Supporting Information for:

β -C(sp^3)-H Arylation of α-Hydroxy Acid Derivatives Utilizing Amino Acid as a Directing Group

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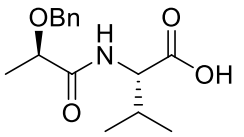
General Information

Solvents were obtained from Sigma-Aldrich, Alfa-Aesar and Acros and used directly without further purification. Amino acids and derivatives were obtained from commercial sources. EDCI (*N*-(3-Dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride), silver acetate, HFIP (hexafluoro-2-propanol) and aryl iodides were commercially available and used without any purification. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. ^1H spectra were recorded on Bruker AMX-400 instrument (400 MHz), and ^{13}C NMR spectra were recorded on Bruker DRX-600 instrument (150 MHz) and were fully decoupled by broadband proton decoupling. Chemical shifts were reported in ppm referenced to tetramethylsilane. The following abbreviations (or combinations thereof) were used to describe multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Coupling constants, *J*, were reported in Hertz unit (Hz). High-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight). HPLC profiles were obtained on a Hitachi LaChrom Elite HPLC system using commercially available chiral columns.

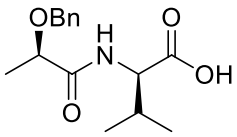
Experimental Procedures and Characterization of Compounds

General Procedure for the Preparation of Substrates

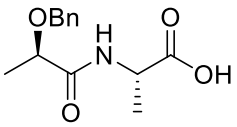
To a solution of *O*-benzyl-lactic acid (1.0 equiv), amino acid ester hydrochloride (1.4 equiv), 1-hydroxybenzotriazole hydrate (1.05 equiv) and 4-methylmorpholine (1.8 equiv) in DMF (0.3 M) was added 1-ethyl-3-[3-(dimethylamino)- propyl]carbodiimide hydrochloride (1.2 equiv) at 0 ºC. After 1 h at 0 ºC and 3 h at room temperature, the mixture was partitioned between EtOAc and H_2O. The EtOAc extract was washed successively with H_2O, 0.5 N HCl, H_2O, saturated aqueous $NaHCO_3$, and brine and then dried over anhydrous Na_2SO_4, filtered, and concentrated to give the corresponding esters as oil. To a solution of the intermediate ester in methanol (4 mL/mmol), lithium hydroxide monohydrate (4.0 equiv) was added. After 4 h at room temperature, methanol was removed under reduced pressure. H_2O was added to the crude residue and was subsequently neutralized by the addition of 0.5 N HCl. The aqueous solution was then extracted three times with EtOAc, and the combined organic layer was dried over anhydrous Na_2SO_4, filtered, concentrated *in vacuo* to give the crude product which was recrystallized from EtOAc/hexane to give the desired substrates (**1a**-**1g**).



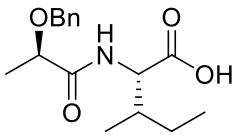
1a



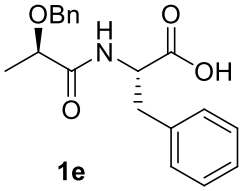
1b



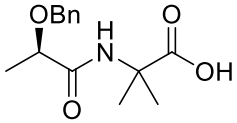
1c



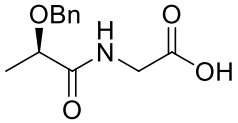
1d



1e



1f



1g

N-[(*R*)-2-(benzyloxy)propionyl]-L-valine (**1a**)

White solid. ^{1}H NMR (400MHz, $CDCl_3$): δ 7.42-7.28 (m, 5H), 7.09 (d, *J* = 8.9 Hz, 1H), 4.63 (d, *J* = 11.7 Hz, 1H), 4.58 (d, *J* = 11.9 Hz, 1H), 4.52 (dd, *J* = 8.9, 4.9 Hz, 1H), 4.03 (q, *J* = 6.8 Hz, 1H), 2.34-2.24 (m, 1H), 1.44 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.9, 173.9, 137.2, 128.6, 128.1, 127.6, 75.9, 72.0, 56.7, 30.6, 19.2, 18.4, 17.6; HRMS (ESI) m/z: calcd. for $C_{15}H_{22}NO_4^+$ ($[M+H]^+$) 280.1543, found 280.1558.

N-[(*R*)-2-(benzyloxy)propionyl]-D-valine (**1b**)

Colorless oil. ^{1}H NMR (400MHz, $CDCl_3$): δ 7.40-7.28 (m, 5H), 7.16 (d, *J* = 9.4 Hz, 1H), 4.64 (d, *J* = 11.3 Hz, 1H), 4.59 (dd, *J* = 9.1, 4.8 Hz, 1H), 4.55 (d, *J* = 11.4 Hz, 1H), 4.01 (q, *J* = 6.8 Hz, 1H), 2.35-2.24 (m, 1H), 1.44 (d, *J* = 6.8 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 175.4, 174.1, 137.1, 128.6, 128.1, 128.0, 76.2, 72.3, 56.4, 30.9, 19.1, 19.1, 17.5;

HRMS (ESI) m/z: calcd. for $C_{15}H_{22}NO_4^+$ ([M+H]$^+$) 280.1543, found 280.1537.

N-[(*R*)-2-(benzyloxy)propionyl]-L-alanine (**1c**)
White solid. ^{1}H NMR (400MHz, $CDCl_3$): δ 7.41-7.29 (m, 5H), 7.10 (d, *J* = 7.3 Hz, 1H), 4.62 (d, *J* = 11.7 Hz, 1H), 4.59-4.51 (m, 2H), 4.02 (q, *J* = 6.8 Hz, 1H), 1.45 (d, *J* = 7.2 Hz, 3H), 1.44 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 175.8, 173.9, 137.1, 128.7, 128.2, 127.9, 75.8, 72.1, 47.7, 18.4, 17.8; HRMS (ESI) m/z: calcd. for $C_{13}H_{18}NO_4^+$ ([M+H]$^+$) 252.1230, found 252.1244.

N-[(*R*)-2-(benzyloxy)propionyl]-L-isoleucine (**1d**)
White solid. ^{1}H NMR (400MHz, $CDCl_3$): δ 7.41-7.29 (m, 5H), 7.11 (d, *J* = 8.9 Hz, 1H), 4.62 (d, *J* = 11.8 Hz, 1H), 4.60-4.54 (m, 2H), 4.02 (q, *J* = 6.8 Hz, 1H), 2.04-1.94 (m, 1H), 1.52-1.45 (m, 1H), 1.43 (d, *J* = 6.8 Hz, 3H), 1.22-1.10 (m, 1H), 0.98-0.90 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 175.3, 173.7, 137.2, 128.6, 128.1, 127.7, 75.9, 72.0, 56.1, 37.3, 25.0, 18.4, 15.7, 11.6; HRMS (ESI) m/z: calcd. for $C_{16}H_{24}NO_4^+$ ([M+H]$^+$) 294.1700, found 294.1702.

N-[(*R*)-2-(benzyloxy)propionyl]-L-phenylalanine (**1e**)
White solid. ^{1}H NMR (400MHz, $CDCl_3$): δ 7.37-7.30 (m, 3H), 7.26-7.20 (m, 3H), 7.19-7.12 (m, 4H), 7.03 (d, *J* = 7.6 Hz, 1H), 4.85 (dt, *J* = 7.7, 5.3 Hz, 1H), 4.36 (d, *J* = 11.8 Hz, 1H), 4.32 (d, *J* = 11.8 Hz, 1H), 3.92 (q, *J* = 6.8 Hz, 1H), 3.30 (dd, *J* = 14.2, 5.3 Hz, 1H), 3.11 (dd, *J* = 14.2, 7.7 Hz, 1H), 1.39 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.4, 174.1, 137.0, 135.6, 129.2, 128.8, 128.5, 128.0, 127.6, 127.3, 75.6, 71.7, 52.7, 37.0, 18.4; HRMS (ESI) m/z: calcd. for $C_{19}H_{22}NO_4^+$ ([M+H]$^+$) 328.1543, found 328.1551.

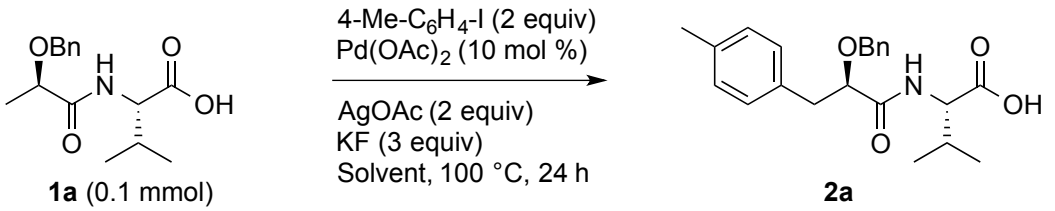
(*R*)-2-[2-(benzyloxy)propanamido]-2-methylpropanoic acid (**1f**)
White solid. ^{1}H NMR (400MHz, $CDCl_3$): δ 7.41-7.30 (m, 5H), 7.06 (s, 1H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.55 (d, *J* = 11.6 Hz, 1H), 3.98 (q, *J* = 6.8 Hz, 1H), 1.56 (d, *J* = 4.9 Hz, 6H), 1.43 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 176.6, 174.4, 137.1, 128.7, 128.3, 128.0, 76.1, 72.3, 56.6, 25.0, 24.8, 18.4; HRMS (ESI) m/z: calcd. for $C_{14}H_{20}NO_4^+$ ([M+H]$^+$) 266.1387, found 266.1393.

N-[(*R*)-2-(benzyloxy)propionyl]-glycine (**1g**)
Pale brown oil. ^{1}H NMR (400MHz, $CDCl_3$): δ 7.39-7.28 (m, 5H), 7.21 (t, *J* = 4.9 Hz, 1H), 4.60 (s, 2H), 4.15 (dd, *J* = 18.3, 6.0 Hz, 1H), 4.10-3.97 (m, 2H), 1.44 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.4, 173.0, 137.1, 128.6, 128.2, 127.9, 75.8, 72.1, 40.8, 18.5; HRMS (ESI) m/z: calcd. for $C_{12}H_{16}NO_4^+$ ([M+H]$^+$) 238.1074, found 238.1084.

General Procedure for the Optimization of the Amino Acid Auxiliary and the Reaction Conditions for the Pd-Catalyzed C–H Arylation of the *O*-benzyl-lactic acid with Amino Acid derivatives

A mixture of **1** (0.1 mmol) and designated amounts of 4-iodotoluene, $Pd(OAc)_2$, AgOAc, KF in HFIP (1.0 mL) in a sealed vial was stirred at 100℃ for 24 h. After cooling down to room temperature, EtOAc (1.5 mL) and acetic acid (0.3 mL) were added and the reaction mixture was filtered through a short pad of Celite®. The Celite® was washed thoroughly with EtOAc (4 × 1.5 mL), and the filtrate was concentrated to dryness.

Table S1*. *Optimization of solvent

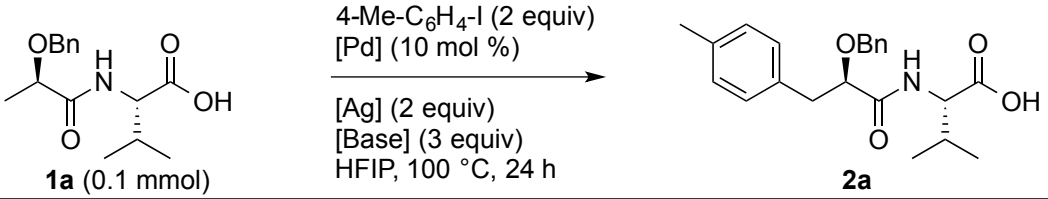


1a (0.1 mmol) **2a**

entry	solvent	yield (%)[a]	entry	solvent	yield (%)[a]
1	Hexane	18	8	*i*-PrOH	2
2	Toluene	13	9	*t*-BuOH	44
3	$PhCF_3$	15	10	*t*-AmylOH	31
4	1,2-Dichloroethane	16	11	CF_3CH_2OH	64
5	1,4-Dioxane	17	12	$CF_3CH_2CH_2OH$	17
6	MeCN	38	13	$CF_3CH(CH_3)OH$	43
7	DMF	71	14	HFIP	79

[a] The yields were determined by ^1H NMR analysis of the crude products using CH_2Br_2 as an internal standard.

Table S2. Optimization of Pd/Ag/Base

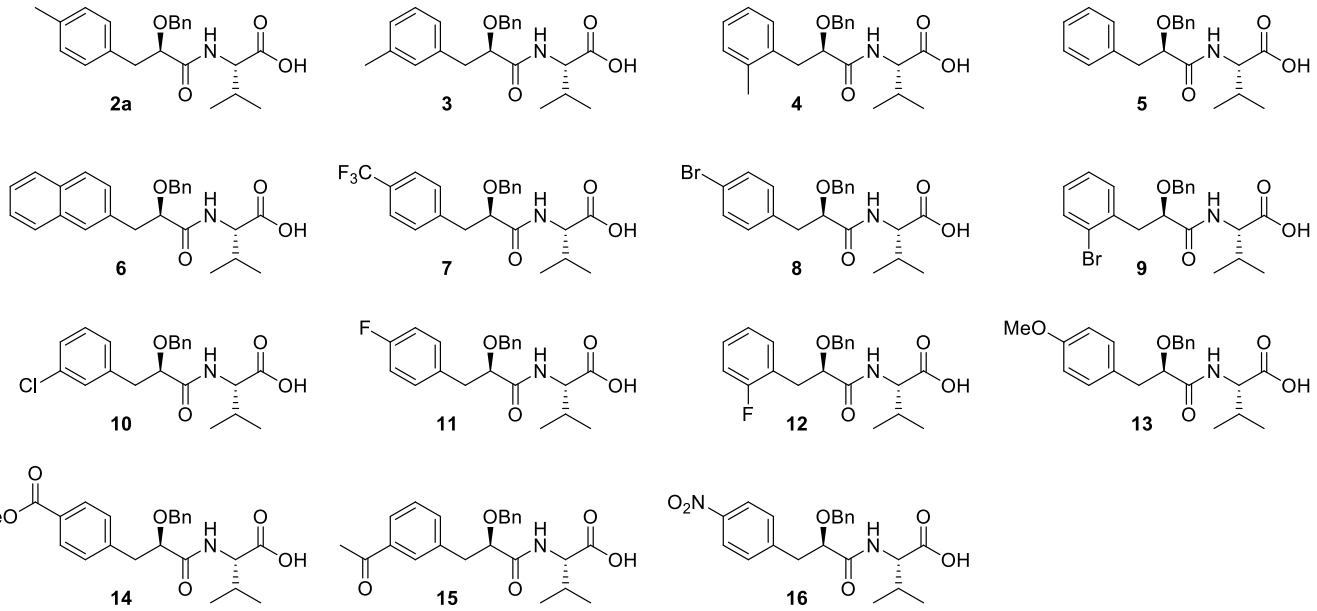


entry	[Pd]	[Ag]	[base]	yield (%)[a]
1	$Pd(OAc)_2$	AgOAc	KF	79
2	$Pd(OAc)_2$	AgOAc	KF[b]	71
3	$Pd(OAc)_2$	AgOAc	KOAc	48
4	$Pd(OAc)_2$	AgOAc	$KHCO_3$	70
5	$Pd(OAc)_2$	AgOAc	K_2CO_3	76
6	$Pd(OAc)_2$	AgOAc	KH_2PO_4	56
7	$Pd(OAc)_2$	AgOAc	tBuOK	60
8	$Pd(OAc)_2$	AgOAc	K_2HPO_4	21
9	$Pd(OAc)_2$	AgOAc	LiF	58
10	$Pd(OAc)_2$	AgOAc	Li_2CO_3	51
11	$Pd(OAc)_2$	AgOAc	$NaHCO_3$	51
12	$Pd(OAc)_2$	AgOAc	Na_2HPO_4	12
13	$Pd(OAc)_2$	AgOAc	CsF	75
14	$Pd(OAc)_2$	AgOAc	CsOAc	60
15	$Pd(OAc)_2$	AgOAc	(None)	59
16	$Pd(OAc)_2$[c]	AgOAc	KF	77
17	$Pd(OCOCF_3)_2$	AgOAc	KF	72
18	$PdCl_2$	AgOAc	KF	58
19	$Pd(OAc)_2$	AgOAc[d]	KF	69
20	$Pd(OAc)_2$	AgOAc[e]	KF	69
21	$Pd(OAc)_2$	Ag_2CO_3	KF	68
22	$Pd(OAc)_2$	Ag_2O	KF	31
23	$Pd(OAc)_2$	AgF	KF	76
24	$Pd(OAc)_2$	Ag_3PO_4	KF	7
25	$Pd(OAc)_2$	AgOTf	KF	66
26	$Pd(OAc)_2$	$Cu(OAc)_2$	KF	0
27[f]	$Pd(OAc)_2$	AgOAc	KF	66
28[g]	$Pd(OAc)_2$	AgOAc	KF	76
29[h]	$Pd(OAc)_2$	AgOAc	KF	78
30[h]	**$Pd(OAc)_2$**	**AgOAc[e]**	**KF**	**85**
31[h]	$Pd(OAc)_2$[c]	AgOAc[e]	KF	81

[a] The yields were determined by ^1H NMR analysis of the crude products using CH_2Br_2 as an internal standard. [b] 2 equiv [c] 5 mol %. [d] 1.5 equiv [e] 3 equiv [f] 16 h. [g] 120 °C. [h] 4-Me-C_6H_4I (3 equiv).

General Procedure for $Pd(OAc)_2$-Catalyzed C–H Arylation of *O*-Benzyl Acid Substrates Using Valine as a Directing Group

A mixture of substrate (55.9 mg, 0.2 mmol), aryl iodide (0.6 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), AgOAc (100 mg, 0.6 mmol), KF (34.9 mg, 0.6 mmol) and HFIP (2.0 mL) in a sealed vial was stirred at 100℃ for 24 h. After cooling down to room temperature, EtOAc (3 mL) and acetic acid (0.6 ml) were added and the reaction mixture was filtered through a short pad of Celite®. The Celite was washed thoroughly with EtOAc (4 × 1.5 mL). To the combined filtrate was added 2 N HCl (4.5 mL), the layers were separated, and the aqueous layer was extracted with EtOAc (3 × 1.5 mL). Combined organic phase was dried over Na_2SO_4, filtered, concentrated and purified by silica gel column chromatography using mixture of hexane, EtOAc and AcOH as eluents (ratios of solvents were varied for different substrates, typically hexane:EtOAc:AcOH = 100:100:0.2 to 100:100:1).



N-[(*R*)-2-(benzyloxy)-3-(*p*-tolyl)propionyl]-L-valine (**2a**)

Light yellow oil, 57.9 mg (77% from 56.5 mg of substrate **1a**)

^{1}H NMR (400MHz, $CDCl_3$): δ 7.33-7.26 (m, 3H), 7.19-7.11 (m, 4H), 7.08 (d, *J* = 7.8 Hz, 2H), 7.00 (d, *J* = 9.0 Hz, 1H), 4.49 (dd, *J* = 8.9, 5.1 Hz, 1H), 4.45 (d, *J* = 11.9 Hz, 1H), 4.41 (d, *J* = 11.6 Hz, 1H), 4.10 (dd, *J* = 8.4, 3.6 Hz, 1H), 3.15 (dd, *J* = 14.2, 3.5 Hz, 1H), 2.90 (dd, *J* = 14.0, 8.3 Hz, 1H), 2.32 (s, 3H), 2.24 (qd, *J* = 11.9, 6.9 Hz, 1H), 0.96 (d, *J* = 6.9 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.4, 172.7, 136.9, 136.1, 134.1, 129.5, 129.0, 128.5, 128.1, 127.8, 81.0, 73.2, 56.8, 38.8, 30.5, 21.1, 19.2, 17.6; HRMS (ESI) m/z: calcd. for $C_{22}H_{28}NO_4^+$ ($[M+H]^+$) 370.2013, found 370.2016.

N-[(*R*)-2-(benzyloxy)-3-(*m*-tolyl)propionyl]-L-valine (**3**)

Light yellow oil, 59.6 mg (80% from 56.0 mg of substrate **1a**)

^{1}H NMR (400MHz, $CDCl_3$): δ 7.33-7.26 (m, 3H), 7.20-7.09 (m, 3H), 7.09-6.99 (m, 4H), 4.52 (dd, *J* = 8.8, 4.9 Hz, 1H), 4.47 (d, *J* = 11.6 Hz, 1H), 4.39 (d, *J* = 11.6 Hz, 1H), 4.12 (dd, *J* = 8.6, 3.3 Hz, 1H), 3.15 (dd, *J* = 14.0, 3.3 Hz, 1H), 2.89 (dd, *J* = 14.0, 8.5 Hz, 1H), 2.31 (s, 3H), 2.29-2.20 (m, 1H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.0, 172.7, 137.8, 137.1, 136.8, 130.4, 128.5, 128.2, 128.1, 127.9, 127.3, 126.6, 80.9, 73.2, 56.8, 39.2, 30.5, 21.3, 19.2, 17.6; HRMS (ESI) m/z: calcd. for $C_{22}H_{28}NO_4^+$ ($[M+H]^+$) 370.2013, found 370.2016.

N-[(*R*)-2-(benzyloxy)-3-(*o*-tolyl)propionyl]-L-valine (**4**)

Light yellow oil 9.4 mg (13% from 56.1 mg of substrate **1a**)

^{1}H NMR (400MHz, $CDCl_3$): δ 7.26-7.19 (m, 4H), 7.16-7.05 (m, 5H), 4.53 (dd, *J* = 8.8, 4.9 Hz, 1H), 4.39 (d, *J* = 11.6 Hz, 1H), 4.30 (d, *J* = 11.6 Hz, 1H), 4.08 (dd, *J* = 9.7, 3.2 Hz, 1H), 3.22 (dd, *J* = 14.3, 3.1 Hz, 1H), 2.92 (dd, *J* = 14.0, 9.8 Hz, 1H), 2.32 (s, 3H), 2.30-2.22 (m, 1H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.1, 172.9, 136.8, 136.7, 135.8, 130.5, 130.3, 128.5, 128.1, 127.8, 126.8, 125.8, 80.5, 73.5, 56.8, 36.9, 30.6, 19.6, 19.2, 17.6; HRMS (ESI) m/z: calcd. for $C_{22}H_{28}NO_4^+$ ($[M+H]^+$) 370.2013, found 370.2013.

N-[(*R*)-2-(benzyloxy)-3-phenylpropionyl]-L-valine (**5**)

Light yellow oil 48.7 mg (68% from 55.9 mg of substrate **1a**)

^{1}H NMR (400MHz, $CDCl_3$): δ 7.33-7.27 (m, 4H), 7.26-7.20 (m, 4H), 7.17-7.12 (m, 2H), 7.01 (d, *J* = 8.9 Hz, 1H), 4.50 (dd, *J* = 8.9, 5.0 Hz, 1H), 4.46 (d, *J* = 11.8 Hz, 1H), 4.40 (d, *J* = 11.8 Hz, 1H), 4.13 (dd, *J* = 8.5, 3.5 Hz, 1H), 3.19 (dd, *J* = 14.1, 3.4 Hz, 1H), 2.93 (dd, *J* = 14.0, 8.6 Hz, 1H), 2.29-2.19 (m, 1H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.9, 172.5, 137.2, 136.8, 129.6, 128.6, 128.3, 128.1, 127.8, 126.6, 80.9, 73.2, 56.8, 39.3, 30.6, 19.2, 17.6; HRMS (ESI) m/z: calcd. for $C_{21}H_{26}NO_4^+$ ($[M+H]^+$) 356.1856, found 356.1857.

N-[(*R*)-2-(benzyloxy)-3-(naphthalen-2-yl)propionyl]-L-valine (**6**)

Light brown oil 39.4 mg (48% from 56.1 mg of substrate **1a**)

^{1}H NMR (400MHz, $CDCl_3$): δ 7.82-7.72 (m, 3H), 7.70 (s, 1H), 7.47-7.37 (m, 3H), 7.24-7.17 (m, 3H), 7.13-7.07 (m, 2H), 7.04 (d, *J* = 8.9 Hz, 1H), 4.53 (dd, *J* = 8.9, 4.9 Hz, 1H), 4.46 (d, *J* = 11.6 Hz, 1H), 4.38 (d, *J* = 11.7 Hz, 1H), 4.22 (dd, *J* = 8.7, 3.4 Hz, 1H), 3.36 (dd, *J* = 14.2, 3.3 Hz, 1H), 3.10 (dd, *J* = 14.1, 8.7 Hz, 1H), 2.29-2.19 (m, 1H), 0.96 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.7, 172.5, 136.7, 134.8, 133.5, 132.3, 128.5, 128.2, 128.1, 127.9, 127.9, 127.8, 127.6, 127.6, 125.9, 125.4, 80.9, 73.3, 56.7, 39.5, 30.6, 19.2, 17.6; HRMS (ESI) m/z: calcd. for $C_{25}H_{28}NO_4^+$ ($[M+H]^+$) 406.2013, found 406.2016.

N-{(*R*)-2-(benzyloxy)-3-[4-(trifluoromethyl)phenyl]propionyl}-L-valine (**7**)
Light yellow oil 57.1 mg (y. 67% from 56.1 mg of substrate **1a**)
^{1}H NMR (400MHz, $CDCl_3$): δ 7.51 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.30-7.26 (m, 3H), 7.12 (dd, *J* = 6.1, 2.9 Hz, 2H), 7.01 (d, *J* = 8.9 Hz, 1H), 4.56-4.47 (m, 2H), 4.41 (d, *J* = 11.7 Hz, 1H), 4.13 (dd, *J* = 8.1, 3.5 Hz, 1H), 3.20 (dd, *J* = 14.1, 3.3 Hz, 1H), 2.99 (dd, *J* = 13.9, 8.3 Hz, 1H), 2.31-2.20 (m, 1H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.9, 172.0, 141.3, 136.4, 130.0, 128.9 (d, *J* = 33.0 Hz), 128.6, 128.3, 127.9, 125.1 (q, *J* = 3.7 Hz), 124.3 (d, *J* = 271.8 Hz), 80.2, 73.2, 56.6, 38.9, 30.7 19.2, 17.6; HRMS (ESI) m/z: calcd. for $C_{22}H_{25}F_3NO_4^+$ ($[M+H]^+$) 424.1730, found 424.1739.

