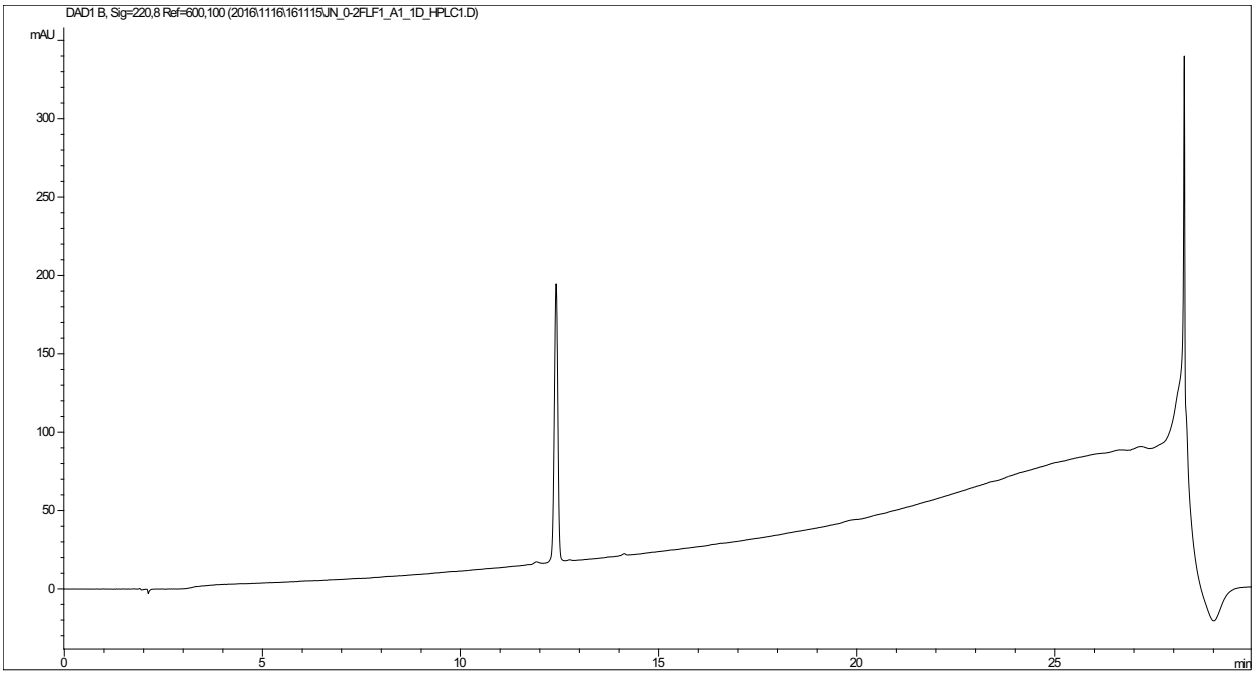
4.2.13. *N*-Acetyl-L-valyl-L-phenylalanyl-L-valine methyl ester (Ac-Val-Phe-Val-OMe (23))



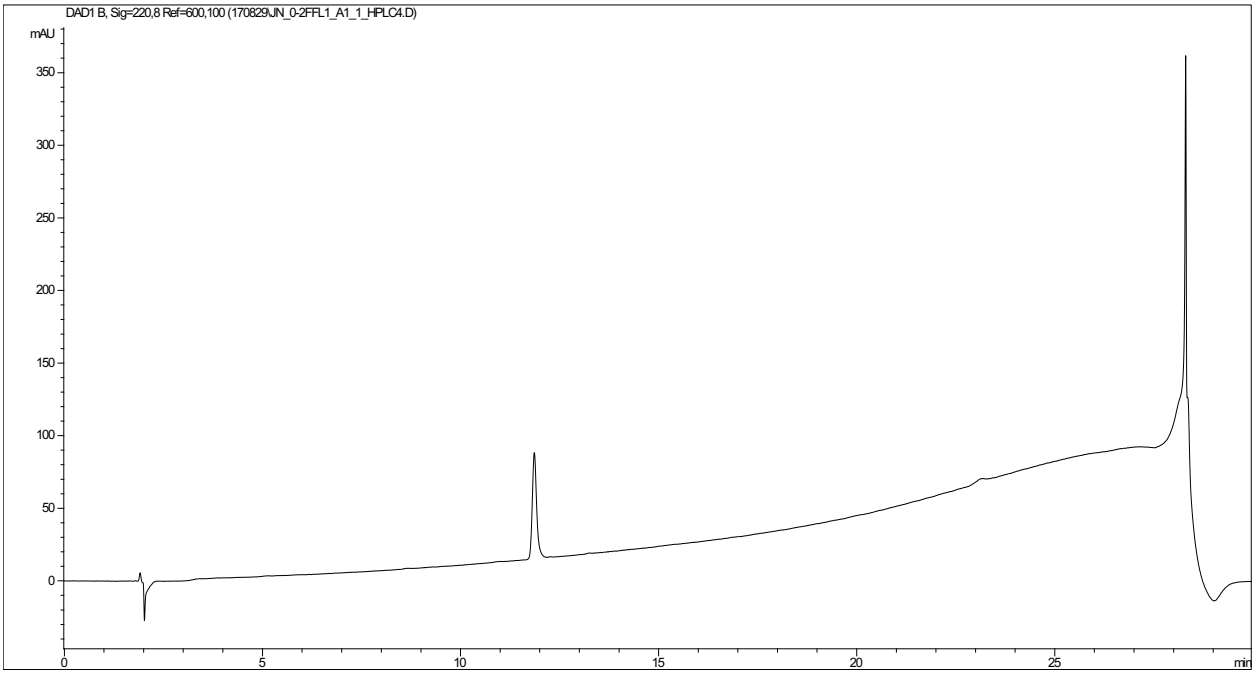
4.2.14. *N*-Acetyl-L-phenylalanyl-L-valyl-L-valine methyl ester (Ac-Phe-Val-Val-OMe (24))



