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Oxidative Peptide Bond Formation of Glycine-Amino Acid using 2-(Aminomethyl)malononitrile as a Glycine Unit

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SUPPORTING INFORMATION

Experimental procedures and Characterization data

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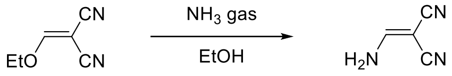
1. Materials and Methods

General Methods

General Remarks: All reactions were carried out under argon atmosphere and monitored by thin-layer chromatography using Merck 60 F254 precoated silica gel plates (0.25 mm thickness). Specific optical rotations were measured using a JASCO P-1020 polarimeter and a JASCO DIP-370 polarimeter. FT-IR spectra were recorded on a JASCO FT/IR-410 spectrometer and a Perkin Elmer spectrum BX FT-IP spectrometer. 1 H and 13C NMR spectra were recorded on an Agilent-400 MR (400 MHz for 1 H NMR, 100 M Hz for 13C NMR) instrument. Data for 1 H NMR are reported as chemical shift (δ ppm), integration multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quintet = quin, septet = sep, dd = doublet of doublets, ddd = doublet of doublet of doublets, dt = double of triplets, td = triplet of doublets, m = multiplet, brs = broad singlet), coupling constant (Hz), Data for ^{13}C NMR are reported as chemical shift. High resolution ESI-TOF mass spectra were measured by Themo Orbi-trap instrument. General Methods. General Remarks: All reactions were carried out under argon atmosphere and monitored by thin-layer chromatography using Merck 60 F254 precoated silica gel plates (0.25 mm thickness). Specific optical rotations were measured using a JASCO P-1020 polarimeter and a JASCO DIP-370 polarimeter. FT-IR spectra were recorded on a JASCO FT/IR-410 spectrometer and a Perkin Elmer spectrum BX FT-IP spectrometer. ^{1} H and ^{13}C NMR spectra were recorded on an Agilent-400 MR (400 MHz for 1 H NMR, 100 M Hz for 13C NMR) instrument. Data for ^{1}H NMR are reported as chemical shift (δ ppm), integration multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quintet = quin, septet = sep, dd = doublet of doublets, ddd = doublet of doublet of doublets, dt = double of triplets, td = triplet of doublets, m = multiplet, brs = broad singlet), coupling constant (Hz), Data for ^{13}C NMR are reported as chemical shift. High resolution ESI-TOF mass spectra were measured by Themo Orbi-trap instrument.

2. Experimental procedure

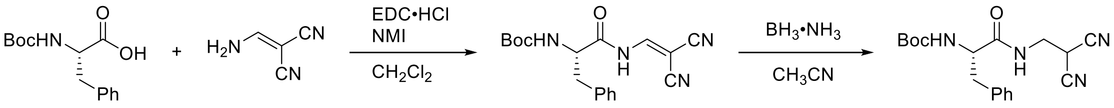
2.1 Synthesis of 2-(aminomethylene)malononitrile SS1[1].



ss1

NH_3 gas was introduced to a saturated solution of 2-(ethoxymethylene)malononitrile[1a] (5.25 g, 43 mmol) in ethanol under stirring. After 12 min, the solvent was removed under reduced pressure. The crude compound was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 25%/75%) and gave compound **SS1**, which was used directly for the next step without further determination of the structure.

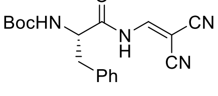
2.2 Synthesis of dicyano compound 1a and physical information



ss1 s1 1a

To a mixture of **SS1** (1.34 g, 14.4 mmol) in CH_2Cl_2 (96 mL) was added *N*-(*tert*-Butoxycarbonyl)-*L*-phenylalanine (4.4 g, 16.6 mmol), 1-Methylimidazole (118 mg, 1.44 mmol), EDC·HCl (3.8 g, 19.8 mmol). The mixture was stirred at room temperature overnight and then evaporated to remove volatiles. After addition of EtOAc, the suspension was filtered and the filtrate was concentrated under reduced pressure. Purification by silica gel column chromatography (EtOAc/Hexane=28%/62%) gave the desired product **S1**. To a mixture of **S1** (1.76 g, 5.17 mmol) in CH_3CN (59 mL) was added $BH_3·NH_3$ (1.6 g, 51.7 mmol). The mixture was stirred at room temperature for 2 h (the reaction was monitored by TLC using MeOH/DCM=1/7). Then the reaction mixture was slowly added to a mixture of cold 1N HCl/EtOAc = 2/1 and extracted with EtOAc. The organic phase was collected and concentrated under reduced pressure. The crude compound was further purified by silica gel column chromatography (EtOAc/Hexane = 50%/50%) and gave compound **1a**.

***tert*-Butyl (*S*)-(1-((2,2-dicyanovinyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate**



s1

S1 was obtained in 63% yield as white solid.

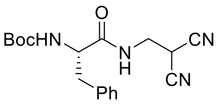
^{1}H NMR (399 MHz, DMSO-d$_6$) δ 12.05 (d, *J* = 12.2 Hz, 1H), 8.38 (d, *J* = 12.0 Hz, 1H), 7.49 – 7.07 (m, 5H), 4.69 – 4.44 (m, 1H), 2.95 (dd, *J* = 13.9, 3.6 Hz, 1H), 2.73 (dd, *J* = 13.7, 10.9 Hz, 1H), 1.28 (s, 9H).

^{13}C NMR (100 MHz, DMSO-d$_6$) δ 172.7, 156.0, 153.7, 137.5, 129.6 (2C), 128.5(2C), 126.9, 114.5, 112.4, 79.0, 63.0, 56.1, 36.2, 28.5 (3C).

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 363.1428; Found: 363.1424
FT-IR (neat): 2361, 2233, 1684, 1614, 1497, 1367, 1252, 1165, 700 cm^{-1}

$[\alpha]_D^{24}$ 2.47 (c 1.0, DMSO)

<u>*tert*-Butyl (*S*)-(1-((2,2-dicyanoethyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate</u>

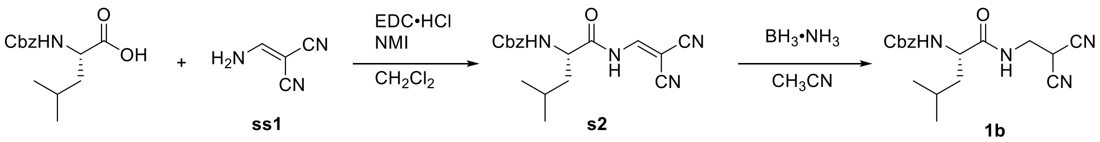


1a

1a was obtained in 65% yield as white solid.
^{1}H NMR (399 MHz, DMSO-d_6) δ 8.66 (t, *J* = 6.1 Hz, 1H), 7.33 – 7.09 (m, 5H), 6.99 (d, *J* = 8.6 Hz, 1H), 4.85 (t, *J* = 6.2 Hz, 1H), 4.16 (td, *J* = 10.7, 4.1 Hz, 1H), 3.77 (dt, *J* = 12.8, 6.3 Hz, 1H), 3.69 – 3.59 (m, 1H), 2.92 (dd, *J* = 13.7, 4.0 Hz, 1H), 2.71 (dd, *J* = 13.7, 10.8 Hz, 1H), 1.25 (s, 9H).
^{13}C NMR (100 MHz, DMSO-d_6) δ 173.4, 155.7, 138.4, 129.6 (2C), 128.5 (2C), 126.7, 113.7(2C), 78.5, 56.1, 38.6, 37.8, 28.5 (3C), 24.1.
HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 365.1584; Found: 365.1586
FT-IR (neat): 3291, 2979, 1668, 1526, 1367, 1249, 1168, 910, 734 cm^{-1}

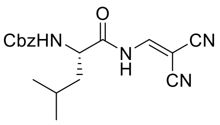
$[\alpha]_D^{27}$ -0.64 (c 1.0 $CHCl_3$)

2.3 Synthesis of dicyano compound 1b and physical information



To a mixture of **SS1** (0.46 g, 4.94 mmol) in CH_2Cl_2 (33 mL) was added N-Benzyloxycarbonyl-*L*-leucine (1.44 g, 5.44 mmol), 1-Methylimidazole (40.6 mg, 0.494 mmol), EDC·HCl (1.56 g, 8.15 mmol). The mixture was stirred at room temperature overnight and then quenched with 1N HCl and extracted with CH_2Cl_2. The organic face was concentrated under reduced pressure. Purification by silica gel column chromatography (EtOAc/Hexane=30%/70%) gave the desired product **S2**. To a mixture of **S2** (1.0 g, 2.94 mmol) in CH_3CN (33 mL) was added $BH_3{\cdot}NH_3$ (0.97 g, 29.4 mmol). The mixture was stirred at room temperature for 1 h. Then the reaction mixture was slowly added to a mixture of cold 1N HCl /EtOAc = 2/1 and extracted with EtOAc. The organic phase was collected and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (EtOAc/Hexane = 50%/50%) and gave compound **1b**.

Benzyl (*S*)-(1-((2,2-dicyanovinyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate



s2

S2 was obtained in 61% yield as white solid.

^{1}H NMR (399 MHz, $CDCl_3$) δ 10.22 (d, *J* = 11.8 Hz, 1H), 8.16 (d, *J* = 12.0 Hz, 1H), 7.56 – 7.02 (m, 5H), 5.36 (d, *J* = 5.4 Hz, 1H), 5.10 (d, *J* = 19.7 Hz, 2H), 4.43 (s, 1H), 1.84 – 1.40 (m, 3H), 0.95 (d, *J* = 6.2 Hz, 3H), 0.91 (d, *J* = 6.1 Hz, 3H).

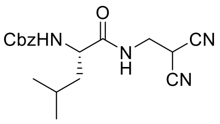
^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 157.1, 151.2, 135.3, 128.7(2C), 128.6 (2C), 128.3, 112.3, 110.6, 68.1, 66.2, 53.5, 39.4, 24.6, 22.8, 21.5.

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 363.1428; Found: 363.1427.

FT-IR (neat): 3020, 2963, 2400, 2235, 1703, 1615, 1508, 1216, 1044, 754, 669 cm^{-1}

$[\alpha]_D^{28}$ 8.97 (c 2.2 $CHCl_3$)

Benzyl (*S*)-(1-((2,2-dicyanoethyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate



1b

1b was obtained in 72% yield as white solid.

^{1}H NMR (399 MHz, $CDCl_3$) δ 7.55 (brs, 1H), 7.43 – 7.21 (m, 5H), 5.48 (d, *J* = 7.6 Hz, 1H), 5.09 (s, 2H), 4.32 – 4.19 (m, 1H), 4.18 – 4.12 (m, 1H), 3.77 – 3.64 (m, 1H), 3.63 – 3.54 (m, 1H), 1.72 – 1.57 (m, 2H), 1.55 – 1.44 (m, 1H), 0.92 (d, *J* = 6.3 Hz, 3H), 0.89 (d, *J* = 6.1 Hz, 3H).

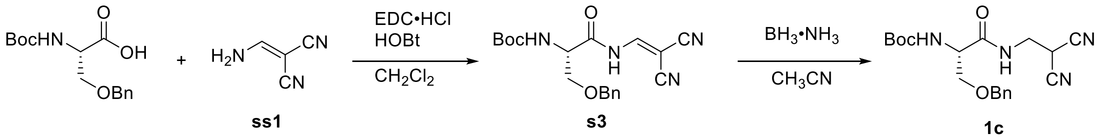
^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 156.5, 135.9, 128.6 (2C), 128.4, 127.9 (2C), 111.3 (2C), 67.4, 53.3, 40.7, 39.7, 24.7 (2C), 22.7, 21.9.

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 365.1584; Found: 365.1586.

FT-IR (neat): 3300, 3067, 2959, 2259, 1672, 1534, 1455, 1368, 1239, 1173, 1122, 1043, 911, 736, 698 cm^{-1}

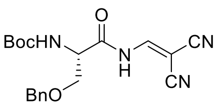
$[\alpha]_D^{25}$ -24.00 (c 1.9 $CHCl_3$)

2.4 Synthesis of dicyano compound 1c and physical information



To a mixture of **SS1** (600 mg, 6.45 mmol) in CH_2Cl_2 (26 mL) was added N-(*tert*-Butoxycarbonyl)-O-benzyl-*L*-serine (2.09 g, 7.09 mmol), 1-Hydroxybenzotriazole Monohydrate (99.0 mg, 0.645 mmol), EDC·HCl (1.63 g, 8.51 mmol). The mixture was stirred at room temperature overnight and then quenched with 1N HCl and extracted with CH_2Cl_2. The organic face was concentrated under reduced pressure. Purification by silica gel column chromatography (EtOAc/Hexane=50%/50%) gave the desired product **S3**. To a mixture of **S3** (400 mg, 1.08 mmol) in CH_3CN (39 mL) was added $BH_3 \cdot NH_3$ (330 mg, 10.8 mmol). The mixture was stirred at room temperature for 4 h. Then the reaction mixture was slowly added to a mixture of cold 1N HCl /EtOAc = 2/1 and extracted with EtOAc. The organic phase was collected, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (EtOAc/Hexane = 35%/65%) and gave compound **1c**.

***tert*-Butyl (*S*)-(3-(benzyloxy)-1-((2,2-dicyanovinyl)amino)-1-oxopropan-2-yl)carbamate**



s3

S3 was obtained in 42% yield as white solid.

^{1}H NMR (399 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.16 (d, *J* = 12.7 Hz, 1H), 7.42 – 7.25 (m, 5H), 5.33 (s, 1H), 4.59 (s, 2H), 4.45 – 4.35 (m, 1H), 3.93 (dd, *J* = 9.3, 3.6 Hz, 1H), 3.63 (dd, *J* = 9.5, 6.1 Hz, 1H), 1.45 (s, 9H).

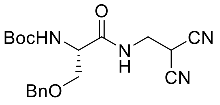
^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 150.4 (2C), 136.2, 128.7 (2C), 128.4, 128.1 (2C), 112.0, 110.2, 82.1, 73.9, 67.6, 66.8, 54.5, 28.2 (3C).

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 393.1533; Found: 393.1534.

FT-IR (neat): 3289, 1719, 1686, 1625, 1498, 1368, 1250, 1131, 738, 696 cm^{-1}

$[\alpha]_D^{27}$-5.27 (c 0.85 $CHCl_3$)

***tert*-Butyl (*S*)-(3-(benzyloxy)-1-((2,2-dicyanoethyl)amino)-1-oxopropan-2-yl)carbamate**



1c

1c was obtained in 84% yield as white solid.

^{1}H NMR (399 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.36 – 7.13 (m, 5H), 5.45 (s, 1H), 4.50 (s, 2H), 4.32 (s, 1H), 4.21 (t, *J* = 6.9 Hz, 1H), 3.83 (dd, *J* = 9.3, 4.0 Hz, 1H), 3.79 – 3.65 (m, 2H), 3.56 (dd, *J* = 9.3, 5.7 Hz, 1H), 1.43 (s, 9H).

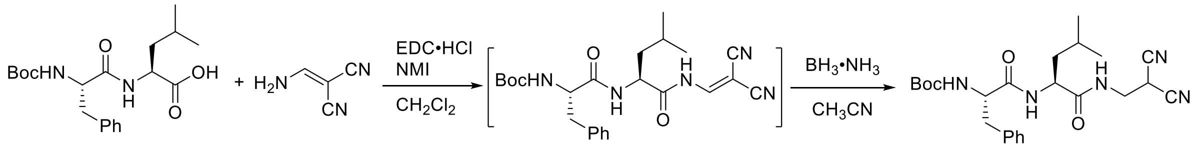
^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 155.6, 137.1, 128.6 (2C), 128.1, 127.9 (2C), 111.3, 111.3, 80.8, 73.5, 69.4, 54.1, 39.9, 28.3 (3C), 22.7.

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 395.1690; Found: 395.1695.

FT-IR (neat): 3310, 2979, 1675, 1523, 1367, 1248, 1166, 1100, 750, 698 cm^{-1}

$[\alpha]_D^{26}$ 1.31 (c 3.7 $CHCl_3$)

2.5 Synthesis of dicyano compound 1d and physical information

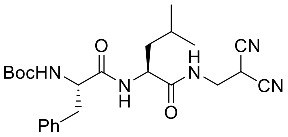


ss1 s4 1d

To a mixture of **SS1** (227 mg, 2.44 mmol) in CH_2Cl_2 (22 mL) was added Boc-Phe-Leu-OH[2] (1.06 g, 5.44 mmol), 1-Methylimidazole (20 mg, 0.244 mmol), EDC·HCl (644 mg, 3.36 mmol). The mixture was stirred at room temperature overnight and then quenched with 1N HCl and extracted with CH_2Cl_2. The organic phase was concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography (EtOAc/Hexane = 30%/70%) and gave compound **S4**. (It was directly used for the next step without further determination of the structure). To a mixture of **S4** (300 mg, 0.661 mmol) in CH_3CN (7.5 mL) was added $BH_3 \cdot NH_3$ (204 mg, 6.61 mmol). The mixture was stirred at room temperature for 1 h. Then the reaction mixture was slowly added to a mixture of cold 1N HCl /EtOAc = 2/1 and extracted with EtOAc. The organic phase was collected and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (CH_2Cl_2/MeOH=92%/8%) and gave compound **1d**.

***tert*-Butyl ((*S*)-1-(((*S*)-1-((2,2-dicyanoethyl)amino)-4-methyl-1-oxopentan-2-yl)amino)- 1-**

oxo-3-phenylpropan-2-yl)carbamate



1d

1d was obtained in 29% yield as white solid (**mixture of two rotamers**).

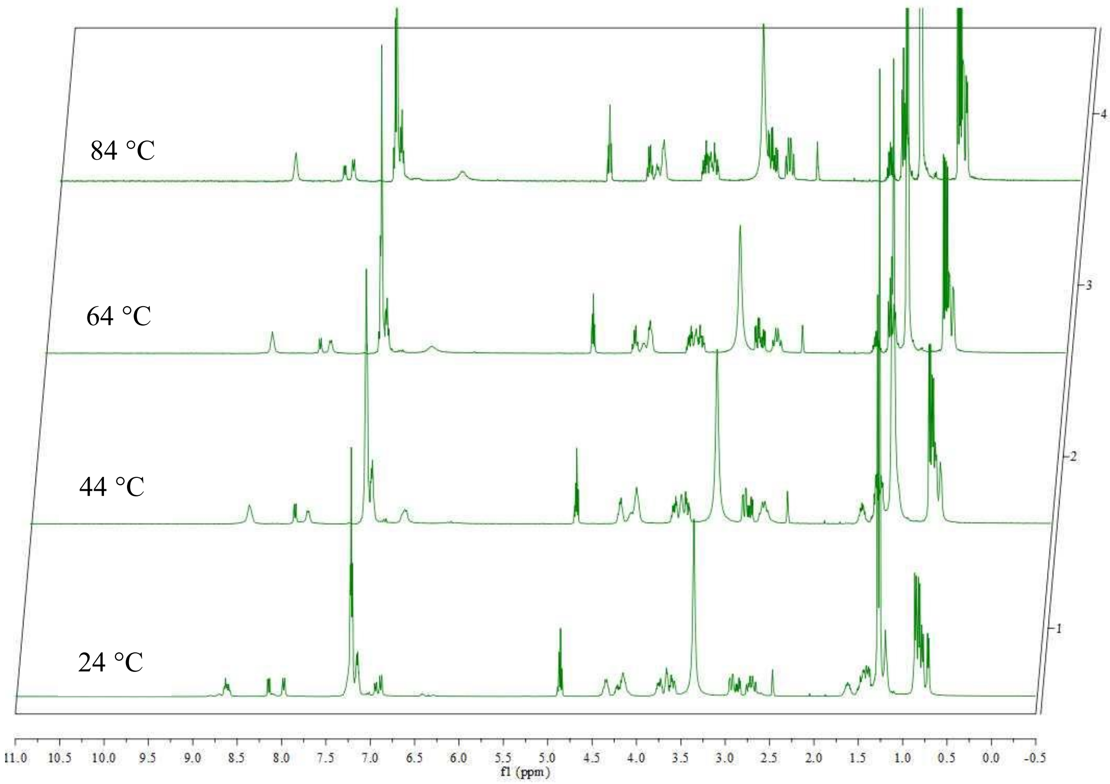
^{1}H NMR (399 MHz, DMSO-d_6) δ 8.83 – 8.54 (m, 1H), (8.14 (d, *J* = 8.3 Hz) and 7.97 (d, *J* = 8.2 Hz), 1H), 7.34 – 7.10 (m, 5H), (6.94 (d, *J* = 8.0 Hz) and 6.88 (d, *J* = 8.4 Hz), 1H), 4.92 – 4.81 and 4.41 – 4.04 (m, 1H), 4.41 – 4.07 (m, 2H), 3.82 – 3.54 (m, 2H), (2.93 (dd, *J* = 13.8, 4.0 Hz) and 2.86 (dd, *J* = 13.5, 5.9 Hz), 1H), 2.79 – 2.61 (m, 1H), 1.73 – 1.56 (m, 1H), 1.53 – 1.36 (m, 2H), 1.28 and 1.26 (s, 9H), (0.86 (d, *J* = 6.8 Hz) and 0.78 (d, *J* = 6.0 Hz), 3H), (0.81 (d, *J* = 6.4 Hz) and 0.71 (d, *J* = 6.4 Hz), 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 173.6 and 173.5 (1C), 172.0 and 171.9 (1C), 155.7 and 155.7 (1C), 138.6 and 138.1 (1C), 129.6 (2C), 128.4 (2C), 126.6 and 126.5 (1C), 113.6 and 113.6 (2C), 78.7 and 78.5 (1C), 56.3 and 56.0 (1C), 51.3 and 51.2 (1C), 41.6 and 41.3 (1C), 38.5, 38.0 and 37.5 (1C), 28.6 and 28.5 (3C), 24.4 and 24.3 (1C), 24.1 and 24.1 (1C), 23.5 and 23.4 (1C), 22.0 and 21.7 (1C).

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 478.2425; Found 478.2424.

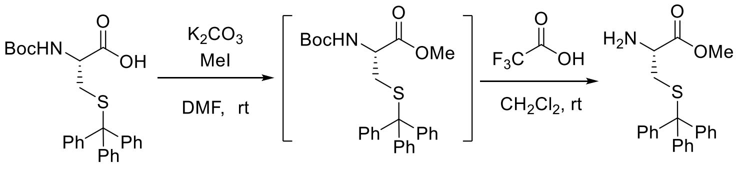
FT-IR (neat): 3287, 2961, 2256, 1650, 1524, 1368, 1251, 1169, 1049, 910, 735, 700 cm^{-1}

$[\alpha]_D^{28}$ -4.81 (c 1.0 $CHCl_3$)



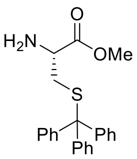
Variable temperature **¹H NMR** (399 Hz, DMSO-d₆) spectra of compound **1d** to prove the rotamer.

2.6 Synthesis of *L*-Cysteine-(S-Trityl)-OMe s5 and physical information



To a mixture of Boc-*L*-Cys-(S-Trityl)-OH (1.00 g, 2.16 mmol) and Iodomethane (403 μL, 6.47 mmol) in DMF (4.3 mL) was added K_2CO_3 (1.34 g, 9.71 mmol). The mixture was stirred at room temperature for 3 h, and then cooled to 0 °C and quenched by saturated NH_4Cl solution. The mixture was then extracted with EtOAc and the organic phase was collected and dried over Na_2SO_4, concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hexane/EtOAc=50%/50%) to give **ss2** as a white solid. It was used directly for the next step without determining the structure. To a mixture of **ss2** (1.03 g, 2.16 mmol) in CH_2Cl_2 (20 mL) was added 2,2,2-trifluoacetic acid (2.46 g, 21.6 mmol). The mixture was stirred at room temperature for 2.5 h and quenched by saturated $NaHCO_3$ solution and extracted with CH_2Cl_2. The organic phase was collected, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hexane/EtOAc=25%/75%) to give **s5** as colorless oil.

Methyl S-trityl-*L*-cysteinate

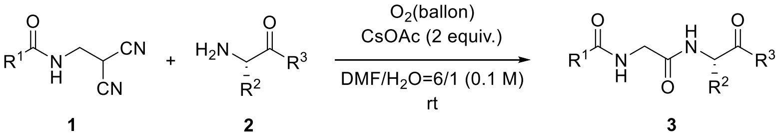


s5

S5 was obtained in 86% yield as colorless oil.
¹H NMR (399 MHz, $CDCl_3$) δ 7.48 – 7.36 (m, 6H), 7.32 – 7.24 (m, 6H), 7.23 – 7.17 (m, 3H), 3.64 (s, 3H), 3.24 – 3.17 (m, 1H), 2.62 (dd, *J* = 12.6, 4.8 Hz, 1H), 2.51 (dd, *J* = 12.6, 7.8 Hz, 1H), 2.35 (s, 2H).
¹³C NMR (100 MHz, $CDCl_3$) δ 173.6, 144.4, 129.6, 128.0, 126.8, 66.9, 53.6, 52.3, 36.5.
HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 400.1342; Found 400.1346.
FT-IR (neat): 3057, 1739, 1595, 1489, 1443, 1200, 1034, 744, 701, 622 cm^{-1}
$[\alpha]_D^{29}$ 41.53 (c 4.4 $CHCl_3$)

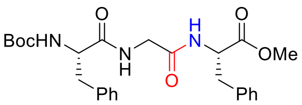
2.7 Typical procedure of oxidative peptide synthesis using amino acid esters/dipeptide and

physical information



To a mixture of the amino acid ester **2** (0.4 mmol) in DMF/H_2O = 6/1 (2 mL) was added CsOAc (76.8 mg, 0.4 mmol). The mixture was stirred and CsOAc dissolved and then was filled with O_2. The dicyano compound **1** (0.2 mmol) was then added and stirred at room temperature. The mixture was then diluted by EtOAc and quenched with 1N HCl and extracted with EtOAc. The organic phase was washed with water/brine = 1/1 and dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by silica gel column chromatography, eluted with Hexane/EtOAc.

Methyl (*tert*-butoxycarbonyl)-*L*-phenylalanylglycyl-*L*-phenylalaninate

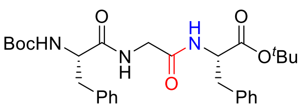


Boc-Phe-Gly-Phe-OMe (3a)

3a was obtained in 58% yield as yellow solid. Purification by EtOAc/Hexane = 65%/35%
^{1}H NMR (399 MHz, DMSO-d_6) δ 8.26 (d, *J* = 7.4 Hz, 1H), 8.10 (s, 1H), 7.29 – 7.09 (m, 10H), 6.96 – 6.87 (m, 1H), 4.46 (dd, *J* = 13.7, 8.0 Hz, 1H), 4.13 (dd, *J* = 12.8, 5.5 Hz, 1H), 3.81 – 3.60 (m, 2H), 3.56 (s, 3H), 3.05 – 2.83 (m, 3H), 2.67 (dd, *J* = 13.3, 11.0 Hz, 1H), 1.25 (s, 9H).
^{13}C NMR (100 MHz, DMSO-d_6) δ 172.3, 172.2, 169.2, 155.7, 138.7, 137.4, 129.6 (2C), 129.5 (2C), 128.7 (2C), 128.4 (2C), 127.0, 126.5, 78.5, 56.1, 54.1, 52.3, 42.1, 37.8, 37.2, 28.5 (3C).
HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 506.2262; Found: 506.2260
FT-IR (neat): 3301, 2979, 1657, 1525, 1455, 1367, 1251, 1171, 1022, 911, 734, 701 cm^{-1}

$[\alpha]_D^{26}$ 30.74 (c 1.1 $CHCl_3$)

tert-Butyl (*tert*-butoxycarbonyl)-*L*-phenylalanylglycyl-*L*-phenylalaninate



Boc-Phe-Gly-Phe-O*t*-Bu (3b)

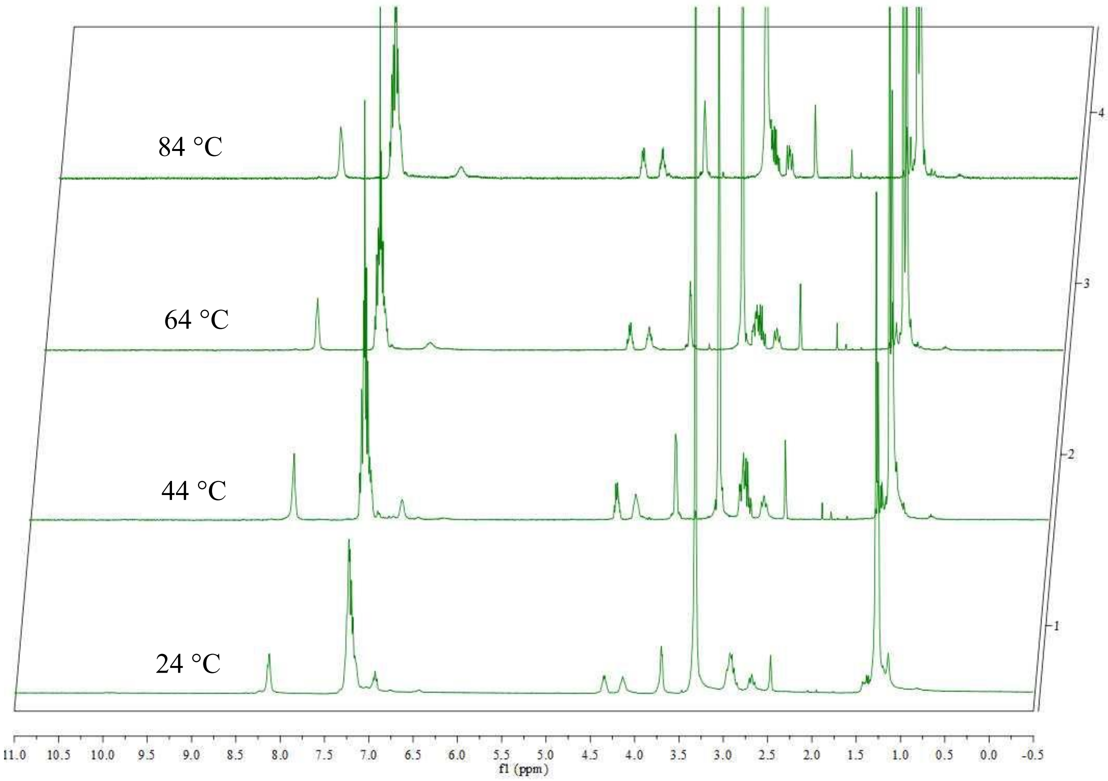
3b was obtained in 50% yield as white solid (**mixture of two rotamers**). Purification by EtOAc/Hexane = 60%/40%;
^{1}H NMR (399 MHz, DMSO-d_6) δ 8.18 – 8.05 (m, 2H), 7.37 – 7.05 (m, 10H), 6.97 – 6.88 (m, 1H), 4.34 (dt, *J* = 7.3, 6.1 Hz, 1H), 4.13 (dd, *J* = 13.0, 6.0 Hz, 1H), 3.70 (d, *J* = 5.5 Hz, 2H), 2.99 – 2.84 (m, 3H), 2.68 (dd, *J* = 13.5, 10.9 Hz, 1H), 1.28 (s, 9H), 1.25 and 1.26 (s, 9H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 172.4, 170.8, 169.1, 155.7, 138.7, 137.4, 129.6 (2C), 129.6 (2C), 128.6 (2C), 128.4 (2C), 127.0, 126.5, 81.2, 78.4, 56.1, 54.5, 42.1, 37.8, 37.6, 28.6 (3C), 27.9 (3C).

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 548.2731; Found: 548.2733

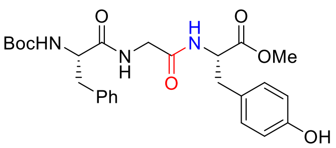
FT-IR (neat): 3299, 2979, 1652, 1523, 1455, 1368, 1252, 1160, 911, 734, 700 cm^{-1}

$[\alpha]_D^{25}$ 28.43 (c 1.0 $CHCl_3$)



Variable temperature **^{1}H NMR** (399 Hz, DMSO-d_6) spectra of compound **3b** to prove the rotamer.

<u>Methyl (*tert*-butoxycarbonyl)-*L*-phenylalanylglycyl-*L*-tyrosinate</u>



Boc-Phe-Gly-Tyr-OMe (**3c**)

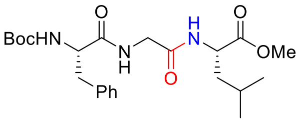
3c was obtained in 52% yield as white solid. Purification by EtOAc/Hexane = 75%/25%

^{1}H NMR (399 MHz, DMSO-d_6) δ 9.20 (s, 1H), 8.25 – 8.15 (m, 1H), 8.11 (t, *J* = 5.2 Hz, 1H), 7.31 – 7.07 (m, 5H), 7.06 – 6.85 (m, 1H) 7.06 – 6.85 (m, 2H), 6.63 (d, *J* = 8.3 Hz, 2H), 4.37 (dd, *J* = 13.9, 8.0 Hz, 1H), 4.13 (dd, *J* = 12.9, 6.0 Hz, 1H), 3.81 – 3.62 (m, 2H), 3.55 (s, 3H), 3.01 – 2.83 (m, 2H), 2.77 (dd, *J* = 13.8, 8.5 Hz, 1H), 2.68 (dd, *J* = 13.4, 11.1 Hz, 1H), 1.25 (s, 9H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 172.3, 169.1, 156.5, 155.7, 138.7 (2C), 130.4 (2C), 129.6 (2C), 128.4 (2C), 127.3, 126.5, 115.5 (2C), 78.5, 56.1, 54.4, 52.2, 42.1, 37.8, 36.6, 28.6 (3C).
HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 522.2211; Found: 522.2211
FT-IR (neat): 3311, 1660, 1517, 1454, 1367, 1250, 1170, 1023, 910, 733 cm^{-1}

$[\alpha]_D^{30}$ 22.72 (c 1.8 $CHCl_3$)

Methyl (*tert*-butoxycarbonyl)-*L*-phenylalanylglycyl-*L*-leucinate

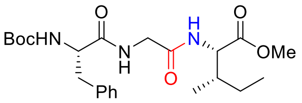


Boc-Phe-Gly-Leu-OMe (3d)

3d was obtained in 65% yield as yellow solid. Purification by EtOAc/Hexane=75%/25%
^{1}H NMR (399 MHz, DMSO-d_6) δ 8.19 – 8.06 (m, 2H), 7.29 – 7.19 (m, 4H), 7.15 (td, *J* = 8.2, 3.8 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 4.33 – 4.25 (m, 1H), 4.18 – 4.09 (m, 1H), 3.72 (d, *J* = 5.7 Hz, 2H), 3.59 (s, 3H), 2.98 (dd, *J* = 13.7, 3.9 Hz, 1H), 2.70 (dd, *J* = 13.6, 10.8 Hz, 1H), 1.64 – 1.41 (m, 3H), 1.26 (s, 9H), 0.86 (d, *J* = 6.4 Hz, 3H), 0.82 (d, *J* = 6.4 Hz, 3H).
^{13}C NMR (100 MHz, DMSO-d_6) δ 173.2, 172.3, 169.2, 155.7, 138.7, 129.6 (2C), 128.4 (2C), 126.5, 78.5, 56.1, 52.3, 50.6, 42.1, 37.7, 28.5 (3C), 24.6, 23.1, 21.8 (2C).
HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 472.2418; Found: 472.2418
FT-IR (neat): 3316, 2959, 2252, 1668, 1518, 1368, 1251, 1160, 1025, 907, 734, 649 cm^{-1}

$[\alpha]_D^{25}$ 1.38 (c 2.4 $CHCl_3$)

Methyl (*tert*-butoxycarbonyl)-*L*-phenylalanylglycyl-*L*-isoleucinate

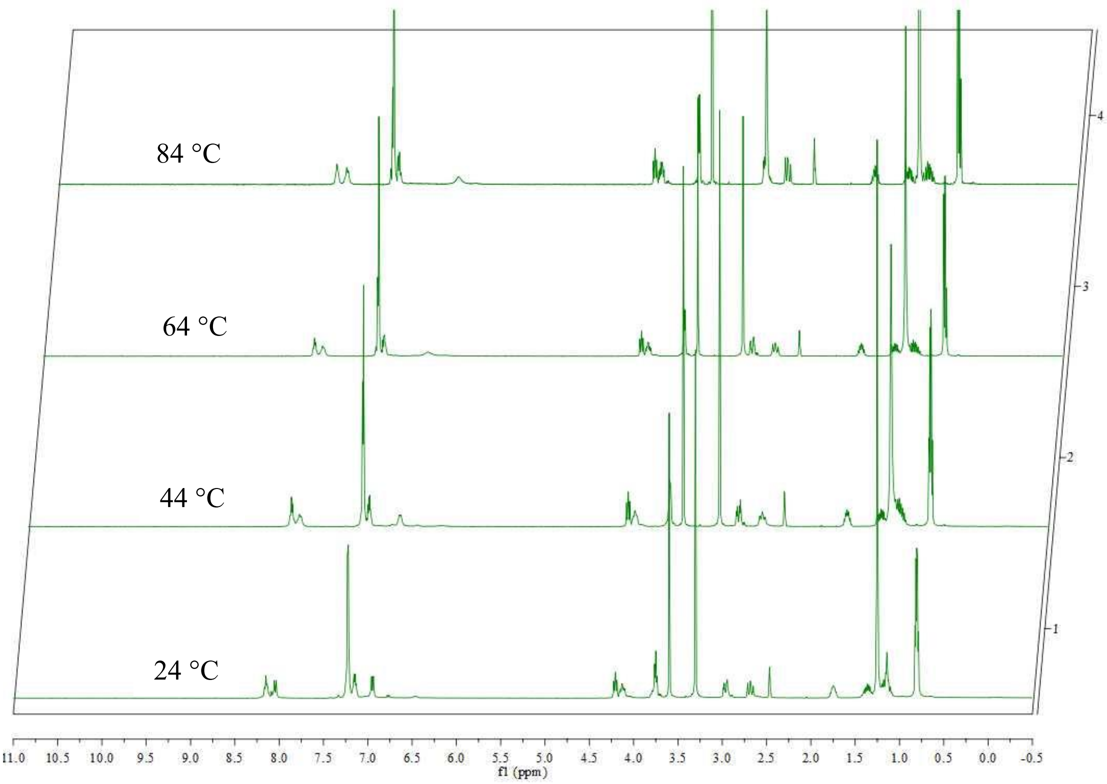


Boc-Phe-Gly-Ile-OMe (3e)

3e was obtained in 60% yield as yellow solid (**mixture of two rotamers**). Purification by EtOAc/Hexane = 75%/25%
^{1}H NMR (399 MHz, DMSO-d_6) δ 8.19 – 8.10 (m, 1H), 8.05 (dd, *J* = 12.8, 8.2 Hz, 1H), 7.29 – 7.19 (m, 4H), 7.15 (td, *J* = 8.3, 4.1 Hz, 1H), 6.93 (d, *J* = 8.5 Hz, 1H), 4.25 – 4.18 (m, 1H), 4.18 – 4.08 (m, 1H), 3.84 – 3.69 (m, 2H), 3.60 and 3.60 (s, 3H), 2.97 (dt, *J* = 13.6, 3.8 Hz, 1H), 2.69 (dd, *J* = 13.5, 11.0 Hz, 1H), 1.81 – 1.69 (m, 1H), 1.47 – 1.31 (m, 2H), 1.25 (s, 9H), 0.89 – 0.71 (m, 6H).
^{13}C NMR (100 MHz, DMSO-d_6) δ 172.4, 172.3, 169.3, 155.7, 138.7, 129.6 (2C), 128.4 (2C), 126.5, 78.4, 56.7, 56.1, 52.1, 42.2, 37.8, 36.8, 28.5 (3C), 25.1, 15.8, 11.5.
HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 472.2418; Found: 472.2417

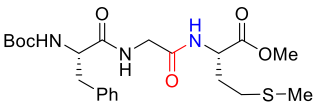
FT-IR (neat): 3304, 2969, 1655, 1526, 1455, 1366, 1252, 1170, 1022, 912, 734, 700 cm^{-1}

$[\alpha]_D^{29}$ 14.23 (c 1.2 $CHCl_3$)



Variable temperature ^{1}**H NMR** (399 Hz, DMSO-d_6) spectra of compound **3e** to prove the rotamer.

<u>Methyl (*tert*-butoxycarbonyl)-*L*-phenylalanylglycyl-*L*-methioninate</u>



Boc-Phe-Gly-Met-OMe (3f)

3f was obtained in 47% yield as yellow solid (**mixture of two rotamers**). Purification by EtOAc/Hexane = 80%/20%

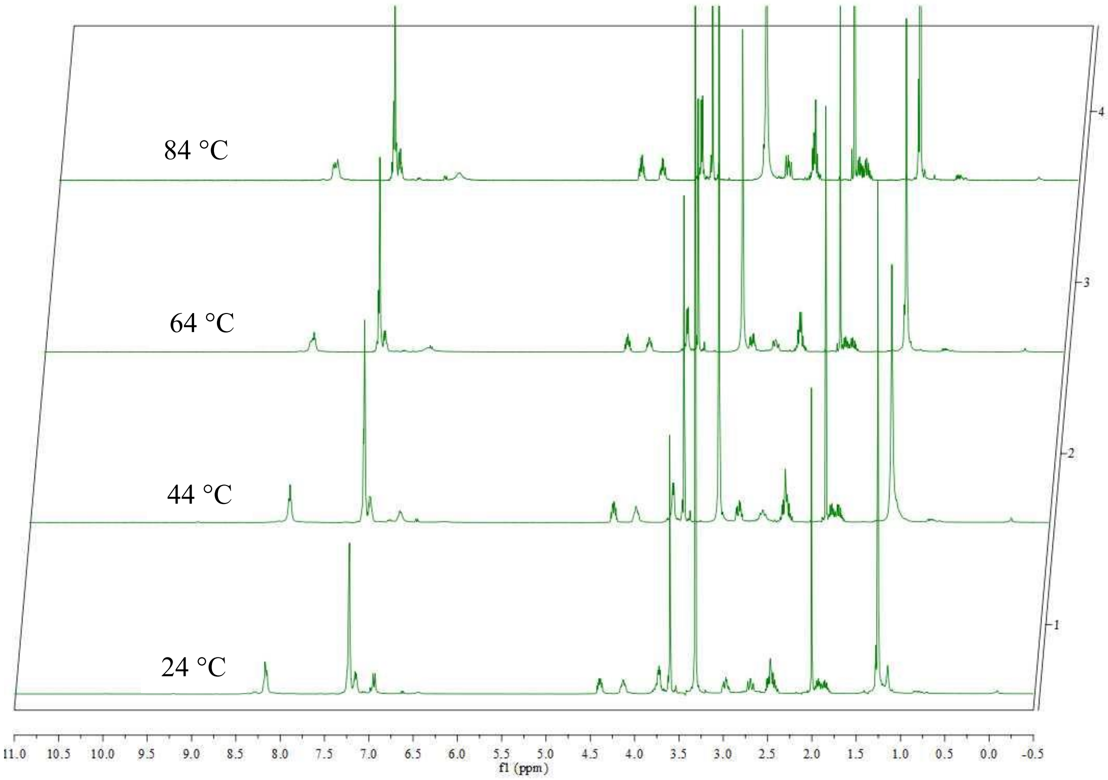
^{1}**H NMR** (399 MHz, DMSO-d_6) δ 8.24 – 8.09 (m, 2H), 7.29 – 7.20 (m, 4H), 7.16 (dd, *J* = 8.1, 4.2 Hz, 1H), 6.95 (dd, *J* = 12.9, 8.3 Hz, 1H), 4.44 – 4.35 (m, 1H), 4.12 (dd, *J* = 12.5, 6.1 Hz, 1H), 3.82 – 3.68 (m, 2H), 3.60 and 3.60 (s, 3H), 3.03 – 2.93 (m, 1H), 2.69 (dd, *J* = 13.5, 10.9 Hz, 1H), 2.54 – 2.38 (m, 2H), 2.00 (s, 3H), 1.97 – 1.79 (m, 2H), 1.26 (s, 9H).

^{13}**C NMR** (100 MHz, DMSO-d_6) δ 172.5, 172.4, 169.4, 155.7, 138.7, 129.6, 128.4, 126.5, 78.5, 56.1, 52.4, 51.2, 42.2, 37.7, 31.1, 29.8, 28.5, 15.0 and 14.9 (1C).

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 490.1982; Found: 490.1981

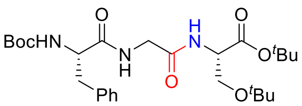
FT-IR (neat): 3308, 2978, 1658, 1527, 1440, 1367, 1251, 1170, 1022, 912, 733, 701 cm^{-1}

$[\alpha]_D^{28}$ 11.35 (c 1.8 $CHCl_3$)



Variable temperature ^{1}**H NMR** (399 Hz, DMSO-d_6) spectra of compound **3f** to prove the rotamer.

<u>*tert*-Butyl N-(*tert*-butoxycarbonyl)-*L*-phenylalanylglycyl-O-(tert-butyl)-*L*-serinate</u>



Boc-Phe-Gly-Ser(O*t*-Bu)-O*t*-Bu (3g)

3g was obtained in 56% yield as yellow solid (**mixture of two rotamers**). Purification by EtOAc/Hexane = 55%/45%

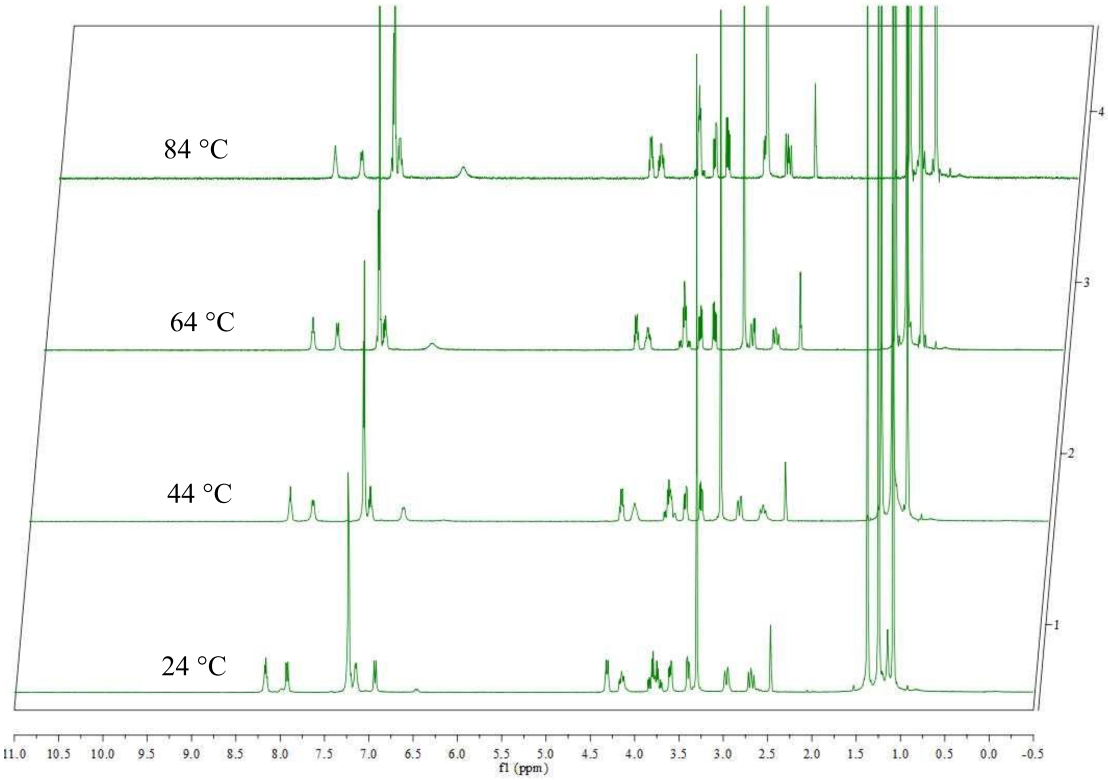
^{1}**H NMR** (399 MHz, DMSO-d_6) δ 8.14 (t, *J* = 5.3 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.34 – 7.19 (m, 4H), 7.18 – 7.09 (m, 1H), 6.89 (d, *J* = 8.6 Hz, 1H), 4.31 (dt, *J* = 8.1, 4.2 Hz, 1H), 4.21 – 4.09 (m, 1H), 3.86 – 3.68 (m, 2H), 3.59 (dd, *J* = 8.9, 4.4 Hz, 1H), 3.40 (dd, *J* = 9.0, 4.3 Hz, 1H), 2.97 (dd, *J* = 13.7, 3.5 Hz, 1H), 2.69 (dd, *J* = 13.5, 10.9 Hz, 1H), 1.37 (s, 9H), 1.25 (s, 9H), 1.08 and 1.08 (s, 9H).

^{13}**C NMR** (100 MHz, DMSO-d_6) δ 172.4, 169.6, 169.2, 155.7, 138.7, 129.6(2C), 128.4(2C), 126.5, 81.1, 78.4, 73.1, 62.2, 56.1, 53.6, 42.2, 37.9, 28.5(3C), 28.1(3C), 27.5(3C).

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 544.2993; Found: 544.2993

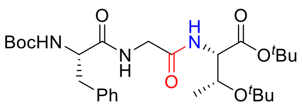
FT-IR (neat): 3299, 2977, 1645, 1521, 1392, 1366, 1249, 1169, 734 cm^{-1}

$[\alpha]_D^{27}$ 18.07 (c 1.1 $CHCl_3$)



Variable temperature ^{1}**H NMR** (399 Hz, DMSO-d$_6$) spectra of compound **3g** to prove the rotamer.

<u>*tert*-Butyl N-(*tert*-butoxycarbonyl)-*L*-phenylalanylglycyl-O-(tert-butyl)-*L*-threoninate</u>



Boc-Phe-Gly-Thr(O*t*-Bu)-O*t*-Bu (3h)

3h was obtained in 51% yield as white solid (**mixture of two rotamers**). Purification by EtOAc/Hexane=50%/50%

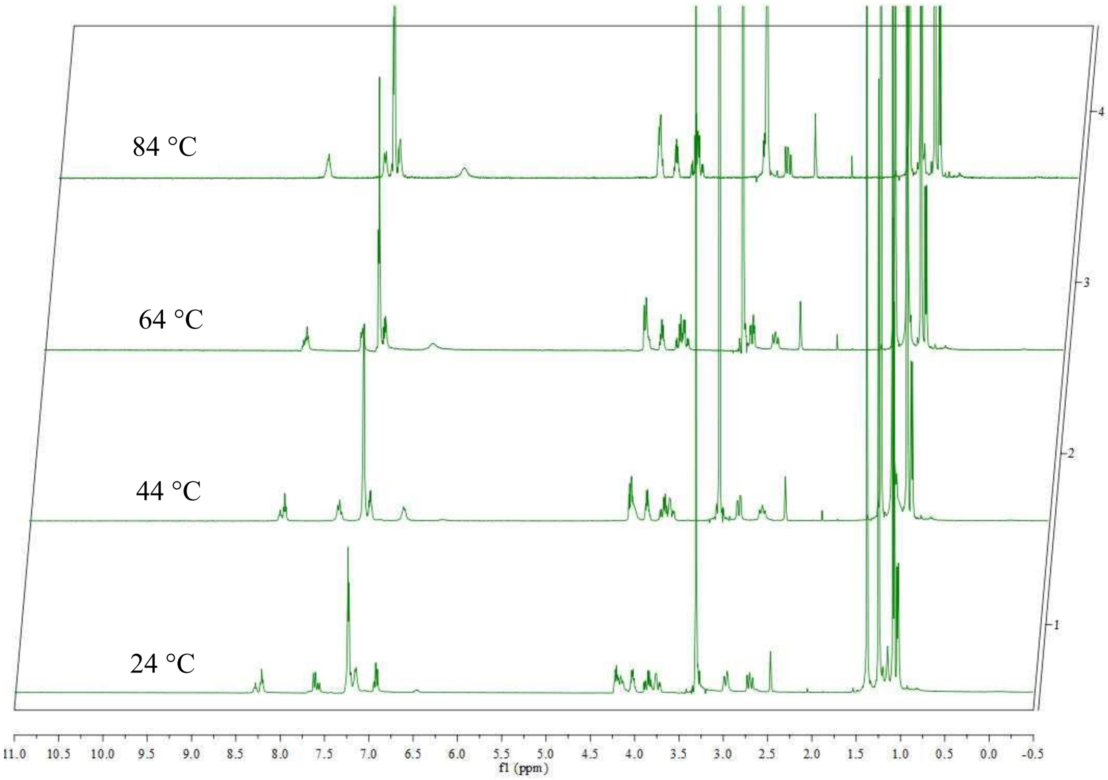
^{1}**H NMR** (399 MHz, DMSO-d$_6$) δ 8.24 (dt, *J* = 28.2, 5.6 Hz, 1H), (7.61 (d, *J* = 8.8 Hz) and 7.56 (d, *J* = 8.8 Hz), 1H), 7.31 – 7.10 (m, 5H), 6.91 (t, *J* = 8.2 Hz, 1H), 4.27 – 4.10 (m, 2H), 4.07 – 3.99 (m, 1H), 3.92 – 3.80 (m, 1H), 3.74 (dd, *J* = 16.9, 5.2 Hz, 1H), 2.97 (dd, *J* = 13.6, 3.0 Hz, 1H), 2.70 (dd, *J* = 13.5, 11.2 Hz, 1H), 1.38 (s, 9H), 1.22 (s, 9H), 1.09 and 1.07 (s, 9H), (1.03 (d, *J* = 6.4 Hz) and 1.02 (d, *J* = 6.0 Hz), 3H).

^{13}**C NMR** (100 MHz, DMSO-d$_6$) δ 172.5, 169.7, 169.5, 155.6, 138.7, 129.6 (2C), 128.4 (2C), 126.5, 81.2 and 81.2 (1C), 78.4, 73.7, 67.3, 58.3, 56.2, 42.4, 38.0, 28.8 (3C), 28.5 (3C), 28.1 (3C), 20.3 and 20.4 (1C).

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 558.3150; Found: 558.3151

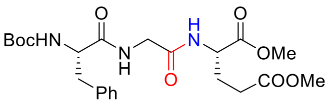
FT-IR (neat): 3299, 2978, 1652, 1520, 1367, 1251, 1169, 1084, 912, 734, 700 cm^{-1}

$[\alpha]_D^{27}$ 4.37 (c 1.2 $CHCl_3$)



Variable temperature ^{1}**H NMR** (399 Hz, DMSO-d_6) spectra of compound **3h** to prove the rotamer.

Dimethyl (*tert*-butoxycarbonyl)-*L*-phenylalanylglycyl-*L*-glutamate



Boc-Phe-Gly-Glu(OMe)-OMe (3i)

3i was obtained in 32% yield as yellow solid (**mixture of two rotamers**). Purification by EtOAc/Hexane = 80%/20%

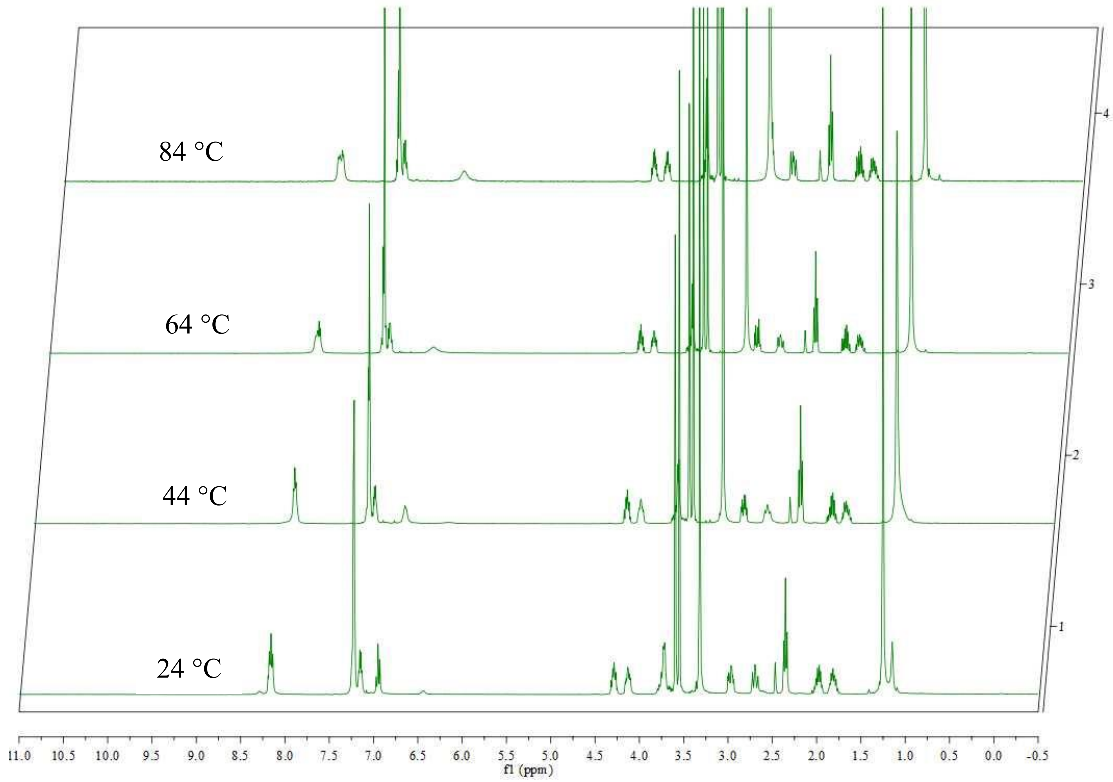
^{1}**H NMR** (399 MHz, DMSO-d_6) δ 8.21 – 8.10 (m, 2H), 7.32 – 7.19 (m, 4H), 7.18 – 7.09 (m, 1H), 6.95 (t, J = 8.3 Hz, 1H), 4.34 – 4.23 (m, 1H), 4.17 – 4.08 (m, 1H), 3.82 – 3.68 (m, 2H), 3.60 and 3.59 (s, 3H), 3.55 (s, 3H), 3.02 – 2.91 (m, 1H), 2.69 (dd, J = 13.4, 10.9 Hz, 1H), 2.35 (t, J = 7.5 Hz, 2H), 1.98 (dt, J = 13.3, 7.7 Hz, 1H), 1.89 – 1.75 (m, 1H), 1.25 (s, 9H).

