Electronic supplementary information for

Trimethylaluminum-Mediated One-Pot Peptide Elongation

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Contents

1. General Information

NMR spectra were recorded on a JEOL 400SS spectrometer operating at 400 MHz and 100 MHz for ^{1}H and ^{13}C acquisitions, respectively. Chemical shifts are reported in ppm with a solvent resonance as an internal standard (^{1}H NMR; tetramethylsilane as internal standard, indicating 0 ppm, ^{13}C NMR; chloroform as internal standard, indicating 77.0 ppm). Data is reported as follows: s = singlet, br = broad, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiplet; coupling constants in Hz; integration. FT-IR spectra were recorded with a Bruker ALPHA (Eco-ATR) spectrometer. Specific rotation was measured with an ATAGO AP-300 digital polarimeter. MS spectra were recorded with a Bruker micrOTOF-12 mass spectrometer with electrospray ionization time-of flight (ESI-TOF) for HRMS measurements. TLC analysis was performed on commercial glass plates bearing a 0.25 mm layer of Merck KGaA TLC silica gel 60 F_{254}. Silica gel chromatography was conducted with silica gel 60N (KANTO CHEMICAL, spherical, neutral, 40-50 or 63-210 μm).

Solvent; Anhydrous CH_2Cl_2 was dried with Glass Contour solvent purification system.

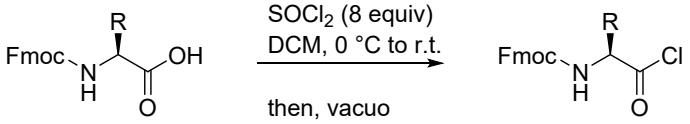
Chemical; Amino acids and their derivatives were purchased from Watanabe Chemical Ind., Ltd. and Tokyo Chemical Industry Co. Ltd (TCI) and Sigma-Aldrich. Trimethylaluminum 2M in Hexane (Sigma-Aldrich), Trifluoromethanesulfonic Acid (TCI), Thionyl Chloride (Fujifilm Wako Pure Chemical Corporation).

Caution
Although trimethylaluminum is a pyrophoric combustible reagent, it is hardly hazardous because of the hexane solution was used.
While, close attention should be paid for using in plants scale.

2. Neutralization of Amino Acid *tert*-Butyl Ester HCl Salts

A flame-dried 300 mL round-bottom flask with a magnetic stirring bar was charged with amino acid *tert*-butyl ester HCl salt (5 g), Amberlyst A21 (10 g), and dichloromethane. The resulting mixture was stirred at room temperature for 4 h, and filtered through a glass filter with dichloromethane. Then the filtrate was concentrated in *vacuo* in a water bath (>70 Torr, without heating), and the residue was transferred into 30 mL vials using a pipette, and further concentrated in *vacuo* at ambient temperature for 4 h. The free amines were stored in a freezer.

3. Preparation of Fmoc-L-Ala-Cl and Fmoc-L-Val-Cl



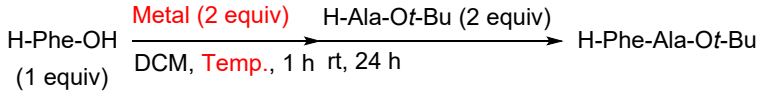
R = Me or *i*-Pr

To a solution of Fmoc-L-Ala-OH (311 mg, 1.00 mmol) or Fmoc-L-Val-OH (339 mg, 1.00 mmol) in DCM (7.00 mL), $SOCl_2$ (0.58 mL, 8.00 mmol) was added slowly under N_2 atmosphere at 0 °C. Then, the mixture was vigorously stirred at room temperature. After 3 h, the solvent and excess $SOCl_2$ were removed under vacuum. DCM (10 mL) was added again and evaporated to completely remove $SOCl_2$. The crude product was washed with DCM to give the Fmoc-L-Ala-Cl or Fmoc-L-Val-OH as a white solid, which was used directly without further purification.

The product was too unstable to be stored for more than 12 h.

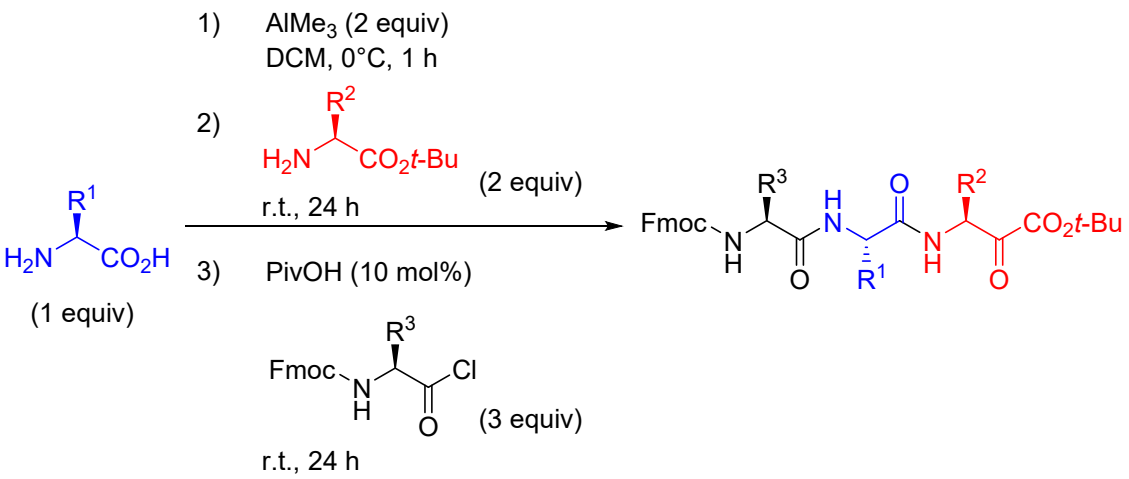
4. Optimization for Dipeptide Synthesis

Table S: Effects of Additives for Dipeptide Synthesis

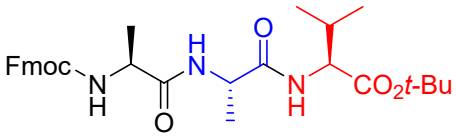


Metal (2 equiv)	Temp. (°C)	Yield (%)
$ZnMe_2$	r.t.	trace
$Ti(O\textit{i}\text{-}Pr)_4$	r.t.	trace H-Phe-O*i*-Pr was observed
$TiCl_4$	r.t.	trace
$MgCl_2$	r.t.	trace
$ZrCl_4$	r.t.	trace
DIBAL	r.t.	trace
Et_2AlCl	r.t.	trace
$AlMe_3$	r.t.	67%
$AlEt_3$	r.t.	55%
$Al(\textit{i}\text{-}Bu)_3$	r.t.	12%
$AlMe_3$	50 °C	57%
$AlMe_3$	0 °C	77%

5. General Procedure for One-Pot Tripeptide Synthesis



General procedure 1: A mixture of L-amino acid (0.250 mmol), trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), and dry DCM (1 mL) in a flame-dried 20 mL test tube equipped with a magnetic stirring bar was stirred vigorously for 1 h at 0 °C under N_2 atmosphere. Then, L-amino acid *tert*-butyl ester (0.500 mmol) was added to the above reaction solution, and t mixture was allowed to stir vigorously under N_2 atmosphere at room temperature. After 24 h, Fmoc-L-amino acid chloride and pivalic acid (2.55 mg, 0.025 mmol) were added to the reaction solution, and stirring was continued under N_2 atmosphere at room temperature for another 24 h. The reaction mixture was then diluted with $CHCl_3$ (4.50 mL) and transferred to a SiO_2 column using a pipette; the used test tube and pipette were washed with $CHCl_3$ (2 x 4.00 mL). The reaction mixture was purified by flash column chromatography (50–100% EtOAc in hexane) to provide the corresponding tripeptide as a white solid.

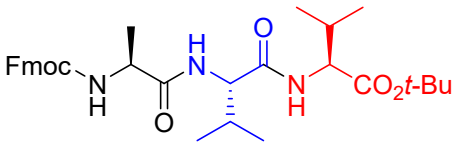


Fmoc-L-Ala-L-Ala-L-Val-O*t*-Bu (5a) was prepared following **General Procedure 1** using H-L-Ala-OH (22.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (56% AcOEt in hexane) to provide the title

compound as a white solid in 93% yield with >20:1 dr (125 mg).

Gram-scale synthesis;
A mixture of H-L-Ala-OH (265 mg, 3.00 mmol), trimethylaluminum 2M in hexane (3.00 mL, 6.00 mmol), and dry DCM (10 mL) in a flame-dried 50 mL flask equipped with a magnetic stirring bar was stirred vigorously for 1 h at 0 °C under N_2 atmosphere. Then, L-Val-O*t*-Bu (1.04 g, 6.00 mmol) was added to the above reaction solution. The mixture was allowed to stir vigorously under N_2 atmosphere at room temperature. After 24 h, Fmoc-L-Ala-Cl (2.96 g, 9.00 mmol) and pivalic acid (30.6 mg, 0.300 mmol) were added to the reaction solution, and stirring was continued under N_2 atmosphere at room temperature for 24 h. The reaction mixture was then diluted with $CHCl_3$ (7.50 mL), transferred onto SiO_2 column using a pipette, and the used test tube and pipette were washed with $CHCl_3$ (2 x 4.00 mL). The reaction mixture was purified by flash column chromatography (56% AcOEt in hexane) to provide the title compound as a white solid in 81% yield with >20:1 dr (1.31 g).

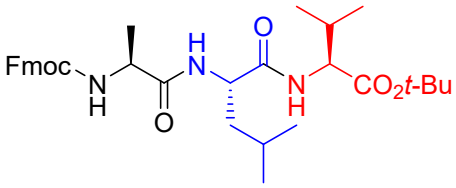
R_f = 0.35 (50% AcOEt in hexane). M.p. 175–180 °C. $[\alpha]_D^{22}$ = –32.4 (*c* 1.05, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.58 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.38 (t, *J* = 7.6 Hz, 1H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.31–7.26 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 6.93 (br d, *J* = 6.9 Hz, 1H, N*H*), 6.85 (br d, *J* = 8.2 Hz, 1H, N*H*), 5.74 (br d, *J* = 7.3 Hz, 1H, N*H*), 4.63 (quin, *J* = 7.1 Hz, 1H, C*H*CH_3), 4.43–4.36 (m, 4H, C*H*CH_3 and C*H*$CH(CH_3)_2$ and $C_{12}H_8CHC\underline{H_2}OCONHCHCH_3$), 4.20 (t, *J* = 7.1 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.18–2.10 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.45 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.40–1.38 (m, 6H, $CHC\underline{H_3}$ and $CHC\underline{H_3}$), 0.89 (d, *J* = 8.0 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.87 (d, *J* = 8.0 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 171.7, 170.7, 155.9, 143.8(2C), 141.3(2C), 127.7(2C), 127.0(2C), 125.1(2C), 119.9(2C), 82.0, 67.1, 57.5, 50.4, 48.9, 47.1, 31.3, 28.0 (3C), 19.1, 18.8, 18.3, 17.6. IR (thin film, cm^{-1}) 3304, 3066, 2974, 2934, 1732, 1703, 1674, 1637, 1516, 1449, 1393, 1369, 1310, 1253, 1218, 1149, 1108, 1049, 756. HRMS (ESI) calculated for $C_{30}H_{39}N_3O_6Na$ $[M+Na]^+$ *m/z* 560.2691, found 560.2736.



Fmoc-L-Ala-L-Val-L-Val-O*t*-Bu (5b) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After

24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (35% AcOEt in hexane) to provide the title compound as a white solid in 88% yield with >20:1 dr (124 mg).

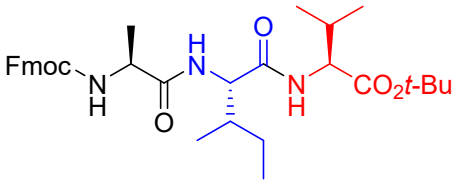
R_f = 0.49 (40% AcOEt in hexane). M.p. 165–170 °C. $[\alpha]_D^{22}$ = –35.4 (*c* 1.01, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.4 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.58 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.36 (t, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.28–7.24 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.19 (br d, *J* = 8.7 Hz, 1H, N*H*), 7.10 (br d, *J* = 8.7 Hz, 1H, N*H*), 6.19 (br d, *J* = 8.0 Hz, 1H, N*H*), 4.55–4.47 (m, 3H, C*H*CH_3 and C*H*$CH(CH_3)_2$ and C*H*$CH(CH_3)_2$), 4.39–4.29 (m, 2H, $C_{12}H_8CHC\underline{H_2}OCONH$), 4.19 (t, *J* = 7.4 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.19–2.00 (m, 2H, $CHC\underline{H}(CH_3)_2$ and $CHC\underline{H}(CH_3)_2$), 1.43 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.36 (d, *J* = 6.9 Hz, 3H, $CHC\underline{H_3}$), 0.96 (d, *J* = 6.6 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.93 (d, *J* = 6.6 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.87 (d, *J* = 6.6 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.85 (d, *J* = 6.6 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 171.2, 170.8, 156.0, 143.8(2C), 141.2(2C), 127.6(2C), 127.0(2C), 125.2, 125.1, 119.8(2C), 81.8, 67.1, 58.7, 57.4, 50.3, 47.0, 31.3, 31.1, 27.9(3C), 19.1, 18.9, 18.8, 18.4, 17.6. IR (thin film, cm^{-1}) 3301, 3054, 2971, 2931, 1731, 1703, 1674, 1635, 1515, 1444, 1390, 1361, 1301, 1241, 1218, 1149, 1108, 1049, 753. HRMS (ESI) calculated for $C_{32}H_{43}N_3O_6Na$ $[M+Na]^+$ *m/z* 588.3049, found 588.3059.



Fmoc-L-Ala-L-Leu-L-Val-O*t*-Bu (5c) was prepared following **General Procedure 1** using H-L-Leu-OH (32.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (40% AcOEt in hexane) to provide the title compound as a white solid in 91% yield with >20:1 dr (132 mg).

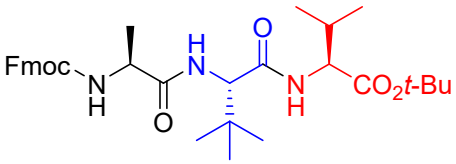
R_f = 0.66 (50% AcOEt in hexane). M.p. 85–90 °C. $[\alpha]_D^{20}$ = +56.8 (*c* 1.20, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.59 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.39–7.25 (m, 5H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N*H*), 7.09 (br d, *J* = 8.0 Hz, 1H, N*H*), 6.18 (br d, *J* = 8.2 Hz, 1H, N*H*), 4.70 (quin, *J* = 6.9 Hz, 1H, C*H*CH_3), 4.51–4.37 (m, 3H, C*H*$CH(CH_3)_2$ and $C_{12}H_8CHC\underline{H_2}OCONHCHCH_3$), 4.30 (t, *J* = 7.3 Hz, 1H, C*H*$CH_2CH(CH_3)_2$), 4.19 (t, *J* = 7.1 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.17–2.08 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.72–1.48 (m, 3H,

CHC$\underline{H_2}$CH$(CH_3)_2$ and CHCH$_2$C$\underline{H}(CH_3)_2$), 1.43 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.35 (d, J = 6.9 Hz, 3H, CHC$\underline{H_3}$), 0.89–0.84 (m, 12H, CHCH$(C\underline{H_3})_2$ and CHCH$_2$CH$(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 172.1, 170.9, 156.0, 143.9, 143.8, 141.2, 141.1, 127.5(2C), 127.0(2C), 125.3, 125.2, 119.8(2C), 81.7, 67.1, 57.3, 51.8, 50.1, 47.0, 41.2, 31.5, 27.9(3C), 24.6, 22.5, 22.3, 19.1, 18.8, 17.5. IR (thin film, cm^{-1}) 3286, 3065, 2962, 2933, 2873, 1705, 1645, 1530, 1449, 1392, 1368, 1312, 1226, 1150, 1109, 1078, 1042, 755. HRMS (ESI) calculated for $C_{33}H_{45}N_3O_6Na$ $[M+Na]^+$ *m/z* 602.3162, found 602.3206.



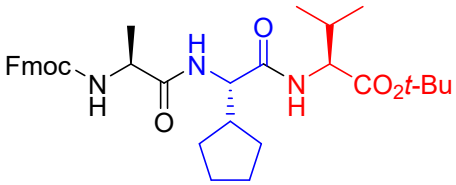
Fmoc-L-Ala-L-Ile-L-Val-O*t*-Bu (5d) was prepared following **General Procedure 1** using H-L-Ile-OH (32.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (33% AcOEt in hexane) to provide the title compound as a white solid in 86% yield with >20:1 dr (125 mg).

R_f = 0.29 (33% AcOEt in hexane). M.p. 95–100 °C. $[\alpha]_D^{20}$ = –50.0 (*c* 1.10, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 7.6 Hz, 2H, $C_{12}\underline{H_8}$CHCH$_2$OCONH), 7.59 (d, J = 7.6 Hz, 2H, $C_{12}\underline{H_8}$CHCH$_2$OCONH), 7.49 (br d, J = 8.9 Hz, 1H, N$\underline{H}$), 7.44 (br d, J = 8.7 Hz, 1H, N$\underline{H}$), 7.34 (t, J = 7.6 Hz, 2H, $C_{12}\underline{H_8}$CHCH$_2$OCONH), 7.26–7.21 (m, 2H, $C_{12}\underline{H_8}$CHCH$_2$OCONH), 6.50 (br d, J = 8.3 Hz, 1H, N$\underline{H}$), 4.66–4.57 (m, 2H, C$\underline{H}$CH(CH_3)CH$_2$CH$_3$ and C$\underline{H}$CH$_3$), 4.52 (dd, J = 5.0 Hz and 8.9 Hz, 1H, C$\underline{H}$CH$(CH_3)_2$), 4.38–4.27 (m, 2H, C_{12}H$_8$CHC$\underline{H_2}$OCONHCHCH$_3$), 4.18 (t, J = 7.4 Hz, 1H, C_{12}H$_8$C$\underline{H}$CH$_2$OCONH), 2.15–2.04 (m, 1H, CHC$\underline{H}(CH_3)_2$), 1.86–1.77 (m, 1H, CHC$\underline{H}(CH_3)$CH$_2$CH$_3$), 1.61–1.52 (m, 1H, CHCH(CH_3)C$\underline{H_2}$CH$_3$), 1.40 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.35 (d, J = 7.1 Hz, 3H, CHC$\underline{H_3}$), 1.17–1.06 (m, 1H, CHCH(CH_3)C$\underline{H_2}$CH$_3$), 0.94 (d, J = 6.6 Hz, 3H, CHCH$(C\underline{H_3})$CH$_2$CH$_3$), 0.88–0.81 (m, 9H, CHCH$(C\underline{H_3})_2$ and CHCH(CH_3)CH$_2$C$\underline{H_3}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 171.5, 170.8, 156.1, 143.9, 143.8, 141.1 (2C), 127.5(2C), 126.9(2C), 125.2, 125.1, 119.8(2C), 81.6, 67.1, 57.8, 57.4, 50.2, 47.0, 37.3, 31.3, 27.9(3C), 25.1, 19.2, 18.8, 17.6, 15.2, 11.2. IR (thin film, cm^{-1}) 3285, 3064, 2965, 2876, 1727, 1703, 1642, 1526, 1449, 1392, 1368, 1252, 1220, 1150, 1109, 1043, 756. HRMS (ESI) calculated for $C_{33}H_{45}N_3O_6Na$ $[M+Na]^+$ *m/z* 602.3158, found 602.3206.



Fmoc-L-Ala-L-Tle-L-Val-O*t*-Bu (5e) was prepared following **General Procedure 1** using H-L-Tle-OH (32.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (33% AcOEt in hexane) to provide the title compound as a white solid in 84% yield with >20:1 dr (122 mg).

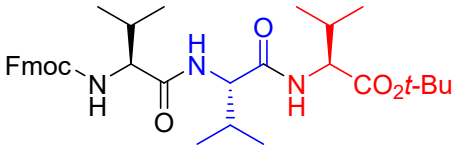
R_f = 0.31 (33% AcOEt in hexane). M.p. 205–210 °C. $[\alpha]_D^{18}$ = –30.9 (*c* 1.10, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.61 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.57 (br d, *J* = 8.9 Hz, 1H, N*H*), 7.37–7.33 (m, 3H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N*H*), 7.24 (br t, *J* = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 6.72 (br d, *J* = 8.7 Hz, 1H, N*H*), 4.78 (d, *J* = 8.7 Hz, 1H, C*H*$(CH_3)_3$), 4.67 (quin, *J* = 7.8 Hz, 1H, C*H*CH_3), 4.50 (dd, *J* = 5.0 Hz and 8.7 Hz, C*H*$CH(CH_3)_2$), 4.38–4.28 (m, 2H, $C_{12}H_8CHC\underline{H_2}OCONHCHCH_3$), 4.20 (t, *J* = 7.6 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.10–2.02 (m, 1H, CHC*H*$(CH_3)_2$), 1.38 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.35 (d, *J* = 7.8 Hz, 3H, $CHC\underline{H_3}$), 1.03 (s, 9H, $CH(C\underline{H_3})_3$), 0.84 (d, *J* = 6.8 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.79 (d, *J* = 6.8 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 170.9, 170.6, 156.2, 143.9, 143.8, 141.1(2C), 127.5(2C), 126.9(2C), 125.2(2C), 119.7(2C), 81.5, 67.0, 60.3, 57.4, 50.2, 47.0, 34.3, 31.4, 27.9(3C), 26.6(3C), 19.1, 18.8, 17.7. IR (thin film, cm^{-1}) 3300, 2966, 1703, 1643, 1523, 1449, 1368, 1252, 1217, 1144, 1078, 753. HRMS (ESI) calculated for $C_{33}H_{45}N_3O_6Na$ $[M+Na]^+$ *m/z* 602.3174, found 602.3206.



Fmoc-L-Ala-L-Gly(*c*-Pent)-L-Val-O*t*-Bu (5f) was prepared following **General Procedure 1** using H-L-Gly(*c*-Pent)-OH (35.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature

for 24 h. The reaction mixture was purified by flash column chromatography (45% AcOEt in hexane) to provide the title compound as a white solid in 86% yield with >20:1 dr (127 mg).

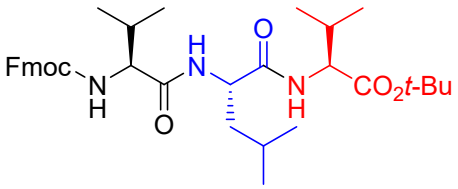
R_f = 0.45 (50% AcOEt in hexane). M.p. 200–205 °C. $[\alpha]_D^{18}$ = –35.9 (*c* 1.01, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.4 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.59 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.44 (br d, *J* = 8.7 Hz, 1H, N*H*), 7.36 (t, *J* = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.28–7.23 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.18 (br d, *J* = 8.2 Hz, 1H, N*H*), 6.32 (br d, *J* = 8.2 Hz, 1H, N*H*), 4.62–4.58 (m, 1H, C*H*$CH(CH_2CH_2)_2$), 4.53–4.48 (m, 2H, C*H*CH_3 and C*H*$CH(CH_3)_2$), 4.39–4.27 (m, 2H, $C_{12}H_8CHC\underline{H_2}OCONH$), 4.18 (t, *J* = 7.3 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.30–2.09 (m, 2H, CHC*H*$(CH_2CH_2)_2$ and CHC*H*$(CH_3)_2$), 1.72–1.66 (m, 2H, CHCH($C\underline{H_2}CH_2)_2$), 1.61–1.20 (m, 6H, CHCH($C\underline{H_2}CH_2)_2$ and CHCH($CH_2C\underline{H_2})_2$), 1.43 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.35 (d, *J* = 6.8 Hz, 3H, CHC$\underline{H_3}$), 0.87 (d, *J* = 6.9 Hz, 3H, CHCH($C\underline{H_3})_2$), 0.84 (d, *J* = 6.9 Hz, 3H, CHCH($C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 171.6, 170.9, 156.1, 143.9, 143.8, 141.2(2C), 127.6(2C), 127.0(2C), 125.3, 125.2, 119.8(2C), 81.7, 67.1, 57.3(2C), 50.2, 47.0, 42.3, 31.4, 29.3, 29.1, 27.9(3C), 25.3, 25.0, 19.0, 18.8, 17.5. IR (thin film, cm^{-1}) 3229, 2961, 1705, 1644, 1524, 1444, 1361, 1221, 1217, 1141, 1075, 756. HRMS (ESI) calculated for $C_{34}H_{45}N_3O_6Na$ $[M+Na]^+$ *m/z* 614.3206, found 614.3208.



Fmoc-L-Val-L-Val-L-Val-O*t*-Bu (5g) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Val-Cl (268 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (35% AcOEt in hexane) to provide the title compound as a white solid in 83% yield with >20:1 dr (123 mg).

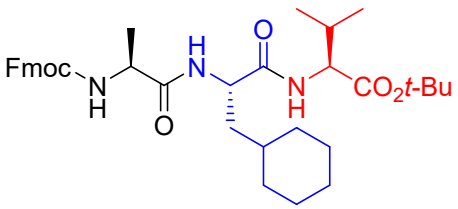
R_f = 0.39 (33% AcOEt in hexane). M.p. 195–200 °C. $[\alpha]_D^{22}$ = –39.4 (*c* 1.01, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.61–7.51 (m, 3H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N*H*), 7.36–7.19 (m, 5H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N*H*), 6.45 (br d, *J* = 9.4 Hz, 1H, N*H*), 4.60 (t, *J* = 8.7 Hz, 1H, C*H*$CH(CH_3)_2$), 4.52 (dd, *J* = 5.0 Hz and 9.0 Hz, 1H, C*H*$CH(CH_3)_2$), 4.40 (dd, *J* = 7.3 Hz and 9.4 Hz, 1H, C*H*$CH(CH_3)_2$), 4.25–4.14 (m, 3H, $C_{12}H_8CHC\underline{H_2}OCONH$ and $C_{12}H_8C\underline{H}CH_2OCONH$), 2.15–1.99 (m, 3H, CHC*H*$(CH_3)_2$ and CHC*H*$(CH_3)_2$ and CHC*H*$(CH_3)_2$), 1.43 (s, 9H, $CO_2C(C\underline{H_3})_3$), 0.96–0.83 (m, 18H, CHCH($C\underline{H_3})_2$ and

CHCH(C$\underline{H_3}$)$_2$ and CHCH(C$\underline{H_3}$)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 171.4, 171.0, 156.6, 144.0 143.9, 141.2, 141.1, 127.5(2C), 127.0(2C), 125.3, 125.2, 119.8(2C), 81.6, 67.0, 60.4, 58.6, 57.3, 47.1, 31.5, 31.3, 30.9, 28.0(3C), 19.1(2C), 18.9, 18.8, 18.4, 17.6. IR (thin film, cm^{-1}) 3294, 3061, 2975, 2931, 1735, 1701, 1676, 1634, 1515, 1448, 1393, 1361, 1315, 1255, 1215, 1149, 1105, 1045, 756. HRMS (ESI) calculated for $C_{34}H_{47}N_3O_6Na$ [M+Na]$^+$ *m/z* 616.3363, found 616.3398.



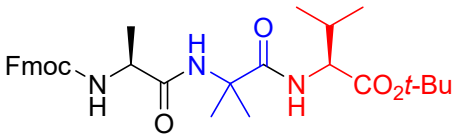
Fmoc-L-Val-L-Leu-L-Val-O*t*-Bu (5h) was prepared following **General Procedure 1** using H-L-Leu-OH (32.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Val-Cl (268 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (30% AcOEt in hexane) to provide the title compound as a white solid in 84% yield with >20:1 dr (128 mg).

R_f = 0.39 (33% AcOEt in hexane). M.p. 205–210 °C. $[\alpha]_D^{22}$ = –35.4 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77–7.62 (m, 5H, $C_{12}\underline{H_8}$CHCH$_2$OCONH and N$\underline{H}$), 7.38–7.23 (m, 5H, $C_{12}\underline{H_8}$CHCH$_2$OCONH and N$\underline{H}$), 6.60 (br d, *J* = 9.4 Hz, 1H, N$\underline{H}$), 4.79 (dd., *J* = 7.4 Hz and 15 Hz, C$\underline{H}$CH$_2$CH(CH$_3$)$_2$), 4.56 (dd, *J* = 4.8 Hz and 9.2 Hz, 1H, C$\underline{H}$CH(CH$_3$)$_2$), 4.50 (dd, *J* = 5.0 Hz and 8.2 Hz, 1H, C$\underline{H}$CH(CH$_3$)$_2$), 4.22–4.11 (m, 3H, $C_{12}H_8$CHC$\underline{H_2}$OCONH and $C_{12}H_8$C$\underline{H}$CH$_2$OCONH), 2.15–1.99 (m, 2H, CHC$\underline{H}$(CH$_3$)$_2$ and CHC$\underline{H}$(CH$_3$)$_2$), 1.73–1.58 (m, 2H, CHC$\underline{H_2}$CH(CH$_3$)$_2$),1.49–1.40 (m, 1H, CHCH$_2$C$\underline{H}$(CH$_3$)$_2$), 1.40 (s, 9H, CO$_2$C(C$\underline{H_3}$)$_3$), 0.98–0.79 (m, 18H, CHCH(C$\underline{H_3}$)$_2$ and CHCH(C$\underline{H_3}$)$_2$ and CHCH$_2$CH(C$\underline{H_3}$)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 171.8, 171.2, 156.6, 144.1 143.8, 141.1(2C), 127.5(2C), 127.0(2C), 125.5, 125.3, 119.7(2C), 81.5, 67.1, 60.2, 57.2, 51.8, 47.1, 41.4, 31.6, 31.4, 27.9(3C), 24.5, 22.7, 22.3, 19.1, 19.0, 18.6, 17.5. IR (thin film, cm^{-1}) 3309, 3055, 2971, 1731, 1701, 1673, 1633, 1515, 1445, 1391, 1361, 1310, 1253, 1215, 1144, 1108, 1049, 756. HRMS (ESI) calculated for $C_{35}H_{49}N_3O_6Na$ [M+Na]$^+$ *m/z* 630.3519, found 630.3493.



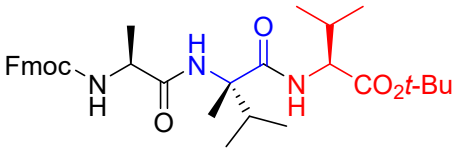
Fmoc-L-Ala-L-Cha-L-Val-O*t*-Bu (5i) was prepared following **General Procedure 1** using H-L-Cha-OH (42.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (40% AcOEt in hexane) to provide the title compound as a white solid in 84% yield with >20:1 dr (130 mg).

R_f = 0.63 (50% AcOEt in hexane). M.p. 205–210 °C. $[\alpha]_D^{18}$ = –35.9 (*c* 1.05, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 6.9 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.61–7.58 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.37 (t, *J* = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.29–7.26 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.18 (br d, *J* = 8.9 Hz, 1H, N*H*), 7.00 (br d, *J* = 7.8 Hz, 1H, N*H*), 6.07 (d, *J* = 8.0 Hz, 1H, N*H*), 4.69 (quin., *J* = 7.3 Hz, 1H, C*H*CH_3), 4.50–4.39 (m, 3H, $C_{12}H_8CHC\underline{H_2}OCONH$ and C*H*$CH(CH_3)_2$), 4.32–4.27 (m, 1H, C*H*$CH_2CH(CH_2CH_2CH_2CH_2CH_2)$), 4.20 (t, *J* = 7.3 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.15–2.10 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.71–1.00 (m, 11H, $CHC\underline{H_2}CH(CH_2CH_2CH_2CH_2CH_2)$ and $CHCH_2C\underline{H}(CH_2CH_2CH_2CH_2CH_2)$ and $CHCH_2CH(C\underline{H_2}CH_2CH_2CH_2CH_2)$ and $CHCH_2CH(CH_2C\underline{H_2}CH_2CH_2CH_2)$ and $CHCH_2CH(CH_2CH_2C\underline{H_2}CH_2CH_2)$ and $CHCH_2CH(CH_2CH_2CH_2C\underline{H_2}CH_2)$), 1.44 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.36 (d, *J* = 7.3 Hz, 3H, $CHC\underline{H_3}$), 0.89–0.79 (m, 8H, $CHCH(C\underline{H_3})_2$ and $CHCH_2CH(CH_2CH_2CH_2CH_2C\underline{H_2})$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 172.0, 170.8, 156.0, 143.8(2C), 141.1(2C), 127.6(2C), 127.0(2C), 125.2, 125.1, 119.8(2C), 81.7, 67.2, 57.3, 51.2, 50.2, 47.0, 39.8, 33.9, 33.2, 32.8, 31.5, 27.9(3C), 26.3, 26.0(2C), 19.1, 18.8, 17.5. IR (thin film, cm^{-1}) 3301, 2965, 1705, 1644, 1521, 1449, 1367, 1251, 1215, 1141, 1075, 753. HRMS (ESI) calculated for $C_{36}H_{49}N_3O_6Na$ $[M+Na]^+$ *m/z* 642.3519, found 642.3492.



Fmoc-L-Ala-Aib-L-Val-O*t*-Bu (5j) was prepared following **General Procedure 1** using H-Aib-OH (25.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (50% AcOEt in hexane) to provide the title compound as a white solid in 90% yield with >20:1 dr (124 mg).

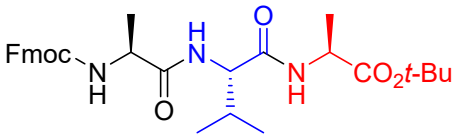
R_f = 0.35 (50% AcOEt in hexane). M.p. 95–100 °C. $[\alpha]_D^{23}$ = –105.0 (*c* 1.00, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.59–7.56 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.39 (t, *J* = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.31–7.27 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 6.82–6.79 (m, 2H, N*H* and N*H*), 5.51 (d, *J* = 7.1 Hz, 1H, N*H*), 4.41–4.37 (m, 3H, C*H*CH_3 and $C_{12}H_8CHC\underline{H_2}OCONH$), 4.22–4.18 (m, 2H, C*H*$CH(CH_3)_2$ and $C_{12}H_8C\underline{H}CH_2OCONH$), 2.22–2.12 (m, 1H, CHC*H*$(CH_3)_2$), 1.59 (s, 3H, $C(C\underline{H_3})_2$), 1.56 (s, 3H, $C(C\underline{H_3})_2$), 1.44 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.38 (d, *J* = 6.9 Hz, 3H, $CHC\underline{H_3}$), 0.91 (d, *J* = 6.8 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.87 (d, *J* = 6.8 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 171.8, 170.9, 156.0, 143.7, 143.6, 141.2(2C), 127.7(2C), 127.0(2C), 125.0(2C), 119.9(2C), 81.8, 67.1, 57.6, 57.3, 50.9, 47.0, 31.3, 27.9(3C), 25.5, 24.7, 18.8, 18.5, 17.5. IR (thin film, cm^{-1}) 3313, 2973, 2937, 1716, 1668, 1511, 1450, 1390, 1368, 1315, 1245, 1157, 1117, 1077, 1033, 982, 755. HRMS (ESI) calculated for $C_{31}H_{41}N_3O_6Na$ $[M+Na]^+$ *m/z* 574.2893, found 574.2880.



Fmoc-L-Ala-L-(Me)Val-L-Val-O*t*-Bu (5k) was prepared following **General Procedure 1** using H-L-(Me)Val-OH (32.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (40% AcOEt in hexane) to provide the title compound as a white solid in 81% yield with >20:1 dr (117 mg).

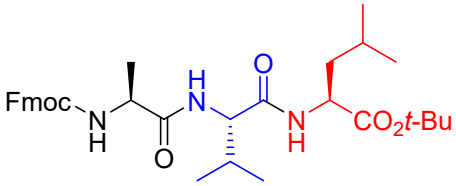
R_f = 0.59 (50% AcOEt in hexane). M.p. 205–210 °C. $[\alpha]_D^{22}$ = –36.4 (*c* 1.01, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.56 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.39 (t, *J* = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.31–7.27 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.09 (br d, *J* = 8.5 Hz, 1H, N*H*), 6.71 (br s, 1H, N*H*), 5.55 (d, *J* = 7.4 Hz, 1H, N*H*), 4.41–4.18 (m, 5H, C*H*CH_3 and C*H*$CH(CH_3)_2$ and $C_{12}H_8CHC\underline{H_2}OCONH$ and $C_{12}H_8C\underline{H}CH_2OCONH$), 2.55–2.46 (m, 1H, $C(CH_3)C\underline{H}(CH_3)_2$), 2.24–2.12 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.47 (s, 3H, $C(C\underline{H_3})CH(CH_3)_2$), 1.44 (s, 9H, $CO_2C(C\underline{H_3})_3$), 0.96–0.89 (m, 12H, $C(CH_3)CH(C\underline{H_3})_2$ and $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 172.1, 170.8, 156.0, 143.7, 143.6, 141.2(2C), 127.7(2C), 127.0(2C), 125.0(2C), 119.9(2C), 81.7, 67.1, 64.2, 57.8, 50.9, 47.0, 33.5, 31.2, 27.9(3C), 18.9, 18.3, 18.0, 17.6, 17.1, 17.0. IR (thin film, cm^{-1}) 3301, 3065, 2971, 2944, 1721, 1703, 1676, 1635, 1515, 1441, 1393, 1360, 1311, 1251, 1218, 1149, 1107, 1049, 753. HRMS (ESI)

calculated for $C_{33}H_{45}N_3O_6Na$ $[M+Na]^+$ *m/z* 602.3174, found 602.3186.



Fmoc-L-Ala-L-Val-L-Ala-O*t*-Bu (5l) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Ala-O*t*-Bu (72.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (45% AcOEt in hexane) to provide the title compound as a white solid in 92% yield with >20:1 dr (124 mg).

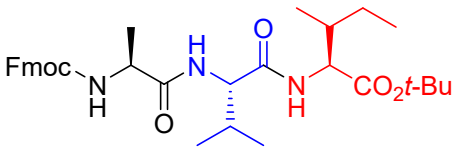
R_f = 0.46 (50% AcOEt in hexane). M.p. 170–175 °C. $[\alpha]_D^{22}$ = –31.4 (*c* 1.03, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.57 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.38 (t, *J* = 7.3 Hz, 1H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.30–7.26 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 6.84 (br d, *J* = 8.3 Hz, 1H, N*H*), 6.70 (br d, *J* = 6.6 Hz, 1H, N*H*), 5.70 (d, *J* = 7.3 Hz, 1H, N*H*), 4.48–4.35 (m, 5H, C*H*CH_3 and C*H*CH_3 and C*H*$CH(CH_3)_2$ and $C_{12}H_8CHC\underline{H_2}OCONHCHCH_3$), 4.20 (t, *J* = 7.1 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.17–2.04 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.44 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.39 (d, *J* = 6.8 Hz, 3H, $CHC\underline{H_3}$),1.33 (d, *J* = 7.1 Hz, 3H, $CHC\underline{H_3}$), 0.95 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.92 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 171.8, 170.2, 156.0, 143.8, 143.7, 141.2(2C), 127.7(2C), 127.0(2C), 125.1(2C), 120.0(2C), 82.0, 67.1, 58.3, 50.5, 48.7, 47.1, 31.3, 27.9(3C), 19.1, 18.7, 18.4, 18.0. IR (thin film, cm^{-1}) 3301, 3065, 2974, 1731, 1705, 1664, 1633, 1515, 1449, 1399, 1369, 1311, 1251, 1212, 1145, 1107, 1045, 756. HRMS (ESI) calculated for $C_{30}H_{39}N_3O_6Na$ $[M+Na]^+$ *m/z* 560.2691, found 560.2639.



Fmoc-L-Ala-L-Val-L-Leu-O*t*-Bu (5m) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Leu-O*t*-Bu (93.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were

added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (40% AcOEt in hexane) to provide the title compound as a white solid in 84% yield with >20:1 dr (122 mg).

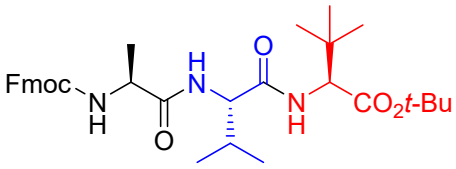
R_f = 0.27 (33% AcOEt in hexane). M.p. 110–115 °C. $[\alpha]_D^{23}$ = –38.9 (*c* 1.05, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.56 (dd, *J* = 2.5 Hz and 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.40 (br d, *J* = 8.9 Hz, 1H, N*H*), 7.36–7.21 (m, 5H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N*H*), 6.37 (d, *J* = 8.2 Hz, 1H, N*H*), 4.60–4.51 (m, 3H, C*H*$CH_2CH(CH_3)_2$ and C*H*$CH(CH_3)_2$ and C*H*CH_3), 4.32–4.30 (m, 2H, $C_{12}H_8CHC\underline{H_2}OCONH$), 4.17 (t, *J* = 7.3 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.14–2.02 (m, 1H, CHC*H*$(CH_3)_2$), 1.62–1.40 (m, 3H, CHC$\underline{H_2}CH(CH_3)_2$ and $CHCH_2C\underline{H}(CH_3)_2$), 1.40 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.37 (d, *J* = 6.8 Hz, 3H, CHC$\underline{H_3}$), 0.95 (d, *J* = 6.6 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.93 (d, *J* = 6.6 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.86–0.83 (m, 6H, $CHCH_2CH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 171.8, 170.9, 156.1, 143.8, 143.7, 141.1 (2C), 127.5 (2C), 126.9 (2C), 125.2 (2C), 119.8 (2C), 81.6, 67.1, 58.4, 51.4, 50.3, 47.0, 41.3, 31.3, 27.8 (3C), 24.8, 22.6, 22.0, 19.0 (2C), 18.4. IR (thin film, cm^{-1}) 3291, 3066, 2961, 2934, 2877, 1725, 1703, 1643, 1528, 1450, 1361, 1301, 1252, 1227, 1151, 1107, 1075, 1041, 753. HRMS (ESI) calculated for $C_{33}H_{45}N_3O_6Na$ $[M+Na]^+$ *m/z* 602.3175, found 602.3184.



Fmoc-L-Ala-L-Val-L-Ile-O*t*-Bu (5n) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Ile-O*t*-Bu (93.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (40% AcOEt in hexane) to provide the title compound as a white solid in 78% yield with >20:1 dr (113 mg).

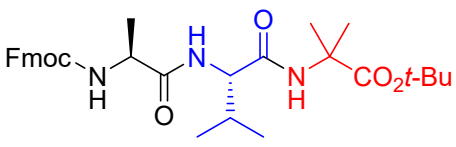
R_f = 0.35 (30% AcOEt in hexane). M.p. 90–95 °C. $[\alpha]_D^{23}$ = –34.9 (*c* 1.09, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.58 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.35 (t, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.27–7.18 (m, 3H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N*H*), 6.25 (d, *J* = 8.0 Hz, 1H, N*H*), 4.57–4.51 (m, 3H, C*H*$CH(CH_3)CH_2CH_3$ and C*H*$CH(CH_3)_2$ and C*H*CH_3), 4.38–4.29 (m, 2H, $C_{12}H_8CHC\underline{H_2}OCONH$), 4.19 (t, *J* = 7.3 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.11–2.01 (m, 1H, CHC*H*$(CH_3)_2$), 1.88–1.78 (m, 1H, CHC*H*$(CH_3)CH_2CH_3$), 1.42 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.36 (d, *J* = 6.8 Hz, 3H, CHC$\underline{H_3}$), 1.19–1.08

(m, 1H, CHCH(CH$_3$)C$\underline{H_2}$CH$_3$), 0.97–0.93 (m, 7H, CHCH(CH$_3$)C$\underline{H_2}$CH$_3$ and CHCH(C$\underline{H_3}$)CH$_2$CH$_3$ and CHCH(CH$_3$)CH$_2$C$\underline{H_3}$), 0.86–0.82 (m, 6H, CHCH(C$\underline{H_3}$)$_2$). ^{13}C NMR (100 MHz, CDCl$_3$) δ 172.7, 171.0, 170.7, 156.1, 143.8(2C), 141.2(2C), 127.6(2C), 127.0(2C), 125.2, 125.1, 119.8(2C), 81.8, 67.1, 58.6, 56.8, 50.3, 47.0, 38.0, 31.2, 27.9(3C), 25.1, 19.1, 19.0, 18.4, 15.2, 11.6. IR (thin film, cm^{-1}) 3293, 3069, 2965, 2933, 2875, 1728, 1703, 1643, 1526, 1450, 1368, 1301, 1252, 1227, 1151, 1107, 1078, 1043, 756. HRMS (ESI) calculated for $C_{33}H_{45}N_3O_6Na$ [M+Na]$^+$ *m/z* 602.3175, found 602.3206.



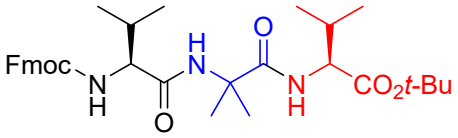
Fmoc-L-Ala-L-Val-L-Tle-O*t*-Bu (5o) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Tle-O*t*-Bu (93.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (40% AcOEt in hexane) to provide the title compound as a white solid in 85% yield with >20:1 dr (123 mg).

R_f = 0.61 (50% AcOEt in hexane). M.p. 195–200 °C. $[\alpha]_D^{20}$ = –39.0 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.6 Hz, 2H, C$_{12}\underline{H_8}$CHCH$_2$OCONH), 7.59–5.57 (m, 2H, C$_{12}\underline{H_8}$CHCH$_2$OCONH), 7.42 (br d, *J* = 9.2 Hz, 1H, N$\underline{H}$), 7.36 (t, *J* = 7.4 Hz, 2H, C$_{12}\underline{H_8}$CHCH$_2$OCONH), 7.27–7.23 (m, 2H, C$_{12}\underline{H_8}$CHCH$_2$OCONH), 7.13 (br d, *J* = 8.7 Hz, 1H, N$\underline{H}$), 6.36 (d, *J* = 8.3 Hz, 1H, N$\underline{H}$), 4.64–4.28 (m, 5H, C$\underline{H}$C(CH$_3$)$_3$ and C$\underline{H}$CH(CH$_3$)$_2$ and C$\underline{H}$CH$_3$ and C$_{12}$H$_8$CHC$\underline{H_2}$OCONH), 4.19 (t, *J* = 7.3 Hz, 1H, C$_{12}$H$_8$C$\underline{H}$CH$_2$OCONH), 2.08–1.98 (m, 1H, CHC$\underline{H}$(CH$_3$)$_2$), 1.42 (s, 9H, CO$_2$C(C$\underline{H_3}$)$_3$), 1.36 (d, *J* = 7.1 Hz, 3H, CHC$\underline{H_3}$), 0.94–0.93 (m, 15H, CHC(C$\underline{H_3}$)$_3$ and CHCH(C$\underline{H_3}$)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 170.8, 170.3, 156.0, 143.8(2C), 141.2(2C), 127.6(2C), 127.0(2C), 125.1(2C), 119.9(2C), 82.0, 67.1, 60.5, 58.7, 50.4, 47.1, 34.9, 31.1, 28.0(3C), 26.6(3C), 19.0, 18.8, 18.4. IR (thin film, cm^{-1}) 3277, 3065, 2966, 2875, 1725, 1707, 1644, 1525, 1449, 1391, 1366, 1251, 1221, 1150, 1109, 1043, 756. HRMS (ESI) calculated for $C_{33}H_{45}N_3O_6Na$ [M+Na]$^+$ *m/z* 602.3206, found 602.3217.



Fmoc-L-Ala-L-Val-Aib-O*t*-Bu (5p) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, Aib-O*t*-Bu (79.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (45% AcOEt in hexane) to provide the title compound as a white solid in 90% yield with >20:1 dr (124 mg).

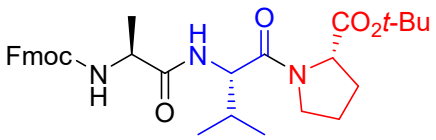
R_f = 0.43 (50% AcOEt in hexane). M.p. 125–130 °C. $[\alpha]_D^{23}$ = –89.0 (*c* 1.01, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.58–7.55 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.38 (t, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.30–7.26 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 6.93 (br d, *J* = 8.5 Hz, 1H, N*H*), 6.77 (br s, 1H, N*H*), 5.75 (br d, *J* = 7.3 Hz, 1H, N*H*), 4.41–4.32 (m, 3H, C*H*CH_3 and $C_{12}H_8CHC\underline{H_2}OCONH$), 4.28–4.25 (m, 1H, C*H*$CH(CH_3)_2$), 4.20 (t, *J* = 7.4 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.16–2.07 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.43 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.38 (d, *J* = 6.9 Hz, 3H, $CHC\underline{H_3}$), 0.96–0.91 (m, 6H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 172.4, 169.6, 156.0, 143.8, 143.7, 141.2 (2C), 127.6 (2C), 127.1 (2C), 125.0 (2C), 119.9 (2C), 81.6, 67.1, 58.5, 56.9, 50.5, 47.0, 31.1, 27.8 (3C), 24.5, 24.2, 19.1, 18.8, 18.0. IR (thin film, cm^{-1}) 3297, 2975, 2931, 1715, 1666, 1513, 1450, 1393, 1369, 1315, 1244, 1155, 1117, 1075, 1033, 982, 755. HRMS (ESI) calculated for $C_{31}H_{41}N_3O_6Na$ $[M+Na]^+$ *m/z* 574.2893, found 574.2921.



Fmoc-L-Val-Aib-L-Val-O*t*-Bu (5q) was prepared following **General Procedure 1** using H-Aib-OH (25.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Val-Cl (268 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (33% AcOEt in hexane) to provide the title compound as a white solid in 91% yield with >20:1 dr (132 mg).

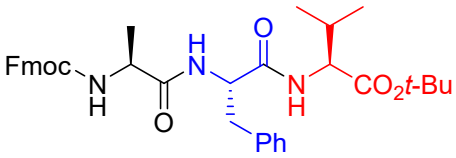
R_f = 0.31 (33% AcOEt in hexane). M.p. 135–140 °C. $[\alpha]_D^{22}$ = –45.4 (*c* 1.01, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.57 (d, *J* = 7.4 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.38 (t, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.31–7.26 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 6.81–7.76 (m, 2H, N*H* and N*H*), 5.50 (d, *J* = 8.2 Hz, 1H, N*H*), 4.45–4.29

(m, 3H, $C_{12}H_8CHC\underline{H_2}OCONH$ and $C\underline{H}CH(CH_3)_2$), 4.20 (dd, *J* = 6.9 Hz and 7.1 Hz, 1H, $C\underline{H}CH(CH_3)_2$), 3.96 (t, *J* = 7.3 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.21–2.08 (m, 2H, $CHC\underline{H}(CH_3)_2$ and $CHC\underline{H}(CH_3)_2$), 1.61 (s, 3H, $C(CH_3)_2$), 1.57 (s, 3H, $C(CH_3)_2$), 1.43 (s, 9H, $CO_2C(C\underline{H_3})_3$), 0.98–0.85 (m, 12H, $CHCH(C\underline{H_3})_2$ and $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 170.8, 170.7, 156.4, 143.7(2C), 141.2(2C), 127.6(2C), 127.0(2C), 125.0, 124.9, 119.8(2C), 81.8, 67.0, 60.7, 57.6, 57.4, 47.1, 31.3, 31.0, 27.9(3C), 25.7, 24.4, 19.1, 18.8, 17.9, 17.5. IR (thin film, cm^{-1}) 3294, 3065, 2969, 2934, 1703, 1674, 1647, 1530, 1449, 1393, 1310, 1253, 1221, 1149, 1108, 1049, 756. HRMS (ESI) calculated for $C_{33}H_{45}N_3O_6Na$ $[M+Na]^+$ *m/z* 602.3206, found 602.3213.



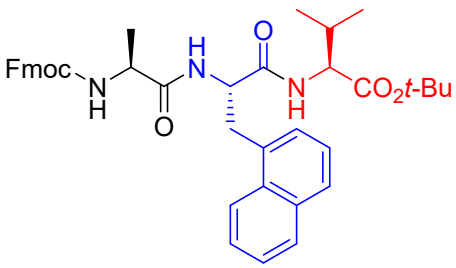
Fmoc-L-Ala-L-Val-L-Pro-O*t*-Bu (5r) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Pro-O*t*-Bu (85.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (50% AcOEt in hexane) to provide the title compound as a white solid in 68% yield with >20:1 dr (95.8 mg).

R_f = 0.35 (50% AcOEt in hexane). M.p. 80–85 °C. $[\alpha]_D^{23}$ = –45.7 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.58 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.38 (t, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.31–7.27 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 6.98 (br d, *J* = 8.7 Hz, 1H, N$\underline{H}$), 5.65 (br d, *J* = 7.6 Hz, 1H, N$\underline{H}$),4.64 (dd, *J* = 5.8 Hz and 8.7 Hz, 1H, $NCHCO_2C(CH_3)_3$), 4.39–4.32 (m, 4H, $C\underline{H}CH(CH_3)_2$ and $C\underline{H}CH_3$ and $C_{12}H_8CHC\underline{H_2}OCONH$), 4.20 (t, *J* = 7.1 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 3.78–3.61 (m, 2H, $N(C\underline{H_2}CH_2CH_2C)$), 2.24–1.87 (m, 5H, $CHC\underline{H}(CH_3)_2$ and $N(CH_2C\underline{H_2}CH_2C)$ and $N(CH_2CH_2C\underline{H_2}C)$), 1.44 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.36 (d, *J* = 7.1 Hz, 3H, $CHC\underline{H_3}$), 1.03 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.93 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 171.0, 170.1, 155.6, 143.8, 143.7, 141.2 (2C), 127.6 (2C), 127.0 (2C), 125.1 (2C), 119.8 (2C), 81.3, 66.9, 59.7, 55.4, 50.4, 47.3, 47.0, 31.3, 29.0, 28.0 (3C), 24.8, 19.4, 18.9, 17.5. IR (thin film, cm^{-1}) 3301, 2967, 2935, 2875, 1725, 1703, 1645, 1525, 1441, 1371, 1305, 1241, 1225, 1150, 1107, 1078, 1043, 756. HRMS (ESI) calculated for $C_{32}H_{41}N_3O_6Na$ $[M+Na]^+$ *m/z* 586.2893, found 586.2889.



Fmoc-L-Ala-L-Phe-L-Val-O*t*-Bu (5s) was prepared following **General Procedure 1** using H-L-Phe-OH (41.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (35% AcOEt in hexane) to provide the title compound as a white solid in 94% yield with >20:1 dr (144 mg).

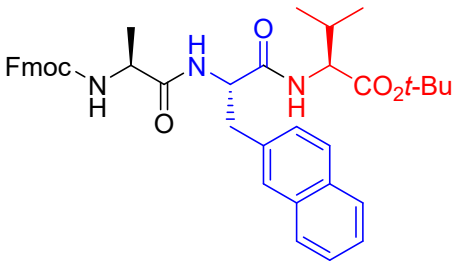
R_f = 0.29 (33% AcOEt in hexane). M.p. 170–175 °C. $[\alpha]_D^{20}$ = –70.0 (*c* 1.20, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.58 (t, *J* = 8.9 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.46 (br d, *J* = 7.8 Hz, 1H, N*H*), 7.38–7.32 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.27–7.23 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.17–7.05 (m, 5H, $CHCH_2C_6\underline{H_5}$), 7.07 (br d, *J* = 6.9 Hz, 1H, N*H*), 6.17 (d, *J* = 8.0 Hz, 1H, N*H*), 4.98 (dd, *J* = 6.9 Hz and 14 Hz 1H, C*H*CH_2Ph), 4.51 (quin, *J* = 7.3 Hz 1H, C*H*CH_3), 4.44–4.27 (m, 3H, $C_{12}H_8CHC\underline{H_2}OCONH$, C*H*$CH(CH_3)_2$), 4.18 (t, *J* = 7.1 Hz, $C_{12}H_8C\underline{H}CH_2OCONH$), 3.08 (dd, *J* = 6.9 Hz and 14 Hz, 1H, $CHC\underline{H_2}Ph$), 2.99 (dd, *J* = 6.9 Hz and 14 Hz, 1H, $CHC\underline{H_2}Ph$), 2.09–2.03 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.41 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.32 (d, *J* = 7.3 Hz, 3H, $CHC\underline{H_3}$), 0.84 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.81 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 170.7, 170.4, 155.9, 143.8(2C), 141.1(2C), 136.3, 129.2(2C), 128.3(2C), 127.5(2C), 126.9 (2C), 126.7, 125.1 (2C), 119.8 (2C), 81.7, 67.1, 57.4, 54.3, 50.2, 46.9, 38.4, 31.4, 27.9 (3C), 19.0, 18.7, 17.6. IR (thin film, cm^{-1}) 3293, 3064, 2969, 2933, 1706, 1645, 1530, 1477, 1450, 1393, 1313, 1221, 1143, 1110, 1078, 1045, 757. HRMS (ESI) calculated for $C_{36}H_{43}N_3O_6Na$ $[M+Na]^+$ *m/z* 636.3022, found 636.3049.



Fmoc-L-Ala-L-Ala(1-Naph)-L-Val-O*t*-Bu (5t) was prepared following **General Procedure 1** using H-L-Ala(1-Naph)-OH (53.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-

Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (40% AcOEt in hexane) to provide the title compound as a white solid in 86% yield with >20:1 dr (143 mg).

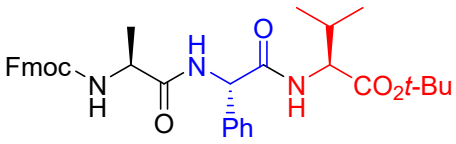
R_f = 0.68 (50% AcOEt in hexane). M.p. 210–215 °C. $[\alpha]_D^{20}$ = –79.0 (*c* 1.01, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.2 Hz, 1H, $CHCH_2NaphH$), 7.78–7.74 (m, 3H, $C_{12}H_8CHCH_2OCONH$ and $CHCH_2NaphH$), 7.66–7.37 (m, 7H, $C_{12}H_8CHCH_2OCONH$ and $CHCH_2NaphH$), 7.32–7.25 (m, 4H, $C_{12}H_8CHCH_2OCONH$ and $CHCH_2NaphH$), 6.94 (br d, *J* = 7.1 Hz, 1H, N*H*), 6.46 (br d, *J* = 7.8 Hz, 1H, N*H*), 5.47 (d, *J* = 7.8 Hz, 1H, N*H*), 4.88 (quin., *J* = 7.1 Hz, 1H, C*H*CH_3), 4.40–4.26 (m, 4H, C*H*CH_2Naph and $C_{12}H_8CHCH_2OCONH$ and C*H*$CH(CH_3)_2$), 4.17 (t, *J* = 6.9 Hz, $C_{12}H_8CHCH_2OCONH$), 3.50 (d, *J* = 6.9 Hz, 2H, $CHCH_2Naph$), 2.06–2.02 (m, 1H, $CHCH(CH_3)_2$), 1.39 (s, 9H, $CO_2C(CH_3)_3$), 1.27 (d, *J* = 7.1 Hz, 3H, $CHCH_3$), 0.80 (d, *J* = 6.2 Hz, 3H, $CHCH(CH_3)_2$), 0.78 (d, *J* = 6.2 Hz, 3H, $CHCH(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 170.6, 170.0, 155.8, 143.8, 143.7, 141.2(2C), 134.0, 132.4, 132.0, 128.7, 127.7(2C), 127.6(2C), 127.0(2C), 125.8(2C), 125.4, 125.2, 125.1, 123.5, 119.9(2C), 81.8, 67.0, 57.5, 54.1, 50.3, 47.0, 35.3, 31.4, 27.9(3C), 18.8, 18.6, 17.7. IR (thin film, cm^{-1}) 3290, 3061, 2966, 2931, 1705, 1644, 1531, 1475, 1453, 1391, 1313, 1221, 1143, 1110, 1078, 1045, 757. HRMS (ESI) calculated for $C_{40}H_{45}N_3O_6Na$ $[M+Na]^+$ *m/z* 686.3206, found 686.3221.