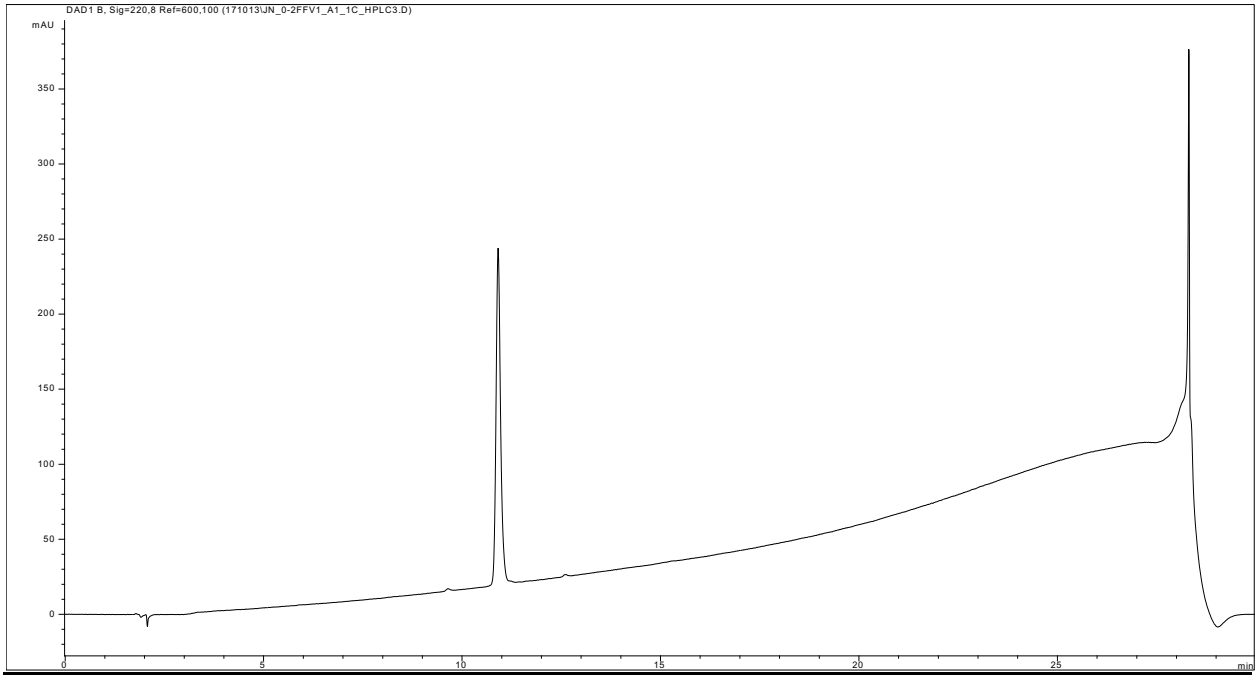
4.2.15. *N*-Acetyl-L-phenylalanyl-L-leucyl-L-phenylalanine methyl ester (Ac-Phe-Leu-Phe-OMe (25))



4.2.16. *N*-Acetyl-L-phenylalanyl-L-phenylalanyl-L-leucine methyl ester (Ac-Phe-Phe-Leu-OMe (26))



4.2.17. *N*-Acetyl-L-phenylalanyl-L-phenylalanyl-L-valine methyl ester (Ac-Phe-Phe-Val-OMe (27))



5. Laser flash photolysis studies

All experiments were performed at 298 ± 1 K on an Edinburgh Instrument LP920 spectrometer using the third harmonic of a Quantel Brilliant B Nd:YAG laser (6 ns pulse, 10 – 30 mJ, λ = 355 nm) to generate the reaction transient. The detection system employed a Hamamatsu R2856 photomultiplier tube (PMT) interfaced with a Tektronix TDS 3012C Digital Phosphor oscilloscope for transient absorption spectra.

Kinetic measurements were carried out under pseudo-first order conditions following the established procedure described in ref [1]. Measurement for each substrate was done three times and the results were reported as the average of the three runs. Due to the very low solubility of tripeptide Ac-Leu-Leu-Phe-OMe (**19**) and Ac-Val-Val-Phe-OMe (**22**), some measurements were not carried out under ideal pseudo-first order conditions. Therefore, the values reported in the manuscript were only based on peptide concentrations in the range of pseudo-first order conditions. However, the rate coefficients obtained do not vary dramatically, e.g., Ac-Leu-Leu-Phe-OMe (**19**) has the rate coefficient of 1.9 x 10^7 M^{-1} s^{-1} (Table 2 in the manuscript), compared to 2.2 x 10^7 M^{-1} s^{-1} when all peptide concentrations are included (Figure S3). Because of this, the error for the rate coefficients for these peptides is given as 30%.

Below are the plots of pseudo-first order rate coefficients of all substrates used with respect of substrate concentrations. The intercept is due to the reaction of $NO_3^{\bullet}$ with the solvent (see ref [1]).

