Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Transition metal-free, visible-light-mediated construction of α,β-diamino esters via decarboxylative radical addition at room-temperature

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Contents

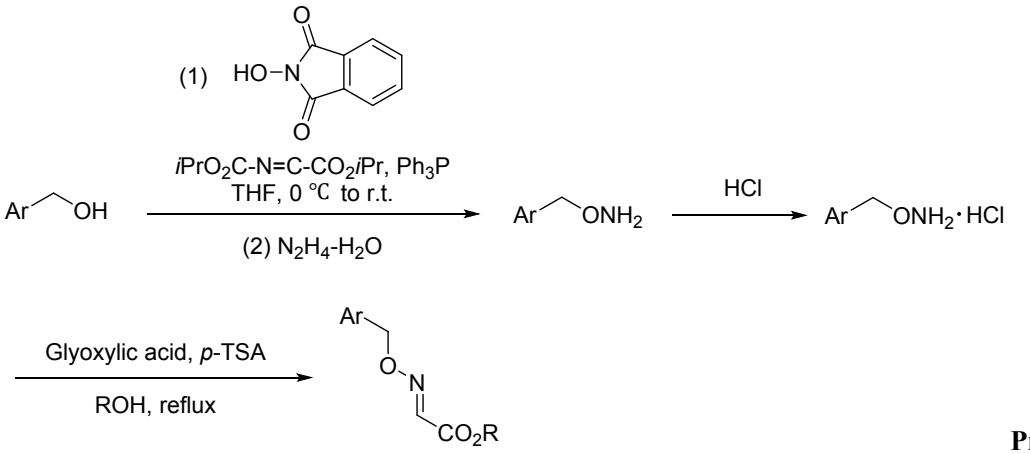
1. General Information

General Information. Proton nuclear magnetic resonance (^{1}H-NMR) spectra and carbon nuclear magnetic resonance (^{13}C-NMR) spectra were recorded on a Bruker AV-400 spectrometer (400 MHz and 100 MHz). Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane or referenced to residual solvent. Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane or referenced to residual solvent. Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz). High resolution mass spectrometry (ESI) were carried out using a Waters Quatro Macro triple quadrupole mass spectrometer Mass spectra (EI) were measured on a Waters Micromass GCT spectrometer. Melting points were measured on a XT3A apparatus. Diastereomeric ratios are determined by spectrums.

Starting Materials. Unless otherwise noted, all reactions were performed under nitrogen atmosphere in Schlenk tube, all chemicals were purchased from commercial sources and used as received. All other solvents, including those for NMR analysis, were used without further purification.

2. Synthesis of Substrates and Photocatalysts

Glyoxylic oxime ethers:



Procedure 1: To a solution of alcohol (20.0 mmol) in freshly distilled THF (100 mL) was added triphenylphosphine (22.0 mmol) and *N*-hydroxylphthalimide (22.0 mmol). After the solution was cooled to 0^{o}C diisopropylazodicarboxylate (22.0 mmol) was added dropwise. The solution was allowed to warm to room temperature over 3 h. Reaction progress was monitored by TLC. Hydrazine monohydrate (22.0 mmol) was then added and the solution was allowed

to stir for 30 min. The resulting reaction mixture was filtered to remove the white precipitate. The filtrate was concentrated and subjected to flash chromatography. The resulting product was dissolved in ether and treated with HCl (2.0 M solution in ether) to afford the HCl salt of the *O*-alkylhydroxylamine.[1]

Procedure 2: Glyoxylic acid (13.4 mmol) was dissolved in ethanol, and then *O*-alkylhydroxylamine hydrochloride (13.4 mmol), *p*-TsOH (1.3 mmol) were successively added. The mixture was heated at reflux for 5 hours. Then ethanol was distilled off. The crude mixture was diluted with CH_2Cl_2. The organic phase was successively washed with saturated $NaHCO_3$ (1x) and the resulting aqueous phase was back-extracted with CH_2Cl_2 (2x). The combined organic extracts were washed with saturated aqueous NaCl (1x), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash chromatography (eluent: petroleum ether/ethyl acetate) yielded glyoxylic oxime ether as a colorless oil.[2]

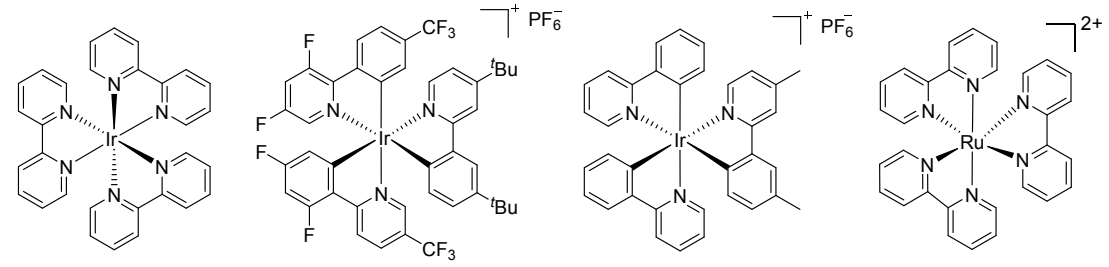
1a, **1f**, **1g**, **1h** were synthesized according to procedure 2. **1b**, **1c**, **1d**, **1e** were synthesized according to procedure 1 and procedure 2.

Alkyl carboxylic acids:

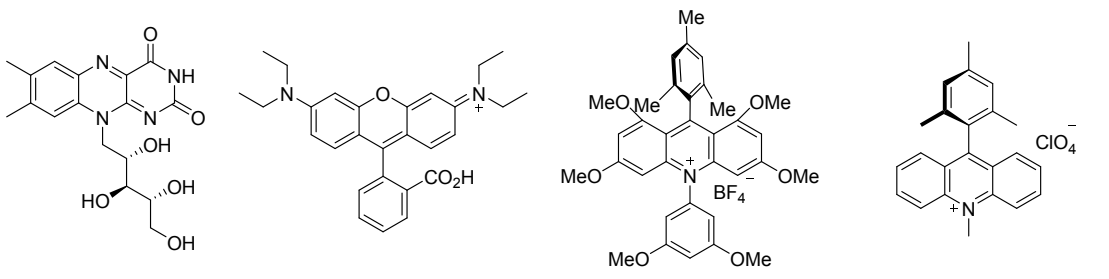
Alkyl carboxylic acids were commercially available while *N*-Cbz-*L*-proline **2i**[3], *N*-Bz-*L*-proline **2j**[4], Boc-*O*-benzyl-*L*-hydroxyproline **2k**[5], *N*-Boc-*L*-Methionine **2n**[6], *N*-Boc-sarcosine **2t**[7] were synthesized according to literature procedures.

Photocatalysts:

fac-$Ir(ppy)_3$[8], $Ir(dF\text{-}CF_3\text{-}ppy)_2(dtbpy)PF_6$[9], $Ir(ppy)_2(dmbpy)PF_6$[10], $Ru(bpy)_3Cl_2{\cdot}6H_2O$[11], $Acr^+BF_4^-$ **I** [12] were syhthesized according to literature procetures, Riboflavin, Rhodamine B, $Acr^+ClO_4^-$ **II**, Eosin-Yellow were commercially available.



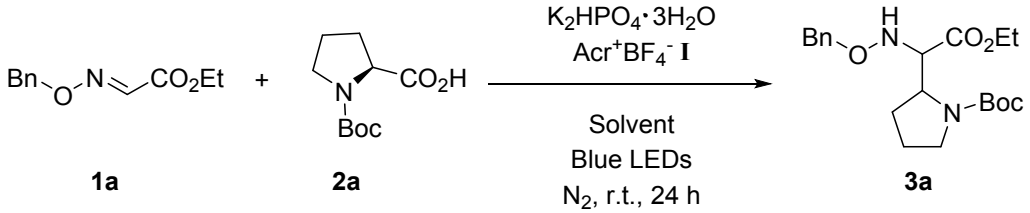
fac-$Ir(ppy)_3$ $Ir(dF\text{-}CF_3\text{-}ppy)_2(dtbpy)PF_6$ $Ir(ppy)_2(dmbpy)(PF_6)$ $[Ru(bpy)_3]^{2+}$



Riboflavin Rhodamine B $Acr^+BF_4^-$ **I** $Acr^+ClO_4^-$ **II**

3. Optimization Studies

3.1 Solvent Screening

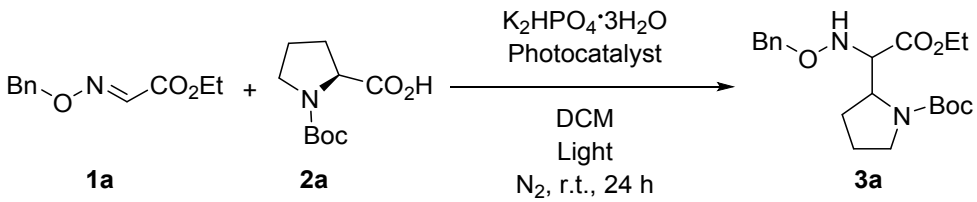


1a **2a** **3a**

Entry[a]	Solvent	Yield[b]
1	MeCN	64 %
2	DCE	40 %
3	EtOH	Trace
4	DMF	25 %
5	THF	47 %
6	EA	60 %
7	1,4-Dioxane	Trace
8	DCM	73 %
9	Toluene	72 %
10	MeOH	Trace
11	Acetone	64 %
12	*n*-Hexane	65 %
13	H_2O	Trace
14	$CHCl_3$	35 %
15	DCM/H_2O (2 mL / 2 mL)	69 %
16	DCM/H_2O (2 mL / 1 mL)	68 %
17[c]	DCM	55 %
18[d]	DCM	61 %

[a] Unless otherwise noted, all reactions were carried out using 1.0 equiv of **1a** (0.2 mmol), 1.0 equiv of **2a** (0.2 mmol), 2.0 mol% $Acr^+BF_4^-$ **I**, 1.5 equiv of $K_2HPO_4{\cdot}3H_2O$ (0.3 mmol), solvent (0.1 M) under N_2, room temperature and irradiation with blue LEDs for 24 h. [b] Isolated yield after silica gel chromatography. [c] The reaction concentration was 0.05 M. [d] The reaction concentration was 0.4 M.

3.2 Photocatalysts and light resource Screening

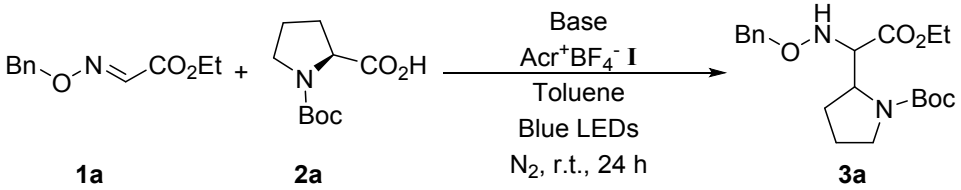


1a **2a** **3a**

Entry[a]	Photocatalyst	Light resource	Usage	Yield[b]
1	*fac*-Ir(ppy)$_3$	Fluorescence	3 mol%	Trace
2	Ir(dF-CF$_3$-ppy)$_2$(dtbpy)PF$_6$	Fluorescence	3 mol%	Trace
3	Ir(ppy)$_2$(dmbpy)PF$_6$	Fluorescence	3 mol%	Trace
4	Ru(bpy)$_3$Cl$_2$.6H$_2$O	Fluorescence	3 mol%	Trace
5	Riboflavin	Fluorescence	2 mol%	Trace
6	Rhodamine B	Fluorescence	2 mol%	Trace
7	Acr$^+$ClO$_4^-$ **II**	Fluorescence	2 mol%	15 %
8	Eosin-Yellow	Fluorescence	2 mol%	Trace
9	Acr$^+$BF$_4^-$ **I**	Fluorescence	2 mol%	24 %
10[c]	-	Fluorescence	0	0
11	*fac*-Ir(ppy)$_3$	Blue	3 mol%	Trace
12	Ir(dF-CF$_3$-ppy)$_2$(dtbpy)PF$_6$	Blue	3 mol%	64 %
13	Ir(ppy)$_2$(dmbpy)PF$_6$	Blue	3 mol%	Trace
14	Ru(bpy)$_3$Cl$_2$.6H$_2$O	Blue	3 mol%	Trace
15	Riboflavin	Blue	2 mol%	Trace
16	Rhodamine B	Blue	2 mol%	Trace
17	Acr$^+$ClO$_4^-$ **II**	Blue	2 mol%	40 %
18	Eosin-Yellow	Blue	2 mol%	Trace
19	Acr$^+$BF$_4^-$ **I**	Blue	2 mol%	73 %
20[c]	-	Blue	0	0
21[d]	Acr$^+$BF$_4^-$ **I**	Blue	2 mol%	75 %

[a] Unless otherwise noted, all reactions were carried out using 1.0 equiv of **1a** (0.2 mmol), 1.0 equiv of **2a** (0.2 mmol), 1.5 equiv of $K_2HPO_4{\cdot}3H_2O$ (0.3 mmol), DCM (0.1 M) as solvent, under N_2, room temperature and irradiation with light for 24 h. [b] Isolated yield after silica gel chromatography. [c] The reaction was carried out without photocatalyst. [d] The reaction was carried out with toluene.

3.3 Additive Screening

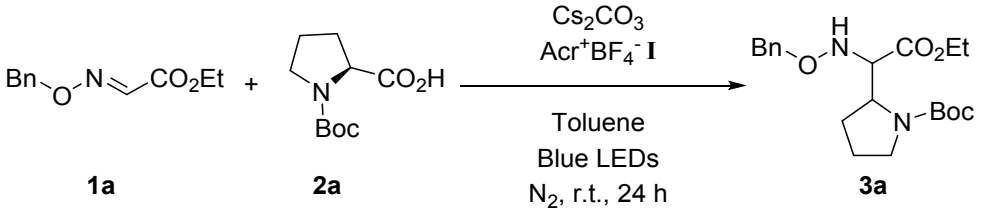


1a **2a** **3a**

Entry[a]	Base	Usage	Yield[b]
1[c]	-	0	5 %
2	Cs_2CO_3	1.5 eq	84 %

3	KH_2PO_4	1.5 eq	54 %
4	$K_3PO_4·3H_2O$	1.5 eq	83 %
5	NaOAc	1.5 eq	69 %
6	$Na_2HPO_4·12H_2O$	1.5 eq	10 %
7	Li_2CO_3	1.5 eq	76 %
8	K_2CO_3	1.5 eq	6 %
9	$NaHPO_4·2H_2O$	1.5 eq	32 %
10	$NaHCO_3$	1.5 eq	69 %
11	$K_2HPO_4·3H_2O$	1.5 eq	72 %
12	Et_3N	1.5 eq	25 %
13	DBU	1.5 eq	84 %
14	2,6-lutidine	1.5 eq	20 %
15	DIPEA	1.5 eq	7 %
16	DABCO	1.5 eq	81 %

[a] Unless otherwise noted, all reactions were carried out using 1.0 equiv of **1a** (0.2 mmol), 1.0 equiv of **2a** (0.2 mmol), 2.0 mol% $Acr^+BF_4^-$ **I**, toluene (0.1 M) as solvent, 1.5 equiv of additive, under N_2, room temperature and irradiation with blue LEDs for 24 h. [b] Isolated yield after silica gel chromatography. [c] The reaction was carried out without base.

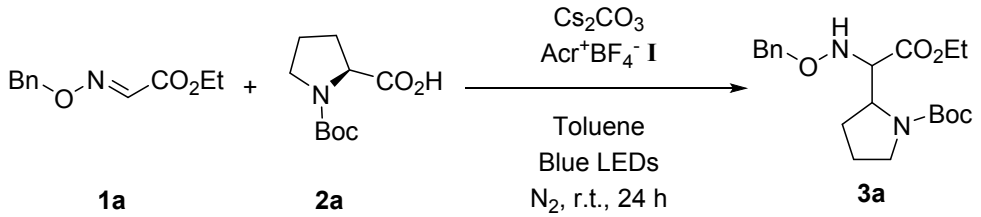


1a **2a** **3a**

Entry[a]	Base	Usage	Yield[b]
1	Cs_2CO_3	0.5 eq	75 %
2	Cs_2CO_3	1.0 eq	82 %
3	Cs_2CO_3	1.5 eq	83 %
4	Cs_2CO_3	2.0 eq	85 %
5	Cs_2CO_3	2.5 eq	93 %
6	Cs_2CO_3	3.0 eq	81 %

[a] Unless otherwise noted, all reactions were carried out using 1.0 equiv of **1a** (0.2 mmol), 1.0 equiv of **2a** (0.2 mmol), 2.0 mol% $Acr^+BF_4^-$ **I**, toluene (0.1 M) as solvent, Cs_2CO_3, under N_2, room temperature and irradiation with blue LEDs for 24 h. [b] Isolated yield after silica gel chromatography.

3.4 Substrate ratio Screening

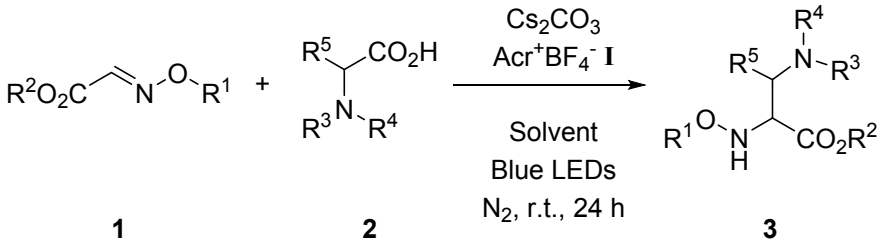


Entry[a]	2-1a	2-2a	Yield[b]
1	0.2 mmol	0.2 mmol	93
2	0.24 mmol	0.2 mmol	80 %
3	0.3 mmol	0.2 mmol	86 %
4	0.36 mmol	0.2 mmol	87 %
5	0.2 mmol	0.24 mmol	88 %
6	0.2 mmol	0.3 mmol	40 %
7	0.2 mmol	0.36 mmol	90 %

[a] Unless otherwise noted, all reactions were carried out using **1a**, **2a**, 2.0 mol% $Acr^+BF_4^-$ **I**, toluene (0.1 M) as solvent, 2.5 equiv of Cs_2CO_3 (0.5 mmol), under N_2 (freeze-pump-thaw cycles), room temperature and irradiation with blue LEDs for 24 h. [b] Isolated yield after silica gel chromatography.

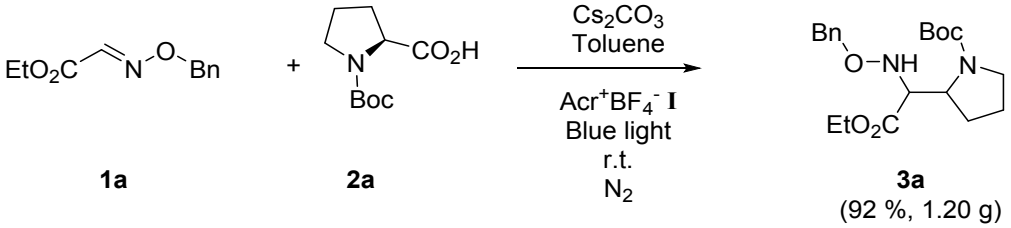
4. General Procedure and Characterization of Products

4.1 General Procedure



Glyoxylic oxime **1** (0.2 mmol, 1.0 equiv), alkyl carboxylic acid **2** (0.2 mmol, 1.0 equiv), Cs_2CO_3 (0.5 mmol, 2.5 equiv), $Acr^+BF_4^-$ **I** (0.002 mmol, 0.02 equiv) and solvent (2 mL) were added to a 10 mL transparent Schlenk tube charged with a magnetic stir bar. The resulting solution was degassed and backfilled with nitrogen via the freeze-pump-thaw procedure for three cycles. The reaction tube was then placed in an irradiation apparatus (at approximately 2 cm away from the light source) equipped with two 30 W blue light LED bulbs (λmax= 450 nm) and stirred at room temperature until TLC showed consumption of starting material. Then reaction mixture was concentrated under reduced pressure and the crude residue was purified by flash chromatography to yield corresponding addition products **3**.

