Supplemental Information for

Late-Stage Peptide Modification and Macrocyclization Enabled by Tertiary Amine Catalyzed Tryptophan Allylation

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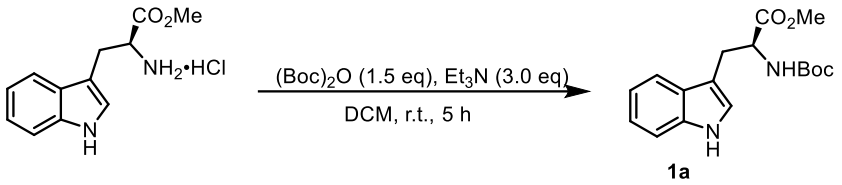
1. General information

Unless stated otherwise, all reactions were carried out in flame-dried glassware. All solvents were purified and dried according to standard methods prior to use. All chemical reagents were purchased from Energy Chemical and GL Biochem and were used without further purification. peptides and MBH-Carbonates were prepared according to literature. Solid phase peptide synthesis was performed on Rink Amind-MBHA Resin (100-200 mesh, 0.42 mmol/g) and 2-Chlorotrityl Chloride Resin (100-200 mesh, 0.97 mmol/g) in a 20 mL filtration tube. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker instrument (300 MHz and 75 MHz, respectively) and internally referenced to tetramethylsilane signal or residual protio solvent signals. Data for ^{1}H NMR were recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet or unresolved, dd = doublet of doublet, td = triplet of doublets, dt = doublet of triplets, coupling constant(s) in Hz, integration). Data for ^{13}C NMR were reported in terms of chemical shift (δ, ppm). High resolution mass spectra (HRMS) were obtained by quadrupole mass spectrometer with ESI ionization sources. Semi-preparative HPLC was performed on a Waters 2996 using a Dubhe C18 (10 μm, 20 × 250 mm) preparative column. Linear gradients using A: MeCN (0.1% CF_3COOH) and B: H_2O (0.1% CF_3COOH) were run over varying periods of time. Purity analysis was performed on Waters e2695/2998 using a XBridge® Peptide BEH C18 (10 μm, 4.6 mm x 250 mm) Column. LC-MS/MS spectra were performed on Agilent 6100 LC/MS using an Agilent 5 HC-C18 (2) (250 x 4.6 mm) column.

2. Experimental Section

2.1 Procedure for Synthesis of Protected Tryptophan and Tryptophan-containing Peptides

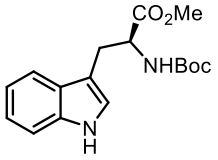
General Procedure A for Synthesis of N-protected Tryptophan



1a

To a 100 mL round-bottom flask, Trp-OMe·HCl (5.08 g, 20 mmol) was dissolved in 40 mL DCM at room temperature, Et_3N (13.9 mL, 60 mmol) was added slowly via syringe and stirred for 5 min. Then $(Boc)_2O$ (6.55 g, 30 mmol) was added dropwise into the mixture. The reaction was stirred at room temperature for 5 h. Upon completion as indicated by TLC, the reaction mixture was added to water and extracted with DCM, and washed with brine twice. The combined organic layer was dried with anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel using hexanes/EtOAc (4/1) as the eluent giving the pure product as a white solid (6.23 g, 98% yield).

methyl (tert-butoxycarbonyl)-L-tryptophanate (1a):



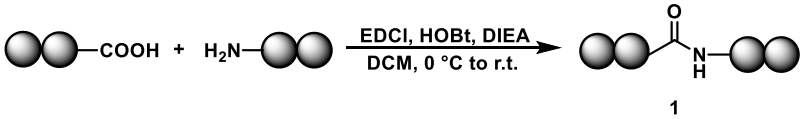
1a

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 7.8 Hz, 1H), 7.15 (dt, *J* = 22.2, 7.2 Hz, 2H), 6.97 (s, 1H), 5.09 (d, *J* = 7.5 Hz, 1H), 4.65 (q, *J* = 6.6 Hz, 1H), 3.67 (s, 3H), 3.28 (d, *J* = 4.8 Hz, 2H), 1.43 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.8, 155.3, 136.1, 127.7, 122.8, 122.2, 119.6, 118.7, 111.2, 110.1, 79.9, 54.2, 52.3, 28.3, 28.0. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{17}H_{22}N_2O_4Na^+$ 341.1472, Found: 341.1462。

The synthetic procedure of tryptophan-containing peptides was prepared following the reported procedure [1].

General Procedure B for Synthesis of Tryptophan-containing peptides (1b-1m, 1o) via LPPS

Tryptophan-containing peptide derivatives were obtained by LPPS strategies. Synthesis of all peptides has been accomplished by performing the active ester reaction.

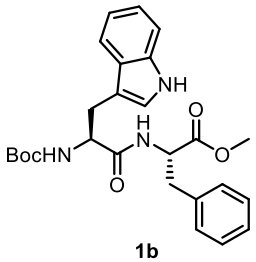


1

To a 100 mL round-bottom flask, Boc-*L*- amino acids (5.0 mmol, 1.0 equiv.), EDCI (6.0 mmol, 1.2 equiv.), and HOBt (6.0 mmol, 1.2 equiv.) were dissolved in 30 mL DCM at 0 ℃, DIEA (15.0 mmol, 3.0 equiv) was added and stirred for 10 min. Corresponding amino acid (1.2 equiv.) or oligopeptide was added. The reaction mixture maintained the temperature for 30 min and then

warmed to room temperature and stirred overnight. After the reaction was completed, the reaction mixture was extracted with DCM and washed with 5% Citric acid (30 mL), saturated $NaHCO_3$ (30 mL), and brine (2 x 40 mL), the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography and the desired product **1** was obtained.

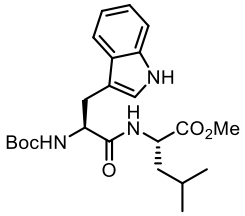
methyl (tert-butoxycarbonyl)-L-tryptophyl-L-phenylalaninate (1b)



1b

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 2.21 g, 95% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.34 (d, *J* =8.1 Hz, 1H), 7.25 – 7.08 (m, 5H), 6.98 (s, 1H), 6.79 (d, *J* = 6.6 Hz, 2H), 6.25 (s, 1H), 5.14 (s, 1H), 4.72 (d, *J* = 5.7 Hz, 1H), 4.44 (s, 1H), 3.60 (s, 3H), 3.30 (d, *J* = 12.0 Hz, 1H), 3.13 (dd, *J* = 14.4, 6.9 Hz, 1H), 2.92 (d, *J* = 5.4 Hz, 2H), 1.41 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.4, 155.4, 136.3, 135.6, 129.2, 128.5, 127.5, 127.0, 123.4, 122.2, 119.7, 118.9, 111.3, 110.3, 80.1, 55.2, 53.2, 52.3, 37.9, 28.3. **HRMS(ESI)** m/z $[M+Na]^+$: Calcd for $C_{26}H_{31}N_5O_3Na^+$ 488.2156, Found: 488.2141.

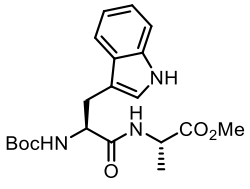
methyl (tert-butoxycarbonyl)-L-tryptophyl-L-leucinate (1c):



1c

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 1.98 g, 92% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.65 (d, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.18 (t, 7.2 Hz, 1H), 7.12 (d, *J* = 7.5 Hz, 1H), 7.06 (s, 1H), 6.29 (d, *J* = 8.1 Hz, 1H), 5.22 (s, 1H), 4.56 - 3.38 (m, 2H), 3.63 (s, 3H), 3.35 – 3.14 (m, 2H), 1.43 (s, 12H), 0.84 (t, *J* = 4.2 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.9, 171.5, 155.5, 136.3, 127.5, 123.4, 122.1, 119.6, 118.8, 111.2, 110.4, 80.1, 55.1, 52.2, 50.8, 41.5, 28.3, 24.6, 22.7, 21.9. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{23}H_{33}N_3O_5Na^+$ 454.2312, Found: 454.2300.

methyl (tert-butoxycarbonyl)-L-tryptophyl-L-alaninate (1d):

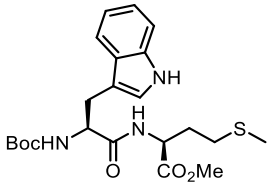


1d

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 1.81 g, 93% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 8.1

Hz, 1H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.11 (t, *J* = 7.8 Hz, 2H), 6.39 (d, *J* = 6.9 Hz, 1H), 5.20 (s, 1H), 4.45 (t, *J* = 6.3 Hz, 2H), 3.64 (s, 3H), 3.32 (d, *J* = 11.1 Hz, 1H), 3.18 (dd, *J* = 14.1, 7.2 Hz, 1H), 1.43 (s, 9H), 1.26 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.8, 171.2, 155.4, 136.2, 123.3, 122.2, 119.7, 118.9, 111.2, 110.5, 80.1, 77.2, 52.4, 48.1, 28.3, 18.3. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{20}H_{27}N_3O_5Na^+$ 412.1843, Found: 412.1833

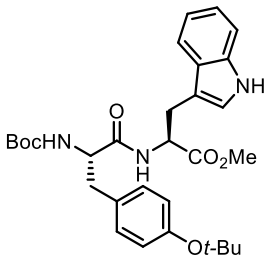
methyl (tert-butoxycarbonyl)-L-tryptophyl-L-methioninate (1e):



1e

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 2.02 g, 90% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 1.52 (dt, *J* = 22.3, 6.9 Hz, 2H), 7.07 (s, 1H), 6.52 (s, 1H), 5.20 (s, 1H), 4.58 (q, *J* = 6.6 Hz, 1H), 4.47 (s, 1H), 3.64 (s, 3H), 3.34 (dd, *J* = 14.1, 4.5 Hz, 1H), 3.17 (dd, *J* = 14.4, 7.2 Hz, 1H), 2.26 (s, 2H), 1.99 (s, 4H), 1.91 - 1.75 (m, 1H), 1.44 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.8, 155.5, 136.3, 127.5, 123.4，122.2, 119.7, 118.7, 111.3, 110.2, 80.2, 55.34, 52.5, 51.6, 31.4, 29.5, 28.3, 15.3. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{22}H_{31}N_3O_5SNa^+$ 472.1877, Found: 472.1862.

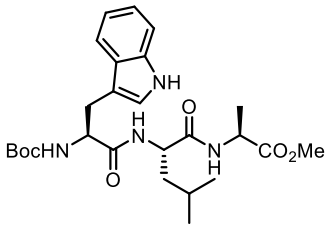
methyl ((S)-3-(4-(tert-butoxy)phenyl)-2-((tert-butoxycarbonyl)amino)propanoyl)-L-tryptophanate (1f):



1f

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:1), 2.44 g, 91% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.18 (t, *J* = 7.8 Hz, 1H), 7.06 (t, *J* = 6.3 Hz, 3H), 6.85 (d, *J* = 8.1 Hz, 2H), 6.78 (s, 1H), 6.26 (d, *J* = 6.9 Hz, 1H), 4.98 (d, *J* = 6.6 Hz, 1H), 4.83 (q, *J* = 6.6 Hz, 1H), 4.31 (d, *J* = 5.7 Hz, 1H), 3.63 (s, 3H), 3.36 – 3.11 (m, 2H), 2.95 (d, *J* = 6.0 Hz, 2H), 1.37 (s, 9H), 1.32 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.7, 170.8, 154.2, 136.0, 131.5, 129.9, 127.4, 124.4, 122.8, 122.2, 119.6, 118.5, 111.3, 109.6, 78.5, 77.2, 52.8, 52.3, 37.8, 28.8, 28.2, 27.5. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{30}H_{39}N_3O_6Na^+$ 560.2742, Found: 560.2718.

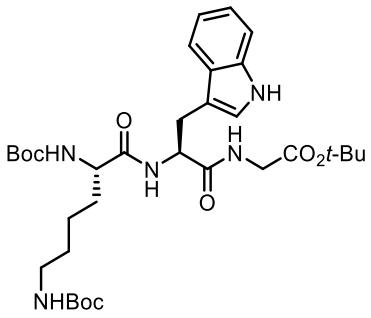
methyl (tert-butoxycarbonyl)-L-tryptophyl-L-leucyl-L-alaninate (1g):



1g

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:1), 1.96 g, 78% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.50 (s, 1H), 7.67 (d, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.22 – 7.10 (m, 2H), 7.09 (s, 1H), 6.90 (d, *J* = 7.8 Hz, 1H), 6.50 (d, *J* = 6.3 Hz, 1H), 5.03 (d, *J* = 6.0 Hz, 1H), 4.76 (q, *J* = 6.8 Hz, 1H), 4.57 – 4.32 (m, 1H), 4.12 (t, *J* = 6.0 Hz, 1H), 3.64 (s, 3H), 3.37 (d, *J* = 13.2 Hz, 1H), 3.16 (dd, *J* = 14.7, 7.5 Hz, 1H), 1.60 – 1.43 (m, 2H), 1.32 (s, 13H), 0.83 (t, *J* = 4.5 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.8, 172.0, 171.0,155.5, 136.3, 127.3, 127.5, 123.6, 122.2, 119.7, 118.8, 113.3, 115.2, 80.2, 53.7, 52.2, 51.0, 41.1, 28.2, 24.6, 22.6, 21.9, 18.3. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{26}H_{38}N_4O_6Na^+$ 525.2684, Found: 525.2671.

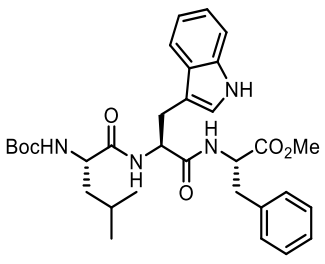
tert-butyl N^2, N^6-bis(tert-butoxycarbonyl)-L-lysyl-L-tryptophylglycinate (1h):



1h

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:1), 2.10 g, 65% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.87 (s, 1H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.21 – 7.07 (m, 3H), 6.95 (s, 1H), 6.73 (d, *J* = 7.2 Hz, 1H), 5.23 (s, 1H), 4.89 – 4.62 (m, 2H), 3.95 (s, 1H), 3.91 – 3.71 (m, 2H), 3.30 (d, *J* = 6.0 Hz, 2H), 3.01 (d, *J* = 5.7 Hz, 2H), 1.45 (d, *J* = 7.5 Hz, 21H), 1.36 (s, 10H), 1.08 (d, *J* = 7.2 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.1, 171.6, 168.5, 136.2, 127.6, 123.5, 122.0, 119.5, 118.5, 111.4, 111.0, 81.9, 80.4, 79.3, 55.3, 53.6, 42.1, 39.61, 31.18, 29.8, 28.5, 28.2, 28.0, 27.4, 22.0. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{33}H_{52}N_5O_8^+$ 646.3810, Found: 646.3797.

methyl (tert-butoxycarbonyl)-L-leucyl-L-tryptophyl-L-phenylalaninate (1i):

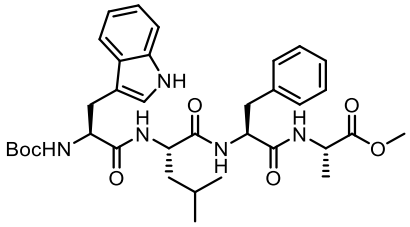


1i

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:1), 2.27 g,

75% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.72 (d, *J* = 7.7 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.24 – 7.05 (m, 5H), 7.03 (s, 1H), 6.80 (d, *J* = 7.0 Hz, 3H), 6.23 (d, *J* = 7.6 Hz, 1H), 4.88 (d, *J* = 7.5 Hz, 1H), 4.80 – 4.65 (m, 2H), 4.09 (s, 1H), 3.61 (s, 3H), 3.35 (dd, *J* = 14.3, 4.9 Hz, 1H), 3.22 – 3.02 (m, 1H), 2.99 – 2.78 (m, 2H), 1.66 – 1.51 (m, 2H), 1.41 (s, 10H), 0.87 (t, *J* = 6.0 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.4, 171.2, 170.6, 155.6, 136.2, 135.6, 129.1, 128.5, 127.4, 127.0, 123.6, 122.3, 119.8, 118.9, 111.3, 110.3, 80.1, 53.6, 53.4, 52.2, 41.3, 37.7, 28.2, 24.7, 22.9, 21.8. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{32}H_{43}N_4O_6^+$ 579.3177, Found: 579.3163.

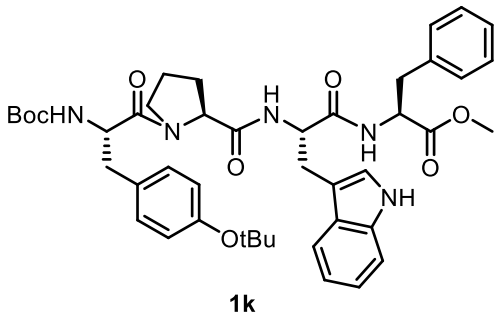
methyl (tert-butoxycarbonyl)-L-tryptophyl-L-leucyl-L-phenylalanyl-L-alaninate (1j):



1j

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:2), 1.65 g, 51% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.25 – 7.09 (m, 5H), 6.99 (d, *J* = 5.7 Hz, 3H), 6.60 (d, *J* = 8.1 Hz, 1H), 6.25 (d, *J* = 6.6 Hz, 1H), 5.24 (d, *J* = 6.9 Hz, 1H), 4.71 (q, *J* = 8.1Hz, 1H), 4.46 (t, *J* = 7.8 Hz, 1H), 4.39 (d, *J* = 6.6 Hz, 1H), 4.37 – 4.24 (m, 1H), 3.71 (s, 3H), 3.19 (d, *J* = 6.6 Hz, 3H), 2.86 – 2.70 (m, 2H), 1.50 – 1.22 (m, 14H), 1.12 (t, *J* = 9.0 Hz, 1H), 0.75 (t, *J* = 6.0 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.9, 172.5, 171.9, 170.7, 155.9, 136.8, 136.3, 129.1, 128.4, 127.2, 126.7, 123.5, 122.3, 119.7, 118.6, 111.6, 109.9, 80.5, 55.5, 53.8, 52.4, 48.4, 40.6, 37.2, 28.3, 27.9, 24.4, 22.8, 21.7, 17.7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{35}H_{48}N_5O_7^+$ 650.3548, Found: 650.3543.

methyl ((S)-3-(4-(tert-butoxy)phenyl)-2-((tert-butoxycarbonyl)amino)propanoyl)-L-prolyl-L-tryptophyl-L-phenylalaninate, (1k):

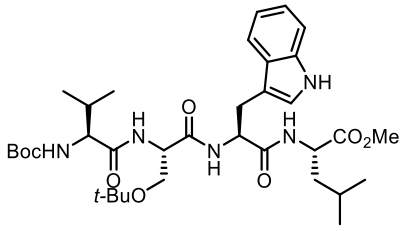


1k

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:1),, 2.11 g, 53% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.67 (t, *J* = 10.1 Hz, 1H), 7.20 (d, *J* = 4.6 Hz, 4H), 7.15 – 6.99 (m, 4H), 6.95 (q, *J* = 5.0, 4.5 Hz, 3H), 6.91 – 6.77 (m, 3H), 6.51 (d, *J* = 7.7 Hz, 1H), 5.16 (d, *J* = 8.7 Hz, 1H), 4.77 (p, *J* = 6.8 Hz, 2H), 4.45 (dt, *J* = 19.6, 8.1 Hz, 2H), 3.65 (d, *J* = 1.9 Hz, 3H), 3.41 (dt, *J* = 20.1, 12.2 Hz, 2H), 3.16 (dd, *J* = 14.5, 7.1 Hz, 1H), 3.02 (dt, *J* = 6.4, 3.9 Hz, 2H), 2.98 – 2.75 (m, 2H), 2.51 – 2.27 (m, 1H), 2.14 – 2.06 (m, 1H), 1.98 – 1.77 (m, 3H), 1.46 (d, *J* = 1.7 Hz, 2H), 1.35 (s, 7H), 1.30 (t, *J* = 2.0 Hz, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.1, 171.5, 170.9, 170.7, 155.1, 154.2, 136.1, 131.1, 129.9, 129.2, 129.1, 128.5, 128.4, 127.5, 126.9, 124.4, 124.2, 123.6, 122.3, 119.8, 118.7, 111.5, 110.1, 79.7, 78.4, 60.6,

53.8, 53.3, 52.3, 47.2, 37.6, 38.2, 37.6, 28.8, 28.5, 28.3, 28.1, 27.3, 25.0. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{44}H_{56}N_5O_8^+$ 782.4123, Found: 782.4123。

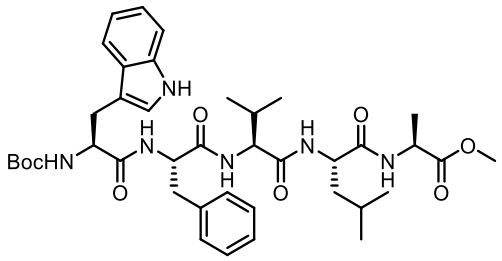
methyl N-((tert-butoxycarbonyl)-L-valyl)-O-(tert-butyl)-L-seryl-L-tryptophyl-L-leucinate (1l):



1l

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:2), 1.51 g, 45% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.24 – 7.08 (m, 3H), 7.07 (s, 1H), 6.91 (s, 1H), 6.63 (s, 1H), 5.03 (d, *J* = 6.9 Hz, 1H), 4.88 (q, *J* = 6.9 Hz, 1H), 4.60 – 4.45 (m, 1H), 4.43 – 4.31 (m, 1H), 3.92 (t, *J* = 7.0 Hz, 1H), 3.87 – 3.79 (m, 1H), 3.65 (s, 3H), 3.47 – 3.30 (m, 2H), 3.22 (dd, *J* = 15.0, 6.0 Hz, 1H), 2.06 – 1.90 (m, 1H), 1.42 (d, *J* = 17.9 Hz, 12H), 1.17 (s, 2H), 1.09 (s, 7H), 0.94 – 0.74 (m, 12H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.9, 171.9, 170.9, 169.7, 156.1, 136.2, 127.6, 123.1, 122.2, 119.7, 118.9, 111.2, 110.5, 80.3, 74.3, 74.2, 61.0, 59.9, 53.6, 52.2, 50.7, 41.2, 30.6, 28.3, 28.2, 27.6, 27.4, 27.2, 24.5, 22.8, 21.8, 19.3, 17.3. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{35}H_{56}N_5O_8^+$ 674.4123, Found: 674.4111.

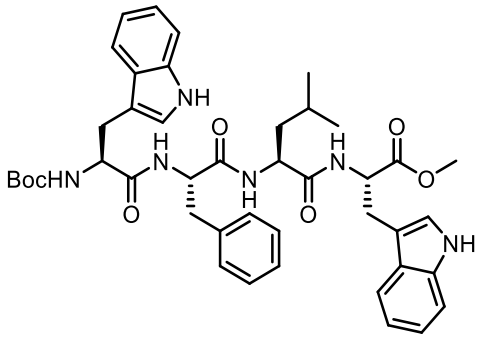
methyl (tert-butoxycarbonyl)-L-tryptophyl-L-phenylalanyl-L-valyl-L-leucyl-L-alaninate (1m):



1m

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:2), 1.41 g, 43% yield. **^{1}H NMR** (300 MHz, DMSO-d_6) δ 10.78 (s, 1H), 8.32 (d, *J* = 6.6 Hz, 1H), 8.17 – 7.84 (m, 3H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 7.2 Hz, 1H), 7.22 (s, 5H), 7.11 – 7.01 (m, 2H), 6.97 (t, *J* =7.2 Hz, 1H), 6.84 (d, *J* = 8.1 Hz, 1H), 4.69 (s, 1H), 4.37 (q, *J* = 7.5 Hz, 1H), 4.23 (s, 2H), 4.11 (s, 1H), 3.60 (s, 3H), 3.13 – 2.89 (m, 2H), 2.89 – 2.72 (m, 2H), 2.07 – 1.86 (m, 1H), 1.74 – 1.58 (m, 1H), 1.46 (t, *J* = 7.2 Hz, 2H), 1.26 (s, 10H), 1.05 (s, 2H), 0.95 – 0.75 (m, 12H). **^{13}C NMR** (75 MHz, DMSO-d_6) δ 172.9, 171.7, 170.6, 170.5, 155.0, 137.5, 136.0, 129.3, 127.9, 126.2, 120.8, 118.1, 110.3, 78.0, 57.5, 55.4, 51.8, 50.5, 47.5, 40.8, 37.5, 30.7, 28.0, 24.1, 23.0, 21.6, 19.1, 18.1, 16.8. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{40}H_{57}N_6O_8^+$ 749.4232, Found: 749.4239.

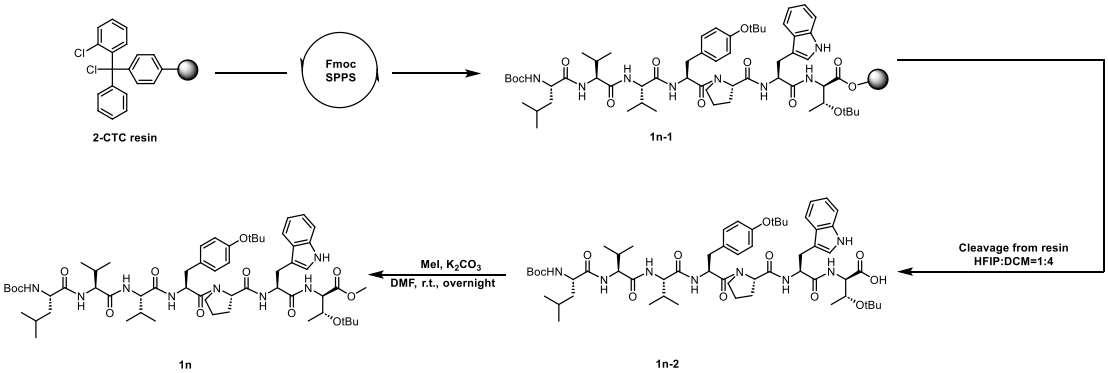
methyl (tert-butoxycarbonyl)-L-tryptophyl-L-phenylalanyl-L-leucyl-L-tryptophanate (1o):



1o

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:1), 1.52 g, 65% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.71 (s, 2H), 7.58 (t, *J* = 6.6 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.22-7.06 (m, 8H), 7.01 (s, 1H), 6.81(d, *J* = 3.9 Hz, 2H), 6.61 (s, 1H), 6.21 (d, *J* = 6.6 Hz, 1H), 6.07 (d, *J* = 7.2 Hz, 1H), 5.05 (d, *J* = 5.1 Hz, 1H), 4.89 (q, *J* = 7.5 Hz, 1H), 4.64 (q, *J* = 6.3 Hz, 1H), 4.48 (t, *J* = 8.7 Hz, 1H), 4.11 (q, *J* = 6.9 Hz, 1H), 3.69 (s, 3H), 3.42 (dd, *J* = 14.7, 3.9 Hz, 1H), 3.33-2.97 (m, 4H), 2.52 (dd, *J* = 13.5,4.5 Hz, 1H), 1.65-1.47 (m, 1H), 1.33 (s, 9H), 1.26 – 1.05 (m, 2H), 0.75 (dd, *J* = 23.4, 6.0 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.7, 172.2, 171.5, 170.6, 155.7, 136.1, 136.1, 135.5, 129.1, 128.7, 127.4, 127.2, 127.0, 123.4, 123.3, 122.4, 121.9, 119.8, 119.3, 118.5, 118.4, 111.6, 111.4, 109.9, 109.4, 80.6, 55.9, 53.8, 52.7, 52.4, 51.5, 39.4, 36.6, 28.2, 27.6, 24.3, 22.7, 21.6. **HRMS(ESI**) m/z $[M+H]^+$: Calcd for $C_{43}H_{53}N_6O_7^+$ 765.3970, Found: 765.3956.

General Procedure C for Synthesis of Tryptophan-containing peptides (1n) via SPPS

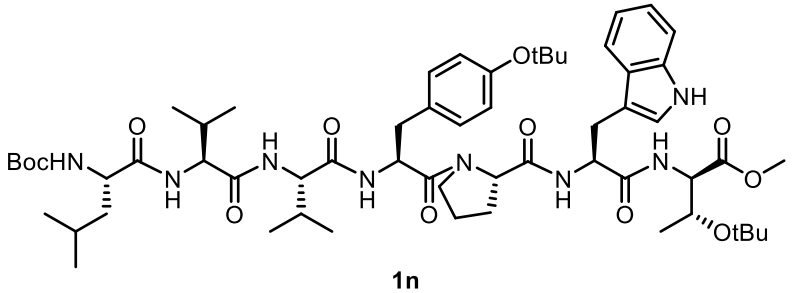


Peptide **1n-1** (1.0 mmol) was prepared via a standard solid-phase peptide synthesis procedure. After cleavage from the resin, the crude peptide **1n-2** was concentrated in vacuo and purified by column chromatography to give the pure product.

To a 10 mL round-bottom flask, the polypeptide **1n-2** (1 equiv) and K_2CO_3 (1.5 equiv) was dissolved in DMF (10 mL), MeI (1.5 equiv) was added dropwise into the mixture. The reaction mixture was stirred at room temperature for 12 h. Upon completion as indicated by TLC, the reaction mixture was poured into water, and extracted with EtOAc (3 x 40 mL). The combined organic layer was washed with brine, and dried with anhydrous Na_2SO_4. The mixture was concentrated under reduced pressure and purified by column chromatography using DCM and MeOH as the eluent giving the pure product **1n** as a white solid.

methyl (3R)-3-(tert-butoxy)-2-((S)-2-((S)-1-((6S,9S,12S,15S)-15-(4-(tert-butoxy)benzyl)-6-

isobutyl-9,12-diisopropyl-2,2-dimethyl-4,7,10,13-tetraoxo-3-oxa-5,8,11,14-tetraazahexadecan-16-oyl)pyrrolidine-2-carboxamido)-3-(1*H*-indol-3-yl)propanamido)butanoate (1n):



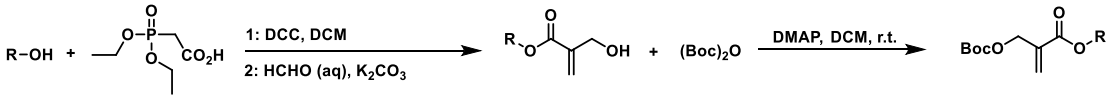
1n

White solid was obtained by silica gel column chromatography (eluent: DCM / MeOH = 20:1), 0.33 g, 30% yield after 15 steps. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.90 (s, 1H), 7.70 (dd, *J* = 15.4, 7.5 Hz, 2H), 7.54 (s, 1H), 7.40 (d, *J* = 8.3 Hz, 1H), 7.32 – 7.21 (m, 2H), 7.20 – 7.02 (m, 4H), 6.98 (d, *J* = 7.9 Hz, 2H), 6.89 (d, *J* = 8.3 Hz, 1H), 6.75 (dd, *J* = 18.7, 7.9 Hz, 2H), 6.59 (d, *J* = 8.9 Hz, 1H), 5.54 (d, *J* = 38.0 Hz, 1H), 4.88 (d, *J* = 7.4 Hz, 1H), 4.75 (d, *J* = 6.6 Hz, 1H), 4.63 (s, 2H), 4.47 (d, *J* = 8.8 Hz, 1H), 4.44 – 4.22 (m, 2H), 4.21 – 4.04 (m, 1H), 3.69 (s, 1H), 3.65 (d, *J* = 1.8 Hz, 3H), 3.48 (d, *J* = 8.1 Hz, 1H), 3.40 – 3.06 (m, 3H), 2.99 – 2.85 (m, 1H), 2.80 (s, 2H), 2.28 (s, 1H), 2.15 (dq, *J* = 19.9, 7.0 Hz, 3H), 1.78 (d, *J* = 31.1 Hz, 3H), 1.70 – 1.51 (m, 3H), 1.43 (s, 9H), 1.32 – 1.17 (m, 11H), 1.06 (q, *J* = 5.4, 4.5 Hz, 14H), 0.89 (dt, *J* = 15.1, 7.9 Hz, 19H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.4, 171.1, 170.7, 166.2, 154.2, 136.3, 136.2, 130.1, 128.2, 126.2, 124.2, 121.9, 119.4, 119.3, 110.1, 78.2, 74.0, 67.3, 60.1, 57.9, 57.8, 54.0, 52.1, 52.0, 47.4, 28.8, 28.3, 28.2, 24.9, 24.7, 23.0, 20.6, 19.4, 19.2, 18.2, 17.9. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{59}H_{91}N_8O_{12}^+$ 1103.6751, Found: 1103.6754.

2.2 Procedure for Synthesis of MBH Carbonates.

The synthetic procedure of MBH-carbonates was prepared following the reported procedure [2].

General Procedure D for Synthesis of MBH Carbonates of 2a - 2n, 2v - 2x

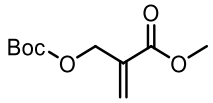


To a 100 mL round-bottom flask, diethylphosphoacetic acid (1.0 equiv.) and alkyl alcohols (1.25 equiv.) were dissolved in DCM (40 mL), DCC (1.1 equiv.) was added slowly in portions, the reaction was stirred at room temperature for 20 min. Upon completion as indicated by TLC, the precipitate was filtered and washed wish DCM (2 x 10 mL). The filtrate was concentrated in vacuo and the residue was used for the next step without further purification.

The crude esterification product was dissolved in THF with 4.0 equiv. of a 30% solution of formaldehyde. Then a saturated solution of K_2CO_3 (2.0 equiv.) was added slowly. At the end of the exothermic addition, the reaction mixture was stirred at room temperature. When the reaction was completion detected by TLC, a saturated solution of ammonium chloride was added and the organic phase was extracted with EtOAc (2 x 40 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4, the mixture was concentrated under reduced pressure and purified by column chromatography using ethyl acetate and petroleum ether as the eluent giving the desired product.

The corresponding allyl alcohol (1.0 equiv.) was dissolved in DCM (40 mL), and $(Boc)_2O$ was added slowly into the mixture, then a catalytic amount of DMAP (0.05 equiv.) was added in one portion. The reaction was stirred at room temperature overnight. Upon completion as indicated by TLC, the reaction mixture was extracted with water and DCM, and the combined layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography using ethyl acetate and petroleum ether as the eluent giving the desired product.

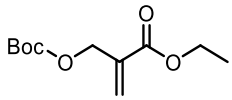
methyl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2a):



2a

Colorless oil was obtained by silica gel column chromatography (eluent: PE / EA = 20:1), 1.03 g, 95% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.38 (s, 1H), 5.89 (s, 1H), 4.80 (s, 2H), 3.79 (s, 3H), 1.50 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.5, 153.0, 135.1, 127.7, 82.5, 64.7, 52.0, 27.7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{10}H_{17}O_5^+$ 217.1071, Found: 217.1067.

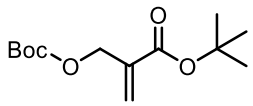
ethyl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2b):



2b

Colorless oil was obtained by silica gel column chromatography (eluent: PE / EA = 20:1), 0.77 g, 71% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.37 (s, 1H), 5.87 (s, 1H), 4.81 (s, 2H), 4.24 (q, *J* = 6.9 Hz, 3H), 1.50 (s, 9H), 1.32 (t, *J* =6.9 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.1, 153.1, 135.3, 127.2, 82.4, 64.7, 60.9, 27.7, 14.1. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{10}H_{17}O_5^+$ 217.1071, Found: 217.1067.

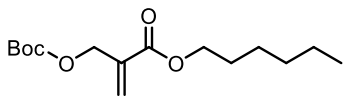
tert-butyl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2c):



2c

Colorless oil was obtained by silica gel column chromatography (eluent: PE / EA = 20:1), 0.90 g, 70% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.27 (s, 1H), 5.78 (s, 1H), 4.77 (s, 2H), 1.50 (s, 18H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 164.2, 153.1, 136.7, 125.9, 82.3, 81.3, 64.8, 28.0, 27.7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{13}H_{23}O_5^+$ 259.1540, Found: 259.1537.

hexyl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2d):

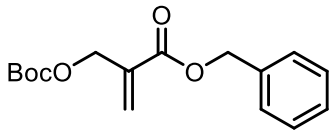


2d

Colorless oil was obtained by silica gel column chromatography (eluent: PE / EA = 20:1), 0.95 g, 67% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.37 (s, 1H), 5.87 (s, 1H), 4.80 (s, 2H), 4.17 (t, *J* = 6.6 Hz, 2H), 1.70 – 1.62 (m, 2H), 1.50 (s, 9H), 1.33 (s, 6H), 0.89 (t, *J* = 3.0 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.2, 153.1, 135.3, 127.2, 82.4, 65.2, 64.8, 31.4, 28.5, 27.7, 25.6, 22.5,

14.0. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{15}H_{27}O_5^+$ 287.1853, Found: 287.1848.

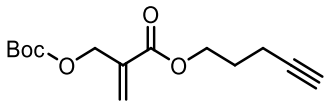
benzyl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2e):



2e

Colourless oil was obtained by silica gel column chromatography (eluent: PE / EA = 20:1), 1.08 g, 74.5% yield after 3 steps. **^{1}H NMR** (300 MHz, CDCl3) δ 7.36 (s, 5H), 6.42 (s, 1H), 5.91 (s, 1H), 5.22 (s, 2H), 4.82 (s, 2H), 1.48 (s, 9H). **^{13}C NMR** (75 MHz, CDCl3) δ 164.9, 153.1, 135.6, 135.1, 128.6, 128.3, 128.1, 127.9, 82.5, 66.7, 64.7, 27.7. **HRMS**(ESI) m/z [M+H]+ : Calcd for C10H17O5+ 293.1384, Found: 293.1375。

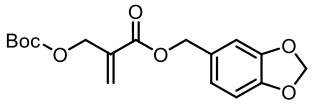
pent-4-yn-1-yl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2f):



2f

Colorless oil was obtained by silica gel column chromatography (eluent: PE / EA = 20:1), 0.93 g, 69% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.39 (d, *J* = 1.0 Hz, 1H), 5.89 (d, *J* = 1.2 Hz, 1H), 4.80 (s, 2H), 4.29 (t, *J* = 6.2 Hz, 2H), 2.32 (td, *J* = 7.0, 2.6 Hz, 2H), 1.98 (t, *J* = 2.7 Hz, 1H), 1.91 (p, *J* = 6.6 Hz, 2H), 1.50 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.0, 153.0, 135.1, 127.7, 82.9, 82.5, 69.1, 64.7, 63.5, 27.7, 27.5, 15.2. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{14}H_{21}O_5^+$ 269.1384, Found: 269.1375.

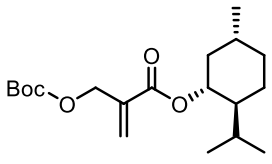
benzo[d][1,3]dioxol-5-ylmethyl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2g):



2g

Colorless oil was obtained by silica gel column chromatography (eluent: PE / EA = 10:1), 0.84 g, 50% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.85 (d, *J* = 7.5 Hz, 2H), 6.78 (d, *J* = 7.5 Hz, 1H), 6.40 (s, 1H), 5.96 (s, 2H), 5.90 (s, 1H), 5.11 (s, 2H), 4.81 (s, 2H), 1.49 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 164.9, 153.0, 147.8, 147.7, 135.1, 129.3, 127.8, 122.3, 109.0, 108.2, 101.2, 82.5, 66.7, 64.7, 27.7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{17}H_{21}O_7^+$ 337.1282, Found: 337.1274.

(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2h):

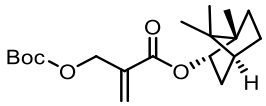


2h

Colorless oil was obtained by silica gel column chromatography (eluent: PE / EA = 10:1), 0.82 g, 48% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.35 (s, 1H), 5.84 (s, 1H), 4.92 – 4.70 (m, 3H), 2.04

(d, *J* = 12.0 Hz, 1H), 1.95 – 1.81 (m, 1H), 1.69 (d, *J* = 10.8 Hz, 2H), 1.50 (s, 10H), 1.41 (d, *J* = 11.7 Hz, 1H), 1.15 – 0.98 (m, 2H), 0.90 (dd, *J* = 6.6, 4.0 Hz, 7H), 0.76 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 164.7, 153.1, 135.6, 126.8, 82.4, 64.8, 47.0, 40.8, 34.2, 31.4, 27.8, 26.3, 23.4, 22.0, 20.8, 16.3. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{19}H_{33}O_5^+$ 341.2323, Found: 341.2316.

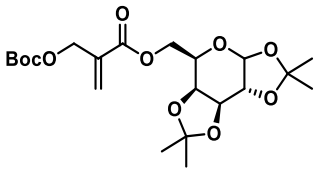
(1S,2S,4S)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2i):



2i

Colorless oil was obtained by silica gel column chromatography (eluent: PE / EA = 10:1), 0.76 g, 45% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.38 (s, 1H), 5.86 (s, 1H), 4.96 (d, *J* = 9.9 Hz, 1H), 4.82 (s, 2H), 2.46 – 2.33 (m, 1H), 2.03 – 1.87 (m, 1H), 1.83 – 1.73 (m, 1H), 1.71 (t, *J* = 6.0 Hz, 1H), 1.50 (s, 9H), 1.40 – 1.20 (m, 2H), 1.03 (dd, *J* = 14.0, 3.3 Hz, 1H), 0.92 (s, 3H), 0.89 (s, 3H), 0.86 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.3, 153.1, 135.6, 127.1, 82.4, 80.7, 64.9, 49.0, 47.8, 44.9, 36.8, 28.0, 27.8, 27.4, 27.3, 19.7, 18.9, 13.5. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{19}H_{31}O_5^+$ 339.2166, Found: 339.2160.

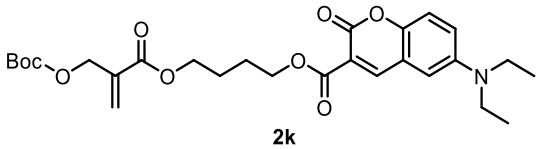
((3aS,5S,5aR,8aR,8bS)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-5-yl)methyl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2j):



2j

Colorless oil was obtained by silica gel column chromatography (eluent: PE / EA = 10:1), 0.99 g, 45% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.40 (s, 1H), 5.90 (s, 1H), 5.53 (d, *J* = 4.8 Hz, 1H), 4.80 (s, 2H), 4.63 (d, *J* = 1.5 Hz, 1H), 4.43 – 4.23 (m, 4H), 4.15 – 4.03 (m, 1H), 1.53 – 1.43 (m, 15H), 1.34 (d, *J* = 3.7 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 164.9, 153.0, 134.9, 127.8, 109.7, 108.8, 96.3, 82.4, 71.0, 70.7, 70.5, 65.9, 64.6, 63.8, 27.7, 26.0, 25.9, 25.0, 24.5. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{21}H_{33}O_{10}^+$ 445.2068, Found: 445.2057.