Fmoc-L-Ala-L-Ala(2-Naph)-L-Val-O*t*-Bu (5u) was prepared following **General Procedure 1** using H-L-Ala(2-Naph)-OH (53.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (35% AcOEt in hexane) to provide the title compound as a white solid in 87% yield with >20:1 dr (144 mg).

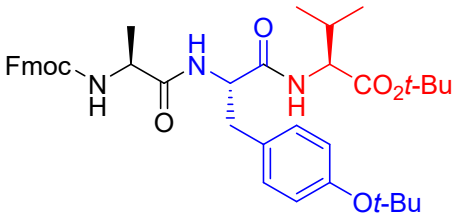
R_f = 0.58 (50% AcOEt in hexane). M.p. 180–185 °C. $[\alpha]_D^{20}$ = –73.3 (*c* 1.01, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.74–7.64 (m, 5H, $C_{12}H_8CHCH_2OCONH$ and $CHCH_2NaphH$), 7.58–7.51 (m, 3H,

$C_{12}\underline{H_8}CHCH_2OCONH$ and $CHCH_2Naph\underline{H}$), 7.39–7.23 (m, 7H, $C_{12}\underline{H_8}CHCH_2OCONH$ and $CHCH_2Naph\underline{H}$), 7.14 (br d, J = 7.6 Hz, 1H, N$\underline{H}$), 6.88 (br d, J = 8.3 Hz, 1H, N$\underline{H}$), 5.76 (d, J = 7.8 Hz, 1H, N$\underline{H}$), 4.94 (quin., J = 7.3 Hz, 1H, C$\underline{H}CH_3$), 4.41–4.31 (m, 3H, $C_{12}H_8CHC\underline{H_2}OCONH$ and C$\underline{H}CH(CH_3)_2$), 4.21 (t, J = 7.1 Hz, 1H, C$\underline{H}CH_2Naph$), 4.12 (t, J = 7.1 Hz, $C_{12}H_8C\underline{H}CH_2OCONH$), 3.24 (dd, J = 6.9 Hz and 14 Hz, 1H, $CHC\underline{H_2}Naph$), 3.15 (dd, J = 6.9 Hz and 14 Hz, 1H, $CHC\underline{H_2}Naph$), 2.10–2.03 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.35 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.30 (d, J = 7.3 Hz, 3H, $CHC\underline{H_3}$), 0.83 (d, J = 6.6 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.79 (d, J = 6.6 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 170.5, 170.3, 155.9, 143.8, 143.7, 141.2(2C), 133.7, 133.3, 132.3, 128.1, 128.0, 127.6, 127.5(2C), 127.4(2C), 127.3, 127.0(2C), 125.9, 125.5, 125.1, 119.9(2C), 81.8, 67.0, 57.5, 54.4, 50.4, 47.0, 38.3, 31.3, 27.9(3C), 18.7(2C), 17.6. IR (thin film, cm^{-1}) 3293, 3061, 2966, 2931, 1705, 1645, 1531, 1478, 1451, 1391, 1313, 1221, 1143, 1109, 1078, 1044, 757. HRMS (ESI) calculated for $C_{40}H_{45}N_3O_6Na$ $[M+Na]^+$ *m/z* 686.3206, found 686.3182.



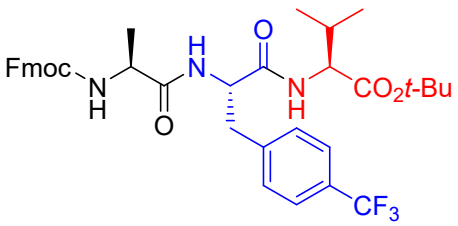
Fmoc-L-Ala-L-Phg-L-Val-O*t*-Bu (5v) was prepared following **General Procedure 1** using H-L-Tyr(*t*-Bu)-OH (37.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (45% AcOEt in hexane) to provide the title compound as a white solid in 93% yield with >20:1 dr (139 mg).

R_f = 0.41 (50% AcOEt in hexane). M.p. 120–125 °C. $[\alpha]_D^{22}$ = –25.7 (*c* 1.13, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73–7.69 (m, 3H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N$\underline{H}$), 7.55 (d, J = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.37–7.22 (m, 10H, $C_{12}\underline{H_8}CHCH_2OCONH$ and $CHC_6\underline{H_5}$ and N$\underline{H}$), 6.85 (br d, J = 8.5 Hz, 1H, N$\underline{H}$), 5.97 (br d, J = 7.6 Hz, 1H, N$\underline{H}$), 5.71 (d, J = 7.4 Hz, 1H, C$\underline{H}$Ph), 4.52 (quin., J = 6.7 Hz, 1H, C$\underline{H}CH_3$), 4.38–4.29 (m, 3H, $C_{12}H_8CHC\underline{H_2}OCONH$ and C$\underline{H}CH(CH_3)_2$), 4.16 (t, J = 7.1 Hz, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.11–2.05 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.36 (d, J = 7.1 Hz, 3H, $CHC\underline{H_3}$), 1.30 (s, 9H, $CO_2C(C\underline{H_3})_3$), 0.89 (d, J = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.86 (d, J = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 170.1, 169.5, 155.9, 143.9, 143.7, 141.1 (2C), 137.4 (2C), 128.8 (2C), 128.2, 127.6 (2C), 126.9 (3C), 125.0 (2C), 119.8 (2C), 81.9, 67.0, 58.1, 56.9, 50.3, 47.0, 31.4, 27.8 (3C), 19.1, 18.7, 17.8. IR (thin film, cm^{-1}) 3296, 3064, 2968, 1726, 1702, 1641, 1521, 1449, 1391, 1367, 1312, 1252, 1217, 1143, 1108, 1078, 1042, 754. HRMS (ESI) calculated for $C_{35}H_{41}N_3O_6Na$ $[M+Na]^+$ *m/z* 622.2867, found 622.2893.



Fmoc-L-Ala-L-Tyr(*t*-Bu)-L-Val-O*t*-Bu (5w) was prepared following **General Procedure 1** using H-L-Tyr(*t*-Bu)-OH (59.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (35% AcOEt in hexane) to provide the title compound as a white solid in 91% yield with >20:1 dr (156 mg).

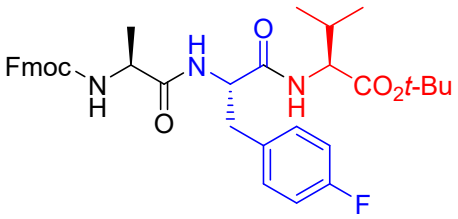
R_f = 0.29 (33% AcOEt in hexane). M.p. 90–95 °C. $[\alpha]_D^{19}$ = –58.2 (*c* 1.10, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 6.9 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.59 (t, *J* = 6.2 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.41–7.36 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.32–7.29 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.07 (d, *J* = 8.5 Hz, 2H, $CHCH_2C_6\underline{H_4}OC(CH_3)_3$), 6.90 (br d, *J* = 7.1 Hz, 1H, N*H*), 6.84 (d, *J* = 8.5 Hz, 2H, $CHCH_2C_6\underline{H_4}OC(CH_3)_3$), 6.66 (br d, *J* = 8.0 Hz, 1H, N*H*), 5.60 (d, *J* = 7.6 Hz, 1H, $C_{12}H_8CHCH_2OCONH$), 4.74 (quin, *J* = 7.1 Hz 1H, $C\underline{H}CH_3$), 4.41–4.31 (m, 4H, $C_{12}H_8CHC\underline{H_2}OCONH$, $C\underline{H}CH(CH_3)_2$, $C\underline{H}CH_2C_6H_4OC(CH_3)_3$), 4.20 (t, *J* = 7.1 Hz, $C_{12}H_8C\underline{H}CH_2OCONH$), 3.03 (d quin., *J* = 6.6 Hz and 14 Hz, 2H, $CHC\underline{H_2}C_6H_4OC(CH_3)_3$), 2.11–2.03 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.44 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.32 (d, *J* = 6.6 Hz, 3H, $CHC\underline{H_3}$), 1.26 (s, 9H, $CHCH_2C_6H_4OC(C\underline{H_3})_3$), 0.84 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.81 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 170.5, 170.3, 155.9, 154.2, 143.8, 143.7, 141.2(2C), 131.1, 129.7(2C), 127.6(2C), 127.0(2C), 125.1(2C), 124.1(2C), 119.8(2C), 81.8, 78.1, 67.0, 57.6, 54.4, 50.4, 47.0, 37.4, 31.2, 28.7(3C), 27.9(3C), 18.8, 18.7, 17.6. IR (thin film, cm^{-1}) 3292, 2975, 2932, 1704, 1644, 1530, 1506, 1391, 1312, 1235, 1160, 1078, 1044, 755. HRMS (ESI) calculated for $C_{40}H_{51}N_3O_7Na$ $[M+Na]^+$ *m/z* 708.3613, found 708.3625.



Fmoc-L-Ala-L-Phe(4-CF_3)-L-Val-O*t*-Bu (5x) was prepared following **General Procedure 1** using

H-L-Phe(4-CF_3)-OH (58.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (40% AcOEt in hexane) to provide the title compound as a white solid in 89% yield with >20:1 dr (152 mg).

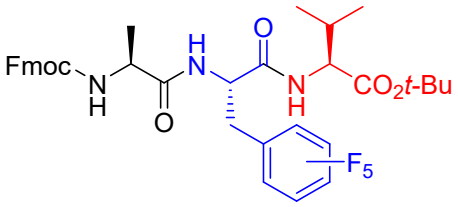
R_f = 0.42 (50% AcOEt in hexane). M.p. 125–130 °C. $[\alpha]_D^{21}$ = –53.9 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.59–7.55 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.44 (d, *J* = 8.0 Hz, 2H, $CHCH_2C_6\underline{H_4}CF_3$), 7.39–7.34 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.28–7.24 (m, 5H, $CHCH_2C_6\underline{H_4}CF_3$ and $C_{12}\underline{H_8}CHCH_2OCONH$ and N$\underline{H}$), 6.99 (br d, *J* = 8.5 Hz, 1H, N$\underline{H}$), 5.95 (br d, *J* = 7.8 Hz, 1H, N$\underline{H}$), 4.93 (quin, *J* = 6.9 Hz 1H, C$\underline{H}CH_3$), 4.45–4.28 (m, 4H, $C_{12}H_8CHC\underline{H_2}OCONH$ and C$\underline{H}CH(CH_3)_2$ and C$\underline{H}CH_2C_6H_4CF_3$), 4.19 (t, *J* = 7.1 Hz, $C_{12}H_8C\underline{H}CH_2OCONH$), 3.13 (dd, *J* = 6.6 Hz and 14 Hz, 1H, $CHC\underline{H_2}C_6H_4CF_3$), 3.02 (dd, *J* = 6.9 Hz and 14 Hz, 1H, $CHC\underline{H_2}C_6H_4CF_3$), 2.10–2.04 (m, 1H, C$\underline{H}(CH_3)_2$), 1.41 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.31 (d, *J* = 6.9 Hz, 3H, $CHC\underline{H_3}$), 0.84 (d, *J* = 6.6 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.81 (d, *J* = 6.6 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 170.4, 170.0, 156.0, 143.8, 143.7, 141.2 (2C), 140.4, 129.7 (2C), 129.1 (J_{FC} = 32.4 Hz), 127.7 (2C), 127.0 (2C), 125.3–125.0, 123.0 (J_{FC} = 270.8 Hz), 119.9 (2C), 82.1, 67.2, 57.5, 54.0, 50.4, 47.0, 38.1, 31.3, 27.9 (3C), 18.7, 17.6 IR (thin film, cm^{-1}) 3291, 2966, 1705, 1644, 1507, 1449, 1391, 1313, 1215, 1113, 1075, 1042, 755. HRMS (ESI) calculated for $C_{37}H_{42}F_3N_3O_6Na$ $[M+Na]^+$ *m/z* 704.2923, found 704.2911.



Fmoc-L-Ala-L-Phe(4-F)-L-Val-O*t*-Bu (5y) was prepared following **General Procedure 1** using H-L-Phe(4-F)-OH (45.5 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (40% AcOEt in hexane) to provide the title compound as a white solid in 93% yield with >20:1 dr (147 mg).

R_f = 0.62 (50% AcOEt in hexane). M.p. 170–175 °C. $[\alpha]_D^{21}$ = –34.9 (*c* 1.03, $CHCl_3$). ^{1}H NMR (400

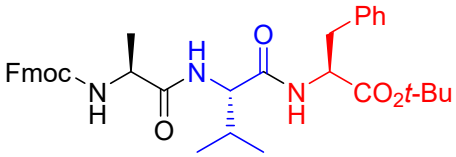
MHz, $CDCl_3$) δ 7.72 (d, *J* = 6.9 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.58 (t, *J* = 8.7 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.39–7.25 (m, 5H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N$\underline{H}$), 7.10–7.06 (m, 3H, $CHCH_2C_6\underline{H_4}F$ and N$\underline{H}$), 6.88–6.85 (m, 2H, $CHCH_2C_6\underline{H_4}F$), 6.08 (br d, *J* = 8.0 Hz, 1H, N$\underline{H}$), 4.91 (quin, *J* = 6.9 Hz 1H, C$\underline{H}CH_3$), 4.50–4.30 (m, 4H, $C_{12}H_8CHC\underline{H_2}OCONH$, C$\underline{H}CH(CH_3)_2$, C$\underline{H}CH_2C_6H_4F$), 4.19 (t, *J* = 7.3 Hz, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.99 (d quin., *J* = 6.9 Hz and 17 Hz, 2H, $CHC\underline{H_2}C_6H_4F$), 2.11–2.04 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.41 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.33 (d, *J* = 6.9 Hz, 3H, $CHC\underline{H_3}$), 0.84 (d, *J* = 6.6 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.81 (d, *J* = 6.6 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 170.5, 170.4, 161.7 (J_{FC} = 243.1 Hz), 156.1, 143.9, 143.7, 141.2 (2C), 131.9, 130.8 (J_{FC} = 7.6 Hz, 2C), 127.6 (2C), 127.0 (2C), 125.1 (2C), 119.8 (2C), 115.1 (J_{FC} = 21.0 Hz, 2C), 81.9, 67.2, 57.3, 54.3, 50.2, 47.0, 37.8, 31.5, 27.9 (3C), 19.0, 18.7, 17.6. IR (thin film, cm^{-1}) 3294, 2969, 1704, 1643, 1509, 1449, 1393, 1313, 1218, 1113, 1078, 1042, 755. HRMS (ESI) calculated for $C_{36}H_{42}FN_3O_6Na$ $[M+Na]^+$ *m/z* 654.2955, found 654.2938.



Fmoc-L-Ala-L-Phe(F_5)-L-Val-O*t*-Bu (5z) was prepared following **General Procedure 1** using H-L-Phe(F5)-OH (63.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (33% AcOEt in hexane) to provide the title compound as a white solid in 89% yield with >20:1 dr (156 mg).

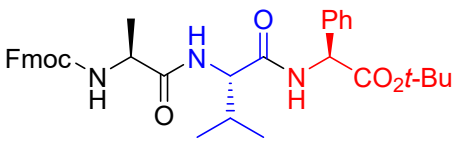
R_f = 0.65 (50% AcOEt in hexane). M.p. 190–195 °C. $[\alpha]_D^{21}$ = –94.1 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.11 (t, *J* = 8.7 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.86 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.68 (t, *J* = 8.2 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.54 (d, *J* = 7.4 Hz, 1H, N$\underline{H}$), 7.42–7.29 (m, 4H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N$\underline{H}$), 4.71 (quin, *J* = 7.6 Hz 1H, C$\underline{H}CH_3$), 4.24–3.97 (m, 5H, $C_{12}H_8C\underline{H}CH_2OCONH$, $C_{12}H_8CHC\underline{H_2}OCONH$, C$\underline{H}CH(CH_3)_2$, C$\underline{H}CH_2C_6F_5$), 3.06 (dd, *J* = 7.1 Hz and 13.7 Hz, 1H, $CHC\underline{H_2}C_6F_5$), 2.92 (dd, *J* = 7.6 Hz and 13.7 Hz, 1H, $CHC\underline{H_2}C_6F_5$), 2.03–1.90 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.38 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.14 (d, *J* = 7.6 Hz, 3H, $CHC\underline{H_3}$), 0.82 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.81 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.2, 170.8, 170.5, 156.4, 146.0 (J_{FC} = 244.1 Hz), 144.6, 144.5, 141.4 (2C), 140.0 (2C, J_{FC} = 241.6 Hz), 137.4 (2C, J_{FC} = 242.2 Hz), 128.3 (2C), 127.8 (2C), 126.0, 125.9, 120.8 (2C),

111.8 (J_{FC} = 16.2 Hz), 81.4, 66.4, 58.4, 50.9, 50.5, 48.7, 31.0, 28.3 (3C), 26.2, 19.5, 18.7, 18.5. IR (thin film, cm^{-1}) 3291, 2966, 1701, 1645, 1505, 1449, 1393, 1311, 1211, 1115, 1075, 1045, 765. HRMS (ESI) calculated for $C_{36}H_{38}F_5N_3O_6Na$ $[M+Na]^+$ *m/z* 726.2578, found 726.2534.



Fmoc-L-Ala-L-Val-L-Phe-O*t*-Bu (5aa) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Phe-O*t*-Bu (111 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (45% AcOEt in hexane) to provide the title compound as a white solid in 92% yield with >20:1 dr (141 mg).

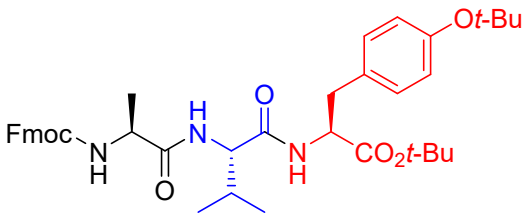
R_f = 0.49 (50% AcOEt in hexane). M.p. 200–205 °C. $[\alpha]_D^{22}$ = –32.4 (*c* 1.03, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.57 (d, *J* = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.44–7.42 (m, 2H, N*H* and N*H*), 7.33 (t, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.25–7.20 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.18–7.05 (m, 5H, $CHCH_2C_6\underline{H_5}$), 6.45 (d, *J* = 8.2 Hz, 1H, N*H*), 4.81 (dd, *J* = 6.2 Hz and 14 Hz 1H, C*H*CH_2Ph), 4.64–4.58 (m, 2H, C*H*$CH(CH_3)_2$ and C*H*CH_3), 4.34–4.24 (m, 2H, $C_{12}H_8CHC\underline{H_2}OCONH$), 4.16 (t, *J* = 7.3 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.98 (d, *J* = 6.2 Hz, 2H, $CHC\underline{H_2}Ph$), 2.10–2.02 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.34 (d, *J* = 6.9 Hz, 3H, $CHC\underline{H_3}$), 1.29 (s, 9H, $CO_2C(C\underline{H_3})_3$), 0.96 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.93 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 170.6, 170.3, 156.0, 143.8(2C), 141.2(2C), 136.0, 129.4(2C), 128.2(2C), 127.6(2C), 126.9 (2C), 126.8, 125.1 (2C), 119.8 (2C), 82.1, 67.1, 58.3, 53.6, 50.4, 47.0, 38.2, 31.4, 27.8(3C), 19.0(2C), 18.3. IR (thin film, cm^{-1}) 3290, 3063, 3019, 2970,1732, 1693, 1643, 1539, 1451, 1392, 1322, 1229, 1216, 1153, 1119, 1085, 1046, 754. HRMS (ESI) calculated for $C_{36}H_{43}N_3O_6Na$ $[M+Na]^+$ *m/z* 636.3031, found 636.3049.



Fmoc-L-Ala-L-Val-L-Phg-O*t*-Bu (5ab) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the

resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Phg-O*t*-Bu (104 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (45% AcOEt in hexane) to provide the title compound as a white solid in 91% yield with >20:1 dr (136 mg).

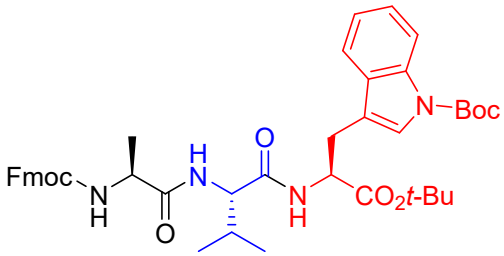
R_f = 0.48 (50% AcOEt in hexane). M.p. 205–210 °C. $[\alpha]_D^{20}$ = –70.0 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (br d, *J* = 7.3 Hz, N*H*), 7.71 (d, *J* = 7.1 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.55 (d, *J* = 6.2 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.36–7.21 (m, 7H, $CHC_6\underline{H_5}$ and $C_{12}\underline{H_8}CHCH_2OCONH$ and N*H*), 7.14–7.12 (m, 3H, $CHC_6\underline{H_5}$), 6.14 (d, *J* = 8.2 Hz, 1H, N*H*), 5.52 (d, *J* = 7.6 Hz, 1H, C*H*Ph), 4.67 (quin., *J* = 7.8 Hz, 1H, C*H*CH_3), 4.46 (t, *J* = 6.2 Hz, 1H, C*H*$CH(CH_3)_2$), 4.32–4.22 (m, 2H, $C_{12}H_8CHC\underline{H_2}OCONH$), 4.14 (t, *J* = 7.3 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.16–2.05 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.34 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.19 (d, *J* = 6.9 Hz, 3H, $CHC\underline{H_3}$), 0.98 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.93 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 170.6, 169.6, 156.0, 143.9, 143.8, 141.1(2C), 136.6, 128.5(3C), 128.0, 127.5(2C), 126.9(3C), 125.1(2C), 119.8(2C), 82.3, 67.0, 58.1, 56.9, 50.2, 47.0, 31.5, 27.7(3C), 19.0, 18.9, 18.3. IR (thin film, cm^{-1}) 3295, 3063, 2966, 2931, 1705, 1645, 1531, 1475, 1455, 1395, 1313, 1221, 1143, 1113, 1078, 1045, 757. HRMS (ESI) calculated for $C_{35}H_{41}N_3O_6Na$ $[M+Na]^+$ *m/z* 622.2867, found 622.2887.



Fmoc-L-Ala-L-Val-L-Tyr(*t*-Bu)-O*t*-Bu (5ac) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Tyr(*t*-Bu)-O*t*-Bu (147 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (40% AcOEt in hexane) to provide the title compound as a white solid in 86% yield with >20:1 dr (142 mg).

R_f = 0.52 (50% AcOEt in hexane). M.p. 120–125 °C. $[\alpha]_D^{19}$ = –65.2 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.57 (dd, *J* = 2.8 Hz and 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.35 (t, *J* = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.29–7.22 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.18 (br d, *J* = 7.6 Hz, 1H, N*H*), 6.97 (d, *J* = 8.5 Hz, 2H,

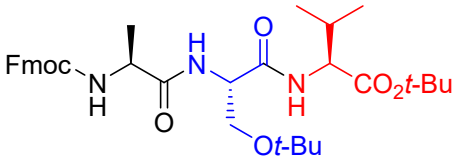
$CHCH_2C_6\underline{H_4}OC(CH_3)_3$), 6.81 (d, J = 8.5 Hz, 2H, $CHCH_2C_6\underline{H_4}OC(CH_3)_3$), 6.23 (br d, J = 7.8 Hz, 1H, N$\underline{H}$), 4.71 (quin, J = 6.4 Hz 1H, C$\underline{H}CH_3$), 4.55–4.53 (m, 2H, C$\underline{H}CH(CH_3)_2$ and C$\underline{H}CH_2C_6H_4OC(CH_3)_3$), 4.37–4.30 (m, 2H, $C_{12}H_8CHC\underline{H_2}OCONH$), 4.19 (t, J = 7.3 Hz, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.98 (dd, J = 5.5 Hz and 14 Hz, 2H, $CHC\underline{H_2}C_6H_4OC(CH_3)_3$), 2.91 (dd, J = 7.4 Hz and 14 Hz, 2H, $CHC\underline{H_2}C_6H_4OC(CH_3)_3$), 2.14–2.04 (m, 1H, CHC$\underline{H}(CH_3)_2$), 1.38 (d, J = 6.9 Hz, 3H, CHC$\underline{H_3}$), 1.29 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.28 (s, 9H, $CHCH_2C_6H_4OC(C\underline{H_3})_3$), 0.94 (d, J = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.92 (d, J = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 170.6, 170.5, 156.0, 154.1, 143.8, 143.7, 141.1(2C), 130.9, 129.8(2C), 127.6(2C), 127.0(2C), 125.1(2C), 124.0(2C), 119.8(2C), 82.0, 78.2, 67.1, 58.3, 53.8, 50.4, 47.0, 37.7, 31.5, 28.7(3C), 27.6(3C), 19.0, 18.9, 18.3. IR (thin film, cm^{-1}) 3231, 3015, 2923, 1704, 1644, 1515, 1391, 1312, 1238, 1160, 1078, 1044, 765. HRMS (ESI) calculated for $C_{40}H_{51}N_3O_7Na$ $[M+Na]^+$ *m/z* 708.3625, found 708.3619.



Fmoc-L-Ala-L-Val-L-Trp(Boc)-O*t*-Bu (5ad) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Trp(Boc)-O*t*-Bu (180 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (45% AcOEt in hexane) to provide the title compound as a white solid in 43% yield with >20:1 dr (80.9 mg).

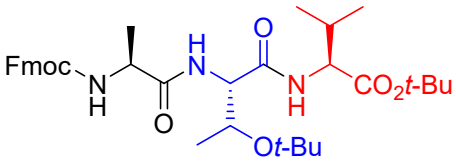
R_f = 0.48 (50% AcOEt in hexane). M.p. 160–165 °C. $[\alpha]_D^{21}$ = –7.7 (*c* 1.04, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (br d, J = 7.8 Hz, 1H, $CHCH_2Ind\underline{H}$(Boc)), 7.72 (d, J = 7.1 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.55 (d, J = 6.4 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.48 (br d, J = 7.8 Hz, 1H, $CHCH_2Ind\underline{H}$(Boc)), 7.40–7.34 (m, 3H, $C_{12}\underline{H_8}CHCH_2OCONH$ and $CHCH_2Ind\underline{H}$(Boc)), 7.30–7.18 (m, 4H, $C_{12}\underline{H_8}CHCH_2OCONH$ and $CHCH_2Ind\underline{H}$(Boc)), 6.87 (br d, J = 8.5 Hz, 1H, N$\underline{H}$), 6.79 (br d, J = 6.9 Hz, 1H, N$\underline{H}$), 5.81 (d, J = 7.6 Hz, 1H, N$\underline{H}$), 4.83 (quin, J = 7.1 Hz 1H, C$\underline{H}CH_3$), 4.39–4.34 (m, 4H, $C_{12}H_8CHC\underline{H_2}OCONH$, C$\underline{H}CH(CH_3)_2$, C$\underline{H}CH_2Ind$(Boc)), 4.18 (t, J = 7.1 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 3.16 (d, J = 5.2 Hz 2H, $CHC\underline{H_2}Ind$(Boc)), 2.14–2.06 (m, 1H, C$\underline{H}(CH_3)_2$), 1.64 (s, 9H, $CHCH_2Ind(CO_2C(C\underline{H_3})_3)$), 1.34 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.34–1.33 (m, 3H,

CHC$\underline{H_3}$), 0.92 (d, J = 6.9 Hz, 3H, CHCH(C$\underline{H_3}$)$_2$), 0.90 (d, J = 6.9 Hz, 3H, CHCH(C$\underline{H_3}$)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 170.5, 170.3, 156.0, 149.4, 143.8, 143.7, 141.2(2C), 135.3, 130.5, 127.6(2C), 127.0(2C), 125.1(2C), 124.5, 124.0, 122.6, 119.9(2C), 119.0, 115.2, 115.1, 83.5, 82.4, 67.0, 58.2, 53.0, 50.5, 47.0, 31.4, 28.1(3C), 27.8(3C), 27.7, 19.0, 18.8, 18.0. IR (thin film, cm^{-1}) 3285, 2975, 2933, 1731, 1639, 1528, 1451, 1368, 1340, 1308, 1253, 1228, 1155, 1085, 1043, 1019, 756. HRMS (ESI) calculated for $C_{43}H_{52}N_4O_8Na$ [M+Na]$^+$ *m/z* 775.3683, found 775.3689.



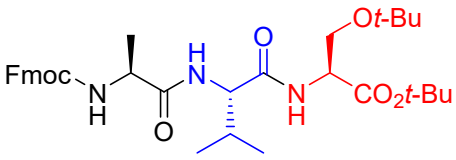
Fmoc-L-Ala-L-Ser(*t*-Bu)-L-Val-O*t*-Bu (5ae) was prepared following **General Procedure 1** using H-L-Ser(*t*-Bu)-OH (40.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (45% AcOEt in hexane) to provide the title compound as a white solid in 93% yield with >20:1 dr (142 mg).

R_f = 0.42 (50% AcOEt in hexane). M.p. 110–115 °C. $[\alpha]_D^{20}$ = –61.5 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.58 (d, J = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N$\underline{H}$), 7.39 (t, J = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.32–7.26 (m, 3H, $C_{12}\underline{H_8}CHCH_2OCONH$), 6.89 (br d, J = 6.0 Hz, 1H, N$\underline{H}$), 5.54 (br d, J = 6.9 Hz, 1H, N$\underline{H}$), 4.46–4.28 (m, 5H, C$\underline{H}CH_2OC(CH_3)_3$ and $C_{12}H_8CHC\underline{H_2}OCONH$ and C$\underline{H}CH_3$ and C$\underline{H}CH(CH_3)_2$), 4.21 (t, J = 6.9 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 3.82 (dd, J = 3.2 Hz, and 8.2 Hz, 1H, CHC$\underline{H_2}$OC(CH$_3$)$_3$), 3.71 (dd, J = 8.0 Hz, and 8.2 Hz, 1H, CHC$\underline{H_2}$OC(CH$_3$)$_3$), 2.19–2.10 (m, 1H, CHC$\underline{H}$(CH$_3$)$_2$), 1.46 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.44 (d, J = 6.9 Hz, 3H, CHC$\underline{H_3}$), 1.21 (s, 9H, $CHCH_2OC(C\underline{H_3})_3$), 0.92 (d, J = 8.7 Hz, 3H, CHCH(C$\underline{H_3}$)$_2$), 0.90 (d, J = 8.7 Hz, 3H, CHCH(C$\underline{H_3}$)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 170.4, 169.9, 155.8, 143.8, 143.7, 141.2(2C), 127.6(2C), 127.0(2C), 125.0(2C), 119.9(2C), 81.7, 74.3, 67.0, 61.2, 57.7, 52.9, 50.6, 47.1, 31.2, 27.9(3C), 27.3(3C), 19.0, 18.9, 17.6. IR (thin film, cm^{-1}) 3291, 3065, 2969, 2935, 1705, 1644, 1535, 1474, 1450, 1391, 1313, 1221, 1143, 1115, 1078, 1045, 757. HRMS (ESI) calculated for $C_{34}H_{47}N_3O_7Na$ [M+Na]$^+$ *m/z* 632.3312, found 632.3310.



Fmoc-L-Ala-L-Thr(*t*-Bu)-L-Val-O*t*-Bu (5af) was prepared following **General Procedure 1** using H-L-Thr(*t*-Bu)-OH (43.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (35% AcOEt in hexane) to provide the title compound as a white solid in 91% yield with >20:1 dr (142 mg).

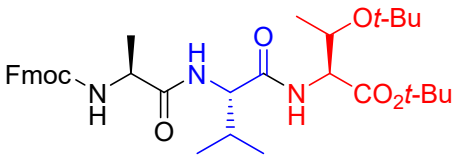
R_f = 0.61 (50% AcOEt in hexane). M.p. 100–105 °C. $[\alpha]_D^{20}$ = –36.7 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.72 (br d, J = 8.7 Hz, 1H, N*H*), 7.59 (d, *J* = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.39 (t, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.32–7.29 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.05 (br d, *J* = 7.0 Hz, 1H, N*H*), 5.53 (d, *J* = 7.3 Hz, 1H, N*H*), 4.38–4.32 (m, 5H, C*H*CH(CH$_3$)OC(CH$_3$)$_3$ and $C_{12}H_8CHC\underline{H_2}OCONH$ and C*H*CH$_3$ and C*H*CH(CH$_3$)$_2$), 4.23–4.19 (m, 2H, $C_{12}H_8C\underline{H}CH_2OCONH$ and CHC*H*(CH$_3$)OC(CH$_3$)$_3$), 2.22–2.12 (m, 1H, CHC*H*(CH$_3$)$_2$), 1.47 (s, 9H, CO$_2$C(C*H*$_3$)$_3$), 1.42 (d, *J* = 6.6 Hz, 3H, CHC*H*$_3$), 1.31 (s, 9H, CHCH(CH$_3$)OC(C*H*$_3$)$_3$), 1.08 (d, *J* = 6.4 Hz, 3H, CHCH(C*H*$_3$)OC(CH$_3$)$_3$), 0.95 (d, *J* = 6.9 Hz, 3H, CHCH(C*H*$_3$)$_2$), 0.92 (d, *J* = 6.9 Hz, 3H, CHCH(C*H*$_3$)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 170.2, 169.3, 155.6, 143.9, 143.8, 141.2(2C), 127.6(2C), 127.0(2C), 125.1(2C), 119.9(2C), 81.6, 75.5, 67.0, 66.2, 58.1, 57.3, 50.4, 47.1, 30.7, 28.2(3C), 28.0(3C), 19.2, 19.1, 17.5, 16.6. IR (thin film, cm^{-1}) 3305, 3034, 2967, 2931, 1705, 1644, 1531, 1475, 1453, 1391, 1311, 1221, 1144, 1110, 1075, 1045, 756. HRMS (ESI) calculated for $C_{35}H_{49}N_3O_7Na$ $[M+Na]^+$ *m/z* 646.3468, found 646.3462.



Fmoc-L-Ala-L-Val-L-Ser(*t*-Bu)-O*t*-Bu (5ag) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Ser(*t*-Bu)-O*t*-Bu (109 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature

for 24 h. The reaction mixture was purified by flash column chromatography (45% AcOEt in hexane) to provide the title compound as a white solid in 91% yield with >20:1 dr (139 mg).

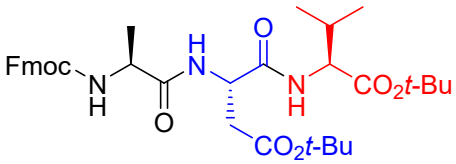
R_f = 0.44 (50% AcOEt in hexane). M.p. 150–155 °C. $[\alpha]_D^{22}$ = –51.4 (*c* 1.07, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.58 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.37 (t, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.30–7.26 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.04 (br d, *J* = 8.7 Hz, 1H, N*H*), 6.81 (br d, *J* = 8.0 Hz, 1H, N*H*), 5.85 (d, *J* = 8.0 Hz, 1H, N*H*), 4.62 (d, *J* = 8.0 Hz, 1H, C*H*$CH_2OC(CH_3)_3$), 4.49–4.33 (m, 4H, $C_{12}H_8CHC\underline{H_2}OCONH$ and C*H*CH_3 and C*H*$CH(CH_3)_2$), 4.20 (t, *J* = 7.4 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 3.73 (dd, *J* = 2.5 Hz, and 8.7 Hz, 1H, $CHC\underline{H_2}OC(CH_3)_3$), 3.47 (dd, *J* = 2.5 Hz, and 6.4 Hz, 1H, $CHC\underline{H_2}OC(CH_3)_3$), 2.17–2.09 (m, 1H, CHC*H*$(CH_3)_2$), 1.44 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.38 (d, *J* = 6.8 Hz, 3H, $CHC\underline{H_3}$), 1.10 (s, 9H, $CHCH_2OC(C\underline{H_3})_3$), 0.97 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.94 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 170.4, 169.1, 155.9, 143.8(2C), 141.2(2C), 127.6(2C), 127.0(2C), 125.1(2C), 119.8(2C), 81.8, 73.0, 67.0, 62.1, 58.1, 53.1, 50.4, 47.0, 31.6, 27.9(3C), 27.2(3C), 19.0(2C), 17.9. IR (thin film, cm^{-1}) 3289, 3067, 2973, 2935, 1706, 1641, 1526, 1449, 1392, 1366, 1249, 1231, 1194, 1152, 1079, 1047, 756. HRMS (ESI) calculated for $C_{34}H_{47}N_3O_7Na$ $[M+Na]^+$ *m/z* 632.3312, found 632.3308.



Fmoc-L-Ala-L-Val-L-Thr(*t*-Bu)-O*t*-Bu (5ah) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Thr(*t*-Bu)-O*t*-Bu (116 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (40% AcOEt in hexane) to provide the title compound as a white solid in 92% yield with >20:1 dr (143.4 mg).

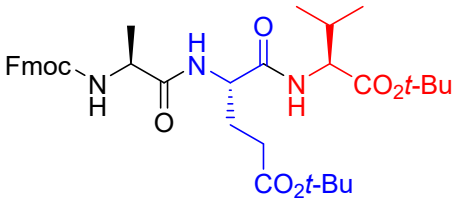
R_f = 0.59 (50% AcOEt in hexane). M.p. 110–115 °C. $[\alpha]_D^{20}$ = –89.0 (*c* 1.01, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.59–7.57 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.37 (t, *J* = 7.1 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.30–7.26 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.08 (br d, J = 8.7 Hz, 1H, N*H*), 6.59 (br d, *J* = 8.9 Hz, 1H, N*H*), 5.85 (d, *J* = 7.6 Hz, 1H, N*H*), 4.47–4.32 (m, 5H, C*H*$CH(CH_3)OC(CH_3)_3$ and $C_{12}H_8CHC\underline{H_2}OCONH$ and C*H*CH_3 and C*H*$CH(CH_3)_2$), 4.22–4.17 (m, 2H, $C_{12}H_8C\underline{H}CH_2OCONH$ and $CHC\underline{H}(CH_3)OC(CH_3)_3$), 2.18–2.10 (m, 1H, C*H*$(CH_3)_2$), 1.44 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.38 (d, *J* = 6.9 Hz, 3H, $CHC\underline{H_3}$), 1.14

(s, 9H, CHCH(CH_3)OC(C$\underline{H_3}$)$_3$), 1.14–1.10 (m, 3H, CHCH(C$\underline{H_3}$)OC(CH_3)$_3$), 0.99 (d, J = 6.9 Hz, 3H, CHCH(C$\underline{H_3}$)$_2$), 0.96 (d, J = 6.9 Hz, 3H, CHCH(C$\underline{H_3}$)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 170.9, 169.4, 155.8, 143.8, 143.7, 141.2(2C), 127.5(2C), 126.9(2C), 125.1(2C), 119.8(2C), 81.8, 73.7, 67.1, 67.0, 58.3, 58.2, 50.3, 47.0, 31.5, 28.6(3C), 28.0(3C), 20.7, 19.0(2C), 18.0. IR (thin film, cm^{-1}) 3291, 3065, 2971, 2935, 1705, 1644, 1535, 1475, 1451, 1391, 1313, 1221, 1143, 1110, 1078, 1045, 757. HRMS (ESI) calculated for $C_{35}H_{49}N_3O_7Na$ [M+Na]$^+$ *m/z* 646.3468, found 646.3464.



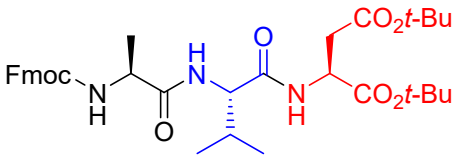
Fmoc-L-Ala-L-Asp(*t*-Bu)-L-Val-O*t*-Bu (5ai) was prepared following **General Procedure 1** using H-L-Asp(*t*-Bu)-OH (47.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (45% AcOEt in hexane) to provide the title compound as a white solid in 87% yield with >20:1 dr (139 mg).

R_f = 0.52 (50% AcOEt in hexane). M.p. 105–110 °C. $[\alpha]_D^{20}$ = –78.9 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.6 Hz, 2H, C$_{12}\underline{H_8}$CHCH$_2$OCONH), 7.59 (t, J = 6.8 Hz, 2H, C$_{12}\underline{H_8}$CHCH$_2$OCONH), 7.43–7.36 (m, 3H, C$_{12}\underline{H_8}$CHCH$_2$OCONH and N$\underline{H}$), 7.32–7.28 (m, 2H, C$_{12}\underline{H_8}$CHCH$_2$OCONH), 7.12 (br d, J = 8.7 Hz, 1H, N$\underline{H}$), 5.58 (d, J = 7.1 Hz, 1H, N$\underline{H}$), 4.83–4.79 (m, 1H, C$\underline{H}$CH$_2$CO$_2$C(CH$_3$)$_3$), 4.42–4.29 (m, 4H, C$_{12}$H$_8$CHC$\underline{H_2}$OCONH and C$\underline{H}$CH(CH$_3$)$_2$ and C$\underline{H}$CH$_3$), 4.21 (t, J = 7.1 Hz, 1H, C$_{12}$H$_8$C$\underline{H}$CH$_2$OCONH), 2.90 (dd, J = 3.4 Hz and 17 Hz, 1H, CHC$\underline{H_2}$CO$_2$C(CH$_3$)$_3$), 2.60 (dd, J = 7.1 Hz and 17 Hz, 1H, CHC$\underline{H_2}$CO$_2$C(CH$_3$)$_3$), 1.44–1.41 (m, 21H, CHCH$_2$CO$_2$C(C$\underline{H_3}$)$_3$ and CO$_2$C(C$\underline{H_3}$)$_3$ and CHC$\underline{H_3}$), 0.90 (d, J = 7.1 Hz, 3H, CHCH(C$\underline{H_3}$)$_2$), 0.88 (d, J = 7.1 Hz, 3H, CHCH(C$\underline{H_3}$)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 171.4, 170.1, 170.0, 155.8, 143.8, 143.7, 141.2(2C), 127.6(2C), 127.0(2C), 125.0(2C), 119.9(2C), 81.8, 81.7, 67.0, 57.8, 50.6, 49.2, 47.0, 36.8, 30.9, 27.9(3C), 27.8(3C), 18.8(2C), 17.4. IR (thin film, cm^{-1}) 3295, 2977, 2931, 1735, 1703, 1677, 1635, 1515, 1451, 1391, 1335, 1311, 1252, 1217, 1149, 1113, 1045, 756. HRMS (ESI) calculated for $C_{35}H_{47}N_3O_8Na$ [M+Na]$^+$ *m/z* 660.3229, found 660.3255.



Fmoc-L-Ala-L-Glu(*t*-Bu)-L-Val-O*t*-Bu (5aj) was prepared following **General Procedure 1** using H-L-Glu(*t*-Bu)-OH (50.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (45% AcOEt in hexane) to provide the title compound as a white solid in 85% yield with >20:1 dr (138 mg).

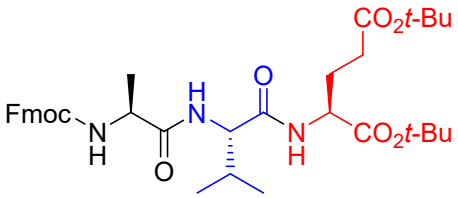
R_f = 0.50 (50% AcOEt in hexane). M.p. 120–125 °C. $[\alpha]_D^{24}$ = –116.5 (*c* 1.03, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.59 (d, *J* = 7.1 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.38 (t, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.31–7.26 (m, 3H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N$\underline{H}$), 7.13 (br d, *J* = 8.7 Hz, N$\underline{H}$), 5.77 (d, *J* = 7.3 Hz, 1H, N$\underline{H}$), 4.57 (quin., *J* = 6.4 Hz, 1H, C$\underline{H}CH_3$), 4.38–4.33 (m, 4H, C$\underline{H}CH(CH_3)_2$ and C$\underline{H}CH_2CH_2CO_2C(CH_3)_3$ and $C_{12}H_8CHC\underline{H_2}OCONH$), 4.21 (t, *J* = 7.1 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.49–2.34 (m, 2H, CHC$\underline{H}(CH_3)_2$ and $CHCH_2C\underline{H_2}CO_2C(CH_3)_3$), 2.19–1.94 (m, 3H, $CHCH_2C\underline{H_2}CO_2C(CH_3)_3$ and $CHC\underline{H_2}CH_2CO_2C(CH_3)_3$), 1.44 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.43 (s, 9H, $CHCH_2CH_2CO_2C(C\underline{H_3})_3$), 1.44–1.39 (m, 3H, CHC$\underline{H_3}$), 0.90 (d, *J* = 7.1 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.88 (d, *J* = 7.1 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 172.4, 170.7, 170.4, 155.8, 143.8, 143.7, 141.2(2C), 127.6(2C), 127.0(2C), 125.1(2C), 119.9(2C), 81.8, 81.0, 67.0, 57.8, 52.5, 50.5, 47.0, 31.7, 31.0, 28.0(3C), 27.9(3C), 19.2, 18.9(2C) 17.5. IR (thin film, cm^{-1}) 3298, 2975, 2933, 1730, 1705, 1676, 1638, 1518, 1450, 1392, 1335, 1311, 1253, 1217, 1149, 1113, 1045, 756. HRMS (ESI) calculated for $C_{36}H_{49}N_3O_8Na$ $[M+Na]^+$ *m/z* 674.3417, found 674.3417.



Fmoc-L-Ala-L-Val-L-Asp(*t*-Bu)-O*t*-Bu (5ak) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Asp(*t*-Bu)-O*t*-Bu (122 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient

temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (45% AcOEt in hexane) to provide the title compound as a white solid in 91% yield with >20:1 dr (145 mg).

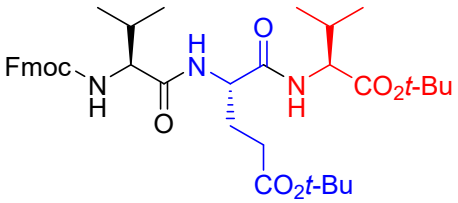
R_f = 0.47 (50% AcOEt in hexane). M.p. 210–215 °C. $[\alpha]_D^{21}$ = –13.8 (*c* 1.09, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.58 (d, *J* = 6.4 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.37 (t, *J* = 7.1 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.29–7.25 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.10–7.05 (m, 2H, N*H* and N*H*), 5.84 (d, *J* = 7.8 Hz, 1H, N*H*), 4.75 (dd, *J* = 3.9 Hz and 8.0 Hz, 1H, $C\underline{H}CH_2CO_2C(CH_3)_3$), 4.48–4.36 (m, 4H, $C_{12}H_8CHC\underline{H_2}OCONH$ and $C\underline{H}CH(CH_3)_2$ and $C\underline{H}CH_3$), 4.19 (t, *J* = 7.1 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.84 (dd, *J* = 4.6 Hz and 17 Hz, 1H, $CHC\underline{H_2}CO_2C(CH_3)_3$), 2.63 (dd, *J* = 3.9 Hz and 17 Hz, 1H, $CHC\underline{H_2}CO_2C(CH_3)_3$), 2.18–2.08 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.42 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.41 (s, 9H, $CHCH_2CO_2C(C\underline{H_3})_3$), 1.38 (d, *J* = 7.3 Hz, 3H, $CHC\underline{H_3}$), 0.97 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.94 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 170.4, 170.2, 169.4, 155.9, 143.8, 143.7, 141.2(2C), 127.6(2C), 126.9(2C), 125.1(2C), 119.8(2C), 82.2, 81.5, 67.0, 58.1, 50.4, 48.9, 47.0, 37.3, 31.6, 27.9(3C), 27.8(3C), 19.0, 18.9, 17.9. IR (thin film, cm^{-1}) 3293, 3017, 2977, 1725, 1644, 1510, 1450, 1393, 1368, 1214, 1150, 1077, 1048, 746. HRMS (ESI) calculated for $C_{35}H_{47}N_3O_8Na$ $[M+Na]^+$ *m/z* 660.3229, found 660.3260.



Fmoc-L-Ala-L-Val-L-Glu(*t*-Bu)-O*t*-Bu (5al) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Glu(*t*-Bu)-O*t*-Bu (130 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (45% AcOEt in hexane) to provide the title compound as a white solid in 89% yield with >20:1 dr (145 mg).

R_f = 0.47 (50% AcOEt in hexane). M.p. 145–150 °C. $[\alpha]_D^{21}$ = –67.7 (*c* 1.02, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.57 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.36 (t, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.28–7.22 (m, 3H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N*H*), 7.13 (br d, *J* = 8.5 Hz, N*H*), 6.07 (d, *J* = 7.8 Hz, 1H, N*H*), 4.49–

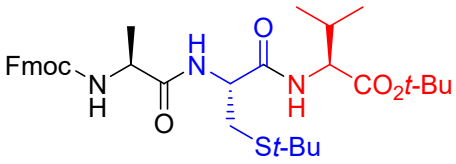
4.34 (m, 5H, C*H*CH(CH$_3$)$_2$ and C*H*CH$_3$ and C*H*CH$_2$CH$_2$CO$_2$C(CH$_3$)$_3$ and C$_{12}$H$_8$CHC*H$_2$*OCONH), 4.19 (t, *J* = 7.3 Hz, 1H, C$_{12}$H$_8$C*H*CH$_2$OCONH), 2.33–2.07 (m, 4H, CHC*H*(CH$_3$)$_2$ and CHC*H$_2$*CH$_2$CO$_2$C(CH$_3$)$_3$ and CHCH$_2$C*H$_2$*CO$_2$C(CH$_3$)$_3$), 1.93–1.84 (m, 1H, CHC*H$_2$*CH$_2$CO$_2$C(CH$_3$)$_3$), 1.42 (s, 9H, CO$_2$C(C*H$_3$*)$_3$), 1.40 (s, 9H, CHCH$_2$CH$_2$CO$_2$C(C*H$_3$*)$_3$), 1.38 (d, *J* = 7.3 Hz, 3H, CHC*H$_3$*), 0.95 (d, *J* = 6.9 Hz, 3H, CHCH(C*H$_3$*)$_2$), 0.94 (d, *J* = 6.9 Hz, 3H, CHCH(C*H$_3$*)$_2$). ^{13}C NMR (100 MHz, CDCl$_3$) δ 172.7, 172.0, 170.9, 170.7, 156.0, 143.9, 143.7, 141.2(2C), 127.5(2C), 126.9 (2C), 125.1 (2C), 119.8 (2C), 82.0, 80.6, 67.0, 58.3, 52.2, 50.3, 46.9, 31.3, 31.2, 27.9(3C), 27.8(3C), 27.4, 19.0(2C) 18.3. IR (thin film, cm^{-1}) 3286, 3067, 2975, 2933, 1729, 1703, 1643, 1531, 1450, 1392, 1367, 1252, 1228, 1150, 1112, 1078, 1041, 846, 756. HRMS (ESI) calculated for C$_{36}$H$_{49}$N$_3$O$_8$Na [M+Na]$^+$ *m/z* 674.3417, found 674.3411.



Fmoc-L-Val-L-Glu(*t*-Bu)-L-Val-O*t*-Bu (5am) was prepared following **General Procedure 1** using H-L-Glu(*t*-Bu)-OH (50.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N$_2$ atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N$_2$ atmosphere at ambient temperature. After 24 h, Fmoc-L-Val-Cl (268 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N$_2$ atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (33% AcOEt in hexane) to provide the title compound as a white solid in 86% yield with >20:1 dr (146 mg).

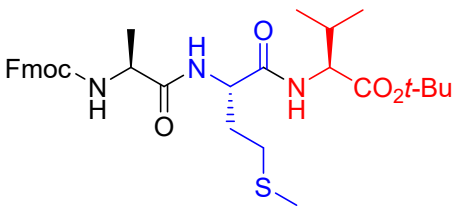
R_f = 0.34 (33% AcOEt in hexane). M.p. 175–180 °C. $[\alpha]_D^{24}$ = –117.1 (*c* 1.01, CHCl$_3$). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.74 (d, *J* = 7.3 Hz, 2H, C$_{12}$*H$_8$*CHCH$_2$OCONH), 7.62–7.59 (m, 2H, C$_{12}$*H$_8$*CHCH$_2$OCONH), 7.38 (t, *J* = 7.6 Hz, 2H, C$_{12}$*H$_8$*CHCH$_2$OCONH), 7.31–7.26 (m, 3H, C$_{12}$*H$_8$*CHCH$_2$OCONH and N*H*), 7.14 (br d, *J* = 8.0 Hz, N*H*), 5.84 (br d, *J* = 8.5 Hz, 1H, N*H*), 4.64–4.60 (m, 1H, C*H*CH(CH$_3$)$_2$), 4.45–4.30 (m, 3H, C*H*CH$_2$CH$_2$CO$_2$C(CH$_3$)$_3$ and C$_{12}$H$_8$CHC*H$_2$*OCONH), 4.23–4.16 (m, 2H, C$_{12}$H$_8$C*H*CH$_2$OCONH and C*H*CH(CH$_3$)$_2$), 2.49–2.34 (m, 2H, CHC*H*(CH$_3$)$_2$ and CHC*H*(CH$_3$)$_2$), 2.21–1.94 (m, 4H, CHCH$_2$C*H$_2$*CO$_2$C(CH$_3$)$_3$ and CHC*H$_2$*CH$_2$CO$_2$C(CH$_3$)$_3$), 1.44 (s, 9H, CO$_2$C(C*H$_3$*)$_3$), 1.42 (s, 9H, CHCH$_2$CH$_2$CO$_2$C(C*H$_3$*)$_3$), 0.94–0.87 (m, 12H, CHCH(C*H$_3$*)$_2$ and CHCH(C*H$_3$*)$_2$). ^{13}C NMR (100 MHz, CDCl$_3$) δ 173.0, 171.4, 170.9, 170.5, 156.3, 143.9, 143.8, 141.2 (2C), 127.6 (2C), 127.0 (2C), 125.2, 125.1, 119.8 (2C), 81.7, 80.9, 67.0, 60.1, 57.8, 52.4, 47.1, 31.7, 31.0, 28.1 (3C), 28.0 (3C), 19.1, 18.9 (2C), 17.9, 17.5 (2C). IR (thin film, cm^{-1}) 3305, 2975, 2930, 1715, 1705, 1675, 1641, 1517, 1441, 1393, 1331, 1311,

1251, 1217, 1149, 1110, 1045, 756. HRMS (ESI) calculated for $C_{38}H_{53}N_3O_8Na$ $[M+Na]^+$ *m/z* 702.3730, found 702.3723.



Fmoc-L-Ala-L-Cys(*t*-Bu)-L-Val-O*t*-Bu (5an) was prepared following **General Procedure 1** using H-L-Cys(*t*-Bu)-OH (53.4 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (40% AcOEt in hexane) to provide the title compound as a white solid in 89% yield with >20:1 dr (139 mg).

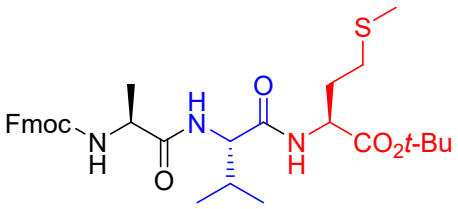
R_f = 0.56 (50% AcOEt in hexane). M.p. 130–135 °C. $[\alpha]_D^{20}$ = –78.9 (*c* 1.01, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.58 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.39 (t, *J* = 7.4 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.32–7.28 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.06–7.03 (m, 2H, N$\underline{H}$), 5.58 (d, *J* = 6.9 Hz, 1H, N$\underline{H}$), 4.58 (quin., *J* = 6.6 Hz, 1H, C$\underline{H}CH_3$), 4.39–4.33 (m, 4H, C$\underline{H}CH_2S(CH_3)_3$ and C$\underline{H}CH(CH_3)_2$ and $C_{12}H_8CHC\underline{H_2}OCONH$), 4.22 (t, *J* = 7.1 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 3.04 (dd, *J* = 5.3 Hz and 13.0 Hz, 1H, $CHC\underline{H_2}S(CH_3)_3$), 2.81 (dd, *J* = 7.3 Hz and 13.0 Hz, 1H, $CHC\underline{H_2}S(CH_3)_3$), 2.16–2.12 (m, 1H, C$\underline{H}(CH_3)_2$), 1.46 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.42 (d, *J* = 6.6 Hz, 3H, $CHC\underline{H_3}$), 1.32 (s, 9H, $CHCH_2S(C\underline{H_3})_3$), 0.92 (d, *J* = 5.5 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.90 (d, *J* = 5.5 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 170.2, 169.8, 155.8, 143.8, 143.7, 141.2(2C), 127.6(2C), 127.0(2C), 125.0(2C), 119.8(2C), 81.8, 67.1, 57.9, 53.1, 50.5, 47.0, 43.0, 31.2, 30.8(3C), 30.3, 27.9(3C), 19.0, 18.8, 17.7. IR (thin film, cm^{-1}) 3301, 3061, 2971, 1723, 1691, 1639, 1525, 1441, 1391, 1366, 1253, 1221, 1151, 1107, 1077, 1043, 756. HRMS (ESI) calculated for $C_{34}H_{47}N_3O_6SNa$ $[M+Na]^+$ *m/z* 648.3083, found 648.3066.



Fmoc-L-Ala-L-Met-L-Val-O*t*-Bu (5ao) was prepared following **General Procedure 1** using H-L-

Met-OH (37.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (40% AcOEt in hexane) to provide the title compound as a white solid in 91% yield with >20:1 dr (136 mg).

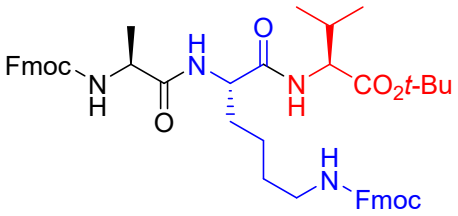
R_f = 0.56 (50% AcOEt in hexane). M.p. 180–185 °C. $[\alpha]_D^{20}$ = –75.5 (*c* 1.01, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.58 (d, *J* = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.38–7.35 (m, 3H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N*H*), 7.29–7.26 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.20 (br d, *J* = 8.7 Hz, N*H*), 6.03 (d, *J* = 7.8 Hz, 1H, N*H*), 4.82 (quin., *J* = 7.4 Hz, 1H, C*H*CH_3), 4.47–4.31 (m, 4H, C*H*$CH_2CH_2SCH_3$ and C*H*$CH(CH_3)_2$ and $C_{12}H_8CHC\underline{H_2}OCONH$), 4.20 (t, *J* = 7.1 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.56 (t, *J* = 7.3 Hz, 2H, $CHCH_2C\underline{H_2}SCH_3$), 2.17–1.96 (m, 3H, $CHC\underline{H_2}CH_2SCH_3$ and $CHC\underline{H}(CH_3)_2$), 2.04 (s, 3H, $CHCH_2CH_2SC\underline{H_3}$), 1.43 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.37 (d, *J* = 6.9 Hz, 3H, $CHC\underline{H_3}$), 0.89 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.86 (d, *J* = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 170.8, 170.5, 156.0, 143.8, 143.7, 141.1(2C), 127.6(2C), 127.0(2C), 125.1(2C), 119.8(2C), 81.8, 67.1, 57.6, 52.1, 50.3, 47.0, 31.6, 31.1, 29.8, 27.9(3C), 19.1, 18.8, 17.6, 14.9. IR (thin film, cm^{-1}) 3289, 3056, 2973, 1725, 1691, 1631, 1525, 1449, 1391, 1365, 1252, 1221, 1151, 1105, 1078, 1043, 756. HRMS (ESI) calculated for $C_{32}H_{43}N_3O_6SNa$ $[M+Na]^+$ *m/z* 620.2770, found 620.2765.



