Electronic Supplementary Material (ESI) for ChemComm.


# Site-specific Indolation of Proline-based Peptides via Copper(II)-Catalyzed oxidative coupling of tertiary amine N-oxides

Xiaowei Wu, ‡ Dengyou Zhang, ‡ Shengbin Zhou, Feng Gao, Hong Liu*

CAS Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zuchongzhi Road, Shanghai 201203, P. R. China.

E-mail: hliu@mail.shcnc.ac.cn

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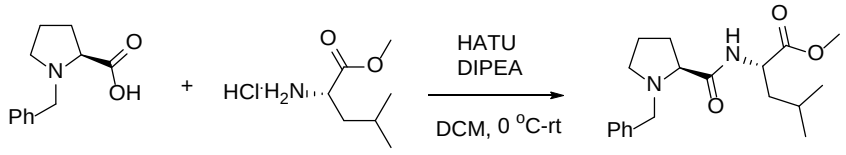
## (A) General Methods

The reagents (chemicals) were purchased from commercial sources, and used without further purification. Analytical thin layer chromatography (TLC) was HSGF 254 (0.15-0.2 mm thickness). Preparative thin layer chromatography (PTLC) was HSGF 254 (0.4-0.5 mm thickness). All products were characterized by their NMR and MS spectra. $^{1}H$ and $^{13}C$ NMR spectra were recorded on a 400 MHz, 500 MHz or 600 MHz instrument. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), doublet of doublets (dd) and broad (br). High-resolution mass spectra (HRMS) were measured on Micromass Ultra Q-TOF spectrometer. The determination of dr was performed via LC/MS analysis using Agilent 6120 spectrometer. Optical rotations were measured using a 1 mL cell with a 10 mm path length on an Auto pol V PLVS matic polarimeter and are reported as follows: $[\alpha]^{25}_{D}$ (c: g/100 mL, in solvent).

## (B) General Procedures

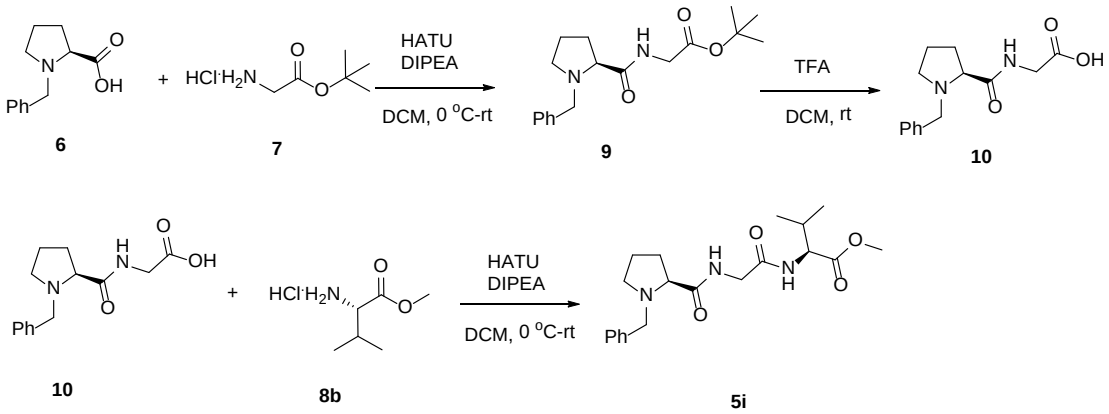
### General Procedure for the Preparation of Dipeptide Derivative 5a-5h.




**6** **8a** **5a**

The synthesis of benzyl-L-prolyl-L-leucine methyl ester **5a** is representative. To a solution of benzyl-L-proline **6** (1 g, 4.87 mmol) and L-leucine methyl ester hydrochloride **8a** (0.97 g, 5.36 mmol) in DIPEA (1.6 mL, 9.74 mmol) and dichloromethane (20 mL) was added HATU (2 g, 5.36 mmol) at 0 °C. After 30 min, the reaction mixture was allowed to warm up to room temperature and the stirring was continued for 12 h. After the reaction was completed, the mixture was portioned between water and dichloromethane. The combined organic layers were washed with brine, dried, filtered and concentrated. The residue was purified by chromatography on silica gel (PE/EA = 4/1- 2/1) to give **5a** as a colorless oil (1.4 g, yield 86%).

### Procedure for the Preparation of Tripeptide Derivative 5i and 5j.




**6** **7** **9** **10**

**10** **8b** **5i**

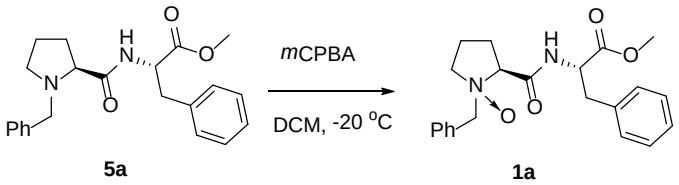
The synthesis of benzyl-L-prolylglycyl-L-valine methyl ester **5i** is representative. To a

solution of benzyl-L-proline **6** (2 g, 9.74 mmol) and glycine tert-butyl ester hydrochloride **7** (1.8 g, 10.72 mmol) in DIPEA (3.2 mL, 19.49 mmol) and dichloromethane (40 mL) was added HATU (4.1 g, 10.72 mmol) at room temperature and the stirring was continued for 12 h. The mixture was portioned between water and dichloromethane. The combined organic layers were washed with brine, dried, filtered and concentrated. The residue was purified by chromatography on silica gel (PE/EA = 6/1- 4/1) to give **9** as a colorless oil (2.8 g, yield 90%).

To a solution of **9** (2.8 g, 8.79 mmol**)** in DCM (10 mL) was added trifluoroacetic acid (6.5 mL, 87.9 mmol), and the mixture was stirred for 5 h at rt. The solvent was removed, and the residue was basified with TEA and purified by chromatography on silica gel (DCM/MeOH = 10/1- 5/1) to get compound **10** as a colorless oil (1.5 g, 65%).

To a mixture of benzyl-L-prolylglycine **10** (700 mg, 2.67 mmol) and L-valine methyl ester hydrochloride **8b** (492 mg, 2.94 mmol) in DIPEA (882 μL, 5.34 mmol) and dichloromethane (20 mL) was added HATU (1.12 g, 2.94 mmol) at 0 °C. After 30 min, the mixture was allowed to warm up to room temperature and the stirring was continued for overnight. The resulting mixture was diluted with dichloromethane and water, washed with saturated $NaHCO_3$ aq. and brine. The organic layers were dried with anhydrous $Na_2SO_4$, filtered and concentrated. The residue was purified by chromatography on silica gel (DCM/MeOH = 30/1) to give crude product **5i** as a yellow oil.

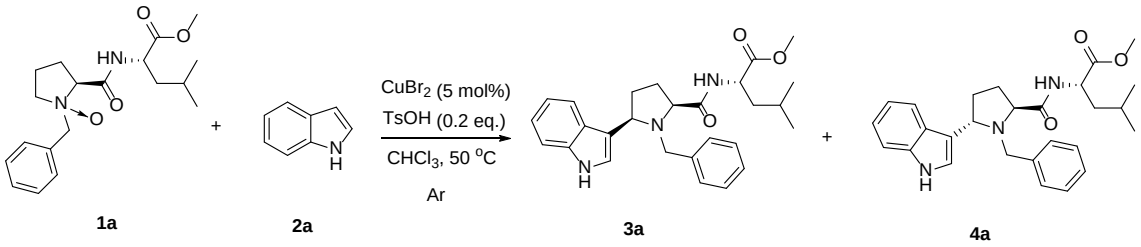
**General Procedure for the Preparation of Amine N-Oxides 1.**[1]




**5a** **1a**

The synthesis of amine N-Oxide **1a** is representative. To a solution of benzyl-L-prolyl-L-leucine methyl ester **5a** (3 g, 9.02 mmol) in DCM (40 mL) was added 3-Chloroperbenzoic acid (m-CPBA, 2.02 g, 11.73 mmol) at -20 °C. The reaction was stirred for 3h, and then diluted with $H_2O$, washed with saturated $Na_2CO_3$ aq. and brine. The combined organic phase was dried over with anhydrous $Na_2SO_4$, filtered and concentrated. The residue was purified by chromatography on silica gel (DCM/MeOH = 30/1) to give product **1a** as a white solid (3 g, 95%).

**General Procedure for the Indolation of Amine N-Oxides 1.**

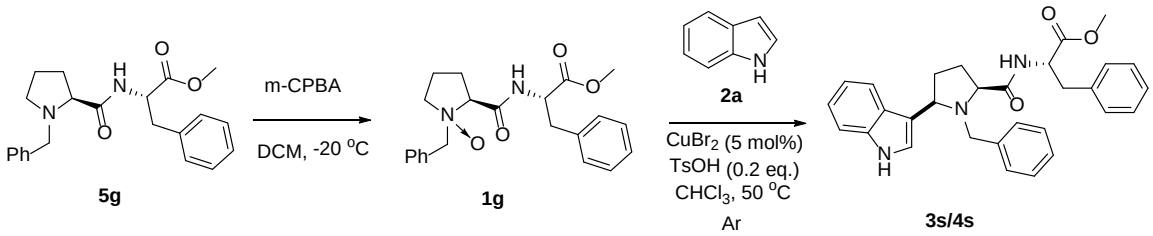



**1a** **2a** **3a** **4a**

The reaction of amine N-Oxide **1a** with indole **2a** is representative. The dry sealed tube was charged with N-Oxide **1a** (70 mg, 0.2 mmol), indole **2a** (71 mg, 0.6 mmol), $CuBr_2$ (2 mg, 0.01 mmol), TsOH (7 mg, 0.04 mmol) and 3mL $CHCl_3$ under Ar atmosphere. The mixture was heated at 50 °C for 36 h. The resulting mixture was diluted with dichloromethane and washed by water. The combined organic layers were dried with $Na_2SO_4$, filtered, concentrated and purified by column

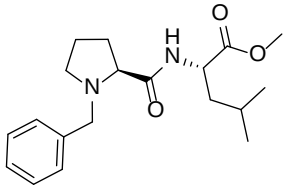
chromatography on silica gel (DCM/MeOH = 50/1- 30/1) to give combined products **3a**/**4a** as a colorless oil (63 mg, yield 70%). The combined products **3a**/**4a** were purified by preparative thin layer chromatography (PTLC) to give the major product **3a** as a colorless oil.

**Procedure of One-pot Reaction.**



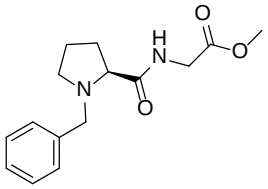

To a solution of benzyl-L-prolyl-L-phenylalanine methyl ester **5g** (560 mg, 1.53 mmol) in DCM (10 mL) was added m-CPBA (263 mg, 1.53 mmol) at -20 °C. The reaction was stirred for 3h, then the solvent was removed, and indole **2a** (537 mg, 4.58 mmol), $CuBr_2$ (17 mg, 0.08 mmol), TsOH (53 mg, 0.3 mmol) and 15 mL $CHCl_3$ were added to the sealed vessel under Ar atmosphere. The reaction was continued for 36 h. The resulting mixture was diluted with dichloromethane and washed with water. The combined organic layers were dried with $Na_2SO_4$, filtered, concentrated and purified by column chromatography on silica gel (DCM/MeOH = 50/1- 30/1) to give combined products **3s/4s** as a colorless oil (503 mg, 68%).

## (C) Analytical Characterization Data of Products



**Methyl benzyl-L-prolyl-L-leucinate 5a.**

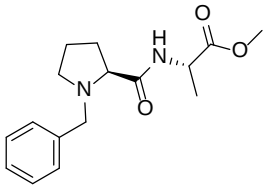
Obtained as a colorless oil by column chromatography (PE/EA = 4/1- 2/1), yield 91%. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.86 (br, 1H), 7.41 – 7.31 (m, 4H), 7.31 – 7.27 (m, 1H), 4.75 – 4.60 (m, 1H), 4.02 (d, *J* = 12.2 Hz, 1H), 3.72 (s, 3H), 3.37 (d, *J* = 12.2 Hz, 1H), 3.25 – 3.15 (m, 1H), 2.99 – 2.91 (m, 1H), 2.38 – 2.18 (m, 2H), 1.83 – 1.53 (m, 6H), 0.99 – 0.93 (m, 6H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.45, 173.32, 138.58, 129.03, 128.43, 127.24, 67.35, 59.62, 53.34, 52.18, 50.01, 41.77, 30.71, 25.03, 23.99, 22.89, 21.92 ppm.



**Methyl benzyl-L-prolylglycinate 5b.**

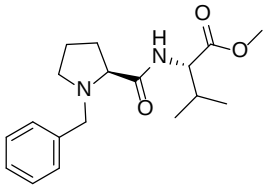
Obtained as a colorless oil by column chromatography (PE/EA = 4/1- 2/1), yield 88%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.93 (br, 1H), 7.38 – 7.30 (m, 4H), 7.29 – 7.25 (m, 1H), 4.05 – 3.99 (m, 2H), 3.95 (d, *J* = 13.0 Hz, 1H), 3.75 (s, 3H), 3.49 (d, *J* = 13.0 Hz, 1H), 3.30 – 3.15 (m, 1H), 3.10 – 2.95 (m, 1H), 2.42 – 2.30 (m, 1H), 2.29 – 2.17 (m, 1H), 1.99 – 1.85 (m, 1H), 1.82 – 1.70 (m, 2H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 175.06, 170.31, 138.39, 128.88, 128.41, 127.28, 67.13, 59.73, 53.68, 52.23, 40.71, 30.54,

23.96 ppm.



**Methyl benzyl-L-prolyl-L-alaninate 5c.**

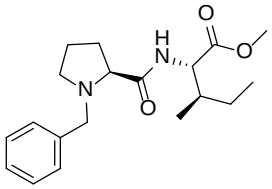
Obtained as a colorless oil by column chromatography (PE/EA = 4/1- 2/1), yield 91%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.99 (br, 1H), 7.40 – 7.28 (m, 4H), 7.26 – 7.21 (m, 1H), 4.62 – 4.52 (m, 1H), 3.98 (d, J = 12.5 Hz, 1H), 3.72 (s, 3H), 3.36 (d, J = 12.5 Hz, 1H), 3.20 – 3.12 (m, 1H), 2.98 – 2.90 (m, 1H), 2.34 – 2.15 (m, 2H), 1.85 – 1.65 (m, 3H), 1.40 (d, J = 7.2 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.38, 173.32, 138.55, 128.97, 128.37, 127.22, 67.26, 59.70, 53.43, 52.34, 47.39, 30.59, 23.90, 18.63 ppm.



**Methyl benzyl-L-prolyl-L-valinate 5d.**

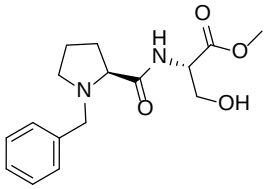
Obtained as a colorless oil by column chromatography (PE/EA = 4/1- 2/1), yield 95%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 9.6 Hz, 1H), 7.41 – 7.30 (m, 4H), 7.30 – 7.24 (m, 1H), 4.56 (dd, J = 9.6, 4.8 Hz, 1H), 4.01 (d, J = 12.5 Hz, 1H), 3.71 (s, 3H), 3.38 (d, J = 12.5 Hz, 1H), 3.21 (dd, J = 10.1, 5.0 Hz, 1H), 2.97 (t, J = 7.6 Hz, 1H), 2.37 – 2.17 (m, 3H), 1.92 – 1.83 (m, 1H), 1.75 – 1.65 (m, 1H), 0.99 – 0.88 (m, 6H)

ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.68, 172.25, 138.57, 128.95, 128.36, 127.19, 67.35, 59.70, 56.30, 53.39, 51.99, 31.37, 30.92, 24.07, 19.09, 17.64 ppm.



**Methyl benzyl-L-prolyl-L-alloisoleucinate 5e.**

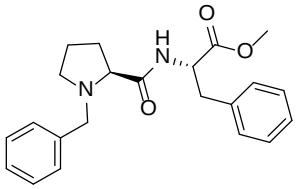
Obtained as a colorless oil by column chromatography (PE/EA = 4/1- 2/1), yield 90%. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 9.5 Hz, 1H), 7.42 – 7.29 (m, 4H), 7.28 – 7.23 (m, 1H), 4.60 (dd, *J* = 9.5, 4.8 Hz, 1H), 4.01 (d, *J* = 12.6 Hz, 1H), 3.71 (s, 3H), 3.38 (d, *J* = 12.6 Hz, 1H), 3.20 (dd, *J* = 10.2, 5.0 Hz, 1H), 2.97 (t, *J* = 7.8 Hz, 1H), 2.38 – 2.16 (m, 2H), 2.01 – 1.63 (m, 4H), 1.52 – 1.37 (m, 1H), 1.25 – 1.10 (m, 1H), 0.96 – 0.88 (m, 6H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.52, 172.25, 138.59, 128.94, 128.36, 127.18, 67.36, 59.68, 55.75, 53.39, 51.94, 37.95, 30.87, 25.04, 24.06, 15.62, 11.57 ppm.



**Methyl benzyl-L-prolyl-L-serinate 5f.**

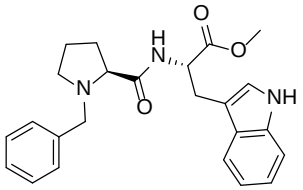
Obtained as a colorless oil by column chromatography (DCM/MeOH = 40/1- 20/1), yield 81%. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.34 (br, 1H), 7.41 – 7.26 (m, 5H), 4.57 (dt, *J* = 7.7, 4.0 Hz, 1H), 4.06 – 3.87 (m, 3H), 3.78 (s, 3H), 3.47 (d, *J* = 12.4 Hz, 1H), 3.26

– 3.20 (m, 1H), 3.05 – 2.90 (m, 2H), 2.43 – 2.17 (m, 2H), 1.99 – 1.85 (m, 1H), 1.82 – 1.72 (m, 2H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$) δ 170.56, 129.15, 128.47, 127.50, 67.25, 63.68, 59.52, 54.77, 53.55, 52.67, 30.53, 23.74 ppm.




**Methyl benzyl-L-prolyl-L-phenylalaninate 5g.**

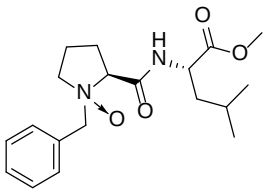
Obtained as a colorless oil by column chromatography (PE/EA = 4/1- 2/1), yield 87%. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.5 Hz, 1H), 7.28 – 7.21 (m, 6H), 7.19 – 7.09 (m, 4H), 4.95 – 4.87 (m, 1H), 3.92 (d, *J* = 12.6 Hz, 1H), 3.70 (s, 3H), 3.32 (d, *J* = 12.6 Hz, 1H), 3.23 – 3.09 (m, 3H), 2.85 (t, *J* = 8.0 Hz, 1H), 2.29 – 2.09 (m, 2H), 1.78 – 1.64 (m, 2H), 1.62 – 1.50 (m, 1H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.10, 171.66, 138.28, 135.76, 129.08, 128.60, 128.27, 128.09, 126.87, 66.89, 59.39, 53.11, 52.01, 51.96, 37.89, 30.31, 23.83 ppm.




**Methyl benzyl-L-prolyl-L-tryptophanate 5h.**

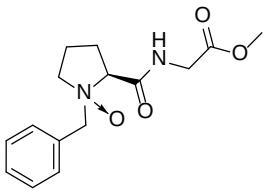
Obtained as a colorless oil by column chromatography (PE/EA = 4/1- 2/1), yield 78%. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.94 (br, 1H), 7.84 (s, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.25 – 7.05 (m, 6H), 6.97 – 6.90 (m, 2H), 6.86 (s, 1H), 4.98 – 4.85 (m, 1H), 3.72 (s,

3H), 3.57 (d, *J* = 12.9 Hz, 1H), 3.44 – 3.32 (m, 1H), 3.31 – 3.22 (m, 2H), 3.21 – 3.13 (m, 1H), 2.95 – 2.87 (m, 1H), 2.28 – 2.14 (m, 2H), 1.97 – 1.87 (m, 1H), 1.77 – 1.60 (m, 2H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$) δ 174.56, 172.59, 138.58, 136.08, 128.40, 128.22, 126.97, 122.18, 119.57, 118.63, 111.17, 110.25, 67.33, 59.46, 53.62, 52.36, 52.13, 30.56, 27.56, 24.03 ppm.



**(2S)-1-benzyl-2-(((S)-1-methoxy-4-methyl-1-oxopentan-2-yl)carbamoyl)pyrrolidine 1-oxide 1a.**

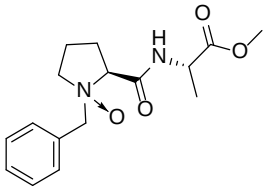
Obtained as a white solid by column chromatography (DCM/MeOH = 40/1- 20/1), yield 97%. $^1$H NMR (400 MHz, $CDCl_3$) δ 11.96 (br, 1H), 7.48 – 7.39 (m, 5H), 4.82 (d, *J* = 13.1 Hz, 1H), 4.68 – 4.56 (m, 2H), 3.75 (s, 3H), 3.65 – 3.55 (m, 1H), 3.43 – 3.33 (m, 1H), 3.27 – 3.20 (m, 1H), 2.50 – 2.27 (m, 3H), 1.86 – 1.72 (m, 4H), 0.99 – 0.92 (m, 6H) ppm.



**(2S)-1-benzyl-2-((2-methoxy-2-oxoethyl)carbamoyl)pyrrolidine 1-oxide 1b.**

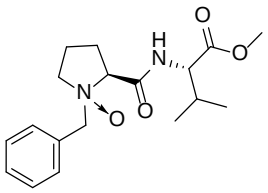
Obtained as a white solid by column chromatography (DCM/MeOH = 40/1- 20/1), yield 95%. $^1$H NMR (400 MHz, $CDCl_3$) δ 11.72 (br, 1H), 7.51 – 7.37 (m, 5H), 4.80 (d,

*J* = 13.1 Hz, 1H), 4.62 (d, *J* = 13.1 Hz, 1H), 4.30 (dd, *J* = 17.7, 7.2 Hz, 1H), 3.86 (dd, *J* = 17.7, 4.8 Hz, 1H), 3.80 – 3.66 (m, 4H), 3.45 – 3.27 (m, 2H), 2.49 – 2.30 (m, 3H), 1.92 – 1.80 (m, 1H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 170.11, 168.87, 132.33, 129.88, 129.82, 128.93, 71.58, 70.17, 65.68, 52.24, 40.43, 26.70, 19.80 ppm.



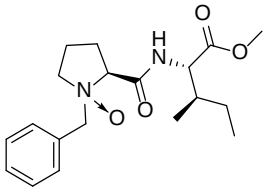
**(2S)-1-benzyl-2-(((S)-1-methoxy-1-oxopropan-2-yl)carbamoyl)pyrrolidine 1-oxide 1c.**

Obtained as a colorless oil by column chromatography (DCM/MeOH = 40/1- 20/1), yield 95%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 11.70 (br, 1H), 7.49 – 7.39 (m, 5H), 4.85 (d, *J* = 13.2 Hz, 1H), 4.72 – 4.53 (m, 2H), 3.76 (s, 3H), 3.68 – 3.58 (m, 1H), 3.43 – 3.25 (m, 2H), 2.50 – 2.30 (m, 3H), 1.89 – 1.80 (m, 1H), 1.50 (d, *J* = 7.4 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 172.77, 167.63, 131.90, 129.56, 129.31, 128.50, 70.94, 69.55, 64.89, 51.89, 47.06, 26.16, 19.30, 16.83 ppm.



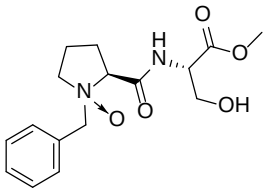
**(2S)-1-benzyl-2-(((S)-1-methoxy-3-methyl-1-oxobutan-2-yl)carbamoyl)pyrrolidine 1-oxide 1d.**

Obtained as a colorless oil by column chromatography (DCM/MeOH = 40/1- 20/1), yield 98%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 12.02 (br, 1H), 7.50 – 7.36 (m, 5H), δ 4.79 (d, J = 13.1 Hz, 1H), 4.69 (d, J = 13.1 Hz, 1H), 4.48 (dd, J = 7.9, 4.3 Hz, 1H), 3.83 – 3.67 (m, 3H), 3.48 – 3.35 (m, 1H), 3.27 (t, J = 9.2 Hz, 1H), 2.54 – 2.30 (m, 4H), 1.92 – 1.80 (m, 1H), 1.05 – 0.96 (m, 6H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 172.25, 168.66, 132.32, 130.03, 129.71, 128.89, 71.74, 69.85, 65.43, 57.33, 52.08, 30.00, 26.89, 19.80, 19.50, 17.65 ppm.



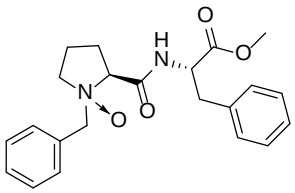

**(2S)-1-benzyl-2-(((2S,3R)-1-methoxy-3-methyl-1-oxopentan-2-yl)carbamoyl)pyrrolidine 1-oxide 1e.**

Obtained as a colorless oil by column chromatography (DCM/MeOH = 40/1- 20/1), yield 95%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 12.01 (br, 1H), 7.48 – 7.43 (m, 2H), 7.42 – 7.37 (m, 3H), 4.80 (d, J = 13.1 Hz, 1H), 4.69 (d, J = 13.1 Hz, 1H), 4.57 – 4.47 (m, 1H), 3.74 (s, 3H), 3.51 – 3.33 (m, 2H), 3.28 (t, J = 9.4 Hz, 1H), 2.53 – 2.29 (m, 3H), 2.14 – 2.03 (m, 1H), 1.92 – 1.79 (m, 1H), 1.53 – 1.41 (m, 1H), 1.38 – 1.26 (m, 1H), 1.23 – 1.15 (m, 2H), 1.01 (d, J = 6.9 Hz, 3H), 0.93 (t, J = 7.3 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 172.30, 168.55, 132.32, 130.04, 129.71, 128.91, 71.64, 69.85, 65.35, 56.76, 52.06, 36.66, 26.83, 25.05, 19.78, 16.27, 11.76 ppm.



**(2S)-1-benzyl-2-(((S)-3-hydroxy-1-methoxy-1-oxopropan-2-yl)carbamoyl)pyrroli dine 1-oxide 1f.**

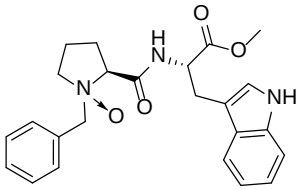
Obtained as a foamy solid by column chromatography (DCM/MeOH = 30/1- 20/1), yield 86%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 11.23 (d, J = 8.1 Hz, 1H), 7.49 – 7.37 (m, 5H), 4.93 (d, J = 13.2 Hz, 1H), 4.75 – 4.61 (m, 2H), 4.10 (dd, J = 11.5, 4.1 Hz, 1H), 3.92 (dd, J = 11.5, 3.0 Hz, 1H), 3.81 – 3.72 (m, 4H), 3.49 – 3.27 (m, 2H), 2.97 – 2.74 (m, 1H), 2.55 – 2.42 (m, 1H), 2.40 – 2.26 (m, 2H), 1.95 – 1.80 (m, 1H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 170.87, 168.11, 132.42, 129.93, 129.58, 129.02, 71.55, 69.63, 65.13, 61.79, 54.65, 52.54, 26.43, 19.68 ppm.



**(2S)-1-benzyl-2-(((S)-1-methoxy-1-oxo-3-phenylpropan-2-yl)carbamoyl)pyrrolidi ne 1-oxide 1g.**

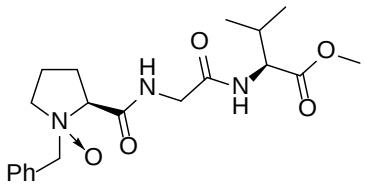
Obtained as a faint yellow oil by column chromatography (DCM/MeOH = 50/1- 30/1), yield 92%. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 12.01 (d, J = 7.3 Hz, 1H), 7.41 – 7.36 (m, 5H), 7.33 – 7.26 (m, 2H), 7.26 – 7.19 (m, 3H), 4.85 – 4.79 (m, 1H), δ 4.63 (d, J = 13.1 Hz, 1H), 4.56 (d, J = 13.1 Hz, 1H), 3.74 (s, 3H), 3.63 – 3.54 (m, 1H), 3.37 – 3.17 (m,

3H), 3.13 – 3.05 (m, 1H), 2.35 – 2.25 (m, 1H), 2.24 – 2.14 (m, 2H), 1.88 – 1.69 (m, 1H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 171.98, 168.18, 136.50, 132.27, 130.07, 129.63, 129.28, 128.80, 128.46, 126.87, 71.89, 69.88, 65.45, 53.27, 52.28, 37.55, 26.55, 19.74 ppm.



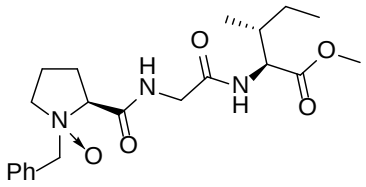

**(2S)-2-(((S)-3-(1H-indol-3-yl)-1-methoxy-1-oxopropan-2-yl)carbamoyl)-1-benzylpyrrolidine 1-oxide 1h.**

Obtained as a faint yellow oil by column chromatography (DCM/MeOH = 50/1- 30/1), yield 84%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 11.15 (d, J = 7.1 Hz, 1H), 9.50 (s, 1H), 7.62 – 7.56 (m, 1H), 7.39 – 7.27 (m, 3H), 7.22 – 7.16 (m, 2H), 7.15 – 7.09 (m, 2H), 7.08 – 6.99 (m, 2H), 4.94 – 4.86 (m, 1H), 4.26 (d, J = 13.1 Hz, 1H), 4.06 (d, J = 13.1 Hz, 1H), 3.71 (s, 3H), 3.69 – 3.63 (m, 1H), 3.35 – 3.24 (m, 4H), 2.48 – 2.35 (m, 1H), 2.34 – 2.20 (m, 2H), 1.85 – 1.73 (m, 1H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 172.07, 167.76, 136.44, 132.10, 129.79, 129.41, 128.79, 127.08, 124.01, 121.81, 119.24, 118.55, 111.38, 109.69, 71.95, 69.93, 66.12, 52.36, 27.36, 26.78, 19.66 ppm.



**(2S)-1-benzyl-2-((2-(((S)-1-methoxy-3-methyl-1-oxobutan-2-yl)amino)-2-oxoethyl )carbamoyl)pyrrolidine 1-oxide 1i.**

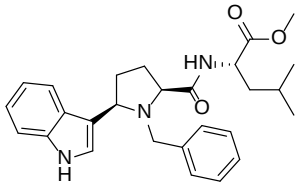
Obtained as a colorless oil by column chromatography (DCM/MeOH = 40/1- 20/1), yield 81%.$^{1}$H NMR (600 MHz, $CDCl_3$) δ 11.29 (br, 1H), 7.49 – 7.45 (m, 2H), 7.43 – 7.38 (m, 3H), 6.85 (d, *J* = 8.7 Hz, 1H), 4.69 (d, *J* = 13.0 Hz, 1H), 4.58 (d, *J* = 13.0 Hz, 1H), 4.53 (dd, *J* = 8.8, 5.1 Hz, 1H), 3.94 – 3.91 (m, 2H), 3.90 – 3.85 (m, 1H), 3.70 (s, 3H), 3.46 – 3.36 (m, 2H), 2.47 – 2.35 (m, 3H), 2.19 – 2.12 (m, 1H), 1.94 – 1.87 (m, 1H), 0.93 (d, *J* = 6.9 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$) δ 172.37, 169.08, 168.85, 132.37, 129.94, 129.59, 128.86, 72.03, 70.51, 66.33, 57.12, 52.12, 42.80, 31.18, 27.05, 19.87, 18.86, 17.81 ppm.




**(2S)-1-benzyl-2-((2-(((2S)-1-methoxy-3-methyl-1-oxopentan-2-yl)amino)-2-oxoeth yl)carbamoyl)pyrrolidine 1-oxide 1j.**

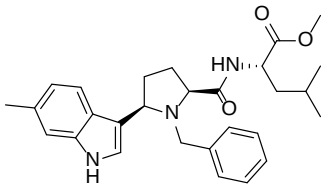
Obtained as a colorless oil by column chromatography (DCM/MeOH = 40/1- 20/1), yield 83%. $^{1}$H NMR (600 MHz, $CDCl_3$) δ 11.36 (br, 1H), 7.47 – 7.44 (m, 2H), 7.43 – 7.39 (m, 3H), 6.82 (d, *J* = 8.6 Hz, 1H), 4.66 (d, *J* = 13.0 Hz, 1H), 4.59 – 4.56 (m, 1H), 4.55 (d, *J* = 13.0 Hz, 1H), 3.91 (d, *J* = 4.2 Hz, 2H), 3.77 – 3.72 (m, 1H), 3.70 (s, 3H), 3.41 – 3.36 (m, 2H), 2.48 – 2.34 (m, 3H), 1.92 – 1.85 (m, 2H), 1.45 – 1.38 (m, 1H), 1.20 – 1.13 (m, 1H), 0.93 – 0.86 (m, 6H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$) δ 172.35, 169.06, 168.80, 132.36, 129.91, 129.73, 128.86, 72.06, 70.66, 66.41, 56.42, 52.08,

42.80, 37.81, 27.09, 25.10, 19.87, 15.35, 11.51 ppm.



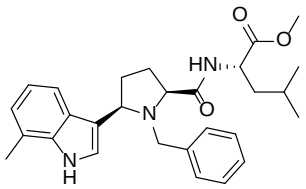
**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3a.**

Colorless oil, combined yield 70%. $[\alpha]^{25}_{D}$ = + 20.7 (c = 0.26, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$) δ 8.36 (br, 1H), 7.94 (d, J = 8.2 Hz, 1H), 7.75 (d, J = 7.9 Hz, 1H), 7.43 (d, J = 8.1 Hz, 1H), 7.35 (d, J = 2.3 Hz, 1H), 7.25 – 7.19 (m, 4H), 7.18 – 7.13 (m, 3H), 4.50 – 4.46 (m, 1H), 4.22 – 4.18 (m, 1H), 3.98 (d, J = 13.5 Hz, 1H), 3.73 (s, 3H), 3.69 (d, J = 13.5 Hz, 1H), 3.52 (dd, J = 10.3, 3.2 Hz, 1H), 2.29 – 2.14 (m, 2H), 2.07 – 1.96 (m, 2H), 1.71 – 1.55 (m, 3H), 0.95 (d, J = 6.3, 6H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.92, 173.17, 136.93, 136.26, 130.15, 128.07, 127.16, 126.26, 122.14, 122.08, 119.35, 116.99, 111.50, 64.84, 61.41, 55.97, 52.13, 50.33, 41.78, 32.68, 29.79, 24.96, 22.77, 22.21 ppm. HRMS (ESI) m/z: calculated for $C_{27}H_{34}N_3O_3^+$ $[M + H]^+$: 448.2595, found: 448.2603. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 11.145 min, $t_R$ (minor diastereomer) = 20.616 min, 93:7 dr.



**Methyl ((2S,5R)-1-benzyl-5-(6-methyl-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3b.**

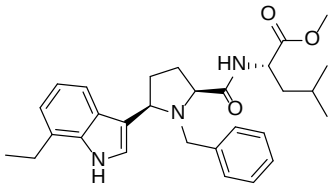
Colorless oil, combined yield 62%. $[\alpha]^{25}_{D}$ = + 21.6 (c = 0.28, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.24 (br, 1H), 7.93 (d, J = 8.2 Hz, 1H), 7.63 (d, J = 8.1 Hz, 1H), 7.27 – 7.14 (m, 7H), 6.99 (d, J = 8.1 Hz, 1H), 4.53 – 4.45 (m, 1H), 4.20 – 4.13 (m, 1H), 3.98 (d, J = 13.4 Hz, 1H), 3.73 (s, 3H), 3.68 (d, J = 13.4 Hz, 1H), 3.57 – 3.46 (m, 1H), 2.50 (s, 3H), 2.31 – 2.09 (m, 2H), 2.06 – 1.93 (m, 2H), 1.74 – 1.53 (m, 3H), 0.95 (d, J = 5.9 Hz, 6H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$) δ 174.87, 173.07, 137.33, 136.14, 131.89, 130.11, 127.97, 127.05, 123.97, 121.43, 121.02, 118.92, 116.66, 111.36, 64.62, 61.30, 55.70, 52.03, 50.22, 41.68, 32.52, 29.69, 24.88, 22.70, 22.10, 21.57 ppm. HRMS (ESI) m/z: calculated for $C_{28}H_{36}N_3O_3^+$ $[M + H]^+$: 462.2757, found: 462.2758. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 9.325 min, $t_R$ (minor diastereomer) = 12.382 min, 94:6 dr.




**Methyl ((2S,5R)-1-benzyl-5-(7-methyl-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3c.**

Colorless oil, combined yield 68%. $[\alpha]^{25}_{D}$ = + 24.2 (c = 0.22, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$) δ 8.23 (br, 1H), 7.94 (d, J = 8.2 Hz, 1H), 7.60 (d, J = 7.4 Hz, 1H), 7.37

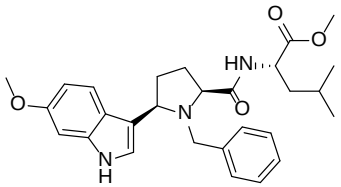
(d, J = 2.3 Hz, 1H), 7.25 – 7.19 (m, 3H), 7.18 – 7.14 (m, 2H), 7.11 – 7.04 (m, 2H), 4.51 – 4.44 (m, 1H), 4.23 – 4.18 (m, 1H), 3.99 (d, J = 13.5 Hz, 1H), 3.74 (s, 3H), 3.69 (d, J = 13.5 Hz, 1H), 3.54 – 3.47 (m, 1H), 2.53 (s, 3H), 2.31 – 2.21 (m, 1H), 2.21 – 2.13 (m, 1H), 2.05 – 1.95 (m, 2H), 1.70 – 1.54 (m, 3H), 0.94 (d, J = 6.3, 6H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.91, 173.18, 136.50, 136.29, 130.18, 128.07, 127.16, 125.83, 122.70, 121.75, 120.68, 119.64, 117.61, 117.09, 64.82, 61.46, 55.93, 52.11, 50.36, 41.81, 32.75, 29.83, 24.96, 22.77, 22.23, 16.63 ppm. HRMS (ESI) m/z: calculated for $C_{28}H_{36}N_3O_3^+$ $[M + H]^+$: 462.2751, found: 462.2756. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 5.375 min, $t_R$ (minor diastereomer) = 7.3 min, 93:7 dr.




**Methyl ((2S,5R)-1-benzyl-5-(7-ethyl-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3d.**

Colorless oil, combined yield 71%. $[\alpha]^{25}_D$ = + 18.9 (c = 0.22, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.34 (br, 1H), 7.97 (d, J = 8.2 Hz, 1H), 7.64 – 7.57 (m, 1H), 7.36 (d, J = 2.4 Hz, 1H), 7.24 – 7.08 (m, 7H), 4.51 – 4.45 (m, 1H), 4.23 – 4.18 (m, 1H), 3.99 (d, J = 13.4 Hz, 1H), 3.74 (s, 3H), 3.70 (d, J = 13.4 Hz, 1H), 3.54 – 3.49 (m, 1H), 2.91 (q, J = 7.6 Hz, 2H), 2.30 – 2.12 (m, 2H), 2.05 – 1.95 (m, 2H), 1.73 – 1.56 (m, 3H), 1.41 (t, J = 7.6 Hz, 3H), 0.95 (d, J = 6.2 Hz, 6H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$) δ 174.97,

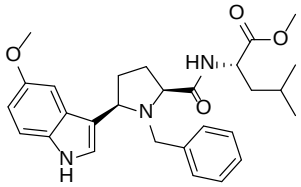
173.20, 136.28, 135.79, 130.19, 128.06, 127.15, 126.90, 126.03, 121.71, 120.66, 119.68, 117.47, 117.10, 64.77, 61.46, 55.90, 52.13, 50.35, 41.80, 32.75, 29.83, 24.98, 24.01, 22.79, 22.22, 13.79 ppm. HRMS (ESI) m/z: calculated for $C_{29}H_{38}N_3O_3^+$ [M + H]$^+$: 476.2913, found: 476.2900. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 18.281 min, $t_R$ (minor diastereomer) = 30.035 min, 93:7 dr.




**Methyl ((2S,5R)-1-benzyl-5-(6- methoxy-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3e.**

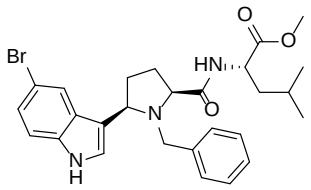
Colorless oil, combined yield 59%. $[\alpha]^{25}_D$ = + 21.8 (c = 0.14, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$) δ 8.08 (br, 1H), 7.88 (d, J = 8.2 Hz, 1H), 7.60 (d, J = 8.7 Hz, 1H), 7.25 – 7.19 (m, 4H), 7.17 – 7.12 (m, 2H), 6.92 (d, J = 2.1 Hz, 1H), 6.81 (dd, J = 8.7, 2.1 Hz, 1H), 4.49 – 4.43 (m, 1H), 4.16 – 4.11 (m, 1H), 3.97 (d, J = 13.5 Hz, 1H), 3.87 (s, 3H), 3.73 (s, 3H), 3.68 (d, J = 13.5 Hz, 1H), 3.53 – 3.46 (m, 1H), 2.31 – 2.19 (m, 1H), 2.18 – 2.09 (m, 1H), 2.05 – 1.92 (m, 2H), 1.67 – 1.53 (m, 3H), 0.93 (d, J = 6.3 Hz, 6H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.86, 173.18, 156.59, 137.70, 136.35, 130.17, 128.08, 127.16, 120.81, 120.63, 119.98, 117.14, 109.51, 94.86, 64.93, 61.49, 56.04, 55.67, 52.12, 50.35, 41.82, 32.71, 29.80, 24.97, 22.79, 22.23 ppm. HRMS (ESI) m/z: calculated for $C_{28}H_{36}N_3O_4^+$ [M + H]$^+$: 478.2700, found: 478.2711. The dr was

determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 9.005 min, $t_R$ (minor diastereomer) = 19.325 min, 93:7 dr.