^{13}**C NMR** (100 MHz, DMSO-d_6) δ 173.0, 172.4, 172.4, 169.4, 155.7, 138.7, 129.6 (2C), 128.4 (2C), 126.5, 78.5, 56.1, 52.4, 51.8, 51.5, 42.2, 37.7, 29.9 and 29.9 (1C), 28.5 (3C), 26.6.

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 502.2160; Found: 502.2159

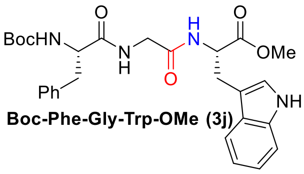
FT-IR (neat): 3310, 2979, 1740, 1659, 1526, 1439, 1367, 1251, 1170, 1022, 915, 734 cm^{-1}

$[\alpha]_D^{28}$ 5.29 (c 2.4 $CHCl_3$)



Variable temperature **^{1}H NMR** (399 Hz, DMSO-d$_6$) spectra of compound **3i** to prove the rotamer.

Methyl (*tert*-butoxycarbonyl)-*L*-phenylalanylglycyl-*L*-tryptophanate



3j was obtained in 51% yield as yellow solid (**mixture of two rotamers**). Purification by EtOAc/Hexane = 60%/40%

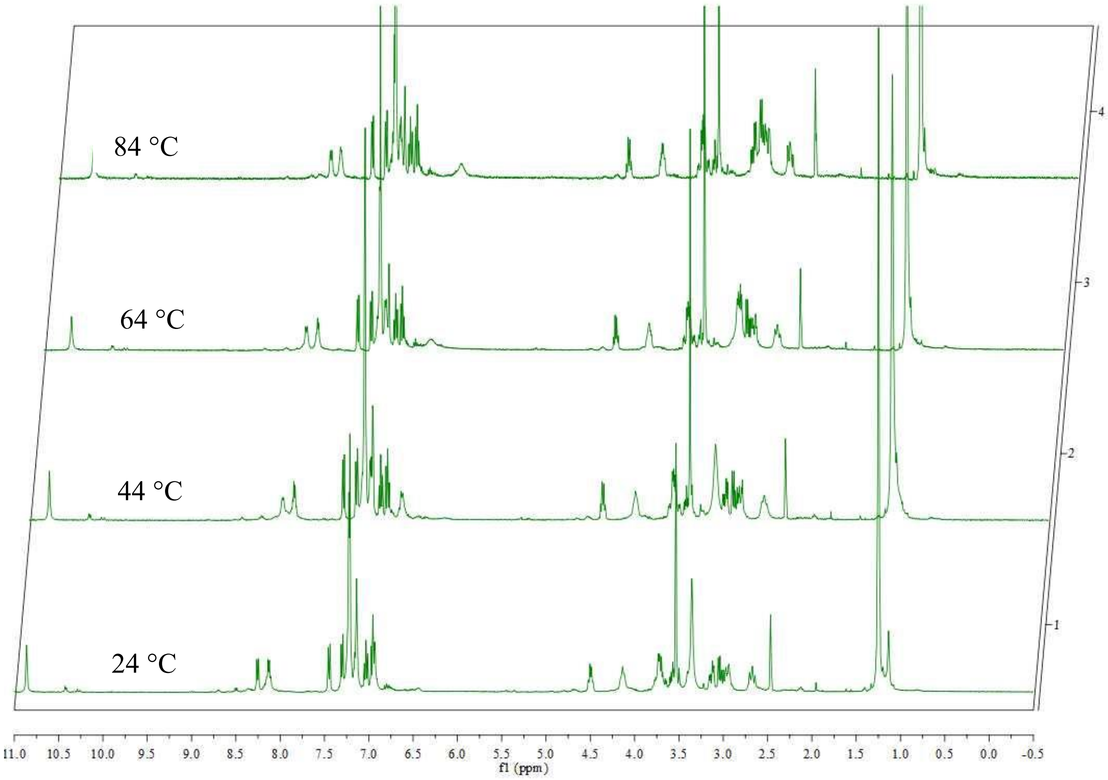
^{1}H NMR (399 MHz, DMSO-d$_6$) δ 10.82 (s, 1H), 8.21 (d, *J* = 7.4 Hz, 1H), 8.09 (d, *J* = 5.9 Hz, 1H), 7.44 (d, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 4.2 Hz, 4H), 7.16 – 7.09 (m, 2H), 7.02 (t, *J* = 7.4 Hz, 1H), 6.95 (t, *J* = 7.4 Hz, 1H), 6.89 (d, *J* = 8.5 Hz, 1H), 4.55 – 4.46 (m, 1H), 4.18 – 4.09 (m, 1H), 3.80 – 3.64 (m, 2H), 3.58 and 3.57 (s, 3H), 3.13 (dd, *J* = 14.5, 6.0 Hz, 1H), 3.07 – 2.90 (m, 2H), 2.76 – 2.63 (m, 1H), 1.24 (s, 9H).

^{13}C NMR (100 MHz, DMSO-d$_6$) δ 172.5, 172.3, 169.1, 155.7, 138.7, 136.5, 129.6 (2C), 128.4 (2C), 127.5, 126.5, 124.2, 121.4, 118.9, 118.3, 111.9, 109.6 and 109.6 (1C), 78.5, 56.1, 53.6, 52.2, 42.2, 37.8, 28.5 (3C), 27.6.

HRMS (ESI) m/z: Calcd for $[M+H]^+$ 523.2551; Found: 523.2547

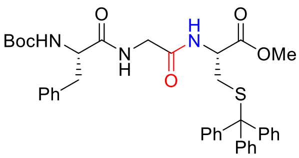
FT-IR (neat): 3308, 2917, 1662, 1523, 1456, 1367, 1251, 1168, 910, 735, 700 cm^{-1}

$[\alpha]_D^{24}$ 21.29 (c 3.6 $CHCl_3$)



Variable temperature **^{1}H NMR** (399 Hz, DMSO-d$_6$) spectra of compound **3j** to prove the rotamer.

Methyl N-(*tert*-butoxycarbonyl)-*L*-phenylalanylglycyl-S-trityl-*L*-cysteinate



Boc-Phe-Gly-Cys(STr)-OMe (3k)

3k was obtained in 43% yield as yellow solid (**mixture of two rotamers**). Purification by EtOAc/Hexane = 80%/20%

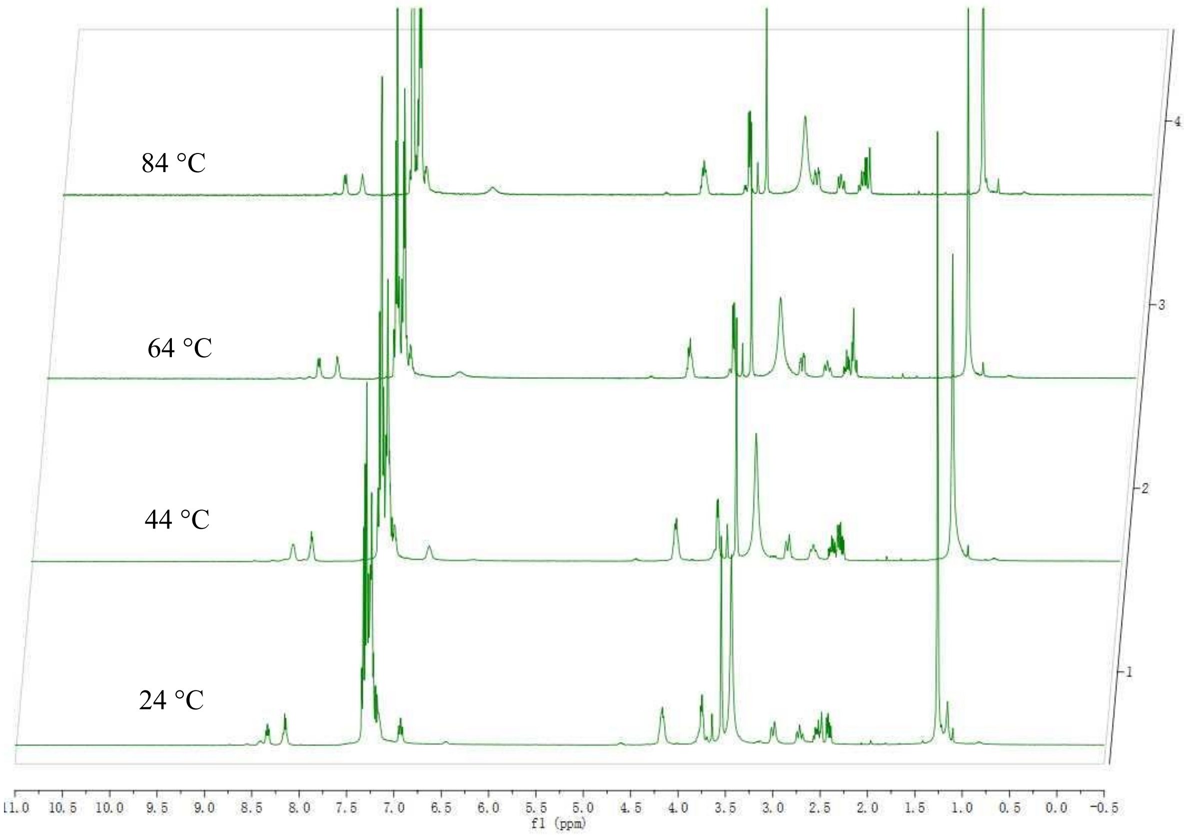
^{1}H NMR 44 °C (399 MHz, DMSO-d$_6$) δ 8.23 (s, 1H), 8.08 – 7.99 (m, 1H), 7.57 – 6.92 (m, 20H), 6.80 (s, 1H), 4.26 – 4.11 (m, 1H), 4.26 – 4.11 (m, 1H), 3.82 – 3.69 (m, 2H), 3.55 and 3.55 (s, 3H), 3.05 – 2.96 (m, 1H), 2.80 – 2.68 (m, 1H), 2.59 – 2.50 (m, 1H), 2.44 (dd, J = 12.4, 5.6 Hz, 1H), 1.27 (s, 9H).

^{13}C NMR (100 MHz, DMSO-d$_6$) δ 172.4 and 172.4 (1C), 170.9 and 170.9 (1C), 169.2 and 169.1 (1C), 155.7 and 155.7 (1C), 148.2, 144.4, 138.7, 129.6, 129.5, 128.5, 128.4, 128.2, 127.9, 127.3, 127.0, 126.5, 81.0 and 78.4 (1C), 66.8 and 66.8 (1C), 56.2 and 56.1 (1C), 52.7 and 52.6 (1C), 51.8 and 51.8 (1C), 42.0, 37.9 and 37.8 (1C), 33.3 and 33.2 (1C), 28.5 and 28.2 (3C).

HRMS (ESI) m/z: Calcd for $[M+H]^+$ 704.2765; Found: 704.2770

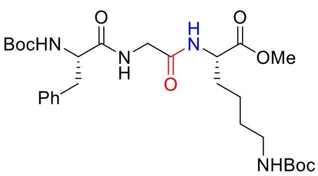
FT-IR (neat): 3298, 1745, 1651, 1519, 1443, 1366, 1170, 751, 700 cm^{-1}

$[\alpha]_D^{27}$ 14.09 (c 1.1 $CHCl_3$)



Variable temperature **^{1}H NMR** (399 Hz, DMSO-d$_6$) spectra of compound **3k** to prove the rotamer.

<u>Methyl N^6-(*tert*-butoxycarbonyl)-N^2-(*tert*-butoxycarbonyl)-*L*-phenylalanylglycyl-*L*-lysinate</u>



Boc-Phe-Gly-Lys(NHBoc)-OMe (3l)

3l was obtained in 53% yield as yellow solid (**mixture of two rotamers**). Purification by EtOAc/Hexane = 66%/34%

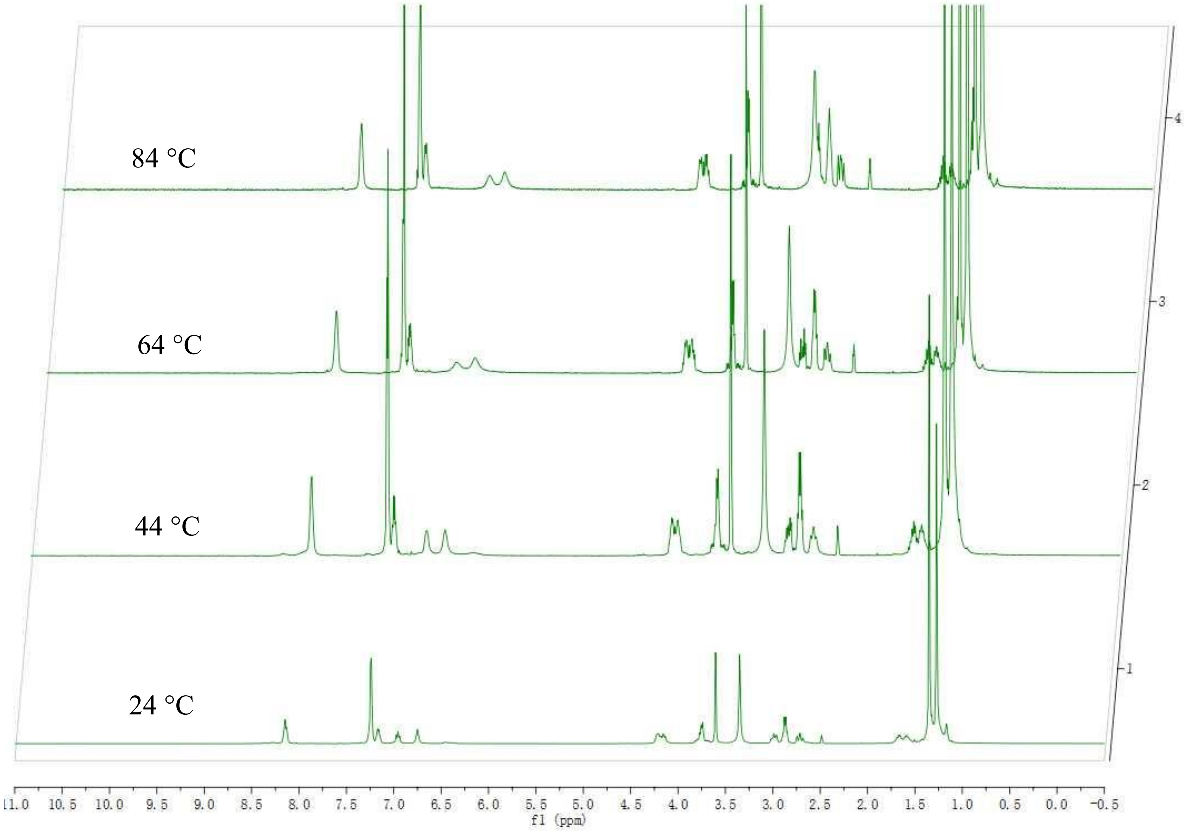
^{1}H NMR (399 MHz, DMSO-d$_6$) δ 8.20 – 8.07 (m, 1H), 8.20 – 8.07 (m, 1H), 7.31 – 7.09 (m, 5H), 7.00 – 6.90 (m, 1H), 6.75 (s, 1H), 4.27 – 4.08 (m, 1H), 4.27 – 4.08 (m, 1H), 3.82 – 3.69 (m, 2H), 3.61 and 3.60 (s, 3H), 3.04 – 2.94 (m, 1H), 2.92 – 2.80 (m, 1H), 2.92 – 2.80 (m, 1H), 2.76 – 2.66 (m, 1H), 1.74 – 1.52 (m, 2H), 1.35 (s, 9H), 1.51 – 0.97 (m, 2H), 1.51 – 0.97 (m, 2H), 1.27 (s, 9H).

^{13}C NMR (100 MHz, DMSO-d$_6$) δ 172.9 and 172.8 (1C), 172.4, 169.3 and 169.2 (1C), 156.0, 155.8 and 155.7 (1C), 138.7 and 138.6 (1C), 129.6 (2C), 128.4 (2C), 126.5, 78.5 and 78.5 (1C), 77.8, 56.2 and 56.1 (1C), 52.3, 52.2, 42.1, 37.8, 31.1 and 31.1 (1C), 29.5, 28.7 (3C), 28.5 (3C), 28.2, 23.0 and 23.0 (1C).

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 587.3051; Found: 587.3057.

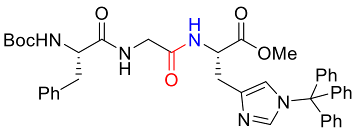
FT-IR (neat): 3315, 2978, 1687, 1524, 1455, 1366, 1251, 1220, 1171, 772 cm^{-1}

$[\alpha]_D^{27}$ -0.83 (c 2.3 $CHCl_3$)



Variable temperature **^{1}H NMR** (399 Hz, DMSO-d$_6$) spectra of compound **3l** to prove the rotamer.

<u>Methyl N$^{\alpha}$-(*tert*-butoxycarbonyl)-*L*-phenylalanylglycyl-N$^{\tau}$-trityl-*L*-histidinate</u>



Boc-Phe-Gly-His(NTr)-OMe (3m)

3m was obtained in 49% yield as yellow solid. Purification method: EtOAc/Hexane = 99%/1% was used at first to remove some impurities, then MeOH was used as eluent to flush the column and collect the MeOH eluent. Next, the collected MeOH eluent was concentrated under reduced pressure. The obtained residue was then purified by DCM/MeOH=94/6.

^{1}H NMR (399 MHz, DMSO-d$_6$) δ 8.25 (d, *J* = 7.5 Hz, 1H), 8.19 (s, 1H), 7.47 – 6.99 (m, 20H), 6.94 (d, *J* = 8.5 Hz, 1H), 6.66 (s, 1H), 4.55 – 4.45 (m, 1H), 4.24 – 4.13 (m, 1H), 3.71 (d, *J* = 4.0 Hz, 2H), 3.53 (s, 3H), 3.02 (d, *J* = 12.3 Hz, 1H), 2.89 – 2.75 (m, 2H), 2.75 – 2.66 (m, 1H), 1.24 (s, 9H).

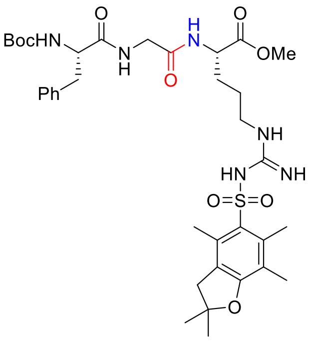
^{13}C NMR (100 MHz, DMSO-d$_6$) δ 172.5, 172.2, 169.0, 155.7, 142.6, 138.7, 138.3, 136.6, 129.6, 129.6, 128.6, 128.4, 128.4, 126.5, 119.7, 78.4, 74.9, 56.1, 52.7, 52.3, 42.2, 37.9, 30.4, 28.5 (3C).

HRMS (ESI) m/z: Calcd for $[M+H]^+$ 716.3443; Found: 716.3446.

FT-IR (neat): 3312, 1670, 1495, 1445, 1366, 1170, 1022, 750, 701, 662 cm^{-1}

$[\alpha]_D^{29}$-0.82 (c 1.6 $CHCl_3$)

Methyl N^2-(*tert*-butoxycarbonyl)-*L*-phenylalanylglycyl-N$^\omega$-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)-*L*-argininate



Boc-Phe-Gly-Arg(Pbf)-OMe (3n)

3n was obtained in 44% yield as yellow solid (**mixture of two rotamers**). Purification by EtOAc/Hexane = 99%/1%

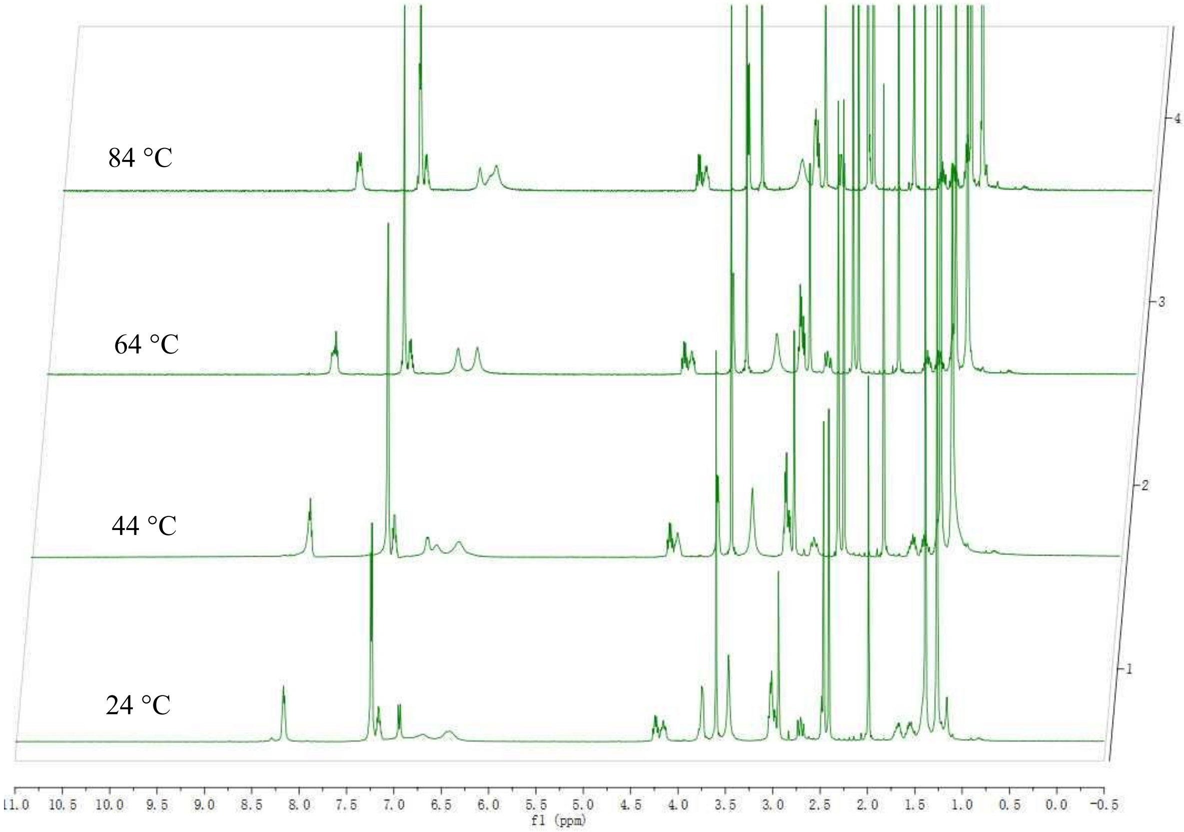
^{1}H NMR 64 °C (399 MHz, DMSO-d$_6$) δ 8.06 – 7.89 (m, 1H), 8.05 – 7.89 (m, 1H), 7.28 – 7.11 (m, 5H), 6.74 – 6.59 (brs, 2H), 6.51 – 6.39 (brs, 2H), 4.30 – 4.23 (m, 1H), 4.22 – 4.15 (m, 1H), 3.76 (d, *J* = 5.6 Hz, 2H), 3.61 (s, 3H), 3.08 – 2.99 (m, 1H), 3.08 – 2.99 (m, 1H), 3.08 – 2.99 (m, 1H), 2.94 (s, 2H), 2.75 (dd, *J* = 13.6, 10.0 Hz, 1H), 2.49 (s, 3H), 2.43 (s, 3H), 2.01 (s, 3H), 1.77 – 1.65 (m, 1H), 1.63 – 1.53 (m, 1H), 1.49 – 1.36 (m, 2H), 1.40 (s, 3H), 1.40 (s, 3H), 1.28 (s, 9H).

^{13}C NMR (100 MHz, DMSO-d$_6$) δ 172.7, 172.4, 169.2, 157.9, 156.5, 155.7, 138.7, 137.7, 134.6, 131.9, 129.6 (2C), 128.4 (2C), 126.6, 124.8, 116.7, 86.7, 78.5, 56.1, 52.3, 52.1, 42.9, 42.1, 37.8, 28.8, 28.7 (2C), 28.6 (3C), 28.2, 25.9, 19.4, 18.0, 12.7.

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 767.3409; Found: 767.3409.

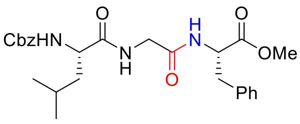
FT-IR (neat): 3330, 2976, 2360, 1662, 1550, 1250, 1166, 1106, 755, 663 cm^{-1}

$[\alpha]_D^{27}$ 10.12 (c 1.5 $CHCl_3$)



Variable temperature **^{1}H NMR** (399 Hz, DMSO-d$_6$) spectra of compound **3n** to prove the rotamer.

<u>Methyl ((benzyloxy)carbonyl)-*L*-leucylglycyl-*L*-phenylalaninate</u>



Cbz-Leu-Gly-Phe-OMe (3o)

3o was obtained in 57% yield as yellow solid. Purification by EtOAc/Hexane = 60%/40%

^{1}H NMR (399 MHz, $CDCl_3$) δ 7.38 – 7.17 (m, 8H), 7.14 – 7.04 (m, 2H), 6.99 – 6.90 (m, 1H), 6.85 (d, *J* = 7.2 Hz, 1H), 5.35 (d, *J* = 7.7 Hz, 1H), 5.14 – 4.97 (m, 2H), 4.83 (dd, *J* = 13.9, 6.3 Hz, 1H), 4.25 – 4.14 (m, 1H), 4.01 (dd, *J* = 17.0, 5.5 Hz, 1H), 3.81 (dd, *J* = 16.7, 4.6 Hz, 1H), 3.67 (s, 3H), 3.12 (dd, *J* = 13.8, 5.9 Hz, 1H), 3.05 (dd, *J* = 13.8, 6.5 Hz, 1H), 1.71 – 1.56 (m, 2H), 1.56 – 1.43 (m, 1H), 0.92 (d, *J* = 5.6 Hz, 6H).

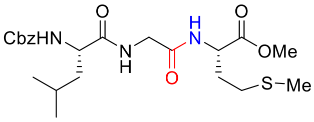
^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 171.7, 168.3, 156.3, 136.0, 135.7, 129.2 (2C), 128.6 (2C), 128.5 (2C), 128.2, 128.0 (2C), 127.1, 67.1, 53.4, 52.3, 42.9, 41.2, 37.8, 29.7, 24.6, 22.9, 21.8.

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 506.2262; Found: 506.2261.

FT-IR (neat): 3303, 2956, 1658, 1531, 1455, 1218, 1043, 910, 733, 699 cm^{-1}

$[\alpha]_D^{29}$ 22.21 (c 1.8 $CHCl_3$)

Methyl ((benzyloxy)carbonyl)-*L*-leucylglycyl-*L*-methioninate

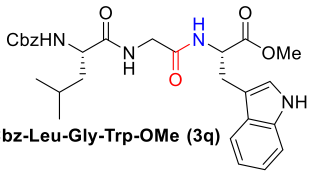


Cbz-Leu-Gly-Met-OMe (3p)

3p was obtained in 43% yield as yellow solid. Purification by EtOAc/Hexane = 50%/50%
^{1}H NMR (399 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 5H), 7.25 – 7.00 (m, 2H), 5.58 (s, 1H), 5.15 – 4.99 (m, 2H), 4.72 – 4.63 (m, 1H), 4.25 – 4.15 (m, 1H), 4.10 (dd, *J* = 16.8, 5.4 Hz, 1H), 3.87 (dd, *J* = 16.8, 4.9 Hz, 1H), 3.69 (s, 3H), 2.57 – 2.42 (m, 2H), 2.21 – 2.09 (m, 1H), 2.05 (s, 3H), 1.98 (dt, *J* = 21.3, 7.2 Hz, 1H), 1.73 – 1.59 (m, 2H), 1.58 – 1.46 (m, 1H), 0.97 – 0.83 (m, 6H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 172.2, 168.9, 156.4, 136.0, 128.5 (2C), 128.2, 128.0 (2C), 67.1, 53.8, 52.5, 51.5, 43.1, 41.1, 31.3, 29.9, 24.6, 22.9, 21.8, 15.4.
HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 490.1982; Found: 490.1982.
FT-IR (neat): 3301, 2956, 1660, 1536, 1439, 1238, 1172, 1121, 1042, 735, 698 cm^{-1}

$[\alpha]_D^{28}$ 11.58 (c 3.0 $CHCl_3$)

Methyl ((benzyloxy)carbonyl)-*L*-leucylglycyl-*L*-tryptophanate

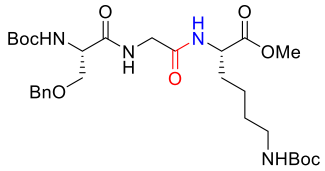


Cbz-Leu-Gly-Trp-OMe (3q)

3q was obtained in 62% yield as yellow solid. Purification by EtOAc/Hexane = 60%/40%
^{1}H NMR (399 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.33 – 7.21 (m, 6H), 7.18 – 7.07 (m, 3H), 7.07 – 7.00 (m, 1H), 6.93 (s, 1H), 5.58 (d, *J* = 6.9 Hz, 1H), 5.04 (t, *J* = 11.4 Hz, 1H), 4.90 (d, *J* = 12.3 Hz, 1H), 4.82 (dd, *J* = 12.9, 5.8 Hz, 1H), 4.23 – 4.11 (m, 1H), 3.86 (dd, *J* = 16.7, 5.4 Hz, 1H), 3.68 (dd, *J* = 16.3, 4.7 Hz, 1H), 3.57 (s, 3H), 3.28 – 3.18 (m, 2H), 1.67 – 1.49 (m, 2H), 1.46 – 1.36 (m, 1H), 0.94 – 0.73 (m, 6H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 172.2, 168.8, 156.5, 136.0, 136.0, 128.5 (2C), 128.1, 127.9 (2C), 127.2, 123.5, 121.9, 119.3, 118.2, 111.4, 109.2, 67.1, 53.6, 52.7, 52.4, 42.8, 41.1, 27.2, 24.6, 22.9, 21.7.
HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 545.2371; Found: 545.2365
FT-IR (neat): 3311, 2956, 1659, 1530, 1439, 1251, 1043, 910, 735 cm^{-1}

$[\alpha]_D^{29}$ 22.28 (c 3.6 $CHCl_3$)

Methyl N^{2}-O-benzyl-N-(*tert*-butoxycarbonyl)-*L*-serylglycyl-N^{6}-(*tert*-butoxycarbonyl)-*L*-lysinate



Boc-Ser(OBn)-Gly-Lys(NHBoc)-OMe (3r)

3r was obtained in 45% yield as yellow solid (**mixture of two rotamers**). Purification by EtOAc/Hexane = 66%/34%

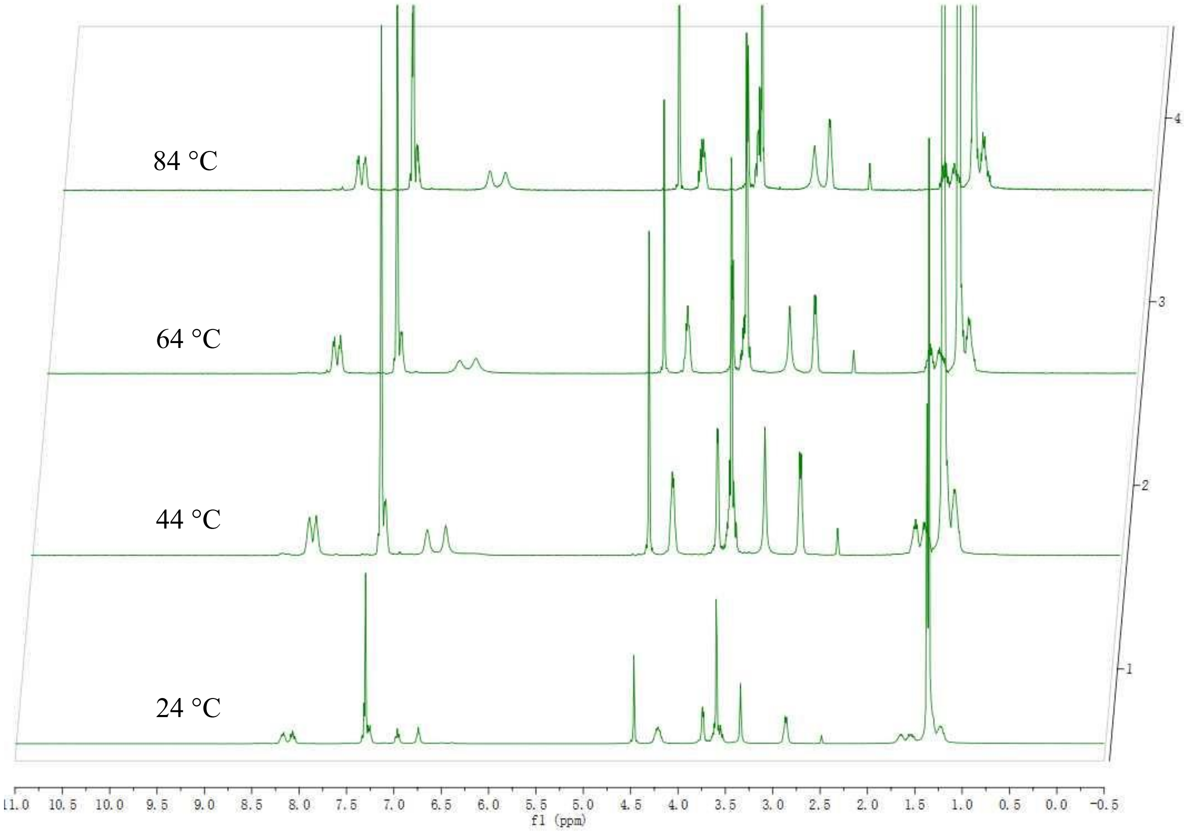
^{1}H NMR (399 MHz, DMSO-d$_6$) δ 8.23 – 8.12 (m, 1H), 8.12 – 8.01 (m, 1H), 7.39 – 7.17 (m, 5H), 6.96 (t, *J* = 7.4 Hz, 1H), 6.74 (t, *J* = 5.1 Hz, 1H), 4.47 (s, 2H), 4.30 – 4.14 (m, 1H), 4.31 – 4.14 (m, 1H), 3.81 – 3.69 (m, 2H), 3.67 – 3.48 (m, 2H), 3.60 and 3.59 (s, 3H), 2.92 – 2.79 (m, 2H), 1.72 – 1.60 (m, 1H), 1.59 – 1.48 (m, 1H), 1.37 (s, 9H), 1.35 (s, 9H), 1.47 – 1.06 (m, 2H), 1.47 – 1.05 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d$_6$) δ 172.8 and 172.8 (1C), 170.6 and 170.5 (1C), 169.2 and 169.1 (1C), 156.0, 155.9 and 155.8 (1C), 138.6 and 138.6 (1C), 128.6 (2C), 127.9 and 127.8 (2C), 127.8, 78.8 and 78.8 (1C), 77.7, 72.3, 70.2 and 70.2 (1C), 54.8 and 54.7 (1C), 52.3, 52.2, 42.2, 31.1 and 31.0 (1C), 29.4, 28.7 (3C), 28.6 (3C), 23.0 and 23.0 (1C).

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 617.3157; Found: 617.3160.

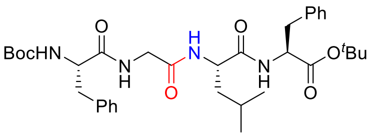
FT-IR (neat): 3326, 2978, 1686, 1525, 1366, 1250, 1170, 752, 699 cm^{-1}

$[\alpha]_D^{26}$5.69 (c 1.8 $CHCl_3$)



Variable temperature ^{1}**H NMR** (399 Hz, DMSO-d$_6$) spectra of compound **3r** to prove the rotamer.

***tert*-Butyl (*tert*-butoxycarbonyl)-*L*-phenylalanylglycyl-*L*-leucyl-*L*-phenylalaninate**



Boc-Phe-Gly-Leu-Phe-O*t*-Bu (3s)

3s was obtained in 67% yield as yellow solid. Purification by EtOAc/Hexane = 50%/50%

^{1}**H NMR** (399 MHz, DMSO-d$_6$) δ 8.33 – 8.19 (m, 1H), 8.16 – 8.04 (m, 1H), 7.86 – 7.77 (m, 1H), 7.38 – 7.08 (m, 10H), 6.95 (dd, *J* = 15.3, 8.3 Hz, 1H), 4.39 – 4.24 (m, 2H), 4.13 (dd, *J* = 12.5, 6.2 Hz, 1H), 3.69 (s, 2H), 3.04 – 2.83 (m, 3H), 2.69 (dd, *J* = 13.6, 10.7 Hz, 1H), 1.54 (dd, *J* = 13.3, 6.7 Hz, 1H), 1.48 – 1.34 (m, 2H), 1.26 (s, 9H), 1.25 (s, 9H), 0.84 (d, *J* = 6.5 Hz, 3H), 0.81 (d, *J* = 6.5 Hz, 3H).

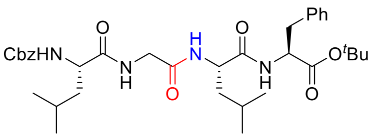
^{13}**C NMR** (100 MHz, DMSO-d$_6$) δ 172.4, 172.3, 170.7, 168.7, 155.7, 138.7, 137.6, 129.6(4C), 128.6 (2C), 128.4 (2C), 126.9, 126.6, 80.9, 78.5, 56.2, 54.6, 50.9, 42.4, 41.6, 37.8, 37.1, 28.6 (3C), 27.9 (3C), 24.5, 23.5, 22.1.

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 661.3572; Found: 661.3570

FT-IR (neat): 3292, 2976, 1641, 1541, 1455, 1367, 1251, 1159, 1048, 910, 851, 734, 699 cm^{-1}

$[\alpha]_D^{28}$ 10.39 (c 2.6 $CHCl_3$)

tert-Butyl ((benzyloxy)carbonyl)-_L_-leucylglycyl-_L_-leucyl-_L_-phenylalaninate



Cbz-Leu-Gly-Leu-Phe-O*t*-Bu (3t)

3t was obtained in 47% yield as yellow solid. Purification by EtOAc/Hexane = 60%/40%

^{1}H NMR (399 MHz, $CDCl_3$) δ 7.39 – 7.26 (m, 4H), 7.24 – 7.09 (m, 5H), 7.03 (s, 1H), 6.94 (s, 1H), 5.69 (d, J = 6.6 Hz, 1H), 5.10 (d, J = 12.2 Hz, 1H), 4.98 (d, J = 12.2 Hz, 1H), 4.71 (dd, J = 14.2, 6.5 Hz, 1H), 4.59 – 4.46 (m, 1H), 4.22 (s, 1H), 4.01 (d, J = 12.8 Hz, 1H), 3.84 (d, J = 15.2 Hz, 1H), 3.10 – 2.92 (m, 2H), 1.75 – 1.43 (m, 6H), 1.34 (s, 9H), 1.10 – 0.62 (m, 12H).

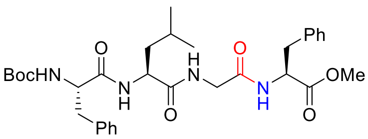
^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 171.6, 170.6, 168.8, 156.5, 136.2, 136.0, 129.5, 128.5, 128.2, 128.2, 128.0, 126.8, 82.4, 67.1, 53.8, 53.6, 51.9, 43.1, 41.2, 41.0, 38.1, 27.9 (3C), 24.7(2C), 22.9, 22.8, 22.0(2C).

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 661.3572; Found: 661.3573.

FT-IR (neat): 3286, 2956, 1639, 1539, 1368, 1233, 1155, 732, 697 cm^{-1}

$[\alpha]_D^{27}$ 14.55 (c 0.9 $CHCl_3$)

Methyl (_tert_-butoxycarbonyl)-_L_-phenylalanyl-_L_-leucylglycyl-_L_-phenylalaninate



Boc-Phe-Leu-Gly-Phe-OMe (3u)

3u was obtained in 50% yield as yellow solid (**mixture of two rotamers**). Purification by EtOAc/Hexane = 75%/25%

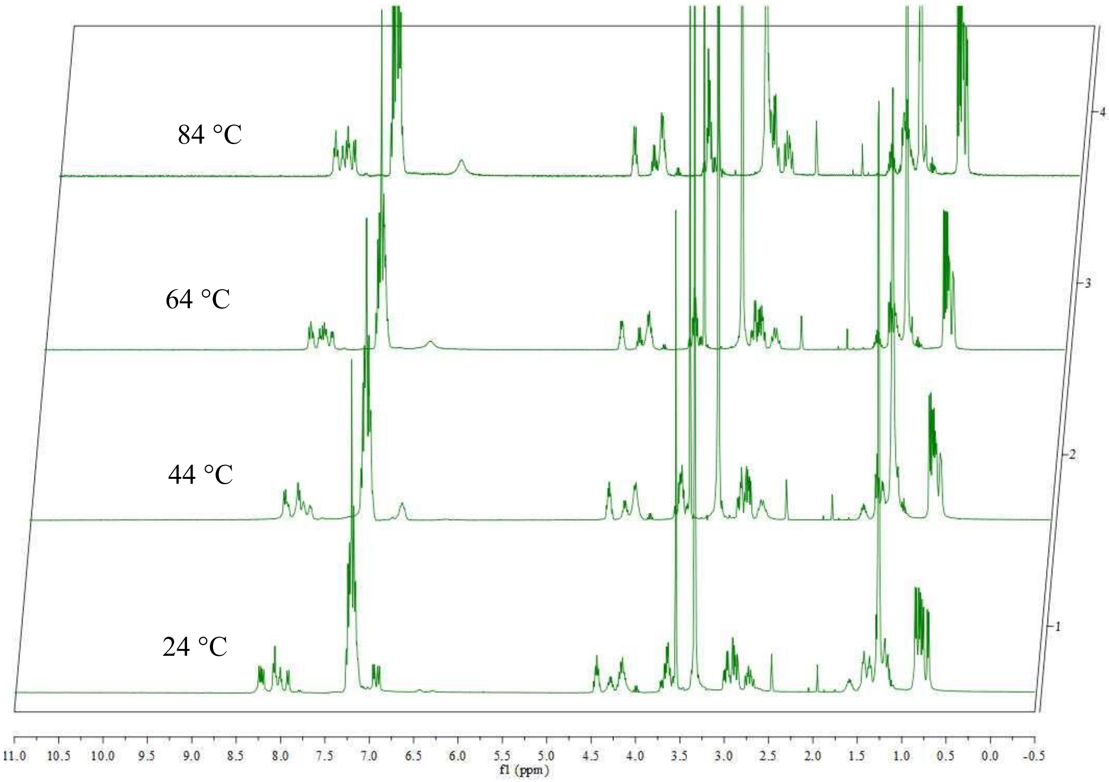
^{1}H NMR (399 MHz, DMSO-d_6) δ (8.23 (d, J = 7.6 Hz) and 8.20 (d, J = 7.6 Hz), 1H), 8.11 – 8.04 (m, 1H), 8.02 – 7.89 (m, 1H), 7.39 – 7.01 (m, 10H), (6.95 (d, J = 7.2 Hz) and 6.90 (d, J = 8.4 Hz), 1H), 4.49 – 4.39 (m, 1H), 4.34 – 4.08 (m, 2H), 3.76 – 3.60 (m, 2H), 3.54 (s, 3H), 3.02 – 2.82 (m, 3H), 2.77 – 2.65 (m, 1H), 1.72 – 1.53 (m, 1H), 1.40 (ddd, J = 14.7, 10.1, 3.5 Hz, 2H), 1.26 and 1.26 (s, 9H), (0.84 (d, J = 6.4 Hz) and 0.76 (d, J = 6.4 Hz), 3H), (0.80 (d, J = 6.4 Hz) and 0.70 (d, J = 6.4 Hz), 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 172.6, 172.2 and 172.2 (1C), 172.0, 169.1 and 169.0 (1C), 155.8 and 155.7 (1C), 138.5 and 138.1 (1C), 137.4, 129.6 (2C), 129.5 (2C), 128.7 (2C), 128.4 (2C), 127.0, 126.6 and 126.5 (1C), 78.7 and 78.5 (1C), 56.4 and 56.1 (1C), 54.1 and 54.0 (1C), 52.3, 51.4 and 51.4 (1C), 41.9, 41.4 and 41.0 (1C), 37.9 and 37.5 (1C), 37.3, 28.5 and 28.5 (3C), 24.3 and 24.3 (1C), 23.6 and 23.5 (1C), 22.0 and 21.7 (1C).

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 619.3102; Found: 619.3096

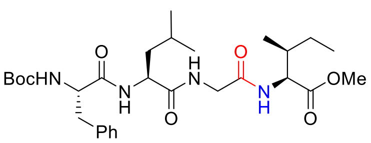
FT-IR (neat): 3287, 2956, 1642, 1528, 1455, 1367, 1250, 1171, 1030, 911, 734, 700 cm^{-1}

$[\alpha]_D^{23}$ 15.10 (c 0.7 $CHCl_3$)



Variable temperature ^{1}**H NMR** (399 Hz, DMSO-d_6) spectra of compound **3u** to prove the rotamer.

Methyl (*tert*-butoxycarbonyl)-*L*-phenylalanyl-*L*-leucylglycyl-*L*-isoleucinate



3v was obtained in 53% yield as yellow solid (**mixture of two rotamers**). Purification by EtOAc/Hexane = 70%/30%

^{1}**H NMR** (399 MHz, DMSO-d_6) δ 8.13 – 7.85 (m, 1H), 8.15 – 7.86 (m, 1H), 8.13 – 7.85 (m, 1H), 7.33 – 7.06 (m, 5H), (6.92 (d, *J* = 7.2 Hz) and 6.86 (d, *J* = 8.4 Hz), 1H), 4.39 – 4.25 (m, 1H), 4.23 – 4.06 (m, 1H), 4.23 – 4.06 (m, 1H), 3.82 – 3.64 (m, 2H), 3.59 (s, 3H), 2.97 – 2.83

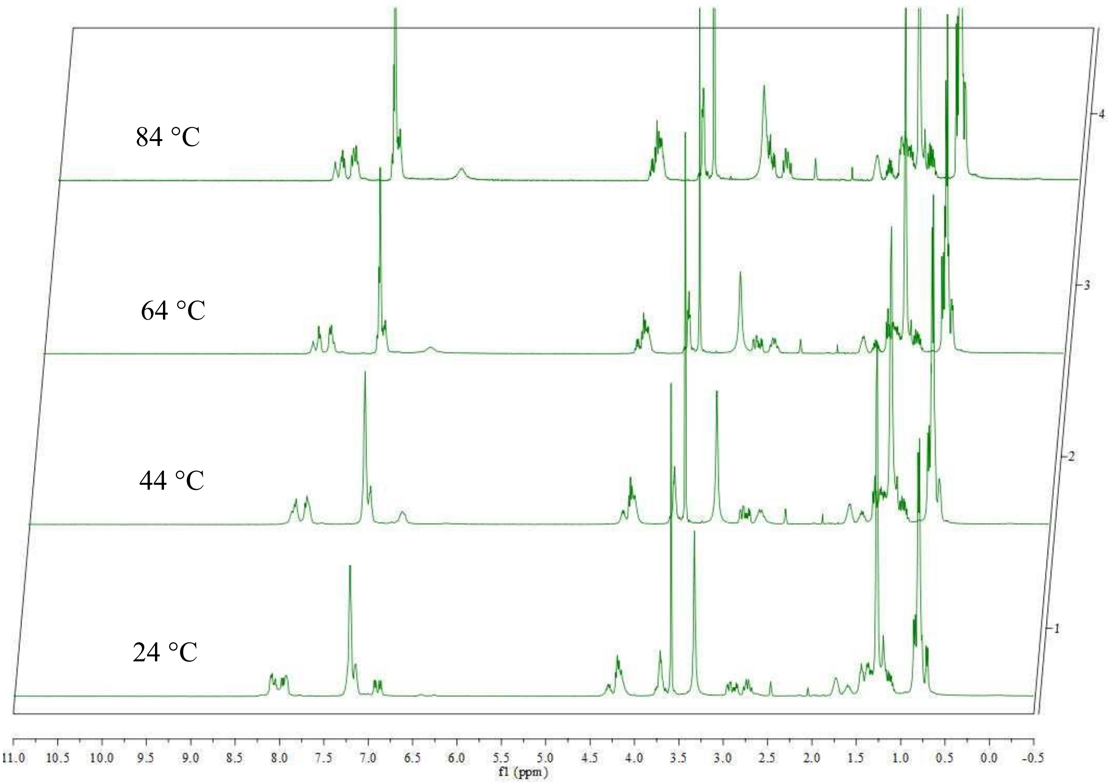
(m, 1H), 2.78 – 2.65 (m, 1H), 1.79 – 1.67 (m, 1H), 1.65 – 1.53 (m, 1H), 1.27 and 1.26 (s, 9H), 1.51 – 1.01 (m, 4H), 0.97 – 0.44 (m, 12H).

^{13}C NMR (100 MHz, DMSO-d$_6$) δ 172.7 and 172.6 (1C), 172.3, 172.0 and 172.0 (1C), 169.2 and 169.2 (1C), 155.7 and 155.6 (1C), 138.5 and 138.0 (1C), 129.6 (2C), 128.4 (2C), 126.6 and 126.5 (1C), 78.6 and 78.5 (1C), 56.7, 56.4 and 56.1 (1C), 52.1, 51.4, 42.1, 41.5 and 41.0 (1C), 37.9 and 37.5 (1C), 36.9 and 36.8 (1C), 28.5 and 28.5 (3C), 25.1, 24.3 and 24.3 (1C), 23.5, 21.9 and 21.7 (1C), 15.8 and 15.8 (1C), 11.5 and 11.5 (1C).

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 585.3259; Found: 585.3254

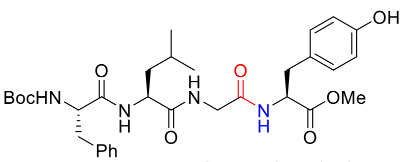
FT-IR (neat): 3289, 2961, 1646, 1530, 1367, 1251, 1170, 911, 734 cm^{-1}

$[\alpha]_D^{26}$ 2.47 (c 0.8 $CHCl_3$)



Variable temperature **^{1}H NMR** (399 Hz, DMSO-d$_6$) spectra of compound **3v** to prove the rotamer.

<u>Methyl (*tert*-butoxycarbonyl)-*L*-phenylalanyl-*L*-leucylglycyl-*L*-tyrosinate</u>



Boc-Phe-Leu-Gly-Tyr-OMe (3w)

3w was obtained in 51% yield as yellow solid (**mixture of two rotamers**). Purification by EtOAc/Hexane = 70%/30%

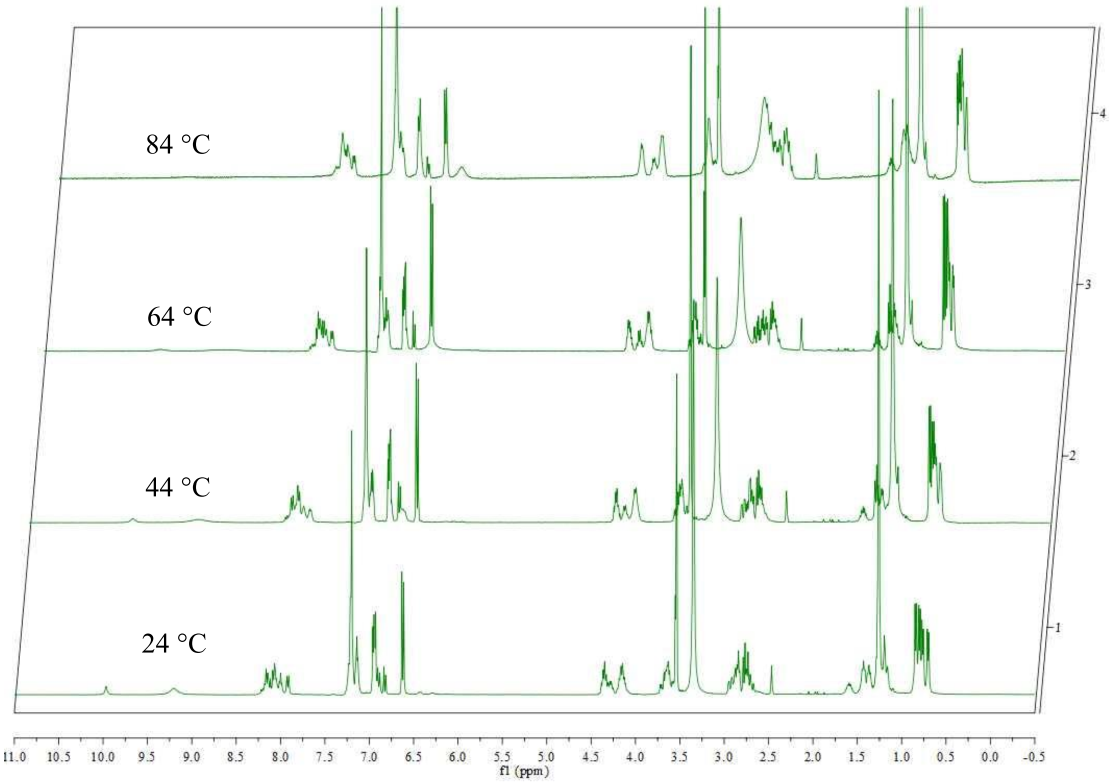
^{1}H NMR (399 MHz, DMSO-d$_6$) δ 9.97 and 9.21 (s, 1H), 8.24 – 8.04 (m, 1H), 8.24 – 8.04 (m, 1H), 8.02 – 7.86 (m, 1H), 7.33 – 7.07 (m, 5H), 7.02 – 6.78 (m, 2H), 7.00 – 6.77 (m, 1H), 6.66 – 6.26 (m, 2H), 4.41 – 4.08 (m, 1H), 4.41 – 4.08 (m, 1H), 4.41 – 4.08 (m, 1H), 3.77 – 3.60 (m, 2H), 3.54 (s, 3H), 2.98 – 2.82 (m, 2H), 2.80 – 2.63 (m, 2H), 1.67 – 1.54 (m, 1H), 1.47 – 1.34 (m, 2H), 1.26 (s, 9H), (0.84 (d, J = 6.4 Hz) and 0.76 (d, J = 6.4 Hz), 3H), (0.80 (d, J = 6.8 Hz) and 0.70 (d, J = 6.0 Hz), 3H).

^{13}C NMR (100 MHz, DMSO-d$_6$) δ 172.6 and 172.4 (1C), 172.3 and 172.0 (1C), 169.0 and 169.0 (1C), 156.4 and 152.1 (1C), 155.8 and 155.7 (1C), 138.5 and 138.1 (1C), 130.7 and 130.4 (2C), 129.6 and 129.1 (2C), 128.4 (2C), 127.4 and 127.3 (1C), 126.6 and 126.5 (1C), 119.7 and 116.9 (1C), 115.5 (2C), 78.7 and 78.5 (1C), 56.4 and 56.1 (1C), 54.4 and 54.4 (1C), 52.3 and 52.2 (1C), 51.4 and 51.4 (1C), 41.9, 41.4 and 41.0 (1C), 37.9 and 37.5 (1C), 36.6 and 36.1 (1C), 28. and, 28.5 (3C), 24.3 and 24.3 (1C), 23.6 and 23.5 (1C), 21.9 and 21.7 (1C).

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 635.3051; Found: 635.3047.