Fmoc-L-Ala-L-Val-L-Met-O*t*-Bu (5ap) was prepared following **General Procedure 1** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Met-O*t*-Bu (103 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (45% AcOEt in hexane) to provide the title compound as a white solid in 90% yield with >20:1 dr (134 mg).

R_f = 0.41 (50% AcOEt in hexane). M.p. 150–155 °C. $[\alpha]_D^{20}$ = –46.2 (*c* 1.17, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.57 (d, *J* = 7.3 Hz, 2H,

$C_{12}\underline{H_8}CHCH_2OCONH$), 7.49 (br d, J = 7.8 Hz, 1H, N$\underline{H}$), 7.44 (br d, J = 8.9 Hz, 1H, N$\underline{H}$), 7.34 (t, J = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.26–7.22 (m, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 6.36 (d, J = 8.2 Hz, 1H, N$\underline{H}$), 4.66–4.51 (m, 3H, C$\underline{H}CH_2CH_2SCH_3$ and C$\underline{H}CH_3$ and C$\underline{H}CH(CH_3)_2$), 4.36–4.29 (m, 2H, $C_{12}H_8CHC\underline{H_2}OCONH$), 4.17 (t, J = 7.4 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.53–2.38 (m, 2H, $CHCH_2C\underline{H_2}SCH_3$), 2.15–2.02 (m, 1H, CHC$\underline{H}(CH_3)_2$), 1.98 (s, 3H, $CHCH_2CH_2SC\underline{H_3}$), 1.95–1.86 (m, 2H, $CHC\underline{H_2}CH_2SCH_3$), 1.40 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.38 (d, J = 7.1 Hz, 3H, $CHC\underline{H_3}$), 0.96 (d, J = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.94 (d, J = 6.9 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 171.0, 170.7, 156.1, 143.8, 143.7, 141.2(2C), 127.5(2C), 126.9(2C), 125.1(2C), 119.8(2C), 82.1, 67.1, 58.5, 52.0, 50.3, 46.9, 31.9, 31.3, 29.8, 27.8(3C), 19.0(2C), 18.4, 15.3. IR (thin film, cm^{-1}) 3287, 3066, 2971, 1729, 1698, 1639, 1530, 1449, 1392, 1368, 1253, 1229, 1151, 1109, 1078, 1043, 756. HRMS (ESI) calculated for $C_{32}H_{43}N_3O_6SNa$ $[M+Na]^+$ *m/z* 620.2770, found 620.2774.

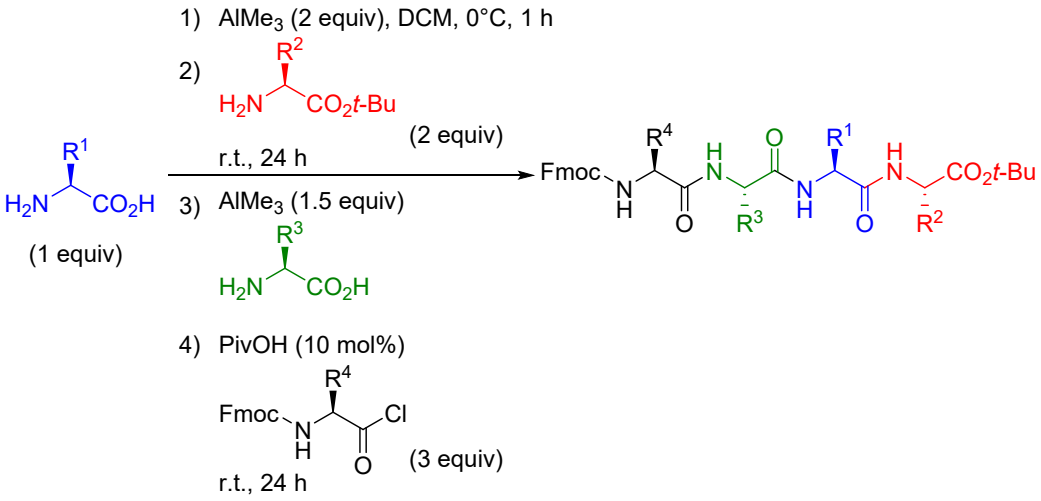


Fmoc-L-Ala-L-Lys(Fmoc)-L-Val-O*t*-Bu (5aq) was prepared following **General Procedure 1** using H-L-Lys(Fmoc)-OH (92.1 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (40% AcOEt in hexane) to provide the title compound as a white solid in 63% yield with >20:1 dr (129 mg).

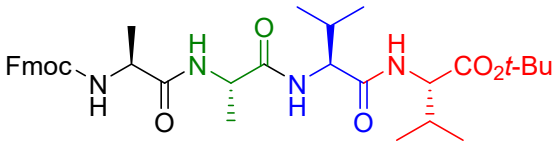
R_f = 0.38 (50% AcOEt in hexane). M.p. 205–210 °C. $[\alpha]_D^{22}$ = –56.4 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.93–7.85 (m, 6H, N$\underline{H}$ and $C_{12}\underline{H_8}CHCH_2OCONH$ and $C_{12}\underline{H_8}CHCH_2OCONH$), 7.73–7.55 (m, 5H, $C_{12}\underline{H_8}CHCH_2OCONH$ and $C_{12}\underline{H_8}CHCH_2OCONH$ and N$\underline{H}$), 7.41–7.23 (m, 9H, $C_{12}\underline{H_8}CHCH_2OCONH$ and $C_{12}\underline{H_8}CHCH_2OCONH$ and N$\underline{H}$), 4.40–4.03 (m, 9H, C$\underline{H}CH_3$ and C$\underline{H}CH_2CH_2CH_2CH_2NHFmoc$ and C$\underline{H}CH(CH_3)_2$ and $C_{12}H_8CHC\underline{H_2}OCONH$ and $C_{12}H_8C\underline{H}CH_2OCONH$ and $C_{12}H_8CHC\underline{H_2}OCONH$ and $C_{12}H_8C\underline{H}CH_2OCONH$), 2.98–2.96 (m, 2H, $CHCH_2CH_2CH_2C\underline{H_2}NHFmoc$), 2.06–1.97 (m, 1H, CHC$\underline{H}(CH_3)_2$), 1.70–1.69 (m, 1H, $CHC\underline{H_2}CH_2CH_2CH_2NHFmoc$), 1.58–1.50 (m, 1H, $CHC\underline{H_2}CH_2CH_2CH_2NHBoc$), 1.38 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.33–1.23 (m, 4H, $CHCH_2C\underline{H_2}CH_2CH_2NHFmoc$ and $CHCH_2CH_2C\underline{H_2}CH_2NHFmoc$), 0.87 (d, J = 6.2 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.85 (d, J = 6.2 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.4, 171.8, 170.4 (2C), 156.1, 155.7, 143.9 (2C), 143.8, 140.7 (2C), 127.6

(4C), 127.1 (4C), 125.3 (2C), 125.1 (2C), 120.0 (6C), 80.5 (2C), 65.7, 65.2, 57.9, 52.2, 50.1, 46.8, 46.7, 31.9, 30.0, 29.2, 27.6 (3C), 22.5, 18.9, 18.2, 18.0. IR (thin film, cm^{-1}) 3292, 3067, 2973, 2933, 1700, 1642, 1520, 1477, 1450, 1392, 1366, 1312, 1247, 1166, 1078, 1042, 756. HRMS (ESI) calculated for $C_{48}H_{56}N_4O_8Na$ $[M+Na]^+$ *m/z* 839.3996, found 839.3991.

6. General Procedure for One-Pot Tetrapeptide Synthesis



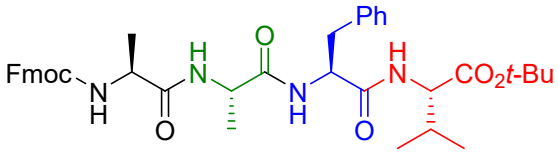
General procedure 2: A mixture of L-amino acid (0.250 mmol), trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), and dry DCM (1 mL) in a flame-dried 20 mL test tube equipped with a magnetic stirring bar was stirred vigorously for 1 h at 0 °C under N_2 atmosphere. Then, L-amino acid *tert*-butyl ester (0.500 mmol) was added to the above reaction solution. The mixture was allowed to stir vigorously under N_2 atmosphere at room temperature for 24 h. Then, a solution of trimethylaluminum 2M in hexane (188 µL, 0.375 mmol) and L-amino acid (0.250 mmol), which was stirred for 1 h, was added. After 24 h, Fmoc-L-amino acid chloride and pivalic acid (2.55 mg, 0.025 mmol) were added to the reaction solution, and stirring continued under N_2 atmosphere at room temperature for 24 h. The reaction mixture was then diluted with $CHCl_3$ (4.50 mL), transferred onto SiO_2 column using ~~by~~ a pipette, and the used test tube ~~vial~~ and pipette were washed with $CHCl_3$ (2 x 4.00 mL). The reaction mixture was purified by flash column chromatography (50–100% EtOAc in hexane) to provide the corresponding tetrapeptide as white solid.



Fmoc-L-Ala-L-Ala-L-Val-L-Val-O*t*-Bu (6a) was prepared following **General Procedure 2** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After

24 h, stirred solution of H-L-Ala-OH (22.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (188 μL, 0.375 mmol) was added into the reaction solution for further 24 h. Then, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (80% AcOEt in hexane) to provide the title compound as a white solid in 59% yield with >20:1 dr (92.4 mg).

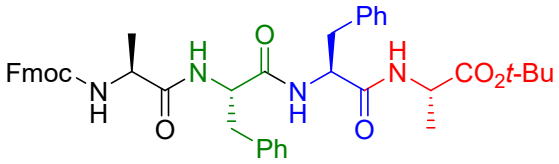
R_f = 0.35 (80% AcOEt in hexane). M.p. 175–180 °C. $[\alpha]_D^{22}$ = –32.9 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74–7.72 (m, 3H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N*H*), 7.58 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.41–7.24 (m, 6H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N*H*), 6.10 (br d, *J* = 8.2 Hz, 1H, N*H*), 4.81–4.78 (m, 1H, C*H*CH(CH$_3$)$_2$), 4.63–4.59 (m, 2H, C*H*CH$_3$ and C*H*CH(CH$_3$)$_2$) 4.49–4.29 (m, 3H, C*H*CH$_3$ and $C_{12}H_8CHC\underline{H_2}OCONH$), 4.19 (t, *J* = 7.3 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.12–2.02 (m, 2H, CHC*H*(CH$_3$)$_2$ and CHC*H*(CH$_3$)$_2$), 1.39 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.37–1.34 (m, 6H, CHC*H*$_3$ and CHC*H*$_3$), 0.95 (d, *J* = 6.9 Hz, 3H, CHCH(C*H*$_3$)$_2$), 0.93 (d, *J* = 6.9 Hz, 3H, CHCH(C*H*$_3$)$_2$), 0.85 (d, *J* = 6.9 Hz, 3H, CHCH(C*H*$_3$)$_2$), 0.81 (d, *J* = 6.9 Hz, 3H, CHCH(C*H*$_3$)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4 (2C), 171.2, 170.8, 155.9, 143.9 (2C), 141.2 (2C), 127.6 (2C), 127.0 (2C), 125.2 (2C), 119.9 (2C), 81.8, 67.1, 58.5, 57.6, 48.7, 47.1, 31.4, 31.3, 27.9 (3C), 19.7 (2C), 19.0 (2C), 18.8, 18.4, 17.7. IR (thin film, cm^{-1}) 3305, 3044, 2969, 2933, 1729, 1705, 1664, 1631, 1515, 1441, 1391, 1355, 1301, 1241, 1217, 1149, 1108, 1049, 753. HRMS (ESI) calculated for $C_{35}H_{48}N_4O_7Na$ $[M+Na]^+$ *m/z* 659.3421, found 659.3429.



Fmoc-L-Ala-L-Ala-L-Phe-L-Val-O*t*-Bu (6b) was prepared following **General Procedure 2** using H-L-Phe-OH (41.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, stirred solution of H-L-Ala-OH (22.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (188 μL, 0.375 mmol) was added into the reaction solution for further 24 h. Then, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (67% AcOEt in hexane) to provide the title compound as a white solid in 54% yield with >20:1 dr (92.4 mg).

R_f = 0.41 (67% AcOEt in hexane). M.p. 205–210 °C. $[\alpha]_D^{22}$ = –72.5 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.04 (d, *J* = 8.2 Hz, 1H, N*H*), 7.95 (d, *J* = 7.3 Hz, 1H, N*H*), 7.88–7.86 (m, 3H,

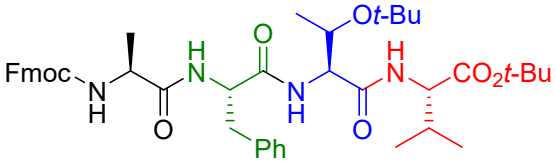
$C_{12}\underline{H_8}CHCH_2OCONH$ and N$\underline{H}$), 7.70 (t, J = 8.5 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.52 (d, J = 7.3 Hz, 1H, N$\underline{H}$), 7.39 (t, J = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.33–7.15 (m, 7H, $C_{12}\underline{H_8}CHCH_2OCONH$ and $CHCH_2C_6\underline{H_5}$), 4.63 (d t, J = 4.4 Hz and 8.9 Hz, 1H, C$\underline{H}CH_2Ph$), 4.26–3.99 (m, 6H, C$\underline{H}CH_3$ and C$\underline{H}CH_3$ and and C$\underline{H}CH(CH_3)_2$ and $C_{12}H_8C\underline{H}CH_2OCONH$ and $C_{12}H_8CHC\underline{H_2}OCONH$), 3.05 (dd, J = 4.4 Hz and 14 Hz, 1H, CHC$\underline{H_2}$Ph), 2.81 (dd, J = 8.9 Hz and 14 Hz, 1H, CHC$\underline{H_2}$Ph), 2.07–1.97 (m, 1H, CHC$\underline{H}(CH_3)_2$), 1.40 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.17 (d, J = 7.3 Hz, 3H, CHC$\underline{H_3}$), 1.14 (d, J = 6.9 Hz, 3H, CHC$\underline{H_3}$), 0.88 (d, J = 5.5 Hz, 3H, CHCH(C$\underline{H_3}$)$_2$), 0.86 (d, J = 5.5 Hz, 3H, CHCH(C$\underline{H_3}$)$_2$). ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.9, 171.7, 170.8, 170.2, 155.5, 143.7, 143.6, 140.5 (2C), 137.3 (2C), 129.0 (2C), 127.7 (2C), 127.4 (2C), 126.8 (2C), 126.0, 125.0, 119.8 (2C), 80.4, 65.4, 57.7, 53.1, 49.7, 47.9, 46.4, 37.2, 29.9, 27.4 (3C), 18.7, 18.0, 17.9, 17.8. IR (thin film, cm^{-1}) 3291, 3054, 2967, 2931, 1705, 1641, 1531, 1475, 1445, 1391, 1313, 1221, 1143, 1110, 1078, 1045, 757. HRMS (ESI) calculated for $C_{39}H_{48}N_4O_7Na$ $[M+Na]^+$ *m/z* 707.3420, found 707.3372.



Fmoc-L-Ala-L-Phe-L-Phe-L-Ala-O*t*-Bu (6c) was prepared following **General Procedure 2** using H-L-Phe-OH (41.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Ala-O*t*-Bu (72.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, stirred solution of H-L-Phe-OH (41.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (188 μL, 0.375 mmol) was added into the reaction solution for further 24 h. Then, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (60% AcOEt in hexane) to provide the title compound as a white solid in 66% yield with >20:1 dr (120.8 mg).

R_f = 0.51 (50% AcOEt in hexane). M.p. 225–230 °C. $[\alpha]_D^{22}$ = –89.5 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.33 (d, J = 6.9 Hz, 1H, N$\underline{H}$), 8.05 (d, J = 8.2 Hz, 1H, N$\underline{H}$), 7.87 (d, J = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.82 (d, J = 8.2 Hz, 1H, N$\underline{H}$), 7.69 (t, J = 7.8 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.45–7.38 (m, 3H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N$\underline{H}$), 7.32–7.10 (m, 12H, $C_{12}\underline{H_8}CHCH_2OCONH$ and $CHCH_2C_6\underline{H_5}$ and $CHCH_2C_6\underline{H_5}$), 4.55 (d t, J = 3.6 Hz and 9.2 Hz, 1H, C$\underline{H}CH_2Ph$), 4.45 (quin., J = 7.1 Hz, 1H, C$\underline{H}CH_3$), 4.29–3.95 (m, 5H, C$\underline{H}CH_2Ph$ and $C_{12}H_8C\underline{H}CH_2OCONH$ and $C_{12}H_8CHC\underline{H_2}OCONH$ and C$\underline{H}CH_3$), 3.06 (dd, J = 3.6 Hz and 14 Hz, 1H, CHC$\underline{H_2}$Ph), 2.93 (dd, J = 4.6 Hz and 14 Hz, 1H, CHC$\underline{H_2}$Ph), 2.83–2.71 (m, 2H, CHC$\underline{H_2}$Ph), 1.39 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.25 (d, J = 7.3 Hz, 3H, CHC$\underline{H_3}$), 1.09 (d, J = 7.1 Hz, 3H, CHC$\underline{H_3}$). ^{13}C NMR

(100 MHz, DMSO-d_6) δ 172.1, 171.6, 170.7, 170.6, 155.6, 143.9, 143.7, 140.7 (2C), 137.6, 137.5, 129.2 (4C), 128.0 (2C), 127.9 (2C), 127.6 (2C), 127.1 (2C), 126.2, 126.1, 125.3 (2C), 120.0 (2C), 80.4, 65.7, 53.6, 53.4, 50.0, 48.3, 46.6, 37.6, 37.4, 27.6 (3C), 18.1, 17.0. IR (thin film, cm^{-1}) 3296, 3033, 2931, 1701, 1644, 1533, 1475, 1441, 1389, 1311, 1213, 1144, 1114, 1078, 1044, 756. HRMS (ESI) calculated for $C_{43}H_{48}N_4O_7Na$ $[M+Na]^+$ *m/z* 755.3421, found 755.3428.

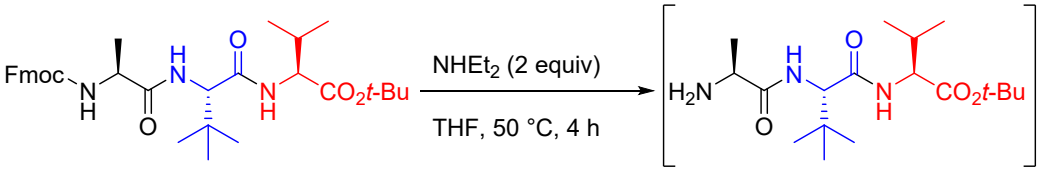


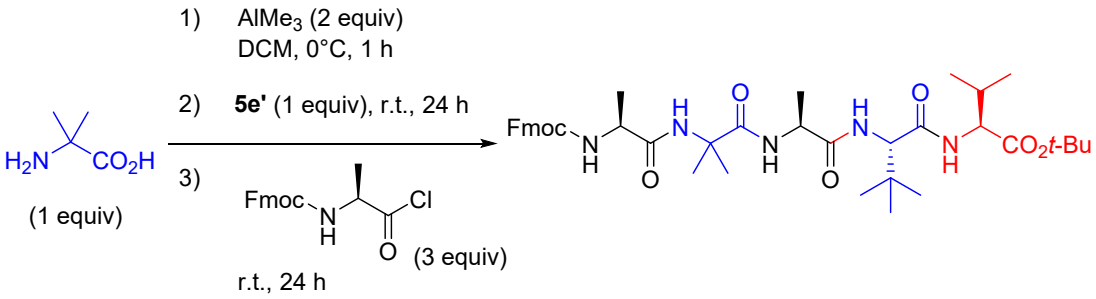
Fmoc-L-Ala-L-Phe-L-Thr(*t*-Bu)-L-Val-O*t*-Bu (6d) was prepared following **General Procedure 2** using H-L-Thr(*t*-Bu)-OH (43.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, stirred solution of H-L-Phe-OH (41.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (188 μL, 0.375 mmol) was added into the reaction solution for further 24 h. Then, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (40% AcOEt in hexane) to provide the title compound as a white solid in 56% yield with >20:1 dr (107.8 mg).

R_f = 0.56 (50% AcOEt in hexane). M.p. 155–160 °C. $[\alpha]_D^{22}$ = –52.8 (*c* 1.01, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.65 (br d, *J* = 8.5 Hz, 1H, N$\underline{H}$), 7.58 (t, *J* = 7.4 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.38 (t, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.31–7.06 (m, 8H, $C_{12}\underline{H_8}CHCH_2OCONH$ and $CHCH_2C_6\underline{H_5}$ and N$\underline{H}$), 6.86 (d, *J* = 7.3 Hz, 1H, N$\underline{H}$), 5.68 (d, *J* = 7.8 Hz, 1H, N$\underline{H}$), 4.86 (quin., *J* = 6.6 Hz, 1H, C$\underline{H}CH_3$), 4.39–4.29 (m, 5H, C$\underline{H}CH(CH_3)OC(CH_3)_3$ and C$\underline{H}CH(CH_3)_2$ and $C_{12}H_8CHC\underline{H_2}OCONH$ and $CHC\underline{H}(CH_3)OC(CH_3)_3$), 4.20–4.12 (m, 2H, C$\underline{H}CH_2Ph$ and $C_{12}H_8C\underline{H}CH_2OCONH$), 3.11 (dd, *J* = 5.7 Hz and 14 Hz, 1H, $CHC\underline{H_2}Ph$), 3.03 (dd, *J* = 6.9 Hz and 14 Hz, 1H, $CHC\underline{H_2}Ph$), 2.19–2.13 (m, 1H, $CHC\underline{H}(CH_3)_2$), 1.44 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.33 (d, *J* = 6.6 Hz, 3H, $CHC\underline{H_3}$), 1.26 (s, 9H, $CHCH(CH_3)OC(C\underline{H_3})_3$), 1.01 (d, *J* = 5.5 Hz, 3H, $CHCH(C\underline{H_3})OC(CH_3)_3$), 0.94 (d, *J* = 6.7 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.90 (d, *J* = 6.7 Hz, 3H, $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 170.3, 170.2, 169.1, 155.8, 143.7, 141.2 (2C), 135.9, 129.1 (2C), 128.4 (2C), 127.6 (2C), 127.0 (2C), 126.9, 125.1, 125.0 (2C), 119.8 (2C), 81.5, 75.3, 66.9, 66.3, 57.8, 57.3, 54.0, 50.3, 47.0, 38.3, 30.8, 28.1 (3C), 28.0 (3C), 19.0, 18.6, 17.5, 16.8. IR (thin film, cm^{-1}) 3302, 3024, 2967, 2931, 1705, 1645, 1531, 1475, 1455, 1391, 1313, 1221, 1144, 1115, 1075, 1045, 756. HRMS (ESI) calculated for $C_{44}H_{58}N_4O_8Na$ $[M+Na]^+$ *m/z* 793.4152, found 793.4159.

7. Procedure for Pentapeptide Synthesis

7-1. Pentapeptide Synthesis





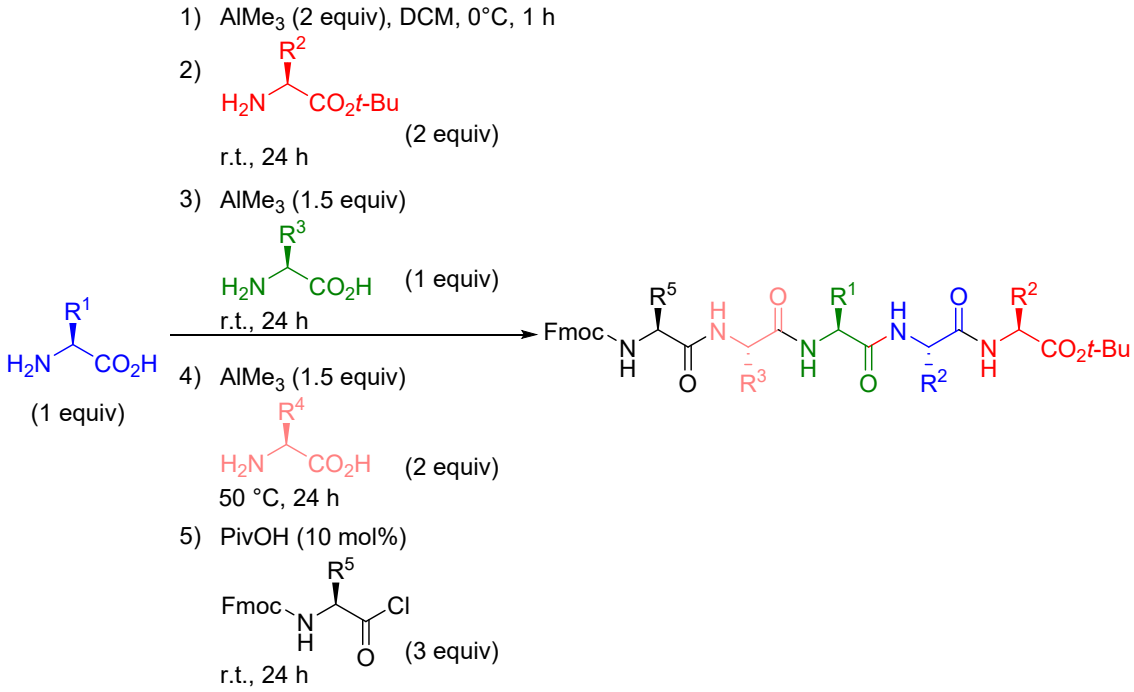
Procedure: To a flame dried round-bottom flask charged with **5e** (145 mg, 0.250 mmol) and THF (5 mL), ~~were added~~ diethylamine (52.2 µL, 0.500 mmol) was added. The reaction mixture was stirred in an oil bath at 50 °C for 4 h. After completion of the reaction, ~~distilled off~~ THF and diethylamine were distilled in vacuo using an evaporator. The residue **5e'** was used for next reaction without purification~~ as 5e'~~.

Fmoc-L-Ala-Aib-L-Ala-L-Tle-L-Val-O*t*-Bu (7a) was prepared as follows ~~procedure~~ ~~below~~. A mixture of H-Aib-OH (25.8 mg, 0.250 mmol), trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), and dry DCM (1 mL) in a flame-dried 20 mL test tube equipped with a magnetic stirring bar was stirred vigorously for 1 h at 0 °C under N_2 atmosphere. Then, **5e'** was added to the above reaction solution. The mixture was allowed to stir vigorously under N_2 atmosphere at room temperature for 24 h. Then, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) was added to the reaction solution, and stirring was continued under N_2 atmosphere at room temperature for 24 h. The reaction mixture was then diluted with $CHCl_3$ (4.50 mL), transferred onto SiO_2 column using ~~by~~ a pipette, and the used test tube ~~vial~~ and pipette were washed with $CHCl_3$ (2 x 4.00 mL). The reaction mixture was purified by flash column chromatography (82% EtOAc in hexane) to provide the corresponding pentapeptide as white solid in 34 % yield with >20:1 dr (62.5 mg).

R_f = 0.26 (80% AcOEt in hexane). M.p. 115–120 °C. $[\alpha]_D^{20}$ = –32.8 (*c* 1.11, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.56 (dd, *J* = 3.9 Hz and 7.4 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.38 (t, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.30–7.21 (m, 4H,

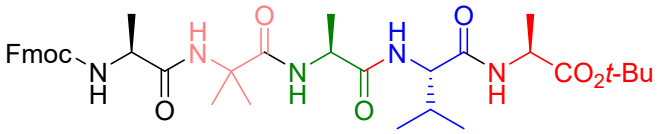
$C_{12}\underline{H_8}CHCH_2OCONH$ and N$\underline{H}$), 7.12 (br s, 1H, N$\underline{H}$), 7.06 (br d, J = 8.5 Hz, 1H, N$\underline{H}$), 6.00 (d, J = 6.0 Hz, 1H, N$\underline{H}$), 4.61–4.52 (m, 2H, C$\underline{H}CH_3$ and C$\underline{H}C(CH_3)_3$), 4.40–4.32 (m, 3H, $C_{12}H_8CHC\underline{H_2}OCONH$ and C$\underline{H}CH(CH_3)_2$), 4.27–4.19 (m, 2H, C$\underline{H}CH_3$ and $C_{12}H_8C\underline{H}CH_2OCONH$), 2.13–2.03 (m, 1H, CHC$\underline{H}(CH_3)_2$), 1.54 (s, 3H, C(C$\underline{H_3}$)$_2$), 1.53 (s, 3H, C(C$\underline{H_3}$)$_2$). 1.42 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.37 (d, J = 7.1 Hz, 3H, CHC$\underline{H_3}$), 1.34 (d, J = 7.1 Hz, 3H, CHC$\underline{H_3}$), 0.99 (s, 9H, CHC(C$\underline{H_3}$)$_3$), 089 (d, J = 6.9 Hz, 3H, CHCH(C$\underline{H_3}$)$_2$), 0.84 (d, J = 6.9 Hz, 3H, CHCH(C$\underline{H_3}$)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 172.6, 172.5, 170.8, 170.5, 156.4, 143.7, 143.6, 141.2 (2C), 127.7 (2C), 127.0 (2C), 125.0 (2C), 119.9 (2C), 81.7, 67.1, 60.6, 57.9, 56.9, 51.2, 49.6, 47.0, 34.6, 31.1, 27.9 (3C), 26.7 (3C), 25.2, 24.9, 18.9, 18.3, 18.1, 18.0. IR (thin film, cm^{-1}) 3305, 3012, 2967, 1707, 1645, 1530, 1478, 1368, 1297, 1192, 1115, 1077, 1045, 764. HRMS (ESI) calculated for $C_{40}H_{57}N_5O_8Na$ [M+Na]$^+$ *m/z* 758.4105, found 758.4120.

7-2. One-Pot Pentapeptide Synthesis



General procedure 3: A mixture of L-amino acid (0.250 mmol), trimethylaluminum 2M in hexane (250 μL, 0.500 mmol), and dry DCM (1 mL) in a flame-dried 20 mL test tube equipped with a magnetic stirring bar was stirred vigorously for 1 h at 0 °C under N_2 atmosphere. Then, L-amino acid *tert*-butyl ester (0.500 mmol) was added to the above reaction solution. The mixture was allowed to stir vigorously under N_2 atmosphere at room temperature for 24 h. Then, a solution of trimethylaluminum 2M in hexane (188 μL, 0.375 mmol) and L-amino acid (0.250 mmol), which was

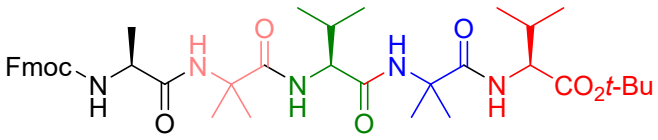
stirred for 1 h, was added. After 24 h, a solution of trimethylaluminum 2M in hexane (250 µL, 0.500 mmol) and L-amino acid (0.500 mmol), which was stirred for 1 h, was added. And the mixture was allowed to stir vigorously under N_2 atmosphere at 50 °C for 24 h. Then, Fmoc-L-amino acid chloride and pivalic acid (2.55 mg, 0.025 mmol) were added to the reaction solution, and stirring continued under N_2 atmosphere at room temperature for 24 h. The reaction mixture was then diluted with $CHCl_3$ (4.50 mL), transferred to a SiO_2 column using pipette; and the used test tube and pipette were washed with $CHCl_3$ (2 x 4.00 mL). The reaction mixture was purified by flash column chromatography (50–100% EtOAc in hexane) to provide the corresponding tetrapeptide as white solid.



Fmoc-L-Ala-Aib-L-Ala-L-Val-L-Ala-O*t*-Bu (7b) was prepared following **General Procedure 3** using H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Ala-O*t*-Bu (72.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, stirred solution of H-L-Ala-OH (22.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (188 µL, 0.375 mmol) was added. After 24 h, a solution of trimethylaluminum 2M in hexane (250 µL, 0.500 mmol) and H-Aib-OH (51.6 mg, 0.500 mmol), which was stirred for 1 h, was added. And the mixture was allowed to stir vigorously under N_2 atmosphere at 50 °C for 24 h. Then, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (AcOEt) to provide the title compound as a white solid in 60% yield with >20:1 dr (104.0 mg).

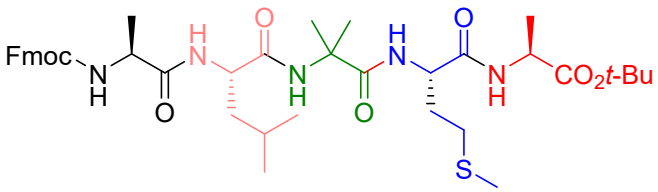
R_f = 0.28 (AcOEt). M.p. 85–90 °C. $[\alpha]_D^{21}$ = –34.5 (*c* 1.16, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.58 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.41–7.23 (m, 8H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N$\underline{H}$ and N$\underline{H}$ and N$\underline{H}$ and N$\underline{H}$), 6.72 (d, *J* = 2.5 Hz, 1H, N$\underline{H}$), 4.48–4.21 (m, 6H, C$\underline{H}CH_3$ and C$\underline{H}CH_3$ and C$\underline{H}CH_3$ and C$\underline{H}CH(CH_3)_2$ and $C_{12}H_8CHC\underline{H_2}OCONH$), 3.98–3.95 (m, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.45–2.36 (m, 1H, CHC$\underline{H}(CH_3)_2$), 1.52 (s, 3H, C(C$\underline{H_3}$)$_2$), 1.44 (s, 3H, C(C$\underline{H_3}$)$_2$), 1.42 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.42–1.36 (m, 9H, CHC$\underline{H_3}$ and CHC$\underline{H_3}$ and CHC$\underline{H_3}$), 0.96 (d, *J* = 6.9 Hz, 3H, CHCH(C$\underline{H_3}$)$_2$), 0.93 (d, *J* = 6.9 Hz, 3H, CHCH(C$\underline{H_3}$)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 173.9, 173.5, 171.7, 171.4, 157.4, 143.6, 143.5, 141.2 (2C), 127.8 (2C), 127.1 (2C), 124.9, 124.8, 119.9 (2C), 81.2, 67.4, 58.6, 56.6, 53.0, 50.9, 49.1, 47.0, 29.8, 27.8 (3C), 26.9, 23.6, 19.3, 17.7, 17.5, 17.4, 16.9. IR (thin film, cm^{-1}) 3307, 2979, 2935, 1642, 1530, 1450, 1382, 1368, 1298, 1251, 1192, 1151, 1118, 1077, 1033, 847.

HRMS (ESI) calculated for $C_{37}H_{51}N_5O_8Na$ $[M+Na]^+$ *m/z* 716.3635, found 716.3607.



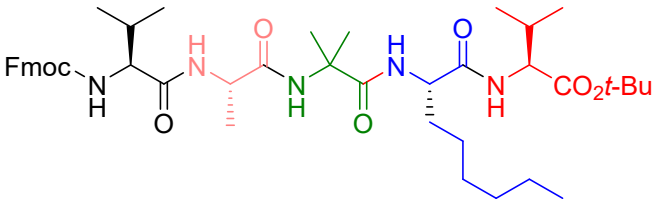
Fmoc-L-Ala-Aib-L-Val-Aib-L-Val-O*t*-Bu (7c) was prepared following **General Procedure 3** using H-Aib-OH (25.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, stirred solution of H-L-Val-OH (29.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (188 µL, 0.375 mmol) was added. After 24 h, a solution of trimethylaluminum 2M in hexane (250 µL, 0.500 mmol) and H-Aib-OH (51.6 mg, 0.500 mmol), which was stirred for 1 h, was added. And the mixture was allowed to stir vigorously under N_2 atmosphere at 50 °C for 24 h. Then, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (82% AcOEt in hexane) to provide the title compound as a white solid in 51% yield with >20:1 dr (93.8 mg).

R_f = 0.23 (80% AcOEt in hexane). M.p. 95–100 °C. $[\alpha]_D^{21}$ = –45.0 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.56 (t, *J* = 6.9 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.38 (t, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.31–7.26 (m, 3H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N*H*), 7.16 (br s, 1H, N*H*), 7.02 (br d, *J* = 8.9 Hz, 1H, N*H*), 6.96 (br d, *J* = 8.5 Hz, 1H, N*H*), 6.63 (d, *J* = 3.0 Hz, 1H, N*H*), 4.36–4.29 (m, 3H, C*H*CH_3 and $C_{12}H_8CHC\underline{H_2}OCONH$), 4.25–4.19 (m, 2H, C*H*$CH(CH_3)_2$ and $C_{12}H_8C\underline{H}CH_2OCONH$), 4.05–3.99 (m, 1H, C*H*$CH(CH_3)_2$), 2.50–2.42 (m, 1H, CHC*H*$(CH_3)_2$), 2.02–1.93 (m, 1H, CHC*H*$(CH_3)_2$), 1.57 (s, 3H, $C(C\underline{H_3})_2$), 1.56 (s, 3H, $C(C\underline{H_3})_2$), 1.47 (s, 3H, $C(C\underline{H_3})_2$), 1.42 (s, 3H, $C(C\underline{H_3})_2$), 1.40 (d, *J* = 6.9 Hz, 3H, $CHC\underline{H_3}$), 1.39 (s, 9H, $CO_2C(C\underline{H_3})_3$), 0.88 (d, *J* = 6.8 Hz, 3H, $CHCH(C\underline{H_3})_2$), 0.83–0.78 (m, 9H, $CHCH(C\underline{H_3})_2$ and $CHCH(C\underline{H_3})_2$ and $CHCH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 174.7, 173.7, 170.9, 170.7, 157.3, 143.6, 143.3, 141.2, 141.1, 127.8 (2C), 127.1 (2C), 124.8 (2C), 120.0 (2C), 81.3, 67.5, 58.9, 57.1, 56.9, 53.0, 46.8, 30.8, 28.8, 27.8 (3C), 27.4, 25.9, 24.9, 23.3, 19.4, 18.9, 18.5, 17.1 (2C), 17.0. IR (thin film, cm^{-1}) 3309, 3018, 1664, 1525, 1451, 1368, 1296, 1214, 1159, 1078, 1035, 744. HRMS (ESI) calculated for $C_{40}H_{57}N_5O_8Na$ $[M+Na]^+$ *m/z* 758.4105, found 758.4128.



Fmoc-L-Ala-L-Leu-Aib-L-Met-L-Ala-O*t*-Bu (7d) was prepared following **General Procedure 3** using H-Met-OH (37.3 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Ala-O*t*-Bu (72.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, stirred solution of H-Aib-OH (25.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (188 µL, 0.375 mmol) was added. After 24 h, a solution of trimethylaluminum 2M in hexane (250 µL, 0.500 mmol) and H- L-Leu-OH (65.6 mg, 0.500 mmol), which was stirred for 1 h, was added. And the mixture was allowed to stir vigorously under N_2 atmosphere at 50 °C for 24 h. Then, Fmoc-L-Ala-Cl (247 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (75% AcOEt in hexane) to provide the title compound as a white solid in 60% yield with >20:1 dr (115.1 mg).

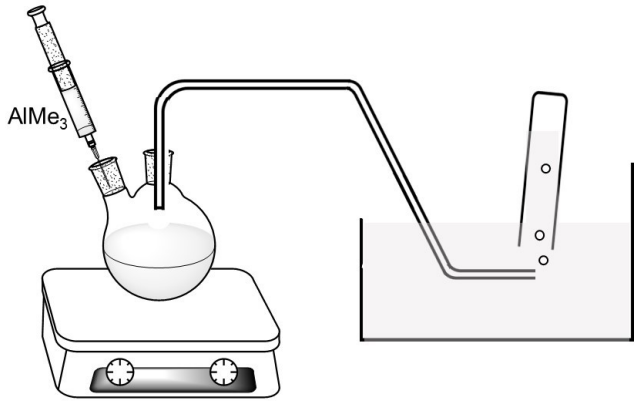
R_f = 0.41 (75% AcOEt in hexane). M.p. 75–80 °C. $[\alpha]_D^{23}$ = –62.1 (*c* 1.03, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.4 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.59 (t, *J* = 8.2 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.46 (br d, *J* = 7.4 Hz, 1H, N*H*), 7.40 (t, *J* = 7.3 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.33–7.23 (m, 3H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N*H*), 7.07 (br s, 1H, N*H*), 6.97 (br d, *J* = 5.3 Hz, 1H, N*H*), 6.09 (br d, *J* = 3.2 Hz, 1H, N*H*), 4.55–4.49 (m, 1H, $C\underline{H}CH_2CH_2SCH_3$), 4.46–4.34 (m, 3H, $C\underline{H}CH_3$ and $C_{12}H_8CHC\underline{H_2}OCONH$), 4.24–4.19 (m, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 4.12–4.06 (m, 2H, $C\underline{H}CH_2CH(CH_3)_2$ and $C\underline{H}CH_3$), 2.61–2.48 (m, 2H, $CHCH_2C\underline{H_2}SCH_3$), 2.36–2.30 (m, 1H, $CHC\underline{H_2}CH_2SCH_3$), 2.13–2.05 (m, 1H, $CHC\underline{H_2}CH_2SCH_3$), 2.02 (s, 3H, $CHCH_2CH_2SC\underline{H_3}$), 1.71–1.53 (m, 3H, $CHC\underline{H_2}CH(CH_3)_2$ and $CHCH_2C\underline{H}(CH_3)_2$), 1.53 (s, 3H, $C(C\underline{H_3})_2$), 1.45–1.37 (m, 18H, $C(C\underline{H_3})_2$ and $CHC\underline{H_3}$ and $CHC\underline{H_3}$ and $CO_2C(C\underline{H_3})_3$), 0.93 (d, *J* = 6.0 Hz, 3H, $CHCH_2CH(C\underline{H_3})_2$), 0.88 (d, *J* = 6.0 Hz, 3H, $CHCH_2CH(C\underline{H_3})_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 172.2, 172.0 (2C), 171.4, 156.9, 143.6, 143.4, 141.2, 127.8 (2C), 127.1 (2C), 124.9, 124.8, 120.0 (2C), 81.3, 67.2, 57.1, 53.9, 52.9, 52.1, 49.1, 47.0, 39.5, 30.7, 30.6, 27.9 (3C), 26.3, 24.9, 24.4, 22.7, 21.8, 17.6, 17.3, 15.2 (2C). IR (thin film, cm^{-1}) 3308, 3018, 1656, 1528, 1450, 1368, 1297, 1214, 1152, 746. HRMS (ESI) calculated for $C_{40}H_{57}N_5O_8SNa$ $[M+Na]^+$ *m/z* 790.3826, found 790.3829.



Fmoc-L-Val-L-Ala-Aib-L-Aoc(2)-L-Val-O*t*-Bu (7e) was prepared following **General Procedure 3** using H-Aoc(2)-OH (39.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (250 µL, 0.500 mmol), the resulting mixture was stirred in DCM under N_2 atmosphere at 0 °C. After 1 h, L-Val-O*t*-Bu (86.6 mg, 0.500 mmol) was added. The mixture was stirred under N_2 atmosphere at ambient temperature. After 24 h, stirred solution of H-Aib-OH (25.8 mg, 0.250 mmol) and trimethylaluminum 2M in hexane (188 µL, 0.375 mmol) was added. After 24 h, a solution of trimethylaluminum 2M in hexane (250 µL, 0.500 mmol) and H- L-Ala-OH (44.6 mg, 0.500 mmol), which was stirred for 1 h, was added. And the mixture was allowed to stir vigorously under N_2 atmosphere at 50 °C for 24 h. Then, Fmoc-L-Val-Cl (268 mg, 0.750 mmol) and pivalic acid (2.55 mg, 0.025 mmol) were added into the reaction solution and stirring under N_2 atmosphere at room temperature for 24 h. The reaction mixture was purified by flash column chromatography (80% AcOEt in hexane) to provide the title compound as a white solid in 53% yield with >20:1 dr (104.9 mg).

R_f = 0.34 (80% AcOEt in hexane). M.p. 135–142 °C. $[\alpha]_D^{23}$ = –48.0 (*c* 1.03, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.57 (d, *J* = 7.6 Hz, 2H, $C_{12}\underline{H_8}CHCH_2OCONH$), 7.40–7.25 (m, 6H, $C_{12}\underline{H_8}CHCH_2OCONH$ and N*H* and N*H*), 7.17 (br d, *J* = 7.4 Hz, 1H, N*H*), 7.06 (br s, 1H, N*H*), 6.00 (br d, *J* = 6.6 Hz, 1H, N*H*), 4.48–4.39 (m, 2H, C*H*CH_3 and C*H*$CH_2CH_2CH_2CH_2CH_2CH_3$), 4.33–4.29 (m, 2H, $C_{12}H_8CHC\underline{H_2}OCONH$), 4.26–4.19 (m, 2H, C*H*$CH(CH_3)_2$ and C*H*$CH(CH_3)_2$), 3.97 (t, *J* = 6.6 Hz, 1H, $C_{12}H_8C\underline{H}CH_2OCONH$), 2.23–2.04 (m, 2H, CHC*H*$(CH_3)_2$ and CHC*H*$(CH_3)_2$), 2.00–1.93 (m, 1H, $CHC\underline{H_2}CH_2CH_2CH_2CH_2CH_3$), 1.75–1.69 (m, 1H, $CHC\underline{H_2}CH_2CH_2CH_2CH_2CH_3$), 1.54 (s, 3H, $C(C\underline{H_3})_2$), 1.47 (s, 3H, $C(C\underline{H_3})_2$), 1.45 (s, 9H, $CO_2C(C\underline{H_3})_3$), 1.38 (d, *J* = 6.9 Hz, 3H, $CHC\underline{H_3}$), 1.33–1.22 (m, 8H, $CHCH_2C\underline{H_2}CH_2CH_2CH_2CH_3$ and $CHCH_2CH_2C\underline{H_2}CH_2CH_2CH_3$ and $CHCH_2CH_2CH_2C\underline{H_2}CH_2CH_3$ and $CHCH_2CH_2CH_2CH_2C\underline{H_2}CH_3$), 0.98–0.92 (m, 12H, $CHCH(C\underline{H_3})_2$ and $CHCH(C\underline{H_3})_2$), 0.82 (t, *J* = 6.6 Hz, 3H, $CHCH_2CH_2CH_2CH_2CH_2C\underline{H_3}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 172.5, 172.3, 172.2, 170.8, 156.9, 143.7, 143.5, 141.2, 127.7 (2C), 127.0 (2C), 125.0, 124.9, 119.9 (2C), 81.5, 67.1, 61.1, 58.5, 57.1, 54.0, 50.8, 47.0, 32.0, 31.6, 30.7, 30.5, 28.9, 27.9 (3C), 26.1, 25.8, 24.4, 22.5 (2C), 19.2, 18.9, 18.2, 17.1, 13.9 (2C). IR (thin film, cm^{-1}) 3315, 2964, 2930, 2248, 1706, 1644, 1524, 1450, 1368, 1275, 1227, 1148, 1031, 907, 726. HRMS (ESI) calculated for $C_{44}H_{65}N_5O_8Na$ $[M+Na]^+$ *m/z* 814.4730, found 814.4721.

8. Procedure for Time Course of Gas Generation



Gases were measured in volume by displacement over water and yields were calculated based on ideal gas (1 mmol = 22.4 mL).

A flame-dried 50 mL two-necked flask with a magnetic stirring bar was charged with substrate (1 mmol) and dichloromethane (5 mL) under N_2 atmosphere. One of the necks of the flask was connected by a tube to an inverted graduated cylinder filled with water. Then, trimethylaluminum 2M in hexane (550 μL, 1.1 mmol) was added under room temperature.

Benzylamine; gas was barely detected.

3-Phenylpropionic acid; 22 mL of gas was gathered within 10 min. And no further gasses were observed.

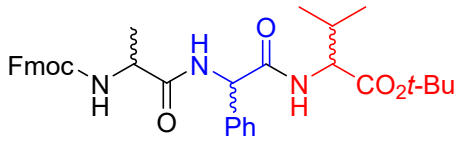
Phenylalanine; 27 mL of gas was gathered within 10 min. Gasses were gradually generated thereafter, and finally 44 mL of gasses could be gathered for one hour.

9. HPLC data

Conditions:

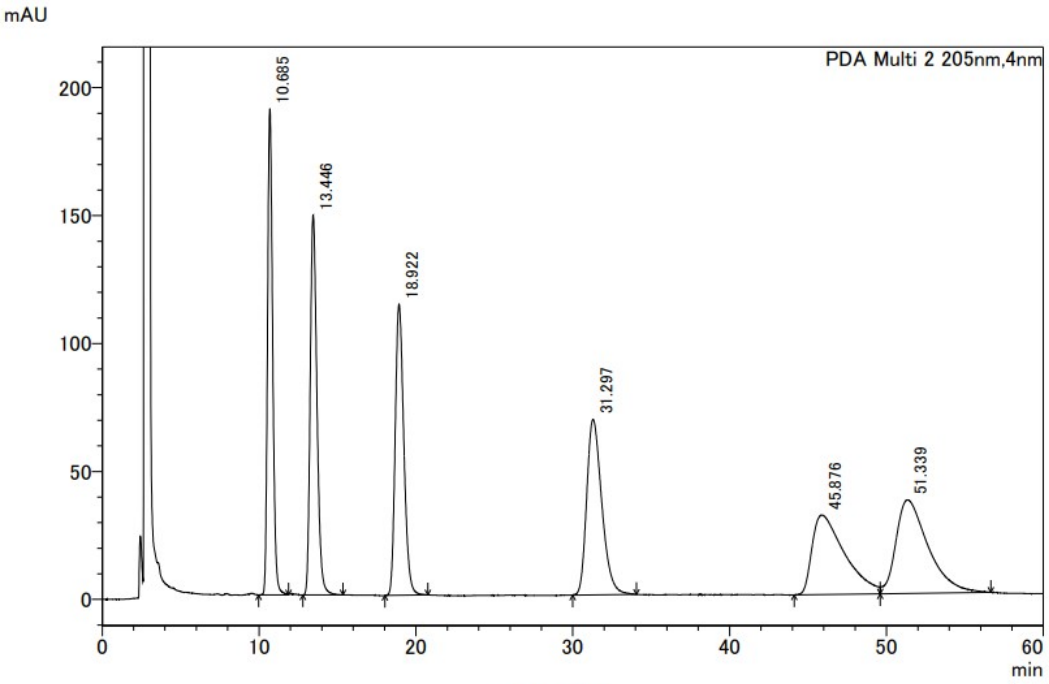
Chiral Column:

Racemic



Sample Information

Injection Volume : 10
Data File : Fmoc-rac.Ala-rac.Phg-rac.Val-OtBu.lcd
Method File : IE 80 20 1.5ml 60min.lcm



Peak Table

PDA Ch2 205nm

Peak#	Ret. Time	Area	Area%
1	10.685	4303848	15.748
2	13.446	4427188	16.199
3	18.922	4330797	15.846
4	31.297	4590956	16.798
5	45.876	4462308	16.327
6	51.339	5215011	19.082
Total		27330107	100.000

Retention time (min.);

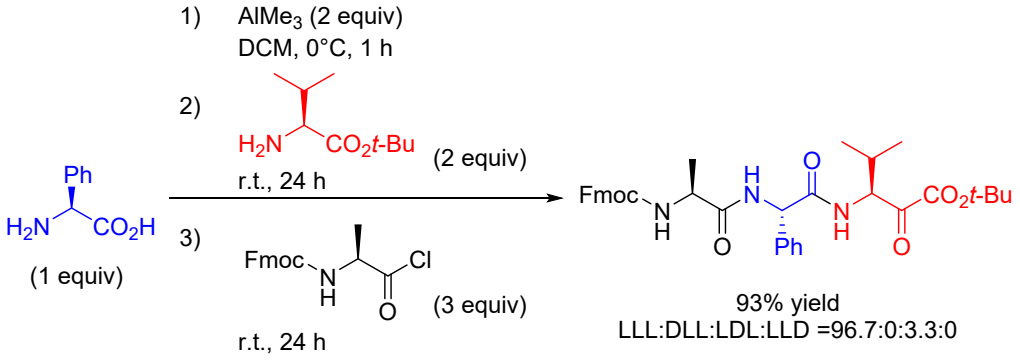
Fmoc-D-Ala-L-Phg-L-Val-O*t*-Bu; 31.297

Fmoc-L-Ala-D-Phg-L-Val-O*t*-Bu; 45.8767

Fmoc-D-Ala-L-Phg-D-Val-O*t*-Bu; 18.922

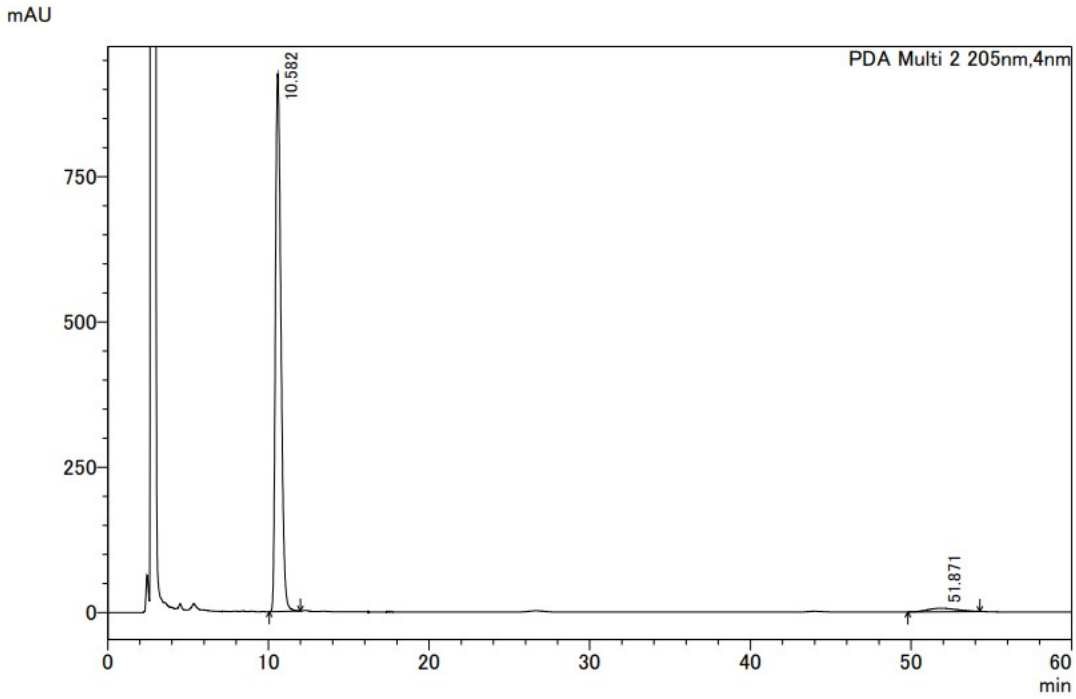
Fmoc-L-Ala-L-Phg-L-Val-O*t*-Bu; 10.685

Result;



Sample Information

Injection Volume	: 10
Data File	: TH19-28.lcd
Method File	: IE 80 20 1.5ml 60min.lcm



Peak Table

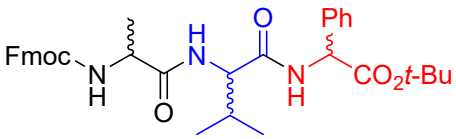
PDA Ch2 205nm

Peak#	Ret. Time	Area	Area%
1	10.582	22151689	96.682
2	51.871	760208	3.318
Total		22911897	100.000

Conditions:

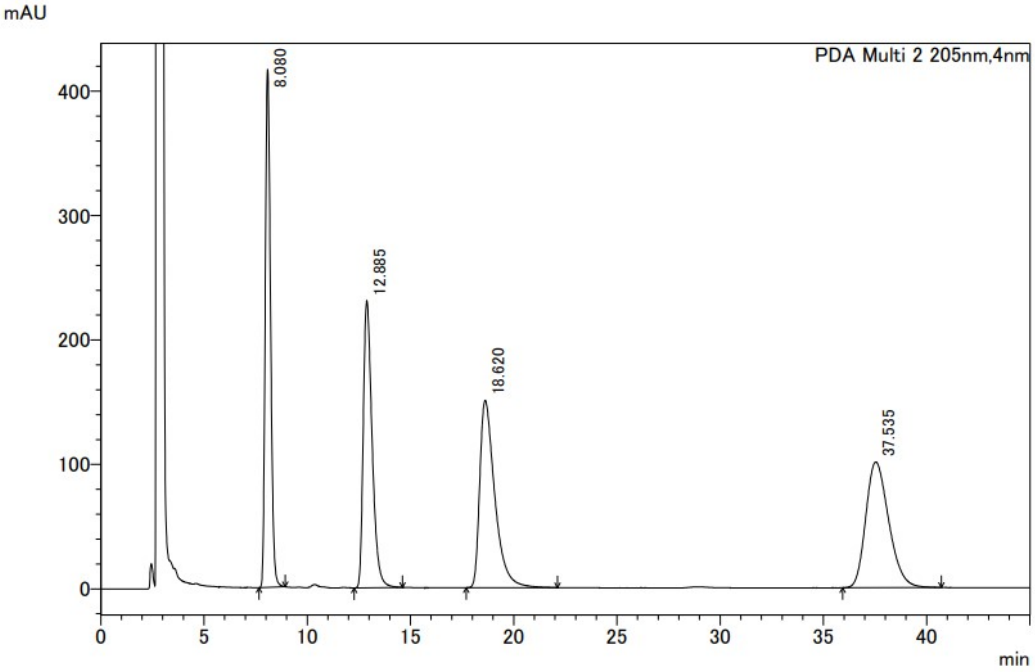
Chiral Column:

Racemic



Sample Information

Injection Volume : 10
Data File : Fmoc-rac.Ala-rac.Val-rac.Phg-OtBu.lcd
Method File : IE 80 20 1.5ml 45min.lcm



Peak Table

PDA Ch2 205nm

Peak#	Ret. Time	Area	Area%
1	8.080	7427979	24.984
2	12.885	6860904	23.076
3	18.620	7626497	25.651
4	37.535	7816088	26.289
Total		29731468	100.000

Retention time (min.);