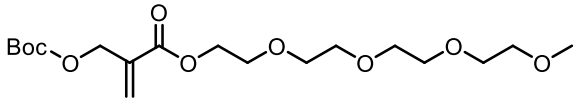
4-((2-(((tert-butoxycarbonyl)oxy)methyl)acryloyl)oxy)butyl 6-(diethylamino)-2-oxo-2*H*-chromene-3-carboxylate (2k):



2k

Yellow solid was obtained by silica gel column chromatography (eluent: PE / EA = 10:1), 0.91 g, 35% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.37 (d, *J* = 9.0 Hz, 1H), 6.62 (d, *J* = 9.0 Hz, 1H), 6.46 (s, 1H), 6.39 (s, 1H), 5.89 (s, 1H), 4.81 (s, 2H), 4.35 (s, 2H), 4.26 (s, 2H), 3.45 (q, *J* = 6.9 Hz, 4H), 1.87 (s, 4H), 1.49 (s, 9H), 1.24 (t, *J* = 6.9 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.1, 164.2, 158.5, 153.0, 152.9, 149.2, 135.2, 131.1, 127.5, 109.5, 108.7, 107.7, 96.7, 82.5, 64.7, 64.6, 64.5, 45.1, 27.7, 25.4, 25.3, 12.4. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{27}H_{36}NO_9^+$ 518.2385, Found: 518.2372.

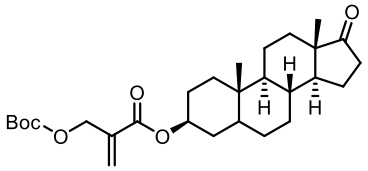
2,5,8,11-tetraoxatridecan-13-yl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2l):



2l

Colorless oil was obtained by silica gel column chromatography (eluent: PE / EA = 10:1), 0.88 g, 45% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.40 (s, 1H), 5.90 (s, 1H), 4.81 (s, 2H), 4.34 (d, *J* = 4.2 Hz, 2H), 3.74 (t, *J* = 3.9 Hz, 2H), 3.66 (s, 10H), 3.53 (t, *J* = 3.0 Hz, 2H), 3.38 (s, 3H), 1.49 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.0, 153.0, 135.0, 127.7, 82.5, 71.9, 70.6, 70.5, 69.0, 64.7, 64.1, 59.0, 27.7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{18}H_{33}O_9^+$ 393.2119, Found: 393.2109.

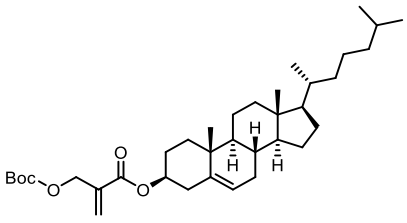
(3S,8R,9S,10S,13S,14S)-10,13-dimethyl-17-oxohexadecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2m):



2m

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 20:1), 0.59 g, 25% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.34 (s, 1H), 5.84 (s, 1H), 4.79 (s, 3H), 2.44 (dd, *J* = 19.2, 9.0 Hz, 1H), 2.15 – 1.99 (m, 1H), 1.99 – 1.87 (m, 2H), 1.80 (d, *J* = 11.3 Hz, 3H), 1.74 – 1.56 (m, 5H), 1.50 (s, 10H), 1.42 (d, *J* = 12.1 Hz, 1H), 1.38 – 1.18 (m, 7H), 0.86 (s, 6H), 0.78 – 0.66 (m, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 164.6, 153.1, 135.6, 126.8, 82.4, 64.8, 54.3, 51.4, 47.8, 44.6, 36.7, 35.8, 35.7, 35.0, 33.9, 31.5, 30.8, 28.3, 27.8, 27.4, 21.8, 20.5, 13.8, 12.2. **HRMS**(ESI) m/z [M+H]+ : Calcd for $C_{28}H_{43}O_6^+$ 475.3054, Found: 475.3042.

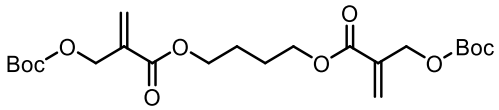
(3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2n):



2n

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 20:1), 0.57 g, 20% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.36 (s, 1H), 5.85 (s, 1H), 5.39 (d, *J* = 5.0 Hz, 1H), 4.80 (s, 2H), 4.79 – 4.63 (m, 1H), 2.36 (d, *J* = 7.9 Hz, 2H), 2.02 (d, *J* = 9.0 Hz, 2H), 1.93 – 1.77 (m, 3H), 1.72 – 1.54 (m, 4H), 1.53 (s, 2H), 1.50 (s, 10H), 1.46 – 1.26 (m, 5H), 1.24 – 1.08 (m, 7H), 1.03 (s, 5H), 0.92 (d, *J* = 6.4 Hz, 3H), 0.88 (s, 3H), 0.86 (s, 3H), 0.68 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 164.5, 153.1, 139.5, 135.6, 126.9, 122.8, 82.5, 64.8, 56.7, 56.1, 50.0, 42.3, 39.7, 39.5, 38.0, 37.0, 36.6, 36.2, 35.8, 31.9, 31.8, 28.2, 28.0, 27.8, 27.4, 24.3, 23.8, 22.8, 22.6, 21.0, 19.3, 18.7, 11.9. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{36}H_{59}O_5^+$ 571.4357, Found: 571.4346.

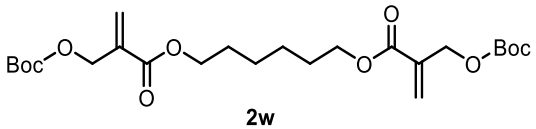
butane-1,4-diyl bis(2-(((tert-butoxycarbonyl)oxy)methyl)acrylate) (2v):



2v

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 10:1), 1.25 g, 27% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.38 (s, 2H), 5.90 (s, 2H), 4.80 (s, 4H), 4.22 (s, 4H), 1.79 (s, 4H), 1.50(s, 18 H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.0, 153.1, 135.1, 127.7, 82.5, 64.7, 64.4, 27.7, 25.2. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{22}H_{35}O_{10}^+$ 459.2225, Found: 459.2219.

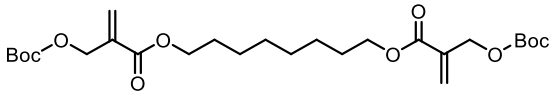
hexane-1,6-diyl bis(2-(((tert-butoxycarbonyl)oxy)methyl)acrylate) (2w):



2w

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 10:1), 1.44 g, 30% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.37 (s, 2H), 5.88 (s, 2H), 4.80 (s, 4H), 4.18 (t, *J* = 6.3 Hz, 4H), 1.69 (t, *J* = 6.0 Hz, 4H), 1.50 (s, 18H), 1.42 (s, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.1, 153.1, 135.2, 127.4, 82.5, 64.9, 64.7, 28.4, 27.7, 25.6. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{24}H_{39}O_{10}^+$ 487.2538, Found: 487.2531.

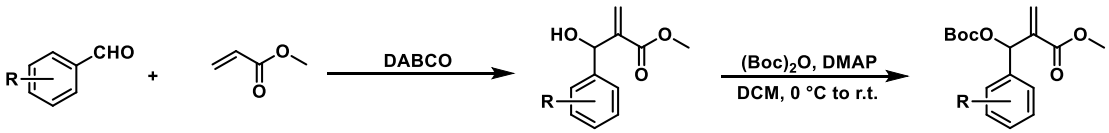
octane-1,8-diyl bis(2-(((tert-butoxycarbonyl)oxy)methyl)acrylate) (2x):



2x

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 10:1), 2.29 g, 44% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6. 37 (s, 2H), 5.87 (s, 2H), 4.80 (s, 4H), 4.17 (t, *J* = 6.6 Hz, 4H), 1.67 (t, *J* = 6.3 Hz, 4H), 1.50 (s, 18H), 1.34 (s, 8H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.2, 153.1, 135.3, 127.3, 82.5, 65.1, 64.8, 29.1, 28.5, 27.7, 25.9. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{26}H_{43}O_{10}^+$ 515.2851, Found: 515.2853.

General Procedure E for Synthesis of MBH Carbonates of 2o – 2u

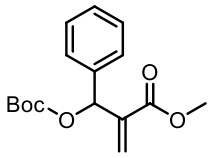


To a 100 mL round-bottom flask equipped with a magnetic stir bar was charged with benzaldehyde (1.0 equiv.), methyl acrylate (3.0 equiv.) and DABCO (1.0 equiv.). The reaction mixture was stirred at room temperature. Upon completion as indicated by TLC, the reaction mixture was diluted with DCM and washed with 1N aq. HCl, saturated aq. $NaHCO_3$ and brine. Then the combined organic layers were dried over anhydrous Na_2SO_4, concentrated under reduced pressure. The residue was purified by column chromatography using ethyl acetate and petroleum ether as the eluent giving the desired product.

The corresponding allyl alcohol (1.0 equiv.) was dissolved in DCM (40 mL), and $(Boc)_2O$ was added slowly into the mixture at 0 ℃, then a catalytic amount of DMAP (0.05 equiv.) was added in one portion. The reaction was warmed to room temperature and stirred overnight. Upon

completion as indicated by TLC, the reaction mixture was extracted with water and DCM, and the combined layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography using ethyl acetate and petroleum ether as the eluent giving the desired product.

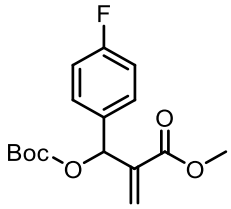
methyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate (2o):



2o

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 20:1), 1.10 g, 80% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.51 – 7.29 (m, 5H), 6.49 (s, 1H), 6.40 (s, 1H), 5.92 (s, 1H), 3.70 (s, 3H), 1.46 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.4, 152.4, 139.7, 137.5, 128.47, 128.45, 127.6, 125.9, 82.6, 75.8, 52.0, 27.8. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{16}H_{21}O_5^+$ 293.1384, Found: 293.1372.

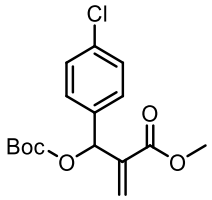
methyl 2-(((tert-butoxycarbonyl)oxy)(4-fluorophenyl)methyl)acrylate (2p):



2p

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 20:1), 1.24 g, 80% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 8.4, 5.4 Hz, 2H), 7.02 (t, *J* = 8.7 Hz, 2H), 6.45 (s, 1H), 6.41 (s, 1H), 5.95 (s, 1H), 3.71 (s, 3H), 1.46 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.3, 152.3, 139.5, 129.6, 129.5, 125.6, 115.5, 115.3, 82.8, 75.1, 52.0, 27.7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{16}H_{20}O_5F^+$ 311.1289, Found: 311.1277.

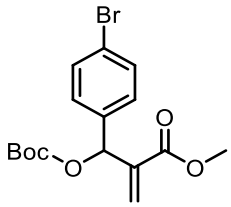
methyl 2-(((tert-butoxycarbonyl)oxy)(4-chlorophenyl)methyl)acrylate (2q):



2q

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 20:1), 1.14 g, 76% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 11.7, 8.7 Hz, 4H), 6.44 (s, 1H), 6.41 (s, 1H), 5.95 (s, 1H), 1.46 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.2,152.2, 139.3, 136.2, 134.3, 129.1, 128.7, 125.9, 82.9, 75.1, 52.1, 27.7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{16}H_{20}O_5Cl^+$ 327.0994, Found: 327.0985.

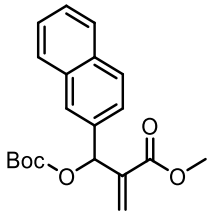
methyl 2-((4-bromophenyl)((tert-butoxycarbonyl)oxy)methyl)acrylate (2r):



2r

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 20:1), 1.41 g, 76% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 6.42 (s, 2H), 5.94 (s, 1H), 3.71 (s, 3H), 1.46 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.2, 152.2, 139.2, 136.7, 131.6, 129.4, 126.0, 122.6, 82.9, 75.1, 52.1, 27.7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{16}H_{20}O_5Br^+$ 371.0489, Found: 371.0477.

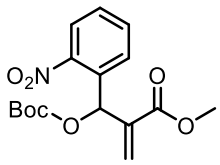
methyl 2-(((tert-butoxycarbonyl)oxy)(naphthalen-2-yl)methyl)acrylate (2s):



2s

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 20:1), 1.11 g, 65% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.1 Hz, 1H), 7.83 (t, *J* = 9.0 Hz, 2H), 7.56 (d, *J* = 6.9 Hz, 1H), 7.46 (td, *J* = 17.4, 8.4 Hz, 3H), 7.34 (s, 1H), 6.48 (s, 1H), 5.74 (s, 1H), 3.72 (s, 3H), 1.47 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.7, 152.6, 139.1, 133.9, 133.2, 130.9, 129.3, 128.8, 128.1, 126.6, 125.9, 125.2, 123.5, 82.8, 72.4, 52.2, 27.8. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{20}H_{23}O_5^+$ 343.1540, Found: 343.1533.

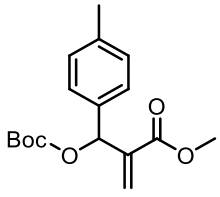
methyl 2-(((tert-butoxycarbonyl)oxy)(2-nitrophenyl)methyl)acrylate (2t):



2t

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 20:1), 0.93 g, 55% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.1 Hz, 1H), 7.66 (s, 2H), 7.58 – 7.46 (m, 1H), 7.18 (s, 1H), 6.45 (s, 1H), 5.58 (s, 1H), 3.78 (s, 3H), 1.48 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.1, 152.0, 147.9, 138.5, 133.6, 133.3, 129.3, 128.6, 128.2, 125.1, 83.3, 71.2, 52.3, 27.7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{16}H_{20}NO_7^+$ 338.1234, Found: 338.1225.

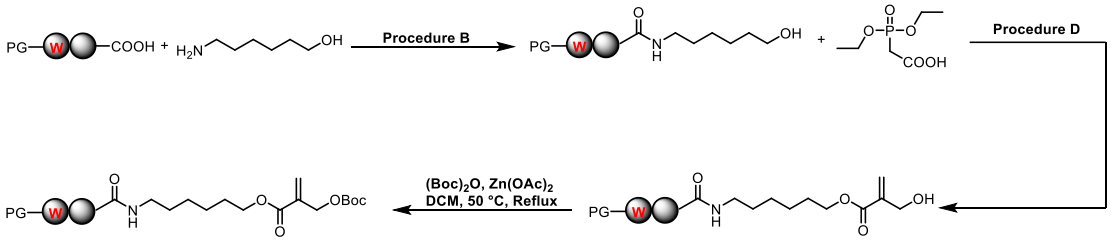
methyl 2-(((tert-butoxycarbonyl)oxy)(p-tolyl)methyl)acrylate (2u):



2u

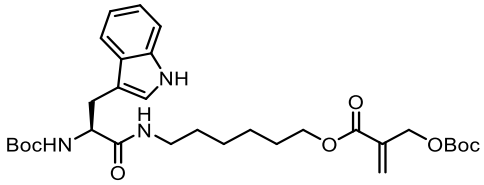
White solid was obtained by silica gel column chromatography (eluent: PE / EA = 20:1), 1.21 g, 79% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.28(d, *J* = 7.8 Hz, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 6.45 (s, 1H), 6.39 (s, 1H), 5.92 (s, 1H), 3.70 (s, 3H), 2.33 (s, 3), 1.48 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.5, 152.5, 139.7, 138.3, 134.5, 129.2, 127.7, 125.6, 82.6, 75.3, 52.0, 27.8, 21.2. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{17}H_{23}O_5^+$ 307.1540, Found: 307.1534.

General Procedure F for Synthesis of MBH Carbonates of 2y – 2aa



The corresponding allyl alcohol (1.0 equiv) prepared by Procedure B and Procedure D was added to a suspension of di-tert-butyl decarbonate (1.1 equiv.) and $Zn(OAc)_2$ (0.1 equiv.) in DCM. The reaction mixture was allowed to reflux at 50 °C for 5 h with an oil bath. Upon the completion detected by TLC, the reaction mixture was cooled to room temperature and diluted with water. Then the mixture was extracted twice with DCM, the combined organic layers was dried by anhydrous Na_2SO_4. The residue was concentrated in vacuo and purified by column chromatography using ethyl acetate and petroleum ether as the eluent giving the desired product.

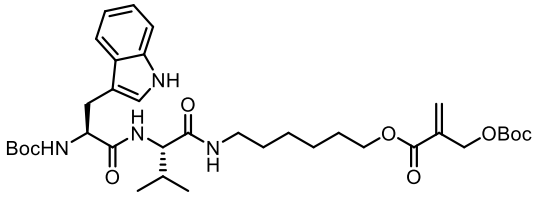
(S)-6-(2-((tert-butoxycarbonyl)amino)-3-(1*H*-indol-3-yl)propanamido)hexyl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2y):



2y

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 1.85 g, 63% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.53 (s, 1H), 7.67 (d, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.15 (dt, *J* = 21.3, 6.9 Hz, 2H), 7.05 (s, 1H), 6.39 (s, 1H), 5.90 (s, 1H), 5.61 (s, 1H), 5.24 (s, 1H), 4.81 (s, 2H), 4.41 (d, *J* = 4.5, 1H), 4.13 (t, *J* = 2.3 Hz, 2H) 3.33 (dd, *J* = 14.4, 4.8 Hz, 1H), 3.18 – 2.97 (m, 3H), 1.56 (q, *J* = 7.2 Hz, 2H), 1.49 (s, 9H), 1.44 (s, 9H), 1.29 – 1.20 (m, 4H), 1.12 – 1.01 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.6, 165.3, 155.5, 153.1, 136.3, 135.2, 127.6, 127.4, 123.3, 122.1, 119.6, 118.9, 111.3, 110.6, 82.6, 80.0, 65.0, 64.8, 55.3, 39.3, 34.0, 29.0, 28.7, 28.27, 28.33, 27.8, 26.1, 25.4. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{31}H_{46}N_3O_8^+$ 588.3279, Found: 588.3266.

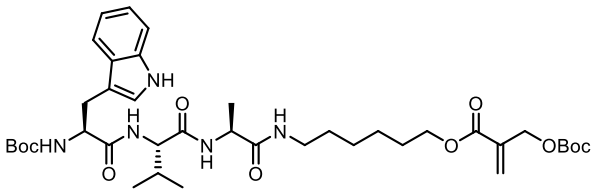
(6S,9S)-6-((1*H*-indol-3-yl)methyl)-9-isopropyl-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazaheptadecan-17-yl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2z):



2z

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 0.68 g, 18% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.70(s, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.11(t, *J* = 7.5 Hz, 1H), 7.06 (s, 1H), 6.53(d, *J* = 7.8 Hz, 2H), 6.36 (s, 1H), 5.87 (s, 1H), 5.23 (d, *J* = 6.3Hz, 1H), 4.80 (s, 2H), 4.52 – 4.36 (m, 1H), 4.25 – 4.17 (m, 1H), 4.13 (t, *J* = 6.6 Hz, 2H), 3.34 – 3.11(m, 3H), 3.10 – 2.95 (m, 1H), 2.28 – 2.11 (m, 1H), 1.63 (t, *J* = 6.6 Hz, 2H), 1.49(s, 9H), 1.42(s, 10H), 1.31(s, 5H), 0.79 (t, *J* = 7.5 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.9, 170.6, 165.2, 153.1, 136.3, 135.2, 127.4, 123.3, 122.2, 119.7, 118.7, 111.4, 109.9, 82.5, 80.5, 65.0, 64.7, 58.7, 55.8, 39.3, 30.1, 29.3, 28.4, 28.3, 27.7, 26.4, 25.5, 19.2. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{36}H_{55}N_4O_9^+$ 687.3964, Found: 687.3951.

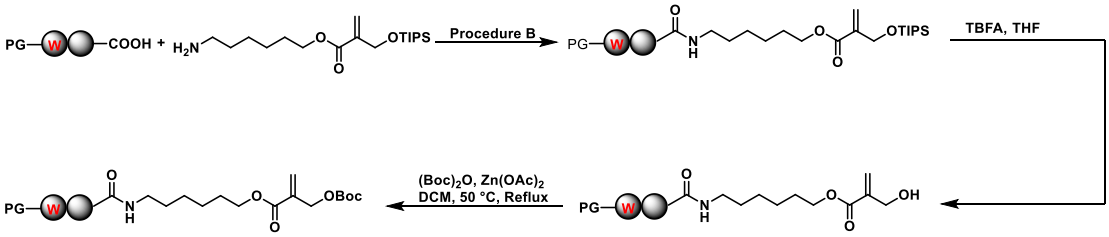
(6S,9S,12S)-6-((1*H*-indol-3-yl)methyl)-9-isopropyl-2,2,12-trimethyl-4,7,10,13-tetraoxo-3-oxa-5,8,11,14-tetraazaicosan-20-yl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2aa):



2aa

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:1), 0.99 g, 22% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.25 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.25 – 7.00 (m, 4H), 6.72(s, 1H), 6.36 (s, 1H), 5.86 (s, 1H), 5.47(s, 1H), 4.80 (s, 2H), 4.66 – 4.50 (m, 1H), 4.41 (d, *J* = 3.6 Hz, 1H), 4.22 – 4.01 (m, 3H), 3.43 – 3.00 (m, 4H), 2.27 – 2.08 (m, 1H), 1.72 – 1.53 (m, 4H), 1.49 (s, 9H), 1.38 (d, *J* = 8.0 Hz, 14H), 1.26 (t, *J* = 6.3 Hz, 2H), 0.73 (dd, *J* = 31.1, 6.9 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 173.3, 172.3, 170.5, 165.2, 156.5, 153.1, 136.5, 135.2, 127.3, 127.2, 123.3, 122.5, 120.0, 118.5, 111.5, 109.4, 82.6, 81.3, 65.1, 64.8, 59.4, 56.5, 49.0, 39.5, 29.2, 29.0, 28.5, 28.2, 27.8, 26.4, 25.6, 19.0, 17.6, 16.9. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{39}H_{60}N_5O_{10}^+$ 758.4335, Found: 758.4317.

General Procedure G for Synthesis of MBH Carbonates of 2ab – 2ae

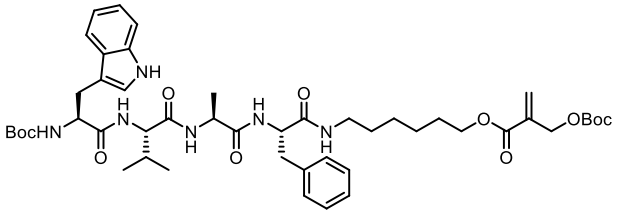


The protected allyl alcohol (1.0 equiv.) prepared via Procedure B was dissolved in THF (10 mL), TBAF (1.05 equiv.) was added slowly and stirred at room temperature for 1 h. Upon the completion detected by TLC, the reaction mixture was extracted with water and EtOAc. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4. The residue was

concentrated in vacuo and purified by column chromatography using ethyl acetate and petroleum ether as the eluent giving the desired product.

After removed the protection group, the corresponding allyl alcohol was performed with Procedure F to prepare the corresponding MBH carbonates.

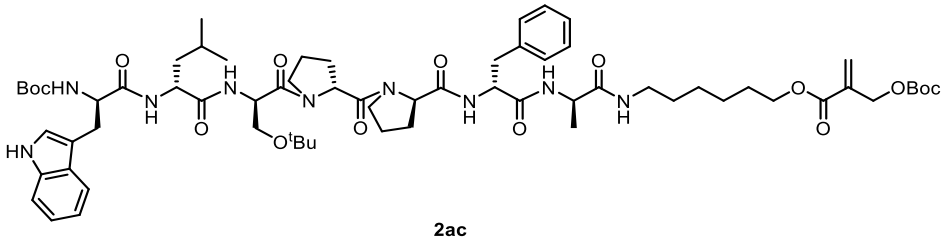
(6S,9S,12S,15S)-6-((1*H*-indol-3-yl)methyl)-15-benzyl-9-isopropyl-2,2,12-trimethyl-4,7,10,13,16-pentaoxo-3-oxa-5,8,11,14,17-pentaazatricosan-23-yl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2ab):



2ab

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:1). 0.82 g, 29% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.29 (s, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.29 (t, *J* = 6.9 Hz, 3H), 7.25 – 7.11 (m, 5H), 7.06 (t, *J* = 7.2 Hz, 2H), 6.35 (s, 1H), 5.86 (s, 1H), 5.41 (s, 1H), 4.79 (s, 2H), 4.49 – 4.20 (m, 1H), 4.14 (t, *J* = 6.0 Hz, 3H), 3.92 (s, 1H), 3.53 (s, 1H), 3.45 – 3.15 (m, 3H), 3.07 (t, *J* = 11.4 Hz, 1H), 2.05 (s, 1H), 1.79 – 1.55 (m, 4H), 1.49 (s, 9H), 1.42 (s, 14H), 0.80 (dd, *J* = 18.6, 5.9 Hz, 10H), 0.62(d, *J* = 5.7 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 174.1, 172.5, 172.1, 171.5, 165.2, 156.7, 153.1, 138.4, 136.7, 135.2, 129.3, 128.2, 127.3, 127.1, 126.3, 123.7, 122.4, 119.7, 118.4, 111.7, 82.5, 82.2, 65.1, 64.7, 60.3, 56.5, 54.8, 53.2, 39.6, 37.5, 29.0, 28.5, 28.1, 27.8, 26.5, 25.6, 24.7, 23.0, 20.8, 18.9, 18.8, 17.4. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{48}H_{69}N_6O_{11}^+$ 905.5019, Found: 905.5024

6-((R)-2-((R)-2-((R)-1-(((6R,9R,12R)-6-((1*H*-indol-3-yl)methyl)-12-(tert-butoxymethyl)-9-isobutyl-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oyl)-D-prolyl)pyrrolidine-2-carboxamido)-3-phenylpropanamido)propanamido)hexyl 2-(((tert-butoxycarbonyl)oxy)methyl)acrylate (2ac):

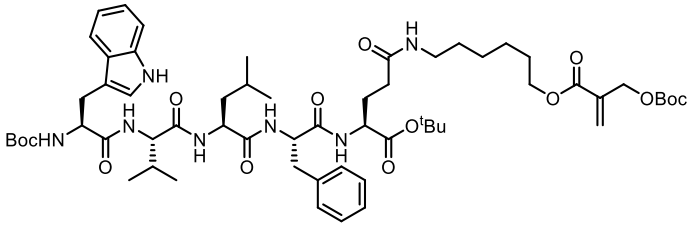


2ac

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:2). 0.62 g, 49% yield after 16 steps. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.56 (s, 1H), 8.02 (d, *J* = 7.2Hz, 1H), 7.60 (s, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.46 (s, 1H), 7.34 (d, *J* = 20.1 Hz, 3H), 7.33 – 7.20 (m, 5H), 7.17 (t, *J* = 6.3 Hz, 2H), 7.11 – 6.99 (m, 2H), 6.35 (d, *J* = 3.9 Hz, 1H), 5.85 (s, 1H), 5.31 – 5.19 (m, 1H), 4.78 (s, 2H), 4.71 (s, 2H), 4.66 – 4.38 (m, 5H), 4.11 (q, *J* = 6.6 Hz, 3H), 3.91 (s, 1H), 3.80 (s, 2H), 3.61 – 3.47 (m, 2H), 3.44 – 3.21 (m, 4H), 3.20 – 3.01 (m, 3H), 2.21 (t, *J* = 6.0 Hz, 2H), 2.02 – 1.77 (m, 3H), 1.74 – 1.56 (m, 4H), 1.49 (s, 12H), 1.41 (s, 9H), 1.40 – 1.23 (m, 8H), 1.17 (s, 9H), 0.84 (t, *J* = 6.6 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.3, 172.0, 171.4, 170.7, 170.0, 165.1, 155.5, 153.1, 129.4, 129.1, 128.3, 127.2, 126.6, 122.6, 121.8, 119.1, 118.6, 111.1, 109.8, 82.5, 80.1, 73.5, 65.0, 64.7, 62.3, 60.6, 58.5, 55.0, 54.7, 52.7, 51.7, 48.7, 47.7, 47.2, 41.3, 39.4, 36.3, 29.5, 29.3, 28.6, 28.4, 28.3, 27.7, 27.4, 26.6, 25.6, 25.5, 24.8, 23.1, 22.9,

22.3, 19.6. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{66}H_{98}N_9O_{15}^+$ 1256.7177, Found: 1256.7179.

tert-butyl N^2-(tert-butoxycarbonyl)-L-tryptophyl-L-valyl-L-leucyl-L-phenylalanyl-N^5-(6-((2-(((tert-butoxycarbonyl)oxy)methyl)acryloyl)oxy)hexyl)-L-glutaminate (2ad):

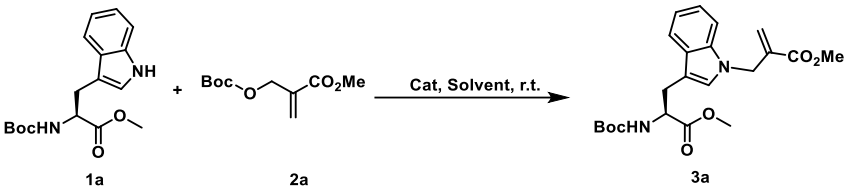


2ad

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:2). 0.17 g, 30% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.26 (s, 1H), 7.55(d, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 8.4 Hz, 2H), 7.28 (s, 3H), 7.25 – 7.13 (m, 7H), 7.05 (d, *J* = 7.2 Hz, 2H), 6.36 (s, 1H), 6.21 (s, 1H), 5.86 (s, 1H), 5.28 (s, 1H), 4.78 (s, 2H), 4.74 – 4.68(m, 1H), 4.47 (t, *J* = 8.4 Hz, 1H), 4.31 (d, *J* = 6.9 Hz, 1H), 4.13 (d, *J* = 6.6 Hz, 4H), 3.84 (s, 1H), 3.50 (dd, J = 14.1, 2.7 Hz, 1H), 3.36 – 2.93 (m, 6H), 2.41 – 2.15 (m, 4H), 2.04 – 1.89 (m, 2H), 1.63 (t, *J* = 7.5 Hz, 3H), 1.49 (s, 9H), 1.46 (s, 8H), 1.43 (s, 8H), 1.34 (s, 5H), 1.08 – 0.92 (m, 1H), 0.82 (dd, *J* = 19.8, 6.8 Hz, 7H), 0.73 (d, J = 6.9 Hz, 2H), 0.55 (d, *J* = 6.9 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 174.1, 172.8, 172.5, 171.9, 171.2, 170.7, 165.1, 156.8, 153.0, 138.2, 136.6, 135.1, 129.3, 128.2, 127.3, 127.0, 126.3, 123.8, 118.3, 111.7, 82.6, 81.8, 81.5, 65.0, 64.7, 60.3, 56.7, 54.0, 52.7, 52.3, 39.4, 35.7, 32.5, 29.6, 28.7, 28.4, 28.0, 27.9, 27.7, 26.6, 25.6, 24.6, 23.2, 20.3, 18.7, 17.0. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{60}H_{90}N_7O_{14}^+$ 1131.6540, Found: 1132.6562.

2.3 Condition Screening for N-Allylation of Trp Reaction

Supplemental Table 1. Optimization studies.



1a 2a 3a

Entry	Cat (10 mol%)	Solvent	Yield (%) [a]
1	DABCO	DCE	96
2	TEA	DCE	48
3	DIEA	DCE	n.r.
4	DBU	DCE	<5
5	$NaHCO_3$	DCE	n.r.
6	K_2CO_3	DCE	n.r.
7	TBAF	DCE	<5
8	PPh_3	DCE	n.r.
9	PBu_3	DCE	<5
10	DABCO	DCM	99
11	DABCO	Tol	99
12	DABCO	MeOH	n.r.
13	DABCO	DMF	99
14	DABCO	EtOAc	99
15	DABCO	DMSO	25
16	DABCO	THF	99
17	DABCO	MeCN	79
18[b]	DABCO	DCM	99

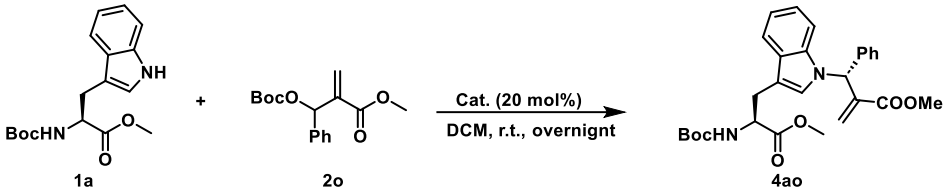
Unless otherwise stated, the reaction was carried out with 1a (0.1 mmol), 2a (0.2 mmol, 2 eq.), catalyst (0.01 mmol, 10 mol%) in 1 mL solvent at room temperature overnight.

[a] Isolated yield.

[b] Reaction was carried out with 1a (0.1 mmol), 2a (0.2 mmol, 2 eq.), catalyst (0.02 mmol, 20 mol%) in 1 mL solvent at room temperature for 1 hour.

The Optimized condition for N-alkylation of tryptophan-containing peptides is: tryptophan-containing peptide **1** (0.1 mmol, 1.0 equiv.), MBH carbonates **2** (0.2 mmol, 2.0 equiv.) and DABCO (0.02 mmol, 20 mol%) was dissolved in 1 mL DCM at room temperature for 1 hour.

Supplemental Table 2. Optimization studies.



Entry	Cat (20 mol%)	Yield (%)[a]	d.r.[b]
1[c]	DABCO	99	1:1
2	*β*-ICD	98	7.1:1
3	Hydroquinine	-	-
4	O-Desmethyl Quinine	-	-
5	Cinchonine	-	-
6	(8α,9R)- 9-(9-phenanthrenyloxy)-Cinchonan-6'-ol	-	-
7	BzQD	-	-
8	$(DHQD)_2PHAL$	49	1:6.5
9	$(DHQD)_2PYR$	60	1:6.5
10	$(DHQD)_2AQN$	47	1:2.8
11	$(DHQ)_2PHAL$	50	5:1
12	$(DHQ)_2AQN$	55	2:1

Unless otherwise stated, the reaction was carried out with 1a (0.1 mmol), 2a (0.2 mmol, 2 eq.), catalyst (0.02 mmol, 20 mol%) in 1 mL solvent at room temperature overnight.

[a] Isolated yield.

[b] d.r. was determined by ^1H NMR.

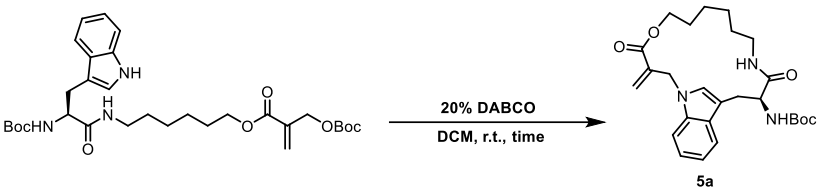
[c] The reaction was carried out for 1h.

DABCO = 1,4-diazabicyclo[2.2.2]octane; β-ICD = beta-Isocupreidine; BzQD = 9-quinidinyl benzoate; $(DHQD)_2PHAL$ = hydroquinidine 1,4-phthalazinediyl diether; $(DHQD)_2PYR$ = hydroquinidine-2,5-diphenyl-4,6-pyrimidinediyl diether; $(DHQD)_2AQN$ = hydroquinidine (anthraquinone-1,4-diyl) diether; $(DHQ)_2PHAL$ = hydroquinine 1,4-phthalazinediyl diether; $(DHQ)_2AQN$ = hydroquinine (anthraquinone-1,4-diyl) diether.

The Optimized condition for N-alkylation of tryptophan-containing peptides is: tryptophan-containing peptide **1** (0.1 mmol, 1.0 equiv.), MBH carbonates **2** (0.2 mmol, 2.0

equiv.) and β-ICD (0.02 mmol, 20 mol%) was dissolved in 1 mL DCM at room temperature for 12 hours. To confirm the absolute configuration, we perform the 1H-1H NOESY and ROESY assay of **4ao**. Combining the results of our experiments with the work reported by Chen group,[3] the absolute configuration was assigned as *(R)*-configuration.

Supplemental Table 3. Optimization studies.



5a

Entry	Solution volume (mL)	Reaction time (h)	Yield (%) [a]	Concentration(mM)
1	1	1	44	100
2	5	1	43	20
3	10	1	77	10
4	20	2.5	75	5

Unless otherwise stated, the reaction was carried out with **1a** (0.1 mmol), catalyst (0.02 mmol, 20 mol%) in DCM at room temperature. [a] Isolated yield.

The Optimized condition for intramolecular macrocyclization of tryptophan-containing peptides is: tryptophan-containing peptide **1** (0.1 mmol, 1.0 equiv.), MBH carbonates **2** (0.2 mmol, 2.0 equiv.) and β-ICD (0.02 mmol, 20 mol%) was dissolved in 1 mL DCM at room temperature for 12 hours.

2.4 Investigation of chemoselectivity of *N*-allylation of Tryptophan

In order to investigation the chemoselectivity of this *N*-allylation of tryptophan reaction, a series of competitive experiments between Boc-Trp-OMe and amounts of nucleophilic competitors (Tyr, Lys, Arg, His, Ser, Cys) were conducted (Figure S1). The results revealed that different nucleophilic competitors had inconsistent impact on the N-allylation of tryptophan reaction, while the addition of Tyr and His led to slight decrease (<10%) in this assay. In contrast, the addition of Lys, Arg, Ser and Cys led to significant decrease in competitive experiments, while the addition of Lys had led to complete disappearance of the target product. To our surprise, the addition of Cys did not lead to the complete disappearance of the target product, but it led to the formation of a complex reaction system.

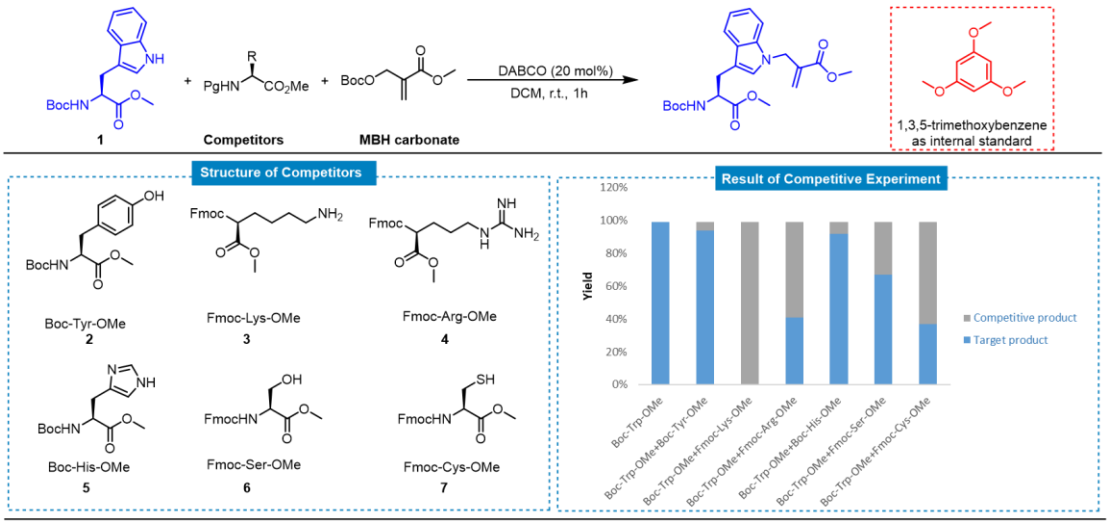


Figure S1. Investigation of the chemoselectivity of the N-allylation of tryptophan reaction. Conditions: Boc-Trp-OMe (0.1 mmol), MBH carbonates (0.2 mmol) and specific competitor (0.1 mmol) was dissolved in 2 mL DCM at room temperature for 1 hour. The yield was determined by 1H NMR with 1,3,5-trimethoxybenzene as an internal standard.

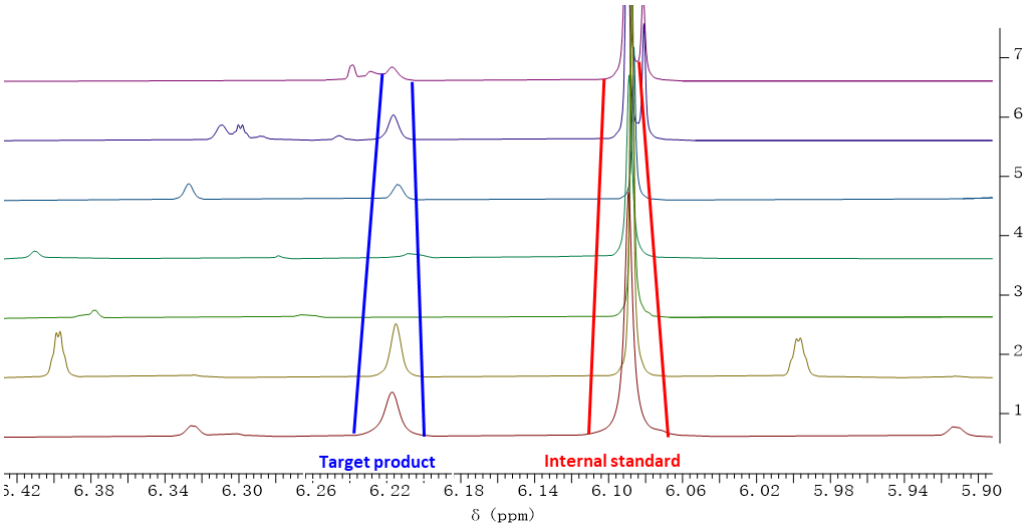


Figure S2. Zoomed spectrum of ^{1}H NMR analysis.