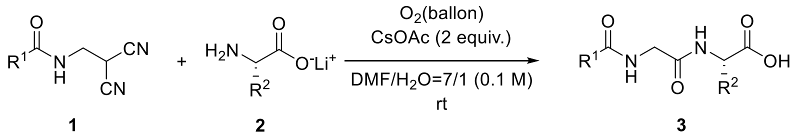
FT-IR (neat): 3296, 2959, 1652, 1517, 1367, 1259, 1170, 910, 801, 735 cm^{-1}

$[\alpha]_D^{18}$ 16.29 (c 1.6 $CHCl_3$)



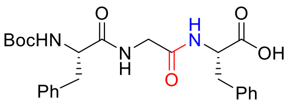
Variable temperature **^{1}H NMR** (399 Hz, DMSO-d$_6$) spectra of compound **3w** to prove the rotamer.

2.8 Typical procedure of oxidative peptide synthesis using unprotected amino acid and physical information



To a mixture of the amino acid lithium salt **2** (0.4 mmol) in DMF/H_2O=7/1 (2 mL) was added CsOAc (76.8 mg, 0.4 mmol). The mixture was stirred and then was filled with O_2. The dicyano compound **1** (0.2 mmol) was then added and stirred at room temperature. The mixture was then diluted by EtOAc and quenched with 1N HCl and extracted with EtOAc/^{t}BuOH=10/1. The organic phase was dried over Na_2SO_4 and concentrated using air blower under 80 °C and then concentrated in vacuo. The crude product was purified by silica gel column chromatography, eluted with CH_2Cl_2/MeOH containing 0.5% acetic acid.

(*tert*-Butoxycarbonyl)-*L*-phenylalanylglycyl-*L*-phenylalanine



Boc-Phe-Gly-Phe-OH (3x)

3x was obtained in 67% yield as white solid. Purification by CH_2Cl_2/MeOH = 91%/9% (0.5% acetic acid was added to the eluent).

^{1}H NMR (399 MHz, DMSO-d$_6$) δ 8.18 – 8.02 (m, 2H), 7.34 – 7.06 (m, 10H), 6.95 – 6.83 (m, 1H), 4.47 – 4.35 (m, 1H), 4.19 – 4.07 (m, 1H), 3.81 – 3.55 (m, 2H), 3.02 (dd, *J* = 13.8, 5.0 Hz, 1H), 2.98 – 2.91 (m, 1H), 2.85 (dd, *J* = 13.7, 8.9 Hz, 1H), 2.67 (dd, *J* = 13.3, 10.9 Hz, 1H), 1.25 (s, 9H).

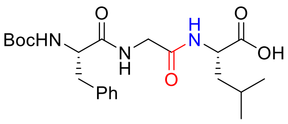
^{13}C NMR (100 MHz, DMSO-d$_6$) δ 173.1, 172.3, 169.0, 155.7, 138.7, 137.8, 129.6 (2C), 129.5 (2C), 128.6 (2C), 128.4 (2C), 126.9, 126.5, 78.5, 56.1, 53.9, 42.1, 37.9, 37.3, 28.6 (3C).

HRMS (ESI) m/z: Calcd for $[M+H]^+$ 470.2286; Found: 470.2284.

FT-IR (neat): 3406, 2499, 2073, 1656, 1456, 1165, 1119, 976, 735, 701 cm^{-1}

$[\alpha]_D^{25}$ 15.13 (c 1.1 DMSO)

(*tert*-Butoxycarbonyl)-*L*-phenylalanylglycyl-*L*-leucine

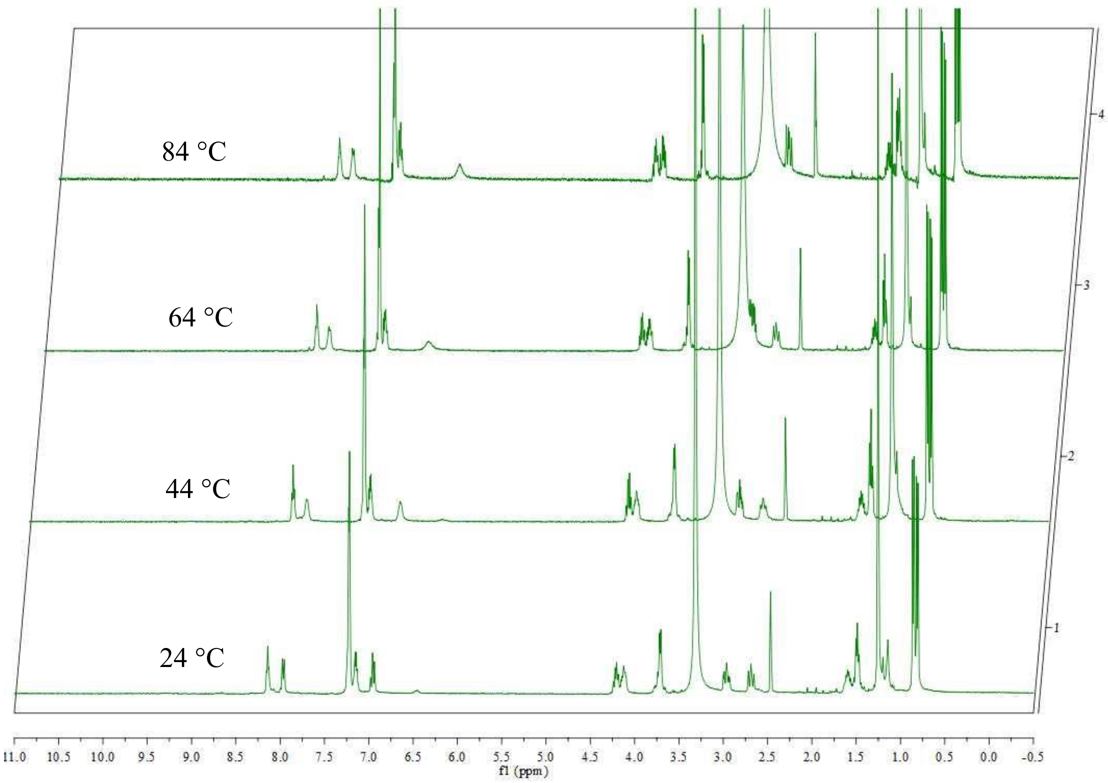


Boc-Phe-Gly-Leu-OH (3y)

3y was obtained in 64% yield as yellow solid (**mixture of two rotamers**). Purification by CH_2Cl_2/MeOH = 92%/8% (0.5% acetic acid was added to the eluent).

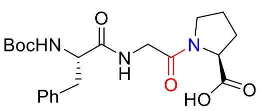
^{1}H NMR (399 MHz, DMSO-d$_6$) δ 8.13 (t, *J* = 5.6 Hz, 1H), 7.95 (d, *J* = 7.9 Hz, 1H), 7.27 – 7.19 (m, 4H), 7.18 – 7.12 (m, 1H), 6.95 (t, *J* = 8.5 Hz, 1H), 4.26 – 4.09 (m, 2H), 3.80 – 3.69 (m, 2H), 3.02 – 2.92 (m, 1H), 2.69 (dd, *J* = 13.5, 11.0 Hz, 1H), 1.66 – 1.44 (m, 3H), 1.26 (s, 9H), 0.86 (d, *J* = 6.5 Hz, 3H), 0.82 (d, *J* = 6.4 Hz, 3H).
^{13}C NMR (100 MHz, DMSO-d$_6$) δ 174.3, 172.3, 169.0, 155.7 and 155.8 (1C), 138.7, 129.6 (2C), 128.4 (2C), 126.5, 78.5, 56.1, 50.6, 42.2, 37.7, 28.6 (3C), 24.6, 23.2 and 23.3 (1C), 21.8 and 21.8 (2C).
HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 458.2262; Found: 458.2260.
FT-IR (neat): 3310, 2956, 2359, 1651, 1455, 1393, 1366, 1251, 1164, 699, 578 cm^{-1}

$[\alpha]_D^{25}$ 9.07 (c 0.83 $CHCl_3$)



Variable temperature **^{1}H NMR** (399 Hz, DMSO-d$_6$) spectra of compound **3y** to prove the rotamer.

(*tert*-Butoxycarbonyl)-*L*-phenylalanylglycyl-*L*-proline



Boc-Phe-Gly-Pro-OH (3z)

3z was obtained in 66% yield as yellow solid (**mixture of two rotamers**). Purification by CH_2Cl_2/MeOH = 91%/9%.

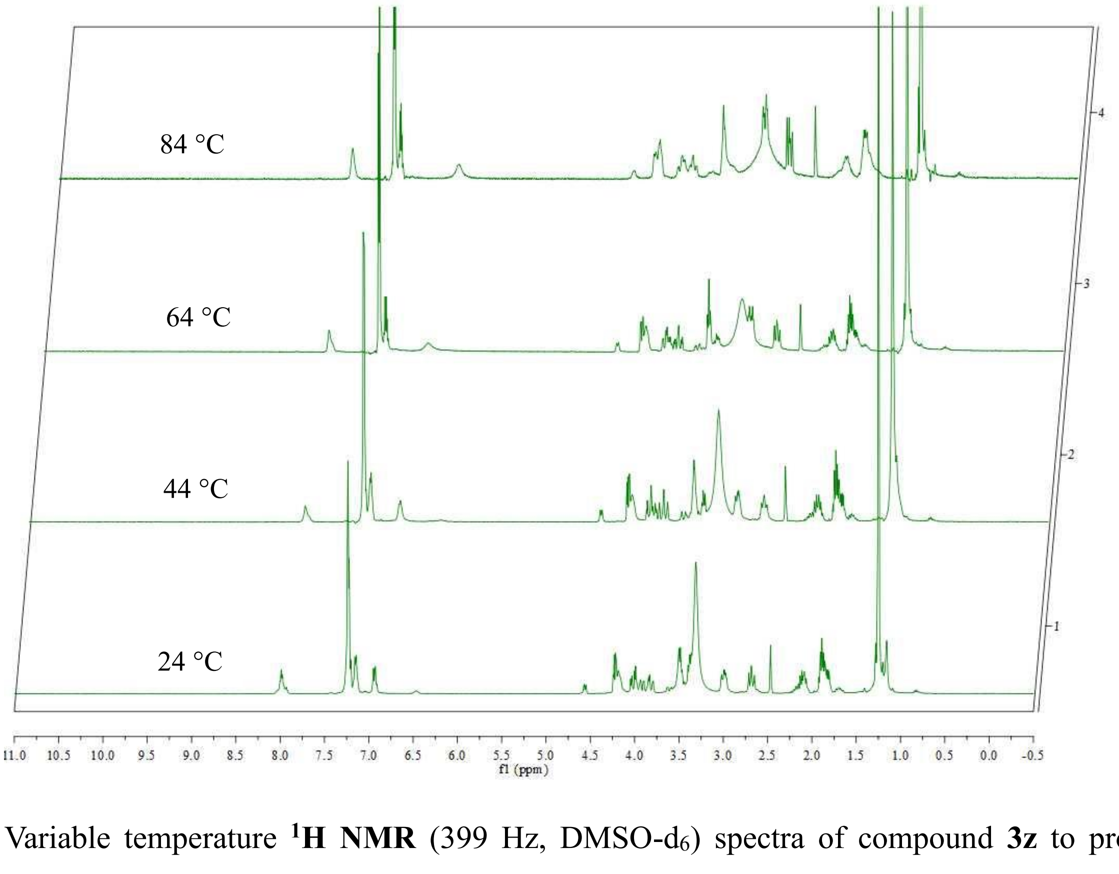
^{1}H NMR 44 °C (399 MHz, DMSO-d_6) δ 7.89 (s, 1H), 7.35 – 7.03 (m, 5H), 6.81, 6.35 (s, 1H), 4.59 – 4.51 and 4.28 – 4.12 (m, 1H), 4.28 – 4.12 (m, 1H), 4.05 – 3.77 and 3.65 – 3.57 (m, 2H), 3.56 – 3.37 (m, 2H), 3.02 (dd, *J* = 13.5, 3.9 Hz, 1H), 2.71 (dd, *J* = 12.8, 11.2 Hz, 1H), 2.30 – 1.98 and 1.75 – 1.64 (m, 2H), 1.95 – 1.78 (m, 2H), 1.26 (s, 9H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 173.9 and 173.6 (1C), 172.3 and 172.2 (1C), 167.4 and 167.1 (1C), 155.7, 138.8 and 138.7 (1C), 129.6 (2C), 128.4 (2C), 126.5, 78.4, 59.0 and 58.4 (1C), 56.1, 46.7 and 45.9 (1C), 41.6 and 41.5 (1C), 37.9, 31.2 and 29.1 (1C), 28.5 and 28.2 (3C), 24.7 and 22.3 (1C).

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 442.1949; Found: 442.1950

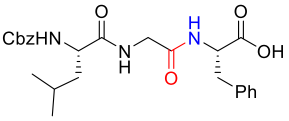
FT-IR (neat): 2918, 2370, 1637, 1456, 1366, 1168, 1022, 753, 700 cm^{-1}

$[\alpha]_D^{24}$ -33.54 (c 0.6 $CHCl_3$)



Variable temperature **^{1}H NMR** (399 Hz, DMSO-d_6) spectra of compound **3z** to prove the rotamer.

((Benzyloxy)carbonyl)-*L*-leucylglycyl-*L*-phenylalanine



Cbz-Leu-Gly-Leu-OH (3aa)

3aa was obtained in 55% yield as yellow solid. Purification by CH_2Cl_2/MeOH = 91%/9%.

^{1}H NMR (399 MHz, DMSO-d_6) δ 8.09 (t, *J* = 5.6 Hz, 1H), 8.02 (d, *J* = 7.9 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.37 – 6.98 (m, 10H), 4.97 (s, 2H), 4.45 – 4.33 (m, 1H), 4.06 – 3.93 (m, 1H), 3.65 (dd, *J* = 16.8, 4.4 Hz, 2H), 3.01 (dd, *J* = 13.8, 5.1 Hz, 1H), 2.84 (dd, *J* = 13.7, 8.8 Hz, 1H), 1.65 – 1.50 (m, 1H), 1.48 – 1.32 (m, 2H), 0.83 (d, *J* = 7.0 Hz, 3H), 0.81 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 173.1, 173.0, 169.0, 156.5, 137.8, 137.4, 129.5 (2C), 128.7 (2C), 128.6 (2C), 128.2 (2C), 128.1, 126.9, 65.8, 53.9, 53.6, 42.1, 41.0, 37.3, 24.6, 23.4, 21.8 (2C).

HRMS (ESI) m/z: Calcd for $[M+Na]^+$ 492.2105; Found: 492.2102.

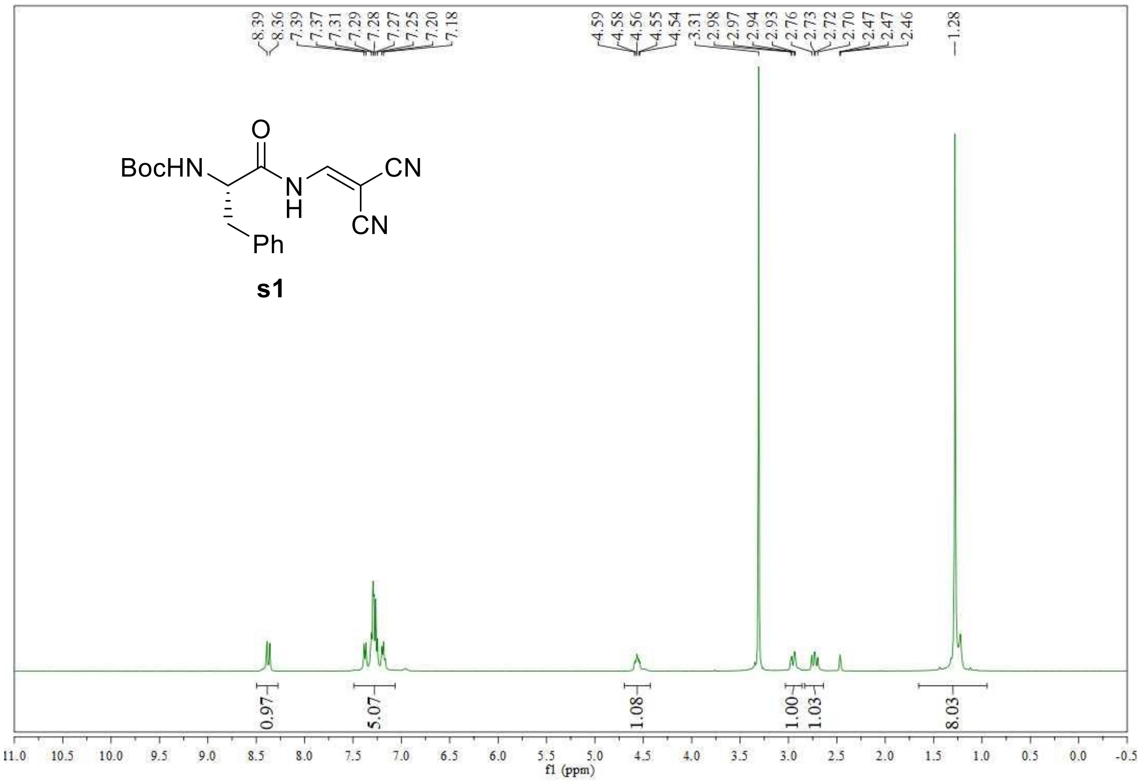
FT-IR (neat): 3324, 2957, 2492, 1655, 1533, 1455, 1256, 1026, 951, 700 cm^{-1}

$[\alpha]_D^{26}$ 5.73 (c 0.47 DMSO)

3. Reference

1. (a) C. B. Mishra, R. K. Mongre, S. Kumari, D. K. Jeong and M. Tiwari, *RSC Adv.*, 2016, **6**, 24491; (b) S. M. Schmitt, K. Stefan and M. Wiese, *J. Med. Chem.*, 2016, **59**, 3018.
2. S. Kokinaki, L. Leondiadis and N. Ferderigos, *Org. Lett.*, 2005, **7**, 1723.

4. Spectra



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8.36
7.39
7.37
7.31
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7.27
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7.20
7.18
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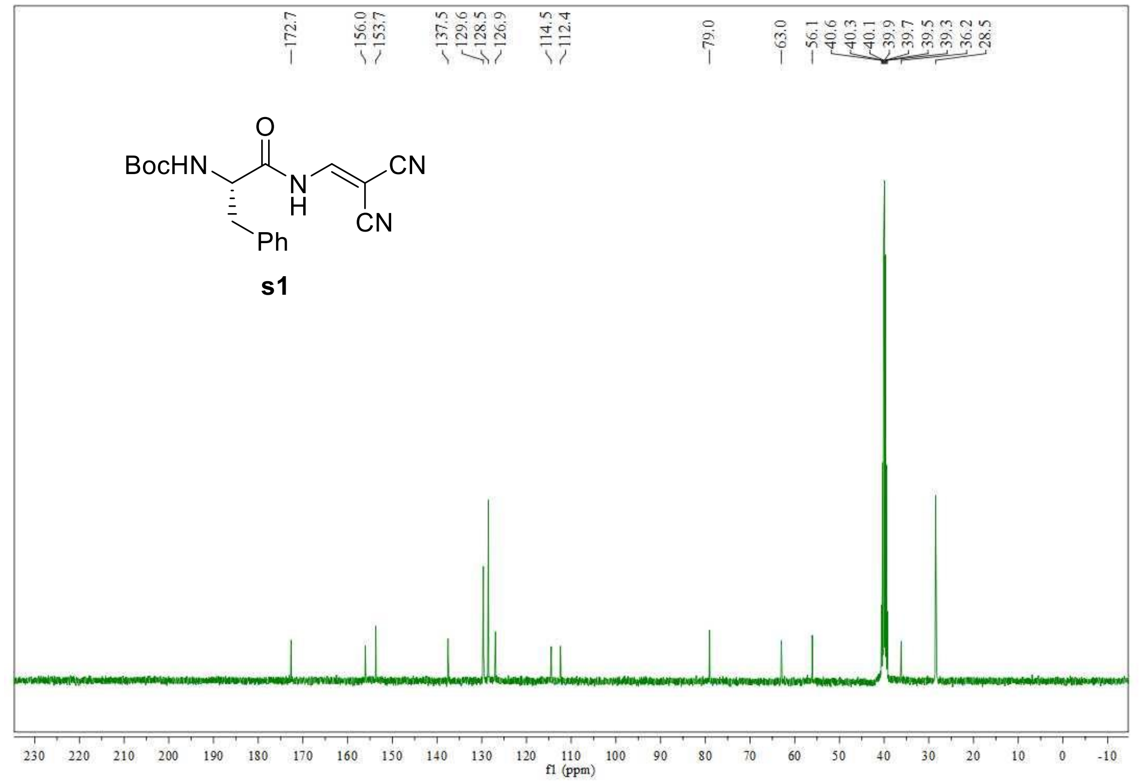
4.58
4.56
4.55
4.54
3.31
2.98
2.97
2.94
2.93
2.76
2.73
2.72
2.70
2.47
2.47
2.46
1.28
BocHN
O
N
H
CN
CN
Ph
s1
0.97
5.07
1.08
1.00
1.03
8.03
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)



172.7
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153.7
137.5
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114.5
112.4
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63.0
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40.6
40.3
40.1
39.9
39.7
39.5
39.3
36.2
28.5
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O
N
H
CN
CN
Ph
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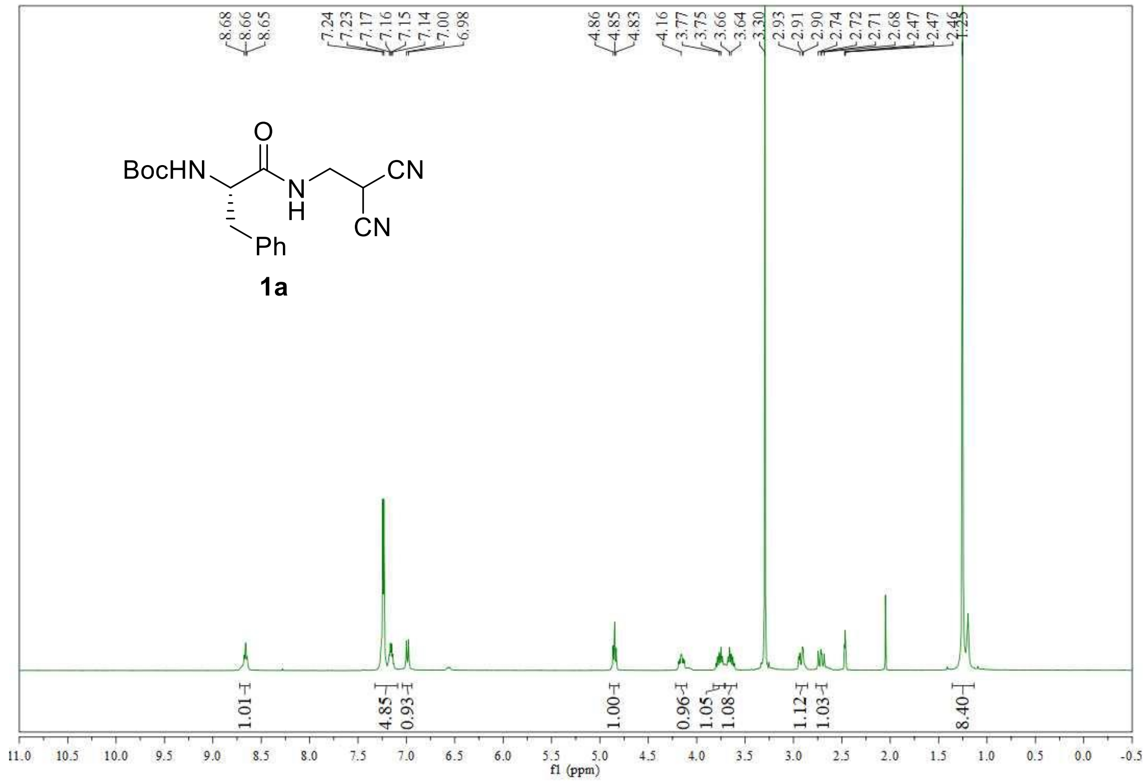
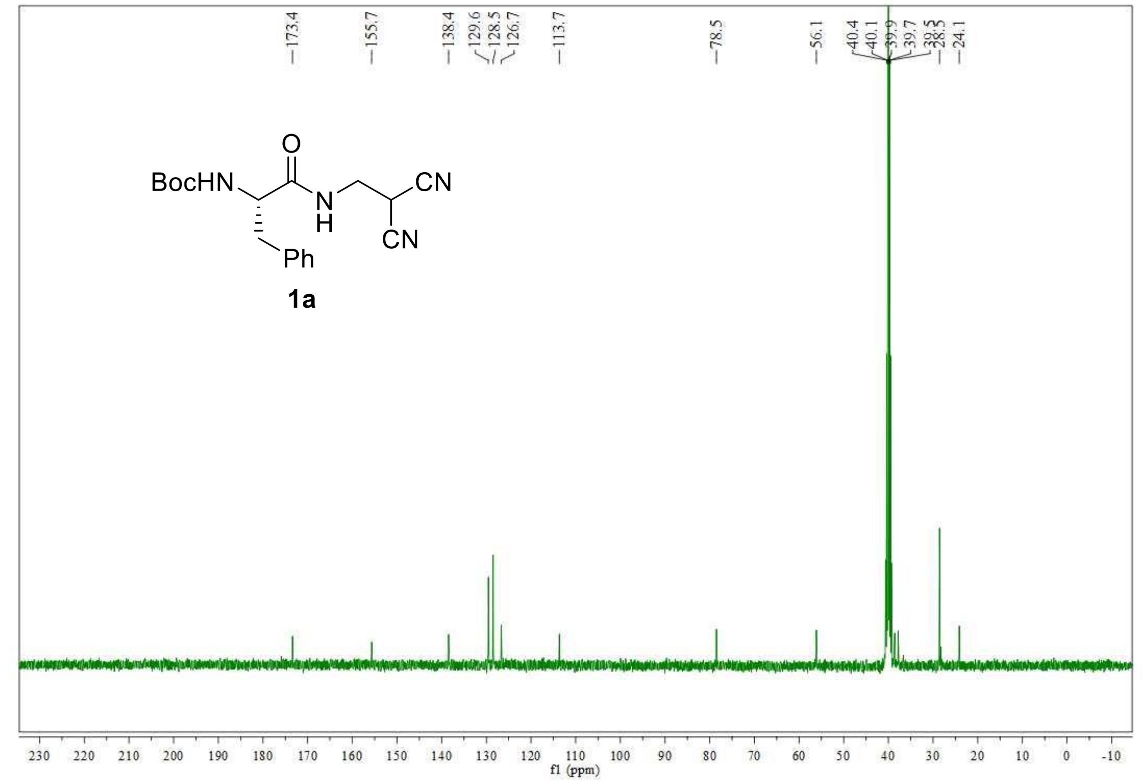
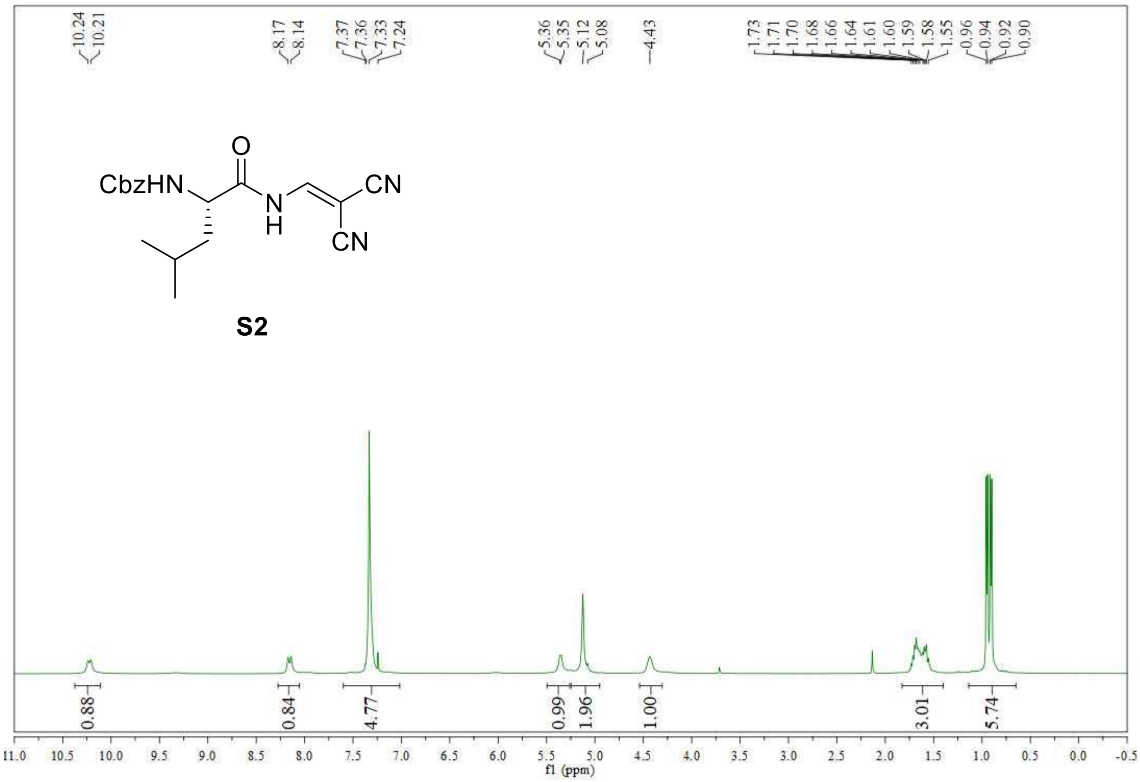
f1 (ppm)



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1.73
1.71
1.70
1.68
1.66
1.64
1.61
1.60
1.59
1.58
1.55
0.96
0.94
0.92
0.90
CbzHN
O
N
H
CN
CN
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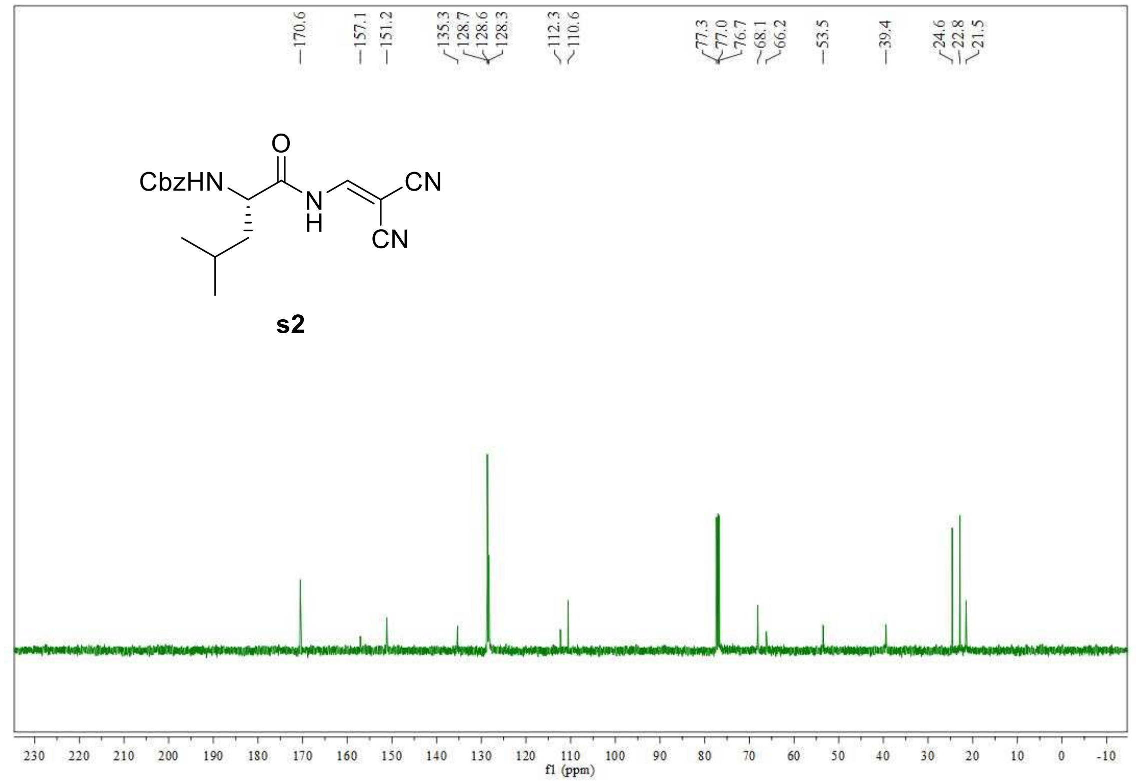
5.74
f1 (ppm)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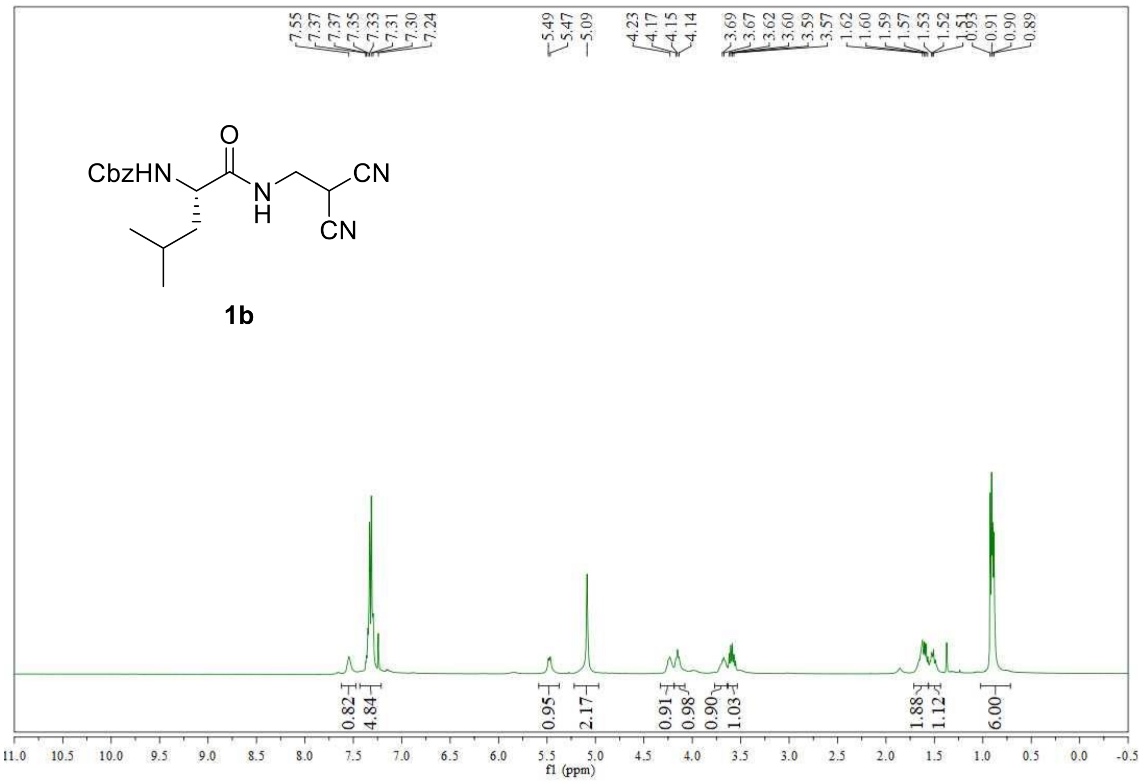
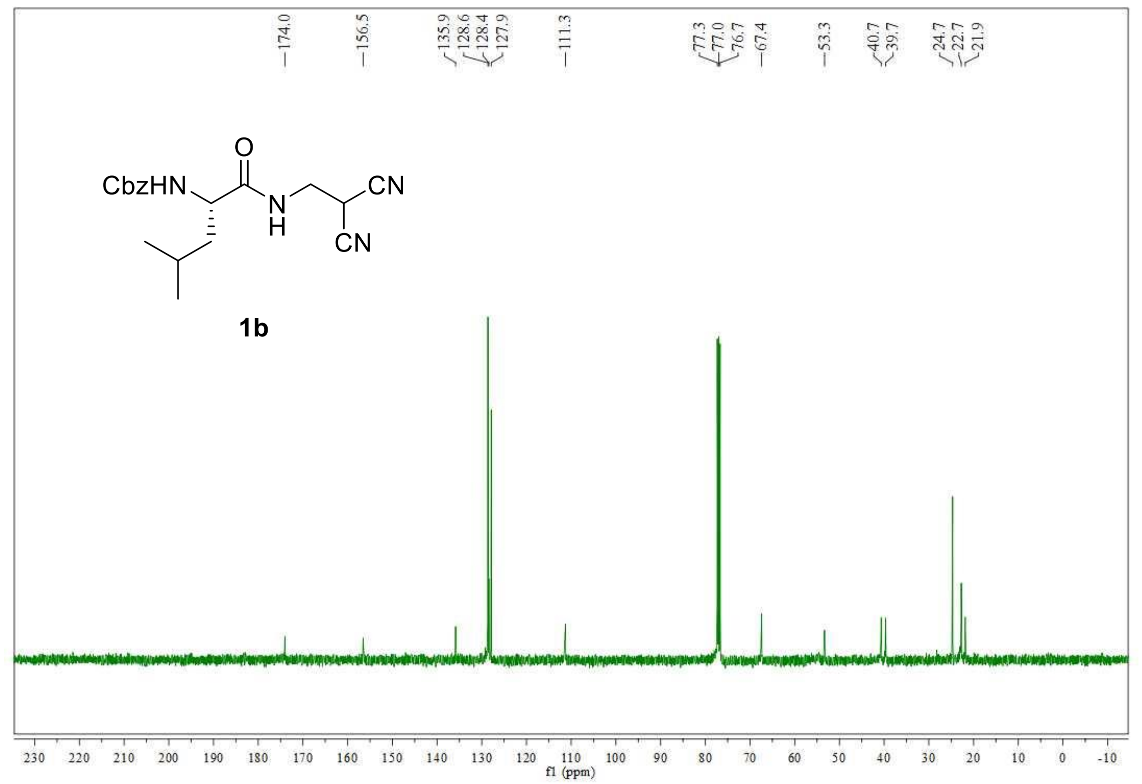
CN
CN
s2
f1 (ppm)



1b



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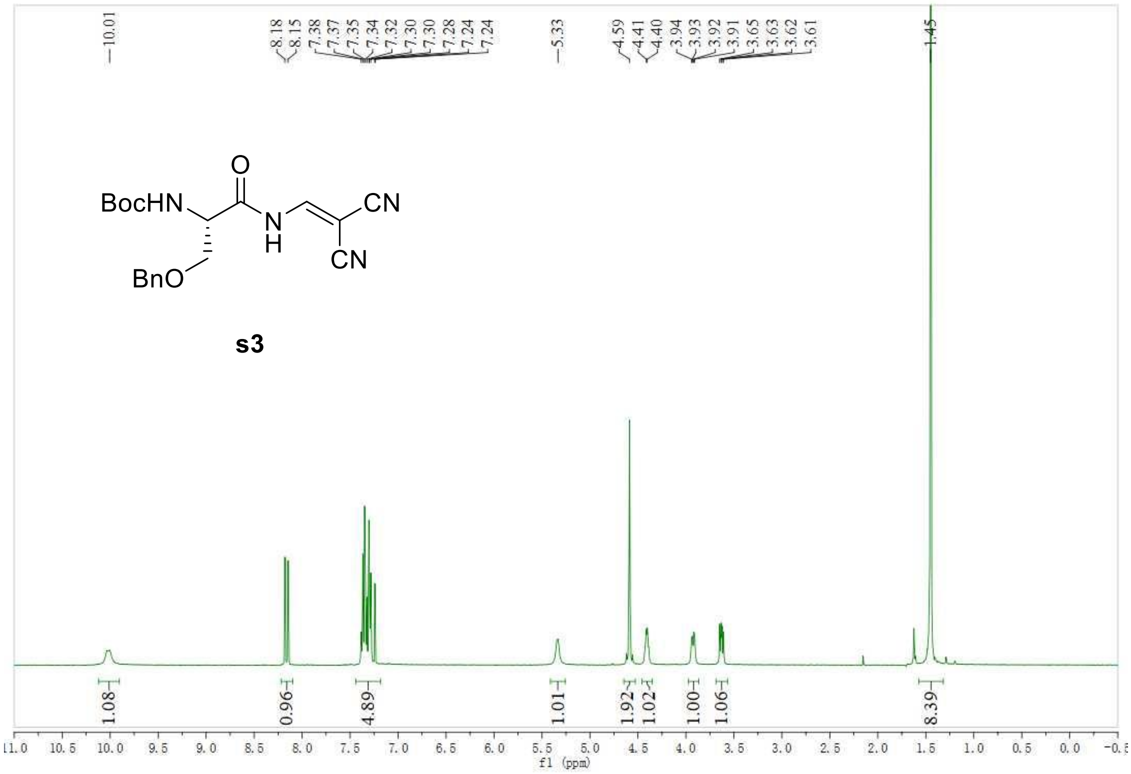
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3.65
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3.62
3.61
1.45
BocHN
O
N
H
CN
CN
BnO
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1.00
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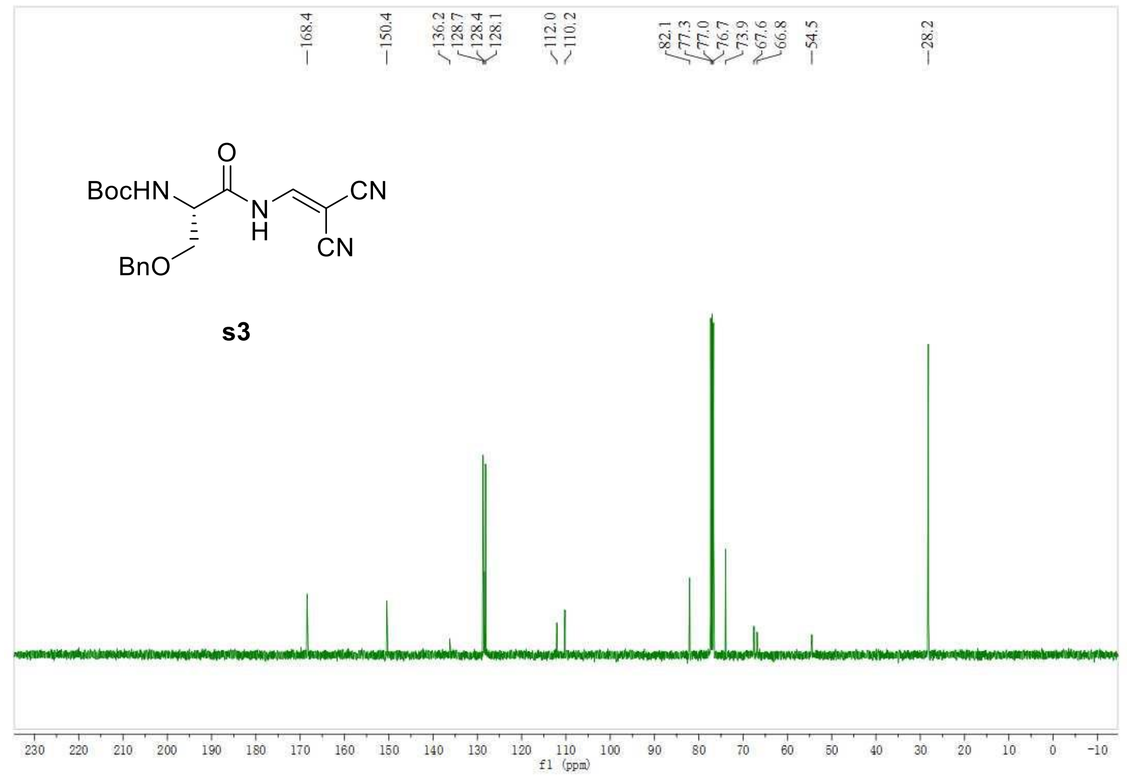
8.39
f1 (ppm)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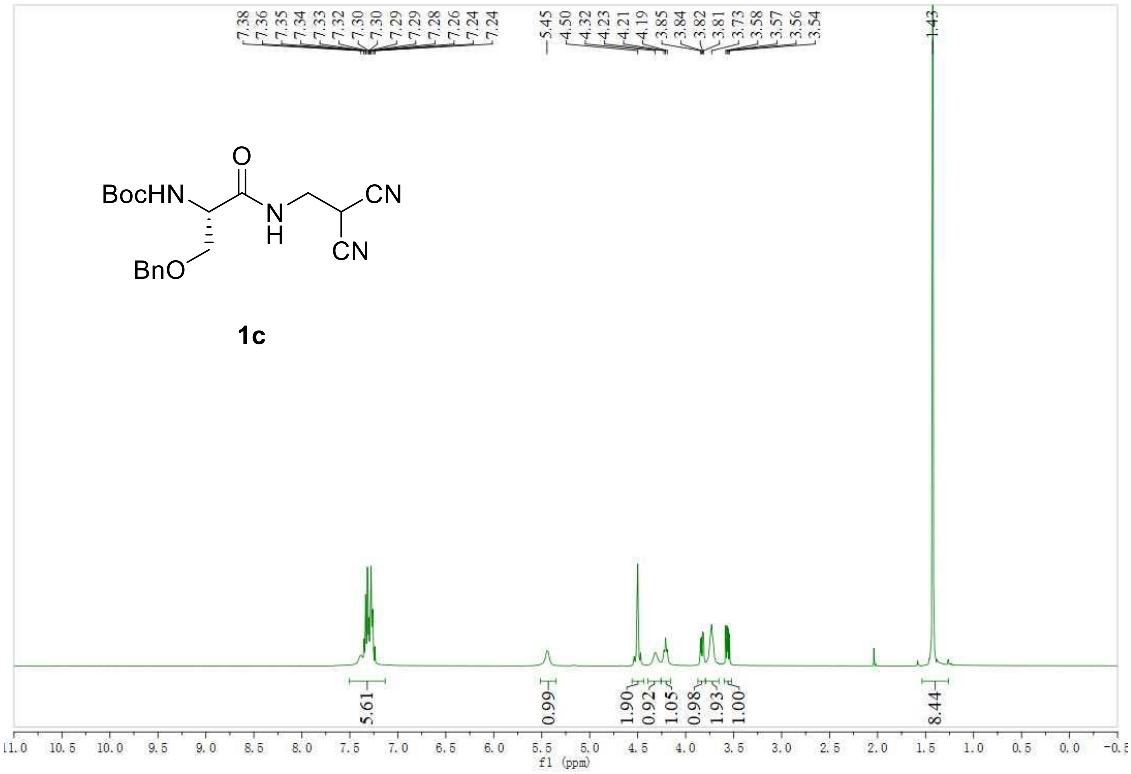
BnO
s3
f1 (ppm)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7.28
7.26
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7.24
5.45
4.50
4.32
4.23
4.21
4.19
3.85
3.84
3.82
3.81
3.73
3.58
3.57
3.56
3.54
1.43
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0.99
1.90
0.92
1.05
0.98
1.93
1.00
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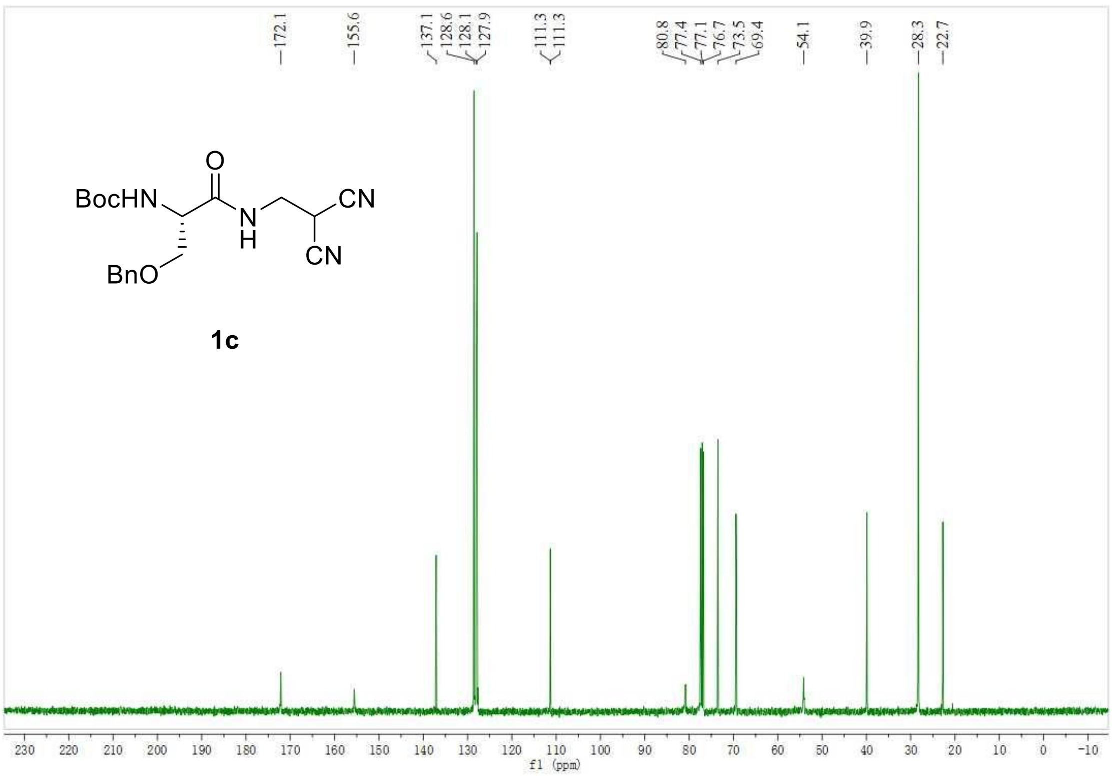
f1 (ppm)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O
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H
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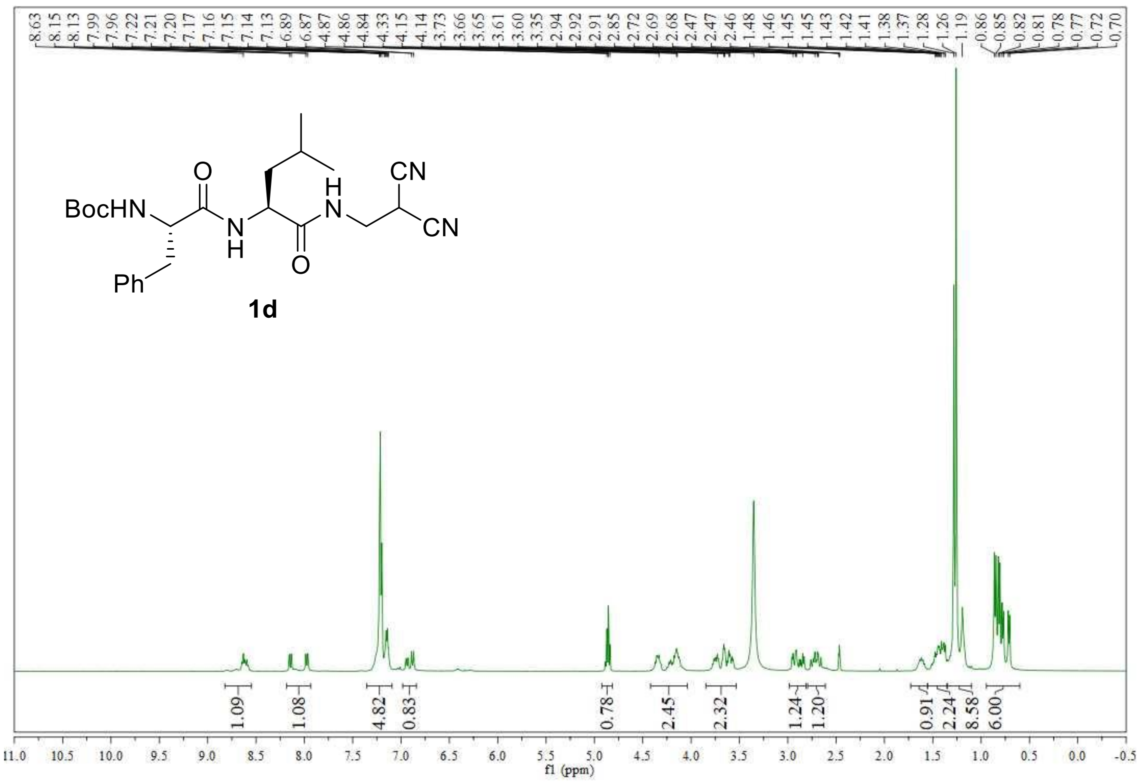
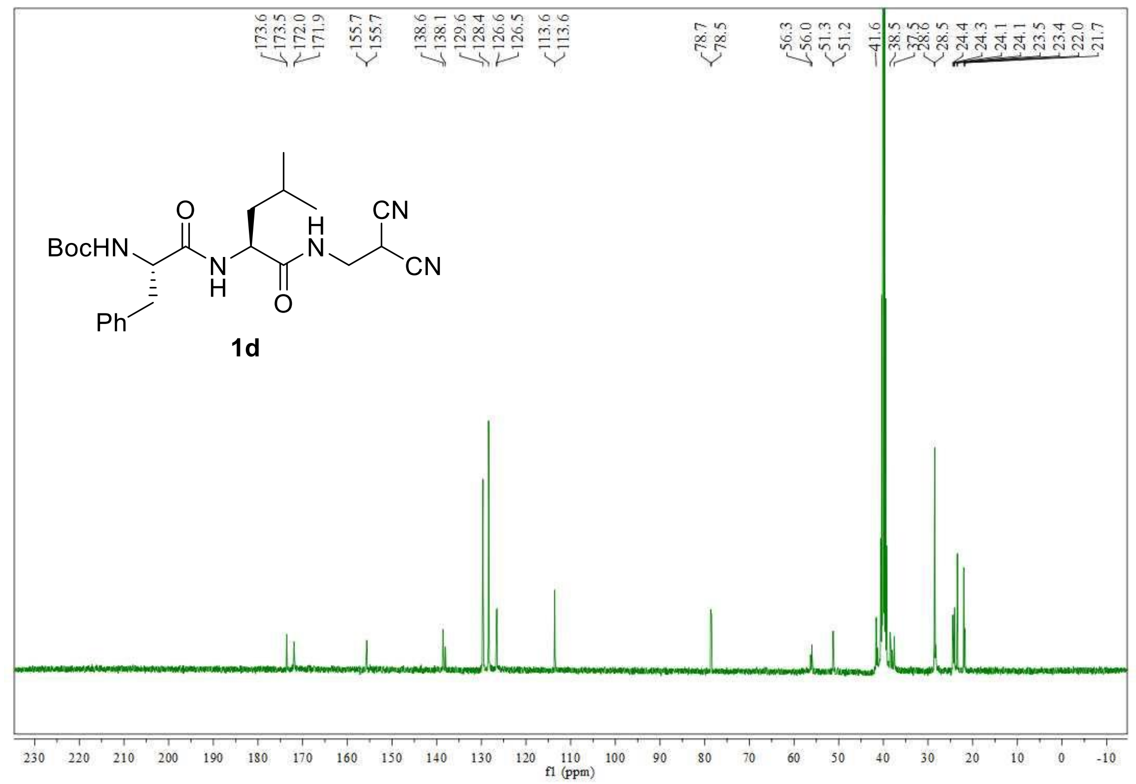
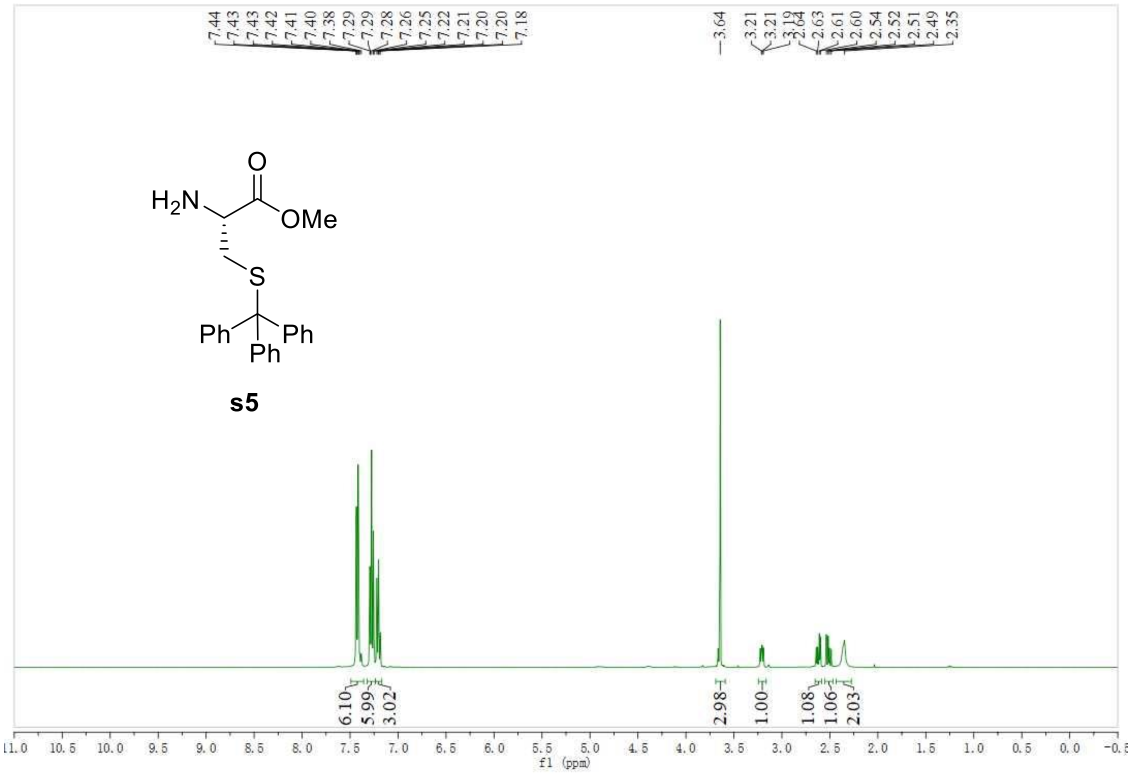
28.3
22.7
f1 (ppm)