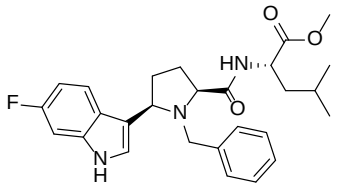

**Methyl ((2S,5R)-1-benzyl-5-(5-methoxy-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3f.**

Colorless oil, combined yield 80%. $[\alpha]^{25}_D$ = + 10.4 (c = 0.14, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.22 (br, 1H), 7.90 (d, J = 8.1 Hz, 1H), 7.35 (s, 1H), 7.31 (d, J = 8.8 Hz, 1H), 7.23 – 7.14 (m, 6H), 6.91 (d, J = 8.8 Hz, 1H), 4.48 – 4.43 (m, 1H), 4.18 – 4.15 (m, 1H), 4.00 (d, J = 13.4 Hz, 1H), 3.88 (s, 3H), 3.73 (s, 3H), 3.70 (d, J = 13.4 Hz, 1H), 3.51 – 3.47 (m, 1H), 2.31 – 2.15 (m, 2H), 1.99 – 1.87 (m, 2H), 1.69 – 1.49 (m, 3H), 0.92 – 0.89 (m, 6H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$) δ 174.82, 173.27, 153.89, 136.32, 131.96, 130.14, 128.07, 127.17, 126.96, 122.43, 116.90, 112.02, 111.95, 101.57, 65.02, 61.21, 56.22, 55.99, 52.13, 50.29, 41.83, 32.81, 29.77, 24.93, 22.66, 22.26 ppm. HRMS (ESI) m/z: calculated for $C_{28}H_{36}N_3O_4^+$ $[M + H]^+$: 478.2706, found: 478.2711. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 15.585 min, $t_R$ (minor diastereomer) = 28.457 min, 93:7 dr.



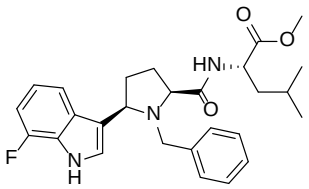

**Methyl ((2S,5R)-1-benzyl-5-(5-bromo-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3g.**

Colorless oil, combined yield 69%. $[\alpha]^{25}_{D}$ = + 36.7 (c = 0.30, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.57 (br, 1H), 7.87 (d, J = 8.2 Hz, 1H), 7.83 (s, 1H), 7.34 – 7.27 (m, 3H), 7.24 – 7.18 (m, 3H), 7.17 – 7.12 (m, 2H), 4.53 – 4.44 (m, 1H), 4.15 – 4.08 (m, 1H), 3.95 (d, J = 13.4 Hz, 1H), 3.73 (s, 3H), 3.68 (d, J = 13.4 Hz, 1H), 3.52 – 3.46 (m, 1H), 2.30 – 2.10 (m, 2H), 2.06 – 1.92 (m, 2H), 1.75 – 1.56 (m, 3H), 0.94 (d, J = 5.9 Hz, 6H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$) δ 174.74, 173.13, 135.98, 135.55, 130.11, 128.08, 127.96, 127.24, 124.97, 123.38, 121.87, 116.63, 112.95, 112.66, 64.92, 61.13, 56.02, 52.17, 50.43, 41.73, 32.54, 29.64, 25.00, 22.70, 22.28 ppm. HRMS (ESI) m/z: calculated for $C_{27}H_{32}N_3O_3BrNa^+$ $[M + Na]^+$: 548.1525, found: 548.1534. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 11.41 min, $t_R$ (minor diastereomer) = 15.844 min, 96:4 dr.




**Methyl ((2S,5R)-1-benzyl-5-(6-fluoro-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3h.**

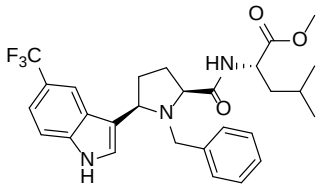
Colorless oil, combined yield 51%. $[\alpha]^{25}_{D}$ = + 23.9 (c = 0.14, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$) δ 8.37 (br, 1H), 7.87 (d, J = 8.1 Hz, 1H), 7.64 (dd, J = 8.7, 5.3 Hz, 1H), 7.30 (d, J = 2.2 Hz, 1H), 7.23 – 7.18 (m, 3H), 7.16 – 7.12 (m, 2H), 7.10 (dd, J = 9.6, 2.2 Hz, 1H), 6.91 (td, J = 9.2, 2.3 Hz, 1H), 4.47 – 4.42 (m, 1H), 4.16 – 4.13 (m, 1H), 3.96 (d, J = 13.4 Hz, 1H), 3.73 (s, 3H), 3.67 (d, J = 13.4 Hz, 1H), 3.50 (dd, J = 10.3, 3.4 Hz, 1H), 2.31 – 2.21 (m, 1H), 2.20 – 2.12 (m, 1H), 2.05 – 1.92 (m, 2H), 1.69 – 1.51 (m, 3H), 0.93 (d, J = 6.3, 6H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.81, 173.18, δ 159.95 (d, J = 237.9 Hz), 136.85 (d, J = 12.5 Hz), 136.30, 130.09, 128.09, 127.22, 122.81, 122.31, 120.03 (d, J = 10.0 Hz), 117.18, 108.16 (d, J = 24.2 Hz), 97.76 (d, J = 25.9 Hz), 65.12, 61.51, 56.32, 52.16, 50.36, 41.83, 32.72, 29.77, 24.96, 22.74, 22.26 ppm. HRMS (ESI) m/z: calculated for $C_{27}H_{33}N_3O_3F^+$ $[M + H]^+$: 466.2500, found: 466.2506. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 18.321 min, $t_R$ (minor diastereomer) = 29.653 min, >93:7 dr.




**Methyl ((2S,5R)-1-benzyl-5-(7-fluoro-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3i.**

Colorless oil, combined yield 46%. $[\alpha]^{25}_{D}$ = + 38.5 (c = 0.16, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.54 (br, 1H), 7.89 (d, J = 8.2 Hz, 1H), 7.49 (d, J = 7.9 Hz, 1H), 7.36

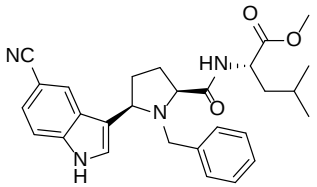
(d, J = 2.3 Hz, 1H), 7.25 – 7.11 (m, 5H), 7.06 – 7.01 (m, 1H), 6.98 – 6.91 (m, 1H), 4.49 – 4.43 (m, 1H), 4.21 – 4.14 (m, 1H), 3.96 (d, J = 13.4 Hz, 1H), 3.73 (s, 3H), 3.69 (d, J = 13.4 Hz, 1H), 3.52 (dd, J = 10.2, 3.4 Hz, 1H), 2.32 – 2.12 (m, 2H), 2.05 – 1.92 (m, 2H), 1.71 – 1.53 (m, 3H), 0.97 – 0.90 (m, 6H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$) δ 174.76, 173.19, δ 149.72 (d, J = 244.2 Hz), 136.22, 130.09, 129.94 (d, J = 5.2 Hz), 128.09, 127.22, 125.26 (d, J = 13.4 Hz), 122.76, 119.65 (d, J = 6.1 Hz), 118.06, 115.13, 106.96 (d, J = 16.2 Hz), 65.11, 61.38, 56.26, 52.15, 50.35, 41.81, 32.71, 29.76, 24.96, 22.75, 22.24 ppm. HRMS (ESI) m/z: calculated for $C_{27}H_{33}N_3O_3F^+$ $[M + H]^+$: 466.2506, found: 466.2502. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 17.124 min, $t_R$ (minor diastereomer) = 24.335 min, 90:10 dr.




**Methyl ((2S,5R)-1-benzyl-5-(5-(trifluoromethyl)-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3j.**

Colorless oil, combined yield 41%. $[\alpha]^{25}_D$ = + 17.4 (c = 0.18, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.69 (br, 1H), 7.98 (s, 1H), 7.85 (d, J = 8.2 Hz, 1H), 7.52 – 7.39 (m, 3H), 7.21 – 7.12 (m, 5H), 4.54 – 4.44 (m, 1H), 4.22 – 4.15 (m, 1H), 3.96 (d, J = 13.4 Hz, 1H), 3.74 – 3.67 (m, 4H), 3.53 – 3.48 (m, 1H), 2.35 – 2.17 (m, 2H), 2.06 – 1.92 (m, 2H), 1.70 – 1.51 (m, 3H), 0.94 – 0.90 (m, 6H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$)

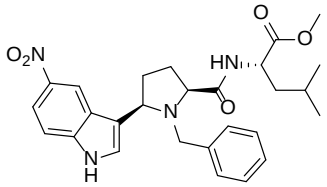
δ 174.61, 173.23, 138.20, 135.97, 130.09, 128.08, 127.27, 125.70, 123.60, 121.68, 118.91, 118.19, 116.92, 111.72, 65.21, 61.05, 56.29, 52.17, 50.38, 41.77, 32.92, 29.65, 24.98, 22.61, 22.24 ppm. HRMS (ESI) m/z: calculated for $C_{28}H_{33}N_3O_3F_3^+$ $[M + H]^+$: 516.2474, found: 516.2480. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 15.035 min, $t_R$ (minor diastereomer) = 22.473 min, 90:10 dr.




**Methyl ((2S,5R)-1-benzyl-5-(5-cyano-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3k.**

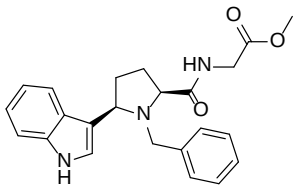
Colorless oil, combined yield 26%. $[\alpha]^{25}_D$ = + 41.1 (c = 0.28, $CHCl_3$). $^1$H NMR (600 MHz, $CDCl_3$) δ 8.96 (br, 1H), 8.05 (s, 1H), 7.88 (d, J = 7.9 Hz, 1H), 7.48 – 7.41 (m, 3H), 7.22 – 7.16 (m, 3H), 7.15 – 7.09 (m, 2H), 4.49 – 4.41 (m, 1H), 4.17 (dd, J = 9.7, 6.1 Hz, 1H), 3.93 (d, J = 13.4 Hz, 1H), 3.75 (s, 3H), 3.68 (d, J = 13.4 Hz, 1H), 3.51 (dd, J = 10.3, 4.0 Hz, 1H), 2.34 – 2.24 (m, 1H), 2.23 – 2.16 (m, 1H), 2.08 – 1.92 (m, 2H), 1.74 – 1.66 (m, 1H), 1.62 – 1.54 (m, 2H), 0.96 – 0.90 (m, 6H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$) δ 174.51, 173.18, 138.57, 136.10, 130.00, 128.12, 127.37, 126.04, 125.08, 124.89, 124.22, 120.58, 118.14, 112.40, 102.60, 65.48, 61.26, 56.72, 52.26, 50.48, 41.86, 32.89, 29.72, 25.02, 22.65, 22.36 ppm. HRMS (ESI) m/z: calculated for $C_{28}H_{33}N_4O_3^+$ $[M + H]^+$: 473.2553, found: 473.2539. The dr was determined by HPLC

with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 10.07 min, $t_R$ (minor diastereomer) = 16.621 min, 92:8 dr.



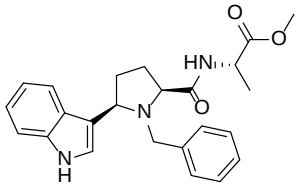

**Methyl ((2S,5R)-1-benzyl-5-(5-nitro-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3l.**

Yellow oil, combined yield 20%. $[\alpha]^{25}_D$ = + 27.4 (c = 0.26, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$) δ 8.97 (br, 1H), 8.66 (d, J = 1.9 Hz, 1H), 8.14 (dd, J = 9.0, 2.1 Hz, 1H), 7.86 (d, J = 7.7 Hz, 1H), 7.48 (s, 1H), 7.43 (d, J = 9.0 Hz, 1H), 7.20 – 7.16 (m, 3H), 7.15 – 7.11 (m, 2H), 4.54 – 4.46 (m, 1H), 4.23 – 4.16 (m, 1H), 3.94 (d, J = 13.4 Hz, 1H), 3.76 – 3.69 (m, 4H), 3.55 – 3.48 (m, 1H), 2.32 – 2.20 (m, 2H), 2.08 – 1.91 (m, 2H), 1.71 – 1.59 (m, 3H), 0.94 – 0.91 (m, 6H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.45, 173.34, 141.47, 139.83, 135.85, 130.04, 128.10, 127.34, 125.63, 125.00, 119.91, 117.86, 116.56, 111.42, 65.38, 61.02, 56.47, 52.22, 50.40, 41.79, 33.10, 29.64, 25.05, 22.67, 22.27 ppm. HRMS (ESI) m/z: calculated for $C_{27}H_{33}N_4O_5^+$ $[M + H]^+$: 493.2451, found: 493.2440. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 21.023 min, $t_R$ (minor diastereomer) = 32.702 min, 91:9 dr.



**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)glycinate 3n.**

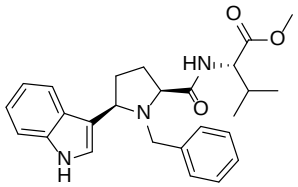
Colorless oil, combined yield 63%. $[\alpha]^{25}_{D}$ = + 34.4 (c = 0.16, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.41 (br, 1H), 7.87 – 7.74 (m, 2H), 7.48 – 7.37 (m, 2H), 7.26 – 7.07 (m, 7H), 4.23 – 4.14 (m, 1H), 4.07 – 3.94 (m, 2H), 3.78 (s, 3H), 3.56 – 3.43 (m, 3H), 2.39 – 2.22 (m, 1H), 2.19 – 1.97 (m, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 175.42, 170.29, 137.28, 136.83, 129.86, 128.17, 127.21, 126.38, 122.42, 122.11, 119.50, 119.41, 116.84, 111.44, 65.69, 62.51, 57.21, 52.23, 40.80, 32.69, 29.76 ppm. HRMS (ESI) m/z: calculated for $C_{23}H_{26}N_3O_3^+$ $[M + H]^+$: 392.1974, found: 392.1966. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 8.494 min, $t_R$ (minor diastereomer) = 12.104 min, 95:5 dr.



**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-alaninate 3o.**

Colorless oil, combined yield 62%. $[\alpha]^{25}_{D}$ = + 59.6 (c = 0.064, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.39 (br, 1H), 8.04 (d, J = 6.2 Hz, 1H), 7.77 (d, J = 7.9 Hz, 1H), 7.46 – 7.37 (m, 2H), 7.25 – 7.13 (m, 7H), 4.32 – 4.24 (m, 1H), 4.23 – 4.16 (m, 1H), 4.00 (d,

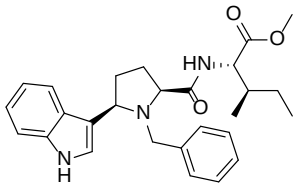
J = 13.2 Hz, 1H), 3.75 (s, 3H), 3.60 (d, J = 13.2 Hz, 1H), 3.52 – 3.44 (m, 1H), 2.35 – 2.22 (m, 1H), 2.20 – 2.13 (m, 1H), 2.08 – 1.96 (m, 2H), 1.38 (d, J = 7.1 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 175.02, 173.24, 136.90, 136.76, 130.08, 128.04, 127.16, 126.32, 122.13, 119.37, 117.01, 111.46, 65.35, 62.00, 56.70, 52.30, 47.71, 32.75, 29.75, 18.58 ppm. HRMS (ESI) m/z: calculated for $C_{24}H_{27}N_3O_3Na^+$ $[M + Na]^+$: 428.1950, found: 428.1916. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 8.535 min, $t_R$ (minor diastereomer) = 15.712 min, >94:6 dr.




**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-valinate 3p.**

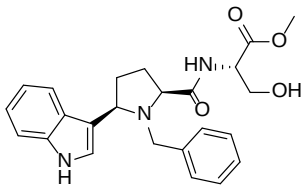
Colorless oil, combined yield 58%. $[\alpha]^{25}_D$ = + 55.8 (c = 0.1, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.33 (br, 1H), 8.11 (d, J = 8.5 Hz, 1H), 7.75 (d, J = 7.9 Hz, 1H), 7.47 – 7.38 (m, 2H), 7.26 – 7.12 (m, 7H), 4.44 – 4.37 (m, 1H), 4.27 – 4.20 (m, 1H), 3.99 (d, J = 13.3 Hz, 1H), 3.75 (s, 3H), 3.70 (d, J = 13.3 Hz, 1H), 3.56 – 3.48 (m, 1H), 2.33 – 2.12 (m, 3H), 2.05 – 1.89 (m, 2H), 0.94 – 0.88 (m, 6H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 175.14, 172.14, 136.85, 136.35, 130.14, 128.05, 127.17, 126.41, 122.17, 121.62, 119.38, 119.30, 117.28, 111.42, 65.10, 61.53, 56.50, 56.32, 51.96, 33.15, 31.64, 30.11, 18.80, 17.81 ppm. HRMS (ESI) m/z: calculated for $C_{26}H_{31}N_3O_3Na^+$ [M

+ Na]$^+$: 456.2263, found: 456.2258. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 13.557 min, $t_R$ (minor diastereomer) = 27.517 min, >94:6 dr.



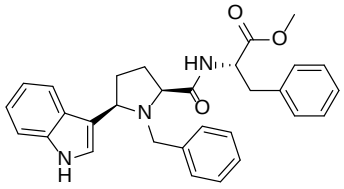

**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-alloisoleucinate 3q.**

Colorless oil, combined yield 61%. $[\alpha]^{25}_D$ = + 34.2 (c = 0.22, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.31 (br, 1H), 8.10 (d, J = 8.7 Hz, 1H), 7.75 (d, J = 7.9 Hz, 1H), 7.49 – 7.36 (m, 2H), 7.25 – 7.12 (m, 7H), 4.47 – 4.40 (m, 1H), 4.26 – 4.18 (m, 1H), 3.99 (d, J = 13.2 Hz, 1H), 3.75 (s, 3H), 3.69 (d, J = 13.2 Hz, 1H), 3.55 – 3.48 (m, 1H), 2.33 – 2.17 (m, 2H), 2.04 – 1.85 (m, 3H), 1.51 – 1.38 (m, 1H), 1.22 – 1.08 (m, 1H), 0.95 – 0.85 (m, 6H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.95, 172.10, 136.88, 136.36, 130.16, 128.05, 127.18, 126.41, 122.18, 121.72, 119.38, 119.35, 117.27, 111.44, 65.10, 61.54, 56.30, 55.91, 51.91, 38.23, 33.09, 30.04, 25.29, 15.31, 11.72 ppm. HRMS (ESI) m/z: calculated for $C_{27}H_{34}N_3O_3^+$ [M + H]$^+$: 448.2600, found: 448.2604. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 5.54 min, $t_R$ (minor diastereomer) = 8.745 min, 95:5 dr.



**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-serinate 3r.**

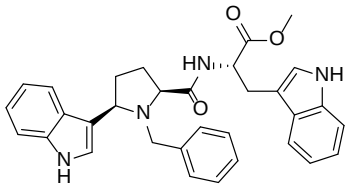
Colorless oil, combined yield 55%. $[\alpha]^{25}_{D}$ = + 34.5 (c = 0.34, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.46 (br, 1H), 8.32 (d, J = 5.7 Hz, 1H), 7.75 (d, J = 7.9 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.26 – 7.11 (m, 7H), 4.25 – 4.19 (m, 1H), 4.18 – 4.12 (m, 1H), 4.02 (d, J = 13.0 Hz, 1H), 3.86 – 3.82 (m, 2H), 3.77 (s, 3H), 3.55 (d, J = 13.0 Hz, 1H), 3.53 – 3.46 (m, 1H), 2.37 – 2.23 (m, 1H), 2.23 – 2.13 (m, 1H), 2.08 – 1.91 (m, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 176.62, 170.46, 137.09, 136.74, 129.99, 128.11, 127.27, 126.45, 122.12, 119.43, 119.20, 116.97, 111.43, 65.66, 63.95, 62.32, 57.31, 55.26, 52.66, 32.99, 29.91 ppm. HRMS (ESI) m/z: calculated for $C_{24}H_{28}N_3O_4^+$ $[M + H]^+$: 422.2080, found: 422.2089. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 7.119 min, $t_R$ (minor diastereomer) = 9.719 min, 96:4 dr.



**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-phenylalaninate 3s.**

Colorless oil, combined yield 76%. $[\alpha]^{25}_{D}$ = + 31.3 (c = 0.24, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.19 (br, 1H), 7.95 (d, J = 6.9 Hz, 1H), 7.50 (d, J = 7.8 Hz, 1H), 7.39

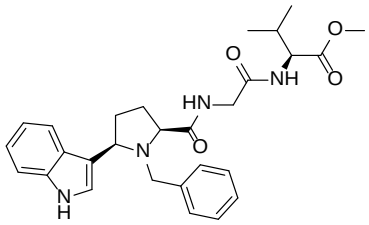
(d, J = 8.3 Hz, 1H), 7.25 – 7.18 (m, 4H), 7.17 – 7.12 (m, 3H), 7.11 – 7.03 (m, 5H), 7.02 (t, J = 7.4 Hz, 1H), 4.67 – 4.57 (m, 1H), 4.18 – 4.08 (m, 1H), 3.89 (d, J = 13.1 Hz, 1H), 3.73 (s, 3H), 3.55 (d, J = 13.1 Hz, 1H), 3.51 – 3.42 (m, 1H), 3.26 – 3.17 (m, 1H), 3.13 – 3.04 (m, 1H), 2.33 – 2.19 (m, 1H), 2.17 – 2.05 (m, 1H), 2.00 – 1.81 (m, 2H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.78, 171.59, 136.71, 136.51, 135.98, 130.11, 129.31, 128.38, 127.94, 127.11, 126.97, 126.30, 122.14, 122.01, 119.41, 119.34, 116.84, 111.26, 65.15, 61.73, 56.51, 52.73, 52.13, 37.88, 32.80, 29.74 ppm. HRMS (ESI) m/z: calculated for $C_{30}H_{32}N_3O_3^+$ $[M + H]^+$: 482.2444, found: 482.2453. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 15.998 min, $t_R$ (minor diastereomer) = 35.412 min, >96:4 dr.




**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-tryptophanate 3t.**

Dark red oil, combined yield 59%. $[\alpha]^{25}_D$ = - 7.1 (c = 0.22, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$) δ 8.33 (br, 1H), 8.23 (s, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 7.9 Hz, 1H), 7.57 (d, J = 7.9 Hz, 1H), 7.42 – 7.33 (m, 2H), 7.24 – 7.18 (m, 2H), 7.16 – 7.05 (m, 5H), 6.99 – 6.93 (m, 2H), 6.89 – 6.82 (m, 2H), 4.80 – 4.73 (m, 1H), 4.19 – 4.11 (m, 1H), 3.73 – 3.67 (m, 2H), 3.63 (s, 3H), 3.59 – 3.53 (m, 1H), 3.50 (d, J = 13.5 Hz, 1H), δ 3.18 (dd, J = 14.9, 5.8 Hz, 1H), 3.09 (dd, J = 14.9, 6.3 Hz, 1H), 2.22 – 2.04

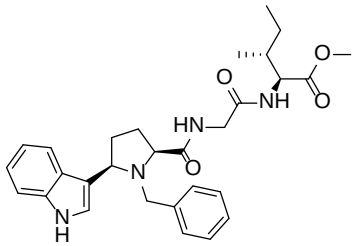
(m, 3H), 1.95 – 1.85 (m, 1H) ppm. $^{13}$C NMR (125MHz, $CDCl_3$) δ 175.27, 172.76, 136.74, 136.56, 136.19, 136.09, 129.83, 128.23, 127.57, 127.24, 126.58, 122.77, 122.20, 122.09, 121.94, 119.64, 119.34, 119.13, 118.80, 117.01, 111.31, 111.19, 110.06, 65.11, 61.31, 56.32, 52.23, 32.91, 29.99, 27.48 ppm. HRMS (ESI) m/z: calculated for $C_{32}H_{32}N_4O_3Na^+$ $[M + Na]^+$: 543.2372, found: 543.2361. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 13.21 min, $t_R$ (minor diastereomer) = 21.701 min, >97:3 dr.




**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)glycyl-L-valinate 3u.**

Colorless oil, combined yield 47%. $[\alpha]^{25}_D$ = + 22.2 (c = 0.24, $CHCl_3$). $^1$H NMR (600 MHz, $CDCl_3$) δ 8.45 (br, 1H), 7.85 – 7.78 (m, 1H), 7.72 (d, J = 7.9 Hz, 1H), 7.45 – 7.42 (m, 2H), 7.34 – 7.30 (m, 1H), 7.23 – 7.16 (m, 4H), 7.13 – 7.07 (m, 2H), 6.80 (d, J = 8.5 Hz, 1H), 4.51 (dd, J = 8.7, 5.0 Hz, 1H), 4.22 – 4.15 (m, 1H), 4.00 (d, J = 12.1 Hz, 1H), 3.86 (dd, J = 16.4, 6.1 Hz, 1H), 3.69 (s, 3H), 3.52 – 3.45 (m, 2H), 3.34 (dd, J = 16.4, 4.7 Hz, 1H), 2.37 – 2.28 (m, 1H), 2.20 – 2.13 (m, 2H), 2.06 – 1.98 (m, 2H), 0.95 (d, J = 6.9 Hz, 3H), 0.91 (d, J = 6.9 Hz, 3H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$) δ 176.24, 172.07, 169.05, 137.44, 136.74, 129.73, 128.31, 127.31, 126.48, 122.38,

122.13, 119.57, 119.09, 116.73, 111.47, 65.89, 62.56, 57.52, 57.18, 52.12, 43.00, 32.78, 31.02, 29.86, 18.92, 17.69 ppm. HRMS (ESI) m/z: calculated for $C_{28}H_{35}N_4O_4^+$ $[M + H]^+$: 491.2658, found: 491.2644. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 11.094 min, $t_R$ (minor diastereomer) = 17.325 min, 95:5 dr.




**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)glycyl-L-alloisleucinate 3v.**

Colorless oil, combined yield 42%. $[\alpha]^{25}_D$ = + 31.5 (c = 0.24, $CHCl_3$). $^1$H NMR (600 MHz, $CDCl_3$) δ 8.43 (br, 1H), 7.83 – 7.77 (m, 1H), 7.72 (d, J = 7.9 Hz, 1H), 7.44 – 7.41 (m, 2H), 7.34 – 7.31 (m, 1H), 7.23 – 7.15 (m, 4H), 7.12 – 7.07 (m, 2H), 6.80 (d, J = 8.5 Hz, 1H), 4.56 (dd, J = 8.6, 4.9 Hz, 1H), 4.21 – 4.17 (m, 1H), 4.00 (d, J = 12.9 Hz, 1H), 3.85 (dd, J = 16.4, 6.2 Hz, 1H), 3.69 (s, 3H), 3.52 – 3.45 (m, 2H), 3.33 (dd, J = 16.4, 5.0 Hz, 1H), 2.38 – 2.26 (m, 1H), 2.21 – 2.12 (m, 1H), 2.08 – 1.98 (m, 2H), 1.91 – 1.88 (m, 1H), 1.45 – 1.37 (m, 1H), 1.21 – 1.14 (m, 1H), 0.94 – 0.88 (m, 6H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$) δ 176.23, 172.05, 168.94, 137.43, 136.75, 129.73, 128.30, 127.31, 126.47, 122.38, 122.14, 119.58, 119.11, 116.73, 111.46, 65.88, 62.55, 57.51, 56.51, 52.07, 43.02, 37.66, 32.76, 29.86, 25.04, 15.46, 15.43, 11.56, 11.54 ppm.

HRMS (ESI) m/z: calculated for $C_{29}H_{37}N_4O_4^+$ $[M + H]^+$: 505.2815, found: 505.2829. The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 16.001 min, $t_R$ (minor diastereomer) = 28.538 min, 95:5 dr.

**(D) The Absolute Configuration of 3d.**

X-ray Single Crystal Stucture Analysis of **3d**:

X-ray crystallographic data of **3d** were solutions at T = 130 K. $C_{29}H_{37}N_3O_3$, triclinic. Space group P1, a = 13.8032(6) Å, b = 14.0849(6) Å, c = 14.8146(6) Å, α = 89.715(3)°, β = 77.329(3)°, γ = 77.339(3)°, V = 2738.9(2) $Å^3$, Z = 4.

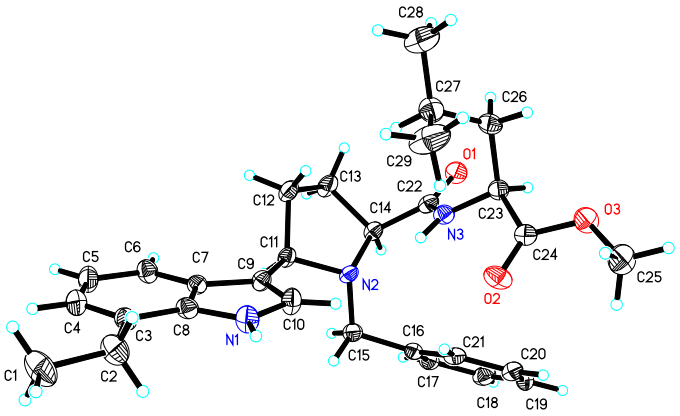


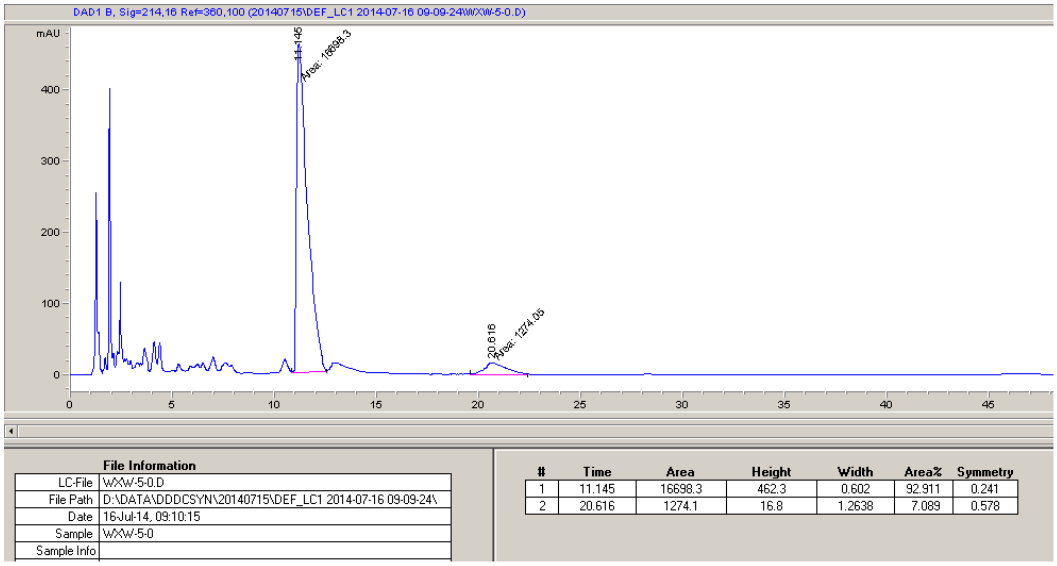

**Figure S1**: The crystal structure of **3d** by X-ray analysis.

These data can be obtained free of charge from the Cambridge Crystallographic Data Centre *via www.ccdc.cam.ac.uk/data_request/cif*, the CCDC number is 1023777.

**(E) HPLC spectra for dr determination.**

**3a/4a**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 11.145 min, $t_R$ (minor diastereomer) = 20.616 min, 93:7 dr.

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| Sample | WXW-5-0 |
| Sample Info | |

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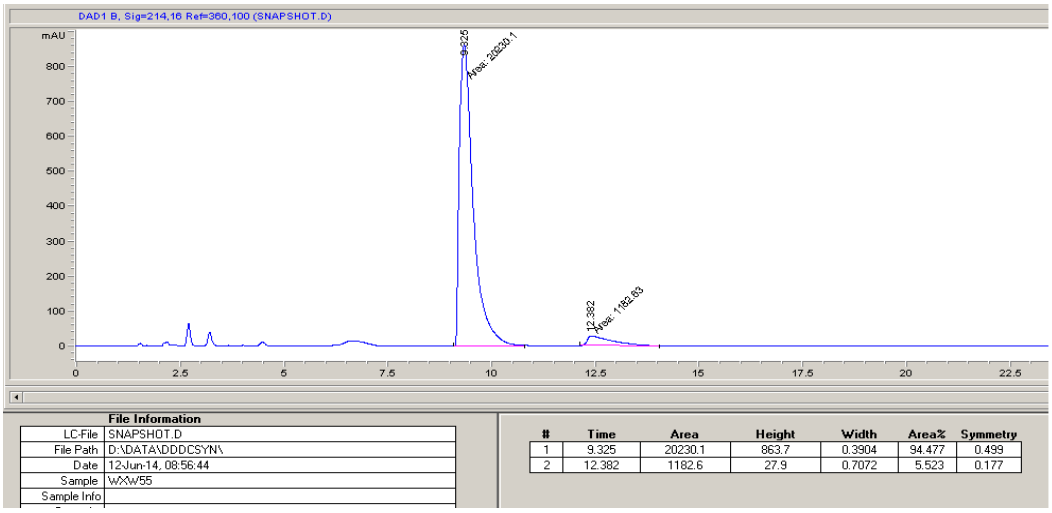
|---|---|---|---|---|---|---|
| 1 | 11.145 | 16698.3 | 462.3 | 0.602 | 92.911 | 0.241 |
| 2 | 20.616 | 1274.1 | 16.8 | 1.2638 | 7.089 | 0.578 |

**3b/4b**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 9.325 min, $t_R$ (minor diastereomer) = 12.382 min, 94:6 dr.

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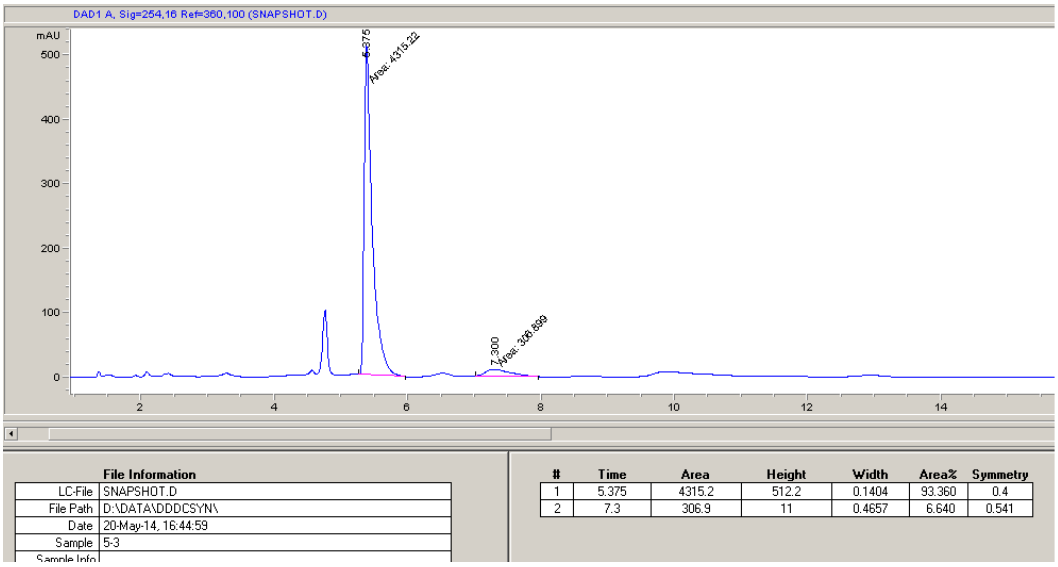
| Sample | WXW55 |
| Sample Info | |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.325 | 20230.1 | 863.7 | 0.3904 | 94.477 | 0.499 |
| 2 | 12.382 | 1182.6 | 27.9 | 0.7072 | 5.523 | 0.177 |

**3c/4c**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 5.375 min, $t_R$ (minor diastereomer) = 7.3 min, 93:7 dr.

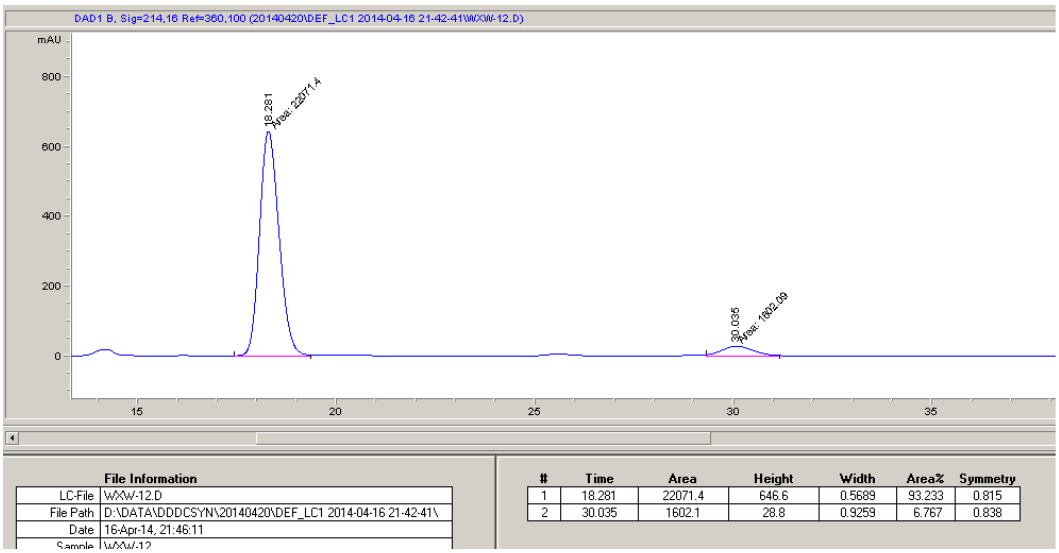



| File Information | |
|---|---|
| LC-File | SNAPSHOT.D |
| File Path | D:\DATA\DDDCSYN\ |
| Date | 20-May-14, 16:44:59 |
| Sample | 5-3 |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.375 | 4315.2 | 512.2 | 0.1404 | 93.360 | 0.4 |
| 2 | 7.3 | 306.9 | 11 | 0.4657 | 6.640 | 0.541 |

**3d/4d**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 18.281 min, $t_R$ (minor diastereomer) = 30.035 min, 93:7 dr.

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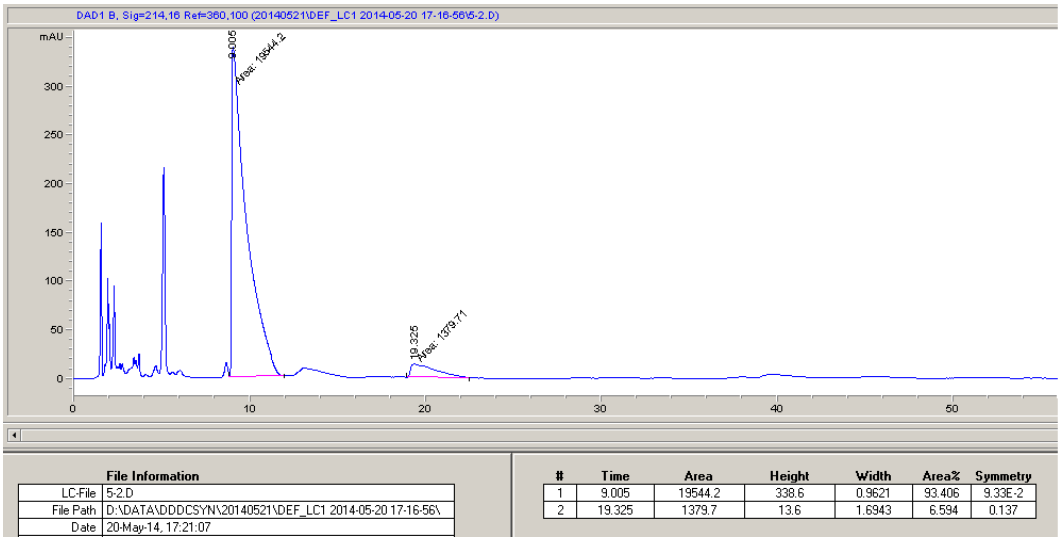
| Sample | WXW-12 |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 18.281 | 22071.4 | 646.6 | 0.5689 | 93.233 | 0.815 |
| 2 | 30.035 | 1602.1 | 28.8 | 0.9259 | 6.767 | 0.838 |

**3e/4e**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 9.005 min, $t_R$ (minor diastereomer) = 19.325 min, 93:7 dr.