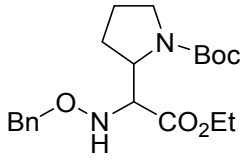
4.2 Gram-Scale Reaction



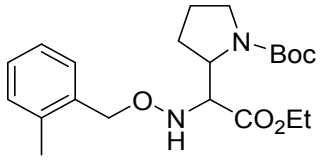
1a **2a** **3a** (92 %, 1.20 g)

Glyoxylic oxime **1a** (698 mg, 3.4 mmol), *N*-Boc-*L*-proline **2a** (725 mg, 3.4 mmol), Cs_2CO_3 (2.70 g, 8.4 mmol), $Acr^+BF_4^-$ **I** (45 mg, 0.07 mmol) and solvent toluene (34 mL) were added to a 100 mL transparent Schlenk tube charged with a magnetic stir bar. The resulting solution was degassed and backfilled with nitrogen via the freeze-pump-thaw procedure for three cycles. The reaction tube was then placed in an irradiation apparatus (at approximately 2 cm away from the light source) equipped with two 30 W blue light LED bulbs (λmax= 450 nm) and stirred at room temperature until TLC showed consumption of starting material. Thenreaction mixture was concentrated under reduced pressure and the crude residue was purified by flash chromatography to yield transparent oil **3a** (1.20 g, 92 %).

4.3 Characterization of Products

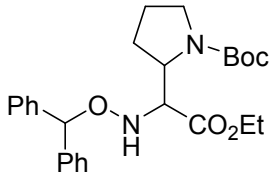


Tert-butyl 2-(1-((benzyloxy)amino)-2-ethoxy-2-oxoethyl) pyrrolidine-1-carboxyl-ate (3a). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 15:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.0:1.0 mixture of diastereomers) δ 7.36 – 7.28 (m, 10H), 6.20 (s, 2H), 4.66 (t, *J* = 8.7 Hz, 4H), 4.27 – 4.15 (m, 4H), 4.07 – 3.90 (m, 4H), 3.51 – 3.21 (m, 3H), 3.16 (s, 1H), 1.89 – 1.68 (m, 8H), 1.46 (s, 9H), 1.45 (s, 9H), 1.276 (t, *J* = 7.2 Hz, 3H), 1.273 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.0:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 172.7, 172.4, 172.2, 154.6, 154.1, 137.9, 137.8, 128.6 (×2), 128.4, 128.2, 127.7, 126.9, 80.0, 79.5, 77.4, 76.1, 66.6, 66.0, 61.2, 61.1, 57.4, 57.1, 47.0, 46.6, 28.4, 27.8, 23.9, 23.3, 14.2 (×2); HRMS (ESI) calcd for $C_{20}H_{31}N_2O_5$ (M+H) 379.2155, found 379.2157.

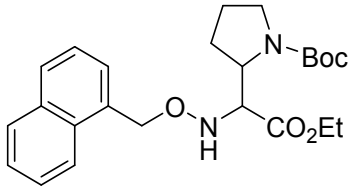


Tert-butyl 2-(2-ethoxy-1-(((2-methylbenzyl)oxy) amino)-2-oxoethyl) pyrrolidine-1-carboxylate (3b). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 15:1);

Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.5:1.0 mixture of diastereomers) δ 7.34 – 7.28 (m, 1H), 7.25 – 7.10 (m, 7H), 6.18 (s, 2H), 4.70 (s, 2H), 4.67 (s, 2H), 4.30 – 4.11 (m, 4H), 4.10 – 3.84 (m, 4H), 3.50 – 3.00 (m, 4H), 2.34 (s, 6H), 1.78 (d, J = 29.8 Hz, 8H), 1.46 (s, 18H), 1.27 (d, J = 5.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.5:1.0 mixture of diastereomers, each diastereomer exists as 1:1 mixture of rotamers) δ 172.7, 172.4, 154.9, 154.6, 137.2, 135.5, 130.1, 129.9, 129.8, 128.0, 125.6, 80.0, 79.5, 74.3, 66.6, 66.1, 61.1 (×2), 57.1, 56.8, 46.9, 46.6, 29.7, 28.4, 27.8, 18.9, 14.2 (×2); HRMS (ESI) calcd for $C_{21}H_{33}N_2O_5$ (M+H) 393.2311, found 393.2312.

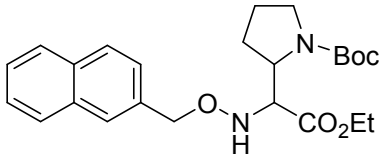


Tert-butyl-2-(1-((benzhydryloxy)amino)-2-ethoxy-2-oxoethyl)pyrrolidine-1-carboxylate (3c). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 10:1); Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.5:1.0 mixture of diastereomers) δ 7.30 (d, J = 18.4 Hz, 20H), 6.20 (t, J = 49.1 Hz, 2H), 5.70 (s, 1H), 5.68 – 5.59 (m, 1 H), 4.38 – 3.86 (m, 8H), 3.53 – 3.00 (m, 4H), 1.73 (br s, 8H), 1.43 (s, 12H), 1.36 (s, 6H), 1.28 (t, J = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.5:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 172.7, 171.2, 154.6, 154.1, 141.6, 141.4, 128.4, 128.2 (×2), 127.5, 127.4, 127.2, 127.1 86.7, 86.6, 79.9, 79.4, 66.2, 61.1, 60.4, 57.2, 56.5, 46.8, 46.2, 28.5, 28.4, 28.1, 27.8, 23.8, 23.0, 14.3, 14.2; HRMS (ESI) calcd for $C_{26}H_{35}N_2O_5$ (M+H) 455.2468, found 455.2467.

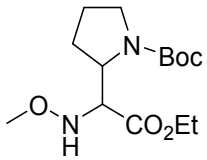


Tert-butyl 2-(2-ethoxy-1-((naphthalen-1-ylmethoxy)amino)-2-oxoethyl)pyrroledi-ne-1-carboxylate (3d). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 10:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.3:1.0 mixture of diastereomers) δ 8.12 (d, J = 7.7 Hz, 2H), 7.82 (dd, J = 16.7, 7.9 Hz, 4H), 7.59 – 7.35 (m, 8H), 6.51 – 6.00 (m, 2H), 5.14 (d, J = 3.0 Hz, 2H), 5.11 (s, 2H), 4.31 – 4.10 (m, 4H), 3.97 (s, 4H), 3.53 – 2.99 (m, 4H), 1.92 – 1.64 (m, 8H), 1.44 (d, J = 7.9 Hz, 18H), 1.24 (t, J = 6.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.3:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 172.4, 171.2, 154.7, 154.3, 133.7, 132.0, 128.7, 128.4, 127.7, 127.6, 126.1 (×2), 125.7, 125.2, 80.0, 79.5, 74.5, 74.2, 66.1, 65.5, 61.1, 60.4, 57.4, 56.8, 47.0, 46.6, 28.5, 27.8, 23.9, 23.3, 21.1, 14.2 (×2); HRMS (ESI)

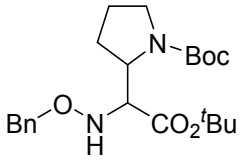
calcd for $C_{24}H_{33}N_2O_5$ (M+H) 429.2311, found 429.2315.



Tert-butyl 2-(2-ethoxy-1-((naphthalen-2-ylmethoxy)amino)-2-oxoethyl)pyrrolidi-ne-1-carboxylate (3e). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 10:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.2:1.0 mixture of diastereomers) δ 7.95 – 7.67 (m, 8H), 7.46 (d, *J* = 4.4 Hz, 6H), 6.56 – 6.02 (m, 2H), 4.83 (s, 2H), 4.80 (s, 2H), 4.33 – 3.86 (m, 8H), 3.55 – 3.02 (m, 4H), 1.94 – 1.63 (m, 8H), 1.51 – 1.39 (m, 18H), 1.28 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) (1.2:1 mixture of diastereomers, each diastereomer exists as 1:1 mixture of rotamers) δ 172.8, 172.5, 154.6, 154.1, 135.4, 135.3, 133.2, 133.0, 128.0, 127.7, 126.7, 126.6, 126.5, 126.0, 125.9, 80.0, 79.5, 76.2, 76.0, 66.7, 65.9, 61.3, 61.2, 57.1, 56.9, 47.0, 46.7, 28.5, 28.3, 23.9, 23.3, 14.2; HRMS (ESI) calcd for $C_{24}H_{33}N_2O_5$ (M+H) 429.2311, found 429.2312.

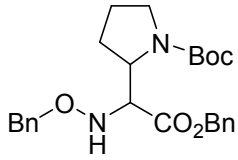


Tert-butyl 2-(2-ethoxy-1-(methoxyamino)-2-oxoethyl)pyrrolidine-1-carboxylate (3f). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 15:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.1:1.0 mixture of diastereomers) δ 6.66 – 5.85 (m, 2H), 4.29 – 3.96 (m, 8H), 3.47 (s, 3H), 3.44 (s, 3H), 3.43 – 2.95 (m, 4H), 1.93 – 1.73 (m, 8H), 1.47 (s, 9H), 1.43 (s, 9H), 1.25 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.1:1.0 mixture of diastereomers, each diastereomer exists as 1:1 mixture of rotamers) δ 172.7, 172.2, 154.7, 154.2, 80.0, 79.5, 65.8, 61.6, 61.2, 58.3, 57.0, 56.8, 47.1, 28.4 (×2), 27.4, 24.0, 18.4, 14.2 (×2); HRMS (ESI) calcd for $C_{14}H_{27}N_2O_5$ (M+H) 303.1842, found 303.1845.

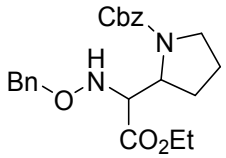


Tert-butyl 2-(1-((benzyloxy)amino)-2-(tert-butoxy)-2-oxoethyl)pyrrolidine-1-carboxylate (3g). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 15:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2.5:1.0 mixture of diastereomers) δ 7.38 – 7.27 (m, 9H), 7.26 – 7.23 (m, 1H), 6.51 – 5.89 (m, 2H), 4.75 – 4.66 (m, 2H), 4.66 – 4.55 (m, 2H), 4.34 – 3.86 (m, 4H), 3.52 – 3.05 (m, 4H), 1.91 – 1.66 (m, 8H), 1.47 (s, 26H), 1.45 (s, 10H); ^{13}C NMR (100 MHz, $CDCl_3$)

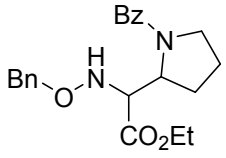
(2.5:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 172.1, 171.2, 154.6, 154.1, 138.0, 137.9, 128.6, 128.5, 128.4, 128.3, 128.2, 127.7, 127.6, 81.7, 79.8, 79.4, 75.9, 67.2, 66.2, 57.7, 56.7, 47.3, 46.9, 28.5, 28.1 (×2), 27.8, 27.3, 24.1, 23.6; HRMS (ESI) calcd for $C_{22}H_{35}N_2O_5$ (M+H) 407.2468, found 407.2469.



Tert-butyl 2-(2-(benzyloxy)-1-((benzyloxy)amino)-2-oxoethyl)pyrrolidine-1-carboxylate (3h). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 15:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.0:1.0 mixture of diastereomers) δ 7.44 – 7.22 (m, 20H), 6.50 – 5.89 (m, 2H), 5.30 – 5.07 (m, 4H), 4.76 – 4.66 (m, 2H), 4.65 – 4.60 (m, 2H), 4.25 – 3.87 (m, 4H), 3.53 – 2.96 (m, 4H), 1.84 – 1.62 (m, 8H), 1.44 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.0:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 172.6, 154.7, 154.3, 137.8, 135.8, 128.6, 128.5, 128.3, 127.7, 80.1, 79.6, 76.1, 67.0 (×2), 65.8, 57.3, 56.7, 47.0, 46.6, 28.5, 28.4, 28.0, 27.7, 23.9, 23.1; HRMS (ESI) calcd for $C_{25}H_{33}N_2O_5$ (M+H) 441.2311, found 441.2313.

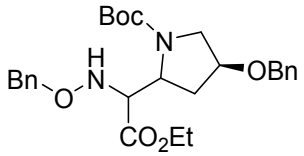


Benzyl 2-(1-((benzyloxy)amino)-2-ethoxy-2-oxoethyl)pyrrolidine-1-carboxylate (3i). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 15:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.19 (m, 10H), 6.14 (s, 1H), 5.24 – 4.95 (m, 2H), 4.82 – 4.42 (m, 2H), 4.30 – 3.72 (m, 4H), 3.57 – 3.05 (m, 2H), 1.98 – 1.61 (m, 4H), 1.26 – 1.18 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 155.3, 155.0, 136.9, 128.7 (×2), 128.5 (×2), 128.3, 128.0, 127.9, 127.8 (×2), 127.7, 76.1, 76.0, 67.1, 66.8, 65.8, 65.7, 61.3, 61.2, 58.2, 57.7, 46.8, 28.3, 27.7, 23.9, 23.2, 14.2 (×2); HRMS (ESI) calcd for $C_{23}H_{29}N_2O_5$ (M+H) 413.1998, found 413.1999.

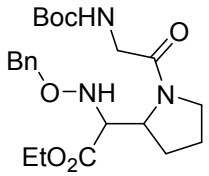


Ethyl 2-(1-benzoylpyrrolidin-2-yl)-2-((benzyloxy)amino)acetate (3j). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 10:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.2:1.0 mixture of diastereomers) δ 7.55 – 7.28 (m, 20H), 6.64 – 6.19 (m, 2H), 4.72 (s, 2H), 4.68 (s, 2H), 4.66 – 4.49 (m, 2H), 4.36 – 4.05 (m, 6H), 3.48 – 3.26 (m, 4H), 2.06 – 1.60 (m,

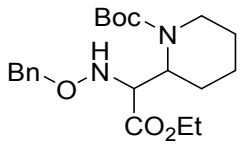
8H), 1.288 (t, J = 14.2 Hz, 3H), 1.286 (t, J = 12.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.2:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 172.3, 172.1, 170.7, 170.3, 137.8, 136.8, 130.2, 130.1, 128.6, 128.5, 128.3 (×2), 127.8 (×2), 127.4, 76.1, 76.0, 65.3, 61.4, 56.8, 56.6, 50.7, 27.5, 27.4, 25.2, 25.0, 14.3; HRMS (ESI) calcd for $C_{22}H_{27}N_2O_4$ (M+H) 383.1893, found 383.1895.



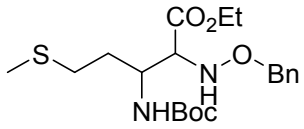
Tert-butyl (4S)-4-(benzyloxy)-2-(1-((benzyloxy)amino)-2-ethoxy-2-oxoethyl)pyro-lidine-1-carboxylate (3k). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 10:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.25 (m, 10H), 6.45 – 5.90 (m, 1H), 4.75 – 4.59 (m, 2H), 4.55 – 4.36 (m, 2H), 4.36 – 4.06 (m, 4H), 4.00 – 3.00 (m, 3H), 2.13 – 1.89 (m, 2H), 1.60 – 1.40 (m, 9H), 1.26 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 172.1, 154.7, 154.4, 128.7, 128.6 (×2), 128.5, 128.3 (×2), 127.8 (×2), 127.6, 79.9, 76.7, 76.2, 71.0, 65.9, 65.4, 61.4, 61.3, 58.3, 56.8, 56.5, 52.4, 34.3, 33.7, 28.5, 28.4, 14.2; HRMS (ESI) calcd for $C_{27}H_{37}N_2O_6$ (M+H) 485.2573, found 485.2576.



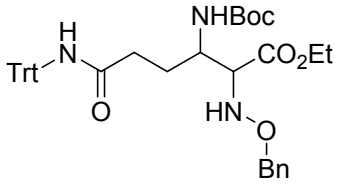
Ethyl 2-((benzyloxy)amino)-2-(1-((tert-butoxycarbonyl)glycyl)pyrrolidin-2-yl)acetate (3l). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 15:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.5:1.0 mixture of diastereomers) δ 7.42 – 7.25 (m, 10H), 6.35 – 6.10 (m, 2H), 5.47 (s, 2H), 4.74 – 4.64 (m, 2H), 4.64 – 4.54 (m, 2H), 4.46 – 4.09 (m, 6H), 4.04 – 3.66 (m, 6H), 3.44 – 3.08 (m, 4H), 1.98 – 1.70 (m, 8H), 1.44 (d, J = 7.7 Hz, 18H), 1.28 (dd, J = 14.2, 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.5:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 172.2, 172.1, 167.8, 167.2, 155.8, 137.8 (×2), 128.7, 128.5, 128.2, 127.8 (×2), 79.6, 76.1, 76.0, 65.5, 61.3, 57.0, 45.9, 43.2 (×2), 28.4, 27.5, 26.7, 24.1, 24.0, 14.2 (×2); HRMS (ESI) calcd for $C_{22}H_{34}N_3O_6$ (M+H) 436.2369, found 436.2370.



Tert-butyl 2-(1-((benzyloxy)amino)-2-ethoxy-2-oxoethyl)piperidine-1-carboxylate (3m). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 15:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.27 (m, 5H), 5.99 (s, 1H), 4.70 – 4.53 (m, 2H), 4.36 – 4.19 (m, 2H), 4.18 – 4.02 (m, 1H), 4.02 – 3.68 (m, 2H), 2.50 – 2.40 (m, 1H), 1.58 – 1.28 (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 173.1, 155.0, 154.3, 138.0, 128.7 (×2), 128.3, 128.2, 127.8, 127.7, 79.7, 79.5, 76.3, 76.0, 63.8, 63.0, 61.1,50.4, 49.2, 39.7, 38.4, 28.4, 28.3, 26.4, 26.0, 25.1, 25.0, 19.2, 19.1, 14.3, 14.1; HRMS (ESI) calcd for $C_{21}H_{33}N_2O_5$ (M+H) 393.2311, found 393.2314.

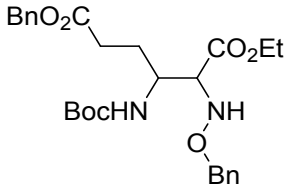


Ethyl 2-((benzyloxy) amino)-3-((tert-butoxycarbonyl) amino)-5-(methylthio) pentanoate (3n). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 10:1); Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.0:1.0 mixture of diastereomers) δ 7.47 – 7.28 (m, 10H), 6.21 (s, 2H), 4.68 (d, J = 6.4 Hz, 4H), 4.60 (d, J = 9.6 Hz, 1H), 4.32 – 3.95 (m, 6H), 3.74 – 3.62 (m, 2H), 2.58 – 2.38 (m, 4H), 2.08 (t, J = 11.0 Hz, 6H), 1.82 – 1.68 (m, 4H), 1.44 (d, J = 5.5 Hz, 9H), 1.41 (s, 9H), 1.29 (t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.0:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 171.9, 171.6, 155.4, 155.2, 137.5 (×2), 128.7, 128.6, 128.4 (×2), 128.0 (×2), 79.6, 79.5, 76.3, 76.1, 66.6, 66.1, 61.6, 61.5, 50.5, 49.6, 30.7, 30.6, 28.4, 28.3, 15.6, 15.5, 14.2, 14.1; HRMS (ESI) calcd for $C_{20}H_{33}N_2O_5S$ (M+H) 413.2032, found 413.2035.

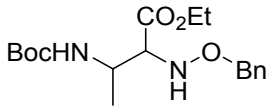


Ethyl 2-((benzyloxy)amino)-3-((tert-butoxycarbonyl)amino)-6-oxo-6-(tritylamin-o)hexaneate (3o). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 10:1); White solid (melting point 146 – 147 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) (1.0:1.0 mixture of diastereomers) δ 7.33 – 7.21 (m, 40H), 6.25 – 6.01 (m, 2H), 5.5 – 4.81 (m, 2H), 4.73 – 4.60 (m, 4H), 4.23 – 3.57 (m, 8H), 2.26 (d, J = 7.1 Hz, 4H), 1.92 – 1.65 (m, 4H), 1.41 (s, 9H), 1.39 (s, 9H), 1.25 – 1.17 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.0:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 171.7, 171.5, 171.4, 171.3, 156.1, 156.0, 144.8, 128.8 (×2), 128.7, 128.6, 128.4 (×2), 127.9, 126.9 (×2), 79.8, 79.6, 76.3, 76.1, 70.6, 70.5, 66.7, 66.5, 61.6, 58.3, 50.8,

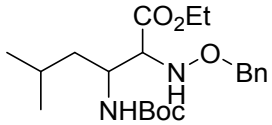
49.7, 34.3, 34.0, 28.4, 28.3, 14.2, 14.1; HRMS (ESI) calcd for $C_{39}H_{46}N_3O_6$ (M+H) 652.3308, found 652.3311.