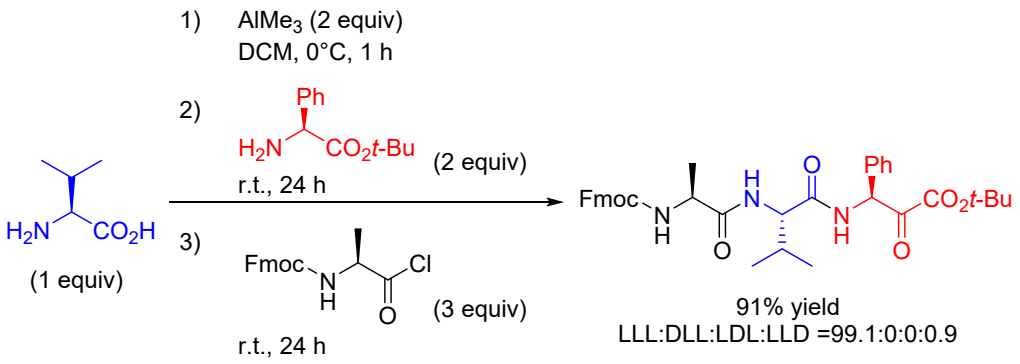
Fmoc-D-Ala-L-Val-L-Phg-O*t*-Bu; 37.535

Fmoc-D-Ala-L-Val-L-Phg-O*t*-Bu; 18.620

Fmoc-D-Ala-L-Val-L-Phg-O*t*-Bu; 12.885

Fmoc-D-Ala-L-Val-L-Phg-O*t*-Bu; 8.080

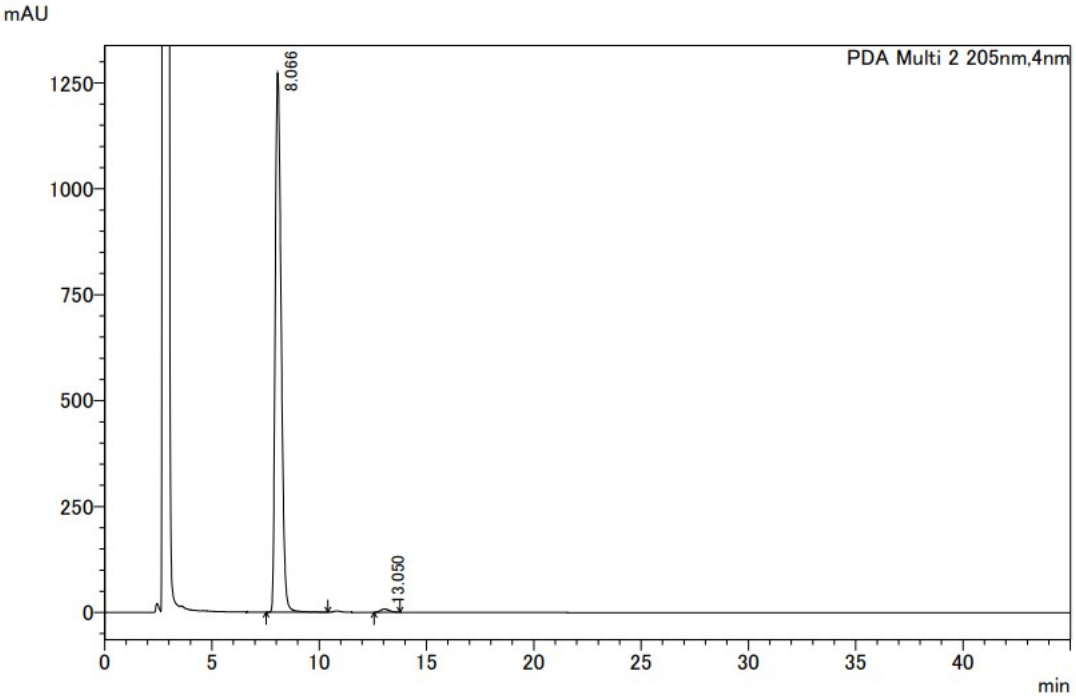
Result;



91% yield
LLL:DLL:LDL:LLD =99.1:0:0:0.9

Sample Information

Injection Volume	: 10
Data File	: Fmoc-L-Ala-L-Val-L-Phg-OtBu.lcd
Method File	: IE 80 20 1.5ml 45min.lcm

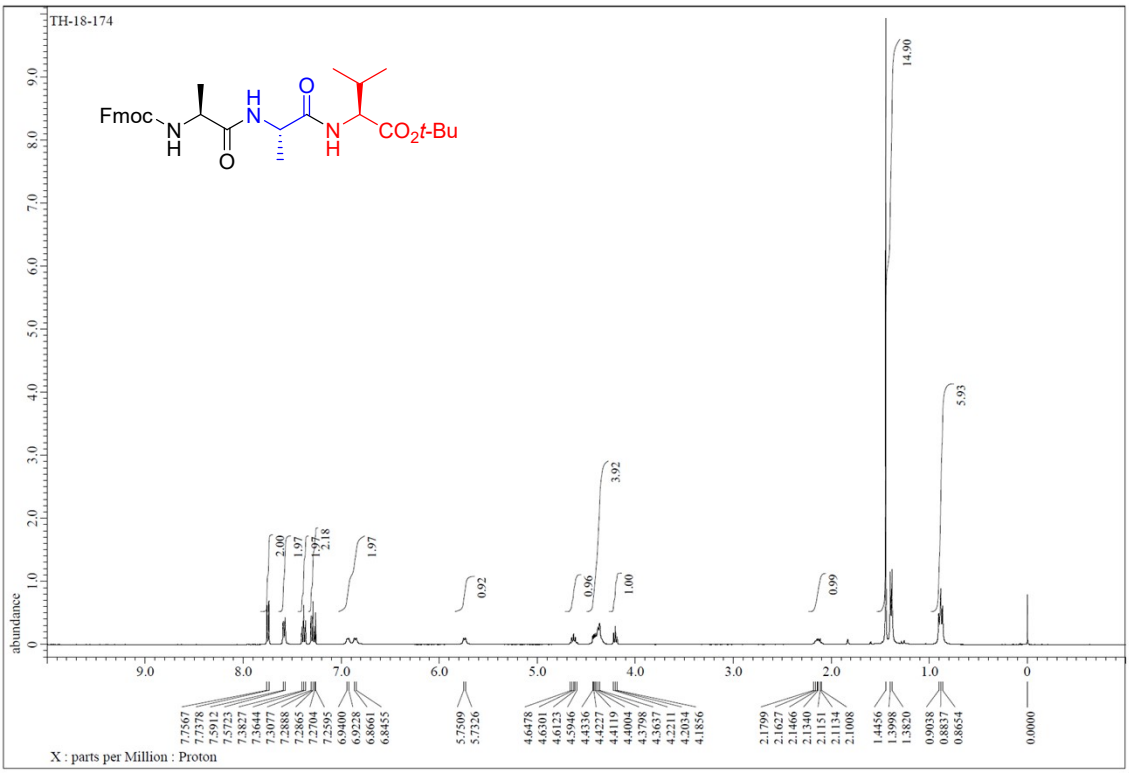


Peak Table

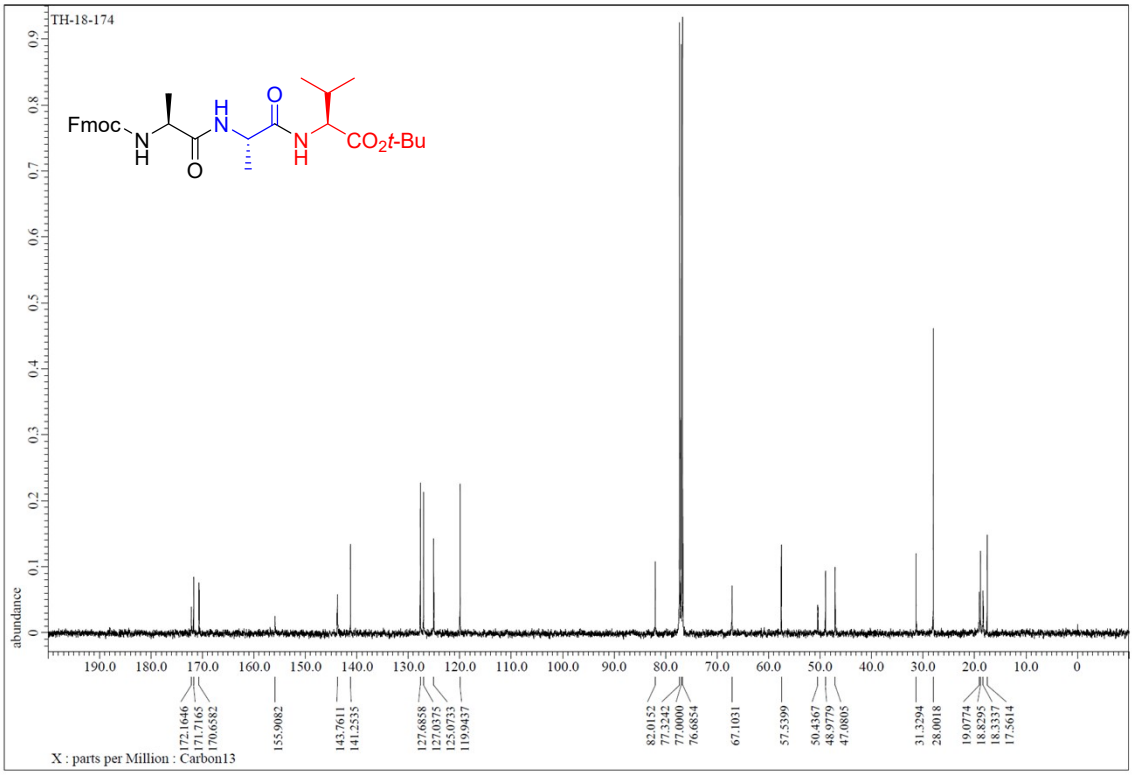
PDA Ch2 205nm

Peak#	Ret. Time	Area	Area%
1	8.066	24664541	99.107
2	13.050	222177	0.893
Total		24886717	100.000

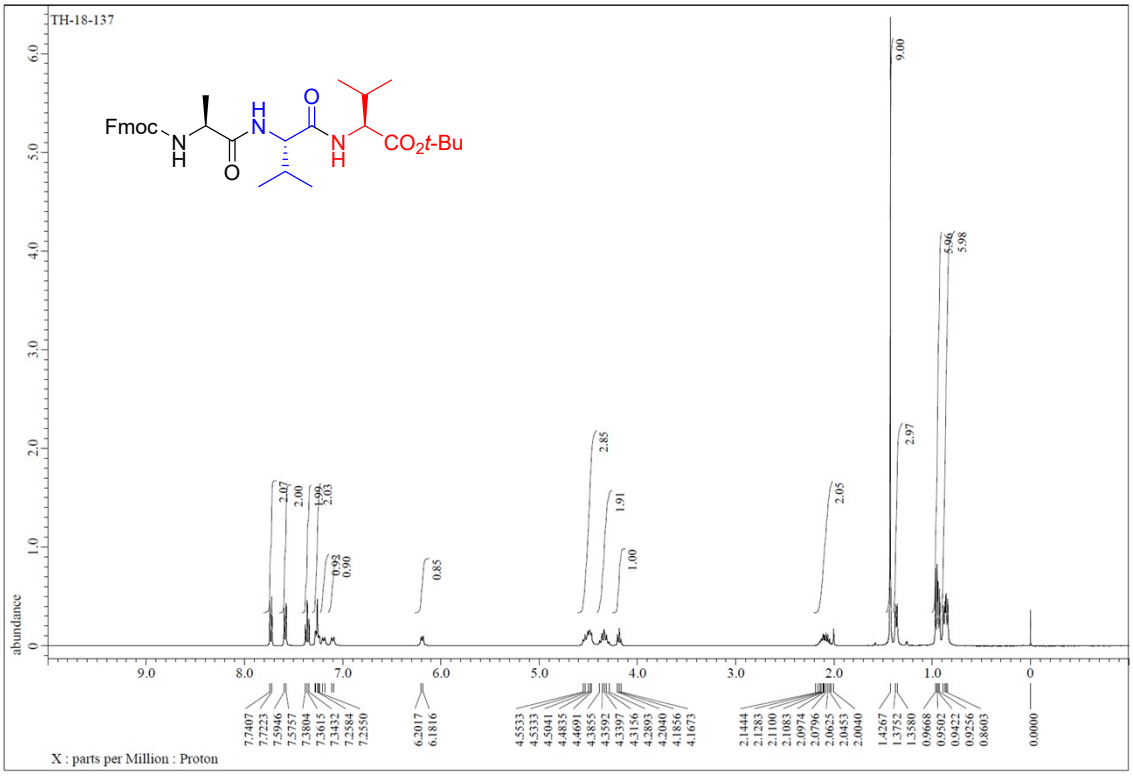
10. NMR data ^{1}H NMR (400 MHz, $CDCl_3$) of **5a**



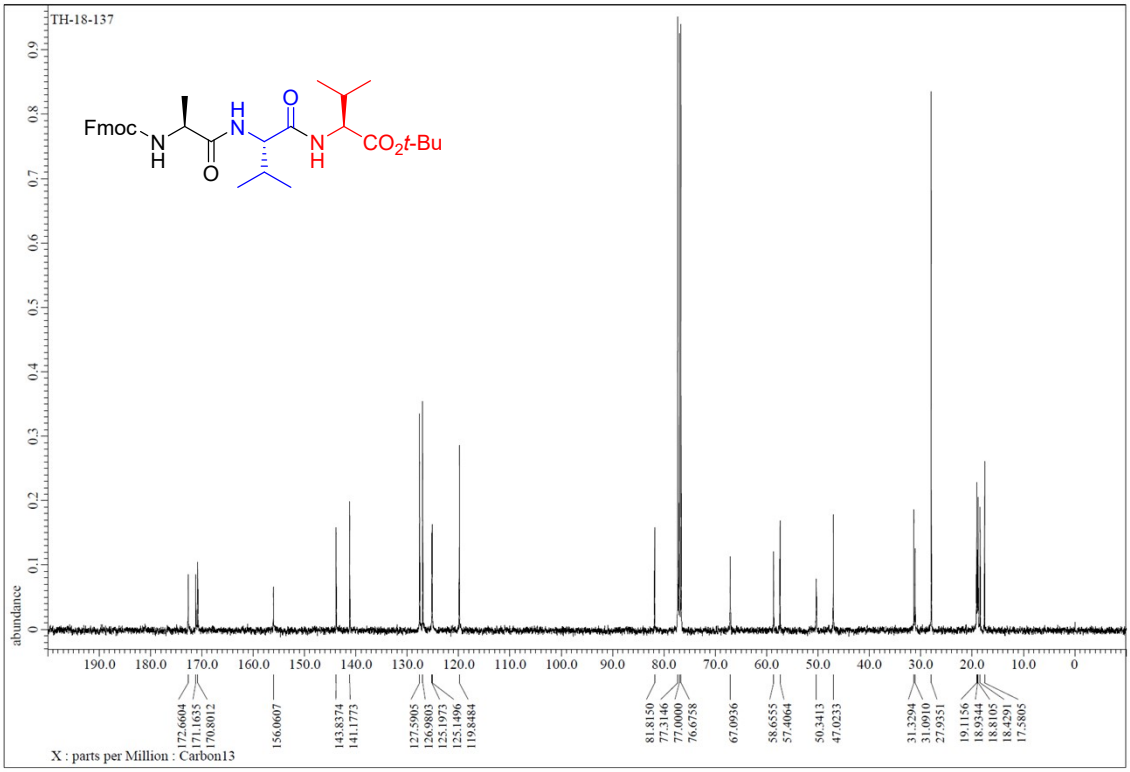
^{13}C NMR (100 MHz, $CDCl_3$) of **5a**



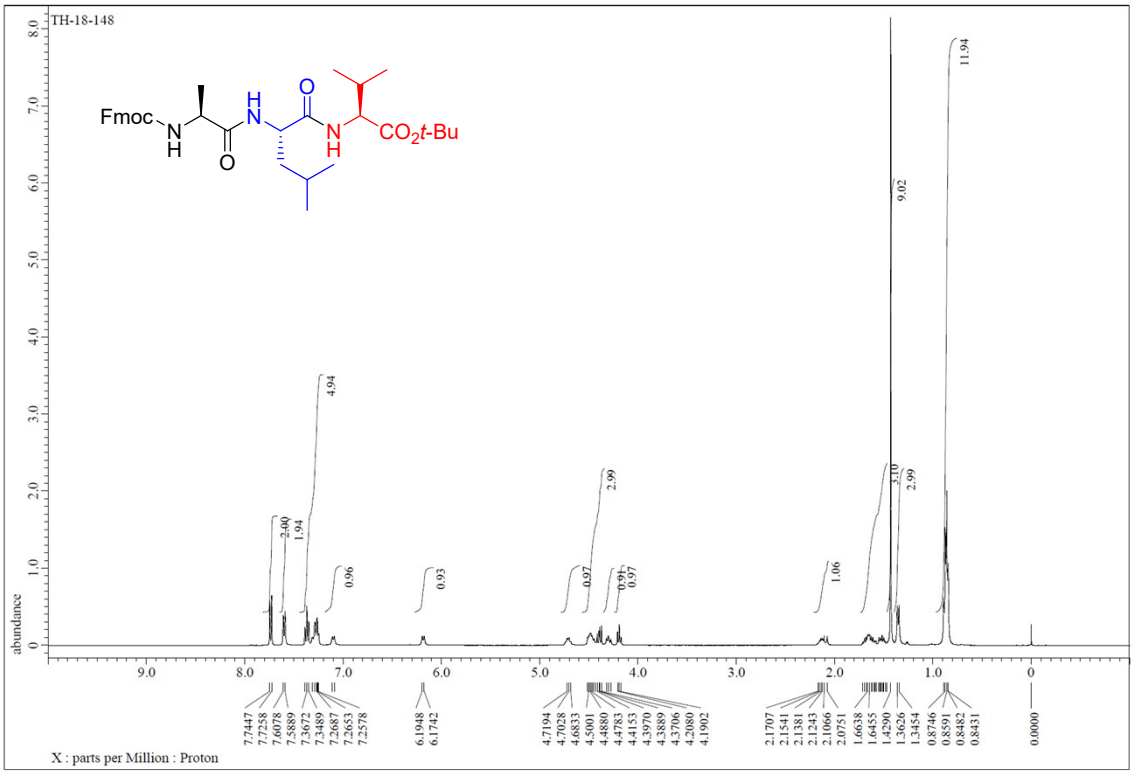
^{1}H NMR (400 MHz, $CDCl_3$) of **5b**



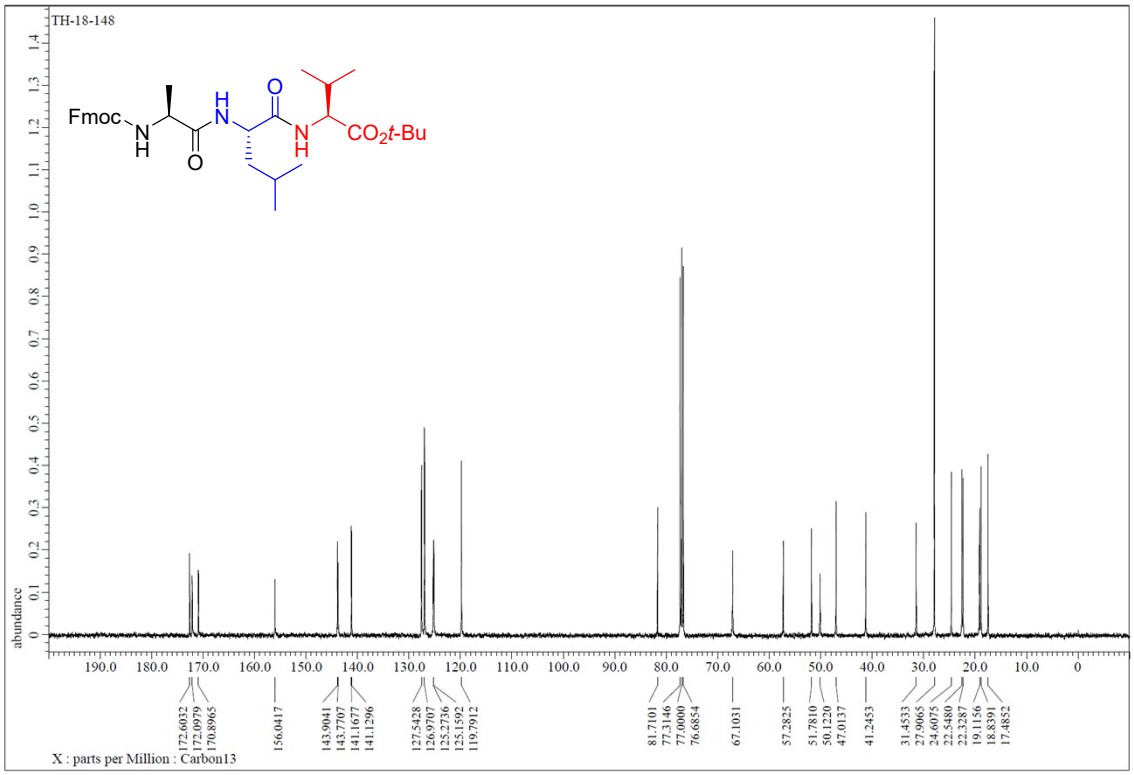
^{13}C NMR (100 MHz, $CDCl_3$) of **5b**



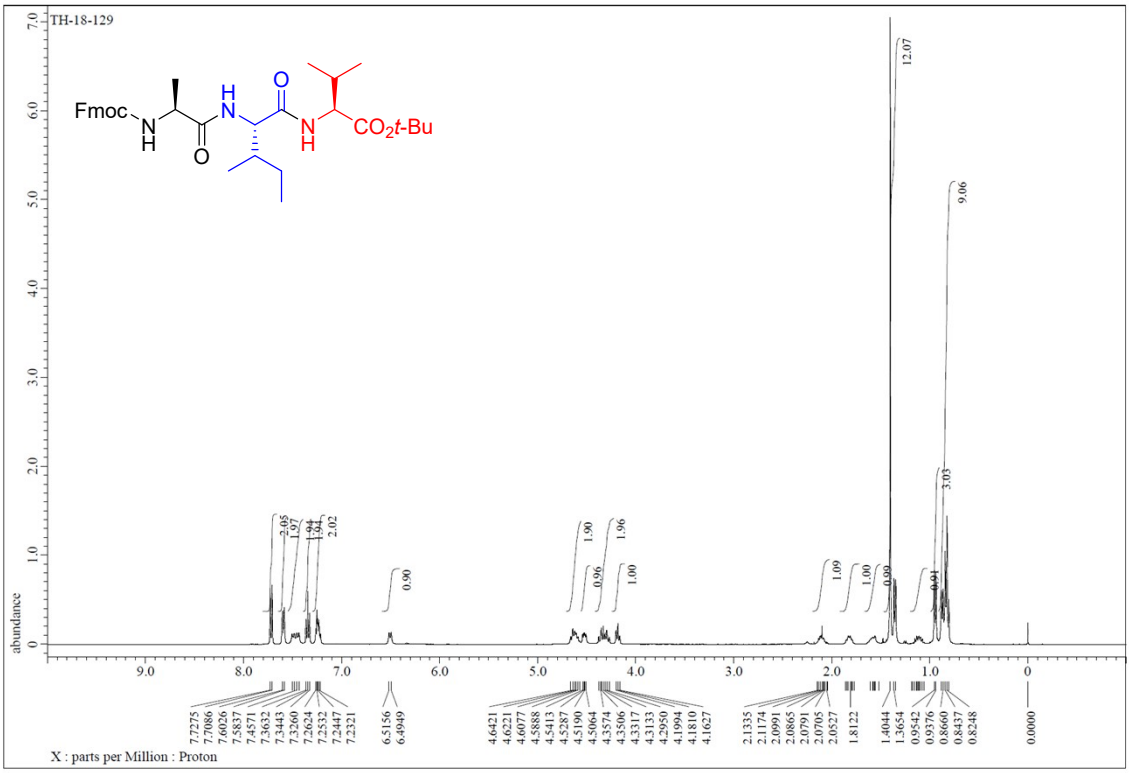
^{1}H NMR (400 MHz, $CDCl_3$) of **5c**



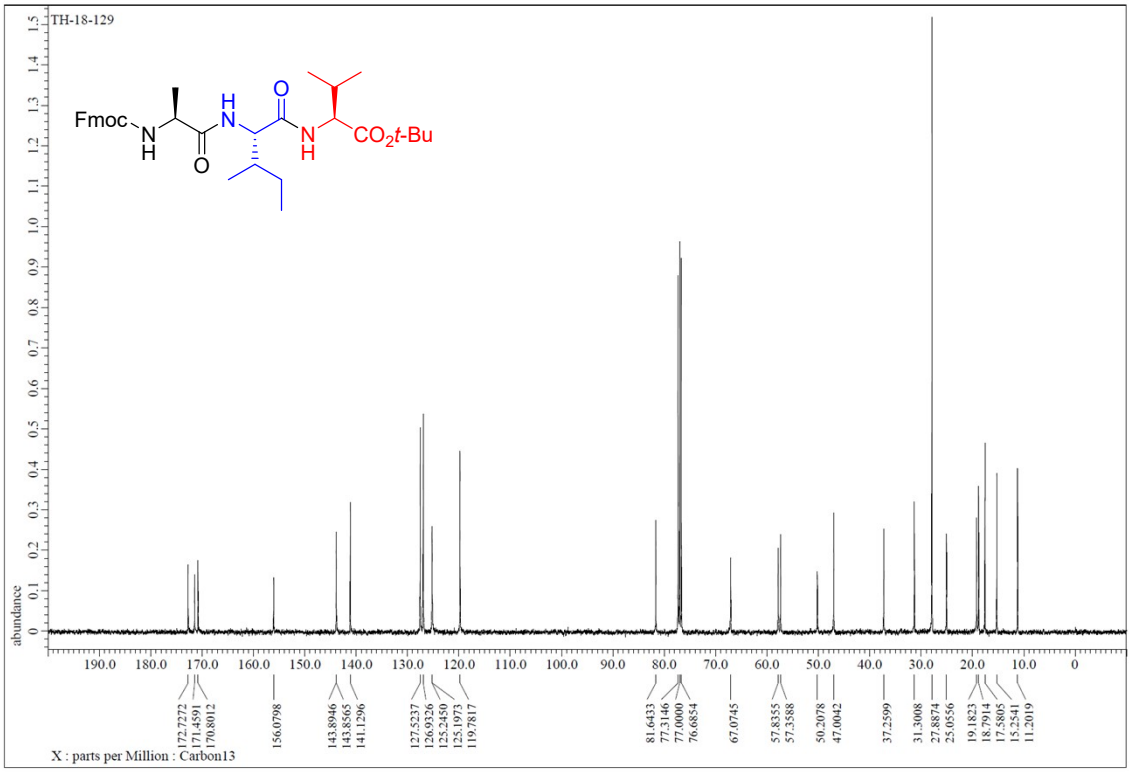
^{13}C NMR (100 MHz, $CDCl_3$) of **5c**



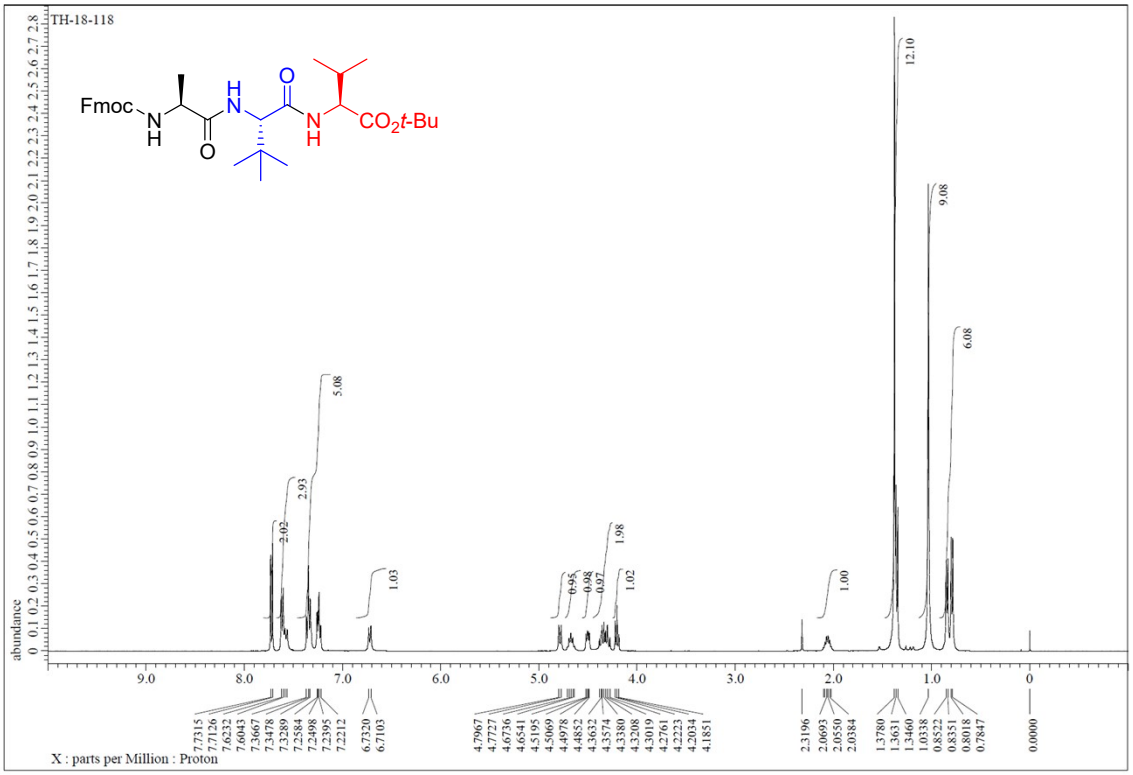
^{1}H NMR (400 MHz, $CDCl_3$) of **5d**



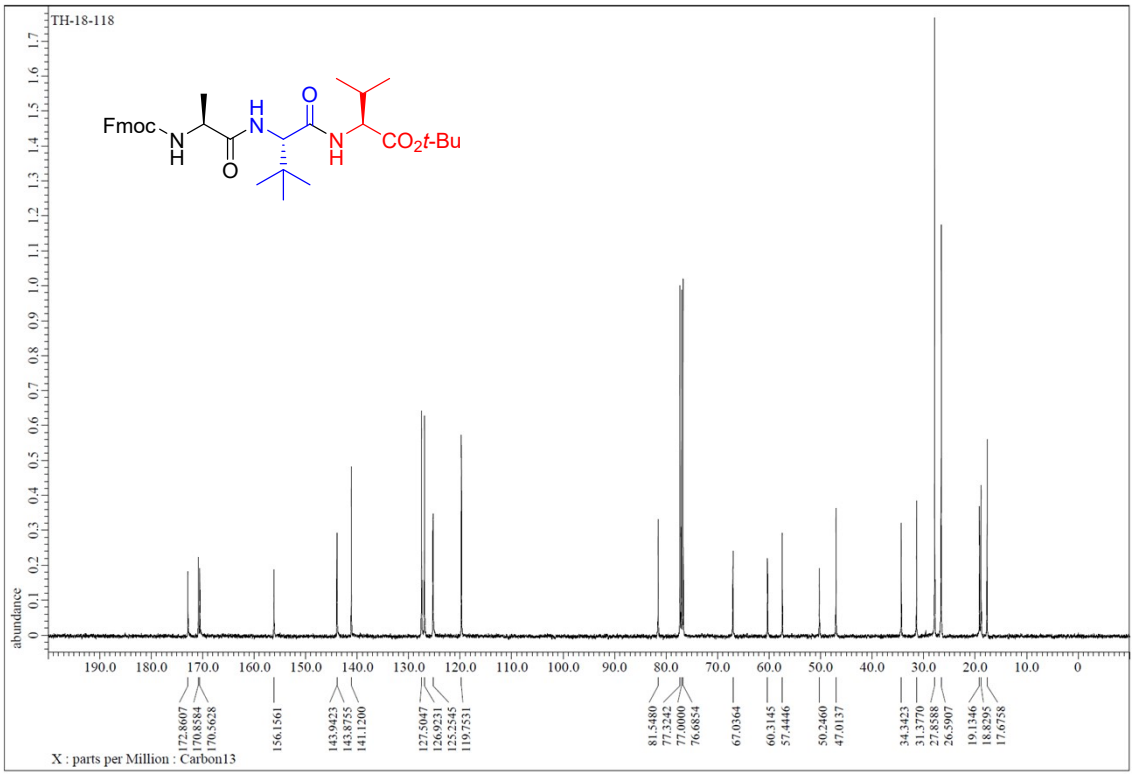
^{13}C NMR (100 MHz, $CDCl_3$) of **5d**



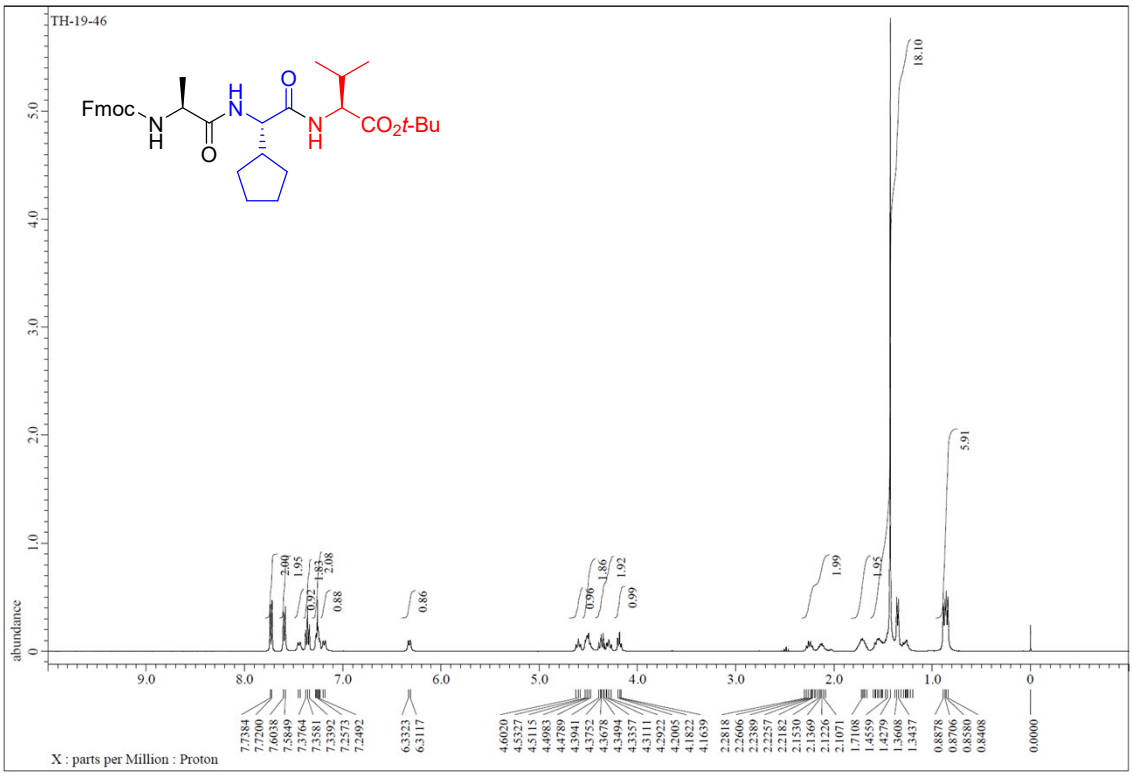
^{1}H NMR (400 MHz, $CDCl_3$) of **5e**



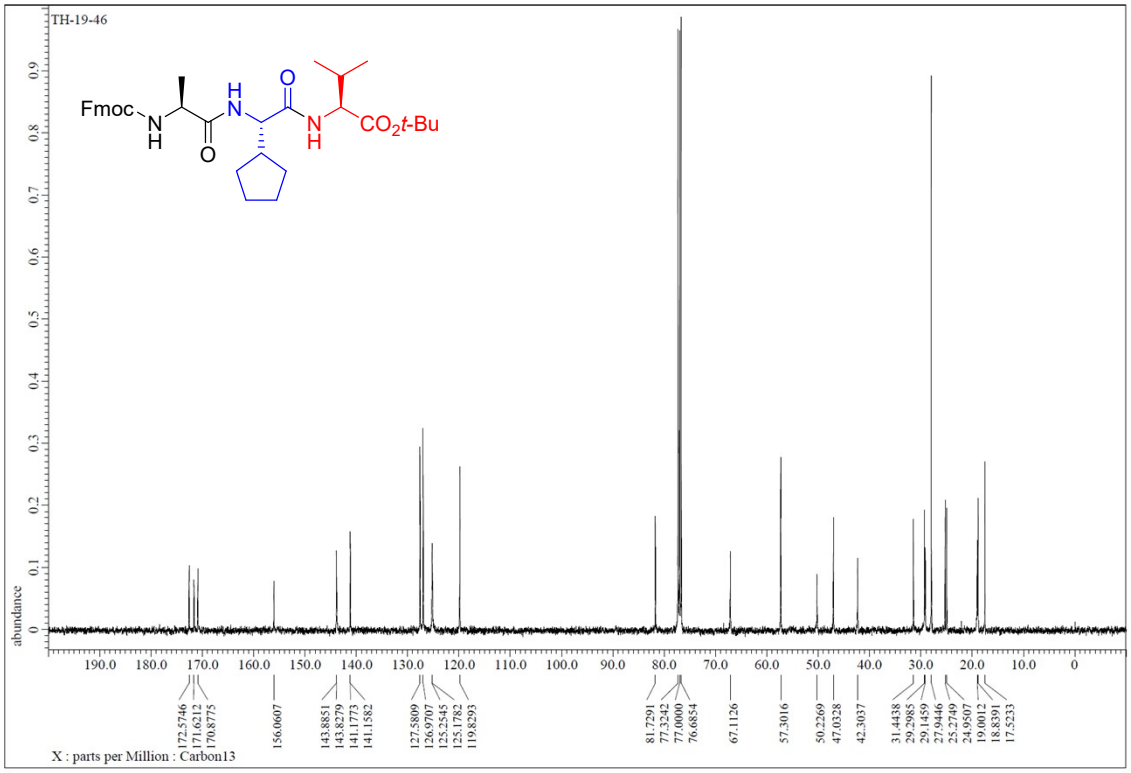
^{13}C NMR (100 MHz, $CDCl_3$) of **5e**



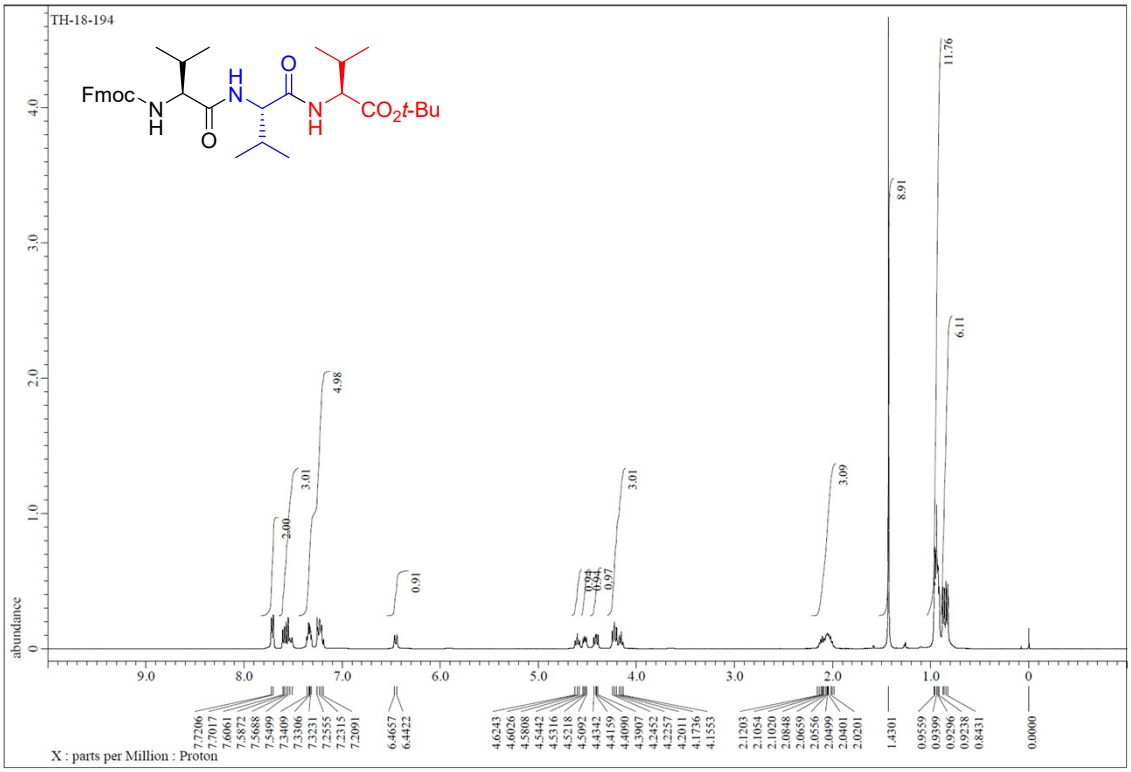
^{1}H NMR (400 MHz, $CDCl_3$) of **5f**



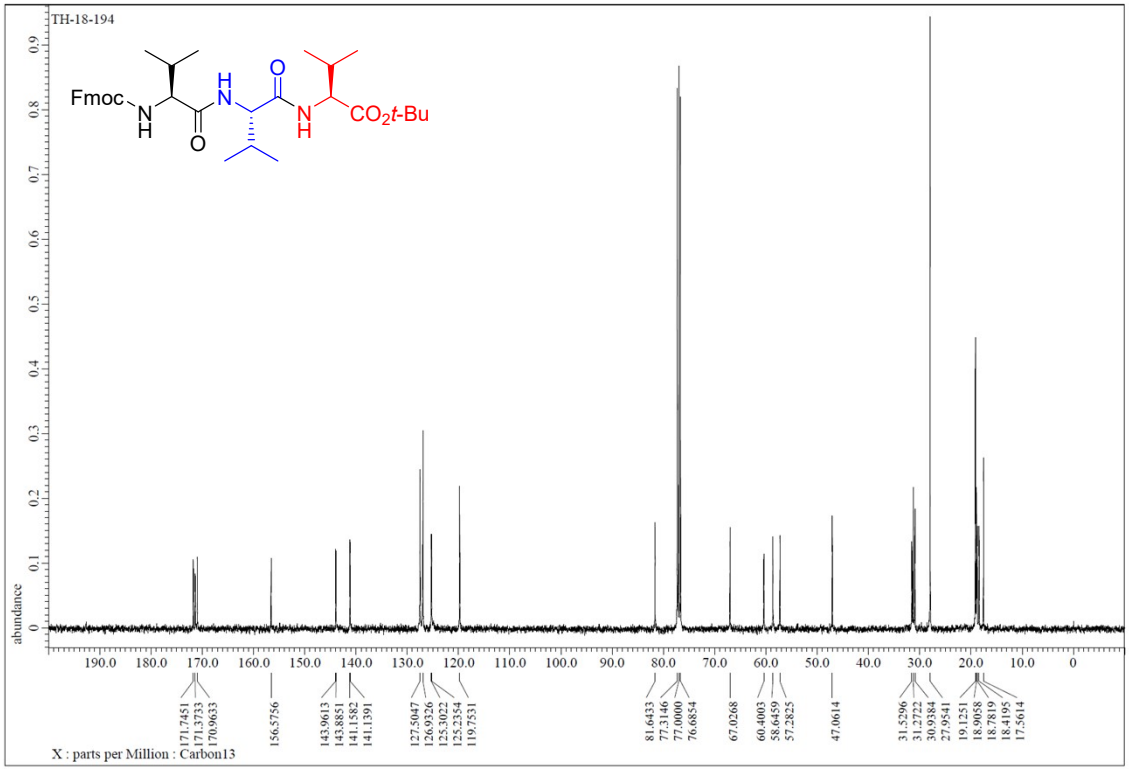
^{13}C NMR (100 MHz, $CDCl_3$) of **5f**



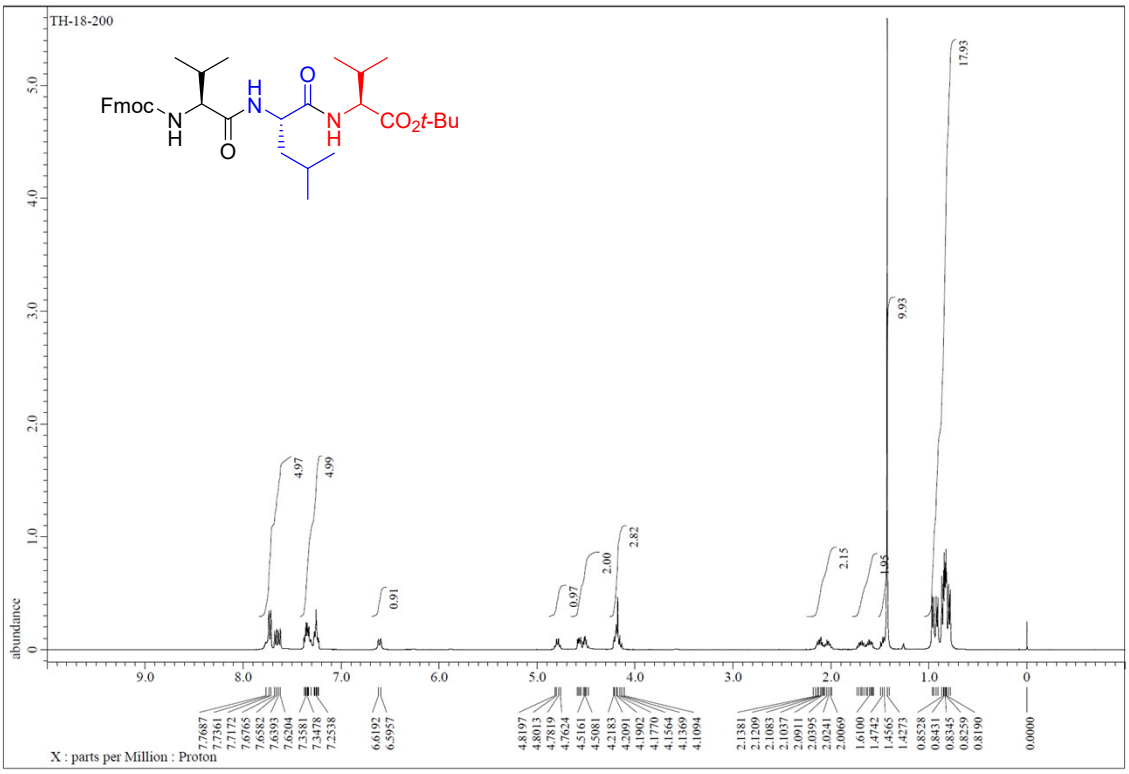
^{1}H NMR (400 MHz, $CDCl_3$) of **5g**



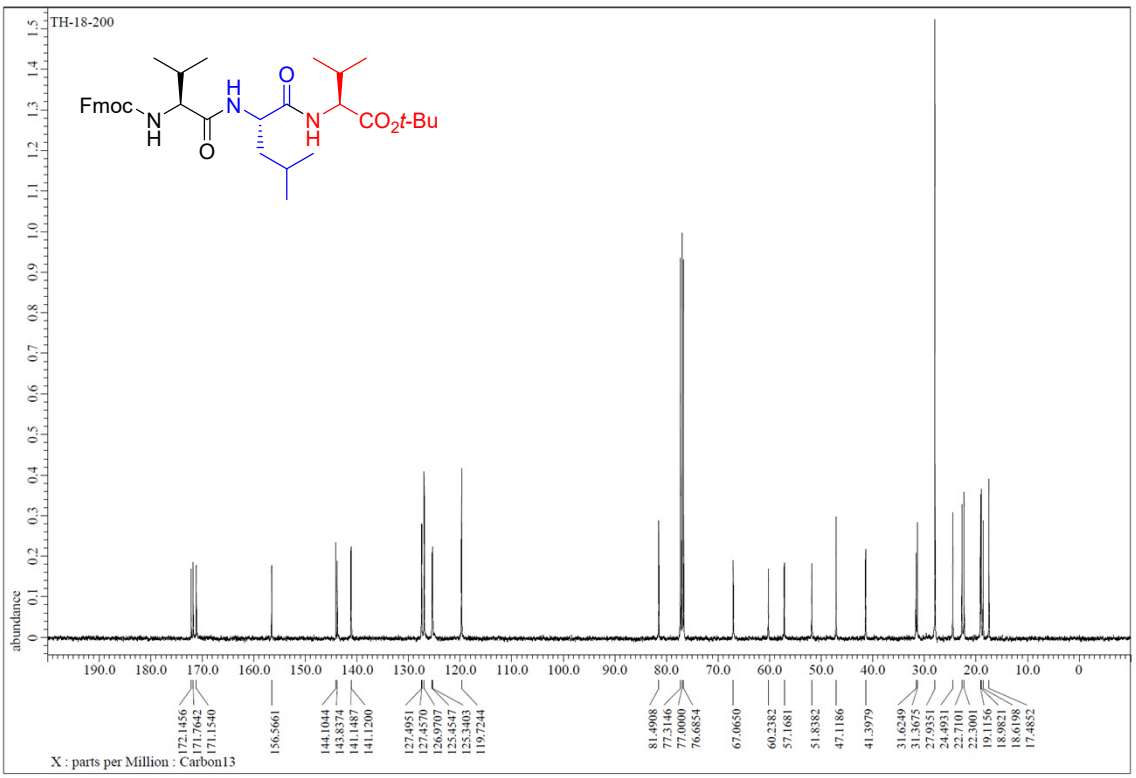
^{13}C NMR (100 MHz, $CDCl_3$) of **5g**



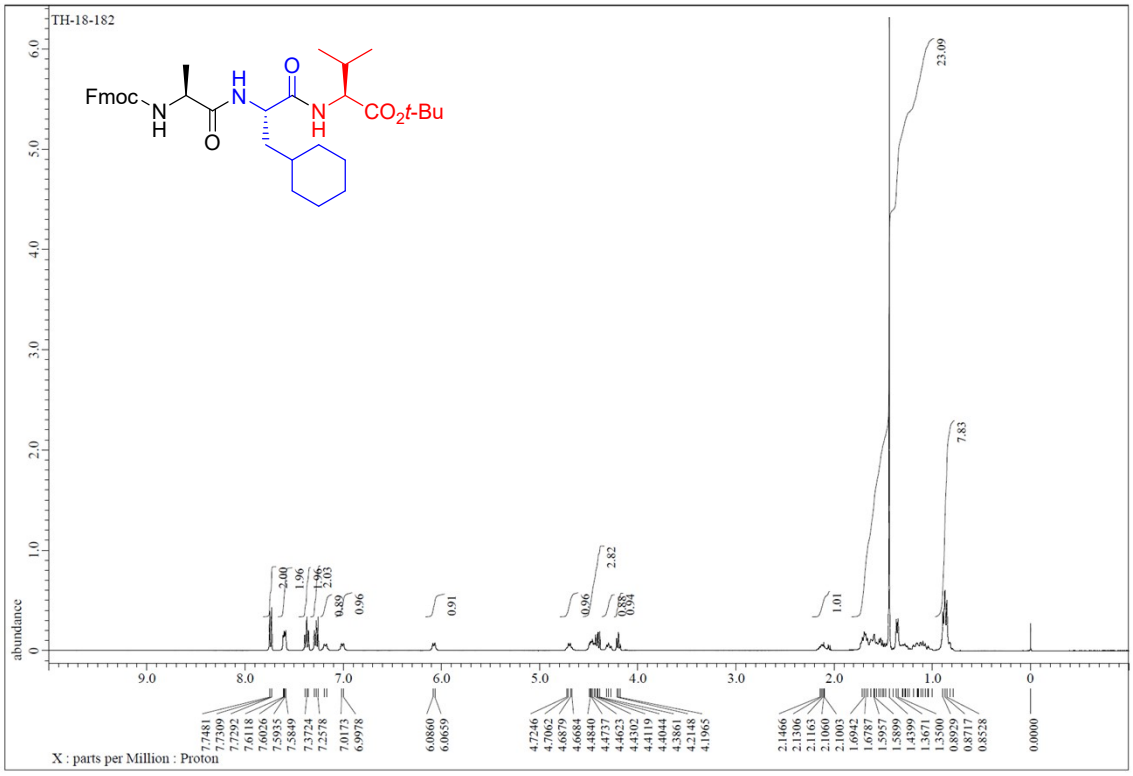
^{1}H NMR (400 MHz, $CDCl_3$) of **5h**



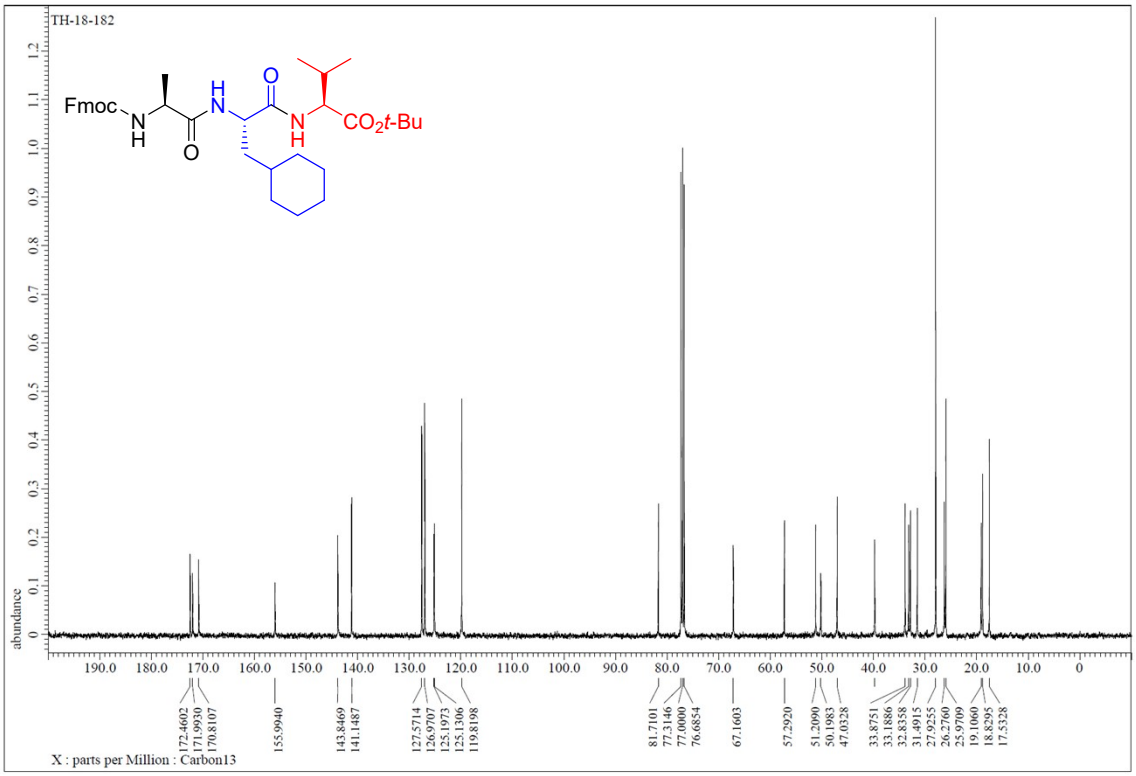
^{13}C NMR (100 MHz, $CDCl_3$) of **5h**



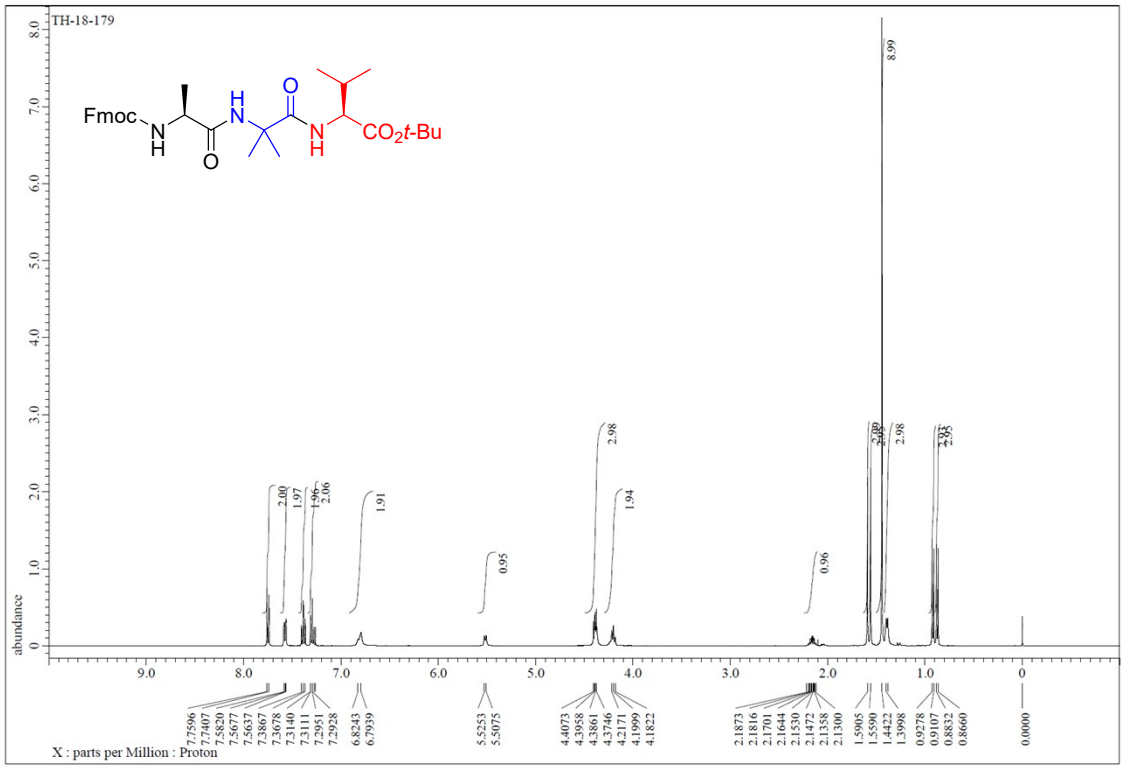
^{1}H NMR (400 MHz, $CDCl_3$) of **5i**



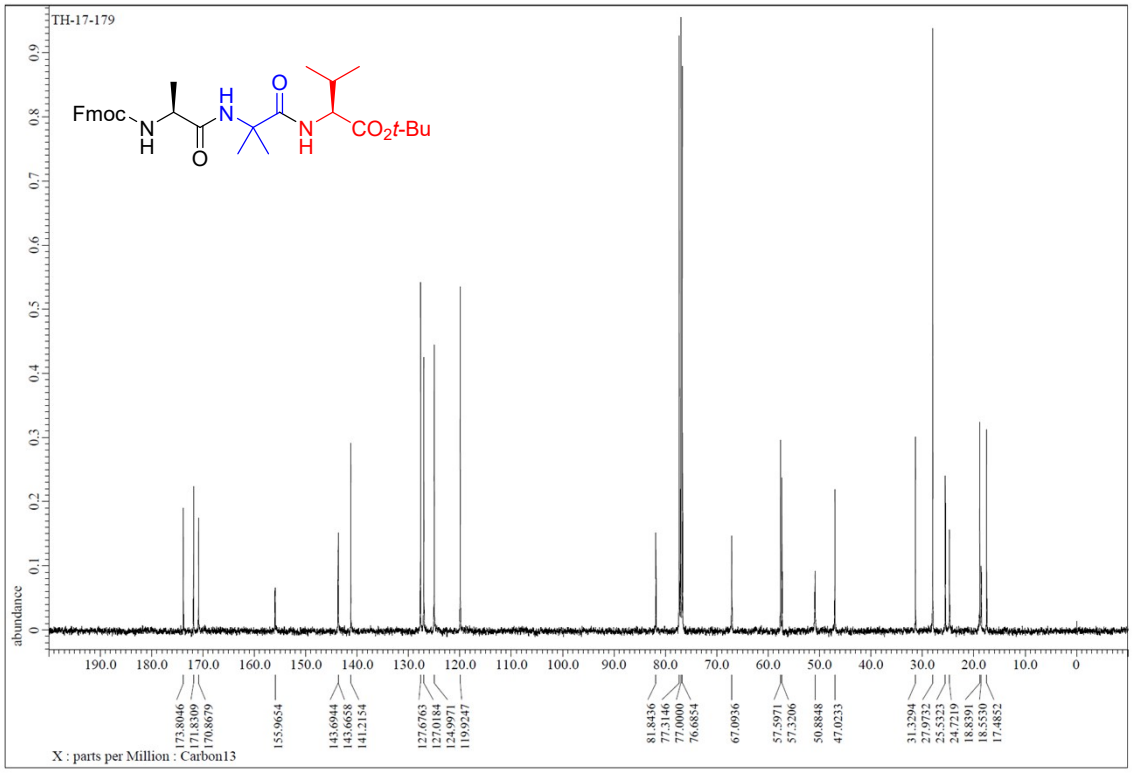
^{13}C NMR (100 MHz, $CDCl_3$) of **5i**