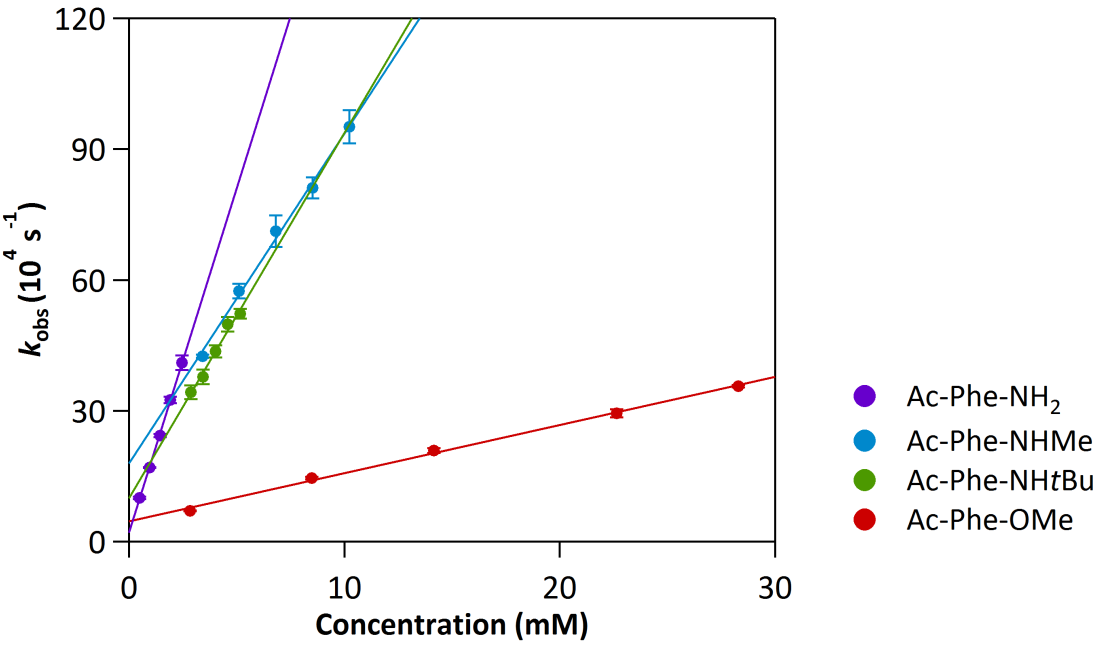


Figure S7. Plot of pseudo-first order rate coefficient (k_{obs}) versus [phenylalanine] with different *C*-terminal protecting groups (see Table 1). Error bars shown are 2σ statistical uncertainties.

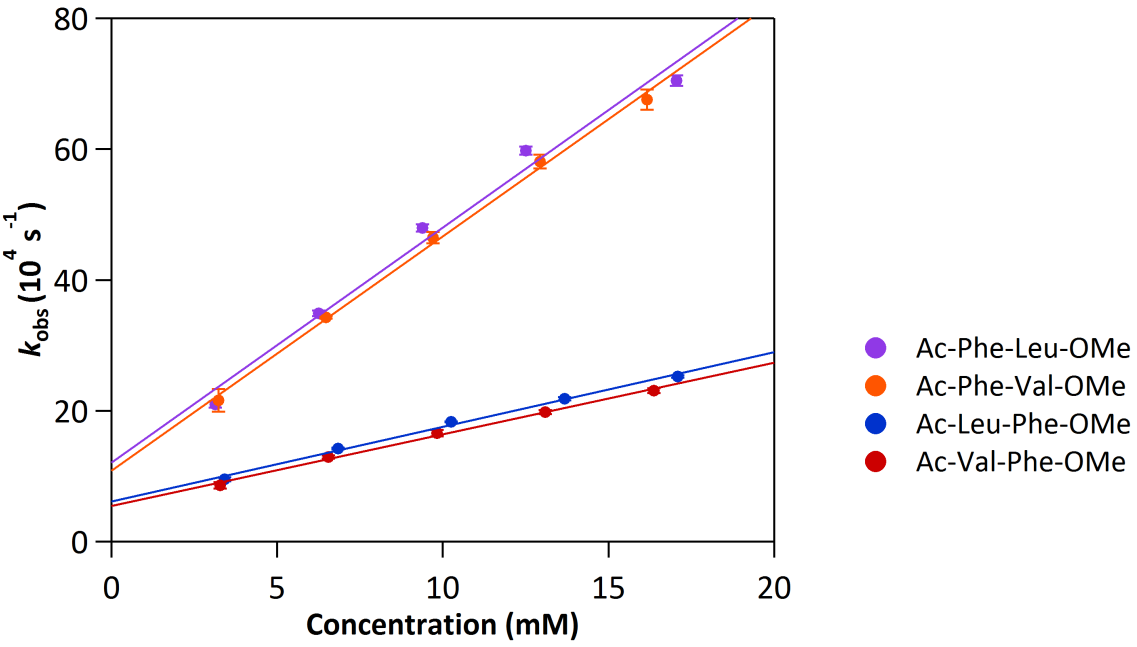


Figure S8. Plot of pseudo-first order rate coefficient (k_{obs}) versus [dipeptides] containing a Phe residue (see Table 2). Error bars shown are 2σ statistical uncertainties.

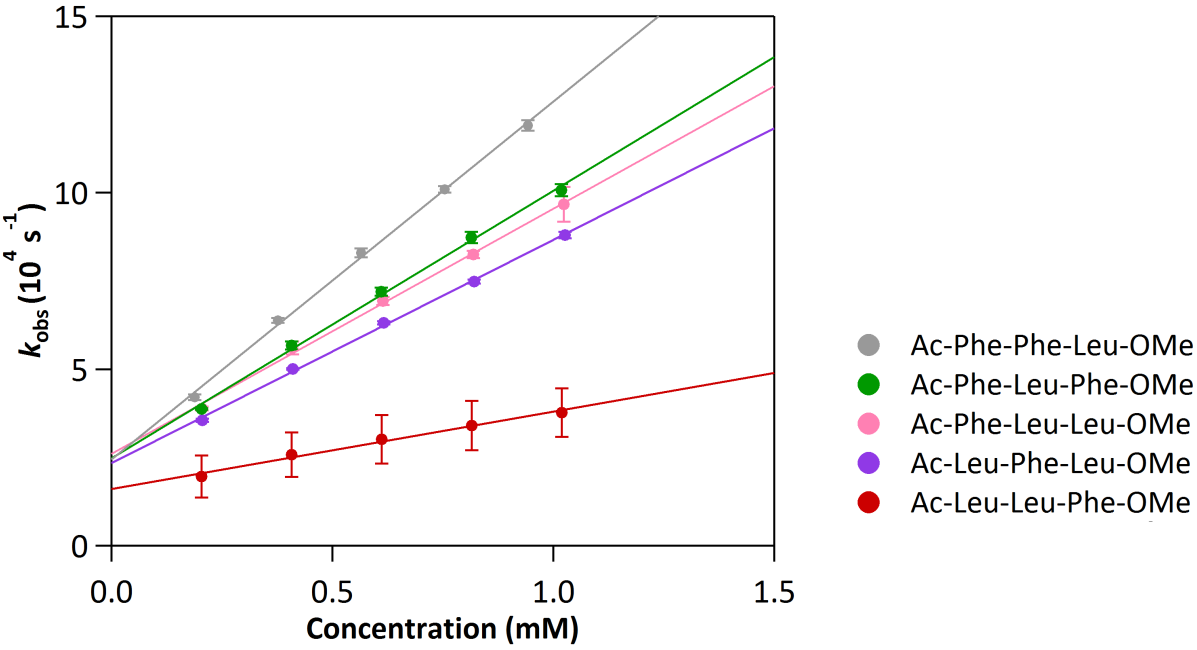


Figure S9. Plot of pseudo-first order rate coefficient (k_{obs}) versus [tripeptides] containing Phe and Leu residues (see Table 2). Error bars shown are 2σ statistical uncertainties.