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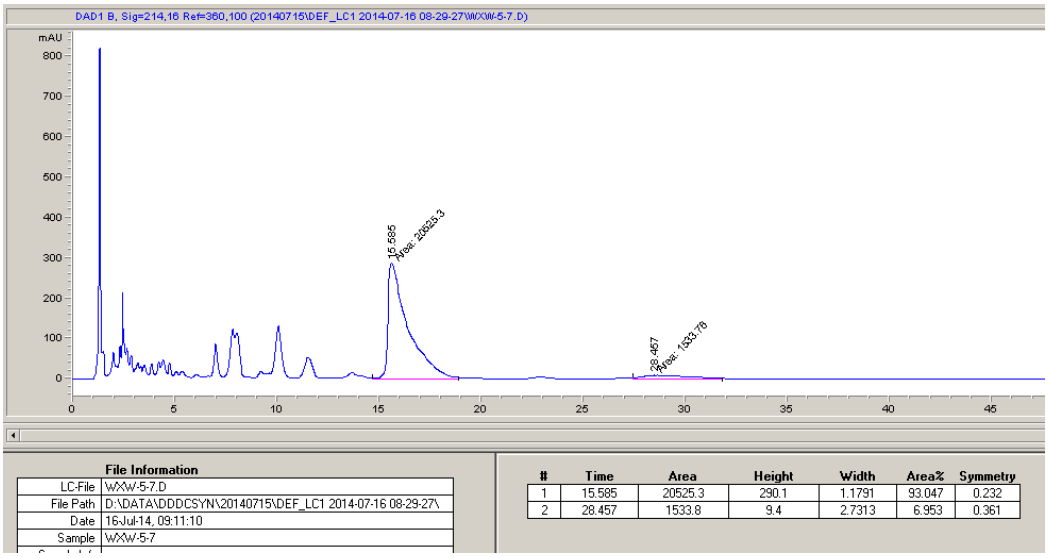
| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.005 | 19544.2 | 338.6 | 0.9621 | 93.406 | 9.33E-2 |
| 2 | 19.325 | 1379.7 | 13.6 | 1.6943 | 6.594 | 0.137 |

**3f/4f**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 15.585 min, $t_R$ (minor diastereomer) = 28.457 min, 93:7 dr.

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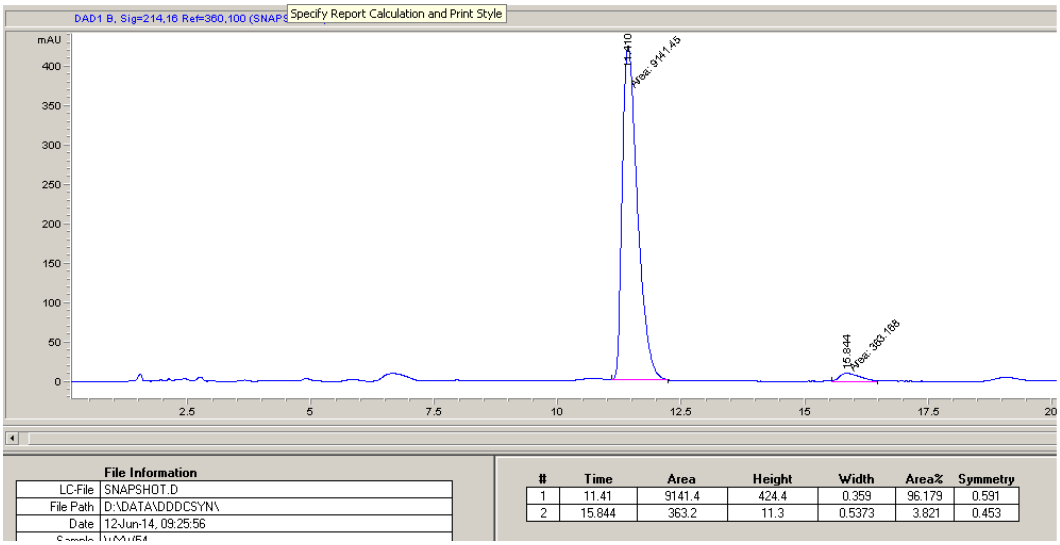
| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 15.585 | 20525.3 | 290.1 | 1.1791 | 93.047 | 0.232 |
| 2 | 28.457 | 1533.8 | 9.4 | 2.7313 | 6.953 | 0.361 |

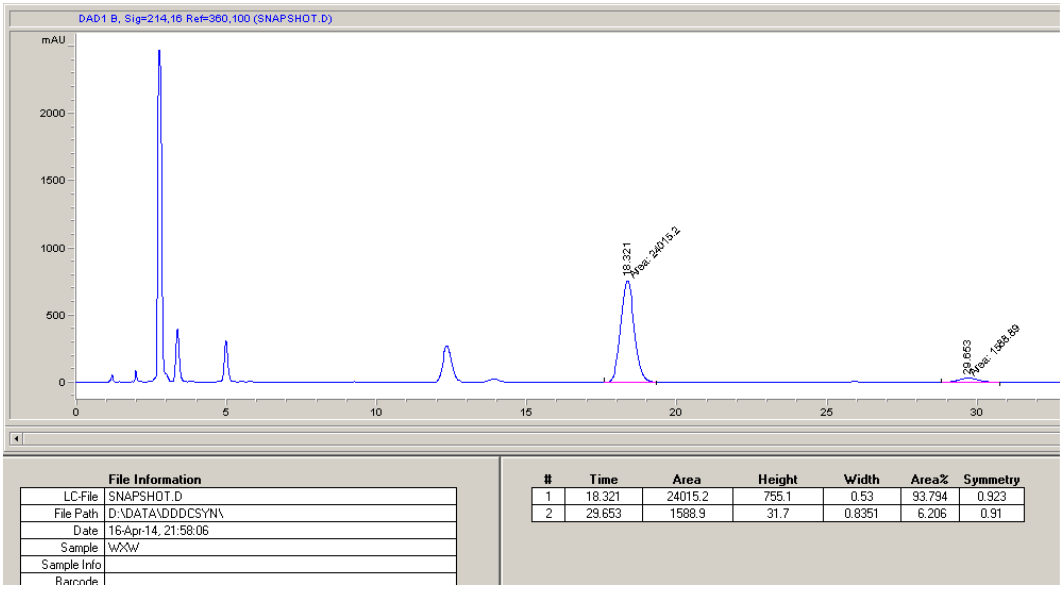
**3g/4g**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 11.41 min, $t_R$ (minor diastereomer) = 15.844 min, 96:4 dr.



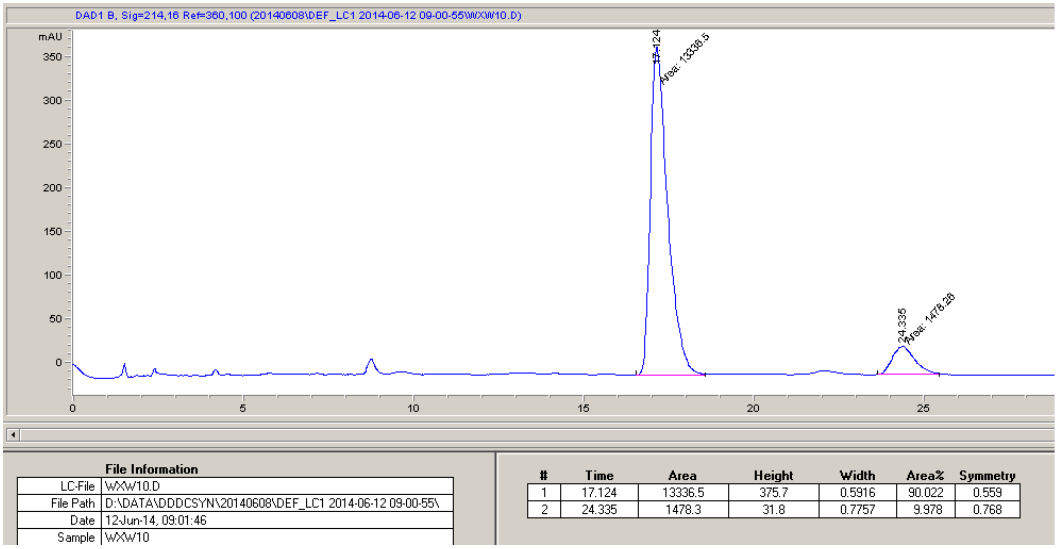

**3h/4h**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 18.321 min, $t_R$ (minor diastereomer) = 29.653 min, >93:7 dr.



**3i/4i**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 17.124 min, $t_R$ (minor diastereomer) = 24.335 min, 90:10 dr.

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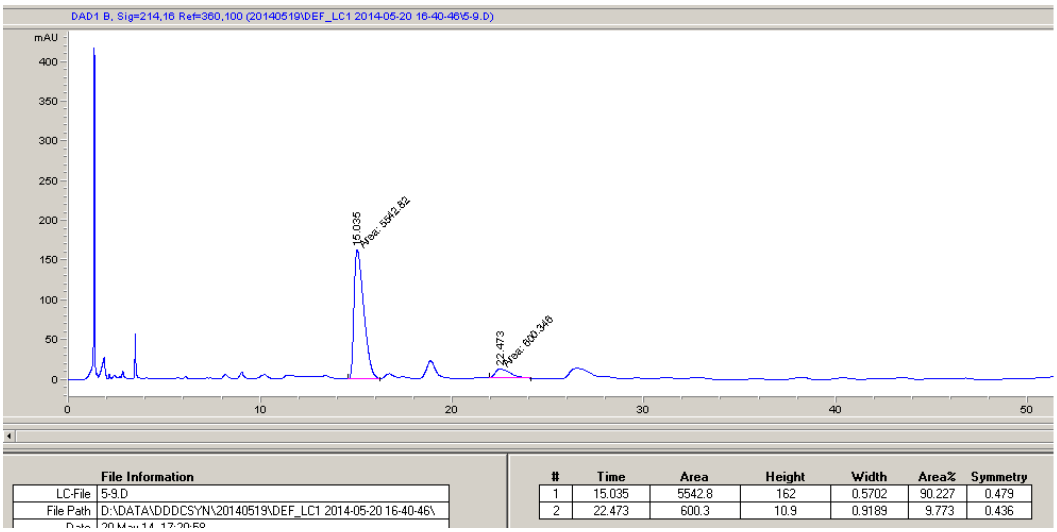
|---|---|---|---|---|---|---|
| 1 | 17.124 | 13336.5 | 375.7 | 0.5916 | 90.022 | 0.559 |
| 2 | 24.335 | 1478.3 | 31.8 | 0.7757 | 9.978 | 0.768 |

**3j/4j**

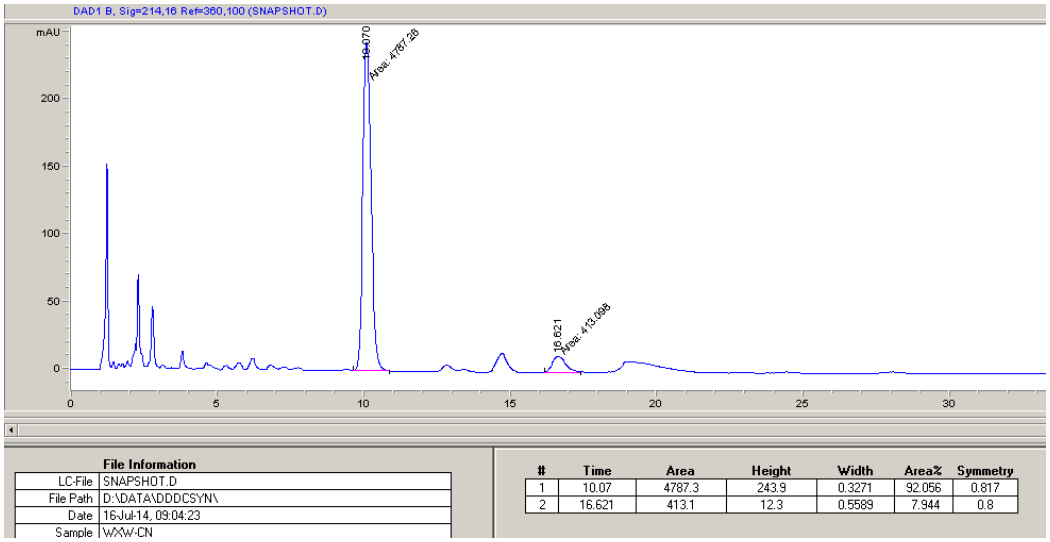
The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 15.035 min, $t_R$ (minor diastereomer) = 22.473 min, 90:10 dr.




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 15.035 | 5542.8 | 162 | 0.5702 | 90.227 | 0.479 |
| 2 | 22.473 | 600.3 | 10.9 | 0.9189 | 9.773 | 0.436 |

**3k/4k**

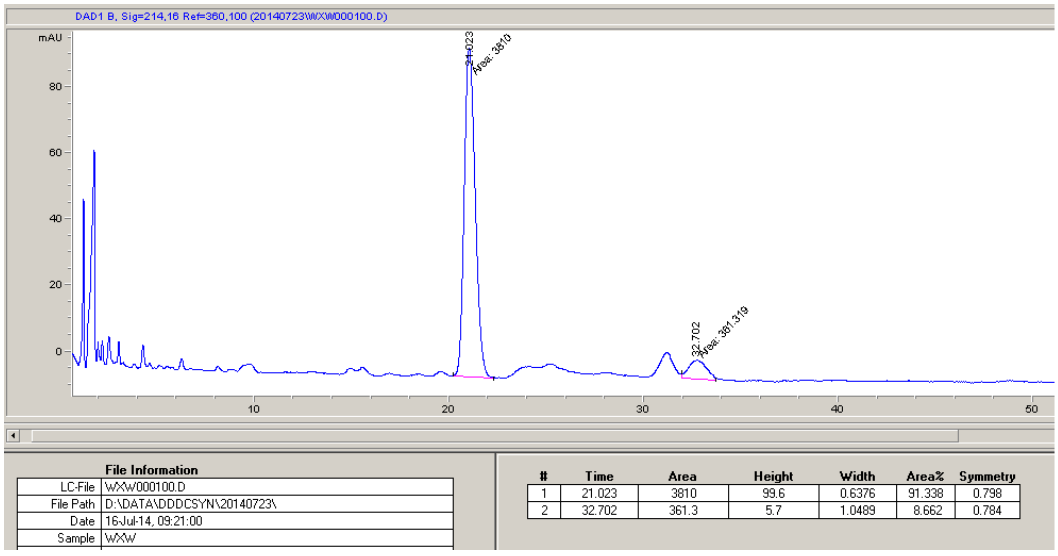
The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 10.07 min, $t_R$ (minor diastereomer) = 16.621 min, 92:8 dr.




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 10.07 | 4787.3 | 243.9 | 0.3271 | 92.056 | 0.817 |
| 2 | 16.621 | 413.1 | 12.3 | 0.5589 | 7.944 | 0.8 |

**3l/4l**

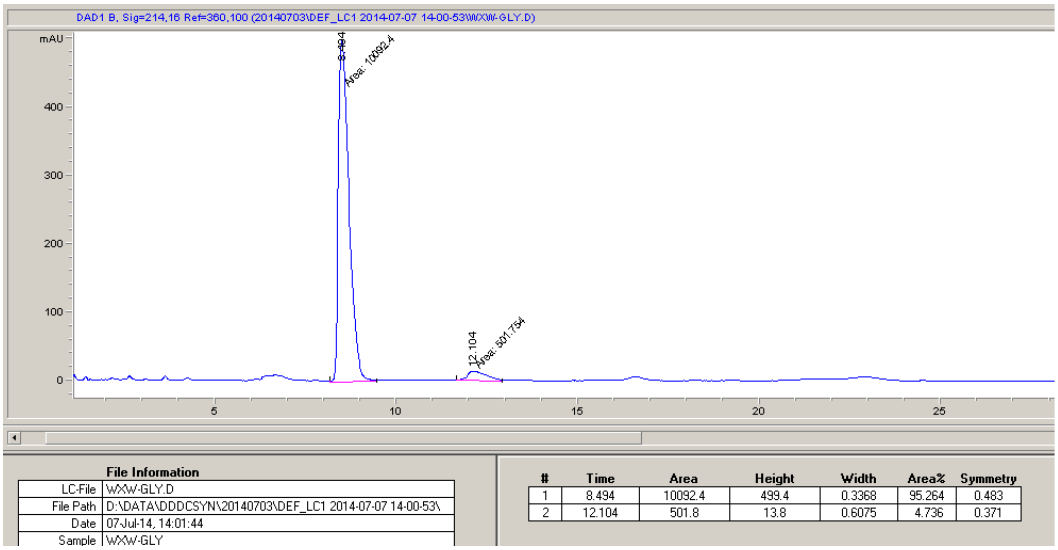
The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 21.023 min, $t_R$ (minor diastereomer) = 32.702 min, 91:9 dr.




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 21.023 | 3810 | 99.6 | 0.6376 | 91.338 | 0.798 |
| 2 | 32.702 | 361.3 | 5.7 | 1.0489 | 8.662 | 0.784 |

**3n/4n**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 8.494 min, $t_R$ (minor diastereomer) = 12.104 min, 95:5 dr.

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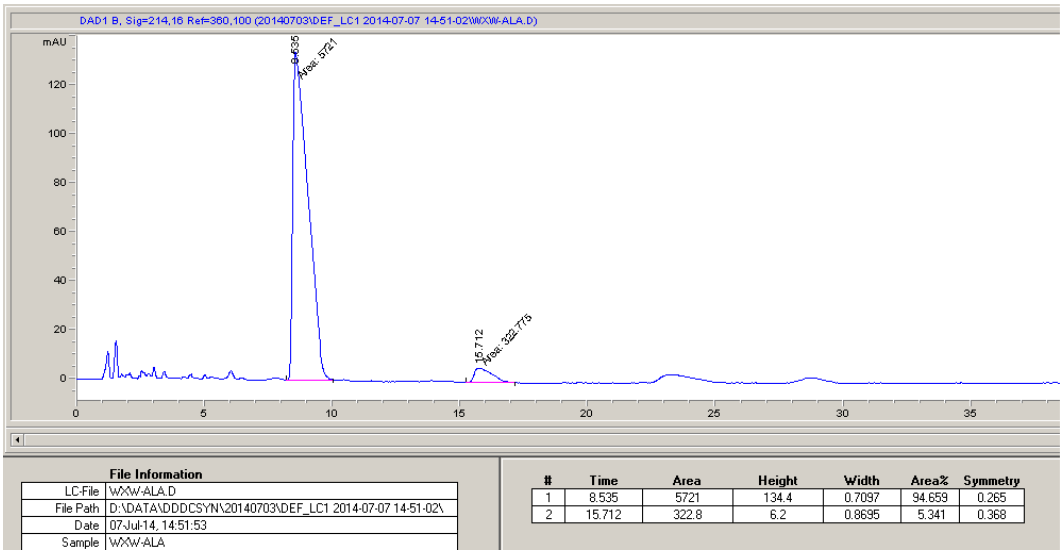
| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 8.494 | 10092.4 | 499.4 | 0.3368 | 95.264 | 0.483 |
| 2 | 12.104 | 501.8 | 13.8 | 0.6075 | 4.736 | 0.371 |

**3o/4o**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 8.535 min, $t_R$ (minor diastereomer) = 15.712 min, >94:6 dr.

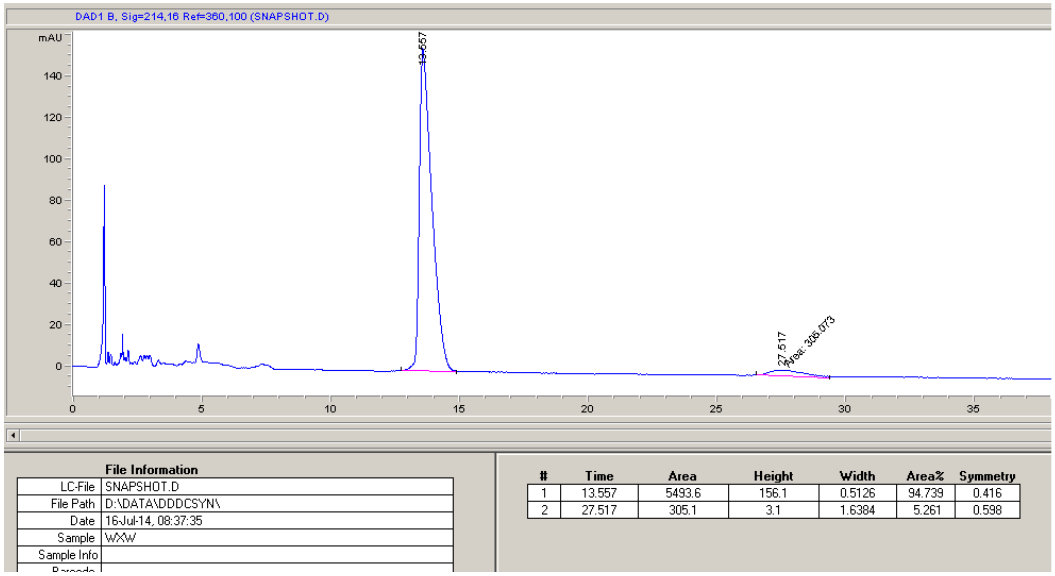



| File Information | |
|---|---|
| LC-File | WXW-ALA.D |
| File Path | D:\DATA\DDDCSYN\20140703\DEF_LC1 2014-07-07 14-51-02\ |
| Date | 07-Jul-14, 14:51:53 |
| Sample | WXW-ALA |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 8.535 | 5721 | 134.4 | 0.7097 | 94.659 | 0.265 |
| 2 | 15.712 | 322.8 | 6.2 | 0.8695 | 5.341 | 0.368 |

**3p/4p**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 13.557 min, $t_R$ (minor diastereomer) = 27.517 min, >94:6 dr.




File Information

| | |
|---|---|
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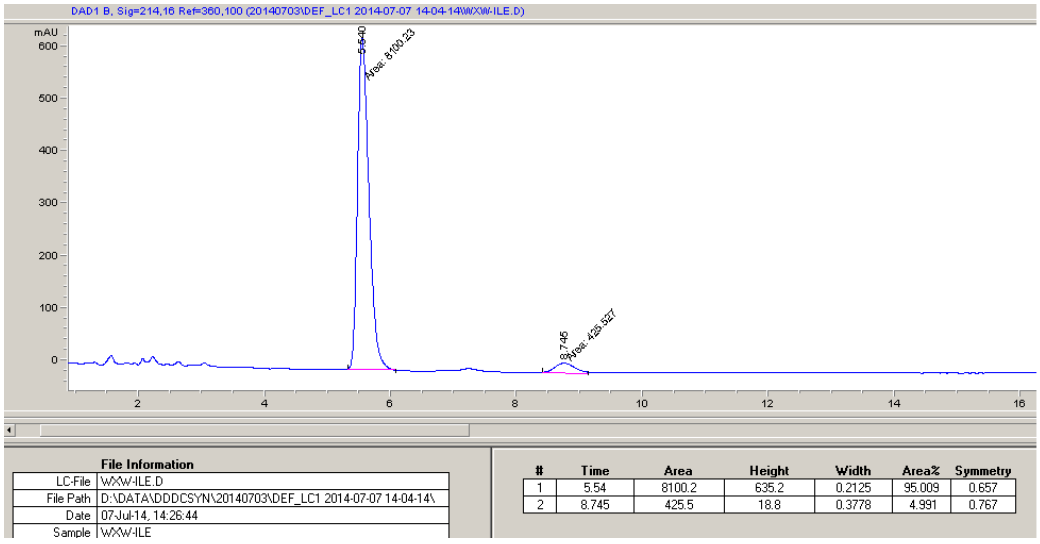
| File Path | D:\DATA\DDDCSYN\ |
| Date | 16-Jul-14, 08:37:35 |
| Sample | WXW |
| Sample Info | |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 13.557 | 5493.6 | 156.1 | 0.5126 | 94.739 | 0.416 |
| 2 | 27.517 | 305.1 | 3.1 | 1.6384 | 5.261 | 0.598 |

**3q/4q**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 5.54 min, $t_R$ (minor diastereomer) = 8.745 min, 95:5 dr.



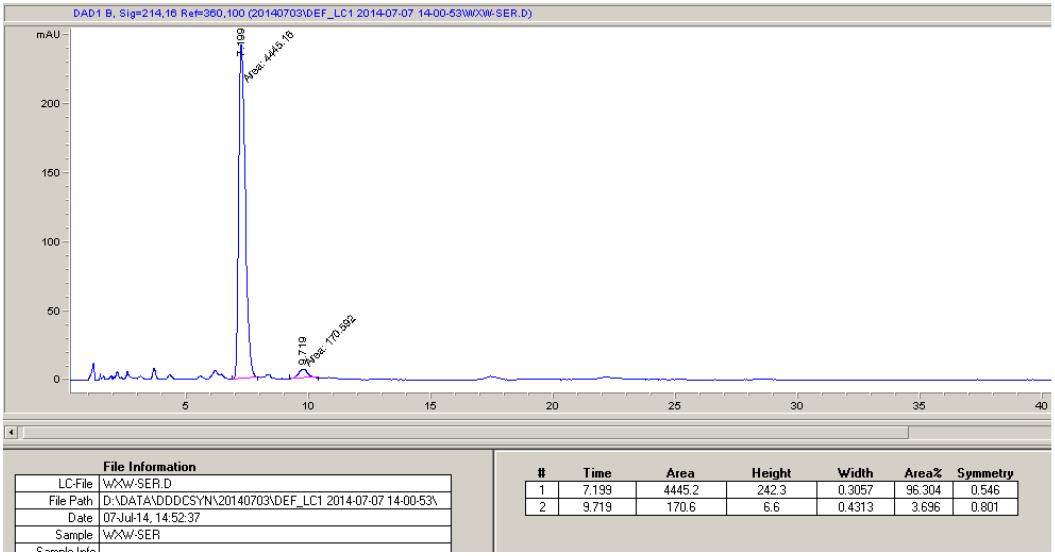

File Information

| | |
|---|---|
| LC-File | WXW-ILE.D |
| File Path | D:\DATA\DDDCSYN\20140703\DEF_LC1 2014-07-07 14-04-14\ |
| Date | 07-Jul-14, 14:26:44 |
| Sample | WXW-ILE |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.54 | 8100.2 | 635.2 | 0.2125 | 95.009 | 0.657 |
| 2 | 8.745 | 425.5 | 18.8 | 0.3778 | 4.991 | 0.767 |

**3r/4r**

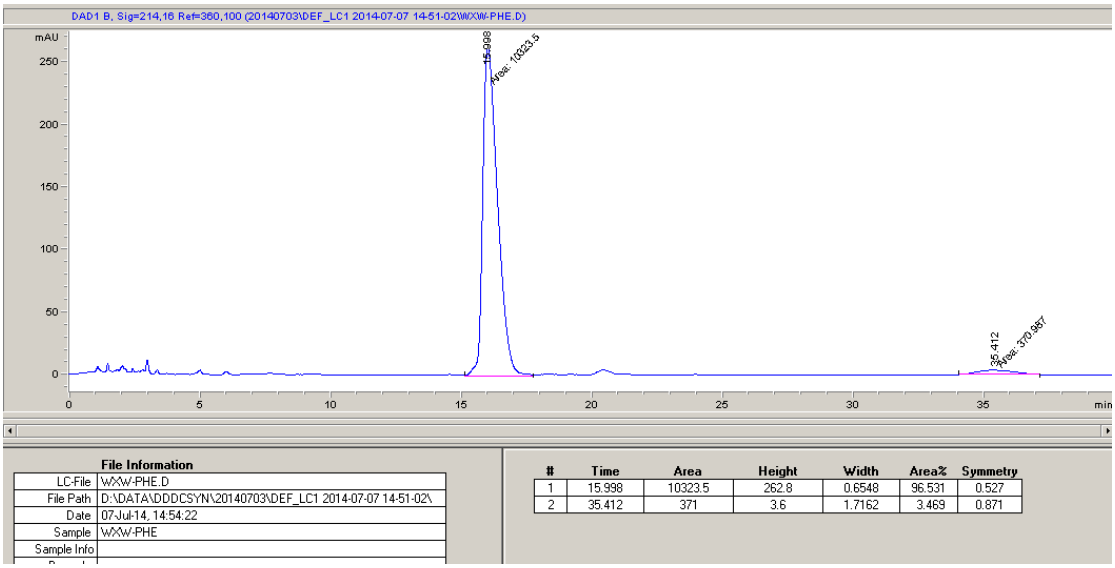
The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 7.119 min, $t_R$ (minor diastereomer) = 9.719 min, 96:4 dr.




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.199 | 4445.2 | 242.3 | 0.3057 | 96.304 | 0.546 |
| 2 | 9.719 | 170.6 | 6.6 | 0.4313 | 3.696 | 0.801 |

**3s/4s**

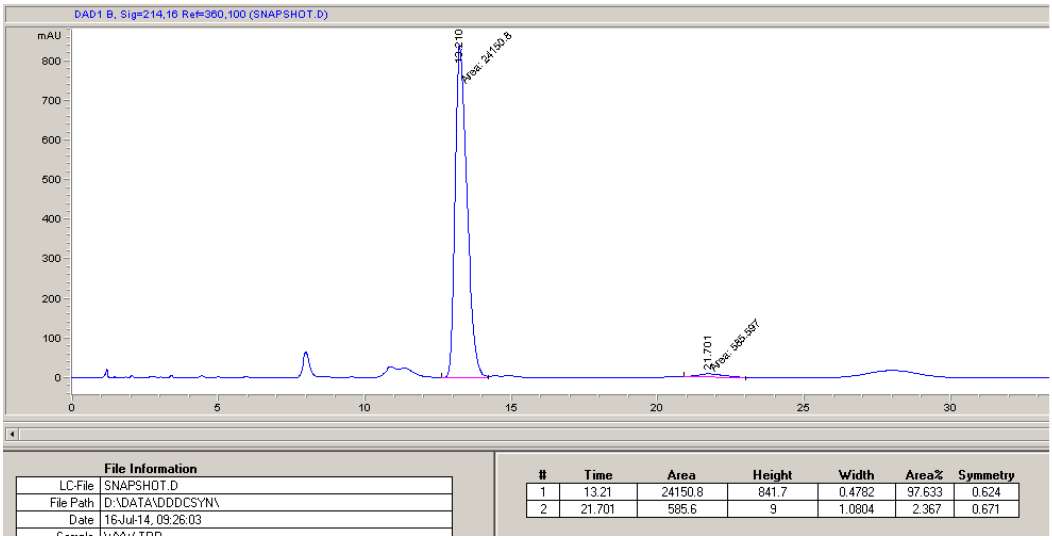
The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 15.998 min, $t_R$ (minor diastereomer) = 35.412 min, >96:4 dr.




| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 15.998 | 10323.5 | 262.8 | 0.6548 | 96.531 | 0.527 |
| 2 | 35.412 | 371 | 3.6 | 1.7162 | 3.469 | 0.871 |

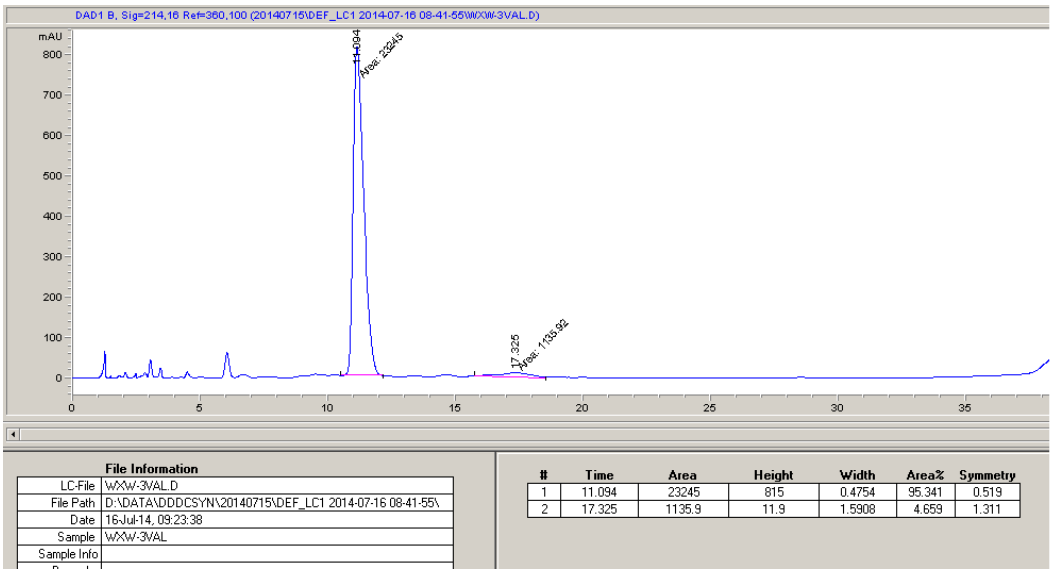
**3t/4t**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 13.21 min, $t_R$ (minor diastereomer) = 21.701 min, >97:3 dr.



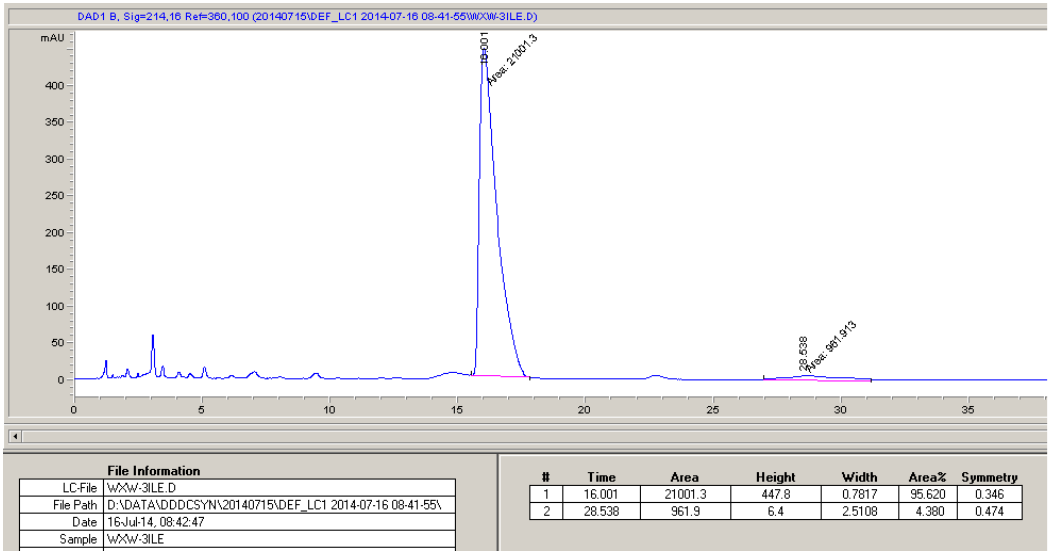

**3u/4u**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 11.094 min, $t_R$ (minor diastereomer) = 17.325 min, 95:5 dr.



**3v/4v**

The dr was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 150 mm) ($H_2O$/MeOH = 30/70, λ = 214 nm, 1.0 mL/min). $t_R$ (major diastereomer) = 16.001 min, $t_R$ (minor diastereomer) = 28.538 min, 95:5 dr.



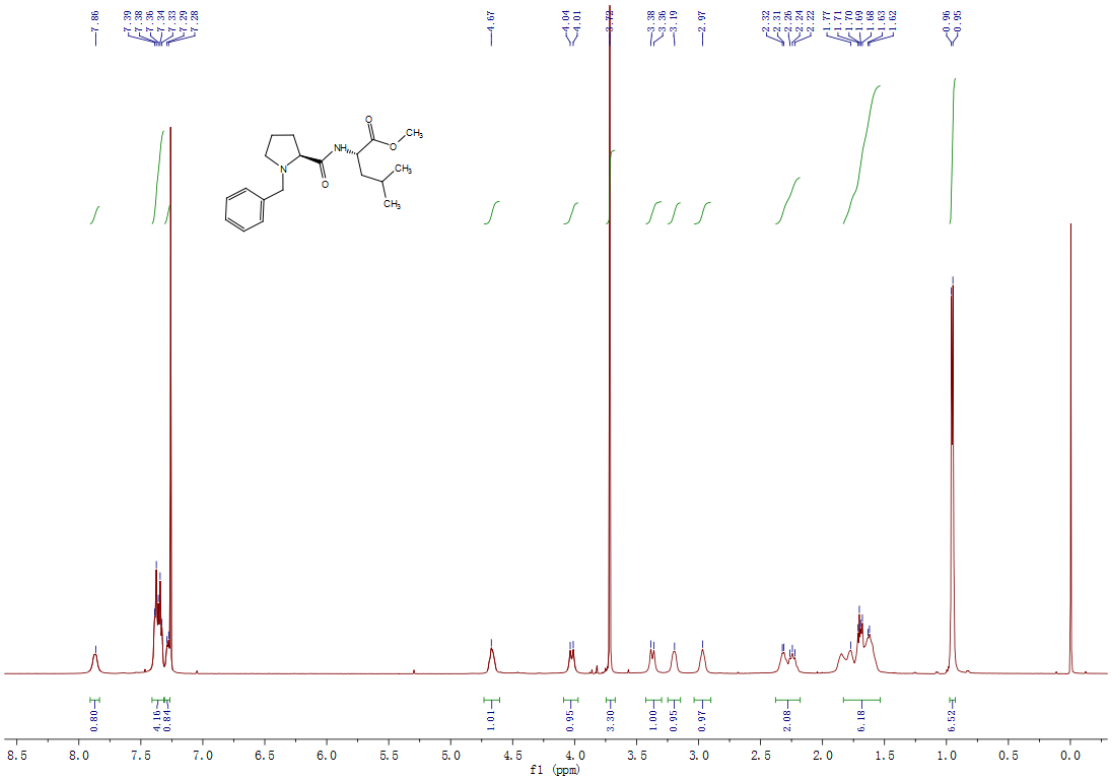

File Information

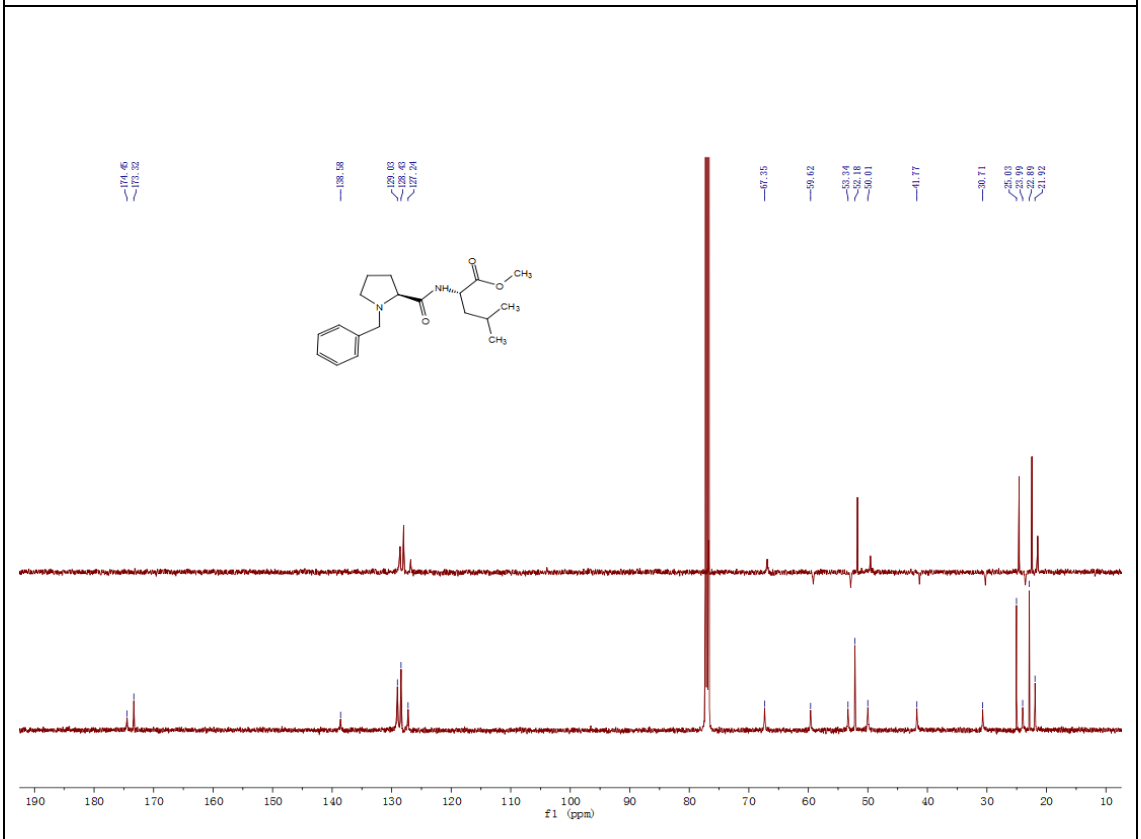
| | |
|---|---|
| LC-File | WXW-3ILE.D |
| File Path | D:\DATA\DDDCSYN\20140715\DEF_LC1 2014-07-16 08-41-55\ |
| Date | 16-Jul-14, 08:42:47 |
| Sample | WXW-3ILE |

| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 16.001 | 21001.3 | 447.8 | 0.7817 | 95.620 | 0.346 |
| 2 | 28.538 | 961.9 | 6.4 | 2.5108 | 4.380 | 0.474 |

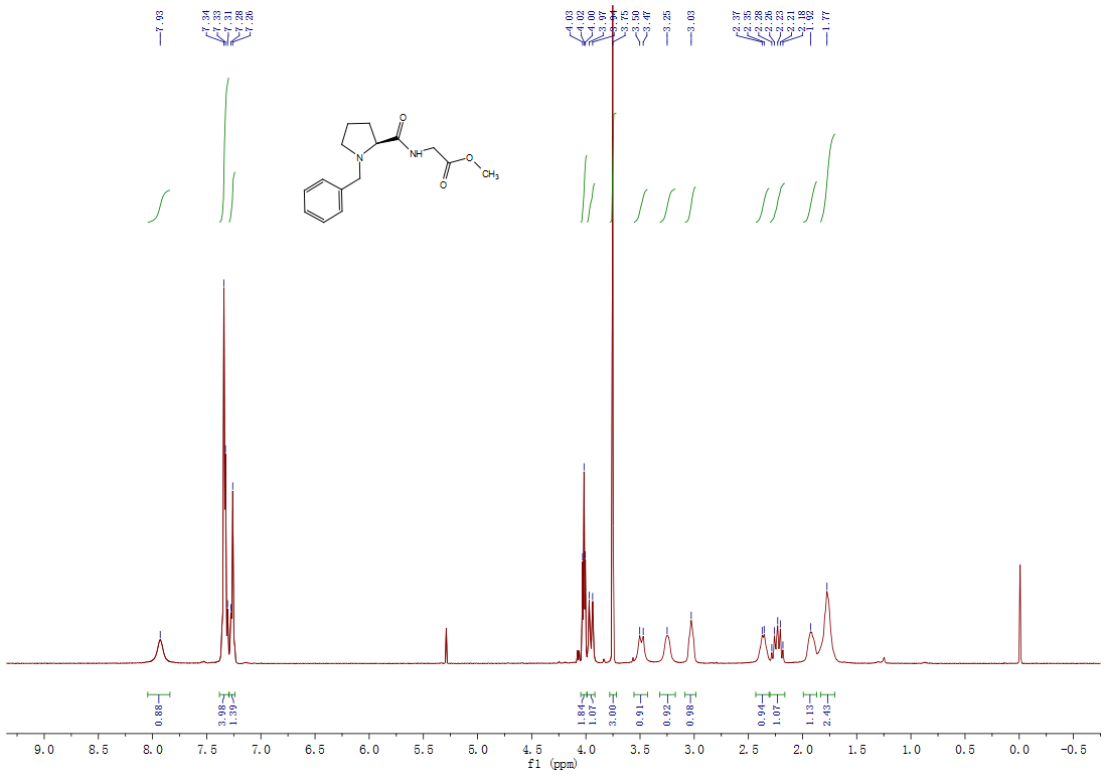
## (F) Copies of $^{1}$H NMR and $^{13}$C NMR Spectra for the Products.