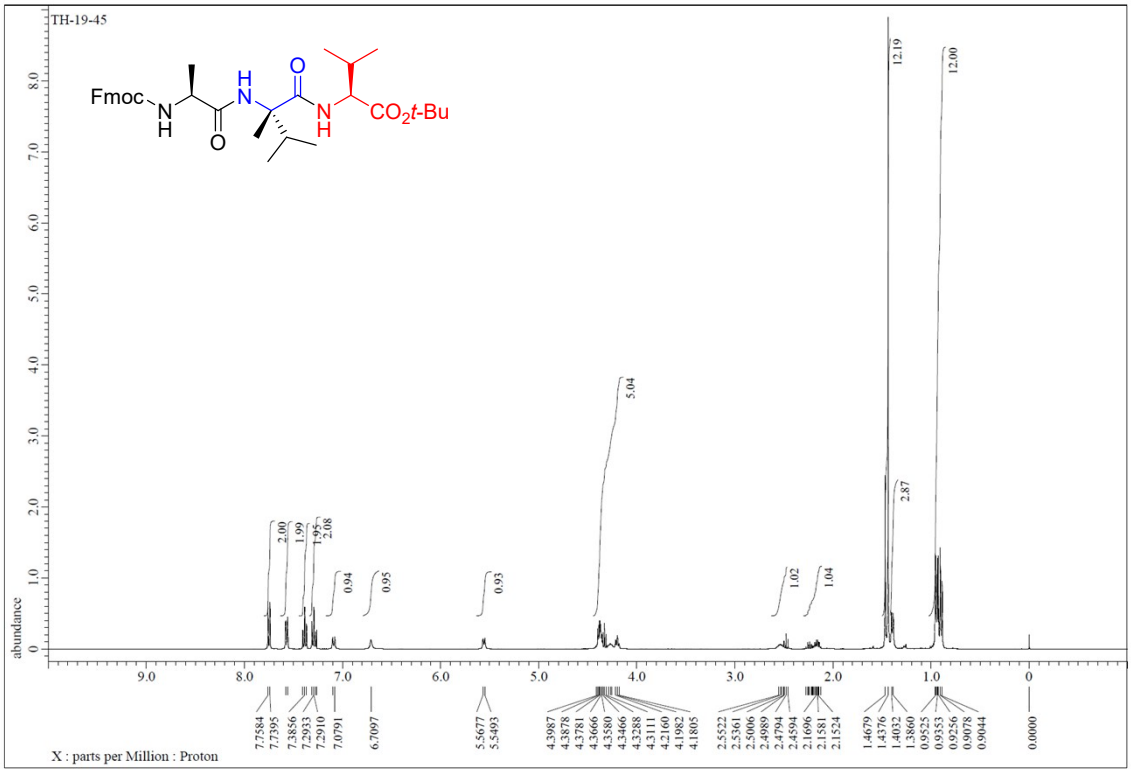
^{1}H NMR (400 MHz, $CDCl_3$) of **5j**



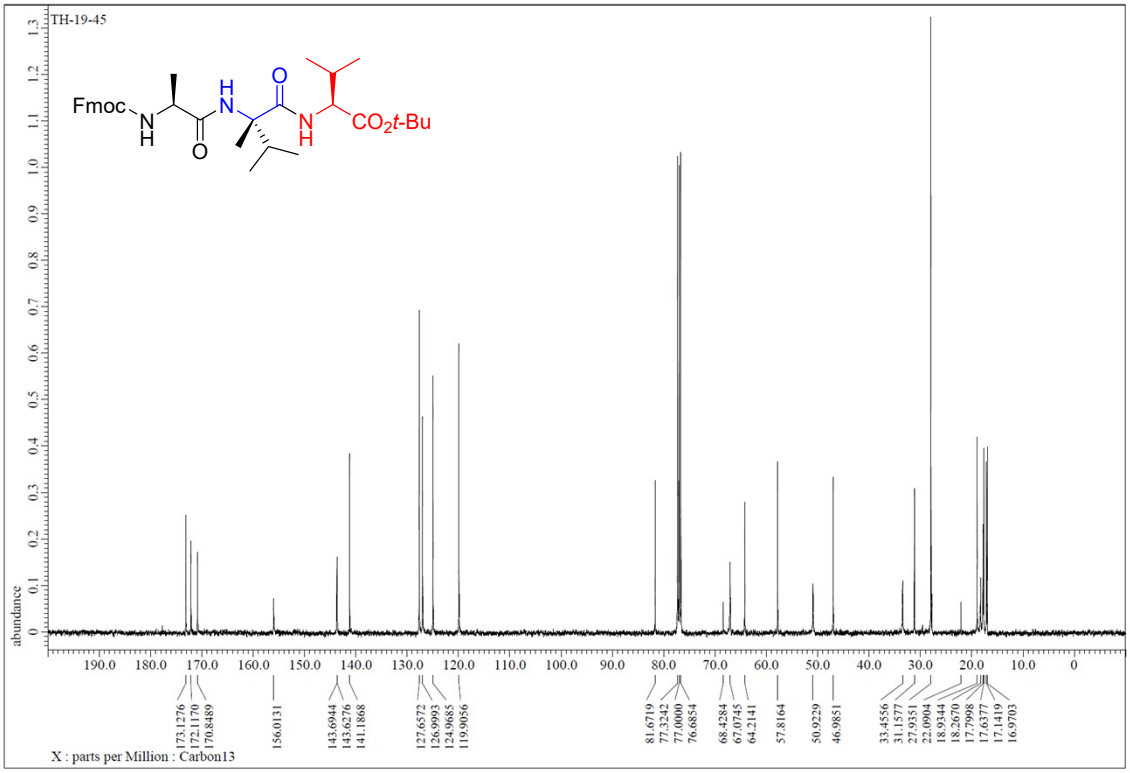
^{13}C NMR (100 MHz, $CDCl_3$) of **5j**



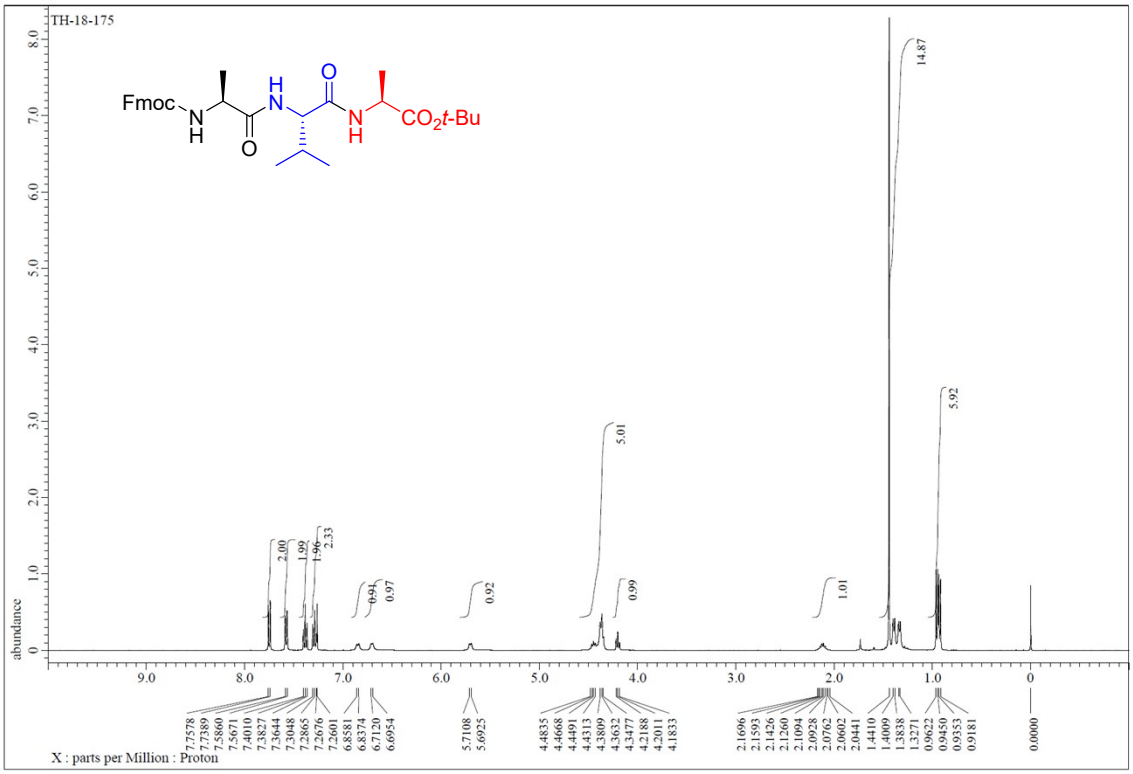
^{1}H NMR (400 MHz, $CDCl_3$) of **5k**



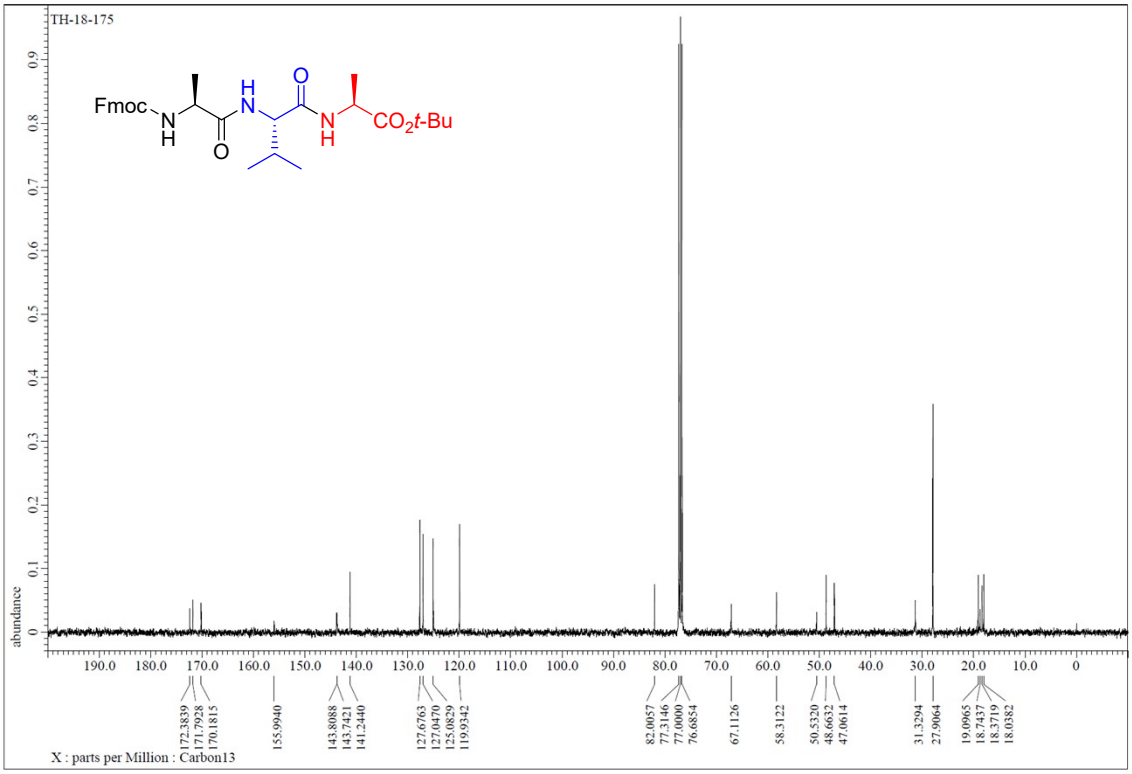
^{13}C NMR (100 MHz, $CDCl_3$) of **5k**



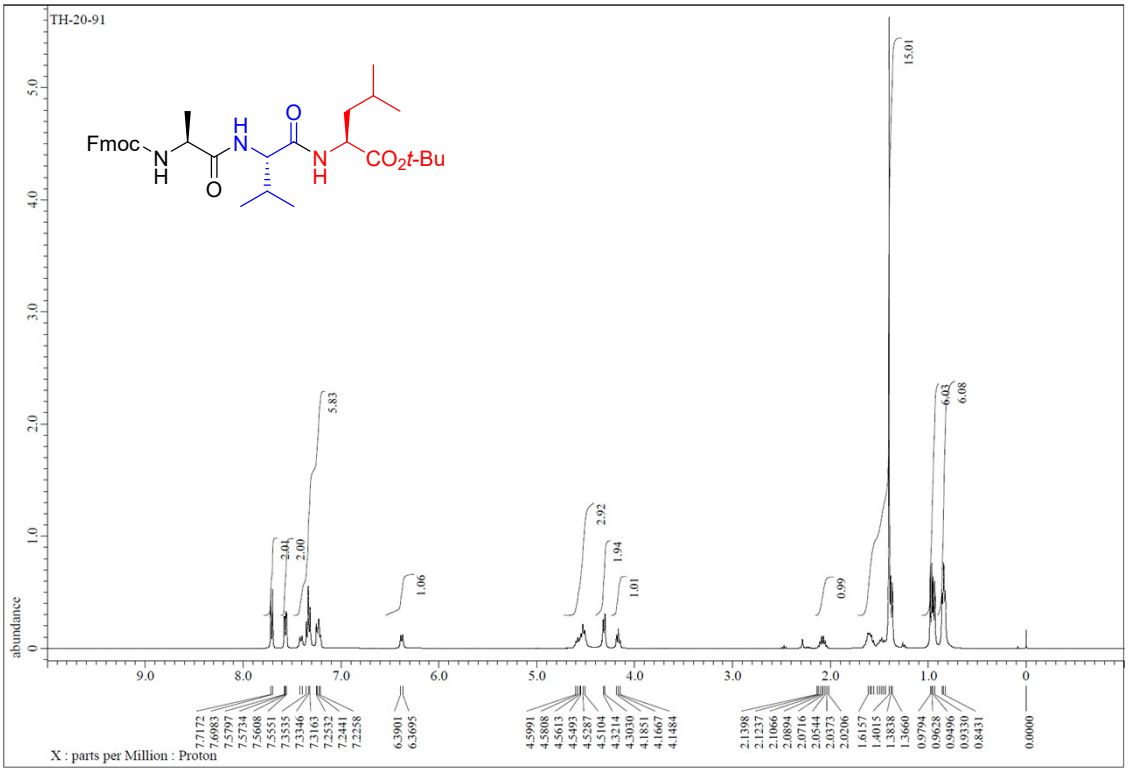
^{1}H NMR (400 MHz, $CDCl_3$) of **5l**



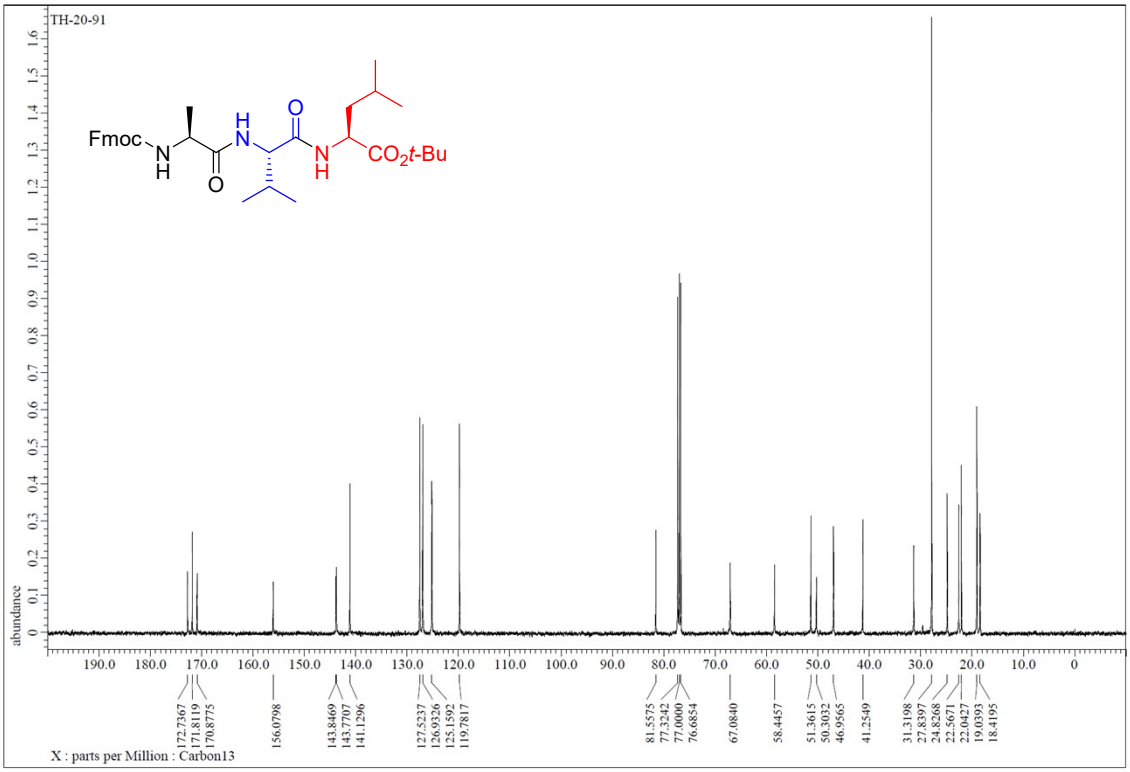
^{13}C NMR (100 MHz, $CDCl_3$) of **5l**



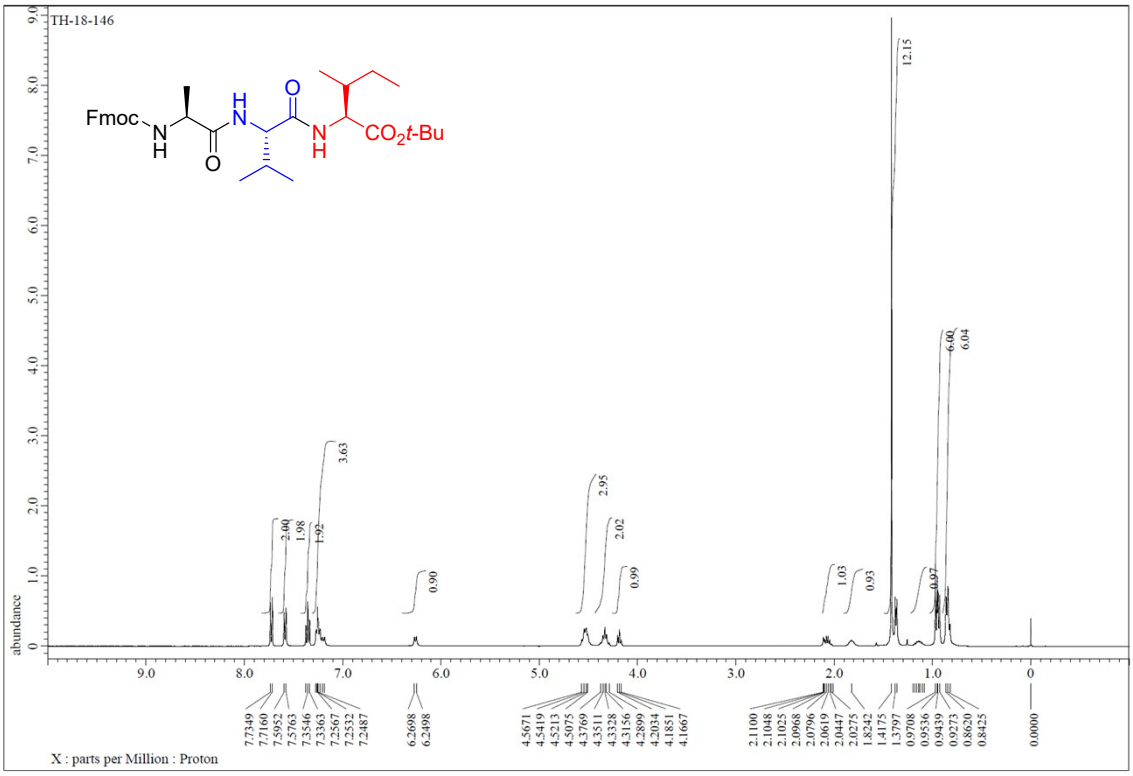
^{1}H NMR (400 MHz, $CDCl_3$) of **5m**



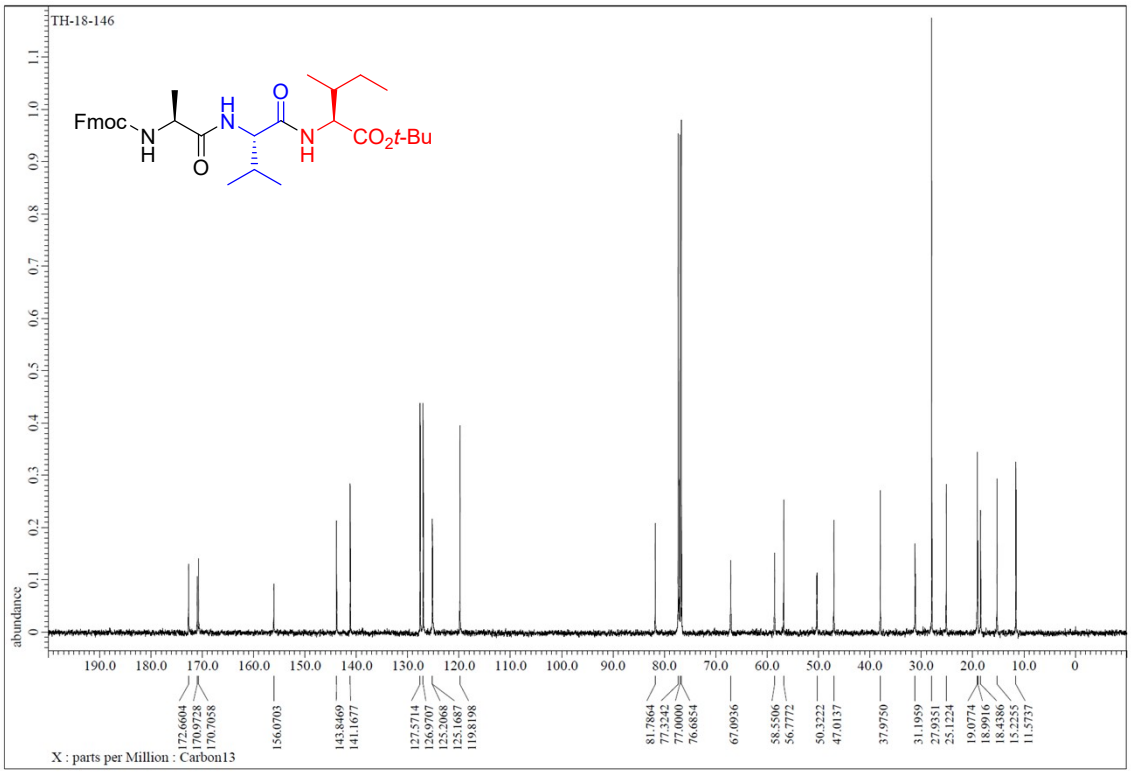
^{13}C NMR (100 MHz, $CDCl_3$) of **5m**



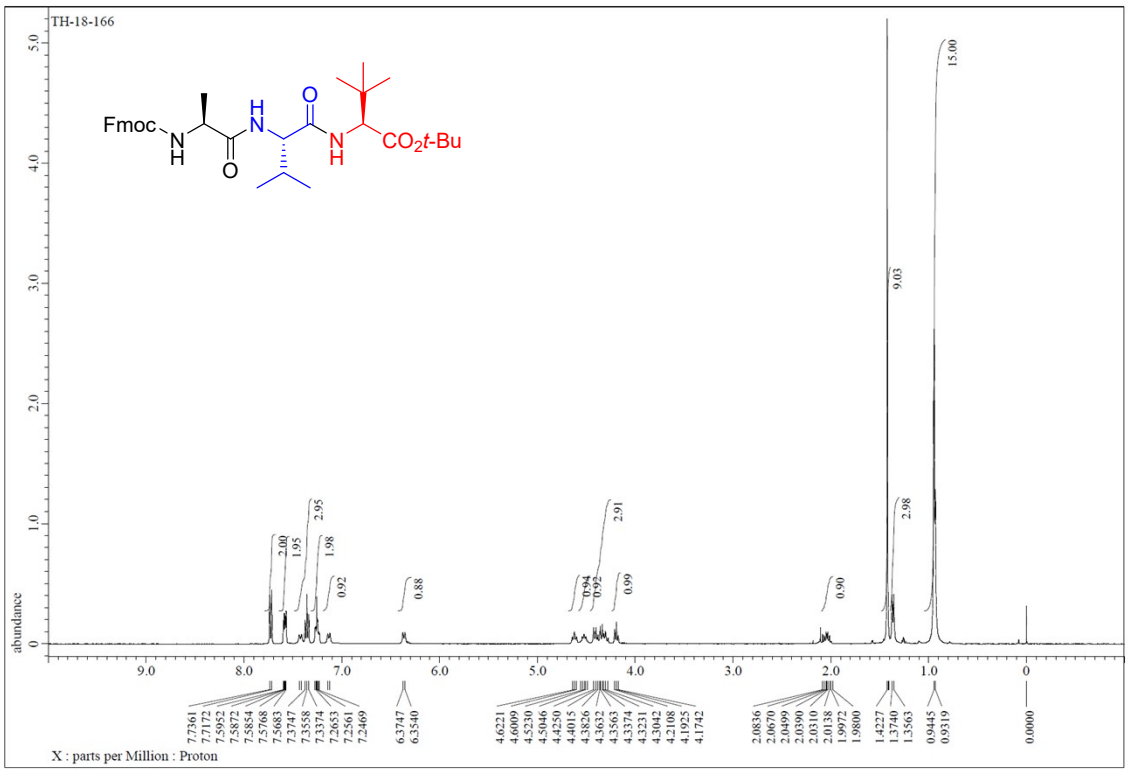
^{1}H NMR (400 MHz, $CDCl_3$) of **5n**



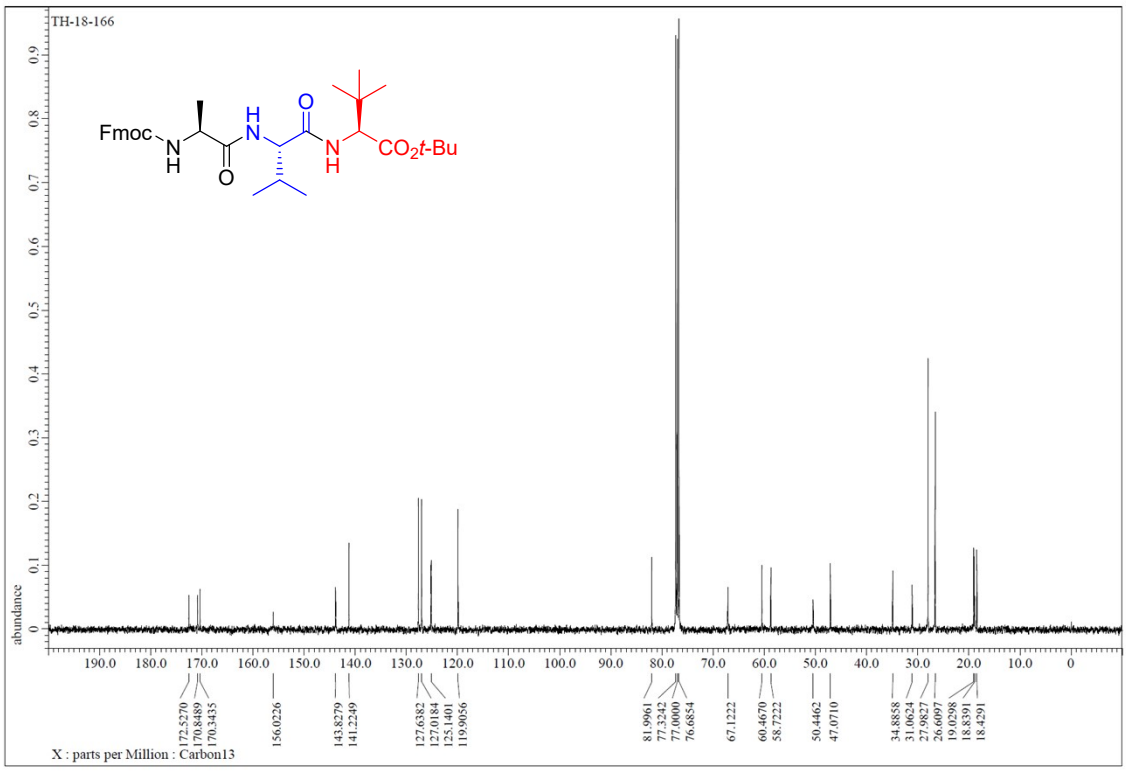
^{13}C NMR (100 MHz, $CDCl_3$) of **5n**



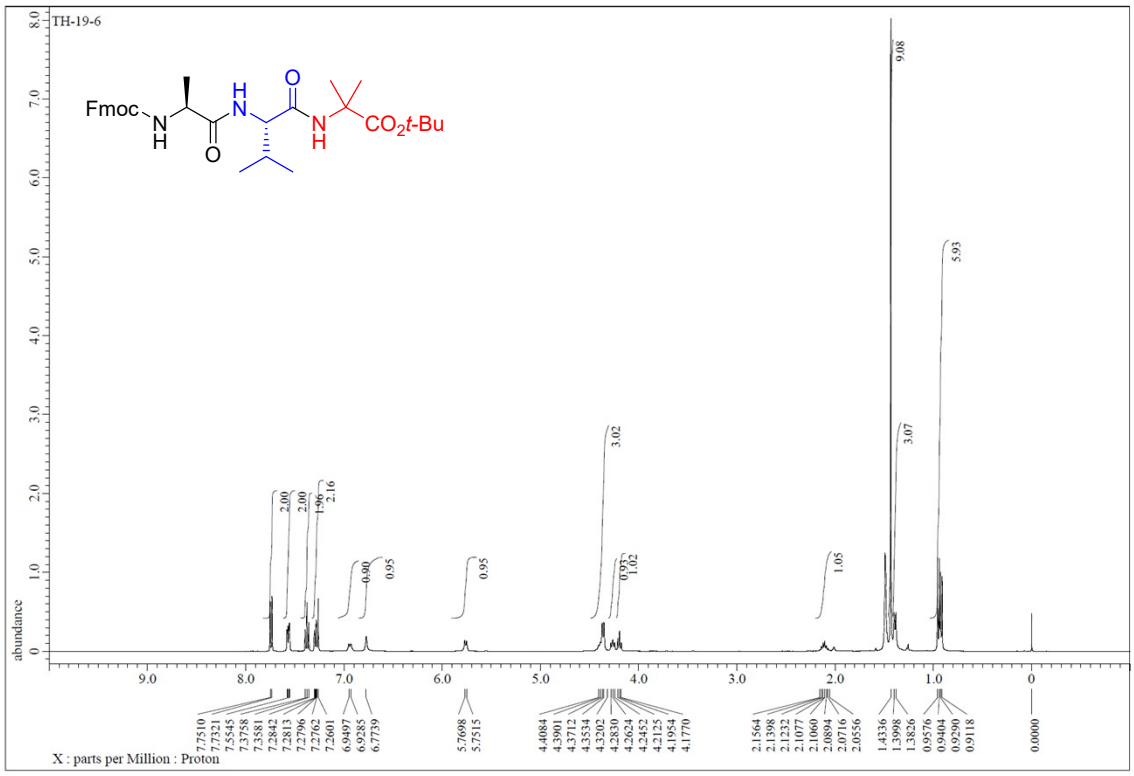
^{1}H NMR (400 MHz, $CDCl_3$) of **5o**



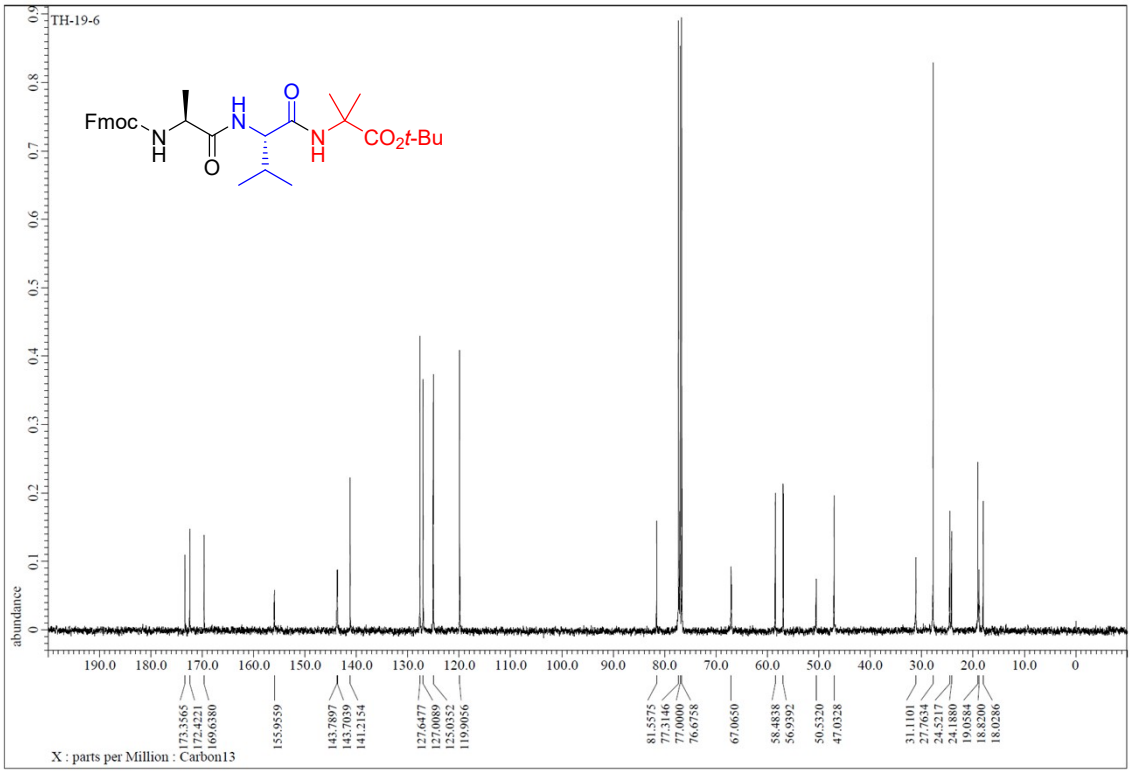
^{13}C NMR (100 MHz, $CDCl_3$) of **5o**



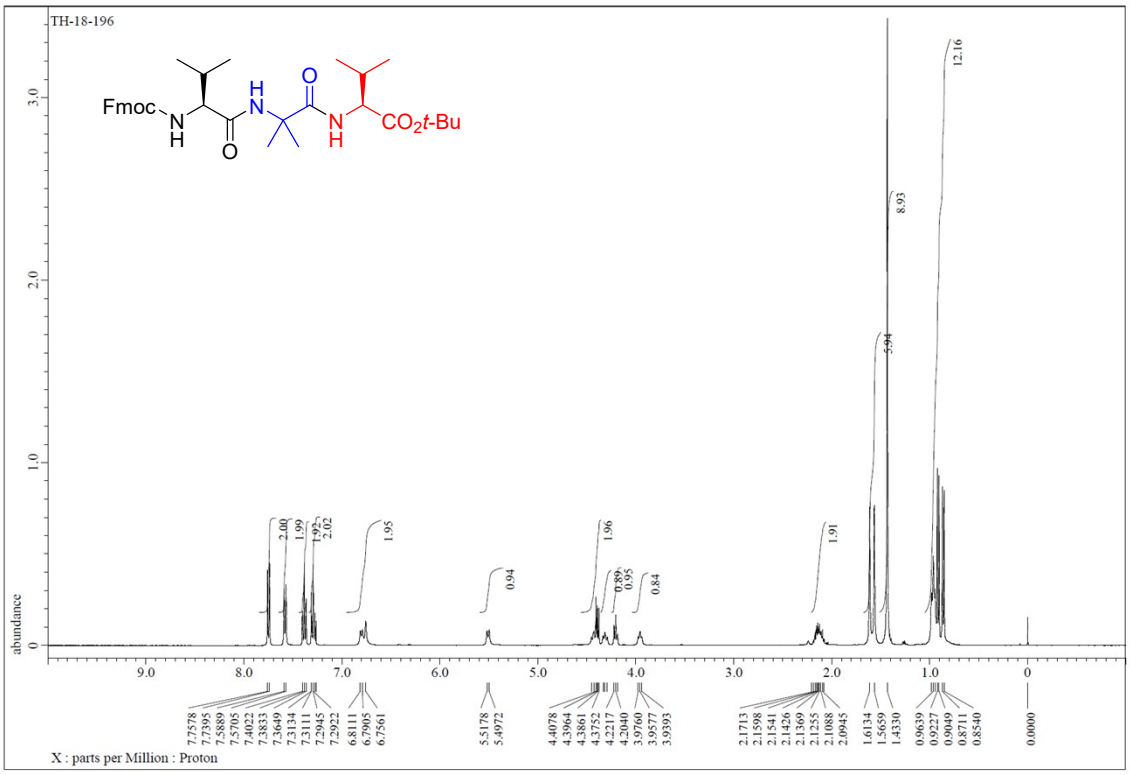
^{1}H NMR (400 MHz, $CDCl_3$) of **5p**



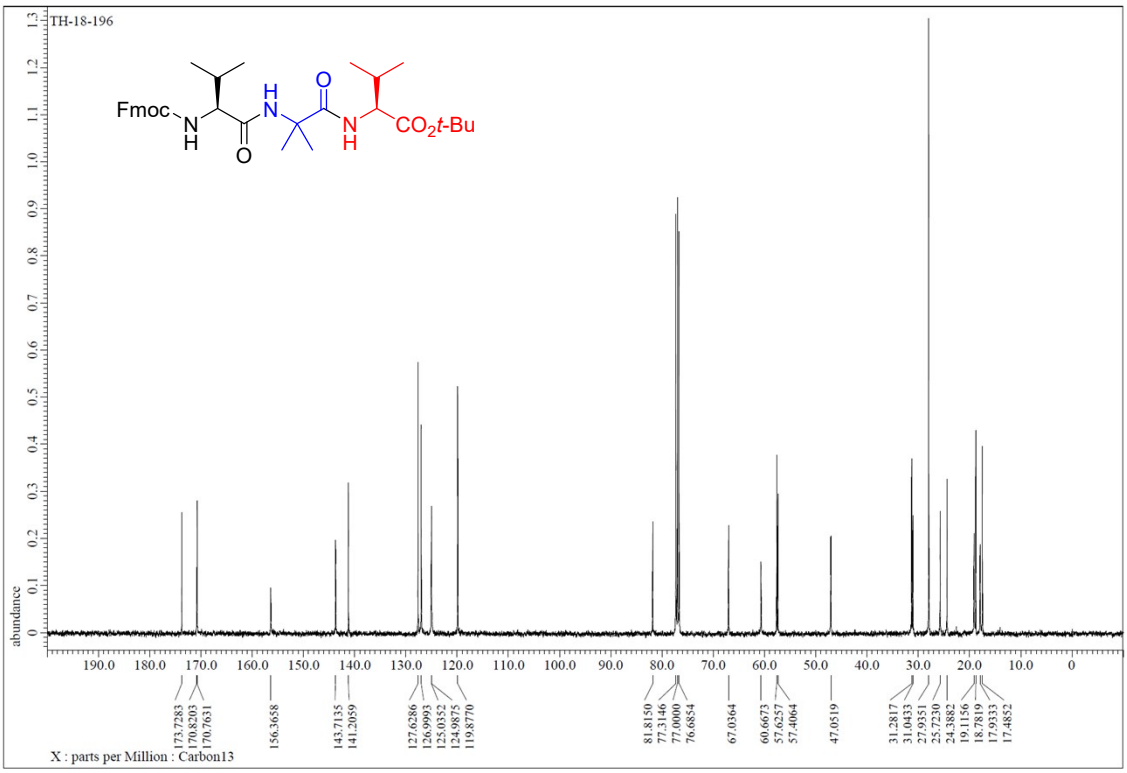
^{13}C NMR (100 MHz, $CDCl_3$) of **5p**



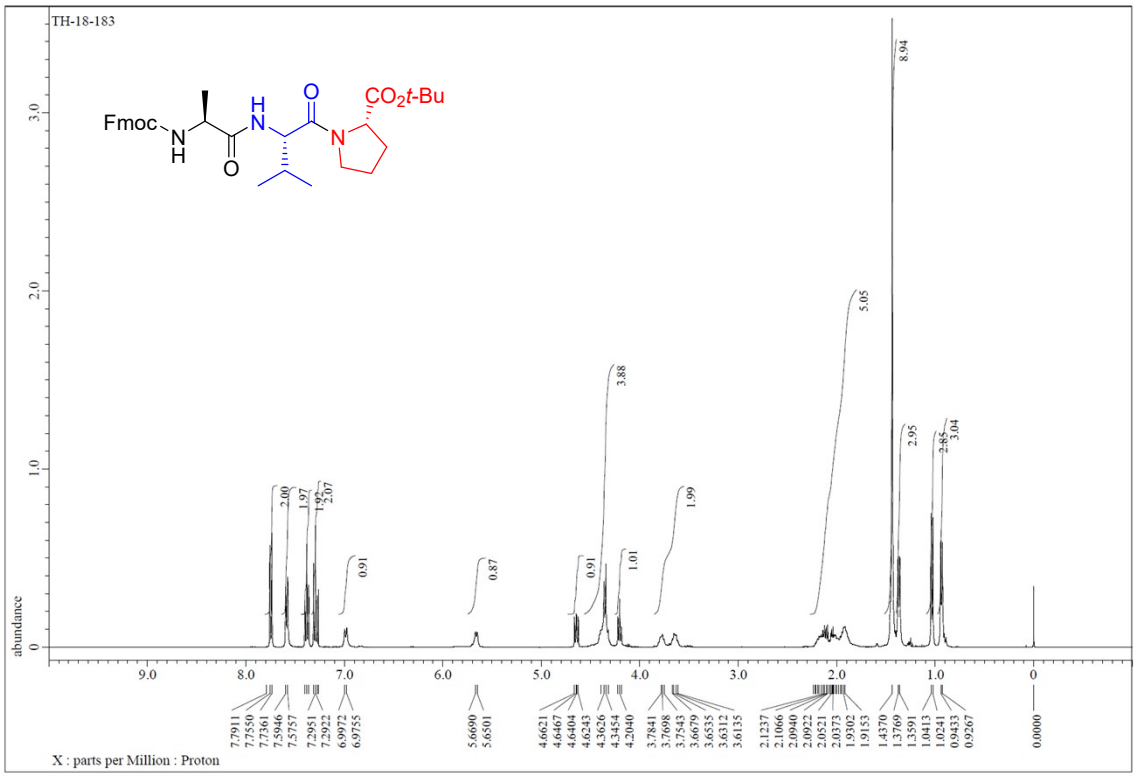
^{1}H NMR (400 MHz, $CDCl_3$) of **5q**



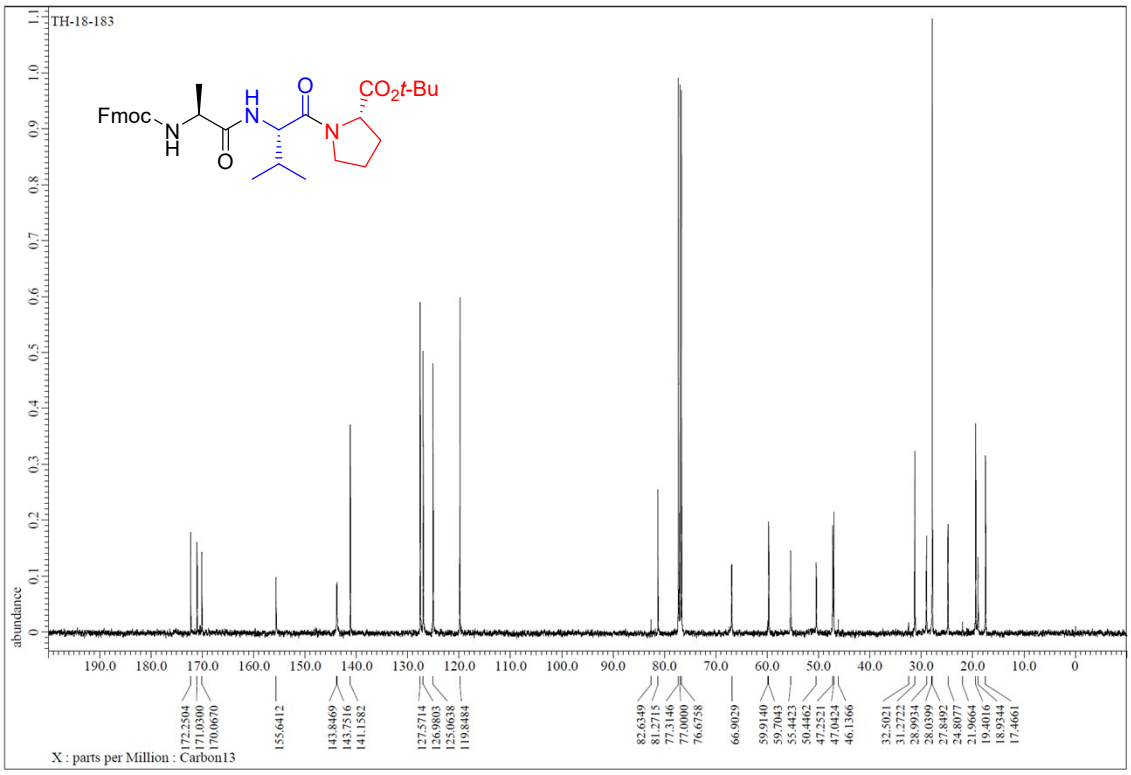
^{13}C NMR (100 MHz, $CDCl_3$) of **5q**



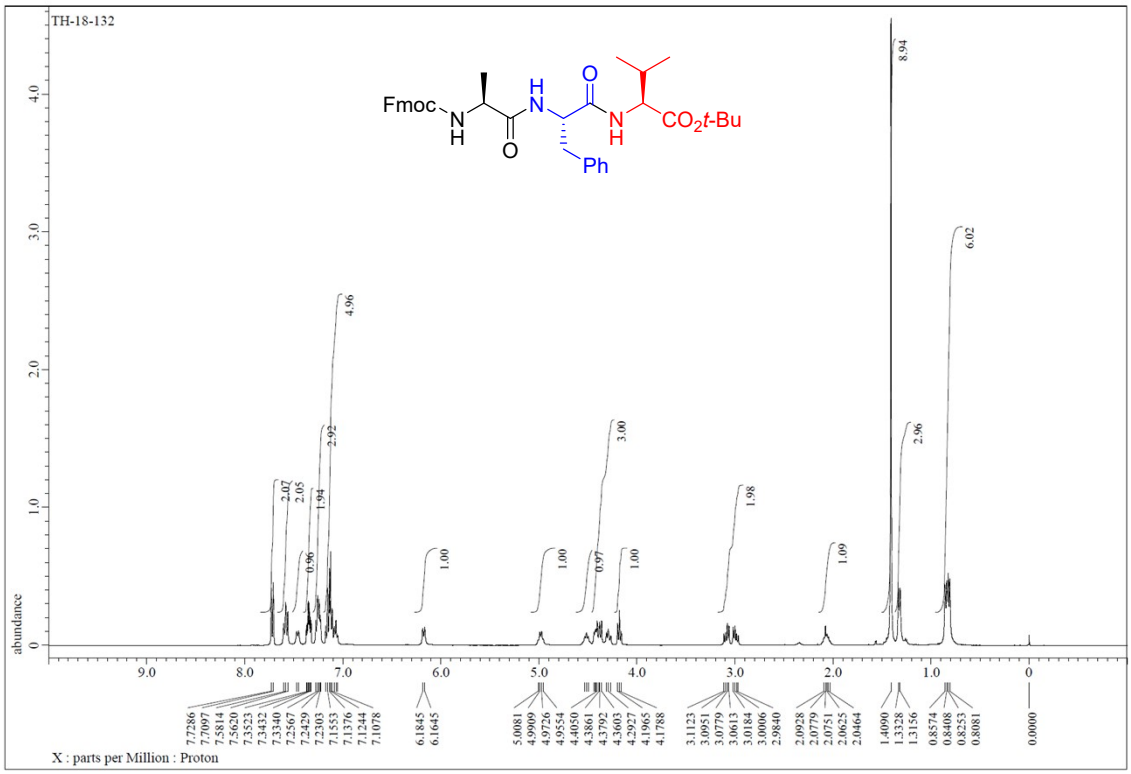
^{1}H NMR (400 MHz, $CDCl_3$) of **5r**



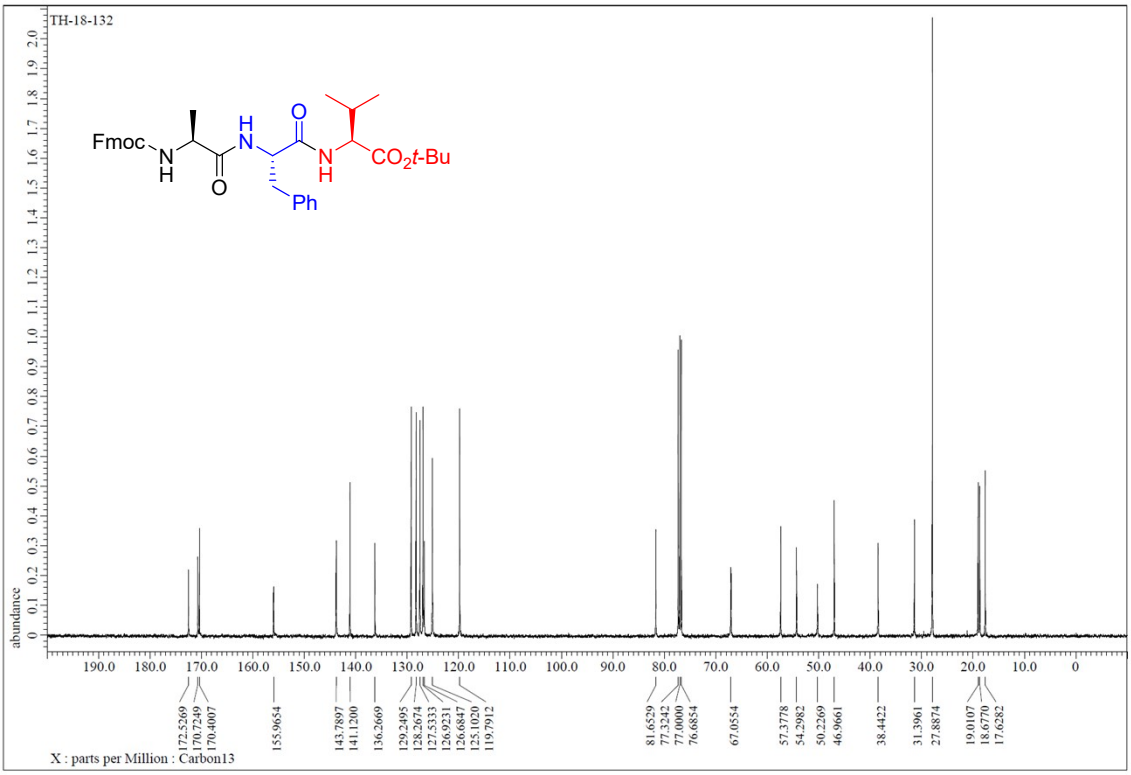
^{13}C NMR (100 MHz, $CDCl_3$) of **5r**



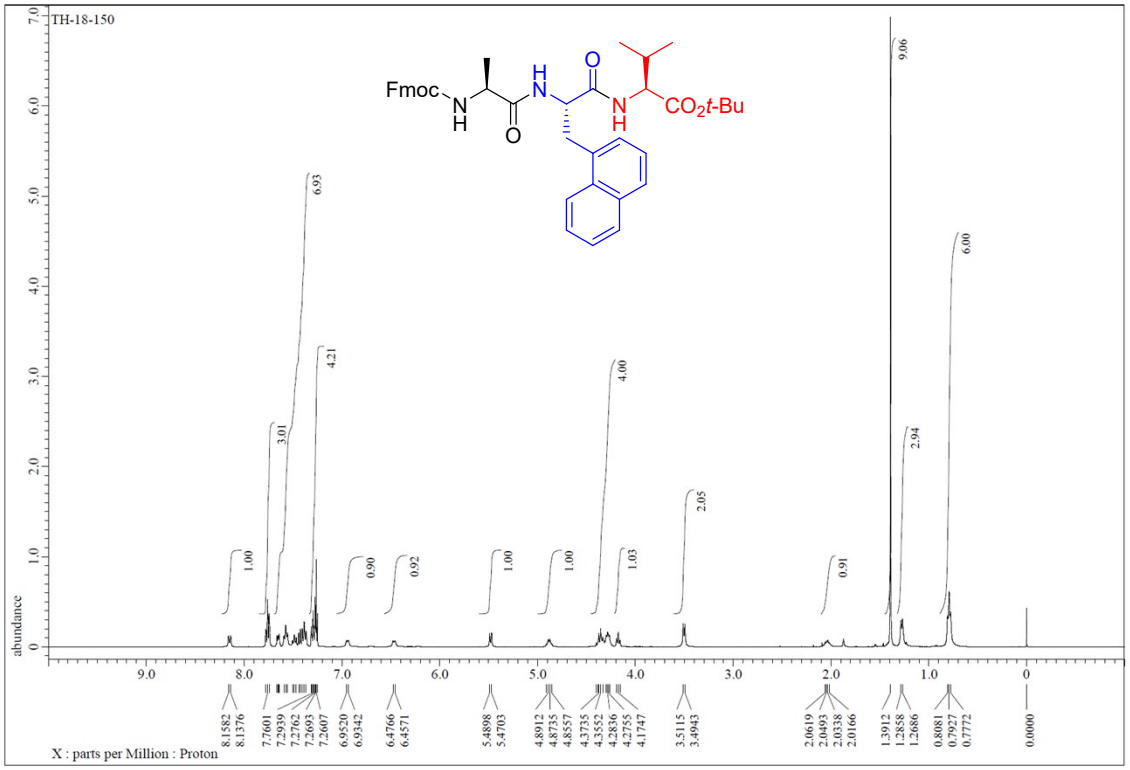
^{1}H NMR (400 MHz, $CDCl_3$) of **5s**



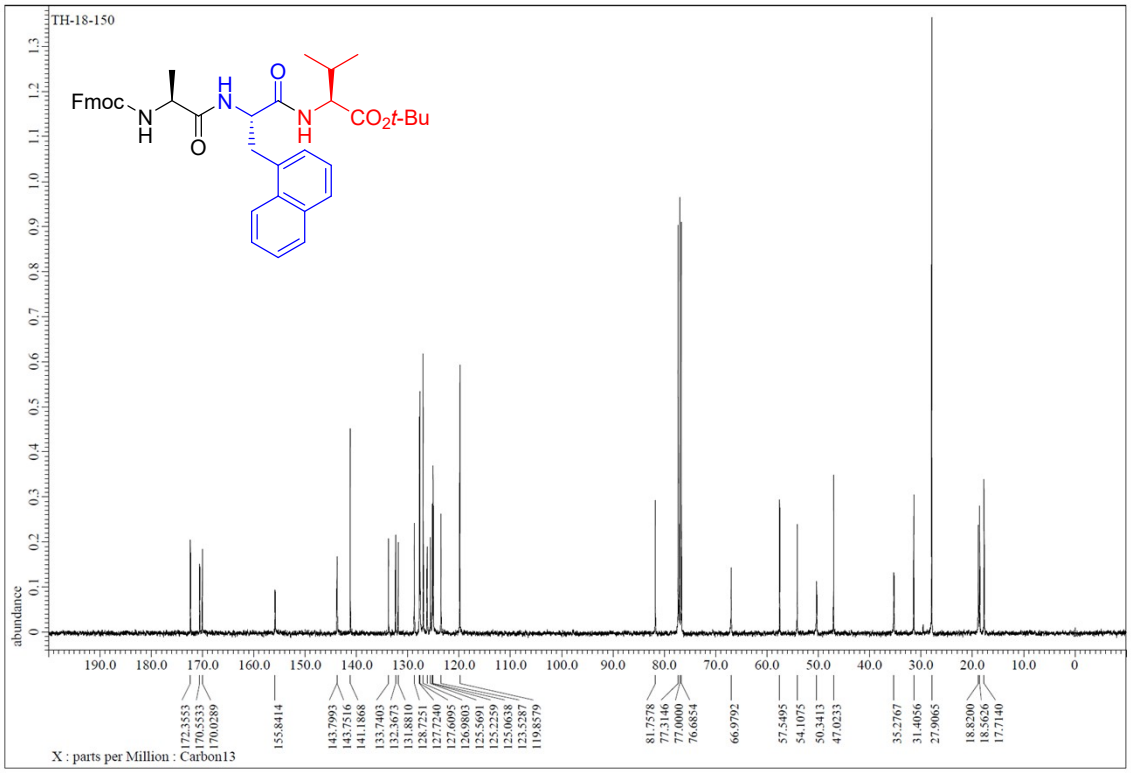
^{13}C NMR (100 MHz, $CDCl_3$) of **5s**