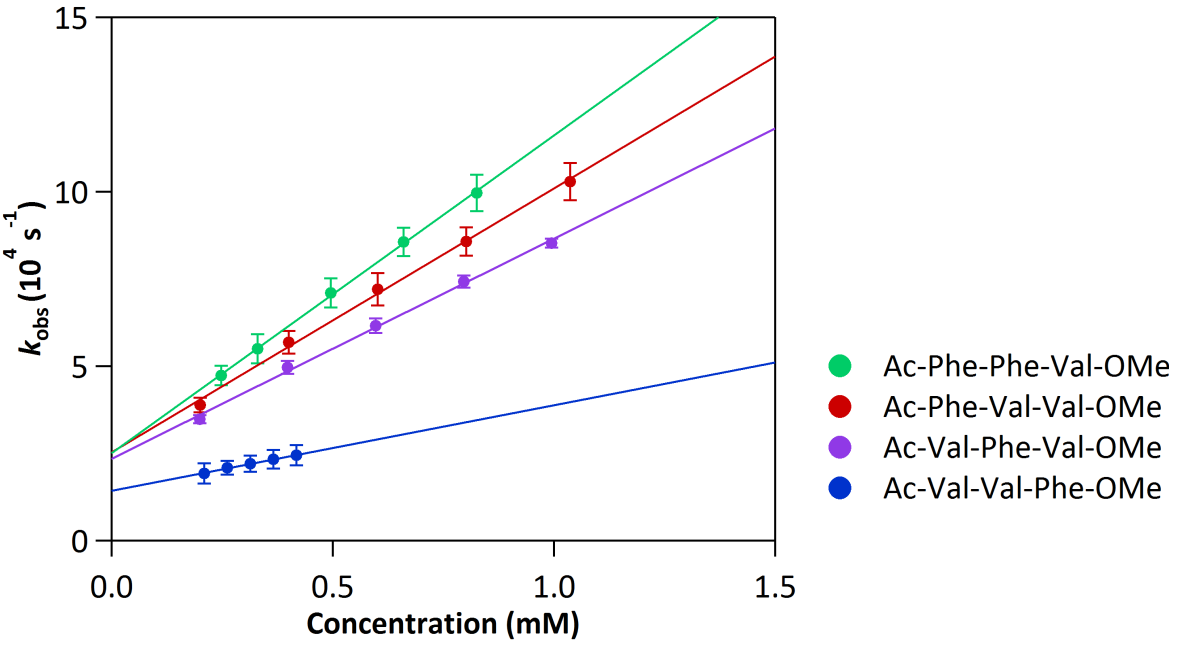


Figure S10. Plot of pseudo-first order rate coefficient (k_{obs}) versus [tripeptides] containing Phe and Val residues (see Table 2). Error bars shown are 2σ statistical uncertainties.

6. Reaction of $NO_3^\bullet$ with Ac-Phe-Phe-OMe (28)

Dipeptide **28** (1 mmol) and CAN (1.10 g, 2 mmol) were dissolved in CH_3CN (100 mL). The mixture was degassed by sparging with argon under sonication and subsequently irradiated at 350 nm in a Rayonet photoreactor for 4 hours. The reaction mixture was concentrated under reduced pressure, resuspended in H_2O (100 mL) and extracted with ethyl acetate (3 x 100 mL). The combined organic fractions were dried with Mg_2SO_4, concentrated under reduced pressure. and the residue was purified by preparative HPLC.

***N*-Acetyl-(*threo*)-β-nitrate-L-phenylalanyl-L-phenylalanine methyl ester (29):** ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.67 (d, *J* = 7.6 Hz, 1H, N*H*), 8.49 (d, *J* = 9.4 Hz, 1H, N*H*), 7.41 – 7.34 (m, 5H, Ar-*H*), 7.28 – 7.17 (m, 5H, Ar-*H*), 6.34 (d, *J* = 5.4 Hz, 1H, $C_\beta H ONO_2$),* 4.98 (dd, *J* = 9.4, 5.4 Hz, 1H, $C_\beta ONO_2C_\alpha H$),* 4.46 (ddd, *J* = 8.9, 7.6, 5.7 Hz, 1H, $C_\beta H_2C_\alpha H$), 3.49 (s, 3H, CO_2CH_3), 3.05 (dd, *J* = 13.9, 5.7 Hz, 1H, CH_2), 2.91 (dd, *J* = 13.9, 9.0 Hz, 1H, CH_2), 1.75 (s, 3H, NHCOCH_3). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.32 (*C*O), 169.36 (*C*O), 167.56 (*C*O), 136.97 (Ar-*C*), 134.46 (Ar-*C*), 128.98 (Ar-*C*), 128.86 (Ar-*C*), 128.36 (Ar-*C*), 128.28 (Ar-*C*), 126.75 (Ar-*C*), 126.60 (Ar-*C*), 84.27 (*C*ONO_2), 54.42 (C_α), 53.65 (C_α), 51.89 (CO_2CH_3), 36.34 (C_β (C-terminal)), 22.15, (NHCO*C*H_3). HRMS (ESI) *m/z* calcd. for [$C_{21}H_{24}N_3O_7^+$]: 430.1609 [M+H$^+$], found 430.1563; HRMS (ESI) *m/z* calcd. for [$C_{21}H_{23}N_3O_7Na^+$]: 452.1428 [M+Na$^+$], found 452.1368.

*The coupling between the α and β protons of ^3J = 5.7 Hz is consistent with an *anti* (*threo*) configuration of the adjacent stereocentres; see: A. G. Griesbeck, S. Bondock, *Can. J. Chem*. **2003**, *81*, 555–559.
The single regioisomer is evidenced by signals showing intact α and β protons at δ = 4.46 ppm and δ = 2.91, 3.05 ppm, where $J_{\alpha\beta}$ = 5.7 and 9.0 Hz, respectively.