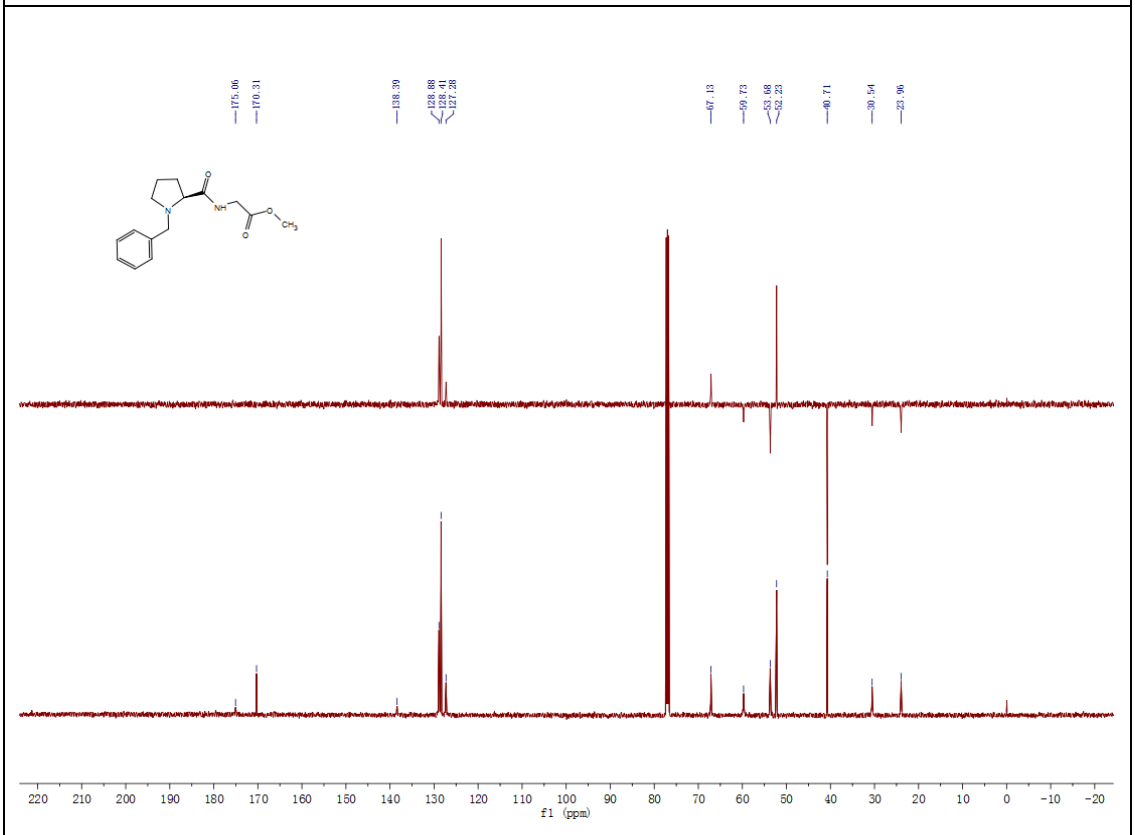
**Methyl benzyl-L-prolyl-L-leucinate 5a:**



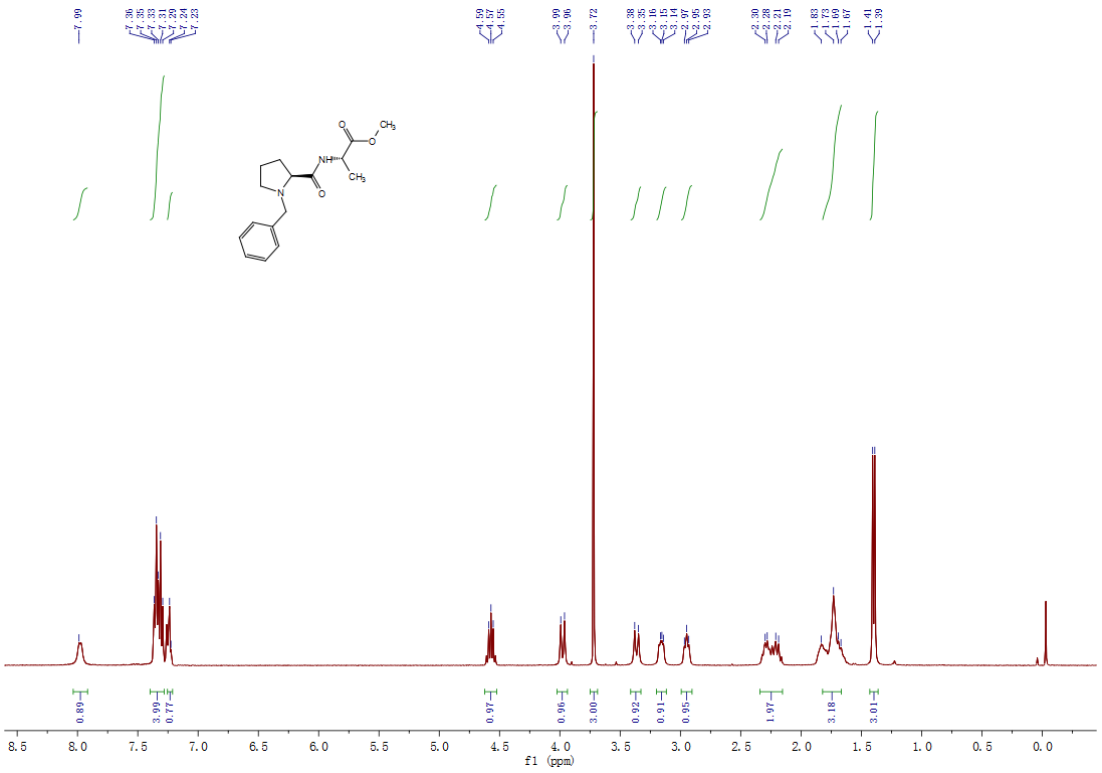


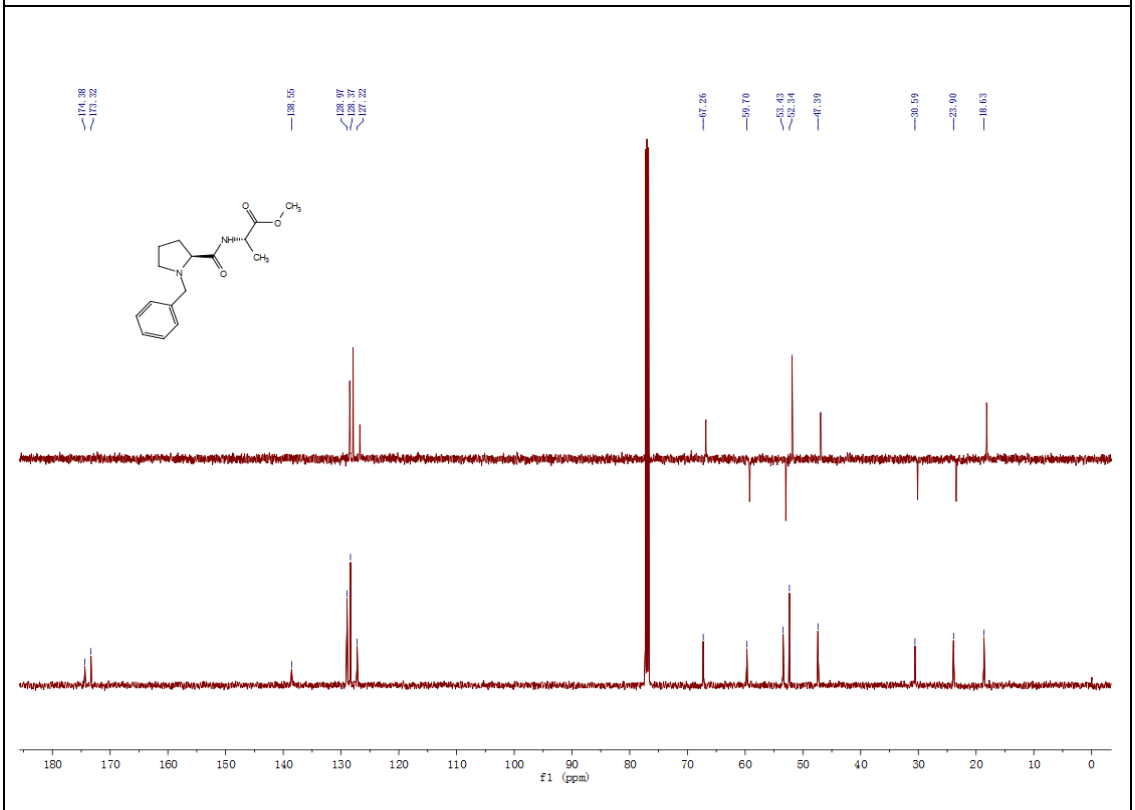
**Methyl benzyl-L-prolylglycinate 5b:**



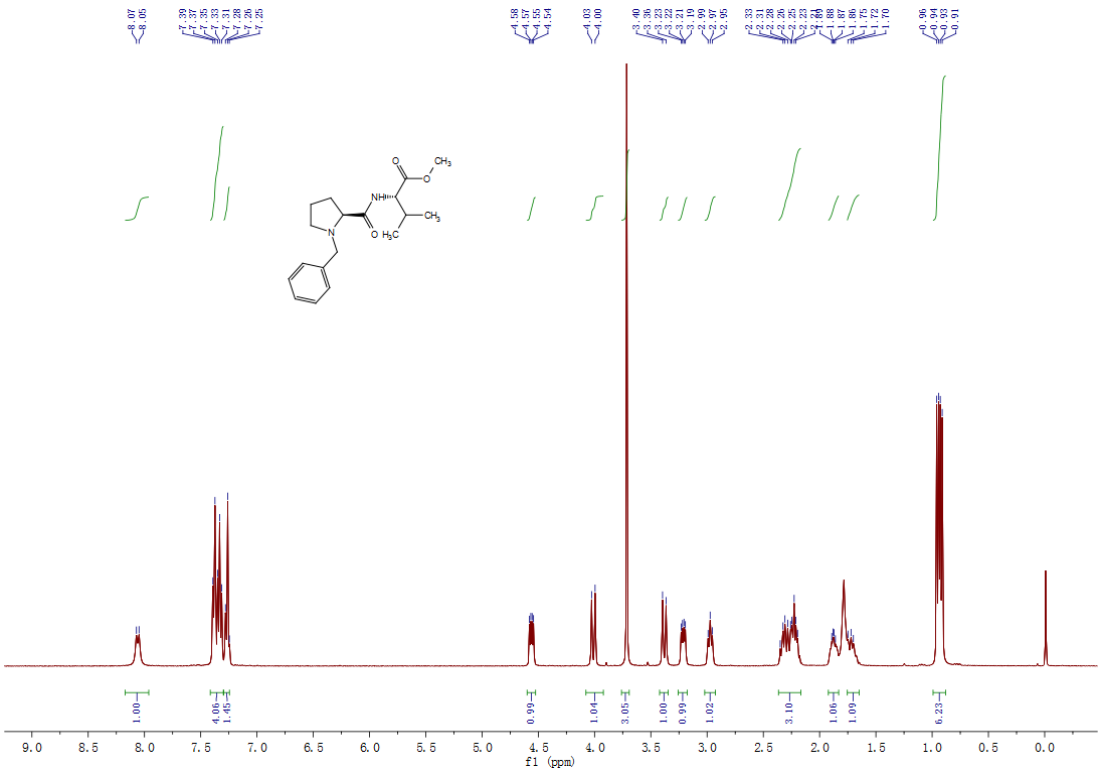



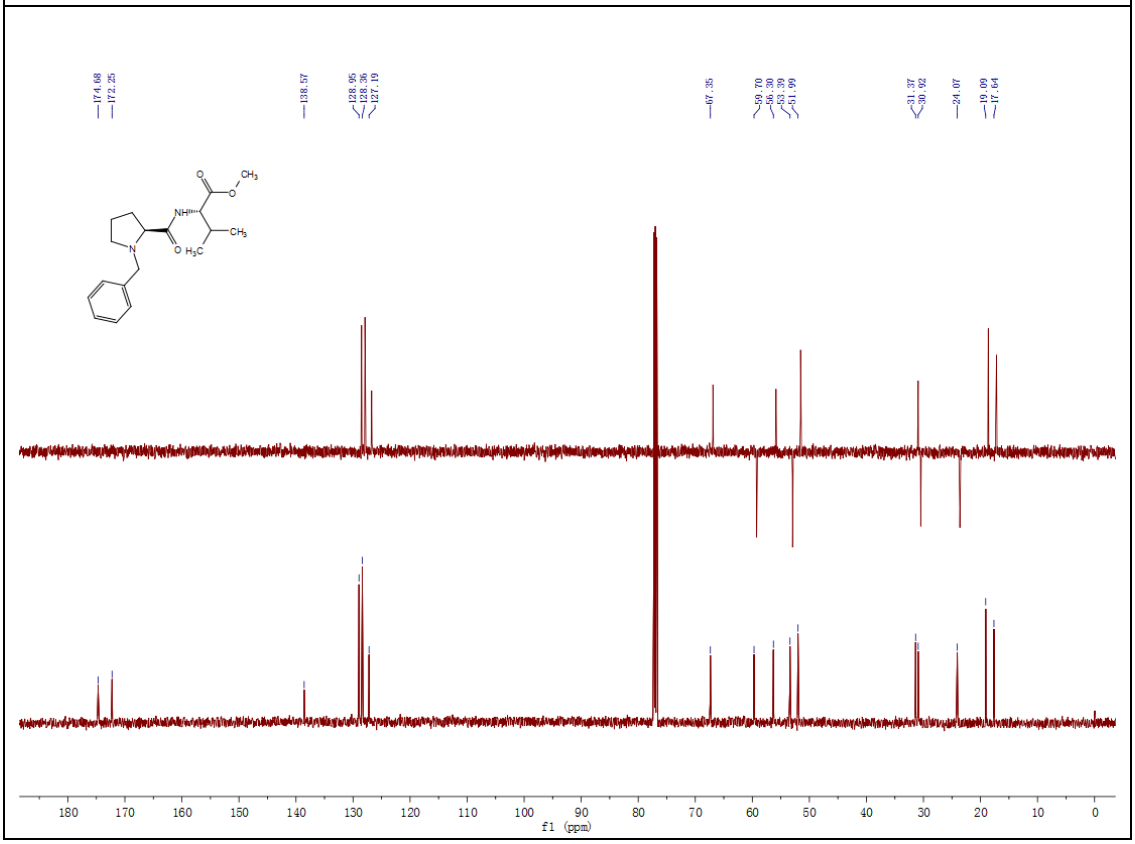
**Methyl benzyl-L-prolyl-L-alaninate 5c:**



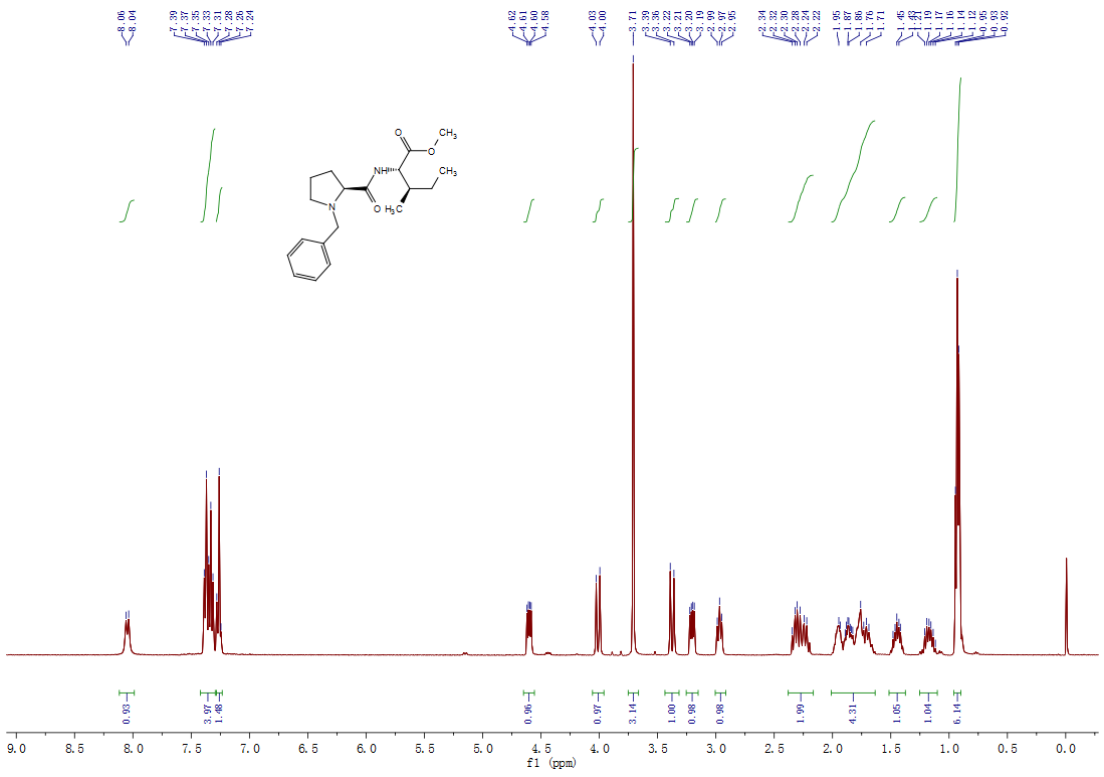



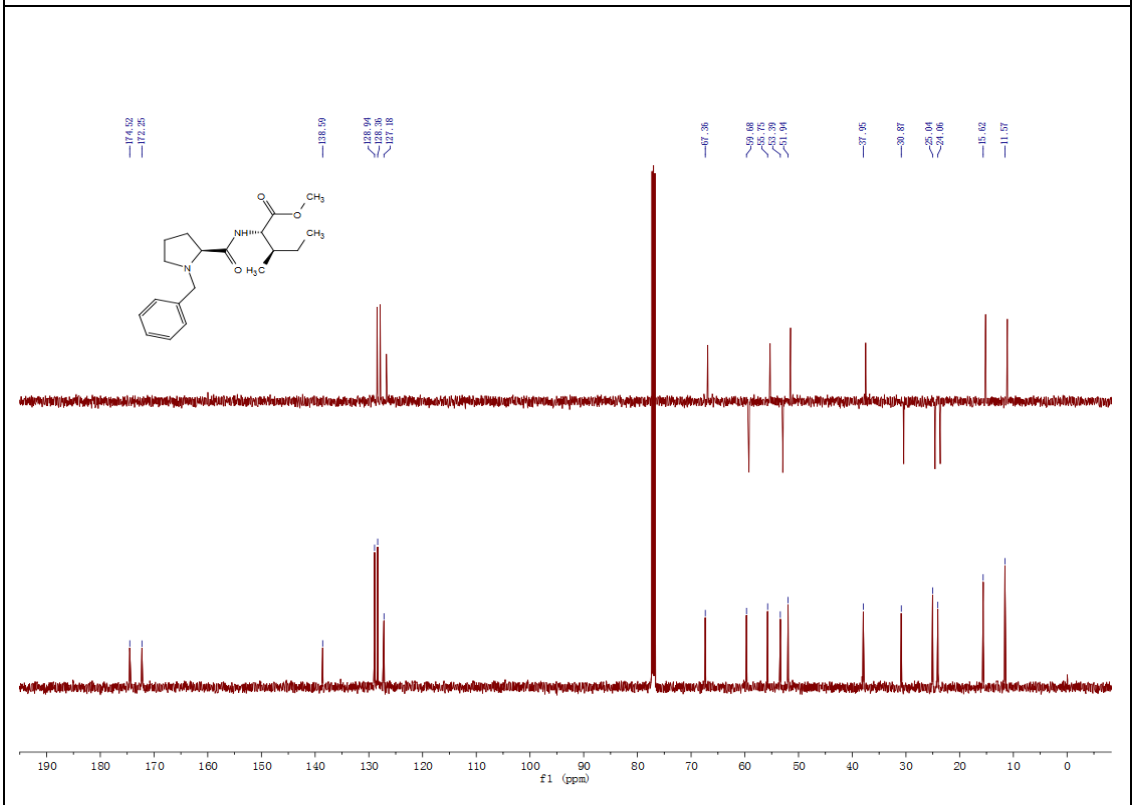
**Methyl benzyl-L-prolyl-L-valinate 5d:**



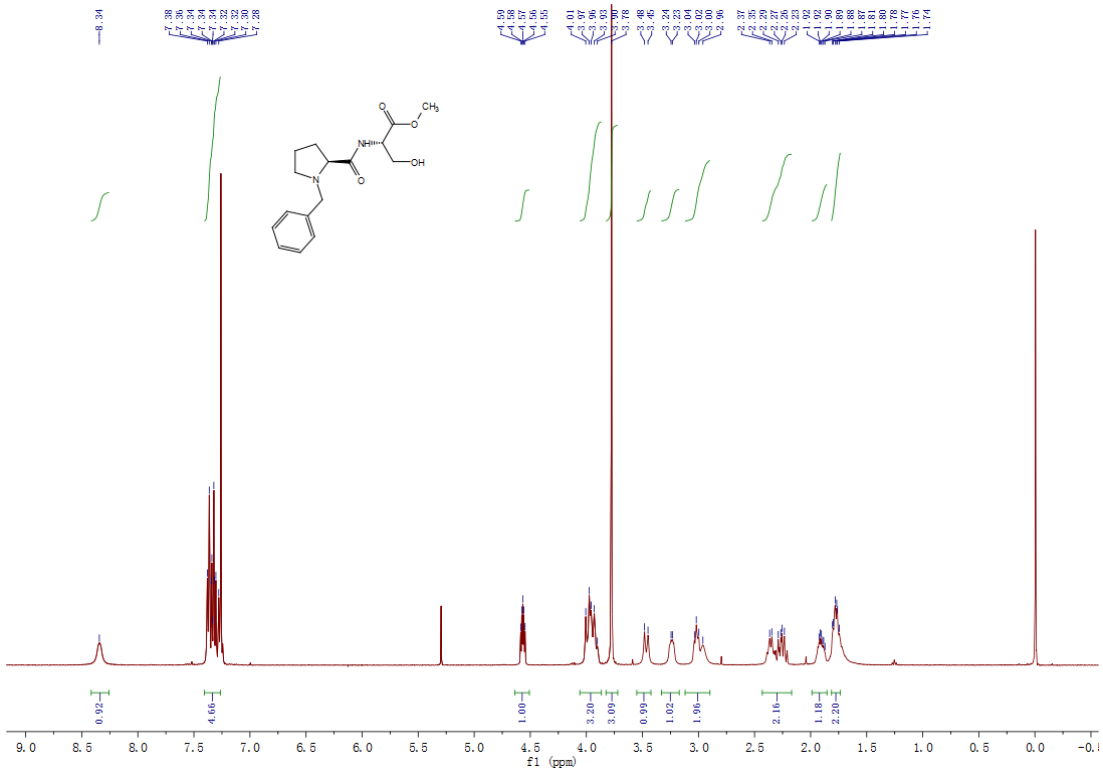



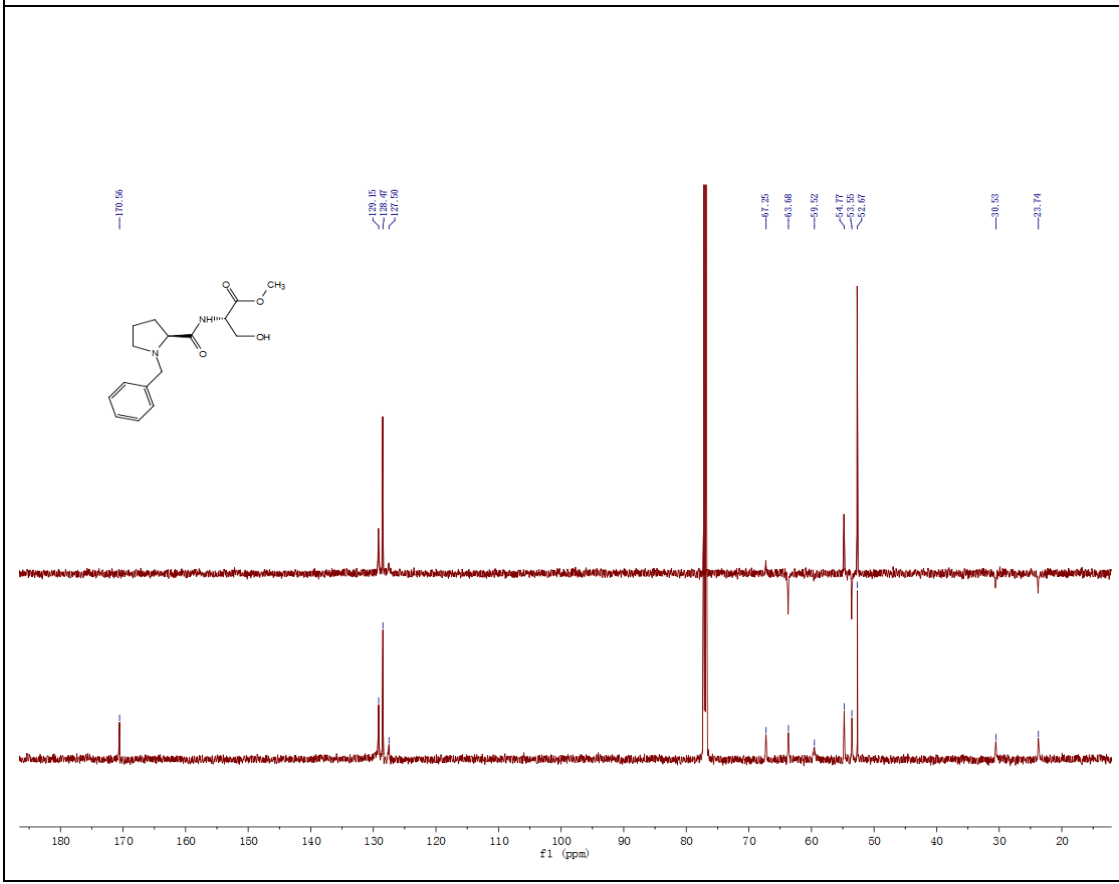
**Methyl benzyl-L-prolyl-L-alloisoleucinate 5e:**



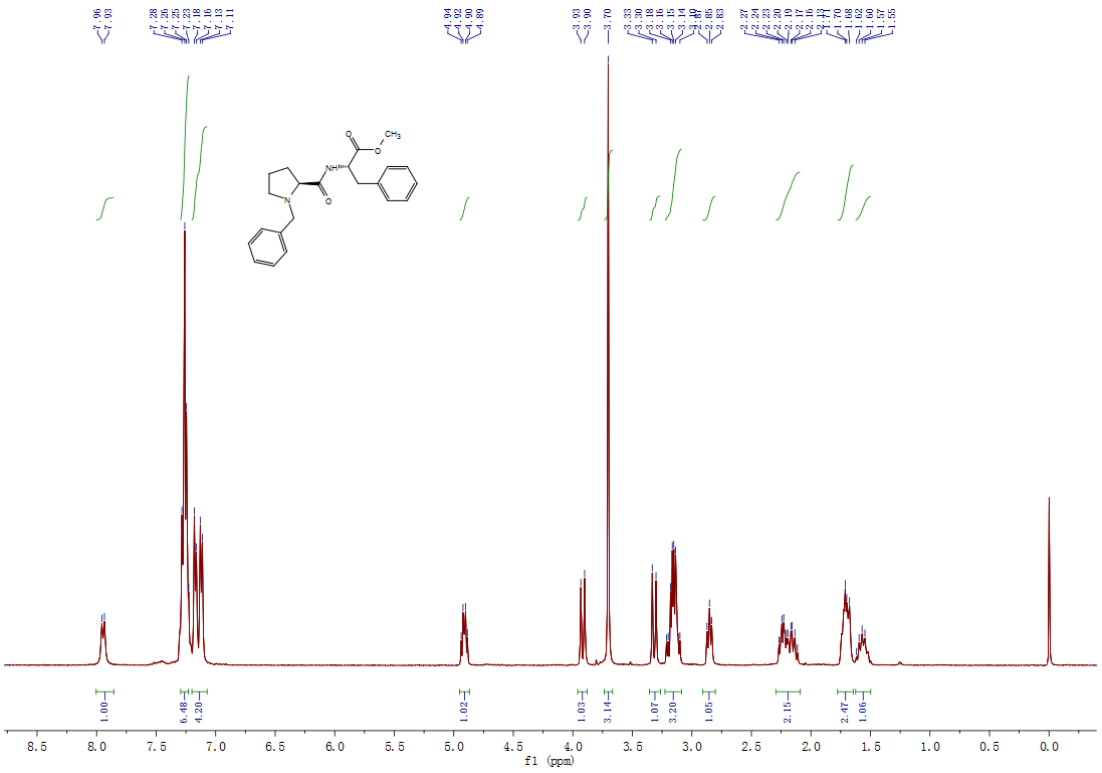



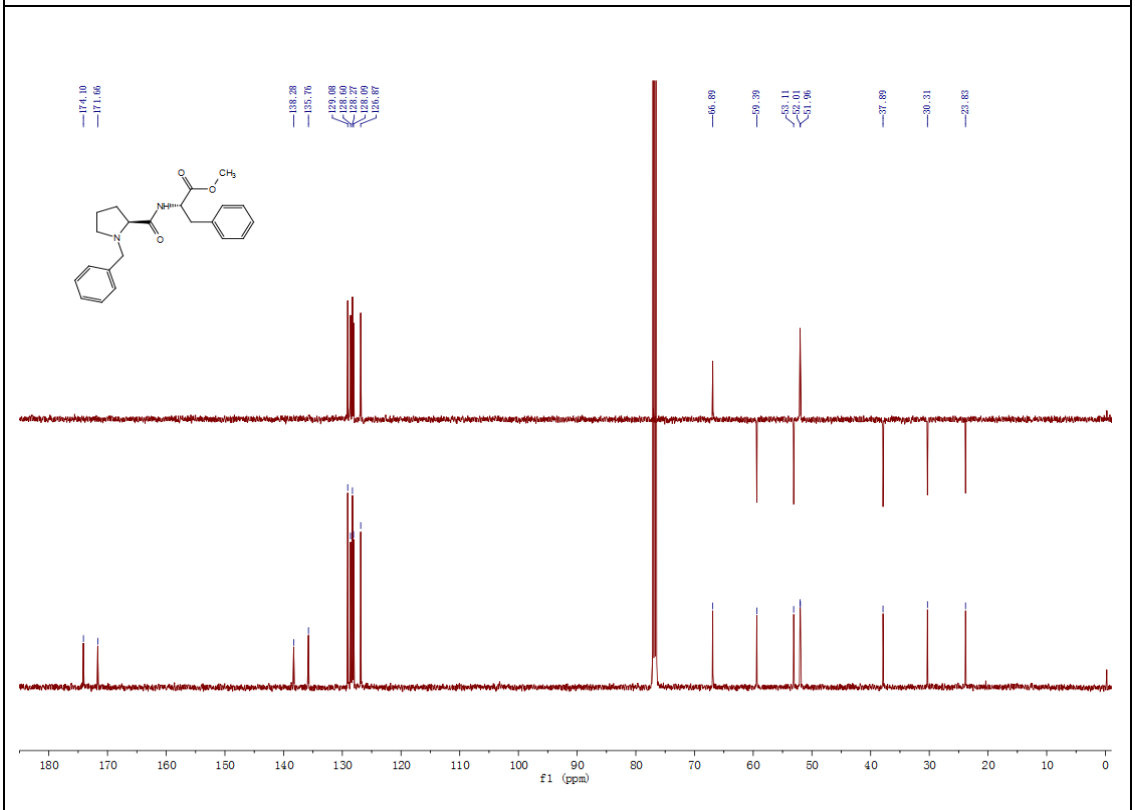
**Methyl benzyl-L-prolyl-L-serinate 5f:**



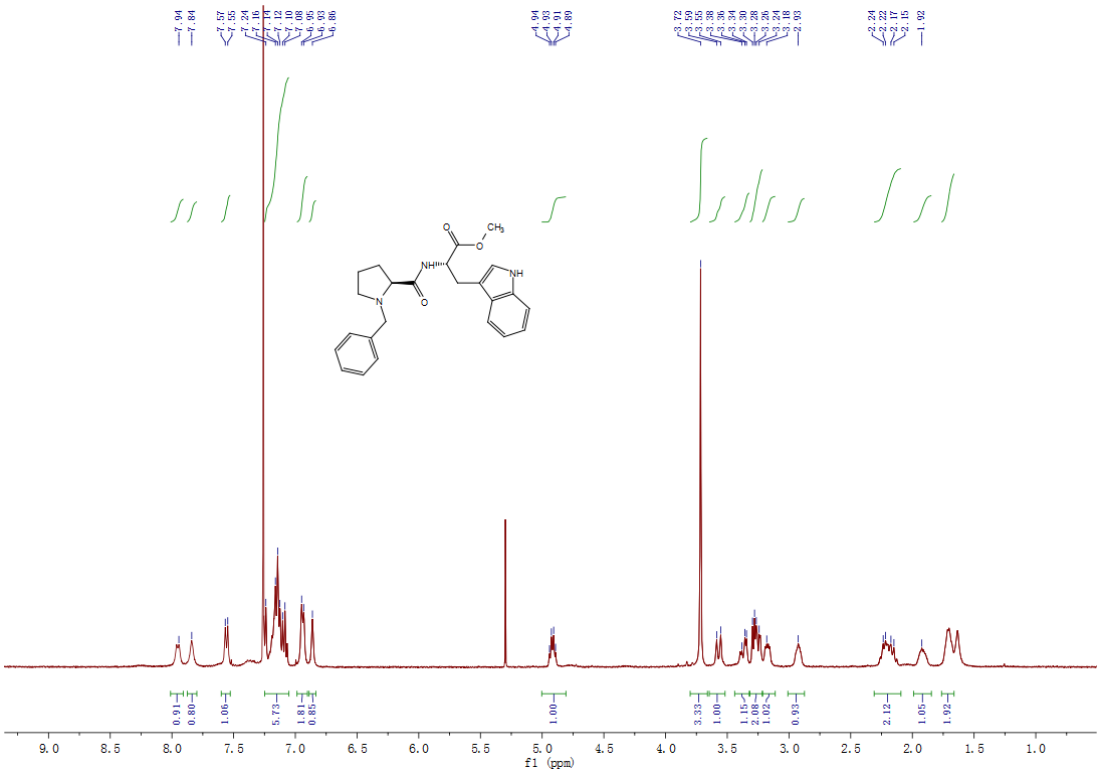



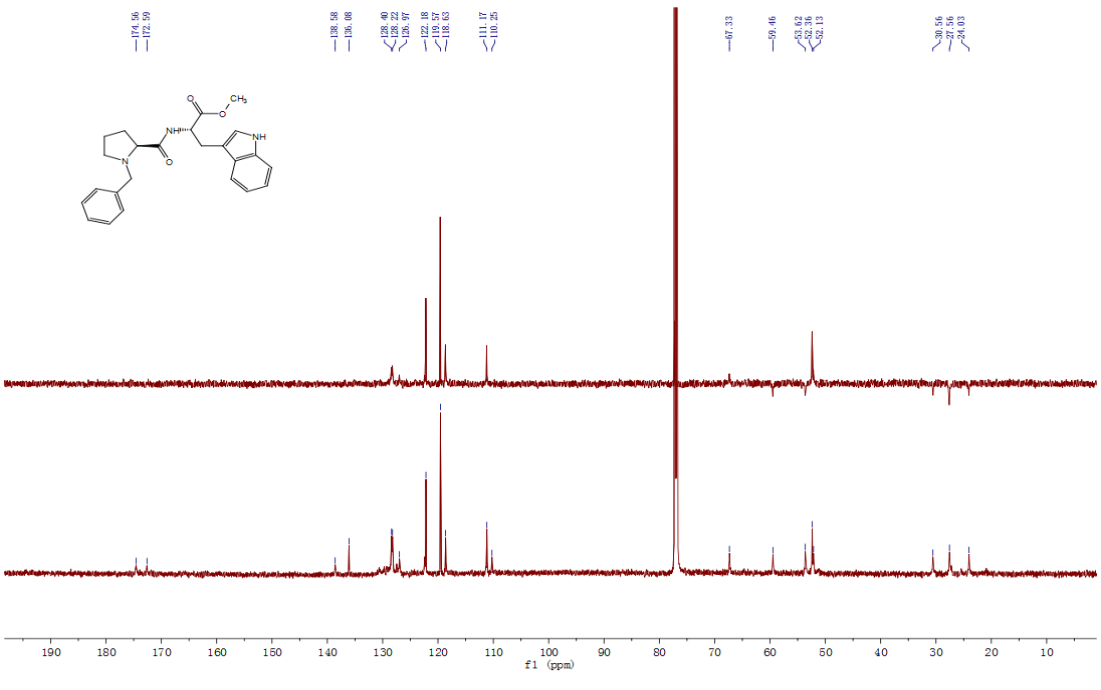
**Methyl benzyl-L-prolyl-L-phenylalaninate 5g:**