6-benzyl 1-ethyl 2-((benzyloxy)amino)-3-((tert-butoxycarbonyl) amino) hexanedioate (3p). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 15:1); Yellow solid (melting point 77 – 78 °C); ^{1}H NMR (400 MHz, $CDCl_3$) (1.0:1.0 mixture of diastereomers) δ 7.49 – 7.14 (m, 20H), 6.20 (s, 2H), 5.18 – 5.04 (m, 4H), 4.73 – 4.63 (m, 4H), 4.61 (d, *J* = 9.8 Hz, 1H), 4.31 – 4.13 (m, 4H), 4.06 – 3.89 (m, 2H), 3.76 – 3.57 (m, 2H), 2.43 – 2.32 (m, 4H), 1.94 – 1.67 (m, 4H), 1.42 (s, 9H), 1.39 (s, 9H), 1.27 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.0:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 172.9, 172.8, 171.7, 171.5, 155.4, 155.3, 137.5, 135.9, 128.7, 128.6 (×3), 128.5, 128.4, 128.3, 128.0, 79.6, 79.5, 76.3, 76.1, 66.7, 66.4, 66.3, 61.6 (×2), 50.7, 49.8, 30.8, 28.4, 28.3, 27.8, 27.0, 14.2, 14.1; HRMS (ESI) calcd for $C_{27}H_{37}N_2O_7$ (M+H) 501.2523, found 501.2526.

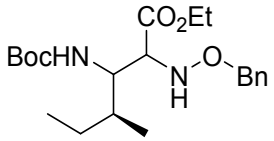


Ethyl 2-((benzyloxy)amino)-3-((tert-butoxycarbonyl)amino)butanoate (3q). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 10:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.0:1.0 mixture of diastereomers) δ 7.41 – 7.29 (m, 10H), 6.18 (s, 2H), 4.92 (s, 1H), 4.70 – 4.66 (m, 4H), 4.32 – 4.14 (m, 4H), 4.03 (s, 2H), 3.73 – 3.65 (m, 1H), 3.59 – 3.57 (m, 1H), 1.44 (s, 9H), 1.42 (s, 9H), 1.31 – 1.26 (m, 6H), 1.15 (d, *J* = 6.8 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.0:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 172.0, 171.8, 155.0, 137.6, 137.5, 128.6, 128.4, 128.3, 127.9 (×2), 79.4, 76.2, 76.1, 67.4, 67.0, 61.4, 46.7, 46.1, 28.4, 28.3, 18.4, 17.0, 14.2 (×2); HRMS (ESI) calcd for $C_{18}H_{29}N_2O_5$ (M+H) 353.1998, found 353.1999.

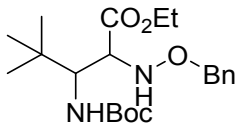


Ethyl 2-((benzyloxy)amino)-3-((tert-butoxycarbonyl)amino)-5-methylhexanoate (3r). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 15:1); Pale yellow oil; ^{1}H NMR

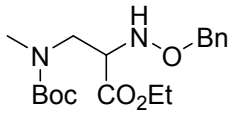
(400 MHz, $CDCl_3$) (1.0:1.0 mixture of diastereomers) δ 7.38 – 7.28 (m, 10H), 6.17 (s, 2H), 4.70 – 4.65 (m, 4H), 4.50 – 4.38 (s, 1H), 4.31 – 4.13 (m, 4H), 4.13 – 3.95 (m, 2H), 1.67 – 1.53 (m, 2H), 1.67 – 1.53 (m, 2H), 1.44 (s, 9H), 1.40 (s, 9H), 1.38 – 1.31 (m, 2H), 1.30 – 1.24 (m, 8H), 0.93 – 0.88 (m, 6H), 0.88 – 0.84 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.0:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 171.1 (×2), 154.4, 154.2, 136.7, 136.6, 127.6 (×2), 127.3, 126.8, 78.3, 78.2, 75.2, 74.9, 65.9, 65.4, 60.4, 60.2, 48.3, 47.6, 40.7, 39.7, 27.4, 27.3, 23.7, 23.6, 22.2, 21.9, 21.0, 20.6, 13.2, 13.1; HRMS (ESI) calcd for $C_{21}H_{35}N_2O_5$ (M+H) 395.2468, found 395.2470.



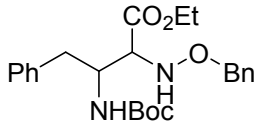
Ethyl (4S)-2-((benzyloxy)amino)-3-((tert-butoxycarbonyl)amino)-4-methylhe-xanoate (3s). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 15:1); Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) (1.2:1.0 mixture of diastereomers) δ 7.59 – 7.27 (m, 10H), 6.30 – 6.02 (m, 2H), 4.75 – 4.67 (m, 2H), 4.66 (s, 2H), 4.35 – 4.35 (m, 1H), 4.35 – 4.10 (m, 4H), 3.83 – 3.65 (m, 4H), 2.07 – 1.42 (m, 6H), 1.41 (s, 12H), 1.40 (s, 6H), 1.28 (t, J = 7.2 Hz, 6H), 0.97 – 0.79 (m, 11H), 0.74 (d, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.2:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 172.7, 172.6, 155.7, 155.5, 137.7 (×2), 128.6 (×2), 128.3 (×3), 127.9, 127.8, 79.3, 79.2, 76.2, 76.1, 65.7, 61.3, 61.2, 54.4, 52.9, 37.2, 36.6, 28.3, 26.6, 24.4, 15.9, 15.7, 14.2, 14.1, 11.4, 11.0; HRMS (ESI) calcd for $C_{21}H_{35}N_2O_5$ (M+H) 395.2468, found 395.2469.



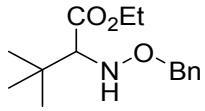
Ethyl 2-((benzyloxy)amino)-3-((tert-butoxycarbonyl)amino)-4,4-dimethylpentan-oate (3t). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 20:1); Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) (2.0:1.0 mixture of diastereomers) δ 7.39 – 7.26 (m, 10H), 6.17 – 6.01 (m, 2H), 4.67 (s, 4H), 4.53 (d, J = 10.7 Hz, 1H), 4.26 – 4.16 (m, 4H), 3.87 – 3.60 (m, 4H), 1.42 (s, 6H), 1.39 (s, 12H), 1.29 (t, J = 7.0 Hz, 6H), 0.92 (s, 13H), 0.86 (s, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) (2.0:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 173.1, 173.0, 155.8, 155.5, 138.0, 137.8, 128.6, 128.4, 128.3, 128.2, 127.8 (×2), 79.3 (×2), 76.1, 76.0, 63.5, 62.8, 61.5, 58.6, 35.2, 35.1, 28.4, 28.3, 26.9, 26.6, 14.1; HRMS (ESI) calcd for $C_{21}H_{35}N_2O_5$ (M+H) 395.2468, found 395.2471.



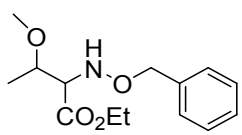
Ethyl 2-((benzyloxy)amino)-3-((tert-butoxycarbonyl)(methyl)amino)propanoate (3u). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 15:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H), 6.15 – 5.94 (m, 1H), 4.69 (s, 2H), 4.27 – 4.13 (m, 2H), 3.92 – 3.64 (m, 1H), 3.47 – 3.21 (m, 2H), 2.83 (s, 3H), 1.43 (s, 9H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 172.2, 155.8, 155.3, 137.7, 137.6, 128.5, 128.3, 127.8, 80.0, 79.7, 76.2, 63.2, 62.7, 61.3, 48.5, 48.2, 35.7, 35.4, 28.3, 14.2; HRMS (ESI) calcd for $C_{18}H_{29}N_2O_5$ (M+H) 353.1998, found 353.2000.



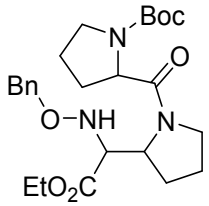
Ethyl 2-((benzyloxy)amino)-3-((tert-butoxycarbonyl)amino)-4-phenylbutanoate (3v). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 15:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.5:1.0 mixture of diastereomers) δ 7.56 – 7.05 (m, 20H), 6.23 (s, 2H), 4.90 (d, *J* = 8.9 Hz, 1H), 4.72 (s, 2H), 4.66 (s, 2H), 4.49 – 3.81 (m, 6H), 3.79 – 3.52 (m, 2H), 2.97 – 2.78 (m, 2H), 2.78 – 2.58 (m, 2H), 1.36 (s, 7H), 1.34 (s, 11H), 1.28 – 1.24 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.5:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 172.0, 171.9, 155.0, 129.5, 129.4, 128.6 (×2), 128.5, 128.4 (×3), 128.0, 127.9, 126.6 (×2), 79.5, 79.4, 76.2, 76.1, 65.5, 61.5, 61.4, 52.4, 51.6, 38.8, 38.0, 28.3 (×2), 14.2, 14.1; HRMS (ESI) calcd for $C_{24}H_{33}N_2O_5$ (M+H) 429.2311, found 429.2312.



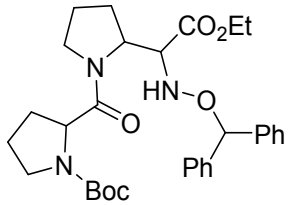
Ethyl 2-((benzyloxy)amino)-3,3-dimethylbutanoate (3w). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 15:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 5H), 6.10 (d, *J* = 11.8 Hz, 1H), 4.65 (s, 2H), 4.27 – 4.16 (m, 2H), 3.30 (d, *J* = 11.8 Hz, 1H), 1.28 (t, *J* = 7.2 Hz, 3H), 0.92 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 138.0, 128.7, 128.2, 127.7, 75.7, 72.0, 60.6, 33.1, 27.0, 14.4; HRMS (ESI) calcd for $C_{15}H_{24}NO_3$ (M+H) 266.1768, found 266.1770.



Ethyl 2-((benzyloxy)amino)-3-methoxybutanoate (3x). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 15:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.2:1.0 mixture of diastereomers) δ 7.37 – 7.28 (m, 10H), 6.29 – 6.12 (m, 2H), 4.71 (s, 2H), 4.70 (s, 2H), 4.33 – 4.14 (m, 4H), 3.71 – 3.48 (m, 4H), 3.28 (s, 3H), 3.26 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 6H), 1.16 (t, *J* = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.2:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 172.0 (×2), 137.8, 137.7, 128.6, 128.5, 128.3 (×2), 127.8 (×2), 76.2 (×2), 75.8, 75.6, 68.3, 67.9, 61.0 (×2), 56.9 (×2), 16.3, 16.0, 14.3 (×2); HRMS (ESI) calcd for $C_{14}H_{22}NO_4$ (M+H) 268.1471, found 268.1472.

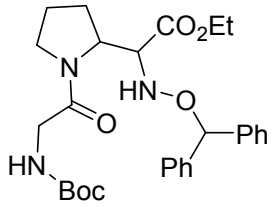


Tert-butyl 2-(2-(1-((benzyloxy)amino)-2-ethoxy-2-oxoethyl)pyrrolidine-1-carbonyl)pyrrolidine-1-carboxylate (3y). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 5:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.2:1.0 mixture of diastereomers) δ 7.39 – 7.29 (m, 10H), 6.39 (d, *J* = 8.6 Hz, 1H), 6.21 (s, 1H), 4.66 (d, *J* = 5.4 Hz, 2H), 4.62 (d, *J* = 4.7 Hz, 2H), 4.52 – 4.41 (m, 2H), 4.40 – 4.29 (m, 2H), 4.26 – 4.12 (m, 4H), 4.10 – 3.87 (m, 2H), 3.78 – 3.65 (m, 2H), 3.63 – 3.55 (m, 2H), 3.50 – 3.28 (m, 4H), 2.16 – 2.00 (m, 5H), 1.92 – 1.79 (m, 11H), 1.45 (s, 10H), 1.37 (s, 8H), 1.30 – 1.26 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.2:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 172.4, 172.1, 171.9, 171.6, 154.5, 153.7, 138.0, 137.7, 128.6, 128.4 (×2), 128.3 (×2), 128.2 (×2), 127.8, 127.7, 79.4, 75.9, 75.8, 65.4, 61.2, 57.8, 56.7, 46.8, 46.6, 30.3, 29.5, 28.5, 28.4, 26.8, 24.5, 24.4, 24.1, 23.5, 14.2, 14.1; HRMS (ESI) calcd for $C_{25}H_{38}N_3O_6$ (M+H) 476.2682, found 475.2684.



Tert-butyl 2-(2-(1-((benzhydryloxy)amino)-2-ethoxy-2-oxoethyl)pyrrolidine-1-carbonyl)pyrrolidine-1-carboxylate (3z). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 5:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.3:1.0 mixture of diastereomers) δ 7.36 – 7.27 (m, 16H), 7.58 – 7.17 (m, 4H), 6.42 – 6.19 (m, 2H), 5.68 (d, *J* = 7.2 Hz, 1H), 5.64 (d, *J* = 6.5 Hz, 1H), 4.50 – 3.95 (m, 10H), 3.67 – 3.26 (m, 8H), 2.06 – 1.74 (m, 16H), 1.45 (s, 9H), 1.42 (s, 2H), 1.37 (d, *J* = 1.8 Hz, 7H), 1.30 (td, *J* = 7.2, 3.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.3:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of

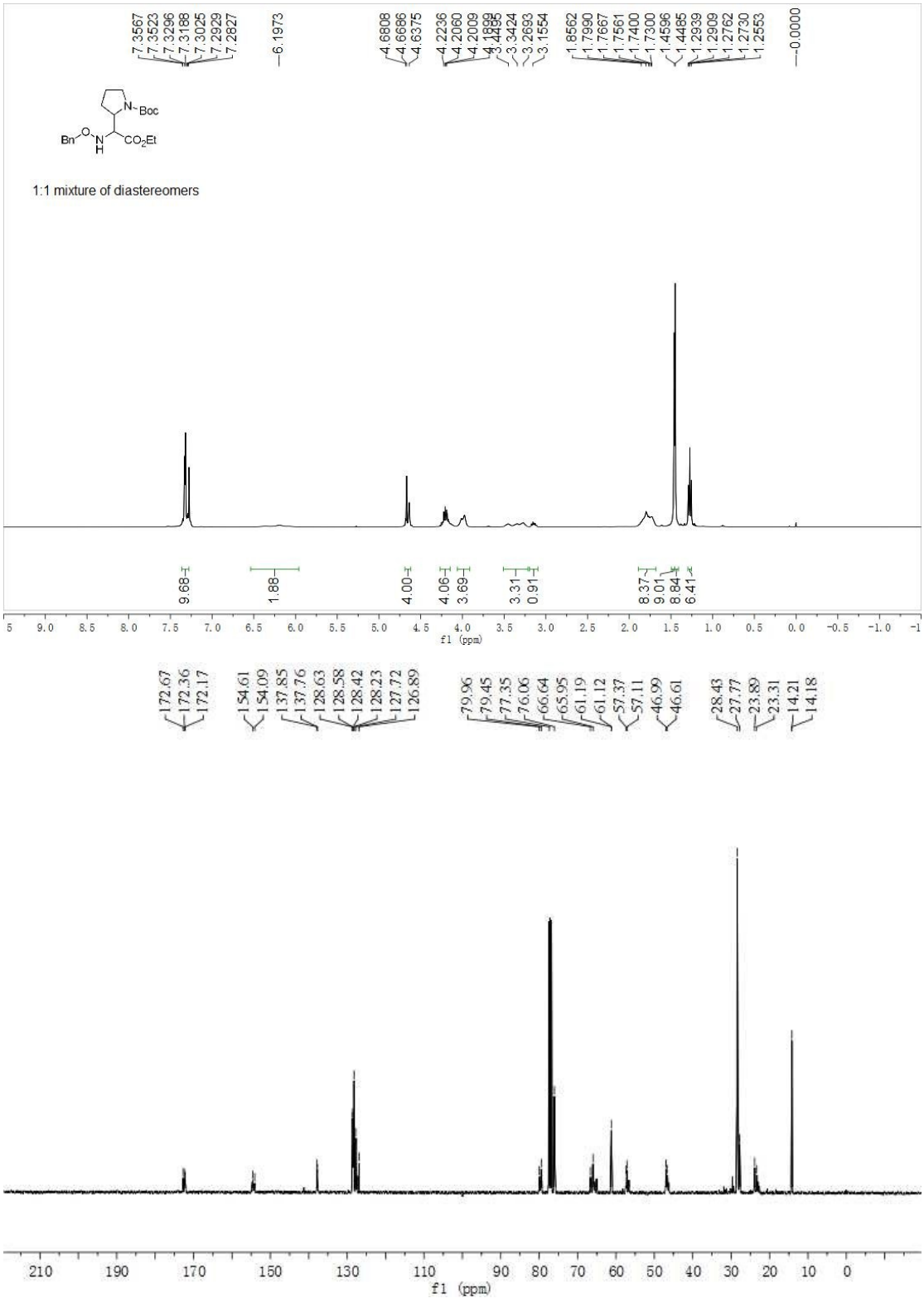
rotamers) δ 172.0, 171.5, 154.5, 141.5, 141.4, 141.3, 128.4, 128.3 (×3), 128.2 (×2), 128.1 (×2), 127.6 (×2), 127.5 (×3), 127.4, 127.1, 127.0 (×2), 86.6 (×2), 79.4, 65.7, 65.5, 61.3, 61.2, 57.7, 57.6, 56.6, 56.1, 46.8, 46.6, 30.3, 29.5, 28.5, 28.4, 27.2, 26.7, 24.4, 24.3, 24.1, 23.5, 14.3 (×2); HRMS (ESI) calcd for $C_{31}H_{42}N_3O_6$ (M+H) 552.2995, found 552.2996.