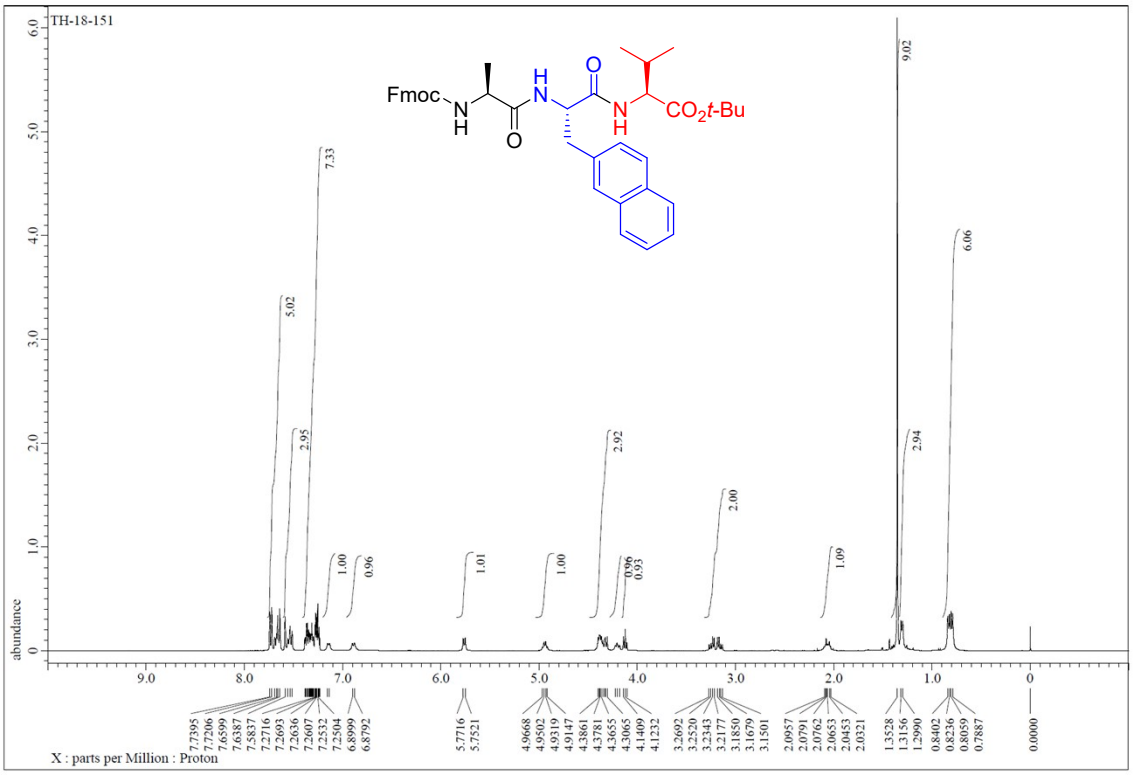
^{1}H NMR (400 MHz, $CDCl_3$) of **5t**



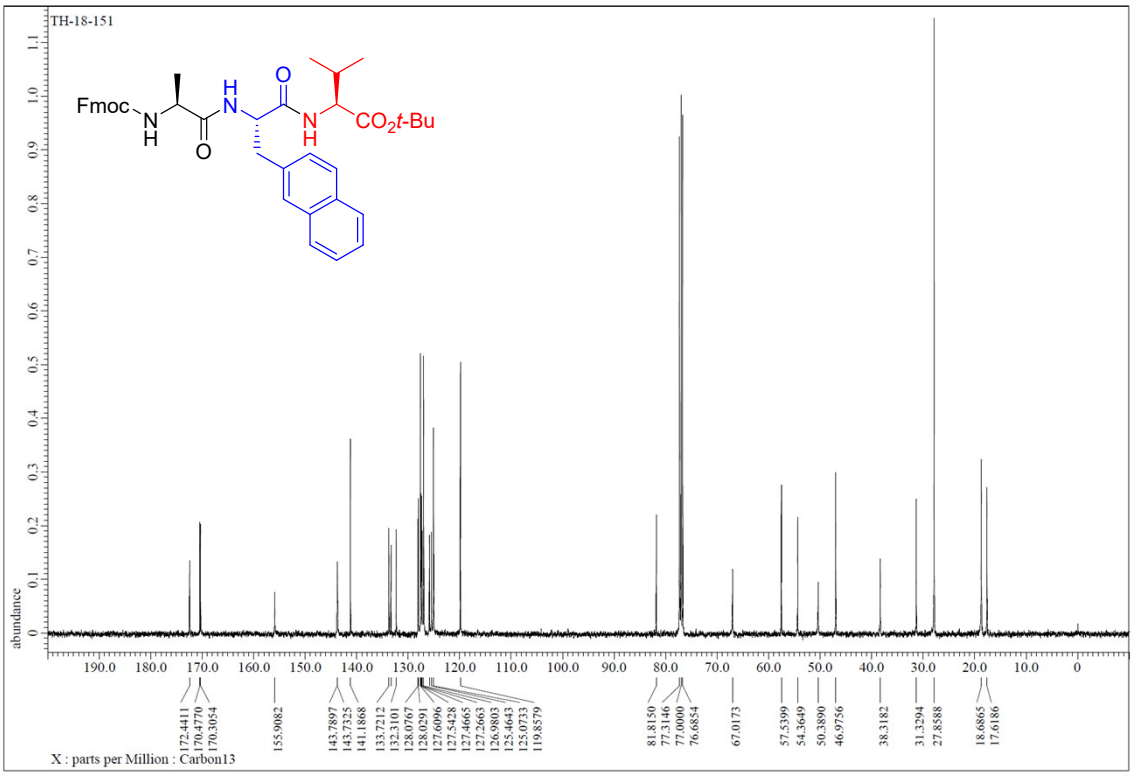
^{13}C NMR (100 MHz, $CDCl_3$) of **5t**



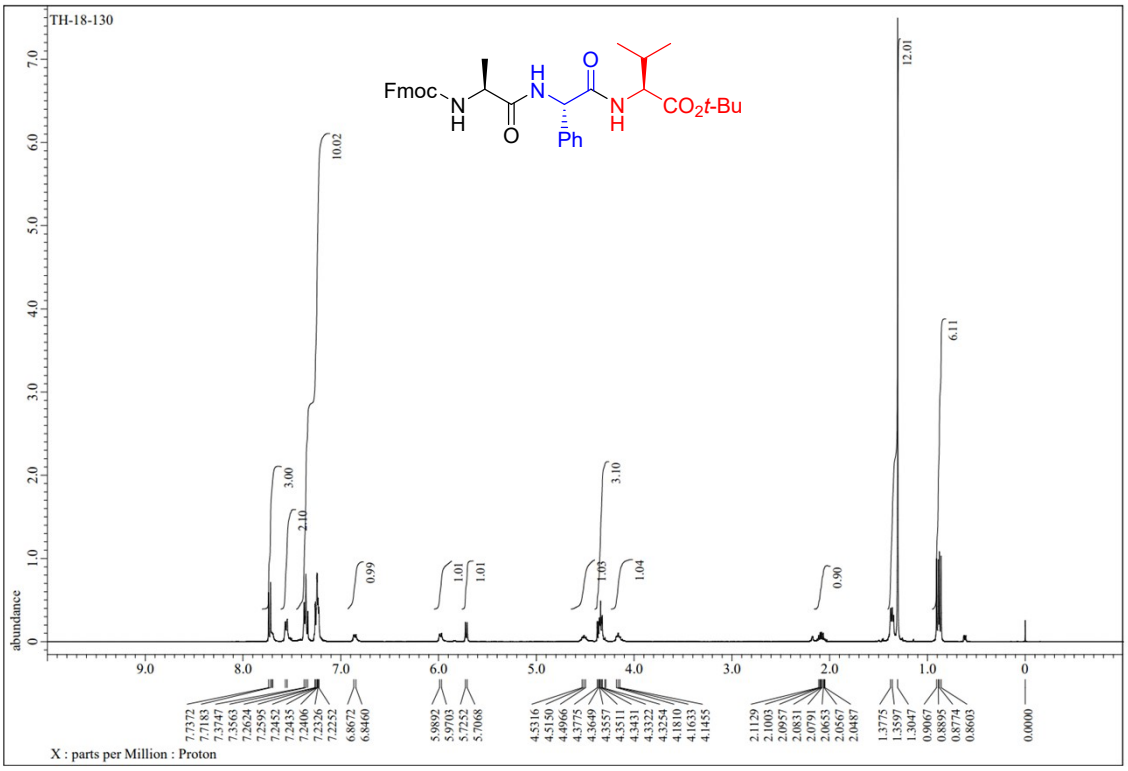
^{1}H NMR (400 MHz, $CDCl_3$) of **5u**



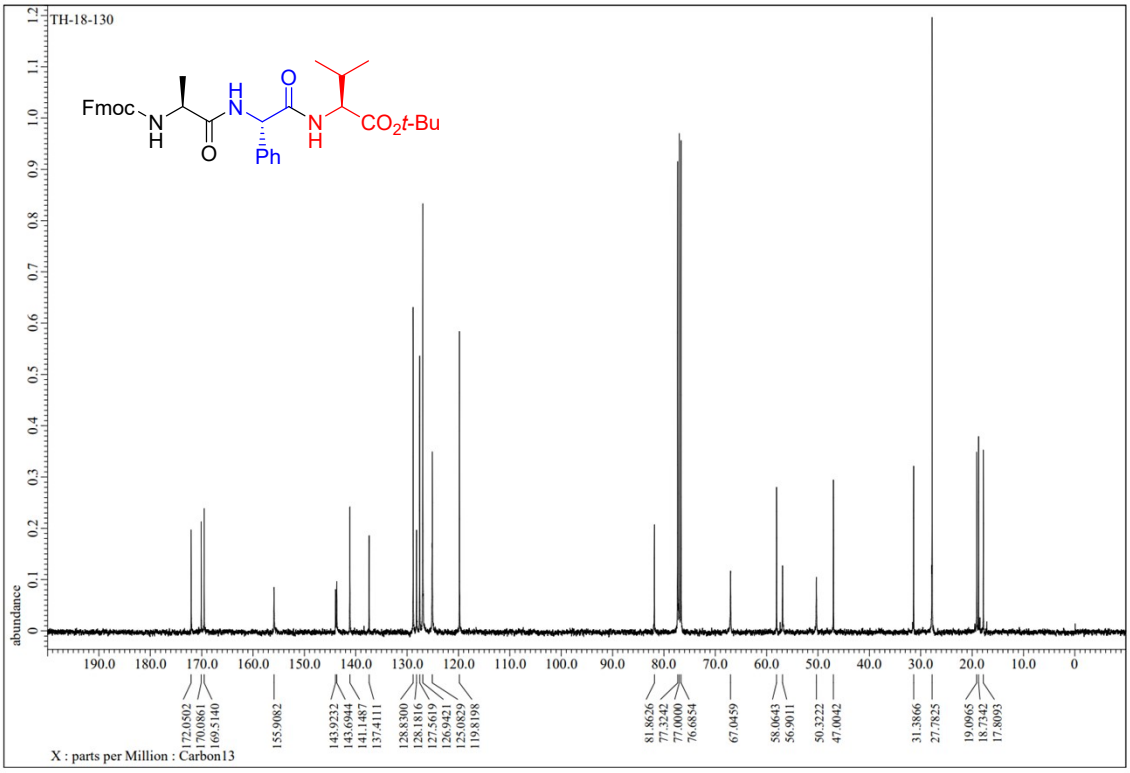
^{13}C NMR (100 MHz, $CDCl_3$) of **5u**



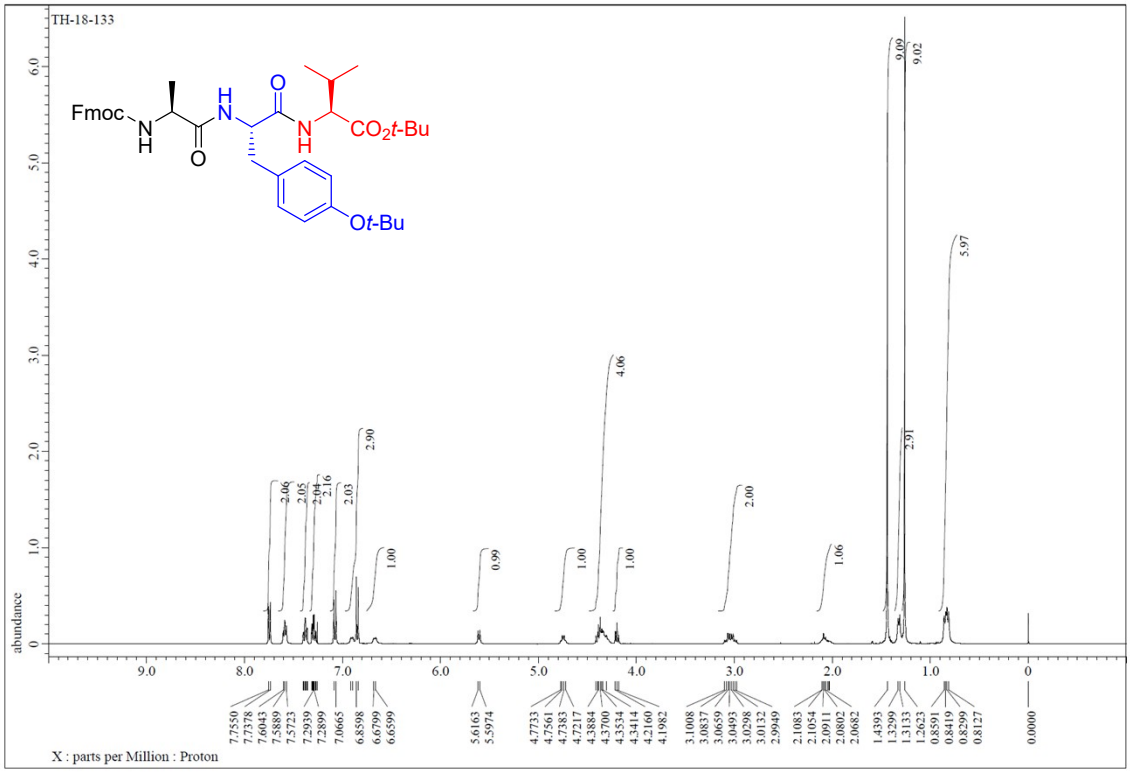
^{1}H NMR (400 MHz, $CDCl_3$) of **5v**



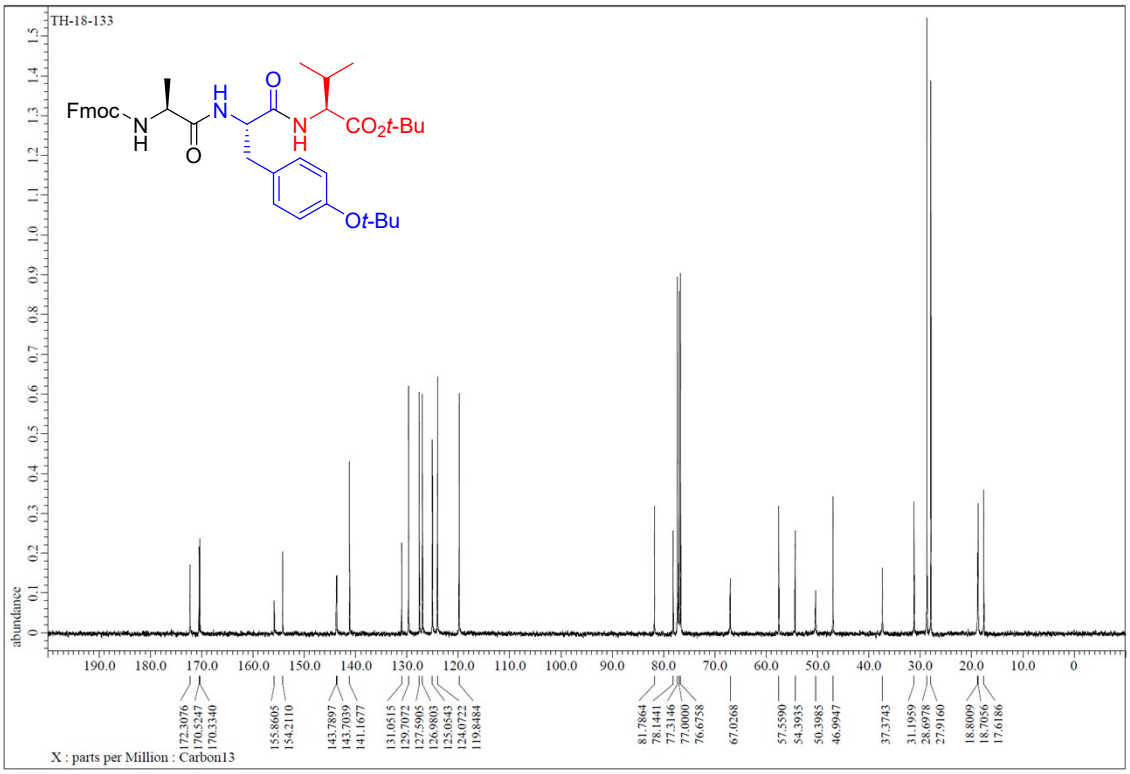
^{13}C NMR (100 MHz, $CDCl_3$) of **5v**



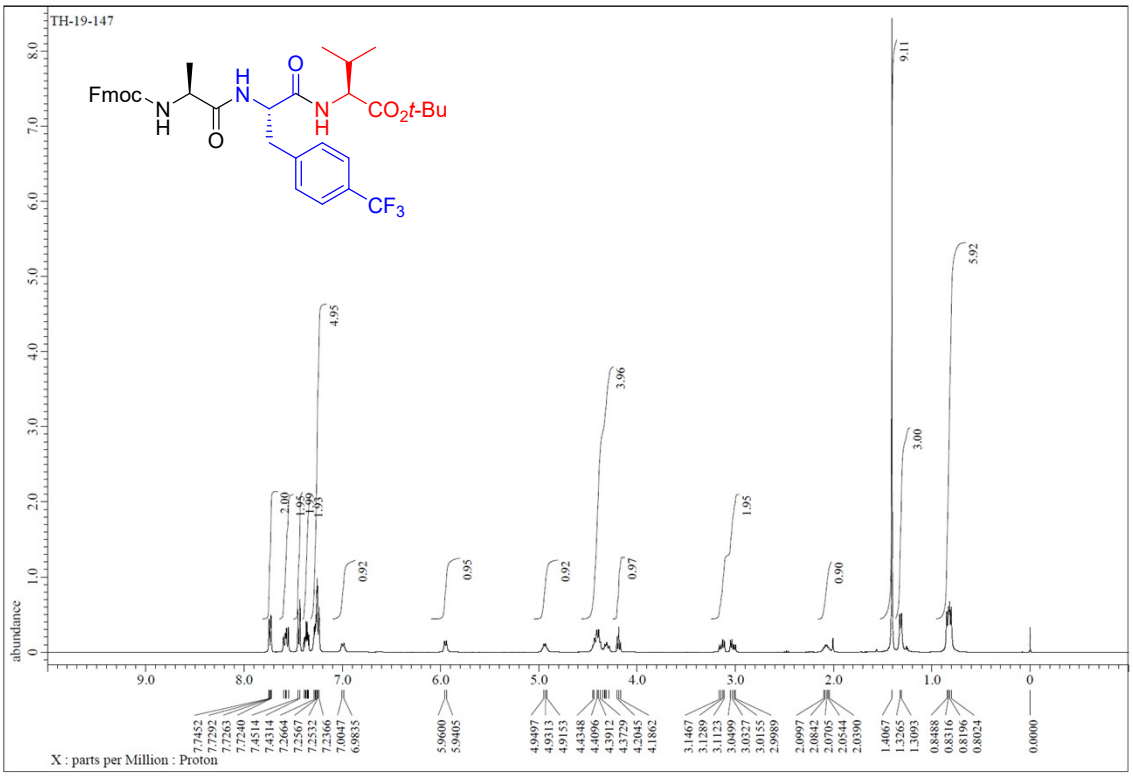
^{1}H NMR (400 MHz, $CDCl_3$) of **5w**



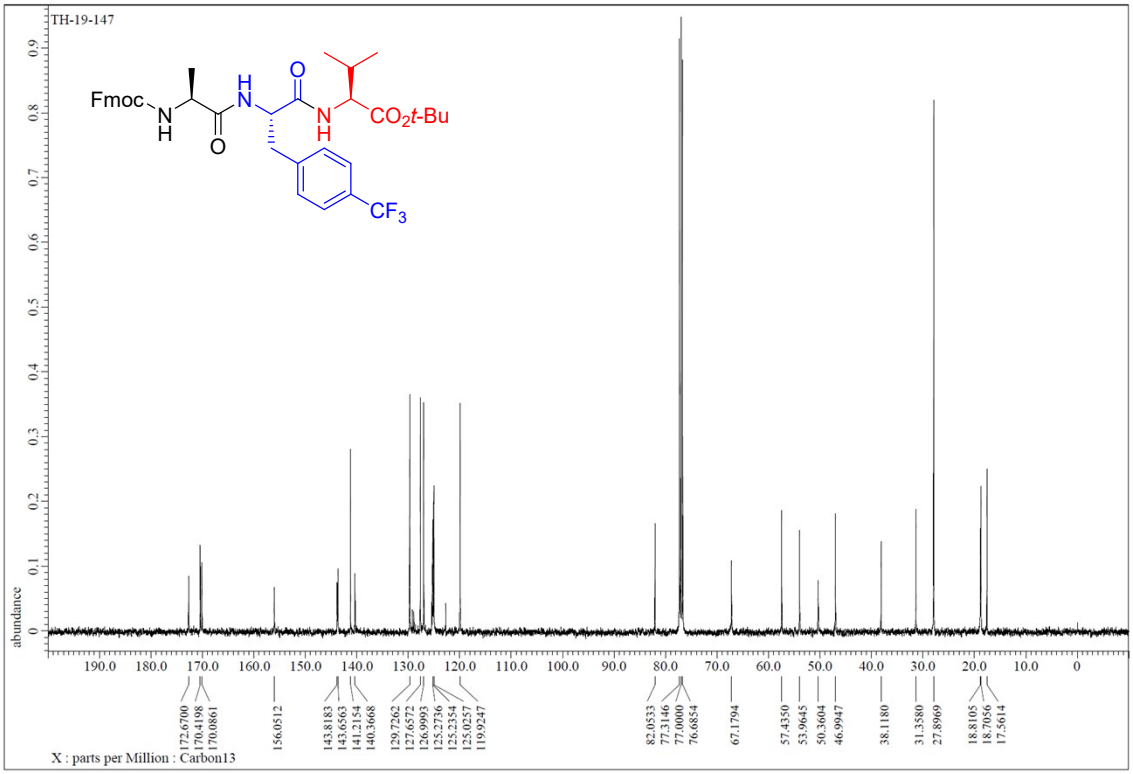
^{13}C NMR (100 MHz, $CDCl_3$) of **5w**



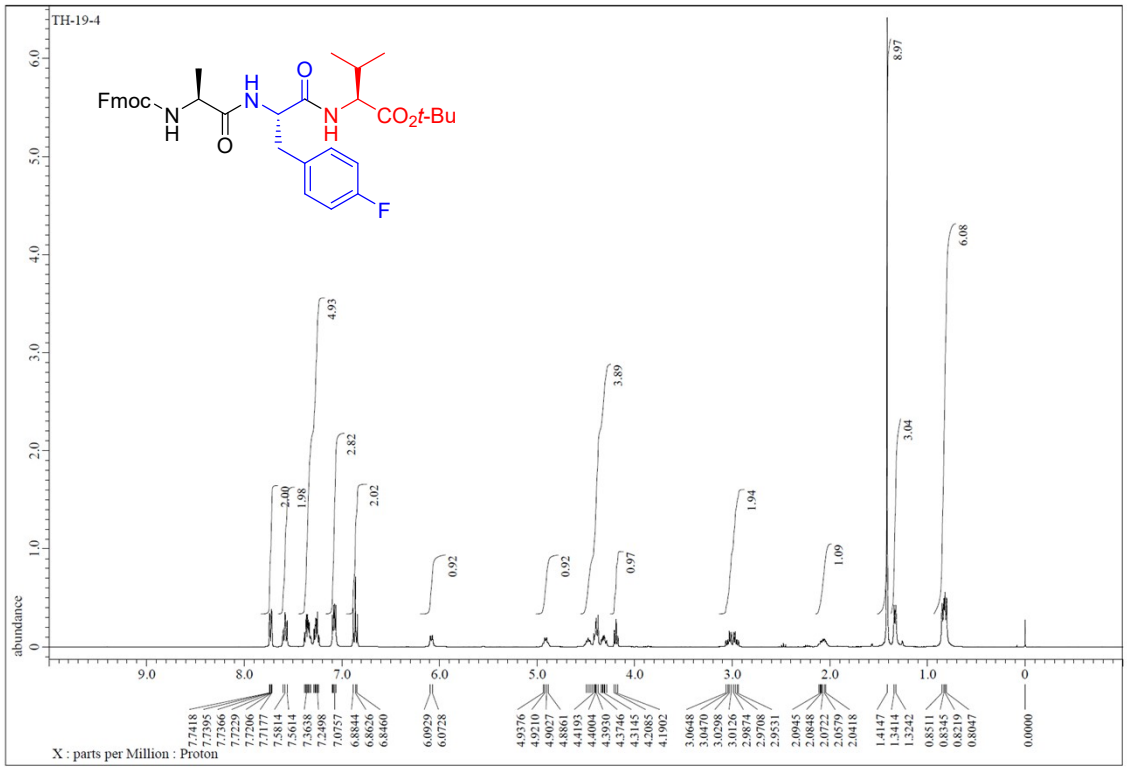
^{1}H NMR (400 MHz, $CDCl_3$) of **5x**



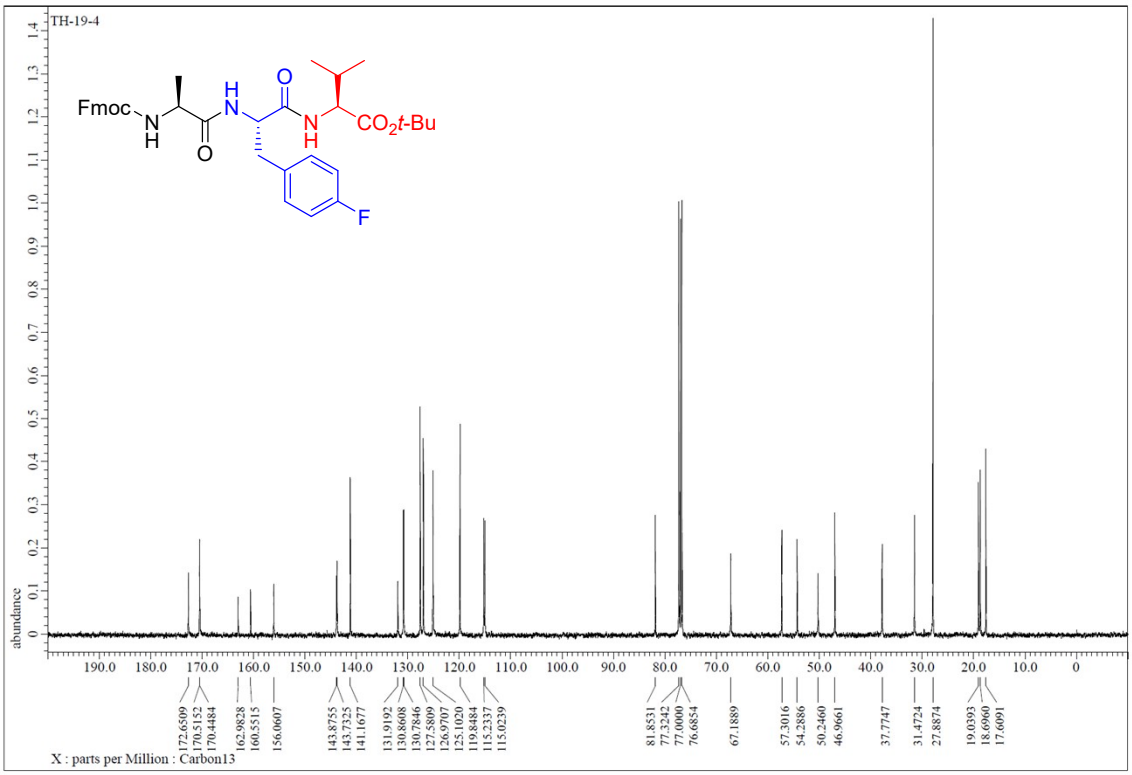
^{13}C NMR (100 MHz, $CDCl_3$) of **5x**



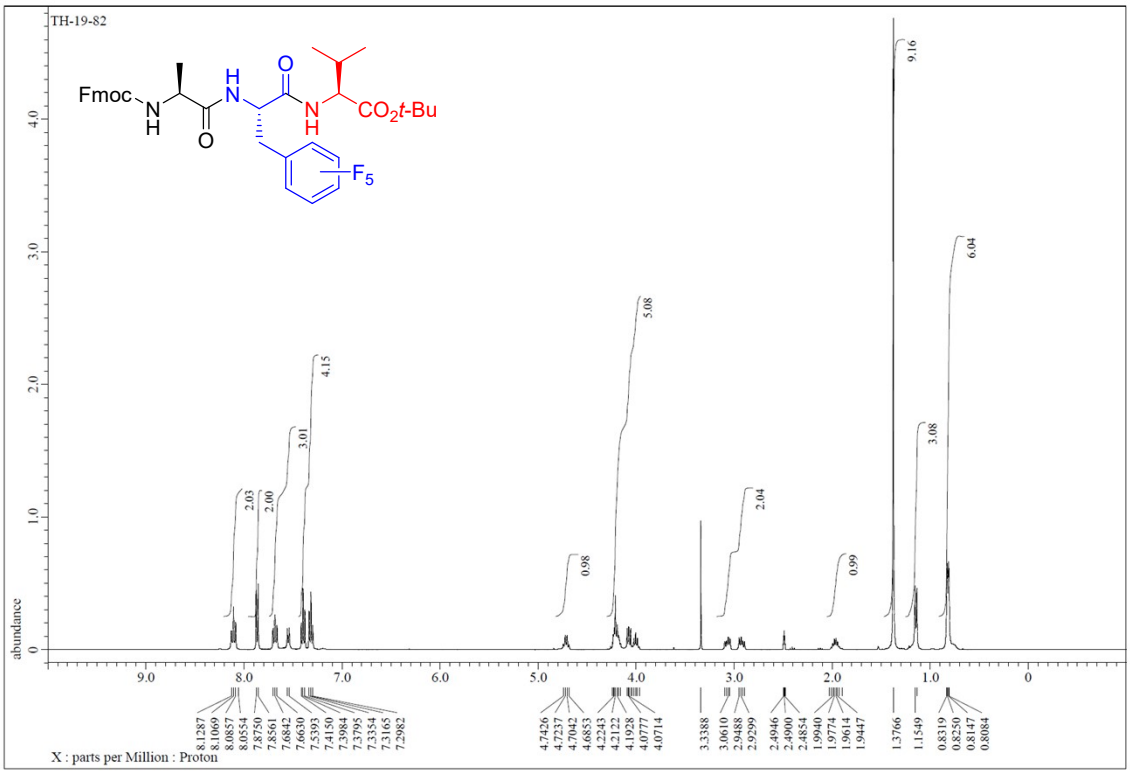
^{1}H NMR (400 MHz, $CDCl_3$) of **5y**



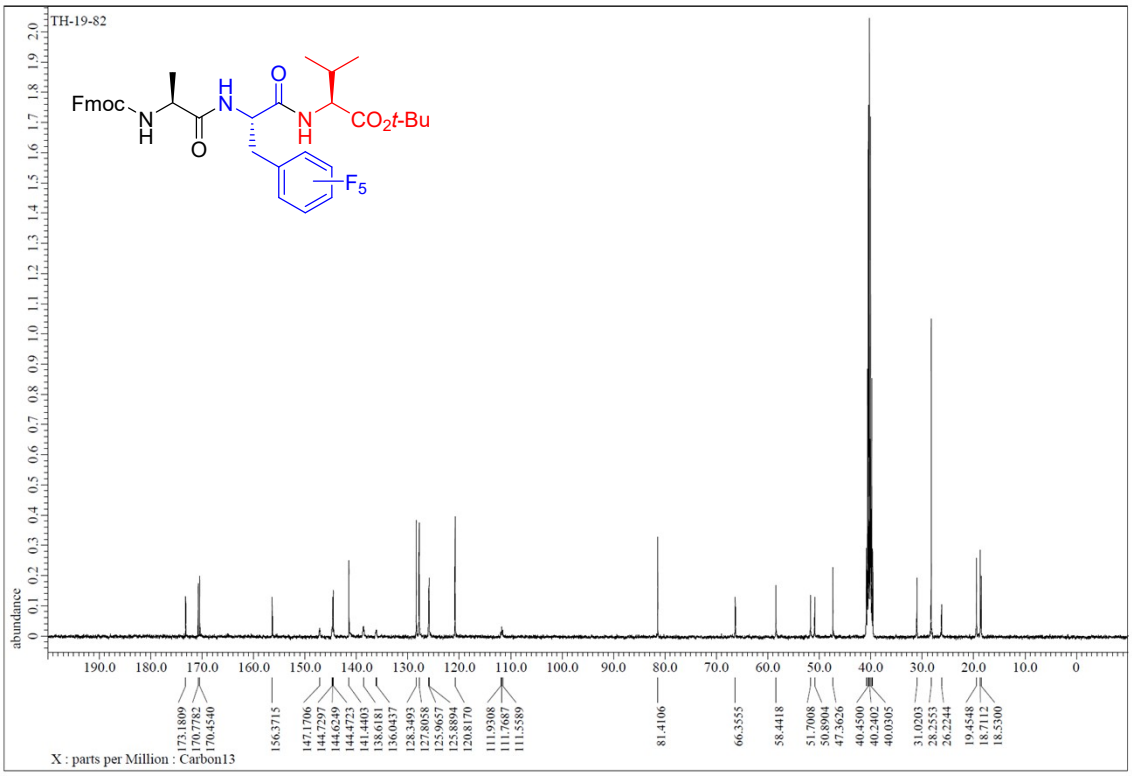
^{13}C NMR (100 MHz, $CDCl_3$) of **5y**



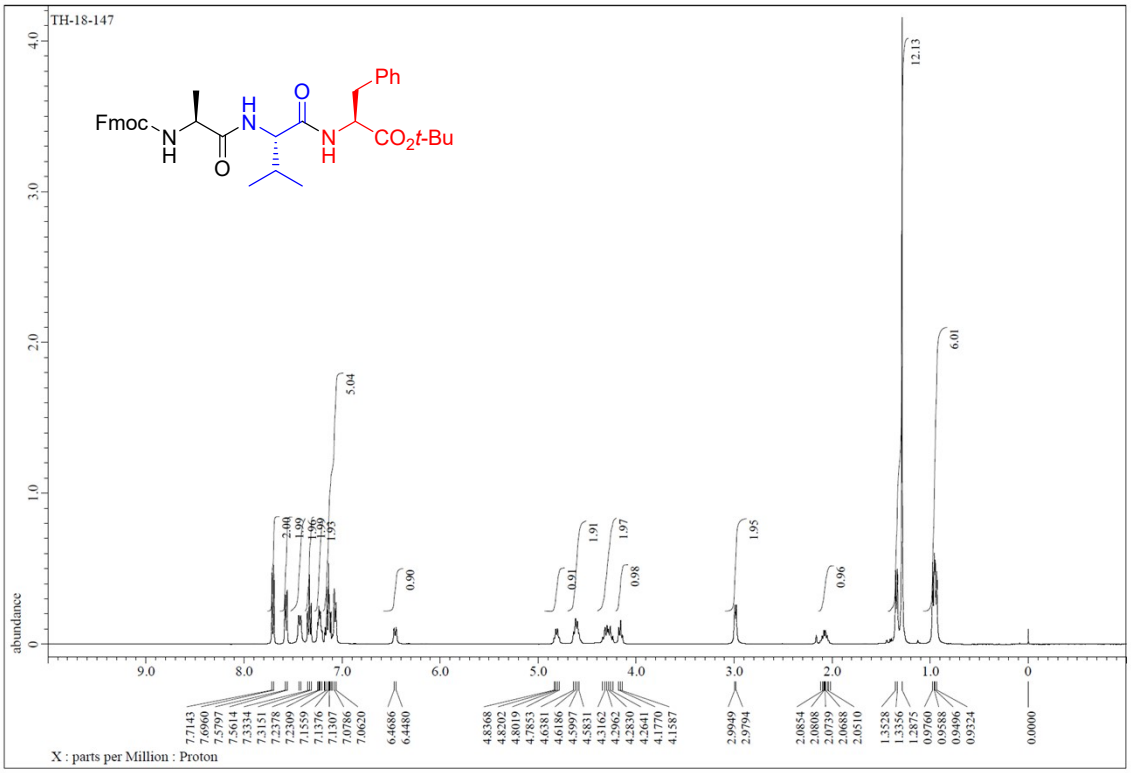
^{1}H NMR (400 MHz, DMSO-d_6) of **5z**



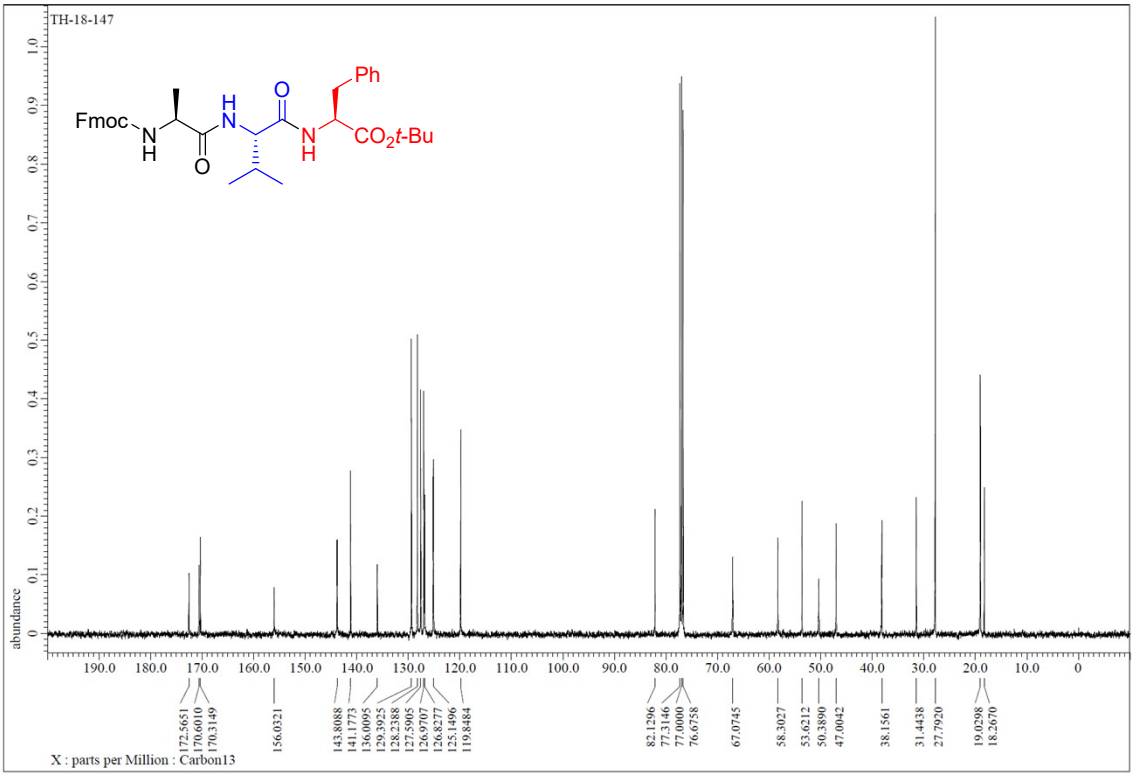
^{13}C NMR (100 MHz, DMSO-d_6) of **5z**



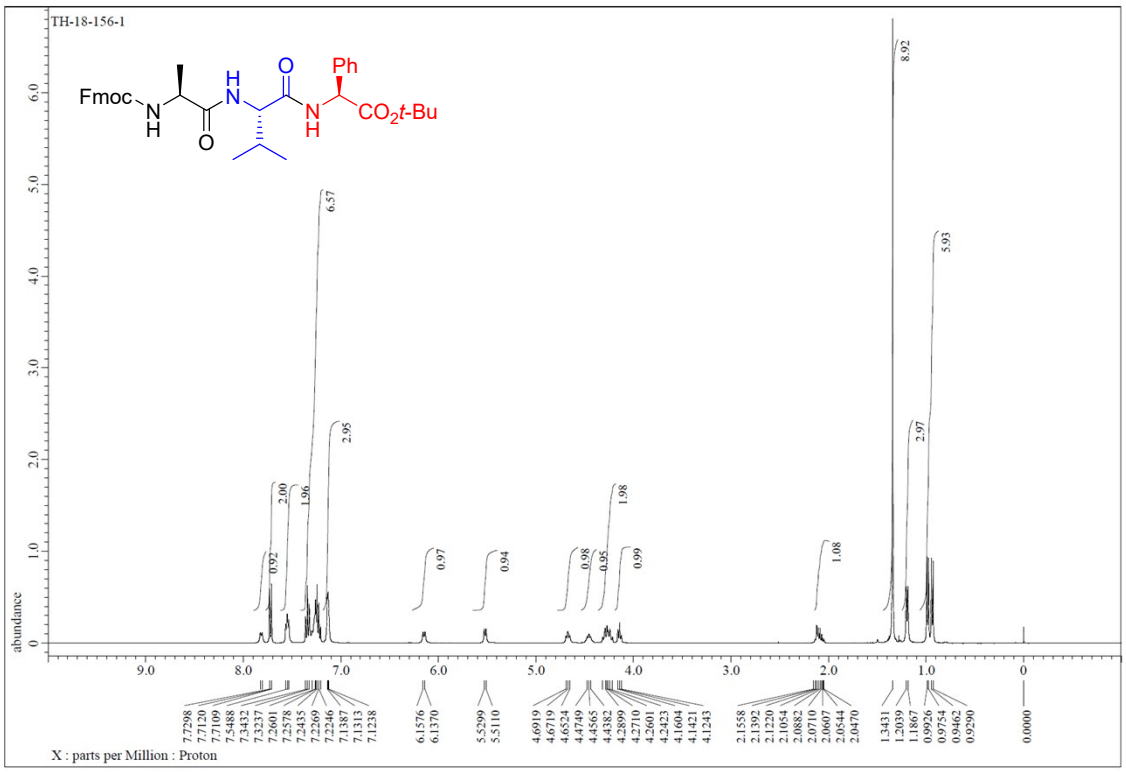
^{1}H NMR (400 MHz, $CDCl_3$) of **5aa**



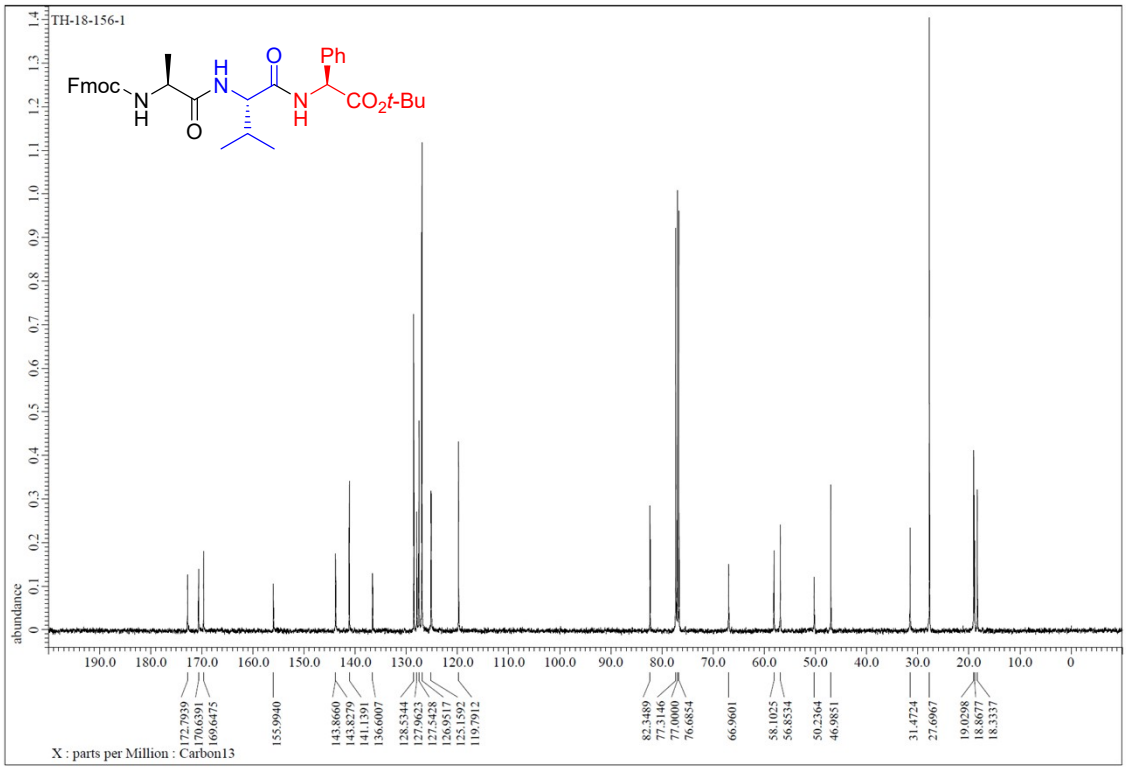
^{13}C NMR (100 MHz, $CDCl_3$) of **5aa**



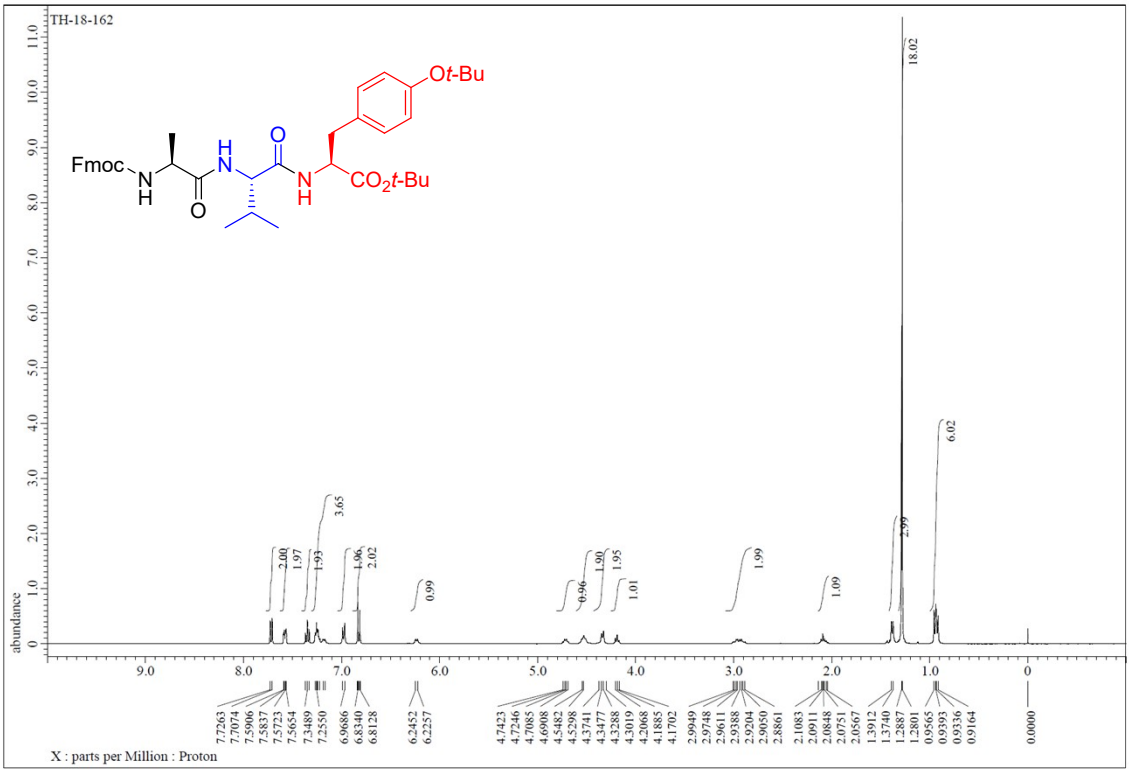
^{1}H NMR (400 MHz, $CDCl_3$) of **5ab**



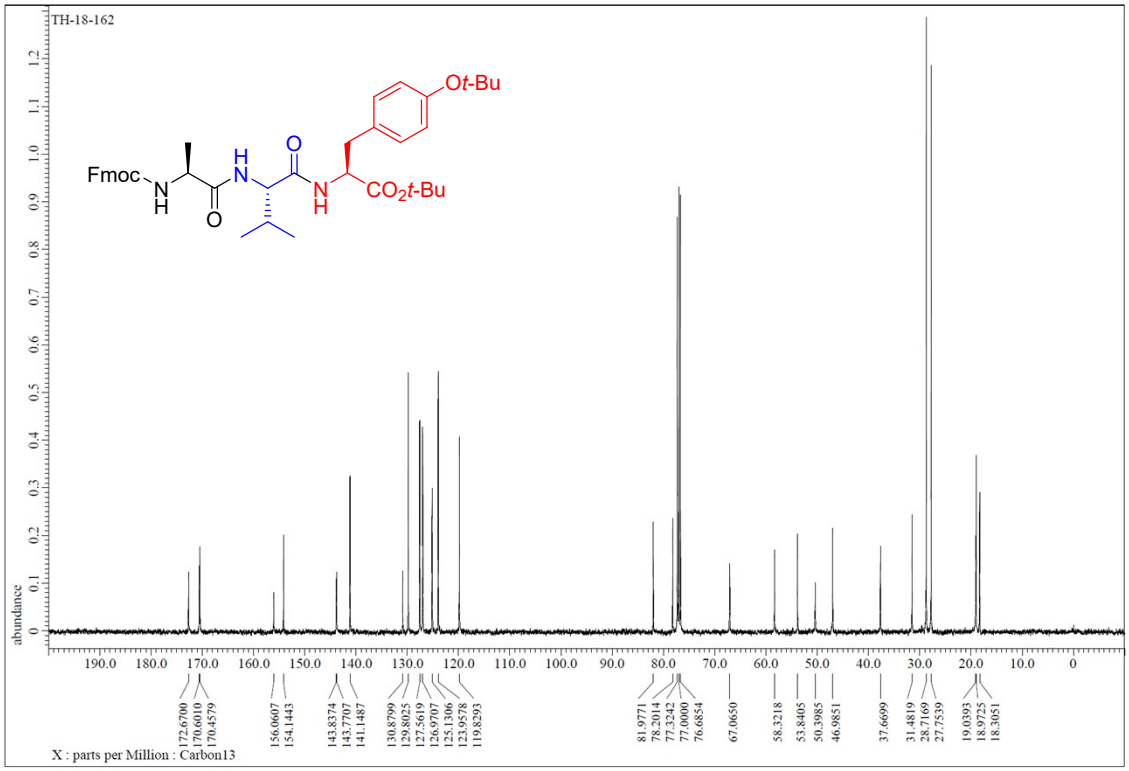
^{13}C NMR (100 MHz, $CDCl_3$) of **5ab**



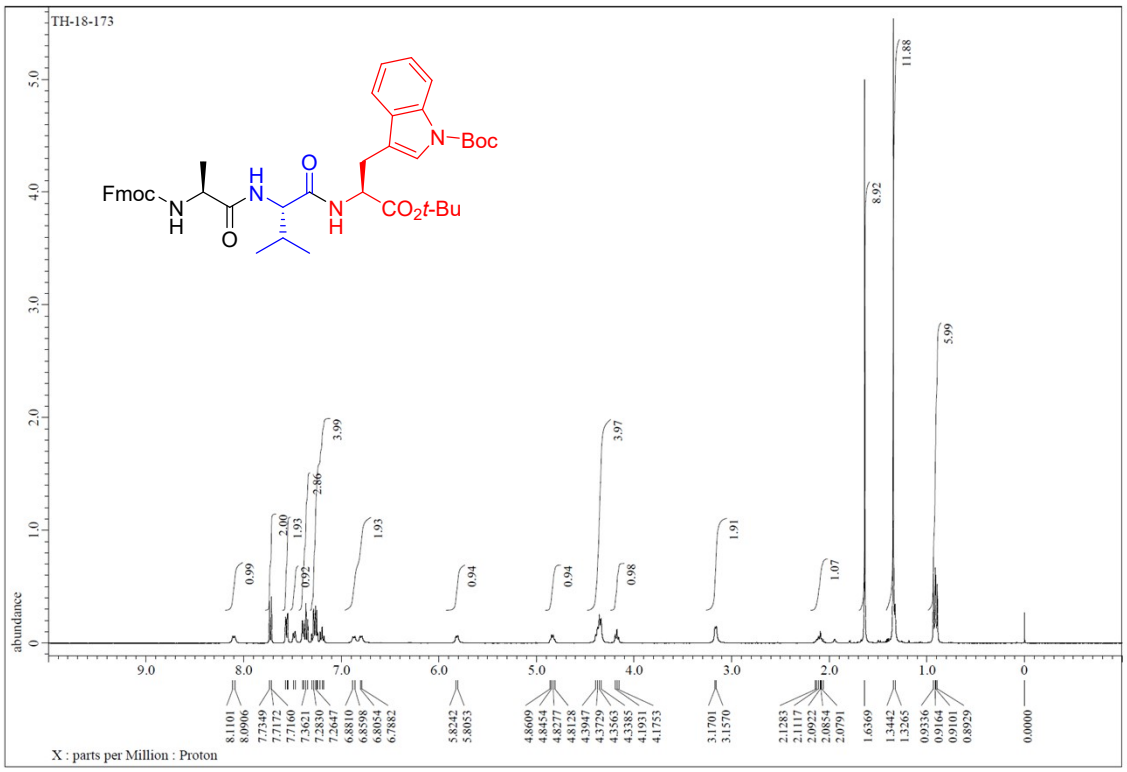
^{1}H NMR (400 MHz, $CDCl_3$) of **5ac**



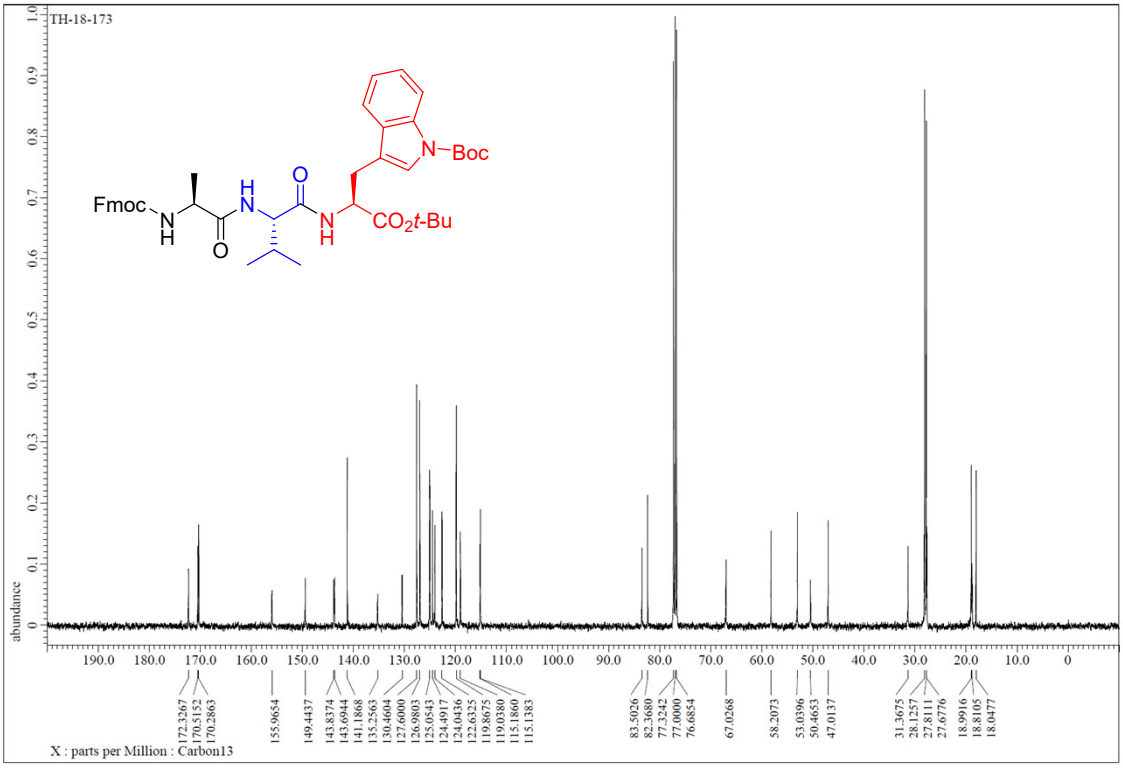
^{13}C NMR (100 MHz, $CDCl_3$) of **5ac**



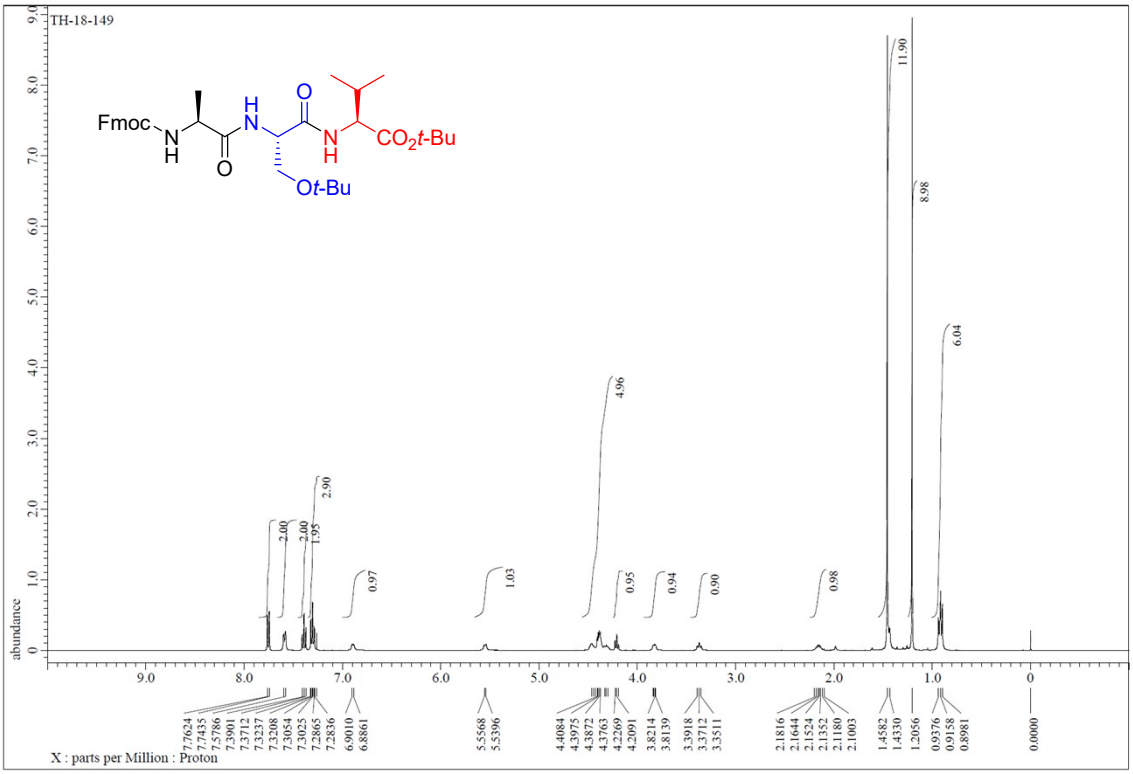
^{1}H NMR (400 MHz, $CDCl_3$) of **5ad**