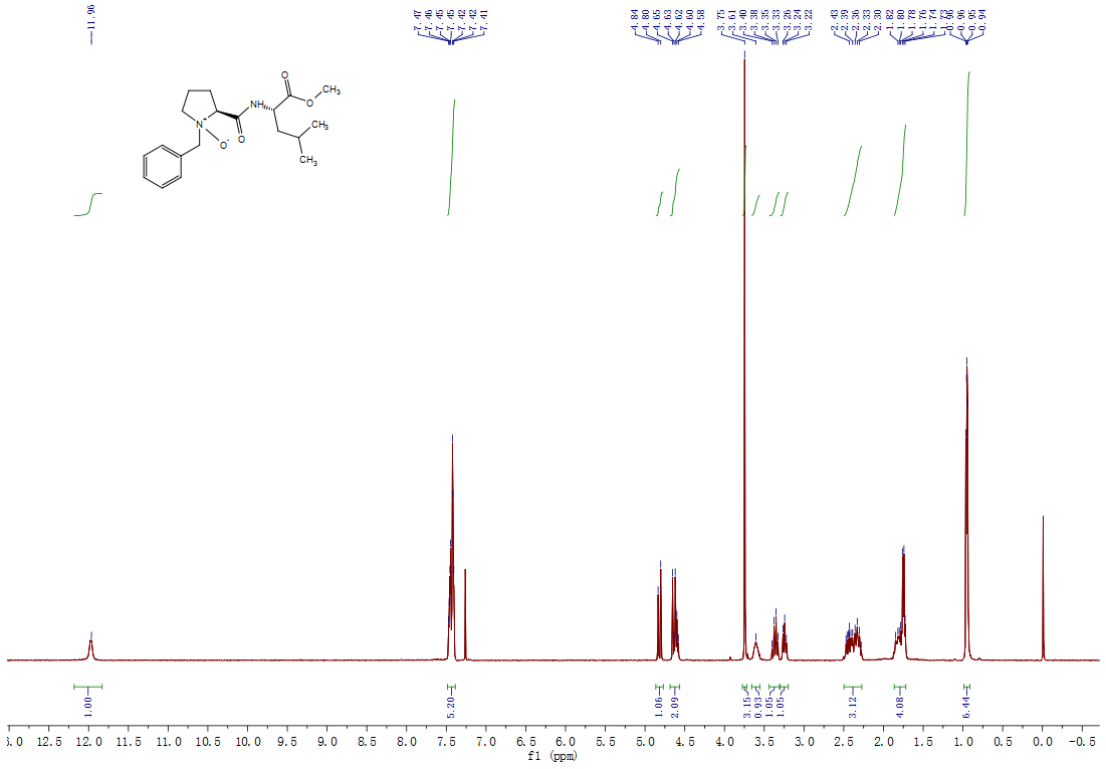


**Methyl benzyl-L-prolyl-L-tryptophanate 5h:**

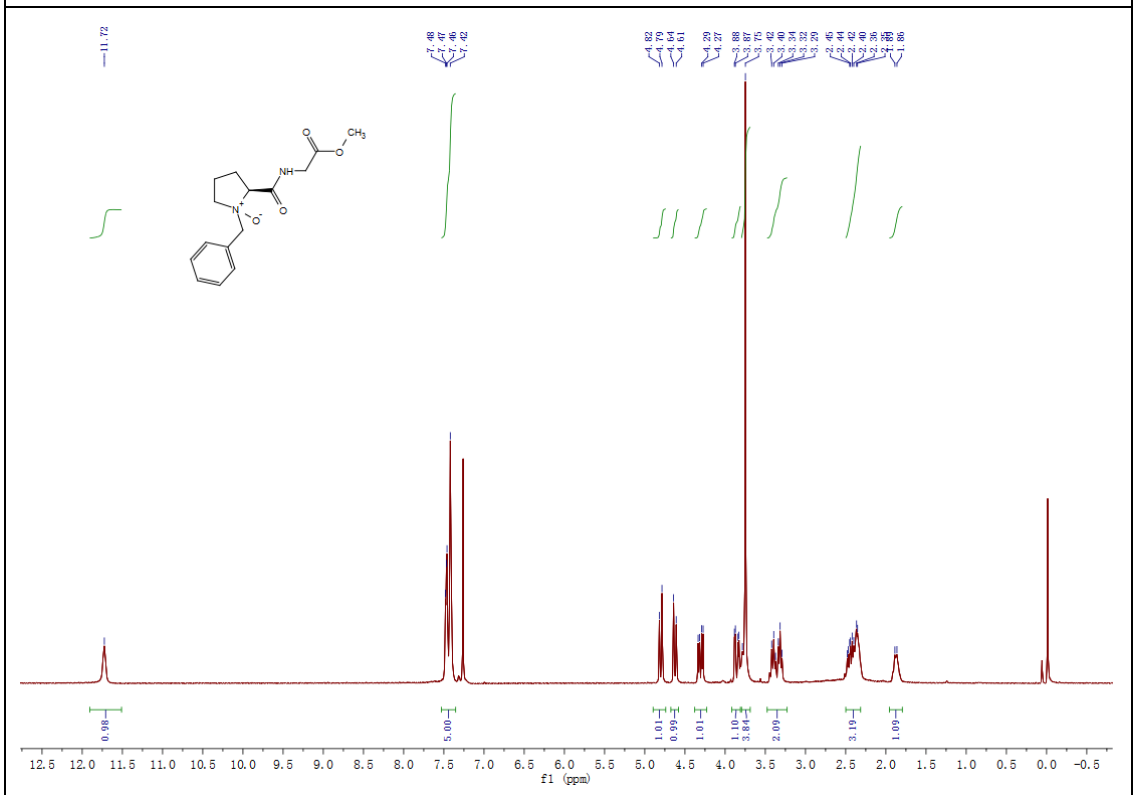


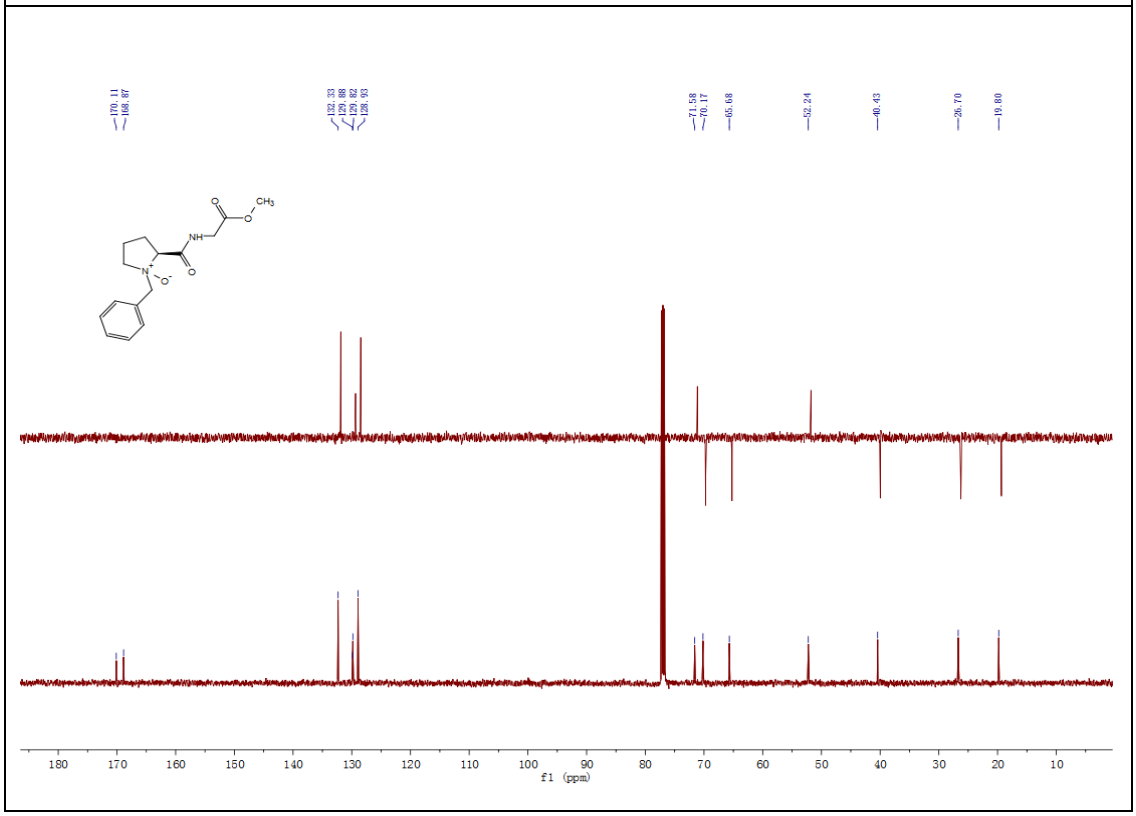



**(2S)-1-benzyl-2-(((S)-1-methoxy-4-methyl-1-oxopentan-2-yl)carbamoyl)pyrrolidine 1-oxide 1a:**

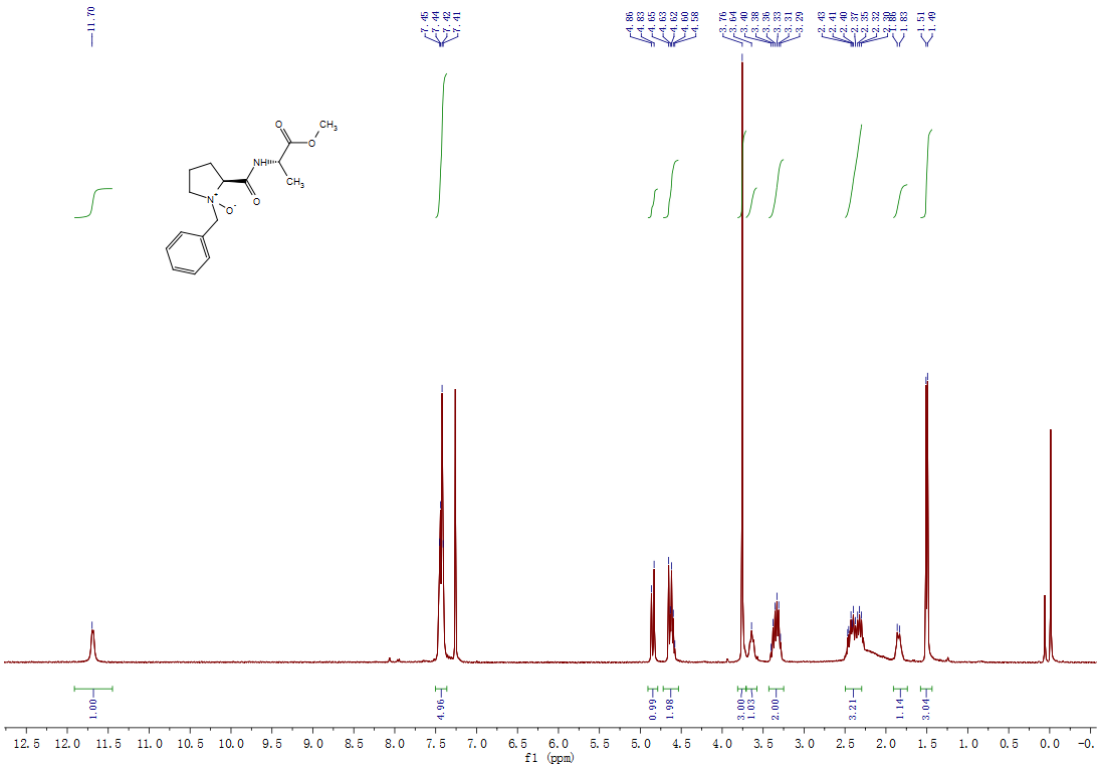


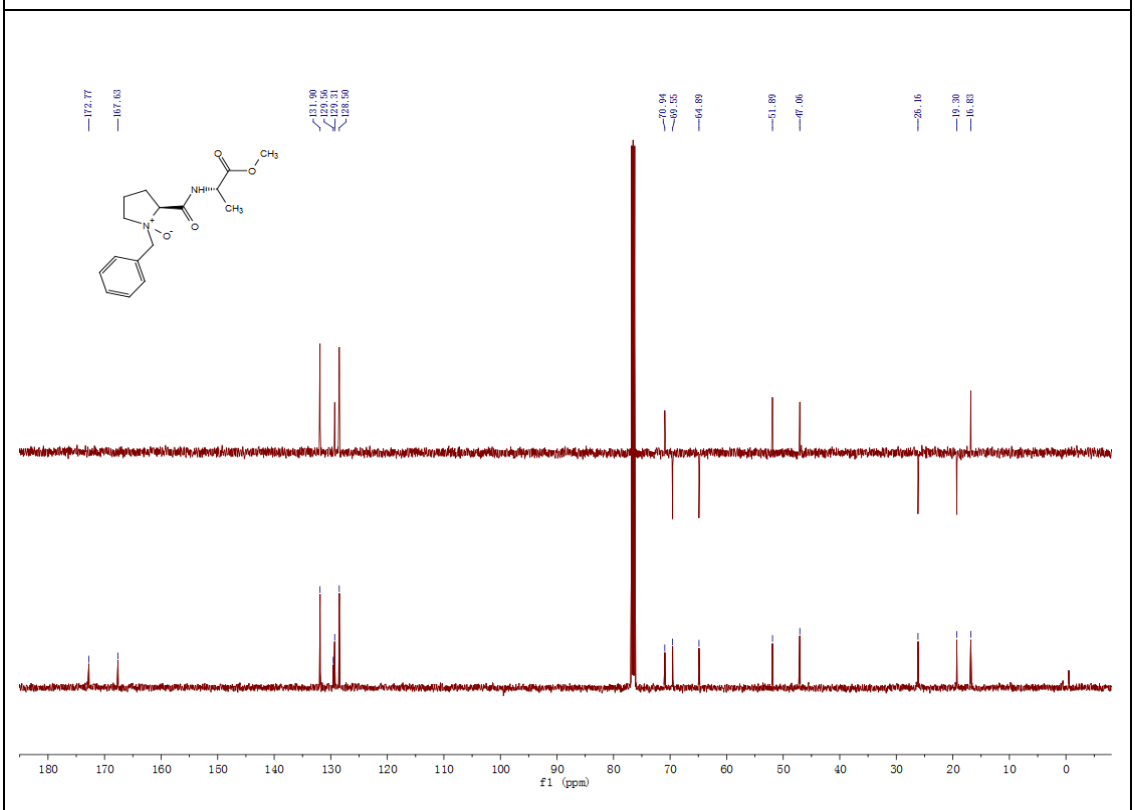
**(2S)-1-benzyl-2-((2-methoxy-2-oxoethyl)carbamoyl)pyrrolidine 1-oxide 1b:**



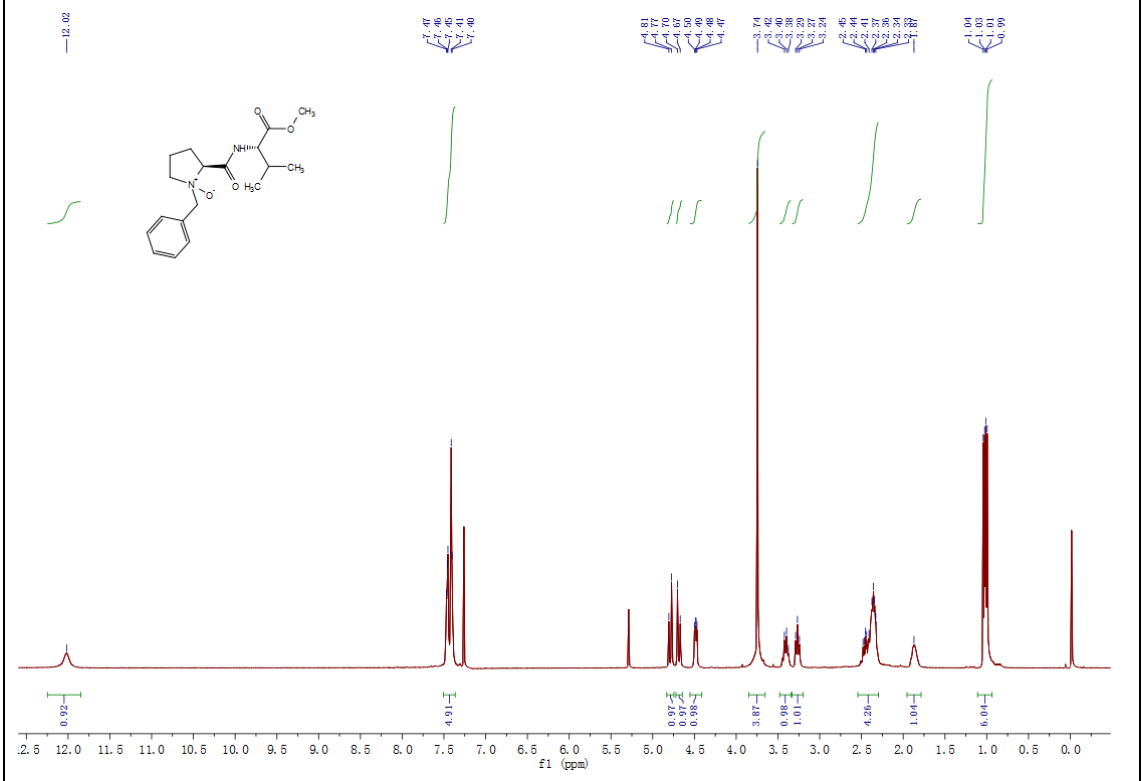



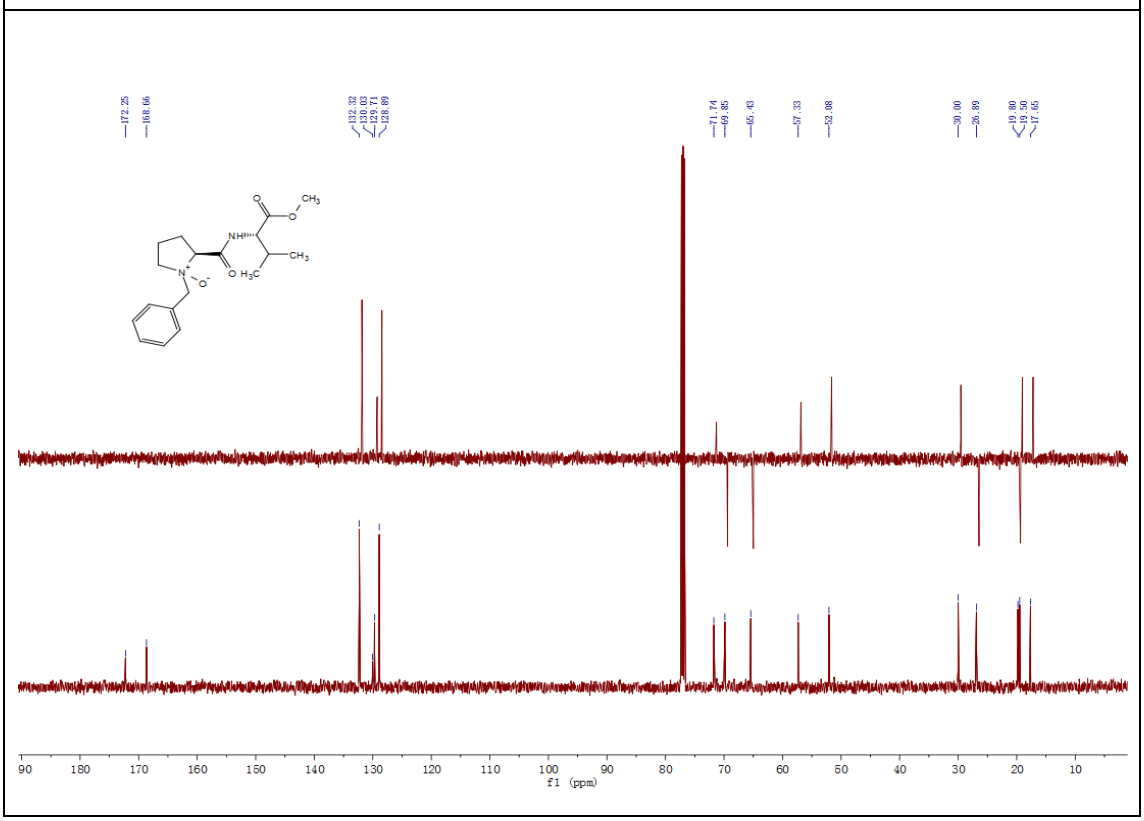
**(2S)-1-benzyl-2-(((S)-1-methoxy-1-oxopropan-2-yl)carbamoyl)pyrrolidine 1-oxide 1c:**



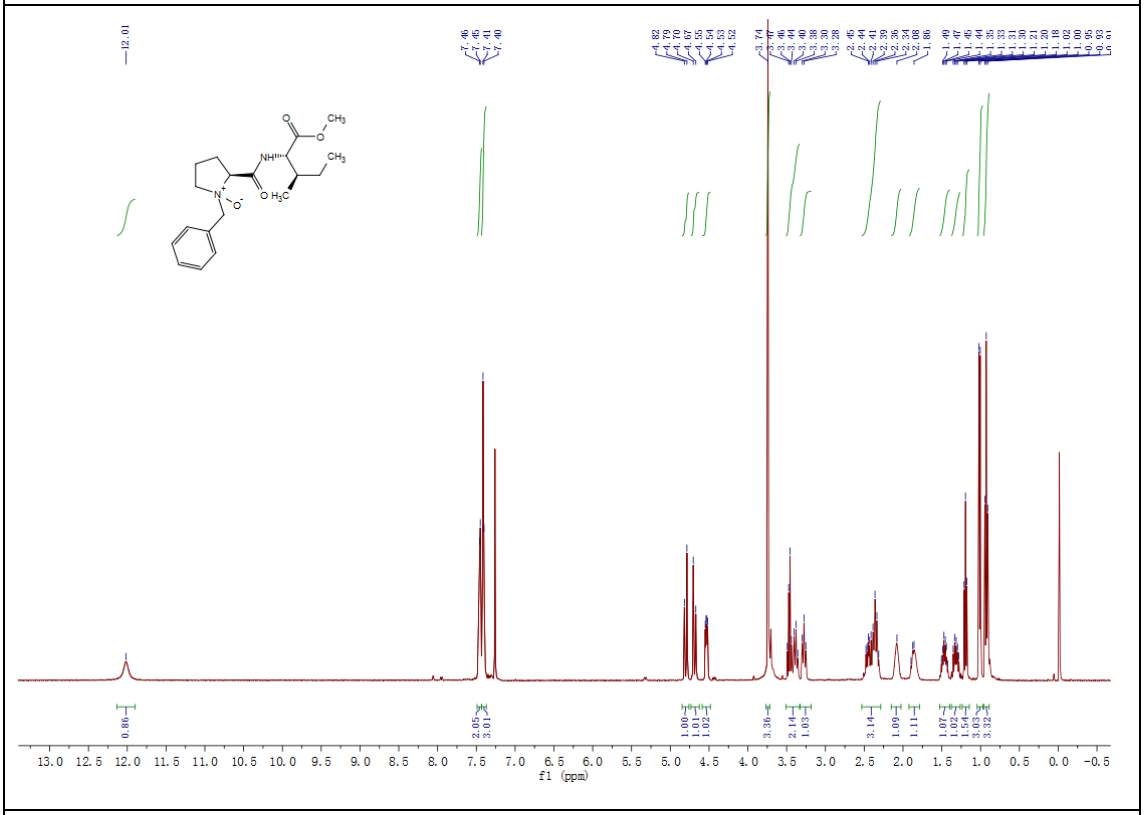


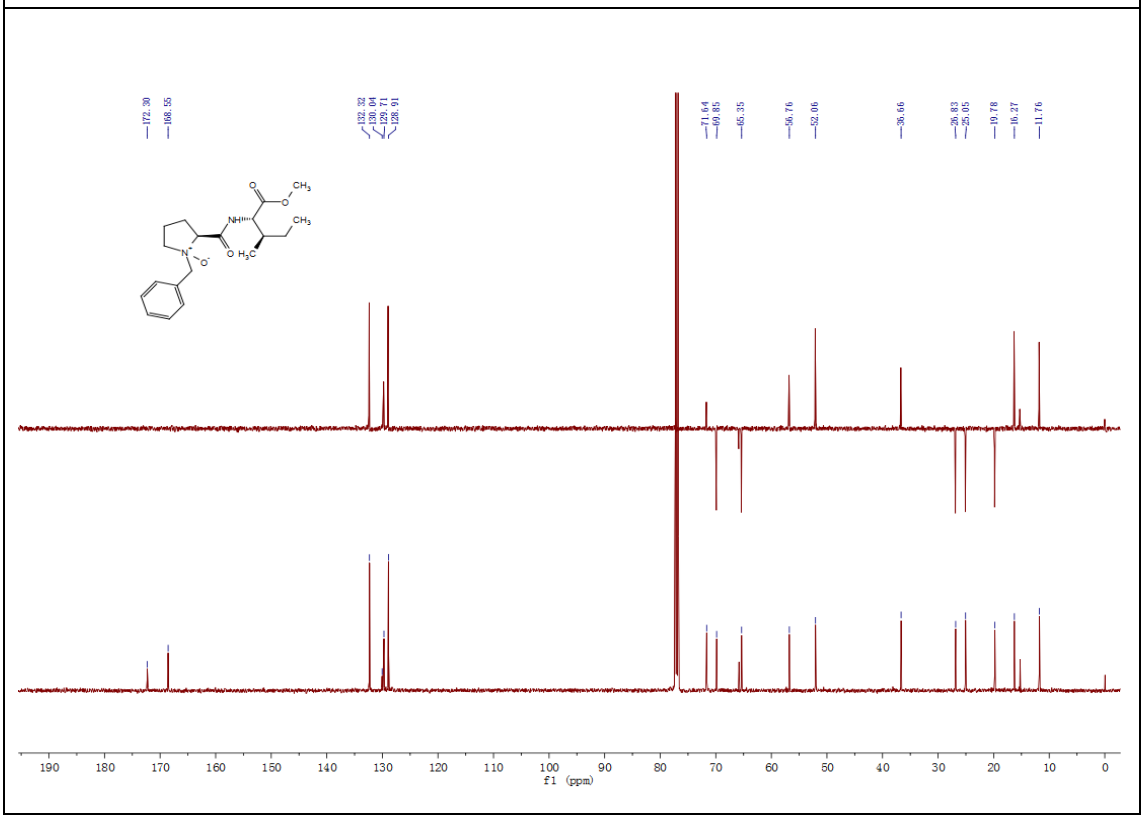
**(2S)-1-benzyl-2-(((S)-1-methoxy-3-methyl-1-oxobutan-2-yl)carbamoyl)pyrrolidin e 1-oxide 1d:**



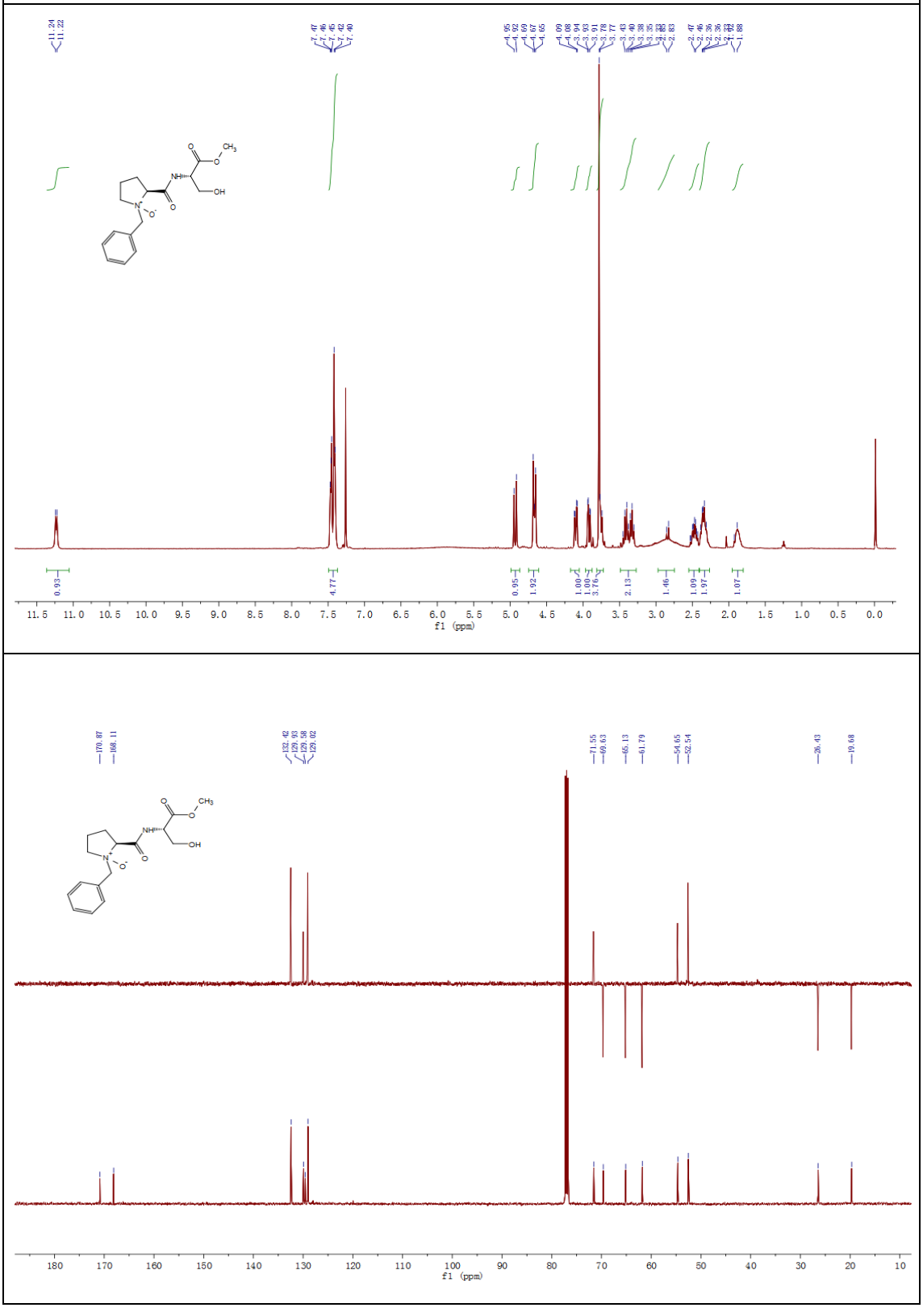


**(2S)-1-benzyl-2-(((2S,3R)-1-methoxy-3-methyl-1-oxopentan-2-yl)carbamoyl)pyrrolidine 1-oxide 1e:**

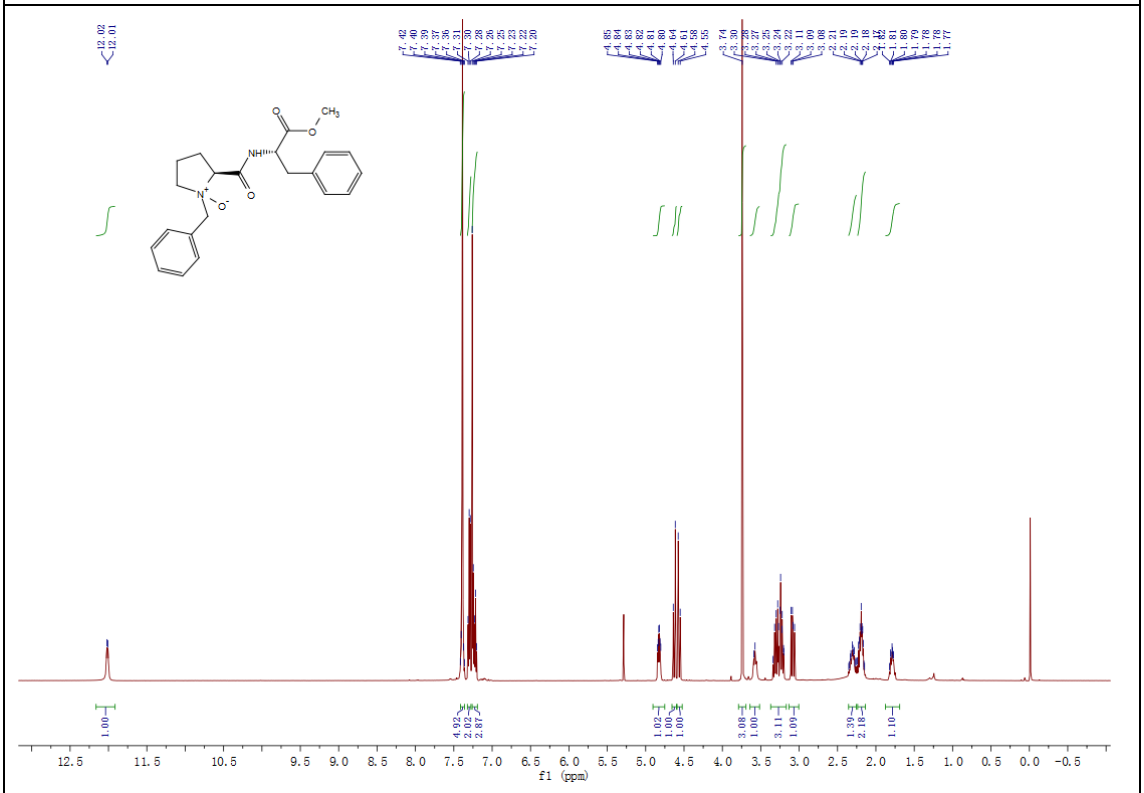


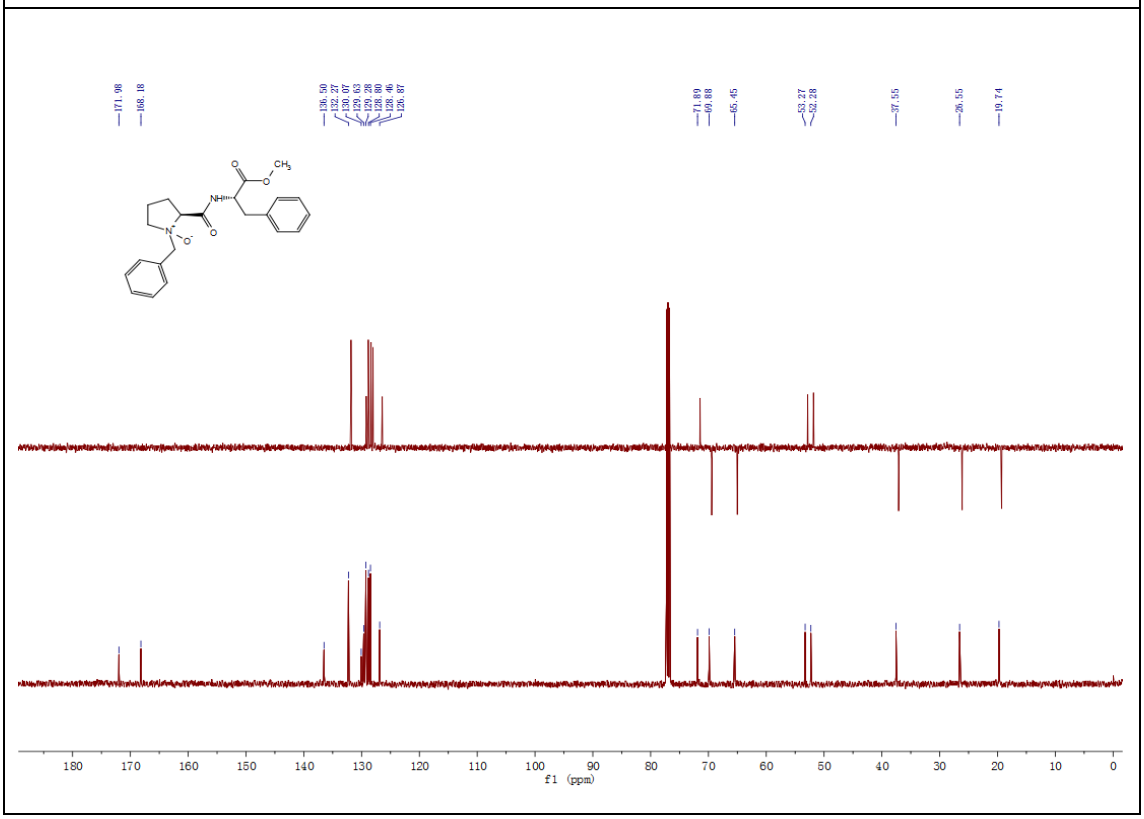


**(2S)-1-benzyl-2-(((S)-3-hydroxy-1-methoxy-1-oxopropan-2-yl)carbamoyl)pyrroli dine 1-oxide 1f:**

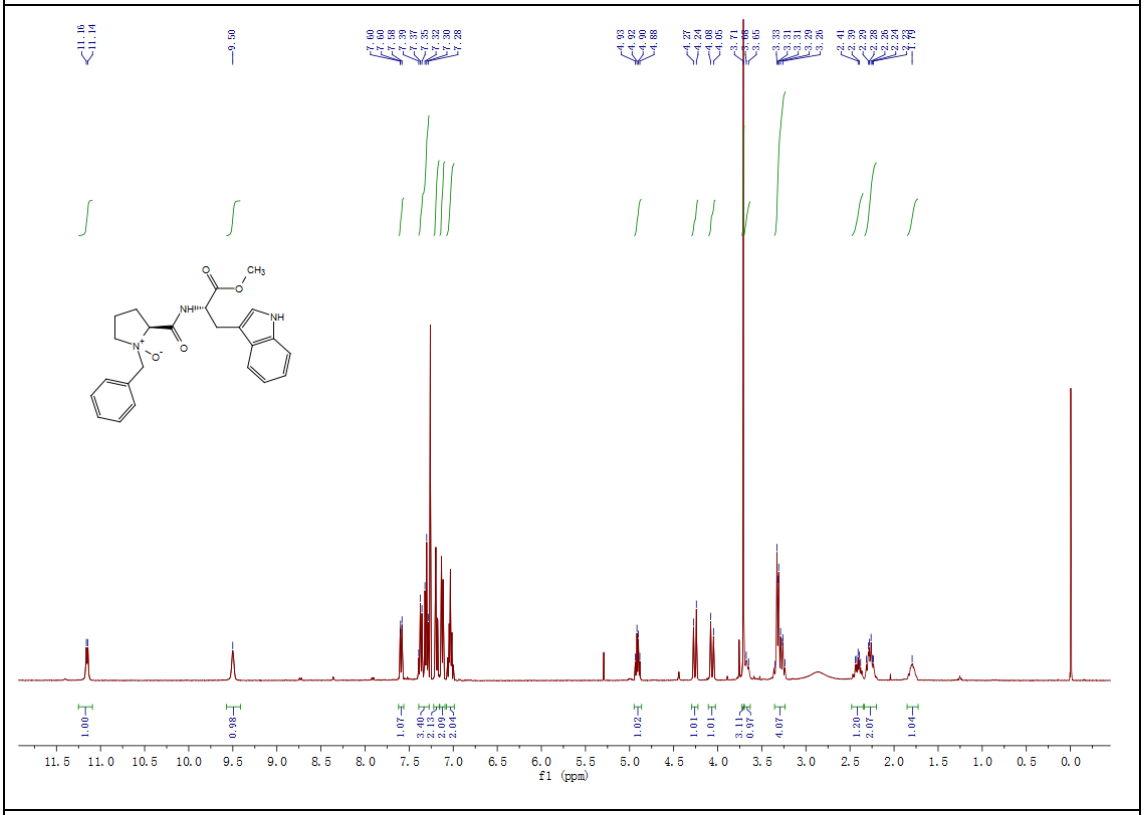


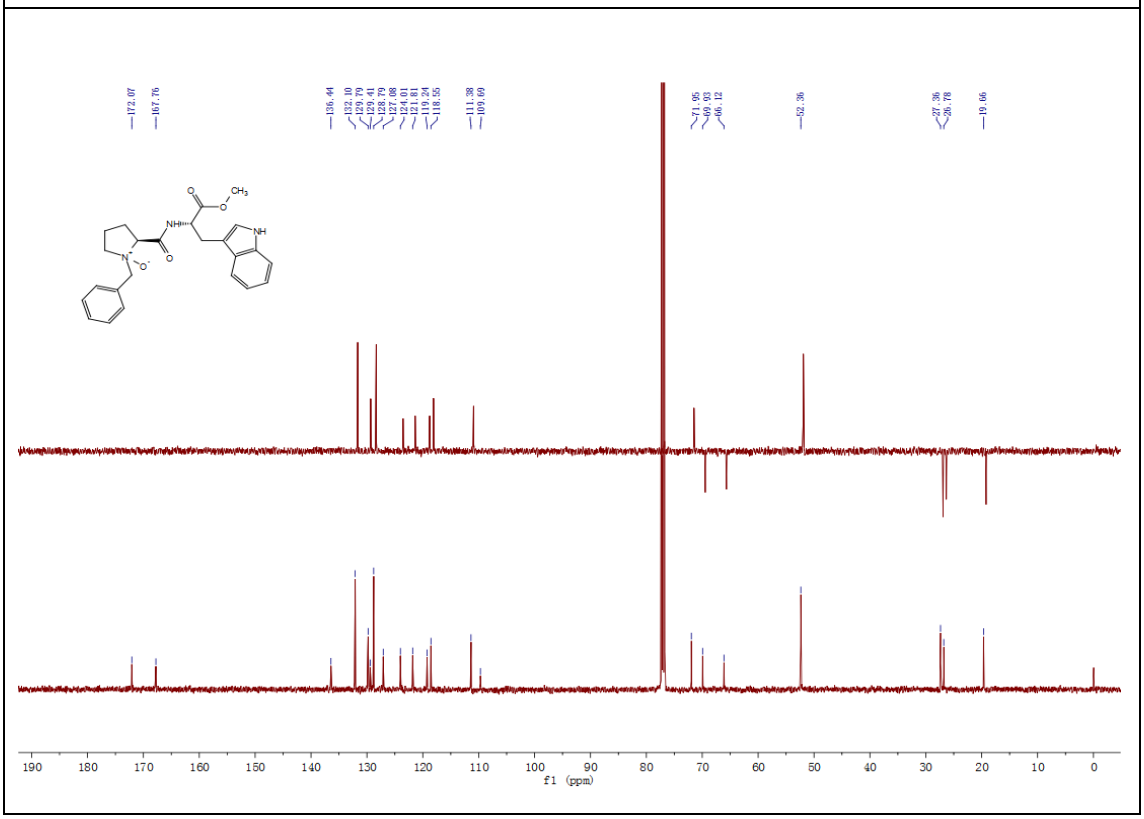
**(2S)-1-benzyl-2-(((S)-1-methoxy-1-oxo-3-phenylpropan-2-yl)carbamoyl)pyrrolidine 1-oxide 1g:**