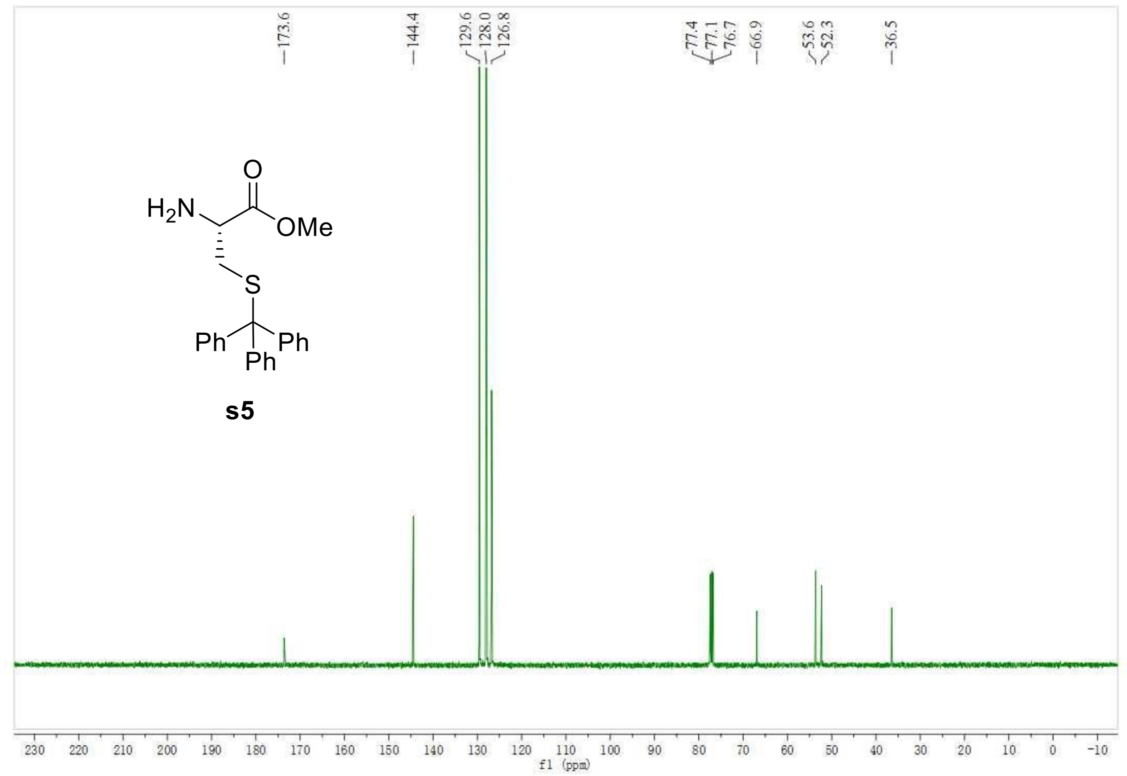
1d



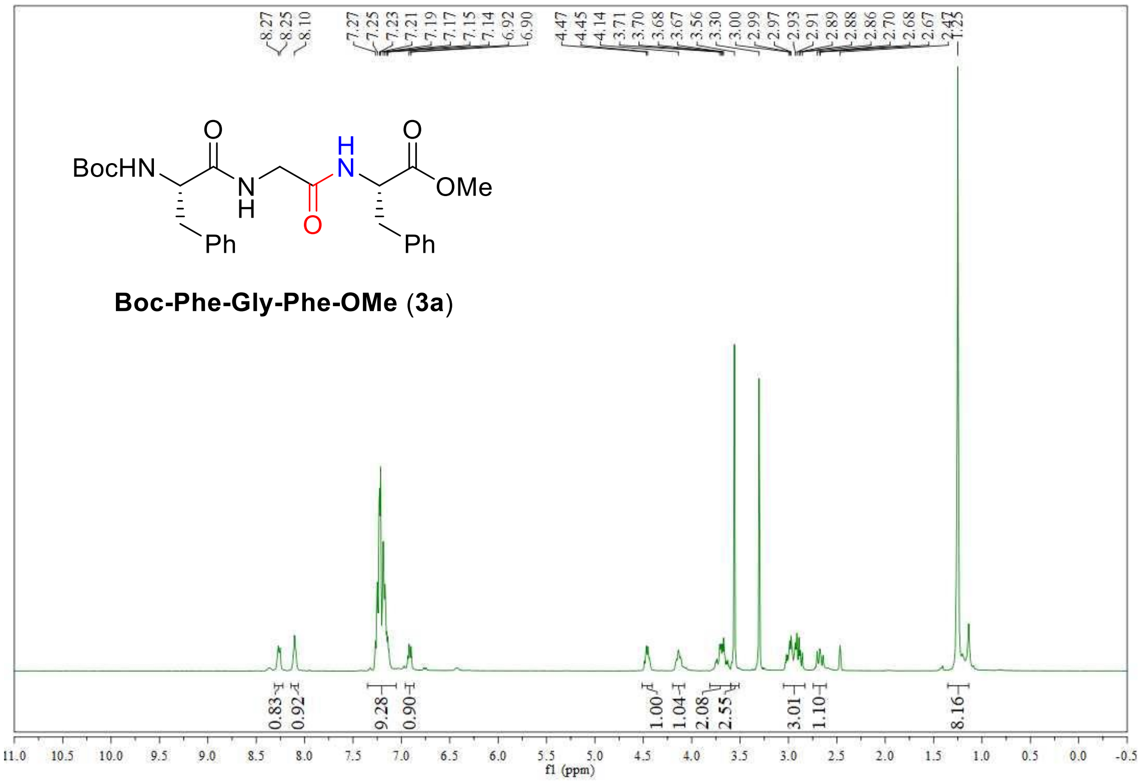
1d

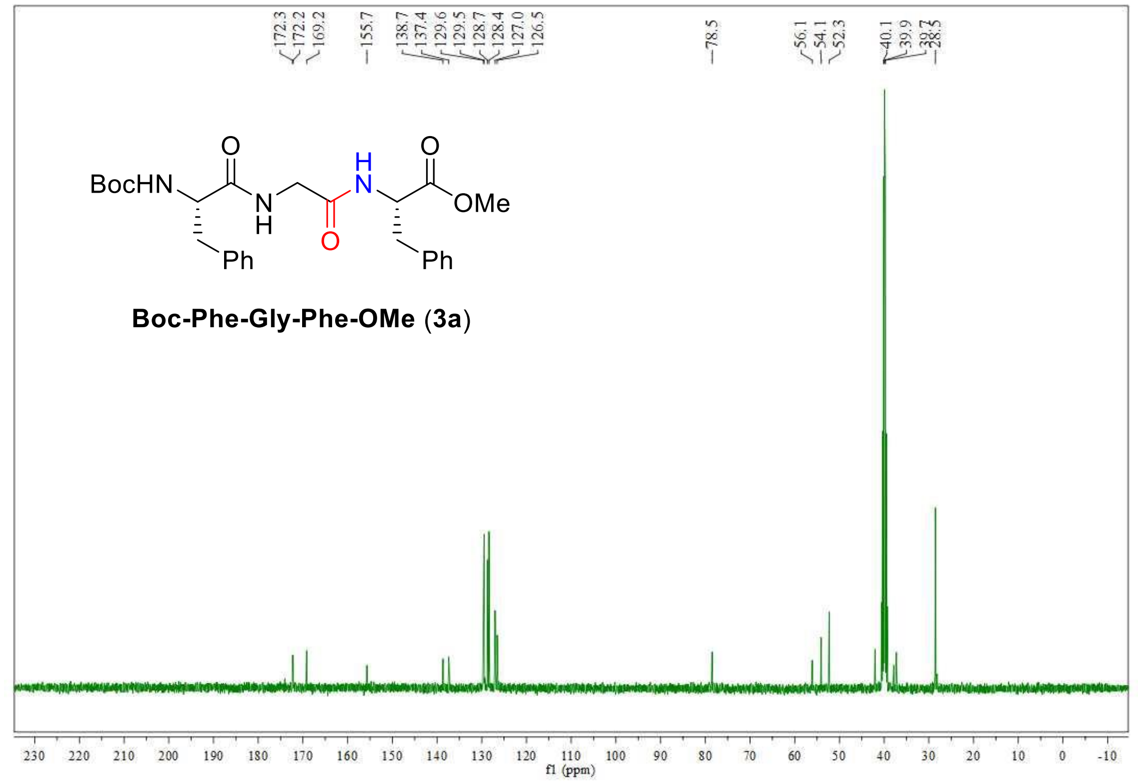


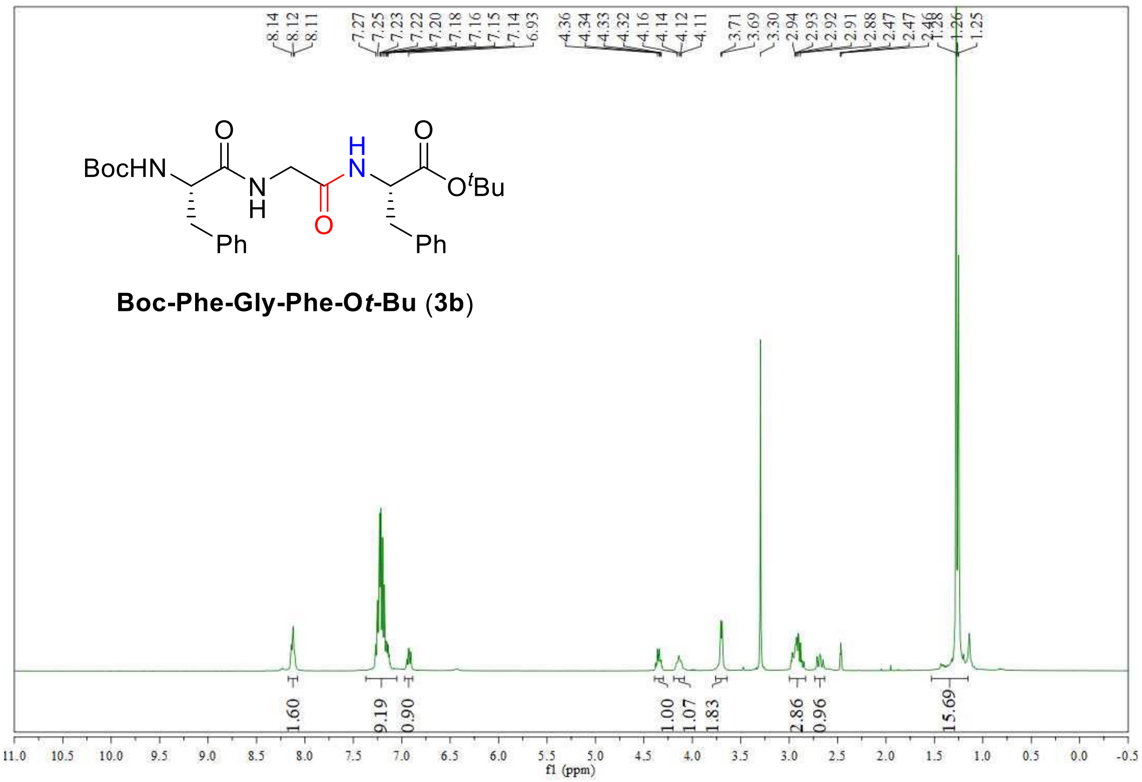
s5

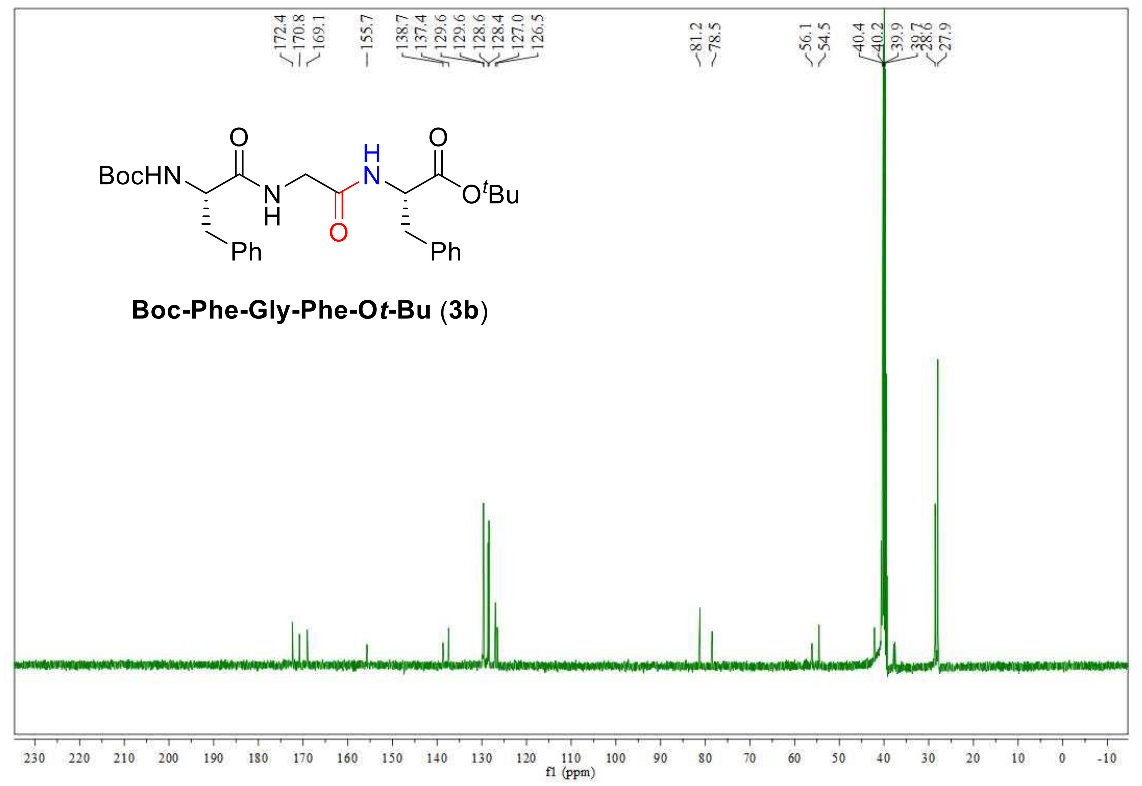


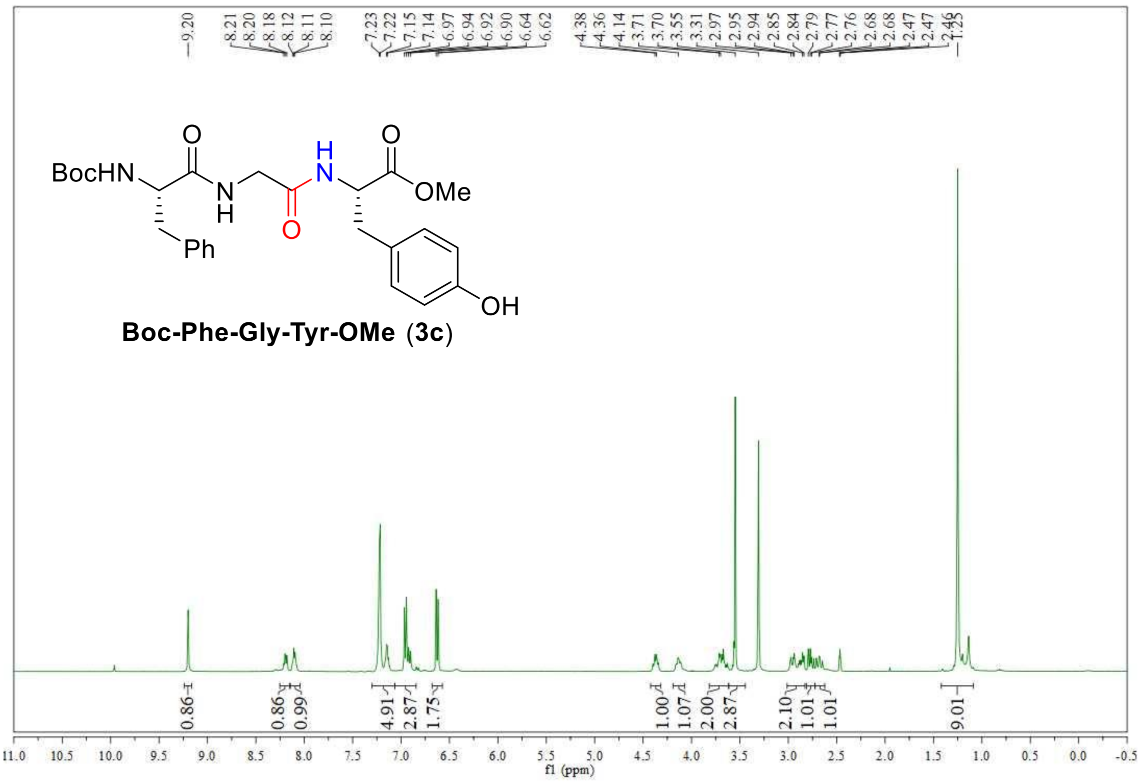
s5

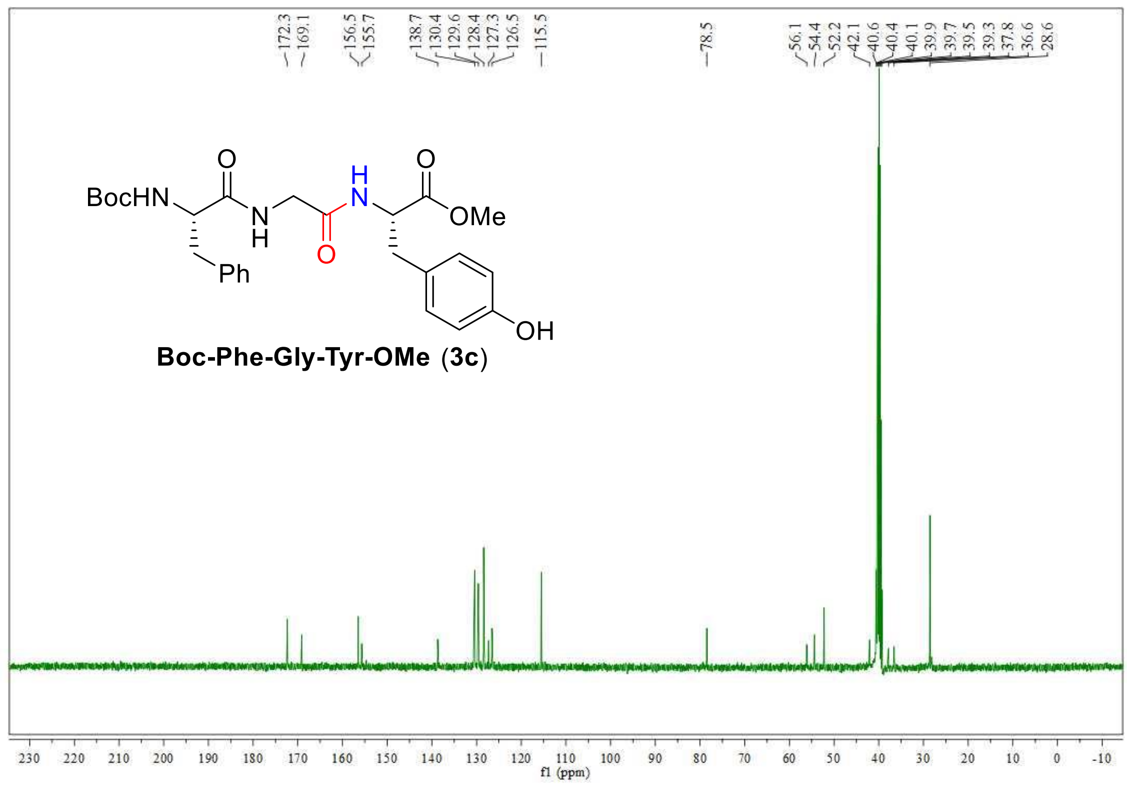


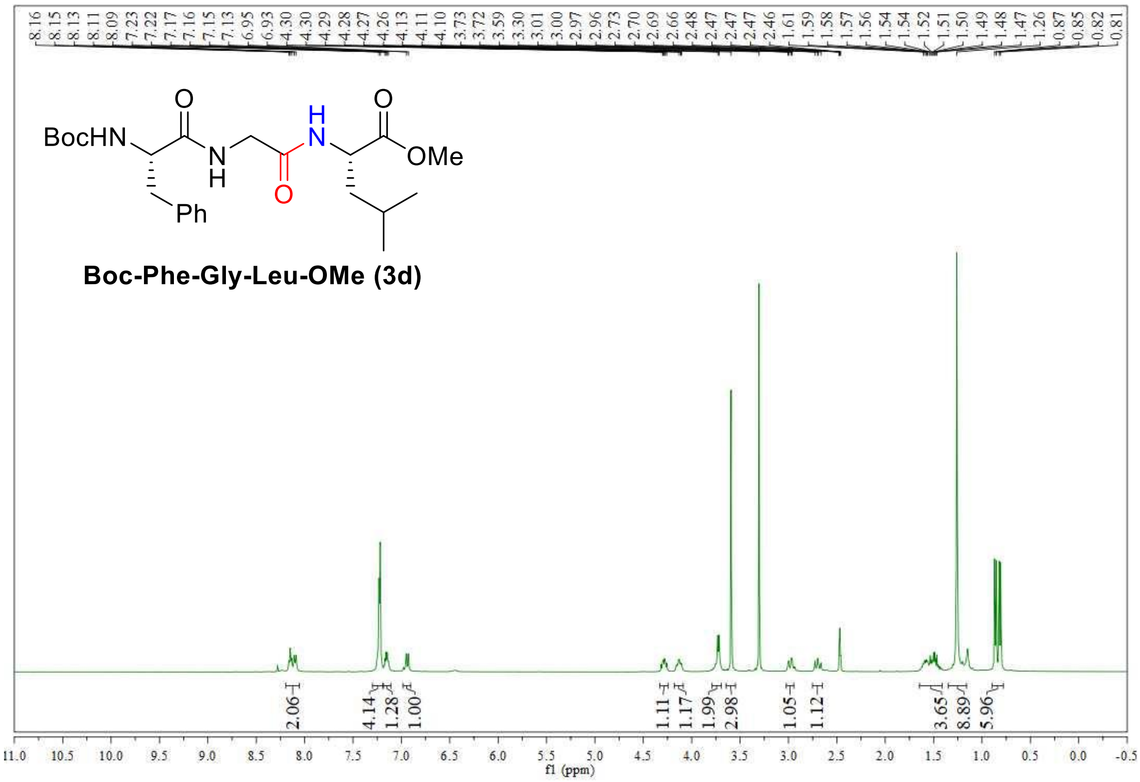


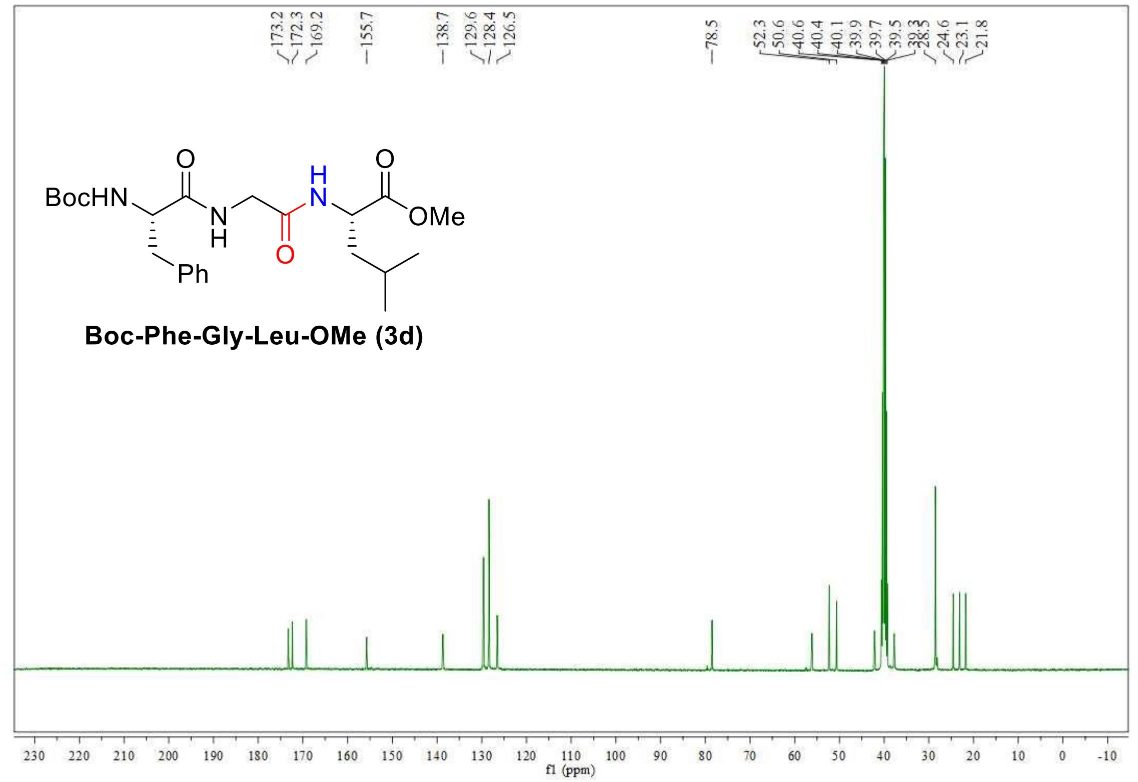

Boc-Phe-Gly-Phe-O*t*-Bu (**3b**)
f1 (ppm)

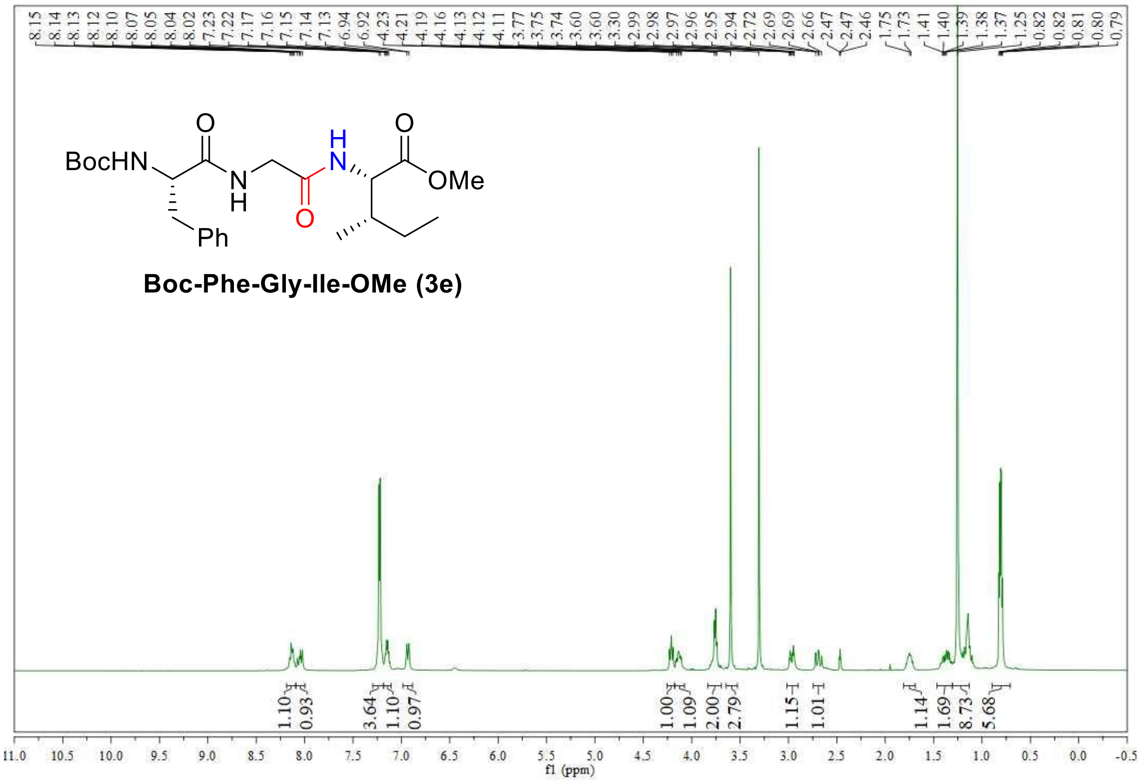

Boc-Phe-Gly-Phe-O*t*-Bu (**3b**)
f1 (ppm)

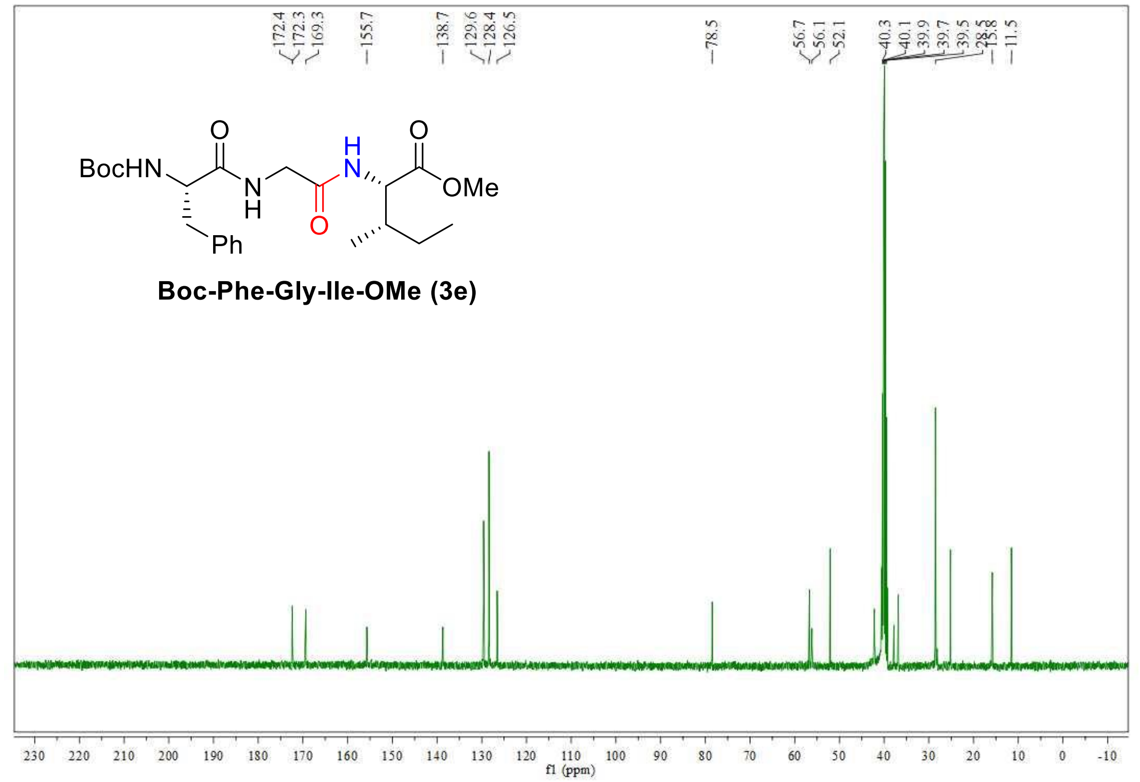

BocHN
Ph
OMe
OH
Boc-Phe-Gly-Tyr-OMe (3c)
f1 (ppm)

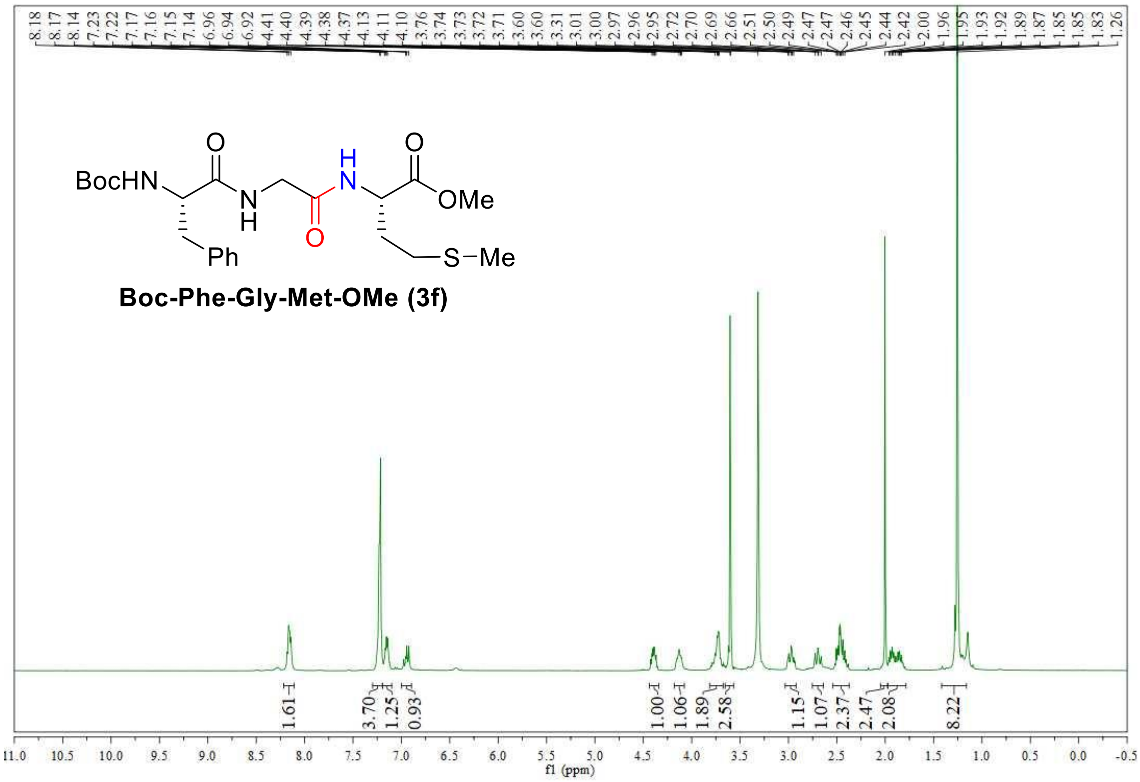

BocHN
Ph
OMe
OH
Boc-Phe-Gly-Tyr-OMe (3c)
f1 (ppm)

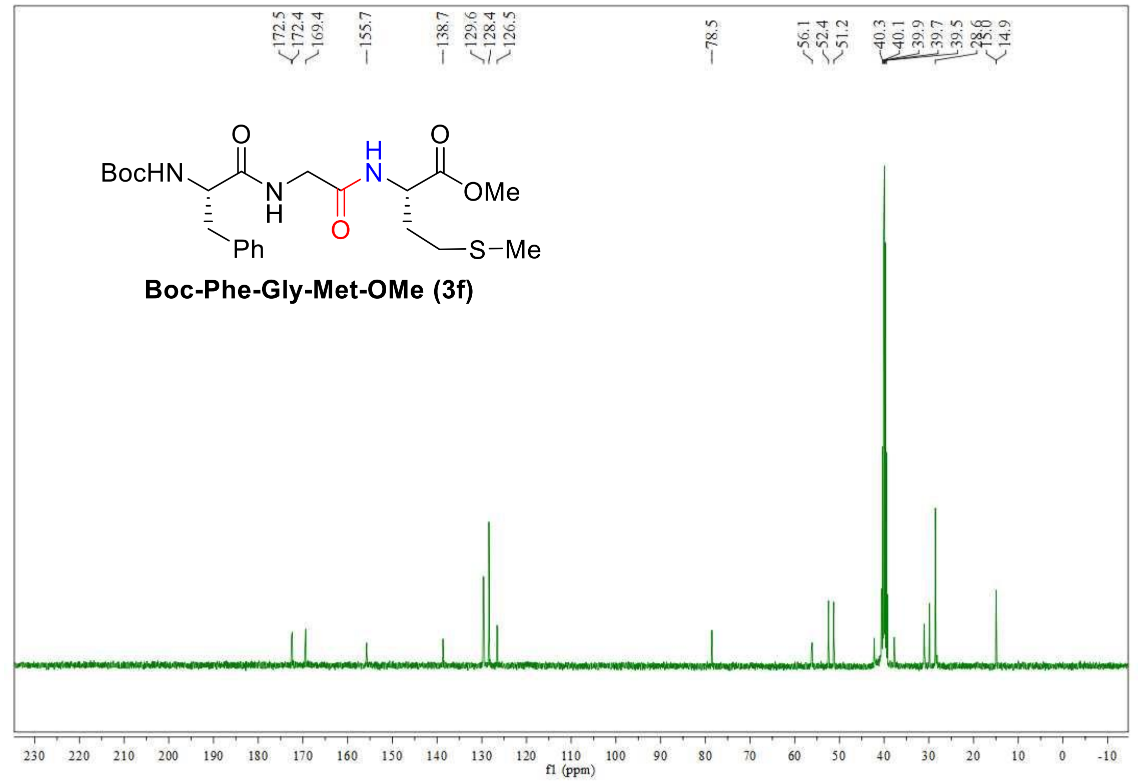

Boc-Phe-Gly-Leu-OMe (3d)
f1 (ppm)

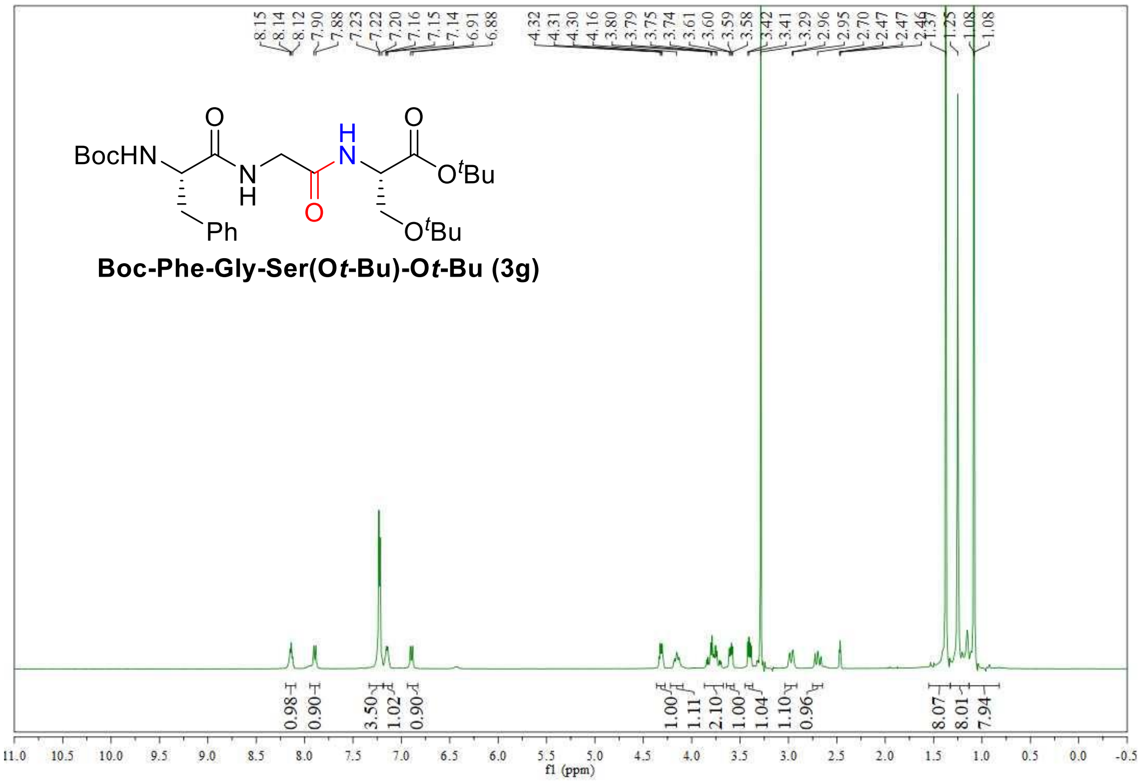

Boc-Phe-Gly-Leu-OMe (3d)
f1 (ppm)

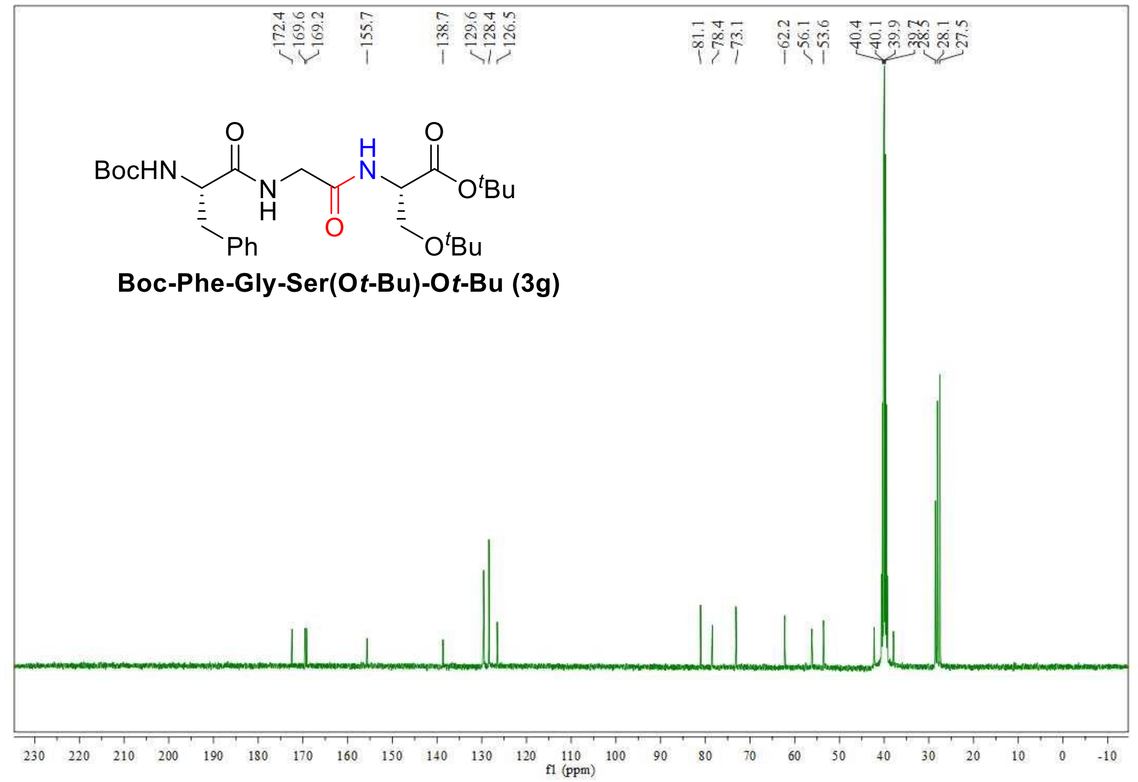

BocHN
Ph
OMe
Boc-Phe-Gly-Ile-OMe (3e)
f1 (ppm)

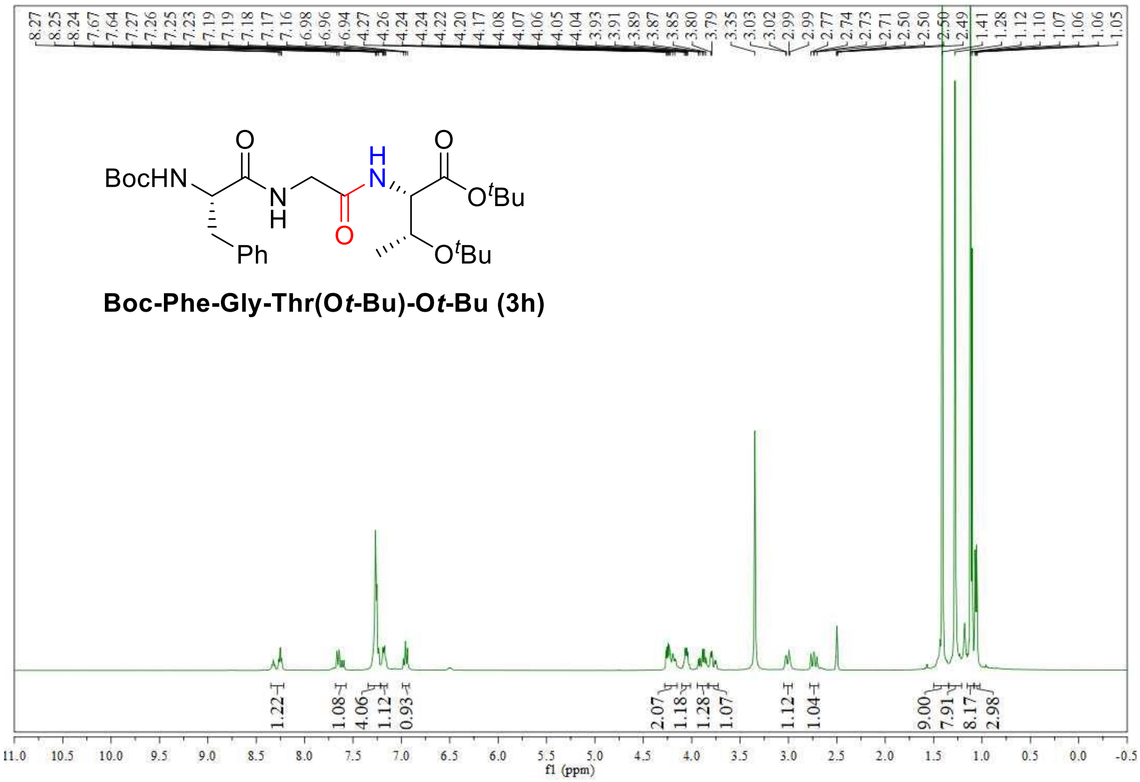

BocHN
Ph
OMe
Boc-Phe-Gly-Ile-OMe (3e)
f1 (ppm)

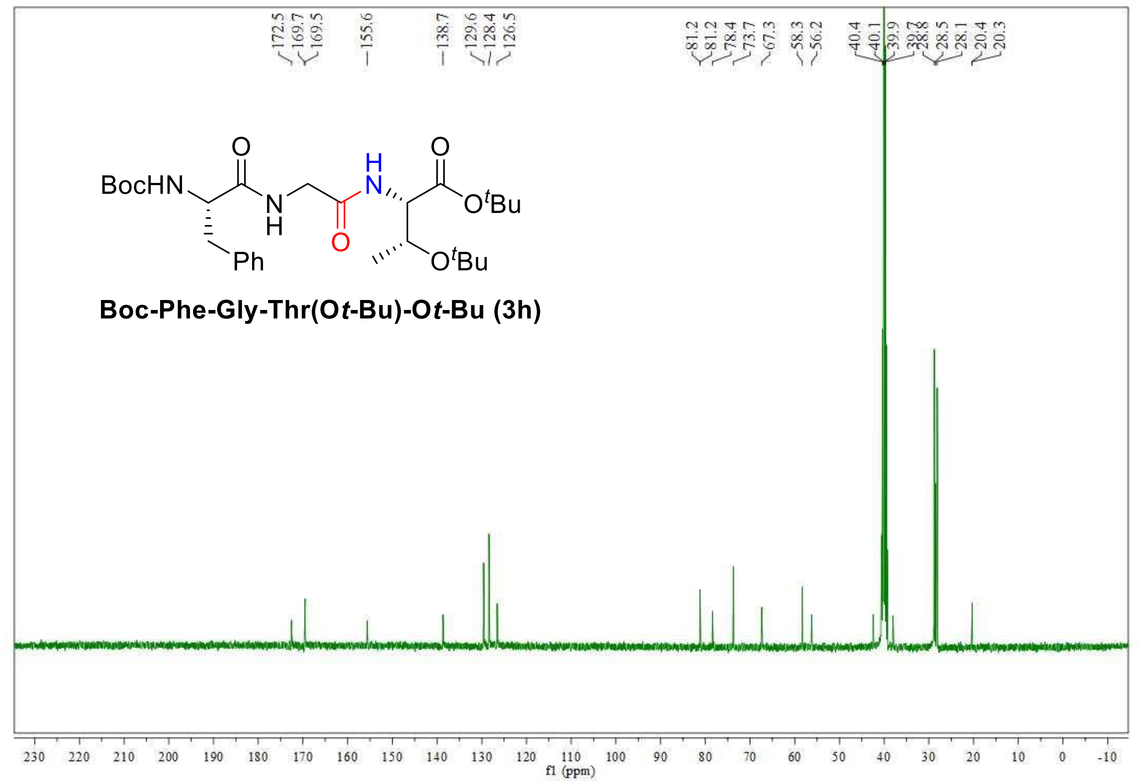

Boc-Phe-Gly-Met-OMe (3f)
f1 (ppm)

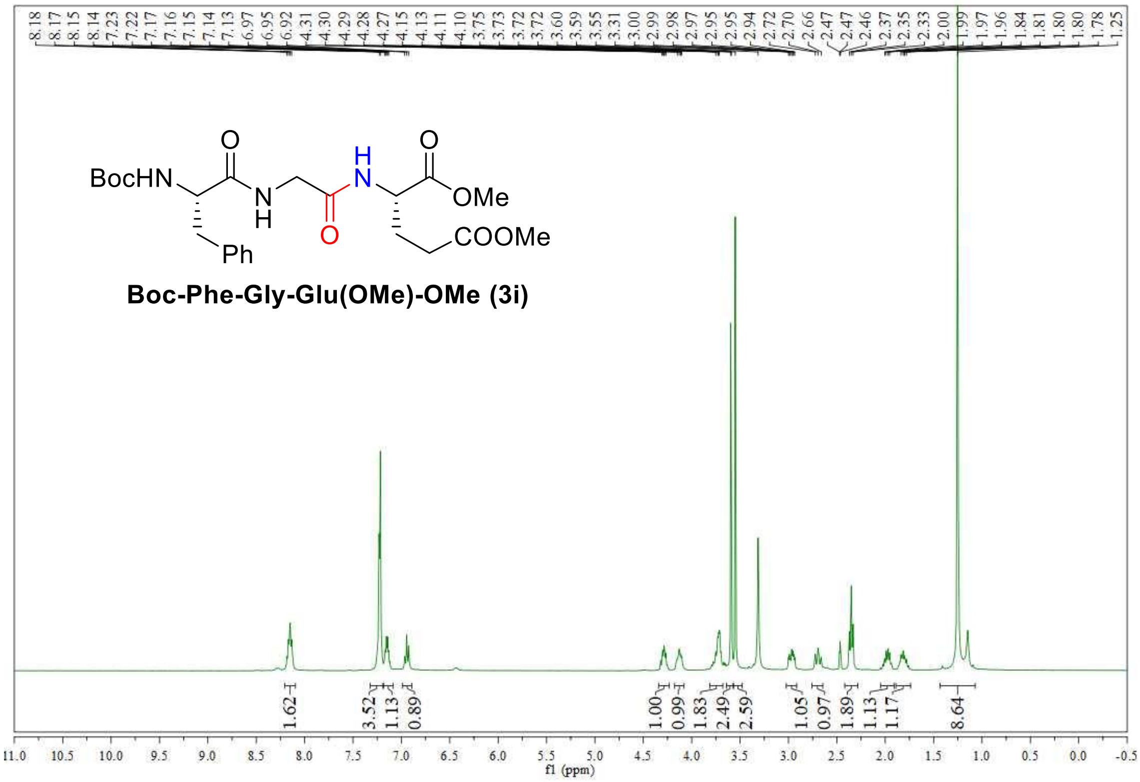

Boc-Phe-Gly-Met-OMe (3f)
f1 (ppm)


BocHN
O^tBu
Ph
Boc-Phe-Gly-Ser(Ot-Bu)-Ot-Bu (3g)
f1 (ppm)

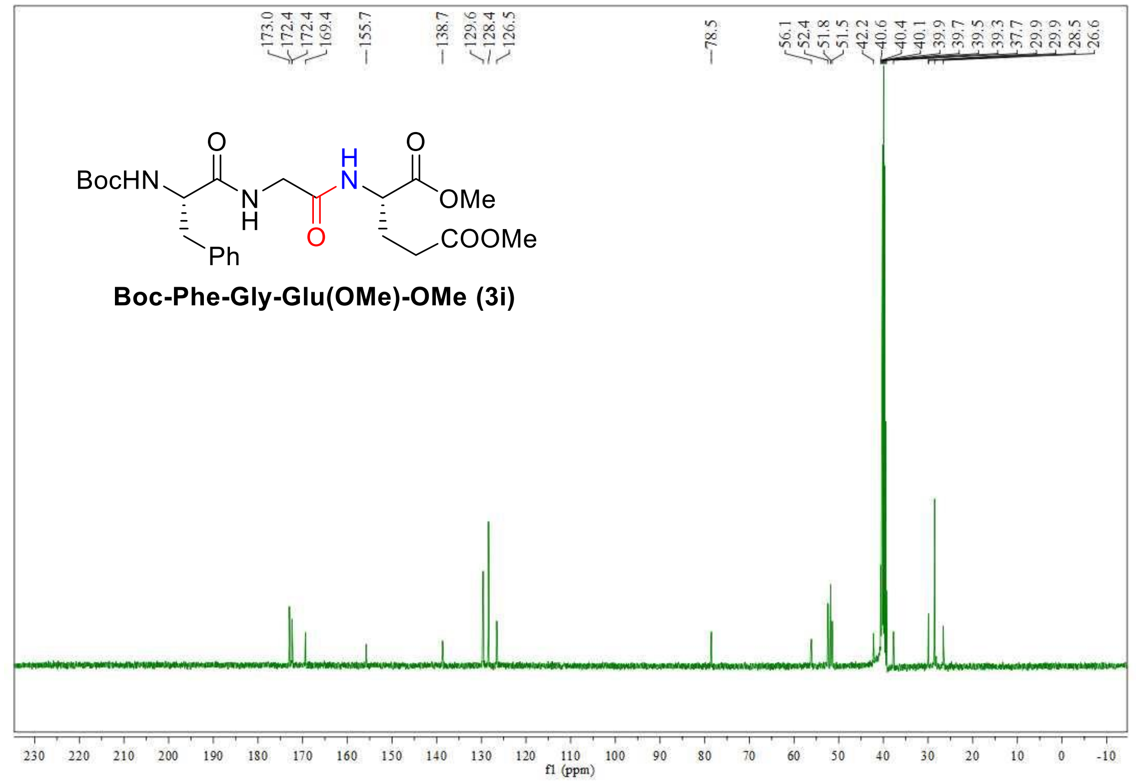

BocHN
O^tBu
Ph
Boc-Phe-Gly-Ser(Ot-Bu)-Ot-Bu (3g)
f1 (ppm)


BocHN
Ph
O^{t}Bu
Boc-Phe-Gly-Thr(O*t*-Bu)-O*t*-Bu (3h)
f1 (ppm)