N-[(*R*)-2-(benzyloxy)-3-(4-bromophenyl)propionyl]-L-valine (**8**)
Light yellow oil 63.6 mg (y. 73% from 55.9 mg of substrate **1a**)
^{1}H NMR (400MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.3 Hz, 2H), 7.35-7.26 (m, 3H), 7.20-7.12 (m, 2H), 7.10 (d, *J* = 8.3 Hz, 2H), 7.00 (d, *J* = 9.1 Hz, 1H), 4.56-4.45 (m, 2H), 4.41 (d, *J* = 11.6 Hz, 1H), 4.09 (dd, *J* = 8.2, 3.4 Hz, 1H), 3.11 (dd, *J* = 14.2, 3.4 Hz, 1H), 2.89 (dd, *J* = 14.2, 8.4 Hz, 1H), 2.25 (dd, *J* = 11.8, 6.7 Hz, 1H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 175.0, 172.2, 136.5, 136.1, 131.4, 131.3, 128.6, 128.2, 127.9, 120.6, 80.5, 73.2, 56.7, 38.5, 30.7, 19.2, 17.6; HRMS (ESI) m/z: calcd. for $C_{21}H_{25}BrNO_4^+$ ($[M+H]^+$) 434.0961, found 434.0966.

N-[(*R*)-2-(benzyloxy)-3-(2-bromophenyl)propionyl]-L-valine (**9**)
Light orange oil 27.7 mg (y. 32% from 55.9 mg of substrate **1a**)
^{1}H NMR (400MHz, $CDCl_3$): δ 7.53 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.32-7.27 (m, 2H), 7.26-7.20 (m, 3H), 7.14-7.05 (m, 4H), 4.56 (dd, *J* = 8.9, 4.8 Hz, 1H), 4.42 (d, *J* = 11.7 Hz, 1H), 4.35 (d, *J* = 11.7 Hz, 1H), 4.27 (dd, *J* = 9.2, 4.0 Hz, 1H), 3.41 (dd, *J* = 14.1, 4.0 Hz, 1H), 3.04 (dd, *J* = 14.0, 9.3 Hz, 1H), 2.34-2.21 (m, 1H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.9, 172.3, 136.7, 136.7, 132.8, 132.3, 128.5, 128.4, 128.1, 127.9, 127.2, 124.8, 79.0, 73.5, 56.7, 39.7, 30.6, 19.2, 17.6; HRMS (ESI) m/z: calcd. for $C_{21}H_{25}BrNO_4^+$ ($[M+H]^+$) 434.0961, found 434.0970.

N-[(*R*)-2-(benzyloxy)-3-(3-chlorophenyl)propionyl]-L-valine (**10**)
Light yellow oil 58.9 mg (y. 75% from 56.0 mg of substrate **1a**)
^{1}H NMR (400MHz, $CDCl_3$): δ 7.35-7.28 (m, 3H), 7.24 (s, 1H), 7.22-7.14 (m, 4H), 7.13-7.09 (m, 1H), 7.00 (d, *J* = 8.9 Hz, 1H), 4.56-4.48 (m, 2H), 4.41 (d, *J* = 12.5 Hz, 1H), 4.10 (dd, *J* = 8.2, 3.5 Hz, 1H), 3.14 (dd, *J* = 14.2, 3.5 Hz, 1H), 2.91 (dd, *J* = 14.1, 8.4 Hz, 1H), 2.25 (dd, *J* = 11.8, 6.8 Hz, 1H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.8, 172.1, 139.2, 136.5, 134.0, 129.8, 129.5, 128.6, 128.3, 127.9, 127.8, 126.8, 80.4, 73.3, 56.7, 38.8, 30.6, 19.2, 17.6; HRMS (ESI) m/z: calcd. for $C_{21}H_{25}ClNO_4^+$ ($[M+H]^+$) 390.1467, found 390.1474.

N-[(*R*)-2-(benzyloxy)-3-(4-fluorophenyl)propionyl]-L-valine (**11**)
Light yellow oil 56.3 mg (y. 75% from 56.0 mg of substrate **1a**)
^{1}H NMR (400MHz, $CDCl_3$): δ 7.35-7.27 (m, 3H), 7.22-7.14 (m, 4H), 7.01-6.90 (m, 3H), 4.53-4.45 (m, 2H), 4.42 (d, *J* = 11.7 Hz, 1H), 4.09 (dd, *J* = 8.0, 3.6 Hz, 1H), 3.13 (dd, *J* = 14.1, 3.4 Hz, 1H), 2.92 (dd, *J* = 14.2, 8.2 Hz, 1H), 2.24 (dd, *J* = 11.9, 7.1 Hz, 1H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.7, 172.3, 161.8 (d, *J* = 244.3 Hz), 136.7, 132.7 (d, *J* = 3.3 Hz), 131.1 (d, *J* = 7.7 Hz), 128.6, 128.2, 127.8, 115.0 (d, *J* = 20.9 Hz), 80.7, 73.2, 56.7, 38.3, 30.6, 19.2, 17.6; HRMS (ESI) m/z: calcd. for $C_{21}H_{25}FNO_4^+$ ($[M+H]^+$) 374.1762, found 374.1771.

N-[(*R*)-2-(benzyloxy)-3-(2-fluorophenyl)propionyl]-L-valine (**12**)
Light yellow oil 47.3 mg (y. 63% from 56.0 mg of substrate **1a**)
^{1}H NMR (400MHz, $CDCl_3$): δ 7.32-7.26 (m, 3H), 7.25-7.10 (m, 4H), 7.10-6.95 (m, 3H), 4.52 (dd, *J* = 8.8, 5.0 Hz, 1H), 4.49 (d, *J* = 11.6 Hz, 1H), 4.45 (d, *J* = 11.6 Hz, 1H), 4.19 (dd, *J* = 8.0, 4.1 Hz, 1H), 3.29 (dd, *J* = 14.3, 4.1 Hz, 1H), 3.00 (dd, *J* = 14.2, 8.1 Hz, 1H), 2.30-2.22 (m, 1H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.9, 172.3, 161.4 (d, *J* = 246.5 Hz), 136.7, 132.0 (d, *J* = 4.4 Hz), 128.5, 128.5 (d, *J* = 7.7 Hz), 128.1, 127.8, 124.1 (d, *J* = 15.4 Hz), 123.9 (d, *J* = 3.3 Hz), 115.2 (d, *J* = 22.0 Hz), 79.5, 73.1, 56.7, 32.3, 30.6, 19.2, 17.6; HRMS (ESI) m/z: calcd. for $C_{21}H_{25}FNO_4^+$ ($[M+H]^+$) 374.1762, found 374.1771.

N-[(*R*)-2-(benzyloxy)-3-(4-methoxyphenyl)propionyl]-L-valine (**13**)
Light yellow oil 45.9 mg (y. 60% from 55.9 mg of substrate **1a**)
^{1}H NMR (400MHz, $CDCl_3$): δ 7.33-7.26 (m, 3H), 7.19-7.13 (m, 4H), 6.99 (d, *J* = 9.1 Hz, 1H), 6.82 (d, *J* = 8.5 Hz, 2H), 4.49 (dd, *J* = 8.8, 4.6 Hz, 1H), 4.46 (d, *J* = 11.6 Hz, 1H), 4.41 (d, *J* = 11.6 Hz, 1H), 4.08 (dd, *J* = 8.3, 3.4 Hz, 1H), 3.78 (s, 3H), 3.12 (dd, *J* = 14.2, 3.4 Hz, 1H), 2.88 (dd, *J* = 14.2, 8.5 Hz, 1H), 2.29-2.19 (m, 1H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.6, 172.6, 158.4, 136.9, 130.6, 129.2, 128.6, 128.1, 127.8, 113.7, 81.1, 73.2, 56.8, 55.2, 38.4, 30.6, 19.2, 17.6; HRMS (ESI) m/z: calcd. for $C_{22}H_{28}NO_5^+$ ($[M+H]^+$) 386.1962, found 386.1959.

N-{(*R*)-2-(benzyloxy)-3-[4-(methoxycarbonyl)phenyl]propionyl}-L-valine (**14**)
Light brown oil 56.1 mg (y. 68% from 55.9 mg of substrate **1a**)
^{1}H NMR (400MHz, $CDCl_3$): δ 7.97-7.92 (m, 2H), 7.34-7.27 (m, 5H), 7.16-7.09 (m, 2H), 7.03 (d, *J* = 8.9 Hz, 1H), 4.52 (dd, *J* = 9.0, 4.9 Hz, 1H), 4.47 (d, *J* = 11.6 Hz, 1H), 4.39 (d, *J* = 11.5 Hz, 1H), 4.15 (dd, *J* = 8.6, 3.5 Hz, 1H), 3.90 (s, 3H), 3.22 (dd, *J* = 14.0, 3.4 Hz, 1H), 2.99 (dd, *J* = 14.0, 8.6 Hz, 1H), 2.30-2.19 (m, 1H), 0.96 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.8, 172.1, 167.3, 142.7, 136.5, 129.7, 129.6, 128.6, 128.5, 128.2, 127.9, 80.4, 73.3, 56.7, 52.1, 39.2, 30.7, 19.2, 17.6; HRMS (ESI) m/z: calcd. for $C_{23}H_{28}NO_6^+$ ($[M+H]^+$) 414.1911, found 414.1911.

N-[(*R*)-2-(benzyloxy)-3-(3-acetylphenyl)propionyl]-L-valine (**15**)

Light yellow oil 40.7 mg (y. 51% from 56.1 mg of substrate **1a**)

^{1}H NMR (400MHz, $CDCl_3$): δ 7.84-7.78 (m, 2H), 7.44 (td, *J* = 7.5, 1.4 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.30-7.27 (m, 3H), 7.17-7.12 (m, 2H), 6.98 (d, *J* = 8.9 Hz, 1H), 4.54 (d, *J* = 11.6 Hz, 1H), 4.49 (dd, *J* = 9.0, 5.1 Hz, 1H), 4.42 (d, *J* = 11.6 Hz, 1H), 4.15 (dd, *J* = 7.9, 3.8 Hz, 1H), 3.21 (dd, *J* = 14.0, 3.7 Hz, 1H), 3.03 (dd, *J* = 14.0, 8.0 Hz, 2H), 2.55 (s, 3H), 2.28-2.18 (m, 1H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 198.7, 174.6, 172.1, 137.6, 137.1, 136.5, 134.6, 129.7, 128.6, 128.5, 128.2, 127.9, 126.6, 80.4, 73.2, 56.7, 38.9, 30.7, 26.7, 19.2, 17.6; HRMS (ESI) m/z: calcd. for $C_{23}H_{28}NO_5^+$ ($[M+H]^+$) 398.1962, found 398.1966.

N-[(*R*)-2-(benzyloxy)-3-(4-nitrophenyl)propionyl]-L-valine (**16**)

Light yellow oil 30.9 mg (y. 39% from 55.9 mg of substrate **1a**)

^{1}H NMR (400MHz, $CDCl_3$): δ 8.12-8.06 (m, 2H), 7.41-7.28 (m, 5H), 7.22-7.16 (m, 2H), 6.95 (d, *J* = 9.2 Hz, 1H), 4.60 (d, *J* = 11.8 Hz, 1H), 4.50 (dd, *J* = 9.1, 4.9 Hz, 1H), 4.49 (d, *J* = 11.8 Hz, 1H), 4.19 (dd, *J* = 7.2, 3.9 Hz, 1H), 3.23 (dd, *J* = 14.1, 4.0 Hz, 1H), 3.11 (dd, *J* = 14.0, 7.2 Hz, 1H), 2.31-2.17 (m, 1H), 0.96 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 175.2, 171.5, 146.9, 144.7, 136.3, 130.7, 128.7, 128.4, 127.9, 123.3, 79.6, 73.2, 56.5, 38.5, 30.6, 19.2, 17.5; HRMS (ESI) m/z: calcd. for $C_{21}H_{25}N_2O_6^+$ ($[M+H]^+$) 401.1707, found 401.1715.

Gram-scale Synthesis of 2a

A mixture of **1a** (1.12 g, 4.0 mmol), 4-iodotoluene (2.62 g, 12.0 mmol), $Pd(OAc)_2$ (89.6 mg, 0.41 mmol), AgOAc (2.01 g, 12.0 mmol), KF (712.6 mg, 12.3 mmol) and HFIP (40 mL) in a sealed vial was stirred at 100 °C for 24 h. After cooling down to room temperature, EtOAc (40 mL) and acetic acid (12 ml) were added and the reaction mixture was filtered through a short pad of Celite®. The Celite was washed thoroughly with EtOAc (4 × 30 mL). To the combined filtrate was added 2 N HCl (60 mL), the layers were separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). Combined organic phase was dried over anhydrous Na_2SO_4, filtered, concentrated and purified by silica gel column chromatography (hexane:EtOAc:AcOH = 100:100:0.2 to 100:100:0.8) to give **2a** as an off-white solid (1.04 g, 70%).

Removal of Amino Acid Auxiliary from 2a

Methyl (*S*)-2-[(*R*)-2-(benzyloxy)-3-(*p*-tolyl)propanamido]-3-methylbutanoate (**18**)

To a solution of **2a** (77.4 mg, 0.21 mmol) in toluene (0.75 mL) and MeOH (0.25 mL) was added dropwise a solution of 2 M $TMSCHN_2$ in hexane (300 μL, 0.6 mmol), and the mixture was stirred at rt for 1 h. Silica gel (ca. 500 mg) was added to quench the reaction, and the mixture was fitered through a cotton plug and the silica gel was washed with EtOAc:MeOH=1:1 solution (10 mL). The eluent was

concentrated under reduced pressure and purified by silica gel column chromatography (hexane:EtOAc = 4:1) to yield **18** as a yellow oil (78.2 mg, 97%)

^{1}H NMR (400MHz, $CDCl_3$): δ 7.32-7.27 (m, 3H), 7.18-7.12 (m, 4H), 7.10-7.06 (m, 2H), 6.99 (d, *J* = 9.3 Hz, 1H), 4.51 (dd, *J* = 9.1, 5.0 Hz, 1H), 4.45 (d, *J* = 11.6 Hz, 1H), 4.39 (d, *J* = 11.6 Hz, 1H), 4.07 (dd, *J* = 8.7, 3.5 Hz, 1H), 3.70 (s, 3H), 3.13 (dd, *J* = 14.0, 3.5 Hz, 1H), 2.89 (dd, *J* = 14.1, 8.7 Hz, 1H), 2.33 (s, 3H), 2.20-2.11 (m, 1H), 0.91 (d, *J* = 6.9 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 172.0, 171.8, 137.0, 136.0, 134.3, 129.5, 128.9, 128.5, 128.0, 127.8, 81.2, 73.2, 56.6, 52.1, 39.0, 31.1, 21.1, 19.1, 17.8; HRMS (ESI) m/z: calcd. for $C_{23}H_{30}NO_4^+$ ($[M+H]^+$) 384.2169, found 384.2183.

(*R*)-2-(benzyloxy)-3-(*p*-tolyl)propanoic acid (**19**)

To a solution of above **18** (78.2 mg, 0.20 mmol) in AcOH:Ac_2O (1:2 v/v) solution (2.0 mL) was added $NaNO_2$ (281.0 mg, 4.1 mmol) portionwise at 0°C. After 1 h of stirring, additional AcOH:Ac_2O (1:2 v/v) solution (1.0 mL) was added. The mixture was stirred for another 2 h at 0 °C, then gradually allowed to warm to rt overnight. Most the volatiles were then removed under reduced pressure, and to the residue was added saturated aqueous $NaHCO_3$ and 2 N NaOH at 0 °C to adjust to pH 8. The mixture was stirred at 0 °C for 45 min. and at rt for 1 h. The mixture was acidified with 2 N HCl, extracted with EtOAc (3 × 30 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (hexane:EtOAc:AcOH = 100:100:1) to give **19** as a pale yellow oil (39.6 mg, 72% or 91% based on recovered **18**).

^{1}H NMR (400MHz, $CDCl_3$): δ 7.33-7.27 (m, 3H), 7.18 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.15-7.09 (m, 4H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.46 (d, *J* = 11.6 Hz, 1H), 4.20 (dd, *J* = 7.8, 4.2 Hz, 1H), 3.15 (dd, *J* = 14.2, 4.2 Hz, 1H), 3.01 (dd, *J* = 14.3, 7.8 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.7, 136.5, 136.4, 133.2, 129.4, 129.1, 128.5, 128.2, 128.0, 78.8, 73.0, 38.2, 21.1; HRMS (ESI) m/z: calcd. for $C_{17}H_{17}O_3^-$ ($[M-H]^-$) 269.1183, found 269.1173; HPLC CHIRALPAK AD-H (2% 2-PrOH + 0.2% TFA in hexane; 0.5 mL/min) t_r = 50.587 min (major), 46 min (minor): 99.7% *ee*.

(*R*)-2-hydroxy-3-(*p*-tolyl)propanoic acid (**17**)

To a solution of **2a** (37.1 mg, 0.10 mmol) in 1,4-dioxane (1.0 mL) was added conc. HCl (1.0 mL, ca. 12 mmol), and the mixture was stirred at 80°C for 24 h. Water (ca. 4.5 mL) was added, and the reaction was extracted with EtOAc (5 × 1.5 mL). Combined organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (hexane:EtOAc:MeOH = 100:200:0 to 100:200:4.5) to yield **17** as an off-white solid (12.7 mg, y. 70%)

^{1}H NMR (400MHz, $CDCl_3$): δ 7.13 (s, 4H), 4.46 (dd, *J* = 6.4, 4.4 Hz, 1H), 3.16 (dd, *J* = 14.1, 4.1 Hz, 1H), 2.95 (dd, *J* = 13.9, 7.1 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 176.9, 136.8, 132.6, 129.4, 129.4, 71.1, 39.7, 21.1; HRMS (ESI) m/z: calcd. for $C_{10}H_{11}O_3^-$ ($[M-H]^-$) 179.0714, found 179.0718; HPLC CHIRALPAK AD-H (10% 2-PrOH + 0.2% TFA in hexane; 0.5 mL/min) t_r = 15.973 min (major), 20.593 min (minor): 98.8% *ee*.

HPLC Spectra

Compound **19**

Area % Report

Data File: C:¥EZChrom Elite¥Enterprise¥Projects¥Default¥Data¥Tetsuya¥TT02-065_chiral_3

Method: C:¥EZChrom Elite¥Enterprise¥Projects¥Default¥Method¥A 90 min without fc 0.5 ml per min.met

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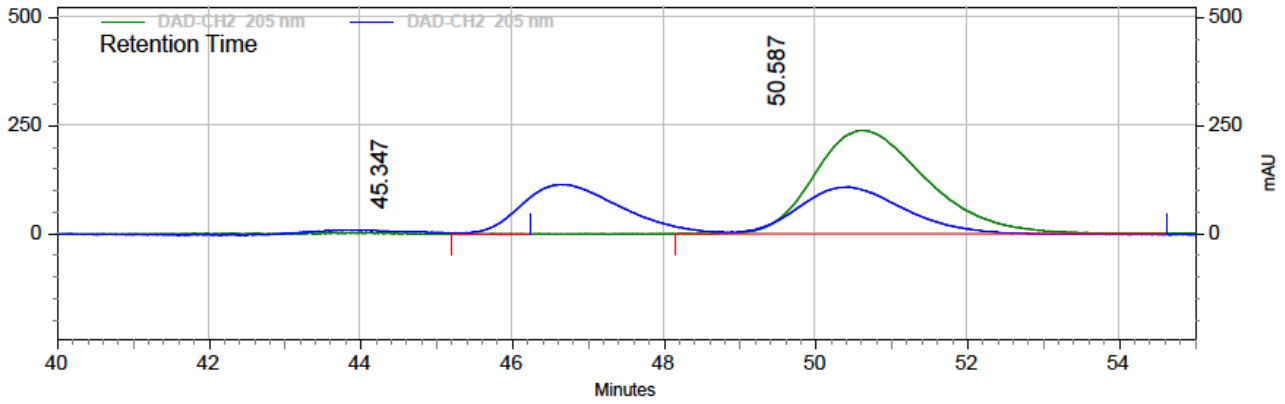
Printed: 8/22/2014 7:49:03 PM



DAD-CH2 205 nm Results

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50.587	99208099	99.83	959804	99.38
Totals	99381283	100.00	965760	100.00

Compound **17**

Area % Report

Data File: C:¥EZChrom Elite¥Enterprise¥Projects¥Default¥Data¥Tetsuya¥TT02-057Px2_chiral

Method: C:¥EZChrom Elite¥Enterprise¥Projects¥Default¥Method¥A 90 min without fc 0.5 ml per min.met

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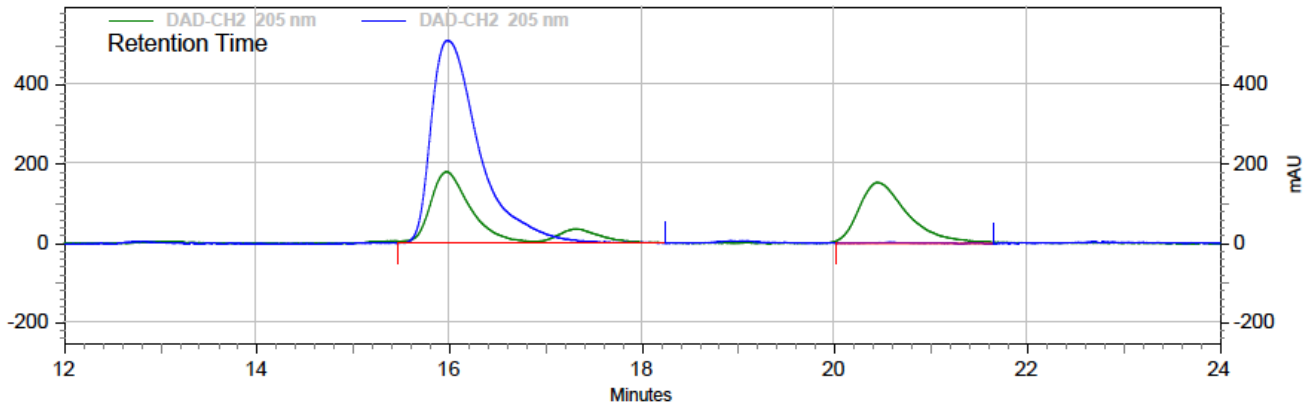
Printed: 8/22/2014 8:26:58 PM