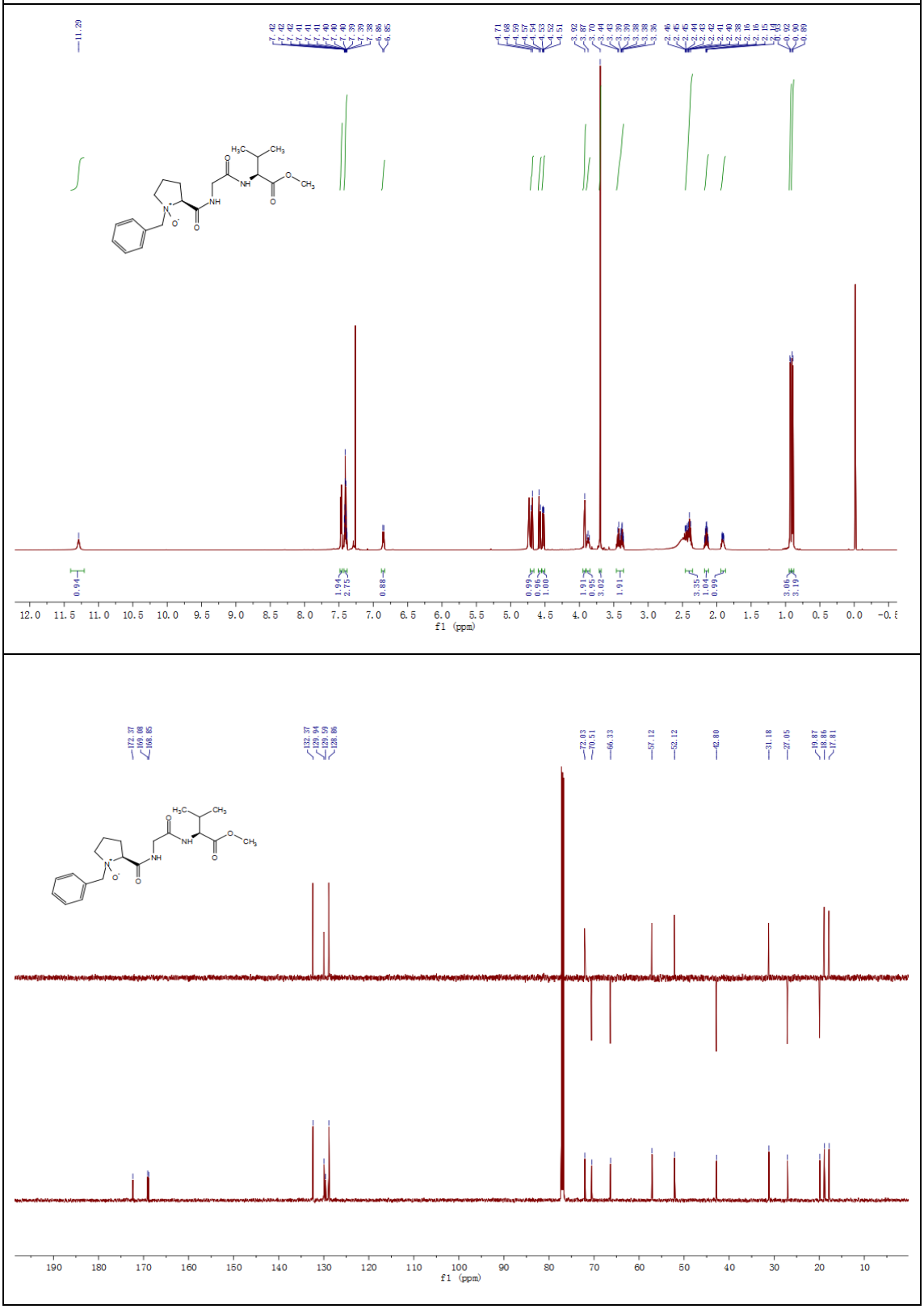


**(2S)-2-(((S)-3-(1H-indol-3-yl)-1-methoxy-1-oxopropan-2-yl)carbamoyl)-1-benzylpyrrolidine 1-oxide 1h:**

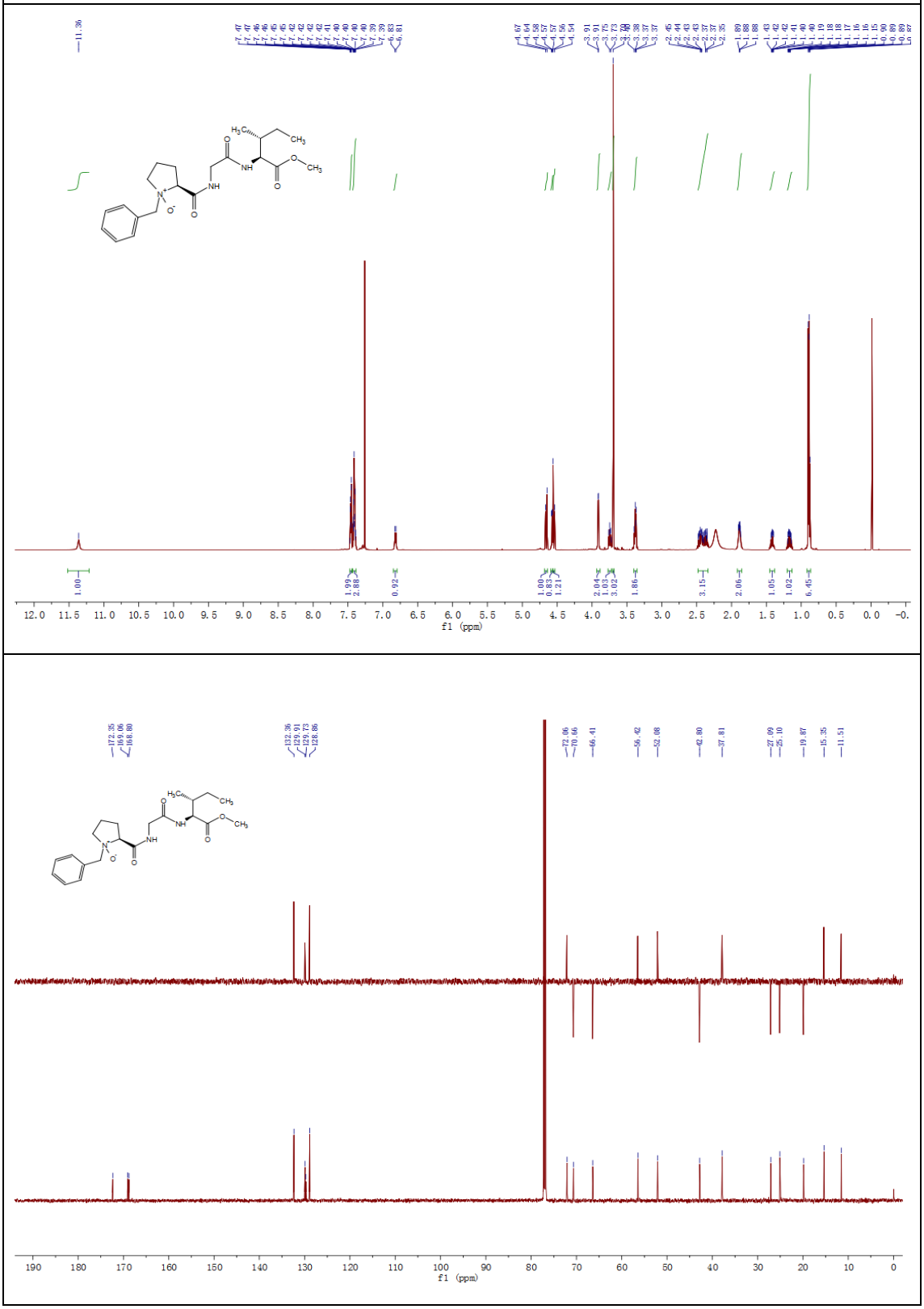


**(2S)-1-benzyl-2-((2-(((S)-1-methoxy-3-methyl-1-oxobutan-2-yl)amino)-2-oxoethyl)carbamoyl)pyrrolidine 1-oxide 1i:**

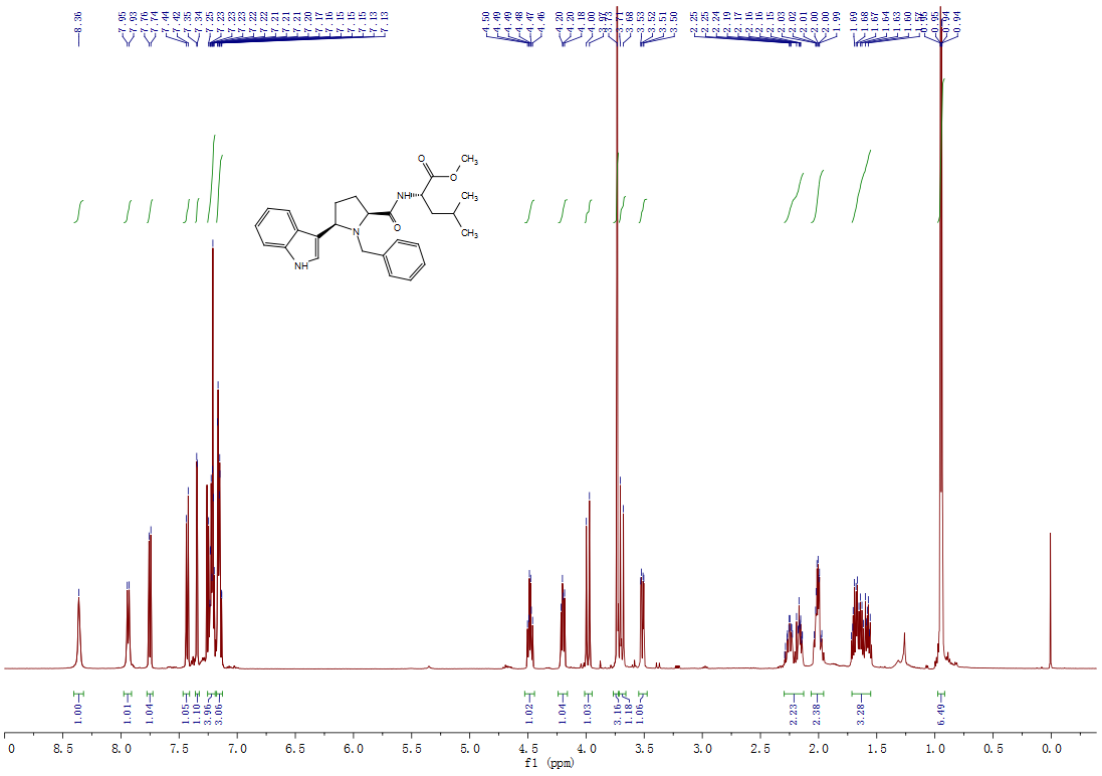


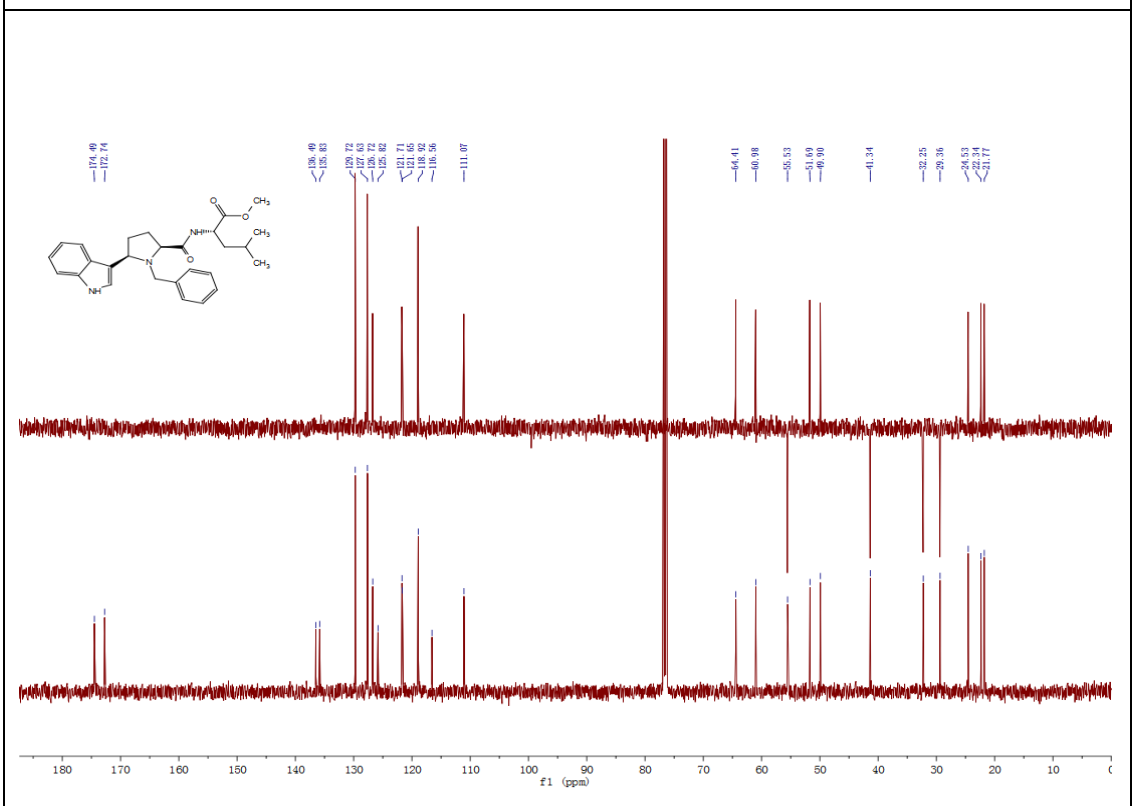
**(2S)-1-benzyl-2-((2-(((2S,3R)-1-methoxy-3-methyl-1-oxopentan-2-yl)amino)-2-oxoethyl)carbamoyl)pyrrolidine 1-oxide 1j:**



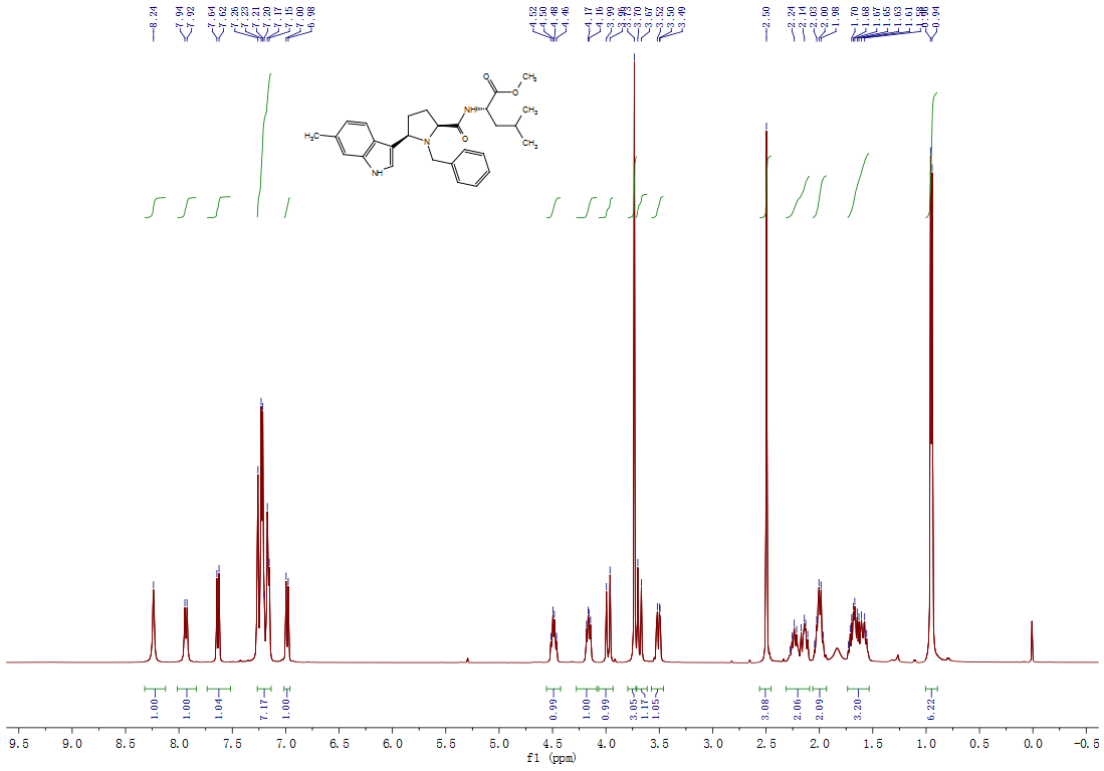
**Methyl ((2S,5S)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate**

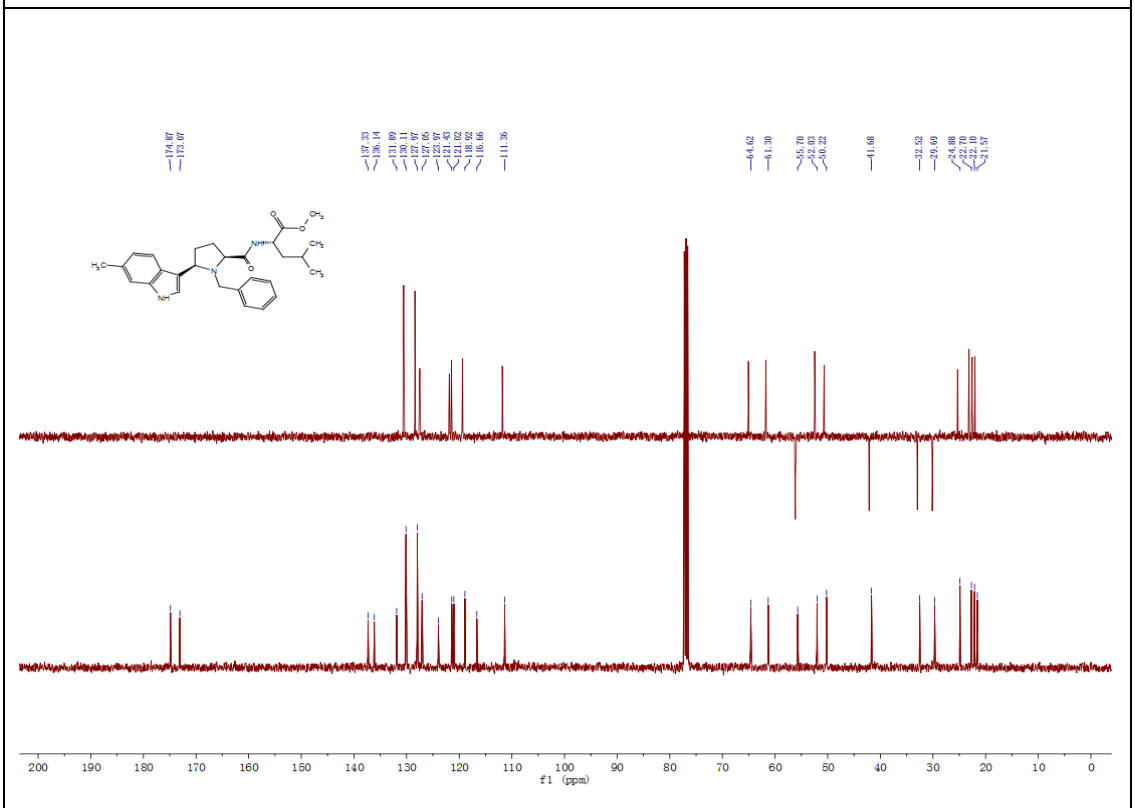
**3a:**



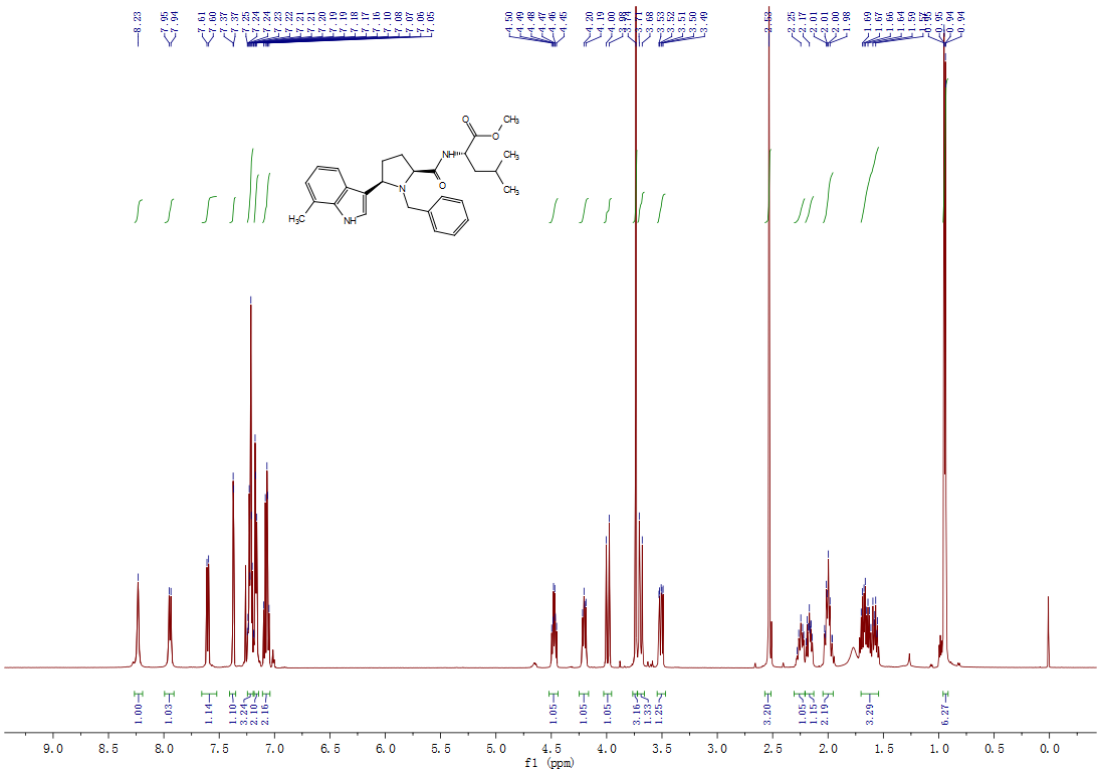


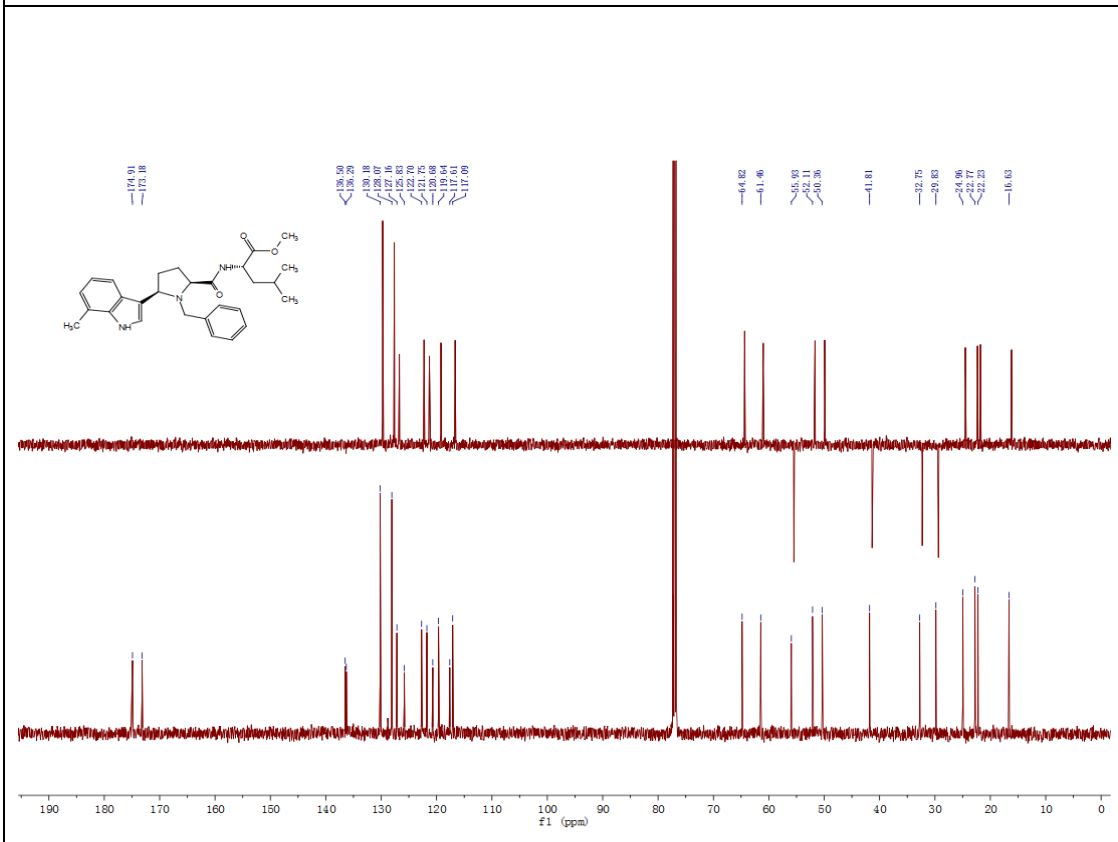
**Methyl ((2S,5R)-1-benzyl-5-(6-methyl-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3b:**