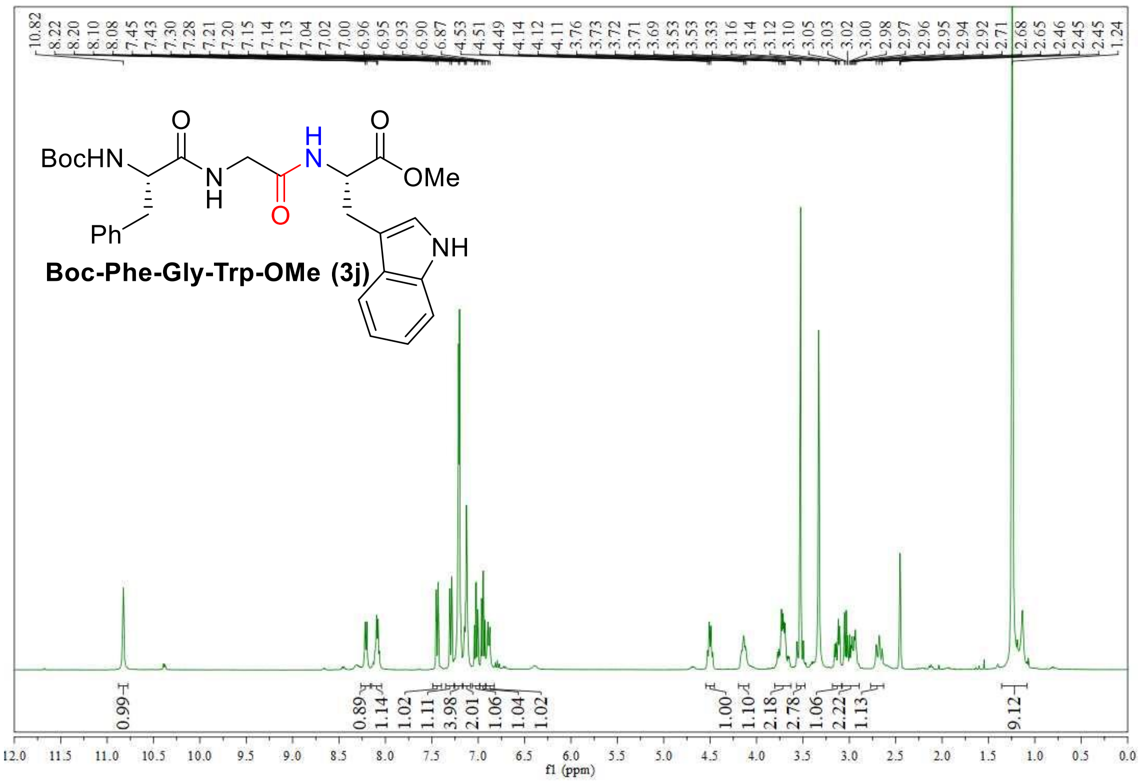

BocHN
Ph
O^{t}Bu
Boc-Phe-Gly-Thr(O*t*-Bu)-O*t*-Bu (3h)
f1 (ppm)

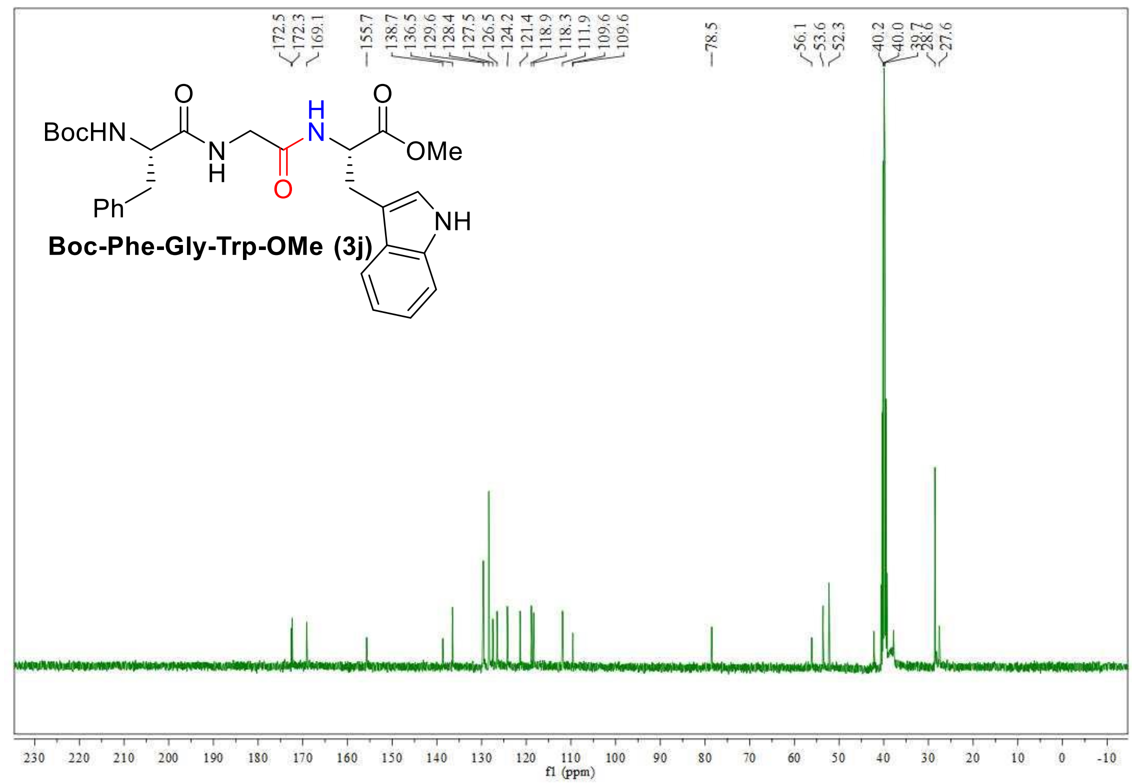


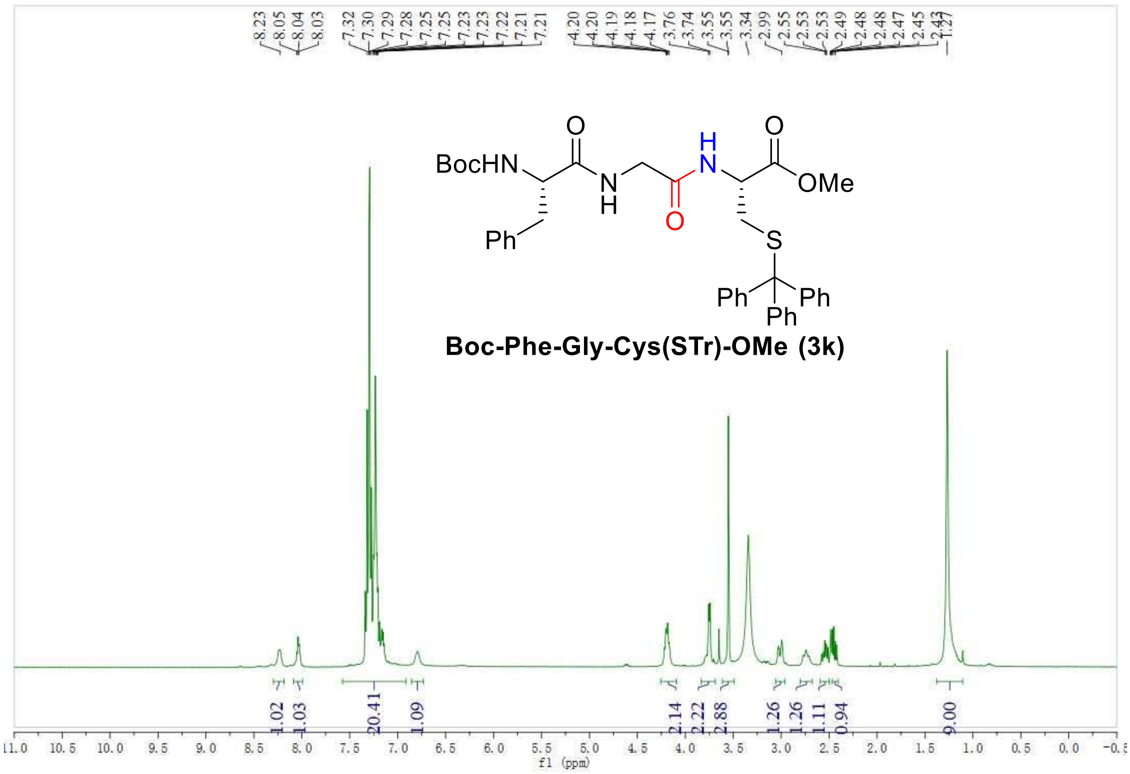
Boc-Phe-Gly-Glu(OMe)-OMe (3i)

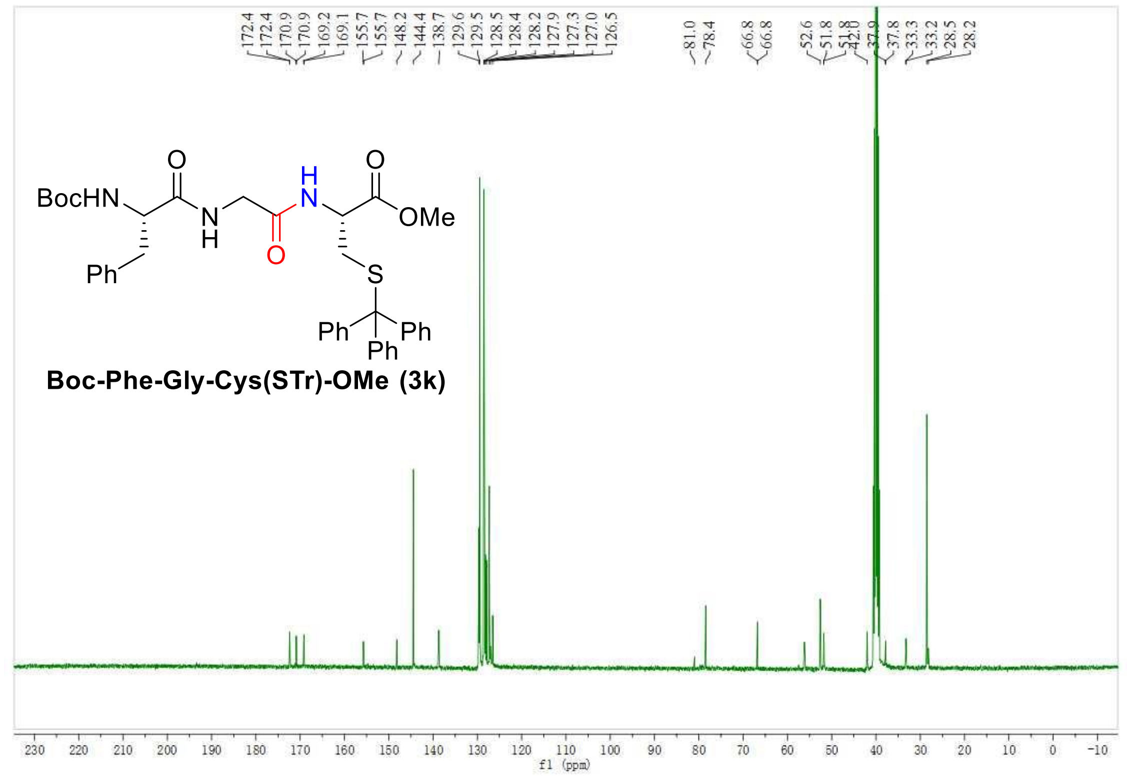


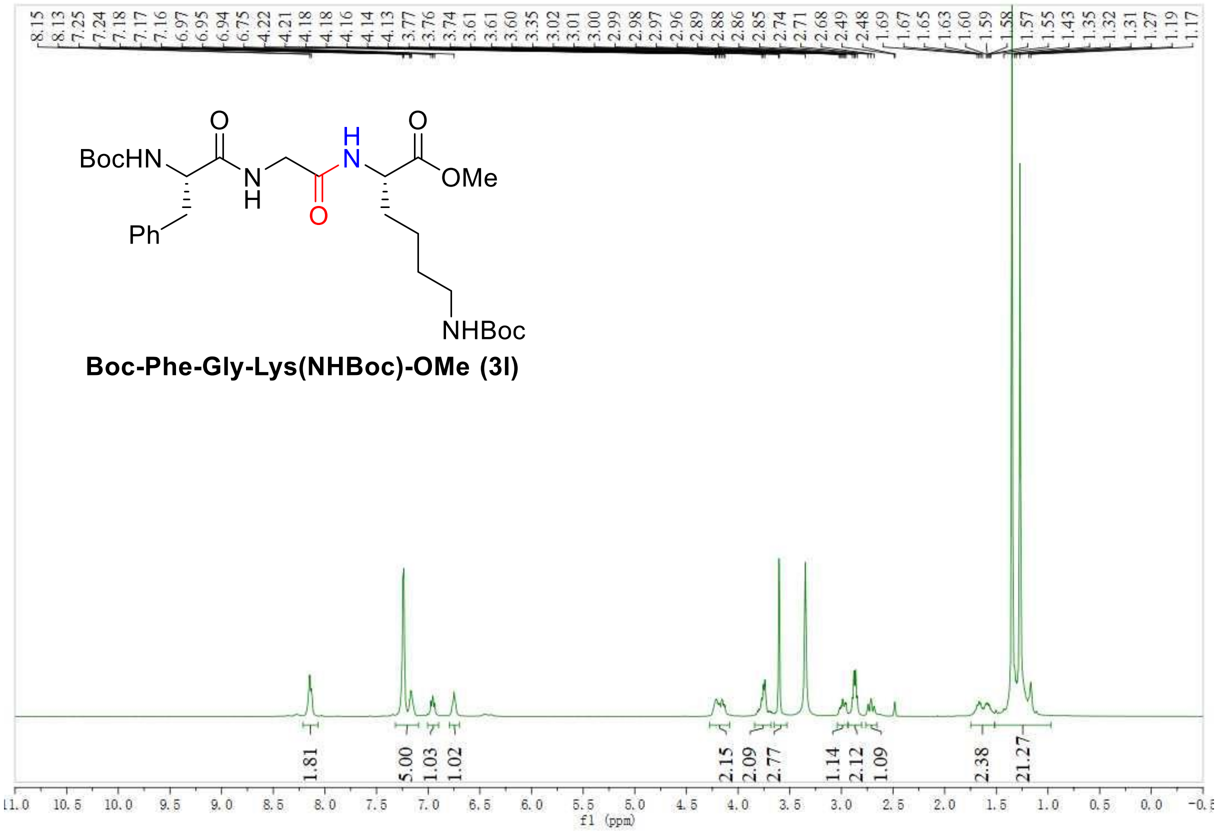
Boc-Phe-Gly-Glu(OMe)-OMe (3i)

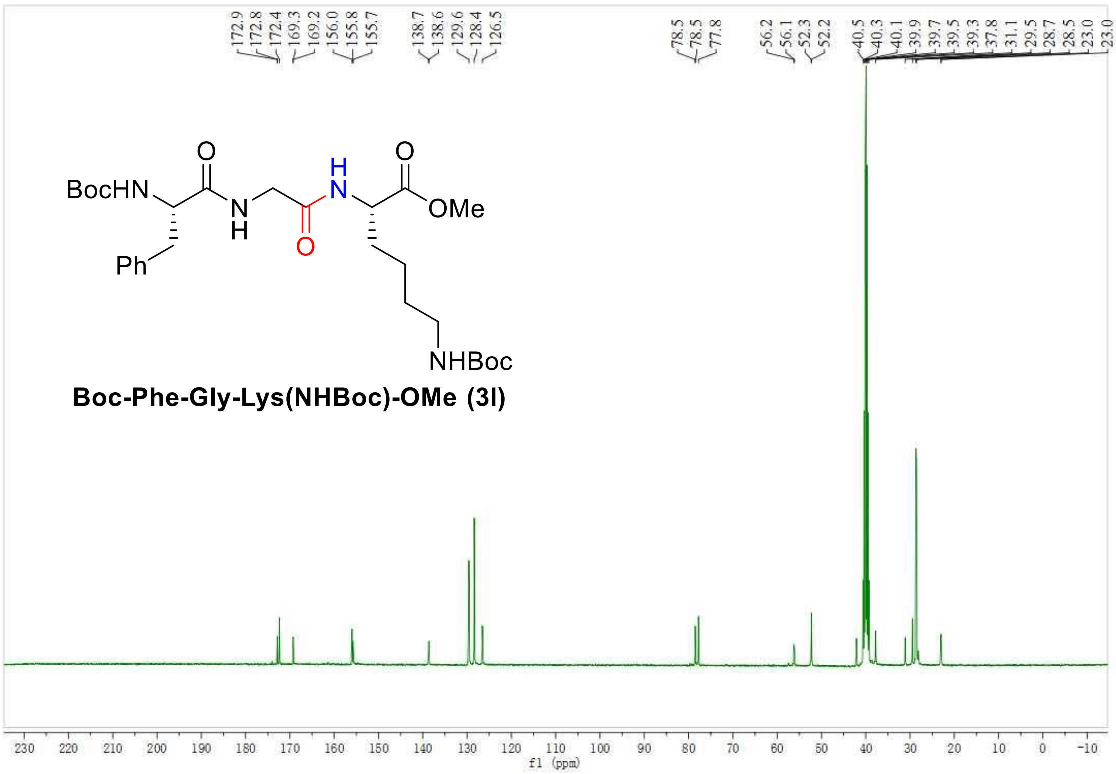


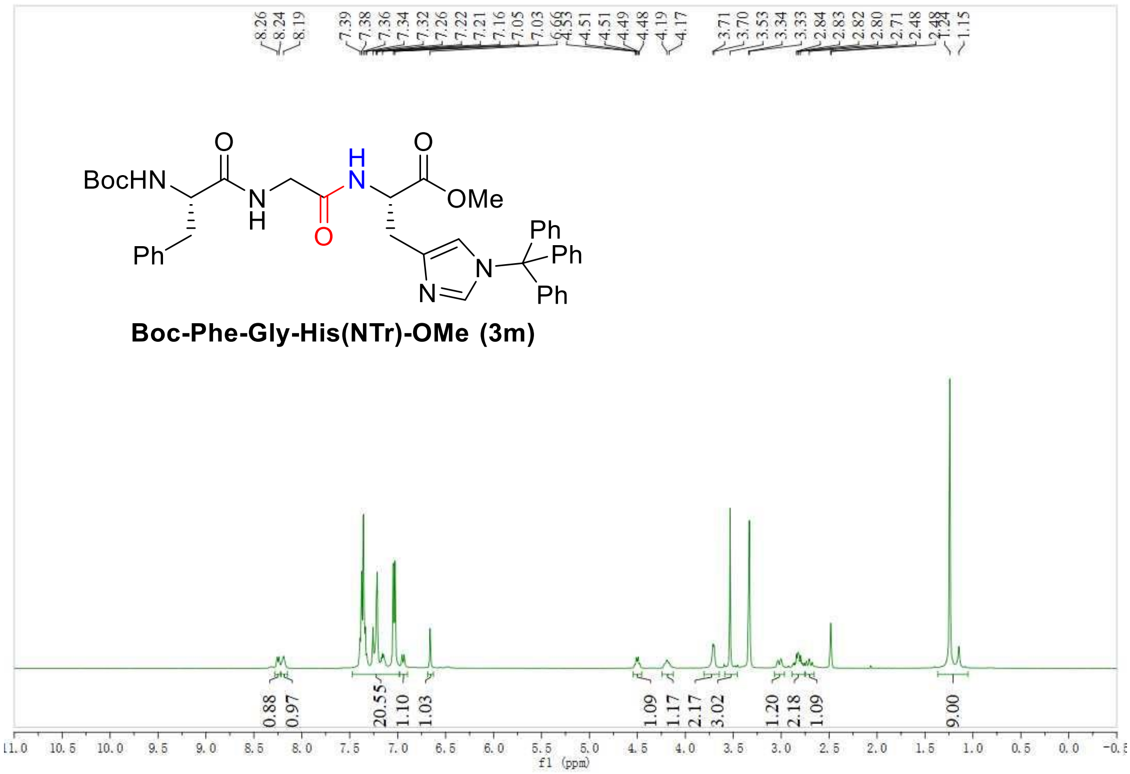



BocHN
Ph
OMe
S
Ph
Ph
Ph
Boc-Phe-Gly-Cys(STr)-OMe (3k)
f1 (ppm)

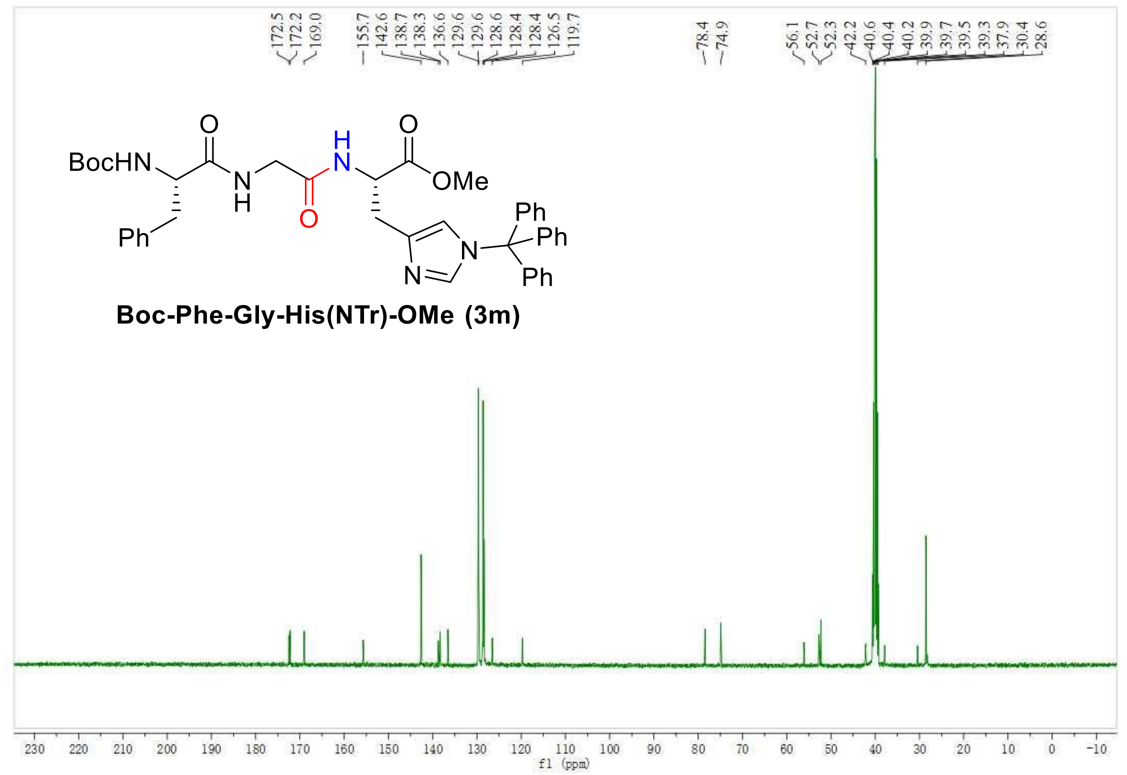

BocHN
Ph
OMe
S
Ph
Ph
Ph
Boc-Phe-Gly-Cys(STr)-OMe (3k)
f1 (ppm)


BocHN
NHBoc
OMe
Boc-Phe-Gly-Lys(NHBoc)-OMe (3l)
f1 (ppm)

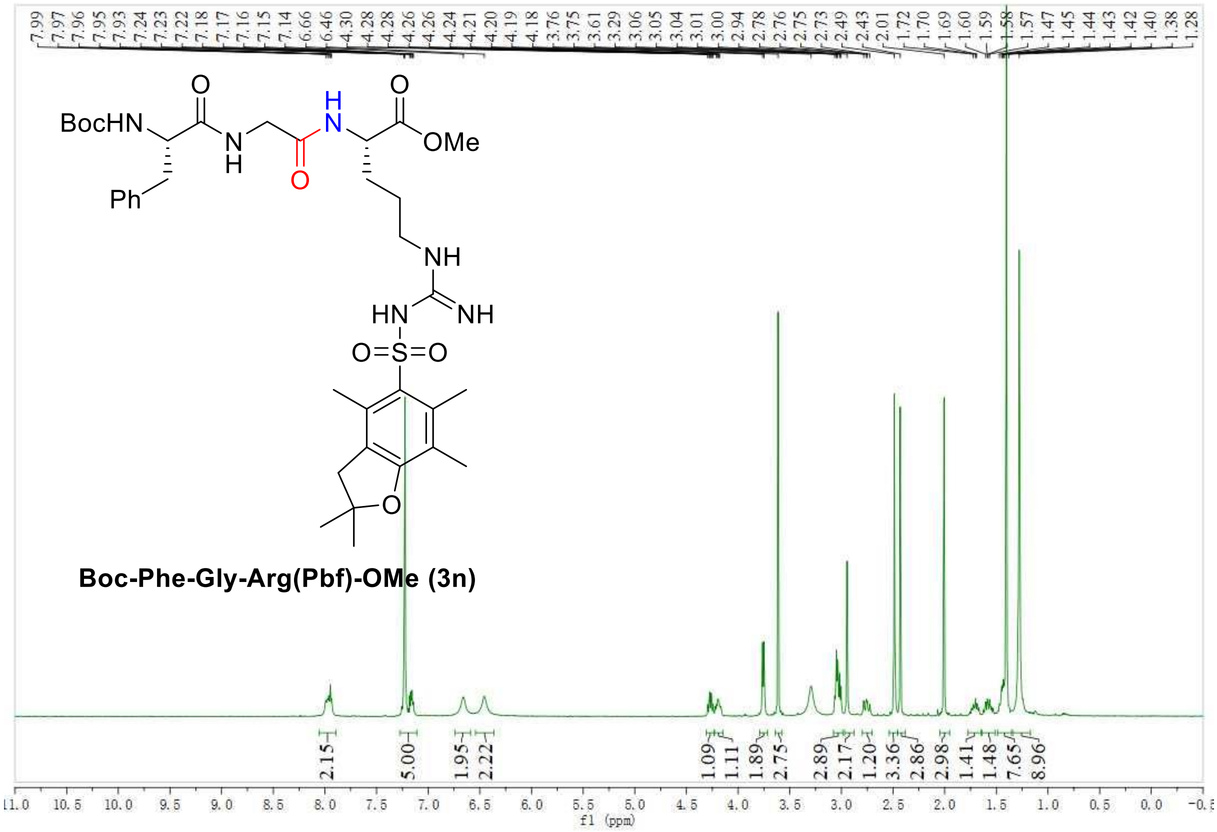

BocHN
NHBoc
OMe
Boc-Phe-Gly-Lys(NHBoc)-OMe (3l)
f1 (ppm)



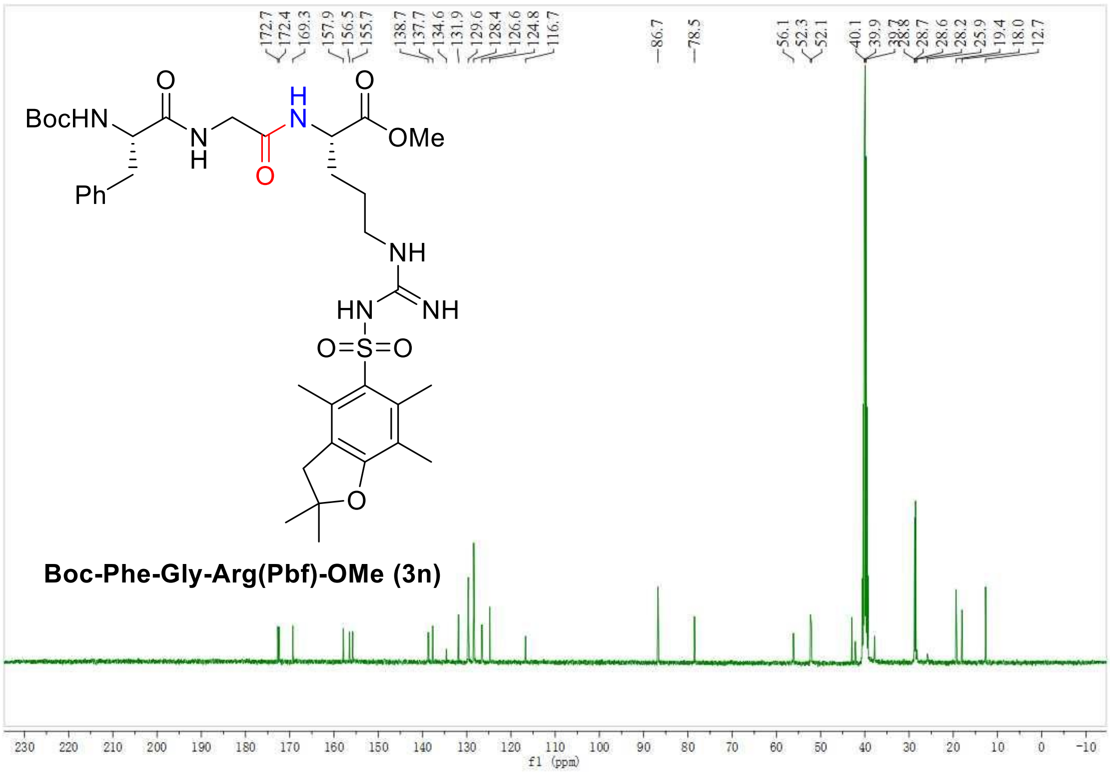
Boc-Phe-Gly-His(NTr)-OMe (3m)
f1 (ppm)

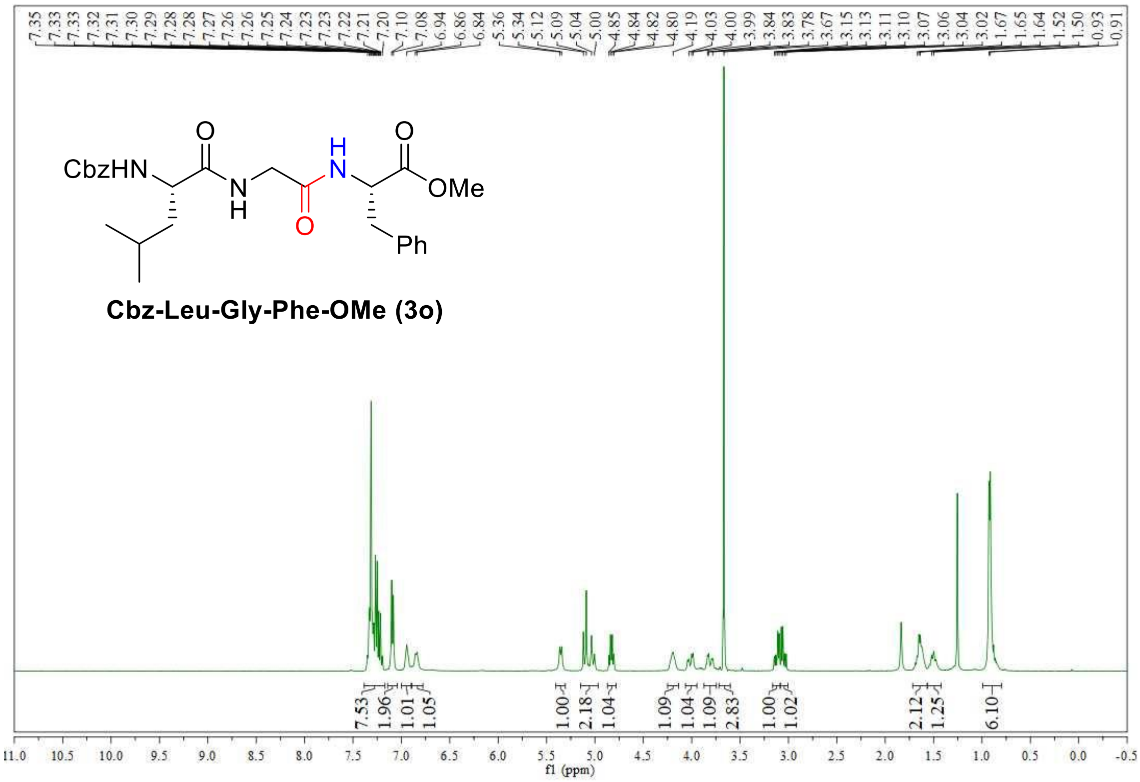


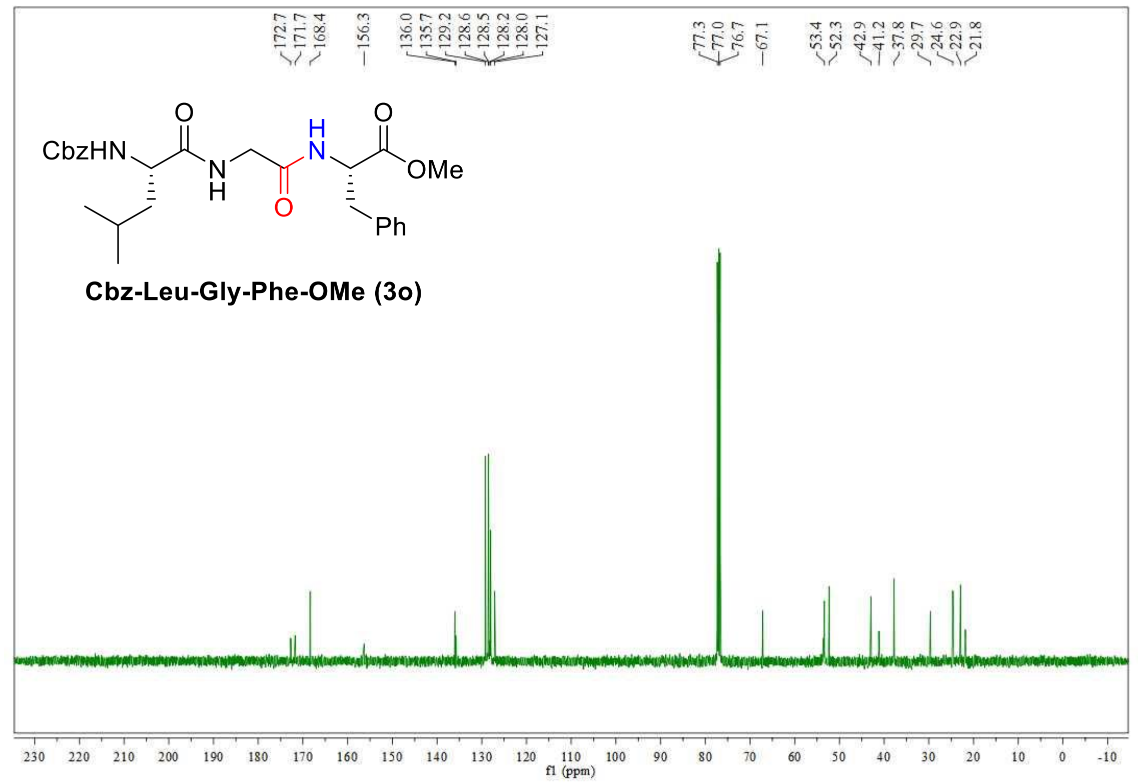
Boc-Phe-Gly-His(NTr)-OMe (3m)
f1 (ppm)

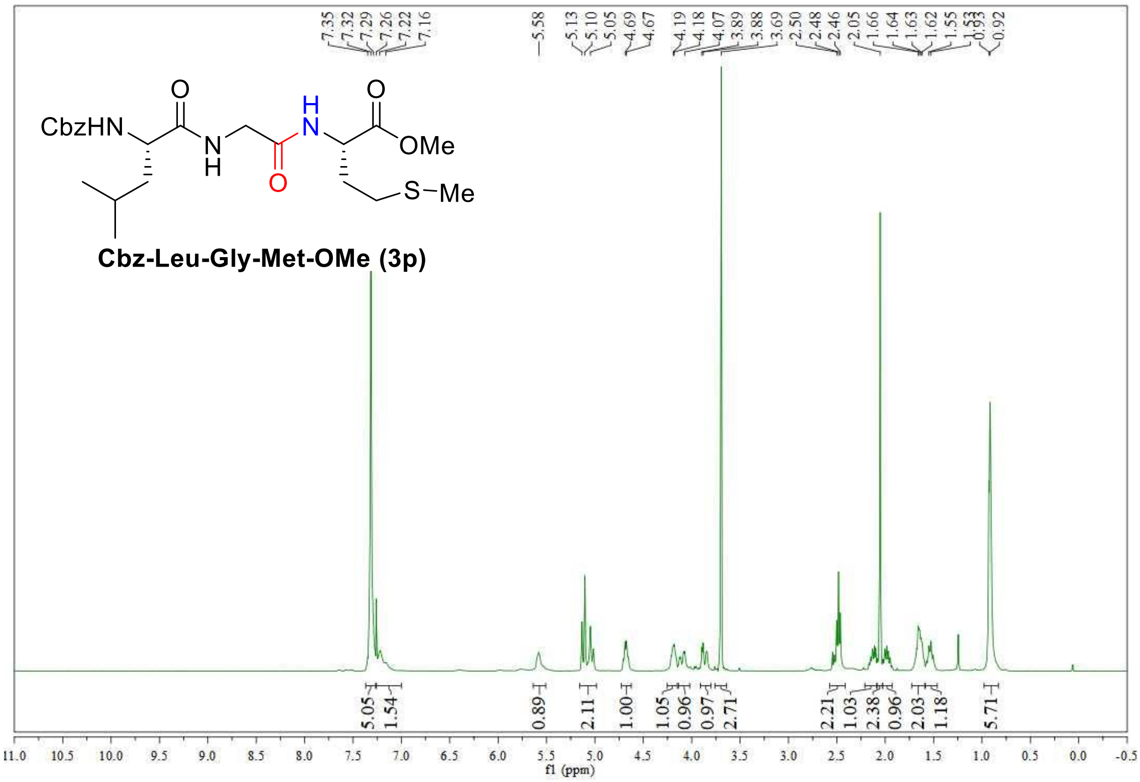


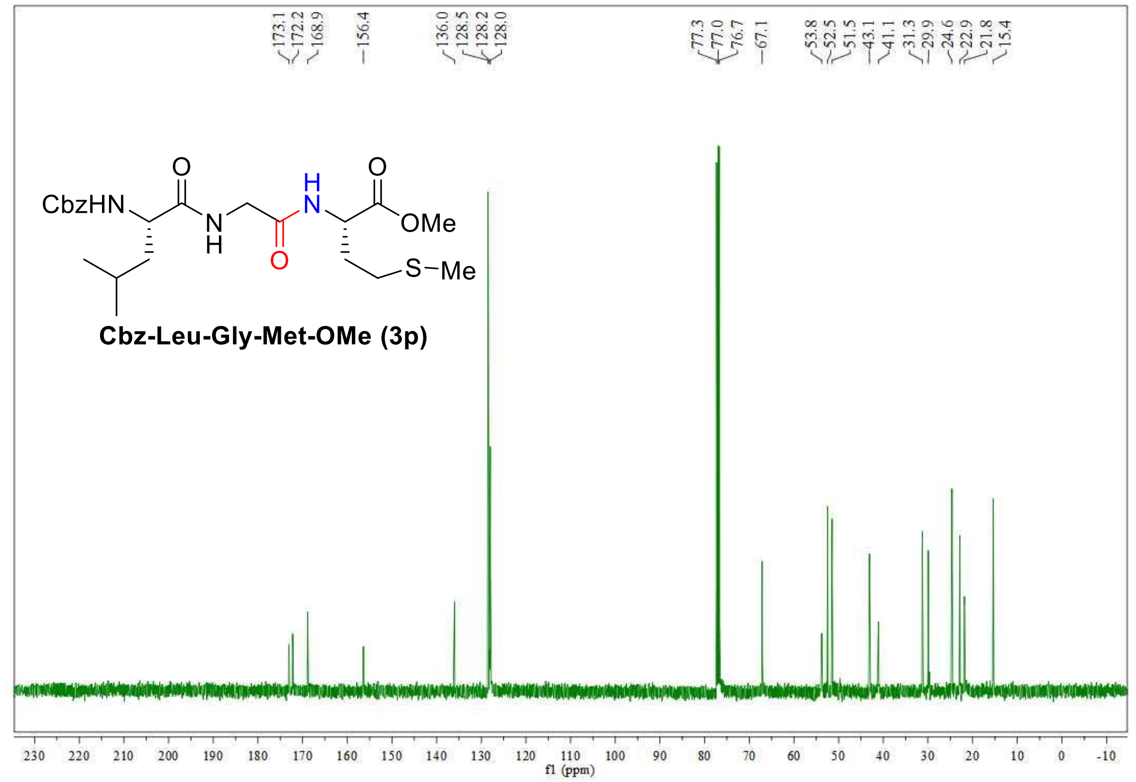
^{1}**H NMR** (399 Hz, DMSO-d$_6$) of compound **3n** at 64 °C

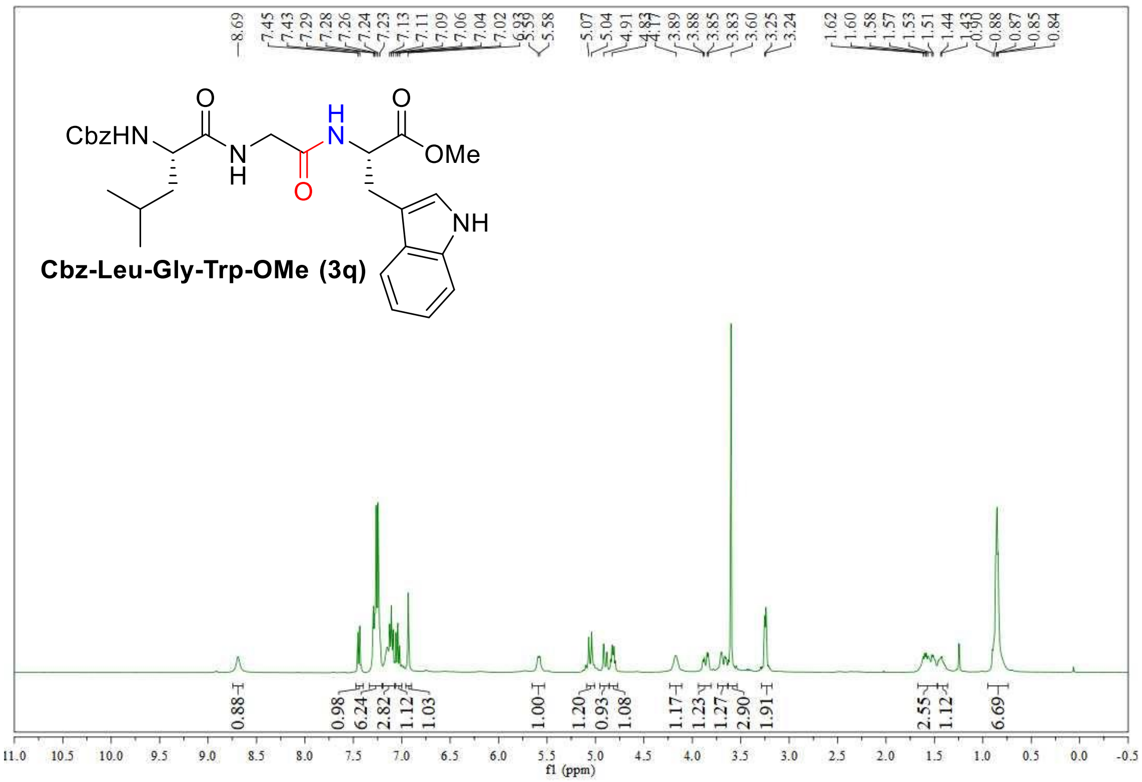


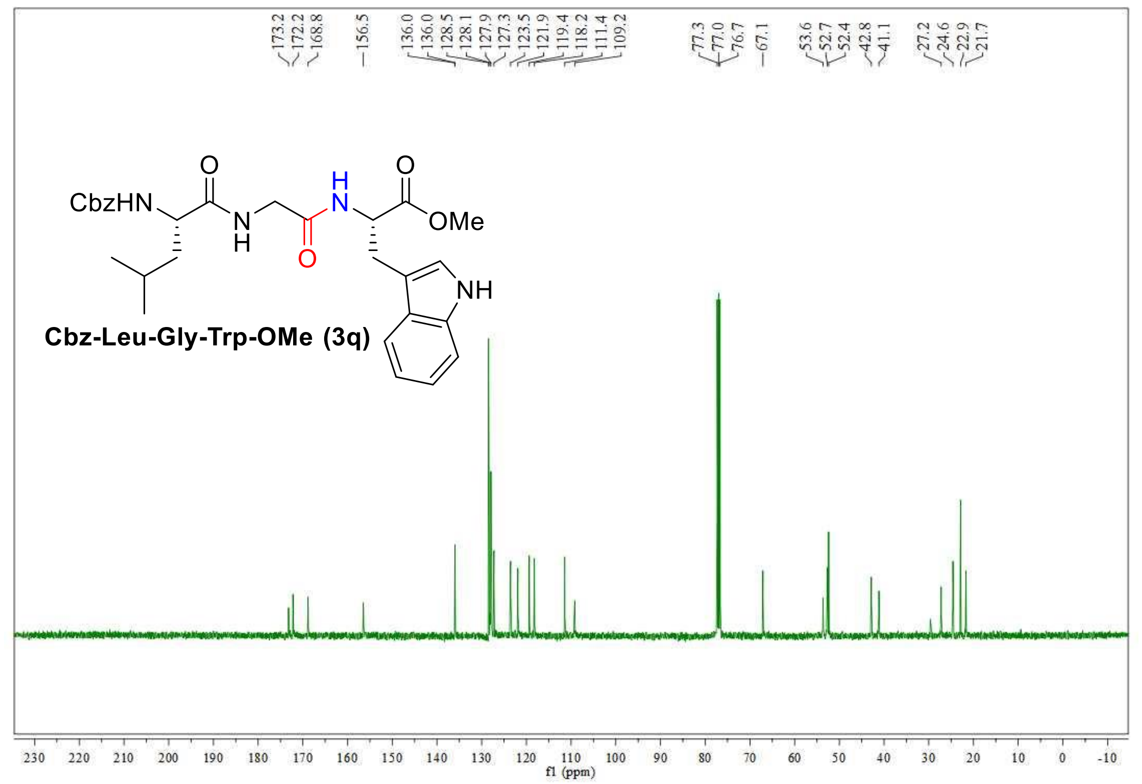

CbzHN
OMe
Ph
Cbz-Leu-Gly-Phe-OMe (3o)
f1 (ppm)

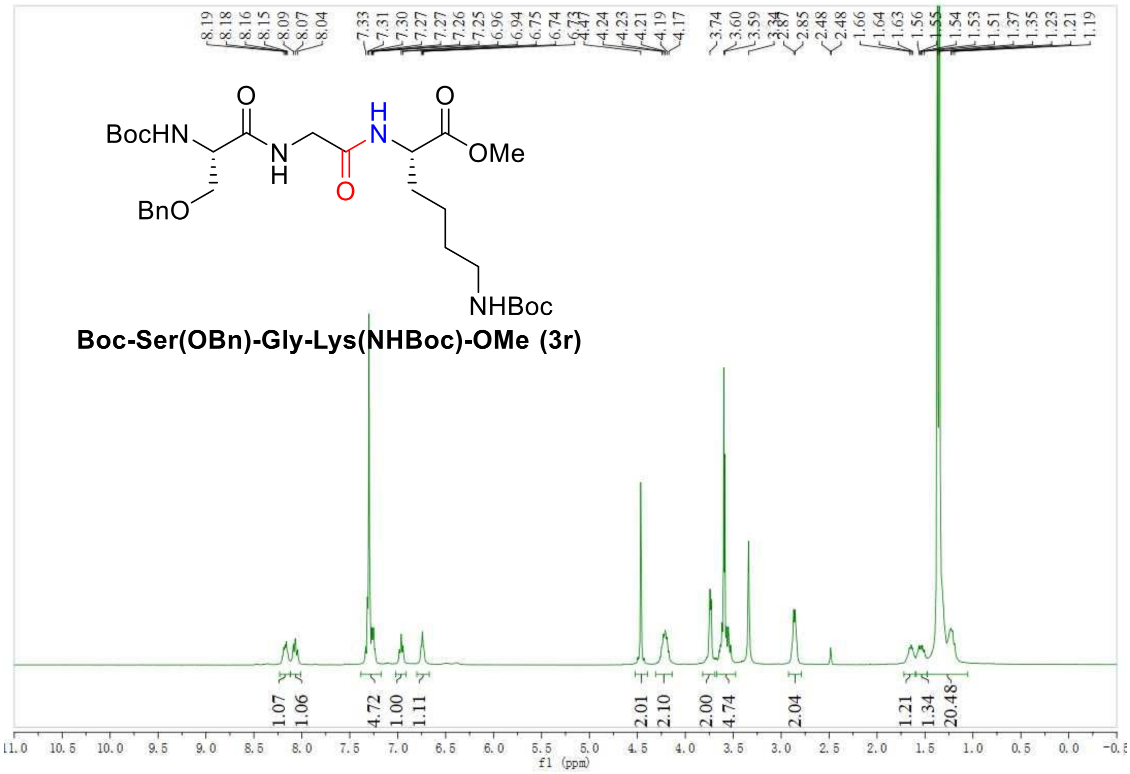

CbzHN
OMe
Ph
Cbz-Leu-Gly-Phe-OMe (3o)
f1 (ppm)

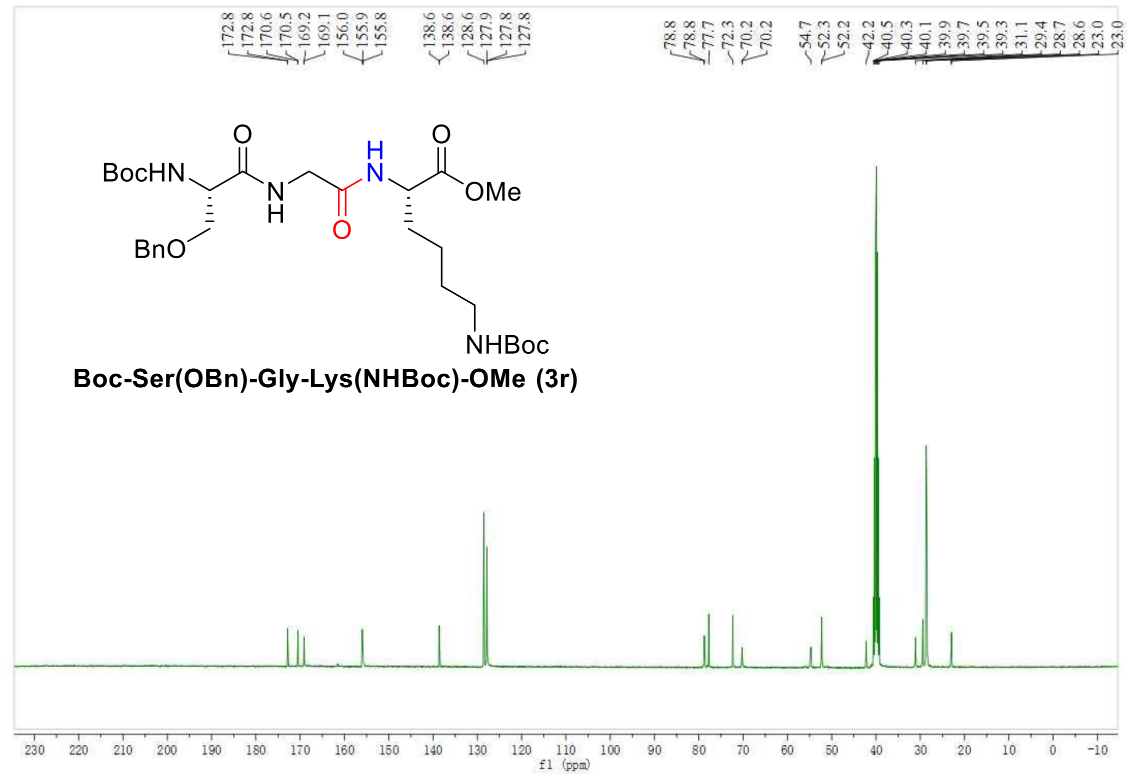

Cbz-Leu-Gly-Met-OMe (3p)
7.35 7.32 7.29 7.26 7.22 7.16
5.58
5.13 5.10 5.05
4.69 4.67
4.19 4.18 4.07 3.89 3.88 3.69
2.50 2.48 2.46 2.05
1.66 1.64 1.63 1.62 1.55 1.53
0.93 0.92
5.05 1.54 0.89 2.11 1.00 1.05 0.96 0.97 2.71 2.21 1.03 2.38 0.96 2.03 1.18 5.71
f1 (ppm)

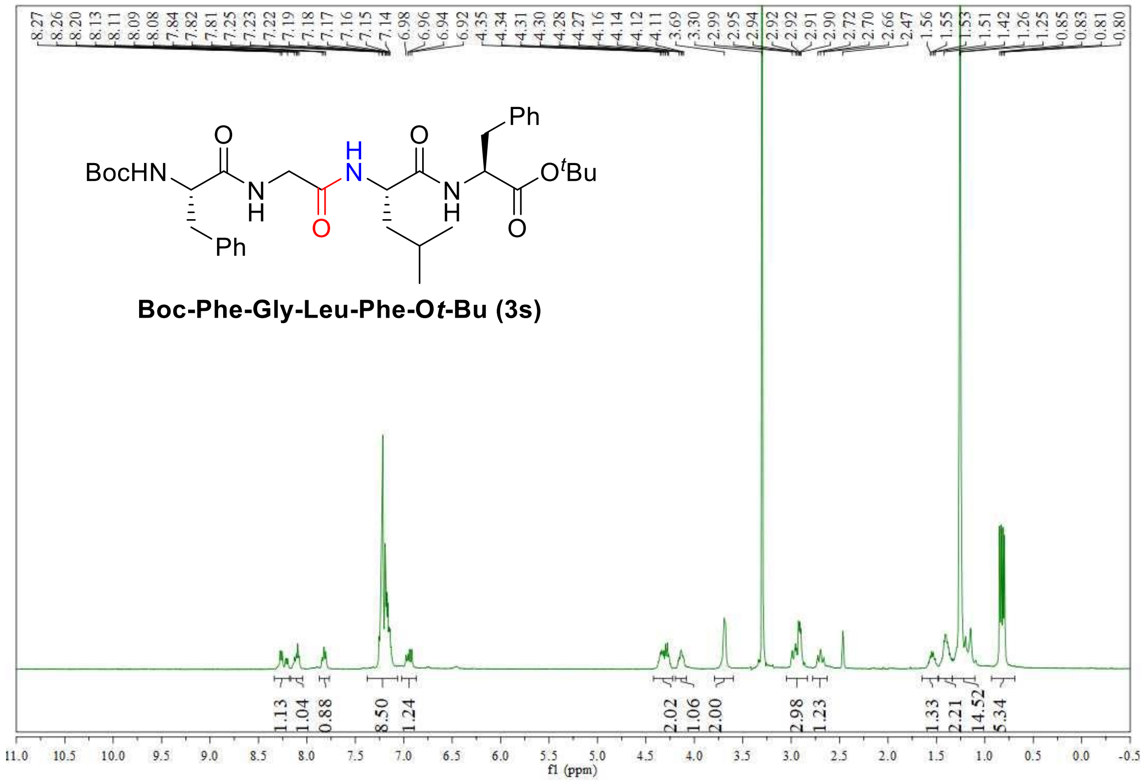

Cbz-Leu-Gly-Met-OMe (3p)
173.1 172.2 168.9
156.4
136.0 128.5 128.2 128.0
77.3 77.0 76.7
67.1
53.8 52.5 51.5 43.1 41.1 31.3 29.9 24.6 22.9 21.8 15.4
f1 (ppm)

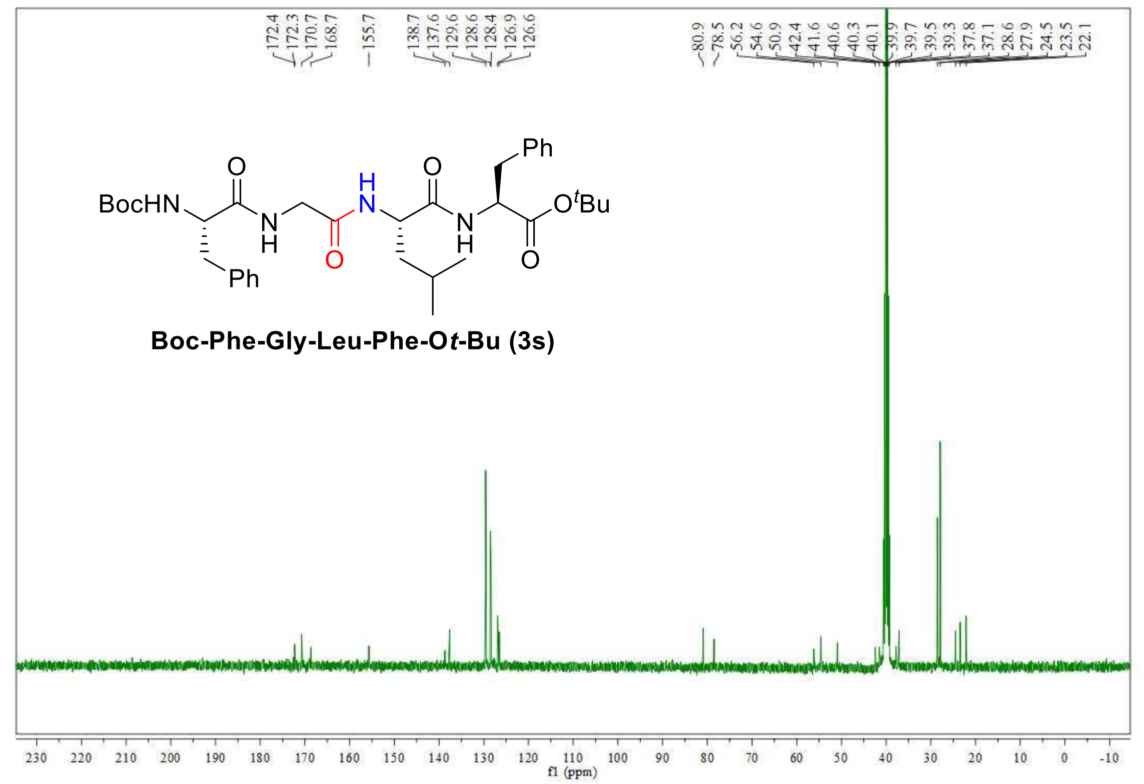

CbzHN
O
N
H
H
N
O
O
OMe
NH
Cbz-Leu-Gly-Trp-OMe (3q)
f1 (ppm)