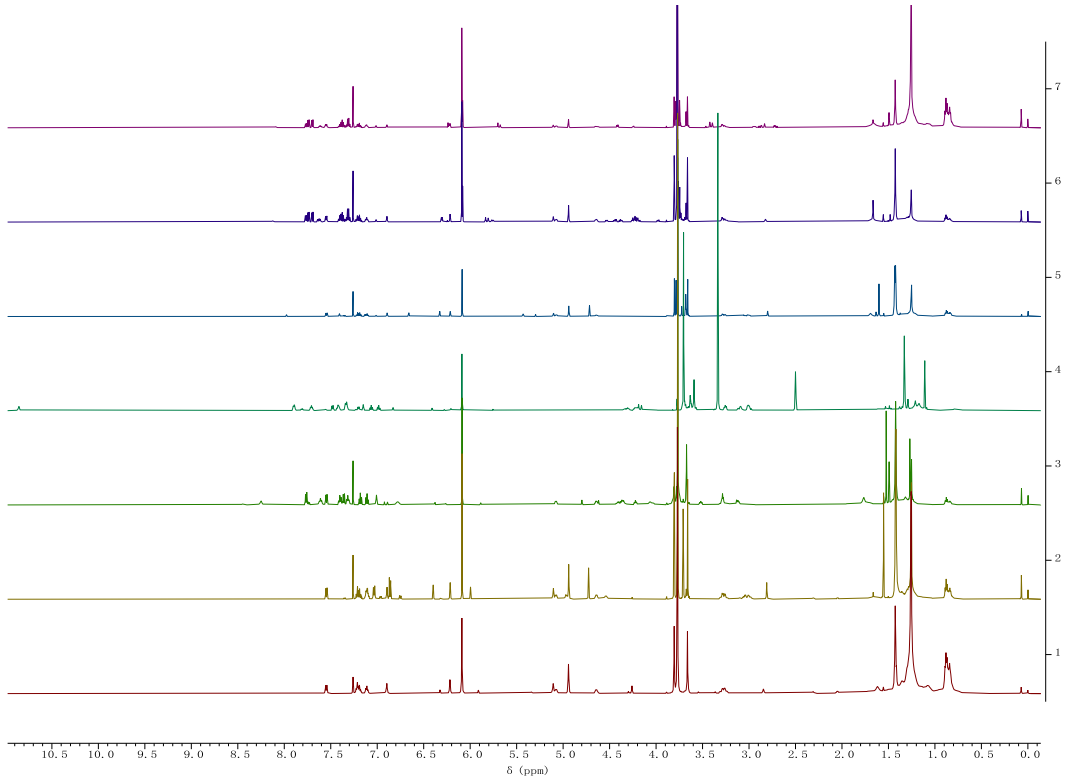
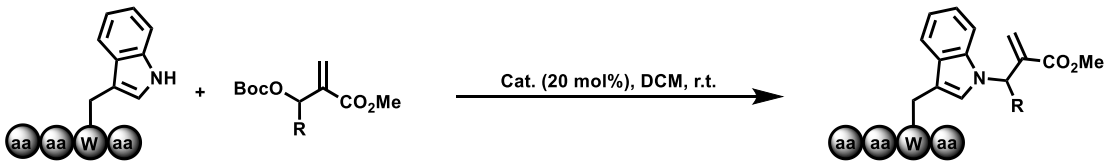


Figure S3. Chemoselectivity study between nucleophilic amino acids and MBH carbonates by ^{1}H NMR analysis.

2.5 General Procedure for N-allylation of Trp-containing peptide

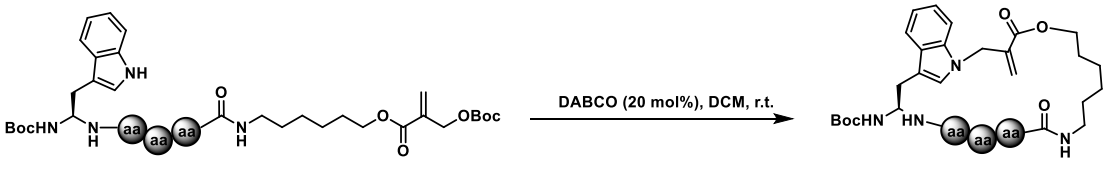
General condition A (Peptide ligation):



1 2a 3

To an oven-dried 10 mL glass test tube with a stirring bar was added peptides derivative **1** (0.1 mmol), MBH carbonate derivative **2** (0.2 mmol) followed by addition of DABCO or β-ICD (0.02 mmol). DCM (1 mL) was added by syringe and the mixture was stirred at room temperature for 1 h or overnight. After the completion of the reaction monitored by TLC, the solvent was removed by reduced pressure and purified by column chromatography to afford product **3** or **4**.

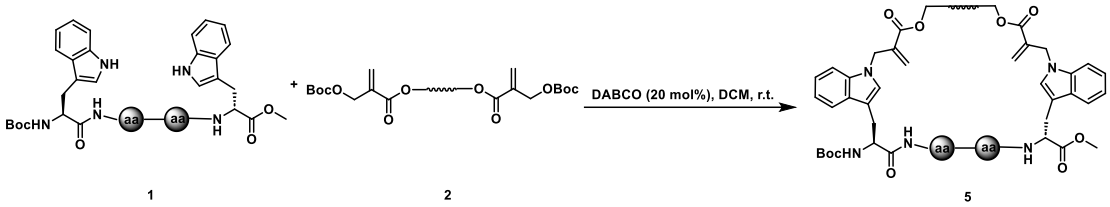
General condition B (Intramolecular Macrocyclization):



2 5

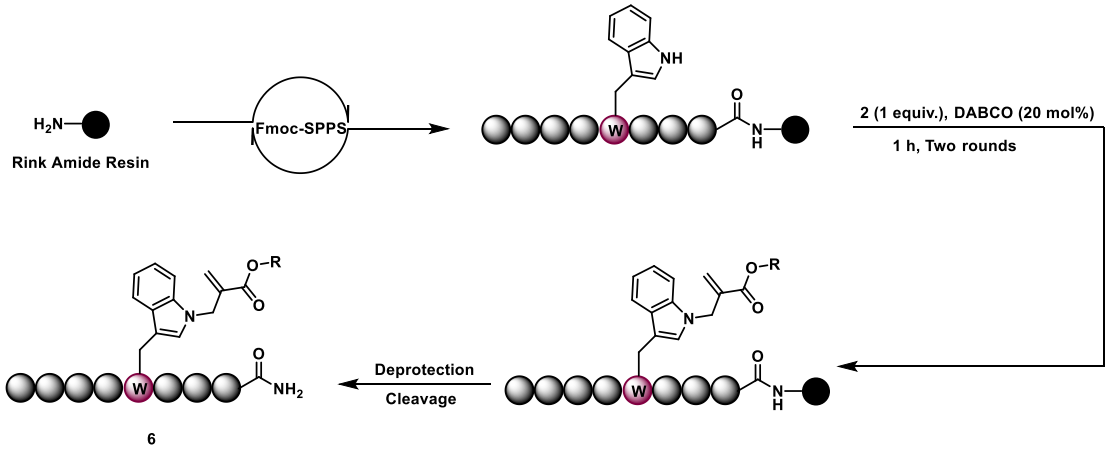
To an oven-dried 10 mL glass test tube with a stirring bar was added MBH carbonate derivative **2** (0.1 mmol) followed by addition of DABCO (0.02 mmol). DCM (10 mL) was added by syringe and the mixture was stirred at room temperature for 1 h. After the completion of the reaction monitored by TLC, the solvent was removed by reduced pressure and purified by column chromatography to afford product **5**.

General condition C (Peptide Stapling):



To an oven-dried 10 mL glass test tube with a stirring bar was added peptides derivative **1** (0.1 mmol), MBH carbonate derivative **2** (0.12 mmol) followed by addition of DABCO (0.02 mmol). DCM (10 mL) was added by syringe and the mixture was stirred at room temperature for 1 h, After the completion of the reaction monitored by TLC, the solvent was removed by reduced pressure and purified by column chromatography to afford product **5**.

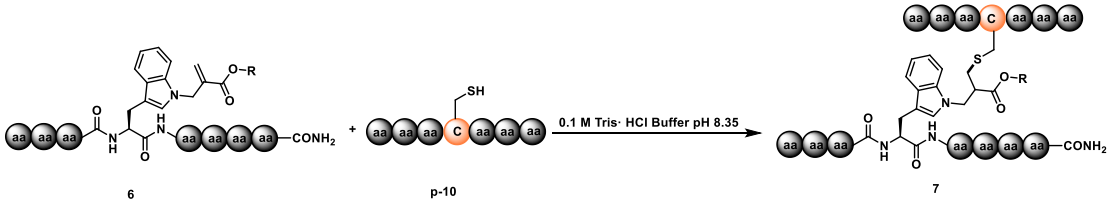
General condition D (N-allylation of Trp-containing peptide on Resin):



A mixture of linear peptide loaded on Rink Amide MBHA Resin (0.2 mmol, 1.0 equiv.), MBH carbonates **2** (0.2 mmol, 1.0 equiv.) was added followed by addition of DABCO (0.02 mmol, 20 mol%) in a 20 mL filtration tube with Luer adapter. DCM (5 mL) was added and shaken for 1 h. Then the mixture was drained and washed with DCM (10 ml x 3). Repeated above procedure once, then the resin was washed with MeOH (10 mL x 3) and drained to dry.

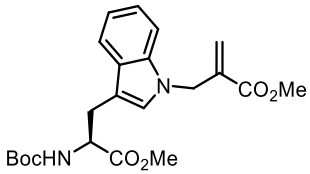
A cleavage solution (10 mL, TAF: Tris: H_2O =95: 2.5: 2.5) was added to the dry resin, the mixture was shaken for 3 h. The reaction mixture was washed with TFA, and combined mixture was concentrated under reduced pressure to afford the crude peptide. The crude peptide was extracted with cold diethyl ether and deionized water, the combined aqueous phase was freeze dried and purified by semi-preparative HPLC and lyophilized to afford the product.

2.6 General Procedure for Peptide-peptide conjugate.



A solution of 0.1 mL of **6** (0.01 M, Tris·HCl pH = 8.35) and 0.1 mL of **p-10** (0.001 M, Tris·HCl pH = 8.35) were pipetted into a 10 ml reaction tube, and added 0.8 ml of Tris·HCl buffer to bring the total volume to 1 ml. The mixture was stirred at 37 ℃ with an oil bath for 1 h. 100 uL reaction mixture was collected and detected by LC-MS at the inital and final time.

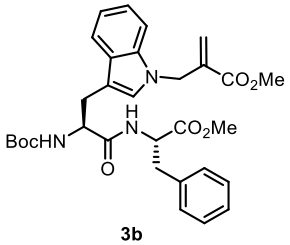
methyl (S)-2-((3-(2-((tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)-1*H*-indol-1-yl)methyl)acrylate (3a):



3a

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 4:1), 41.2 mg, 99% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.8 Hz, 1H), 7.20 (dd, *J* = 13.2, 7.5 Hz, 2H), 7.10 (td, *J* = 8.1, 2.1 Hz, 1H), 6.90 (s, 1H), 6.22 (s, 1H), 5.10 (s, 1H),5.08 (s, 1H), 4.94 (s, 2H), 4.64 (t, *J* = 5.4 Hz, 1H), 3.80 (s, 3H), 3.66 (s, 3H), 3.37 – 3.11 (m, 2H), 1.43 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.7, 166.0, 155.2, 136.3, 136.2, 128.3, 127.0, 126.1, 122.1, 119.5, 119.1, 109.7, 109.6, 54.4, 52.2, 52.1, 46.7, 28.3, 28.0. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{22}H_{29}N_2O_6^+$ 417.2020, Found: 417.2010.

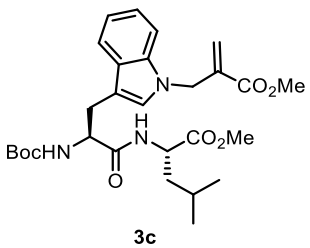
methyl 2-((3-((S)-2-((tert-butoxycarbonyl)amino)-3-(((S)-1-methoxy-1-oxo-3-phenylpropan-2-yl)amino)-3-oxopropyl)-1*H*-indol-1-yl)methyl)acrylate (3b):



3b

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 4:1), 54.0 mg, 96% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.5Hz, 1H), 7.26 – 7.18 (m, 2H), 7.18 – 7.03 (m, 4H), 6.97 (s, 1H), 6.82 (d, *J* = 6.6 Hz, 2H), 6.26 (d, *J* = 6.6 Hz, 1H), 6.21 (s, 1H), 5.13 (s, 2H), 4.91 (s, 2H), 4.73 (q, *J* = 5.7 Hz, 1H), 4.42 (d, *J* = 4.5 Hz, 1H), 3.78 (s, 3H), 3.61 (s, 3H), 3.36 – 3.22 (m, 1H), 3.14 (dd, *J* = 14.1, 6.9 Hz, 1H), 2.96 (d, *J* = 5.4 Hz, 2H), 1.41 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.3, 171.1, 166.0, 155.4, 136.4, 136.1, 135.6, 129.2, 128.5, 128.1, 127.5, 127.1, 126.3, 122.2, 119.7, 119.2, 110.0, 109.6, 80.1, 55.1, 53.2, 52.2, 52.2, 46.7, 37.9, 28.3. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{31}H_{38}N_3O_7^+$ 564.2704, Found: 564.2692.

methyl N^a-(tert-butoxycarbonyl)-1-(2-(methoxycarbonyl)allyl)-L-tryptophyl-L-leucinate (3c):

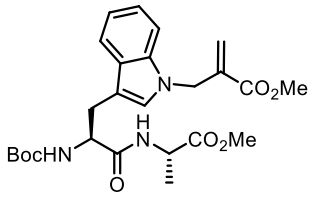


3c

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 4:1), 52.4 mg, 99% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.8 Hz, 1H), 7.20 (dd, *J* = 12.9, 7.5 Hz, 2H), 7.11 (td, *J* = 8.2, 2.1 Hz, 1H), 7.00 (s, 1H), 6.30 (d, *J* = 8.4 Hz, 1H), 6.22 (s, 1H), 5.16 (s, 1H), 5.13 (s, 1H), 4.93 (s, 2H), 4.58 – 4.48 (m, 1H), 4.44 (d, *J* = 6.3 Hz, 1H), 3.80 (s, 3H), 3.65

(s, 3H), 3.32 – 3.13 (m, 2H), 1.42 (s, 12H), 0.86(t, *J* = 2.1 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.8, 171.3, 166.0, 155.4, 136.3, 136.1, 128.1, 127.4, 126.1, 122.0, 119.5, 119.1, 110.0, 109.5, 80.0, 52.12, 52.05, 50.7, 46.6, 41.5, 28.2, 27.9, 24.6, 22.6, 21.8. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{28}H_{40}N_3O_7^+$ 530.2861, Found: 530.2849.

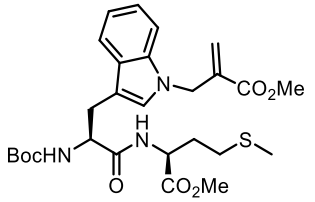
methyl 2-((3-((S)-2-((tert-butoxycarbonyl)amino)-3-(((S)-1-methoxy-1-oxopropan-2-yl)amino)-3-oxopropyl)-1H-indol-1-yl)methyl)acrylate (3d):



3d

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 4:1), 48.1 mg, 99% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.8 Hz, 1H), 7.20 (dd, *J* = 15.0, 8.4 Hz, 2H), 7.11 (t, *J* = 7.8 Hz, 1H), 7.00 (s, 1H), 6.50 (d, *J* = 6.6 Hz, 1H), 6.22 (s, 1H), 5.21 (s, 1H), 5.15 (s, 1H), 4.93 (s, 2H), 4.48 (q, *J* = 6.9 Hz, 2H), 3.80 (s, 3H), 3.66 (s, 3H), 3.35 – 3.11 (m, 2H), 1.42 (s, 9H), 1.27 (d, J = 6.9 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.9, 171.2, 166.0, 155.4, 136.3, 136.2, 128.2, 127.5, 126.3, 122.1, 119.6, 119.2, 110.0, 109.6, 80.0, 55.1, 52.4, 52.1, 48.1, 46.6, 28.3, 18.4. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{25}H_{34}N_3O_7^+$ 488.2391, Found: 488.2381.

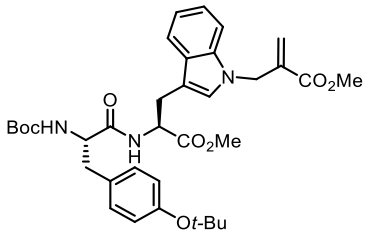
methyl N^a-(tert-butoxycarbonyl)-1-(2-(methoxycarbonyl)allyl)-L-tryptophyl-L-methioninate (3e):



3e

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 4:1), 53.6 mg, 98% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.8 Hz, 1H), 7.20 (dd, *J* = 15.3, 8.1 Hz, 2H), 7.11 (t, *J* = 7.8 Hz, 1H), 7.00 (s, 1H), 6.61 (d, *J* = 7.8 Hz, 1H), 6.22 (s, 1H), 5.20 (s, 1H), 5.15 (s, 1H), 4.94 (s, 2H), 4.59 (q, *J* = 6.9 Hz, 1H), 4.44 (d, *J* = 6.0 Hz, 1H), 3.80 (s, 3H), 3.66 (s, 3H), 3.33 - 3.13 (m, 2H), 2.33 (s, 2H), 2.05 (d, *J* = 7.2 Hz, 1H), 2.00 (s, 3H), 1.93- 1.80 (m, 1H), 1.42 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.8, 171.6, 166.0, 155.4, 136.3, 136.2, 128.1, 127.5, 126.3, 122.1, 119.6, 119.1, 109.9, 109.6, 80.1, 55.1, 52.4, 52.1, 51.5, 46.7, 31.5, 29. 6, 28.3, 28.0, 15.3. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{27}H_{38}N_3O_7S^+$ 548.2425, Found: 548.2416.

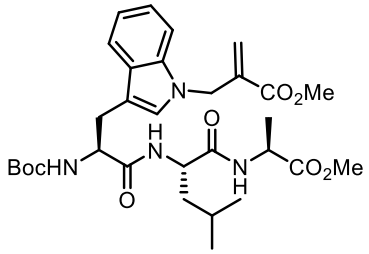
methyl 2-((3-((S)-2-((S)-3-(4-(tert-butoxy)phenyl)-2-((tert-butoxycarbonyl)amino)propanamido)-3-methoxy-3-oxopropyl)-1*H*-indol-1-yl)methyl)acrylate (3f):



3f

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 60.3 mg, 95% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.7 Hz, 1H), 7.19 (t, *J* = 7.2 Hz, 2H), 7.09 (q, *J* = 8.1 Hz, 3H), 6.88 (d, *J* = 7.8 Hz, 2H), 6.79 (s, 1H), 6.46 (d, *J* = 7.5 Hz, 1H), 6.21 (s, 1H), 5.11 (s, 1H), 5.07 – 5.00 (m, 1H), 4.92 (s, 2H), 4.84 (d, *J* = 6.3 Hz, 1H), 4.34 (s, 1H), 3.78 (s, 3H), 3.66 (s, 1H), 3.61 (s, 2H), 3.24 (d, *J* = 5.1 Hz, 2H), 3.10 – 2.74 (m, 2H), 1.35 (s, 9H), 1.31 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.7, 170.8, 166.0, 155.3, 154.3, 136.3, 131.4, 130.1, 129.8, 128.2, 127.4, 126.2, 124.3, 122.1, 119.5, 118.8, 109.7, 109.0, 80.0, 78.3, 55.3, 53.0, 52.3, 52.1, 46.8, 37.6, 28.8, 28.2, 27.6. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{35}H_{46}N_3O_8^+$ 636.3279 Found: 636.3266.

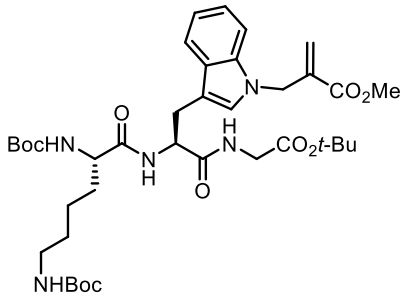
methyl (6S,9S,12S)-9-isobutyl-6-((1-(2-(methoxycarbonyl)allyl)-1*H*-indol-3-yl)methyl)-2,2,12-trimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (3g):



3g

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 60.3 mg, 95% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.9 Hz, 1H), 7.26 – 7.15 (m, 2H), 7.15 – 7.08 (m, 1H), 6.99 (s, 1H), 6.88 (d, *J* = 7.4 Hz, 1H), 6.54 (d, *J* = 8.1 Hz, 1H), 6.21 (s, 1H), 5.17 (d, *J* = 7.7 Hz, 1H), 5.13 (s, 1H), 4.93 (s, 2H), 4.54 – 4.36 (m, 3H), 3.80 (s, 3H), 3.73 (s, 2H), 3.70 (s, 1H), 3.24 (d, *J* = 6.2 Hz, 2H), 1.65 – 1.47 (m, 2H), 1.41 – 1.30 (m, 12H), 0.86 (dd, *J* = 6.2, 3.7 Hz, 5H), 0.78 (s, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 173.0, 171.7, 171.2, 165.9, 155.6, 136.1, 128.1, 127.3, 126.2, 122.1, 119.5, 119.1, 109.8, 109.6,80.2, 52.3, 52.1, 51.6, 48.0, 46.6, 41.0, 28.2, 24.5, 22.7, 22.0, 17.9. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{31}H_{44}N_4O_8Na^+$ 623.3051, Found: 623.3057.

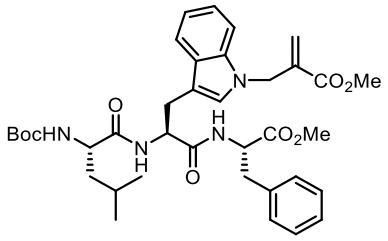
tert-butyl (10S,13S)-10-((tert-butoxycarbonyl)amino)-13-((1-(2-(methoxycarbonyl)allyl)-1*H*-indol-3-yl)methyl)-2,2-dimethyl-4,11,14-trioxo-3-oxa-5,12,15-triazaheptadecan-17-oate (3h):



3h

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:1), 73.4 mg, 99%. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.5 Hz, 1H), 7.26 – 7.11 (m, 3H), 7.08 (s, 1H), 6.88 (s, 1H), 6.80 (d, *J* = 7.2 Hz, 1H), 6.22 (s, 1H), 5.37 (s, 1H), 5.18 (s, 1H), 4.94 (s, 2H), 4.81 (d, *J* = 5.4 Hz, 2H), 3.99 (s, 1H), 3.87 (dd, *J* = 18.3, 5.1 Hz, 1H), 3.79 (s, 3H), 3.70 (d, *J* = 16.2 Hz, 1H), 3.36 (dd, *J* = 14.4, 4.8 Hz, 1H), 3.22 (dd, *J* = 14.4, 6.0 Hz, 1H), 3.06 (d, *J* = 5.1 Hz, 2H), 1.76 (q, *J* = 8.4 Hz, 1H), 1.43 (s, 22H), 1.32 (s, 8H), 1.26 (t, *J* = 6.9 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.0, 171.3, 168.4, 166.0, 156.4, 156.2, 136.22, 136.16, 128.2, 127.9, 126.4, 122.0, 119.6, 118.9, 109.7, 109.5, 81.8, 80.2, 79.1, 55.2, 53.6, 52.1, 46.7, 41.9, 39.4, 29.7, 28.5, 28.3, 28.2, 28.0, 22.2. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{38}H_{58}N_5O_{10}^+$ 744.4178, Found: 744.4163.

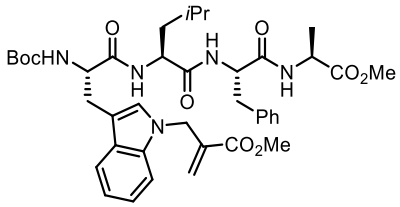
methyl (6S,9S,12S)-12-benzyl-6-isobutyl-9-((1-(2-(methoxycarbonyl)allyl)-1*H*-indol-3-yl)methyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (3i):



3i

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 66.2 mg, 98% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.5 Hz, 1H), 7.21 (t, *J* = 6.9 Hz, 2H), 7.18 – 7.08 (m, 4H), 7.00 (s, 1H), 6.89 – 6.82 (m, 2H), 6.79 (d, *J* = 7.2 Hz, 1H), 6.22 (d, *J* = 7.4 Hz, 2H), 5.17 (s, 1H), 4.89 (s, 3H), 4.67 (q, *J* =7.2 Hz 2H), 4.09 (s, 1H), 3.77 (s, 3H), 3.61 (s, 3H), 3.31 (dd, *J* = 14.7, 5.1 Hz, 1H), 3.11 (dd, *J* = 14.4, 7.5 Hz, 1H), 3.01 - 2.85 (m, 2H), 1.71 - 1.51 (m, 2H), 1.40 (s, 10H), 0.89 (t, *J* = 5.1 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.9, 170.7, 170.0, 165.5, 155.1, 135.8, 135.6, 135.1, 128.6, 128.0, 127.6, 127.2, 126.6, 126.0, 121.7, 119.2, 118.7, 109.3, 109.2, 79.6, 53.2, 52.9, 51.7, 51.6, 46.2, 40.8, 37.3, 27.8, 27.6, 24.2, 22.5, 21.3. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{37}H_{48}N_4O_8Na^+$ 699.3364, Found: 699.3389.

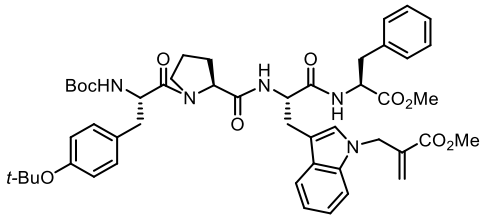
methyl (6S,9S,12S,15S)-12-benzyl-9-isobutyl-6-((1-(2-(methoxycarbonyl)allyl)-1H-indol-3-yl)methyl)-2,2,15-trimethyl-4,7,10,13-tetraoxo-3-oxa-5,8,11,14-tetraazahexadecan-16-oate (3j):



3j

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:1), 43.3 mg, 58% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.8 Hz, 1H), 7.26 – 7.10 (m, 6H), 7.09 – 6.83 (m, 5H), 6.60 (s, 1H), 6.22 (s, 1H), 5.18 (s, 1H), 4.90 (d, *J* = 11.2 Hz, 3H), 4.73 (d, *J* = 7.0 Hz, 1H), 4.64 (d, *J* = 6.3 Hz, 1H), 4.56 – 4.38 (m, 1H), 4.03 (s, 1H), 3.79 (s, 3H), 3.70 (s, 3H), 3.26 – 3.09 (m, 2H), 3.08 – 2.98 (m, 1H), 2.82 (dd, *J* = 15.1, 7.5 Hz, 1H), 1.67 – 1.52 (m, 1H), 1.48 – 1.23 (m, 14H), 0.84 (dd, *J* = 11.1, 6.3 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.8, 172.2, 171.7, 170.5, 166.0, 136.8, 136.4, 136.2, 129.2, 128.4, 128.0, 127.4, 126.7, 126.3, 122.3, 119.7, 119.1, 109.7, 80.5, 55.4, 53.9, 52.4, 52.1, 48.2, 46.7, 40.9, 37.7, 29.7, 28.3, 27.7, 24.6, 22.8, 22.0, 17.9. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{40}H_{54}N_5O_9^+$ 748.3916, Found: 744.748.3017.

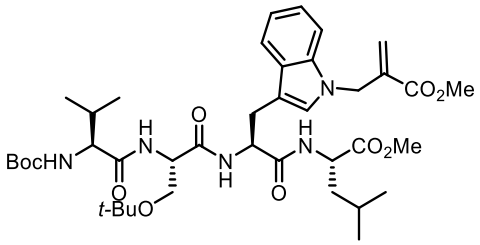
methyl 2-((3-((S)-2-((S)-1-((S)-3-(4-(tert-butoxy)phenyl)-2-((tert-butoxycarbonyl)amino)propanoyl)pyrrolidine-2-carboxamido)-3-(((S)-1-methoxy-1-oxo-3-phenylpropan-2-yl)amino)-3-oxopropyl)-1*H*-indol-1-yl)methyl)acrylate (3k):



3k

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:1), 87 mg, 99% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.73 – 7.63 (m, 1H), 7.26 – 7.15 (m, 4H), 7.15 (s, 3H), 7.00 (d, *J* = 3.6 Hz, 2H), 6.99 – 6.88 (m, 5H), 6.86 (d, *J* = 2.4 Hz, 1H), 6.47 (d, *J* = 7.6 Hz, 1H), 6.18 (d, *J* = 6.5 Hz, 1H), 5.21 (d, *J* = 8.7 Hz, 1H), 5.10 (s, 1H), 4.93 – 4.67 (m, 4H), 4.52 – 4.39 (m, 2H), 3.78 (s, 1H), 3.76 (s, 2H), 3.63 (s, 3H), 3.49 (q, *J* = 7.7 Hz, 1H), 3.37 (dd, *J* = 14.7, 5.2 Hz, 1H), 3.17 (dd, *J* = 14.5, 7.3 Hz, 1H), 3.01 (d, *J* = 6.1 Hz, 2H), 2.97 – 2.89 (m, 1H), 2.49 (d, J = 7.0 Hz, 1H), 2.18 – 2.04 (m, 1H), 1.99 – 1.76 (m, 3H), 1.46 (s, 2H), 1.36 (s, 7H), 1.31 (s, 2H), 1.28 (s, 7H). **^{13}C NMR (75 MHz, $CDCl_3$) δ** 172.0, 171.3, 170.7, 165.9, 155.0, 154.2, 136.2, 136.0, 135.9, 131.0, 129.9, 129.0, 128.4, 128.1, 127.7, 126.8, 126.3, 124.1, 122.0, 119.5, 119.0, 109.7, 79.6, 78.3, 60.4, 53.8, 53.3, 53.2, 52.1, 52.0, 47.2, 46.5, 38.2, 37.6, 28.7, 28.4, 28.2, 27.9, 27.3, 25.0. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{49}H_{61}N_5O_{10}Na^+$ 902.4311, Found: 902.4316.

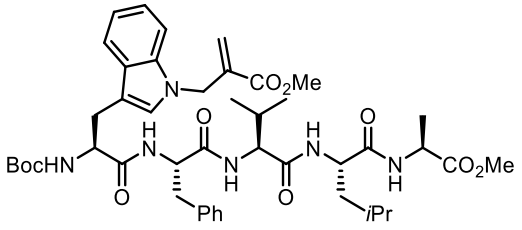
methyl N^a-(N-((tert-butoxycarbonyl)-L-valyl)-O-(tert-butyl)-L-seryl)-1-(2-(methoxycarbonyl)allyl)-L-tryptophyl-L-leucinate (3l):



3l

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:1). 87 mg, 99% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.67 (d, *J* = 4.2 Hz, 1H), 7.16 m, 4H), 7.04 – 6.92 (m, 2H), 6.63 (d, *J* = 7.8 Hz, 1H), 6.21 (d, *J* = 3.5 Hz, 1H), 5.25 – 5.06 (m, 2H), 4.89 (s, 3H), 4.64 – 4.46 (m, 1H), 4.46 – 4.38 (m, 1H), 3.95 (q, 5.7 Hz, 1H), 3.79 (d, *J* = 7.7 Hz, 4H), 3.65 (d, *J* = 7.5 Hz, 3H), 3.44 – 3.18 (m, 3H), 1.94 (q, *J* = 6.5 Hz, 1H), 1.55 – 1.48 (m, 2H), 1.42 (d, *J* = 11.7 Hz, 9H), 1.19 (s, 2H), 1.09 (s, 7H), 0.94 – 0.69 (m, 12H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.9, 172.8, 171.8, 170.8, 169.8, 166.0, 156.0, 136.4, 136.1, 128.3, 127.5, 126.2, 122.1, 119.6, 119.2, 110.0, 109.7, 80.0, 74.4, 61.1, 59.7, 53.9, 53.5, 52.2, 50.2, 46.6, 41.3, 31.0, 28.3, 27.2, 24.6, 22.8, 21.8, 19.3, 17.4. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{40}H_{61}N_5O_{10}Na^+$ 794.4311, Found: 794.4324.

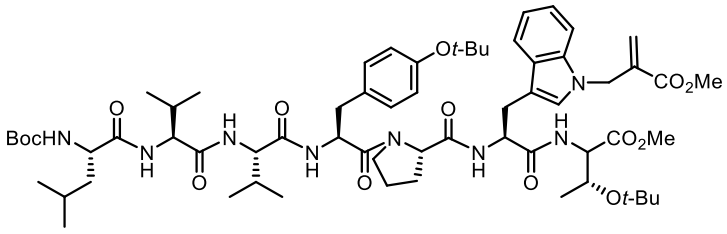
methyl (6S,9S,12S,15S,18S)-9-benzyl-15-isobutyl-12-isopropyl-6-((1-(2-(methoxycarbonyl)allyl)-1H-indol-3-yl)methyl)-2,2,18-trimethyl-4,7,10,13,16-pentaoxo-3-oxa-5,8,11,14,17-pentaazanonadecan-19-oate (3m):



3m

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:2). 65 mg, 77% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.56 – 7.96 (m, 2H), 7.51 (s, 1H), 7.11 (s, 2H), 7.03 (s, 3H), 6.97 (s, 3H), 6.86 (s, 1H), 6.10 (s, 1H), 6.00 – 5.66 (m, 1H), 5.27 – 5.06 (m, 1H), 4.97 (s, 1H), 4.75 (s, 4H), 4.59 (s, 3H), 3.73 (s, 3H), 3.69 (s, 3H), 3.07 (s, 2H), 2.97 – 2.83 (m, 2H), 2.04 (s, 1H), 1.88 (s, 1H), 1.72 (s, 1H), 1.57 (s, 1H), 1.27 (s, 13H), 0.91 (s, 12H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 173.1, 172.4, 171.8, 171.4, 166.0, 155.6, 136.5, 136.2, 136.1, 129.6, 128.1, 127.0, 126.4, 125.9, 121.7, 119.3, 110.8, 109.3, 79.1, 58.2, 54.3, 52.3, 52.0, 47.8, 46.3, 41.4, 38.7, 31.8, 29.7, 28.4, 24.9, 23.2, 22.3, 19.0, 18.7, 17.7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{45}H_{63}N_6O_{10}^+$ 847.4600, Found: 847.4602.

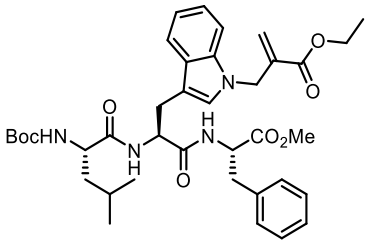
methyl (3R)-3-(tert-butoxy)-2-((S)-2-((S)-1-((6S,9S,12S,15S)-15-(4-(tert-butoxy)benzyl)-6-isobutyl-9,12-diisopropyl-2,2-dimethyl-4,7,10,13-tetraoxo-3-oxa-5,8,11,14-tetraazahexadecan-16-oyl)pyrrolidine-2-carboxamido)-3-(1-(2-(methoxycarbonyl)allyl)-1*H*-indol-3-yl)propanamido)butanoate (3n):



3n

White solid was obtained by silica gel column chromatography (eluent: DCM / MeOH = 20:1), 115.2 mg, 96% yield, **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.0 Hz, 1H), 7.47 (s, 1H), 7.21 – 6.99 (m, 7H), 6.82 (d, *J* = 8.0 Hz, 3H), 6.43 (d, *J* = 8.9 Hz, 1H), 6.19 (s, 1H), 5.34 (s, 1H), 5.11 (s, 1H), 4.92 (s, 3H), 4.80 (q, *J* = 6.9 Hz, 1H), 4.68 – 4.50 (m, 2H), 4.46 (d, 1H), 4.37 – 4.16 (m, 2H), 4.18 – 4.06 (m, 1H), 3.80 (s, 3H), 3.64 (d, *J* = 15.3 Hz, 3H), 3.52 (d, *J* = 9.6 Hz, 1H), 3.25 (d, *J* = 7.5 Hz, 1H), 3.04 (s, 1H), 2.85 (d, *J* = 6.0 Hz, 2H), 2.22 – 2.07 (m, 2H), 2.04 (s, 2H), 1.96 – 1.75 (m, 3H), 1.68 – 1.50 (m, 3H), 1.44 (s, 9H), 1.30 (s, 1H), 1.23 (s, 9H), 1.04 (d, *J* = 8.0 Hz, 12H), 0.95 – 0.81 (m, 18H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.4, 171.1, 170.7, 170.5, 166.2, 154.2, 136.3, 136.2, 131.0, 130.1, 128.2, 127.8, 124.2, 121.9, 119.4, 119.3, 110.1, 109.4, 78.2, 74.0, 67.3, 60.1, 57.9, 57.8, 54.0, 52.1, 52.0, 47.4, 46.5, 31.2, 28.8, 28.3, 28.2, 24.9, 24.7, 23.0, 22.1, 20.6, 19.4, 19.2, 18.2, 18.0.3 **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{64}H_{97}N_8O_{14}^+$ 1201.7119, Found: 1201.7137.

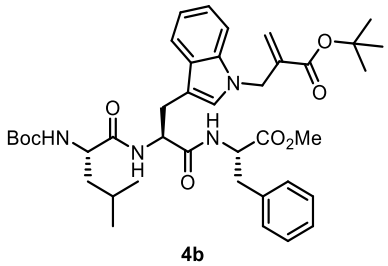
methyl (6S,9S,12S)-12-benzyl-9-((1-(2-(ethoxycarbonyl)allyl)-1*H*-indol-3-yl)methyl)-6-isobutyl-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (4a):



4a

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 50.6 mg, 73% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.7 Hz, 1H), 7.22 (t, *J* = 8.1 Hz, 6H), 6.99 (s, 1H), 6.90 - 6.83 (m, 2H) 6.79 (d, *J* = 7.2Hz, 1H), 6.23 (s, 1H), 6.20 (s, 1H), 5.15 (s, 1H), 4.89 (s, 3H), 4.67 (q, *J* = 6.0 Hz, 2H), 4.23 (q, *J* = 6.9 Hz, 2H), 4.10 (s, 1H), 3.61 (s, 3H), 3.31 (dd, *J* = 14.4, 5.1 Hz, 1H), 3.11 (dd, *J* = 14.4, 7.8 Hz, 1H), 3.02 - 2.85 (m, 2H), 1.69-1.52 (m, 2H), 1.40 (s, 9H), 1.30 (t, *J* = 7.2 Hz, 4H), 0.89 (t, 5.1 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.4, 171.2, 170.5, 165.6, 155.6, 136.40, 136.37, 135.6, 129.1, 128.5, 128.1, 127.7, 127.1, 126.2, 122.2, 119.7, 119.2, 109.7, 80.1, 61.1, 53.7, 53.4, 52.2, 46.7, 41.3, 37.8, 28.3, 28.1, 24.7, 23.0, 21.8, 14.2. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{38}H_{50}N_4O_8Na^+$ 713.3521, Found: 713.3515.

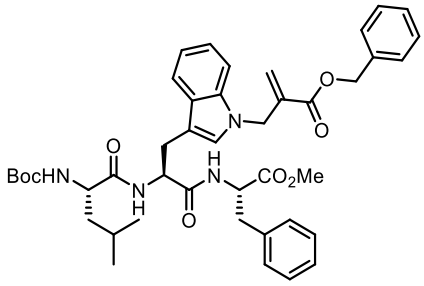
methyl (6S,9S,12S)-12-benzyl-9-((1-(2-(tert-butoxycarbonyl)allyl)-1*H*-indol-3-yl)methyl)-6-isobutyl-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (4b):



4b

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 51.7 mg, 72% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.7 Hz, 1H), 7.21 (t, *J* = 8.1 Hz, 2H), 7.17 – 7.08 (m, 4H), 6.97 (s, 1H), 6.90 – 6.82 (m, 2H), 6.79 (d, *J* = 7.2 Hz, 1H), 6.24 (d, *J* = 6.0 Hz, 1H), 6.08 (s, 1H), 4.97 (s, 1H), 4.85 (s, 3H), 4.68 (q, *J* = 6.9 Hz, 2H), 4.09 (s, 1H), 3.61 (s, 3H), 3.31 (dd, *J* = 14.4, 8.1 Hz, 1H), 3.11 (dd, *J* = 14.4, 7.8 Hz, 1H), 3.02 - 2.85 (m, 2H), 1.67 – 1.54 (m, 2H), 1.49 (s, 9H), 1.41 (s, 10H), 0.89 (t, J = 5.7 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.4, 171.2, 170.5, 164.8, 155.6, 137.8, 136.4, 135.6, 129.1, 128.5, 128.0, 127.6, 127.1, 124.9, 122.1, 119.6, 119.2, 109.8, 109.7, 81.5, 80.1, 53.8, 53.4, 52.2, 46.6, 41.3, 37.8, 28.3, 28.1, 24.7, 23.0, 21.8. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{40}H_{54}N_4O_8Na^+$ 741.3834, Found: 741.3833.

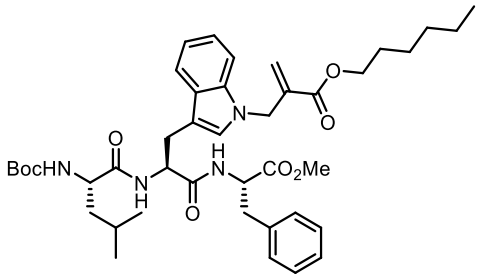
methyl (6S,9S,12S)-12-benzyl-9-((1-(2-((benzyloxy)carbonyl)allyl)-1*H*-indol-3-yl)methyl)-6-isobutyl-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (4c):



4c

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 60.6 mg, 81% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.8 Hz, 1H), 7.35 (s, 5H), 7.20 (t, *J* = 7.5 Hz, 2H), 7.17 – 7.08 (m, 4H), 6.97 (s, 1H), 6.90 – 6.82 (m, 2H), 6.79 (d, *J* = 7.2 Hz, 1H), 6.25 (s, 1H), 6.21 (s, 1H), 5.20 (s, 2H), 5.17 (s, 1H), 4.90 (s, 2H), 4.85 (s, 1H), 4.67 (q, *J* = 6.3 Hz, 2H), 4.09 (s, 1H), 3.59 (s, 3H), 3.30 (dd, *J* = 14.7, 5.1 Hz, 1H), 3.09 (dd, *J* = 14.4, 7.8 Hz, 1H), 3.03 – 2.85 (m, 2H), 1.71 – 1.51 (m, 2H), 1.39 (s, 10H), 0.88 (t, *J* = 5.7 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.4, 171.1, 170.4, 165.4, 155.6, 136.3, 136.2, 135.6, 135.5, 129.1, 128.6, 128.5, 128.4, 128.3, 128.1, 127.7, 127.0, 126.7, 122.2, 119.7, 119.2, 109.8, 109.7, 80.1, 66.8, 53.7, 53.4, 52.2, 46.7, 41.3, 37.8, 28.2, 28.1, 24.7, 23.0, 21.8. **HRMS**(ESI) m/z [M+H]+ : Calcd for C43H53N4O8+ 753.3858, Found: 753.3845.