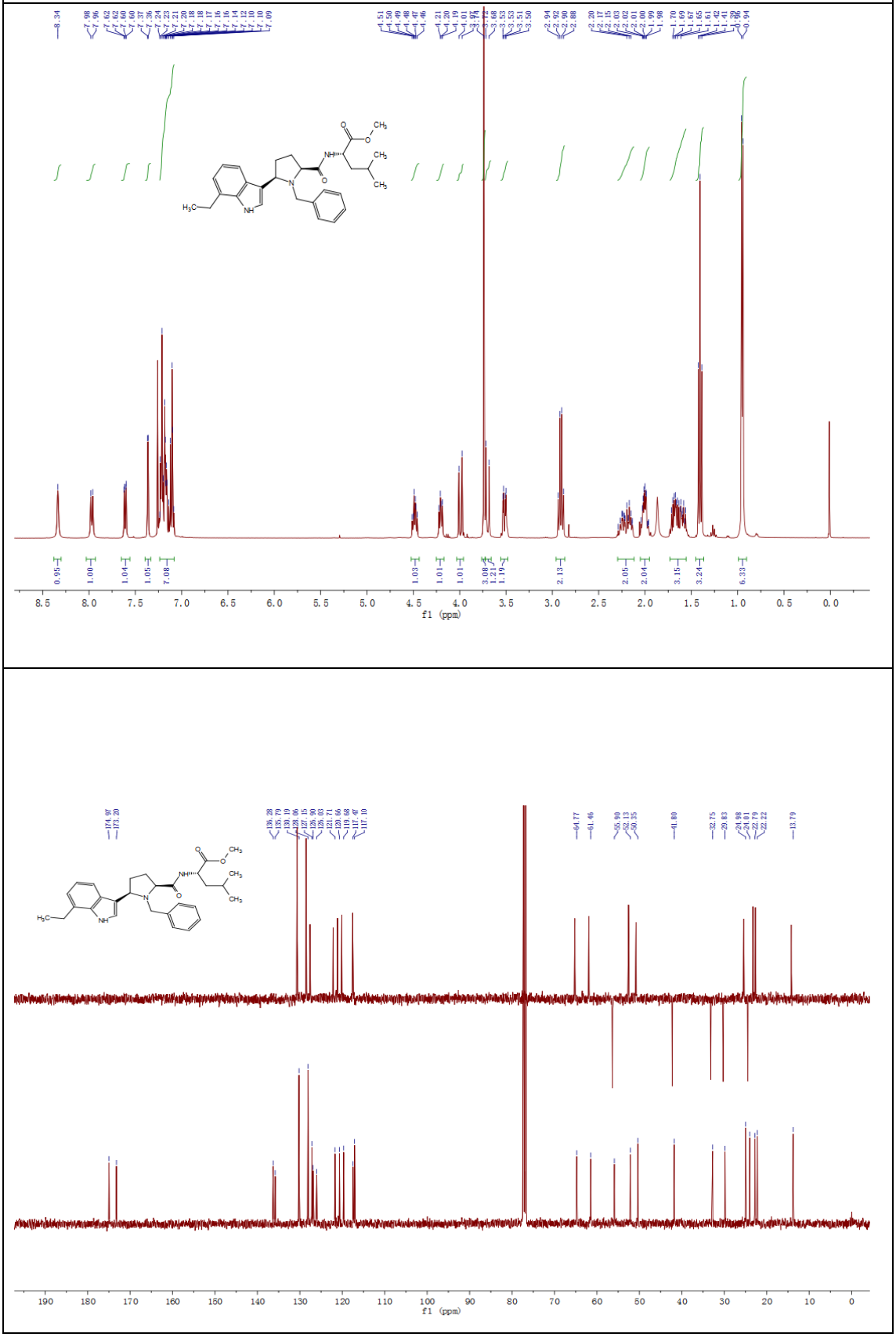


**Methyl ((2S,5R)-1-benzyl-5-(7-methyl-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3c:**

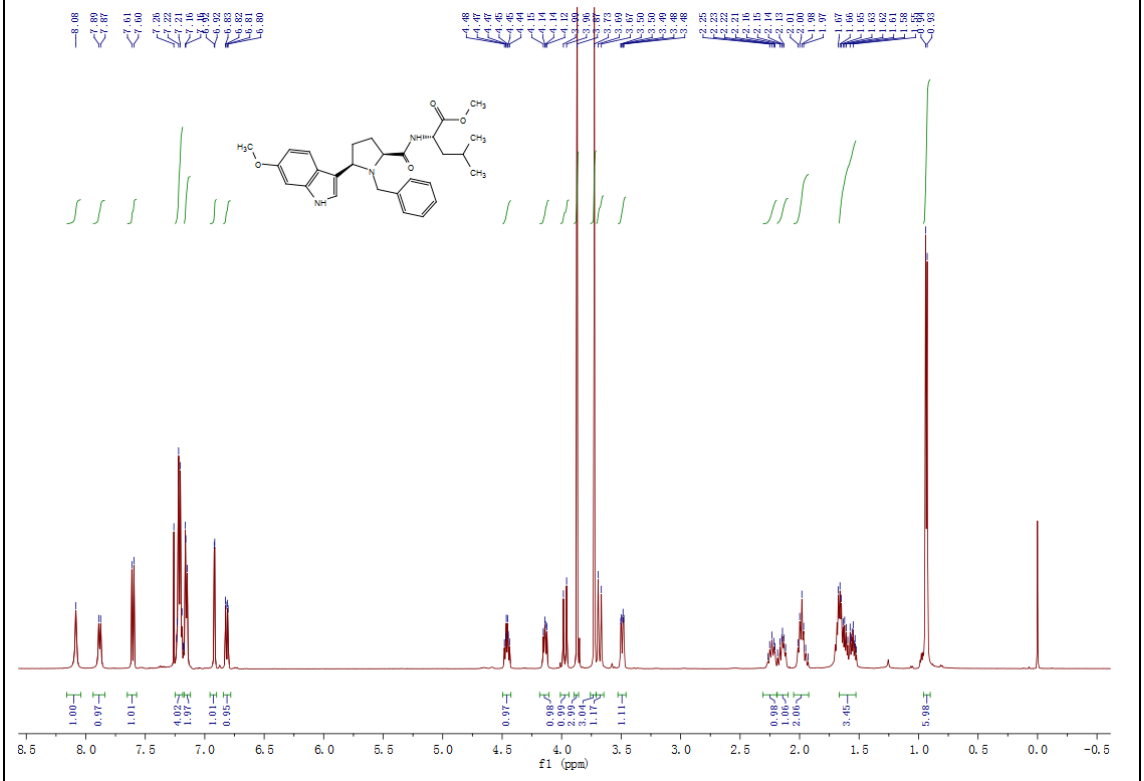


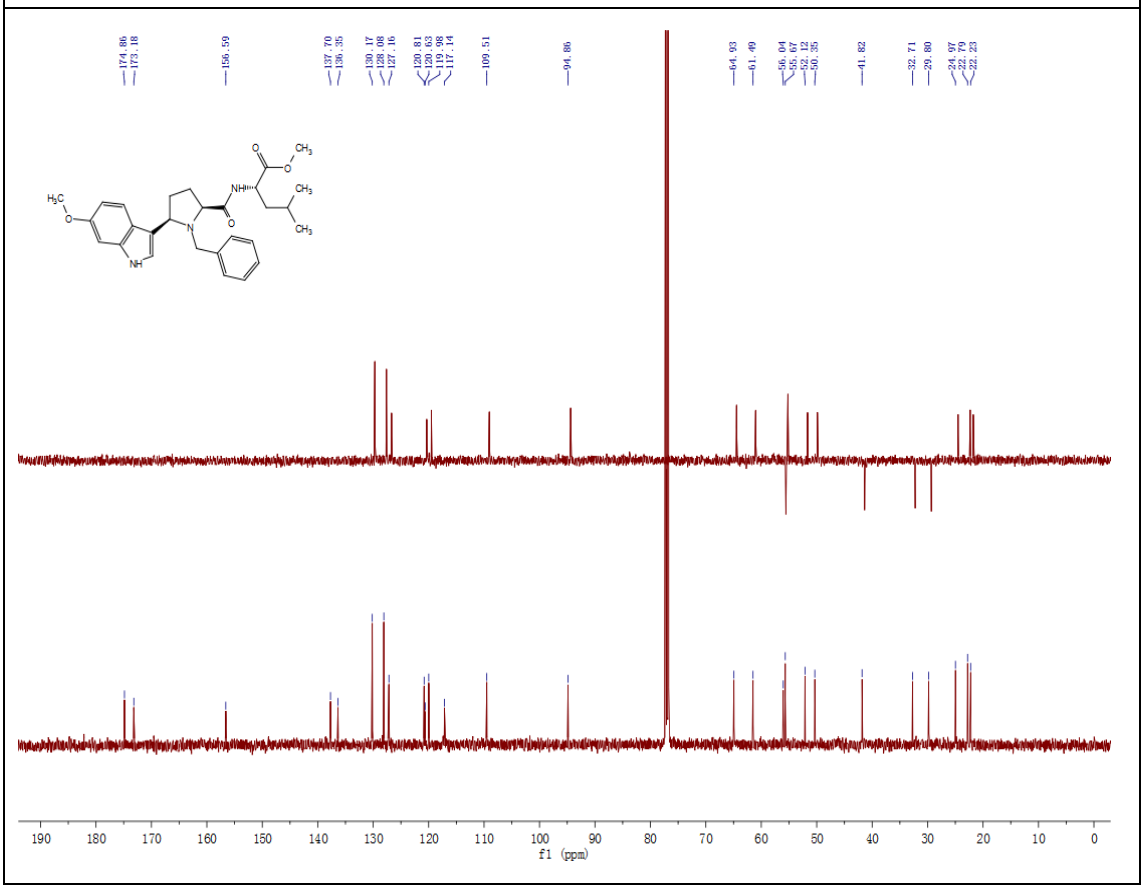



**Methyl ((2S,5R)-1-benzyl-5-(7-ethyl-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3d:**

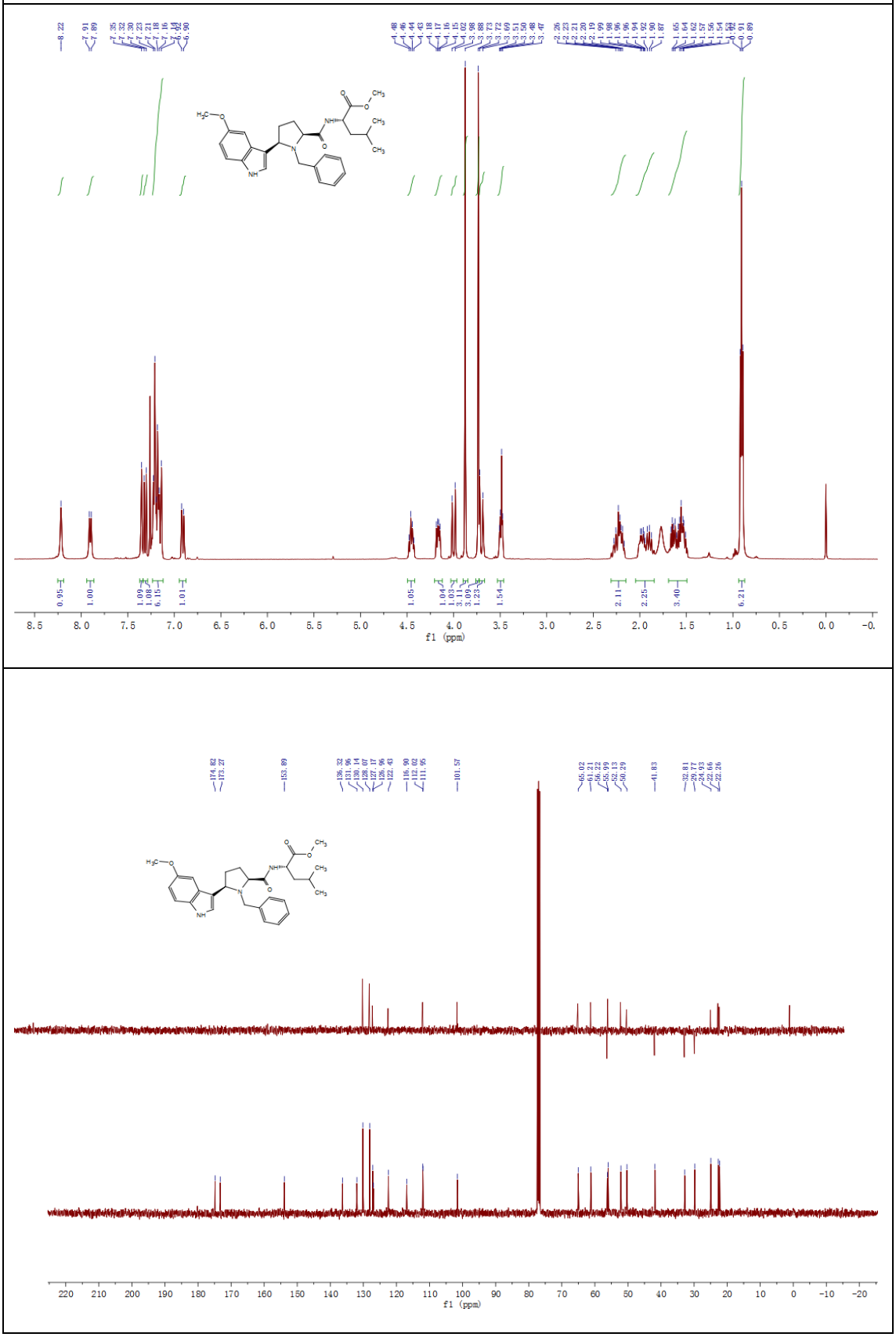


**Methyl ((2S,5R)-1-benzyl-5-(6-methoxy-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3e:**

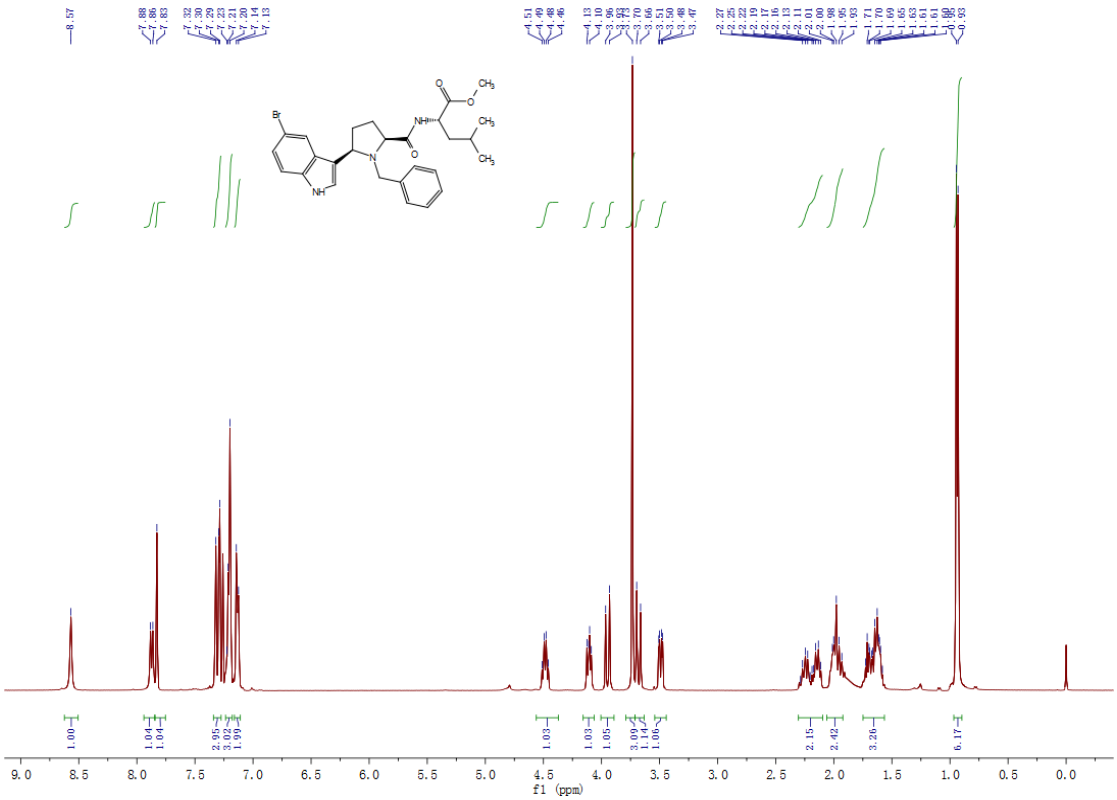


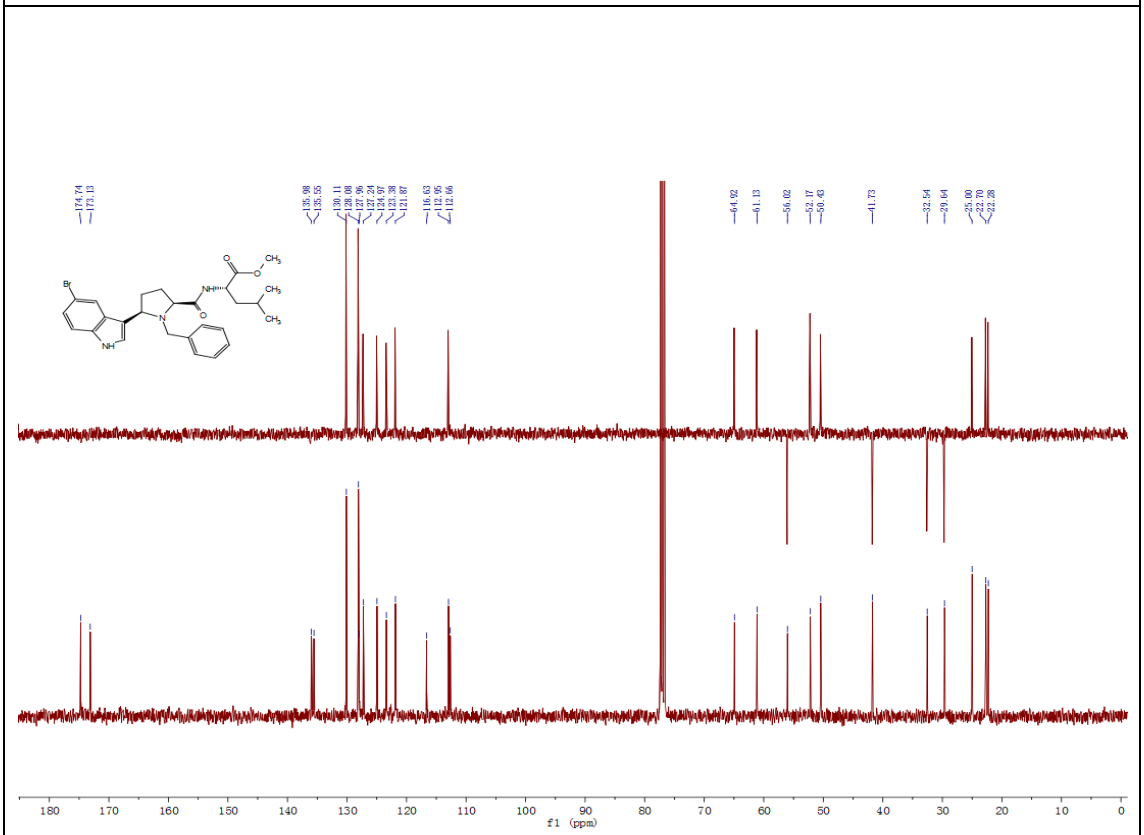



**Methyl ((2S,5R)-1-benzyl-5-(5-methoxy-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3f:**

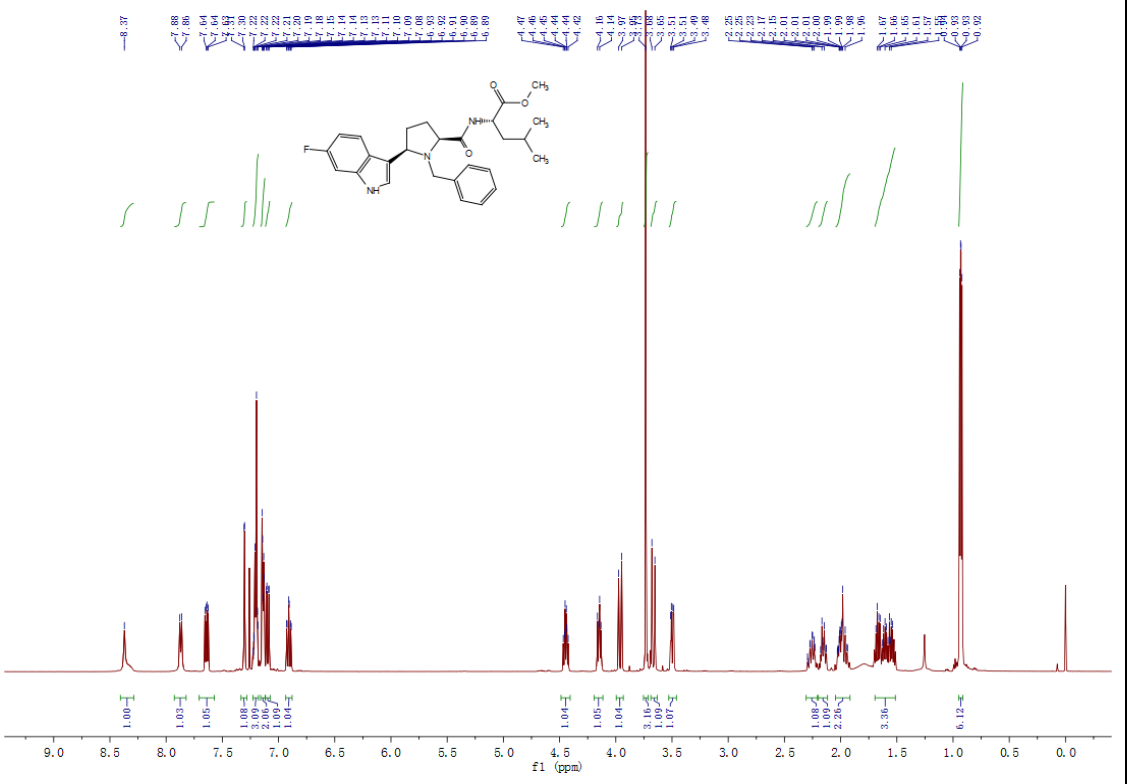


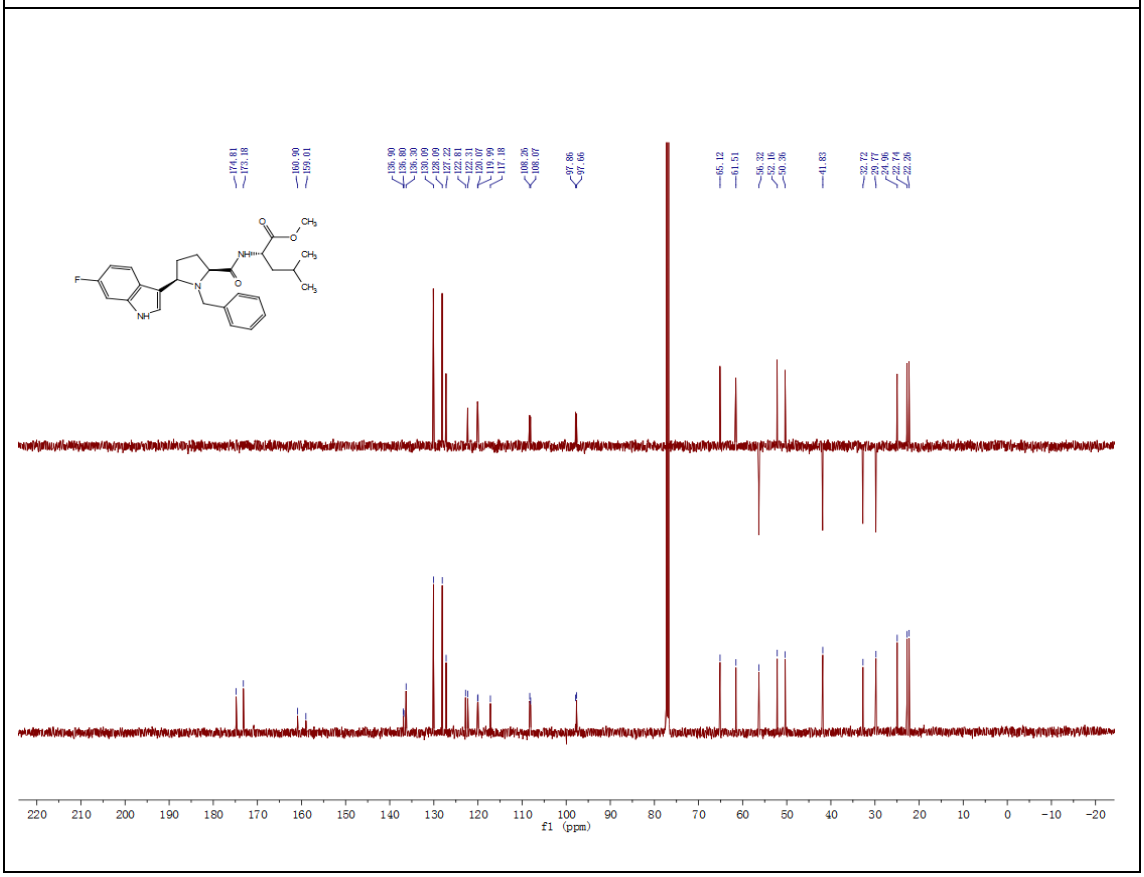
**Methyl ((2S,5R)-1-benzyl-5-(5-bromo-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L -leucinate 3g:**



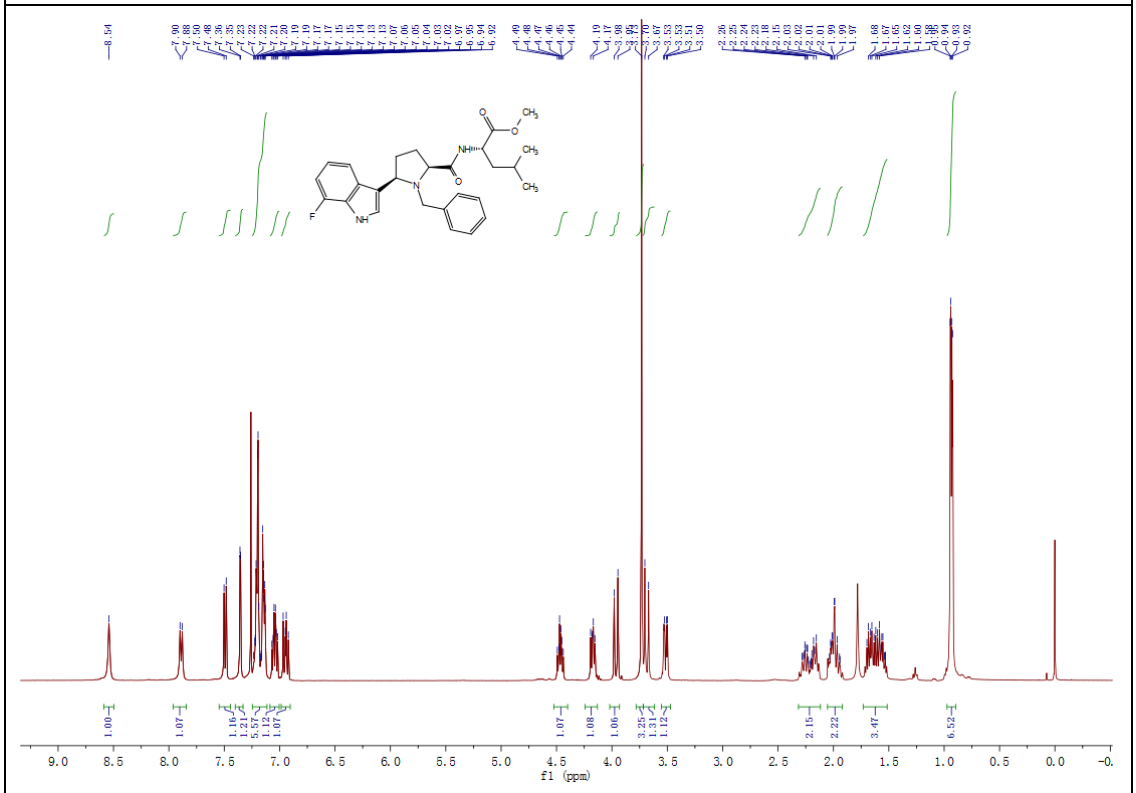



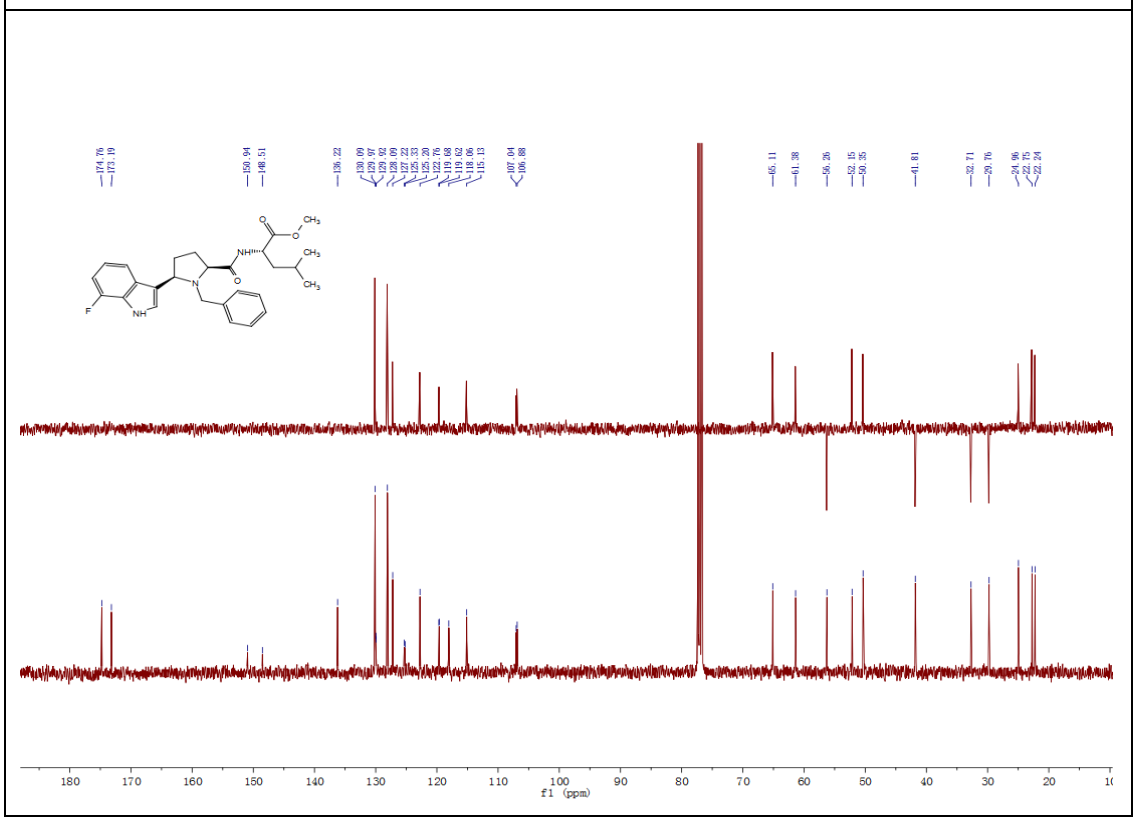
**Methyl ((2S,5R)-1-benzyl-5-(6-fluoro-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3h:**



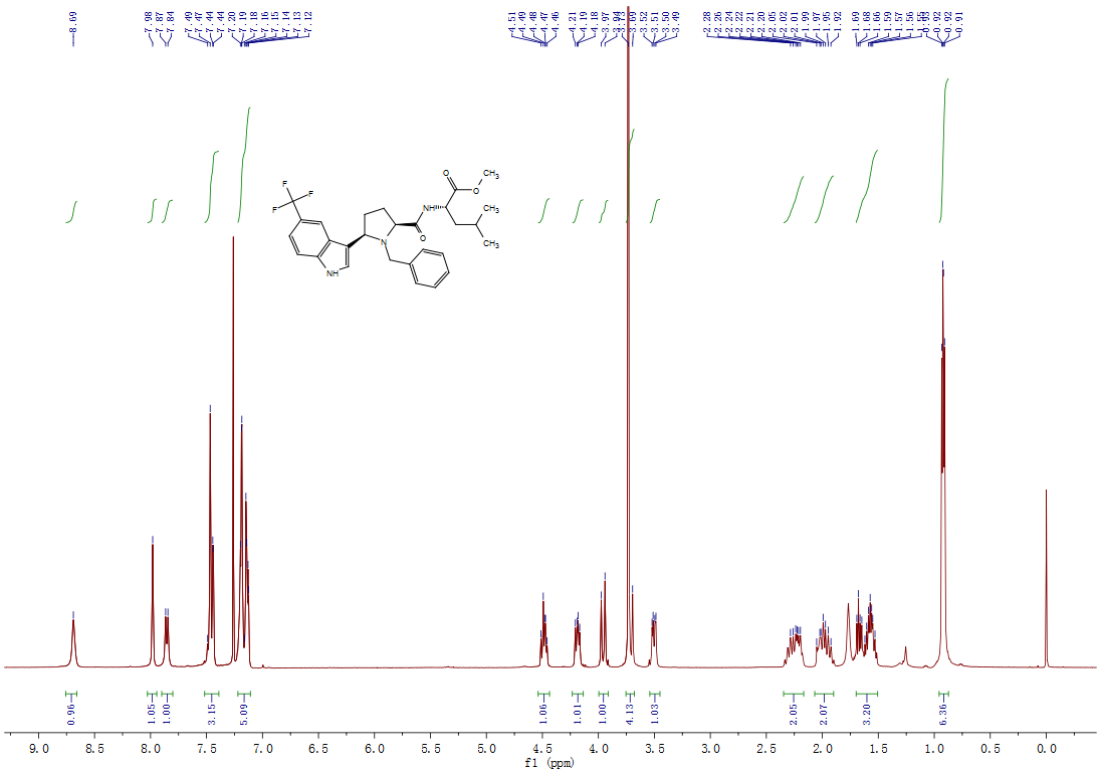



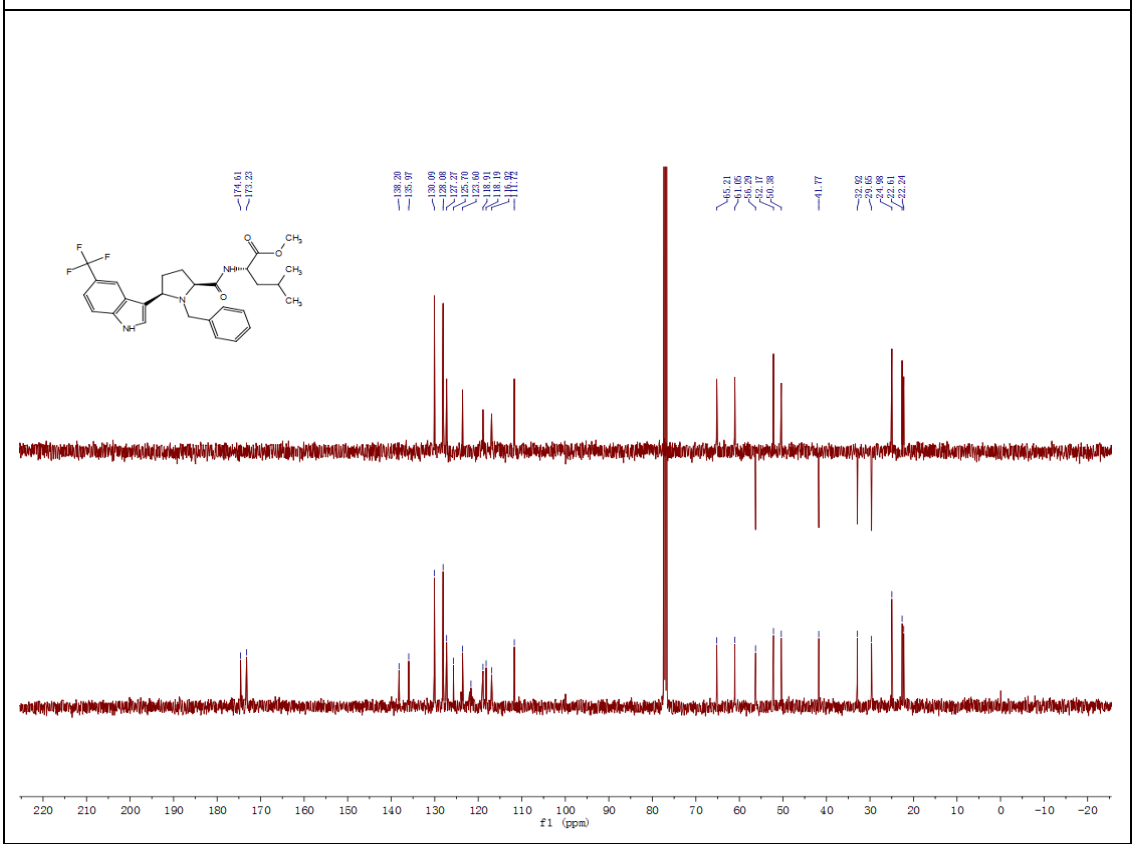
**Methyl ((2S,5R)-1-benzyl-5-(7-fluoro-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3i:**



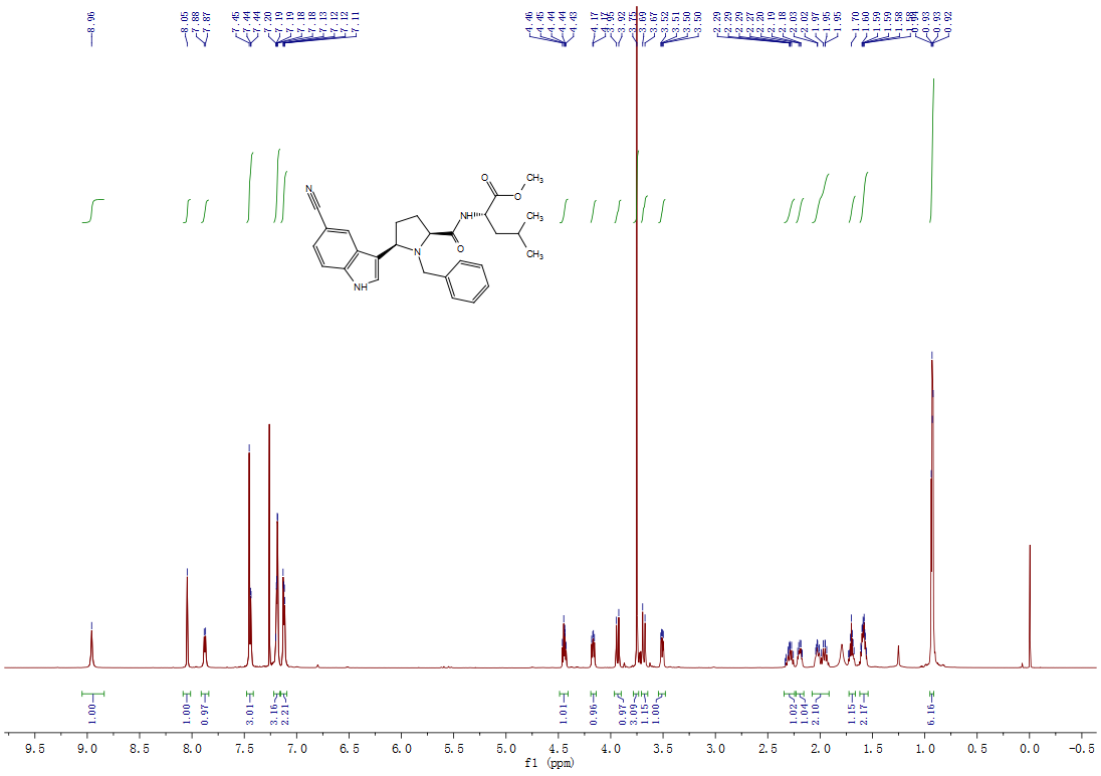



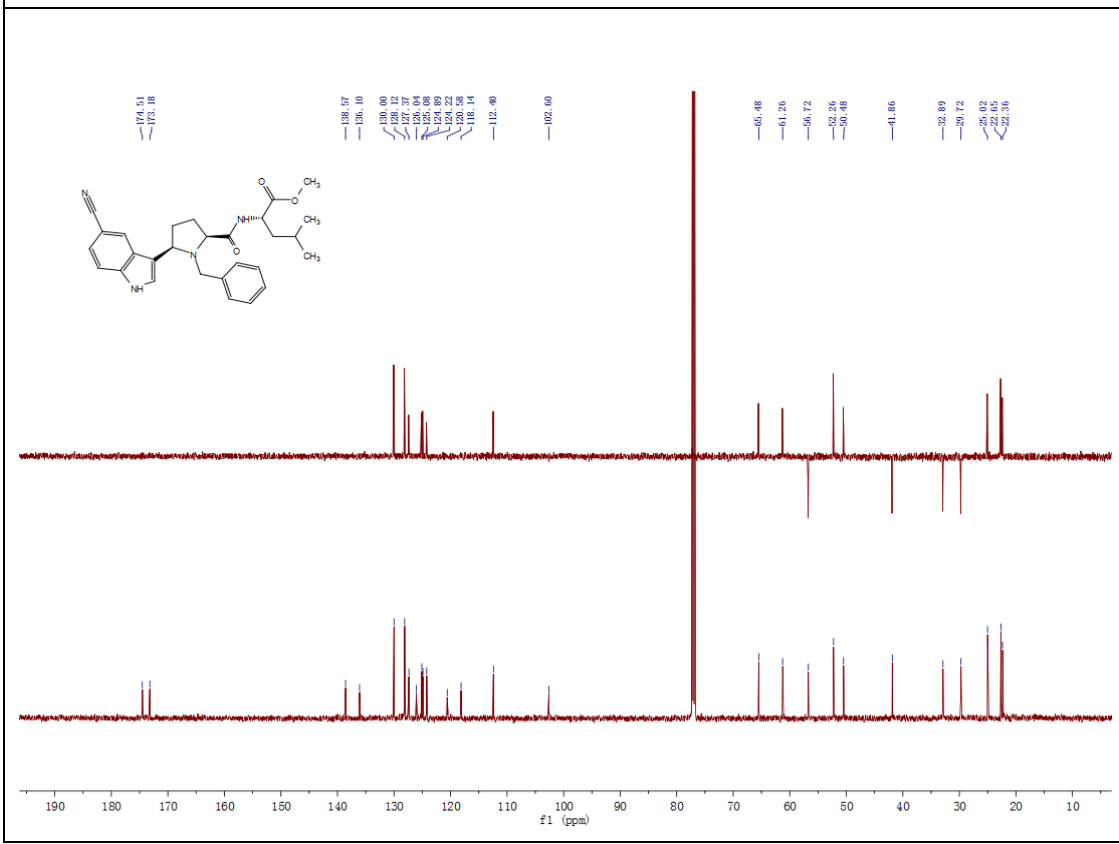
**Methyl ((2S,5R)-1-benzyl-5-(5-(trifluoromethyl)-1H-indol-3-yl)pyrrolidine-2-car -bonyl)-L-leucinate 3j:**



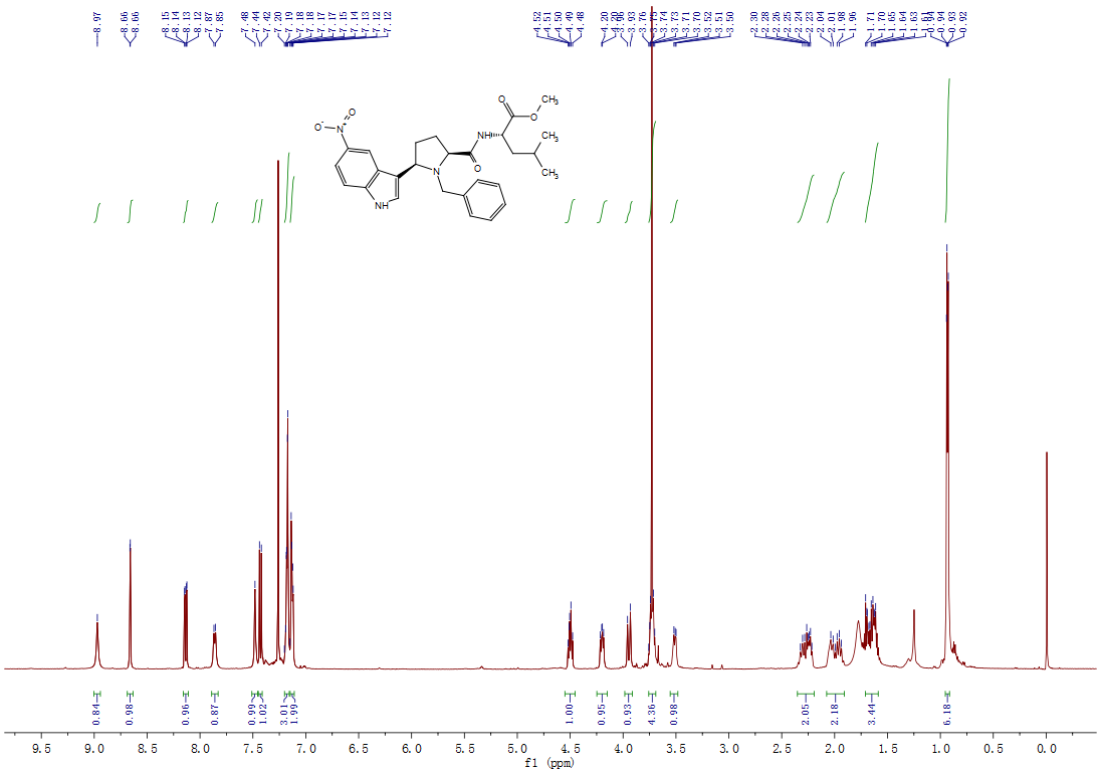



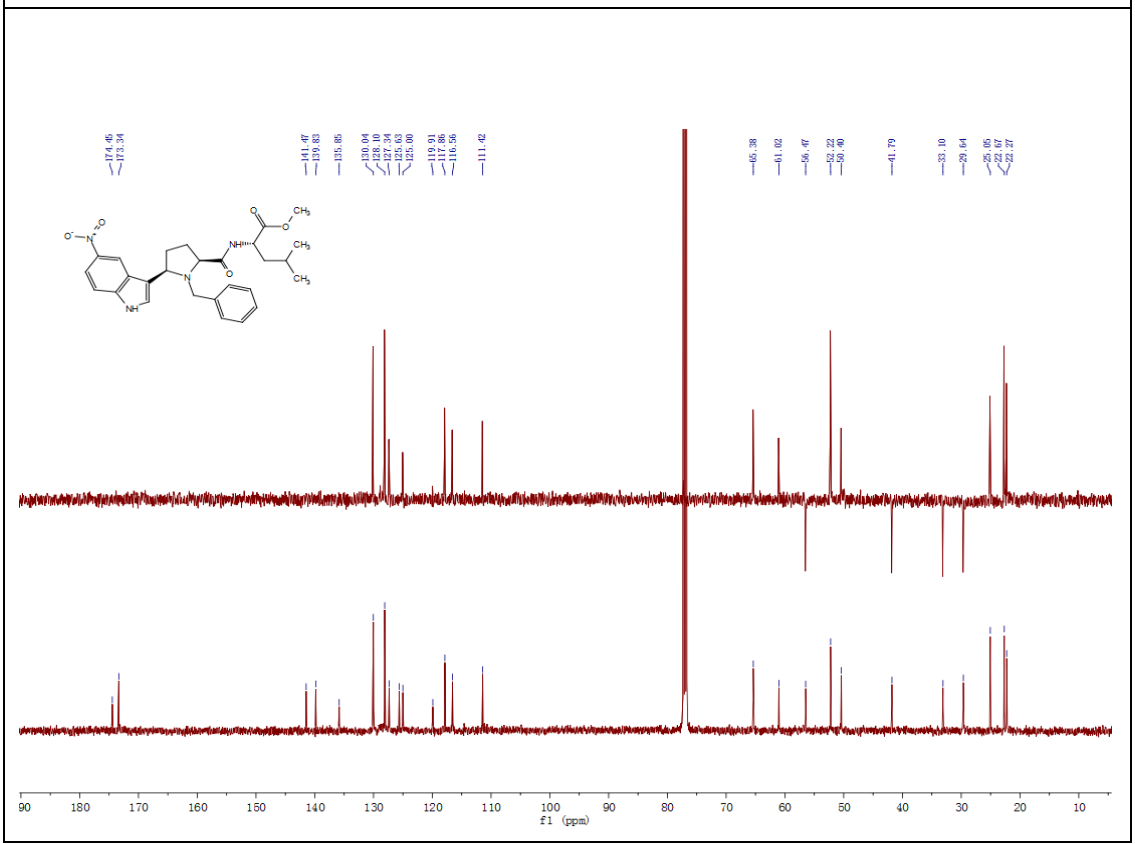
**Methyl ((2S,5R)-1-benzyl-5-(5-cyano-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-leucinate 3k:**



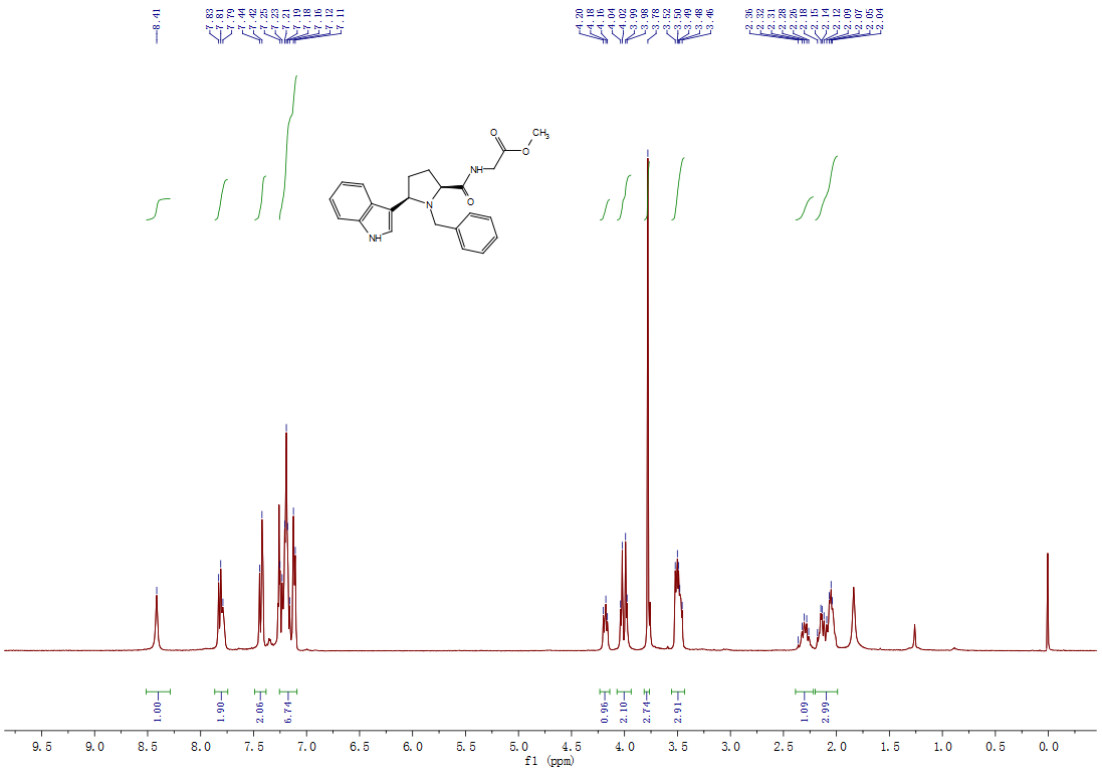



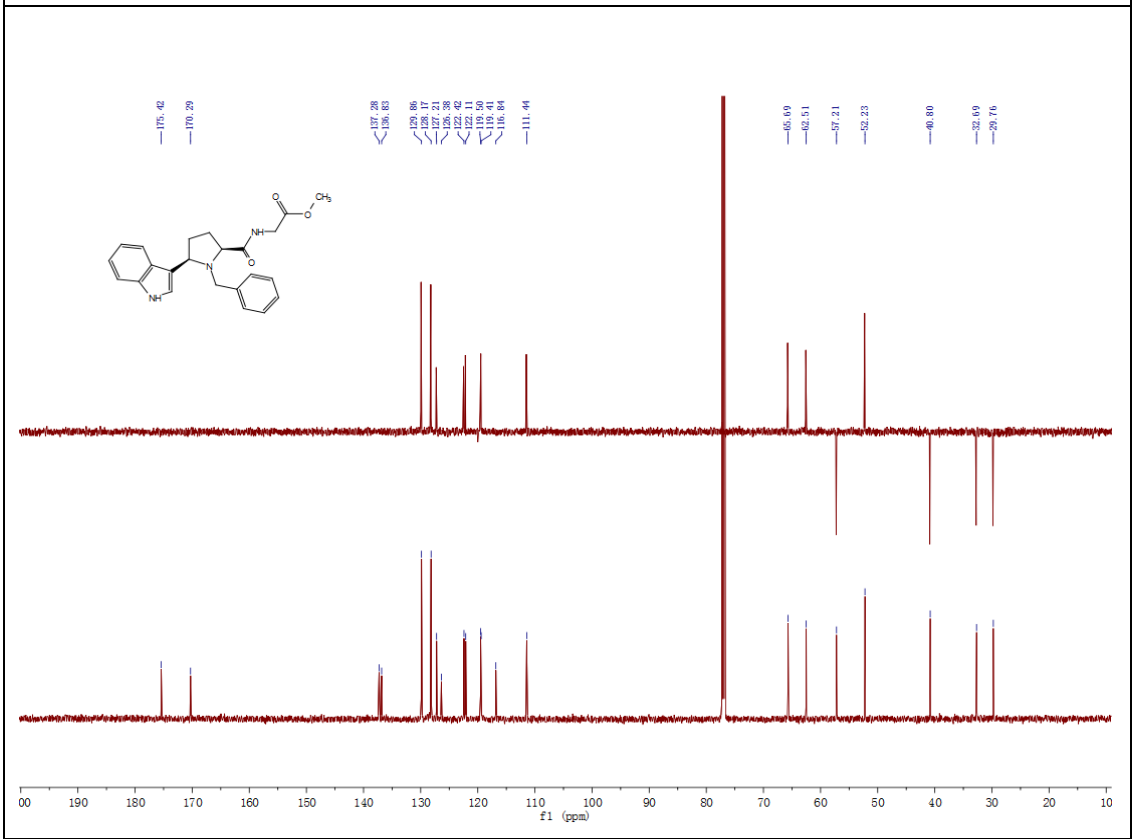
**Methyl ((2S,5R)-1-benzyl-5-(5-nitro-1H-indol-3-yl)pyrrolidine-2-carbonyl)-L -leucinate 3l:**



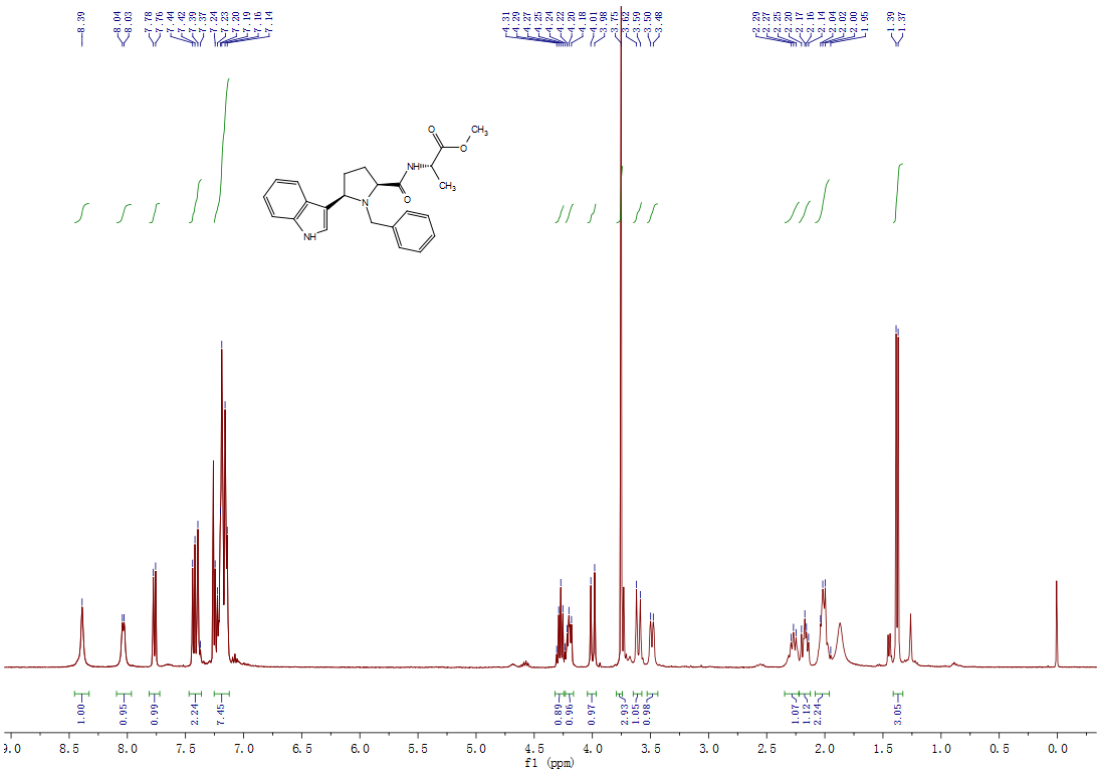



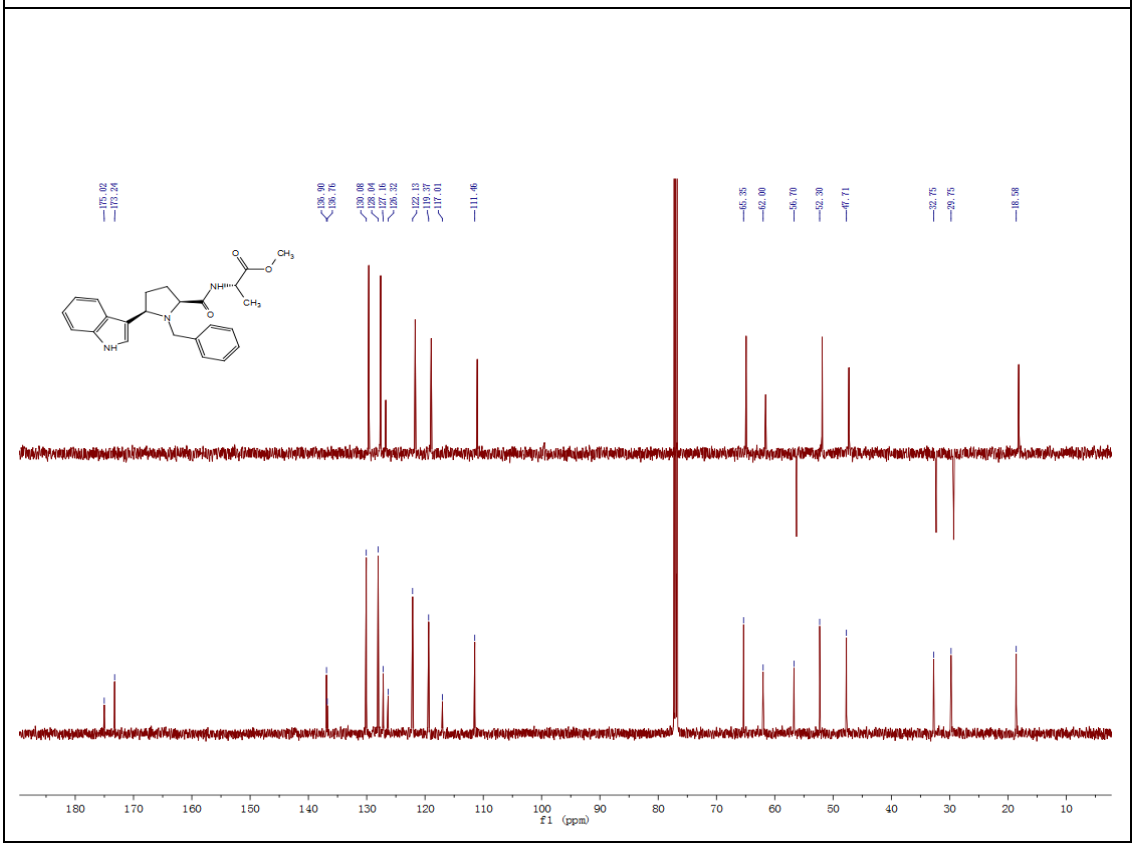
**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)glycinate 3n:**