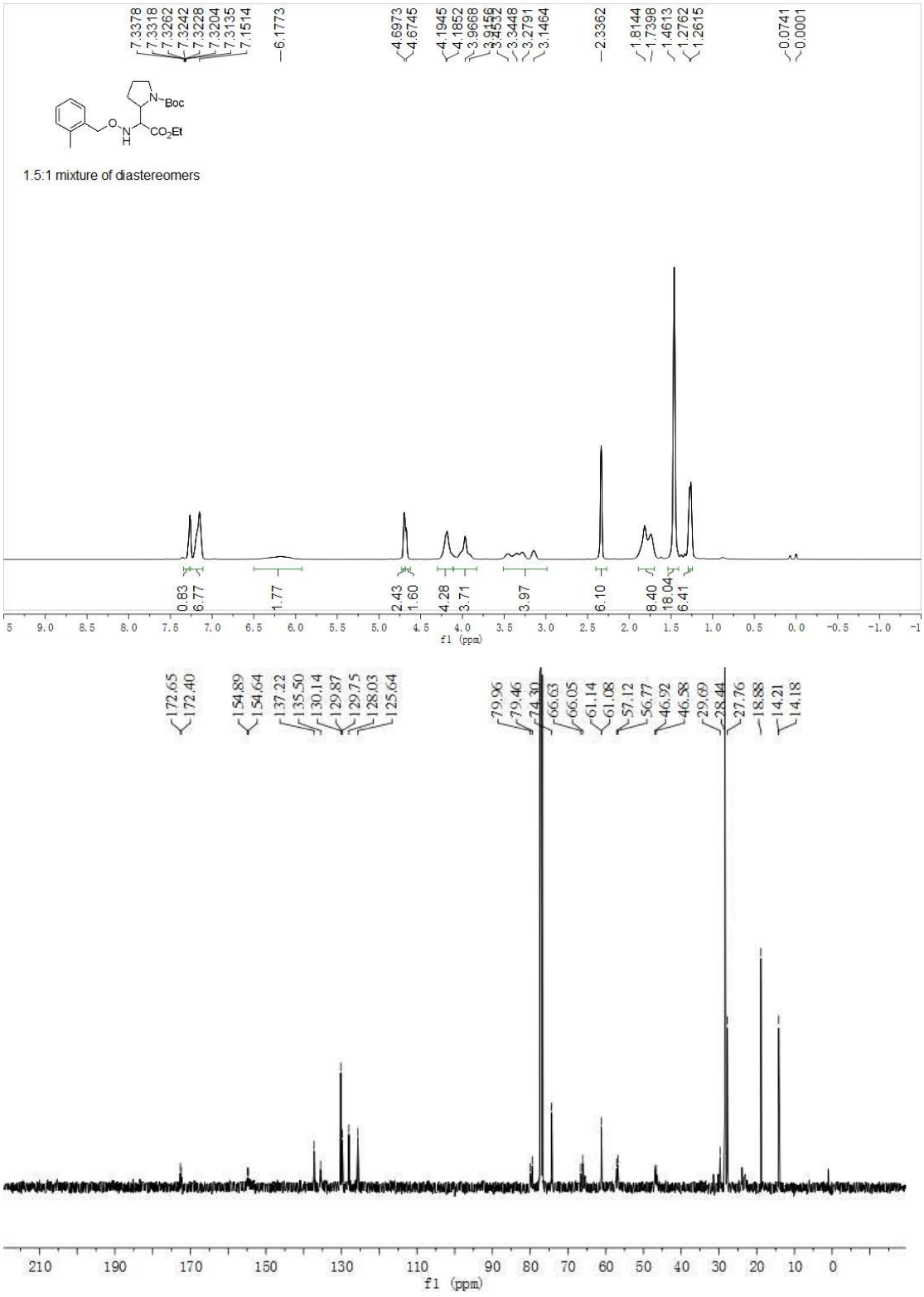
Ethyl 2-((benzhydryloxy)amino)-2-(1-((tert-butoxycarbonyl)glycyl)pyrrolidin-2-yl)acetate (3ab). Isolated by silica gel chromatography (petroleum ether/ethyl acetate = 5:1); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (1.6:1.0 mixture of diastereomers) δ 7.40 – 7.27 (m, 16H), 7.26 – 7.20 (m, 4H), 6.34 (d, *J* = 8.6 Hz, 1H), 6.21 (d, *J* = 8.6 Hz, 1H), 5.66 (d, *J* = 13.7 Hz, 1H), 5.59 (s, 1H), 5.49 – 5.37 (m, 2H), 4.39 – 4.12 (m, 6H), 3.96 – 3.55 (m, 6H), 3.37 – 3.05 (m, 4H), 1.92 – 1.64 (m, 8H), 1.44 (s, 18H), 1.29 (t, *J* = 6.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (1.6:1.0 mixture of diastereomers, each diastereomer exists as 1.0:1.0 mixture of rotamers) δ 172.2, 172.1, 167.7, 167.1, 155.8, 141.5, 141.4, 141.3, 128.3 (×2), 128.2 (×2), 127.7, 127.5, 127.1, 127.0, 86.8, 86.7, 79.6, 65.6, 61.3, 57.3, 57.0, 45.8 (×2), 43.2, 28.4, 24.0, 18.4, 14.2; HRMS (ESI) calcd for $C_{28}H_{38}N_3O_6$ (M+H) 512.2682, found 512.2684.

5. NMR Spectra of Products

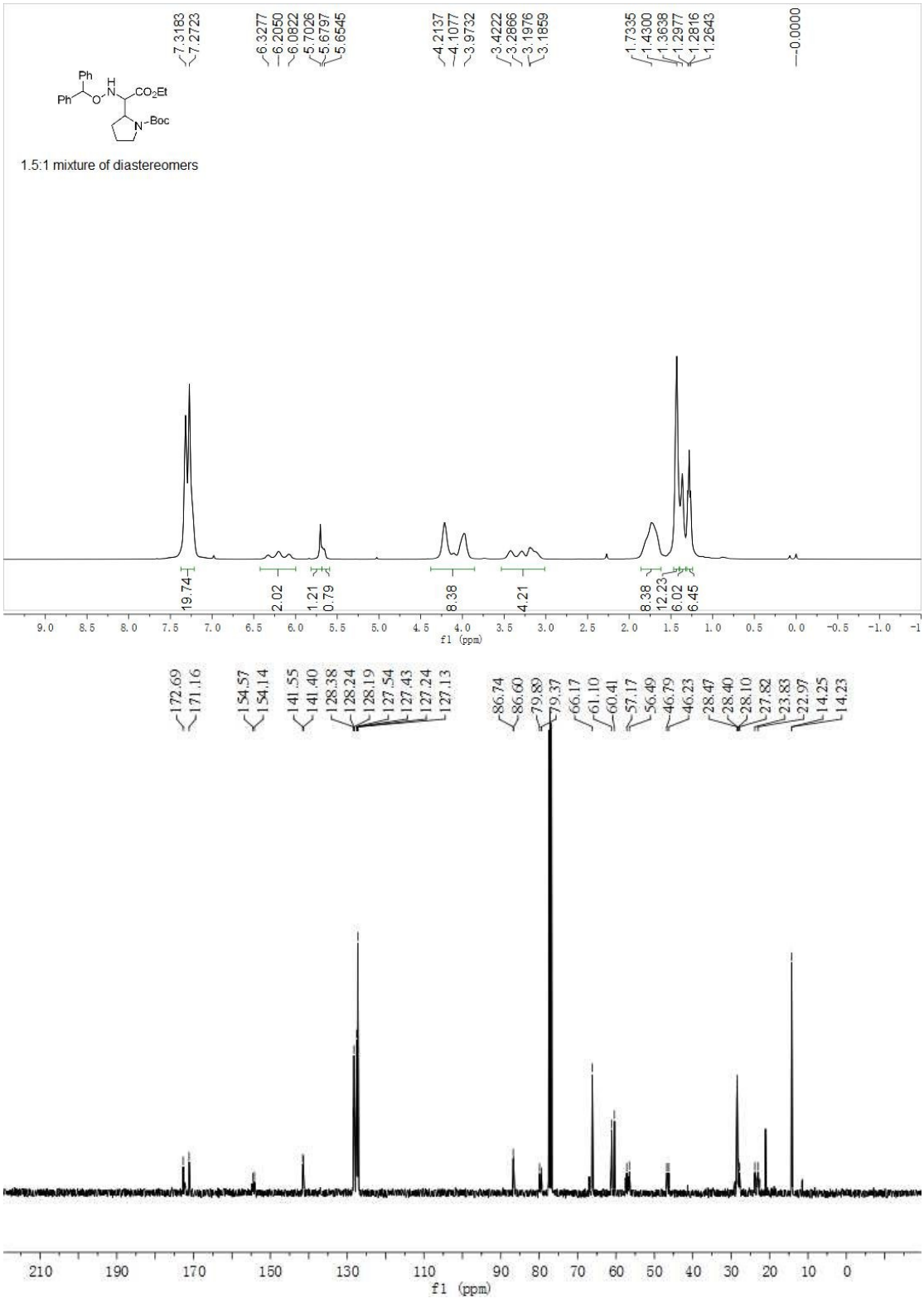
Tert-butyl 2-(1-((benzyloxy)amino)-2-ethoxy-2-oxoethyl) pyrrolidine-1-carboxylate (3a).



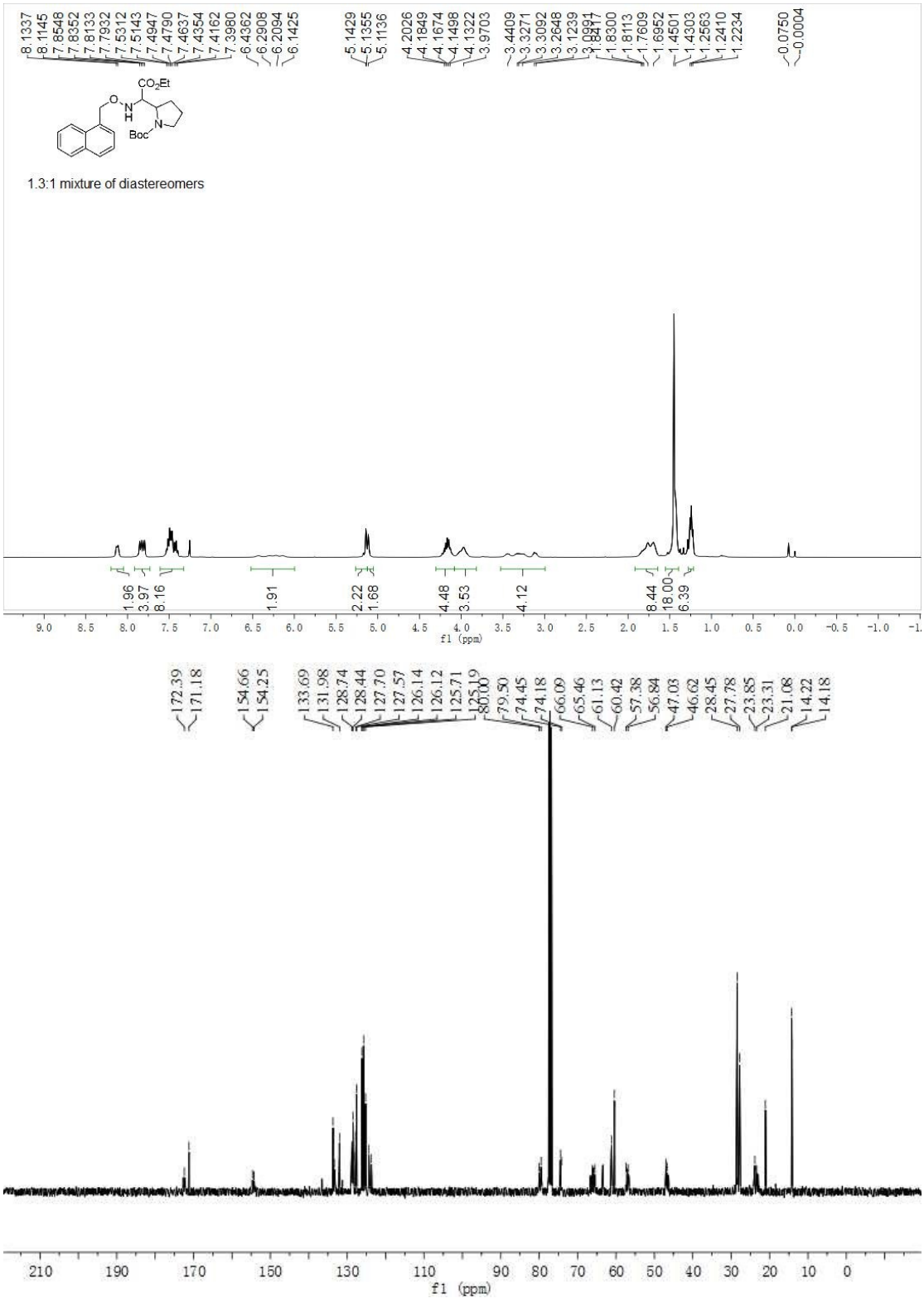
Tert-butyl 2-(2-ethoxy-1-(((2-methylbenzyl)oxy) amino)-2-oxoethyl) pyrrolidine-1-carboxylate (3b).



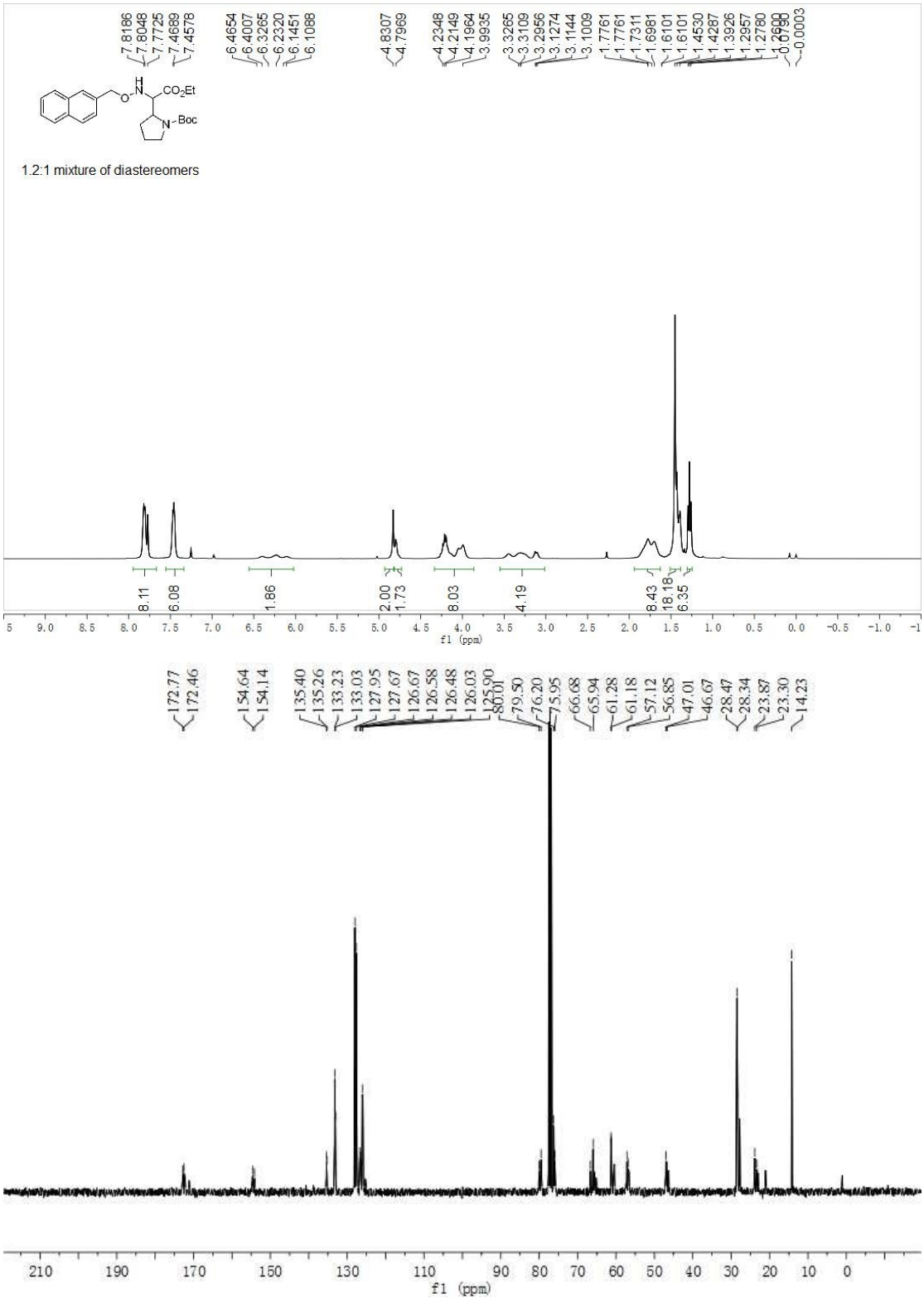
Tert-butyl-2-(1-((benzhydryloxy)amino)-2-ethoxy-2-oxoethyl)pyrrolidine-1-carboxylate (3c)



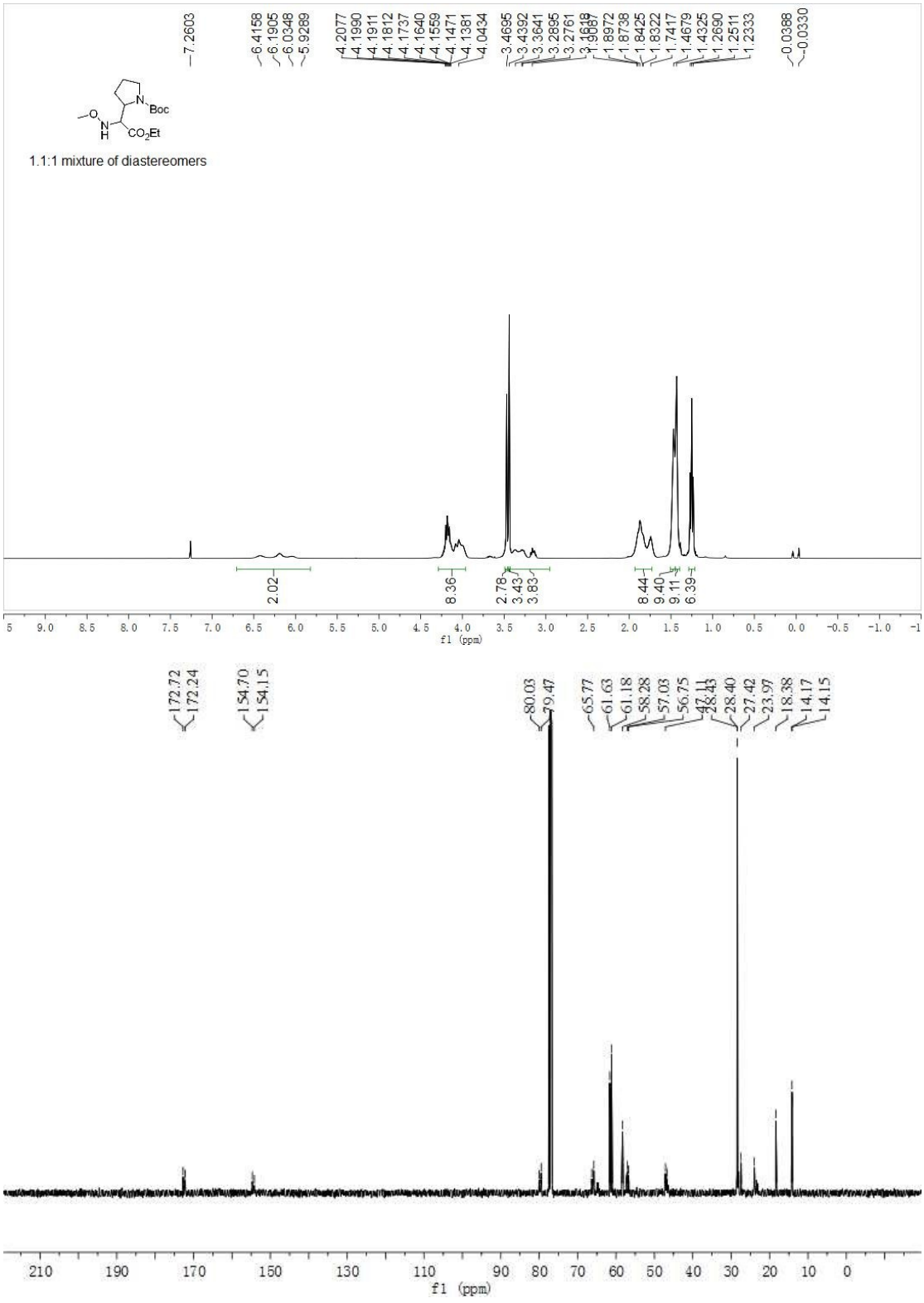
Tert-butyl 2-(2-ethoxy-1-((naphthalen-1-ylmethoxy)amino)-2-oxoethyl)pyrrolidine-1-carboxylate (3d).