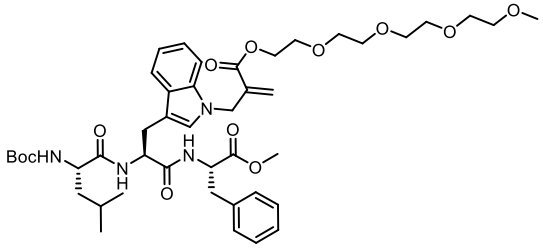
methyl (6S,9S,12S)-12-benzyl-9-((1-(2-((hexyloxy)carbonyl)allyl)-1*H*-indol-3-yl)methyl)-6-isobutyl-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (4d):



4d

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 62.6 mg, 84% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.5 Hz, 1H), 7.21 (t, *J* = 7.8 Hz, 2H), 7.17 – 7.08 (m, 4H), 6.99 (s, 1H), 6.89 – 6.81 (m, 2H), 6.80 (d, *J* = 7.5 Hz, 1H), 6.25 (d, *J* = 6.3 Hz, 1H), 6.20 (s, 1H), 5.13 (s, 1H), 4.89 (s, 3H), 4.68 (q, *J* = 6.0 Hz, 2H), 4.16 (t, *J* = 6.9 Hz, 2H), 4.10 (s, 1H), 3.61 (s, 3H), 3.31 (dd, *J* = 14.7, 5.1 Hz, 1H), 3.11 (dd, *J* = 14.7, 7.8 Hz, 1H), 3.05 – 2.86 (m, 2H), 1.70 – 1.51 (m, 4H), 1.40 (s, 10H), 1.31 (s, 6H), 0.89 (t, *J* = 6.3 Hz, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.4, 171.2, 170.5, 165.7, 155.6, 136.41, 136.37, 135.6, 129.1, 128.5, 128.1, 127.7, 127.1, 126.1, 122.2, 119.7, 119.2, 109.75, 109.72, 80.1, 65.3, 53.7, 53.4, 53.3, 52.2, 46.7, 41.3, 37.8, 31.4, 28.5, 28.3, 25.6, 24.7, 23.0, 22.5, 21.8, 14.0. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{42}H_{58}N_4O_8Na^+$ 769.4147, Found: 769.4147.

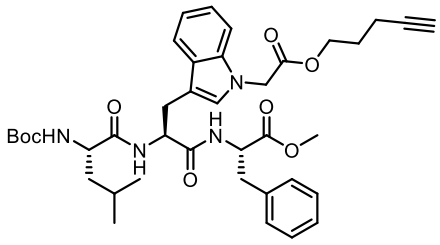
methyl (6S,9S,12S)-12-benzyl-6-isobutyl-2,2-dimethyl-9-((1-(16-methylene-15-oxo-2,5,8,11,14-pentaoxaheptadecan-17-yl)-1*H*-indol-3-yl)methyl)-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (4e):



4e

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 55.6 mg, 65% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.8 Hz, 1H), 7.27 – 7.08 (m, 6H), 7.00 (s, 1H), 6.92 – 6.76 (m, 3H), 6.24 (s, 2H), 5.18 (s, 1H), 4.90 (s, 3H), 4.78 – 4.63 (m, 2H), 4.32 (t, *J* = 4.8 Hz, 2H), 4.09 (s, 1H), 3.72 (t, *J* = 4.8 Hz, 2H), 3.68 – 3.57 (s, 13H), 3.56 – 3.49 (m, 2H), 3.36 (s, 3H), 3.30 (dd, *J* = 14.7, 5.4 Hz, 1H), 3.11 (dd, *J* = 14.7, 7.8 Hz, 1H), 3.01 – 2.85 (m, 2H), 1.70 – 1.51 (m, 2H), 1.40 (s, 10H), 0.89 (t, *J* = 5.1 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.4, 171.1, 170.5, 165.5, 155.6, 136.4, 136. 1, 135.6, 129.2, 129.1, 128.5, 128.1, 127.7, 127.0, 126.7, 122.2, 119.7, 119.2, 109.8, 109.7, 80.0, 71.9, 70.6, 70.5, 68.9, 64.2, 59.0, 53.7, 53.4, 52.2, 46.7, 41.3, 37.8, 28.3, 24.7, 23.0, 21.8. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{45}H_{64}N_4O_{12}Na^+$ 875.4413, Found: 875.4432.

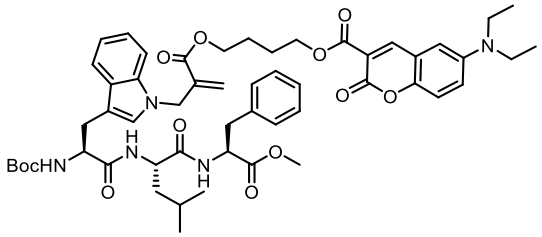
methyl N^a-((tert-butoxycarbonyl)-L-leucyl)-1-(2-oxo-2-(pent-4-yn-1-yloxy)ethyl)-L-tryptophyl-L-phenylalaninate (4f):



4f

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 64.8 mg, 94% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.8 Hz, 1H), 7.21 (t, *J* = 6.6 Hz, 2H), 7.18 – 7.09 (m, 4H), 6.99 (s, 1H), 6.90 – 6.75 (m, 3H), 6.25 (s, 1H), 6.21 (s, 1H), 5.16 (s, 1H), 4.89 (s, 3H), 4.67 (q, *J* = 6.0 Hz, 2H), 4.28 (t, *J* = 6.3 Hz, 2H), 4.13 (s, 1H), 3.61 (s, 3H), 3.30 (dd, *J* = 14.4, 5.1 Hz, 1H), 3.11 (dd, *J* = 14.7, 7.8 Hz, 1H), 3.02 – 2.84 (m, 2H), 2.28 (td, *J* = 6.9, 2.4 Hz, 2H), 1.99 (t, *J* = 2.7 Hz, 1H), 1.96 –1.81 (m, 2H), 1.70 – 1.51 (m, 2H), 1.40 (s, 10H), 0.89 (t, *J* = 6.0 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.4, 171.2, 170.5, 165.5, 155.6, 136.4, 136.2, 135.6, 129.1, 128.5, 128.1, 127.7, 127.1, 126.5, 122.2, 119.7, 119.2, 109.8, 109.7, 82.8, 80.1, 69.3, 63.6, 53.7, 53.4, 52.2, 46.7, 41.3, 37.8, 28.3, 28.1, 27.4, 24.7, 23.0, 21.8, 15.3. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{41}H_{52}N_4O_8Na^+$ 751.3677, Found: 751.3678.

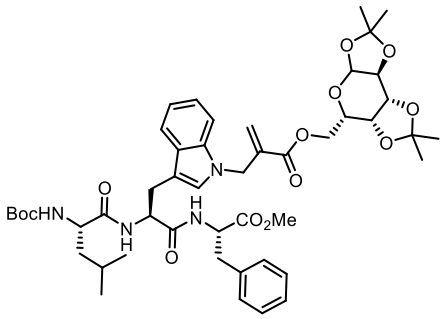
4-((2-((3-((S)-2-((tert-butoxycarbonyl)amino)-3-(((S)-1-(((S)-1-methoxy-1-oxo-3-phenylpropan-2-yl)amino)-4-methyl-1-oxopentan-2-yl)amino)-3-oxopropyl)-1*H*-indol-1-yl)methyl)acryloyl)oxy)butyl 6-(diethylamino)-2-oxo-2*H*-chromene-3-carboxylate (4g):



4g

Yellow solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 67.0 mg, 68% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.69 (d, *J* = 7.5Hz, 1H), 7.36 (dd, *J* = 9.0, 4.5 Hz, 1H), 7.27 – 7.08 (m, 6H), 7.00 (s, 1H), 6.89 – 6.83 (m, 2H), 6.60 (d, *J* = 1.8 Hz, 1H), 6.45 (s, 1H), 6.29 (d, *J* = 7.2 Hz, 1H), 6.22 (s, 1H), 5.16 (s, 1H), 4.90 (s, 3H), 4.76 – 4.63 (m, 2H), 4.34 (d, *J* = 5.4 Hz, 2H), 4.24 (s, 2H), 4.10 (s, 1H), 3.61 (s, 3H), 3.44 (q, *J* = 6.9 Hz, 4H), 3.31 (dd, *J* = 14.4, 5.1 Hz, 1H), 3.12 (dd, *J* = 14.7, 7.5 Hz, 1H), 3.03 – 2.87 (m, 2H), 1.85 (s, 3H), 1.68 – 1.51 (m, 2H), 1.39 (s, 9H), 1.23 (t, *J* = 7.5 Hz, 9H), 0.89 (t, *J* = 4.5 Hz, 6H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.4, 171.2, 170.5, 165.6, 164.4, 158.5, 158.3, 155.6, 153.0, 149.4, 136.4, 136.3, 135.6, 131.2, 129.1, 128.5, 128.0, 127.7, 127.0, 126.4, 122.1, 119.6, 119.2, 109.8, 109.7, 109.6, 108.5, 107.6, 96.7, 80.0, 64.7, 64.5, 53.7, 53.4, 52.2, 46.7, 45.1, 41.3, 37.8, 29.7, 28.3, 25.4, 25.3, 24.7, 23.0, 21.8, 12.4. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{54}H_{67}N_5O_{12}Na^+$ 1000.4684, Found: 1000.4692.

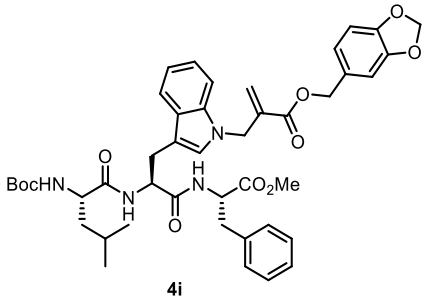
methyl (6S,9S,12S)-12-benzyl-6-isobutyl-2,2-dimethyl-4,7,10-trioxo-9-((1-(2-((((3aS,5S,5aR,8aR,8bS)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-5-yl)methoxy)carbonyl)allyl)-1*H*-indol-3-yl)methyl)-3-oxa-5,8,11-triazatridecan-13-oate (4h):



4h

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 75.6 mg, 83% yield. The reaction was carried out for 24 h. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.8 Hz, 1H), 7.21 (t, *J* = 7.8 Hz, 2H), 7.18 – 7.08 (m, 4H), 7.00 (s, 1H), 6.84 (dd, *J* = 7.5, 2.4 Hz, 2H), 6.77 (d, *J* = 7.5 Hz, 1H), 6.24 (s, 1H), 6.16 (d, *J* = 6.3 Hz, 1H), 5.54 (d, *J* = 5.1 Hz, 1H), 5.15 (s, 1H), 4.90 (s, 2H), 4.82 (d, *J* = 6.6 Hz, 1H), 4.71 – 4.55 (m, 3H), 4.39 – 4.28 (m, 3H), 4.20 (dd, *J* = 7.8, 1.8 Hz, 1H), 4.15 – 3.98 (m, 2H), 3.61 (s, 3H), 3.32 (dd, *J* = 14.4, 5.1 Hz, 1H), 3.09 (dd, *J* = 14.7, 8.1 Hz, 1H), 3.01 – 2.84 (m, 2H), 1.75 (d, *J* = 7.5 Hz, 1H), 1.67 – 1.52 (m, 2H), 1.47 (d, *J* = 7.8 Hz, 6H), 1.40 (s, 9H), 1.33 (s, 7H), 0.89 (t, *J* = 5.7 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.3, 171.1, 170.4, 165.4, 155.6, 136.3, 136.0, 135.6, 129.1, 128.5, 128.0, 127.7, 127.1, 126.8, 119.7, 119.2, 109.8, 109.7, 108.8, 96.3, 80.1, 66.0, 64.1, 53.7, 53.4, 52.2, 46.6, 41.3, 37.7, 28.2, 26.0, 25.9, 25.0, 24.7, 24.4, 23.0, 21.8. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{48}H_{64}N_4O_{13}Na^+$ 927.4362, Found: 927.4359.

methyl (6S,9S,12S)-9-((1-(2-((benzo[d][1,3]dioxol-5-ylmethoxy)carbonyl)allyl)-1*H*-indol-3-yl)methyl)-12-benzyl-6-isobutyl-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (4i):

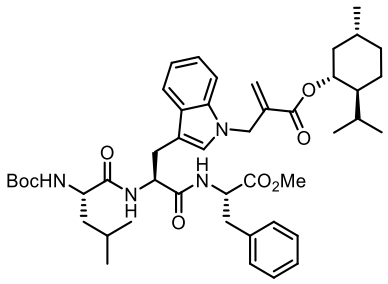


4i

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 56.9 mg, 72% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.5 Hz, 1H), 7.22 (t, *J* = 6.3 Hz, 2H), 7.17 – 7.07 (m, 4H), 6.97 (s, 1H), 6.91 – 6.70 (m, 6H), 6.23 (s, 2H), 5.96 (s, 2H), 5.17 (s, 1H), 5.09 (s, 2H), 4.88 (s, 3H), 4.67 (q, *J* = 6.3 Hz, 2H), 4.11 (t, *J* = 7.2 Hz, 1H), 3.60 (s, 3H), 3.30 (dd, *J* = 14.7, 5.1 Hz, 1H), 3.09 (dd, *J* = 14.4, 7.8 Hz, 1H), 3.01 – 2.85 (m, 2H), 1.70 – 1.52 (m, 2H), 1.40 (s, 10H), 0.88 (t, *J* = 5.7 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.4, 171.2, 170.5, 155.6, 147.84, 147.79, 136.4, 136.2, 135.6, 129.2, 129.1, 128.5, 128.1, 127.6, 127.1, 126.8, 122.4, 122.2, 119.7, 119.2, 109.8, 109.1, 108.3, 101.2, 80.1, 66.9, 53.7, 53.4, 52.2, 46.7, 41.3, 37.8, 28.3, 28.1, 24.74, 23.0, 21.8. **HRMS**(ESI) m/z $[M+Na]^+$: Calcd for $C_{44}H_{52}N_4O_{10}Na^+$ 829.3589, Found: 819.3588.

methyl (6S,9S,12S)-12-benzyl-6-isobutyl-9-((1-(2-((((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)oxy)carbonyl)allyl)-1*H*-indol-3-yl)methyl)-2,2-dimethyl-4,7,10-trioxo-3-

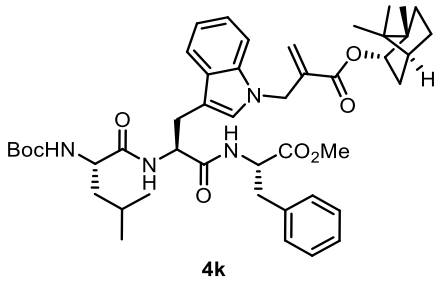
oxa-5,8,11-triazatridecan-13-oate (4j):



4j

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 65.0 mg, 81% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.5 Hz, 1H), 7.20 (d, *J* = 6.6 Hz, 2H), 7.19 – 7.07 (m, 4H), 6.98 (s, 1H), 6.95 – 6.73 (m, 3H), 6.27 (s, 1H), 6.17 (s, 1H), 5.06 (s, 1H), 4.88 (s, 3H), 4.84 – 4.73 (m, 1H), 4.68 (q, *J* = 6.0 Hz, 2H), 4.19 – 3.98 (m, 1H), 3.61 (s, 3H), 3.30 (dd, *J* = 14.4, 4.8 Hz, 1H), 3.11 (dd, *J* = 14.4, 7.5 Hz, 1H), 3.02 – 2.85 (m, 2H), 2.03 – 1.94 (m, 1H), 1.83 – 1.73 (m, 1H), 1.73 – 1.53 (m, 4H), 1.41 (s, 12H), 1.13 – 0.95 (m, 2H), 0.95 – 0.83 (m, 13H), 0.75 (d, *J* = 6.9 Hz, 3H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.4, 171.2, 170.5, 165.1, 155.6, 136.8, 136.4, 135.6, 129.1, 128.5, 128.0, 127.6, 127.1, 125.6, 122.1, 119.7, 119.2, 109.8, 109.7, 80.0, 75.1, 53.8, 53.4, 52.2, 47.0, 46.7, 41.3, 40.8, 37.8, 34.2, 31.4, 28.3, 26.4, 24.7, 23.5, 23.0, 22.0, 21.8, 20.8, 16.4. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{46}H_{65}N_4O_8^+$: 801.4797, Found: 801.4786.

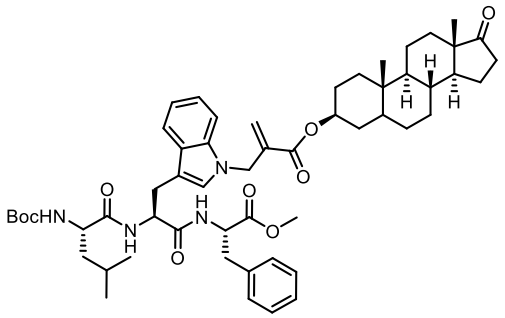
methyl (6S,9S,12S)-12-benzyl-6-isobutyl-2,2-dimethyl-4,7,10-trioxo-9-((1-(2-((((1S,2S,4S)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)oxy)carbonyl)allyl)-1*H*-indol-3-yl)methyl)-3-oxa-5,8,11-triazatridecan-13-oate (4k):



4k

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 48.2 mg, 61% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.8 Hz, 1H), 7.22 (d, 2H), 7.19 – 7.10 (m, 4H), 6.99 (s, 1H), 6.91 – 6.83 (m, 2H), 6.78 (d, *J* = 7.8 Hz, 1H), 6.18 (s, 2H), 5.07 (s, 1H), 4.97 (d, *J* = 8.7 Hz, 1H), 4.90 (d, *J* = 6.9 Hz, 2H), 4.85 – 4.76 (m, 1H), 4.75 – 4.61 (m, 2H), 4.17 – 3.98 (m, 1H), 3.61 (s, 3H), 3.31 (dd, *J* = 14.4, 4.8 Hz, 1H), 3.10 (dd, *J* = 14.4, 7.8 Hz, 1H), 3.05 – 2.85 (m, 2H), 2.47 – 2.33 (m, 1H), 1.98 – 1.85 (m, 1H), 1.81 – 1.75 (m, 1H), 1.72 (d, *J* = 4.2 Hz, 1H), 1.66 – 1.52 (m, 2H), 1.40 (s, 10H), 1.31 – 1.16 (m, 2H), 1.01 (dd, *J* = 13.8, 3.3 Hz, 1H), 0.96 – 0.81 (m, 15H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.3, 171.1, 170.4, 165.8, 155.5, 136.7, 136.4, 135.5, 129.0, 128.5, 128.0, 127.6, 127.0, 125.6, 122.2, 119.7, 119.2, 109.8, 109.7, 80.8, 80.1, 53.7, 53.3, 52.2, 49.0, 47.8, 46.6, 44.8, 41.3, 37.7, 36.7, 28.2, 28.0, 27.2, 24.7, 22.9, 21.7, 19.6, 18.8, 13.5. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{46}H_{63}N_4O_8^+$ 799.4640, Found: 799.4624.

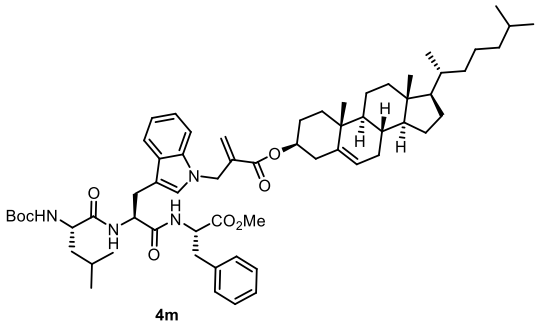
methyl (6S,9S,12S)-12-benzyl-9-((1-(2-((((3S,8R,9S,10S,13S,14S)-10,13-dimethyl-17-oxohexadecahydro-1*H*-cyclopenta[a]phenanthren-3-yl)oxy)carbonyl)allyl)-1*H*-indol-3-yl)methyl)-6-isobutyl-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (4l):



4l

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 63.4 mg, 68% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.5 Hz, 1H), 7.26 – 7.09 (m, 6H), 6.99 (s, 1H), 6.84 (d, *J* = 6.3 Hz, 2H), 6.75 (d, *J* = 6.9 Hz, 1H), 6.16 (s, 2H), 5.12 (s, 1H), 4.88 (s, 2H), 4.85 – 4.71 (m, 2H), 4.66 (d, *J* = 6.9 Hz, 2H), 4.09 (s, 1H), 3.62 (s, 3H), 3.31 (dd, *J* = 14.1, 4.5 Hz, 1H), 3.09 (dd, *J* = 14.4, 7.8 Hz, 1H), 3.02 – 2.84 (m, 2H), 2.45 (dd, *J* = 19.5, 9.0 Hz, 1H), 2.15 – 2.01 (m, 1H), 1.85 – 1.75 (m, 3H), 1.71 – 1.56 (m, 5H), 1.56 – 1.46 (m, 3H), 1.40 (s, 10H), 1.36 – 1.18 (m, 9H), 1.12 – 0.96 (m, 2H), 0.94 – 0.81 (m, 12H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.4, 171.1, 170.4, 165.1, 136.8, 136.4, 135.6, 129.1, 128.5, 128.0, 127.6, 127.1, 126.0, 122.2, 119.7, 119.2, 109.8, 80.1. 74.4, 54.3, 53.7, 53.4, 52.2, 51.3, 47.8, 46.7, 44.6, 37.8, 36.6, 35.9, 35.6, 35.0, 33.8, 31.5, 30.8, 28.3, 27.3, 24.7, 23.0, 21.8, 20.5, 13.8, 12.2. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{55}H_{75}N_4O_9^+$ 935.5529, Found: 935.5534.

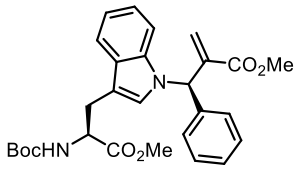
methyl (6S,9S,12S)-12-benzyl-9-((1-(2-((((3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[a]phenanthren-3-yl)oxy)carbonyl)allyl)-1*H*-indol-3-yl)methyl)-6-isobutyl-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (4m):



4m

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 90.0 mg, 87% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.5 Hz, 1H), 7.32 – 7.09 (m, 6H), 6.98 (s, 1H), 6.93 – 6.82 (m, 2H), 6.79 (d, *J* = 6.9 Hz, 1H), 6.21 (s, 2H), 5.38 (s, 1H), 5.12 (s, 1H), 4.88 (s, 3H), 4.67 (d, *J* = 6.0 Hz, 3H), 4.11 (s, 1H), 3.61 (s, 3H), 3.31 (dd, *J* = 14.7, 4.5 Hz, 1H), 3.10 (dd, *J* = 14.4, 7.5 Hz, 1H), 3.02 – 2.83 (m, 2H), 2.33 (d, *J* = 6.6 Hz, 2H), 1.99 (t, *J* = 11.4 Hz, 2H), 1.87 (d, *J* = 10.8 Hz, 3H), 1.71 – 1.46 (m, 9H), 1.40 (s, 13H), 1.26 (s, 2H), 1.13 (q, *J* = 6.9 Hz, 6H), 1.02 (s, 6H), 0.88 (t, *J* = 7.7 Hz, 15H), 0.68 (s, 3H). **^{13}C NMR** (75 MHz,$CDCl_3$) δ 172.4, 171.2, 170.5, 139.4, 136.8, 136.4, 135.6, 129.1, 128.5, 128.0, 127.7, 127.1, 126.0, 122.9, 122.1, 119.7, 119.2, 109.8, 80.1, 74.9, 56.7, 56.1, 53.7, 53.4, 52.2, 50.0, 46.7, 42.3, 41.3, 39.7, 39.5, 38.0, 37.8, 36.9, 36.6, 36.2, 35.8, 31.9, 31.8, 28.3, 28.0, 27.7, 24.7, 24.3, 23.8, 23.0, 22.9, 22.6, 21.8, 21.0, 19.3, 18.7, 11.9. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{63}H_{91}N_4O_8^+$ 1031.6831, Found: 1031.6844.

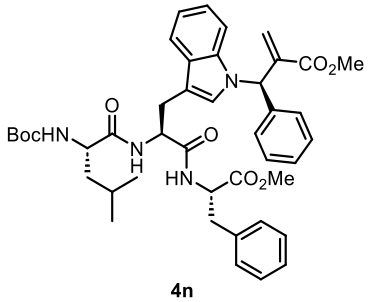
methyl 2-((R)-(3-((S)-2-((tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)-1H-indol-1-yl)(phenyl)methyl)acrylate (4ao):



4ao

White Solid was obtained by silica gel column chromatography (eluent: PE / EA = 4:1), 48.2 mg, 98 % yield. d. r.= 7.1:1 determined by **^{1}H NMR**. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.5 Hz, 1H), 7.37 (d, *J* = 6.0 Hz, 3H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.28 – 7.18 (m, 3H), 7.14 (q, *J* = 7.5Hz, 1H), 6.68 (s, 1H), 6.59 (s, 1H), 6.44 (s, 1H), 5.11 (d, *J* = 7.5 Hz, 1H), 5.03 (d, *J* = 7.8Hz, 1H), 4.58 (d, *J* = 6.9 Hz, 1H), 3.73 (s, 3H), 3.60 (s, 2.63H), 3.47(s, 0.37H) 3.31-3.09 (m, 2H), 1.41 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172,6, 166.0, 155.0, 139.7, 137.3, 136.3, 128.9, 128.5, 128.3, 128.0, 122.1, 119.8, 119.1, 110.0, 109.4, 79.7., 59.3, 54.5, 52.4, 52.1, 28.3, 28.1. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{28}H_{33}N_2O_6^+$ 493.2333, Found: 493.2322

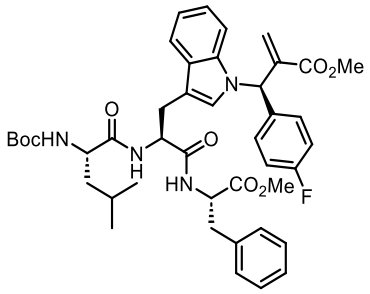
methyl (6S,9S,12S)-12-benzyl-6-isobutyl-9-((1-((R)-2-(methoxycarbonyl)-1-phenylallyl)-1H-indol-3-yl)methyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (4n):



4n

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 87.8 mg, 99% yield, d. r. = 5.3:1 determined by **^{1}H NMR**. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.5 Hz, 1H), 7.40 – 7.31 (m, 4H), 7.28 – 7.20 (m, 2H), 7.20 – 7.03 (m, 5H), 6.90 – 6.80 (m, 2H), 6.78 (s, 1H), 6.72 (d, *J* = 7.5 Hz, 1H), 6.65 (s, 1H), 6.43 (s, 1H), 6.17 (d, = 5.1 Hz, 1H), 5.16 (s, 1H), 4.71 – 4.49 (m, 3H), 4.02 (s, 1H), 3.70 (s, 0.47H), 3.68 (s, 2.51H), 3.55 (s, 3H), 3.22 (dd, *J* = 14.7, 5.7 Hz, 1H), 3.08 (dd, *J* = 14.4, 7.5 Hz, 1H), 3.03 – 2.70 (m, 2H), 1.74 – 1.46 (m, 2H), 1.39 (d, *J* = 9.9 Hz, 9H), 1.29 – 1.17 (m, 1H), 0.86 (t, *J* = 6.0 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.3, 171.0, 170.4, 166.1, 155.5, 139.4, 137.4, 136.5, 135.6, 129.2, 129.1, 129.0, 128.5, 128.4, 128.3, 128.2, 127.0, 125.3, 122.3, 120.0, 119.3, 110.1, 109.9, 80.1, 59.6, 53.6, 53.5, 52.3, 52.2, 41.0, 37.7, 28.3, 28.2, 24.7, 23.0, 21.7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{43}H_{53}N_4O_8^+$ 753.3858, Found: 753.3847.

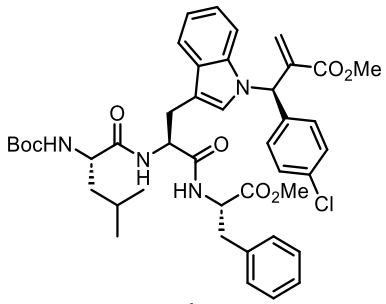
methyl (6S,9S,12S)-12-benzyl-9-((1-((R)-1-(4-fluorophenyl)-2-(methoxycarbonyl)allyl)-1H-indol-3-yl)methyl)-6-isobutyl-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (4o):



4o

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 63.8 mg, 81% yield, d. r.= 4.2:1 determined by **^{1}H NMR**. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.5 Hz, 1H), 7.37 – 7.24 (m, 2H), 7.22 – 7.09 (m, 5H), 7.07 – 6.90 (m, 3H), 6.89 – 6.79 (m, 3H), 6.77 (d, *J* = 6.0 Hz, 1H), 6.64 (s, 1H), 6.46 (s, 1H), 6.22 (d, *J* = 5.1 Hz, 1H), 5.22 (s, 1H), 4.78 (d, *J* = 7.5 Hz, 1H), 4.73 – 4.55 (m, 2H), 4.06 (s, 1H), 3.71 (s, 0.58H), 3.69 (s, 2.42H), 3.57 (s, 3H), 3.23 (dd, *J* = 14.7, 5.2 Hz, 1H), 3.09 (dd, *J* = 14.4, 5.1 Hz, 1H), 3.03 – 2.80 (m, 2H), 1.68 – 1.47 (m, 2H), 1.39 (d, *J* = 6.3 Hz, 9H), 1.31 – 1.21 (m, 1H), 0.86 (t, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.3, 171.1, 170.4, 166.0, 164.2, 160.9, 155.5, 139.4, 136.4, 135.6, 133.20, 133.16, 130.2, 130.1, 129.1, 128.5, 128.3, 127.1, 125.1, 122.3, 120.1, 119.3, 116.1, 115.7, 110.1, 80.1, 58.9, 53.6, 53.5, 52.3, 52.2, 41.2, 37.8, 28.2, 24.7, 23.0, 21.7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{43}H_{52}N_4O_8F^+$ 771.3764, Found: 771.3748.

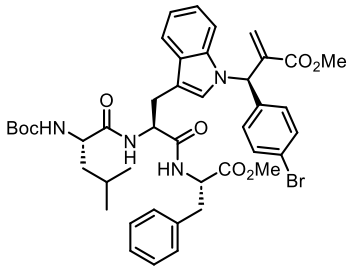
methyl (6S,9S,12S)-12-benzyl-9-((1-((R)-1-(4-chlorophenyl)-2-(methoxycarbonyl)allyl)-1H-indol-3-yl)methyl)-6-isobutyl-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (4p):



4p

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 46.2 mg, 58% yield, d. r.= 6.1:1 determined by **^{1}H NMR**. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.5 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 1H), 7.24 – 7.08 (m, 7H), 7.03 (t, *J* = 8.4 Hz, 2H), 6.90 – 6.82 (m, 2H), 6.77 (s, 2H), 6.63 (s, 1H), 6.42 (s, 1H), 6.22 (d, *J* = 5.7 Hz, 1H), 5.15 (s, 1H), 4.75 (d, *J* = 7.8 Hz, 1H), 4.70 – 4.53 (m, 2H), 4.15 – 3.91 (m, 1H), 3.71 (s, 0.42H), 3.69 (s, 2.56H), 3.56 (s, 3H), 3.29 – 3.02 (m, 2H), 3.02 – 2.74 (m, 2H), 1.71 – 1.47 (m, 2H), 1.40 (d, *J* = 6.0 Hz, 9H), 1.33 – 1.23 (m, 1H), 0.87 (t, *J* = 6.6 Hz, 6H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.4, 171.1, 170.4, 165.9, 155.5, 139.1, 136.4, 136.0, 135.6, 134.3, 129.7, 129.6, 129.2, 129.1, 128.5, 127.1, 125.1, 122.4, 120.2, 119.4, 119.2, 110.2, 110.0, 80.1, 58.9, 53.5, 52.3, 52.2, 41.2, 37.8, 28.3, 24.7, 23.0, 21.7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{43}H_{52}N_4O_8Cl^+$ 787.3468, Found: 787.3453.

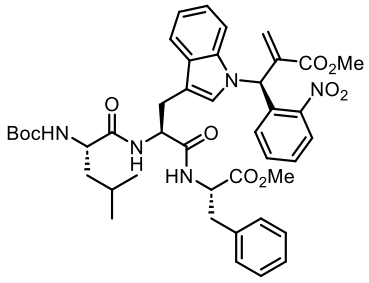
methyl (6S,9S,12S)-12-benzyl-9-((1-((R)-1-(4-bromophenyl)-2-(methoxycarbonyl)allyl)-1H-indol-3-yl)methyl)-6-isobutyl-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (4q):



4q

White solid, 68.1 mg, 82% yield, d. r. = 10.1:1 determined by **^{1}H NMR**. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7. 2Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.23 – 6.92 (m, 8H), 6.81 – 6.72 (m, 3H), 6.68 (d, *J* = 7.8 Hz, 1H), 6.52 (s, 1H), 6.37 (s, 1H), 6.07 (d, *J* = 6.3 Hz, 1H), 5.11 (d, *J* = 0.9 Hz, 1H), 4.73 – 4.46 (m, 3H), 3.95 (s, 1H), 3.64 (s, 0.27H), 3.62 (s, 2.73H), 3.51 (s, 2.70H), 3.49 (s, 0.31H), 3.13 (dd, *J* = 14.7, 5.7 Hz, 1H), 3.02 (dd, *J* = 14.4, 7.5 Hz, 1H), 2.89 (dd, *J* = 13.8, 6.0 Hz, 1H), 2.75 (dd, *J* = 13.8, 6.0 Hz, 1H), 1.60-1.39 (m, 2H), 1.32 (s, 9H), 1.27 – 1.14 (m, 1H), 0.79 (t, *J* = 6.6 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.3, 170.0, 169.3, 164.9, 154.5, 138.0, 135.5, 135.4, 134.5, 131.1, 129.0, 128.1, 128.1, 127.6, 127.5, 126.0, 124.0, 121.5, 121.4, 119.2, 118.4, 109.2, 109.0, 79.1, 57.9, 52.6, 52.5, 51.3, 51.2, 40.1, 36.7, 27.2, 23.7, 21.9, 20.7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{43}H_{52}N_4O_8Br^+$ 831.2963, Found: 831.2951.

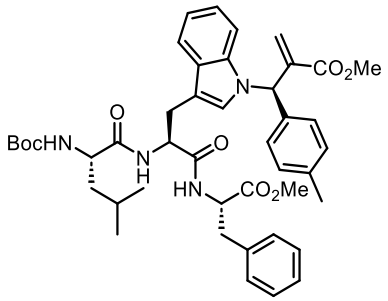
methyl (6S,9S,12S)-12-benzyl-6-isobutyl-9-((1-((R)-2-(methoxycarbonyl)-1-(2-nitrophenyl)allyl)-1H-indol-3-yl)methyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (4r):



4r

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 42.2 mg, 53% yield, d. r.= 3.3:1 determined by **^{1}H NMR**. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.07 (d, *J* = 27.9, 6.3 Hz, 2H), 7.61 (t, *J* = 6.4 Hz, 1H), 7.53 – 7.37 (m, 2H), 7.08 (t, *J* = 5.2 Hz, 5H), 6.87 – 6.64 (m, 5H), 6.47 (s, 1H), 6.14 (s, 1H), 5.22 (s, 1H), 4.79 (d, *J* = 6.2 Hz, 1H), 4.68 – 4.39 (m, 2H), 3.98 (s, 1H), 3.73 – 3.59 (m, 3H), 3.51 (s, 0.70H), 3.49 (s, 2.31H), 3.27 – 2.96 (m, 2H), 2.96 – 2.73 (m, 2H), 1.65 – 1.40 (m, 2H), 1.33 (q, *J* = 2.9 Hz, 9H), 1.26 – 1.17 (m, 2H), 0.79 (t, *J* = 4.9 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.4, 170.1, 169.3, 164.7, 154.5, 147.61, 147.56, 139.0, 137.5, 135.4, 134.5, 133.2, 129.0, 128.6, 128.1, 127.6, 126.1, 126.0, 123.9, 123.8, 122.4, 122.1, 121.6, 119.4, 118.5, 109.7, 108.8, 79.0, 57.7, 52.6, 52.4, 51.5, 51.1, 40.3, 36.7, 27.2, 23.7, 21.9, 20.7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{43}H_{52}N_5O_{10}^+$ 798.3709, Found: 798.3699.

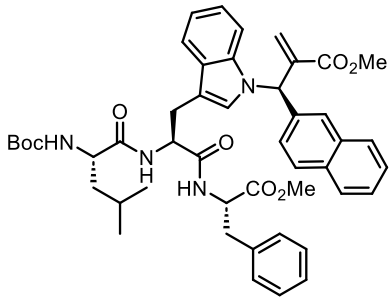
methyl (6S,9S,12S)-12-benzyl-6-isobutyl-9-((1-((R)-2-(methoxycarbonyl)-1-(p-tolyl)allyl)-1H-indol-3-yl)methyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (4s):



4s

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 65.8 mg, 86% yield, d. r.= 6.3:1 determined by **^{1}H NMR**. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.8 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 1H), 7.13 – 7.00 (m, 9H), 6.84 – 6.73 (m, 2H), 6.74 – 6.61 (m, 2H), 6.53 (s, 1H), 6.32 (s, 1H), 6.13 (d, *J* = 5.7 Hz, 1H), 5.05 (s, 1H), 4.68 – 4.38 (m, 3H), 3.98 (s, 1H), 3.62 (s, 0.41H), 3.60 (s, 2.58H), 3.47 (s, 3H), 3.14 (dd, *J* = 14.4, 5.4 Hz, 1H), 2.99 (dd, *J* = 14.7, 7.5 Hz, 1H), 2.88 (dd, *J* = 13.5, 6.0 Hz, 1H), 2.74 (dd, *J* = 13.5, 6.0 Hz, 1H), 2.27 (s, 2.59H), 2.24 (s, 0.41H), 1.58 – 1.38 (m, 2H), 1.31 (d, *J* = 9.6 Hz, 9H), 1.20 – 1.10 (m, 1H), 0.79 (t, *J* = 6.3 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.3, 170.0, 169.4, 165.1, 154.5, 138.7, 138.5, 137.2, 135.4, 134.7, 133.2, 128.6, 128.14, 128.06, 127.5, 127.4, 127.3, 126.7, 126.0, 124.3, 121.1, 118.9, 118.2, 118.0, 109.1, 108.7, 79.1, 58.3, 52.6, 51.2, 51.1, 40.1, 36.7, 27.2, 23.7, 21.9, 20.7, 20.1. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{44}H_{55}N_4O_8^+$ 767.4014, Found: 767.4000.

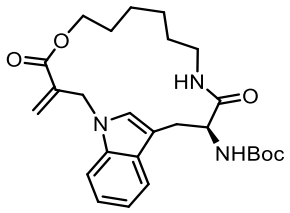
methyl (6S,9S,12S)-12-benzyl-6-isobutyl-9-((1-((R)-2-(methoxycarbonyl)-1-(naphthalen-2-yl)allyl)-1H-indol-3-yl)methyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (4t):



4t

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 59.9 mg, 73% yield, d. r.= 10:1 determined by **^{1}H NMR**. **^{1}H NMR** (300 MHz,$CDCl_3$) δ 7.88 – 7.76 (m, 3H), 7.69 (d, *J* = 6.9 Hz, 2H), 7.56 – 7.45 (m, 2H), 7.45 – 7.29 (m, 2H), 7.20 (t, *J* = 6.9 Hz, 1H), 7.14 (s, 4H), 6.83 (s, 4H), 6.74 (d, *J* = 7.7 Hz, 1H), 6.48 (s, 1H), 6.17 (s, 1H), 5.22 (s, 1H), 4.73 – 4.44 (m, 3H), 3.99 (s, 1H), 3.68 (s, 3H), 3.49 (s, 0.27H), 3.45 (s, 2.7H), 3.21 (dd, *J* = 14.6, 5.6 Hz, 1H), 3.07 (dd, *J* = 14.6, 7.4 Hz, 1H), 2.90 (dd, *J* = 13.8, 6.1 Hz, 1H), 2.76 (d, *J* = 12.9Hz, 2H), 1.36 (s, 9H), 1.16 – 0.96 (m, 1H), 0.79 (dd, *J* = 13.6, 5.9 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.3, 171.0, 170.5, 166.1, 155.5, 139.4, 136.6, 135.7, 134.8, 133.3, 133.1, 129.1, 128.8, 128.5, 128.3, 127.7, 127.4, 126.64, 126.59, 126.3, 125.4, 122.3, 120.1, 119.4, 110.1, 110.0, 80.1, 59.7, 53.7, 53.4, 53.1, 52.3, 52.1, 40.9, 37.7, 28.2, 24.6, 22.9, 21,7. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{47}H_{55}N_4O_8^+$ 803.4014, Found: 803.4002

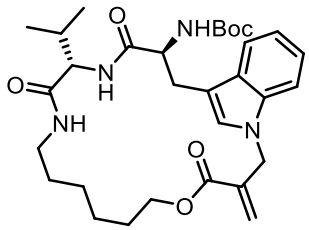
tert-butyl ((14S,*Z*)-3-methylene-4,13-dioxo-1^1*H*-5-oxa-12-aza-1(1,3)-indolacyclopentadecaphane-14-yl)carbamate (5a):



5a

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 55.8 mg, 77% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 1H)7.13 (t, *J* = 7.5 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.96 (s, 1H), 6.39 (s, 1H), 5.97 (s, 1H), 5.41 (d, *J* = 7.2 Hz, 1H), 5.06 (s, 1H), 4.80 (d, *J* = 14.1 Hz, 2H), 4.32 – 4.19 (m, 1H), 4.18 – 4.00 (m, 2H), 3.27 (d, *J* = 13.2 Hz, 1H), 2.90 (dd, *J* = 13.8, 10.5 Hz, 2H), 2.83 – 2.65 (m, 1H), 1.40 (s, 11H), 1.08 – 0.90 (m, 1H), 0.86 – 0.59 (m, 5H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.0, 165.5, 136.5, 136.3, 130.0, 128.3, 126.2, 122.0, 119.6, 119.3, 110.4, 110.0,79.8, 64.0, 55.8, 47.5, 38.5, 29.3, 28.4, 27.8, 27.6, 24.7, 24.5. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{26}H_{36}N_3O_5^+$ 470.2650, Found: 470.2640.