DAD-CH2

205 nm

Results

Retention Time	Area	Area %	Height	Height %
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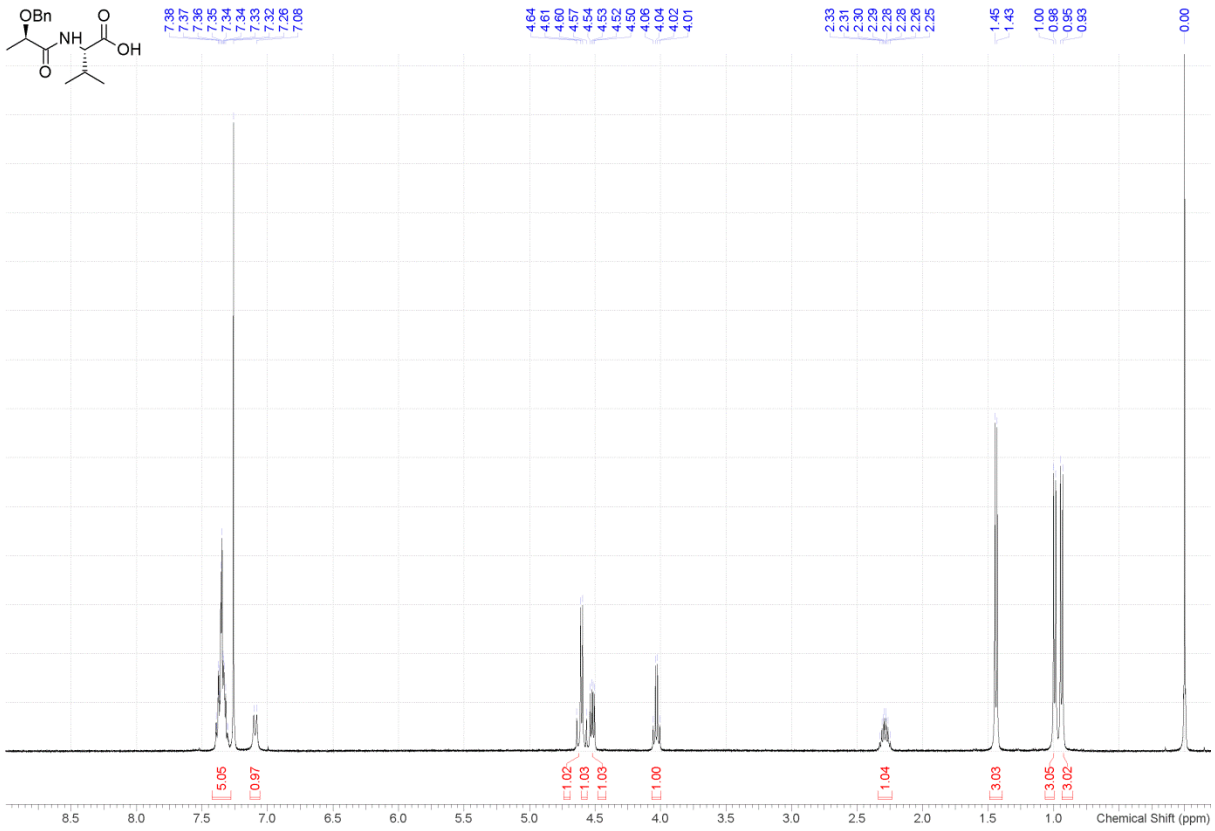
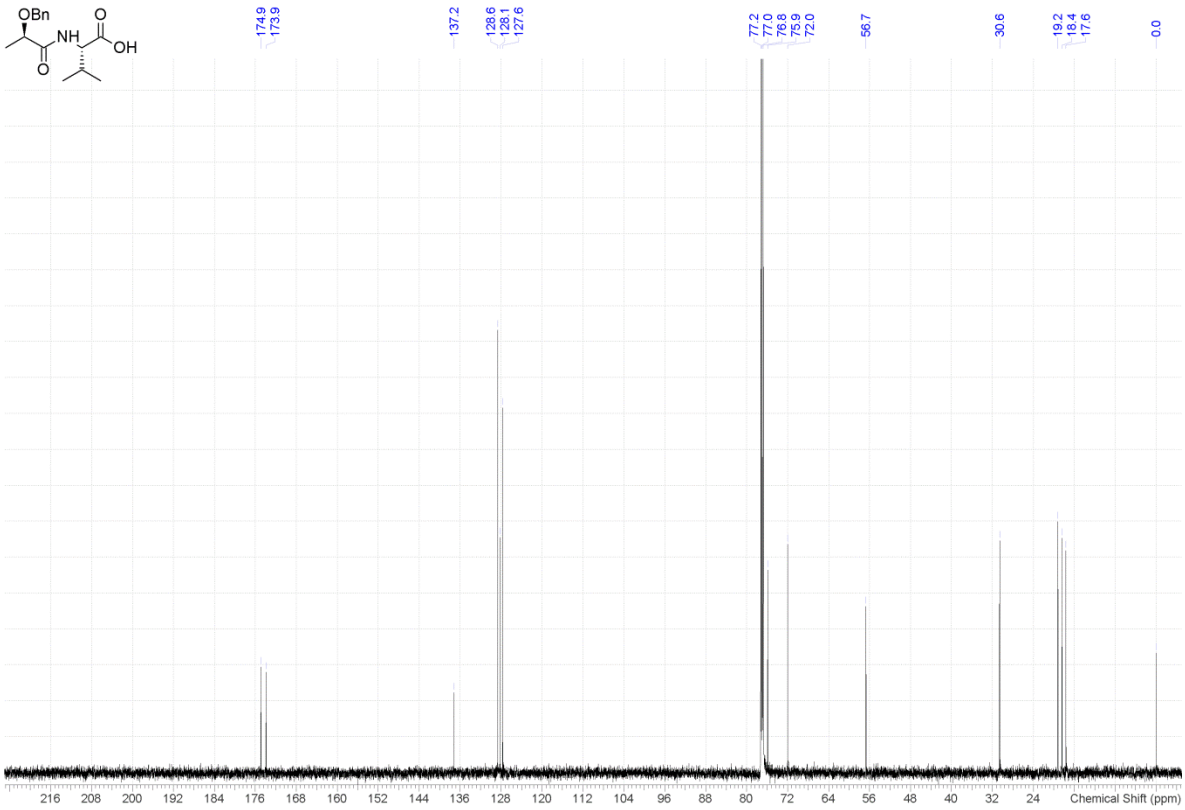
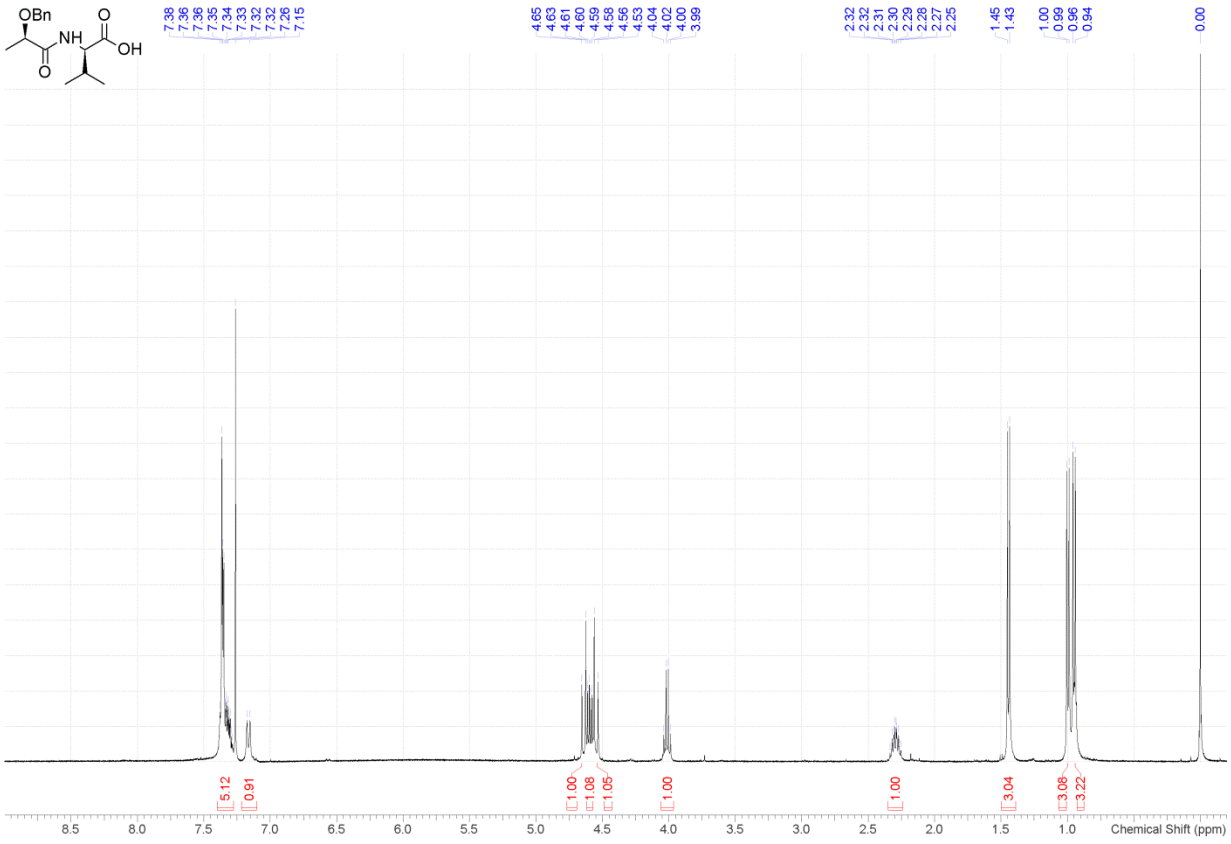
NMR Spectra

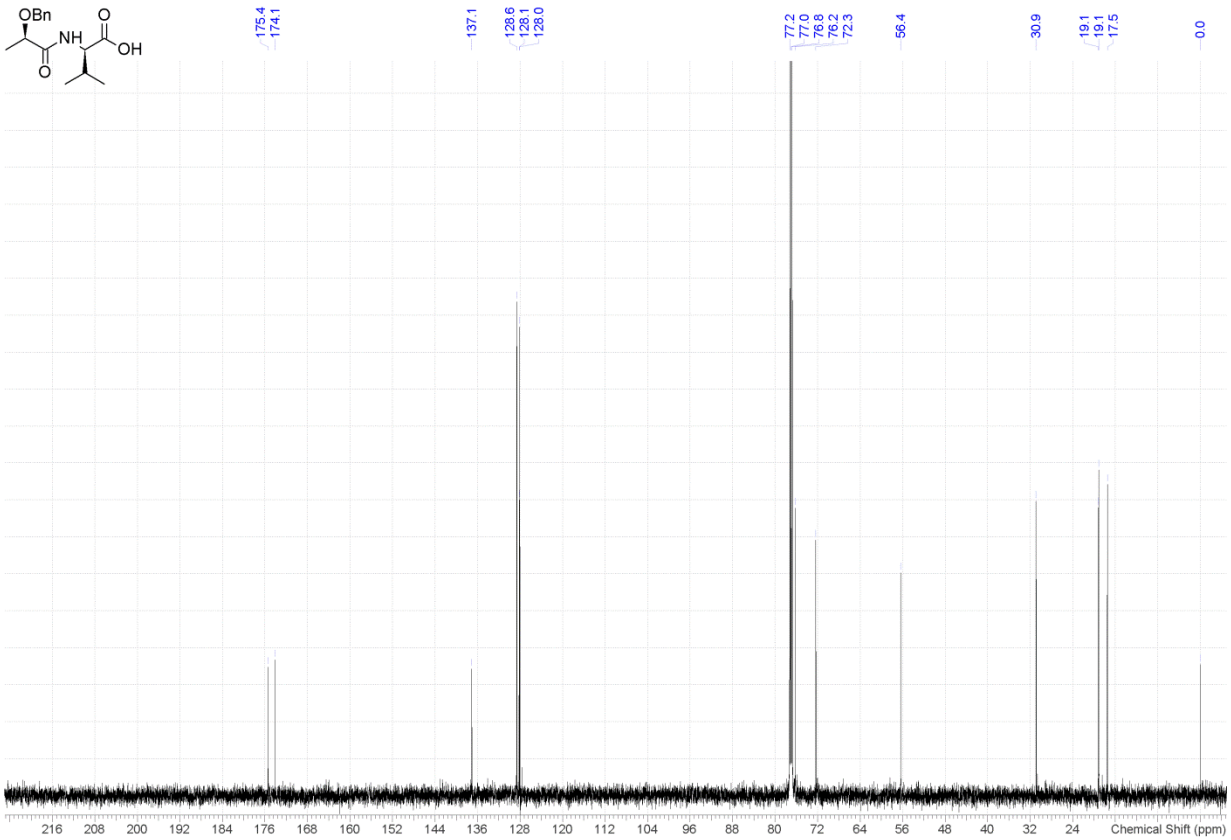
N-[(*R*)-2-(benzyloxy)propionyl]-L-valine (**1a**)



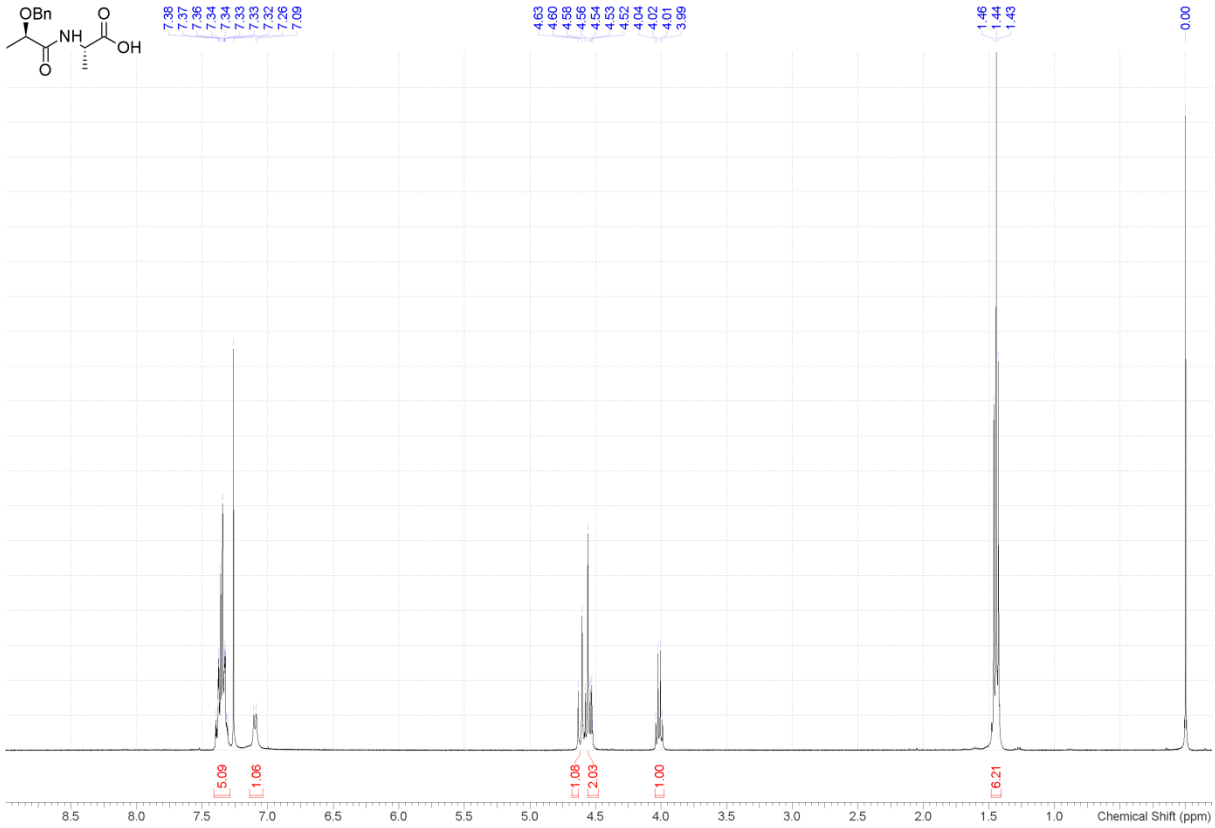


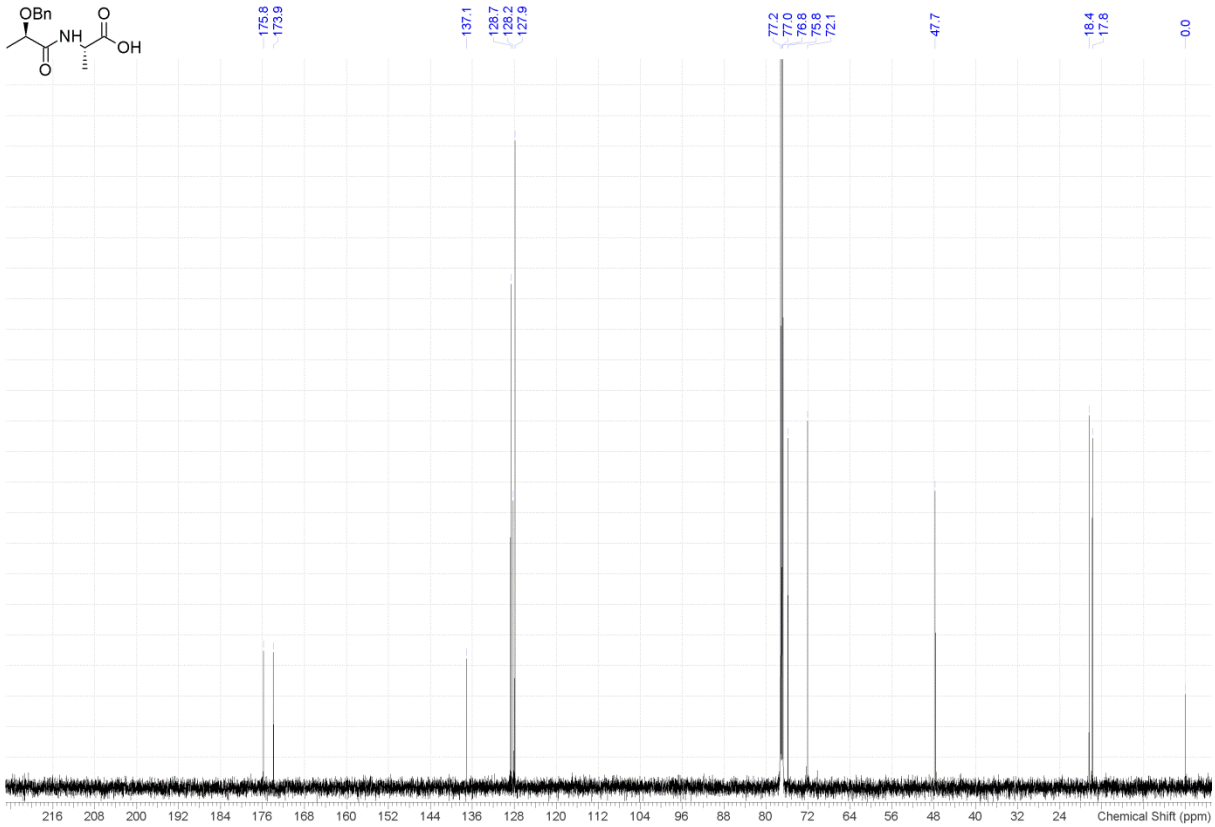
N-[(*R*)-2-(benzyloxy)propionyl]-D-valine (**1b**)



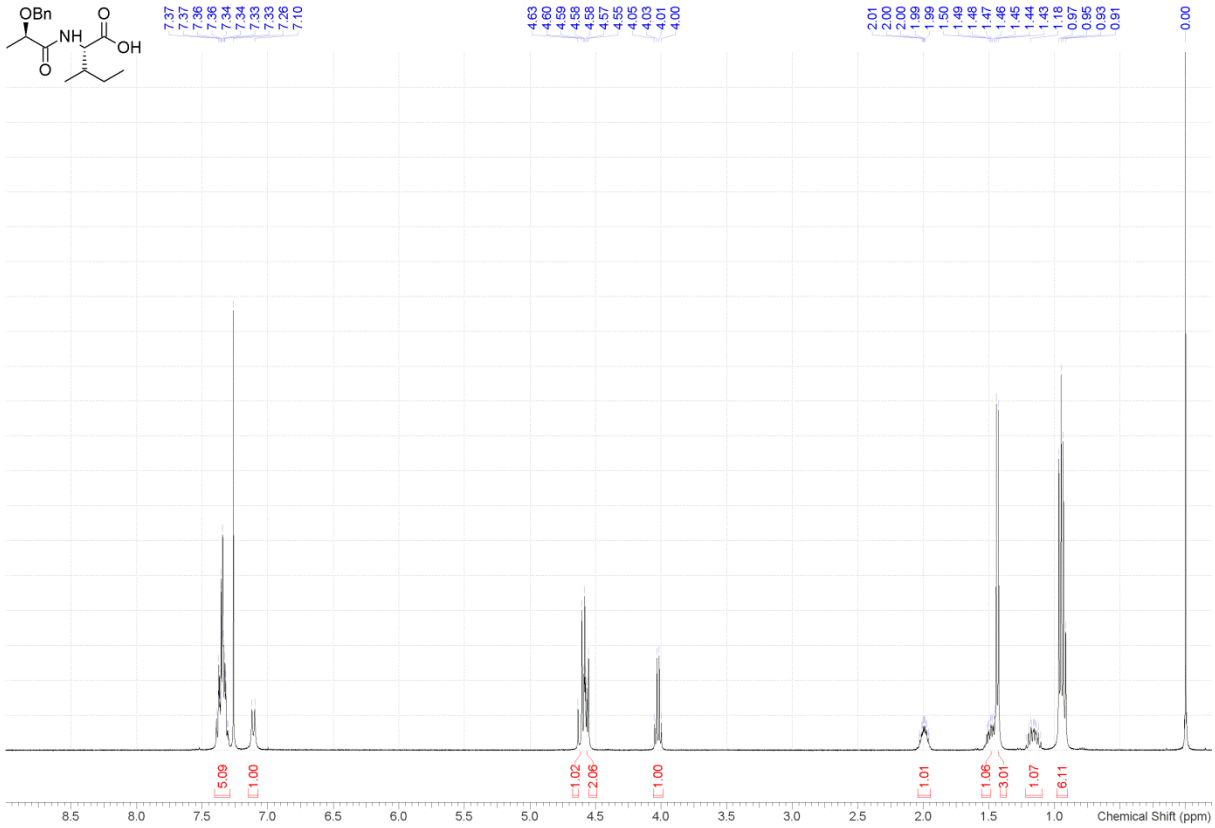


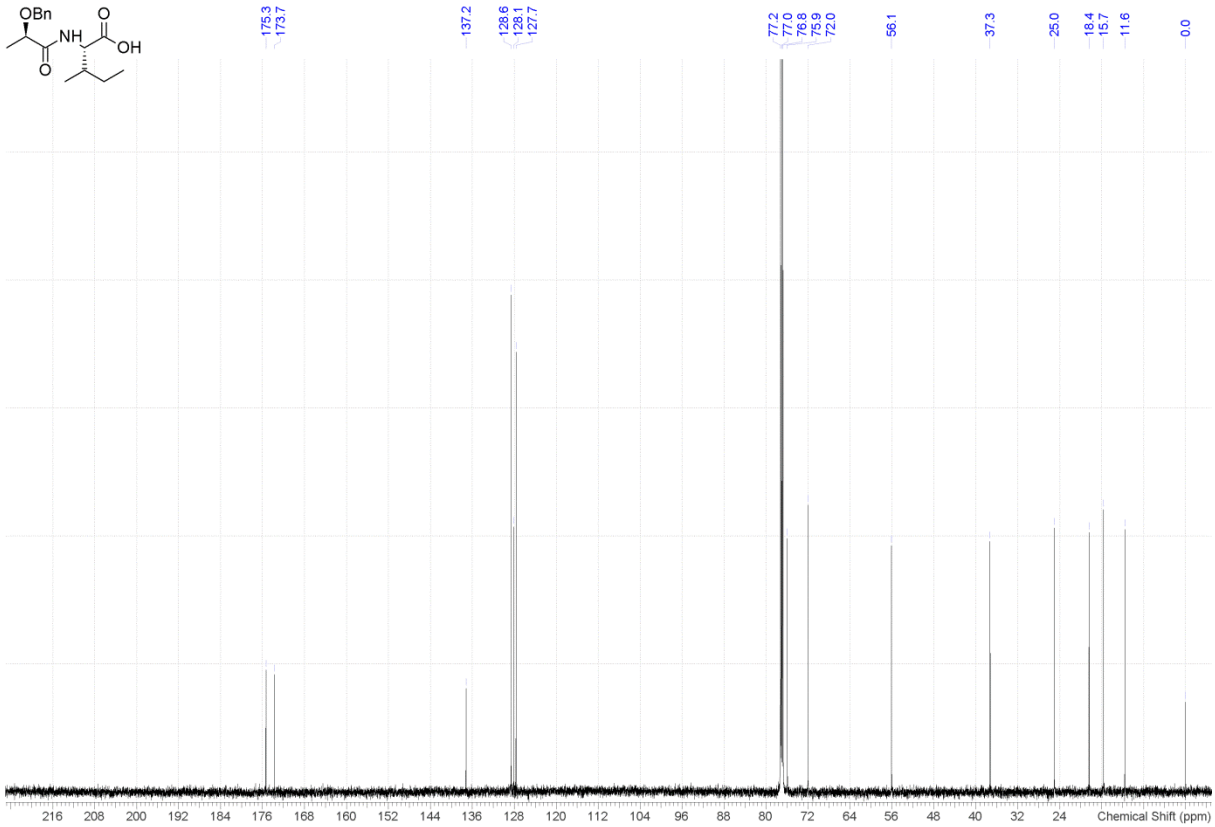
N-[(*R*)-2-(benzyloxy)propionyl]-L-alanine (**1c**)