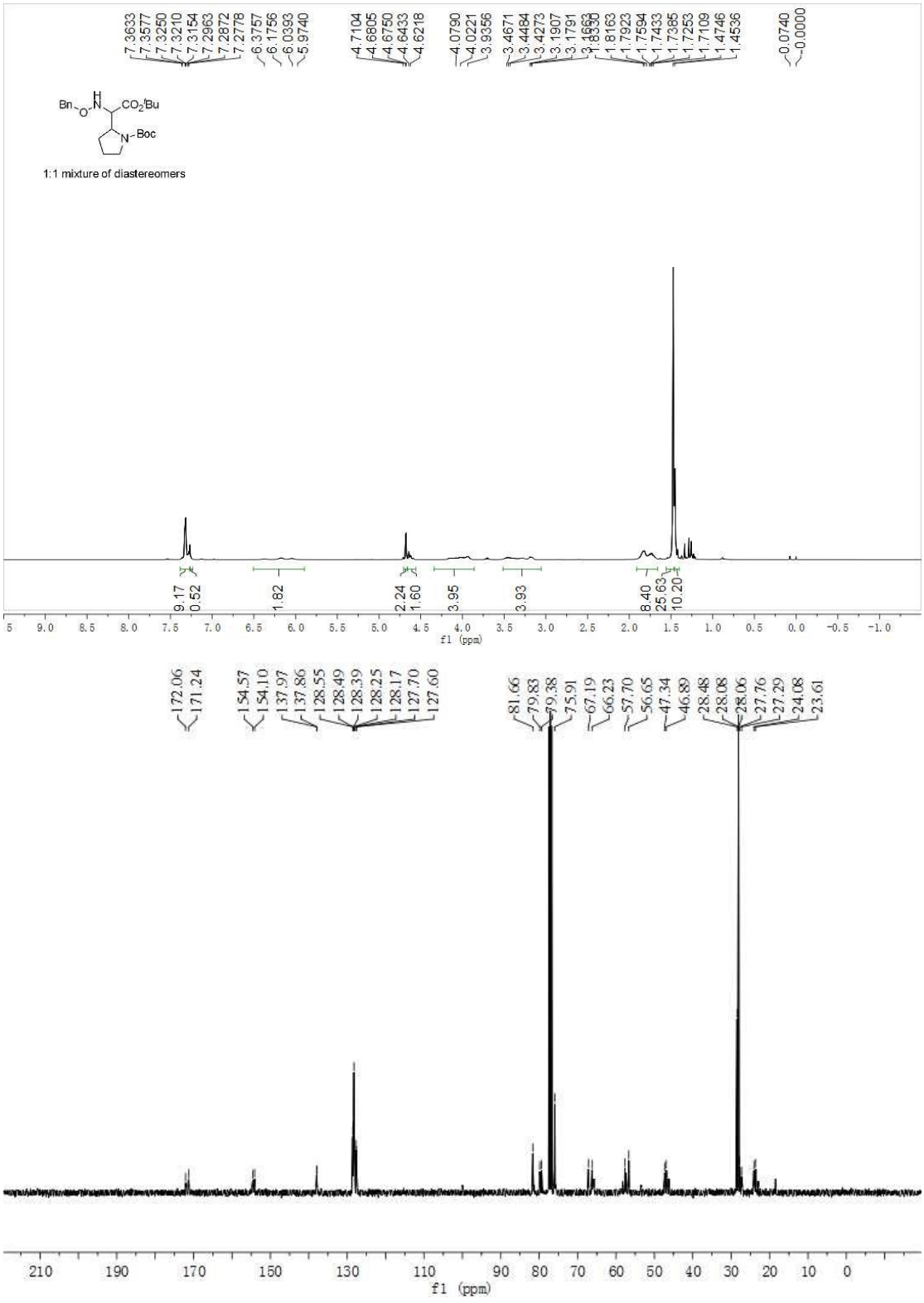
Tert-butyl 2-(2-ethoxy-1-((naphthalen-2-ylmethoxy)amino)-2-oxoethyl)pyrrolidine-1-carboxylate (3e).



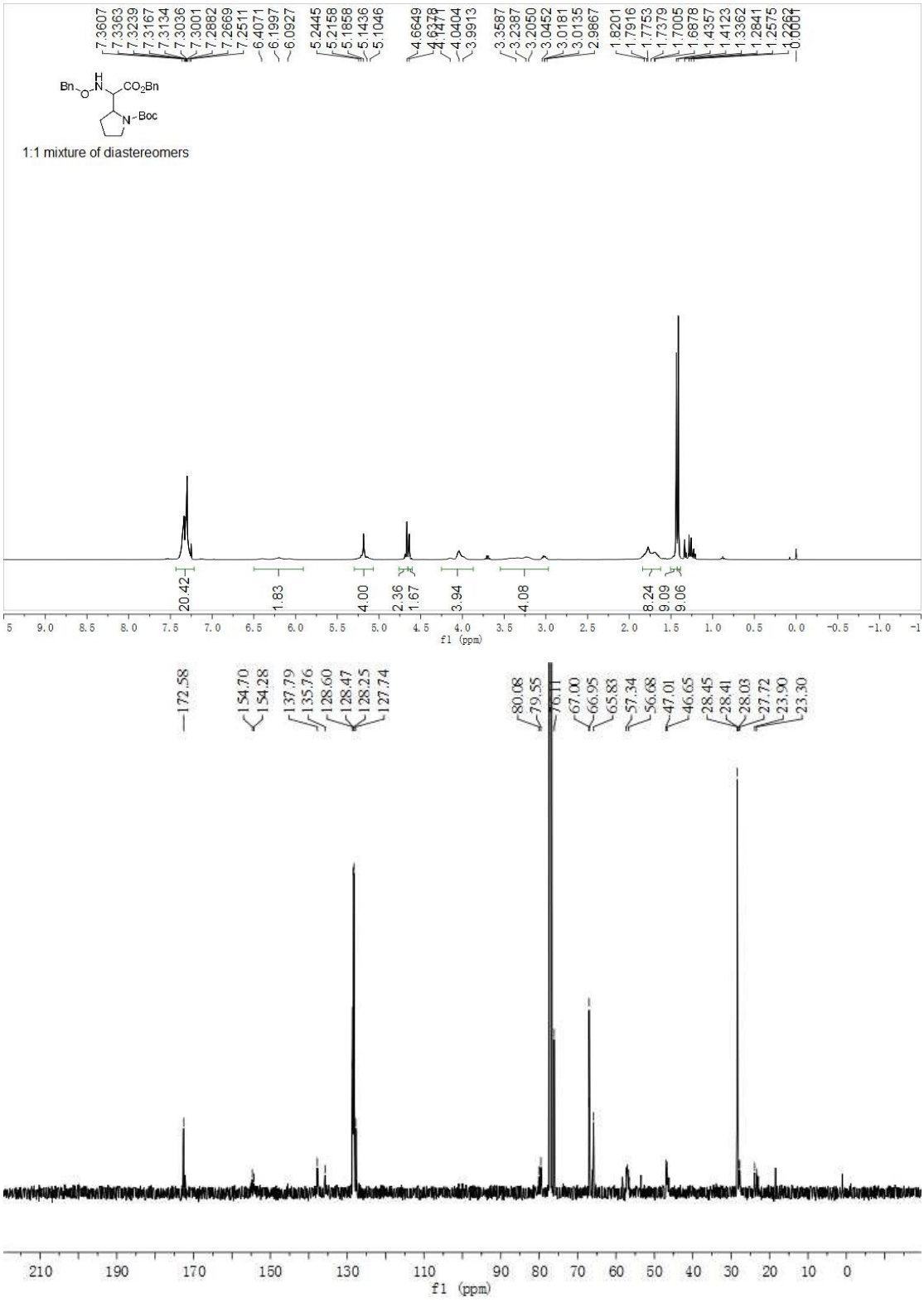
Tert-butyl 2-(2-ethoxy-1-(methoxyamino)-2-oxoethyl)pyrrolidine-1-carboxylate (3f).



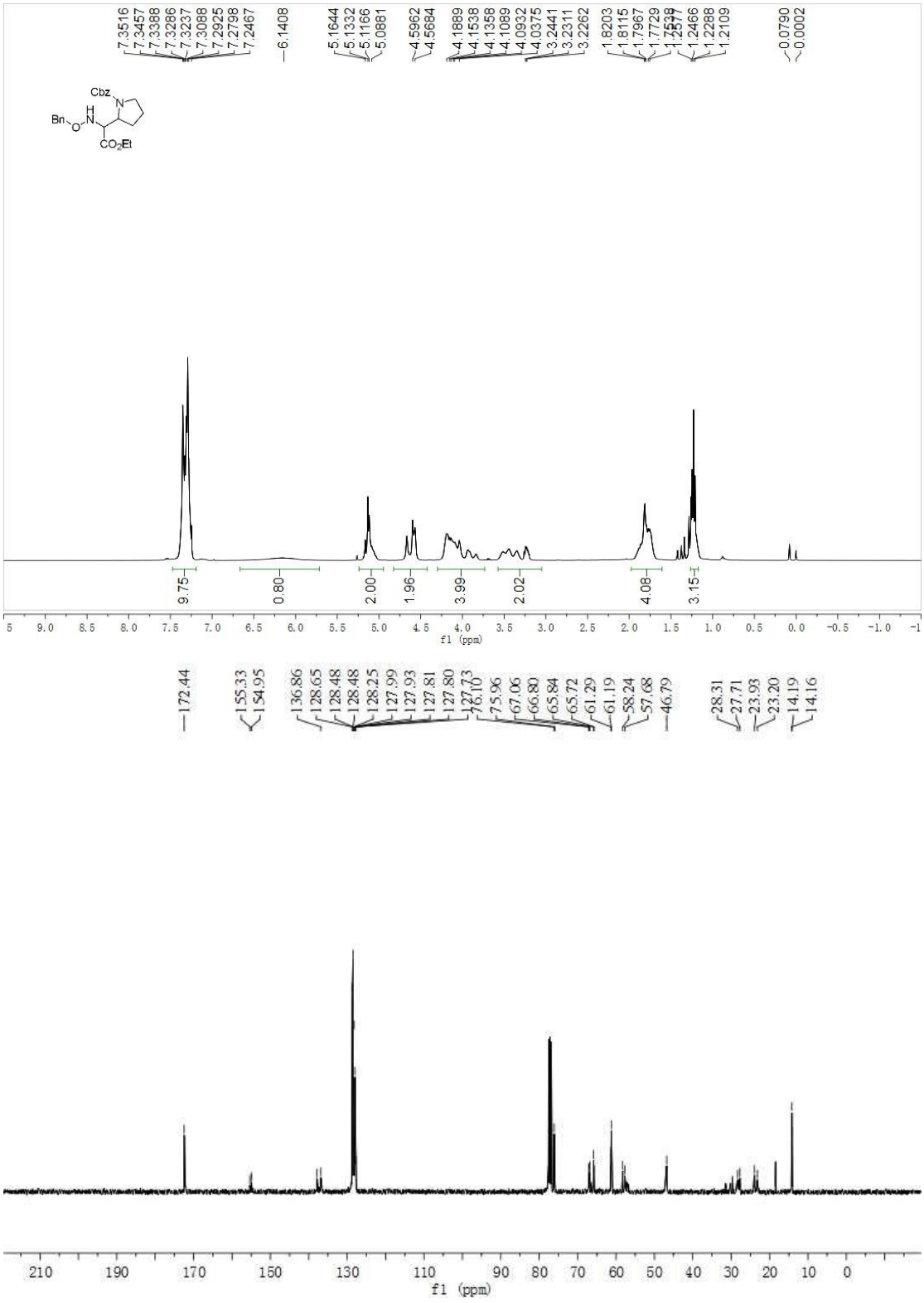
Tert-butyl 2-(1-((benzyloxy)amino)-2-(tert-butoxy)-2-oxoethyl)pyrrolidine-1-carboxylate (3g).



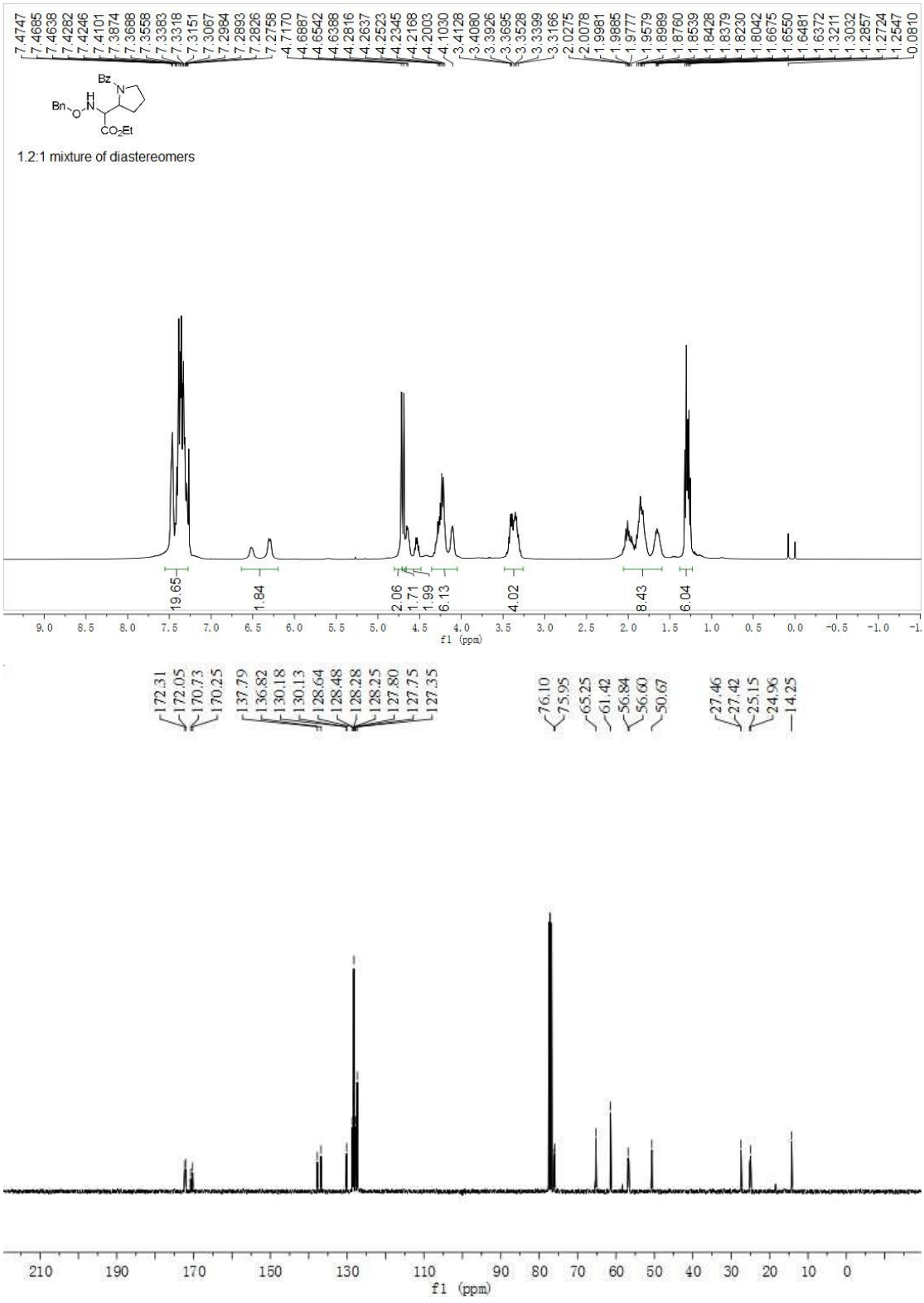
Tert-butyl 2-(2-(benzyloxy)-1-((benzyloxy)amino)-2-oxoethyl)pyrrolidine-1-carboxylate (3h).



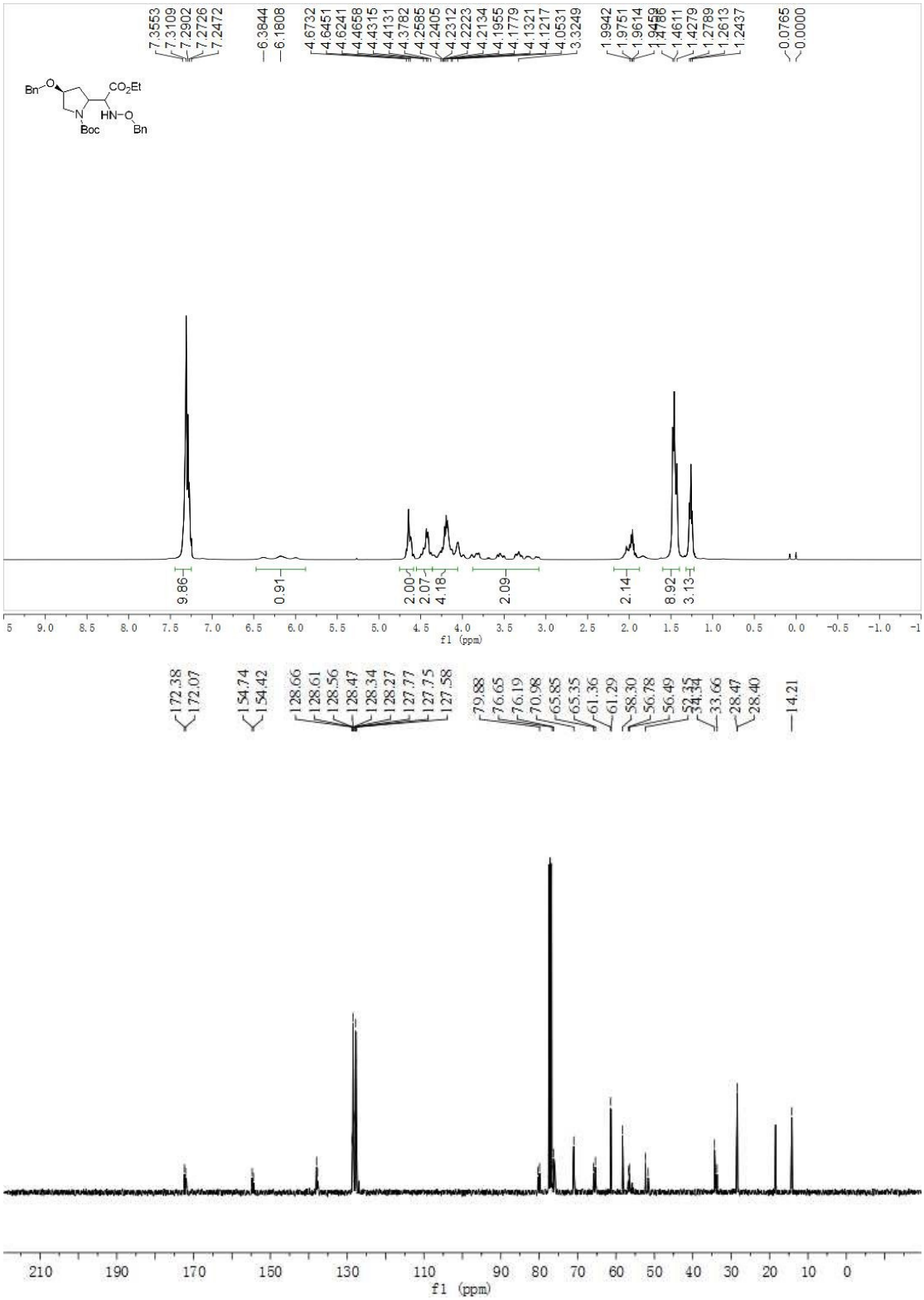
Benzyl 2-(1-((benzyloxy)amino)-2-ethoxy-2-oxoethyl)pyrrolidine-1-carboxylate (3i).



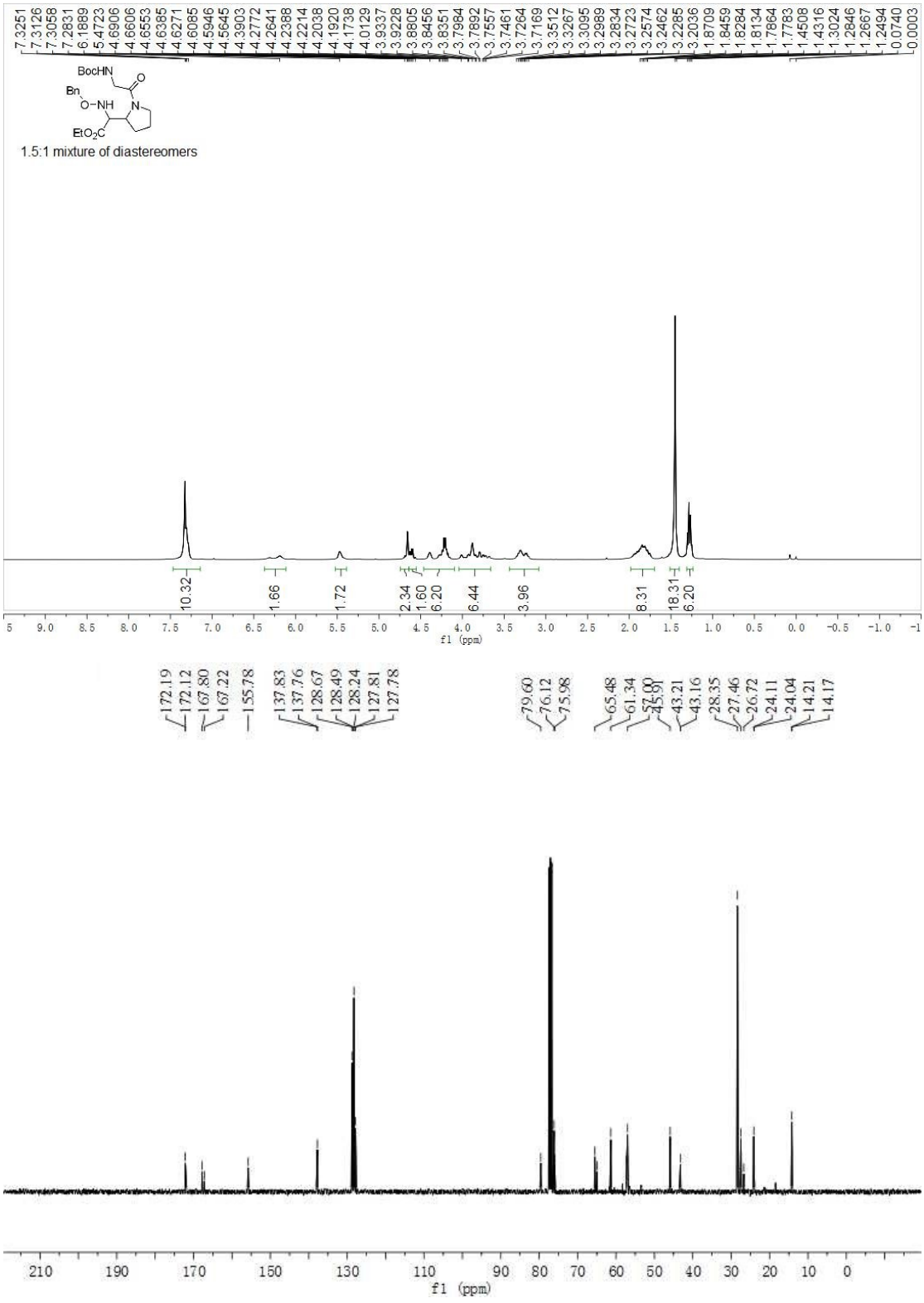
Ethyl 2-(1-benzoylpyrrolidin-2-yl)-2-((benzyloxy)amino)acetate (3j).