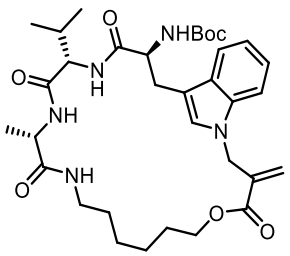
tert-butyl ((3S,6S,Z)-6-isopropyl-17-methylene-4,7,16-trioxo-1^1*H*-15-oxa-5,8-diaza-1(3,1)-indolacyclooctadecaphane-3-yl)carbamate (5b):



5b

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 34.6 mg, 61% yield. **^{1}H NMR** (300 MHz, DMSO-d_6) δ 7.90 (s, 2H), 7.54 (d, *J* = 6.9Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 7.01 (d, *J* = 11.7 Hz, 2H), 6.48 (d, *J* = 7.2 Hz, 1H), 6.11 (s, 1H), 5.30 (s, 1H), 5.00 (s, 2H), 4.28 (s, 1H), 4.10 (d, *J* = 19.2 Hz, 3H), 3.30 – 3.06 (m, 2H), 2.93 (d, *J* = 10.2 Hz, 2H), 1.90 (d, *J* = 6.0 Hz 1H), 1.60 (s, 2H), 1.37 (s, 15H), 0.83 (d, *J* = 5.7 Hz, 6H). **^{13}C NMR** (75 MHz, DMSO-d_6) δ 171.6, 170.5, 166.9, 155.0, 137.3, 137.0, 136.0, 129.4, 129.1, 128.1, 127.9, 127.3, 126.4, 126.2, 123.4, 120.8, 118.4, 118.1, 111.2, 110.3, 78.0, 63.0, 55.3, 53.2, 51.6, 37.7, 28.1, 27.5. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{31}H_{45}N_4O_6^+$ 569.3334, Found: 569.3322.

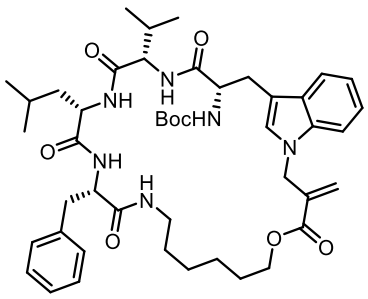
tert-butyl ((3S,6S,9S,Z)-6-isopropyl-9-methyl-20-methylene-4,7,10,19-tetraoxo-1^1*H*-18-oxa-5,8,11-triaza-1(3,1)-indolacyclohenicosaphane-3-yl)carbamate (5c):



5c

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:1), 38.3 mg, 60% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.57 (d, *J* = 6.8 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.23 (d, *J* = 7.8Hz, 1H), 7.17 (d, *J* = 7.5 Hz, 1H), 7.13 (s, 1H), 6.85 (s, 1H), 6.56 (d, *J* = 5.9 Hz, 1H), 6.43 (s, 1H), 5.89 (s, 1H), 5.43 – 5.19 (m, 1H), 4.96 (s, 2H), 4.65 – 4.49 (m, 1H), 4.35 – 4.19 (m, 2H), 4.19 – 4.02 (m, 3H), 3.64 – 3.48 (m, 1H), 3.32 (dd, *J* = 15.3, 4.3 Hz, 1H), 3.12 – 2.94 (m, 2H), 2.48 – 2.26 (m, 1H), 1.77 – 1.49 (m, 4H), 1.41 (s, 15H), 1.26 (s, 1H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 173.1, 172.0, 170.2, 165.6, 156.9, 136.2, 136.1, 129.8, 128.3, 126.9, 122.2, 119.8, 118.2, 109.9, 109.2, 81.6, 77.3, 65.5, 59.8, 58.6, 48.6, 47.8, 39.3, 29.7, 29.1, 29.0, 28.6, 28.1, 27.2, 26.4, 25.8, 19.4, 17.9, 17.0. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{34}H_{50}N_5O_7^+$ 640.3705, Found: 640.3695.

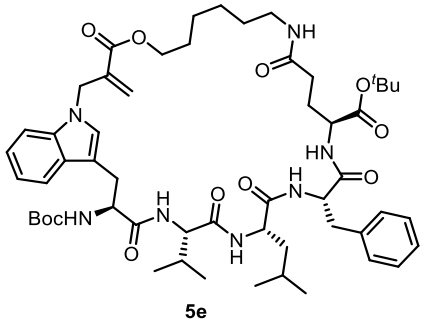
tert-butyl ((3S,6S,9S,12S,Z)-12-benzyl-6-isopropyl-9-methyl-23-methylene-4,7,10,13,22-pentaoxo-1^1*H*-21-oxa-5,8,11,14-tetraaza-1(3,1)-indolacyclotetracosaphane-3-yl)carbamate (5d):



5d

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:1), 50.3 mg, 64% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.5 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.34 – 7.16 (m, 8H), 7.10 (d, *J* = 9.9 Hz, 2H), 7.00 – 6.88 (m, 2H), 6.45 (s, 1H), 6.35 (d, *J* = 3.9 Hz, 1H), 5.97 (s, 1H), 5.18 (s, 1H), 4.90 (s, 2H), 4.78 (t, *J* = 9.0 Hz 1H), 4.26 (s, 1H), 4.23 – 4.10 (m, 3H), 4.00 (s, 1H), 3.86 – 3.70 (m, 1H), 3.61 (d, *J* = 14.1 Hz, 1H), 3.44 (d, *J* = 15.3 Hz, 1H), 3.25 (dd, *J* = 15.3, 5.1 Hz, 1H), 2.97 (t, *J* = 12.9 Hz, 2H), 2.32 – 2.11 (m, 2H), 1.80 – 1.67 (m, 2H), 1.65 – 1.48 (m, 6H), 1.43 (s, 10H), 0.90 – 0.76 (m, 12H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 173.8, 172.0, 172.0, 171.1, 165.4, 156.7, 138.5, 136.0, 135.7, 130.6, 129.4, 128.8, 128.2, 127.7, 126.3, 122.4, 120.3, 117.7, 110.1, 107.1, 81.6, 66.0, 60.8, 58.0, 54.1, 53.5, 47.5, 39.4, 37.5, 29.4, 28.9, 28.6, 28.0, 26.7, 26.5, 25.5, 24.6, 23.1, 20.6, 19.5, 17.1. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{46}H_{65}N_6O_8^+$ 829.4858, Found: 829.4846

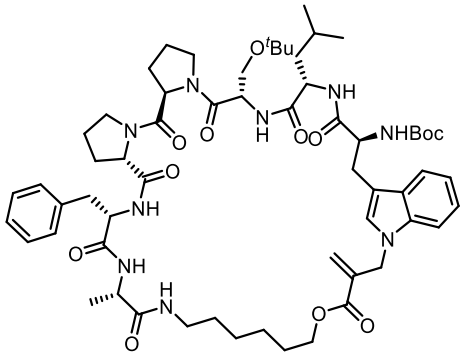
tert-butyl (3S,6S,9S,12S,15S,Z)-12-benzyl-3-((tert-butoxycarbonyl)amino)-9-isobutyl-6-isopropyl-28-methylene-4,7,10,13,18,27-hexaoxo-1^1*H*-26-oxa-5,8,11,14,19-pentaaza-1(3,1)-indolacyclononacosaphane-15-carboxylate (5e):



5e

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:1), 49.6 mg, 49% yield. **^{1}H NMR** (300 MHz, DMSO-d_6) δ 7.80 (d, *J* = 7.8 Hz, 1H), 7.67 (d, *J* = 6.6 Hz, 2H), 7.55 (d, *J* = 7.2 Hz, 1H), 7.44 (s, 1H), 7.31 (d, *J* = 7.5Hz, 1H), 7.14 (d, *J* = 8.1 Hz, 1H), 6.98 (s, 5H), 6.88 (d, *J* = 6.9 Hz, 1H), 6.83 (d, *J* = 5.7 Hz, 1H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.50 (d, *J* = 7.5 Hz, 1H), 5.93 (s, 1H), 5.25 (s, 1H), 4.72 (s, 2H), 4.31 – 4.16 (m, 1H), 4.13 – 4.02 (m, 1H), 3.97 (d, *J* = 7.1 Hz, 1H), 3.93 – 3.78 (m, 5H), 2.92 – 2.62 (m, 7H), 2.00 – 1.82 (m, 3H), 1.81 – 1.65 (m, 3H), 1.66 – 1.46 (m, 2H), 1.16 (s, 15H), 1.11 (s, 9H), 0.58 – 0.49 (m, 12H). **^{13}C NMR** (75 MHz, DMSO-d_6) δ 172.1, 171.6, 171.0, 170.8, 170.7, 165.1, 155.2, 137.7, 136.6, 135.8, 129.0, 128.0, 127.2, 126.2, 118.8, 118.5, 109.9, 80.6, 78.3, 64.4, 51.3, 31.5, 29.0, 28.0, 27.6, 27.2, 25.9, 25.1, 24.0, 22.8, 21.4, 19.0, 17.8. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{55}H_{80}N_7O_{11}^+$ 1014.5910, Found: 1014.5926.

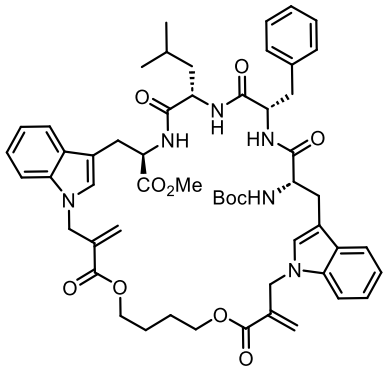
tert-butyl ((1^{2}S,3^{2}R,5S,8S,11S,26S,29S,Z)-29-benzyl-5-(tert-butoxymethyl)-8-isobutyl-26-methyl-15-methylene-2,4,7,10,16,25,28,31-octaoxo-13^1*H*-17-oxa-6,9,24,27,30-pentaaza-13(3,1)-indola-1(1,2),3(2,1)-dipyrrolidinacyclohentriacontaphane-11-yl)carbamate (5f):



5f

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 1:2), 69.3 mg, 61% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.58 (d, *J* = 8.1 Hz, 1H), 7.88 (d, *J* = 8.7 Hz, 1H), 7.79 (s, 1H), 7.55 (d, *J* = 7.5 Hz, 1H), 7.44 – 7.30 (m, 3H), 7.27 – 7.20 (m, 4H), 7.19 – 7.04 (m, 4H), 7.02 (s, 1H), 6.43 (s, 1H), 5.96 (s, 1H), 5.08 (s, 1H), 4.91 (s, 4H), 4.69 – 4.61 (m, 1H), 4.58 – 4.50 (m, 2H), 4.45 (s, 1H), 4.19 – 4.09 (m, 2H), 3.87 – 3.75 (m, 3H), 3.69 – 3.60 (m, 1H), 3.59 – 3.52 (m, 1H), 3.39 – 3.27 (m, 4H), 3.16 – 3.05 (m, 3H), 2.28 – 2.19 (m, 1H), 2.15 – 2.06 (m, 1H), 2.06 – 1.86 (m, 4H), 1.85 – 1.71 (m, 2H), 1.69 – 1.55 (m, 5H), 1.54 – 1.50 (m, 2H), 1.49 – 1.45 (m, 3H), 1.37 (s, 10H), 1.16 (s, 12H), 0.93(s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.7, 172.3, 171.4, 171.2, 171.0, 170.7, 169.4, 165.7, 155.6, 137.9, 136.3, 136.2, 129.8, 129.5, 128.6, 128.2, 127.0, 126.5, 121.9, 119.4, 118.8, 109.8, 109.4, 80.3, 73.3, 65.1, 61.8, 60.3, 58.0, 54.7, 51.9, 51.1, 48.6, 47.9, 47.5, 46.8, 43.2, 39.6, 37.2, 29.7, 29.3, 29.2, 28.4, 28.3, 28.1, 27.7, 27.5, 27.4, 26.6, 25.8, 25.4, 24.8, 23.0, 22.8, 19.9. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{61}H_{88}N_9O_{12}^+$: 1138.6547, Found: 1138.6567.

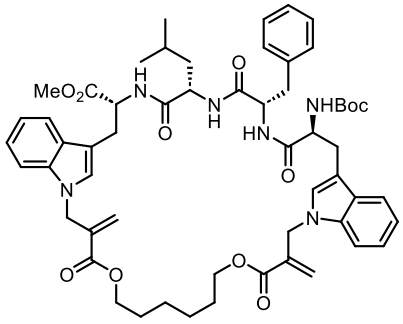
methyl (1^{2}Z,14^{2}Z,3R,6S,9S,12S)-9-benzyl-12-((tert-butoxycarbonyl)amino)-6-isobutyl-16,25-dimethylene-5,8,11,17,24-pentaoxo-1^1*H*,14^1*H*-18,23-dioxa-4,7,10-triaza-1,14(3,1)-diindolacyclohexacosaphane-3-carboxylate (5g):



5g

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 36 mg, 36% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.2 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 1H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.18 – 7.05 (m, 7H), 7.05 – 6.94 (m, 2H), 6.93 (s, 3H), 6.65 (d, *J* = 6.6 Hz, 1H), 6.37 (s, 2H), 5.98 (s, 1H), 5.61 (s, 1H), 4.97 (s, 1H), 4.95 – 4.85 (m, 4H), 4.81 (dd, *J* = 12.0, 6.0 Hz, 1H), 4.66 – 4.42 (m, 2H), 4.26 – 3.95 (m, 5H), 3.71 (s, 3H), 3.47 – 3.32 (m, 2H), 3.28 – 3.11 (m, 2H), 3.01 (dd, *J* = 15.0, 7.8 Hz, 1H), 2.78 (dd, *J* = 13.2, 5.4 Hz, 1H), 1.69 (s, 1H), 1.64 – 1.50 (m, 3H), 1.47 – 1.34 (m, 3H), 1.26 (s, 9H), 0.85 (dd, *J* = 13.8, 6.0 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.2, 172.0, 171.9, 170.3, 165.43, 165.35, 156.1, 136.6,136.3, 136.2, 136.0, 135.7, 129.1, 128.8, 128.4, 128.2, 127.73, 127.65, 127.3, 126.9, 125.9, 122.4, 121.8, 119.8, 119.3, 118.9, 118.8, 109.9, 109.8, 109.5, 109.1, 80.8, 76.6, 64.6, 64.4, 56.0, 54.2, 53.1, 52.4, 51.9, 47.2, 46.5, 40.1, 36.6, 28.1,27.7, 26.9, 25.1, 25.0, 24.4, 23.0, 21.4. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{55}H_{67}N_6O_{11}^+$ 987.4862, Found: 987.4870.

methyl (1^{2}Z,14^{2}Z,3R,6S,9S,12S)-9-benzyl-12-((tert-butoxycarbonyl)amino)-6-isobutyl-16,27-dimethylene-5,8,11,17,26-pentaoxo-1^1*H*,14^1*H*-18,25-dioxa-4,7,10-triaza-1,14(3,1)-diindolacyclooctacosaphane-3-carboxylate (5h):

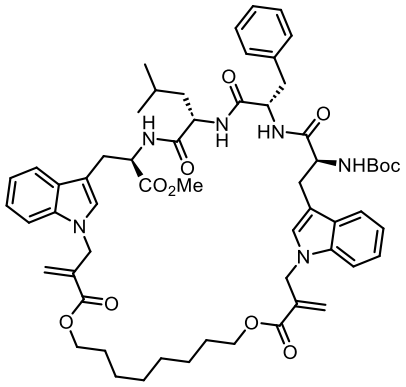


5h

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 33 mg, 33% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 15.0, 7.5 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.24 (d, *J* = 8.1 Hz, 1H), 7.15 (s, 5H), 7.12 – 6.97 (m, 4H), 6.91 – 6.78 (m, 3H), 6.59 (d, *J* = 8.0 Hz, 1H), 6.32 (s, 2H), 6.15 (s, 1H), 5.47 (s, 1H), 5.01 (s, 1H), 4.92 (d, *J* = 10.2 Hz, 4H), 4.81 (dd, *J* = 12.0, 6.3 Hz, 1H), 4.61 – 4.38 (m, 2H), 4.25 – 4.06 (m, 5H), 3.69 (s, 3H), 3.46 – 3.27 (m, 2H), 3.27 – 3.14 (m, 1H), 3.14 – 2.91 (m, 2H), 2.59 (dd, *J* = 14.0, 6.1 Hz, 1H), 1.75 – 1.66(m, 1H), 1.59 – 1.50 (m, 3H), 1.37 (d, *J* = 11.4 Hz, 2H), 1.26 (s, 14H), 0.84 (dd, *J* = 12.6, 6.0 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.1, 172.0, 171.7, 170.4, 165.6, 165.5, 136.5,136.4, 136.1, 135.7, 129.1, 128.8, 128.2, 127.9,127.7, 127.5, 127.3, 126.9, 125.9, 122.4, 121.8, 119.8, 119.3, 118.9, 109.8, 109.5, 109.1, 80.8, 77.3, 64.9, 64.6, 55.9, 54.0, 53.1, 52.3, 51,7, 47.1, 46.5,

40.0, 36.4, 29.7, 28.3, 28.1, 27.5, 27.2, 25.3, 24.4, 23.0, 21.4. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{57}H_{71}N_6O_{11}^+$: 1015.5175, Found: 1015.5185.

methyl (1^{2}Z,14^{2}Z,3R,6S,9S,12S)-9-benzyl-12-((tert-butoxycarbonyl)amino)-6-isobutyl-16,29-dimethylene-5,8,11,17,28-pentaoxo-1^{1}H,14^{1}H-18,27-dioxa-4,7,10-triaza-1,14(3,1)-diindolacyclotriacontaphane-3-carboxylate (5i):

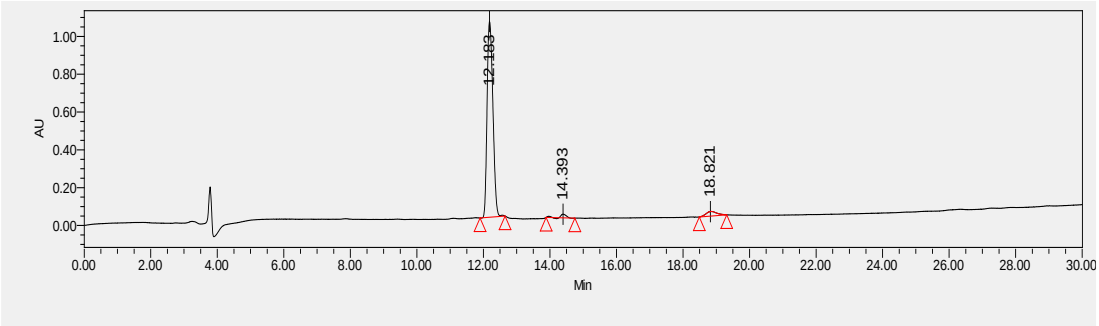


5i

White solid was obtained by silica gel column chromatography (eluent: PE / EA = 2:1), 40 mg, 38% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 13.2, 5.4 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 1H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.17 (s, 5H), 7.13 – 6.98 (m, 4H), 6.90 (s, 3H), 6.64 (d, *J* = 6.9 Hz, 1H), 6.37 (d, *J* = 4.8 Hz, 1H), 6.30 (s, 1H), 6.15 (s, 1H), 5.40 (s, 1H), 5.03 (s, 1H), 4.93 (d, *J* = 8.4 Hz, 4H), 4.81 (dd, *J* =12.0, 6.9Hz, 1H), 4.61 – 4.41 (m, 2H), 4.17 (m, 5H), 3.69 (s, 3H), 3.45 – 3.26 (m, 2H), 3.26 – 3.00 (m, 3H), 2.63 (dd, *J* = 14.1, 6.0 Hz, 1H), 1.76 – 1.51 (m, 6H), 1.41 – 1.30 (m, 4H), 1.24 (d, *J* = 7.2 Hz, 14H), 0.85 (dd, *J* = 15.3, 6.0 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.2, 172.1, 171.6, 165.7, 165.5, 156.1, 136.5, 136.4, 136.1, 135.8, 129.1, 128.8, 128.2, 127.9, 127.4,127.3, 127.0, 126.0, 122.4, 121.8, 119.8, 118.9, 109.8, 109.5, 109.1, 80.8, 77.3, 65.0, 64.9, 56.1, 54.1, 53.0, 52.3, 51.7, 47.1, 46.6, 40.0, 36.4, 28.6, 28.3, 28.2, 28.1, 27.7, 27.5, 27.3, 25.8, 25.61, 25.55, 24.4, 23.0, 21.4. **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{59}H_{75}N_6O_{11}^+$ 1043.5488, Found: 1043.5492.

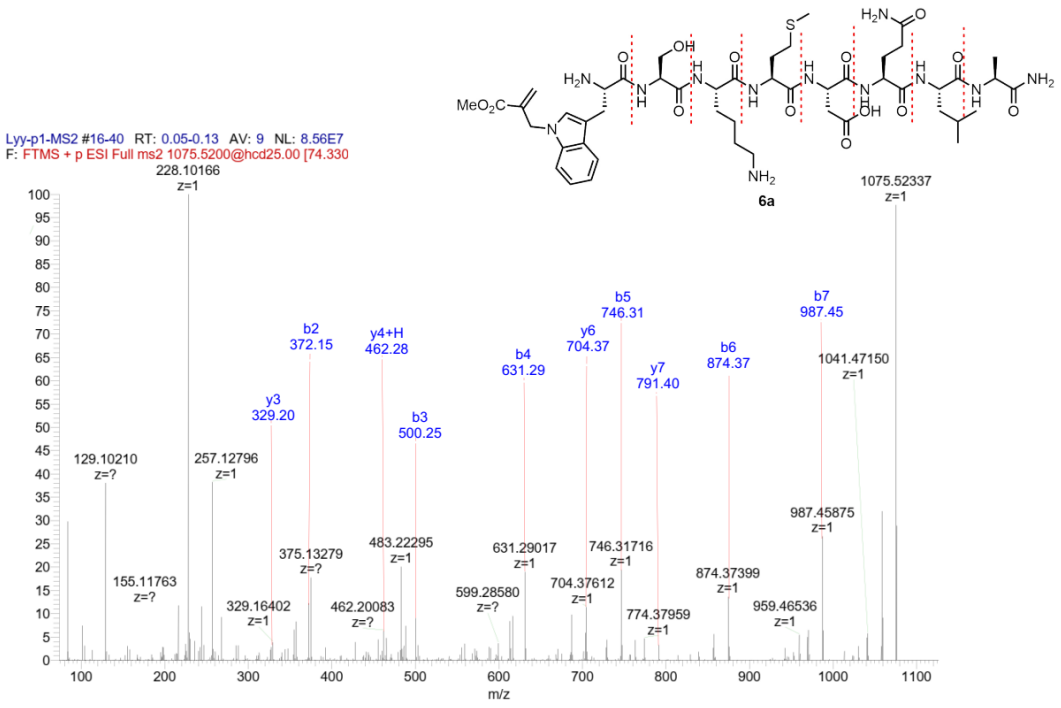
2.7 HPLC Spectra and MS/MS Spectra for the products of solid support allylation.

6a: White solid, 15.3 mg, 7% yield, 92.6% purity, **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{48}H_{75}O_{14}N_{12}S$ 1075.5241, Found 1075.5227.



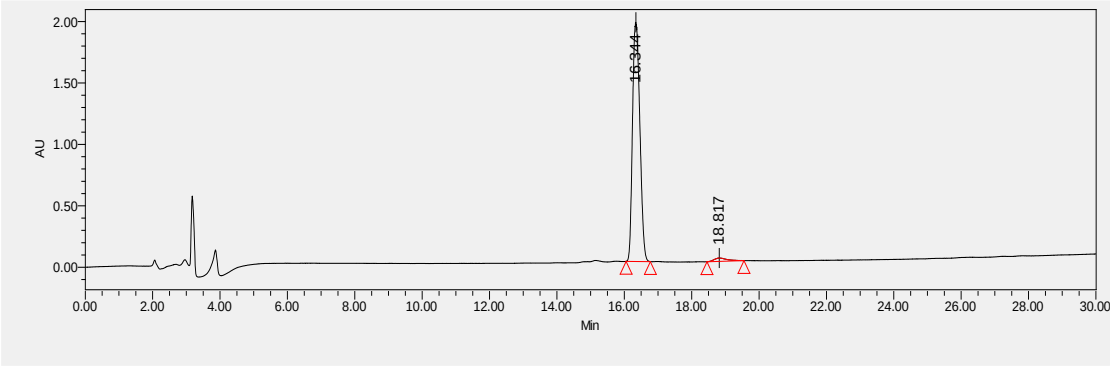
	Retention time (Min)	Area	% Area	Height	Type
1	12.183	12560188	92.58	1035433	bb
2	14.393	386093	2.85	21983	bb
3	18.846	621113	4.58	25229	bb

HPLC spectrum of **6a**



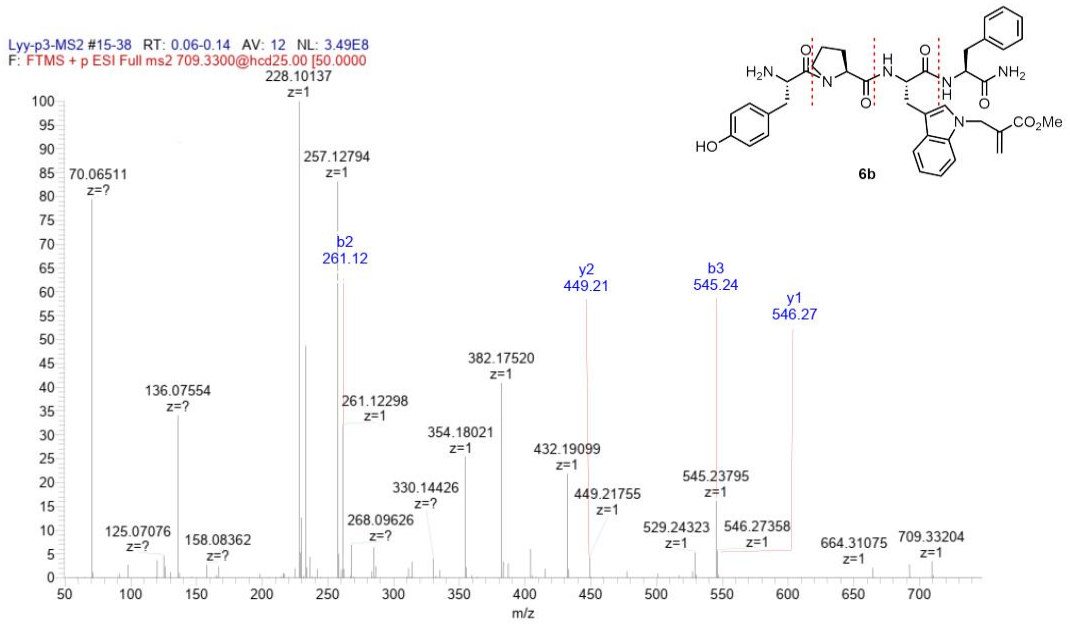
MS/MS spectrum of **6a**

6b: White solid, 58.8 mg, 42% yield, 97.6% purity, **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{39}H_{45}O_7N_6$ 709.3344, Found 709.3341.



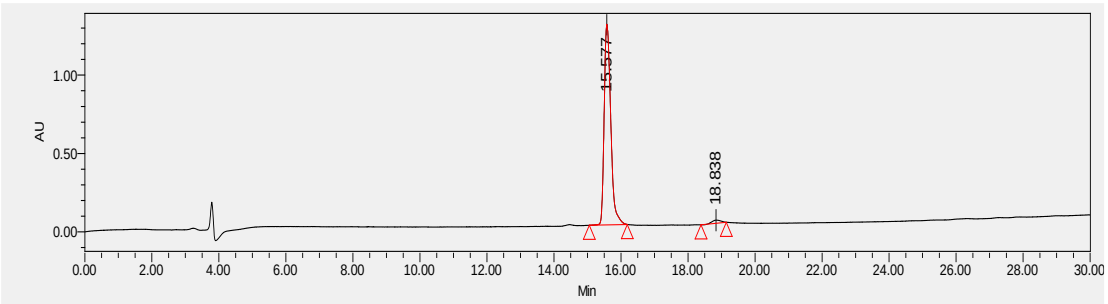
	Retention time (Min)	Area	% Area	Height	Type
1	16.344	29387224	97.64	1941059	bb
2	18.817	709131	2.36	27177	bb

HPLC spectrum of **6b**



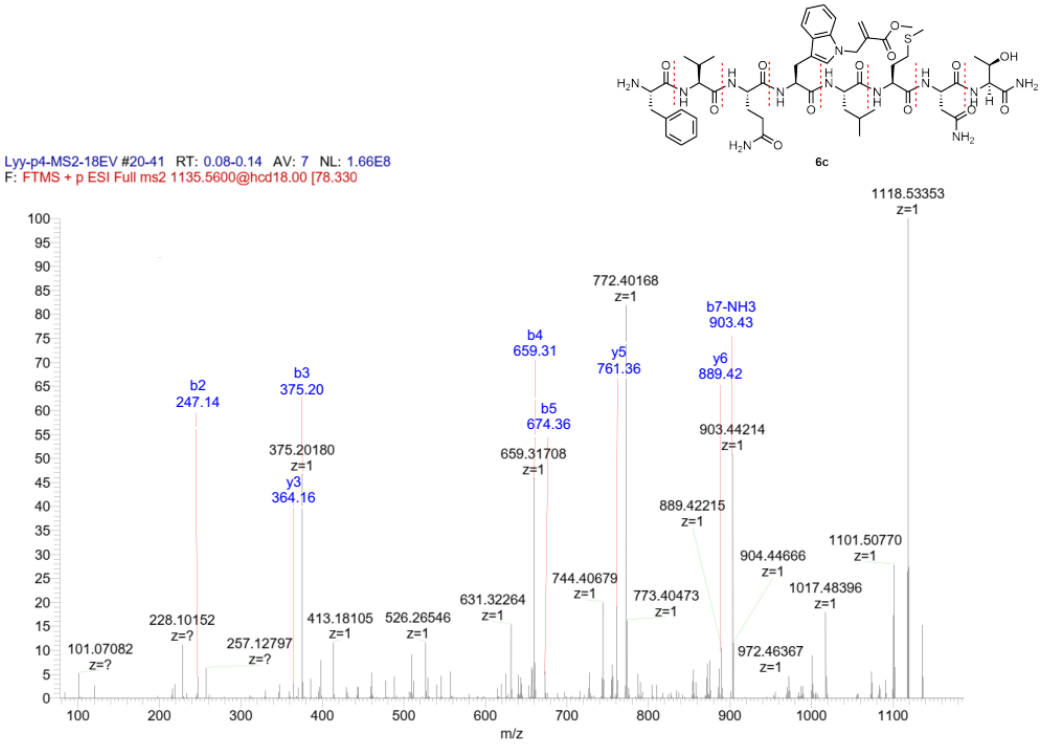
MS/MS spectrum of **6b**

6c: White solid, 48.1 mg, 18% yield, 97.9% purity, **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{54}H_{79}O_{13}N_{12}S$ 1135.5605, Found 1135.56



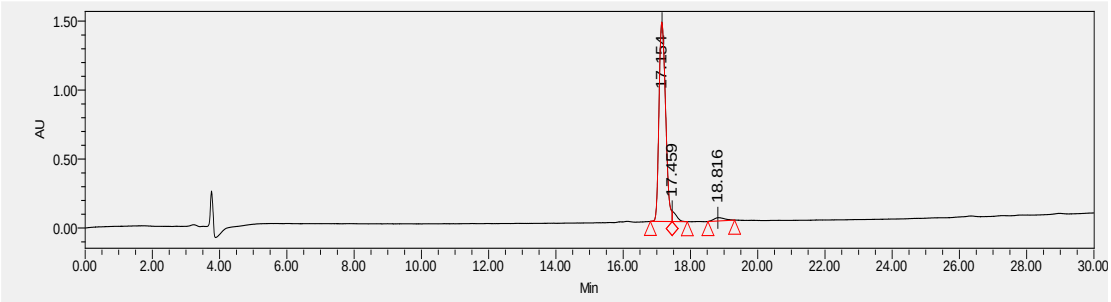
	Retention time (Min)	Area	% Area	Height	Type
1	15.577	17447150	97.88	1279208	bb
2	18.838	378106	2.12	20062	bb

HPLC spectrum of **6c**



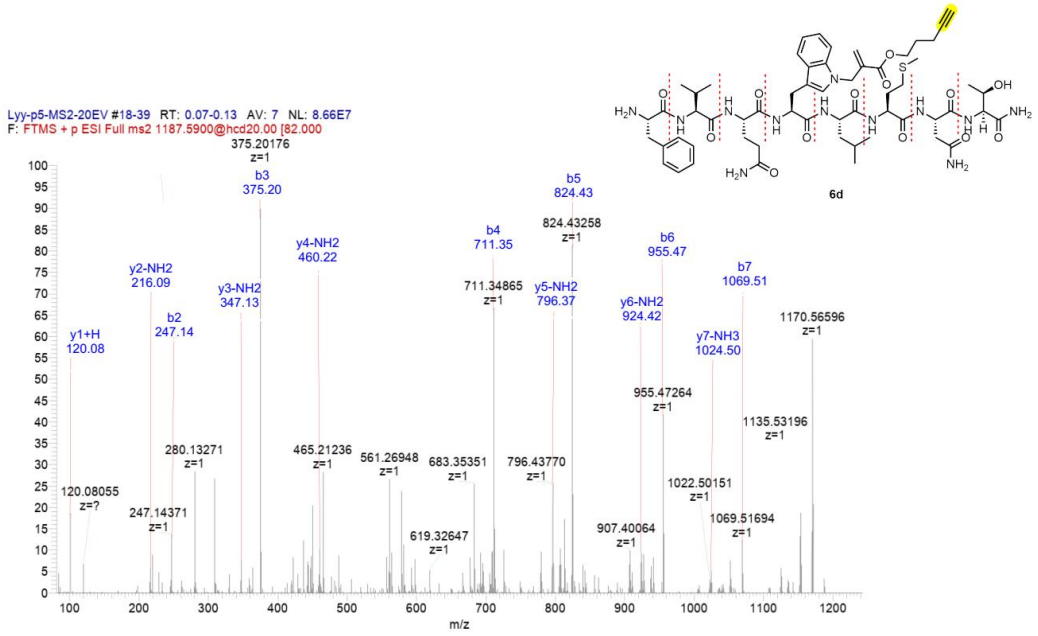
MS/MS spectrum of **6c**

6d: White solid, 35.6 mg, 15% yield, 94.3% purity, **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{58}H_{83}O_{13}N_{12}S$ 1187.5918, Found 1187.5928.



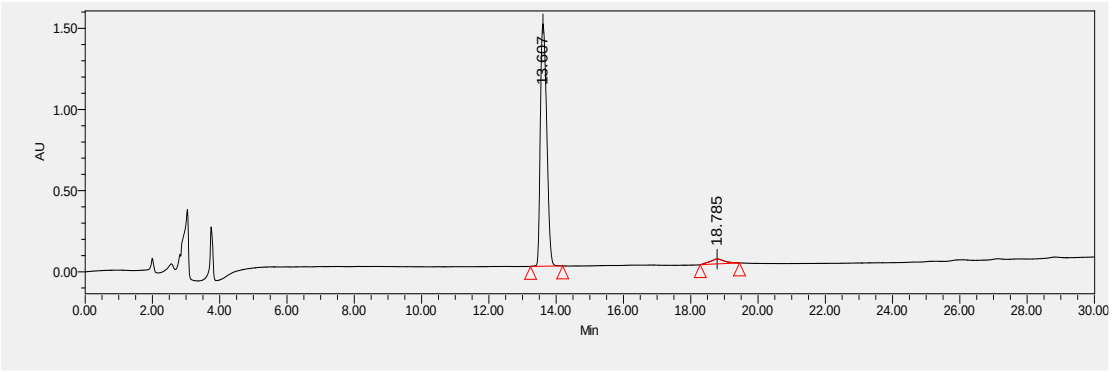
	Retention time (Min)	Area	% Area	Height	Type
1	17.154	19742042	94.34	1444256	bv
2	17.459	650407	3.11	74796	vb
3	18.816	534407	2.55	23812	bb

HPLC spectrum of **6d**



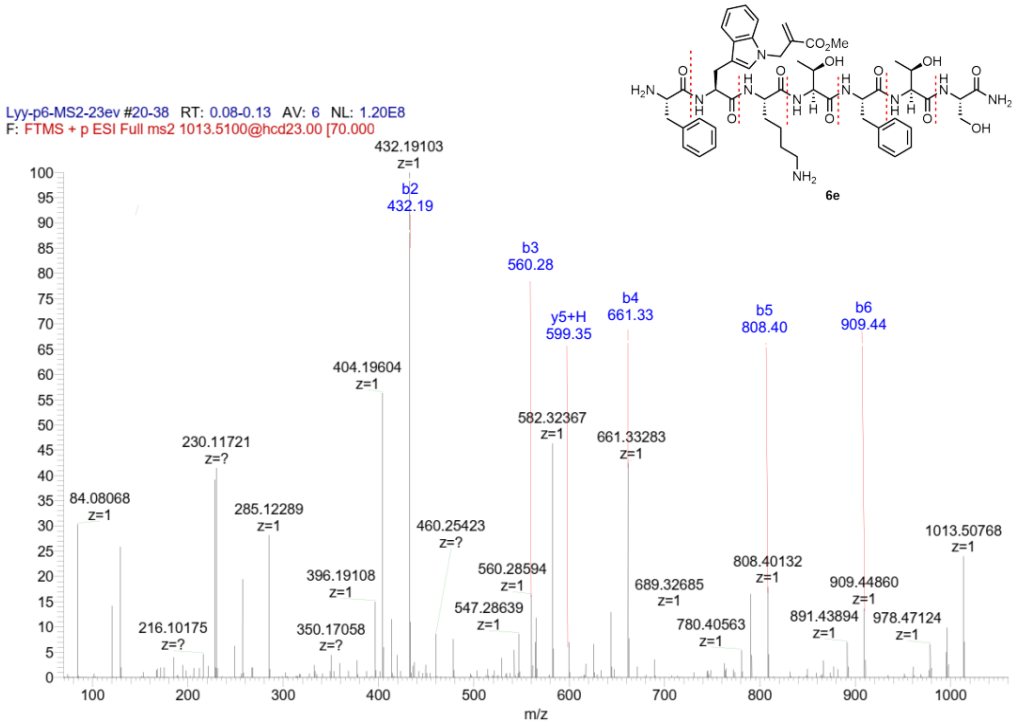
MS/MS spectrum of **6d**

6e: White solid, 68.2 mg, 34% yield, 95.6% purity, **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{51}H_{69}O_{12}N_{10}$ 1013.5091, Found 1013.5081.



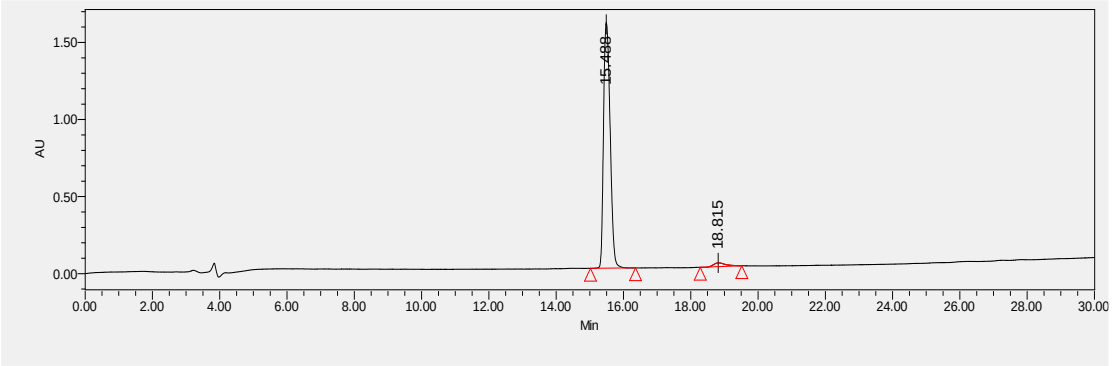
	Retention time (Min)	Area	% Area	Height	Type
1	13.607	19620749	95.57	1491257	bb
2	18.785	909178	4.43	29847	bb

HPLC spectrum of **6e**



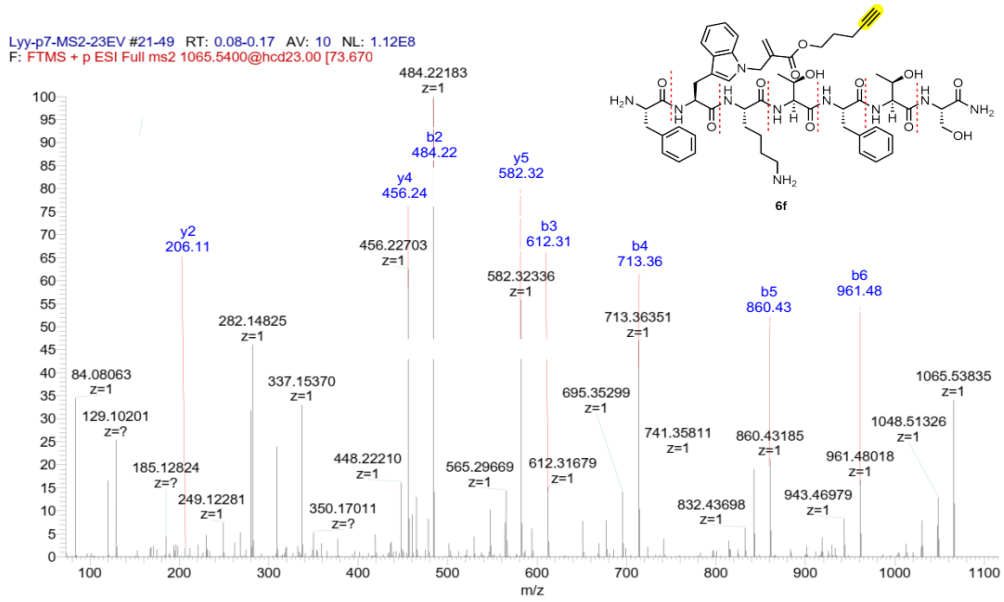
MS/MS spectrum of **6e**

6f: White solid, 66.0 mg, 30% yield, 97.2% purity, **HRMS**(ESI) m/z $[M+H]^+$: Calcd for $C_{55}H_{73}O_{12}N_{12}$ 1065.5404, Found 1065.5392.