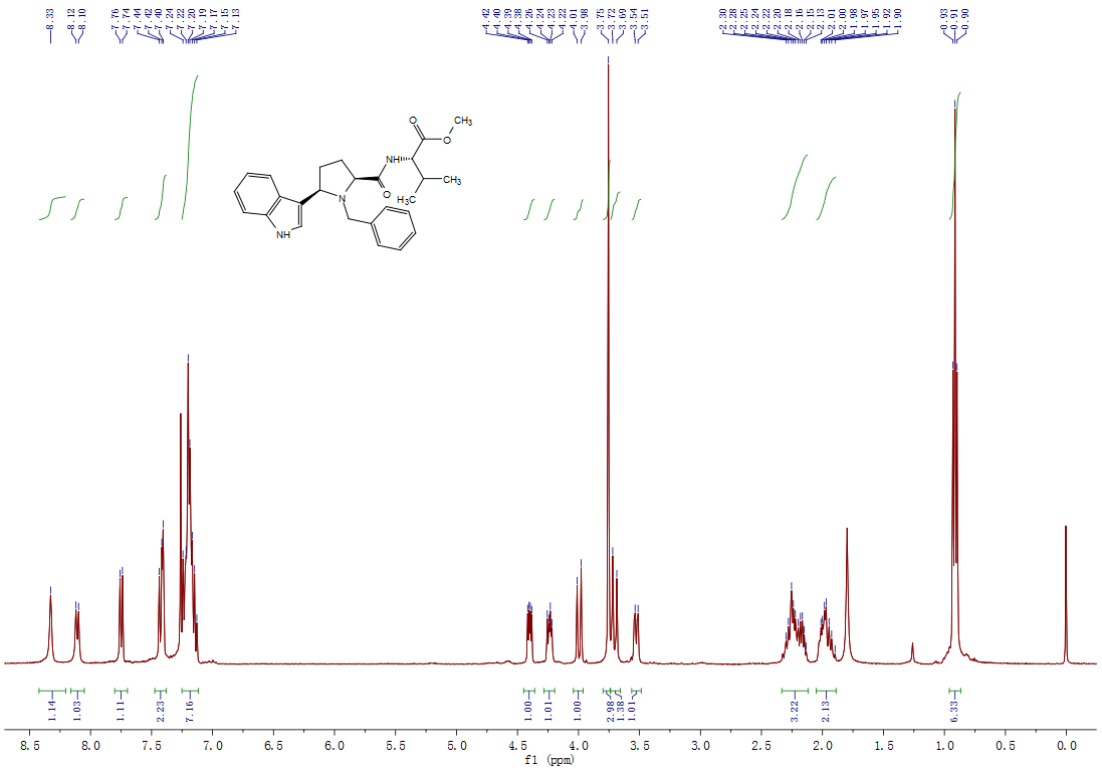



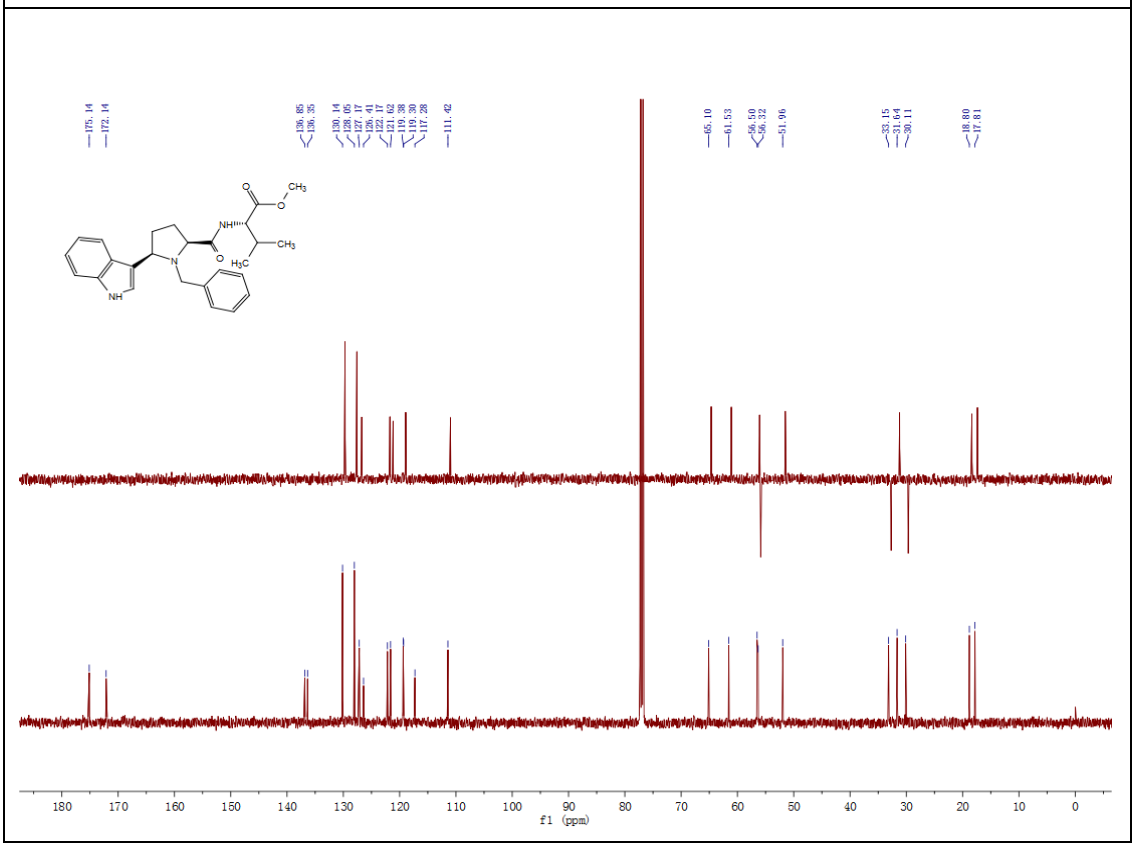
**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-alaninate 3o:**



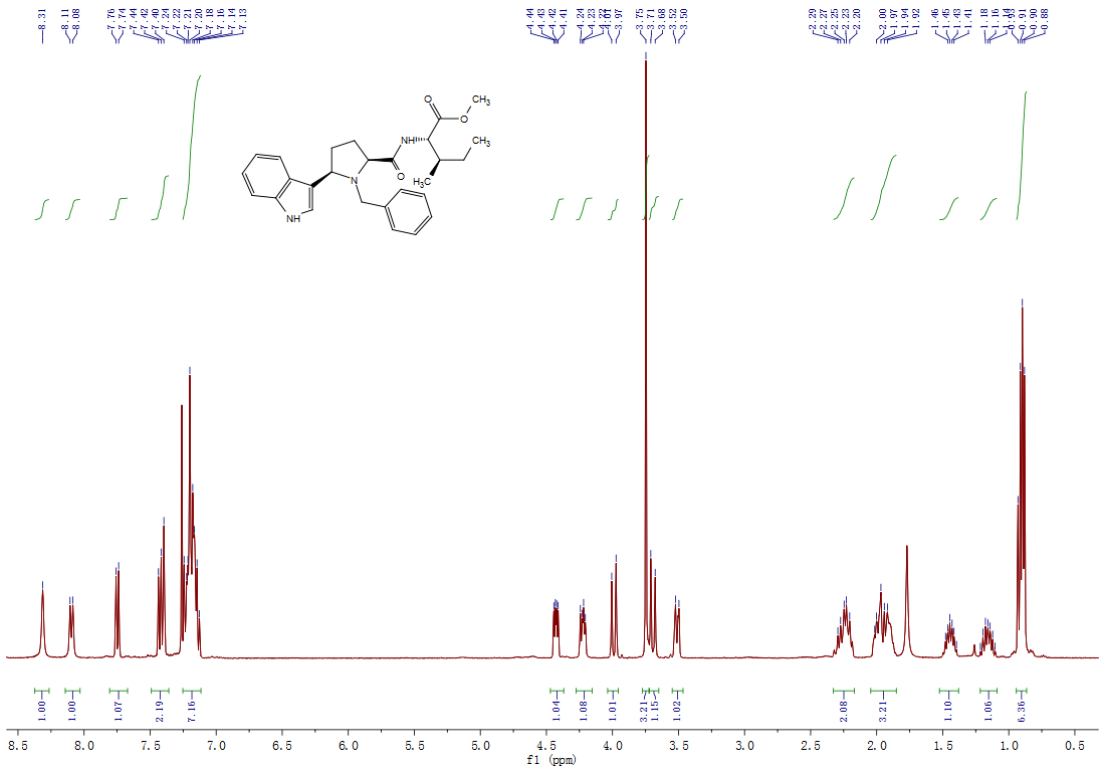


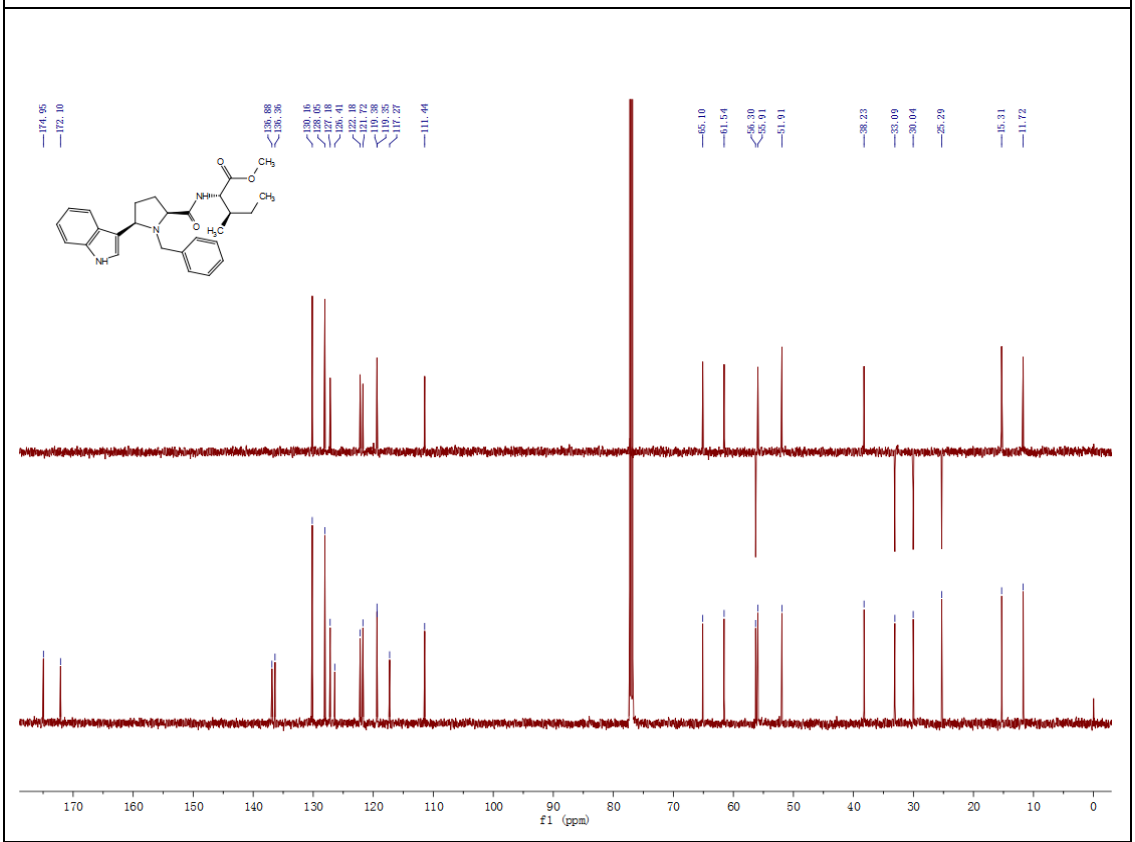
**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-valinate 3p:**



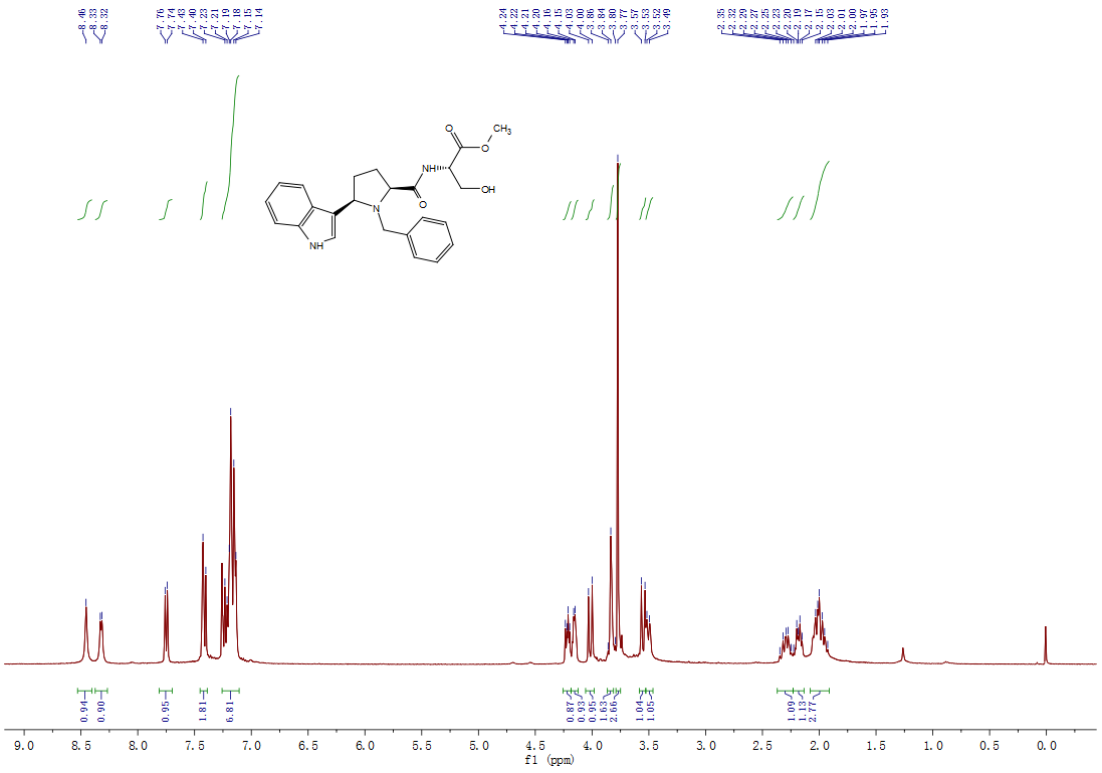


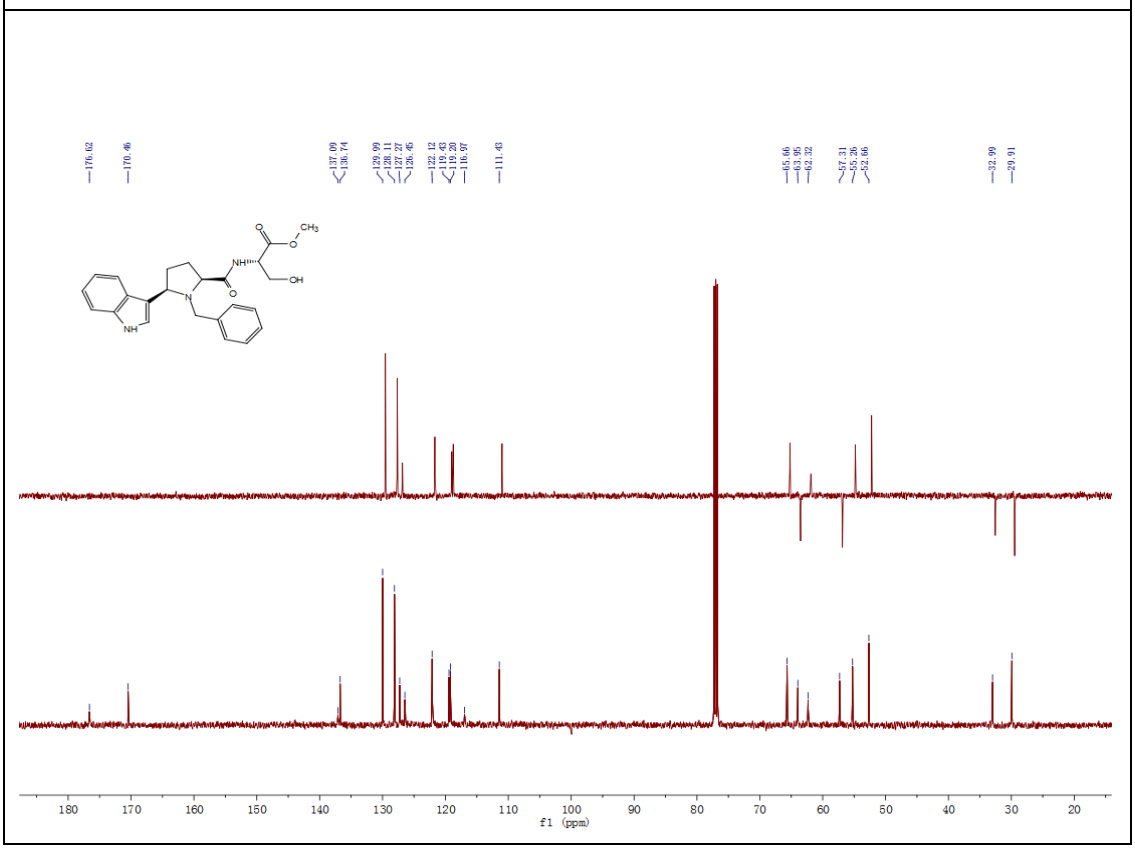
**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-alloisol-eucinate 3q:**



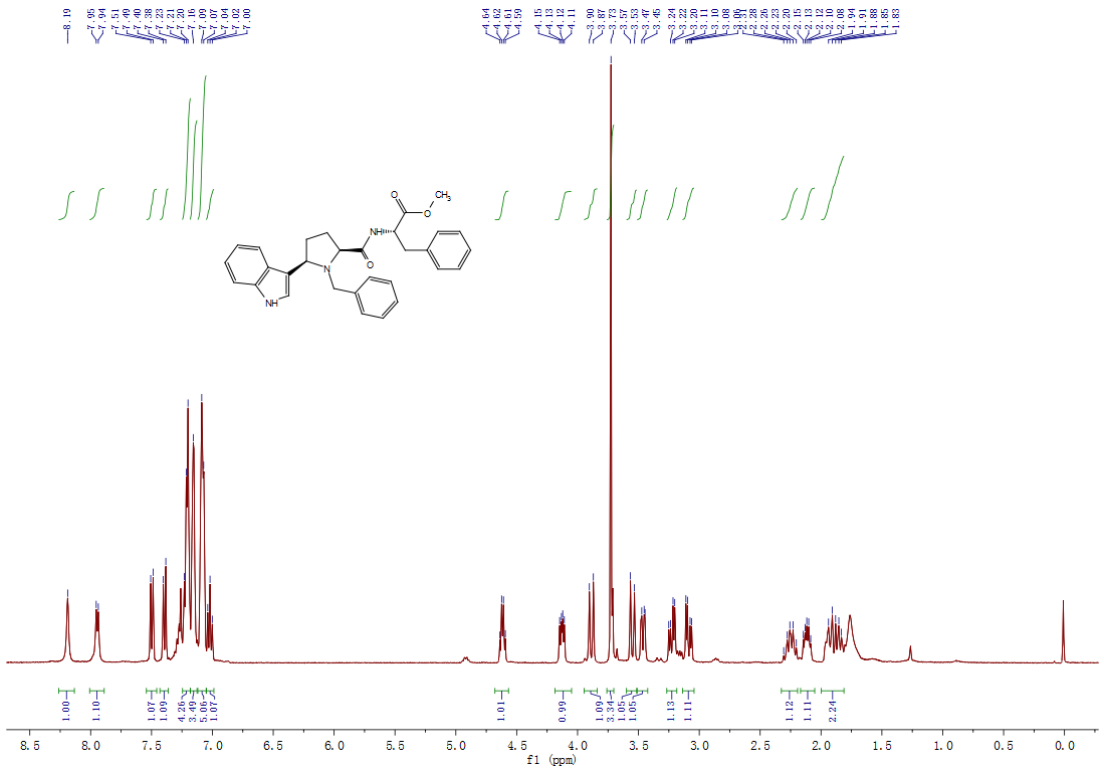



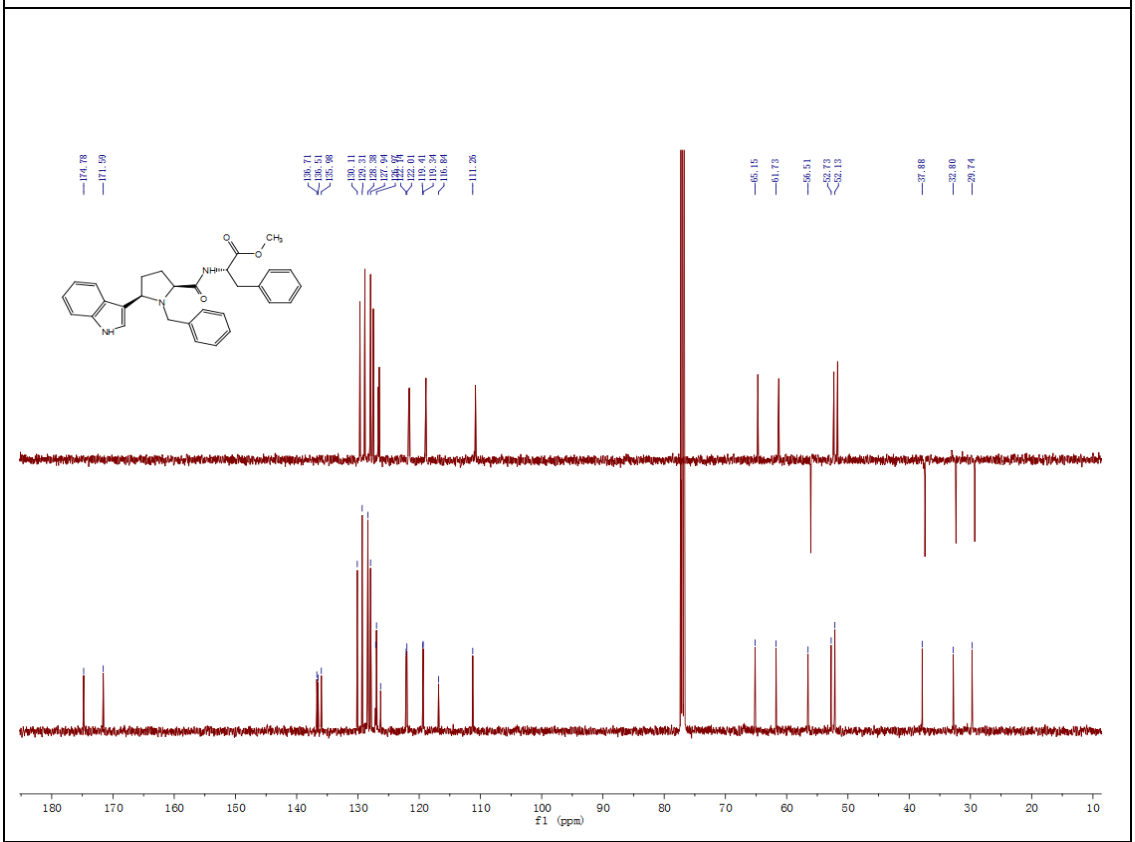
**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-serinate 3r:**



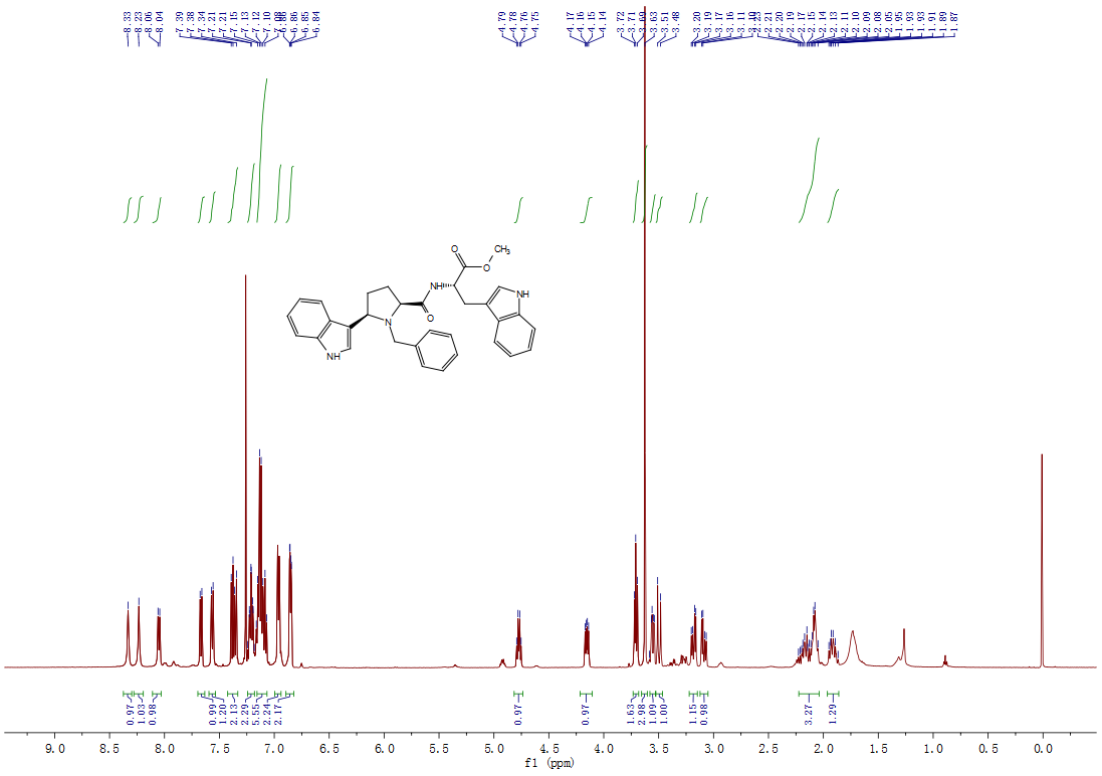


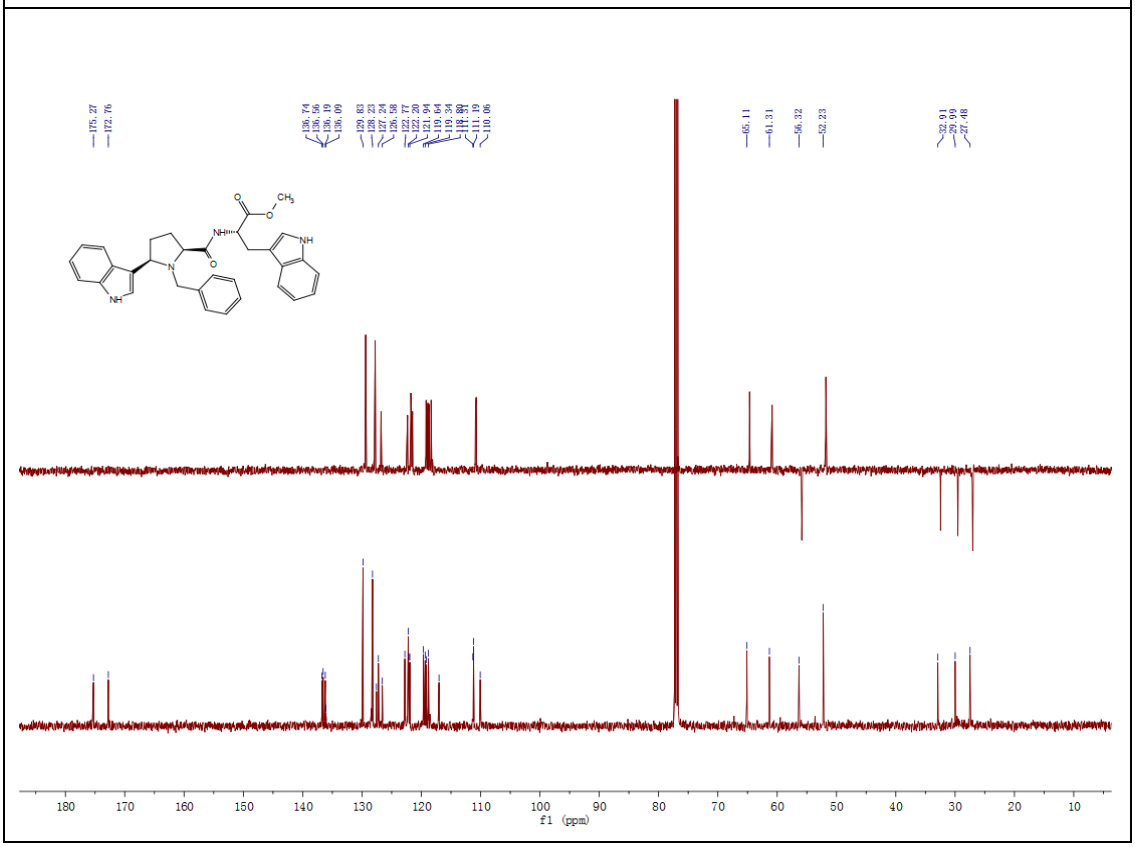
**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-phenylalaninate 3s:**



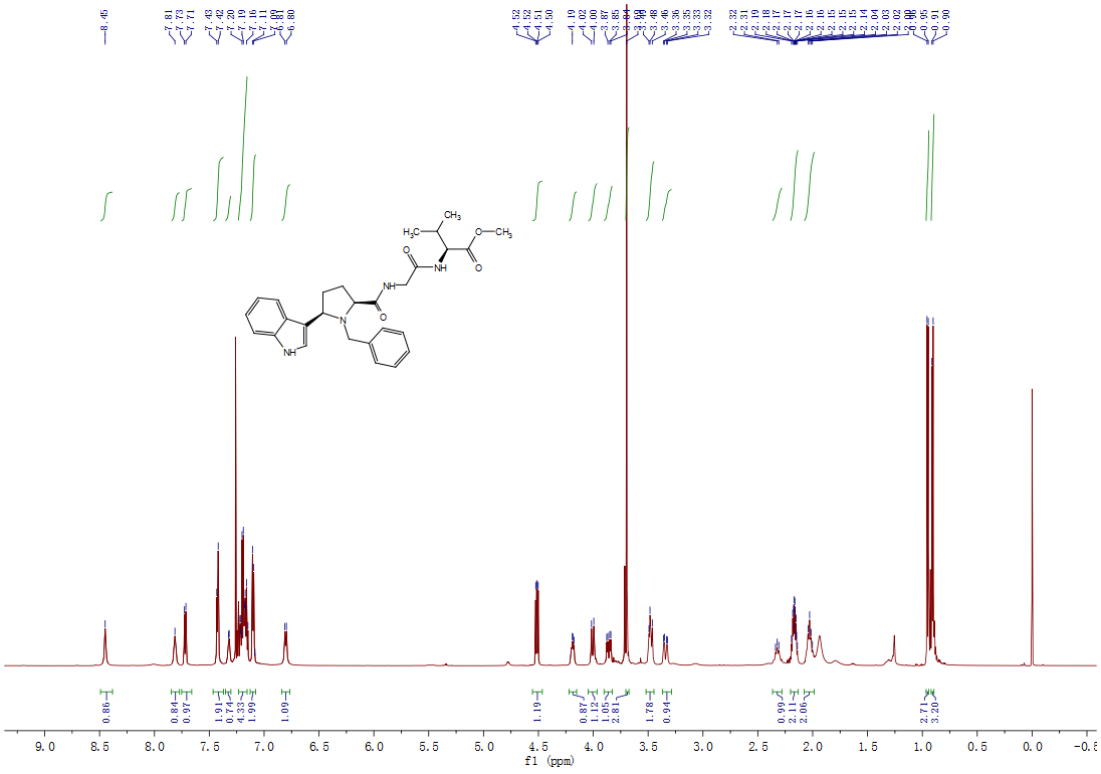



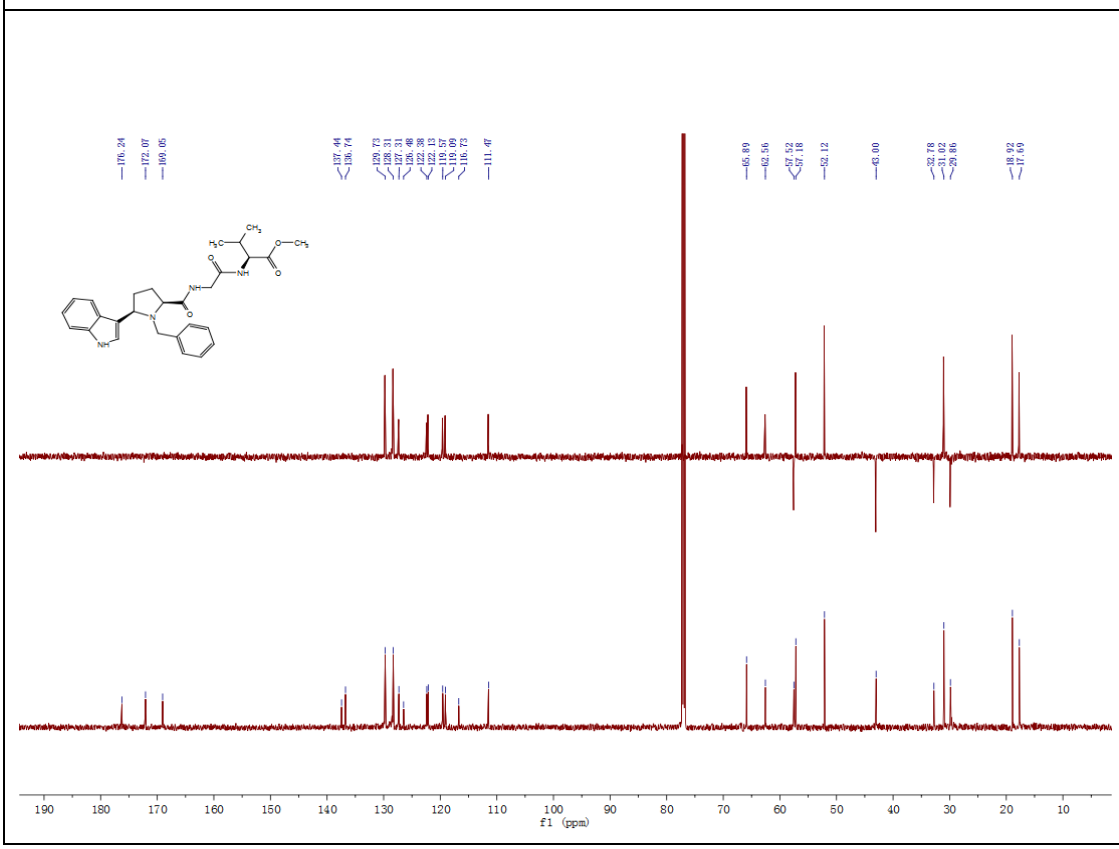
**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)-L-tryptophanate 3t:**



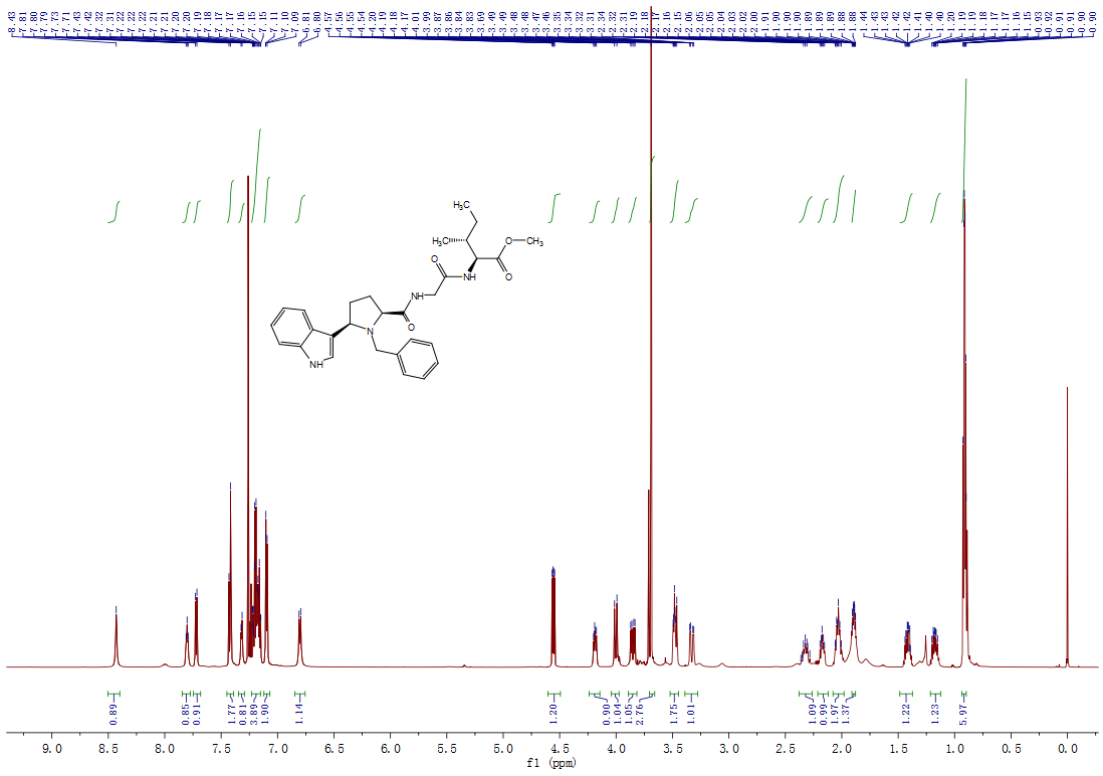


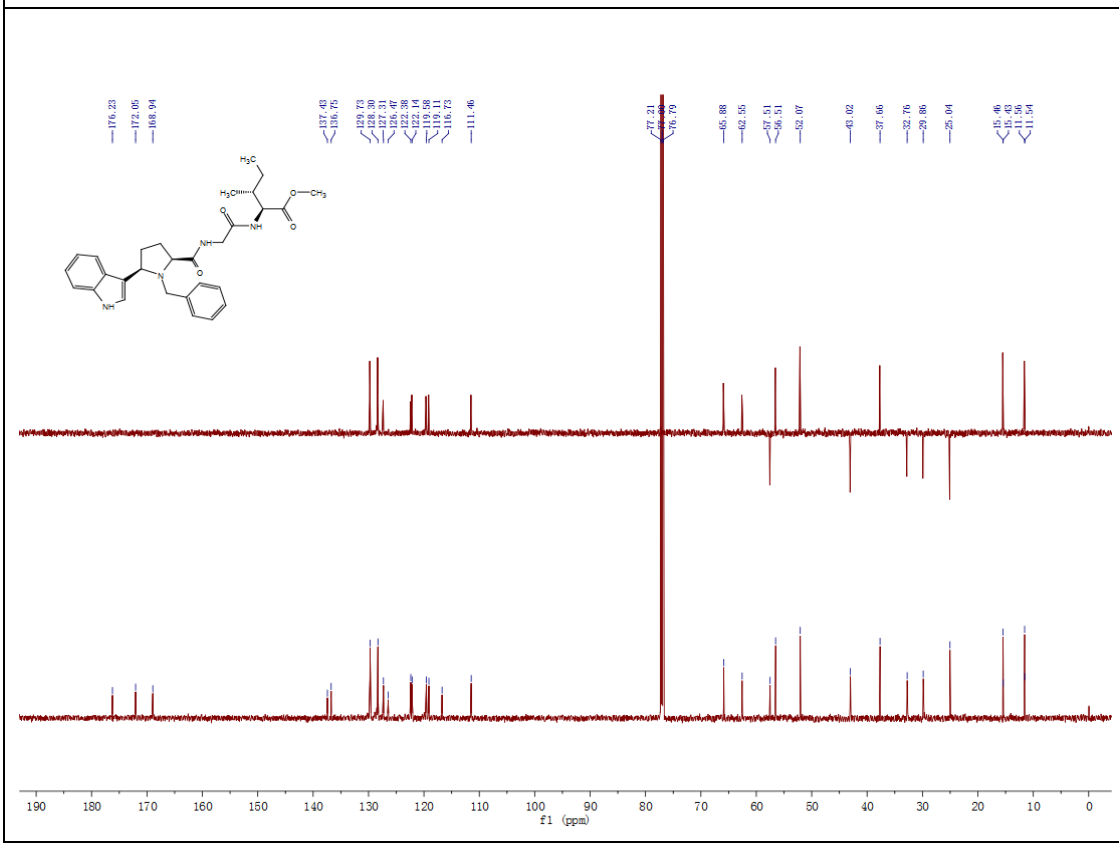
**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)glycyl-L-valinate 3u:**





**Methyl ((2S,5R)-1-benzyl-5-(1H-indol-3-yl)pyrrolidine-2-carbonyl)glycyl-L-all-oisoleucinate 3v:**





## (G) Reference

1 J. S. Chen, R. Properzi, D. P. Uccello, J. A. Young, R. G. Dushin, J. T. Starr, Org. Lett., 2014, 16, 4146−4149.