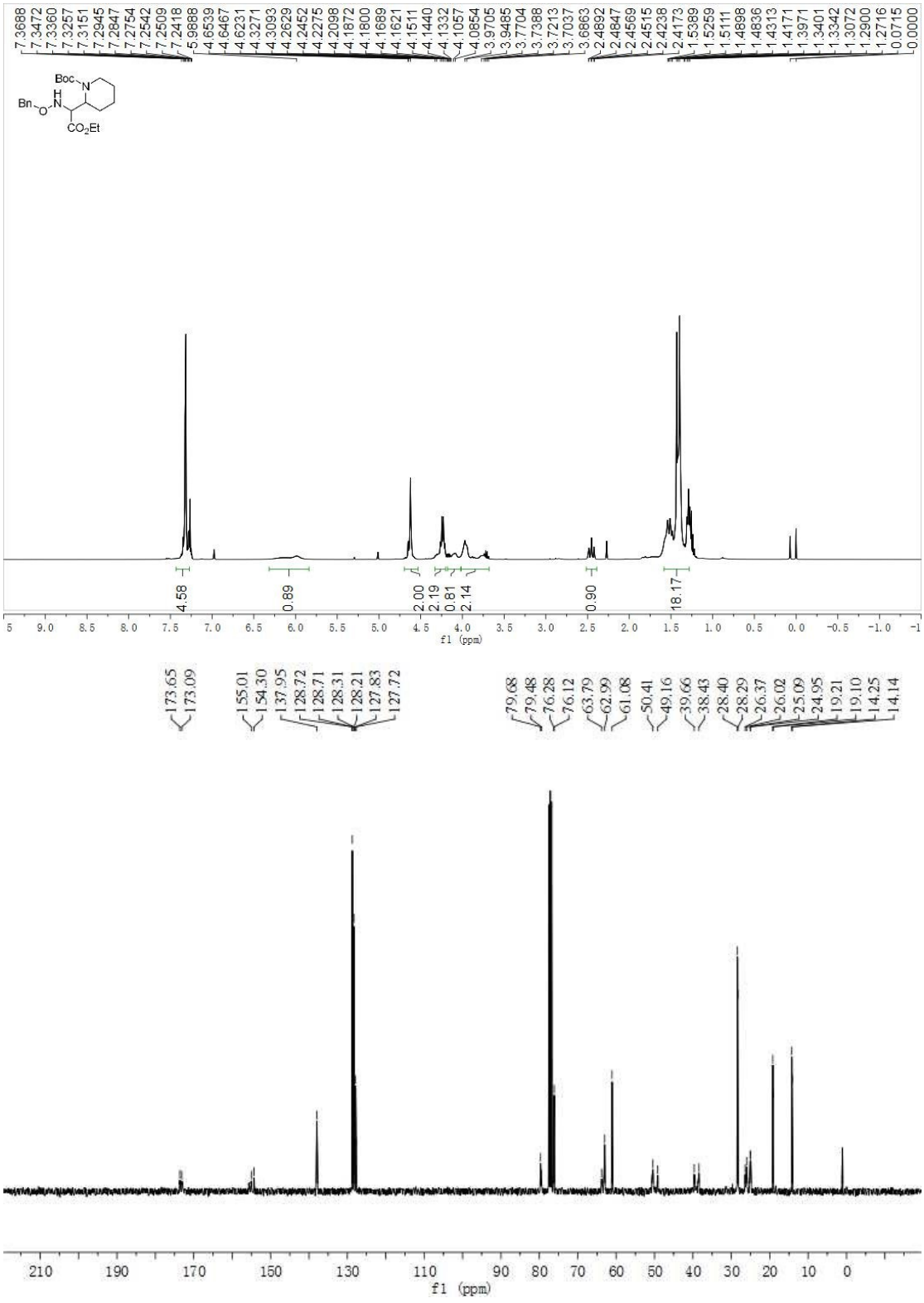
Tert-butyl (4S)-4-(benzyloxy)-2-(1-((benzyloxy)amino)-2-ethoxy-2-oxoethyl)pyrolidine-1-carboxylate (3k).



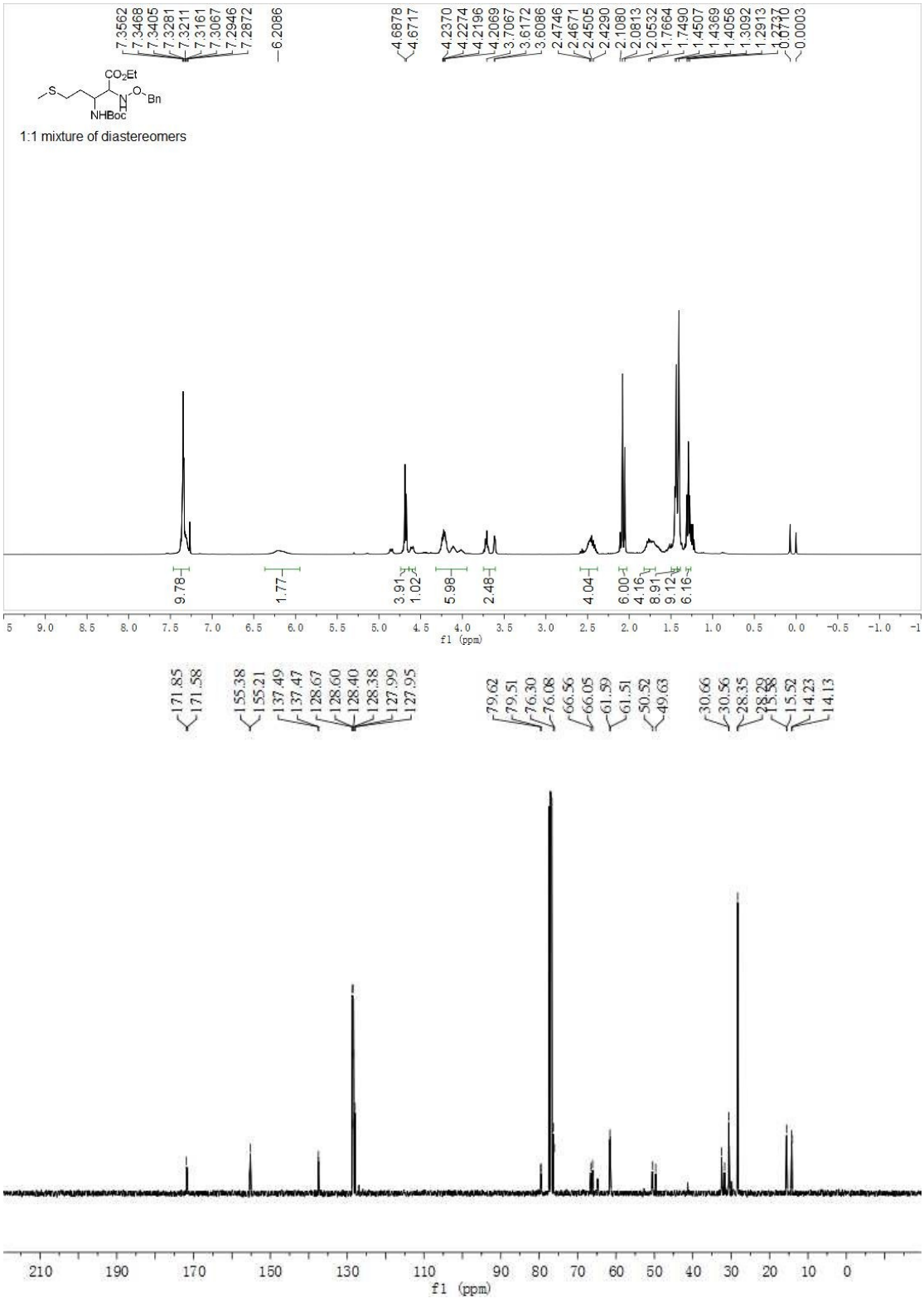
Ethyl 2-((benzyloxy)amino)-2-(1-((tert-butoxycarbonyl)glycyl)pyrrolidin-2-yl)acetate (3l).



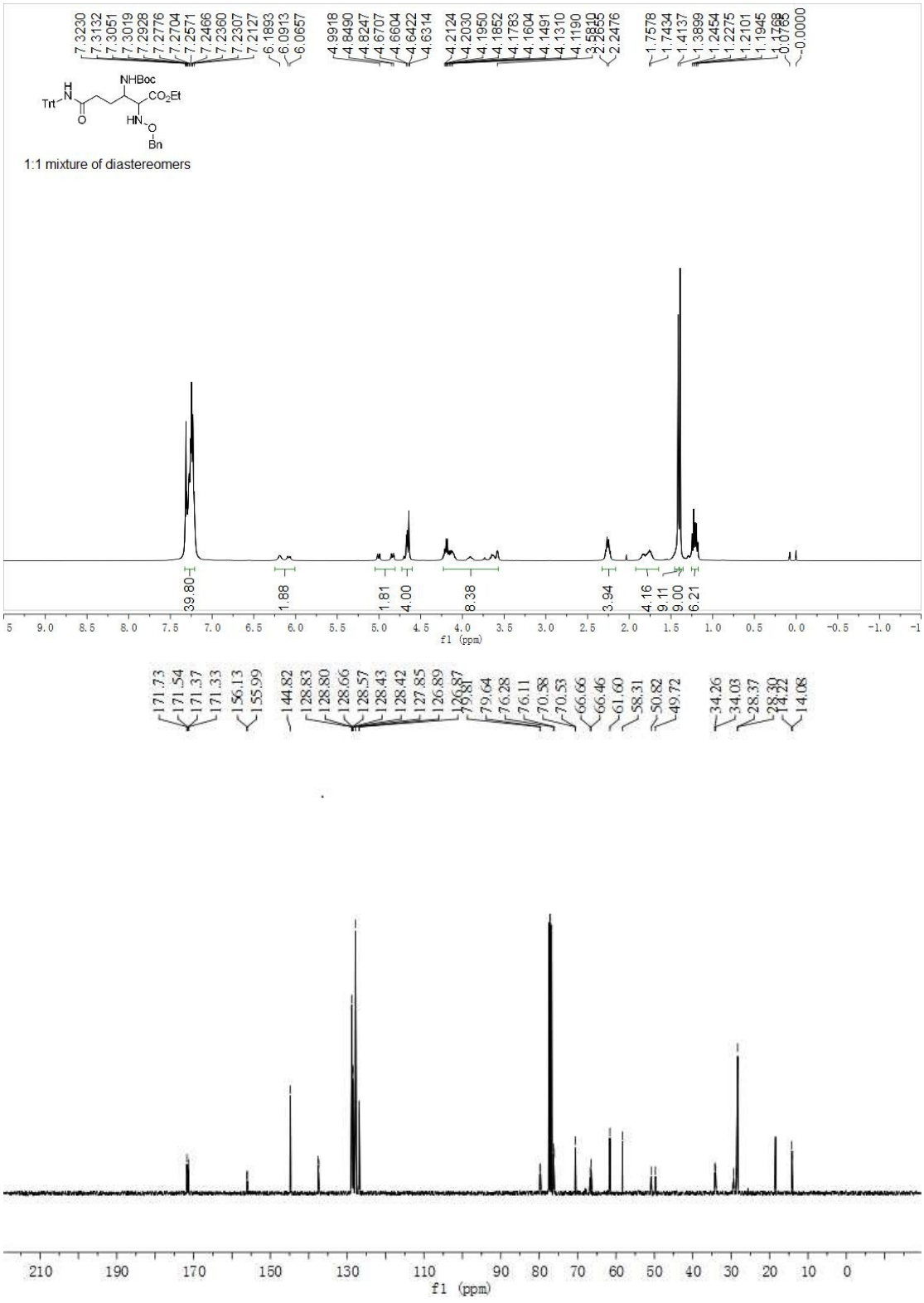
Tert-butyl 2-(1-((benzyloxy)amino)-2-ethoxy-2-oxoethyl)piperidine-1-carboxylate (3m).



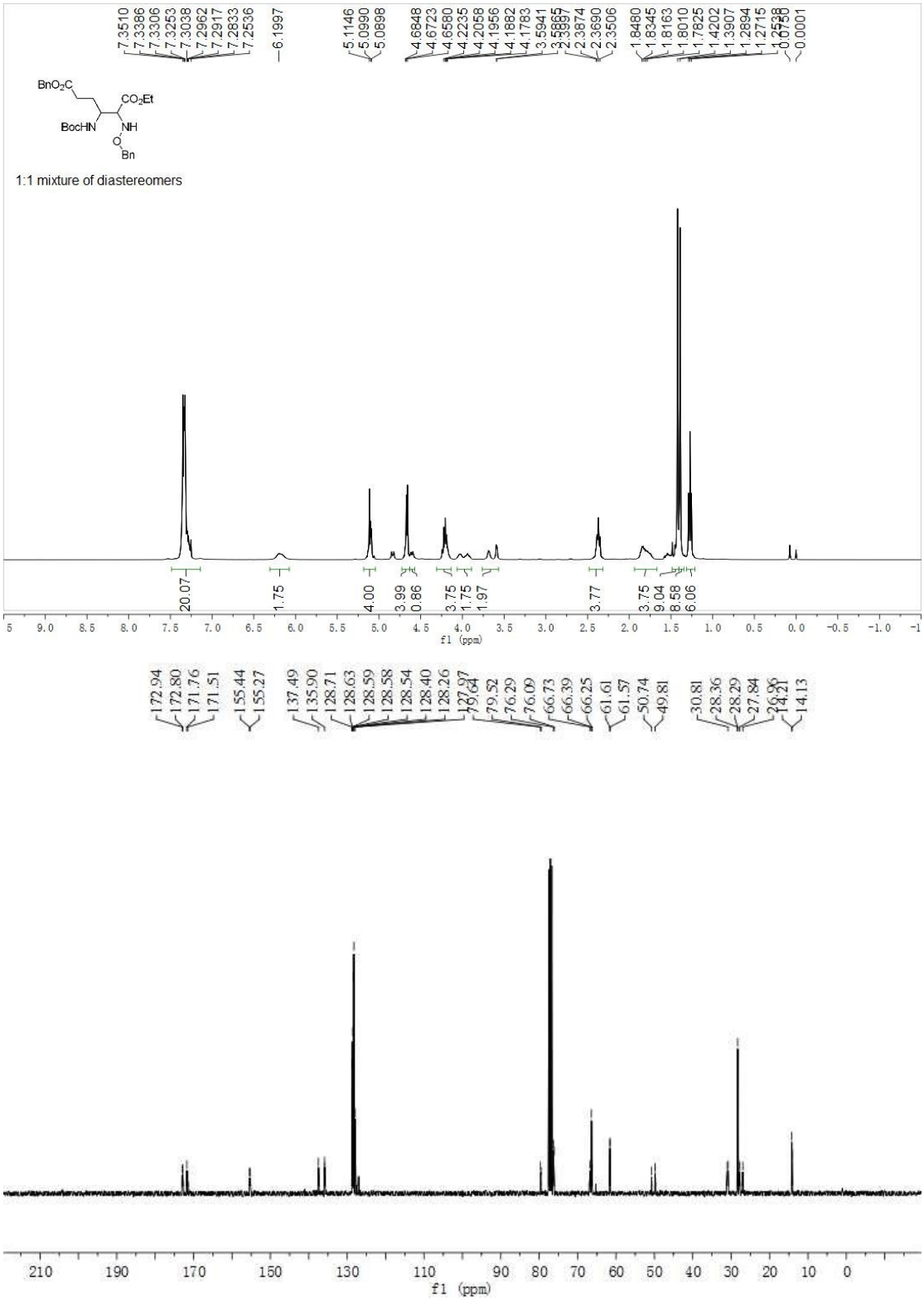
Ethyl 2-((benzyloxy) amino)-3-((tert-butoxycarbonyl) amino)-5-(methylthio) pentanoate (3n).



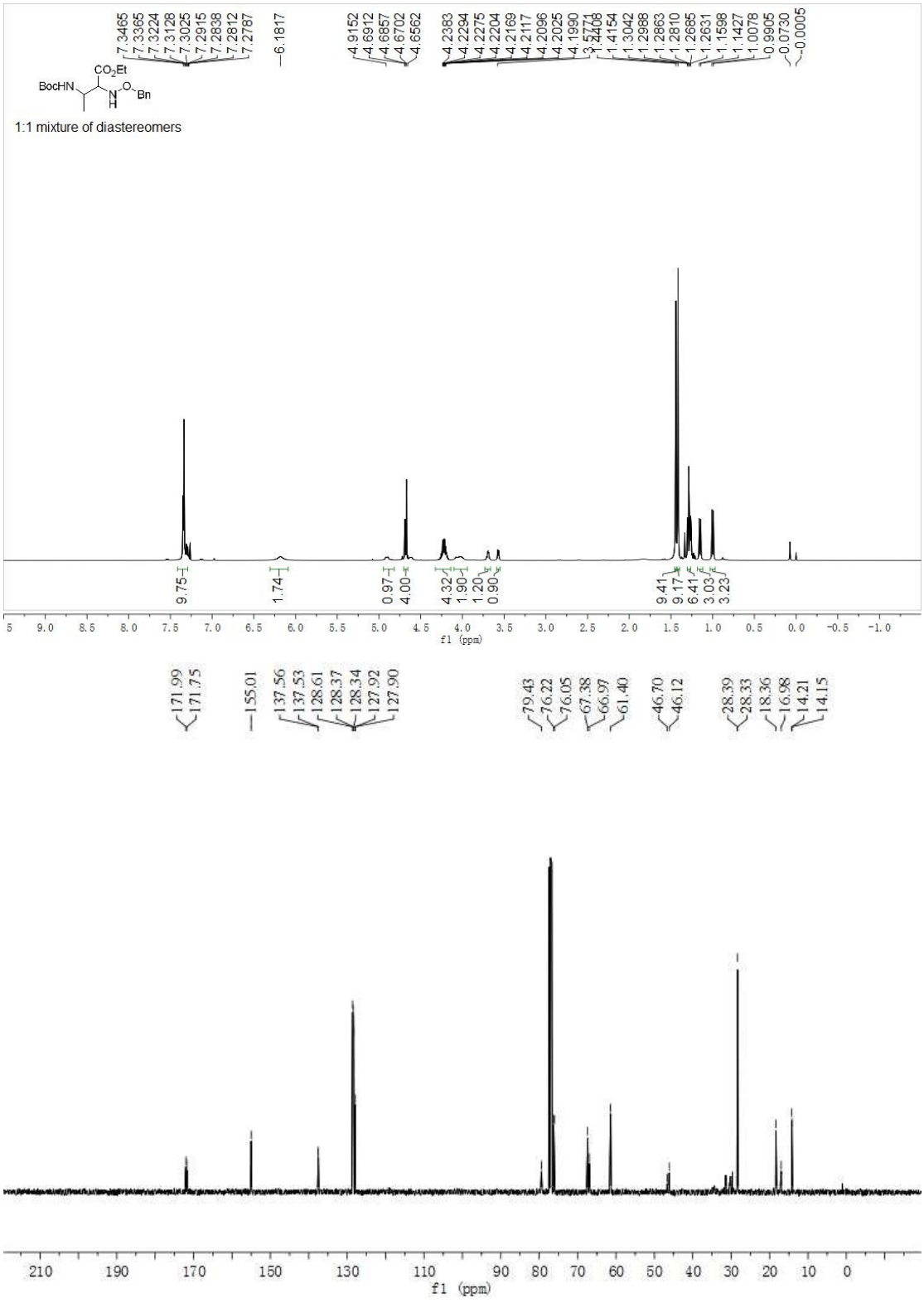
Ethyl 2-((benzyloxy)amino)-3-((tert-butoxycarbonyl)amino)-6-oxo-6-(tritylamino)hexaneate (3o).