	Retention time (Min)	Area	% Area	Height	Type
1	15.488	21688620	97.15	1587898	bb
2	18.815	635836	2.85	24902	bb

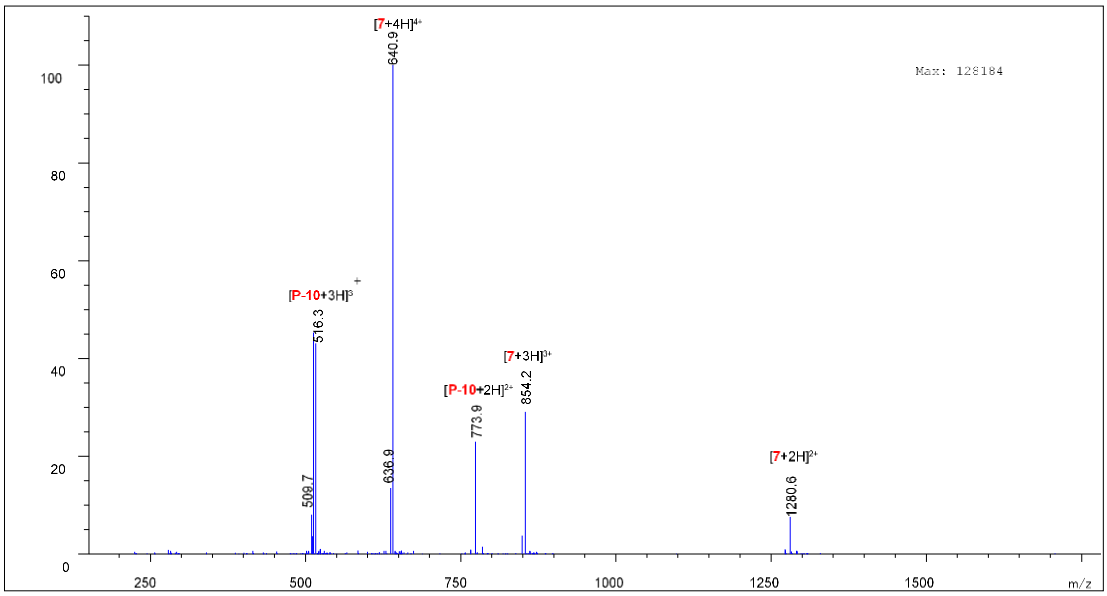
HPLC spectrum of **6f**



MS/MS spectrum of **6f**

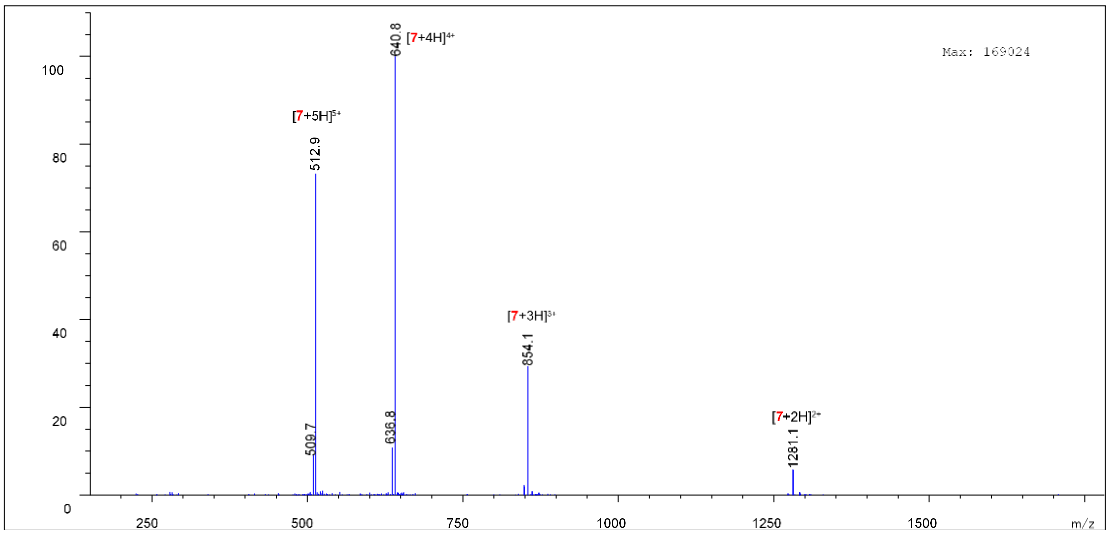
2.8 LC-MS Spectra of peptide-peptide conjugate.

*MSD1 SPC, time=4.738 of lyyome-0h. ES-API, Pos, Scan, Frag: 70

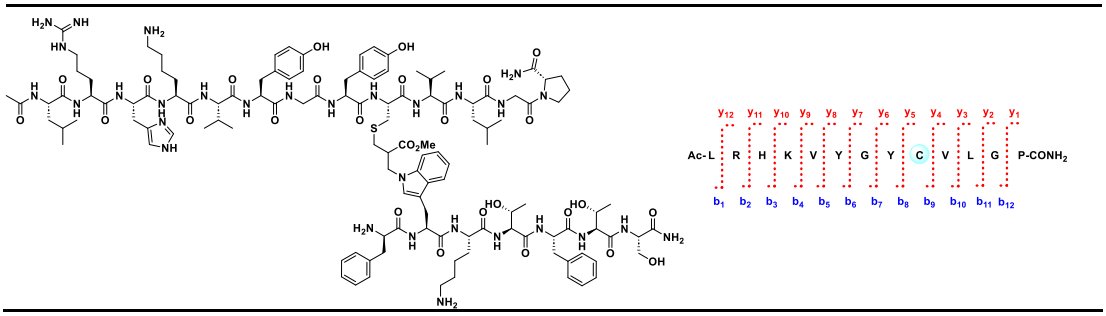


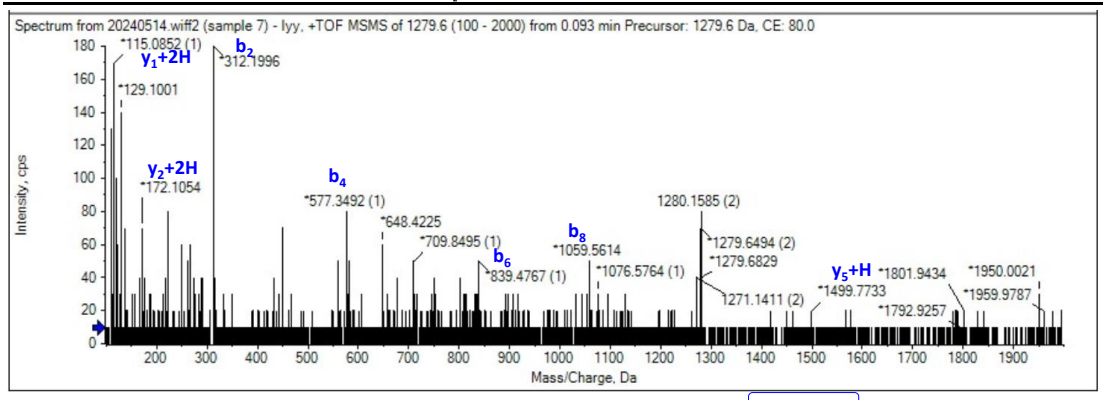
LC-MS trace of 0 h

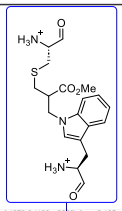
*MSD1 SPC, time=4.737 of lyyome-1h. ES-API, Pos, Scan, Frag: 70

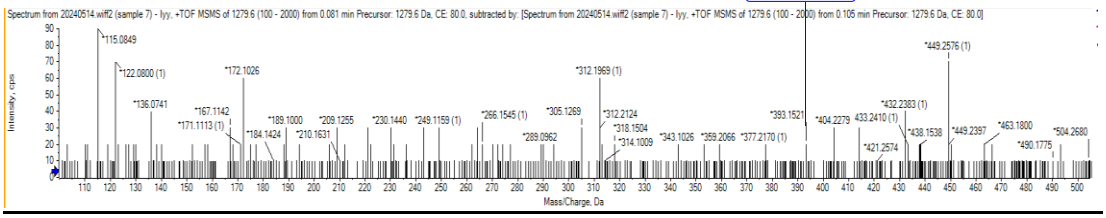


LC-MS trace of 1 h









MS/MS spectrum of **7**

3. References

(1) a) K-J. Xiao, D. W. Lin, M. Miura, R-Y. Zhu, W. Gong, Masayuki Wasa, and J-Q. Yu. *J. Am. Chem. Soc*. **2014**, *136*, 8138 – 8142; b) Y. Wang, Y-H. Xing, X. Liu, H. Ji, M. Kai, Z-Y Chen, J. Yu, D-P. Zhao, H. Ren, R. Wang. *J. Med. Chem*. **2012**, *55*, 6224 – 6236; c) Y. Liu, Z. He, W. Ma, G. Bao, Y. Li, C. Yu, J. Li, R. E, Z. Xu, R. Wang, W. Sun. *Org. Lett*. **2022**, *24*, 9248–9253. d) M. Wang, C. Wang, Y. Huo, H. Xue, L. Liu, H. Chai, X. Xie, Z. Li, D. Lu, Z. Xu. *Nat Commun*., **2021**, *12*, 6873. e) S. J. McCarver, J. X. Qiao, J. Carpenter, R. Borzilleri, M. A. Poss, M. D. Eastgate, M. M. Miller, D. W. C. MacMillan. *Angew. Chem. Int. Ed*. **2017**, 56,7 28 –732.

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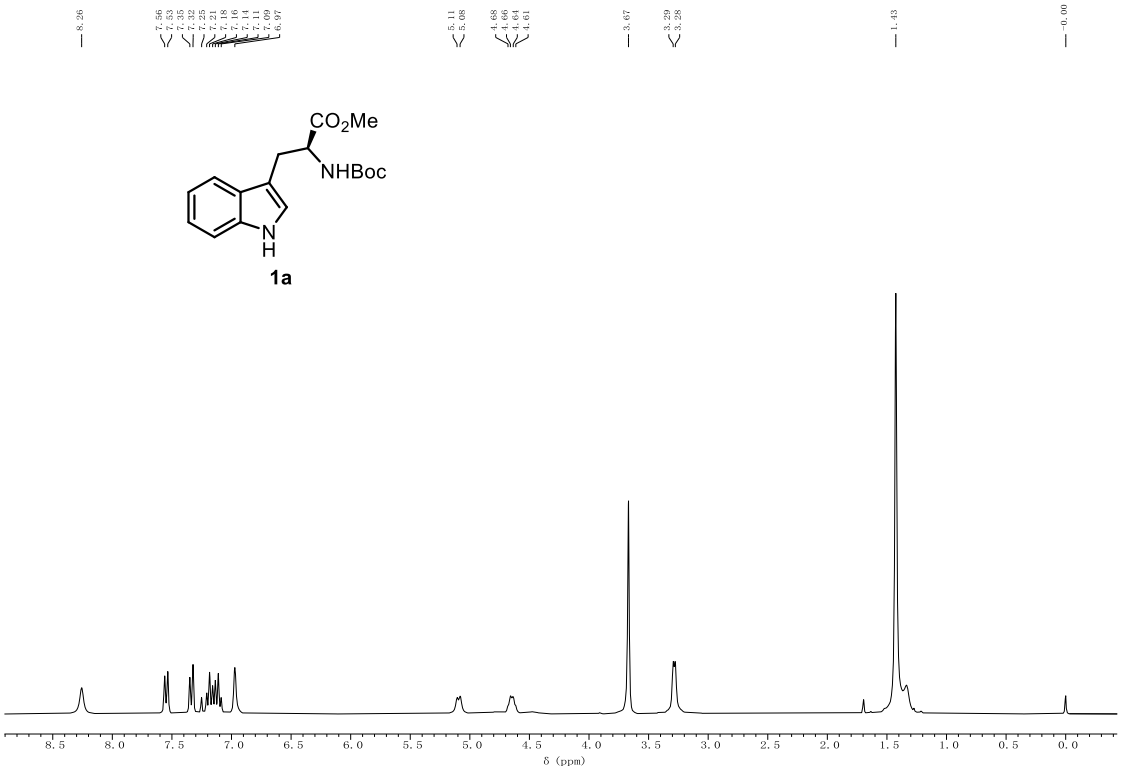
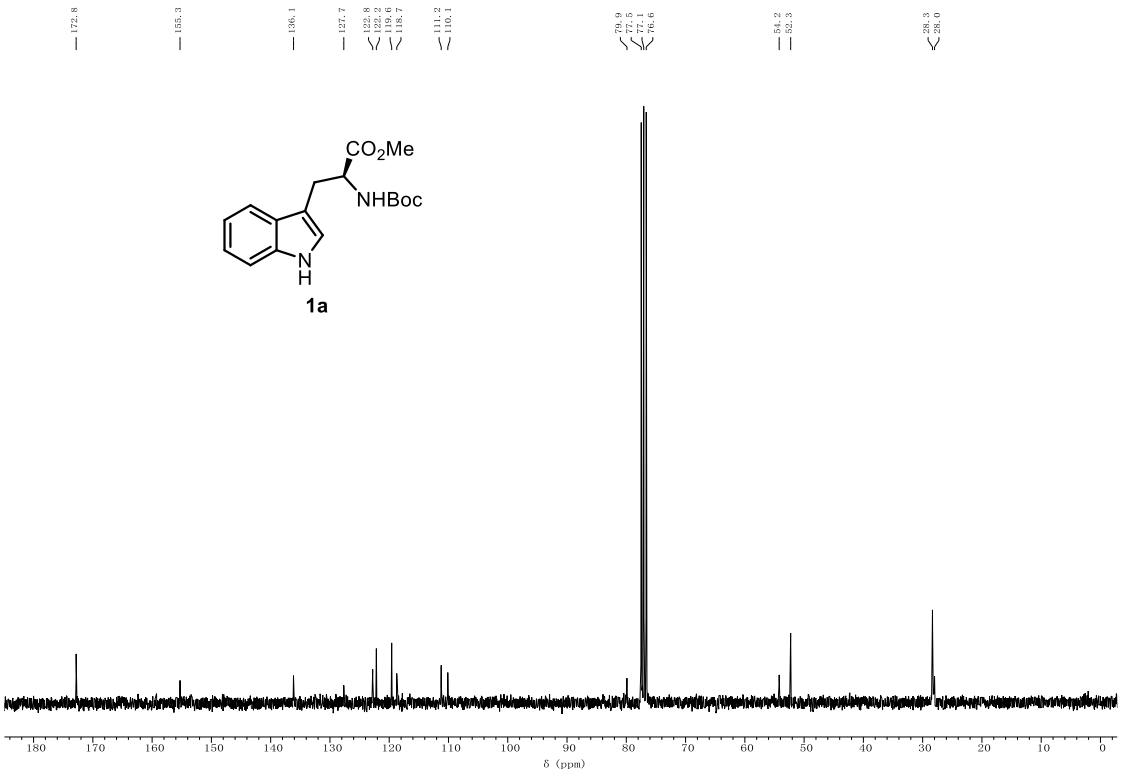
(3) H.-l. Cui, X. Feng, J. Peng, J. Lei, K. Jiang, Y.-C. Chen. Angew. Chem. Int. Ed. 2009, 48, 5737 –5740.

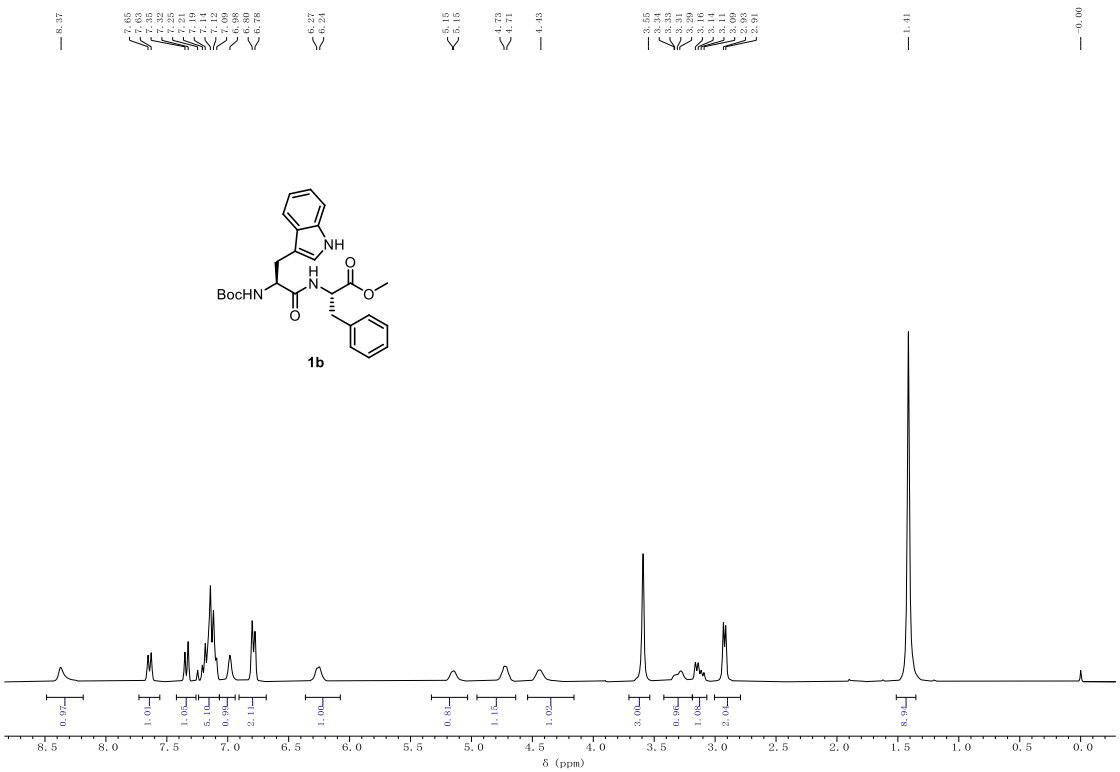
4. NMR spectra



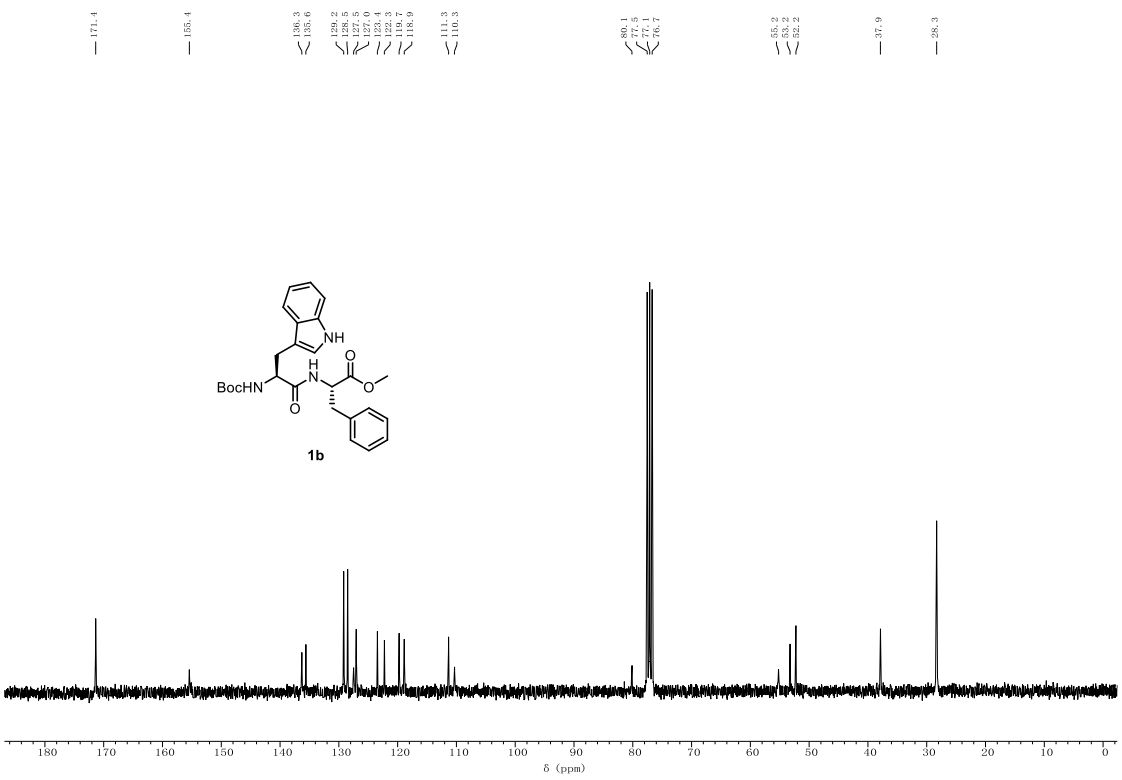
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **1a**



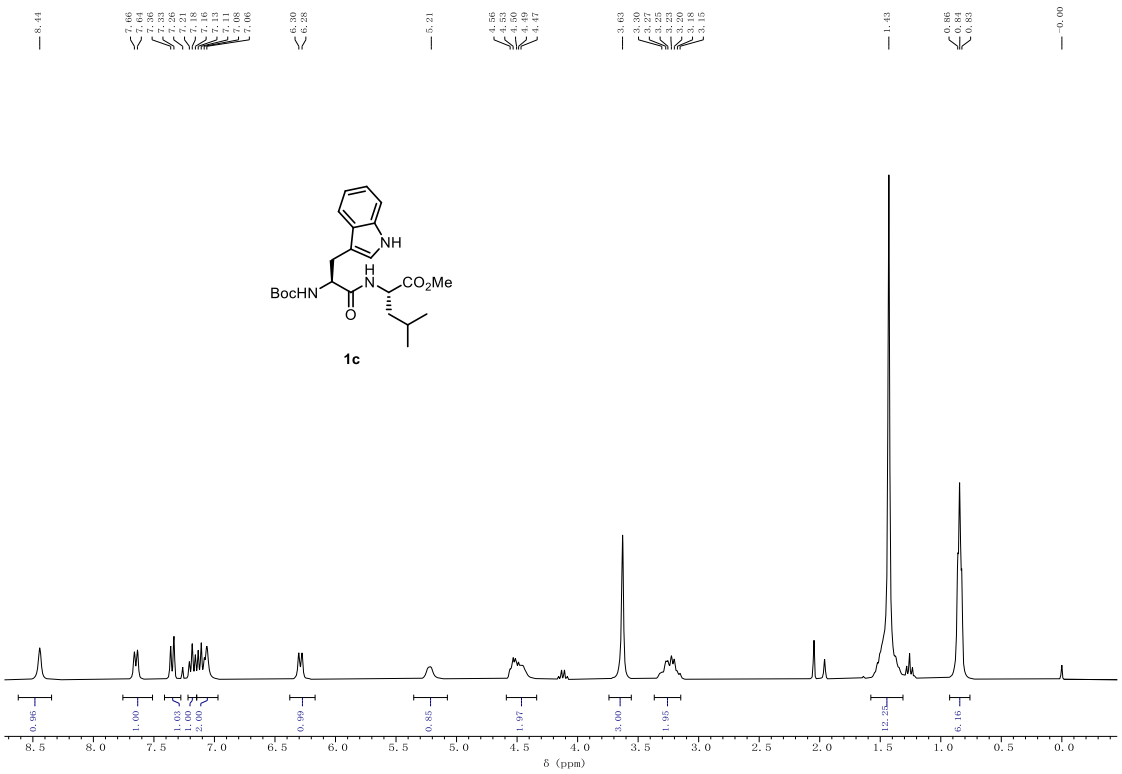
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **1a**



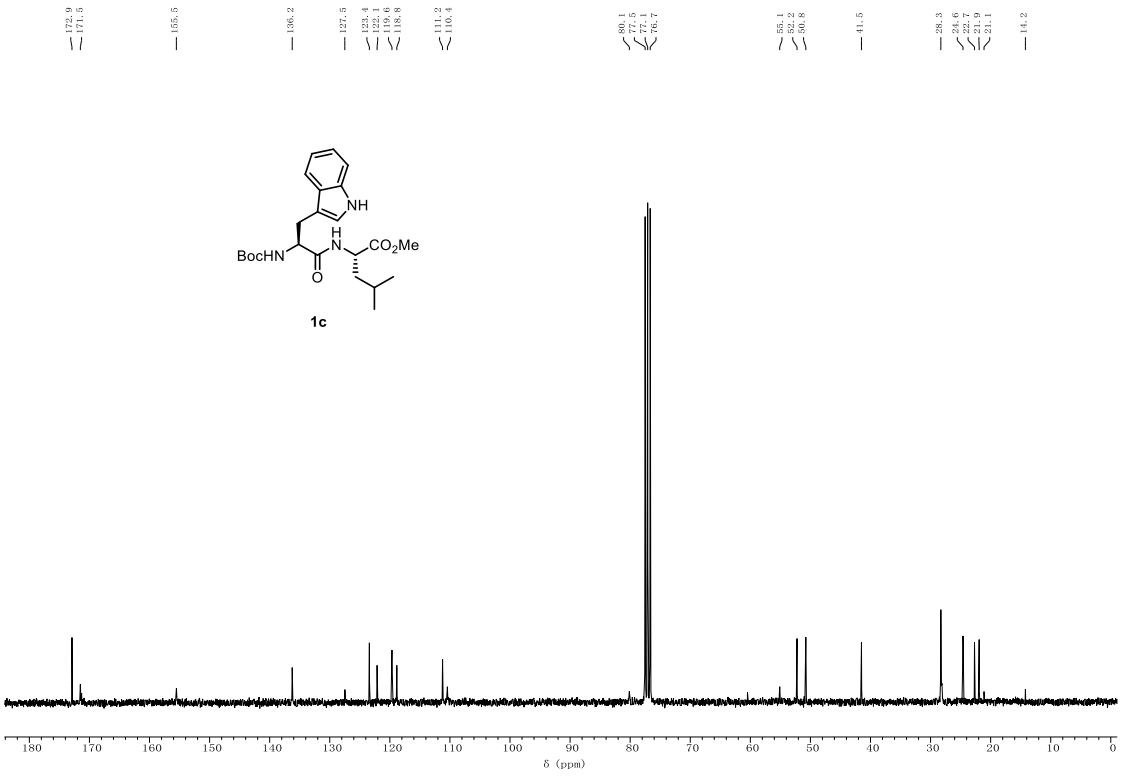
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **1b**



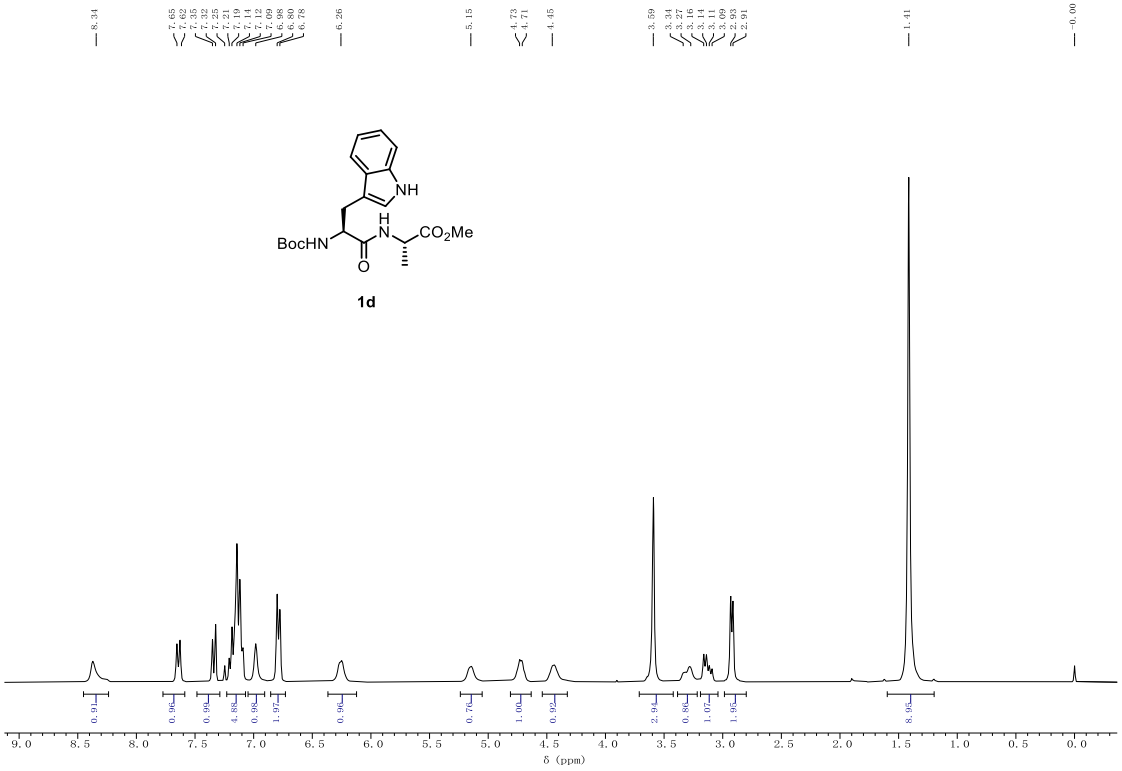
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **1b**



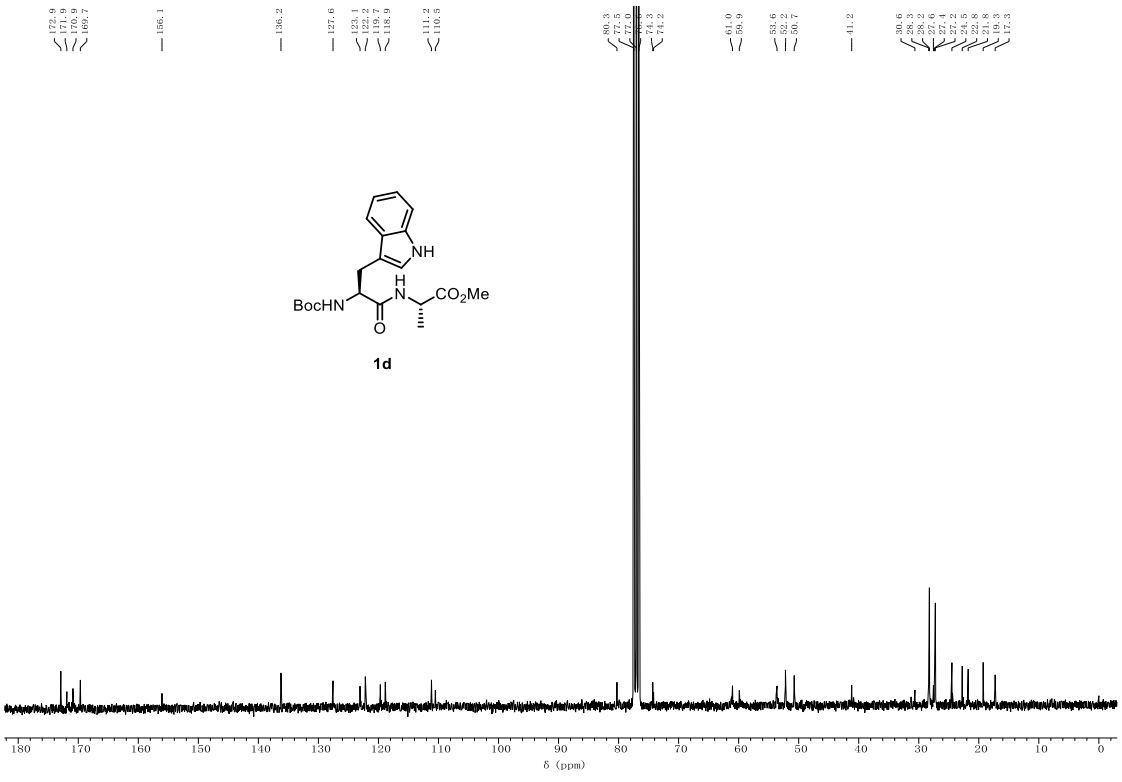
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **1c**



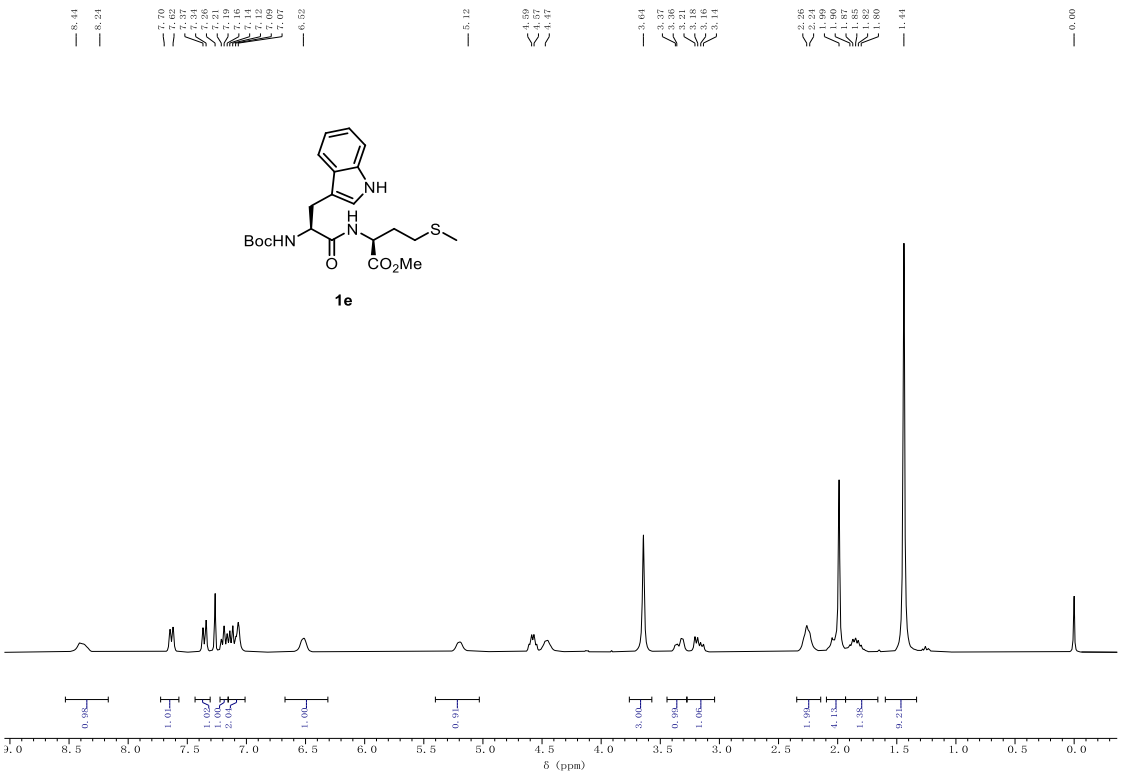
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **1c**



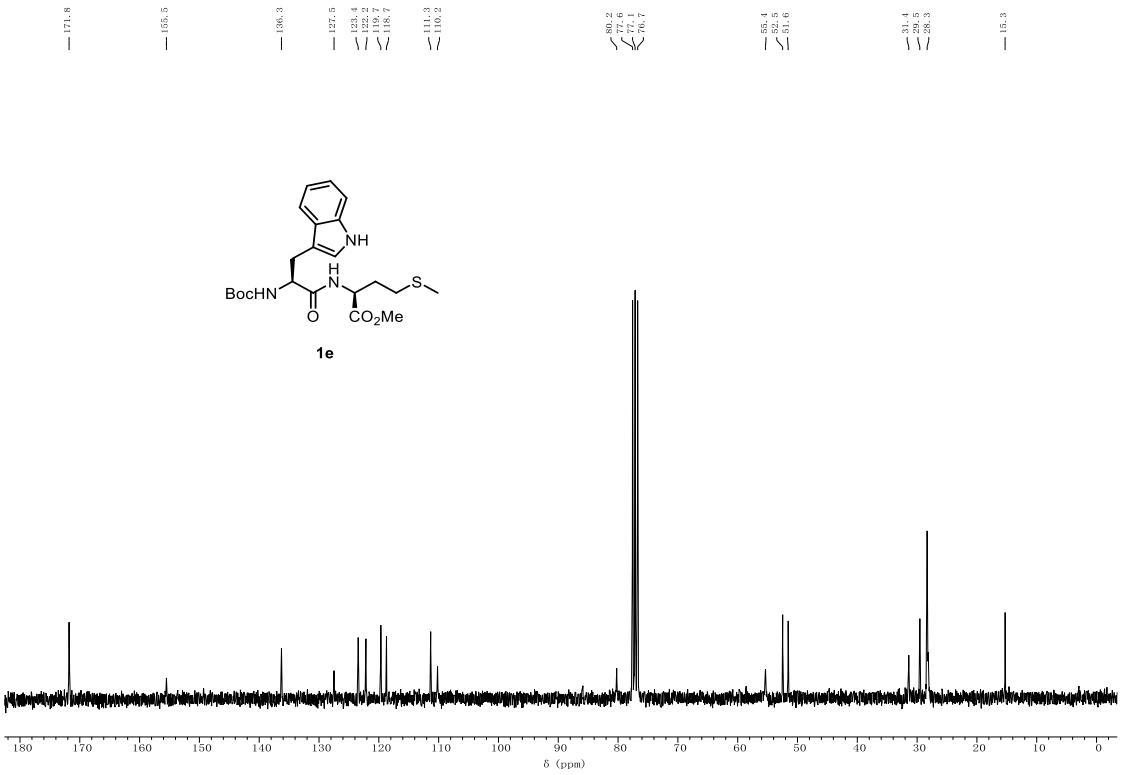
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **1d**



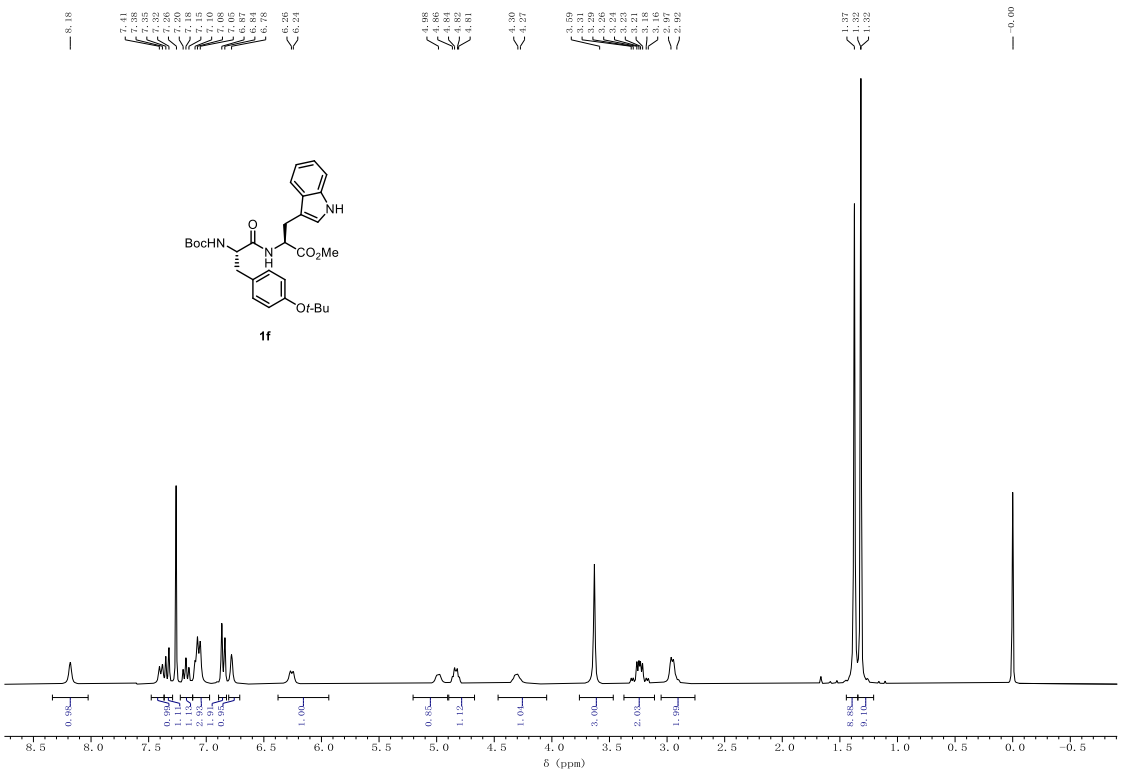
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **1d**



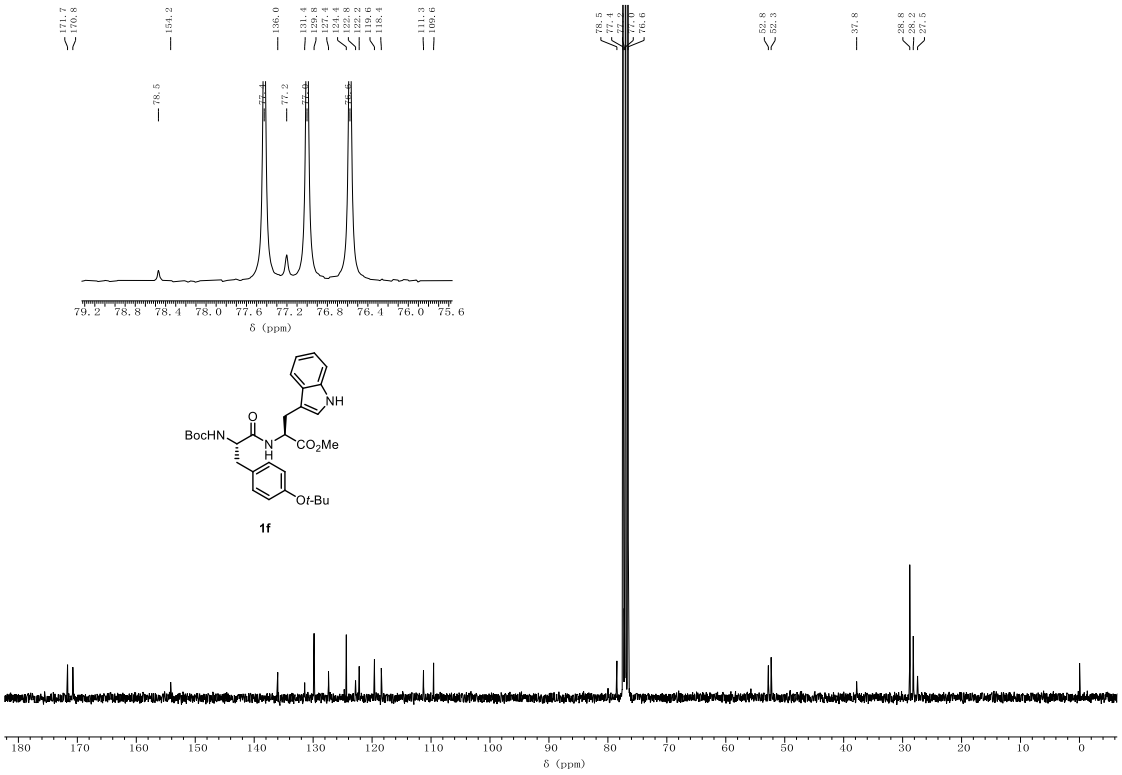
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **1e**