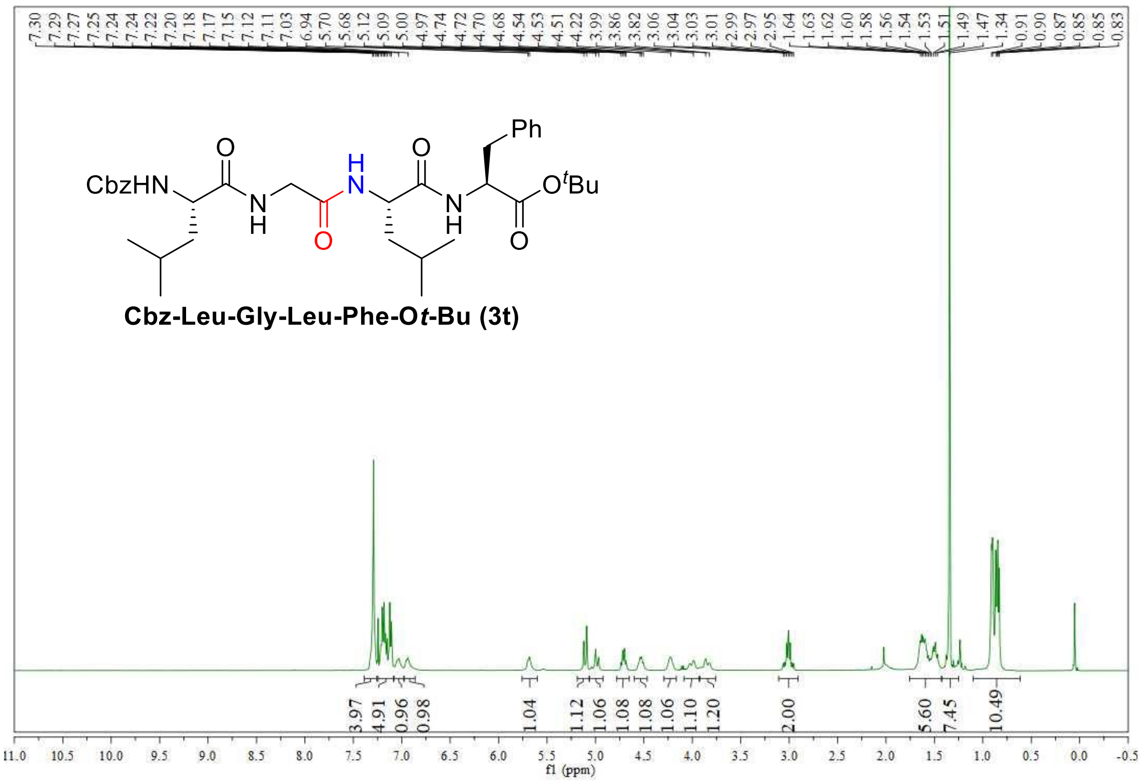

CbzHN
O
N
H
H
N
O
O
OMe
NH
Cbz-Leu-Gly-Trp-OMe (3q)
f1 (ppm)

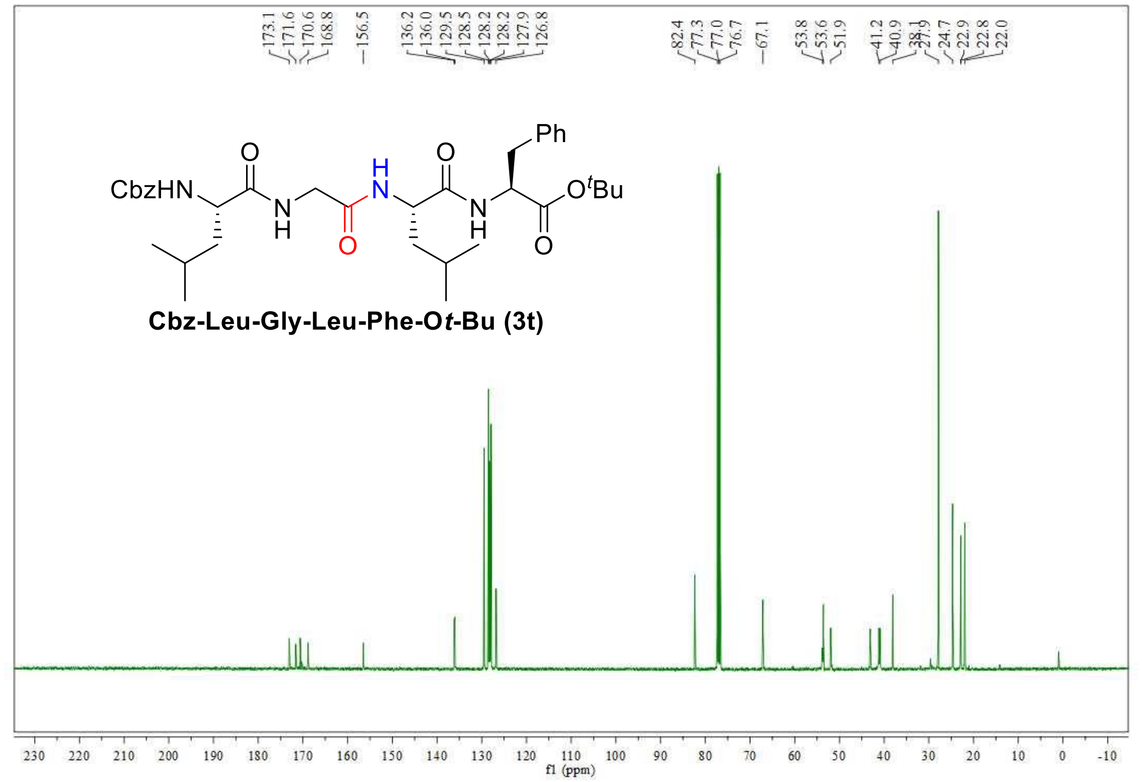

BocHN
BnO
NHBoc
OMe
Boc-Ser(OBn)-Gly-Lys(NHBoc)-OMe (3r)
f1 (ppm)

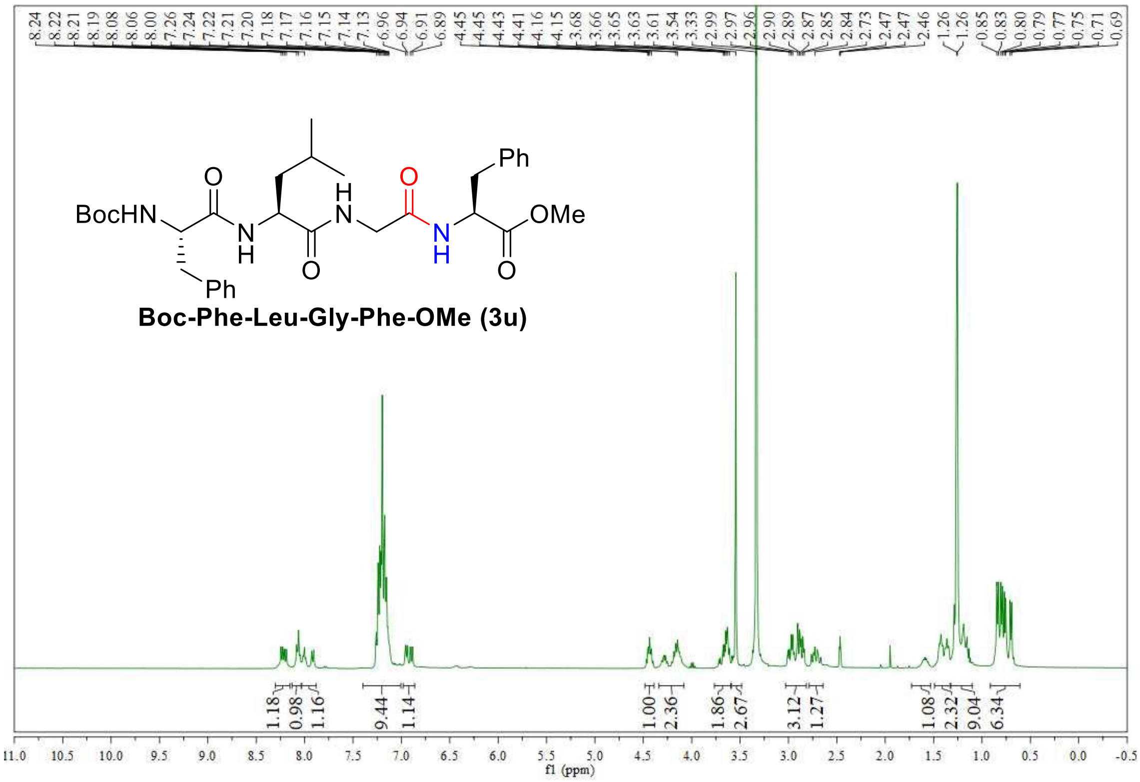

BocHN
BnO
NHBoc
OMe
Boc-Ser(OBn)-Gly-Lys(NHBoc)-OMe (3r)
f1 (ppm)

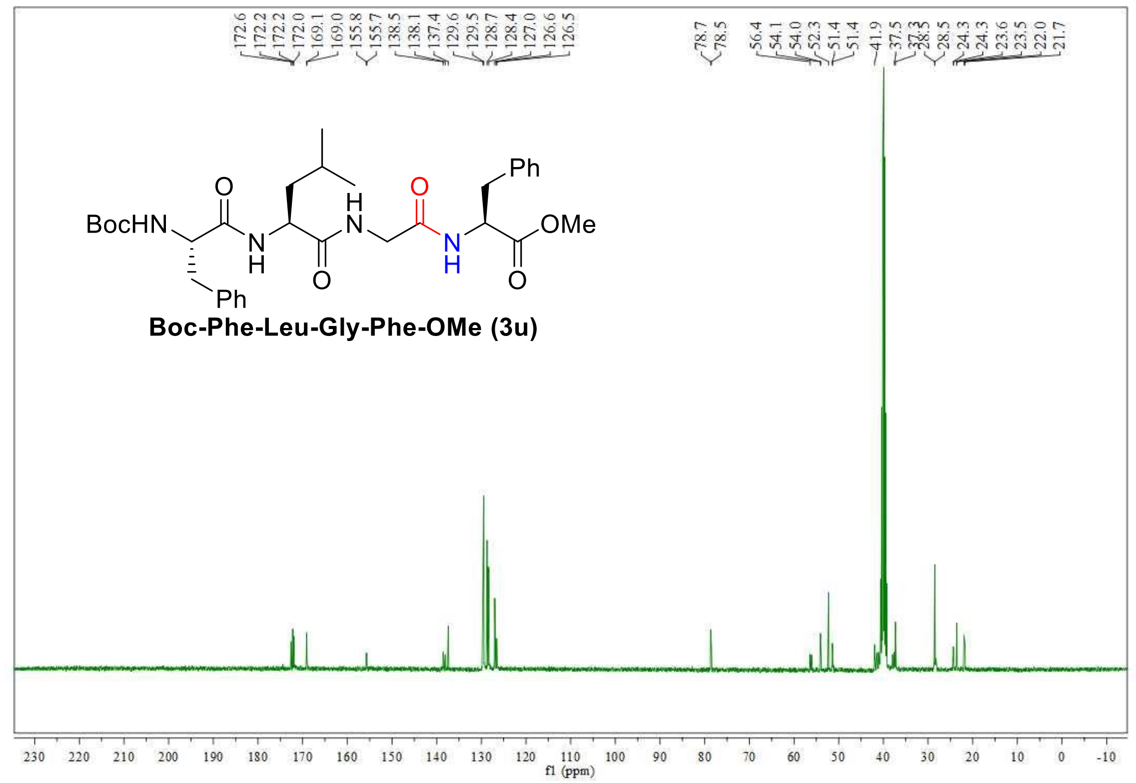

Boc-Phe-Gly-Leu-Phe-O*t*-Bu (3s)
f1 (ppm)

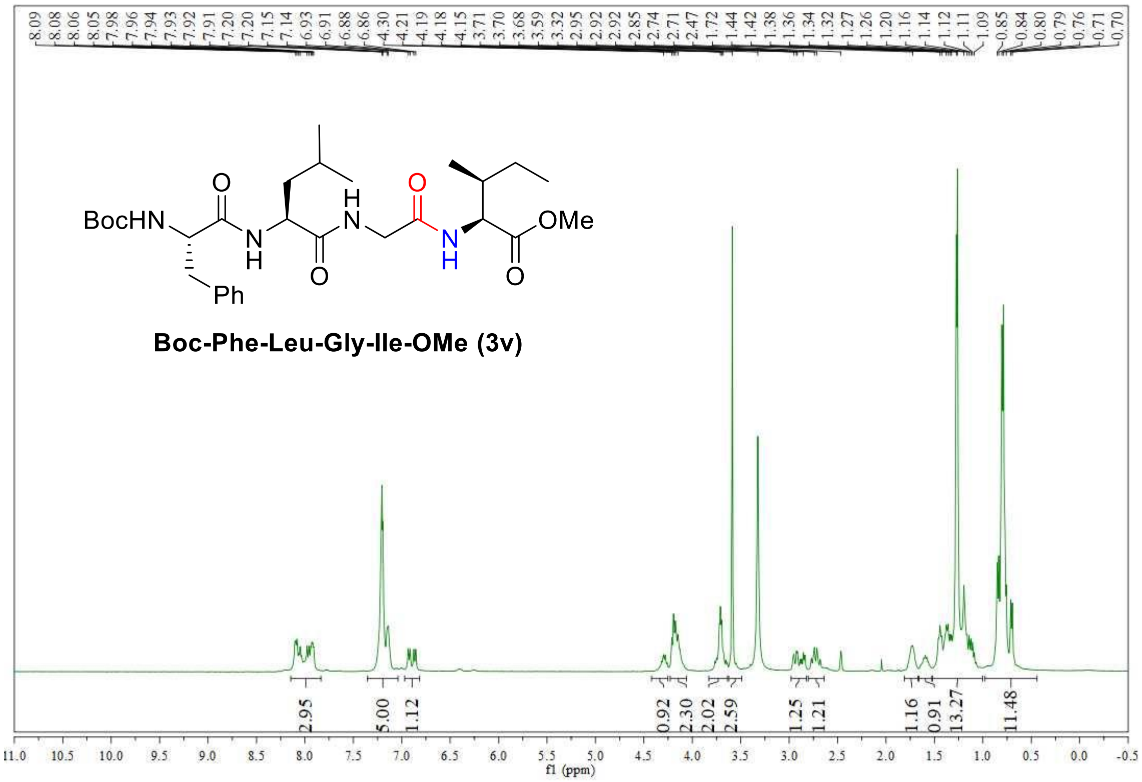

Boc-Phe-Gly-Leu-Phe-O*t*-Bu (3s)
f1 (ppm)

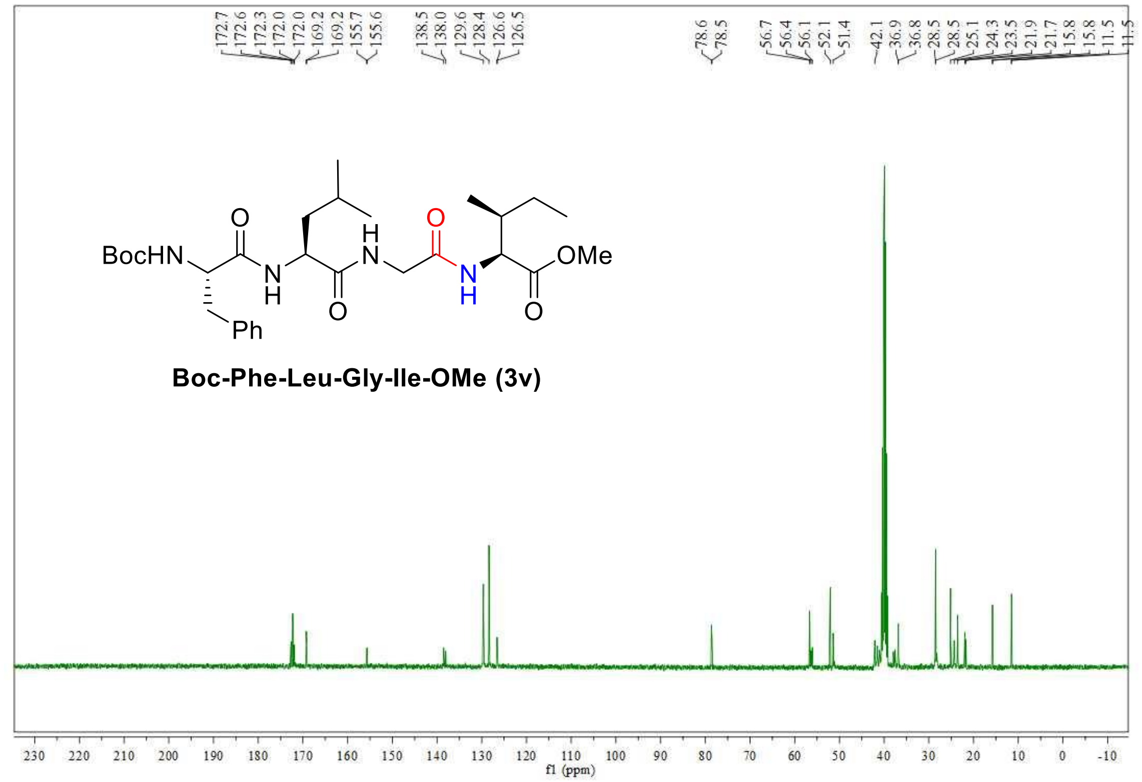

CbzHN
Ph
O^{t}Bu
Cbz-Leu-Gly-Leu-Phe-O*t*-Bu (3t)
7.30 7.29 7.27 7.25 7.24 7.24 7.22 7.20 7.18 7.17 7.15 7.12 7.11 7.03 6.94 5.70 5.68 5.12 5.09 5.00 4.97 4.74 4.72 4.70 4.68 4.54 4.53 4.51 4.22 3.99 3.86 3.82 3.06 3.04 3.03 3.01 2.99 2.97 2.95 1.64 1.63 1.62 1.60 1.58 1.56 1.54 1.53 1.51 1.49 1.47 1.34 0.91 0.90 0.87 0.85 0.85 0.83
3.97 4.91 0.96 0.98 1.04 1.12 1.06 1.08 1.08 1.06 1.10 1.20 2.00 5.60 7.45 10.49
f1 (ppm)

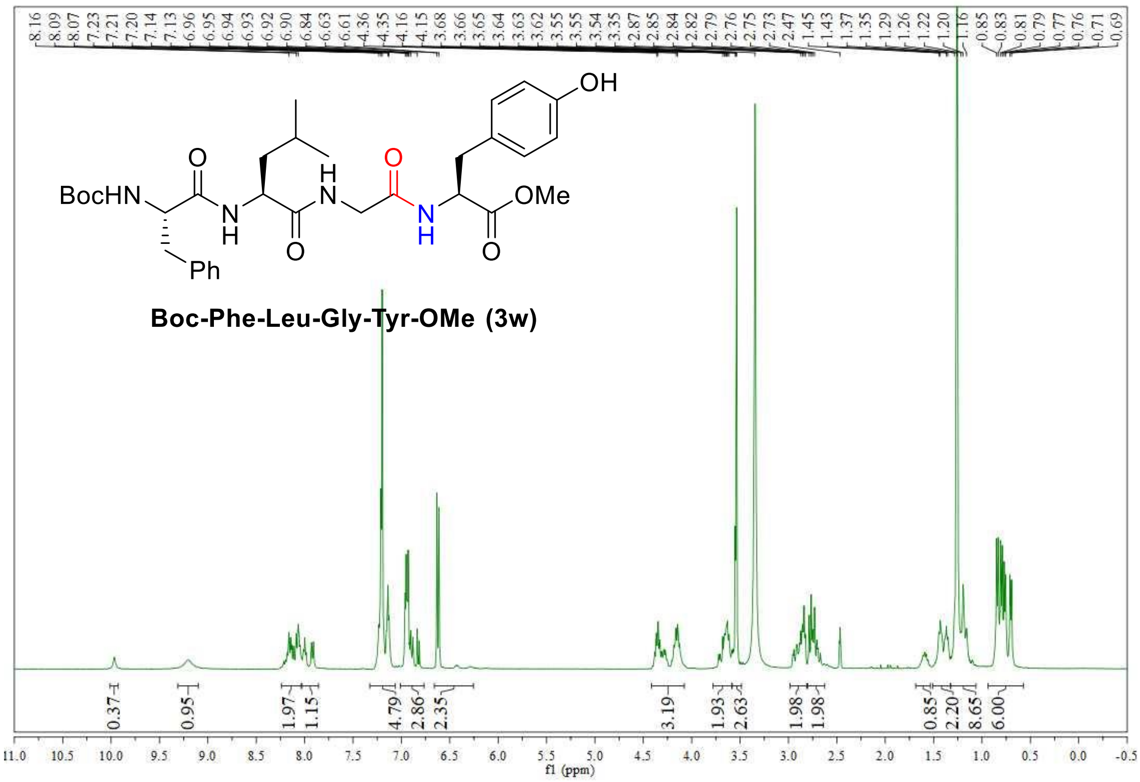

CbzHN
Ph
O^{t}Bu
Cbz-Leu-Gly-Leu-Phe-O*t*-Bu (3t)
173.1 171.6 170.6 168.8 156.5 136.2 136.0 129.5 128.5 128.2 128.2 127.9 126.8 82.4 77.3 77.0 76.7 67.1 53.8 53.6 51.9 41.2 40.9 38.1 27.9 24.7 22.9 22.8 22.0
f1 (ppm)

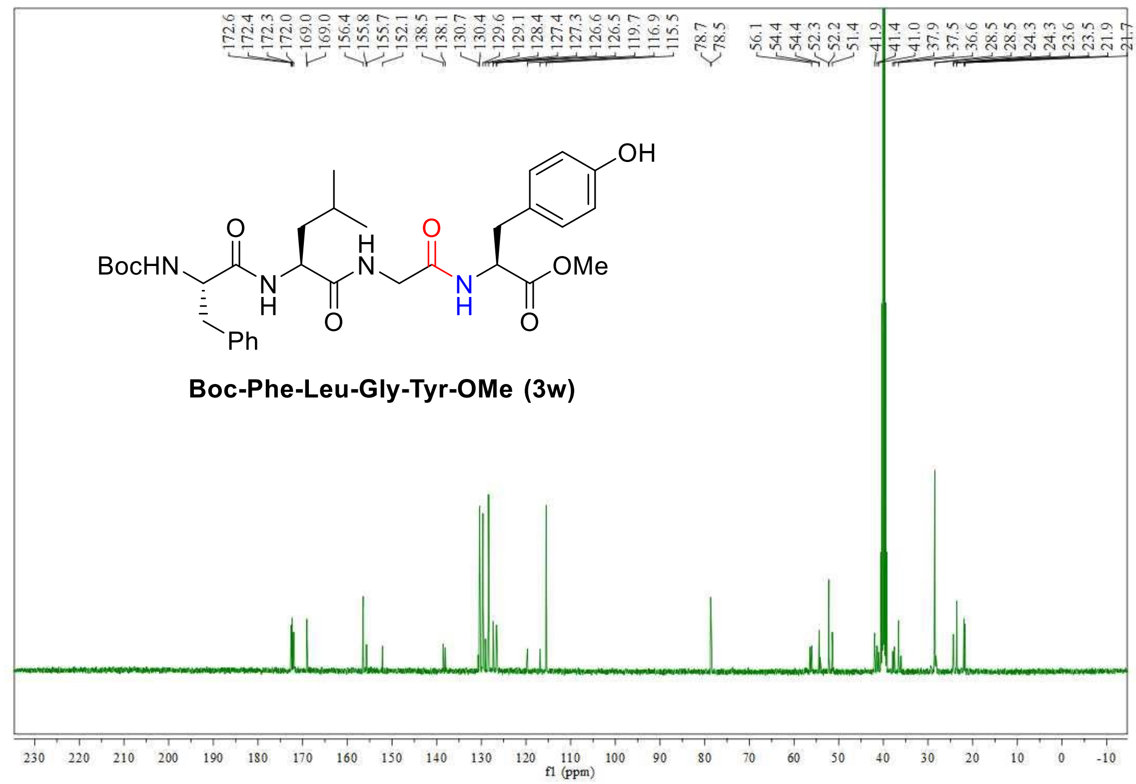

Boc-Phe-Leu-Gly-Phe-OMe (3u)

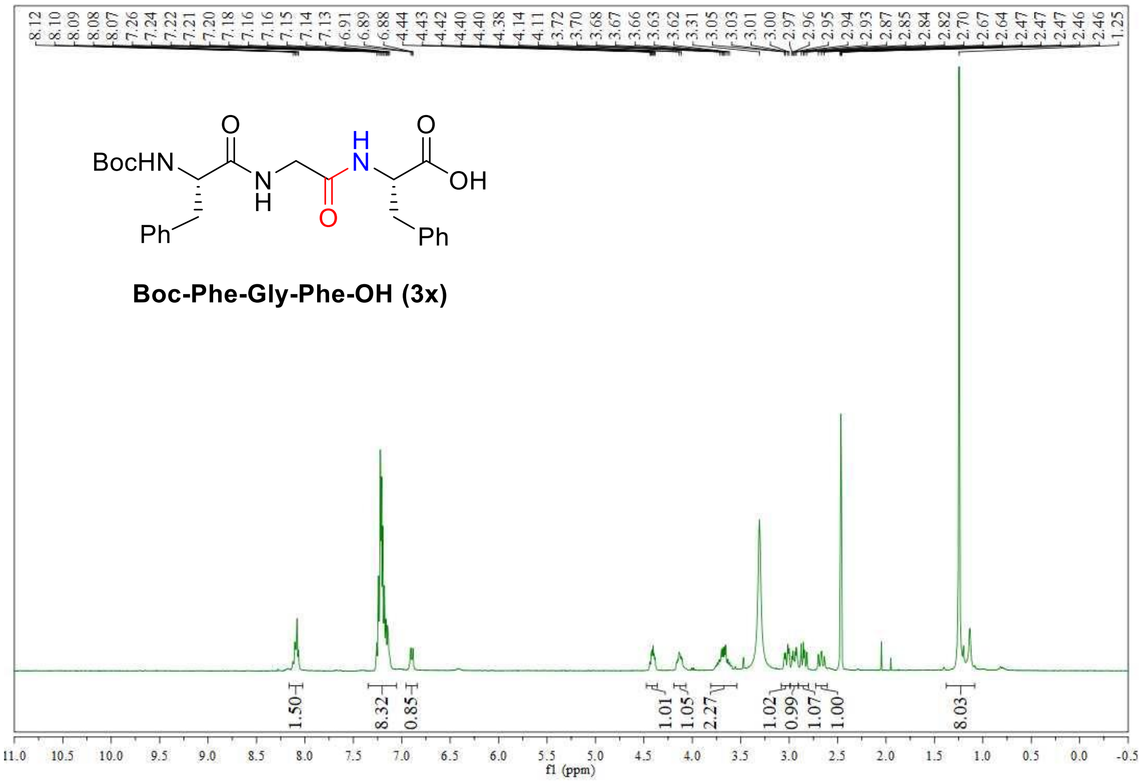

Boc-Phe-Leu-Gly-Phe-OMe (3u)

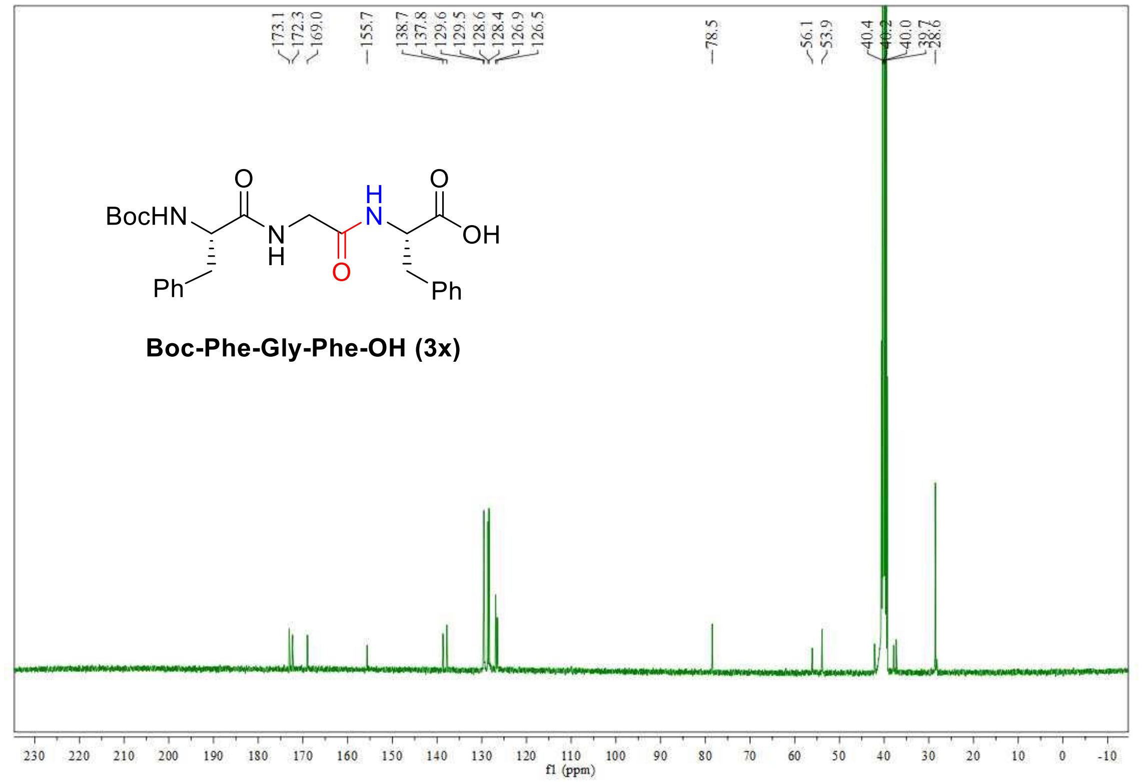

8.09 8.08 8.06 8.05 7.98 7.96 7.94 7.93 7.92 7.91 7.20 7.20 7.15 7.14 6.93 6.91 6.88 6.86 4.30 4.21 4.19 4.18 4.15 3.71 3.70 3.68 3.59 3.32 2.95 2.92 2.92 2.92 2.85 2.74 2.71 2.47 1.72 1.44 1.42 1.38 1.36 1.34 1.32 1.27 1.26 1.20 1.16 1.14 1.12 1.11 1.09 0.85 0.84 0.80 0.79 0.76 0.71 0.70
BocHN
H
N
O
O
OMe
Ph
Boc-Phe-Leu-Gly-Ile-OMe (3v)
2.95
5.00
1.12
0.92
2.30
2.02
2.59
1.25
1.21
1.16
0.91
13.27
11.48
f1 (ppm)

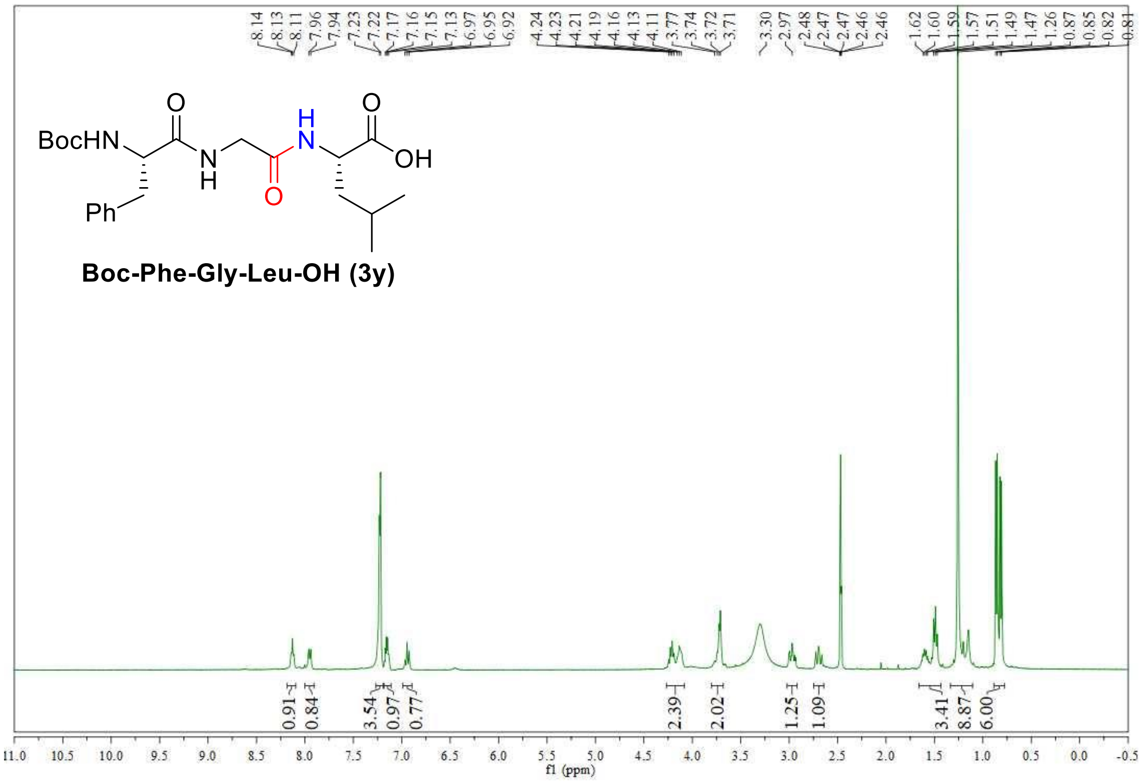

172.7 172.6 172.3 172.0 172.0 169.2 169.2 155.7 155.6 138.5 138.0 129.6 128.4 126.6 126.5 78.6 78.5 56.7 56.4 56.1 52.1 51.4 42.1 36.9 36.8 28.5 28.5 25.1 24.3 23.5 21.9 21.7 15.8 15.8 11.5 11.5
BocHN
H
N
O
O
OMe
Ph
Boc-Phe-Leu-Gly-Ile-OMe (3v)
f1 (ppm)


BocHN
Ph
OH
OMe
Boc-Phe-Leu-Gly-Tyr-OMe (3w)
f1 (ppm)

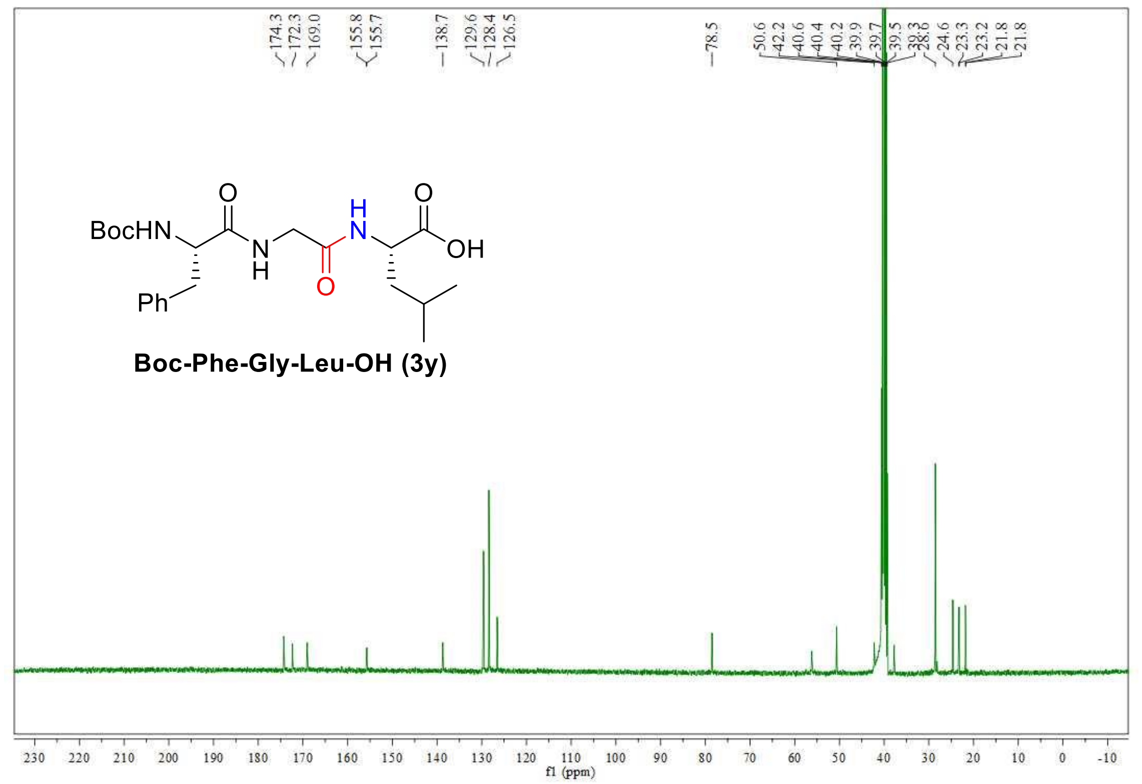

BocHN
Ph
OH
OMe
Boc-Phe-Leu-Gly-Tyr-OMe (3w)
f1 (ppm)



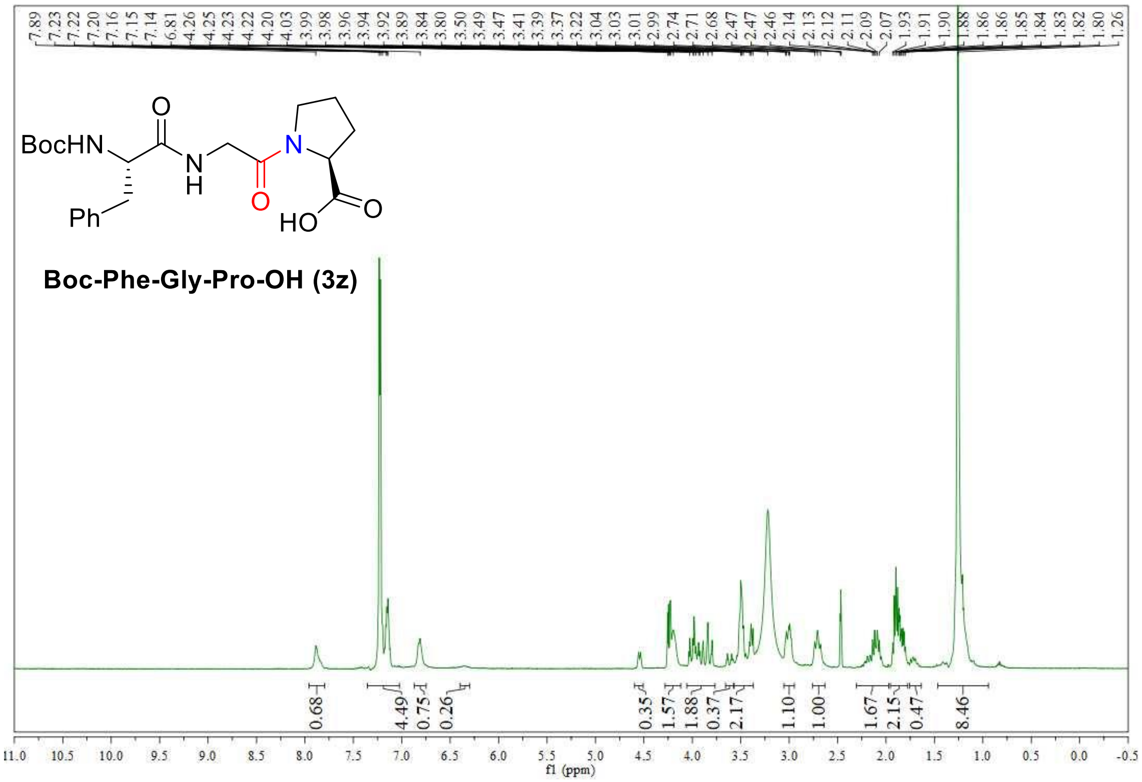




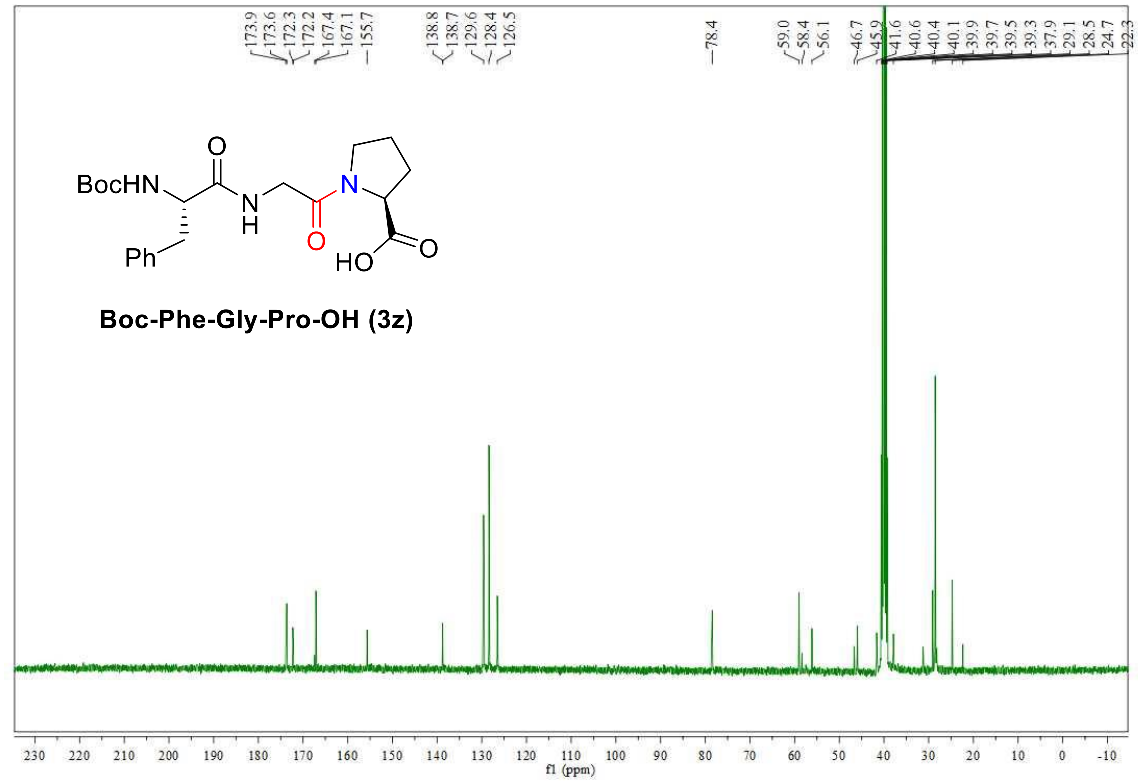
BocHN
Ph
OH
Boc-Phe-Gly-Leu-OH (3y)
f1 (ppm)

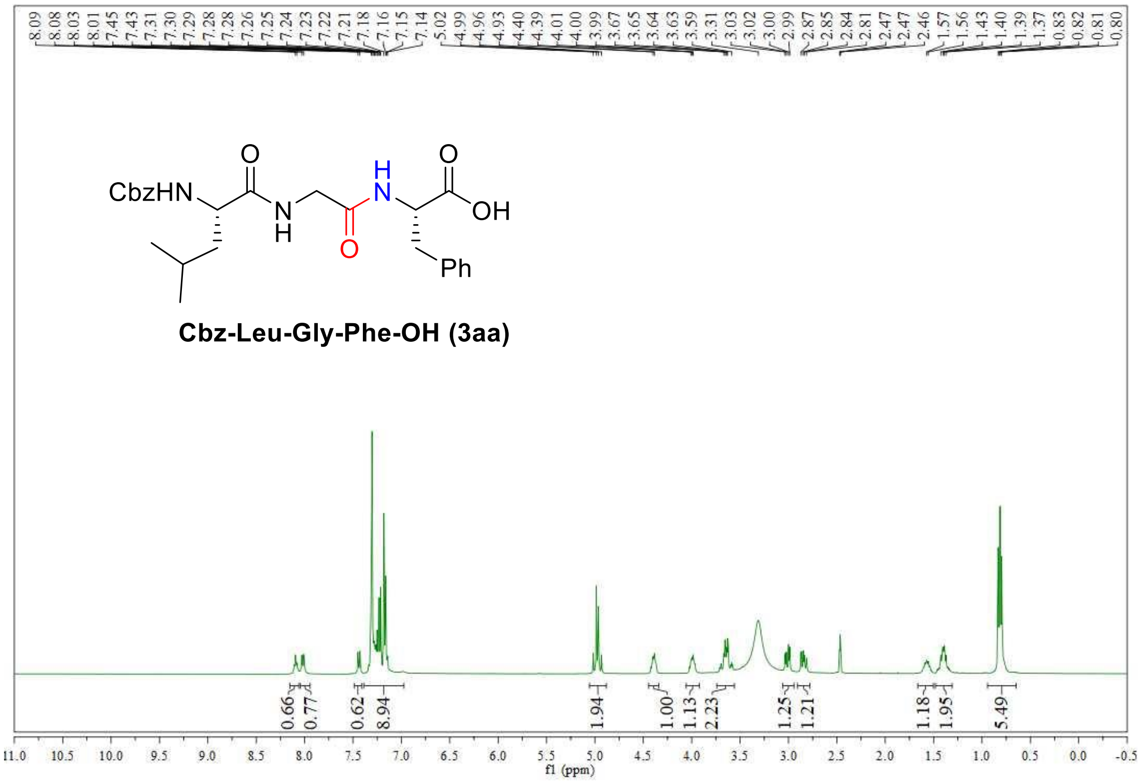


BocHN
Ph
OH
Boc-Phe-Gly-Leu-OH (3y)
f1 (ppm)

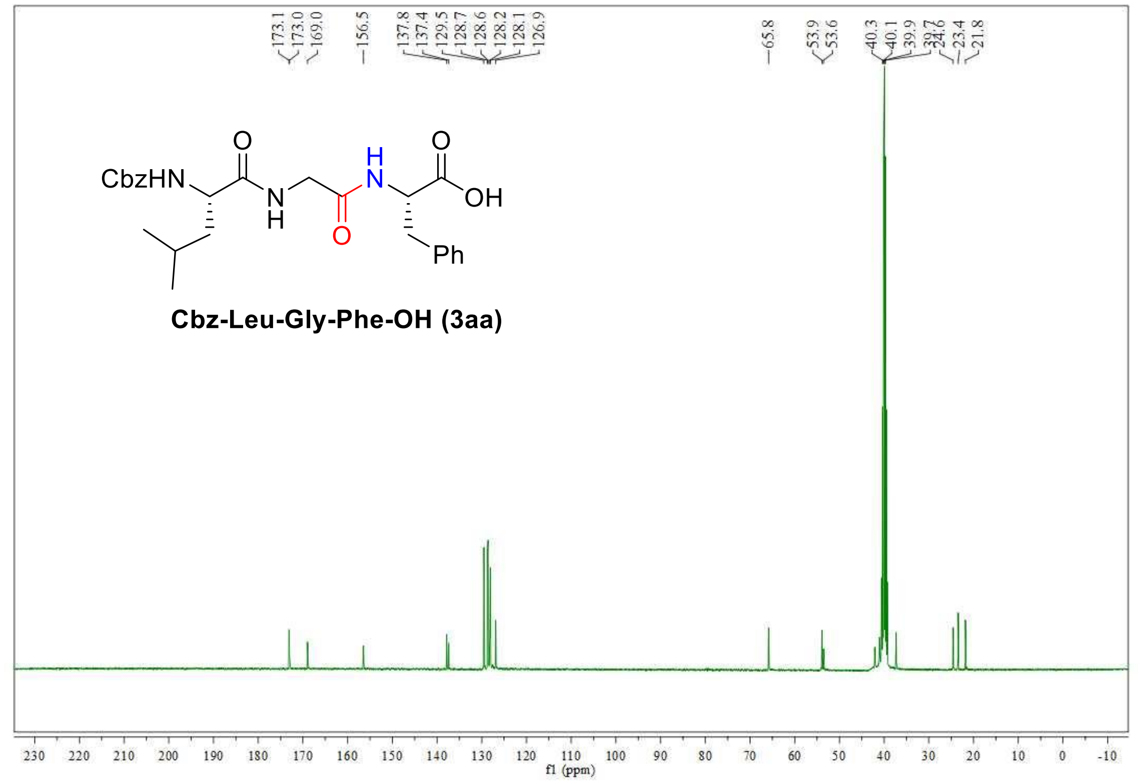


^{1}H NMR (399 Hz, DMSO-d6) of compound **3z** at 44 °C

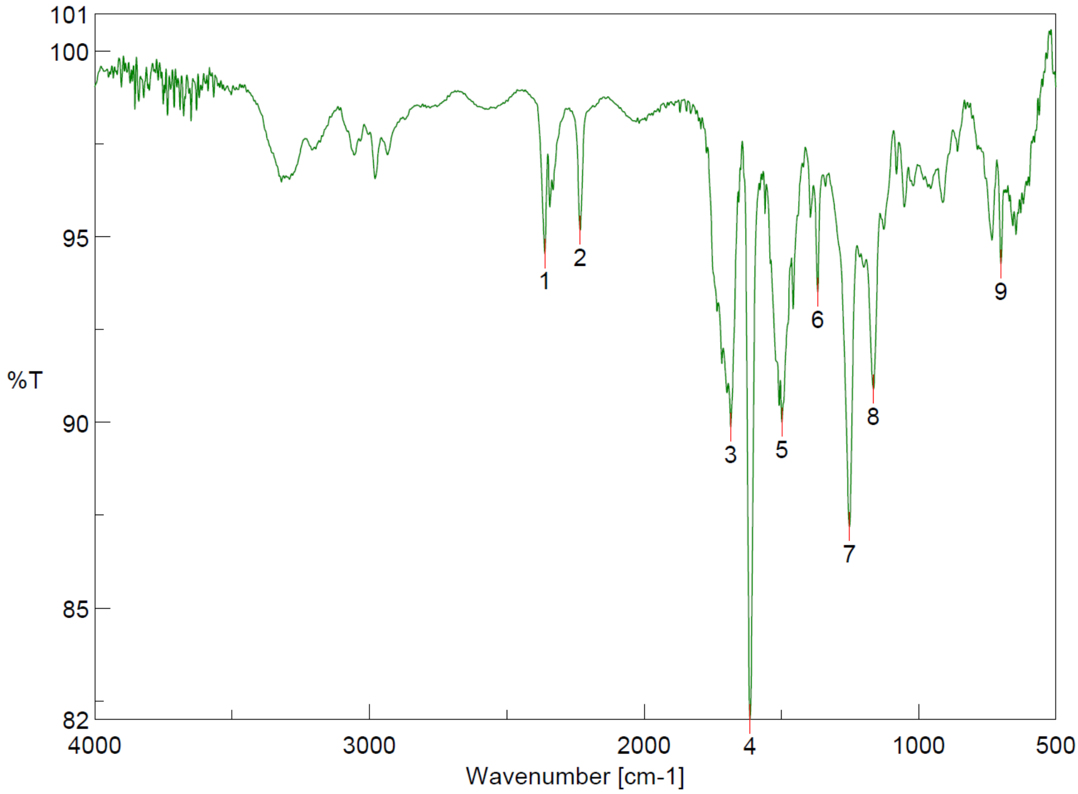




CbzHN
O
N
H
H
N
O
O
OH
Ph
Cbz-Leu-Gly-Phe-OH (3aa)
f1 (ppm)

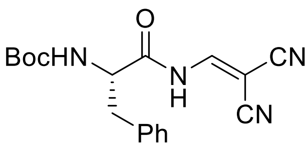


CbzHN
O
N
H
H
N
O
O
OH
Ph
Cbz-Leu-Gly-Phe-OH (3aa)
f1 (ppm)

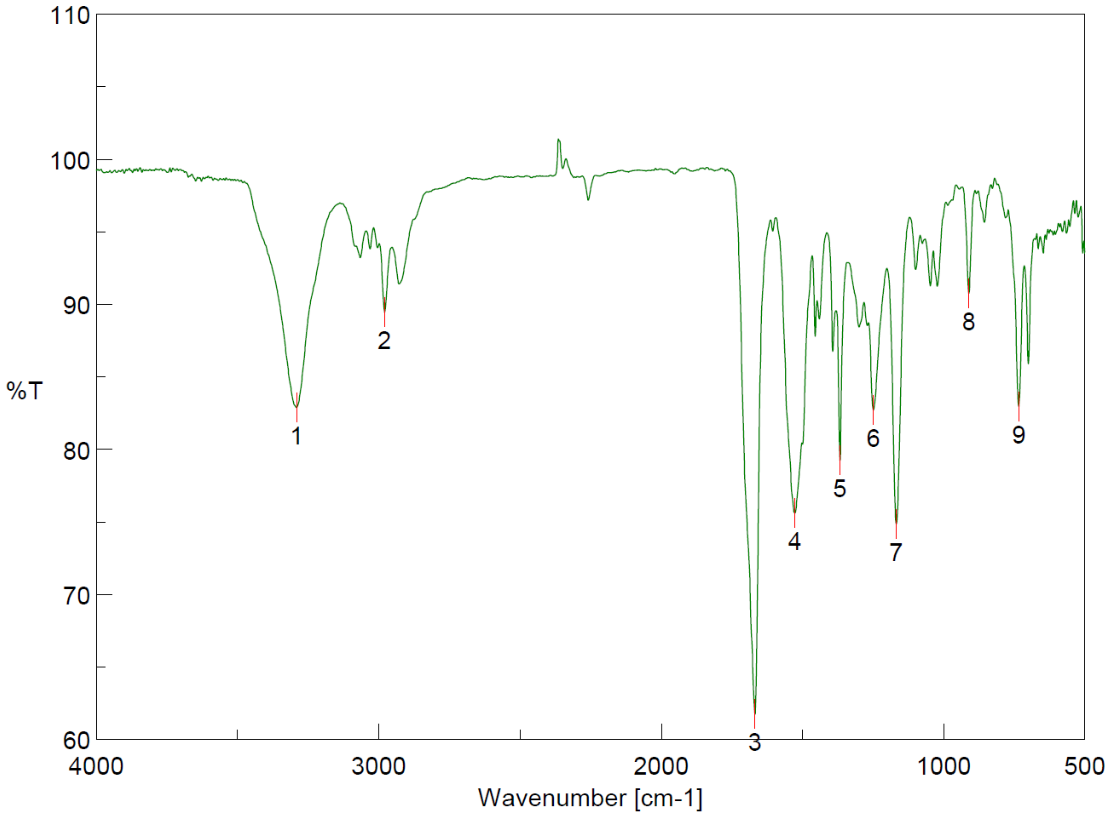


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	2361.41	94.5398	2	2233.16	95.1702
3	1683.55	89.8756	4	1614.13	82.0058
5	1497.45	89.9942	6	1367.28	93.5045
7	1251.58	87.1849	8	1164.79	90.8964
9	700.034	94.2641			

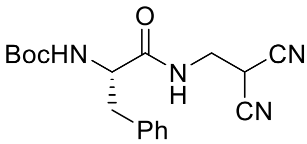


s1

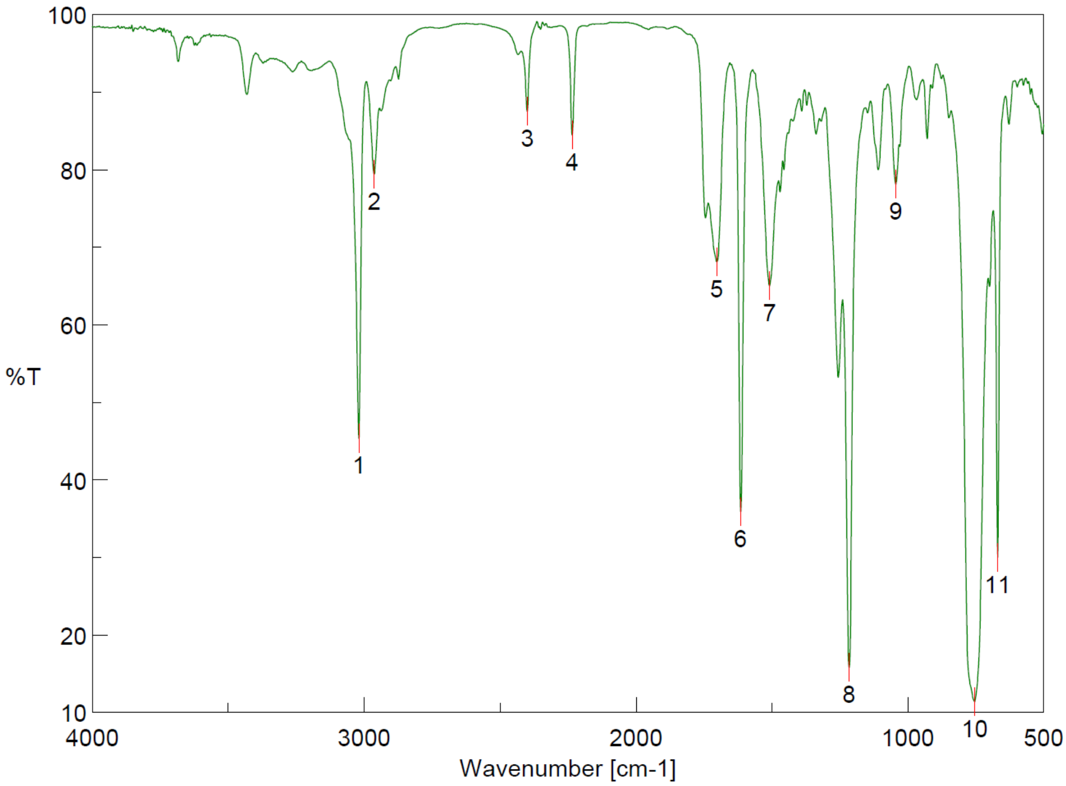


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3290.93	82.8717	2	2979.48	89.4431
3	1668.12	61.7319	4	1526.38	75.6103
5	1367.28	79.2345	6	1248.68	82.6922
7	1167.69	74.8617	8	910.236	90.744
9	733.782	82.9559			