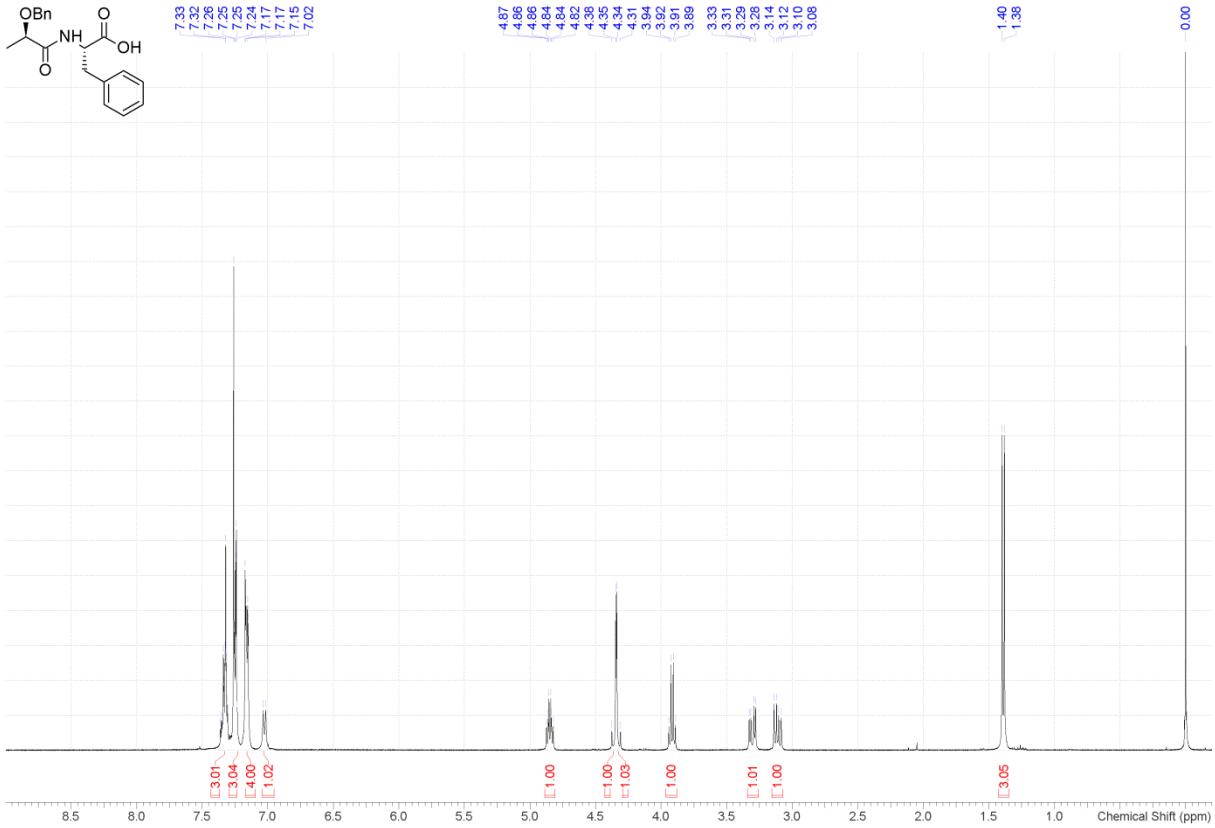


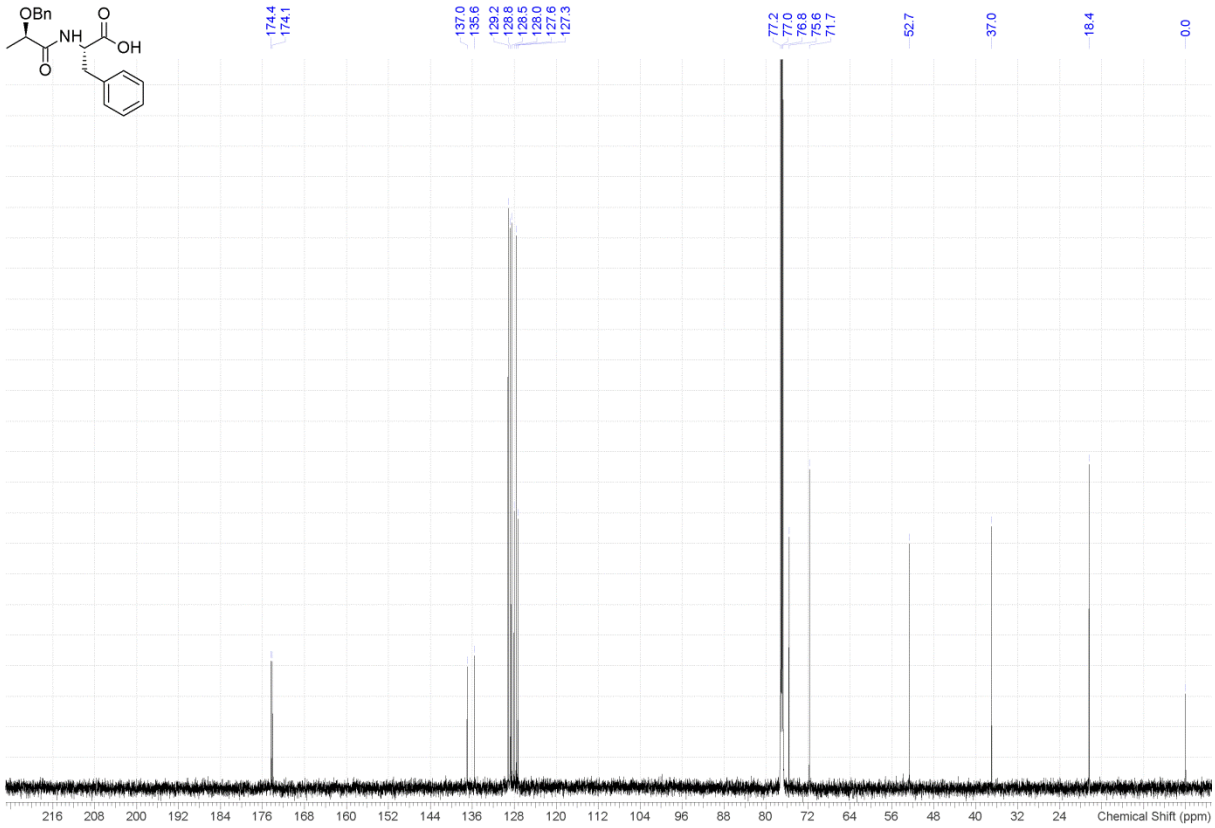
N-[(*R*)-2-(benzyloxy)propionyl]-L-isoleucine (**1d**)



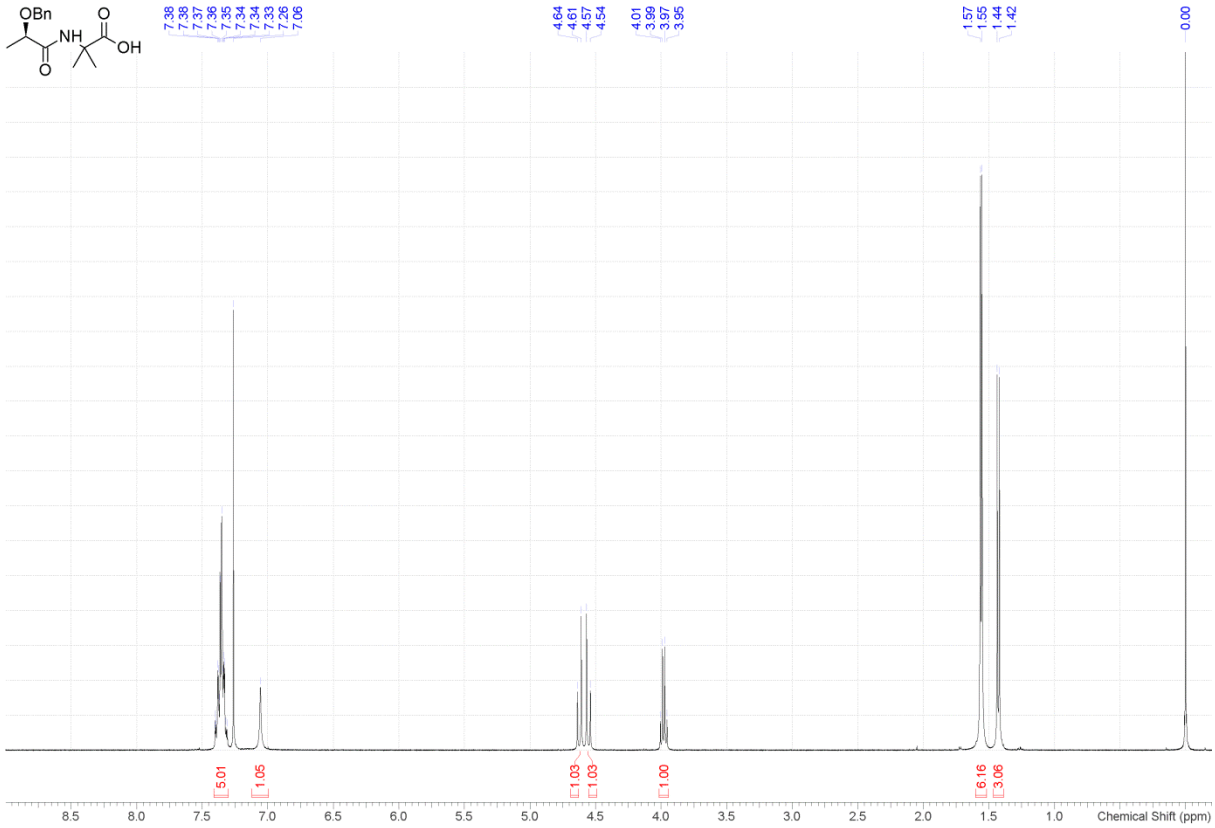


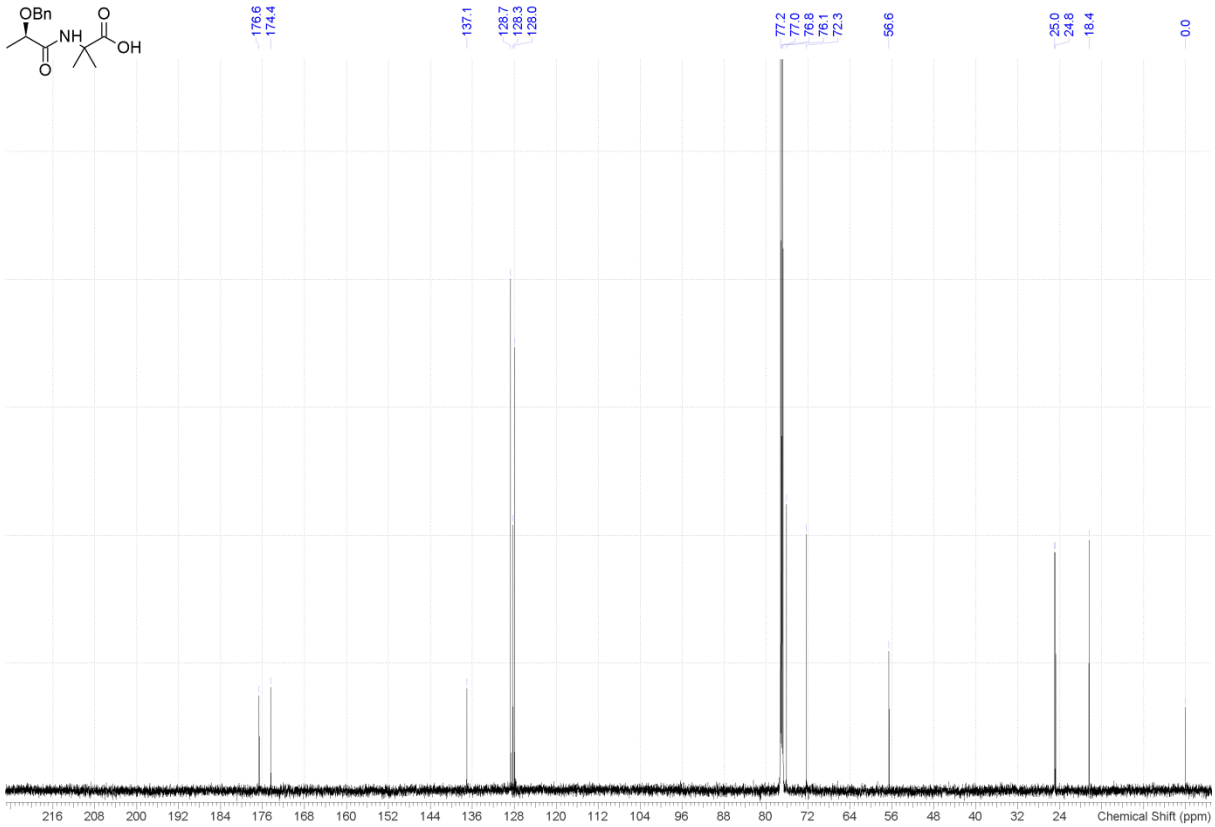
N-[(*R*)-2-(benzyloxy)propionyl]-L-phenylalanine (**1e**)



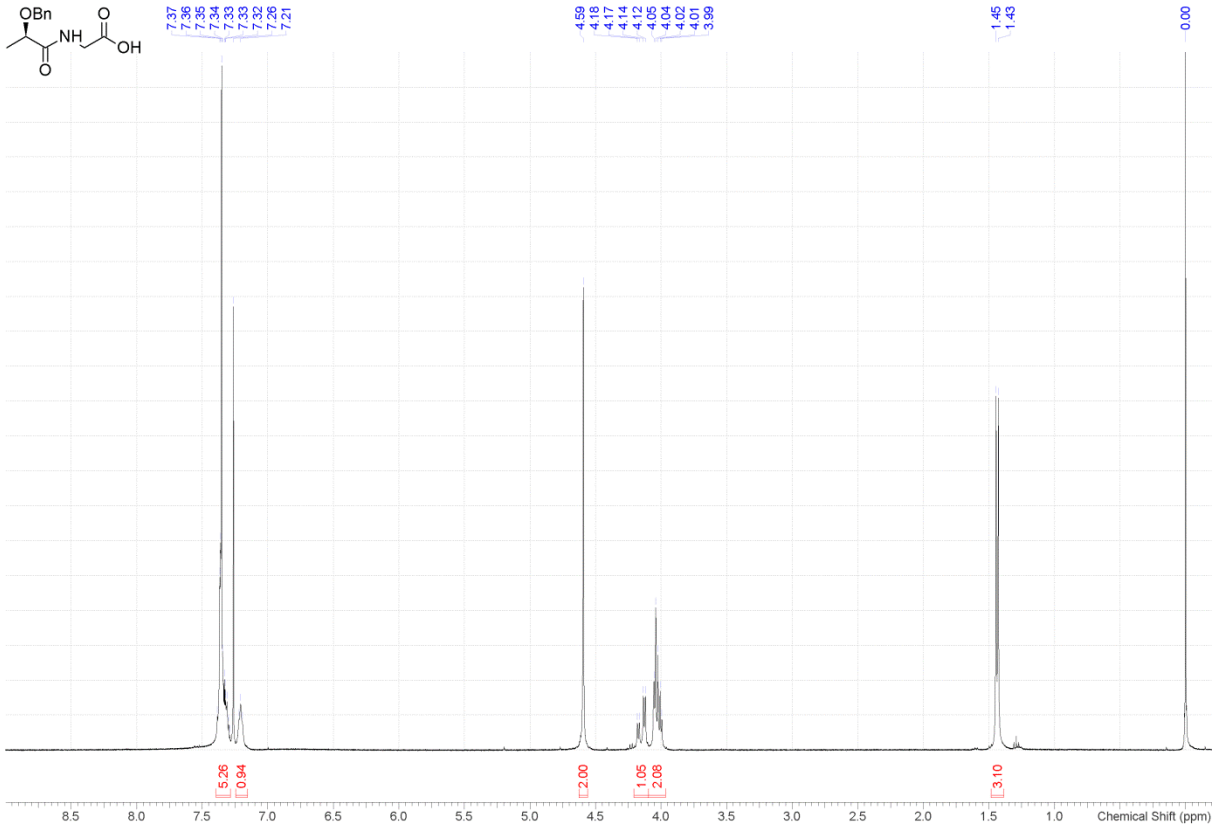


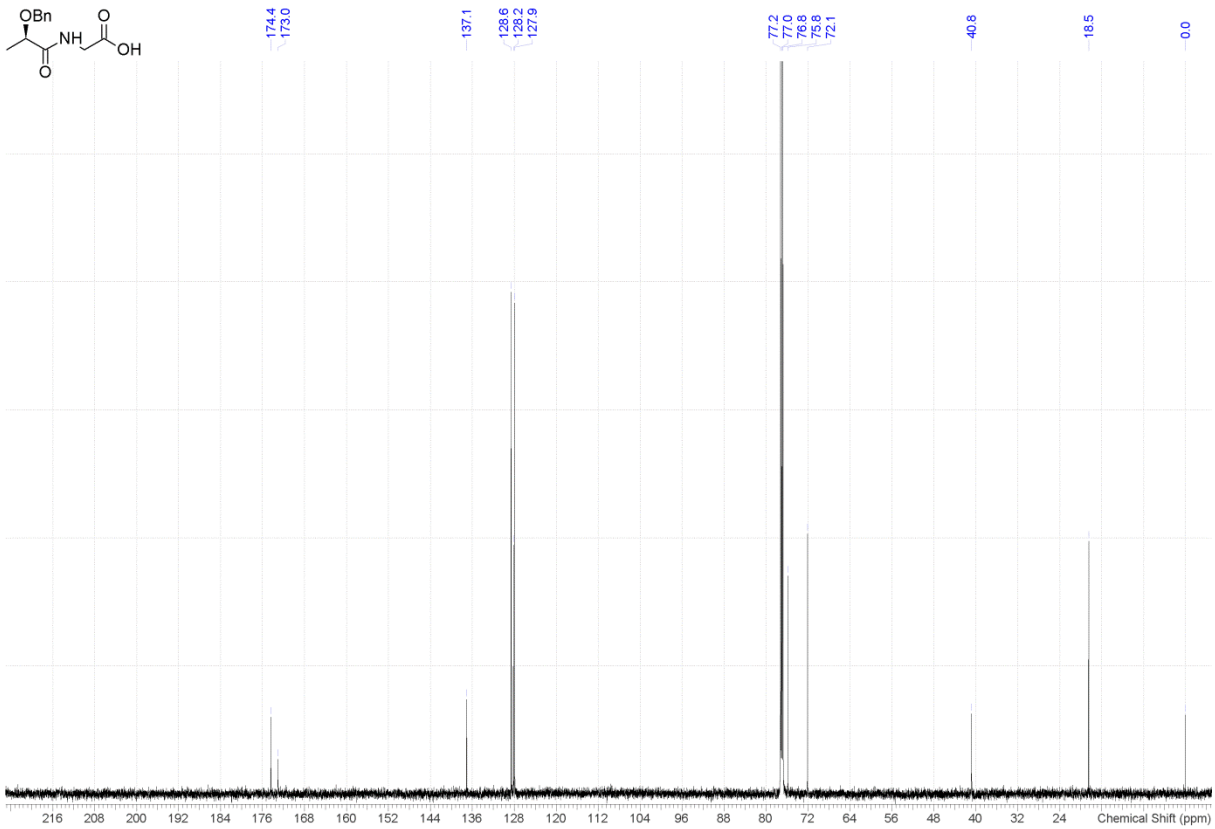
(*R*)-2-[2-(benzyloxy)propanamido]-2-methylpropanoic acid (**1f**)



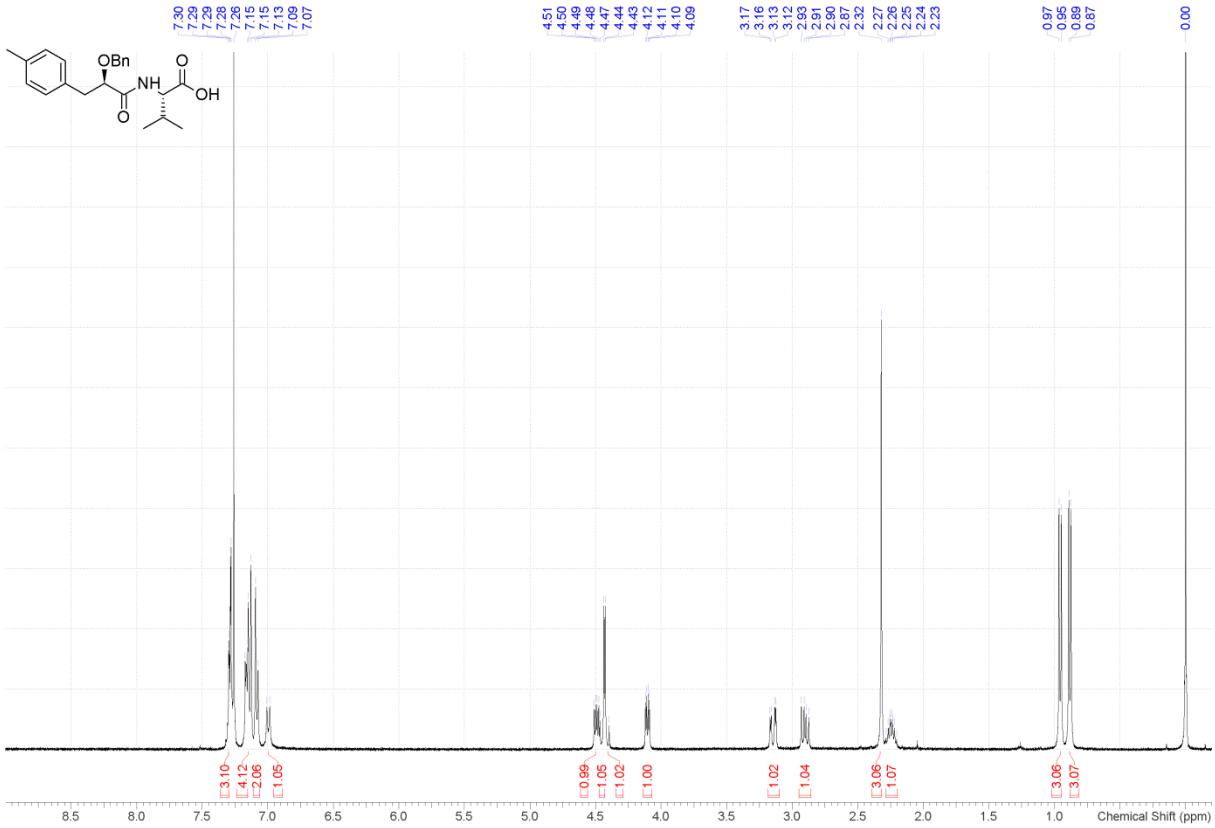


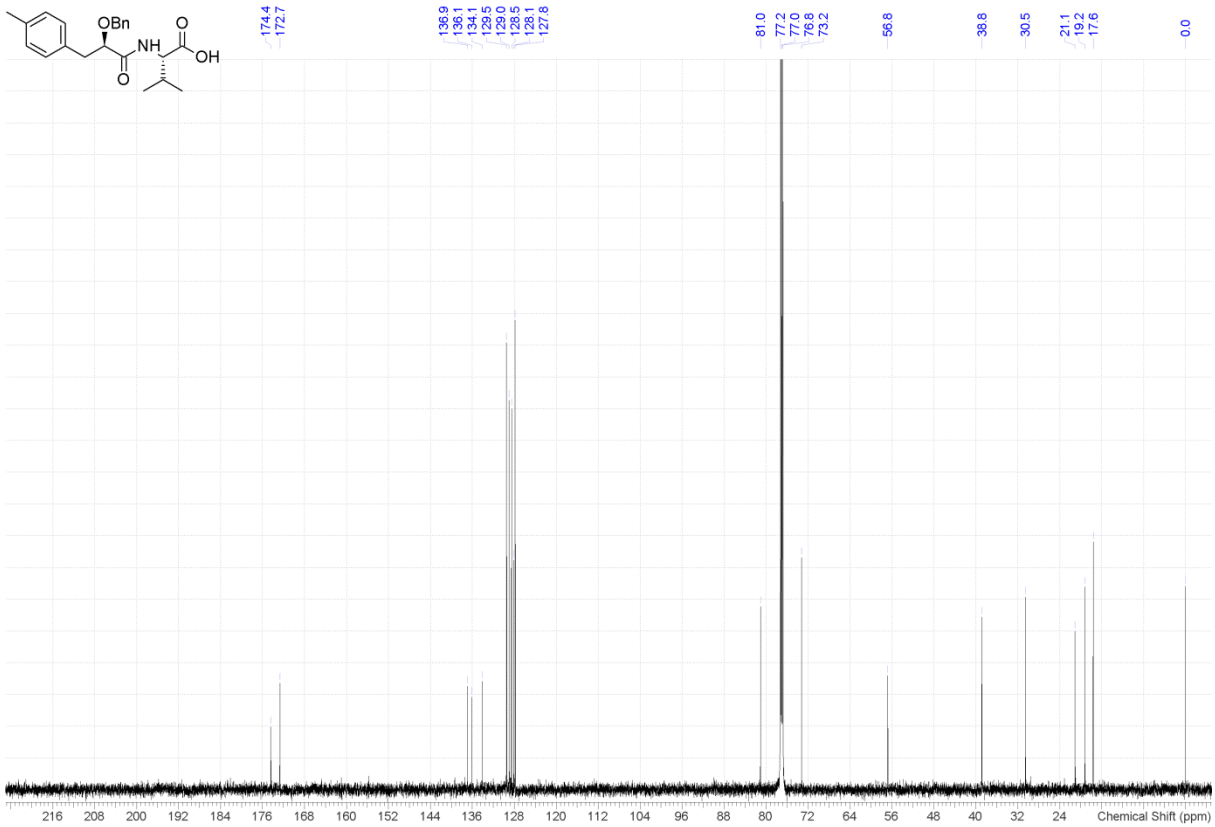
N-[(*R*)-2-(benzyloxy)propionyl]-glycine (**1g**)