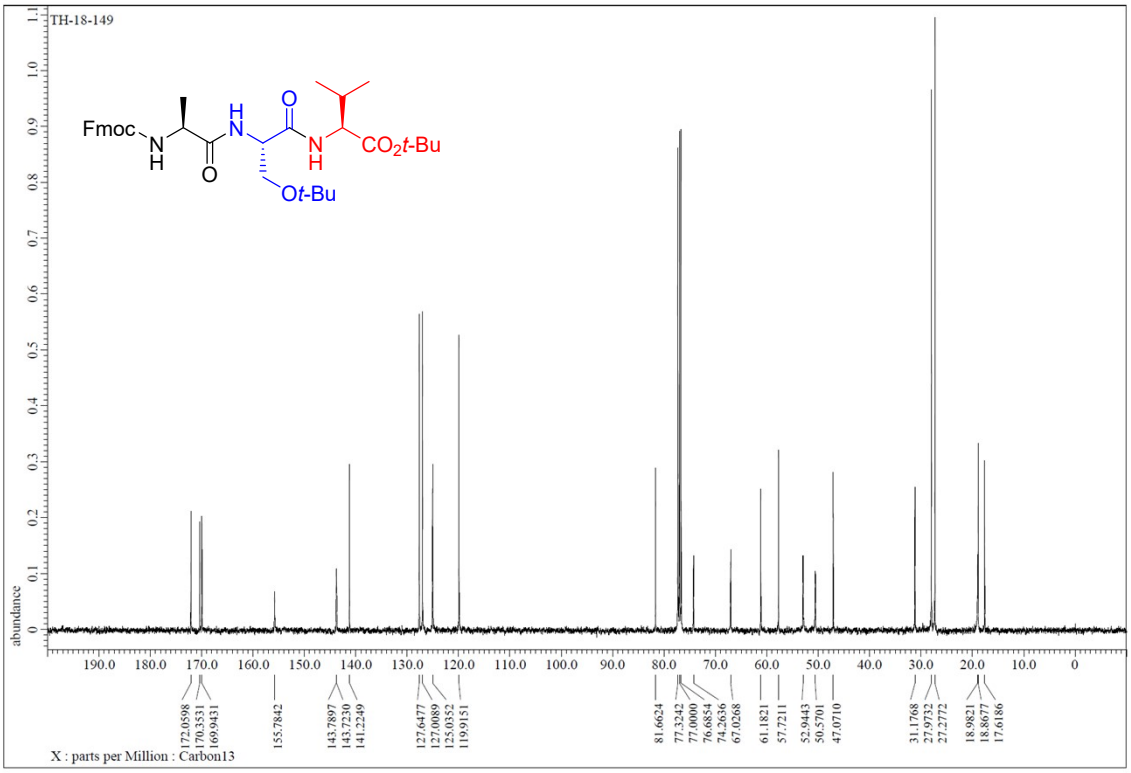
^{13}C NMR (100 MHz, $CDCl_3$) of **5ad**



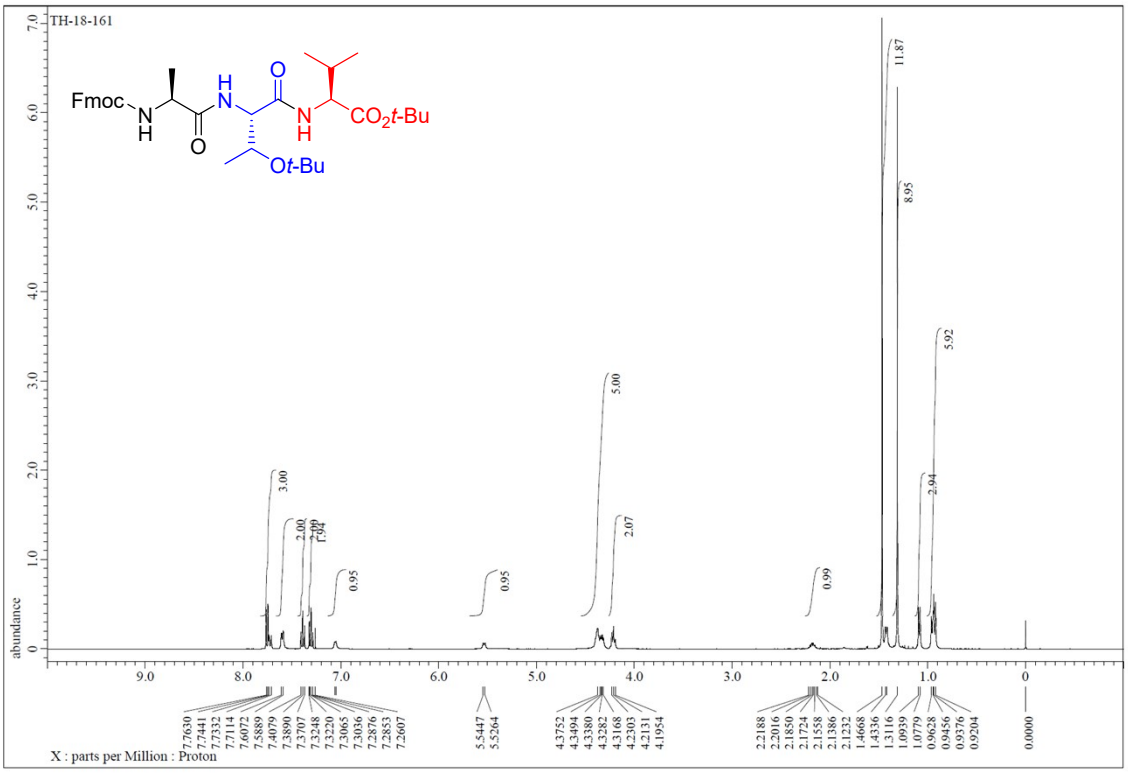
^{1}H NMR (400 MHz, $CDCl_3$) of **5ae**



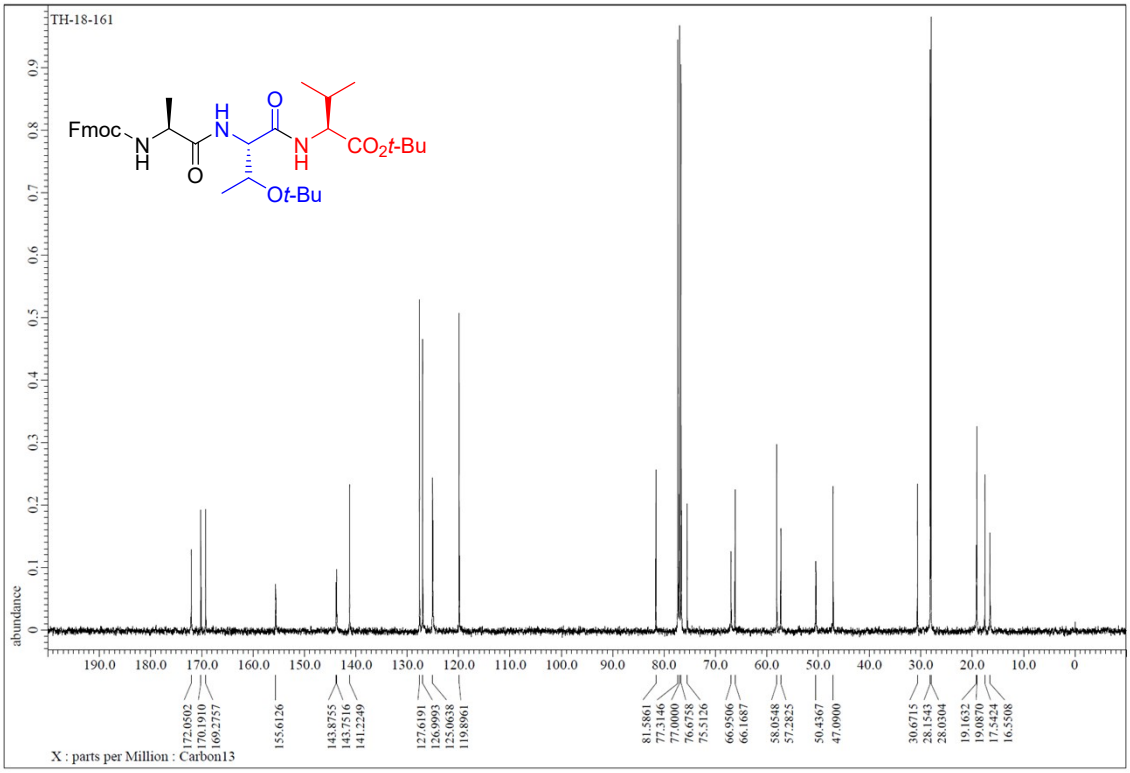
^{13}C NMR (100 MHz, $CDCl_3$) of **5ae**



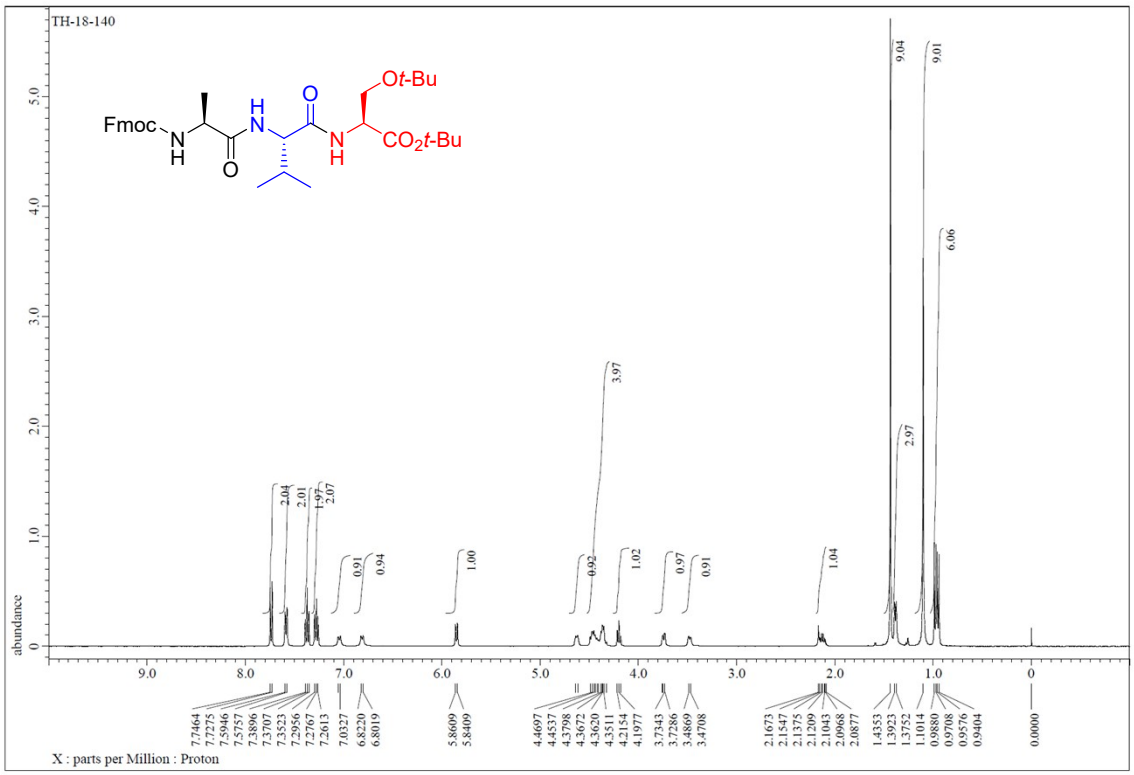
^{1}H NMR (400 MHz, $CDCl_3$) of **5af**



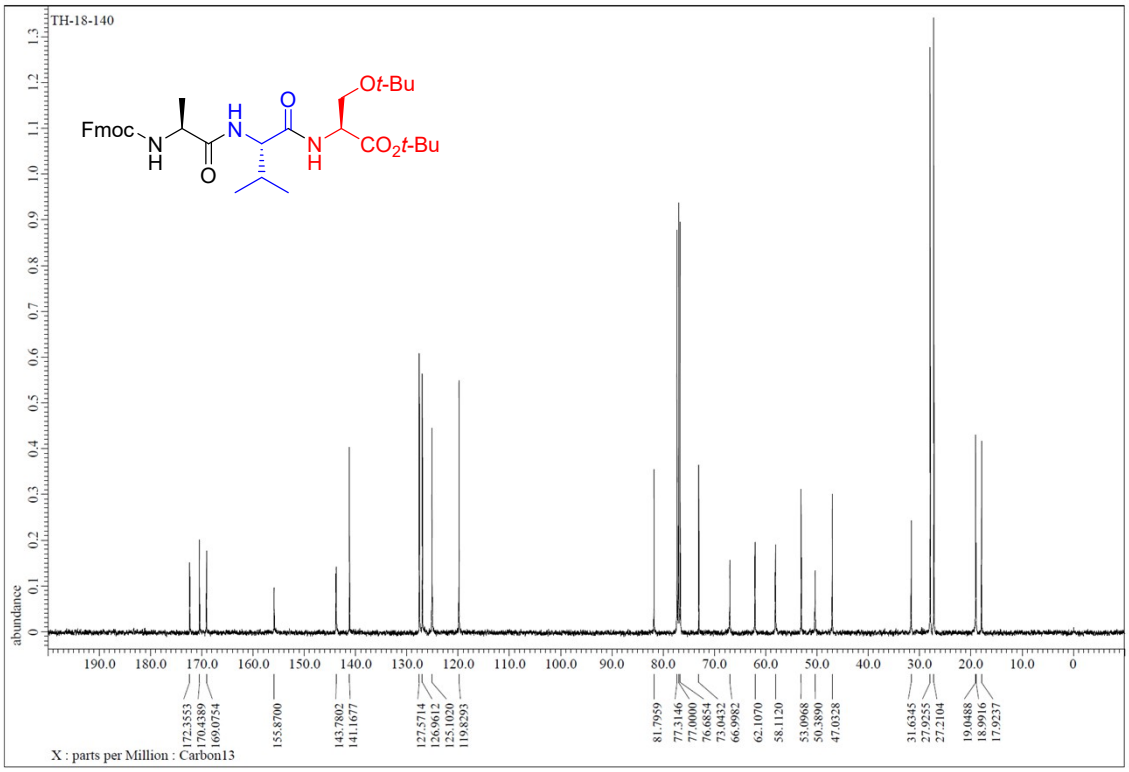
^{13}C NMR (100 MHz, $CDCl_3$) of **5af**



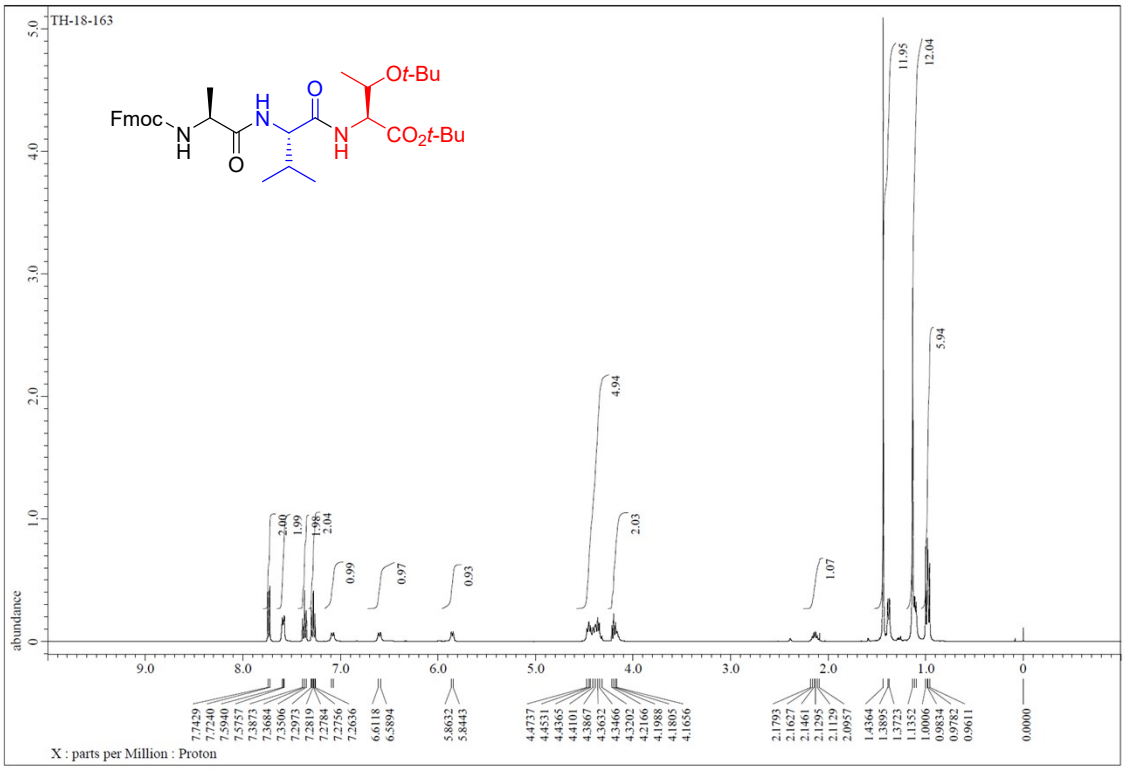
^{1}H NMR (400 MHz, $CDCl_3$) of **5ag**



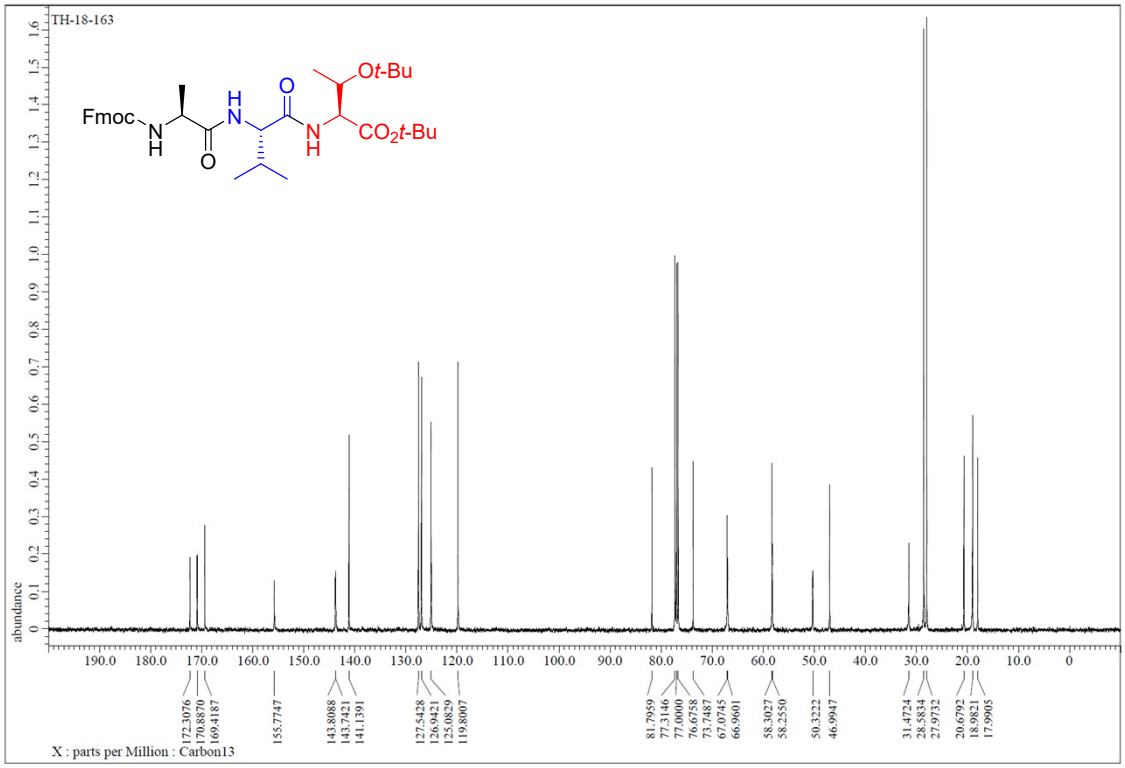
^{13}C NMR (100 MHz, $CDCl_3$) of **5ag**



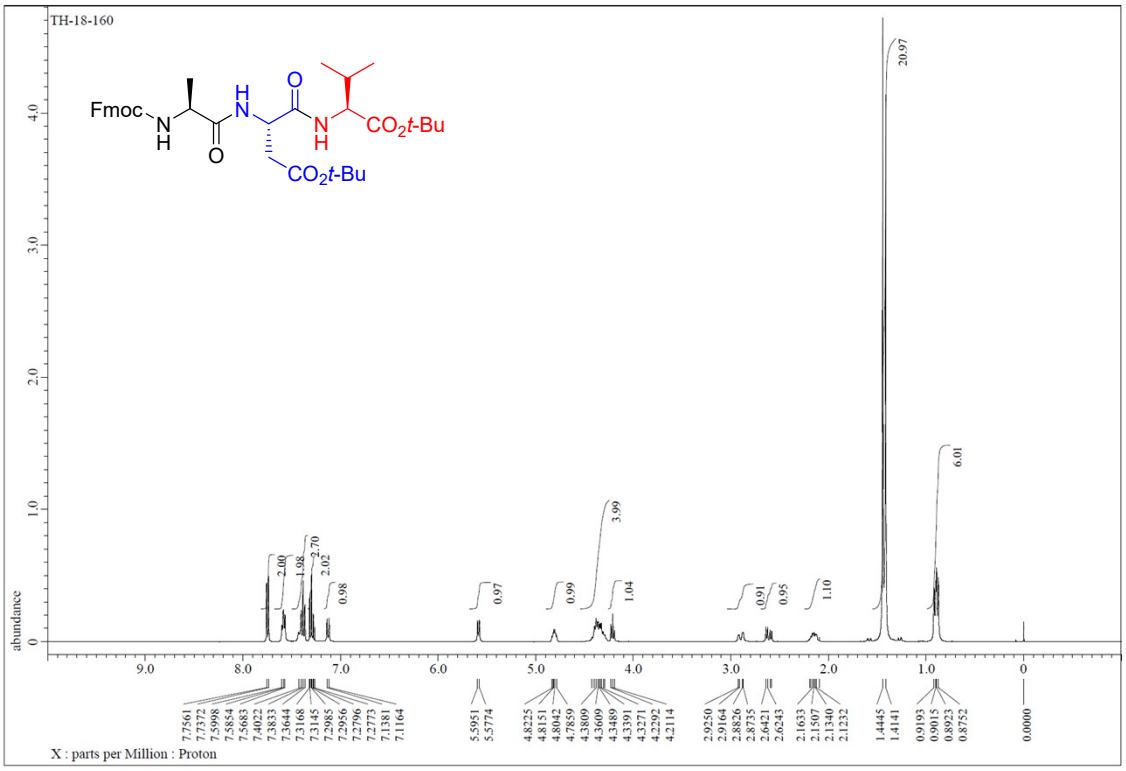
^{1}H NMR (400 MHz, $CDCl_3$) of **5ah**



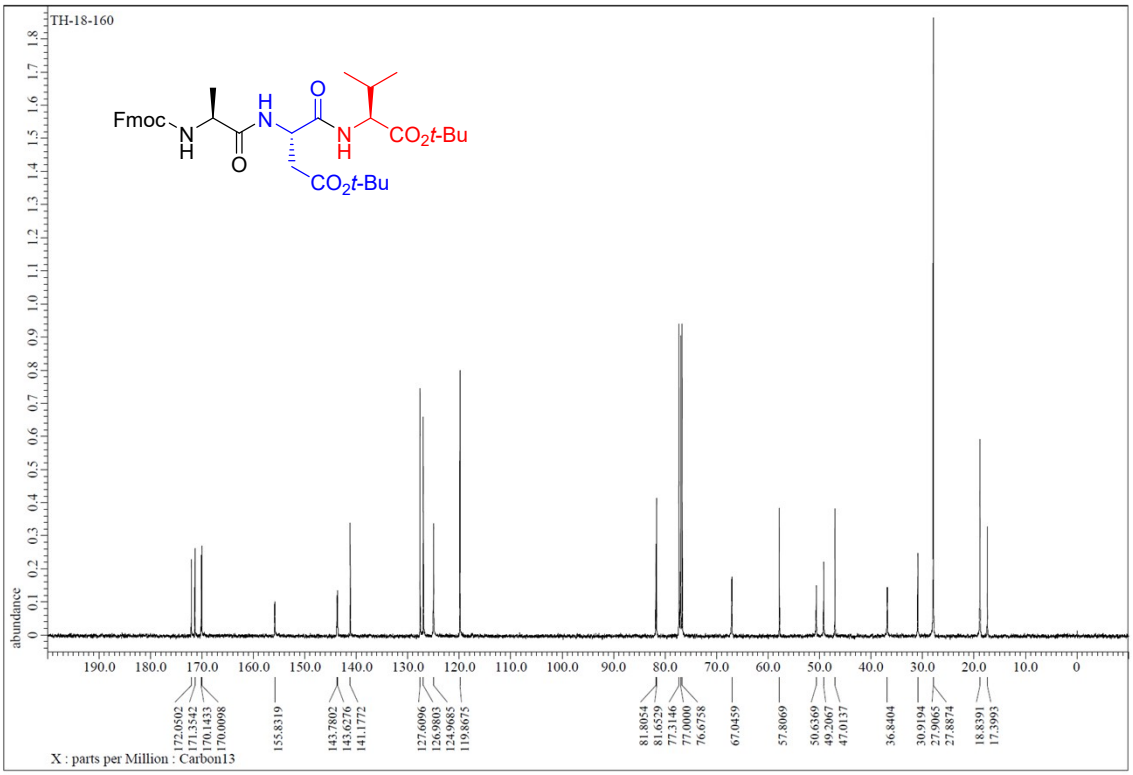
^{13}C NMR (100 MHz, $CDCl_3$) of **5ah**



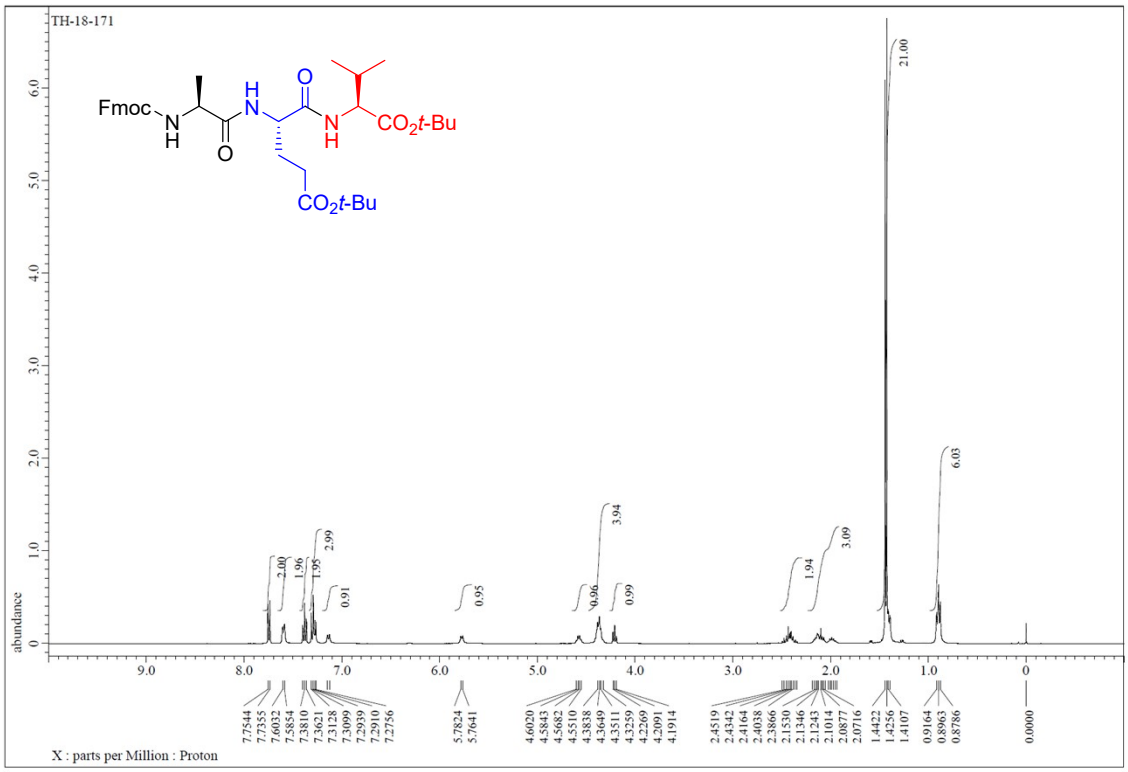
^{1}H NMR (400 MHz, $CDCl_3$) of **5ai**



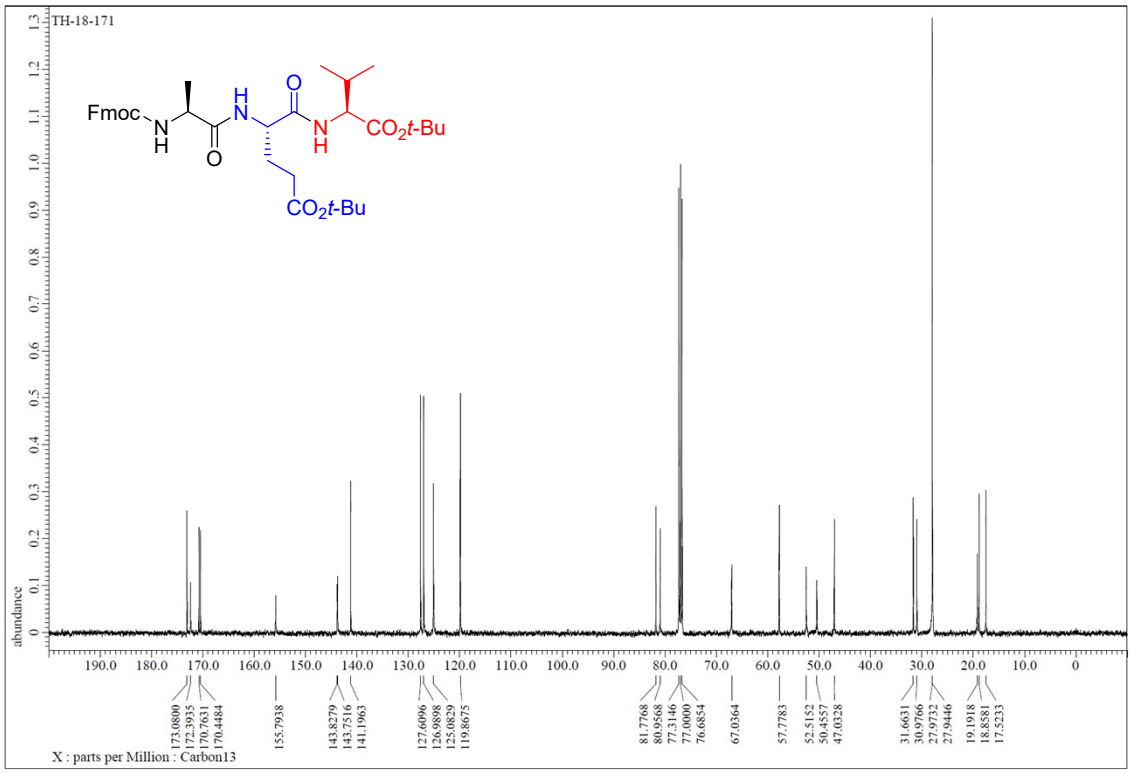
^{13}C NMR (100 MHz, $CDCl_3$) of **5ai**



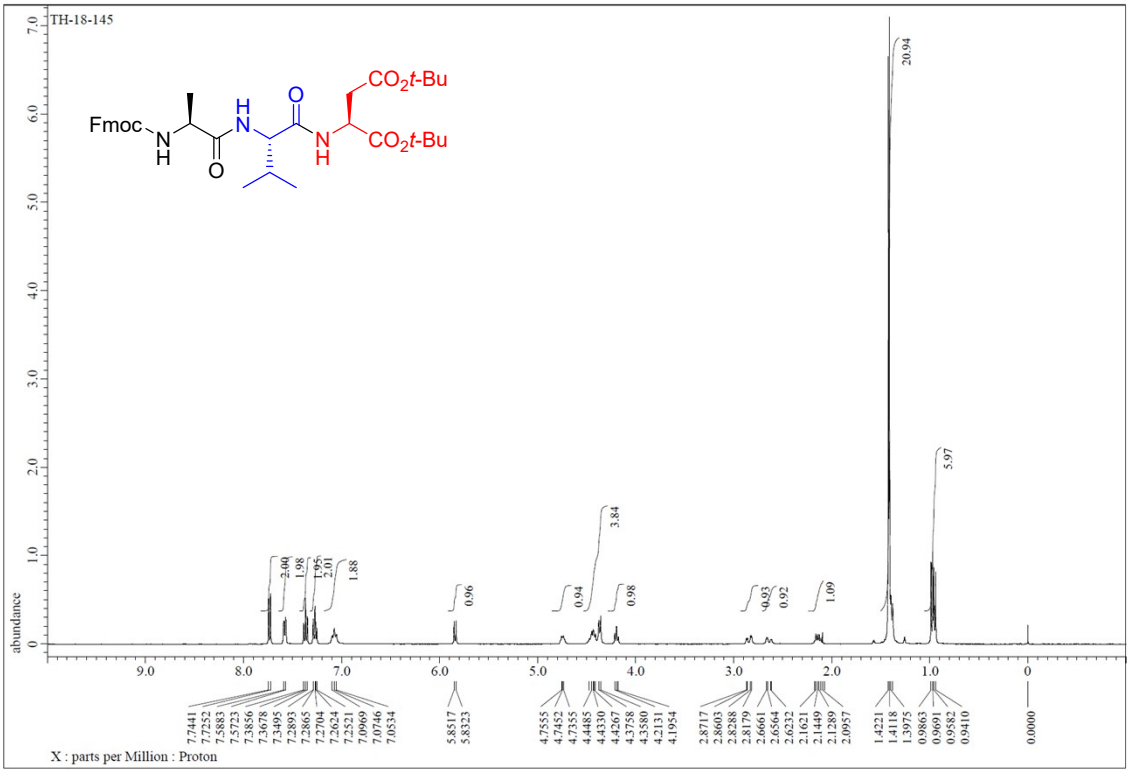
^{1}H NMR (400 MHz, $CDCl_3$) of **5aj**



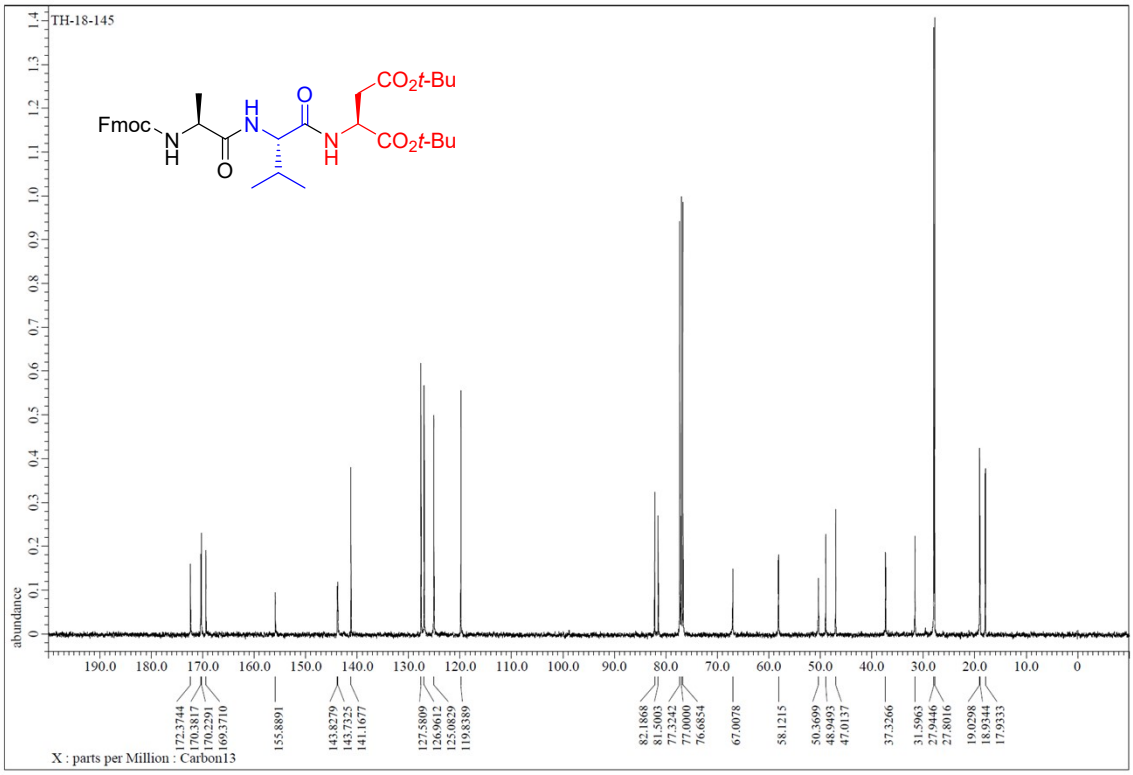
^{13}C NMR (100 MHz, $CDCl_3$) of **5aj**



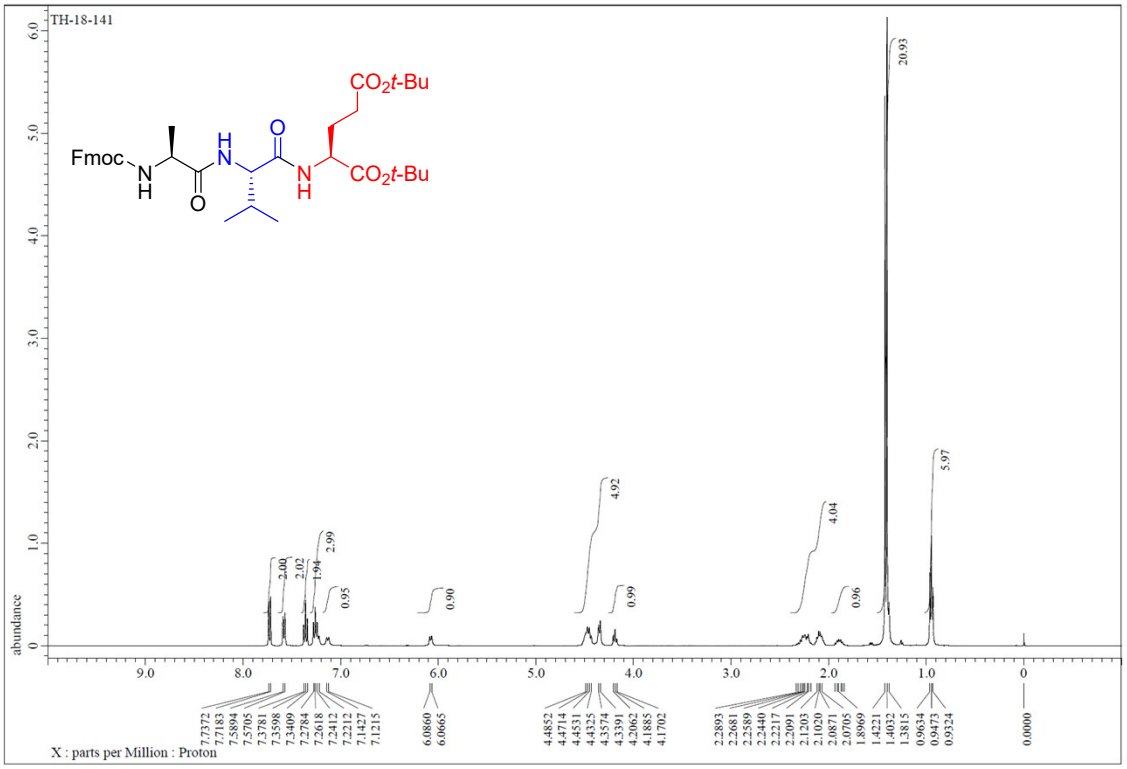
^{1}H NMR (400 MHz, $CDCl_3$) of **5ak**



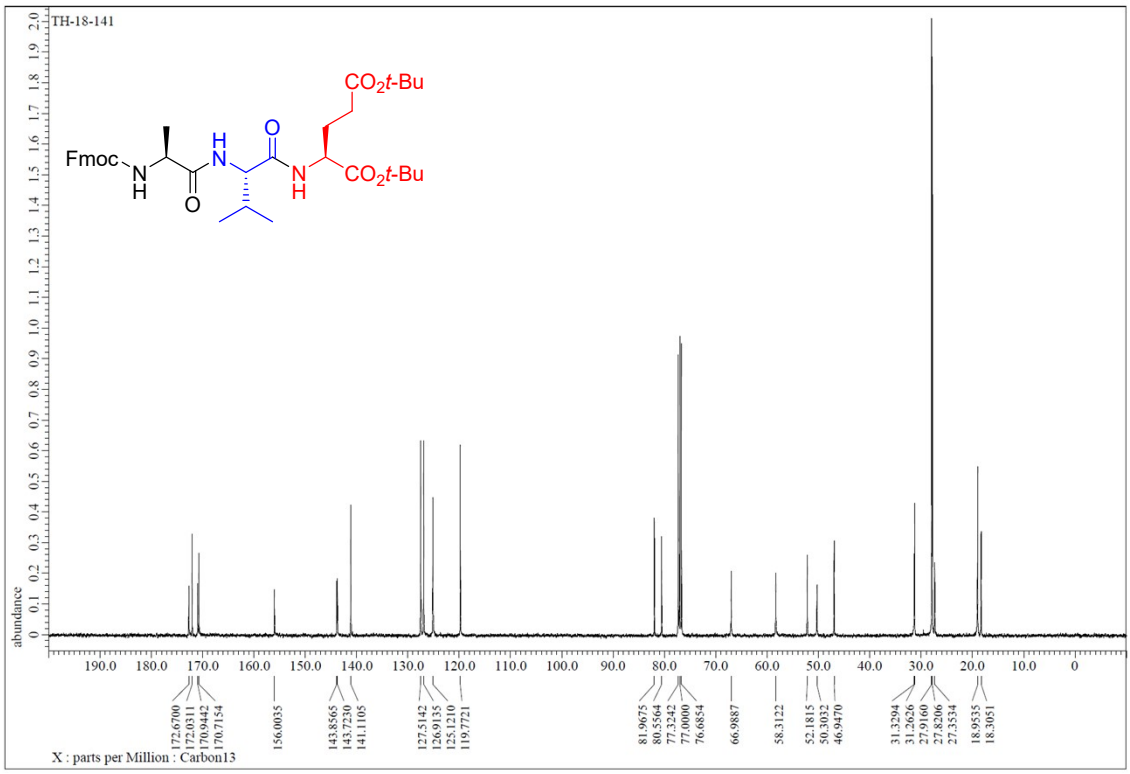
^{13}C NMR (100 MHz, $CDCl_3$) of **5ak**



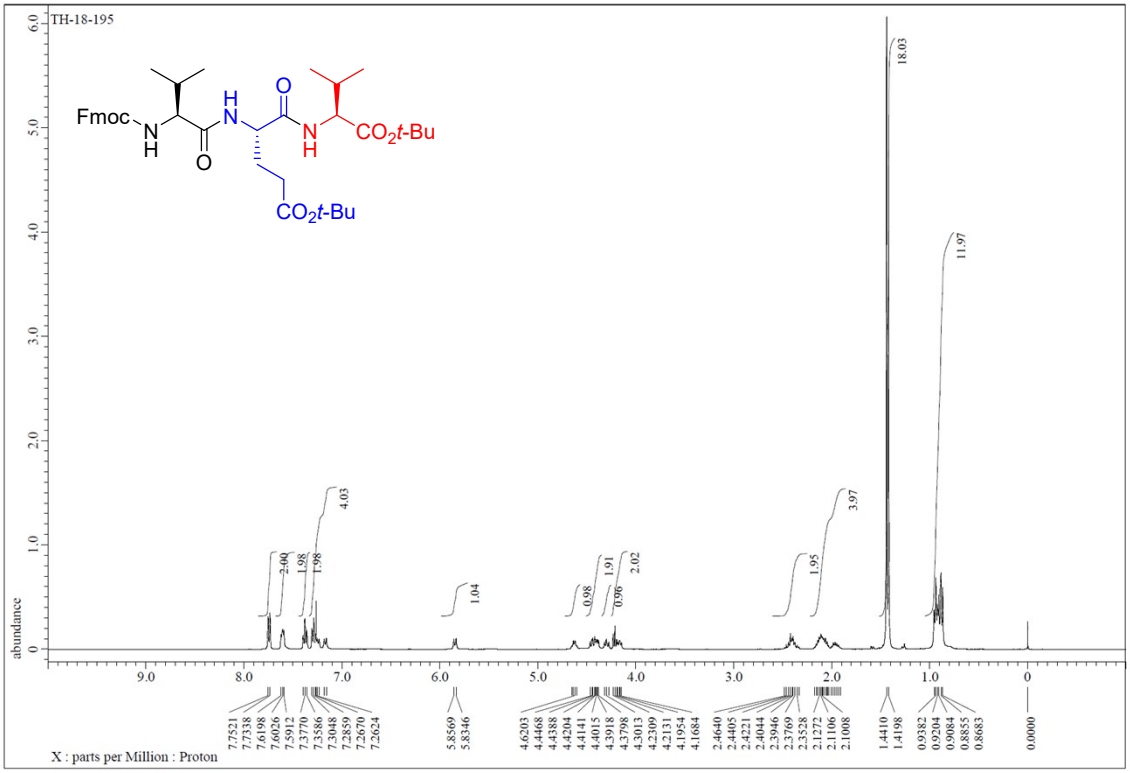
^{1}H NMR (400 MHz, $CDCl_3$) of **5al**



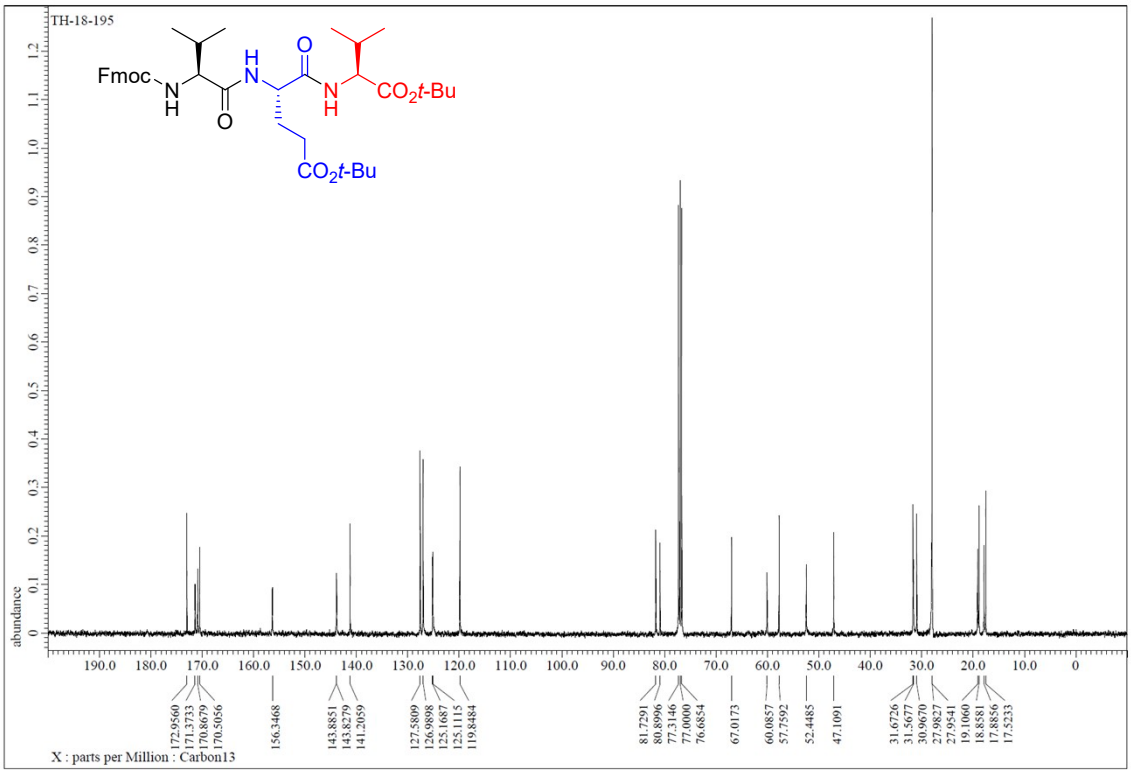
^{13}C NMR (100 MHz, $CDCl_3$) of **5al**



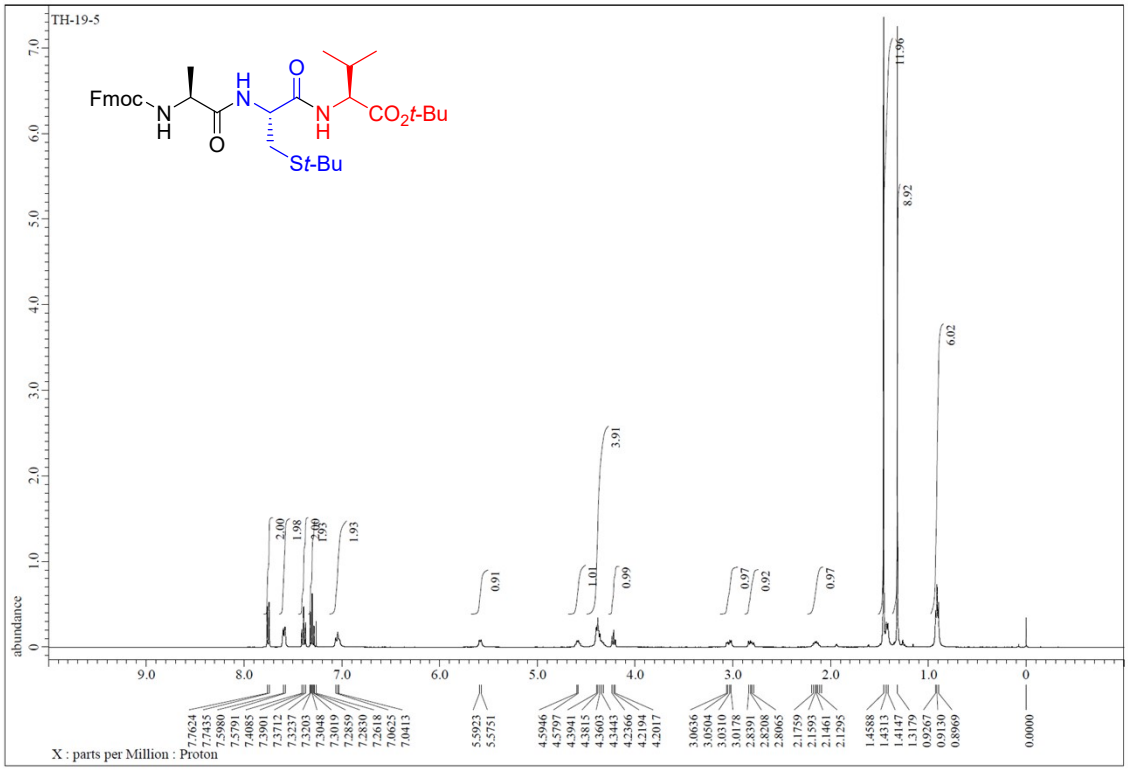
^{1}H NMR (400 MHz, $CDCl_3$) of **5am**



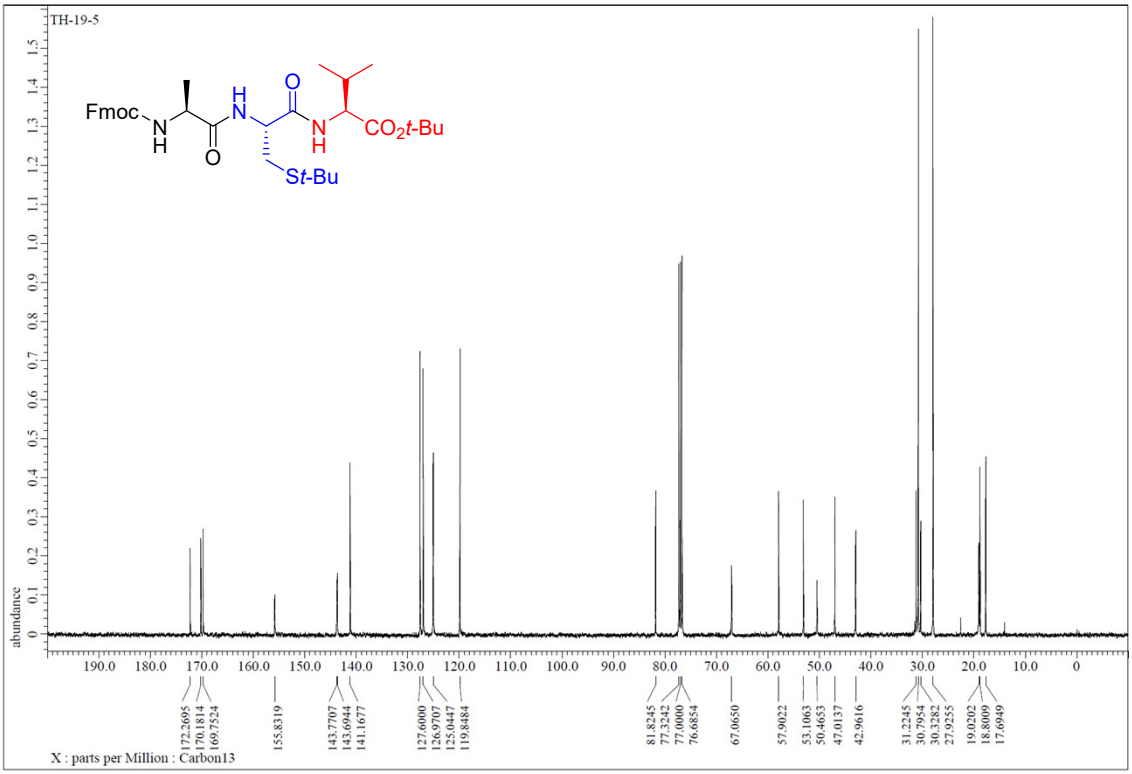
^{13}C NMR (100 MHz, $CDCl_3$) of **5am**



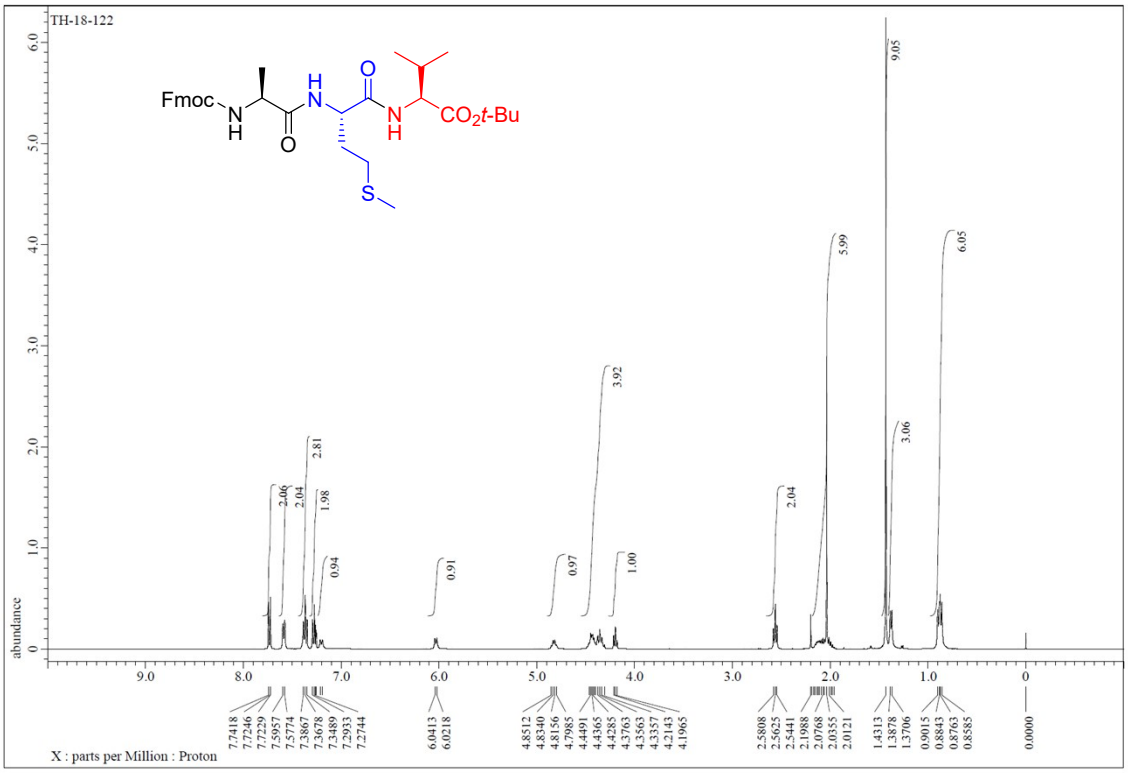
^{1}H NMR (400 MHz, $CDCl_3$) of **5an**



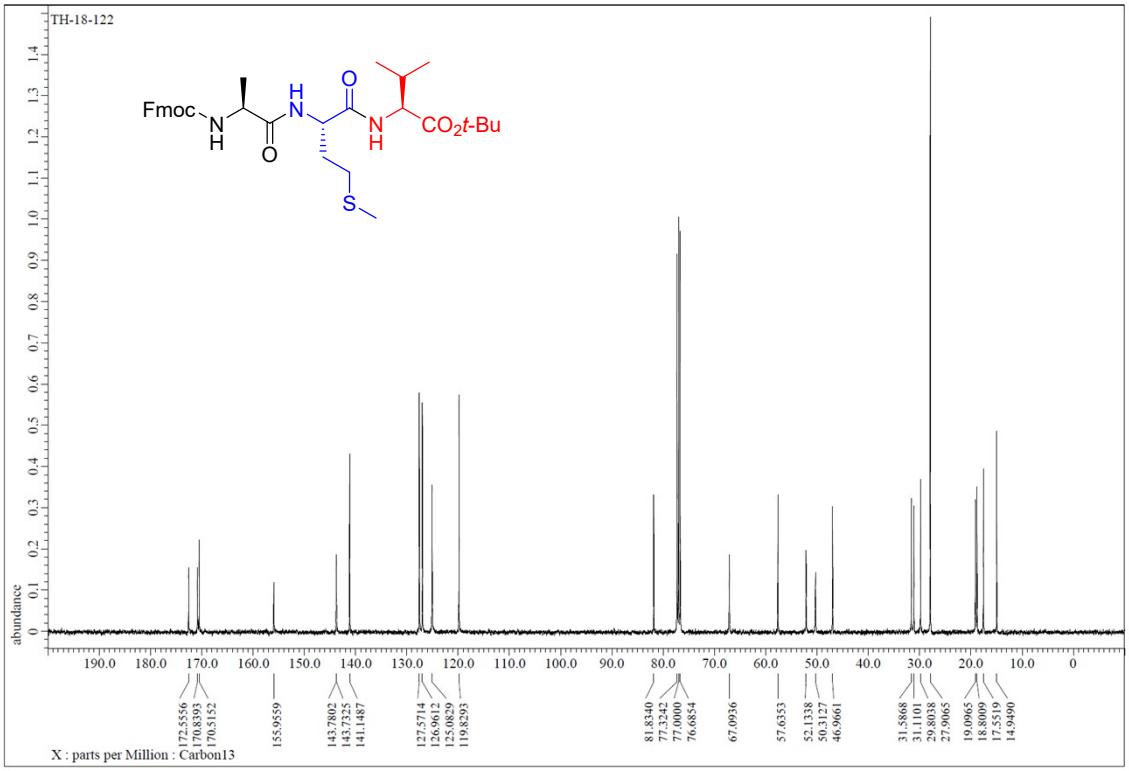
^{13}C NMR (100 MHz, $CDCl_3$) of **5an**