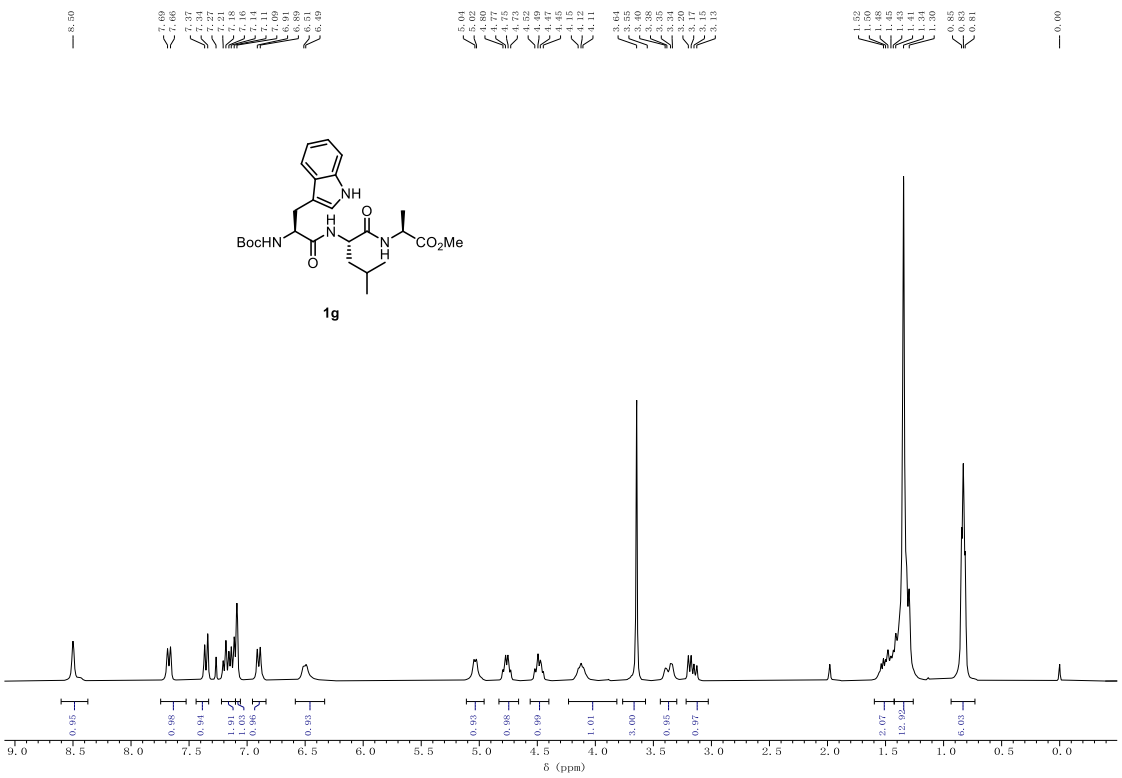
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **1e**



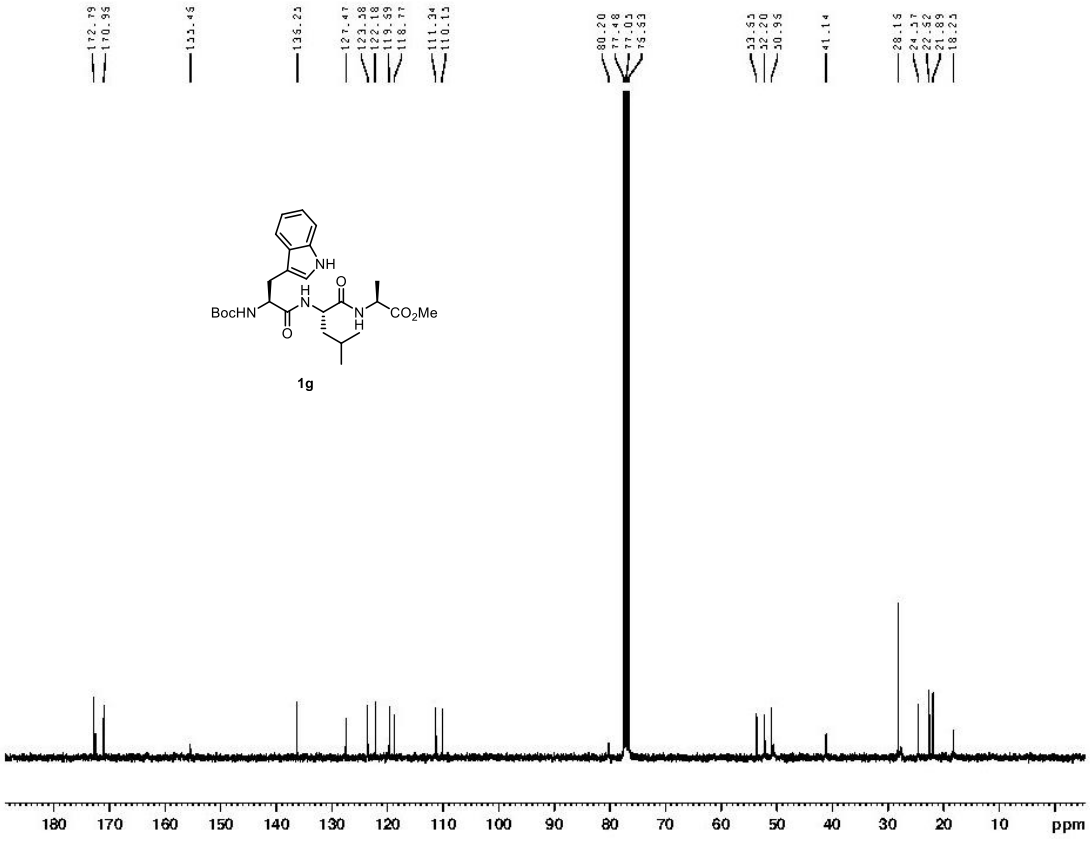
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **1f**



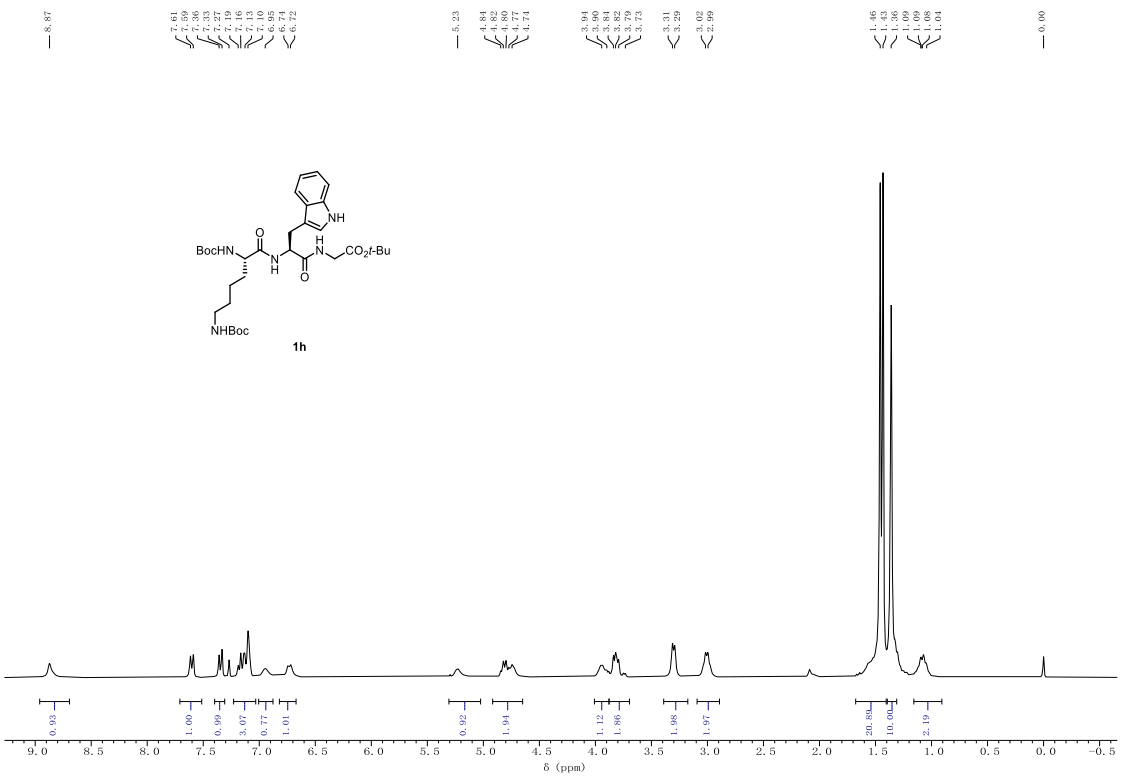
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **1f**



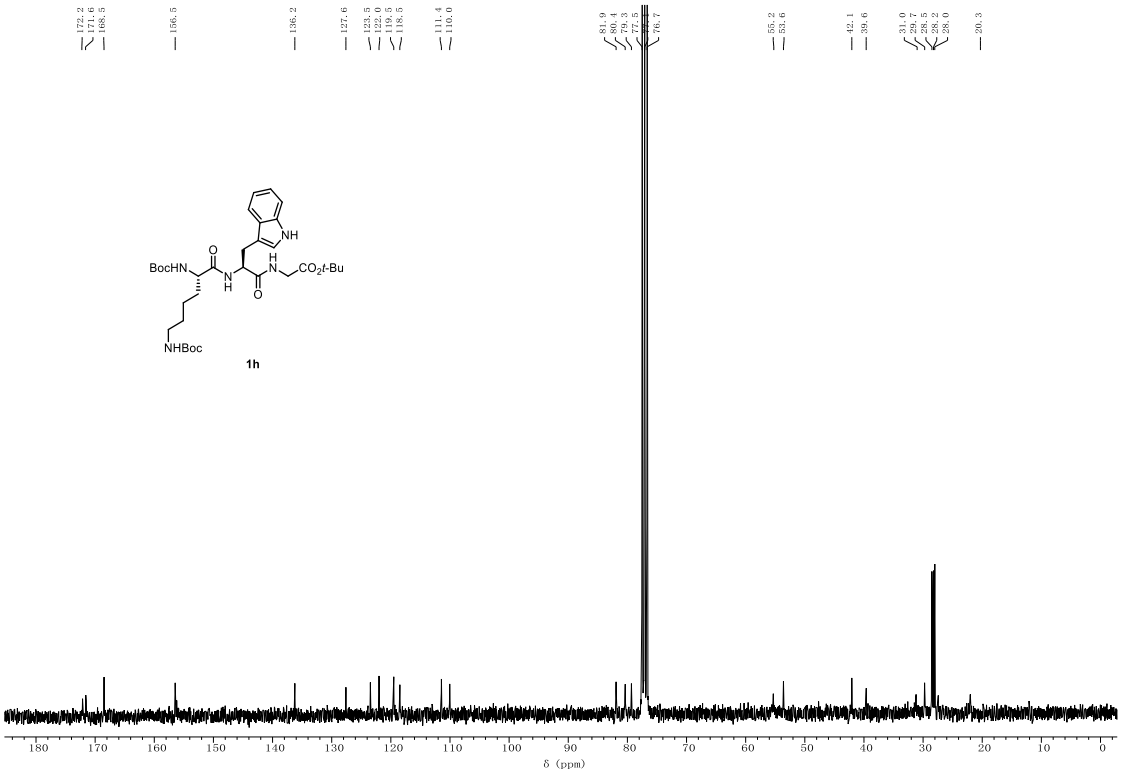
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **1g**



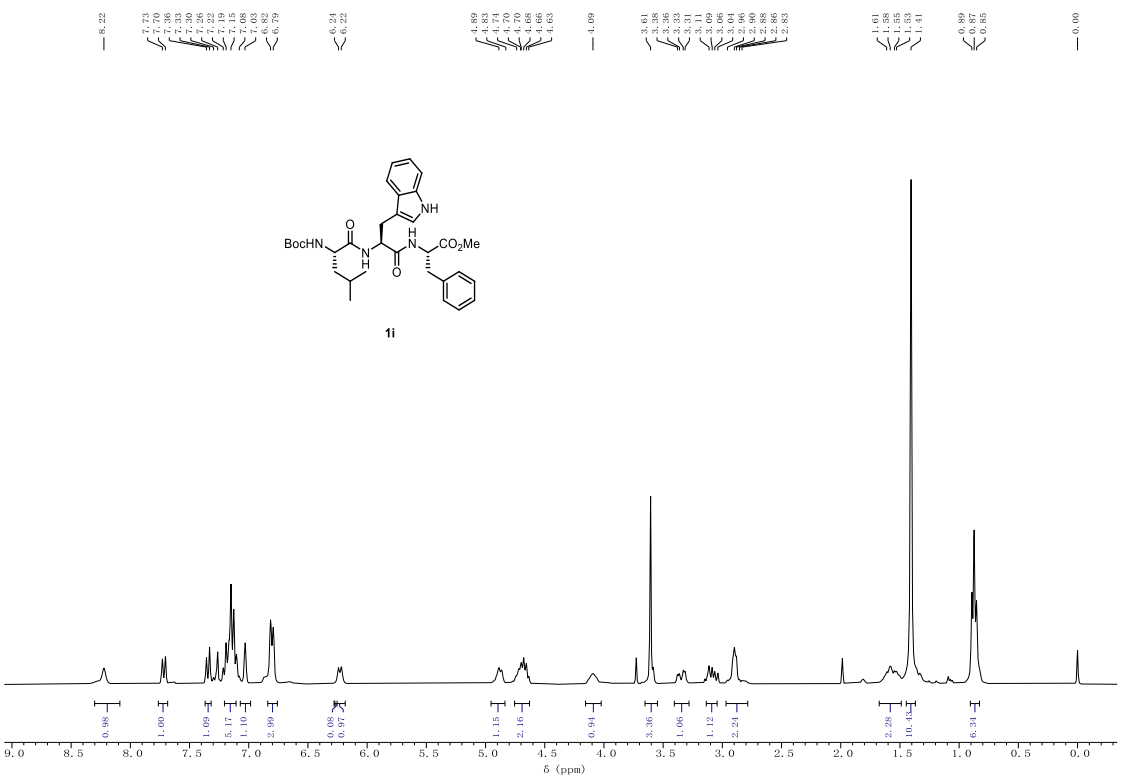
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **1g**



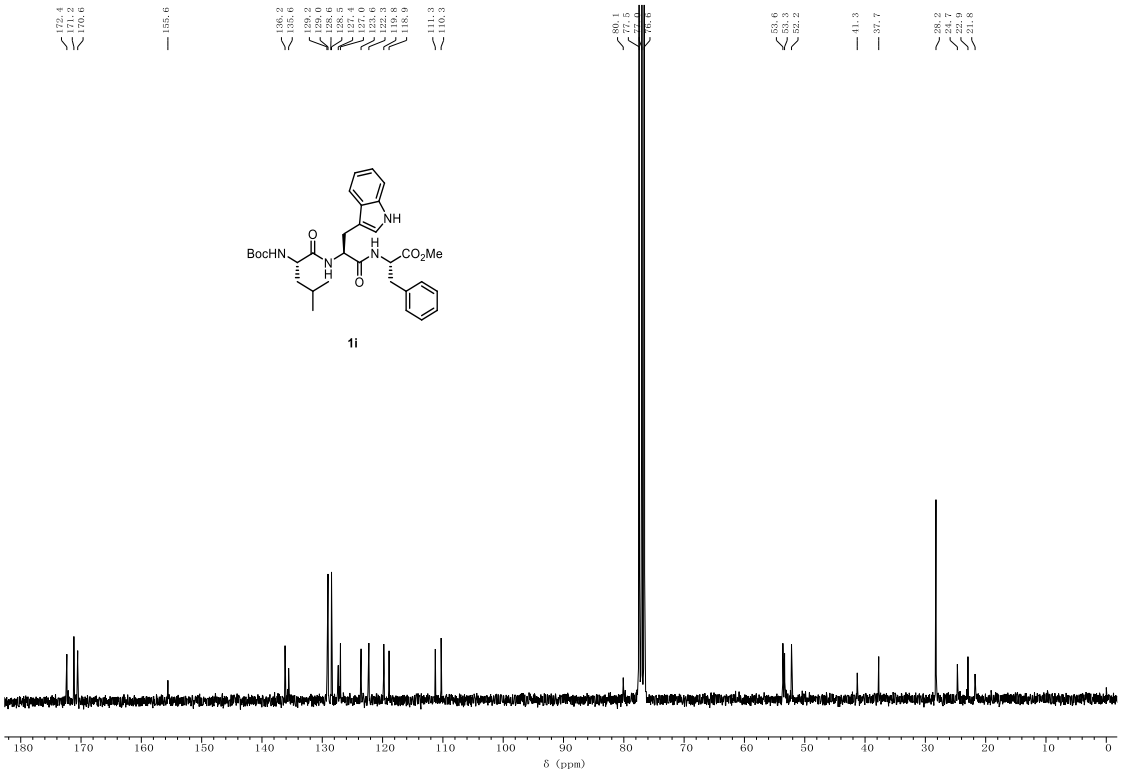
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **1h**



^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **1h**



^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **1i**



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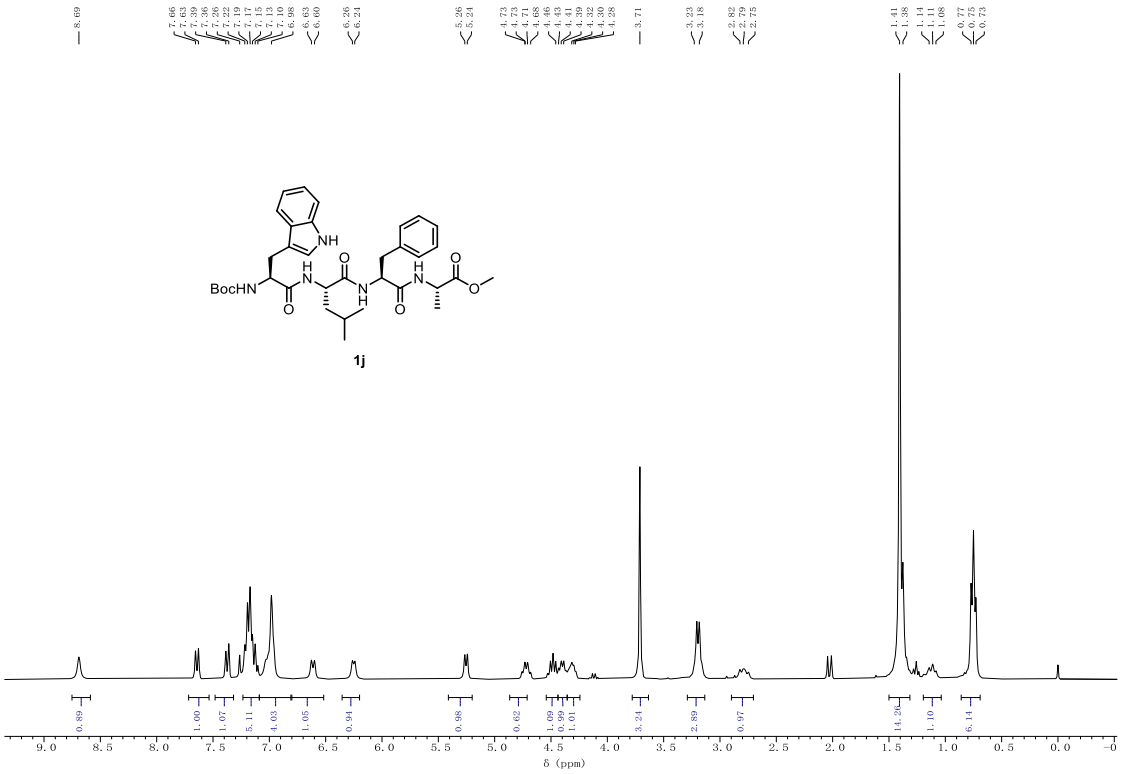
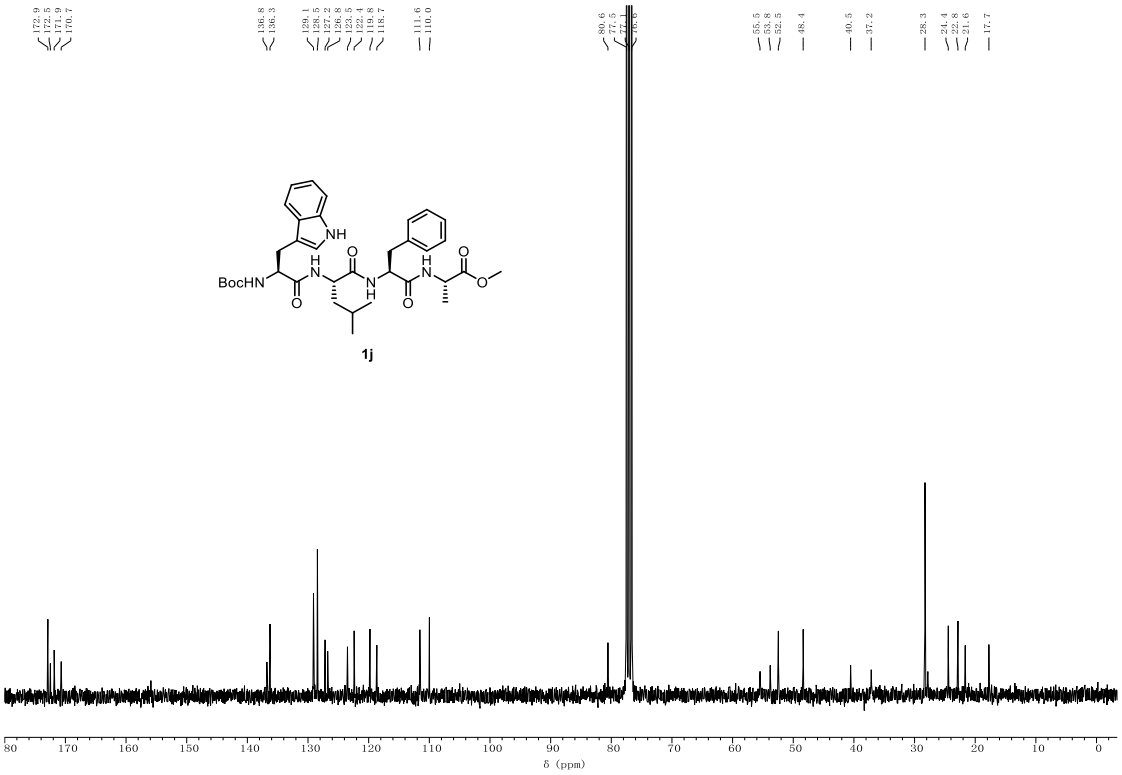
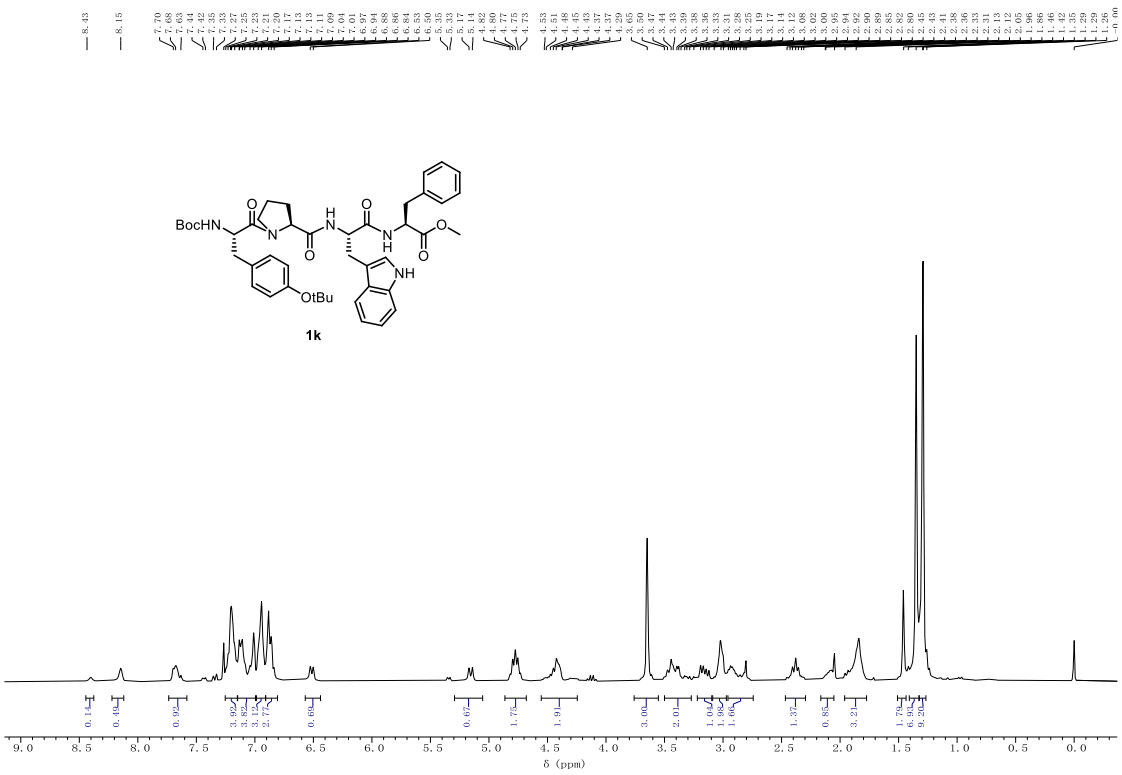


^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **1j**



^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **1j**



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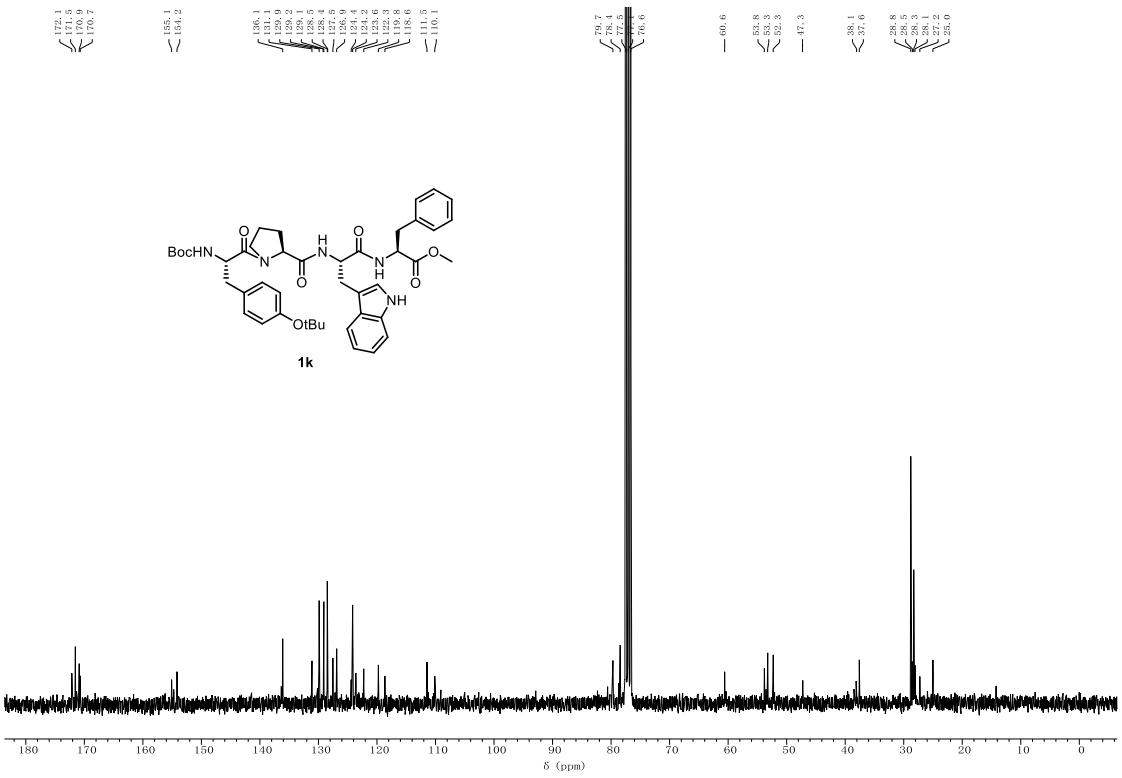

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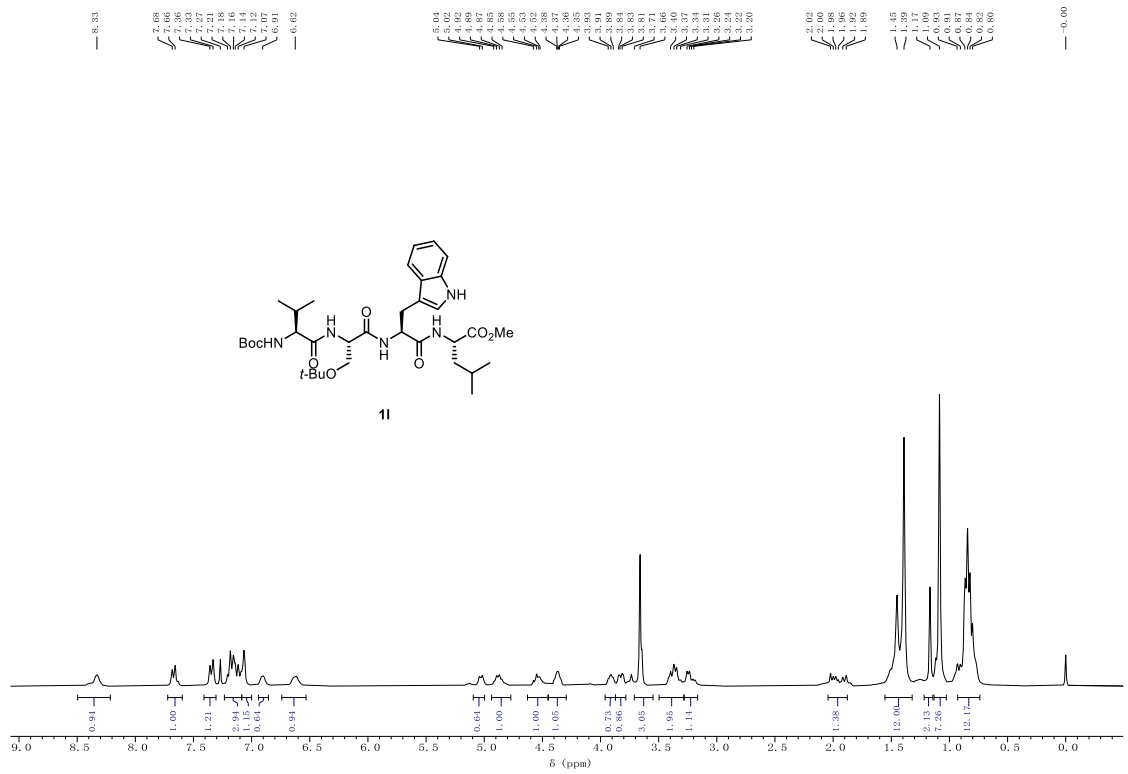
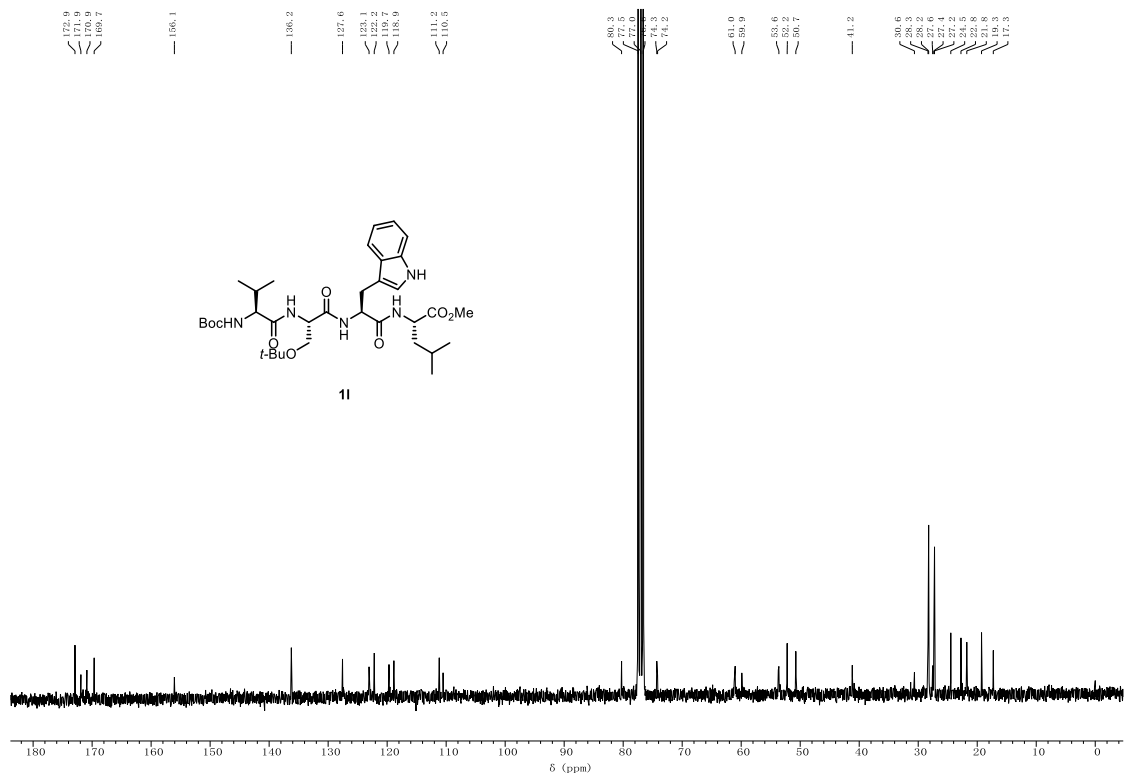


^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **1l**



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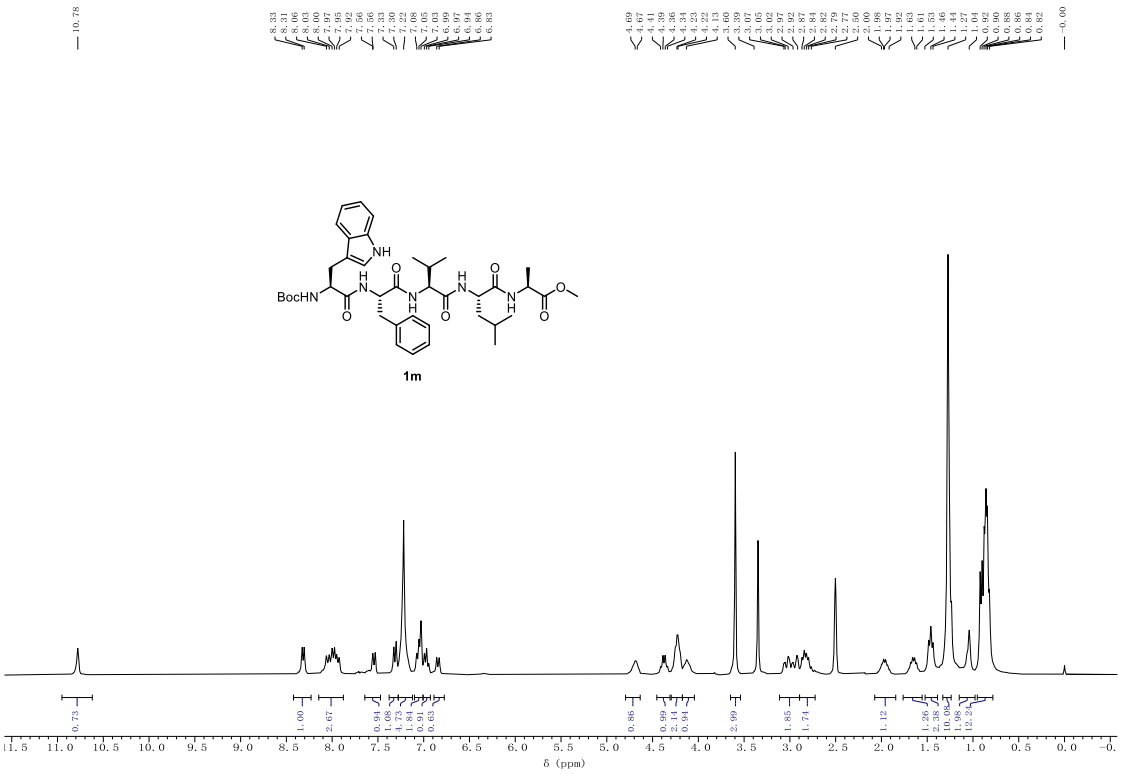
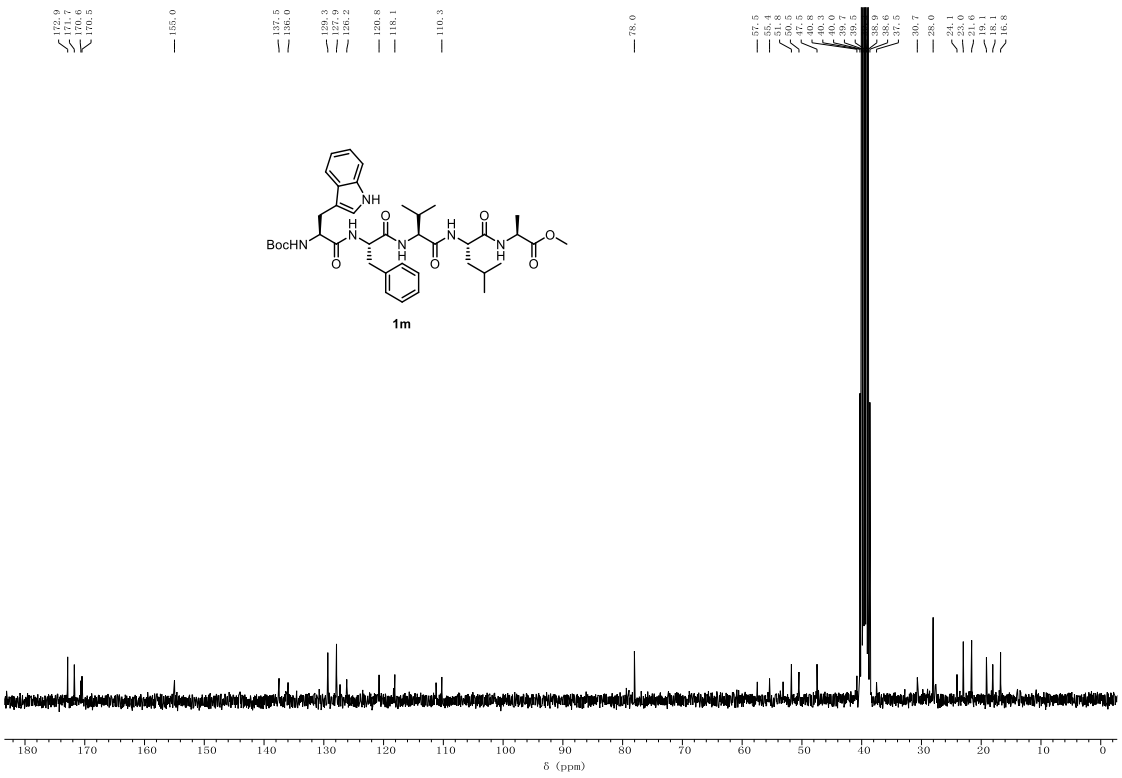
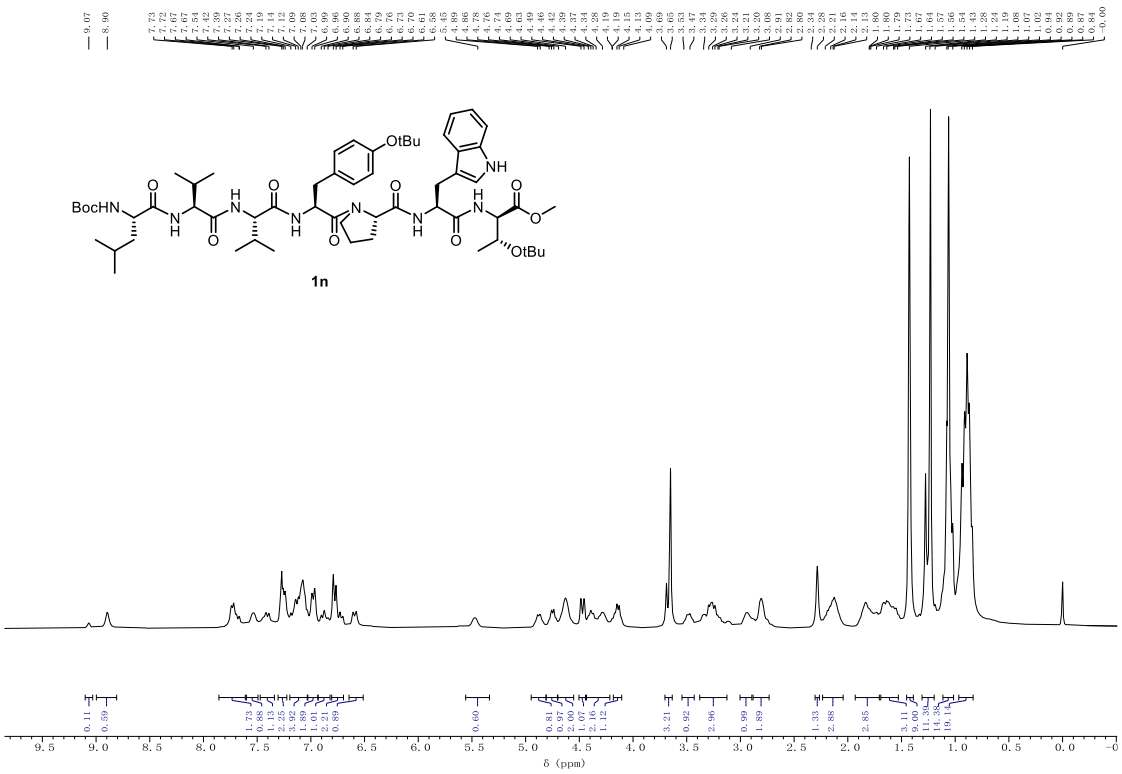