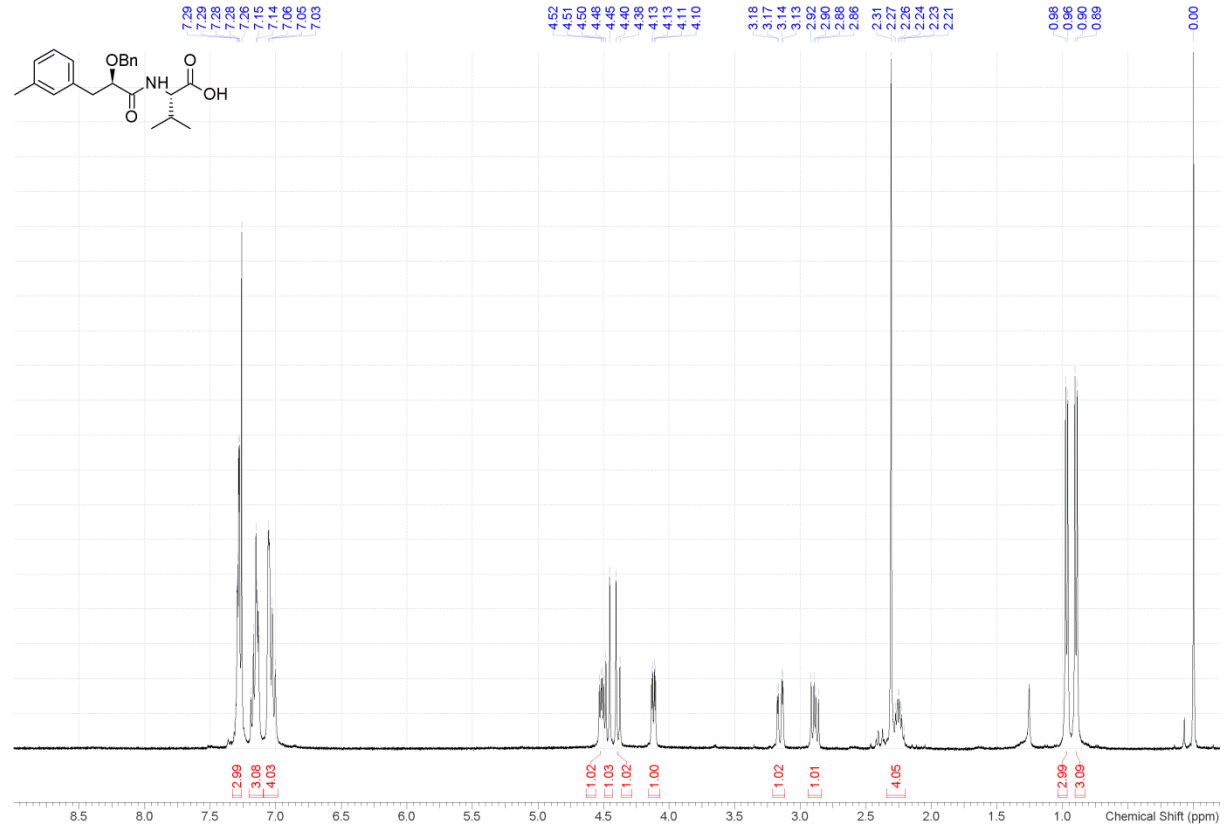


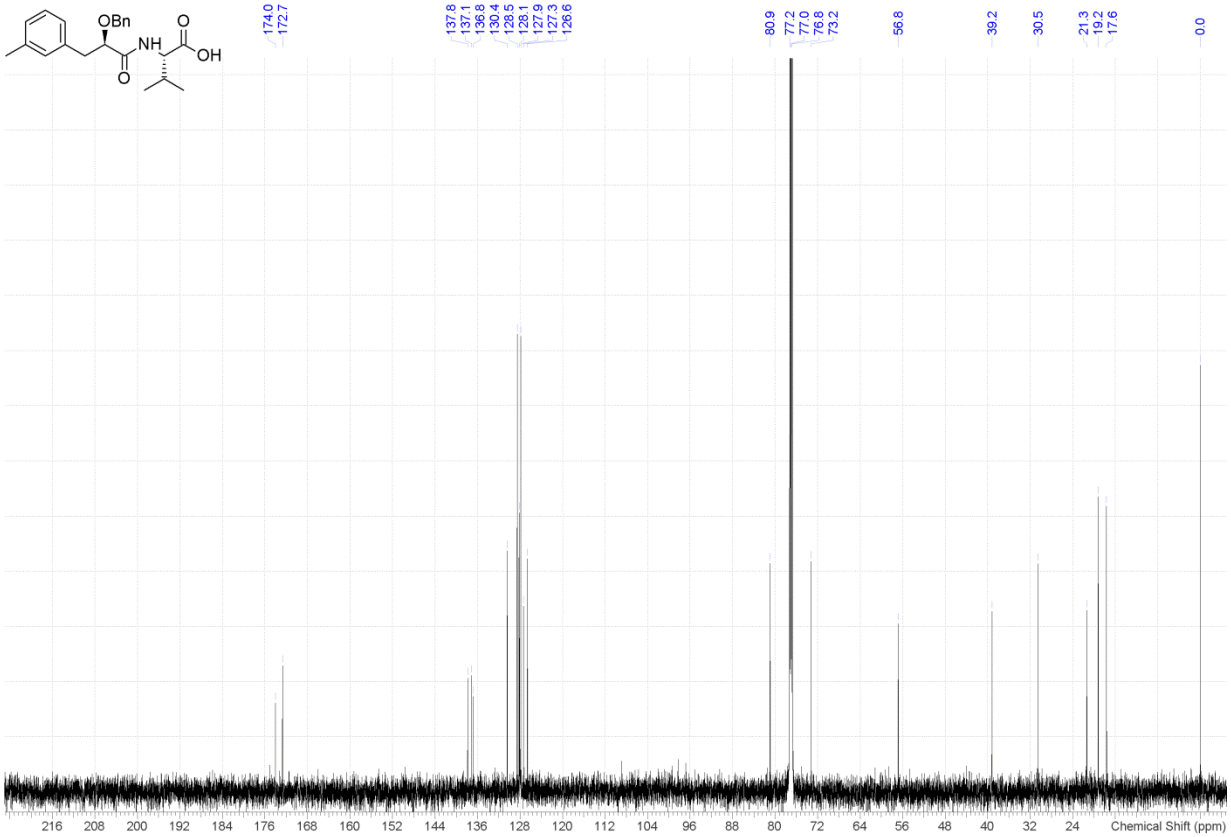
N-[(*R*)-2-(benzyloxy)-3-(*p*-tolyl)propionyl]-L-valine (**2a**)



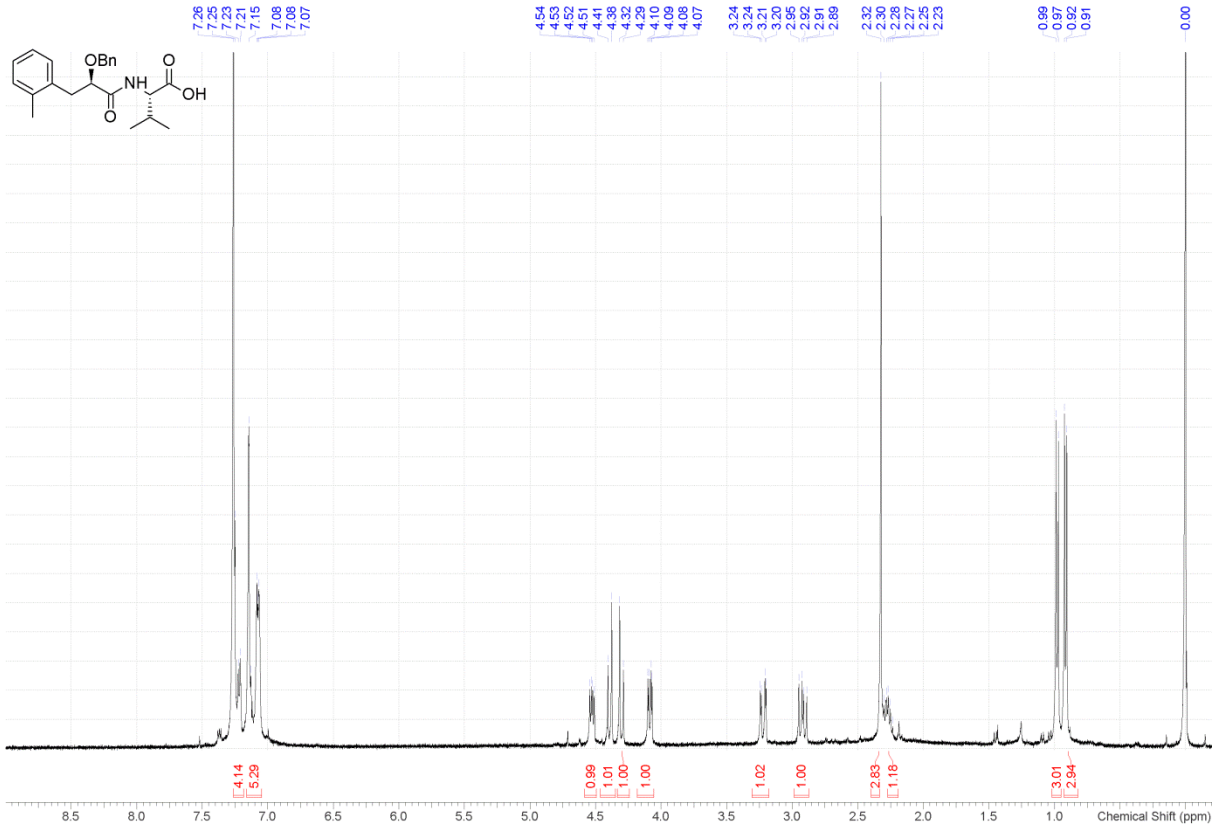


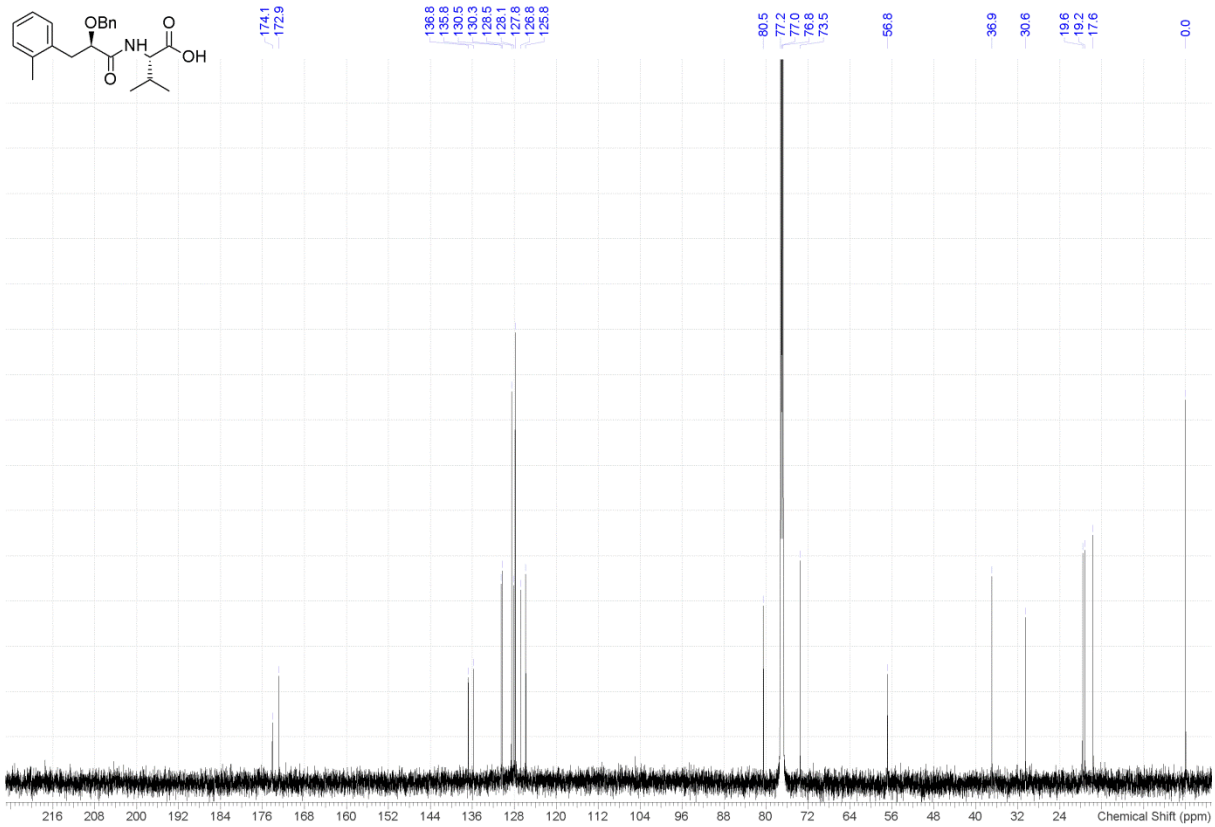
N-[(*R*)-2-(benzyloxy)-3-(*m*-tolyl)propionyl]-L-valine (**3**)



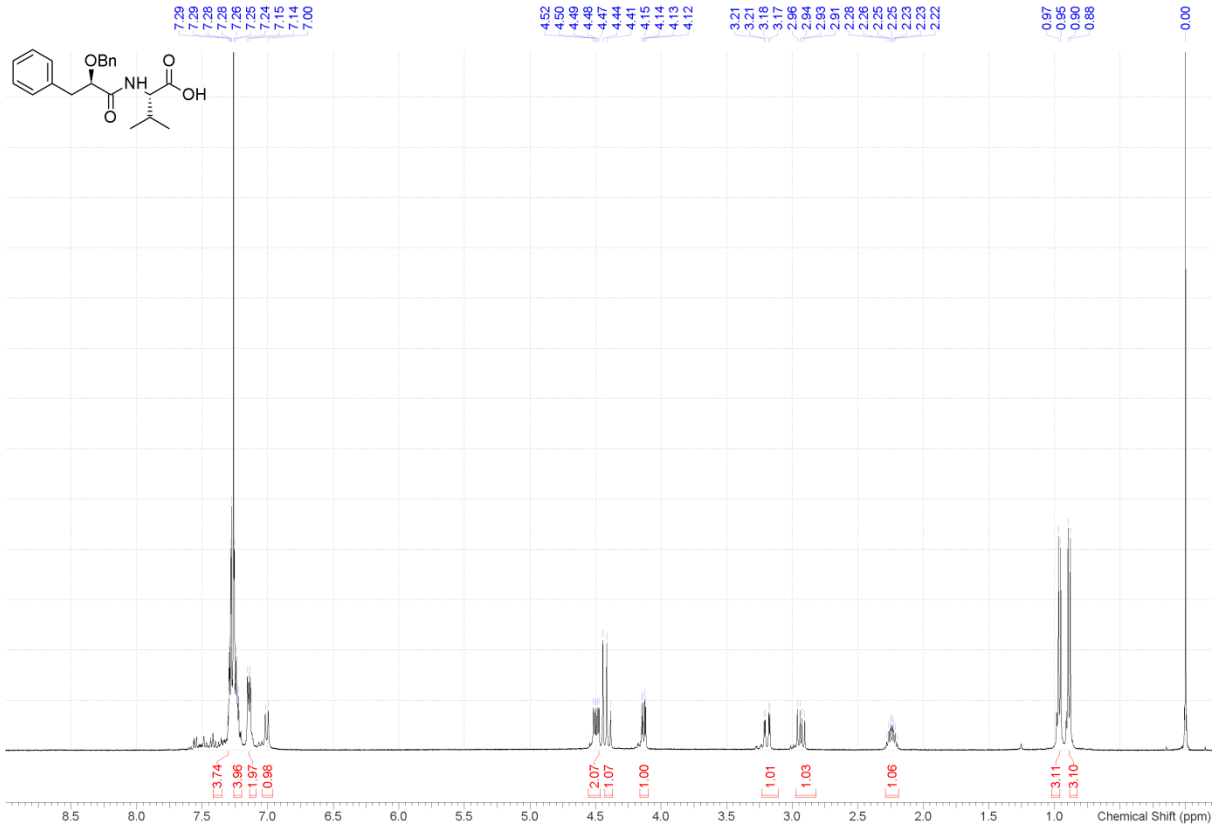


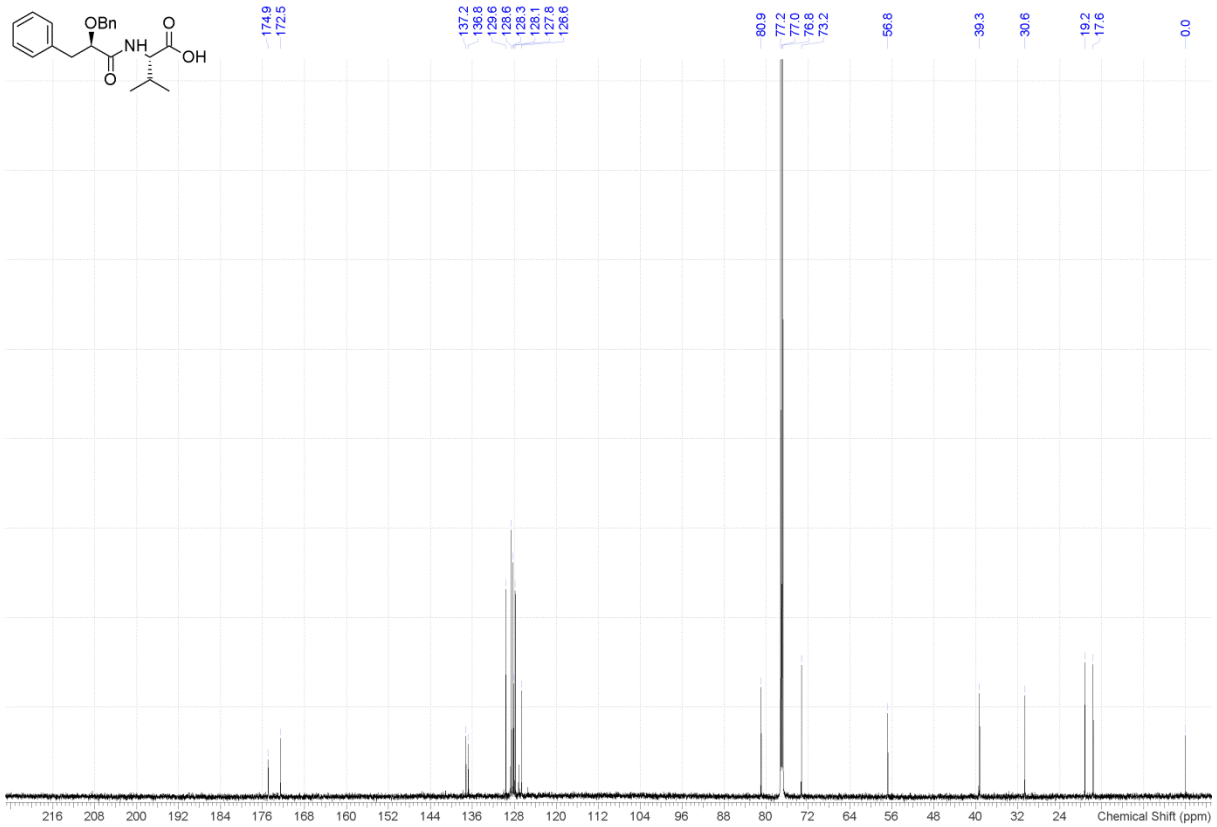
N-[(*R*)-2-(benzyloxy)-3-(*o*-tolyl)propionyl]-L-valine (**4**)



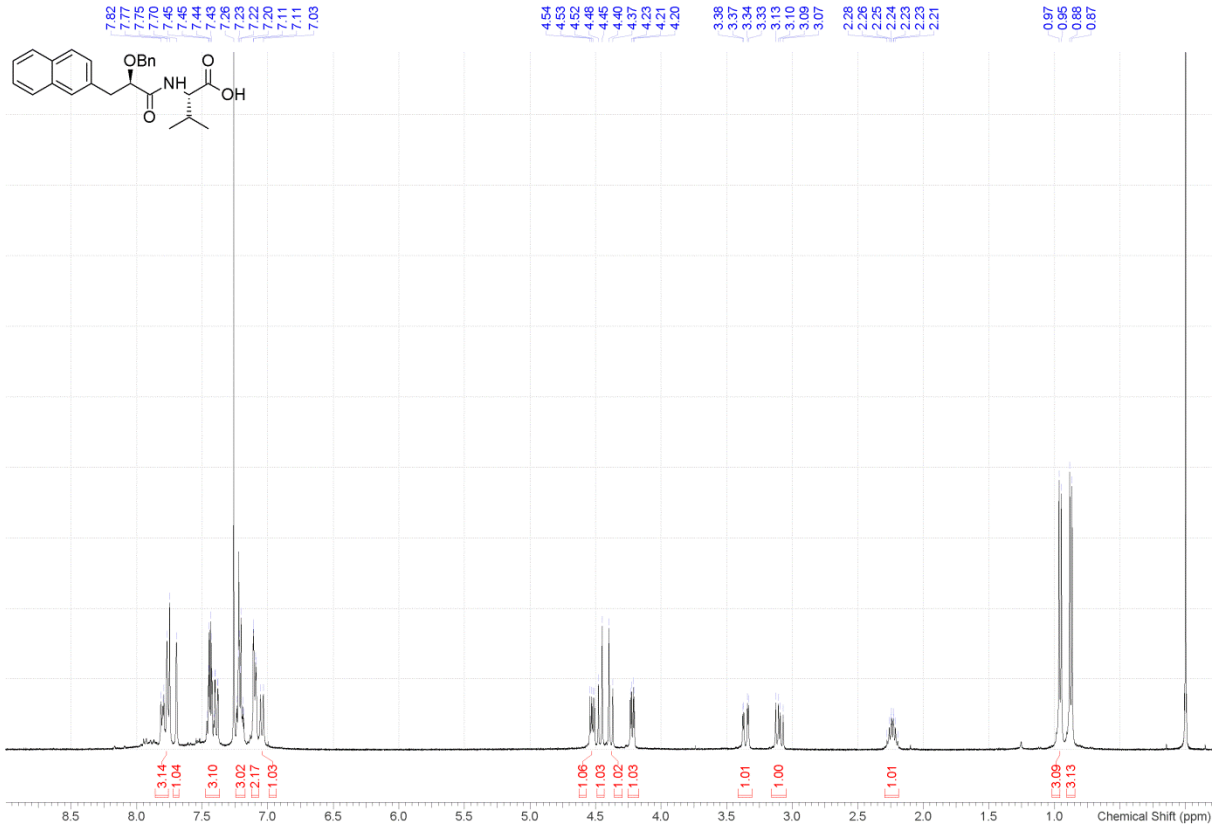


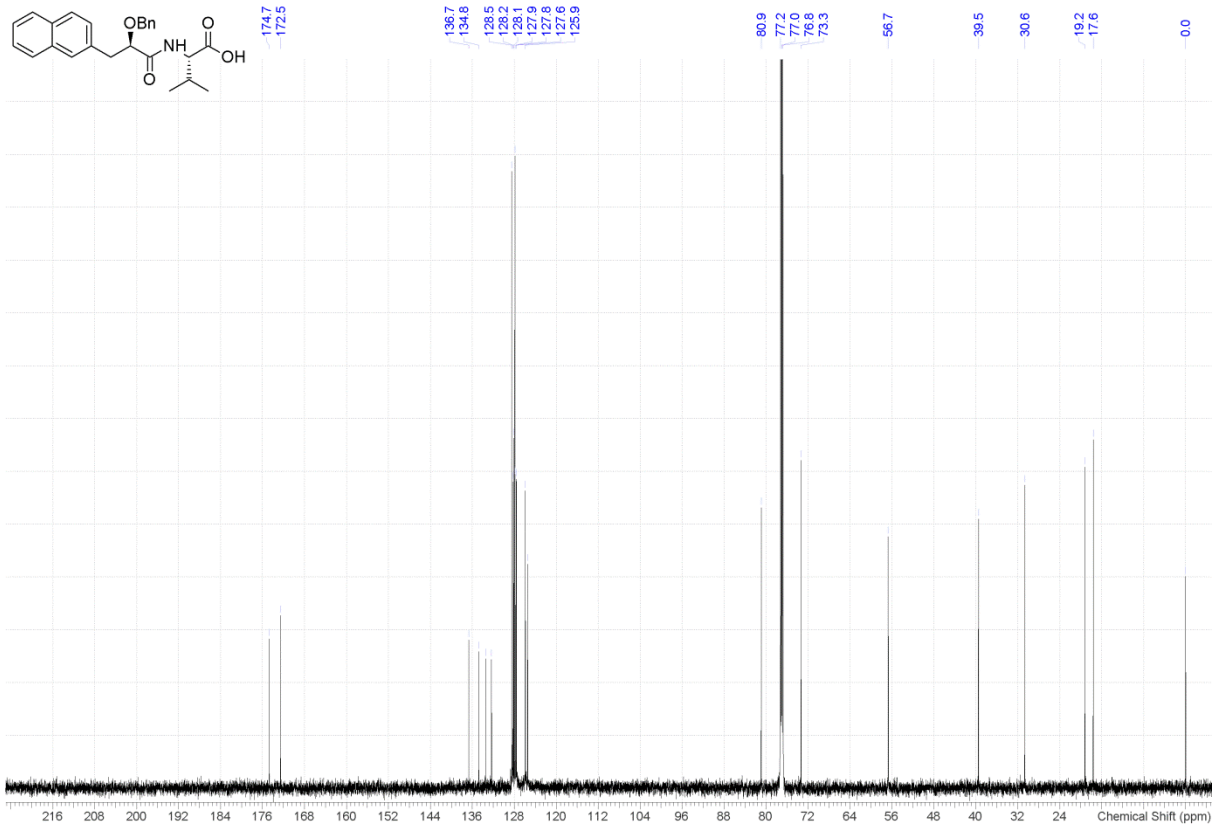
N-[(*R*)-2-(benzyloxy)-3-phenylpropionyl]-L-valine (**5**)