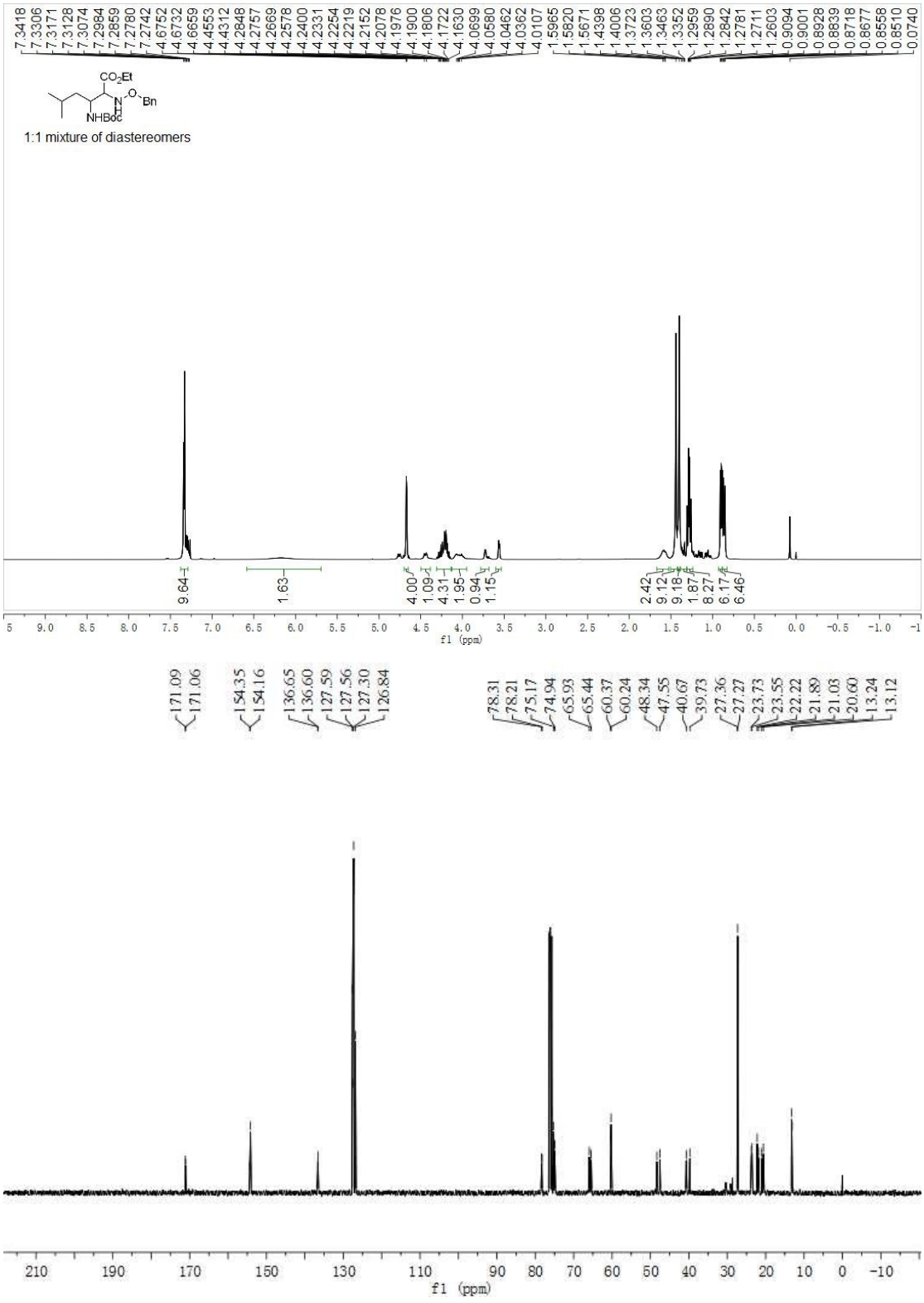
6-benzyl 1-ethyl 2-((benzyloxy)amino)-3-((tert-butoxycarbonyl) amino) hexanedioate (3p).



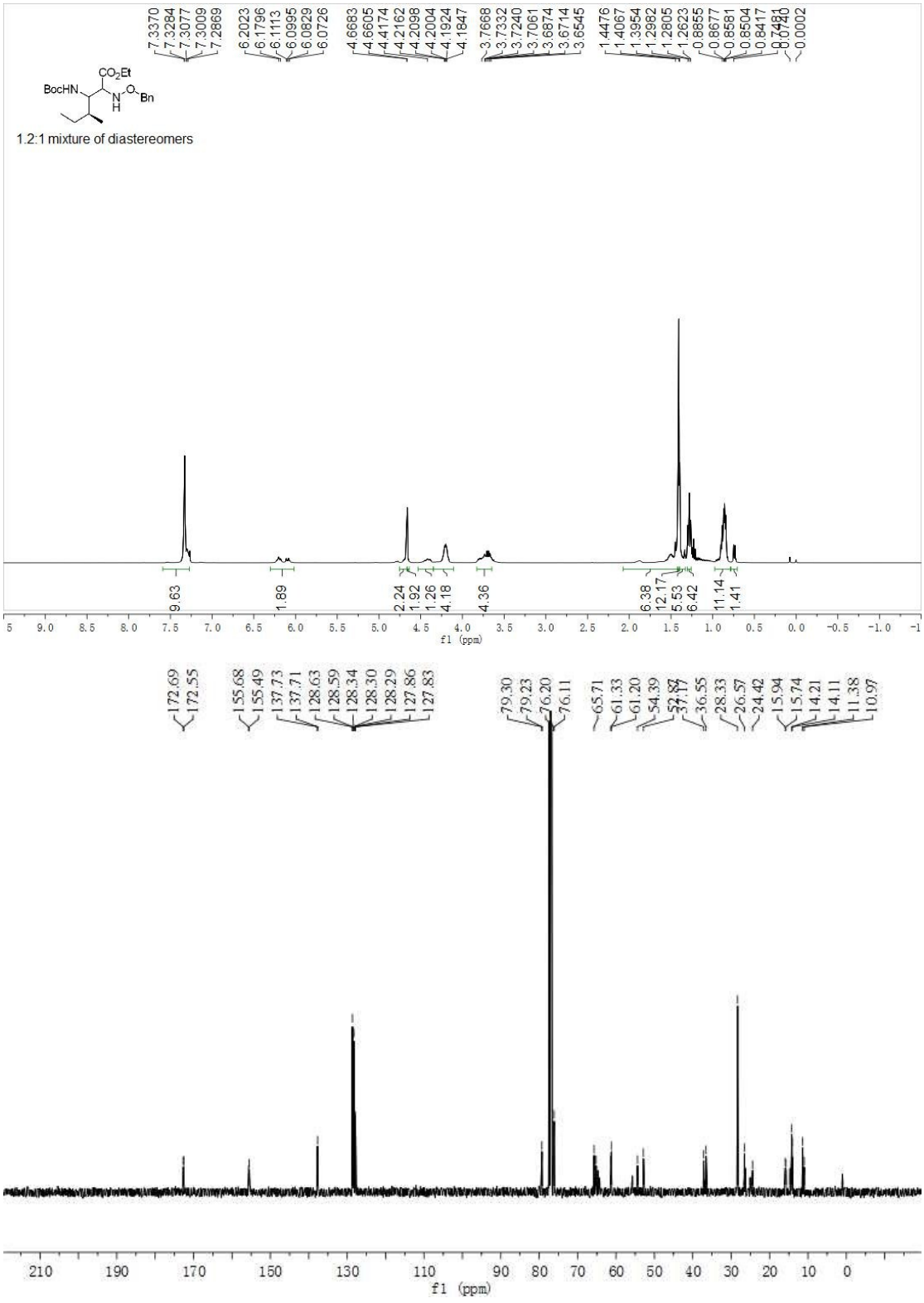
Ethyl 2-((benzyloxy)amino)-3-((tert-butoxycarbonyl)amino)butanoate (3q).



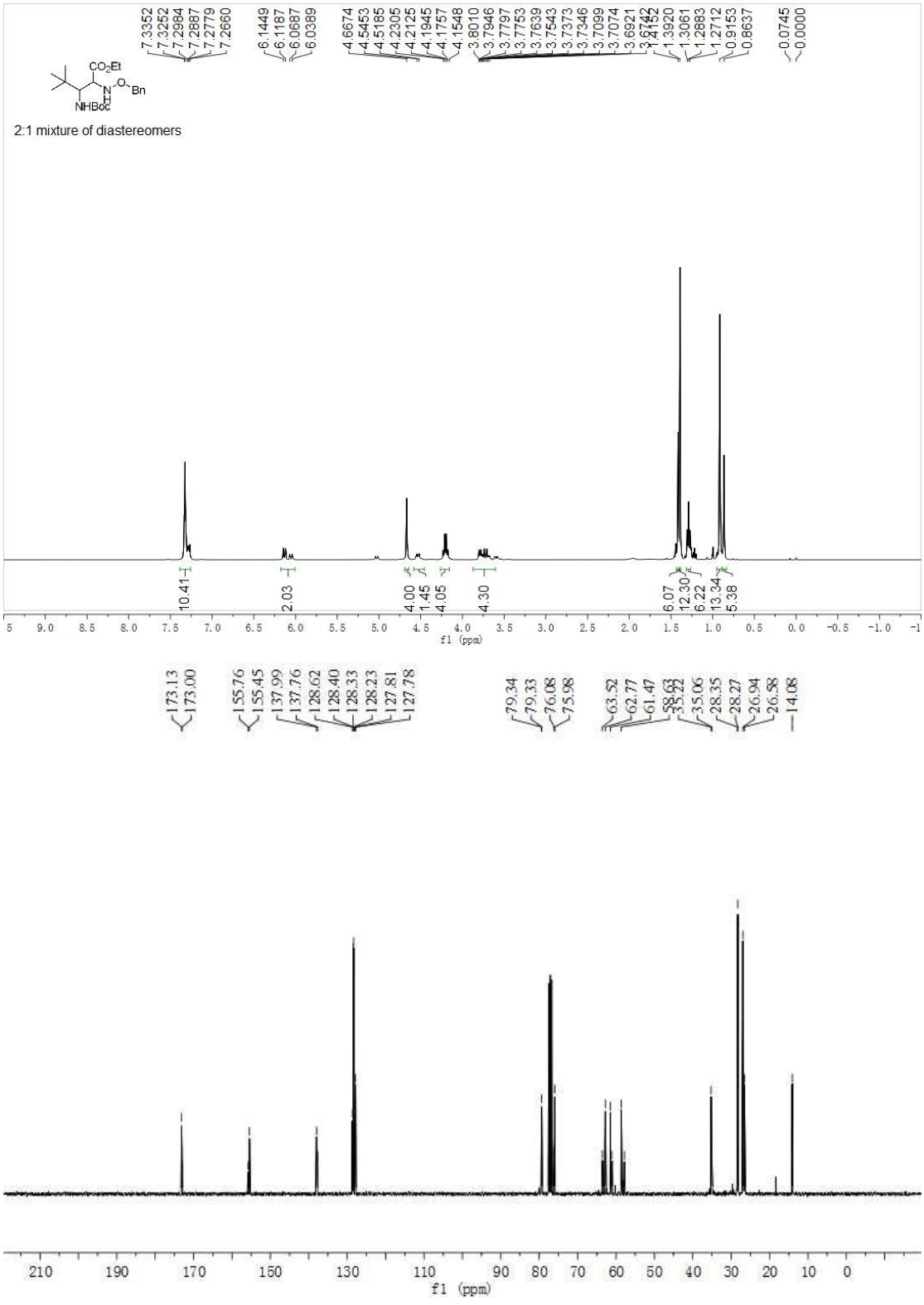
Ethyl 2-((benzyloxy)amino)-3-((tert-butoxycarbonyl)amino)-5-methylhexanoate (3r).



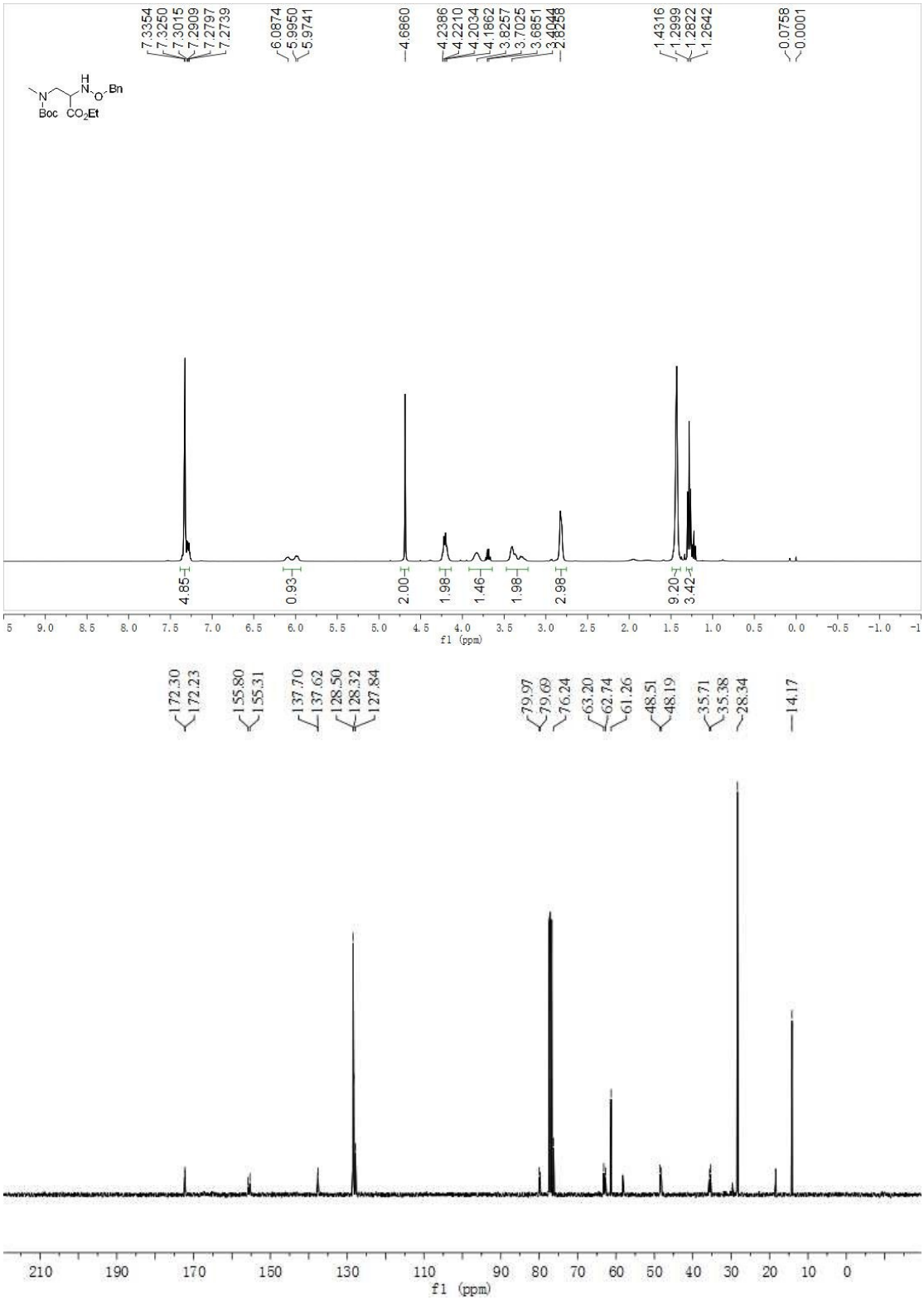
Ethyl (4S)-2-((benzyloxy)amino)-3-((tert-butoxycarbonyl)amino)-4-methylhexanoate (3s).



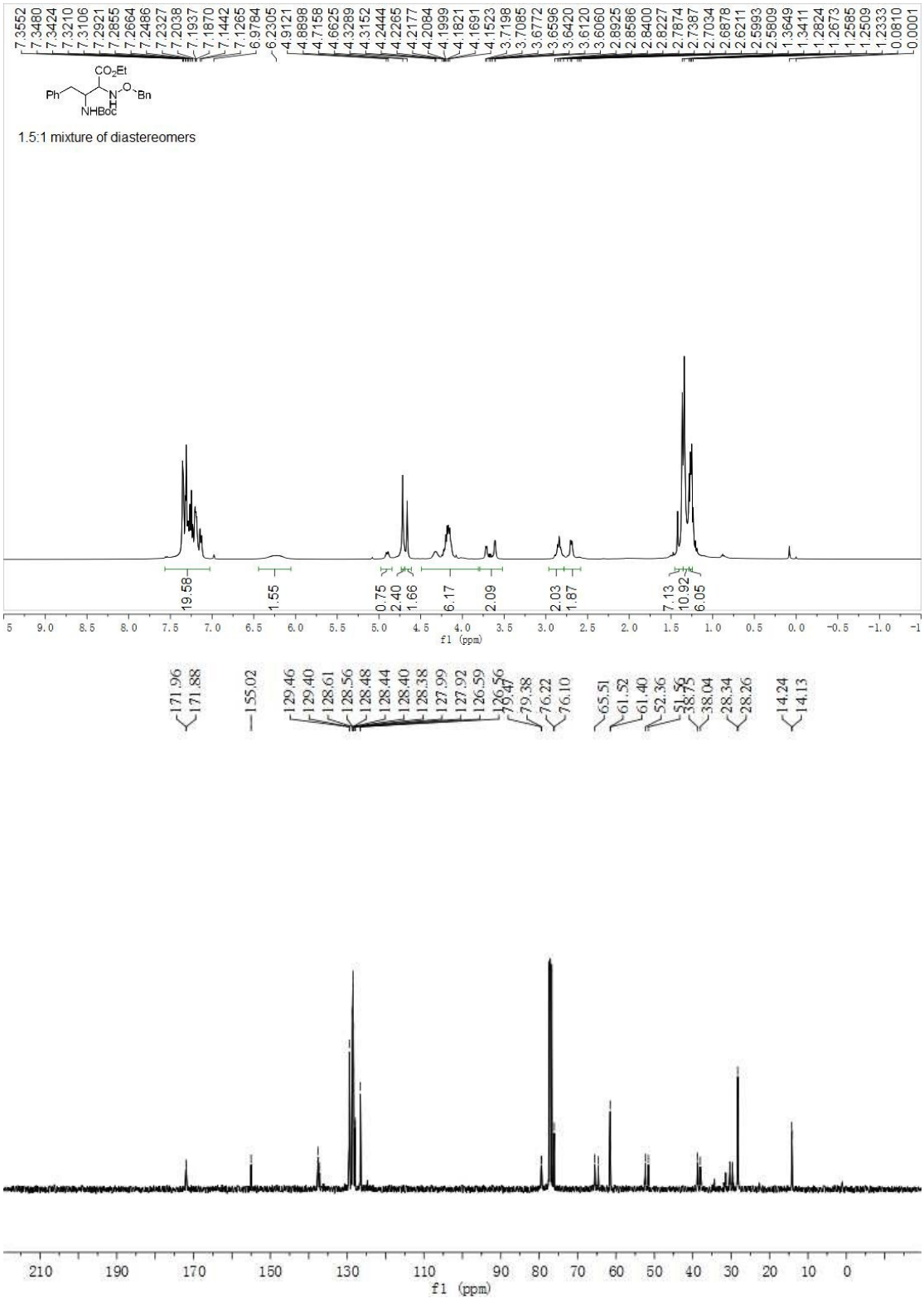
Ethyl 2-((benzyloxy)amino)-3-((tert-butoxycarbonyl)amino)-4,4-dimethylpentanoate (3t).