7. Gaussian Archive Entries for Computational Data

The calculations were performed using the Gaussian software package.[2]

Structure 6:

M062X/6-31G(d) SCRF(solvent=acetonitrile) optimization and frequency calculation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	-1.678383	0.366646	-0.431881
2	6	0	-0.805200	1.055440	0.486526
3	6	0	0.257232	1.768407	-0.350819
4	8	0	0.431374	1.493819	-1.534841
5	6	0	-0.139030	0.084285	1.494973
6	6	0	0.745015	-0.929369	0.814694
7	6	0	2.101743	-0.665522	0.599943
8	6	0	2.907074	-1.580043	-0.074299
9	6	0	2.364333	-2.774201	-0.545267
10	6	0	1.014471	-3.049177	-0.334636
11	6	0	0.212488	-2.132184	0.340887
12	6	0	-2.883953	-0.111262	-0.051839
13	6	0	-3.659523	-0.860839	-1.113068
14	8	0	-3.314471	0.035203	1.089901
15	1	0	-1.323254	0.241298	-1.372298
16	1	0	-1.392499	1.787157	1.053353
17	1	0	0.435907	0.669689	2.220506
18	1	0	-0.951473	-0.408903	2.036354
19	1	0	2.528076	0.265785	0.967244
20	1	0	3.959244	-1.361397	-0.230215
21	1	0	2.991271	-3.488721	-1.069899
22	1	0	0.586500	-3.980256	-0.694017
23	1	0	-0.838739	-2.352538	0.512447
24	1	0	-4.695649	-0.517494	-1.100485
25	1	0	-3.244192	-0.734339	-2.114354
26	1	0	-3.656203	-1.925144	-0.860203
27	7	0	1.016741	2.662071	0.307129
28	6	0	2.107732	3.345896	-0.363839
29	1	0	0.791960	2.907333	1.261179
30	1	0	2.662355	3.925861	0.372525
31	1	0	2.775863	2.614416	-0.825403
32	1	0	1.732824	4.015466	-1.143504

SCF Done: E(RM062X) = -726.604908016 A.U. after 1 cycles

- Thermochemistry -

Zero-point correction= 0.271571 (Hartree/Particle)
Thermal correction to Energy= 0.287767
Thermal correction to Enthalpy= 0.288712
Thermal correction to Gibbs Free Energy= 0.226015
Sum of electronic and zero-point Energies= -726.333337
Sum of electronic and thermal Energies= -726.317141
Sum of electronic and thermal Enthalpies= -726.316196
Sum of electronic and thermal Free Energies= -726.378893
CBS-QB3 calculation at M062X/6-31G(d) scrf(solvent=acetonitrile) geometry:
Temperature= 298.150000 Pressure= 1.000000
E(ZPE)= 0.268855 E(Thermal)= 0.285172
E(SCF)= -722.656483 DE(MP2)= -2.793234
DE(CBS)= -0.268409 DE(MP34)= -0.094069
DE(CCSD)= -0.093948 DE(Int)= 0.089486
DE(Empirical)= -0.130094
CBS-QB3 (0 K)= -725.677895 CBS-QB3 Energy= -725.661578
CBS-QB3 Enthalpy= -725.660634 CBS-QB3 Free Energy= -725.723586

Structure 6a:

M062X/6-31G(d) SCRF(solvent=acetonitrile) optimization and frequency calculation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z

1	7	0	-2.299586	-0.558811	1.010799
2	6	0	-1.005107	0.004651	1.294089
3	6	0	-0.671968	1.106475	0.312294
4	8	0	0.532215	1.081667	-0.133947
5	6	0	0.203088	-0.942803	1.152401
6	6	0	1.274677	-0.200152	0.313562
7	6	0	2.444373	0.268662	1.104701
8	6	0	3.722416	0.080545	0.678174
9	6	0	3.995520	-0.583539	-0.543641
10	6	0	2.926507	-1.071867	-1.334013
11	6	0	1.632414	-0.905365	-0.946520
12	6	0	-2.530836	-1.068960	-0.236100
13	6	0	-3.822283	-1.816859	-0.429930
14	8	0	-1.697696	-0.908055	-1.121614
15	1	0	-2.924835	-0.763550	1.778300
16	1	0	-1.041865	0.455217	2.289541
17	1	0	0.606373	-1.211926	2.129023
18	1	0	-0.100986	-1.854629	0.637618
19	1	0	2.230224	0.765716	2.046964
20	1	0	4.548091	0.433345	1.287811
21	1	0	5.019590	-0.721972	-0.869121
22	1	0	3.145009	-1.595354	-2.259285
23	1	0	0.799530	-1.277934	-1.535690
24	1	0	-3.630381	-2.885301	-0.292555
25	1	0	-4.590590	-1.506307	0.280167
26	1	0	-4.171825	-1.658485	-1.450344
27	7	0	-1.502492	2.041063	-0.030340
28	6	0	-1.194401	3.117609	-0.970831
29	1	0	-2.431204	1.996948	0.380306
30	1	0	-2.088653	3.330679	-1.553729
31	1	0	-0.885085	4.009861	-0.424091
32	1	0	-0.391397	2.788656	-1.628761

SCF Done: E(UM062X) = -726.367082300 A.U. after 1 cycles

- Thermochemistry -

Zero-point correction=	0.271532 (Hartree/Particle)
Thermal correction to Energy=	0.287117
Thermal correction to Enthalpy=	0.288061
Thermal correction to Gibbs Free Energy=	0.226683
Sum of electronic and zero-point Energies=	-726.095550
Sum of electronic and thermal Energies=	-726.079966
Sum of electronic and thermal Enthalpies=	-726.079021
Sum of electronic and thermal Free Energies=	-726.140399

CBS-QB3 calculation at M062X/6-31G(d) scrf(solvent=acetonitrile) geometry:

Temperature=	298.150000	Pressure=	1.000000
E(ZPE)=	0.268817	E(Thermal)=	0.284526
E(SCF)=	-722.464422	DE(MP2)=	-2.707212
DE(CBS)=	-0.260060	DE(MP34)=	-0.121689
DE(CCSD)=	-0.100444	DE(Int)=	0.085106
DE(Empirical)=	-0.131889		
CBS-QB3 (0 K)=	-725.431793	CBS-QB3 Energy=	-725.416084
CBS-QB3 Enthalpy=	-725.415139	CBS-QB3 Free Energy=	-725.476771

Structure 6b:

M062X/6-31G(d) SCRF(solvent=acetonitrile) optimization and frequency calculation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	0.921955	1.432084	0.394622
2	6	0	1.105524	-0.011212	0.491125
3	6	0	2.588025	-0.265672	0.166535
4	8	0	3.372568	0.676113	0.130766
5	6	0	0.108108	-0.684907	-0.443634
6	6	0	-1.310731	-0.144147	-0.205043

7	6	0	-2.234470	-0.574089	-1.295882
8	6	0	-3.412923	-1.201352	-1.040096
9	6	0	-3.836109	-1.458012	0.287803
10	6	0	-3.022726	-1.047006	1.372715
11	6	0	-1.832723	-0.420995	1.168077
12	6	0	-0.160350	2.015893	-0.034550
13	6	0	-0.236635	3.492789	-0.200763
14	8	0	-1.235874	1.363096	-0.344519
15	1	0	1.770832	1.981043	0.537614
16	1	0	0.937823	-0.319208	1.529735
17	1	0	0.393159	-0.504791	-1.485824
18	1	0	0.083281	-1.763537	-0.274074
19	1	0	-1.906455	-0.374308	-2.311605
20	1	0	-4.041683	-1.510276	-1.868869
21	1	0	-4.780866	-1.954278	0.472650
22	1	0	-3.356146	-1.234851	2.388301
23	1	0	-1.228667	-0.099990	2.012068
24	1	0	-0.438326	3.714201	-1.251604
25	1	0	-1.073681	3.865647	0.393604
26	1	0	0.687131	3.977289	0.112061
27	7	0	2.940587	-1.539447	-0.032787
28	6	0	4.331531	-1.888370	-0.281566
29	1	0	2.258661	-2.279562	0.056545
30	1	0	4.391207	-2.958422	-0.471603
31	1	0	4.701736	-1.343216	-1.152422
32	1	0	4.951527	-1.635396	0.582276

SCF Done: E(UM062X) = -726.365699134 A.U. after 1 cycles

- Thermochemistry -

Zero-point correction=	0.271564 (Hartree/Particle)
Thermal correction to Energy=	0.287113
Thermal correction to Enthalpy=	0.288057
Thermal correction to Gibbs Free Energy=	0.227207
Sum of electronic and zero-point Energies=	-726.094135
Sum of electronic and thermal Energies=	-726.078586
Sum of electronic and thermal Enthalpies=	-726.077642
Sum of electronic and thermal Free Energies=	-726.138492

CBS-QB3 calculation at M062X/6-31G(d) scrf(solvent=acetonitrile) geometry:

Temperature=	298.150000	Pressure=	1.000000
E(ZPE)=	0.268849	E(Thermal)=	0.284522
E(SCF)=	-722.464892	DE(MP2)=	-2.706213
DE(CBS)=	-0.260270	DE(MP34)=	-0.121636
DE(CCSD)=	-0.100227	DE(Int)=	0.085131
DE(Empirical)=	-0.131974		
CBS-QB3 (0 K)=	-725.431233	CBS-QB3 Energy=	-725.415560
CBS-QB3 Enthalpy=	-725.414616	CBS-QB3 Free Energy=	-725.475719

Structure 6c:

M062X/6-31G(d) SCRF(solvent=acetonitrile) optimization and frequency calculation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	-1.715154	0.323014	-0.436128
2	6	0	-0.831297	1.001264	0.457066
3	6	0	0.251283	1.696206	-0.373289
4	8	0	0.426653	1.385637	-1.546650
5	6	0	-0.154823	0.026344	1.508959
6	6	0	0.755479	-0.911288	0.827289
7	6	0	2.155609	-0.610311	0.716067
8	6	0	2.988969	-1.456084	0.040229
9	6	0	2.455056	-2.630321	-0.556589
10	6	0	1.069639	-2.943885	-0.459620
11	6	0	0.235083	-2.097389	0.213012
12	6	0	-2.929820	-0.127397	-0.016702
13	6	0	-3.784855	-0.800772	-1.062577

14	8	0	-3.277493	-0.012158	1.152705
15	1	0	-1.413255	0.252094	-1.402021
16	1	0	-1.396234	1.715637	1.065622
17	1	0	0.379122	0.634217	2.242436
18	1	0	-0.987131	-0.495467	1.990538
19	1	0	2.532086	0.297905	1.176901
20	1	0	4.047753	-1.244863	-0.050670
21	1	0	3.113912	-3.297762	-1.100822
22	1	0	0.694763	-3.849465	-0.921688
23	1	0	-0.824287	-2.312019	0.306509
24	1	0	-4.802249	-0.413758	-0.983094
25	1	0	-3.413240	-0.650673	-2.077252
26	1	0	-3.815734	-1.873111	-0.849452
27	7	0	1.009879	2.588921	0.281283
28	6	0	2.088901	3.285381	-0.401914
29	1	0	0.733469	2.903115	1.201959
30	1	0	2.684130	3.816335	0.339302
31	1	0	2.717478	2.558518	-0.920359
32	1	0	1.697715	3.997453	-1.134018

SCF Done: E(UM062X) = -726.355641462 A.U. after 1 cycles

- Thermochemistry -

Zero-point correction=	0.269336 (Hartree/Particle)
Thermal correction to Energy=	0.286086
Thermal correction to Enthalpy=	0.287030
Thermal correction to Gibbs Free Energy=	0.221448
Sum of electronic and zero-point Energies=	-726.086306
Sum of electronic and thermal Energies=	-726.069555
Sum of electronic and thermal Enthalpies=	-726.068611
Sum of electronic and thermal Free Energies=	-726.134193

CBS-QB3 calculation at M062X/6-31G(d) scrf(solvent=acetonitrile) geometry:

Temperature=	298.150000	Pressure=	1.000000
E(ZPE)=	0.266642	E(Thermal)=	0.283515
E(SCF)=	-722.450948	DE(MP2)=	-2.725914
DE(CBS)=	-0.261328	DE(MP34)=	-0.110536
DE(CCSD)=	-0.094022	DE(Int)=	0.086658
DE(Empirical)=	-0.129317		
CBS-QB3 (0 K)=	-725.418764	CBS-QB3 Energy=	-725.401891
CBS-QB3 Enthalpy=	-725.400947	CBS-QB3 Free Energy=	-725.466792