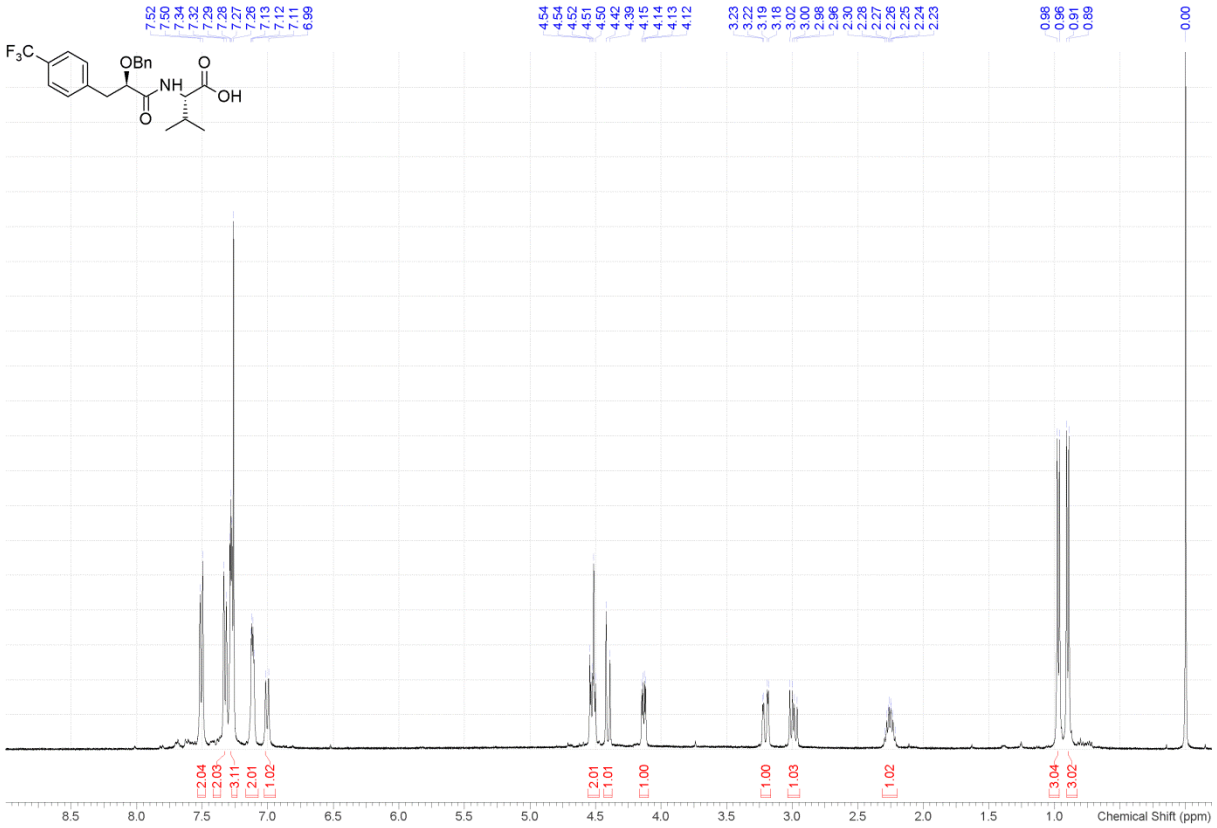


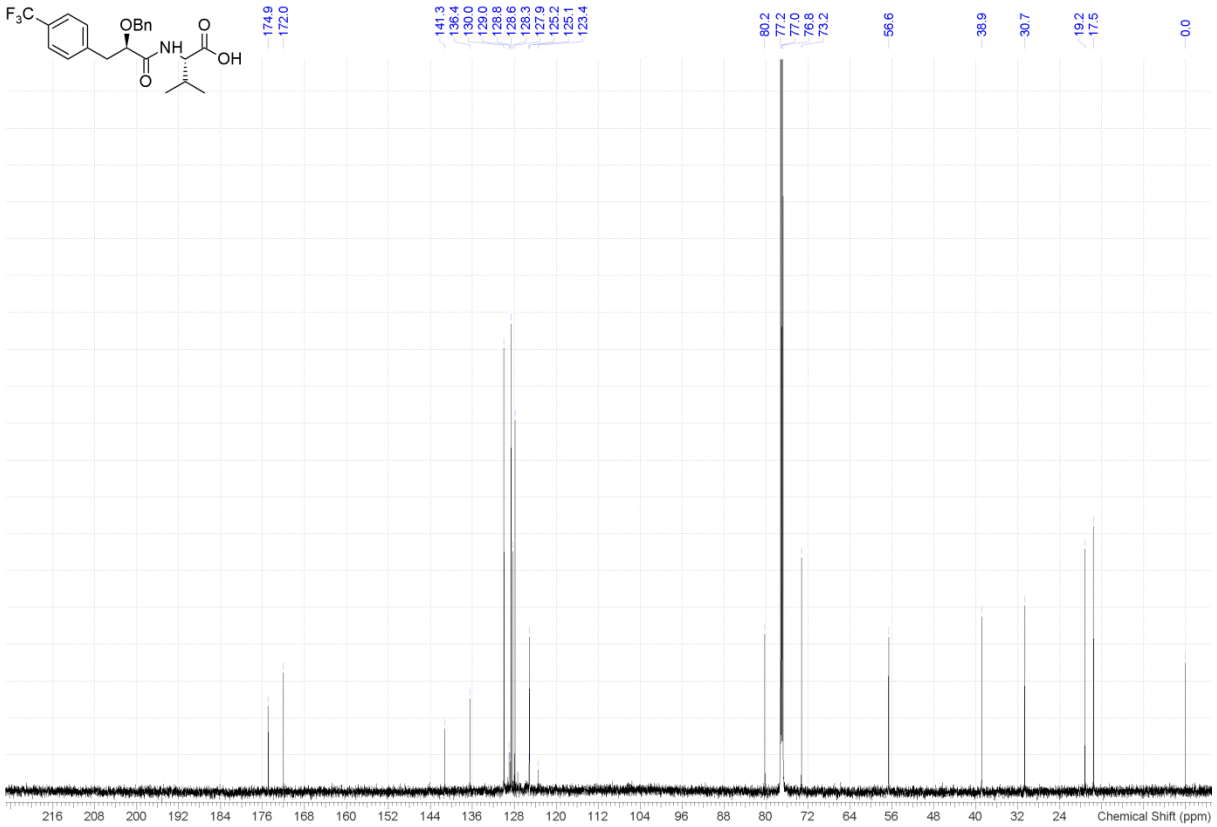
N-[(*R*)-2-(benzyloxy)-3-(naphthalen-2-yl)propionyl]-L-valine (**6**)



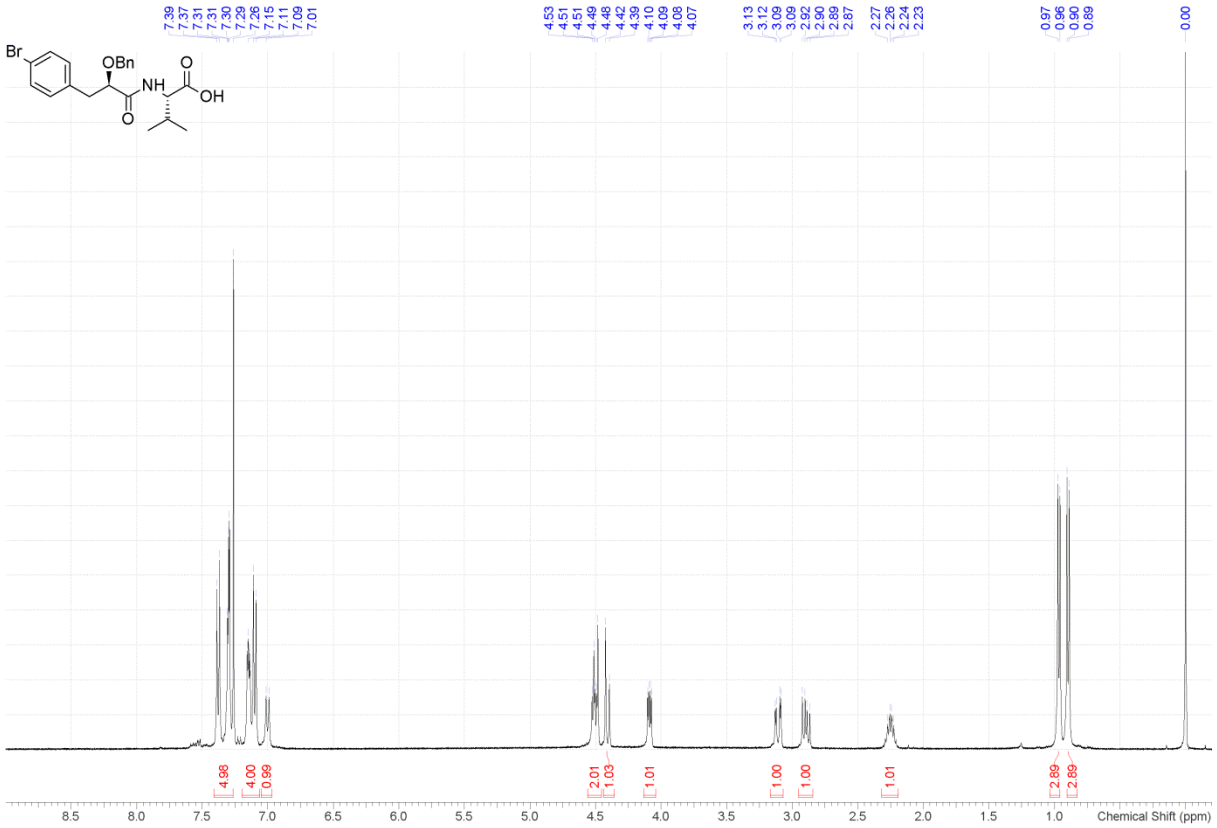


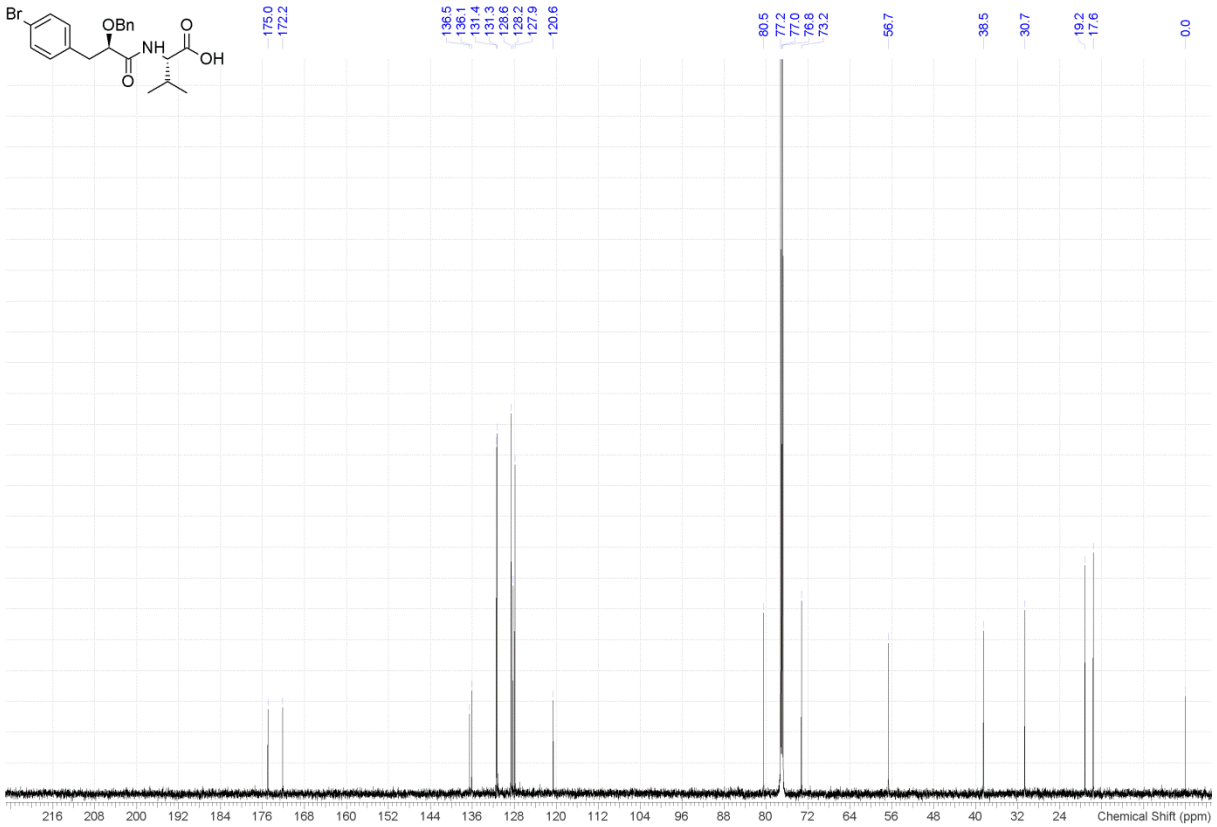
N-{(*R*)-2-(benzyloxy)-3-[4-(trifluoromethyl)phenyl]propionyl}-L-valine (**7**)



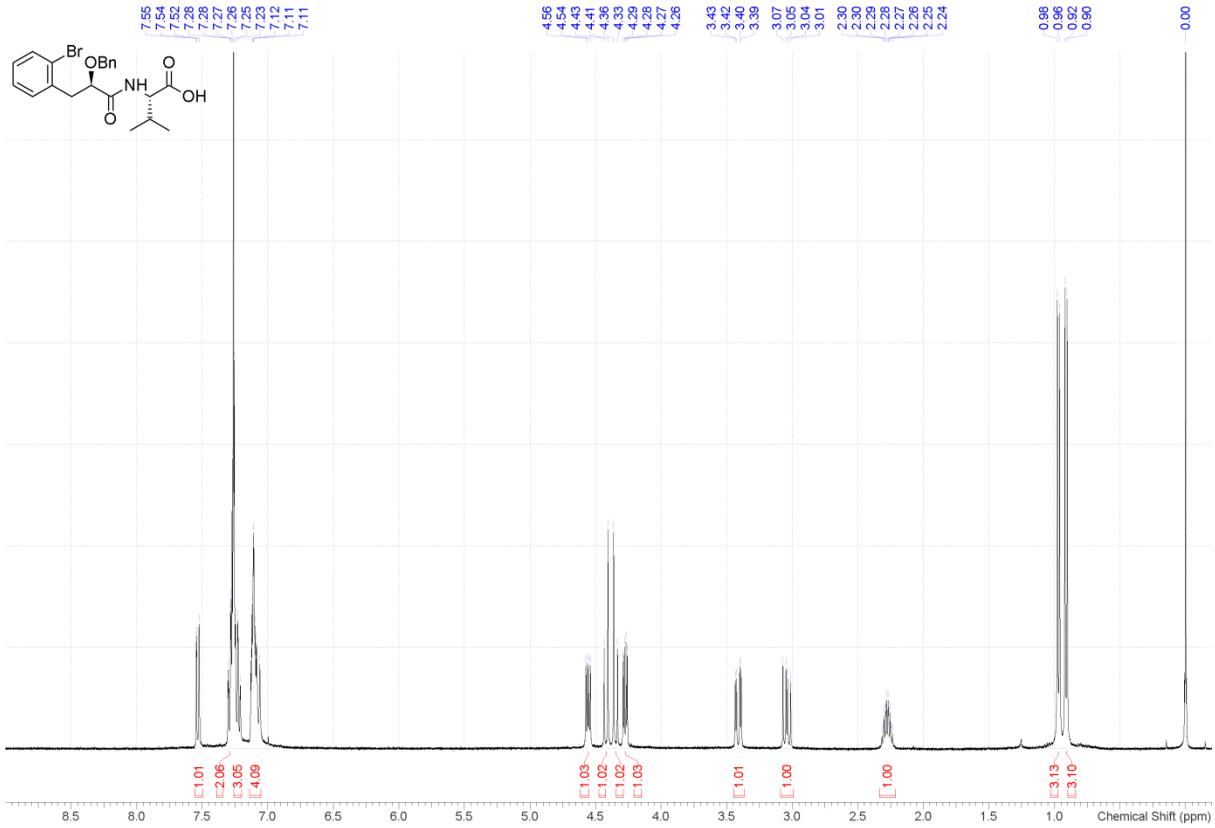


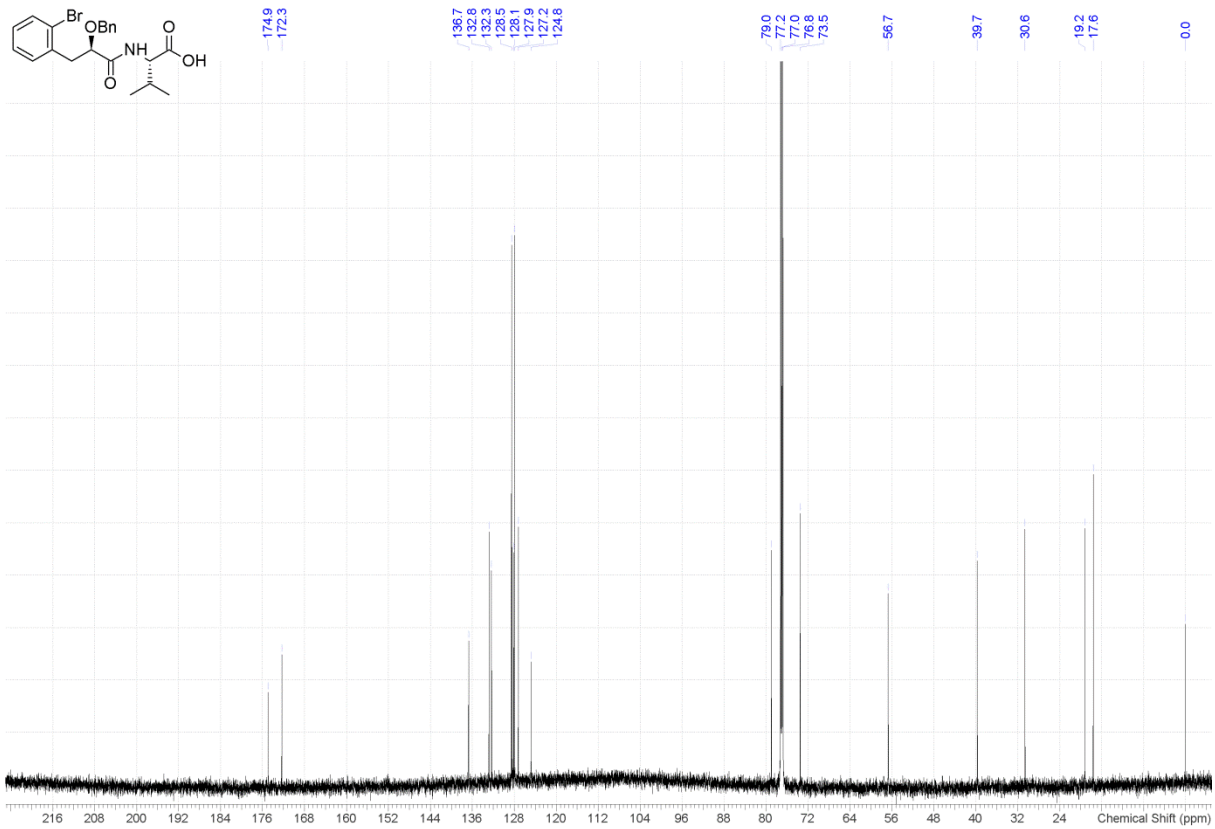
N-[(*R*)-2-(benzyloxy)-3-(4-bromophenyl)propionyl]-L-valine (**8**)



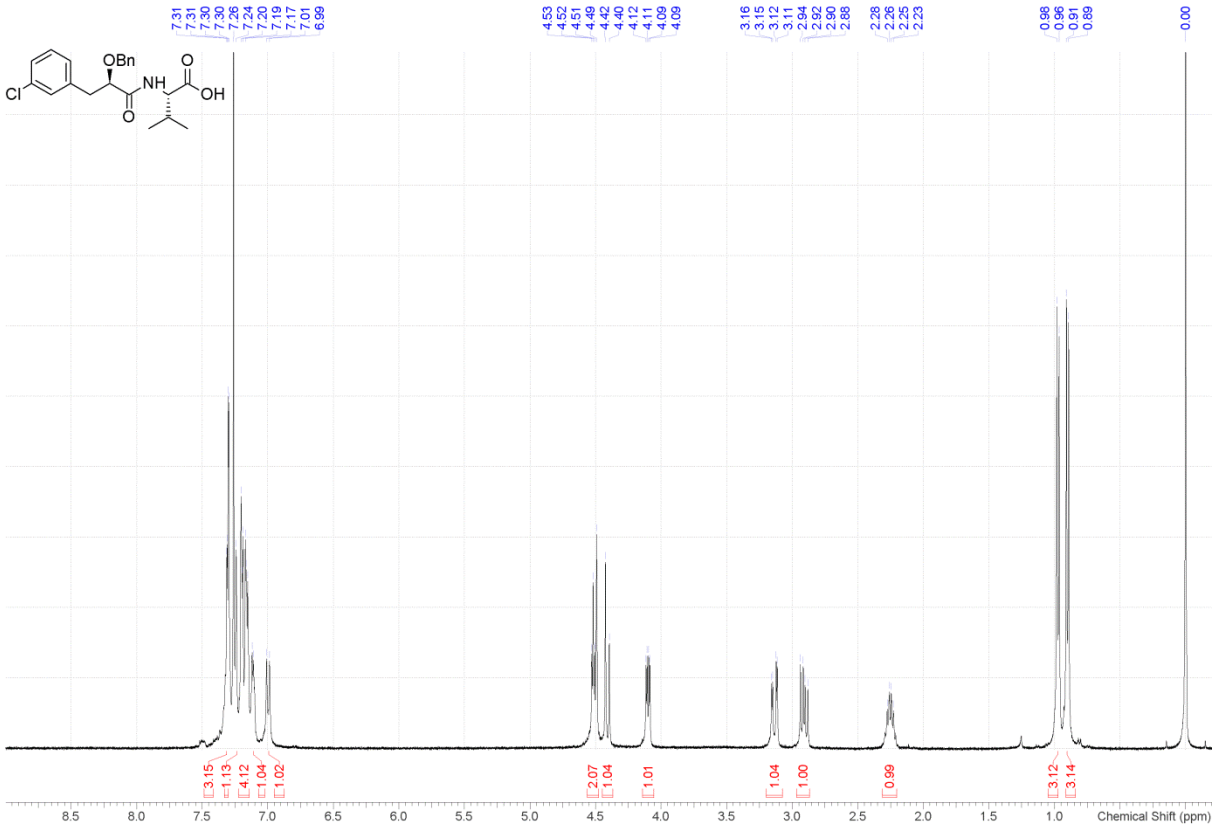


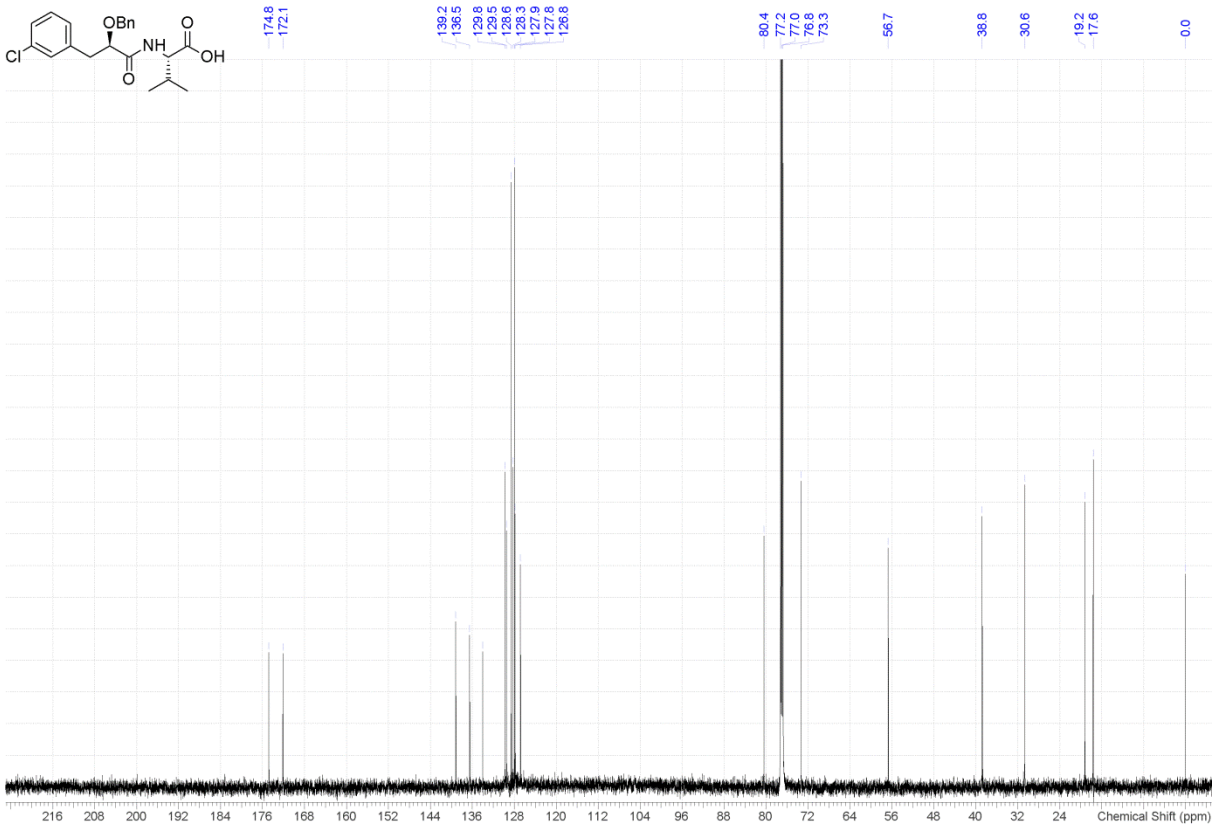
N-[(*R*)-2-(benzyloxy)-3-(2-bromophenyl)propionyl]-L-valine (**9**)