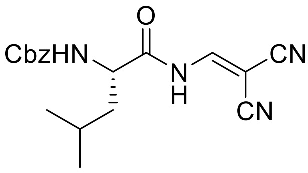


1a

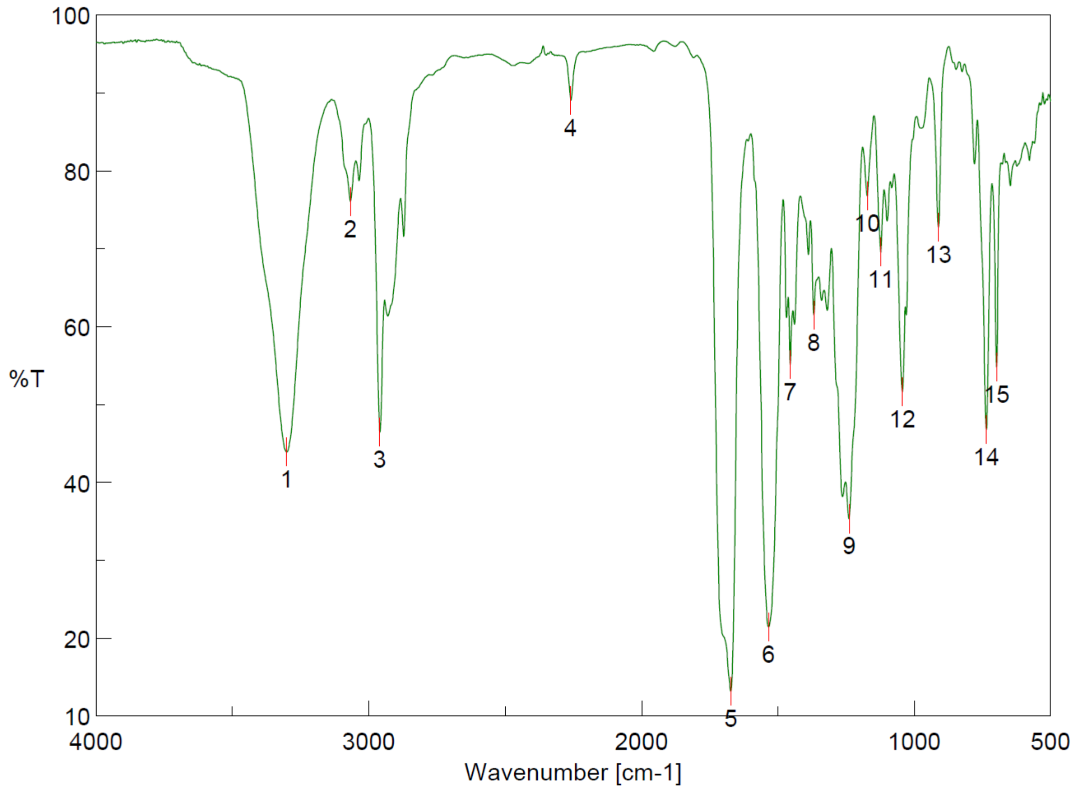


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3019.98	45.3128	2	2963.09	79.3906
3	2399.98	87.4939	4	2235.09	84.4156
5	1702.84	68.0827	6	1615.09	35.88
7	1508.06	64.9972	8	1215.9	15.752
9	1044.26	78.0936	10	754.031	11.349
11	669.178	29.9544			

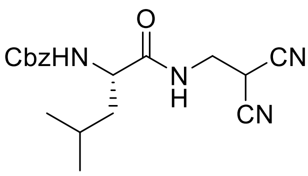


S2

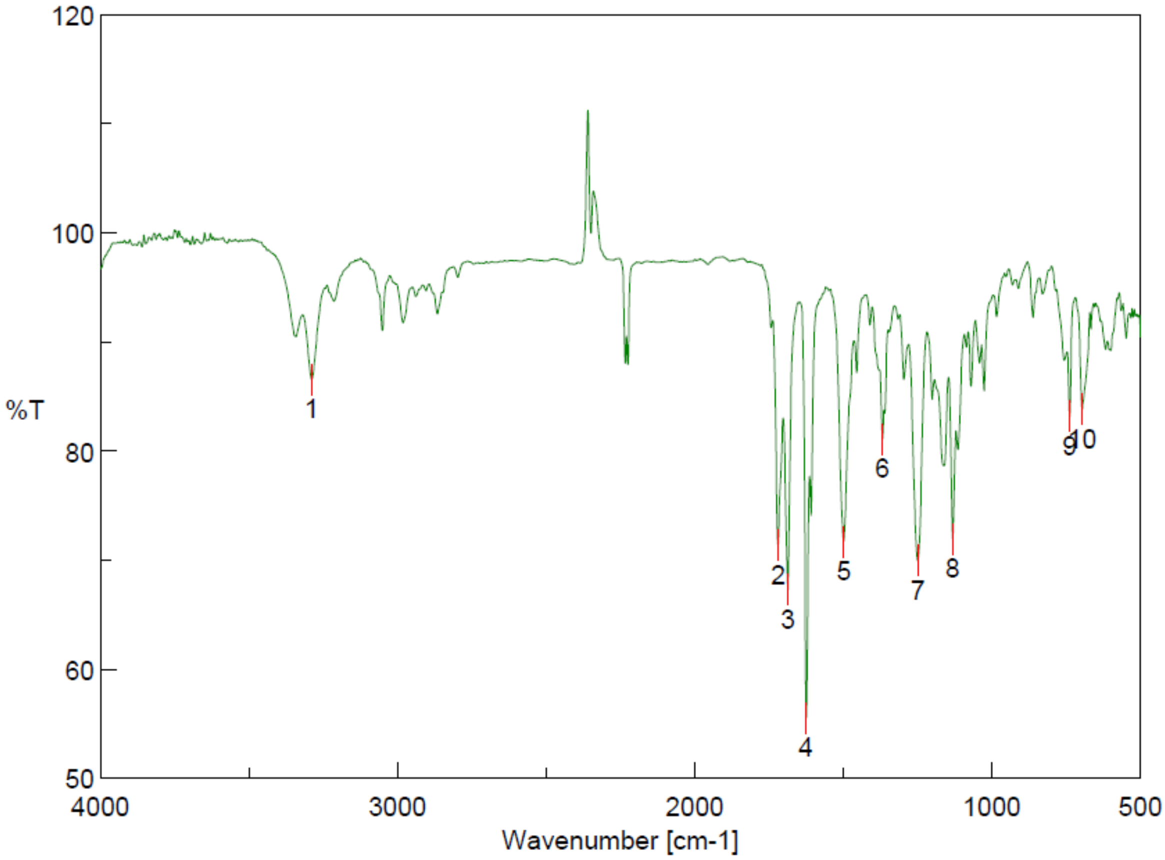


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3300.57	43.8452	2	3067.23	76.0267
3	2959.23	46.4196	4	2259.2	89.0162
5	1671.98	13.1513	6	1534.1	21.4172
7	1455.03	55.0796	8	1368.25	61.4621
9	1239.04	35.2847	10	1172.51	76.7304
11	1122.37	69.5005	12	1043.3	51.5826
13	911.201	72.7499	14	735.71	46.7239
15	698.105	54.7491			

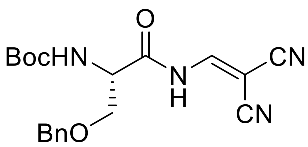


1b

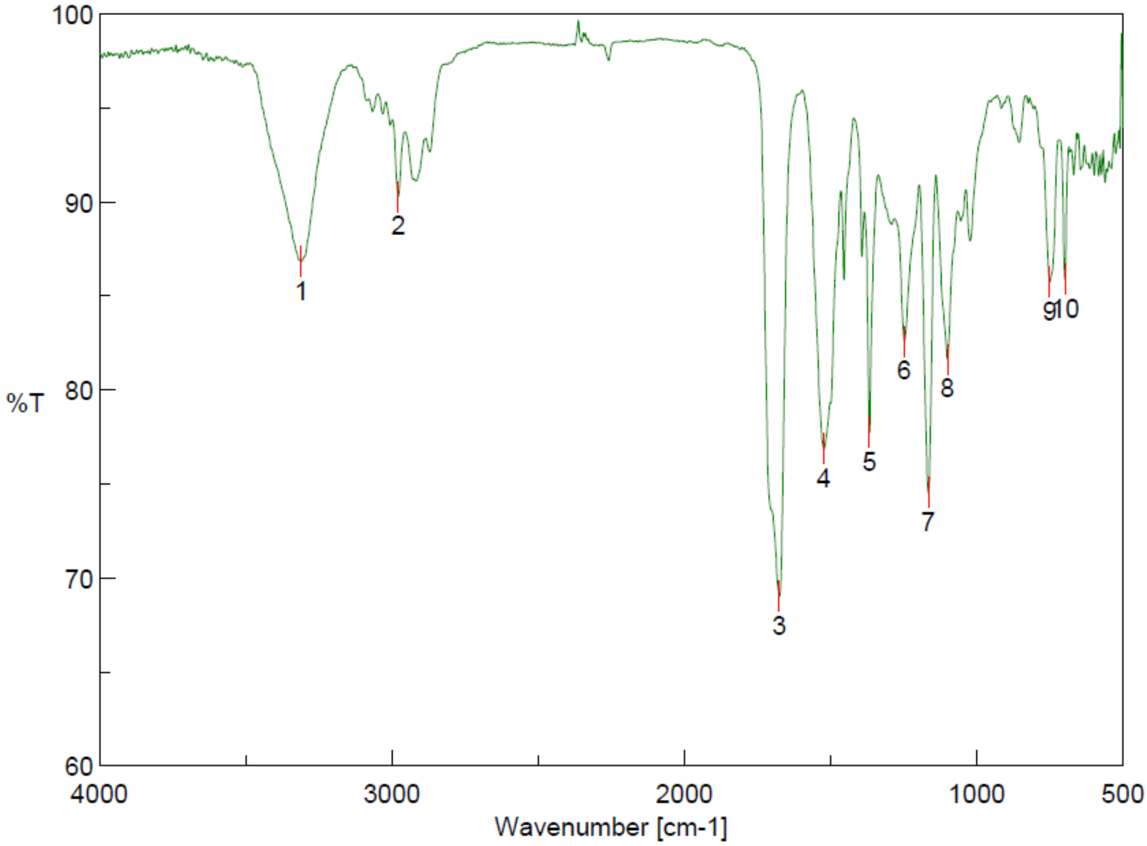


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3289	86.5589	2	1719.23	71.3863
3	1686.44	67.2831	4	1624.73	55.548
5	1498.42	71.7012	6	1368.25	81.075
7	1249.65	69.9421	8	1131.05	71.8968
9	737.639	83.1544	10	696.177	83.8107

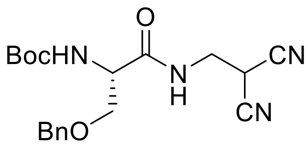


s3

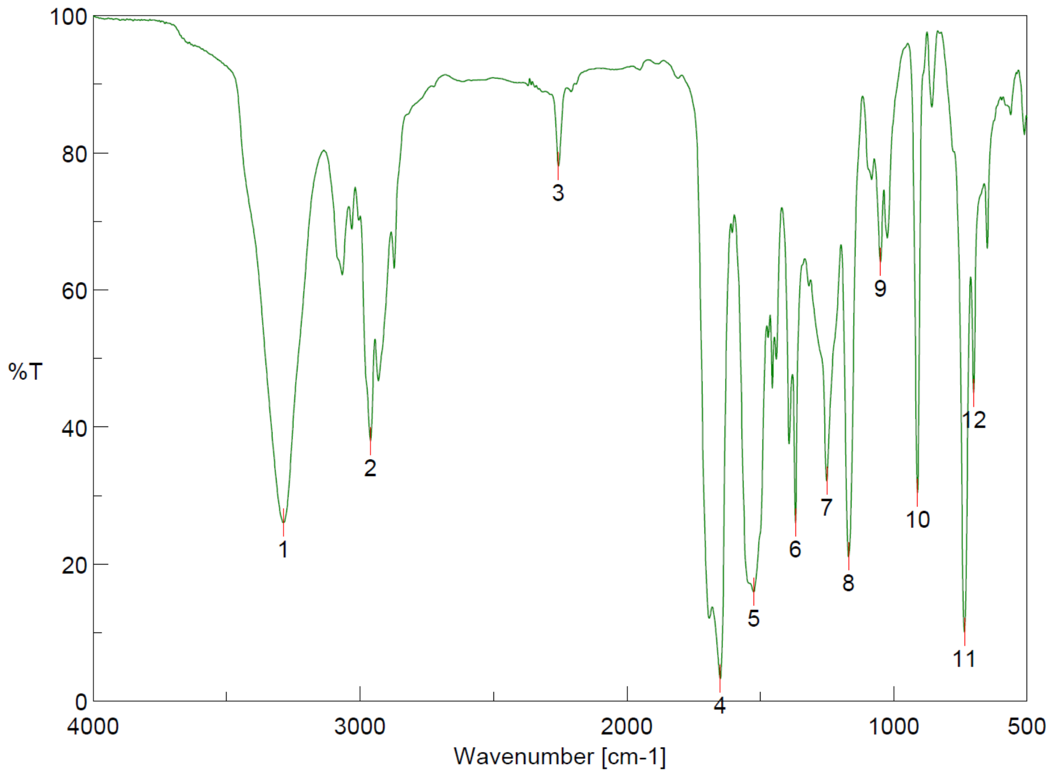


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3310.21	86.7925	2	2978.52	90.2527
3	1674.87	69.0025	4	1522.52	76.841
5	1367.28	77.7134	6	1247.72	82.5589
7	1165.76	74.5069	8	1100.19	81.625
9	750.174	85.6964	10	698.105	85.8536

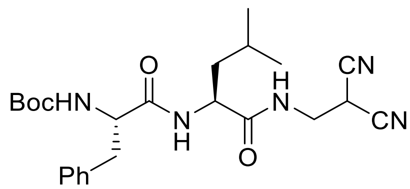


1c

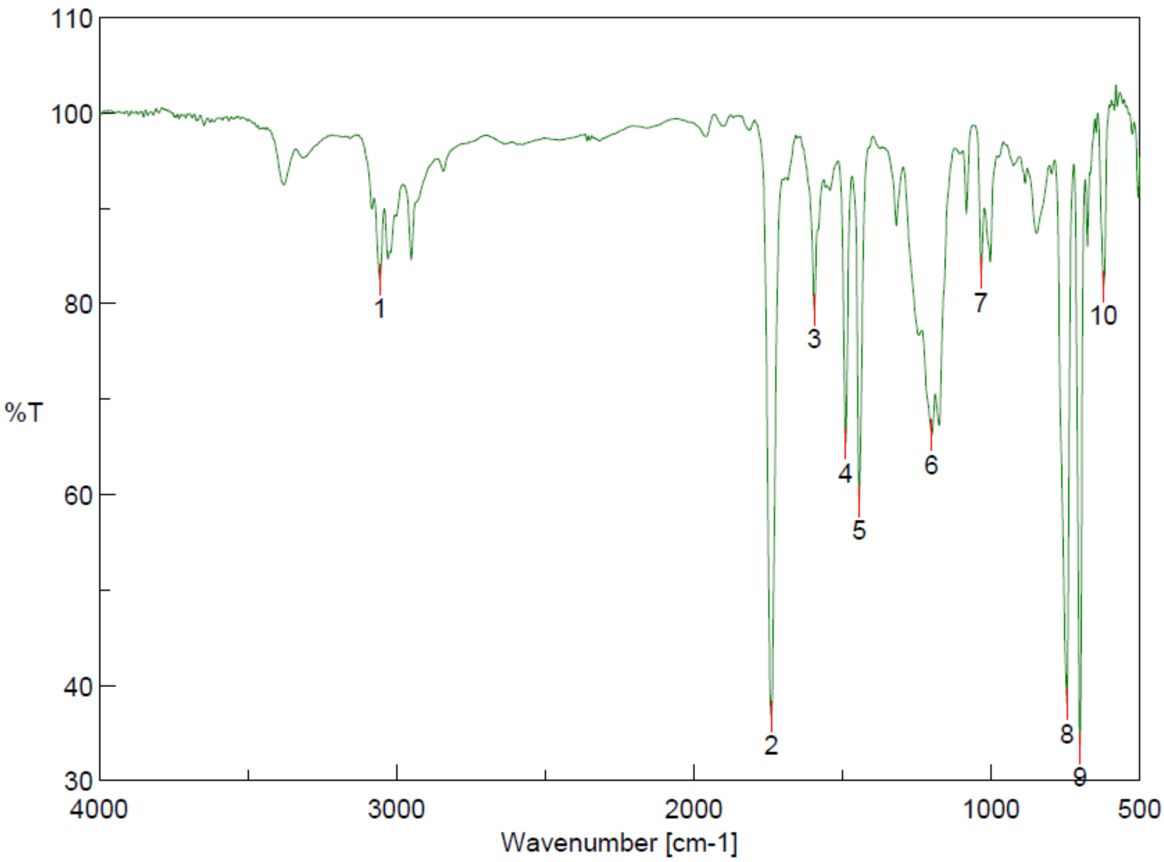


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3287.07	26.0277	2	2961.16	37.9286
3	2256.31	78.0101	4	1649.8	3.2532
5	1524.45	15.903	6	1368.25	25.9993
7	1250.61	32.091	8	1168.65	21.0487
9	1049.09	64.0349	10	910.236	30.4007
11	734.746	10.0449	12	700.034	44.9413

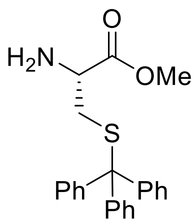


1d

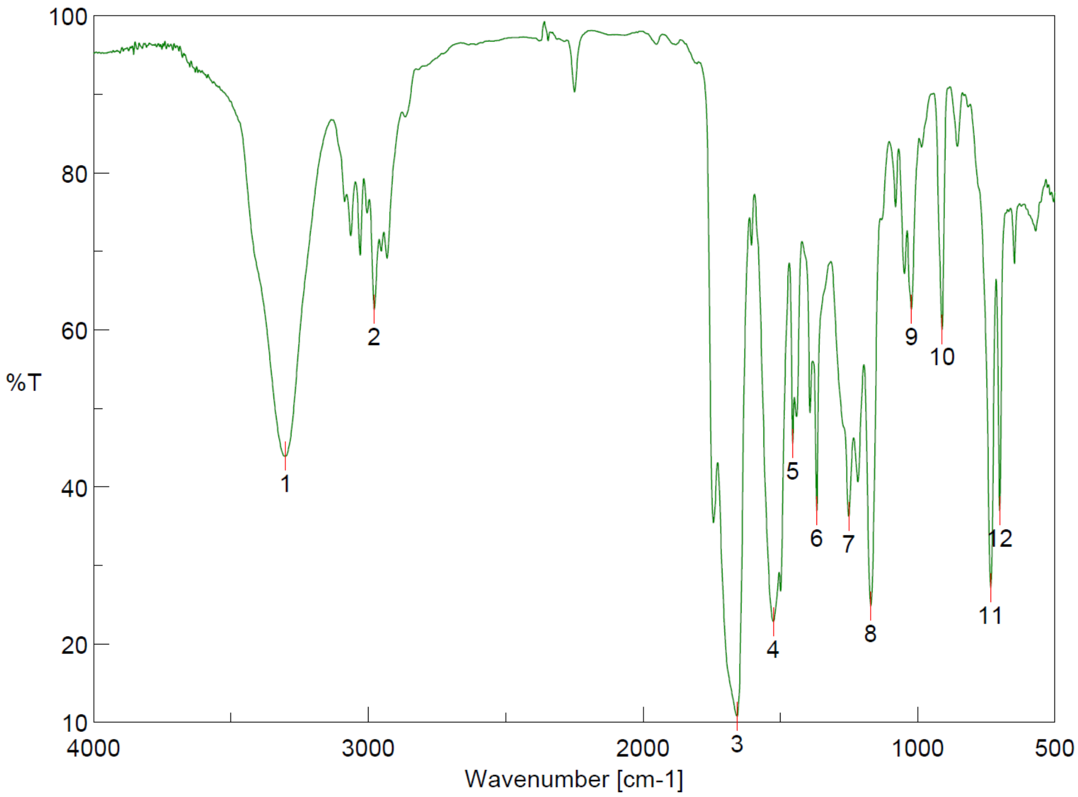


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3056.62	82.5047	2	1739.48	36.7543
3	1594.84	79.2915	4	1488.78	65.3172
5	1443.46	59.2991	6	1199.51	66.2018
7	1033.66	83.1977	8	744.388	38.0137
9	700.998	33.4192	10	621.931	81.7548

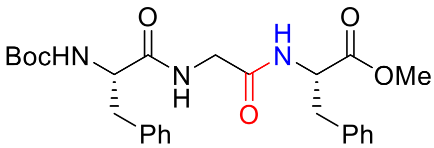


s5

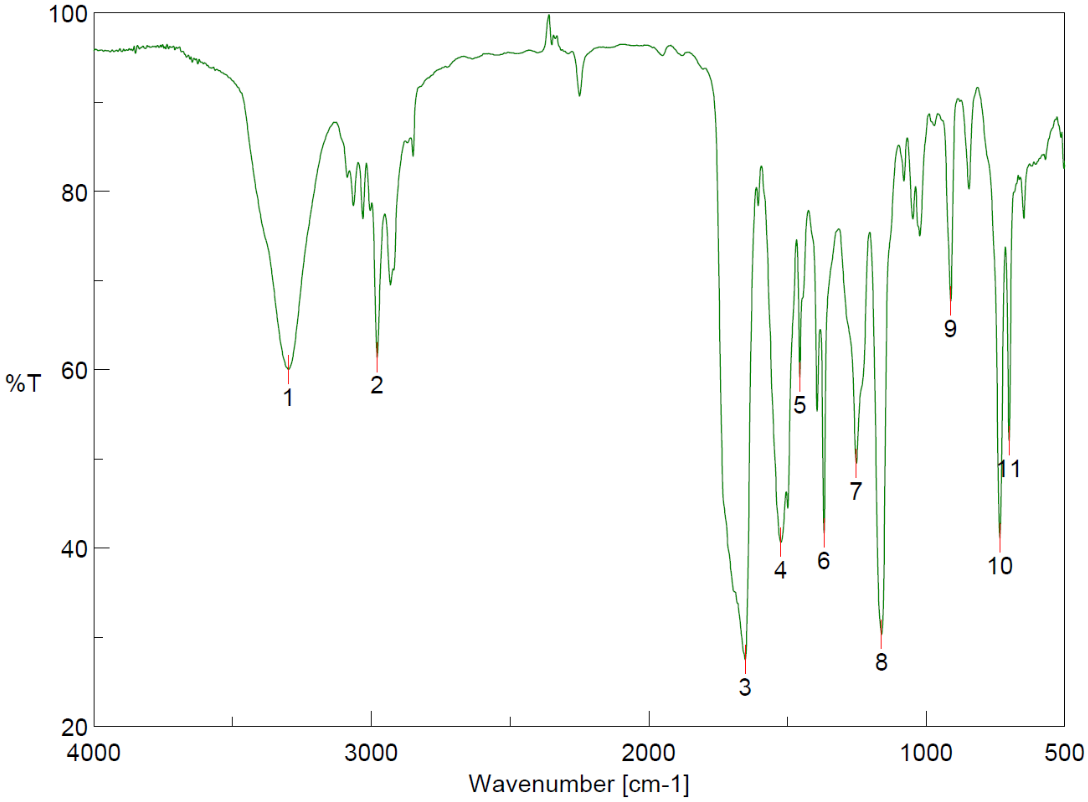


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3301.54	43.8714	2	2978.52	62.5503
3	1656.55	10.7298	4	1525.42	22.8094
5	1455.03	45.4611	6	1367.28	36.9288
7	1250.61	36.1734	8	1170.58	24.7846
9	1022.09	62.5819	10	911.201	59.9884
11	733.782	27.123	12	700.998	36.9299

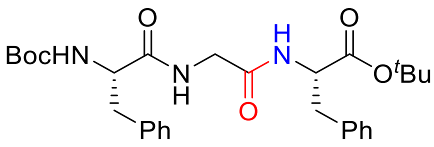


Boc-Phe-Gly-Phe-OMe (**3a**)

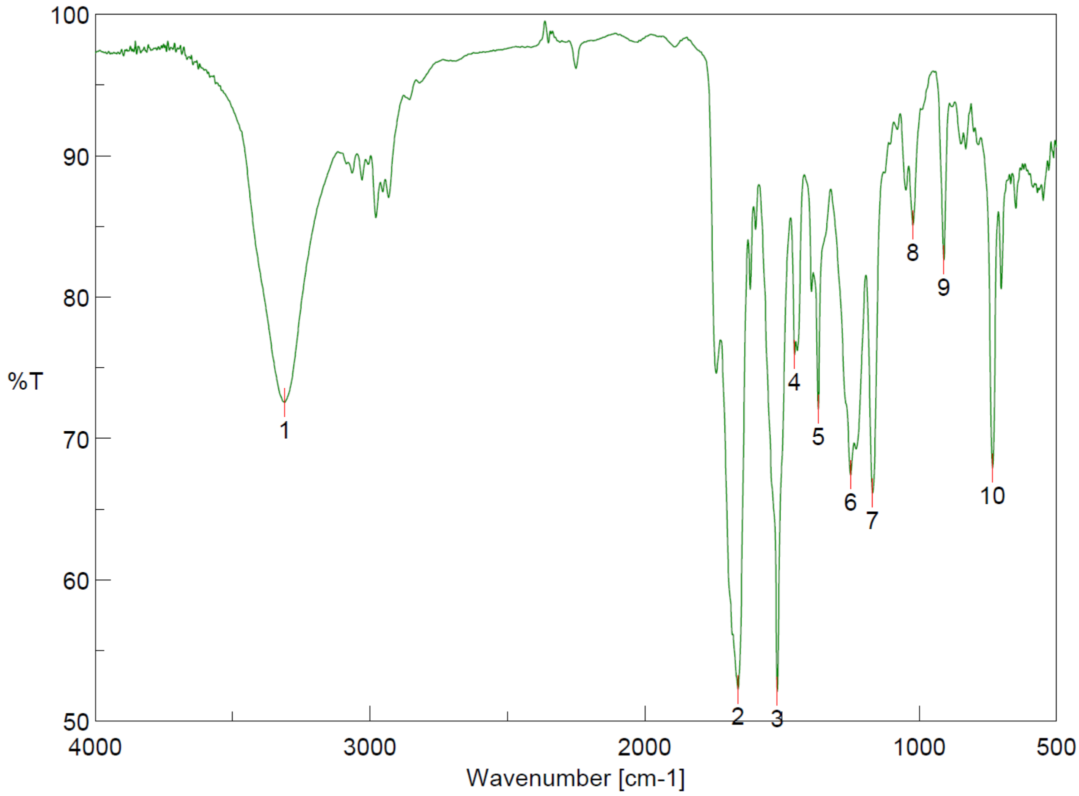


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3298.64	60.0093	2	2978.52	61.3614
3	1651.73	27.4668	4	1523.49	40.6265
5	1455.03	59.1203	6	1368.25	41.7211
7	1251.58	49.5033	8	1159.97	30.2829
9	911.201	67.674	10	733.782	41.0872
11	700.034	51.9936			

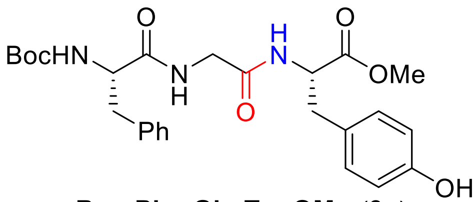


Boc-Phe-Gly-Phe-O*t*-Bu (**3b**)

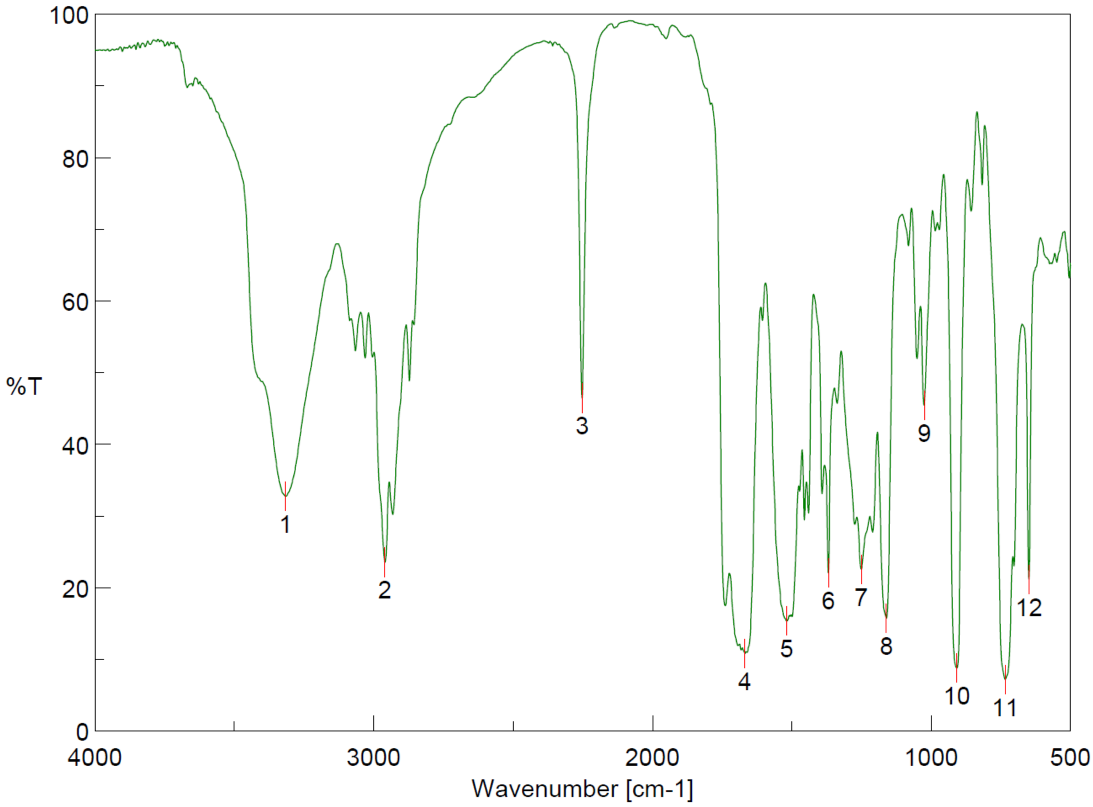


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3311.18	72.5242	2	1660.41	52.2481
3	1516.74	52.0785	4	1454.06	75.9124
5	1367.28	72.0527	6	1249.65	67.3978
7	1169.62	66.1049	8	1023.05	85.067
9	910.236	82.6095	10	732.817	67.8636

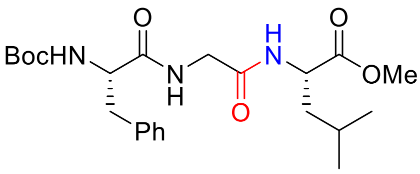


Boc-Phe-Gly-Tyr-OMe (**3c**)

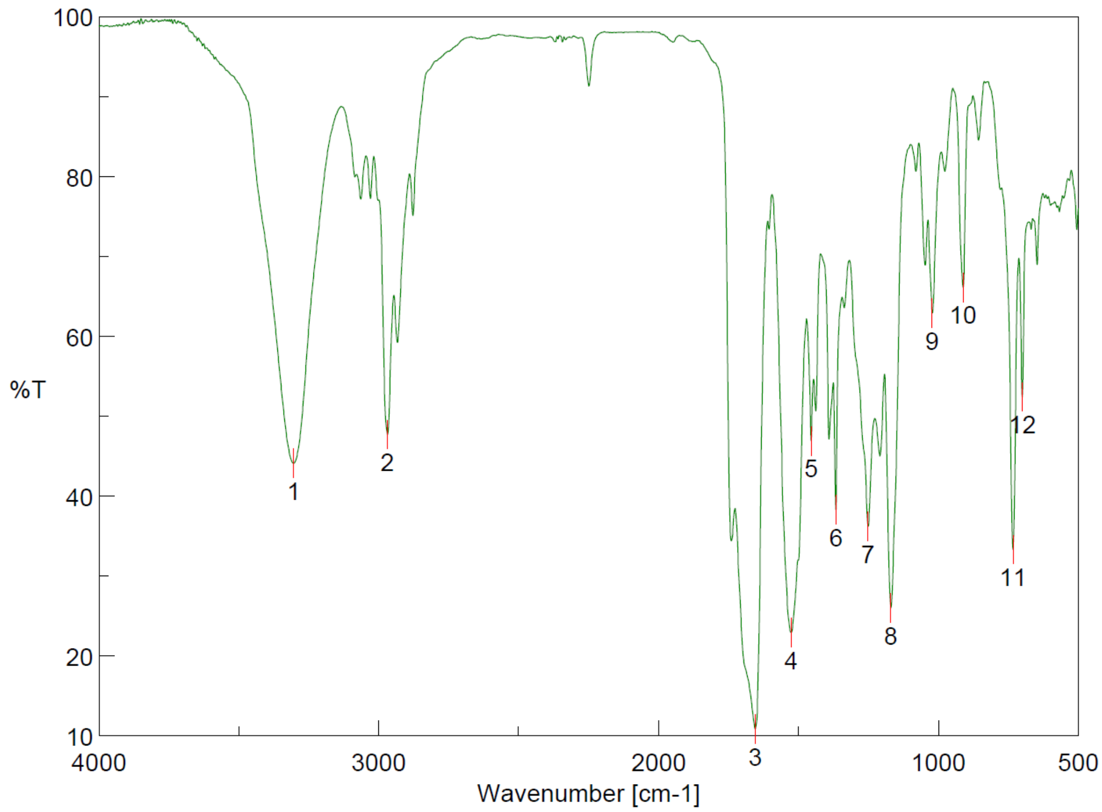


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3316	32.7416	2	2959.23	23.5087
3	2252.45	46.4209	4	1668.12	10.8064
5	1517.7	15.3303	6	1368.25	22.0287
7	1250.61	22.5466	8	1159.97	15.7076
9	1024.98	45.4259	10	907.344	8.72998
11	733.782	7.17211	12	648.929	21.1374

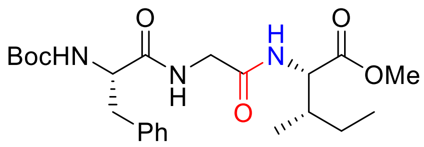


Boc-Phe-Gly-Leu-OMe (3d)

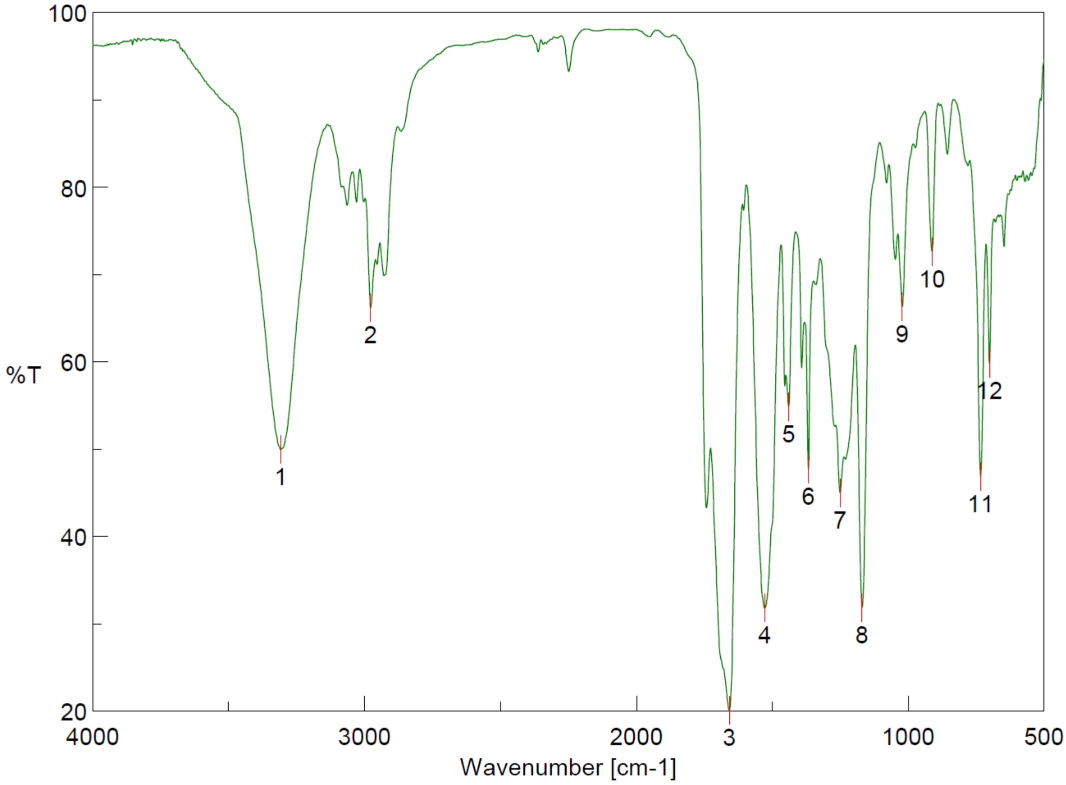


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3304.43	44.096	2	2968.87	47.6925
3	1654.62	10.8463	4	1526.38	22.9138
5	1455.03	46.8776	6	1366.32	38.3292
7	1251.58	36.1985	8	1169.62	26.0006
9	1022.09	62.8908	10	912.165	66.1071
11	733.782	33.304	12	700.034	52.4097

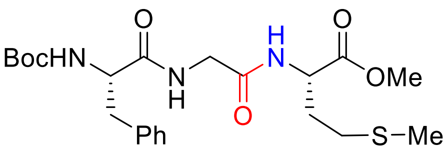


Boc-Phe-Gly-Ile-OMe (3e)

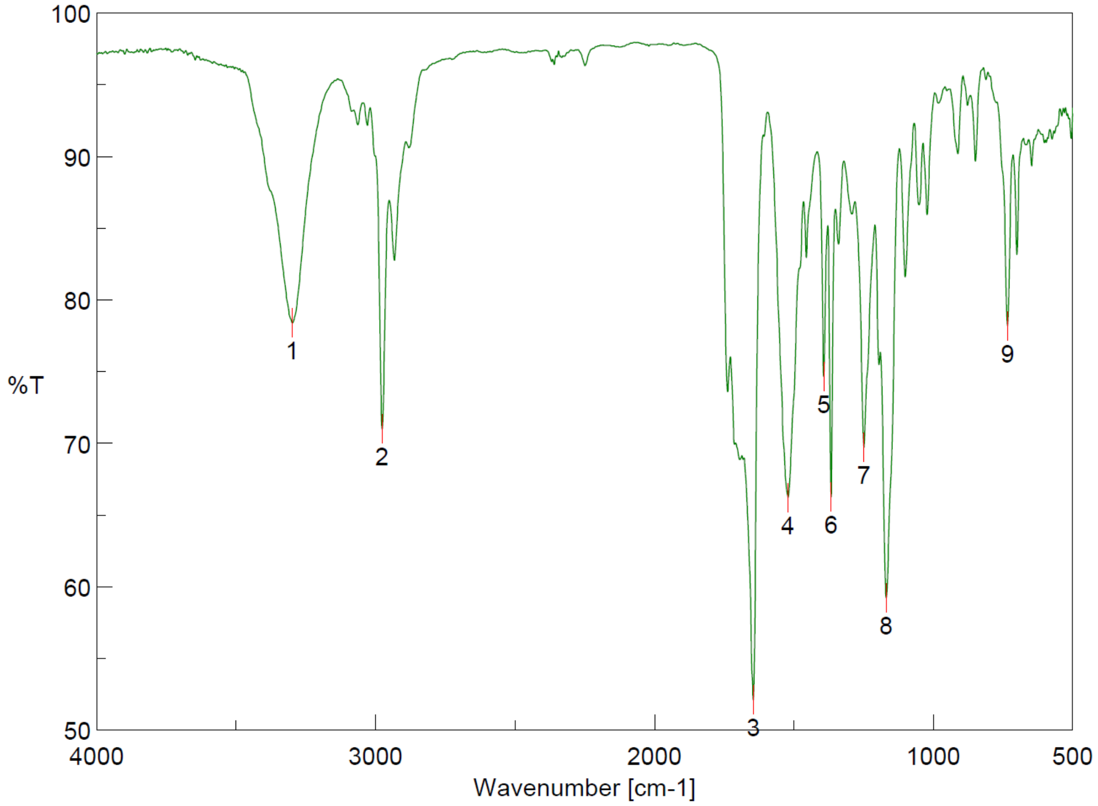


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3308.29	49.9198	2	2977.55	66.1941
3	1658.48	20.1148	4	1527.35	31.7812
5	1439.6	54.863	6	1367.28	47.6799
7	1250.61	44.9626	8	1169.62	31.8551
9	1022.09	66.2899	10	912.165	72.6073
11	732.817	46.8598	12	700.998	59.8015

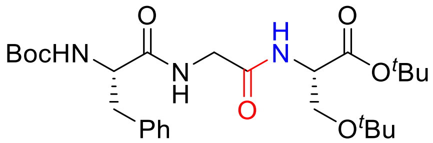


Boc-Phe-Gly-Met-OMe (3f)

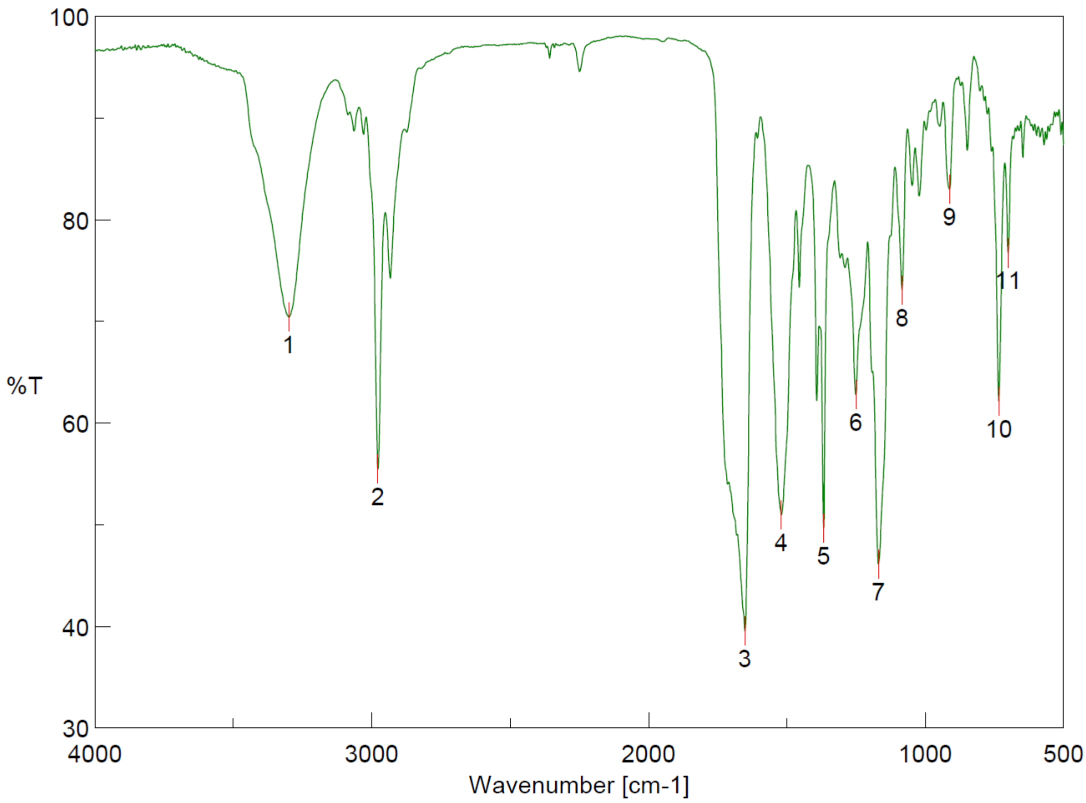


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3298.64	78.3825	2	2976.59	70.9697
3	1644.98	52.0729	4	1520.6	66.2115
5	1392.35	74.6342	6	1366.32	66.2503
7	1248.68	69.7086	8	1168.65	59.2233
9	733.782	78.1645			

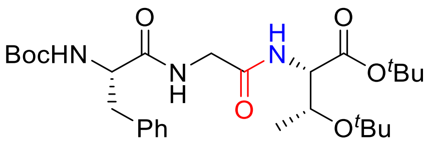


Boc-Phe-Gly-Ser(O*t*-Bu)-O*t*-Bu (3g)

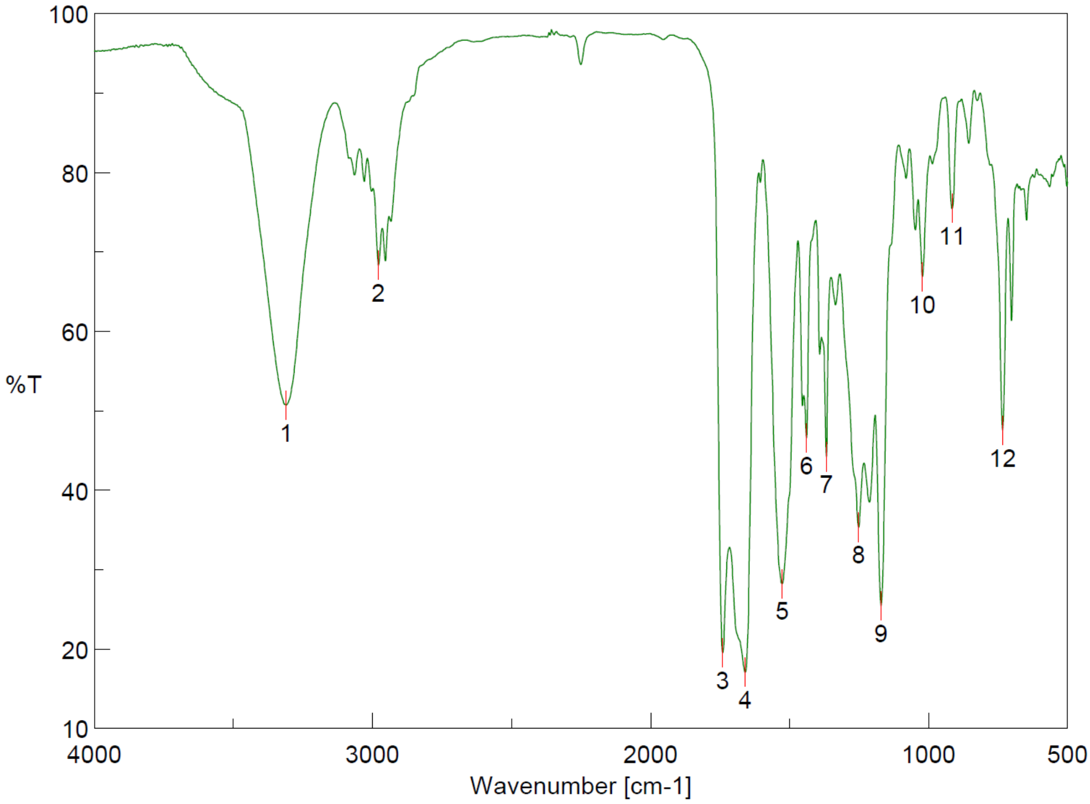


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3299.61	70.391	2	2977.55	55.4201
3	1651.73	39.4972	4	1519.63	50.9488
5	1367.28	49.6368	6	1250.61	62.7666
7	1168.65	46.111	8	1083.8	73.0417
9	912.165	82.9818	10	733.782	62.0768
11	700.034	76.708			

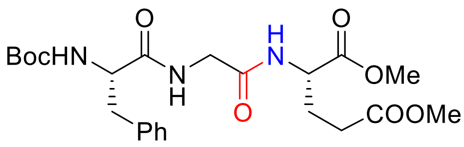


Boc-Phe-Gly-Thr(O*t*-Bu)-O*t*-Bu (3h)

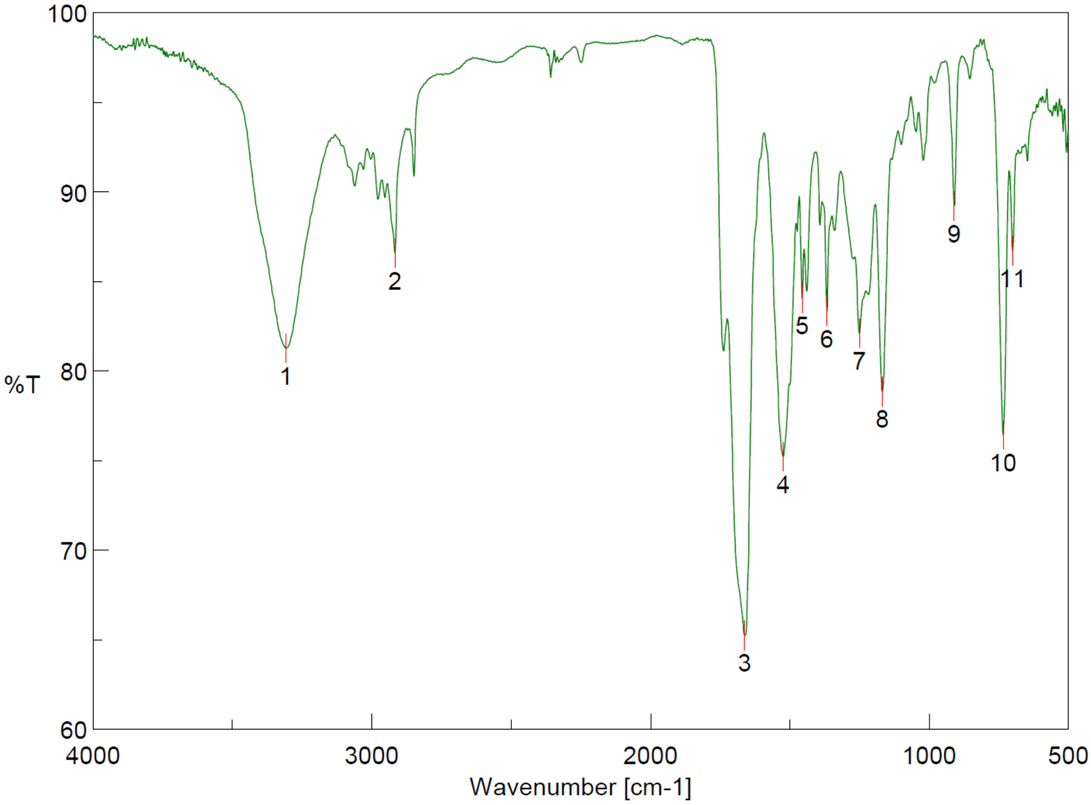


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3310.21	50.6815	2	2978.52	68.2958
3	1740.44	19.4793	4	1659.45	17.035
5	1526.38	28.1887	6	1438.64	46.5453
7	1367.28	44.1716	8	1251.58	35.2838
9	1170.58	25.4031	10	1022.09	66.8709
11	915.058	75.4201	12	733.782	47.5129

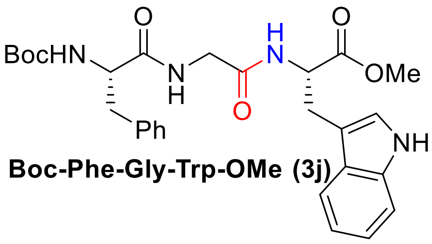


Boc-Phe-Gly-Glu(OMe)-OMe (3i)

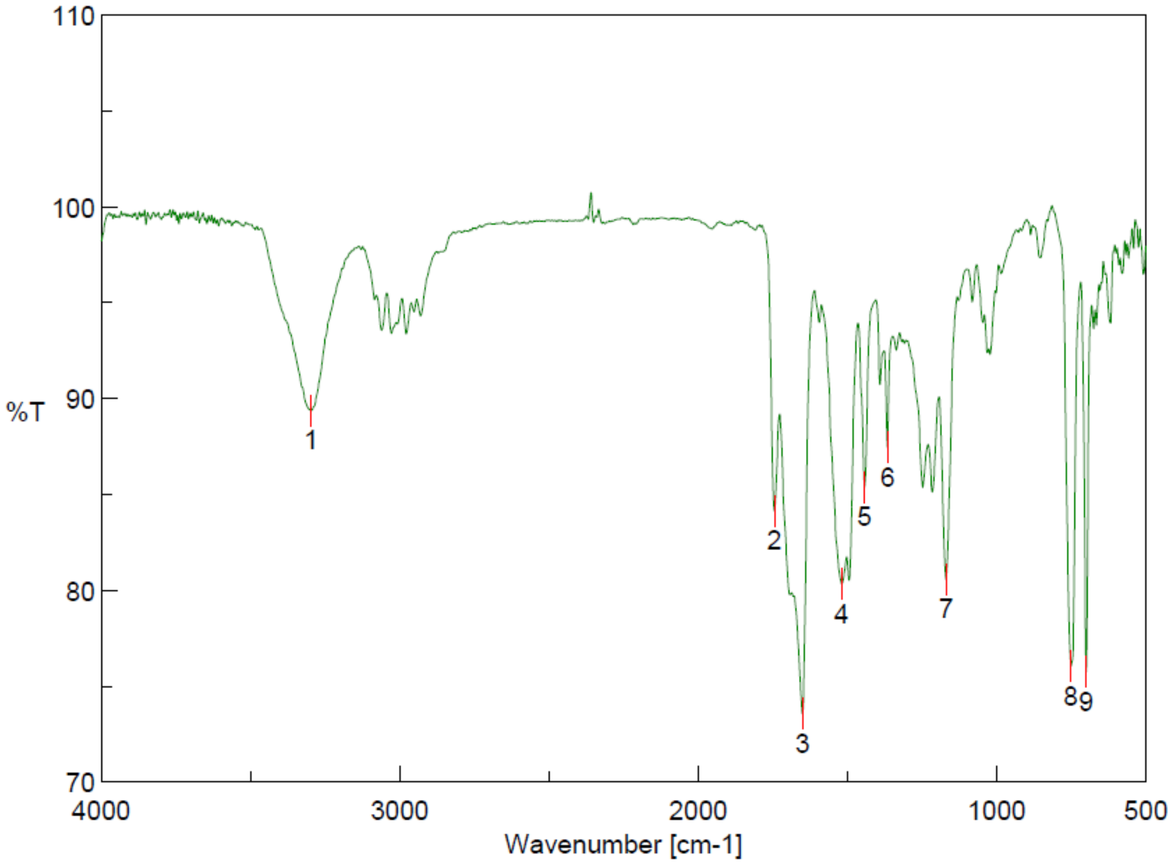


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3308.29	81.275	2	2916.81	86.59
3	1662.34	65.2255	4	1523.49	75.2082
5	1455.99	84.0545	6	1367.28	83.3322
7	1250.61	82.0954	8	1167.69	78.8467
9	910.236	89.2091	10	734.746	76.4169
11	700.034	86.6986			

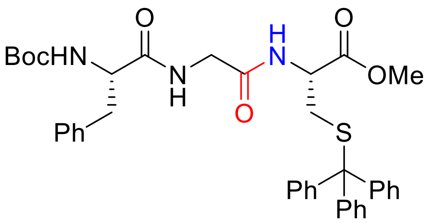


Boc-Phe-Gly-Trp-OMe (3j)