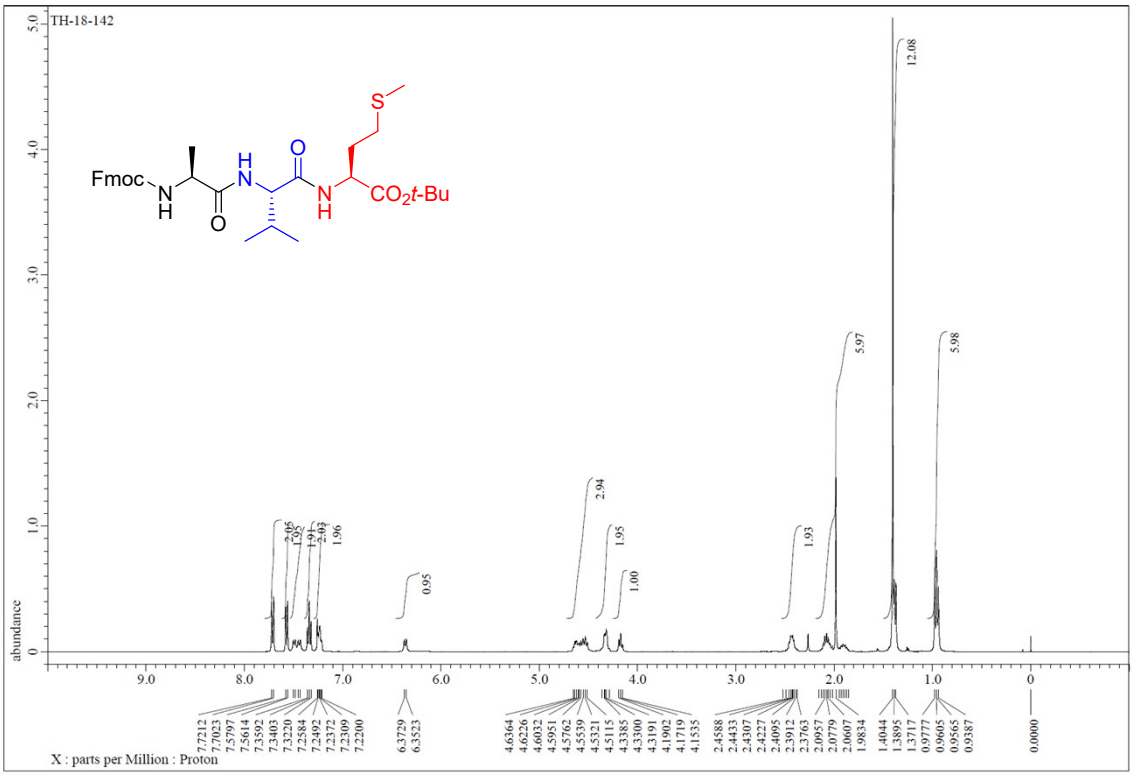
^{1}H NMR (400 MHz, $CDCl_3$) of **5ao**



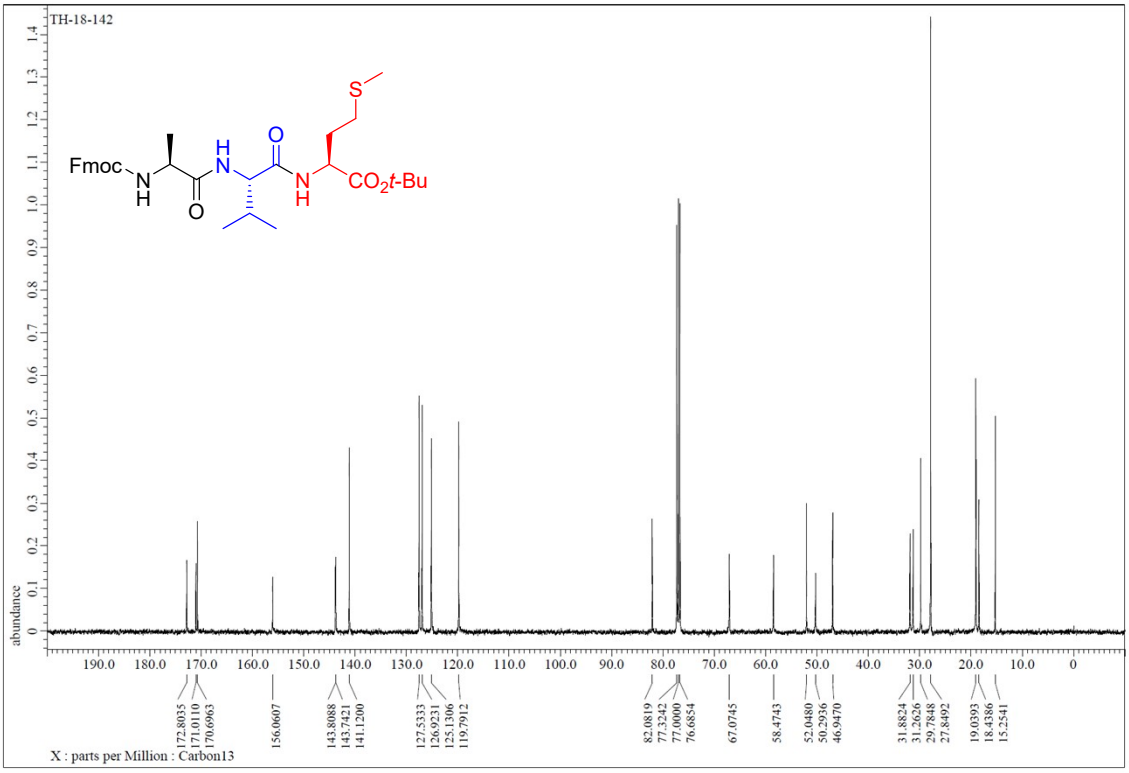
^{13}C NMR (100 MHz, $CDCl_3$) of **5ao**



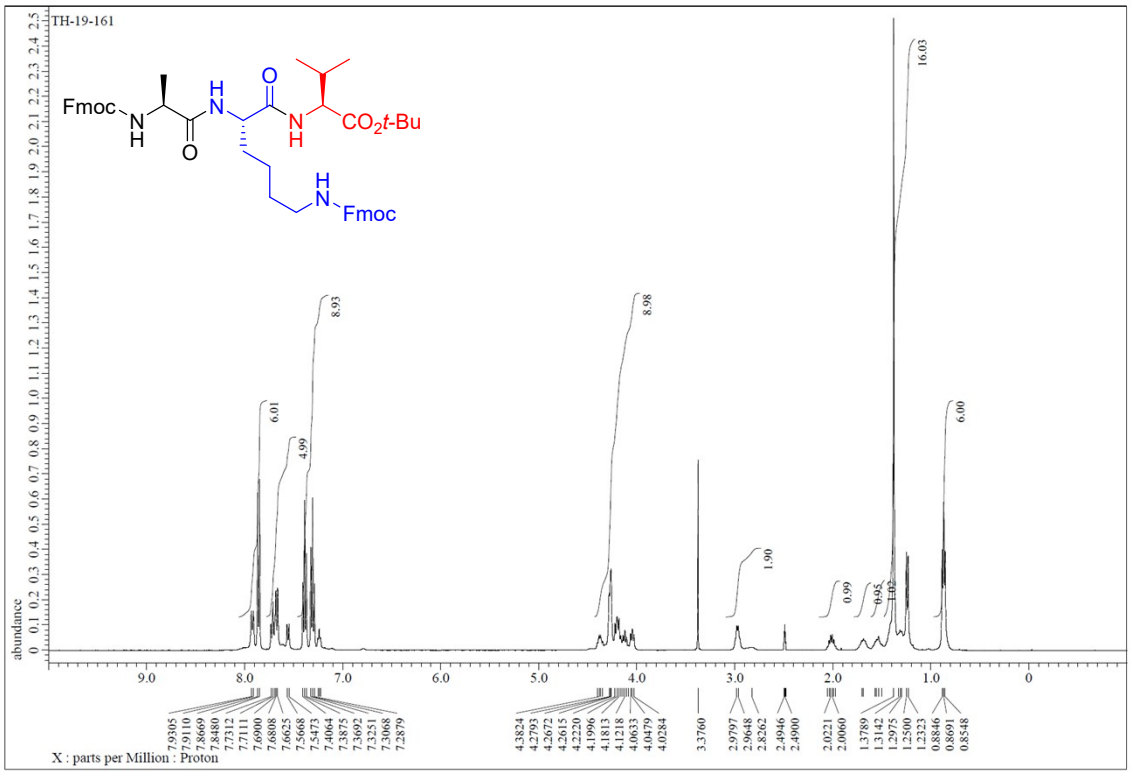
^{1}H NMR (400 MHz, $CDCl_3$) of **5ap**



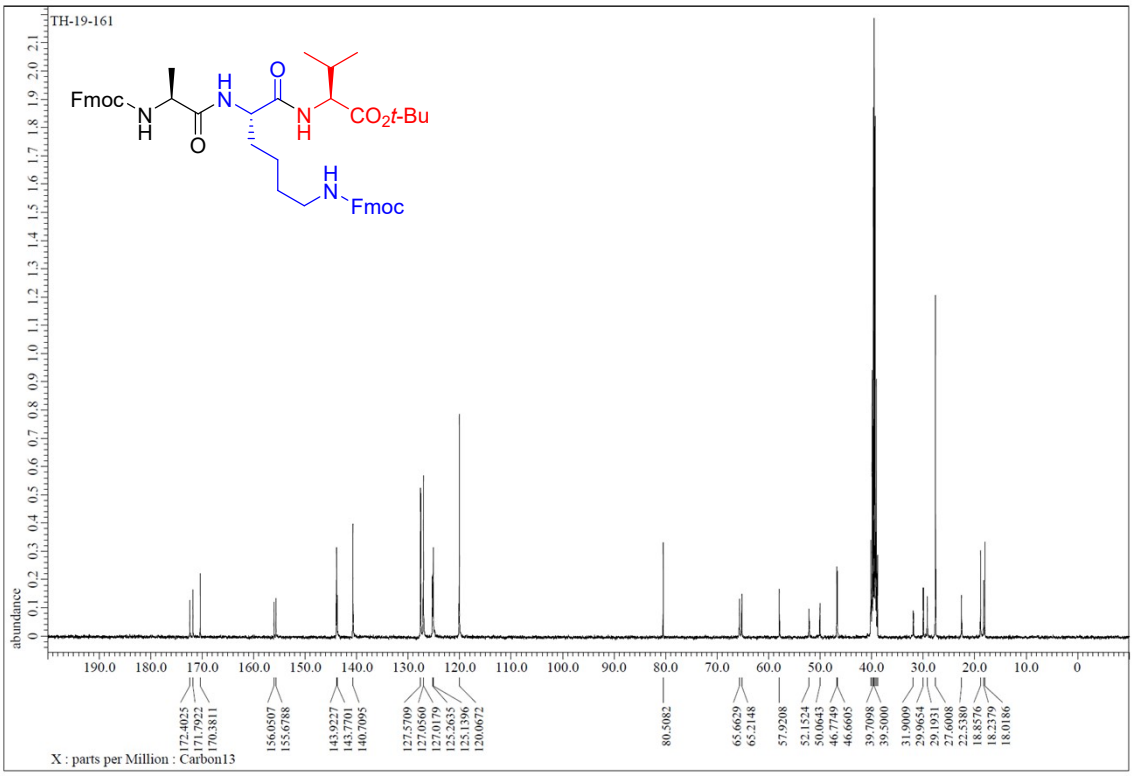
^{13}C NMR (100 MHz, $CDCl_3$) of **5ap**



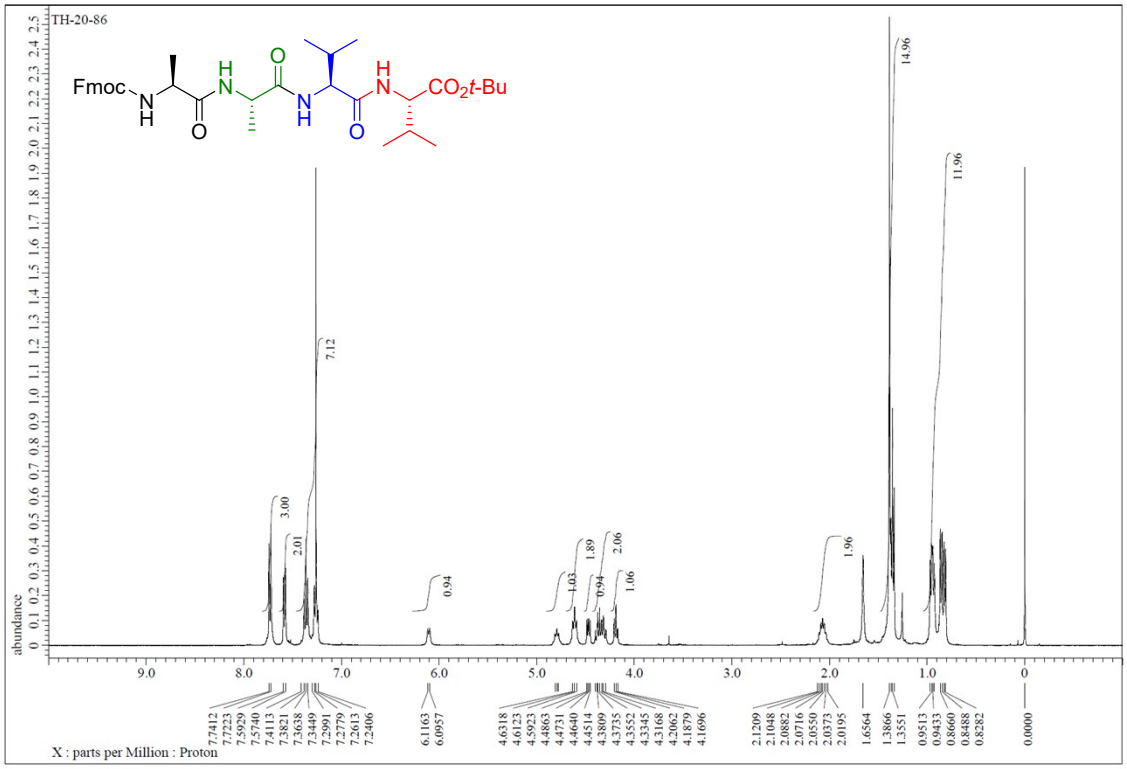
^{1}H NMR (400 MHz, DMSO-d$_6$) of **5aq**



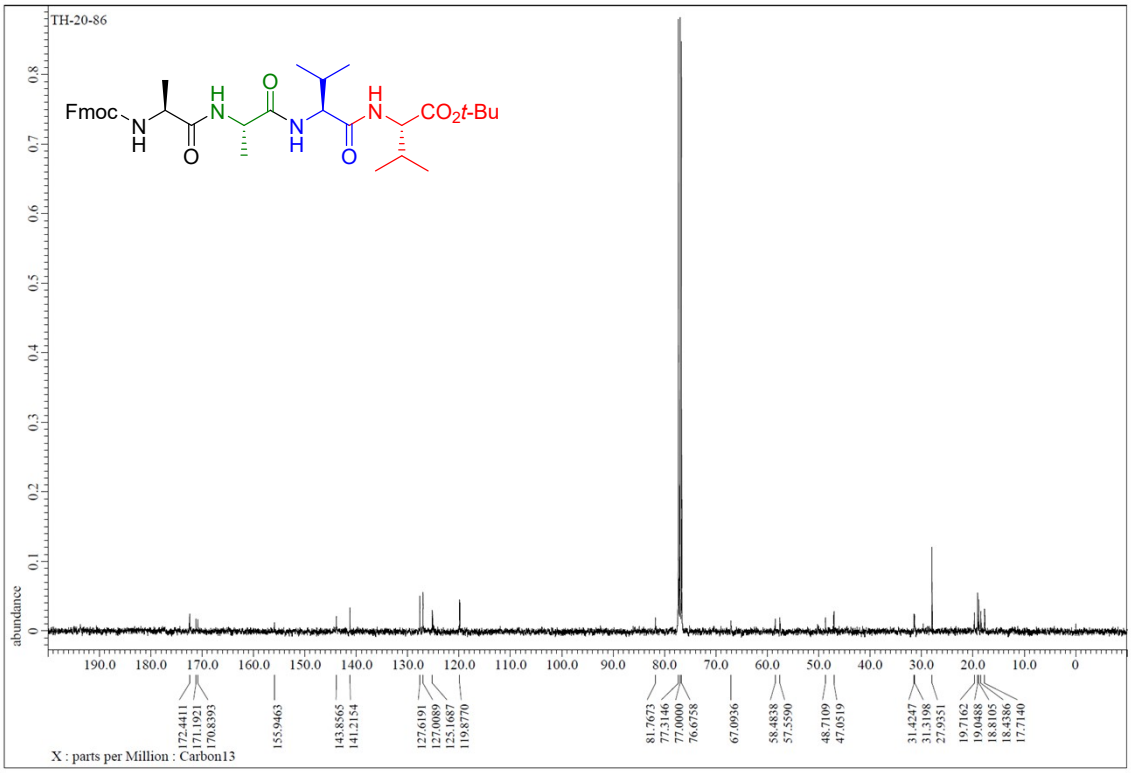
^{13}C NMR (100 MHz, DMSO-d$_6$) of **5aq**



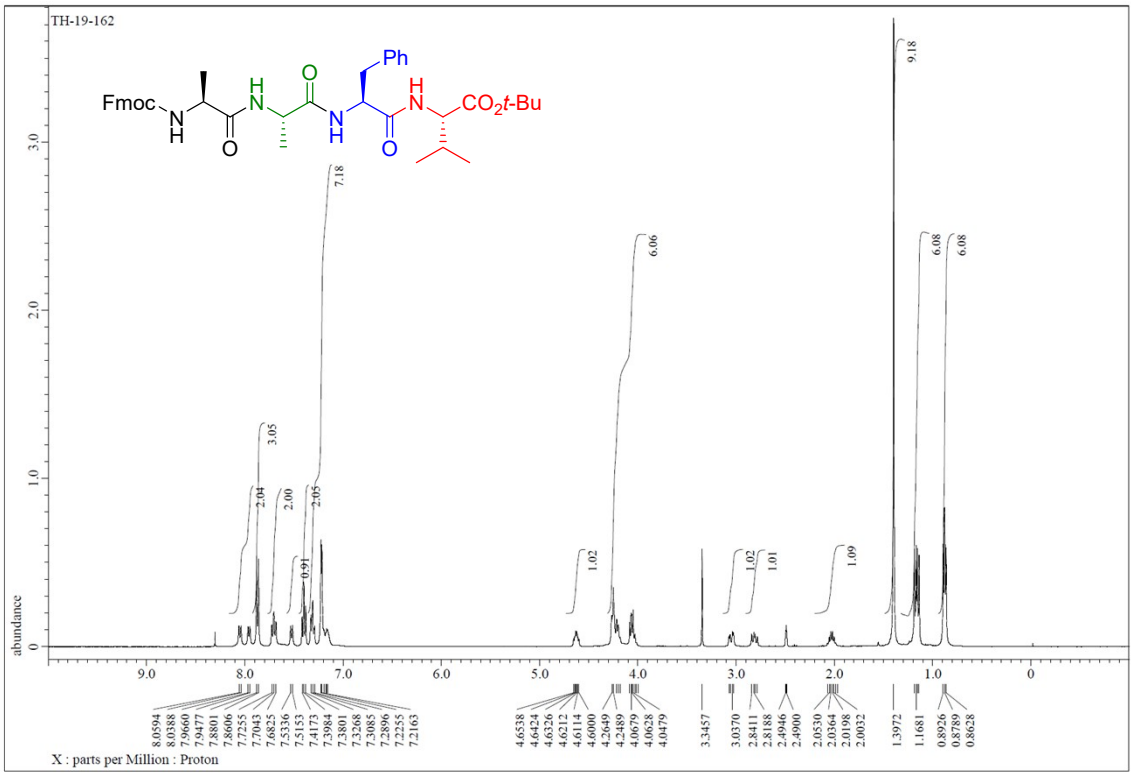
^{1}H NMR (400 MHz, $CDCl_3$) of **6a**



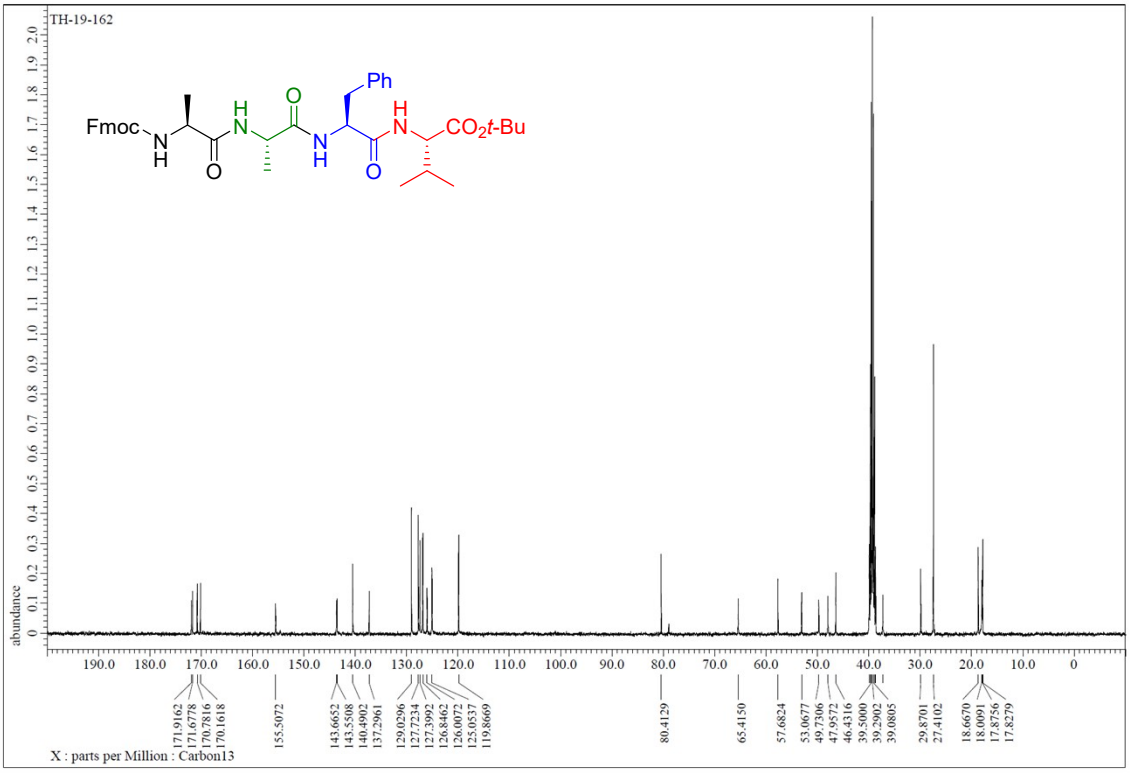
^{13}C NMR (100 MHz, $CDCl_3$) of **6a**



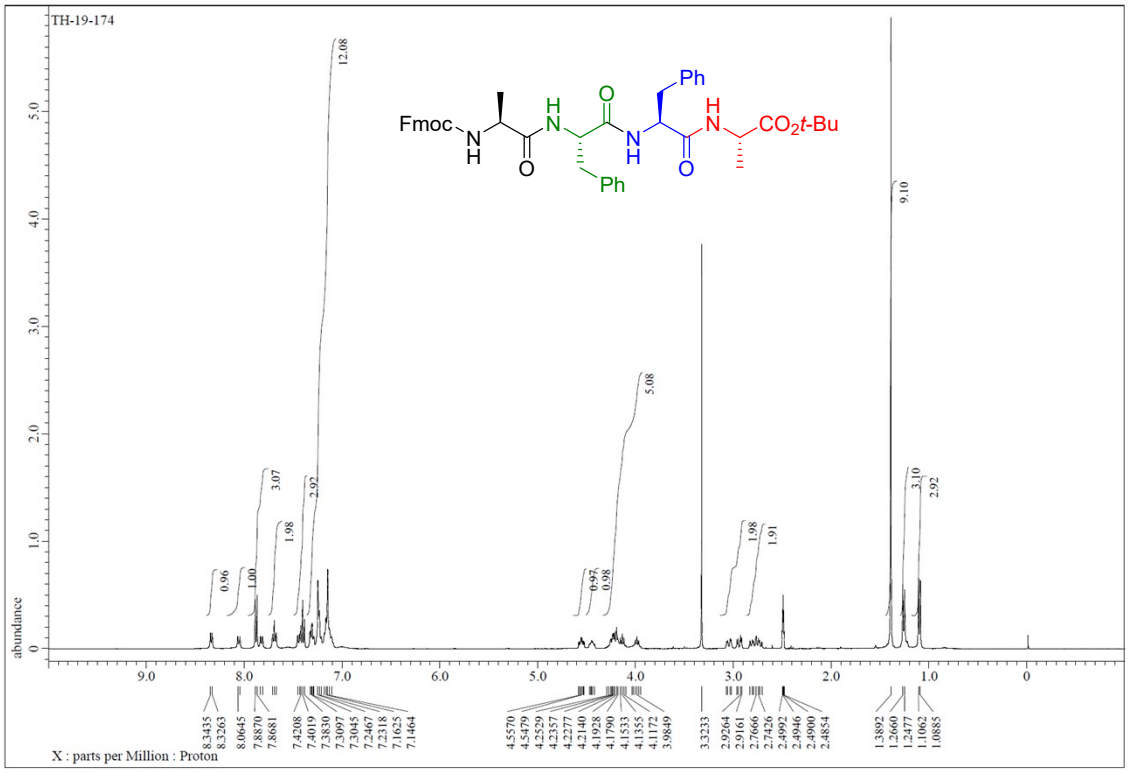
^{1}H NMR (400 MHz, DMSO-d_6) of **6b**



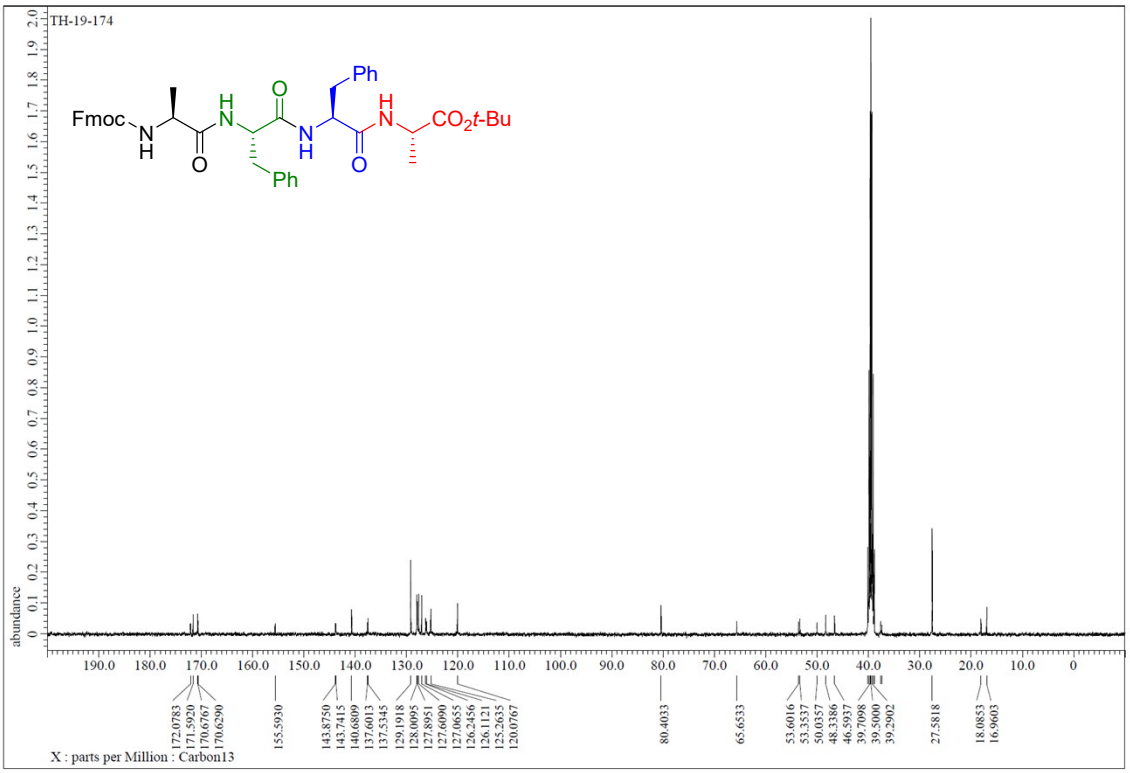
^{13}C NMR (100 MHz, DMSO-d_6) of **6b**



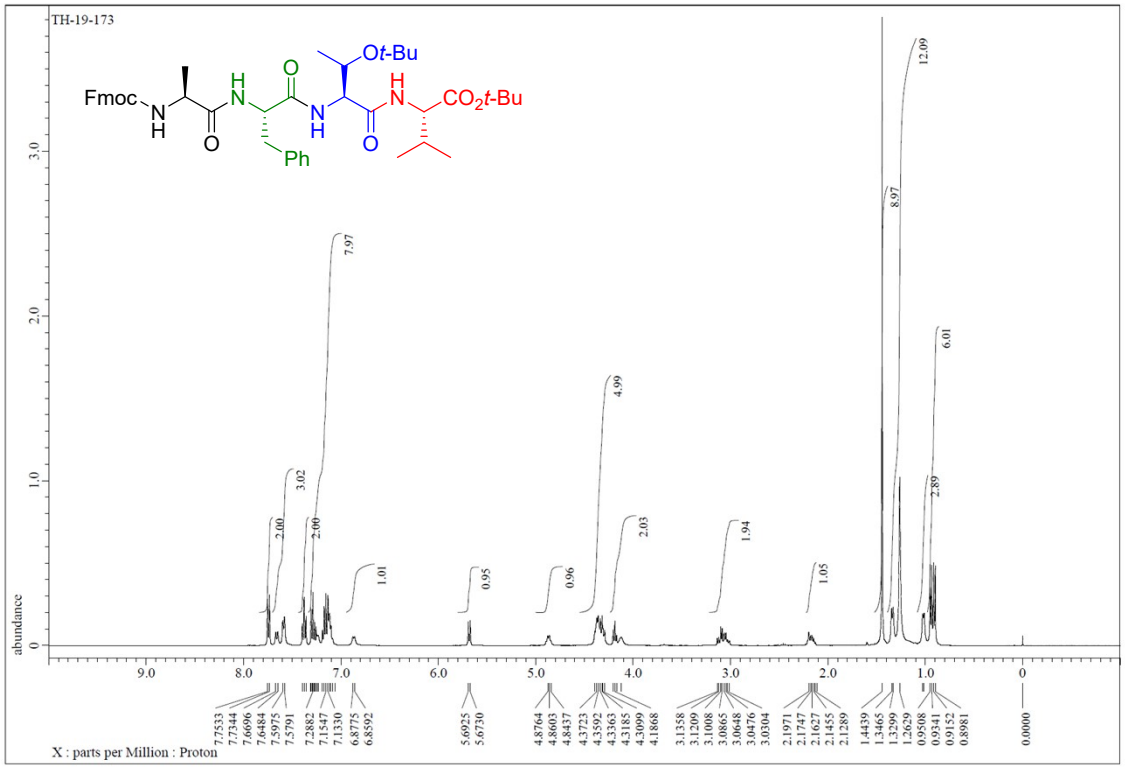
^{1}H NMR (400 MHz, DMSO-d_6) of **6c**



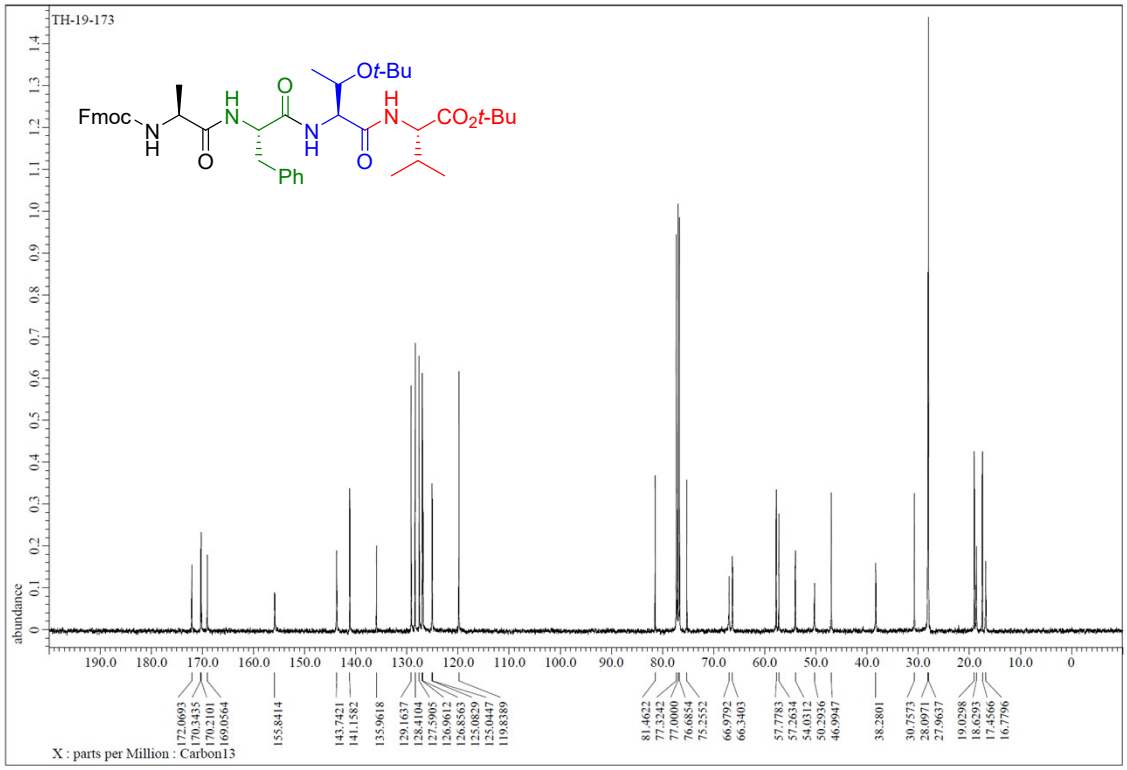
^{13}C NMR (100 MHz, DMSO-d_6) of **6c**



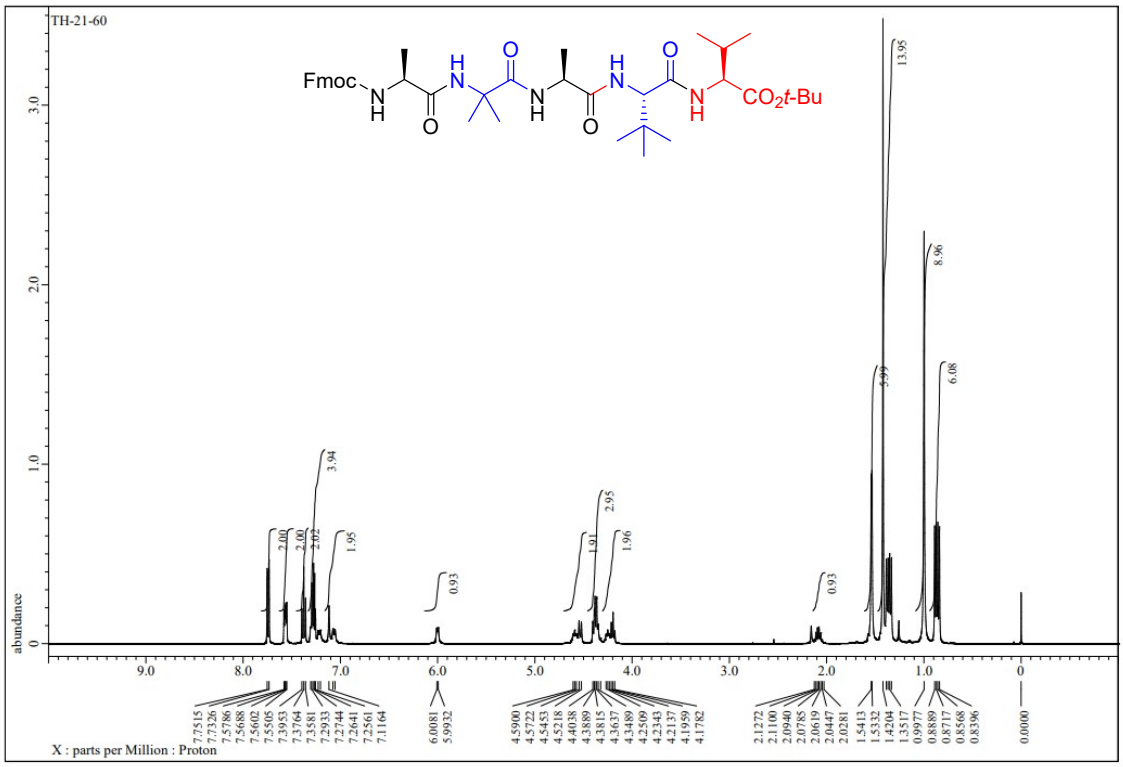
^{1}H NMR (400 MHz, $CDCl_3$) of **6d**



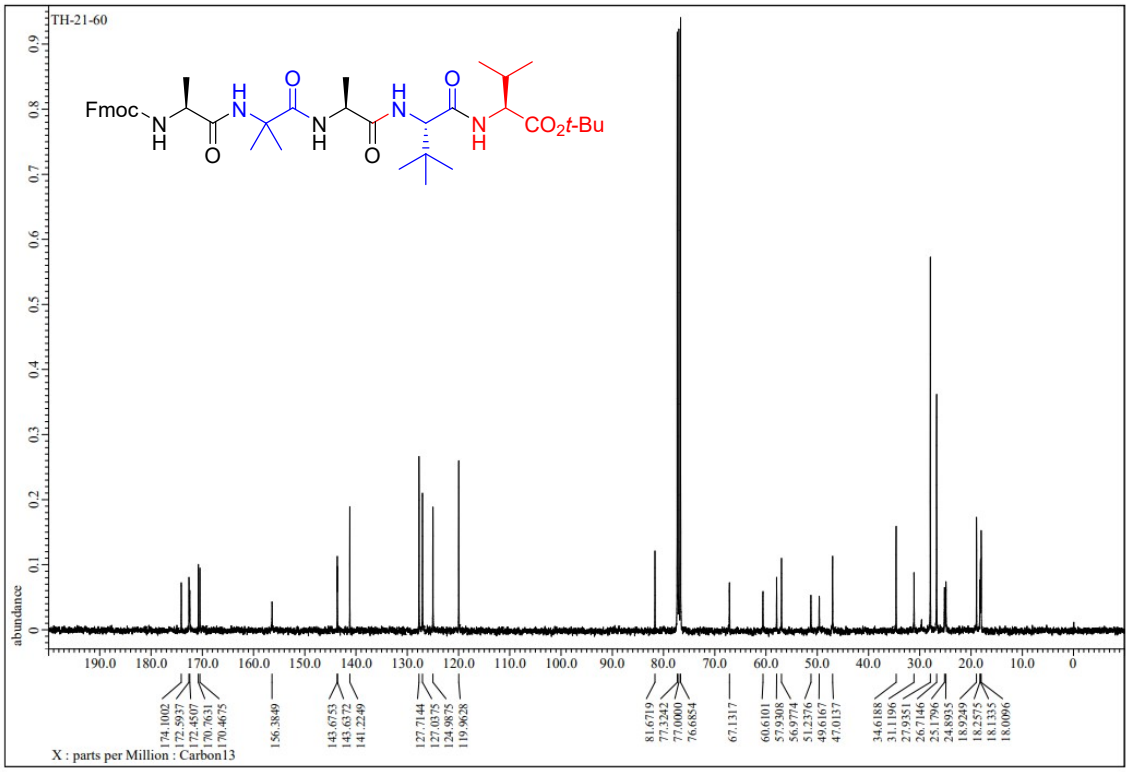
^{13}C NMR (100 MHz, $CDCl_3$) of **6d**



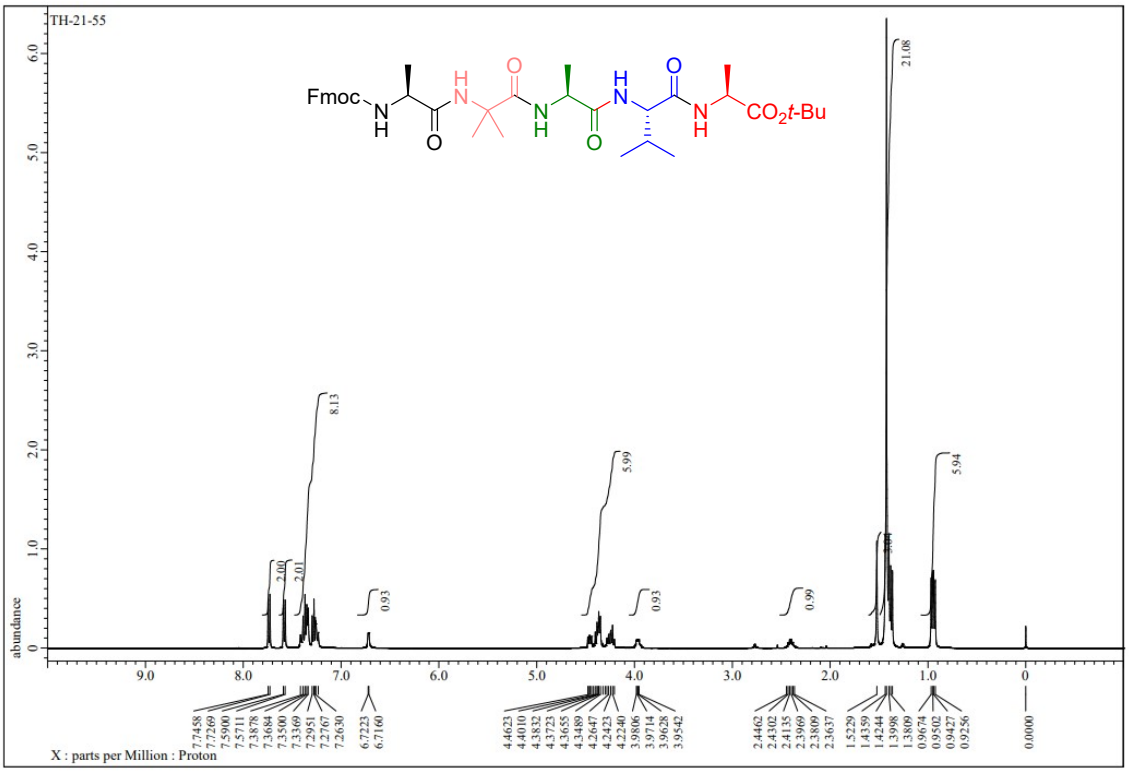
^{1}H NMR (400 MHz, $CDCl_3$) of **7a**



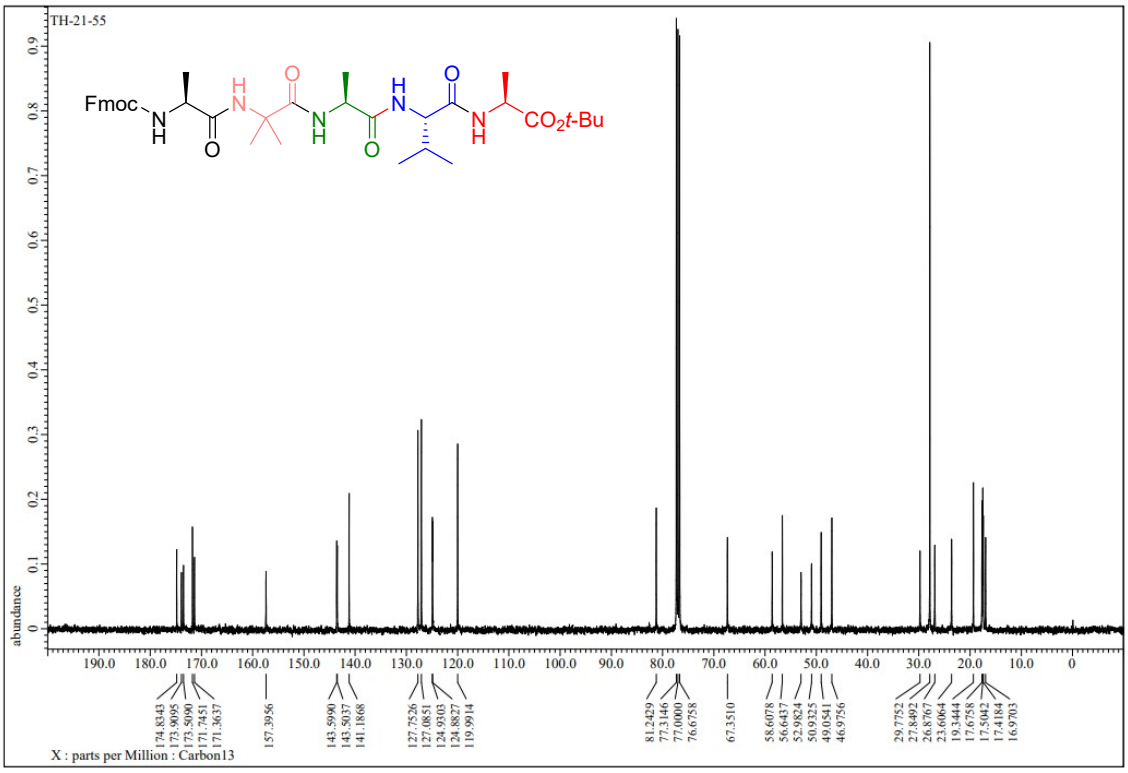
^{13}C NMR (100 MHz, $CDCl_3$) of **7a**



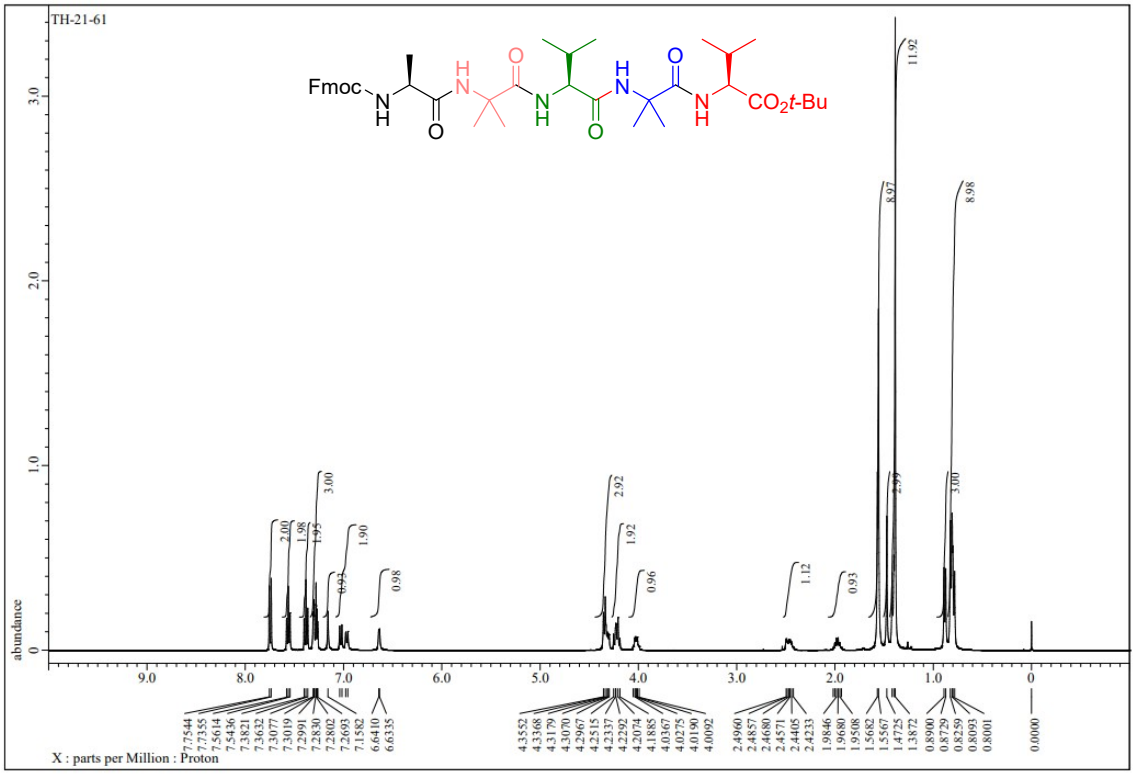
^{1}H NMR (400 MHz, $CDCl_3$) of **7b**



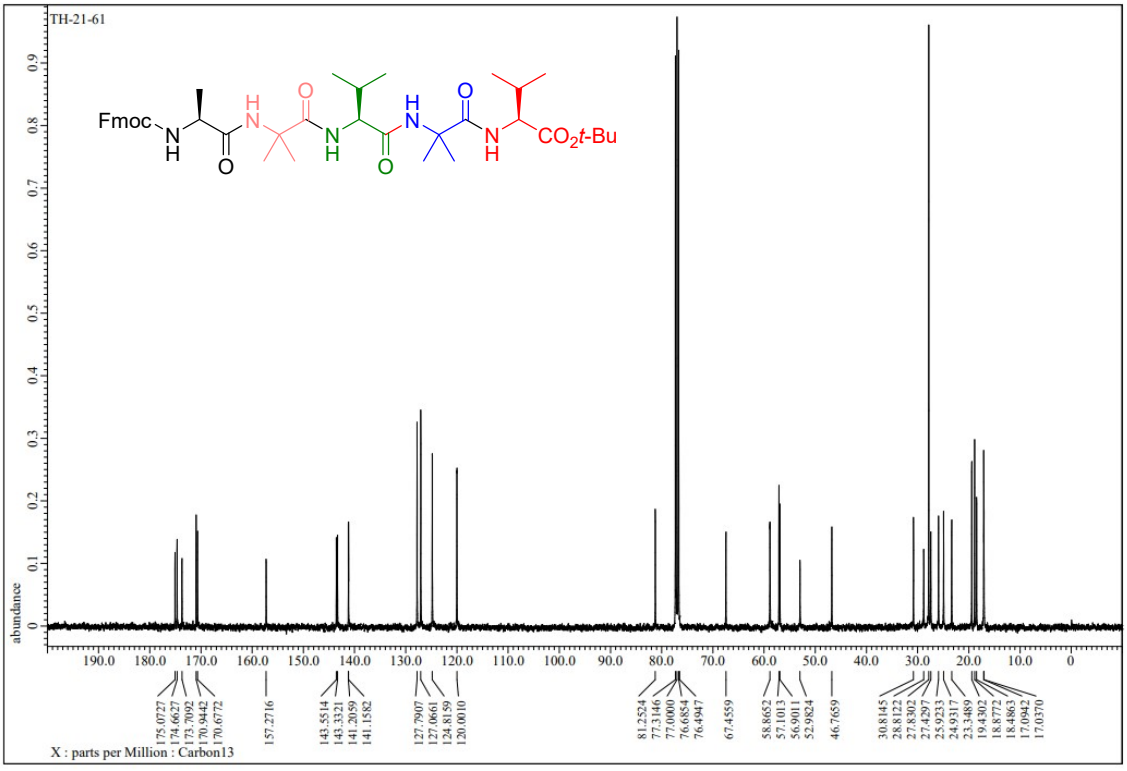
^{13}C NMR (100 MHz, $CDCl_3$) of **7b**



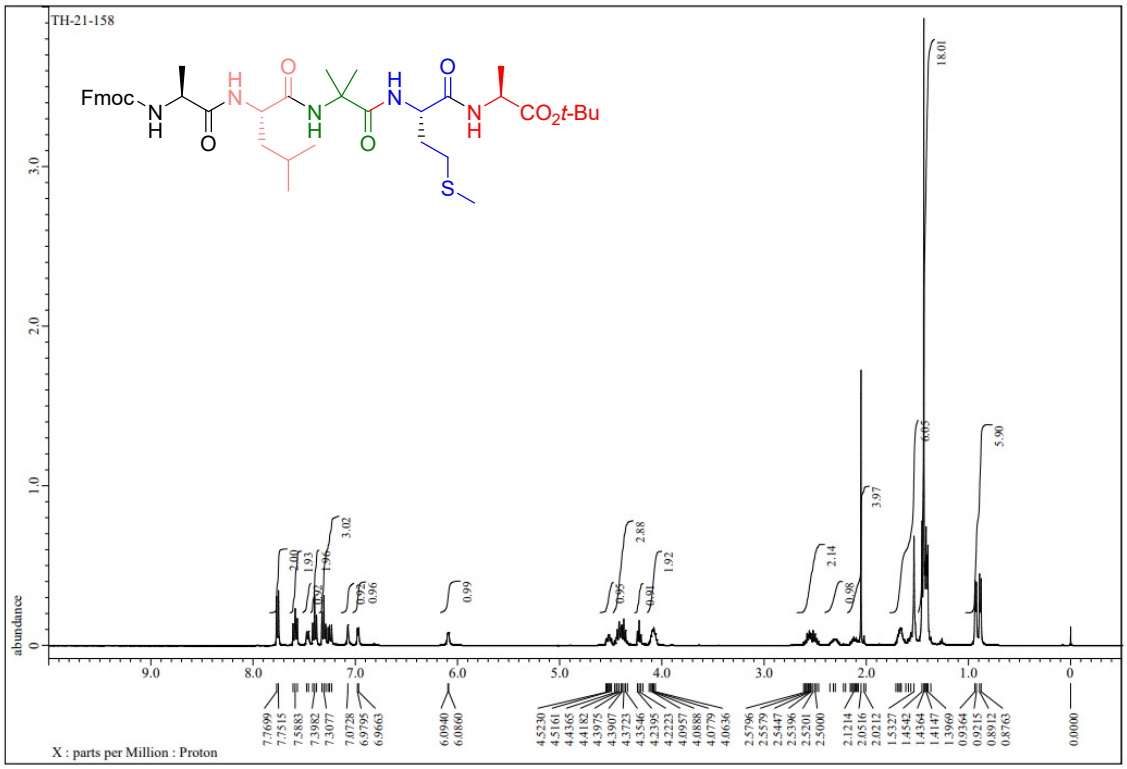
^{1}H NMR (400 MHz, $CDCl_3$) of **7c**



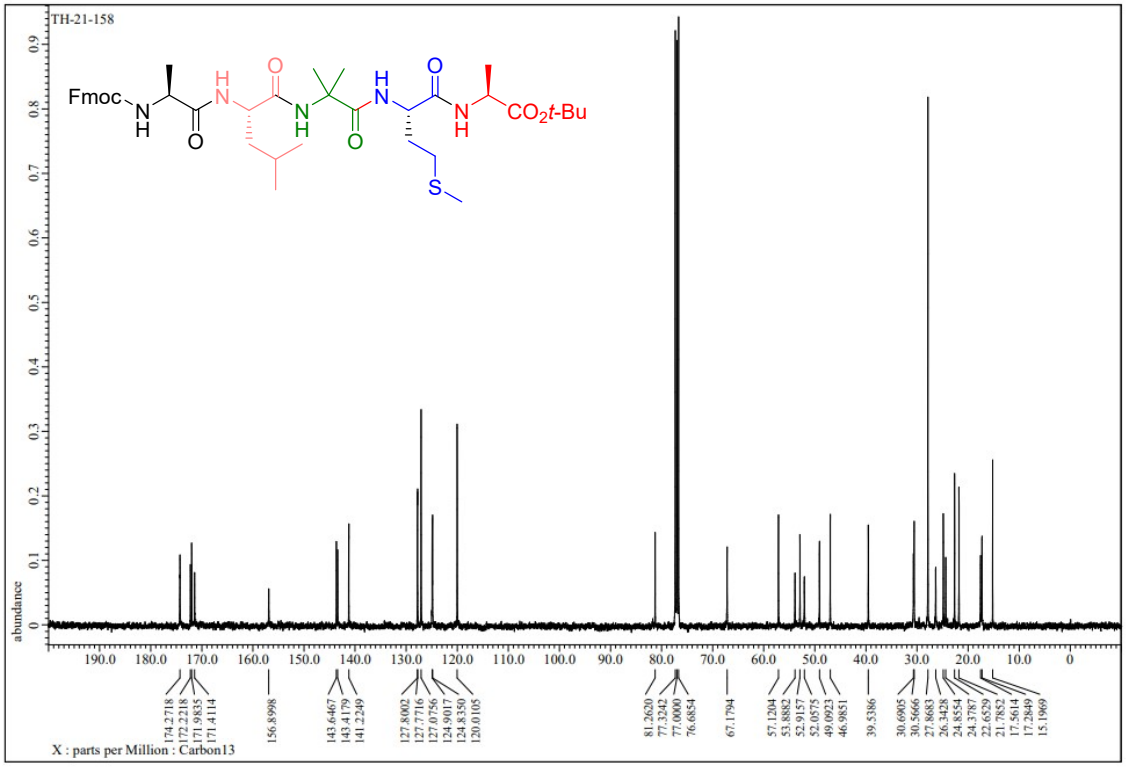
^{13}C NMR (100 MHz, $CDCl_3$) of **7c**



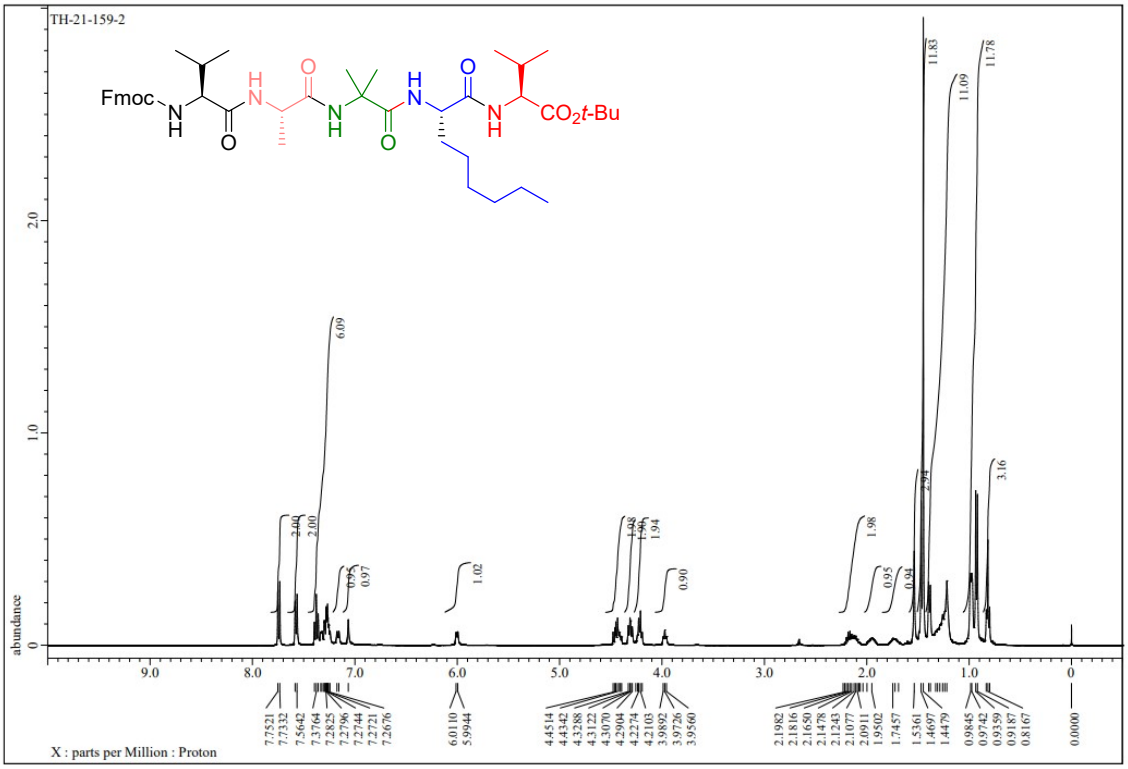
^{1}H NMR (400 MHz, $CDCl_3$) of **7d**



^{13}C NMR (100 MHz, $CDCl_3$) of **7d**



^{1}H NMR (400 MHz, $CDCl_3$) of **7e**



^{13}C NMR (100 MHz, $CDCl_3$) of **7e**