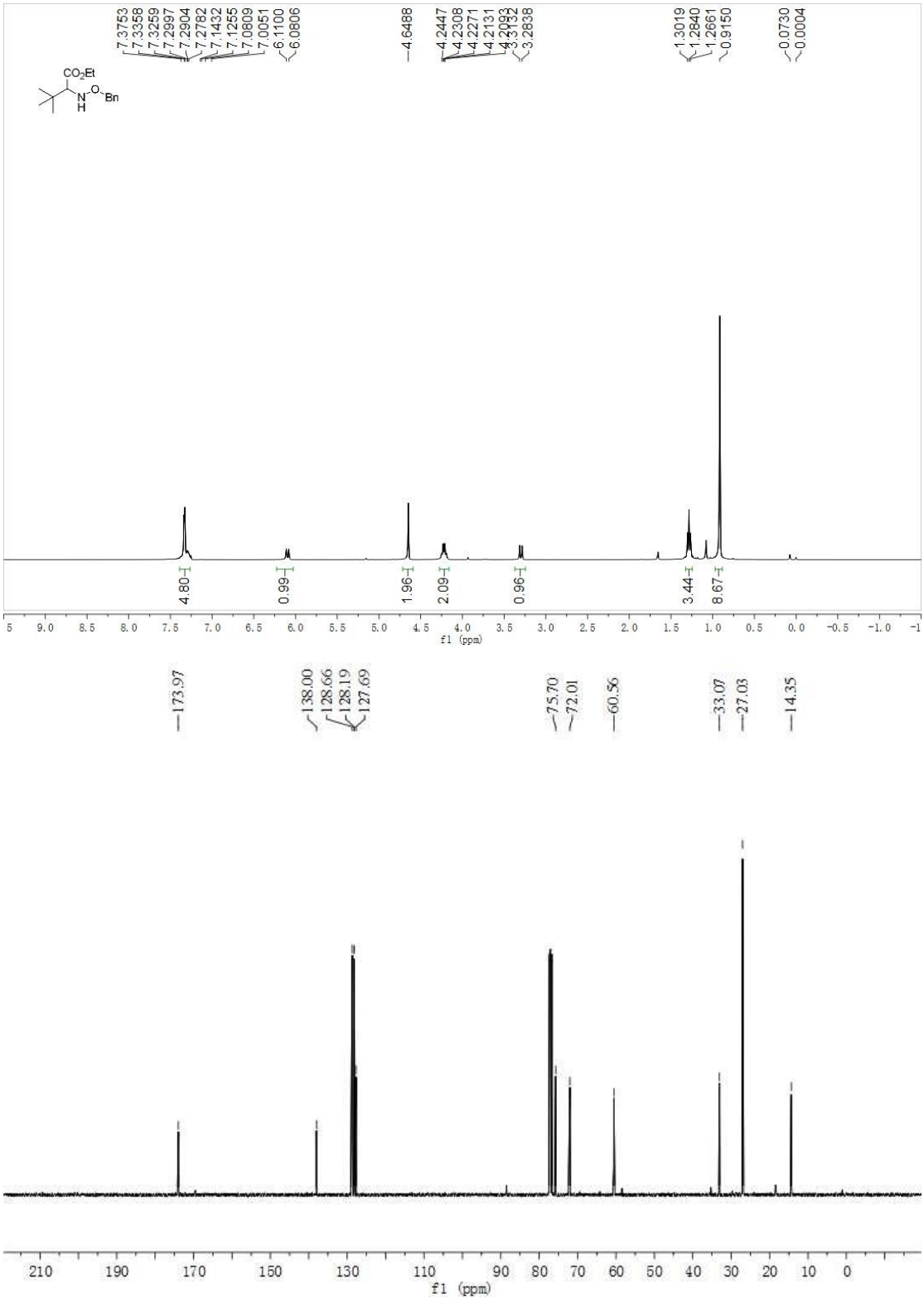
Ethyl 2-((benzyloxy)amino)-3-((tert-butoxycarbonyl)(methyl)amino)propanoate (3u).



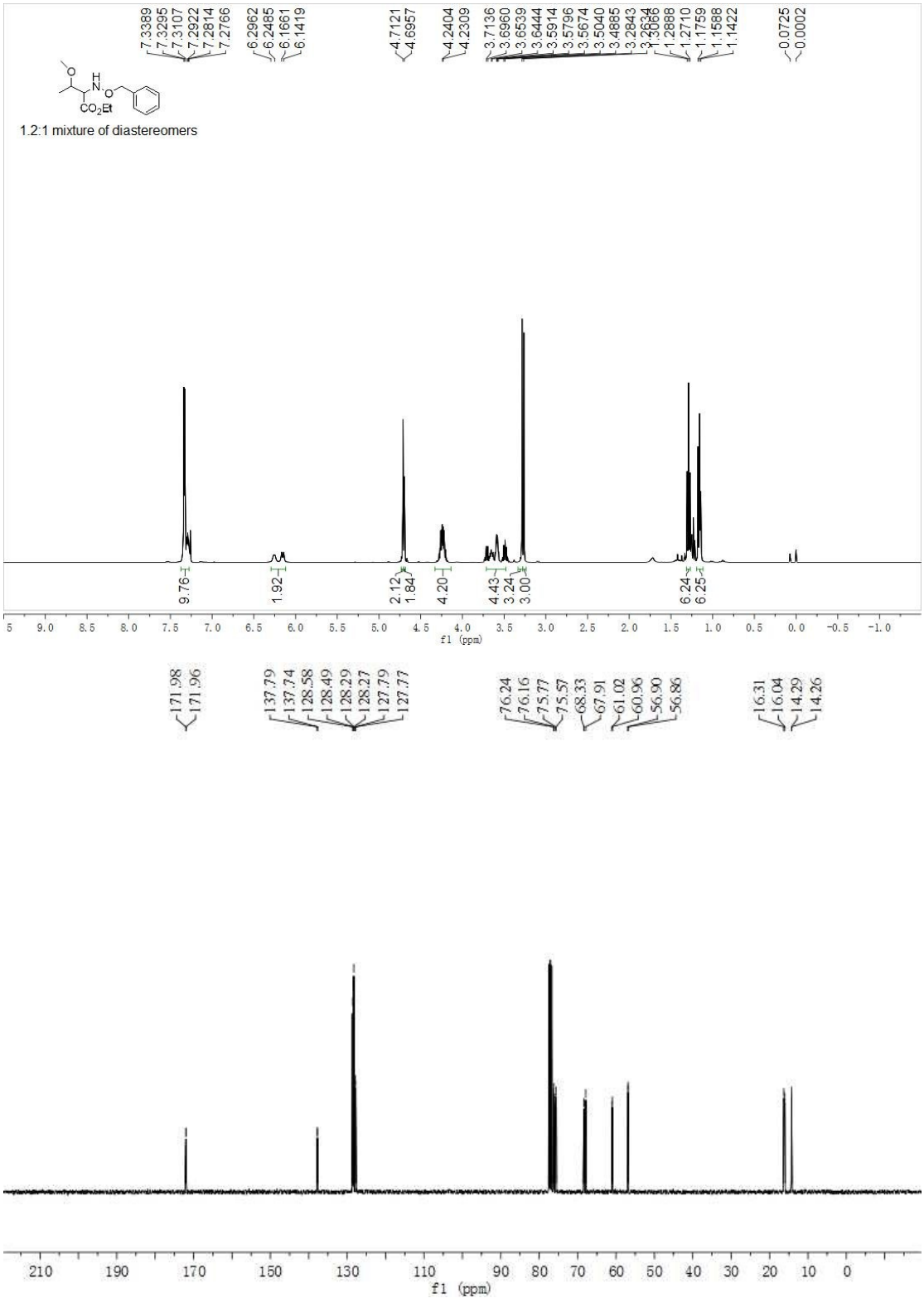
Ethyl 2-((benzyloxy)amino)-3-((tert-butoxycarbonyl)amino)-4-phenylbutanoate (3v).



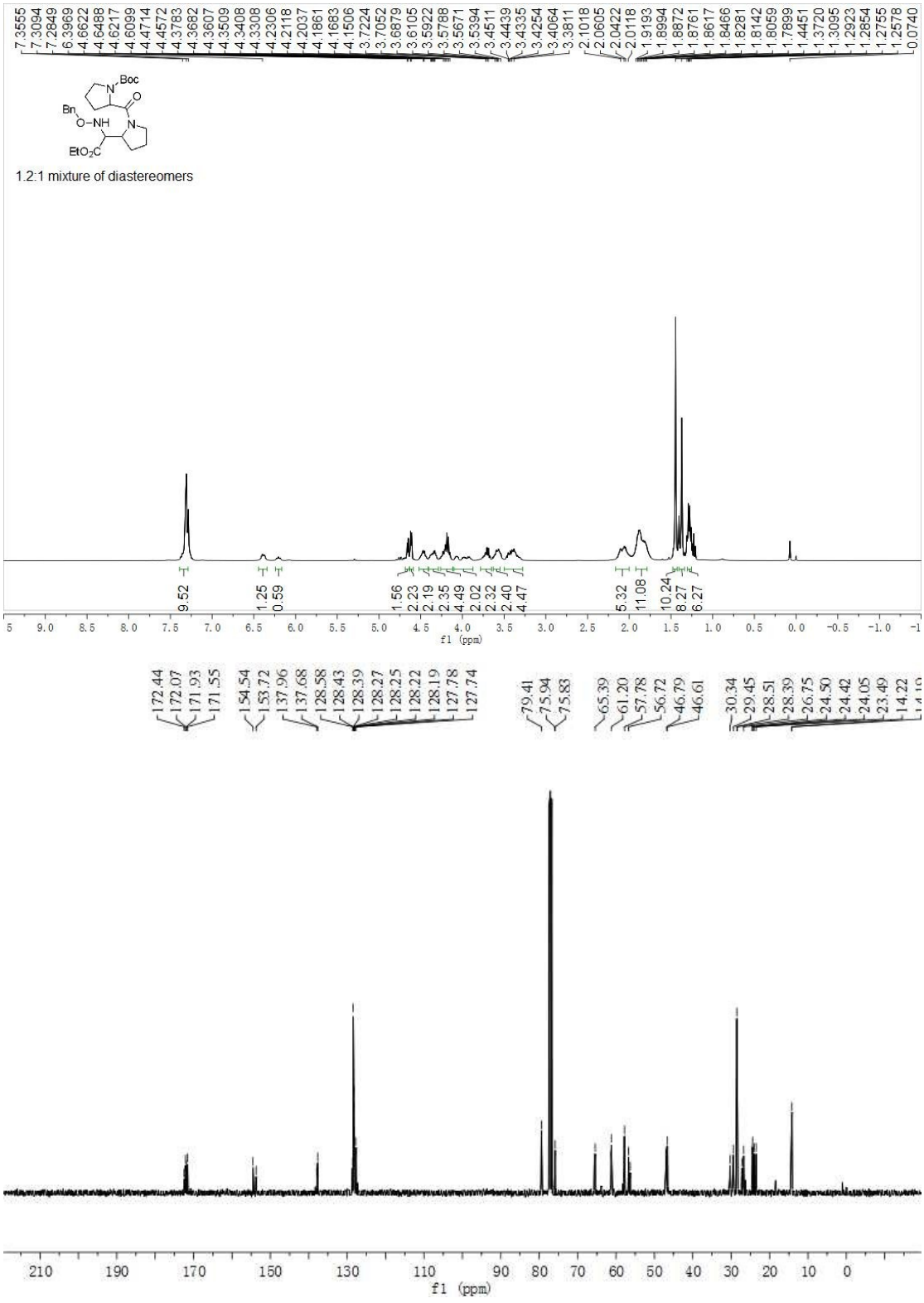
Ethyl 2-((benzyloxy)amino)-3,3-dimethylbutanoate (3w).



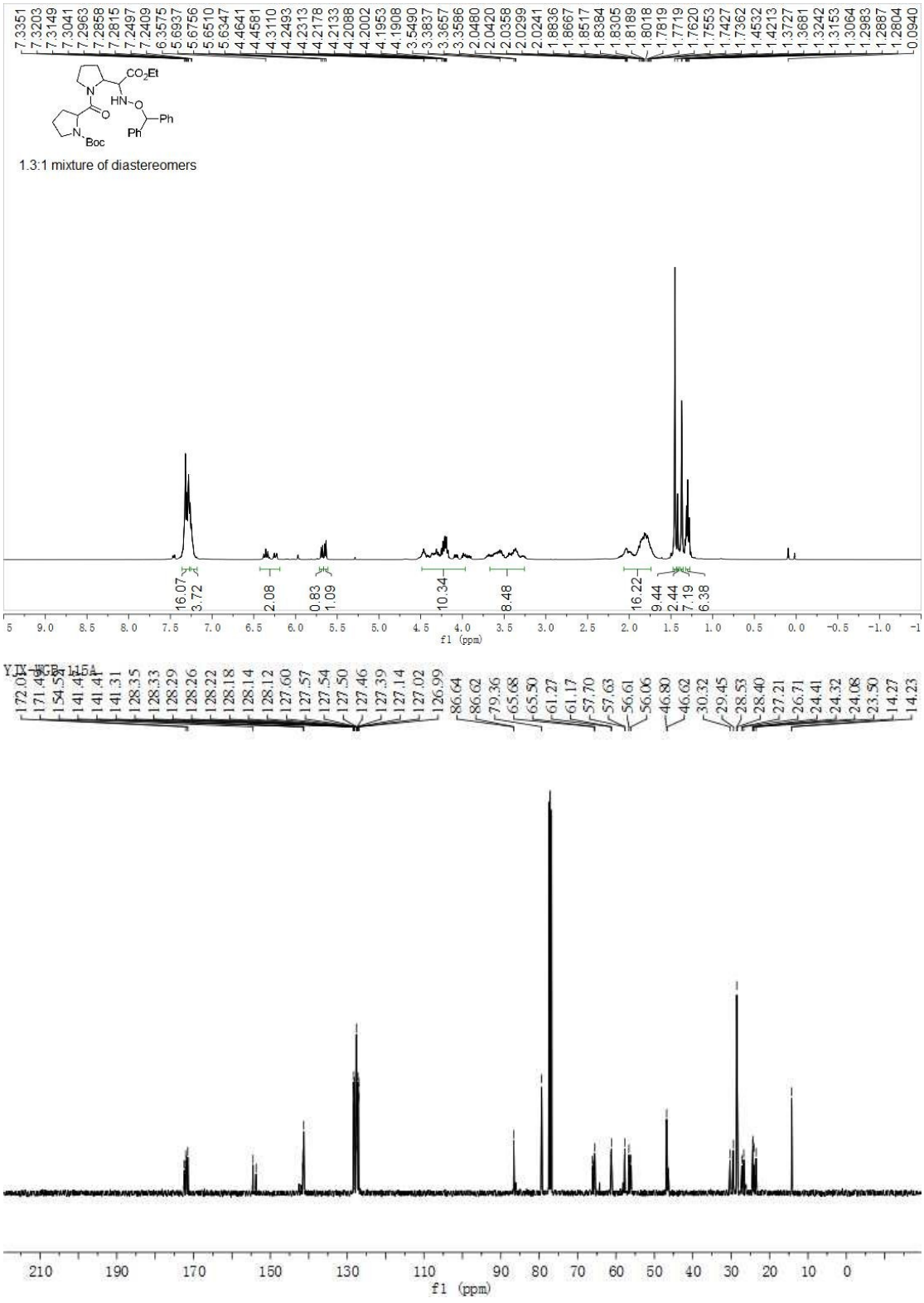
Ethyl 2-((benzyloxy)amino)-3-methoxybutanoate (3x).



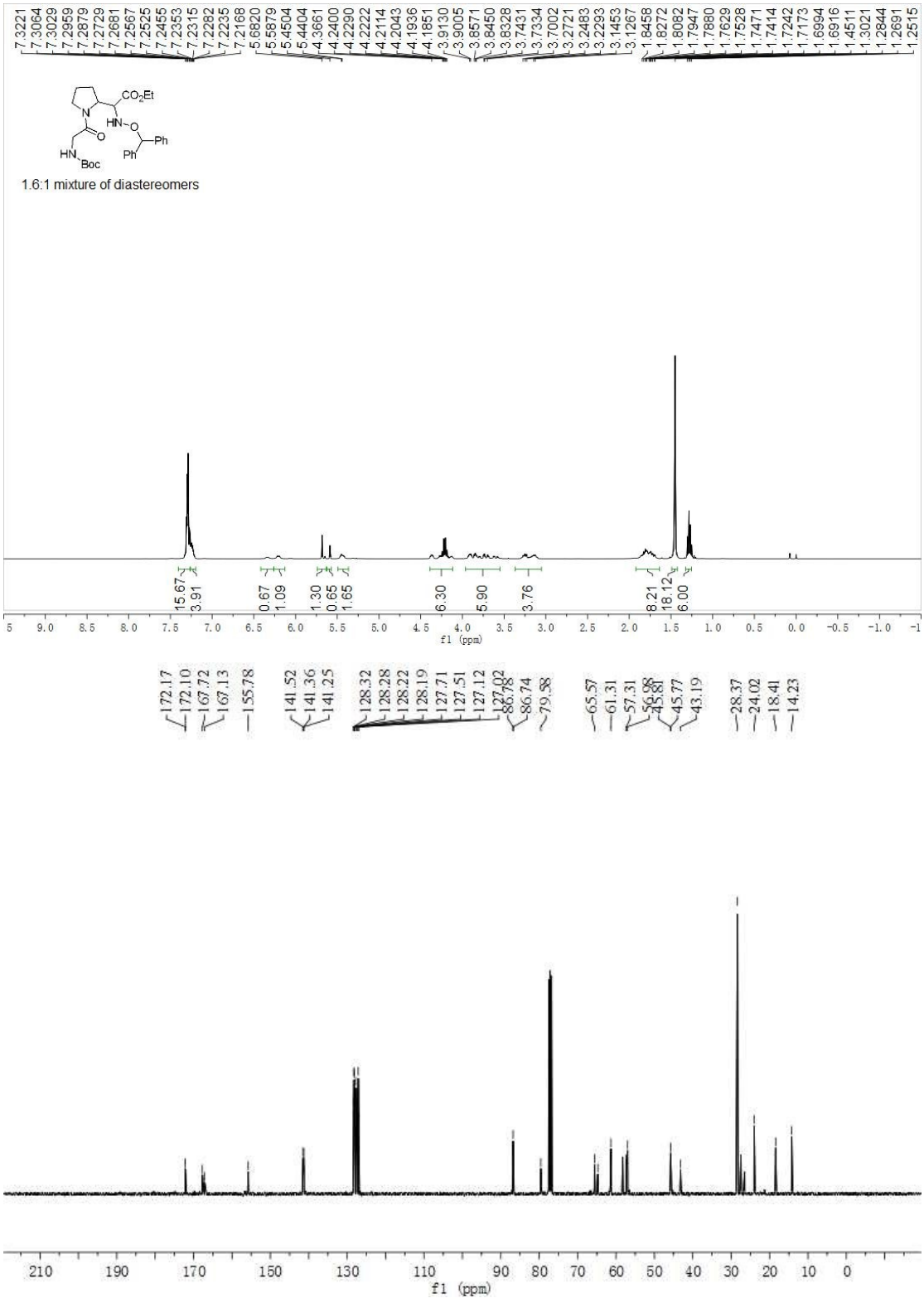
Tert-butyl 2-(2-(1-((benzyloxy)amino)-2-ethoxy-2-oxoethyl)pyrrolidine-1-carbo-yl)pyrrolidine-1-carboxylate (3y).



Tert-butyl 2-(2-(1-((benzhydryloxy)amino)-2-ethoxy-2-oxoethyl)pyrrolidine-1-carbonyl)pyrrolidine-1-carboxylate (3z).



Ethyl 2-((benzhydryloxy)amino)-2-(1-((tert-butoxycarbonyl)glycyl)pyrrolidin-2-yl)acetate (3ab).


1.6:1 mixture of diastereomers
f1 (ppm)

6. Reference

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