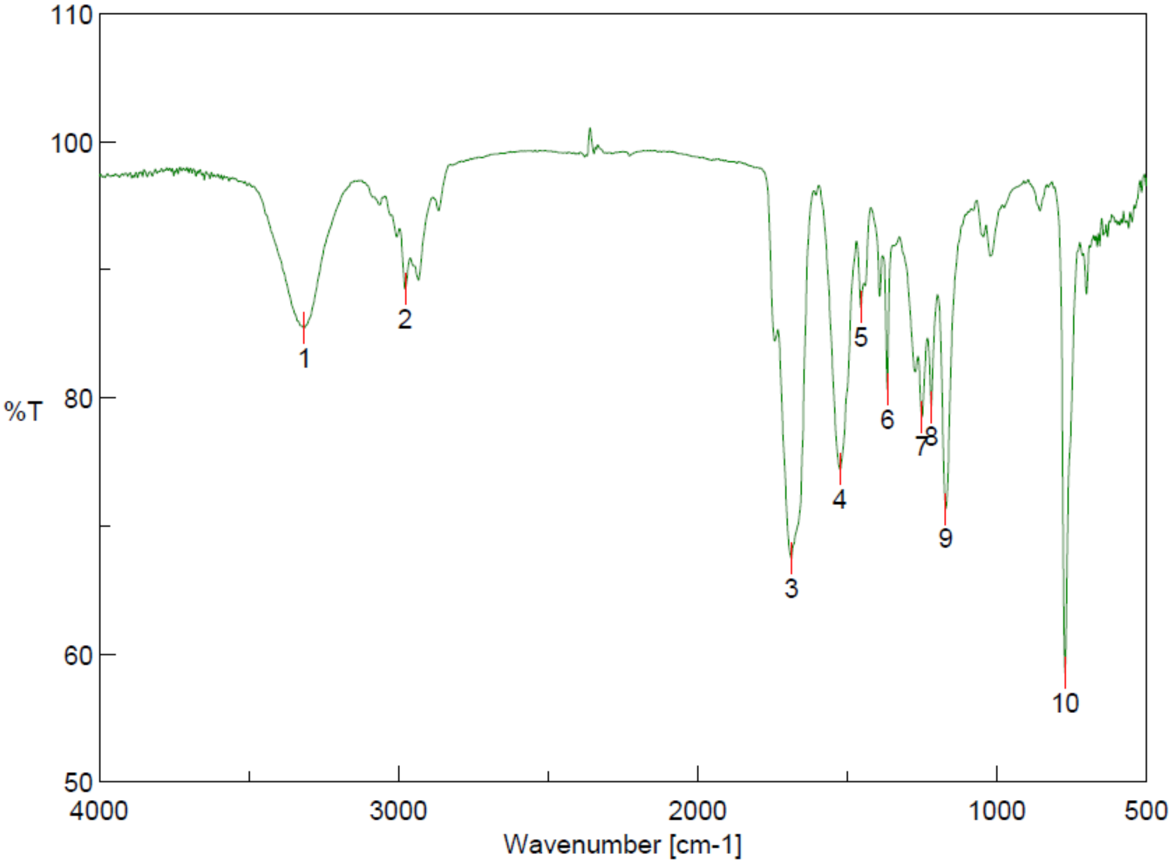


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3297.68	89.366	2	1745.26	84.1273
3	1650.77	73.5398	4	1518.67	80.331
5	1442.49	85.3644	6	1366.32	87.4338
7	1169.62	80.5739	8	751.138	76.033
9	700.034	75.7426			

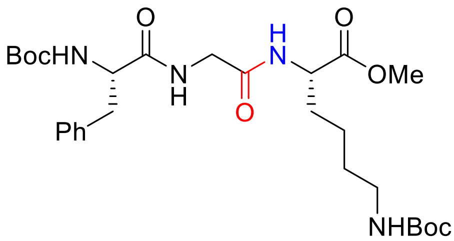


Boc-Phe-Gly-Cys(STr)-OMe (3k)

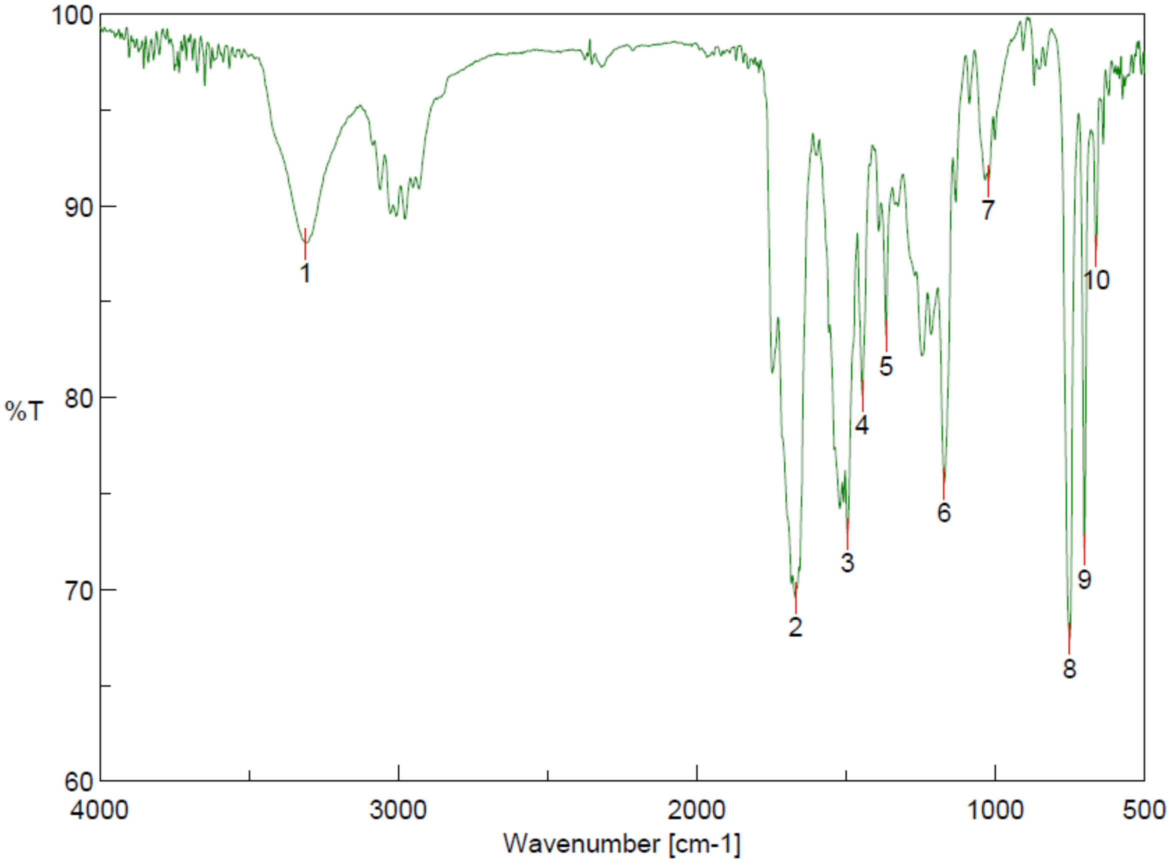


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3315.03	85.4422	2	2977.55	88.4715
3	1687.41	67.4625	4	1524.45	74.3915
5	1455.03	87.0301	6	1366.32	80.6165
7	1250.61	78.4828	8	1219.76	79.2566
9	1170.58	71.3235	10	772.351	58.5079

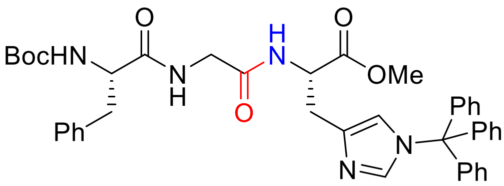


Boc-Phe-Gly-Lys(NHBoc)-OMe (3l)

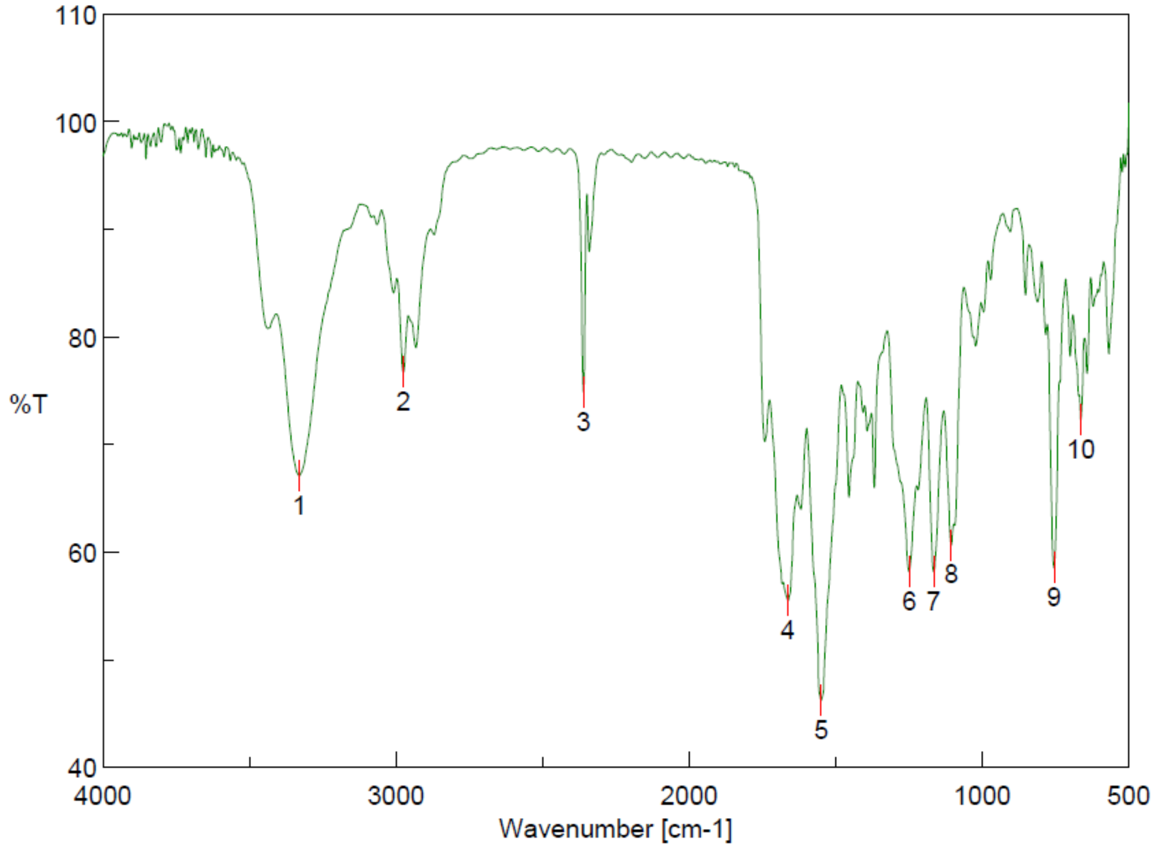


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3312.14	88.0061	2	1670.05	69.561
3	1495.53	72.8783	4	1445.39	80.0703
5	1366.32	83.1778	6	1170.58	75.5172
7	1022.09	91.2757	8	750.174	67.4112
9	700.998	72.0437	10	662.428	87.6546

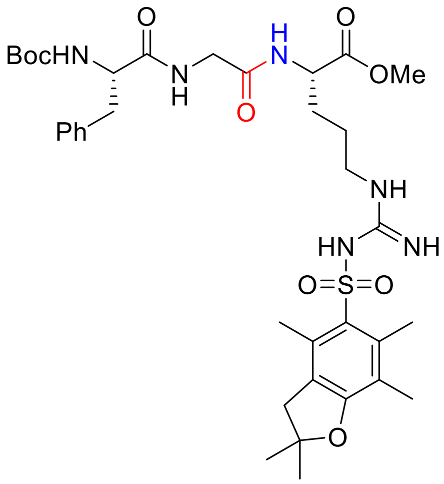


Boc-Phe-Gly-His(NTr)-OMe (3m)

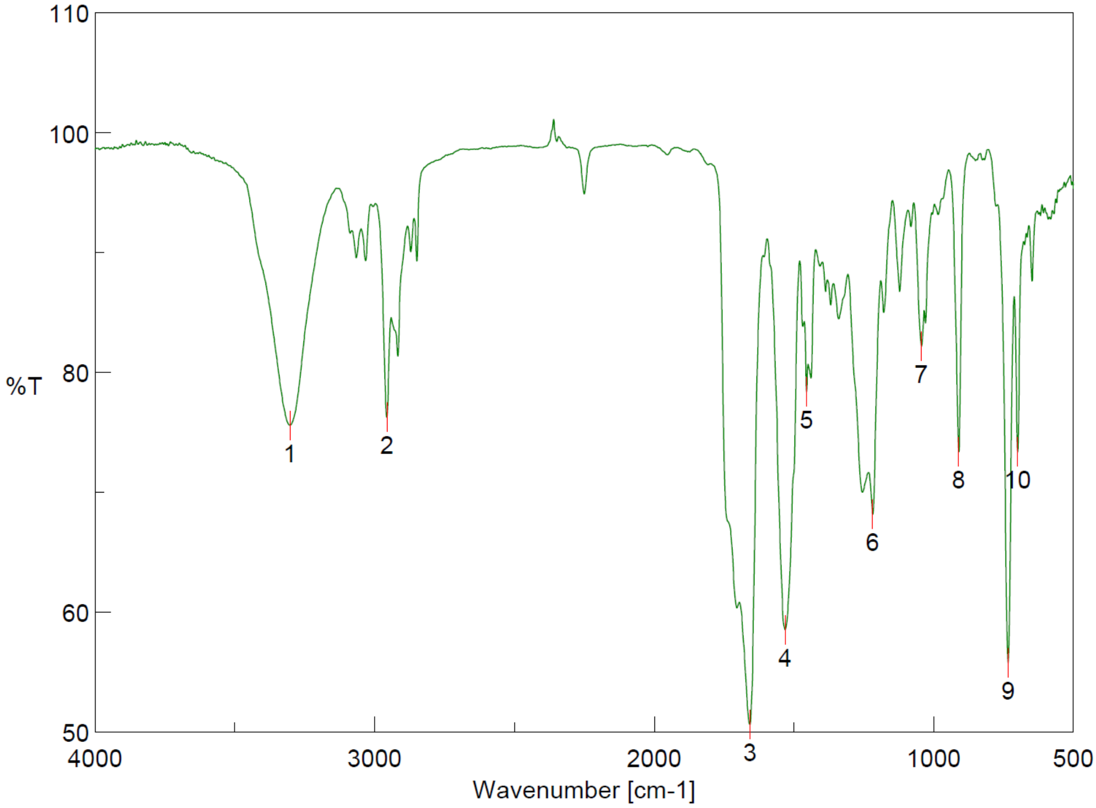


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3330.46	67.0803	2	2975.62	76.6946
3	2360.44	74.8292	4	1662.34	55.4888
5	1550.49	46.2182	6	1249.65	58.1851
7	1165.76	58.1771	8	1105.98	60.6509
9	754.995	58.5308	10	663.393	72.2808

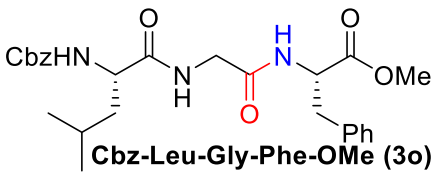


Boc-Phe-Gly-Arg(Pbf)-OMe (3n)

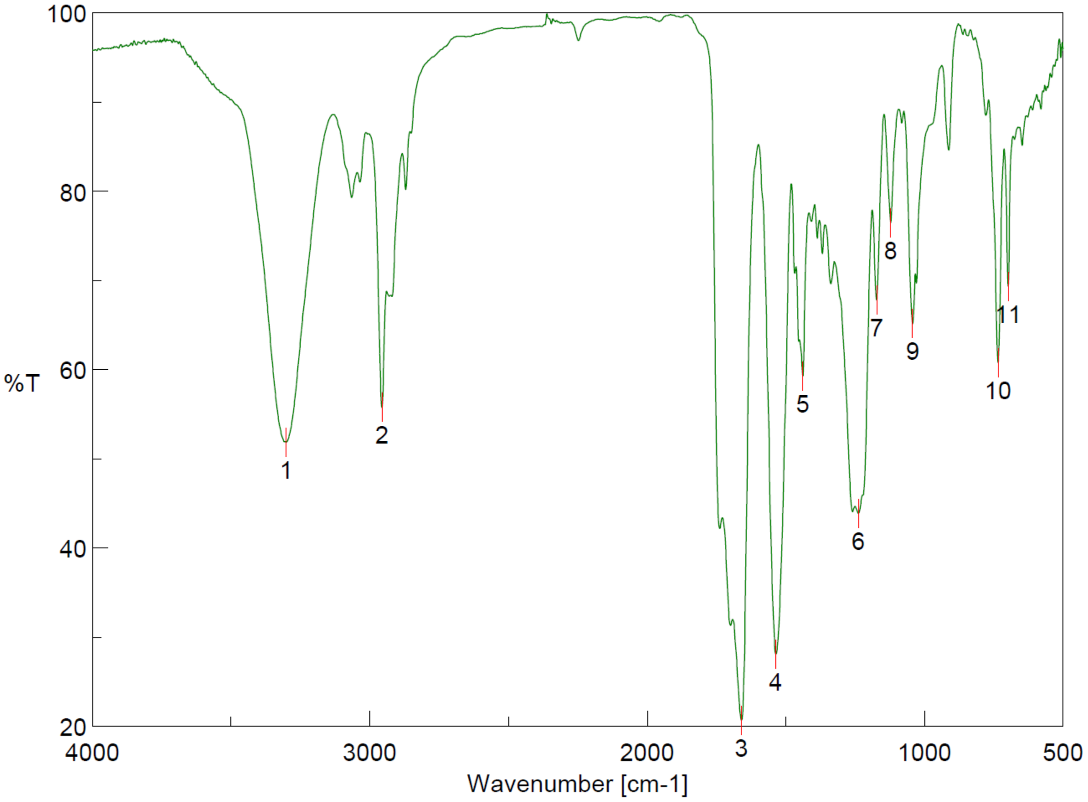


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3303.46	75.58	2	2956.34	76.2501
3	1657.52	50.6284	4	1531.2	58.5182
5	1455.03	78.3637	6	1217.83	68.1593
7	1043.3	82.1589	8	910.236	73.3698
9	732.817	55.7579	10	699.069	73.3381

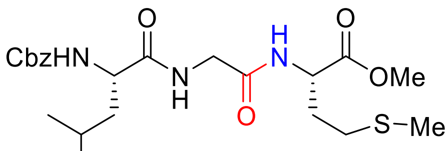


Cbz-Leu-Gly-Phe-OMe (3o)

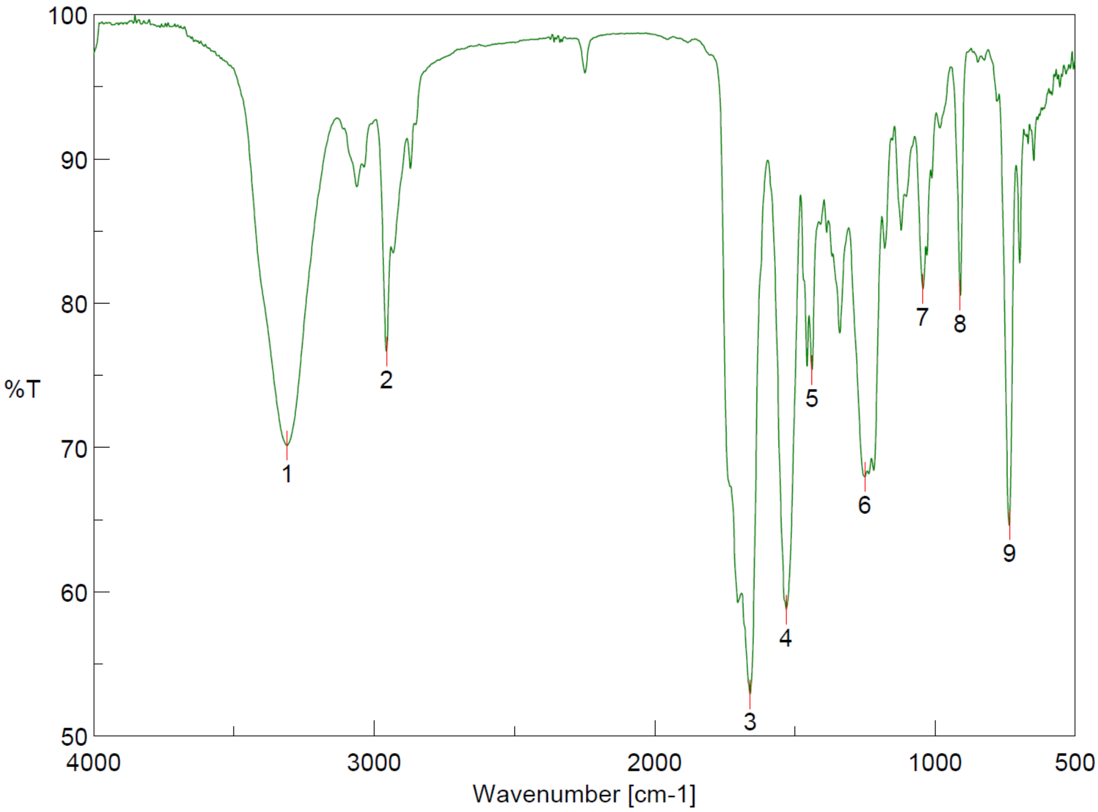


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3301.54	51.839	2	2956.34	55.7298
3	1660.41	20.6665	4	1536.02	28.0911
5	1438.64	59.25	6	1238.08	43.841
7	1172.51	67.7781	8	1121.4	76.4294
9	1042.34	65.1036	10	734.746	60.7577
11	698.105	69.3008			

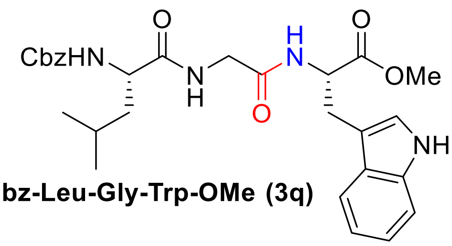


Cbz-Leu-Gly-Met-OMe (3p)

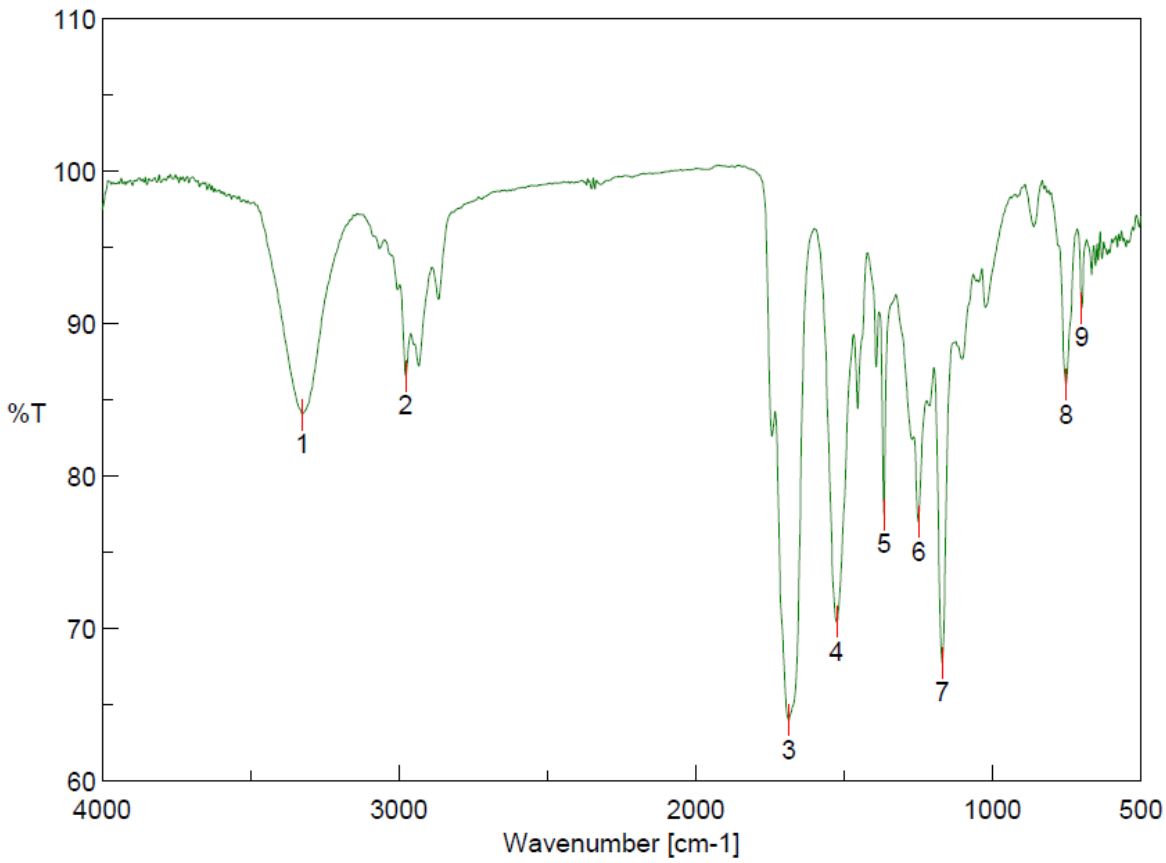


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3311.18	70.1075	2	2956.34	76.6451
3	1659.45	52.9004	4	1530.24	58.7539
5	1438.64	75.3581	6	1250.61	67.9598
7	1043.3	80.9608	8	910.236	80.5249
9	734.746	64.5908			

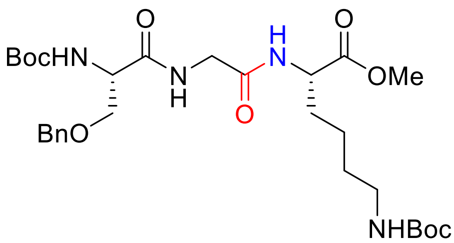


Cbz-Leu-Gly-Trp-OMe (3q)

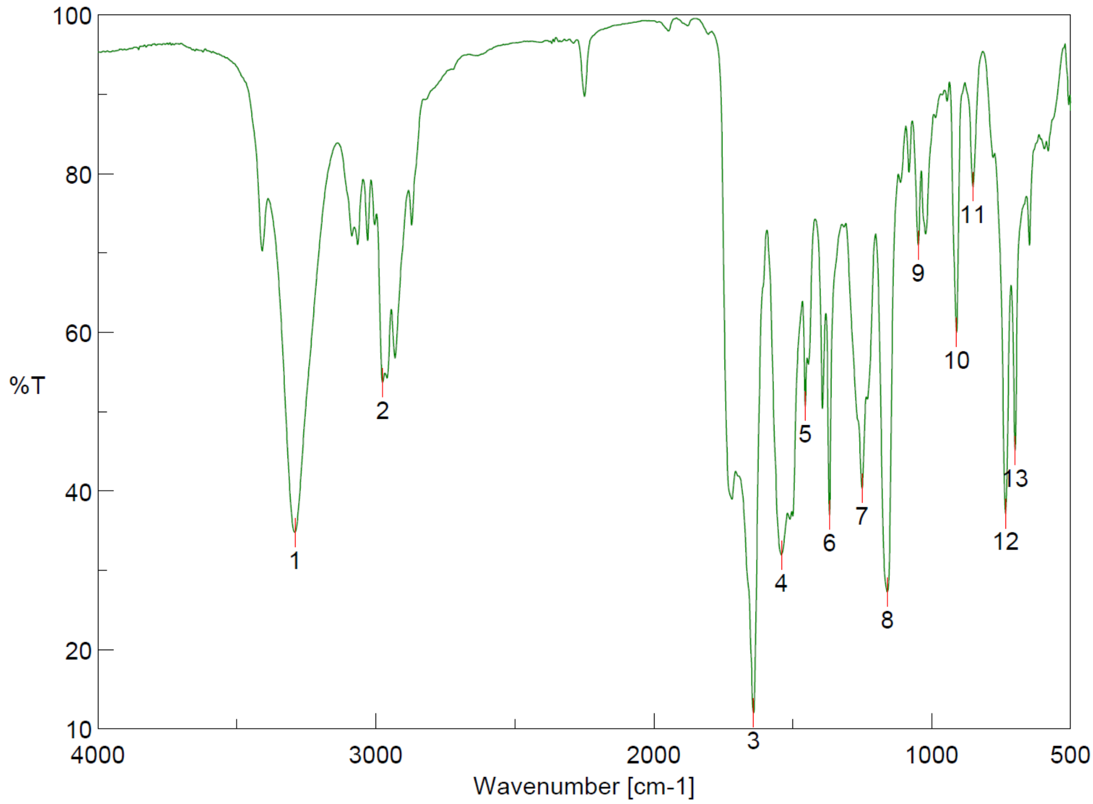


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3325.64	84.0348	2	2977.55	86.5813
3	1686.44	63.9845	4	1525.42	70.4228
5	1366.32	77.4767	6	1249.65	77.0054
7	1169.62	67.79	8	752.102	85.958
9	699.069	91.0233			

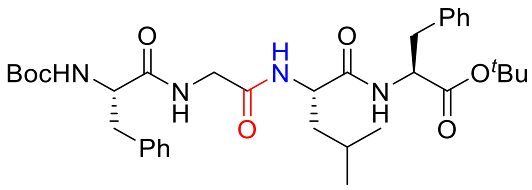


Boc-Ser(OBn)-Gly-Lys(NHBoc)-OMe (3r)

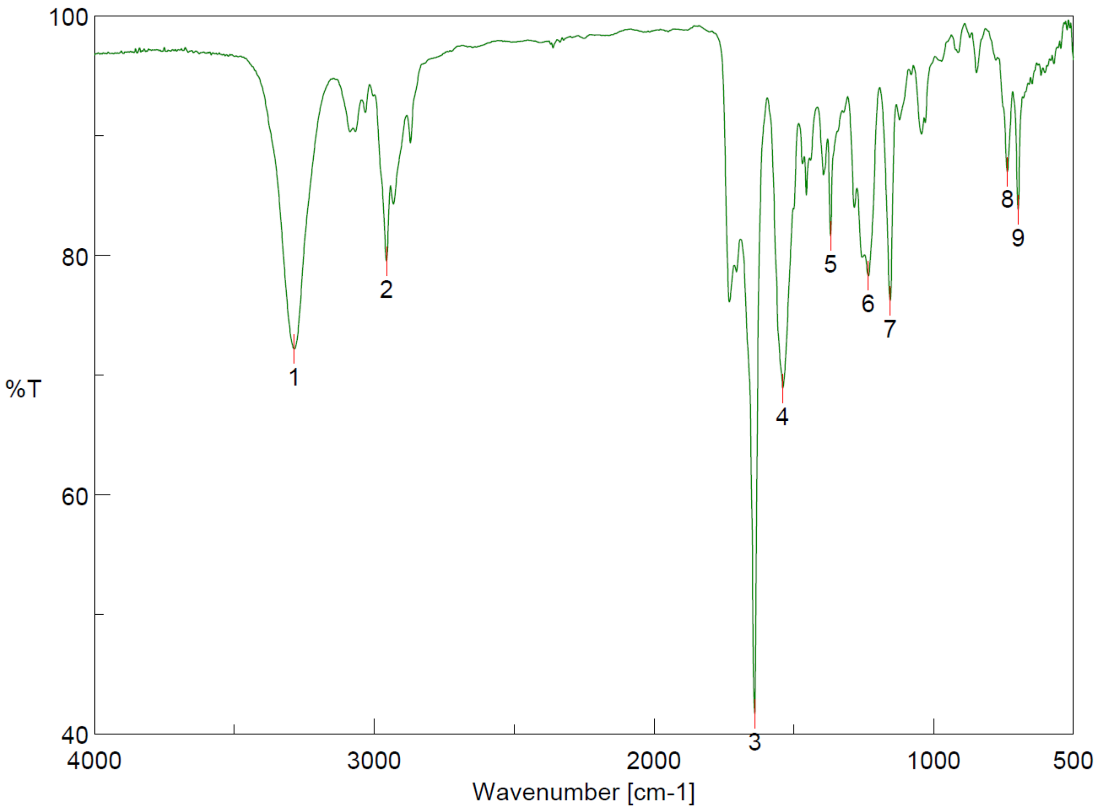


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3291.89	34.7281	2	2975.62	53.6266
3	1641.13	11.9959	4	1540.85	31.8723
5	1455.03	50.6314	6	1367.28	36.9033
7	1250.61	40.3131	8	1159.01	27.2415
9	1048.12	70.9378	10	910.236	59.9538
11	851.418	78.3084	12	733.782	37.0725
13	699.069	45.1068			

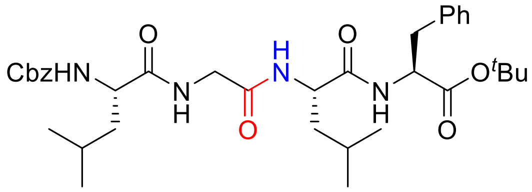


Boc-Phe-Gly-Leu-Phe-O*t*-Bu (3s)

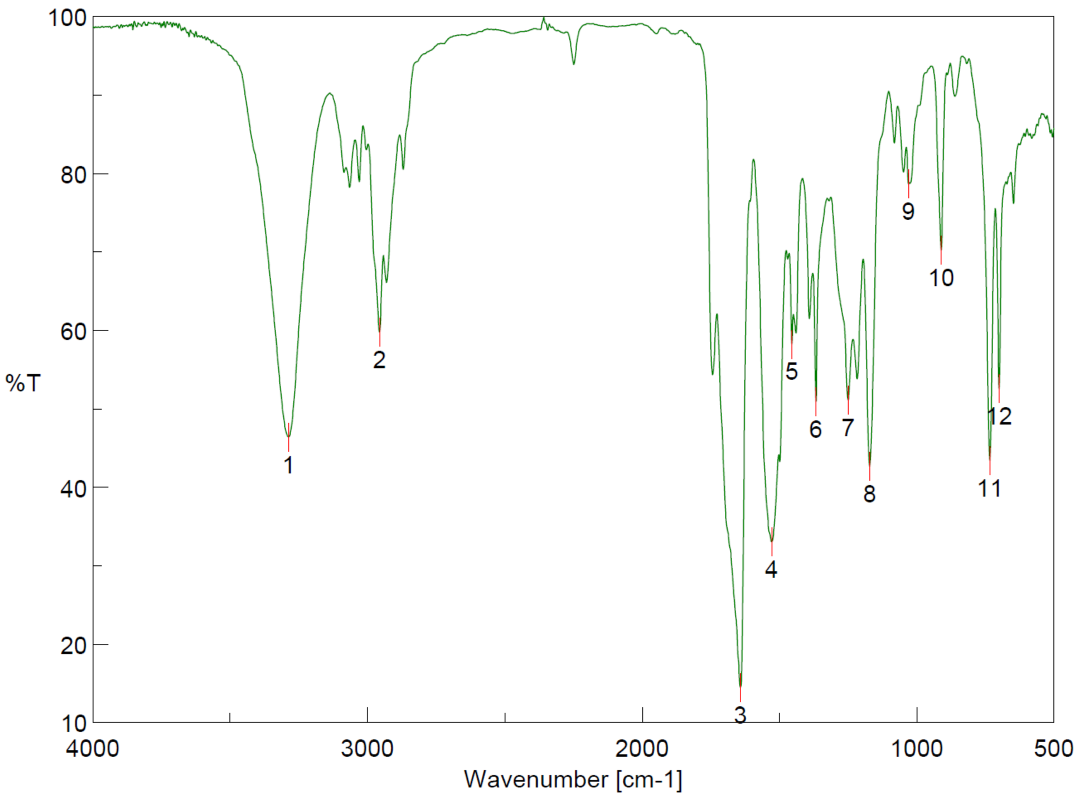


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3286.11	72.1915	2	2956.34	79.5364
3	1639.2	41.6939	4	1538.92	68.8885
5	1368.25	81.6261	6	1233.25	78.2821
7	1155.15	76.1955	8	735.71	86.9833
9	697.141	83.8246			

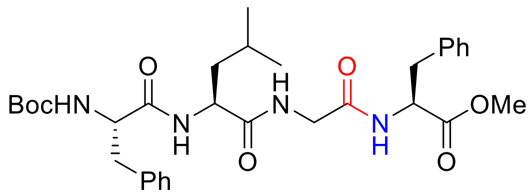


Cbz-Leu-Gly-Leu-Phe-O*t*-Bu (3t)

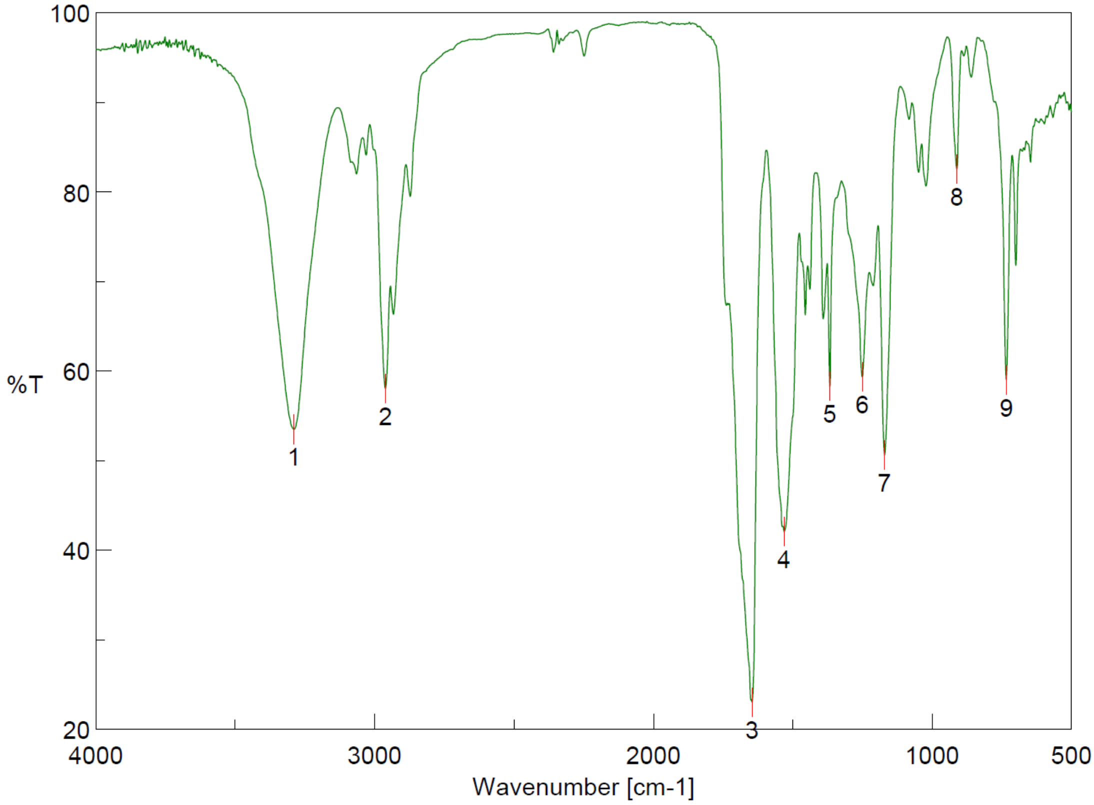


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3287.07	46.3847	2	2956.34	59.7417
3	1642.09	14.4701	4	1528.31	33.0283
5	1455.03	58.1901	6	1367.28	50.9039
7	1249.65	51.0945	8	1171.54	42.625
9	1029.8	78.6058	10	911.201	70.1885
11	733.782	43.3694	12	700.034	52.4965

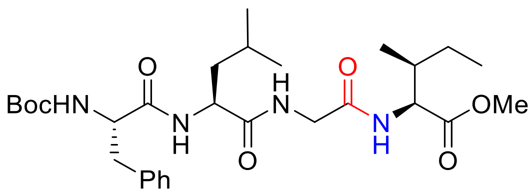


Boc-Phe-Leu-Gly-Phe-OMe (3u)

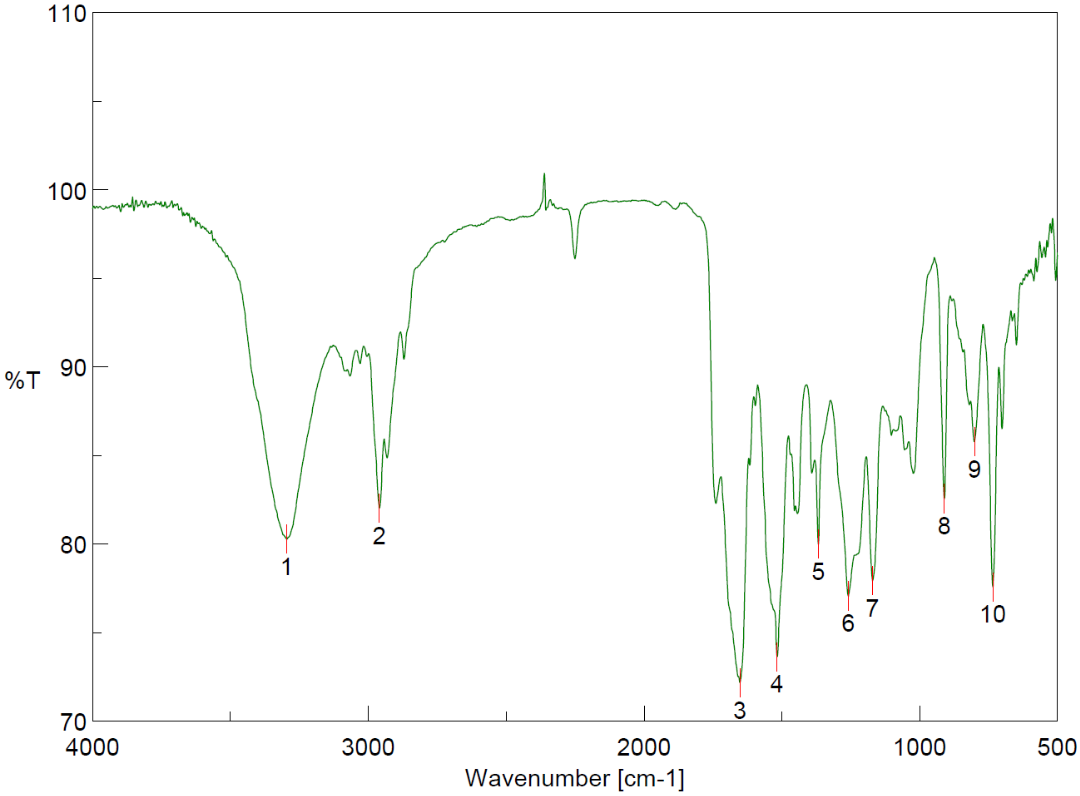


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3289	53.4656	2	2961.16	57.9913
3	1645.95	23.0177	4	1530.24	42.0124
5	1367.28	58.253	6	1250.61	59.3112
7	1170.58	50.5711	8	911.201	82.532
9	733.782	58.9794			

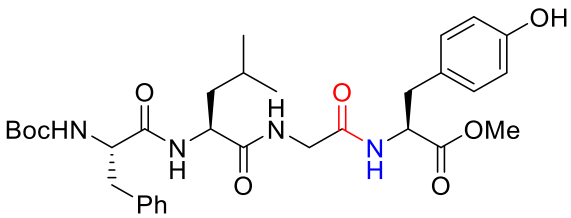


Boc-Phe-Leu-Gly-Ile-OMe (3v)

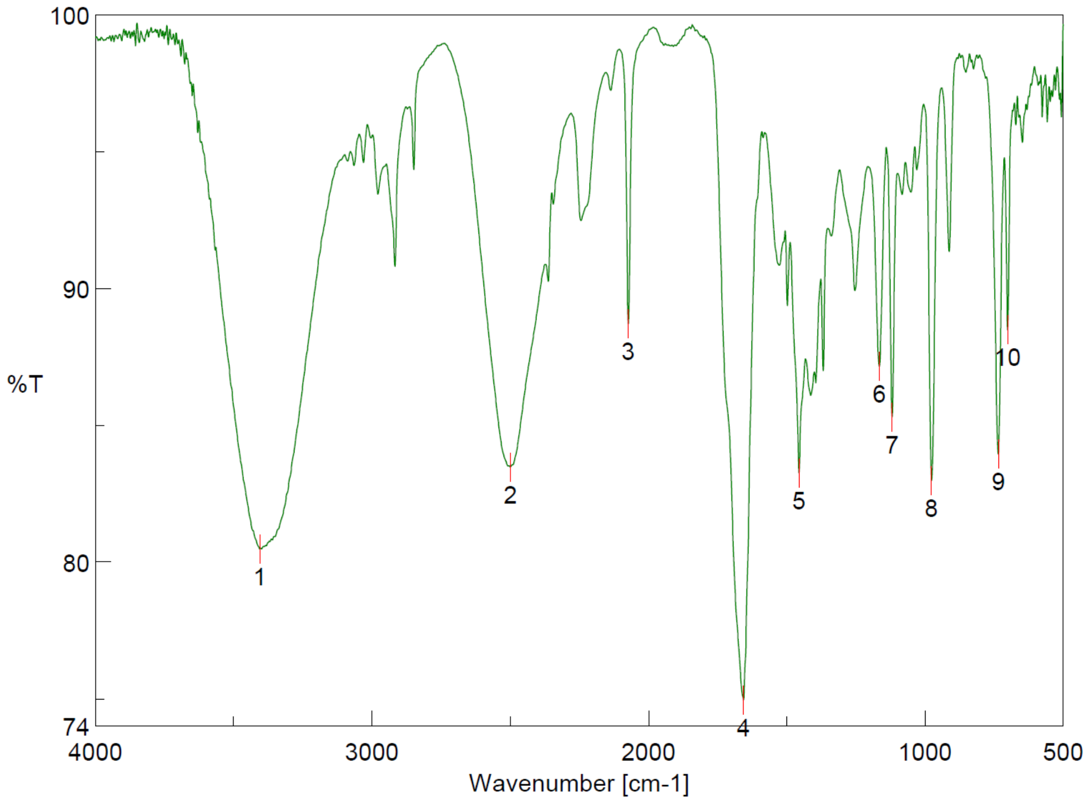


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3295.75	80.2578	2	2959.23	82.0158
3	1651.73	72.164	4	1516.74	73.6263
5	1367.28	79.9733	6	1259.29	77.0601
7	1170.58	77.913	8	910.236	82.543
9	801.278	85.7612	10	734.746	77.5714

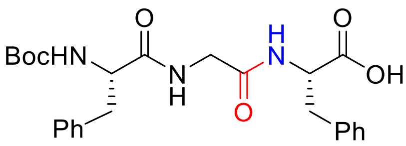


Boc-Phe-Leu-Gly-Tyr-OMe (3w)

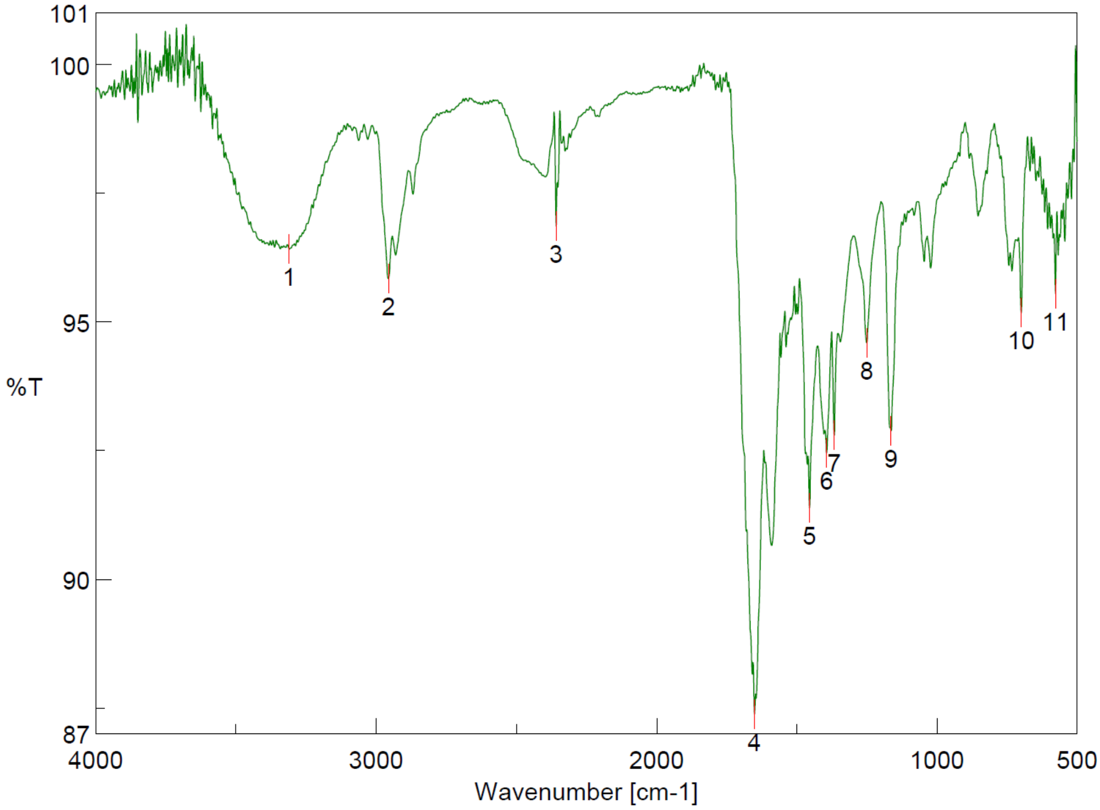


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3405.67	80.4743	2	2499.29	83.4713
3	2073.1	88.7074	4	1655.59	74.948
5	1455.99	83.2477	6	1164.79	87.1448
7	1118.51	85.2991	8	975.804	82.9677
9	734.746	83.9333	10	700.998	88.4719

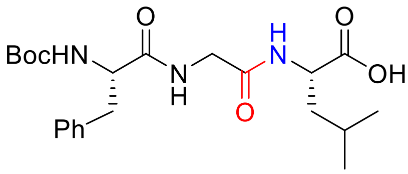


Boc-Phe-Gly-Phe-OH (3x)

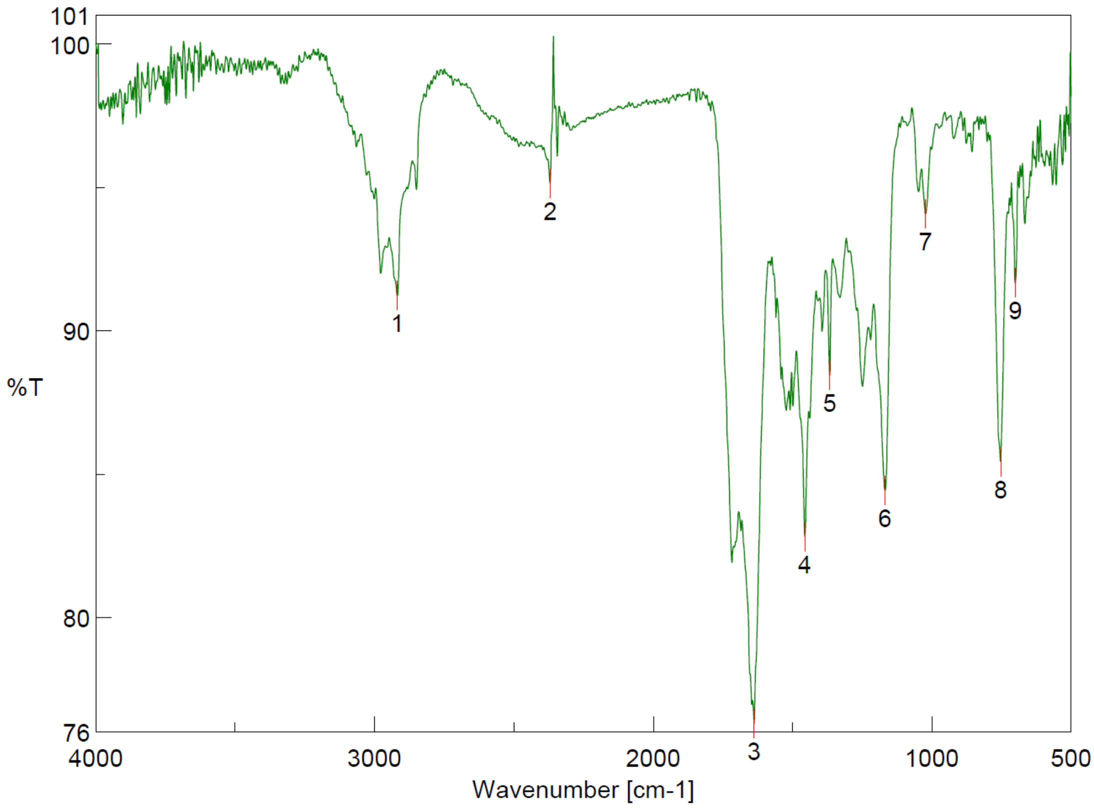


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3310.21	96.4073	2	2956.34	95.8378
3	2358.52	96.8568	4	1650.77	87.3806
5	1455.03	91.3791	6	1393.32	92.4463
7	1366.32	92.7953	8	1250.61	94.5888
9	1163.83	92.8854	10	699.069	95.1729
11	577.576	95.5465			

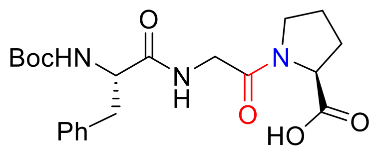


Boc-Phe-Gly-Leu-OH (3y)

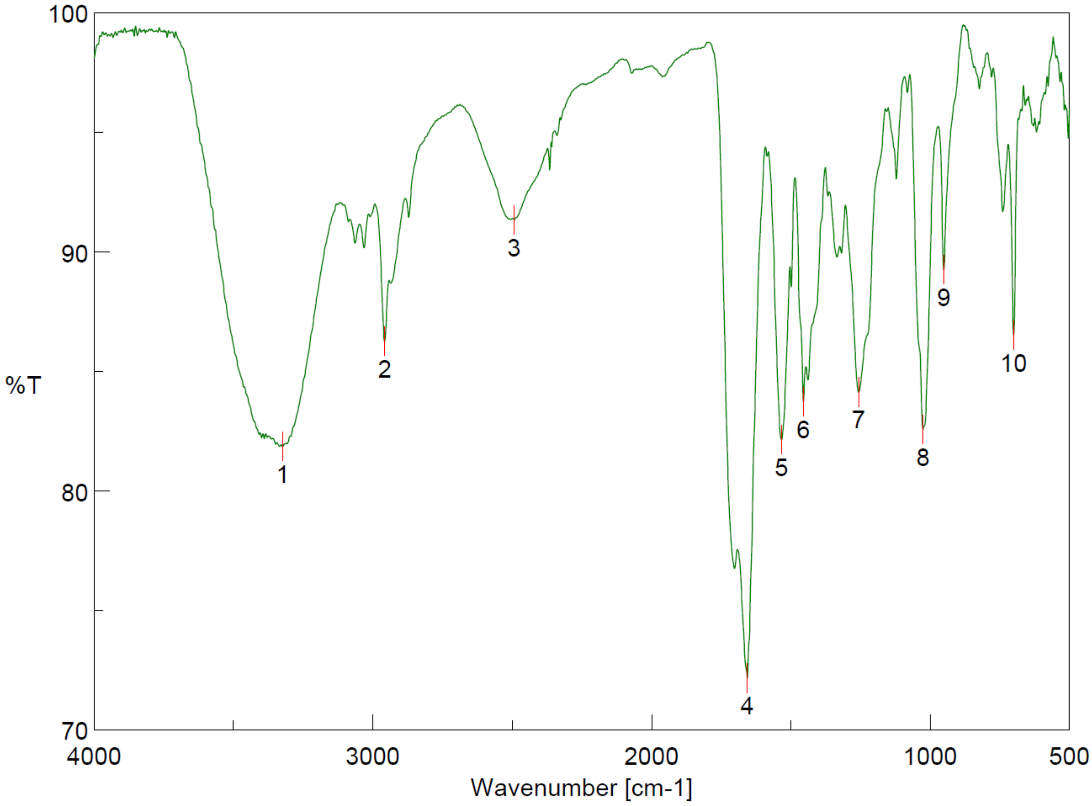


[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	2917.77	91.2052	2	2370.09	95.1349
3	1637.27	76.2818	4	1455.99	82.8108
5	1366.32	88.4422	6	1167.69	84.4209
7	1022.09	94.0591	8	753.066	85.421
9	700.034	91.6616			

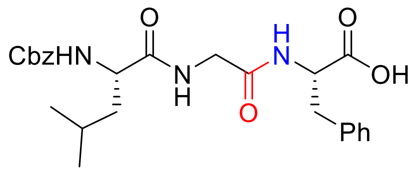


Boc-Phe-Gly-Pro-OH (3z)



[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	3323.71	81.8571	2	2957.3	86.2596
3	2492.54	91.3369	4	1655.59	72.1555
5	1533.13	82.1429	6	1455.03	83.7237
7	1256.4	84.1271	8	1025.94	82.5779
9	950.734	89.2438	10	700.034	86.5



Cbz-Leu-Gly-Phe-OH (3aa)