Structure 7:

M062X/6-31G(d) SCRF(solvent=acetonitrile) optimization and frequency calculation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	-1.711485	0.292520	-0.438475
2	6	0	-0.855933	1.021998	0.465718
3	6	0	0.168508	1.768504	-0.368810
4	8	0	0.293970	1.648670	-1.565929
5	6	0	-0.140921	0.101648	1.485555
6	6	0	0.793292	-0.869573	0.809587
7	6	0	2.135505	-0.537468	0.597582
8	6	0	2.985327	-1.407349	-0.081933
9	6	0	2.502251	-2.624227	-0.559211
10	6	0	1.167684	-2.967234	-0.349952
11	6	0	0.320833	-2.094718	0.329225
12	6	0	-2.901422	-0.211383	-0.032946
13	6	0	-3.664112	-1.005590	-1.069871
14	8	0	-3.313419	-0.057816	1.113197
15	1	0	-1.384155	0.171008	-1.388354
16	1	0	-1.456907	1.749151	1.023289
17	1	0	0.402973	0.734352	2.192853
18	1	0	-0.926670	-0.425004	2.034001
19	1	0	2.516872	0.408197	0.977176
20	1	0	4.025739	-1.136633	-0.234933

21	1	0	3.163757	-3.303924	-1.087628
22	1	0	0.786293	-3.916442	-0.714021
23	1	0	-0.718607	-2.366652	0.498053
24	1	0	-4.732077	-0.834771	-0.928534
25	1	0	-3.381219	-0.746886	-2.092011
26	1	0	-3.465782	-2.070226	-0.911865
27	8	0	0.940545	2.542122	0.391177
28	6	0	1.993155	3.229808	-0.298504
29	1	0	2.533490	3.782259	0.466906
30	1	0	2.649043	2.508068	-0.789849
31	1	0	1.573873	3.909563	-1.041973

SCF Done: E(RM062X) = -746.462734356 A.U. after 1 cycles

- Thermochemistry -

Zero-point correction=	0.258971 (Hartree/Particle)
Thermal correction to Energy=	0.274938
Thermal correction to Enthalpy=	0.275882
Thermal correction to Gibbs Free Energy=	0.213527
Sum of electronic and zero-point Energies=	-746.203763
Sum of electronic and thermal Energies=	-746.187797
Sum of electronic and thermal Enthalpies=	-746.186853
Sum of electronic and thermal Free Energies=	-746.249207

CBS-QB3 calculation at M062X/6-31G(d) scrf(solvent=acetonitrile) geometry:

Temperature=	298.150000	Pressure=	1.000000
E(ZPE)=	0.256381	E(Thermal)=	0.272464
E(SCF)=	-742.487723	DE(MP2)=	-2.814234
DE(CBS)=	-0.271233	DE(MP34)=	-0.090479
DE(CCSD)=	-0.093321	DE(Int)=	0.089568
DE(Empirical)=	-0.131142		
CBS-QB3 (0 K)=	-745.542181	CBS-QB3 Energy=	-745.526098
CBS-QB3 Enthalpy=	-745.525154	CBS-QB3 Free Energy=	-745.587757

Structure 7a:

M062X/6-31G(d) SCRF(solvent=acetonitrile) optimization and frequency calculation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	2.122305	-0.801296	-0.934606
2	6	0	0.766629	-0.331744	-0.958030
3	6	0	0.601683	0.989181	-0.198971
4	8	0	-0.410426	1.254493	0.419935
5	6	0	-0.214771	-1.366774	-0.354218
6	6	0	-1.580597	-0.819590	-0.138920
7	6	0	-2.340084	-0.300648	-1.240532
8	6	0	-3.623780	0.126913	-1.048121
9	6	0	-4.203948	0.048343	0.244011
10	6	0	-3.480859	-0.473589	1.341231
11	6	0	-2.193781	-0.899062	1.156973
12	6	0	2.790809	-0.884846	0.251472
13	6	0	4.190178	-1.441705	0.192128
14	8	0	2.247636	-0.539316	1.294696
15	1	0	2.570523	-1.066695	-1.800133
16	1	0	0.507462	-0.120527	-2.000466
17	1	0	-0.277473	-2.205205	-1.059803
18	1	0	0.201825	-1.729919	0.586447
19	1	0	-1.886222	-0.261498	-2.225690
20	1	0	-4.207030	0.519243	-1.872896
21	1	0	-5.221625	0.393295	0.390327
22	1	0	-3.949118	-0.528017	2.316869
23	1	0	-1.609139	-1.294773	1.980787
24	1	0	4.150568	-2.514944	0.401113
25	1	0	4.657005	-1.293632	-0.783100
26	1	0	4.789912	-0.963393	0.966891
27	8	0	1.613035	1.813543	-0.365198

28	6	0	1.509529	3.073241	0.320393
29	1	0	2.410534	3.621837	0.057792
30	1	0	0.617998	3.606375	-0.012231
31	1	0	1.460645	2.898845	1.396374

SCF Done: E(UM062X) = -746.215221166 A.U. after 1 cycles

- Thermochemistry -

Zero-point correction= 0.257950 (Hartree/Particle)
Thermal correction to Energy= 0.274073
Thermal correction to Enthalpy= 0.275017
Thermal correction to Gibbs Free Energy= 0.212714
Sum of electronic and zero-point Energies= -745.957271
Sum of electronic and thermal Energies= -745.941148
Sum of electronic and thermal Enthalpies= -745.940204
Sum of electronic and thermal Free Energies= -746.002507

CBS-QB3 calculation at M062X/6-31G(d) scrf(solvent=acetonitrile) geometry:

Temperature=	298.150000	Pressure=	1.000000
E(ZPE)=	0.255371	E(Thermal)=	0.271613
E(SCF)=	-742.283264	DE(MP2)=	-2.738573
DE(CBS)=	-0.264074	DE(MP34)=	-0.112185
DE(CCSD)=	-0.097415	DE(Int)=	0.086373
DE(Empirical)=	-0.131282		
CBS-QB3 (0 K)=	-745.285049	CBS-QB3 Energy=	-745.268806
CBS-QB3 Enthalpy=	-745.267862	CBS-QB3 Free Energy=	-745.330419

Structure 7b:

M062X/6-31G(d) SCRF(solvent=acetonitrile) optimization and frequency calculation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	0.941027	1.459101	0.393859
2	6	0	1.127477	0.016533	0.490334
3	6	0	2.586419	-0.269257	0.154773
4	8	0	3.424731	0.595968	0.074198
5	6	0	0.139157	-0.672418	-0.442493
6	6	0	-1.282508	-0.147583	-0.204710
7	6	0	-2.203457	-0.581539	-1.295263
8	6	0	-3.384511	-1.203764	-1.038807
9	6	0	-3.810268	-1.453606	0.289424
10	6	0	-2.995994	-1.043414	1.373804
11	6	0	-1.803788	-0.421746	1.168236
12	6	0	-0.151808	2.031407	-0.032988
13	6	0	-0.247071	3.508418	-0.187175
14	8	0	-1.215723	1.366755	-0.348044
15	1	0	1.763041	2.033790	0.571135
16	1	0	0.969742	-0.298818	1.528436
17	1	0	0.420887	-0.488834	-1.484924
18	1	0	0.155044	-1.748935	-0.265362
19	1	0	-1.872471	-0.388620	-2.311311
20	1	0	-4.012424	-1.515196	-1.867242
21	1	0	-4.756736	-1.946366	0.474901
22	1	0	-3.329358	-1.230000	2.389602
23	1	0	-1.198213	-0.104599	2.012561
24	1	0	-0.458559	3.734172	-1.235149
25	1	0	-1.085562	3.865270	0.414927
26	1	0	0.671758	4.003941	0.122915
27	8	0	2.790545	-1.564617	0.002796
28	6	0	4.149784	-1.953457	-0.266336
29	1	0	4.791120	-1.643133	0.559506
30	1	0	4.129040	-3.036499	-0.356584
31	1	0	4.488473	-1.492170	-1.194812

SCF Done: E(UM062X) = -746.221498069 A.U. after 1 cycles

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- Thermochemistry -
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Zero-point correction=                           0.259358 (Hartree/Particle)
Thermal correction to Energy=                    0.274545
Thermal correction to Enthalpy=                  0.275489
Thermal correction to Gibbs Free Energy=         0.215310
Sum of electronic and zero-point Energies=           -745.962140
Sum of electronic and thermal Energies=              -745.946953
Sum of electronic and thermal Enthalpies=            -745.946009
Sum of electronic and thermal Free Energies=         -746.006188

CBS-QB3 calculation at M062X/6-31G(d) scrf(solvent=acetonitrile) geometry:
Temperature=               298.150000 Pressure=                       1.000000
E(ZPE)=                      0.256764 E(Thermal)=                     0.272072
E(SCF)=                   -742.295419 DE(MP2)=                       -2.726457
DE(CBS)=                    -0.263009 DE(MP34)=                      -0.118031
DE(CCSD)=                   -0.099560 DE(Int)=                        0.085196
DE(Empirical)=              -0.133032
CBS-QB3 (0 K)=            -745.293548 CBS-QB3 Energy=              -745.278240
CBS-QB3 Enthalpy=         -745.277296 CBS-QB3 Free Energy=         -745.337720
```

Structure 7c:

M062X/6-31G(d) SCRF(solvent=acetonitrile) optimization and frequency calculation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	-1.798389	0.142260	-0.402806
2	6	0	-0.933128	0.879461	0.467021
3	6	0	0.023238	1.703093	-0.383468
4	8	0	0.002818	1.721169	-1.590471
5	6	0	-0.146380	-0.037029	1.479073
6	6	0	0.879982	-0.842049	0.787070
7	6	0	2.254976	-0.428860	0.813261
8	6	0	3.197499	-1.135178	0.121992
9	6	0	2.802747	-2.280996	-0.624493
10	6	0	1.445032	-2.709237	-0.656790
11	6	0	0.501393	-2.003451	0.033176
12	6	0	-2.977030	-0.366037	0.065369
13	6	0	-3.867726	-0.993665	-0.978909
14	8	0	-3.256936	-0.306715	1.255144
15	1	0	-1.606749	0.189211	-1.397545
16	1	0	-1.521135	1.551630	1.102813
17	1	0	0.305940	0.608364	2.233444
18	1	0	-0.910777	-0.671924	1.938333
19	1	0	2.522932	0.447487	1.394212
20	1	0	4.239869	-0.839709	0.133557
21	1	0	3.550077	-2.838719	-1.177723
22	1	0	1.177963	-3.588913	-1.229962
23	1	0	-0.540099	-2.306355	0.028208
24	1	0	-4.688007	-1.509944	-0.482191
25	1	0	-4.272949	-0.217889	-1.635338
26	1	0	-3.305352	-1.698856	-1.596621
27	8	0	0.891093	2.364066	0.373281
28	6	0	1.860857	3.151395	-0.339419
29	1	0	2.462257	3.635336	0.426260
30	1	0	2.476276	2.501212	-0.963774
31	1	0	1.353914	3.890398	-0.960955

```
SCF Done:  E(UM062X) =  -746.211259854     A.U. after    1 cycles
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- Thermochemistry -
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Zero-point correction=                           0.257793 (Hartree/Particle)
Thermal correction to Energy=                    0.274159
Thermal correction to Enthalpy=                  0.275104
Thermal correction to Gibbs Free Energy=         0.211217
Sum of electronic and zero-point Energies=           -745.953467
```

Sum of electronic and thermal Energies= -745.937100
Sum of electronic and thermal Enthalpies= -745.936156
Sum of electronic and thermal Free Energies= -746.000043

CBS-QB3 calculation at M062X/6-31G(d) scrf(solvent=acetonitrile) geometry:

Temperature=	298.150000	Pressure=	1.000000
E(ZPE)=	0.255215	E(Thermal)=	0.271700
E(SCF)=	-742.281037	DE(MP2)=	-2.746734
DE(CBS)=	-0.264130	DE(MP34)=	-0.106817
DE(CCSD)=	-0.092588	DE(Int)=	0.086774
DE(Empirical)=	-0.130254		
CBS-QB3 (0 K)=	-745.279571	CBS-QB3 Energy=	-745.263086
CBS-QB3 Enthalpy=	-745.262142	CBS-QB3 Free Energy=	-745.326283

8. References

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