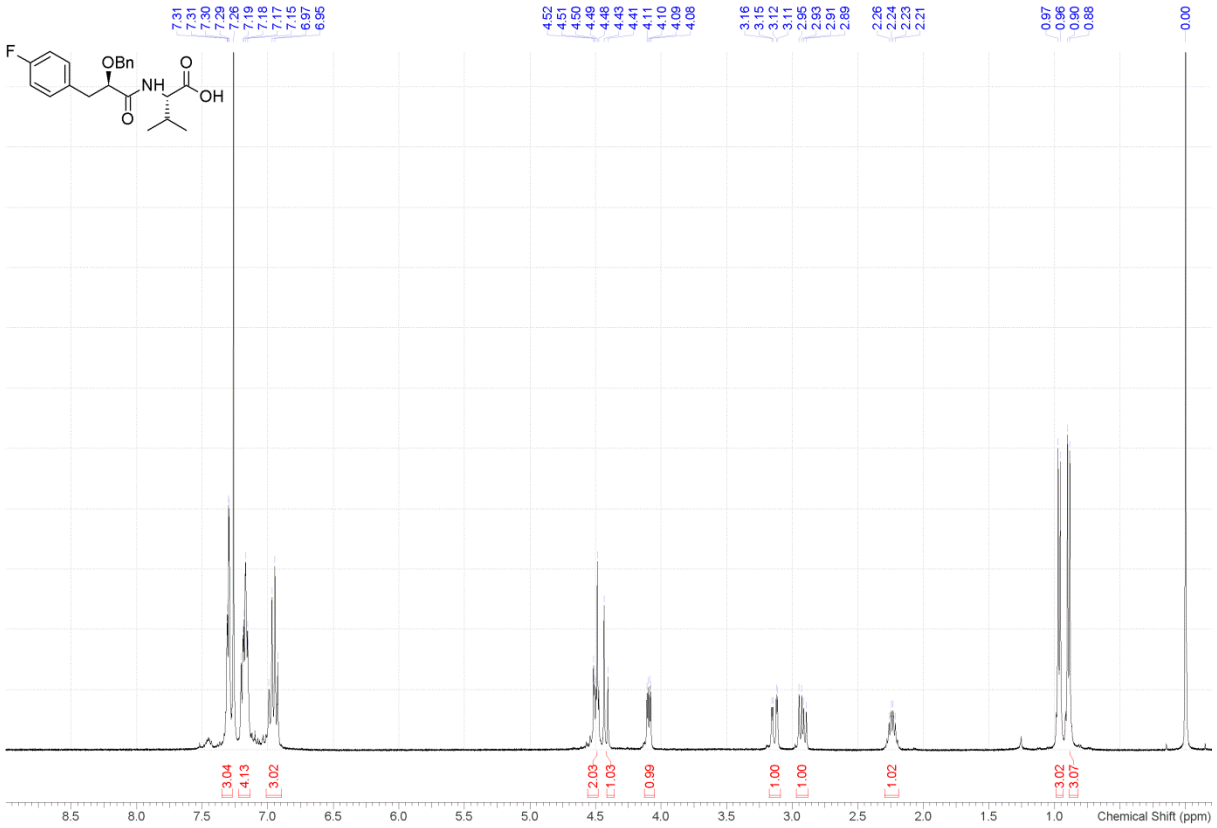


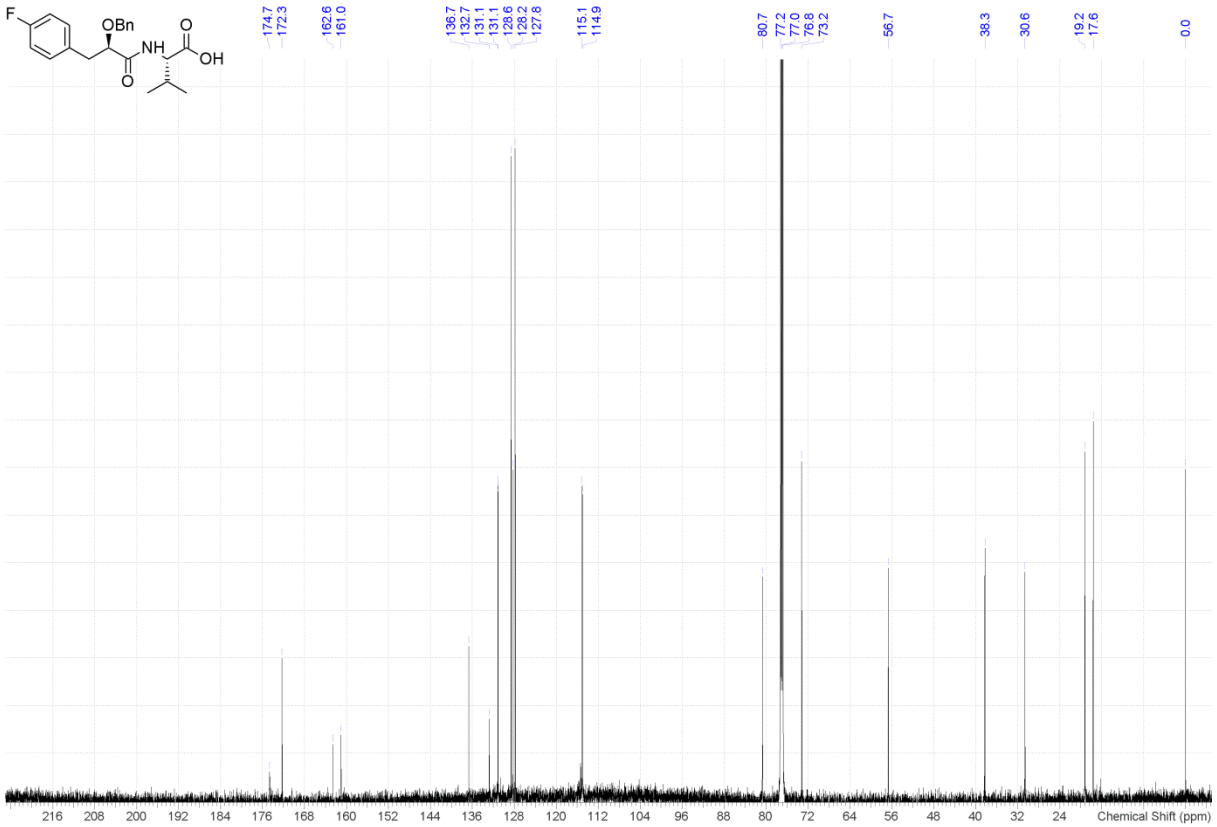
N-[(*R*)-2-(benzyloxy)-3-(3-chlorophenyl)propionyl]-L-valine (**10**)



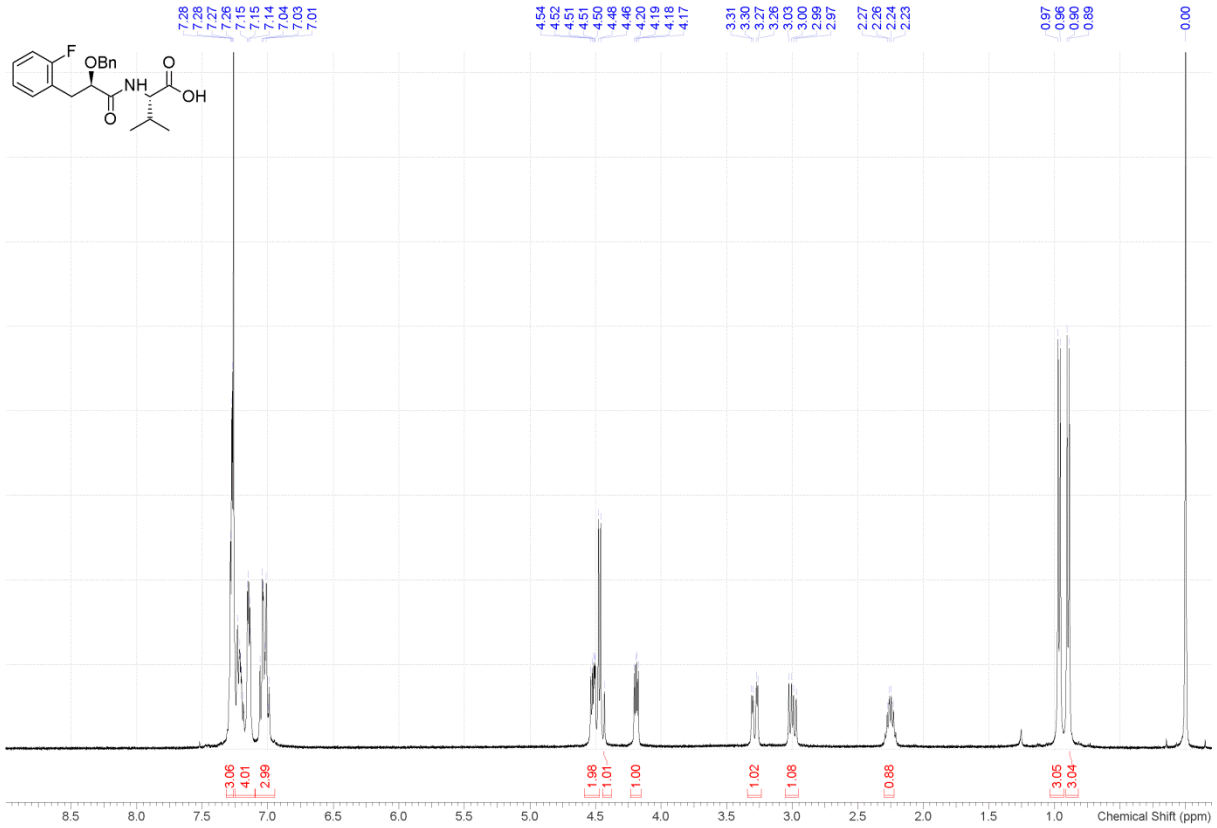


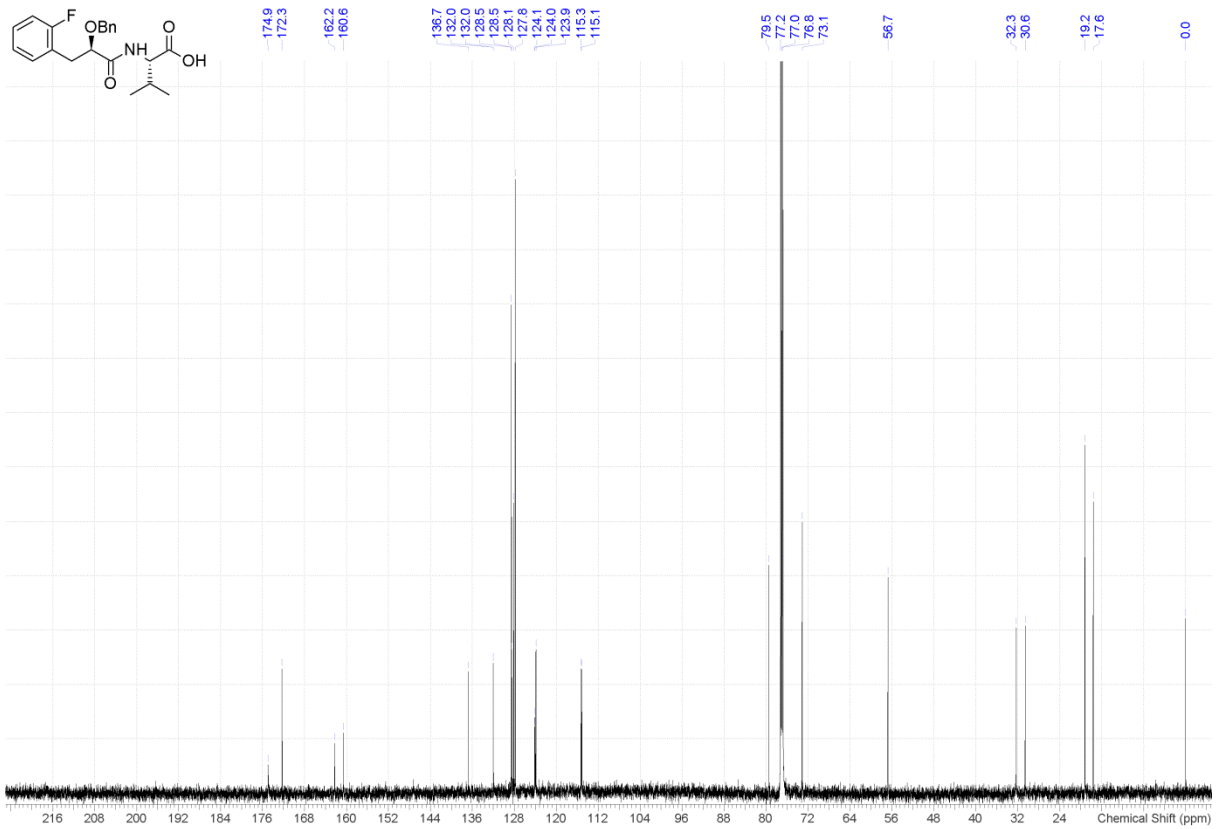
N-[(*R*)-2-(benzyloxy)-3-(4-fluorophenyl)propionyl]-L-valine (**11**)



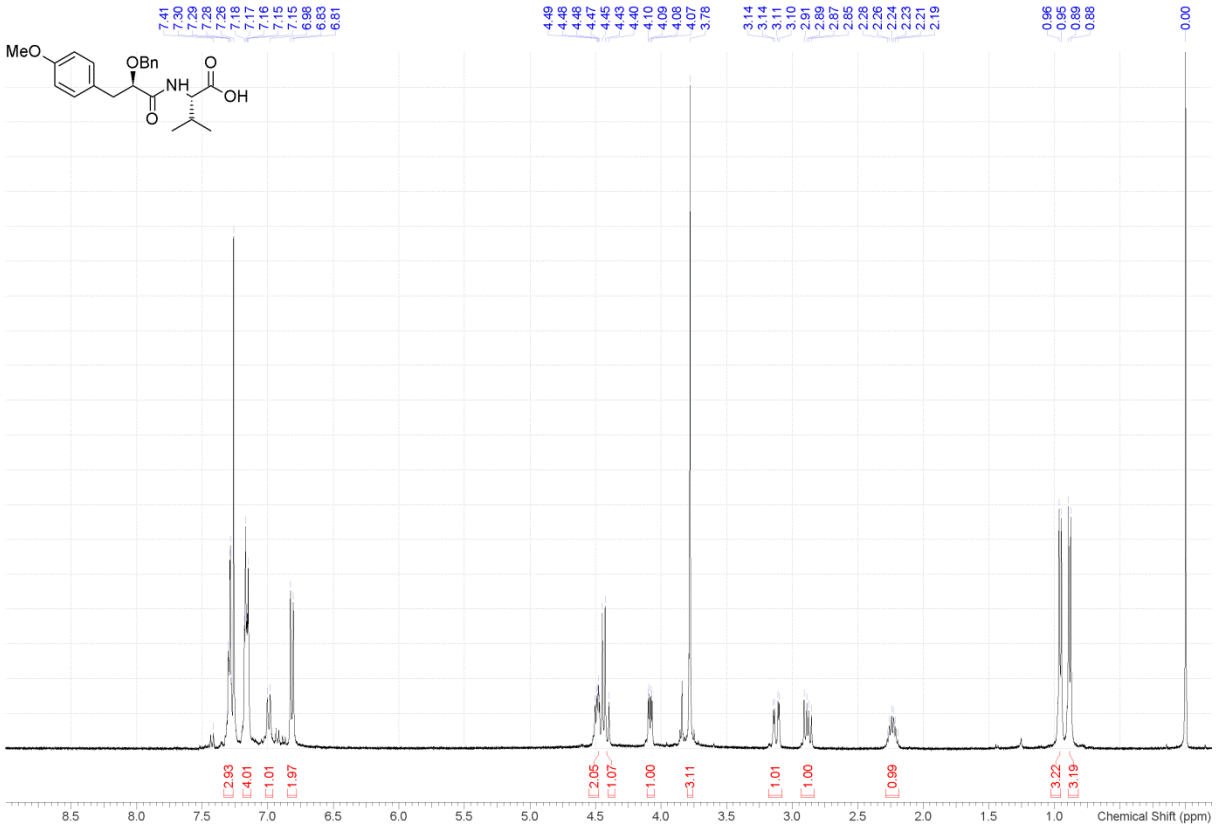


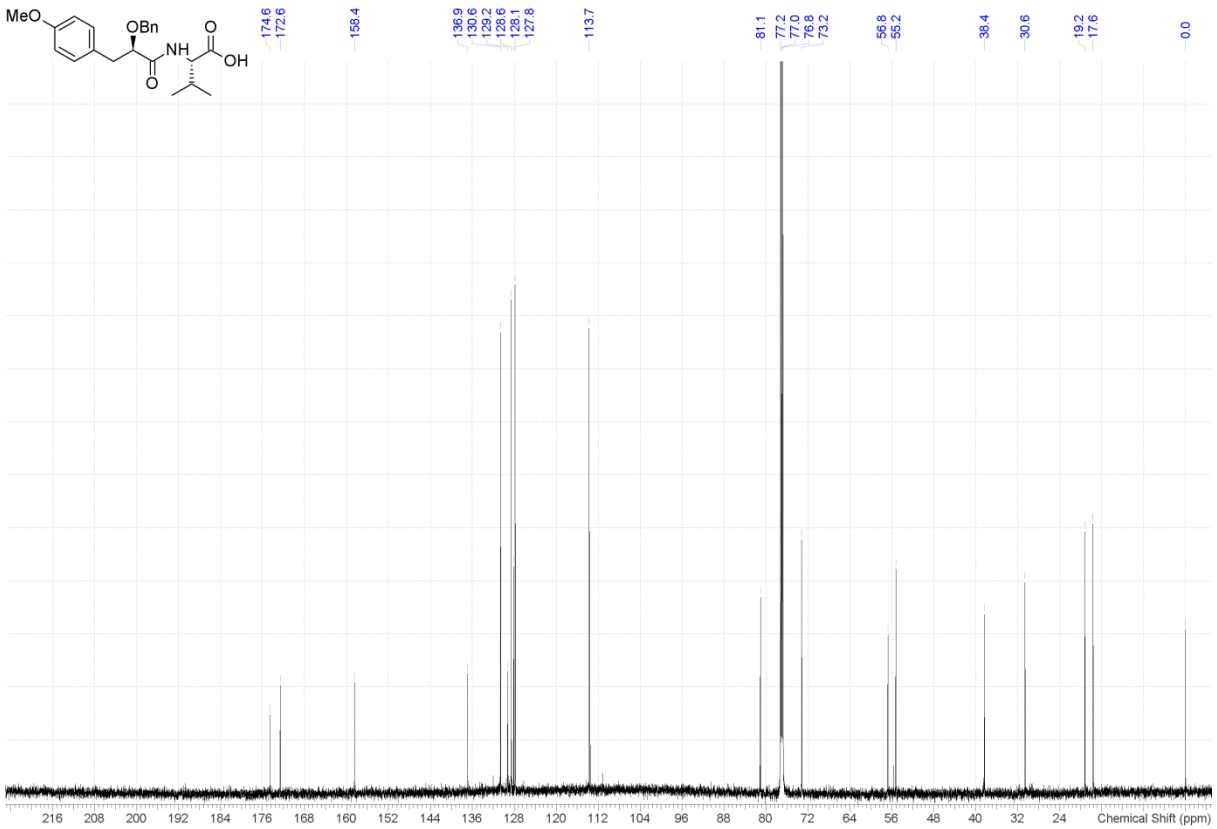
N-[(*R*)-2-(benzyloxy)-3-(2-fluorophenyl)propionyl]-L-valine (**12**)



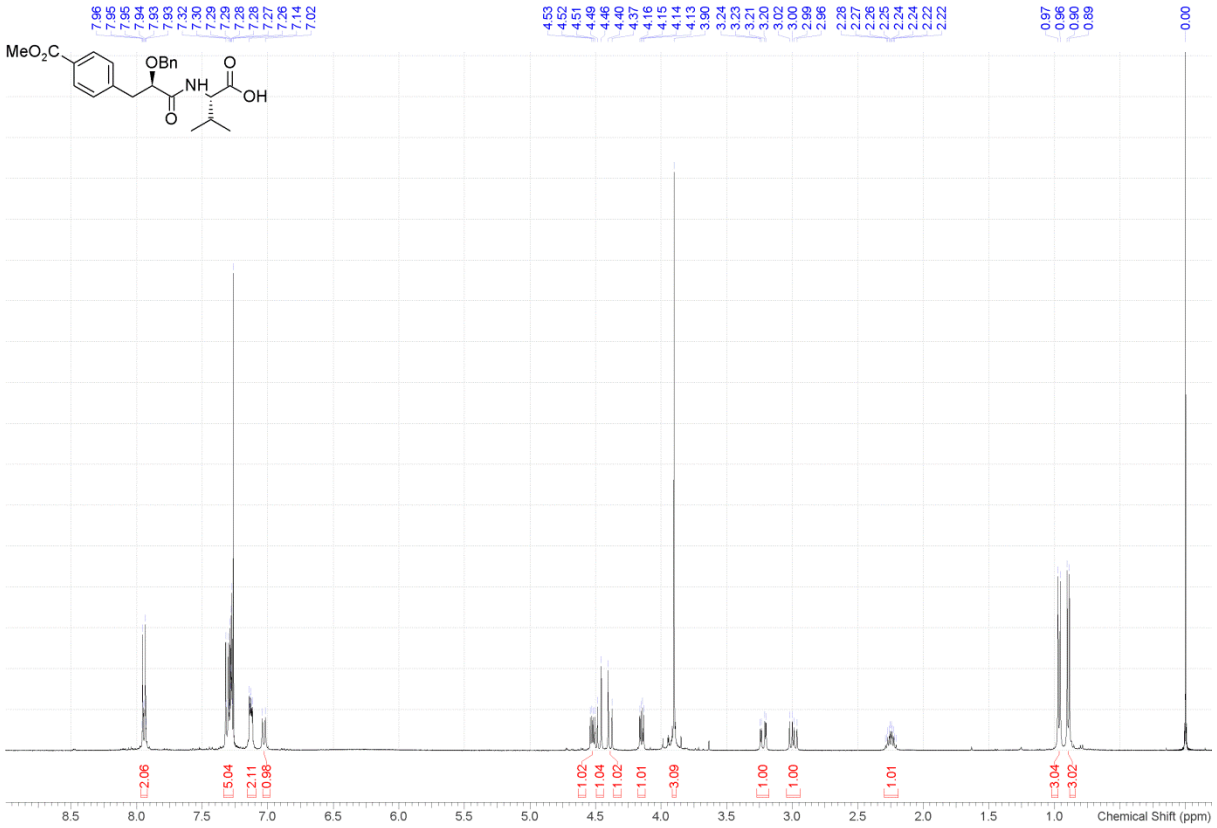


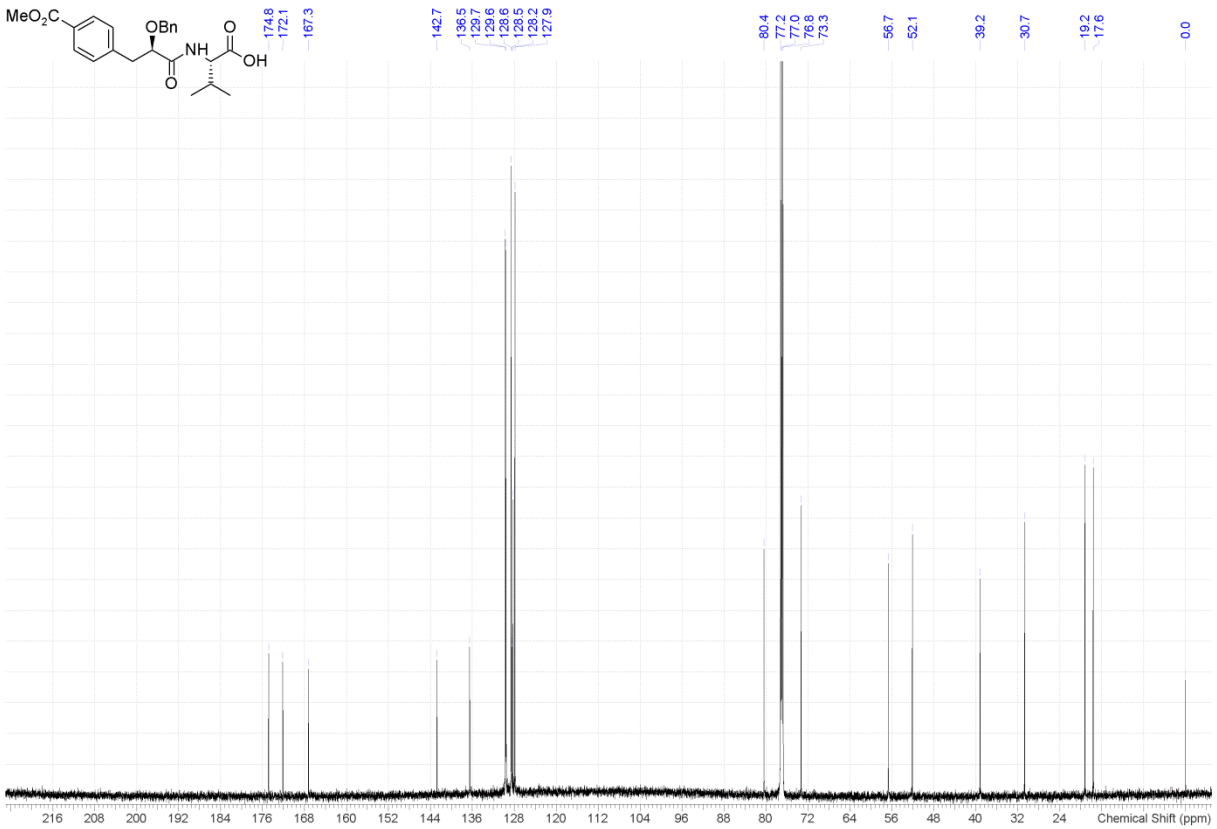
N-[(*R*)-2-(benzyloxy)-3-(4-methoxyphenyl)propionyl]-L-valine (**13**)



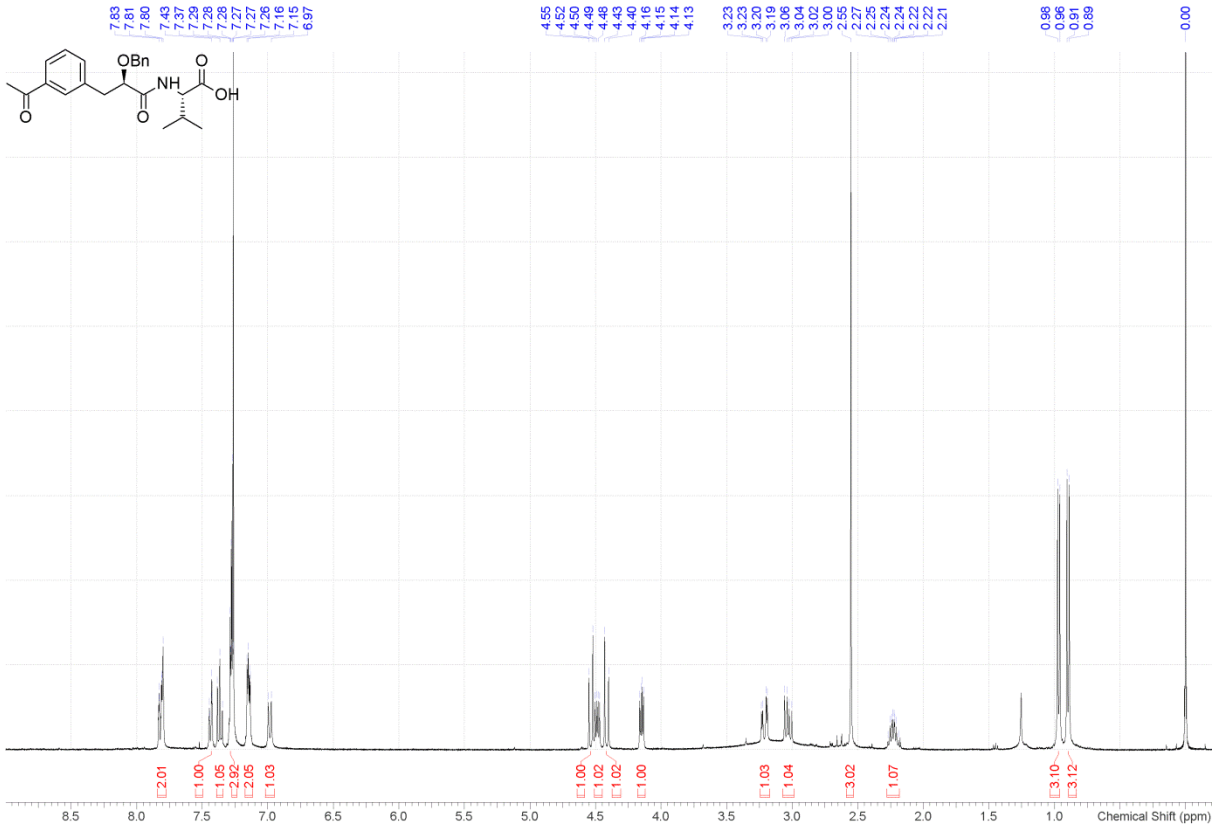


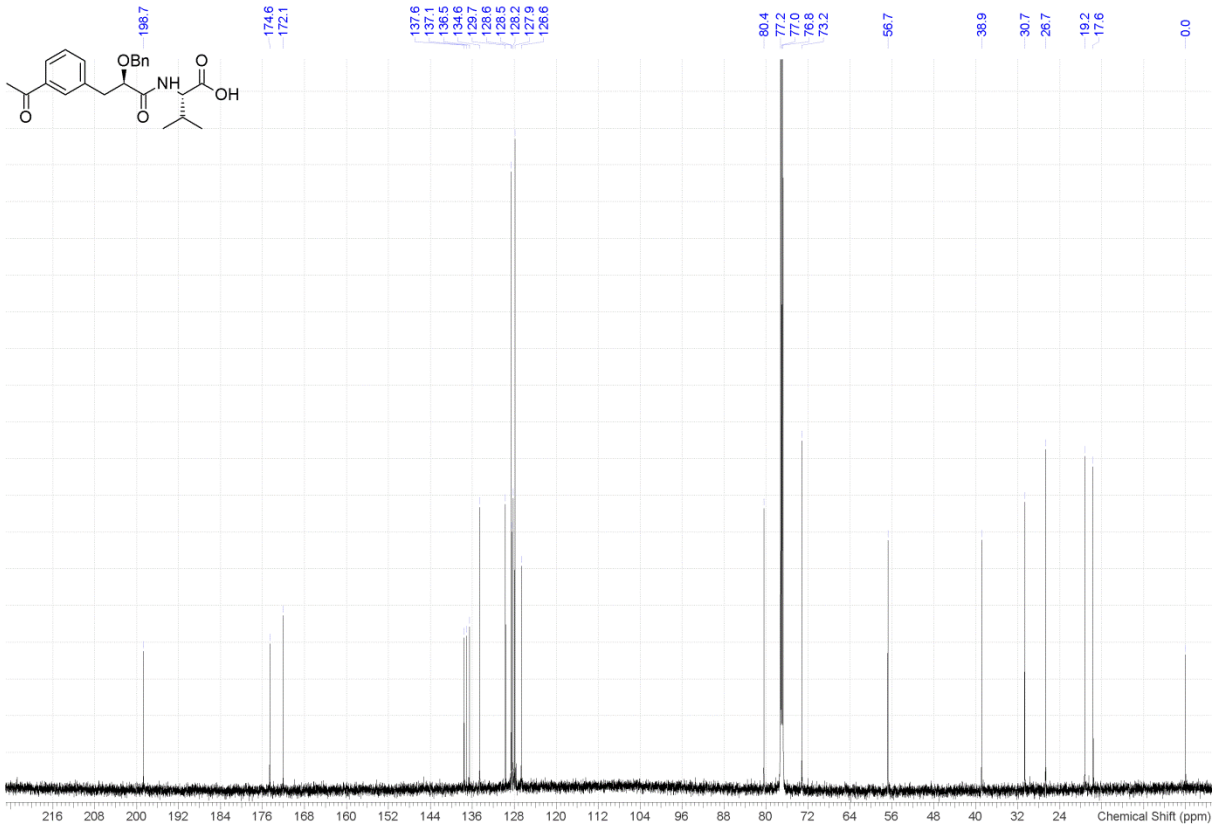
N-{(*R*)-2-(benzyloxy)-3-[4-(methoxycarbonyl)phenyl]propionyl}-L-valine (**14**)



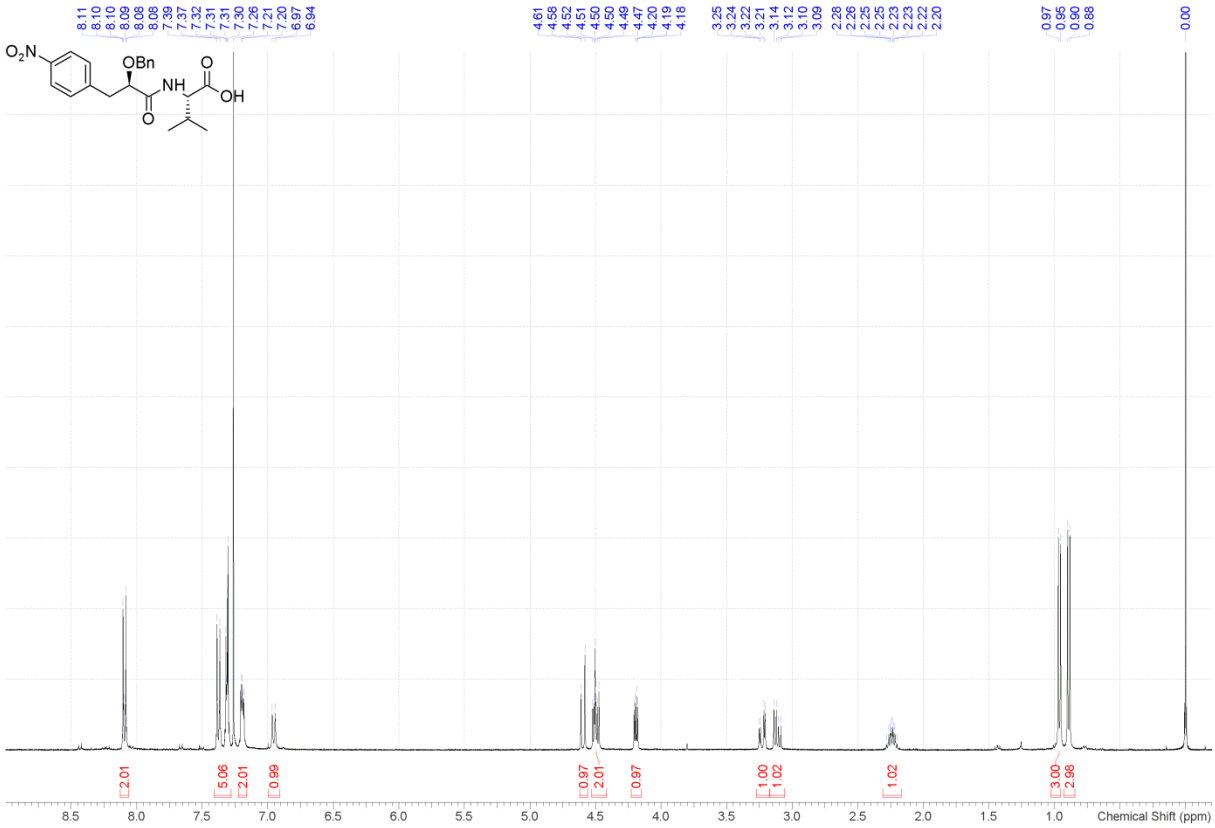


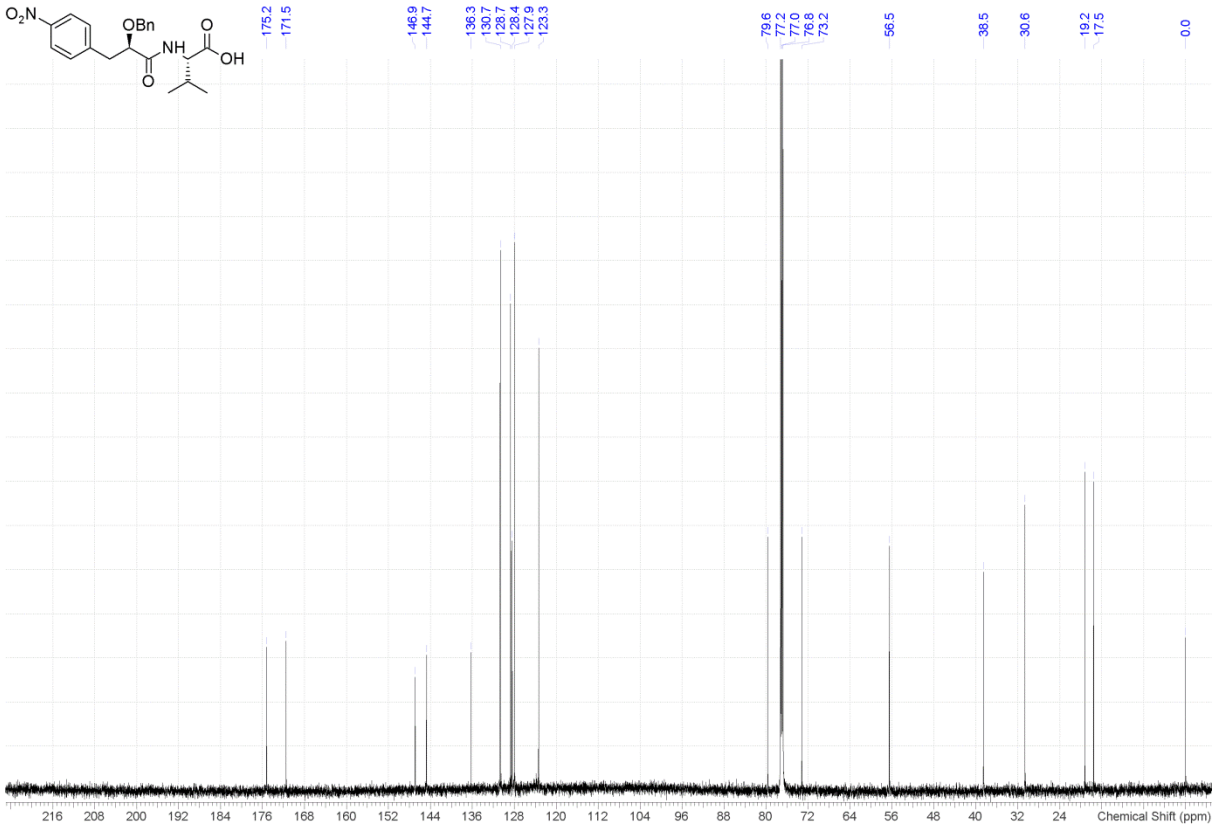
N-[(*R*)-2-(benzyloxy)-3-(3-acetylphenyl)propionyl]-L-valine (**15**)



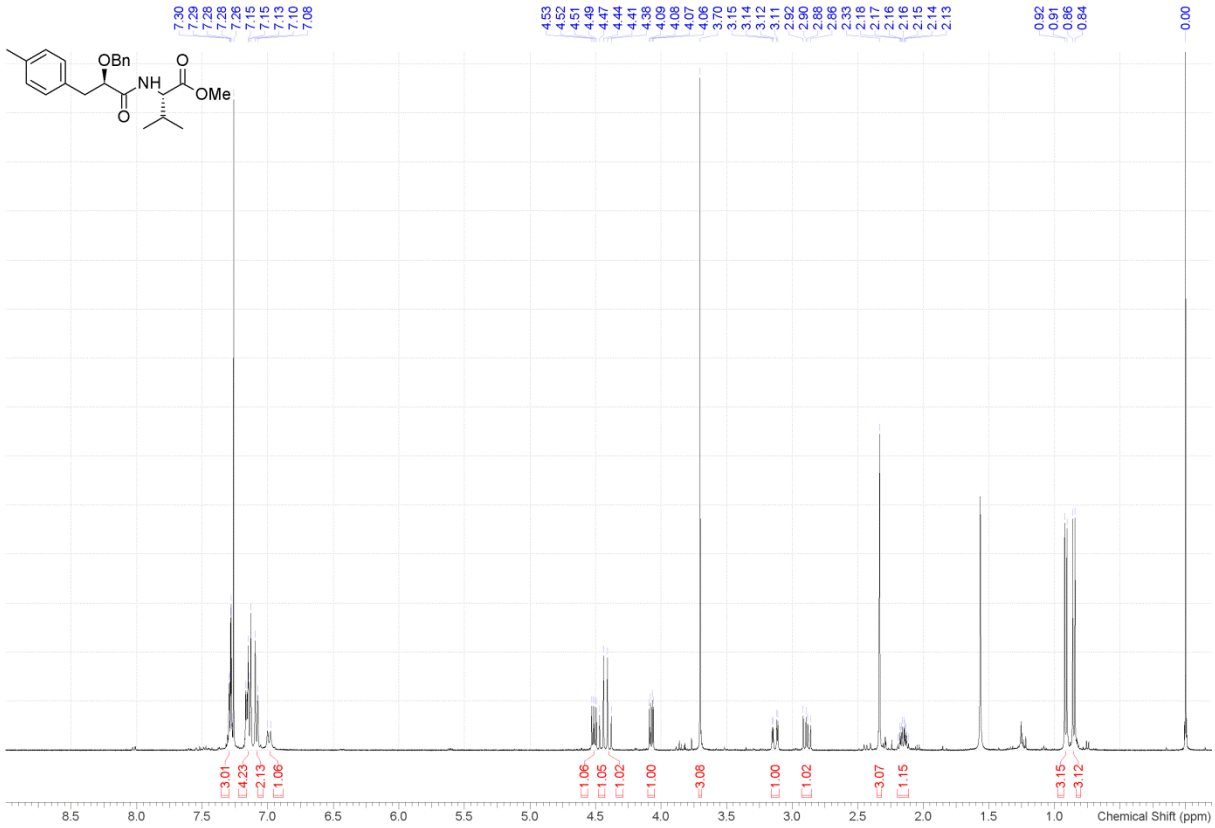


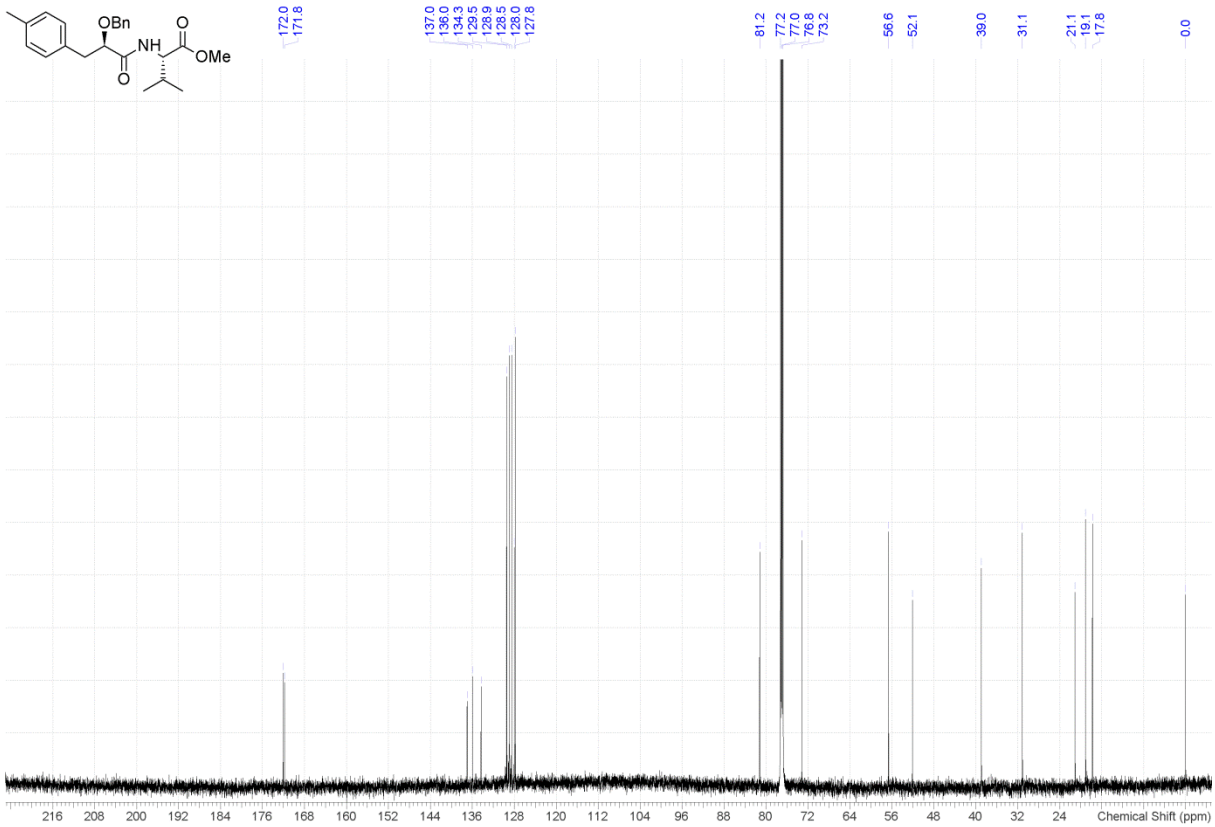
N-[(*R*)-2-(benzyloxy)-3-(4-nitrophenyl)propionyl]-L-valine (**16**)



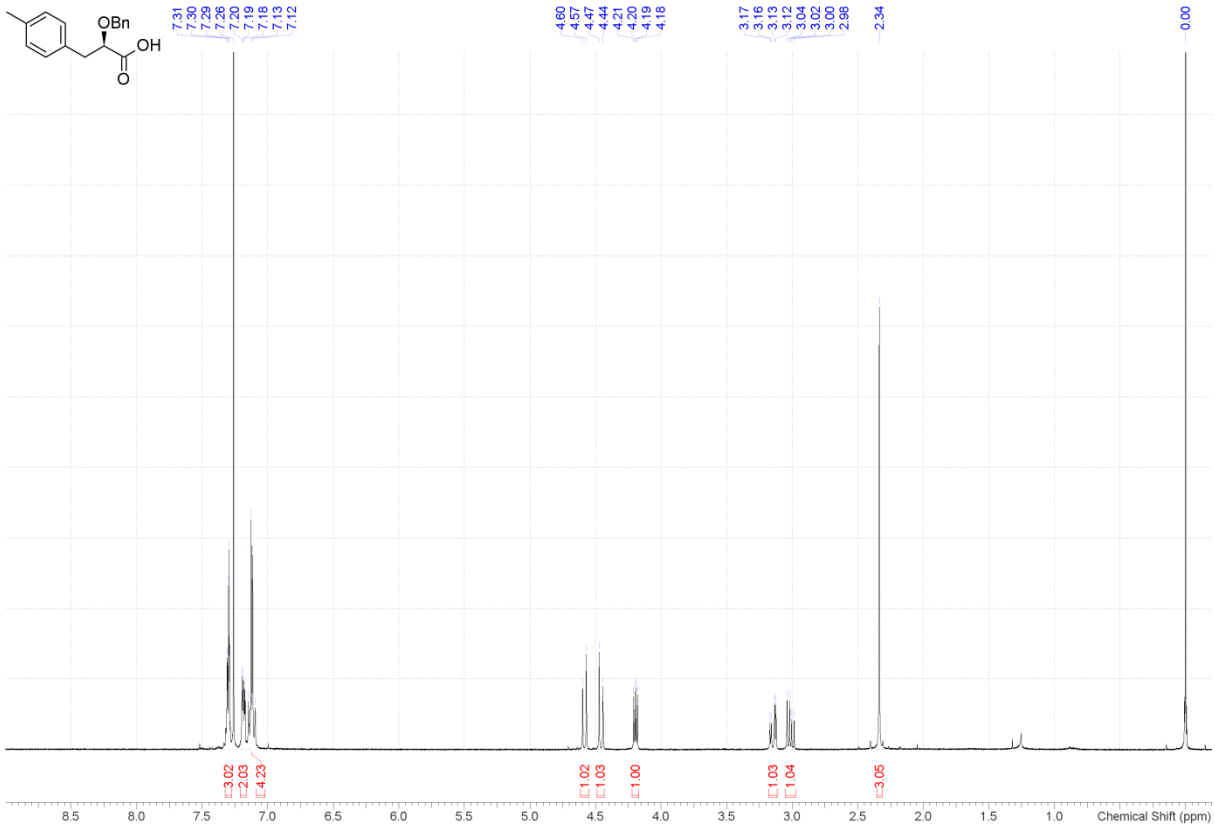


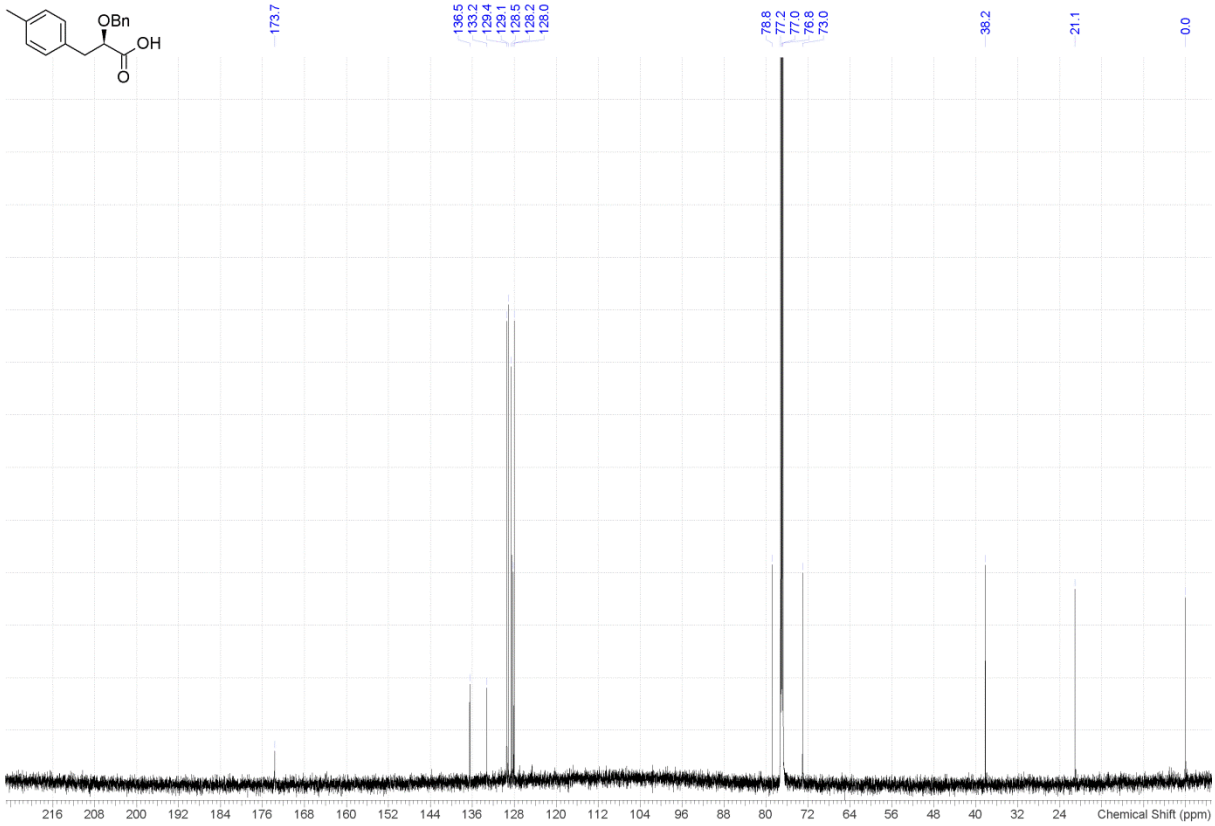
Methyl (*S*)-2-[(*R*)-2-(benzyloxy)-3-(*p*-tolyl)propanamido]-3-methylbutanoate (**18**)





(*R*)-2-(benzyloxy)-3-(*p*-tolyl)propanoic acid (**19**)





(*R*)-2-hydroxy-3-(*p*-tolyl)propanoic acid (**17**)