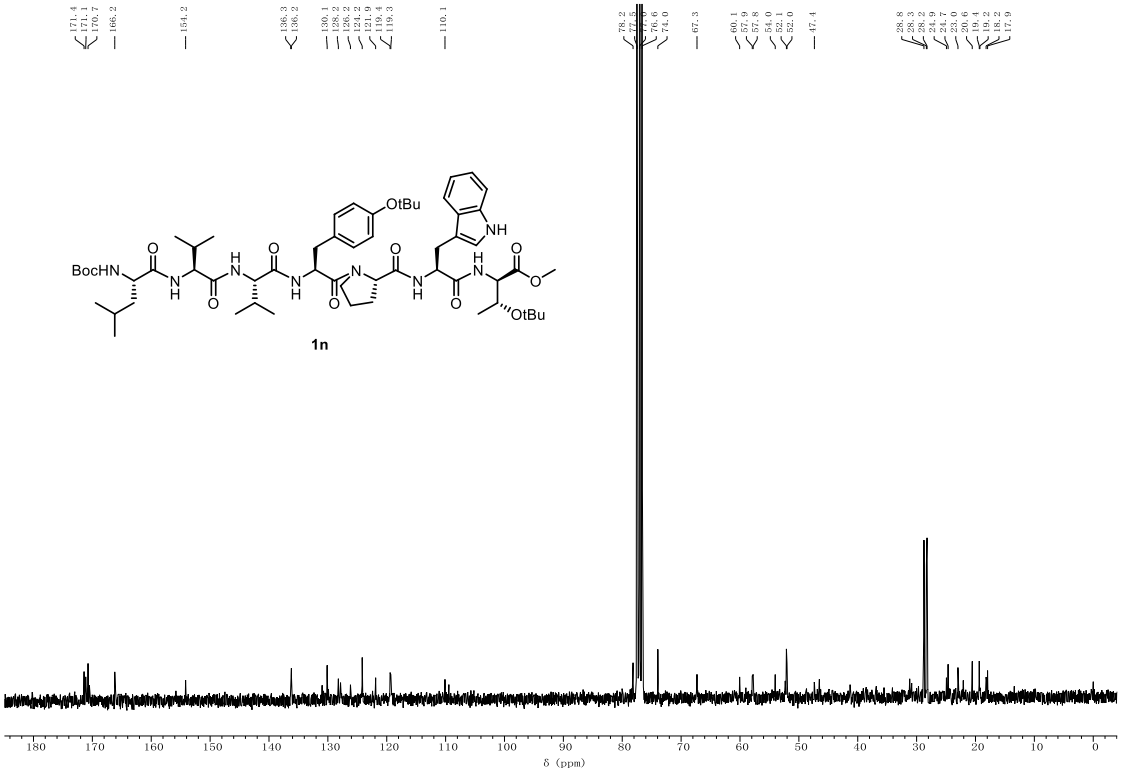
^{1}H NMR (300 MHz, DMSO-d_6) spectrum of **1m**



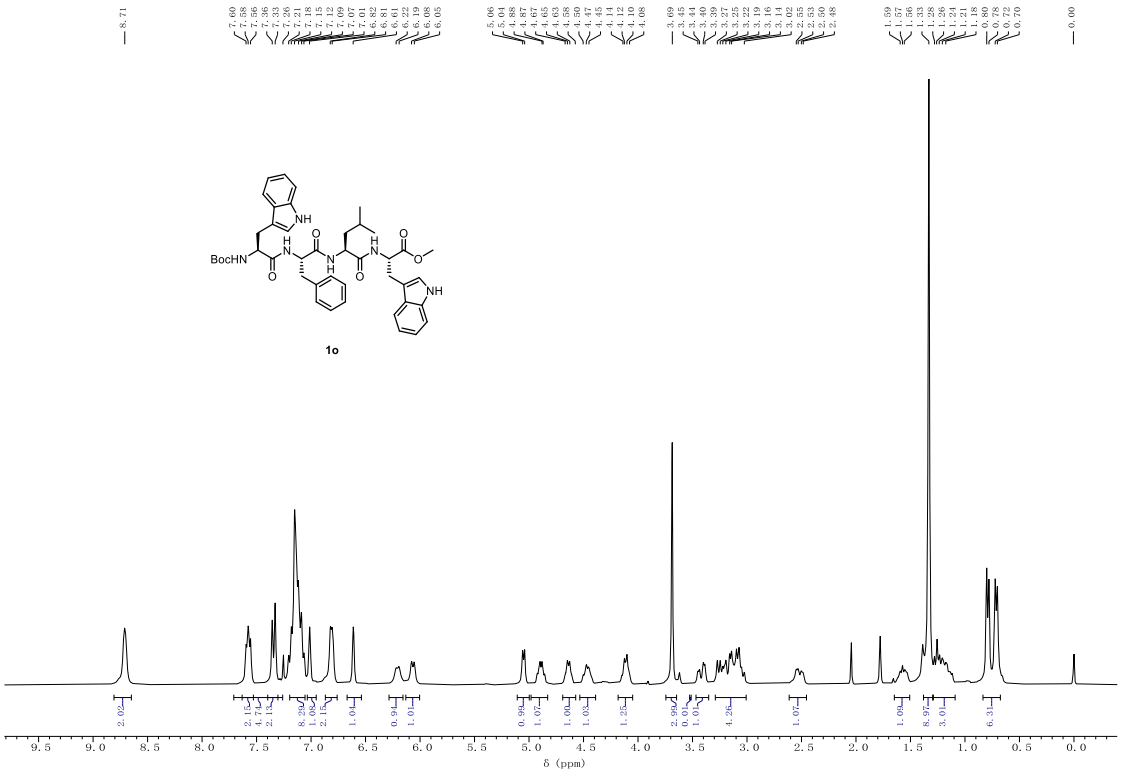
^{13}C NMR (75 MHz, DMSO-d_6) spectrum of **1m**



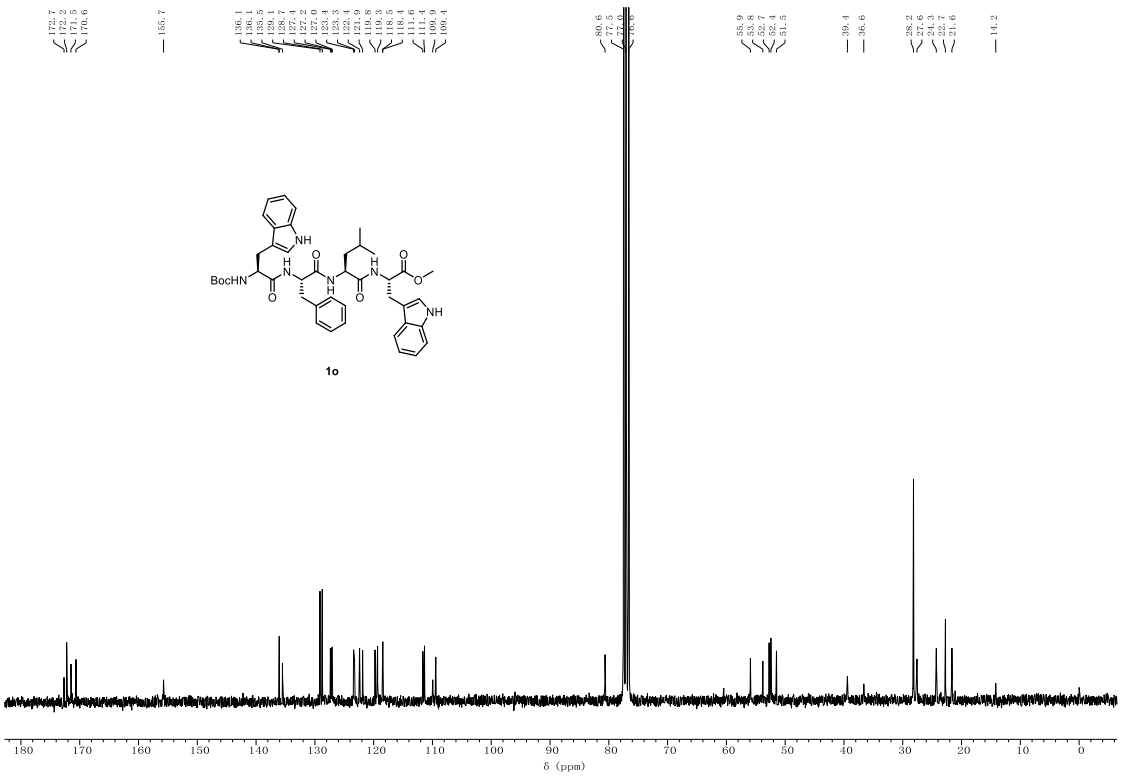
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **1n**



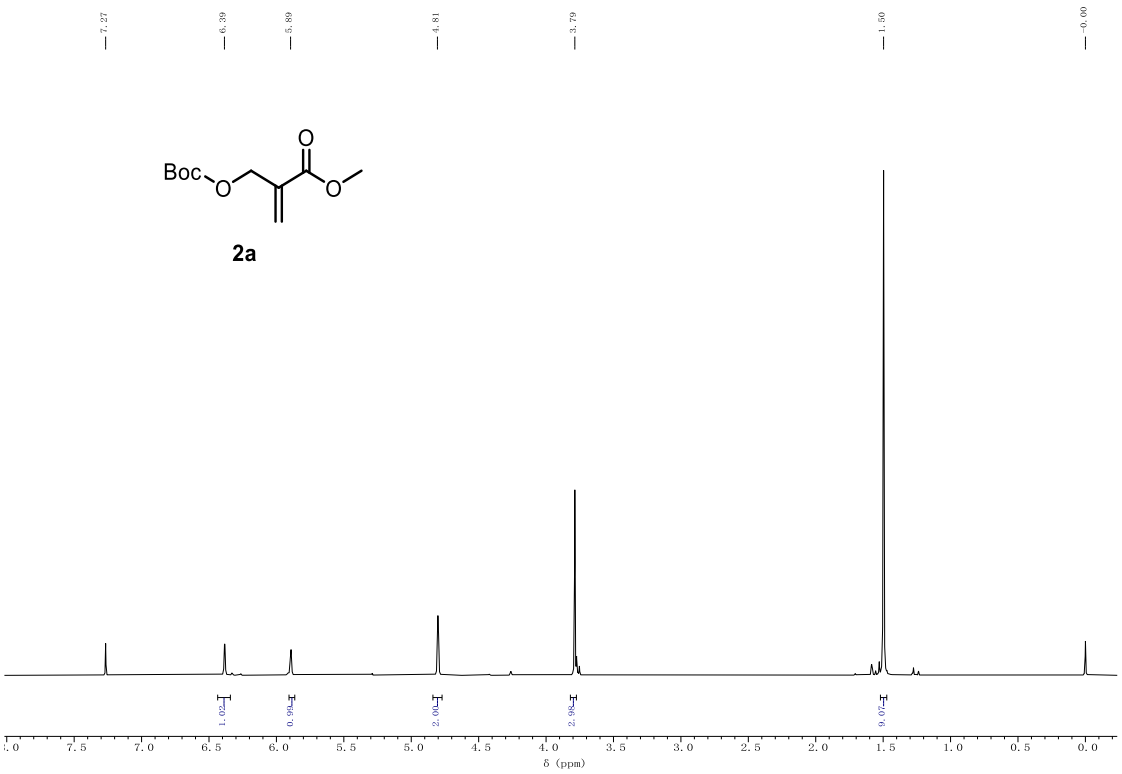
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **1n**



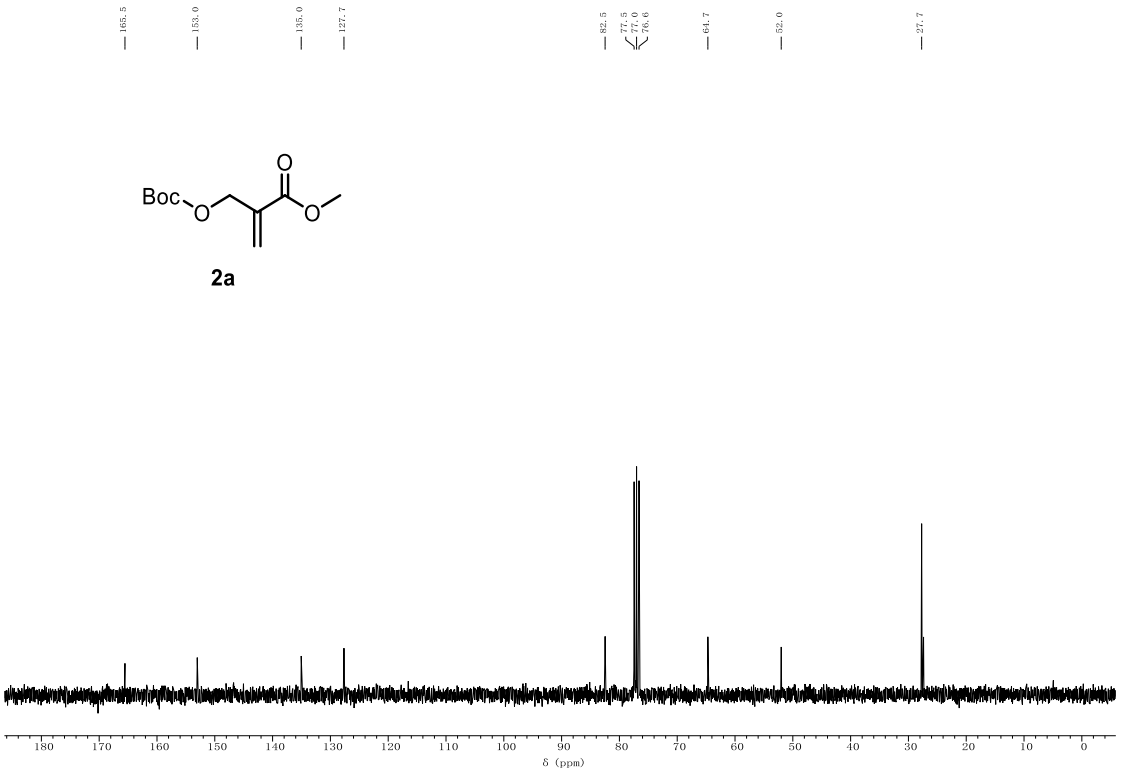
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **1o**



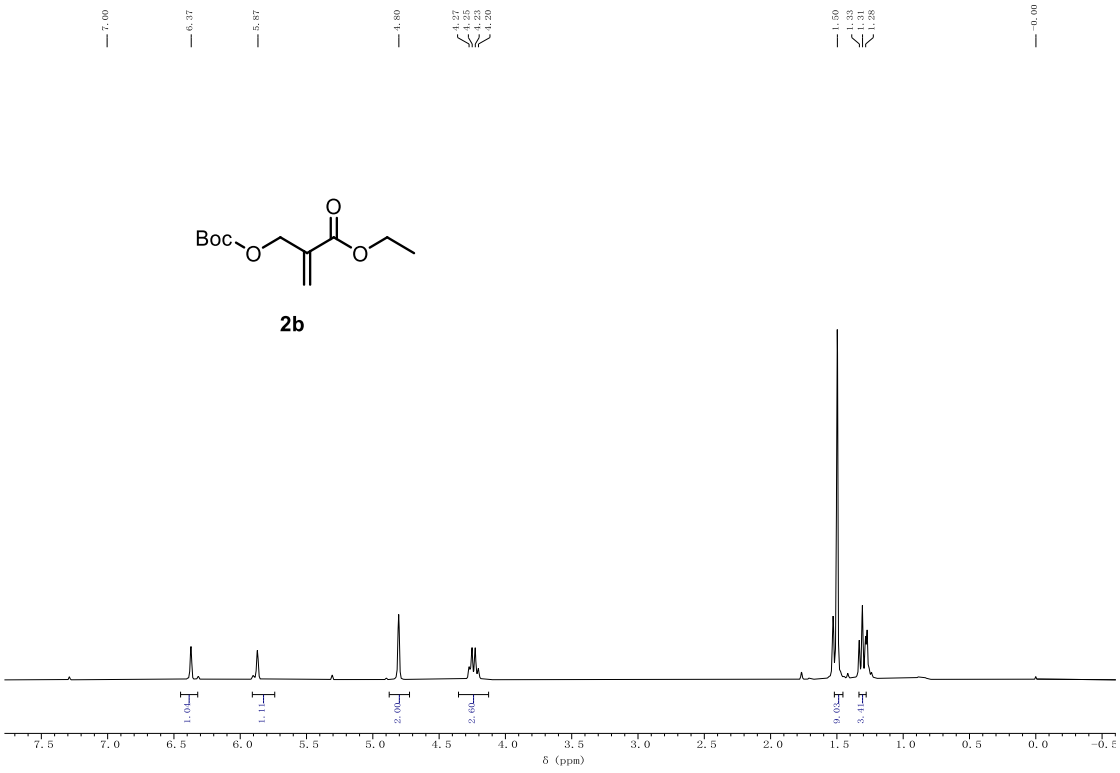
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **1o**



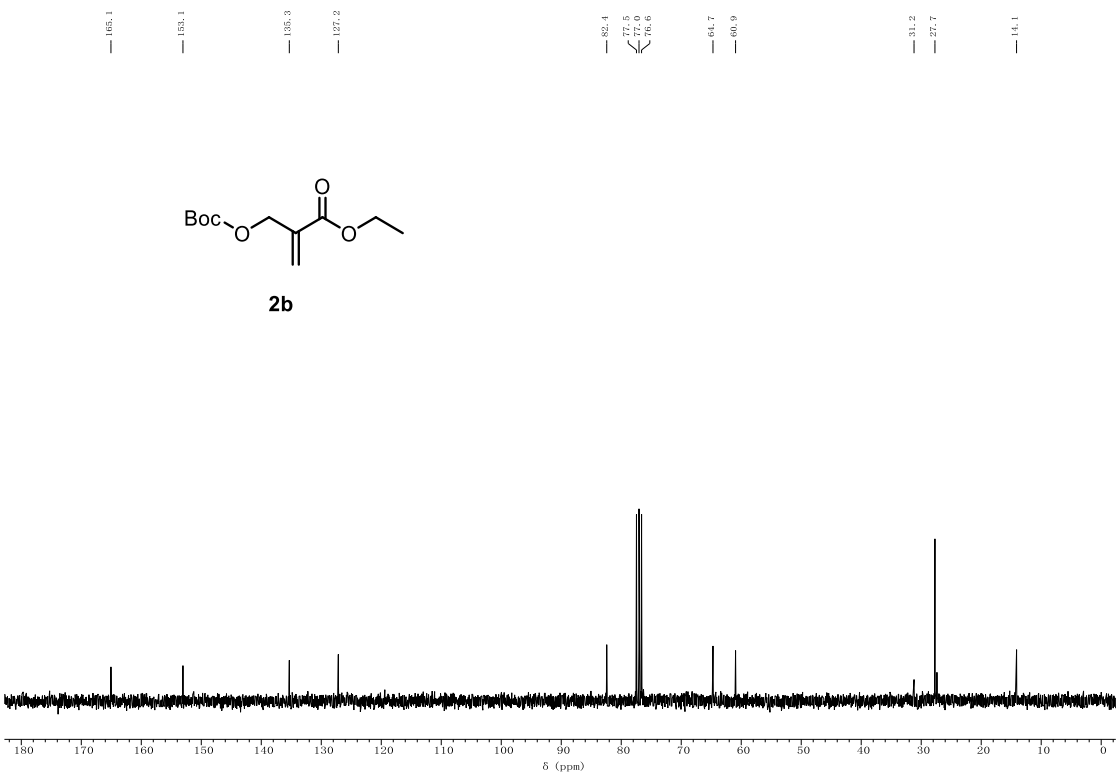
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2a**



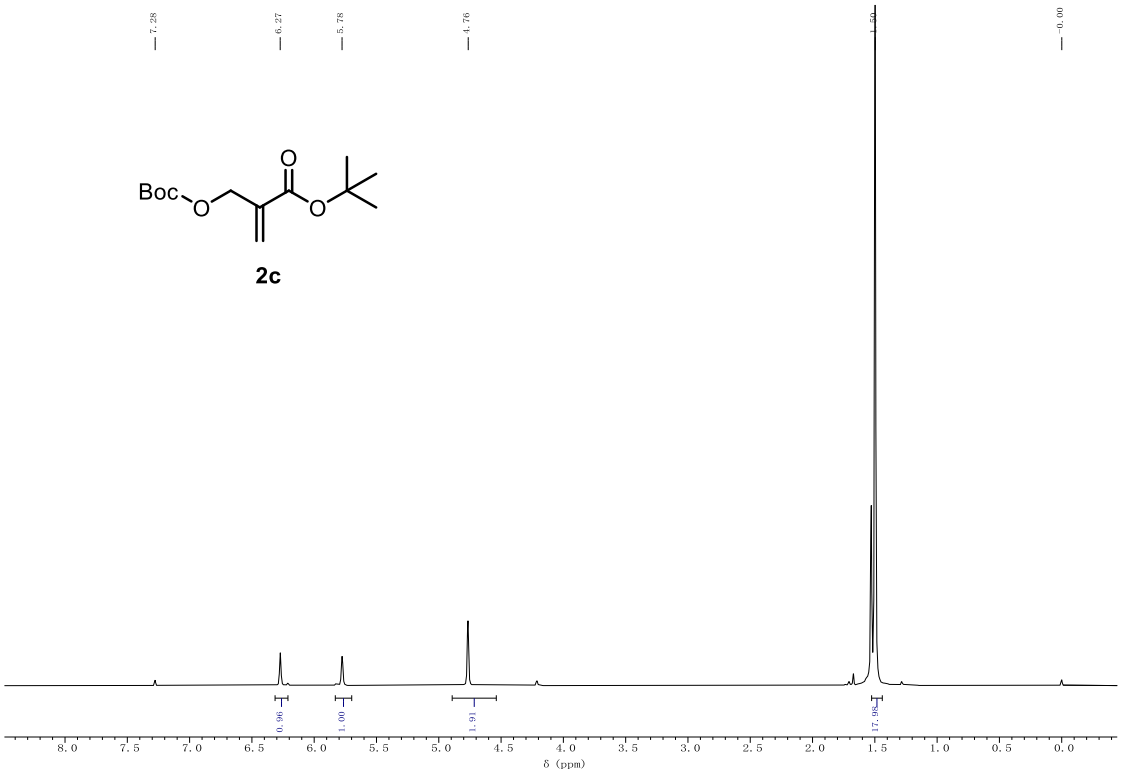
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2a**



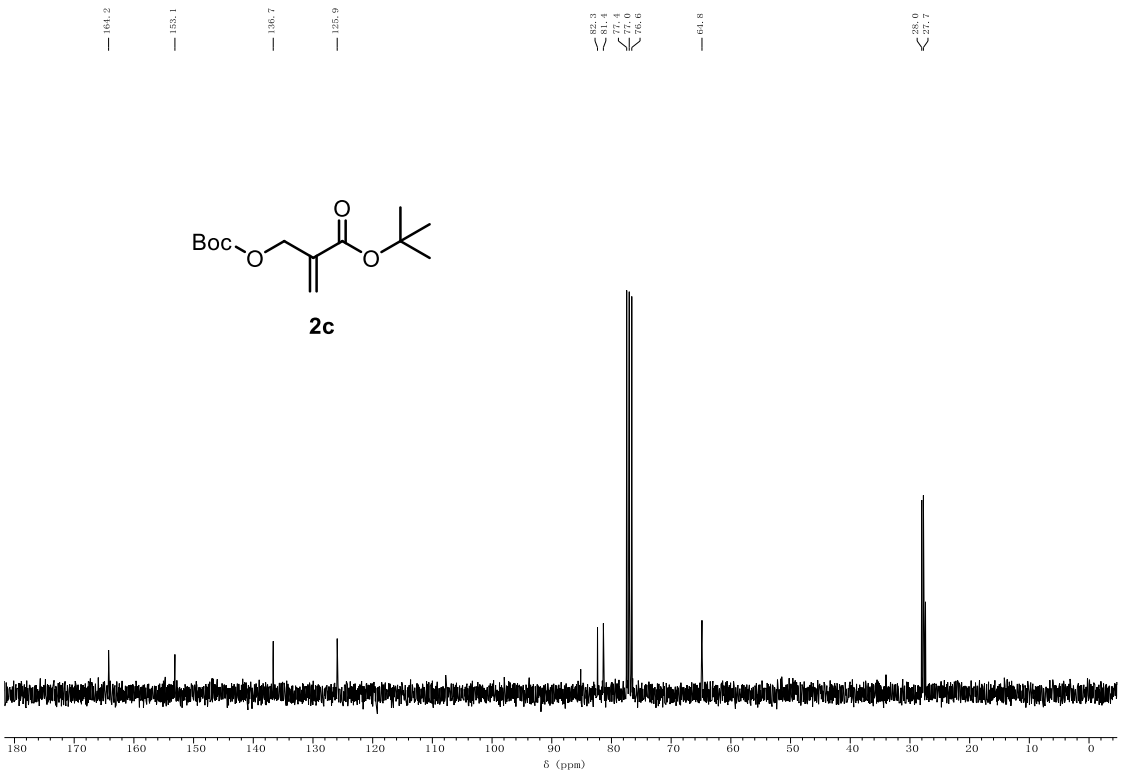
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2b**



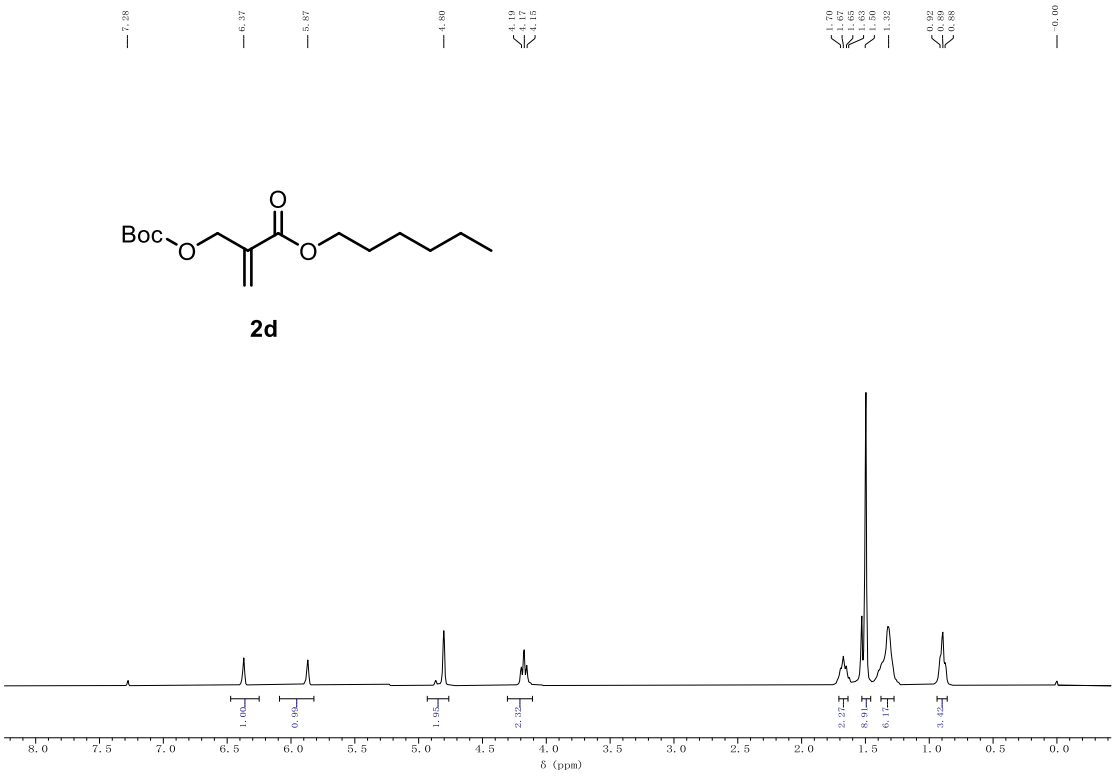
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of 2b



^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2c**

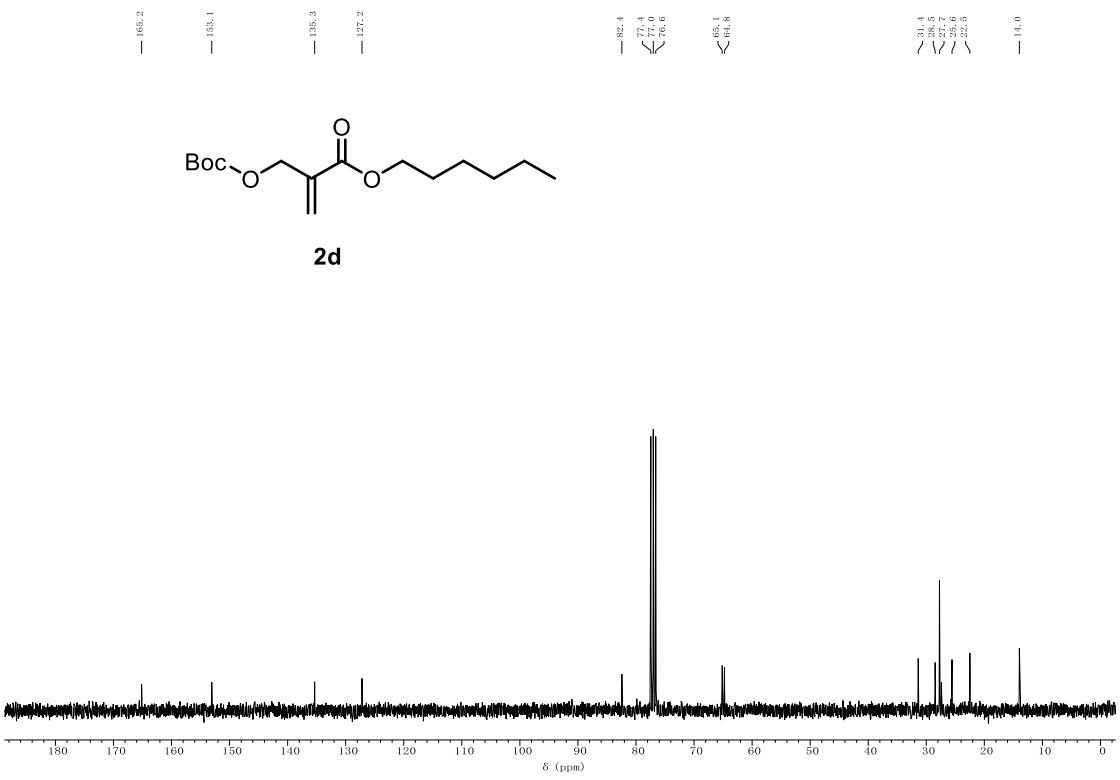


^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2c**



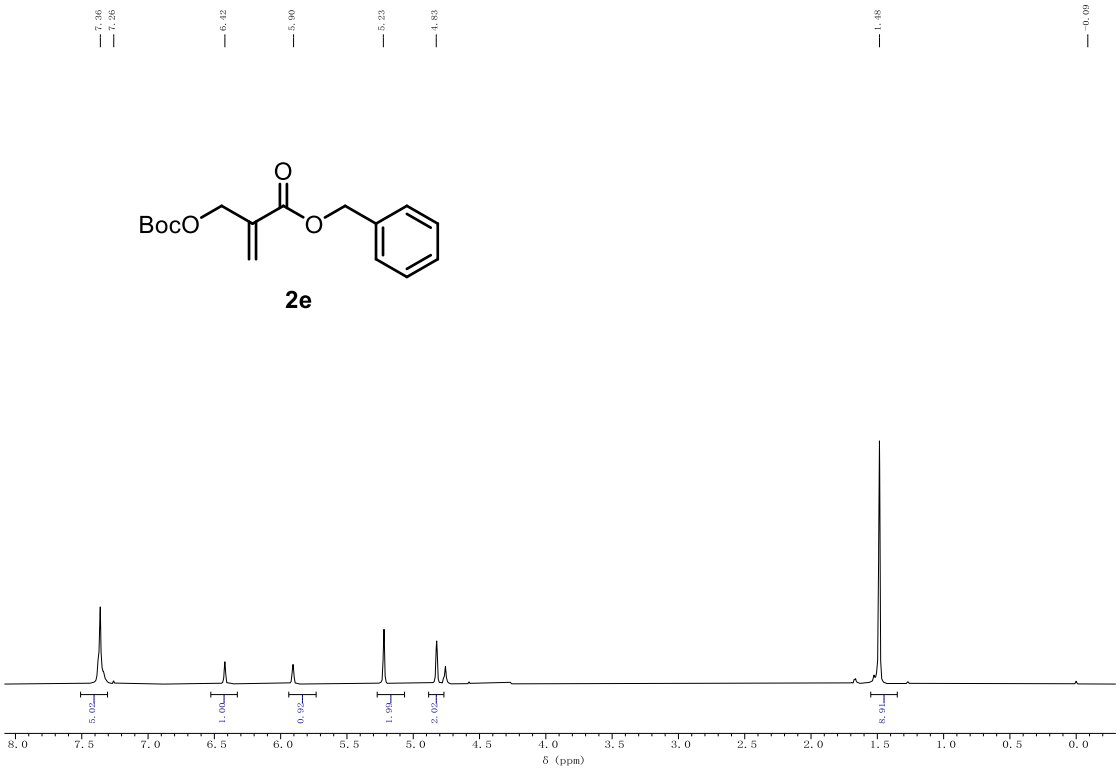
2d

^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2d**



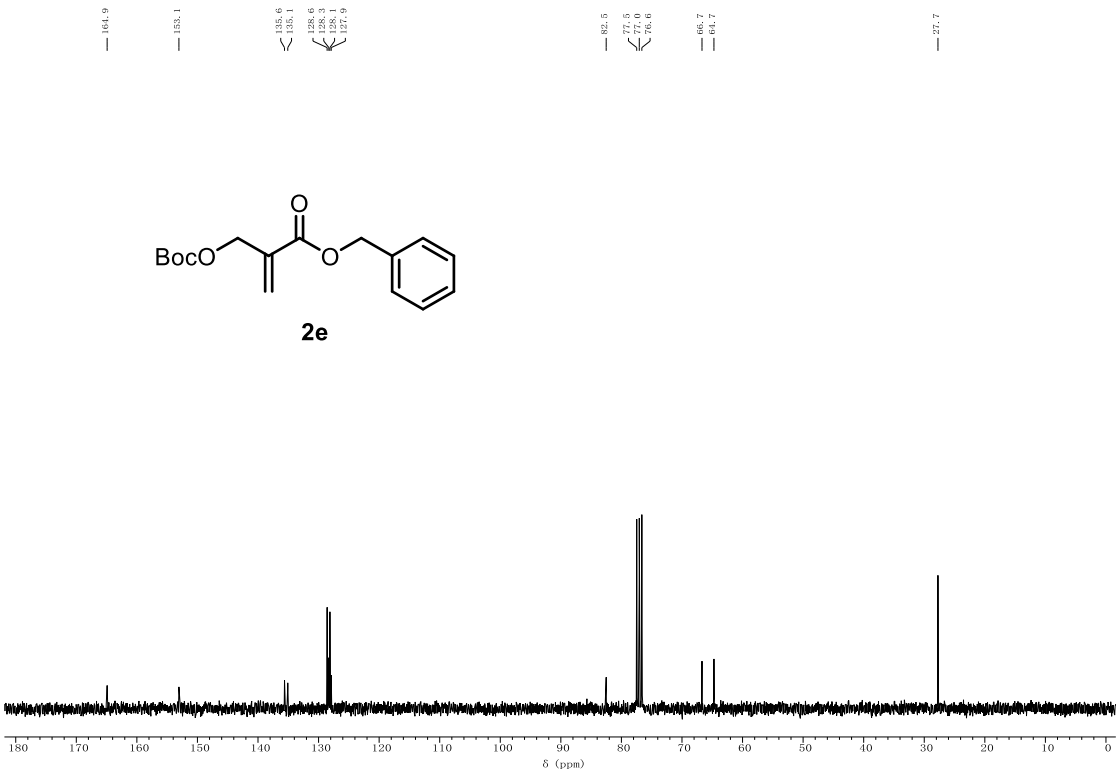
2d

^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2d**



2e

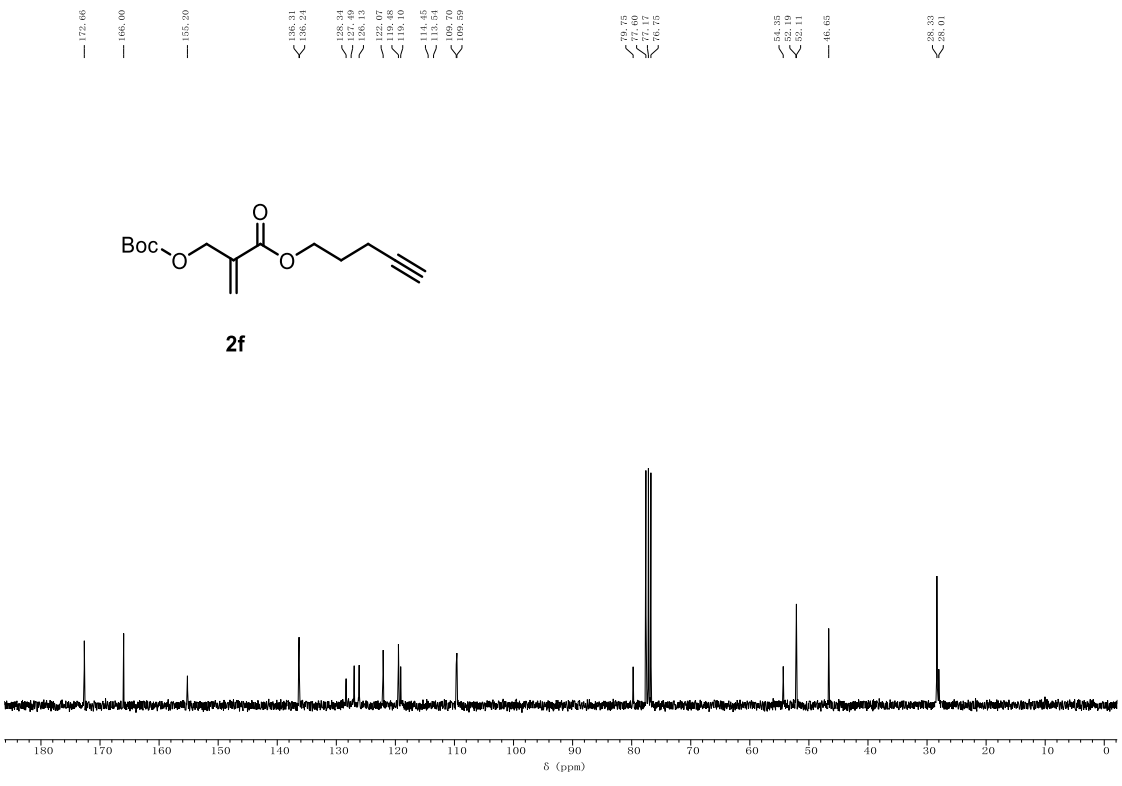
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2e**



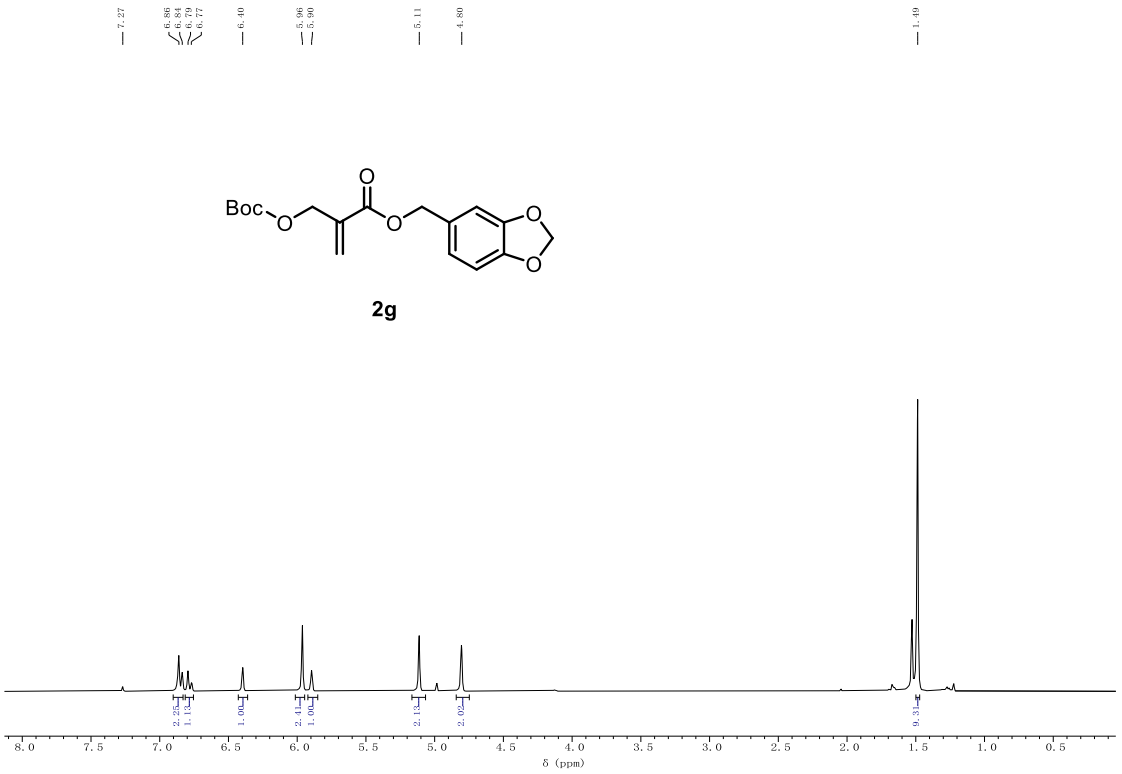
2e

^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2e**

^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2f**

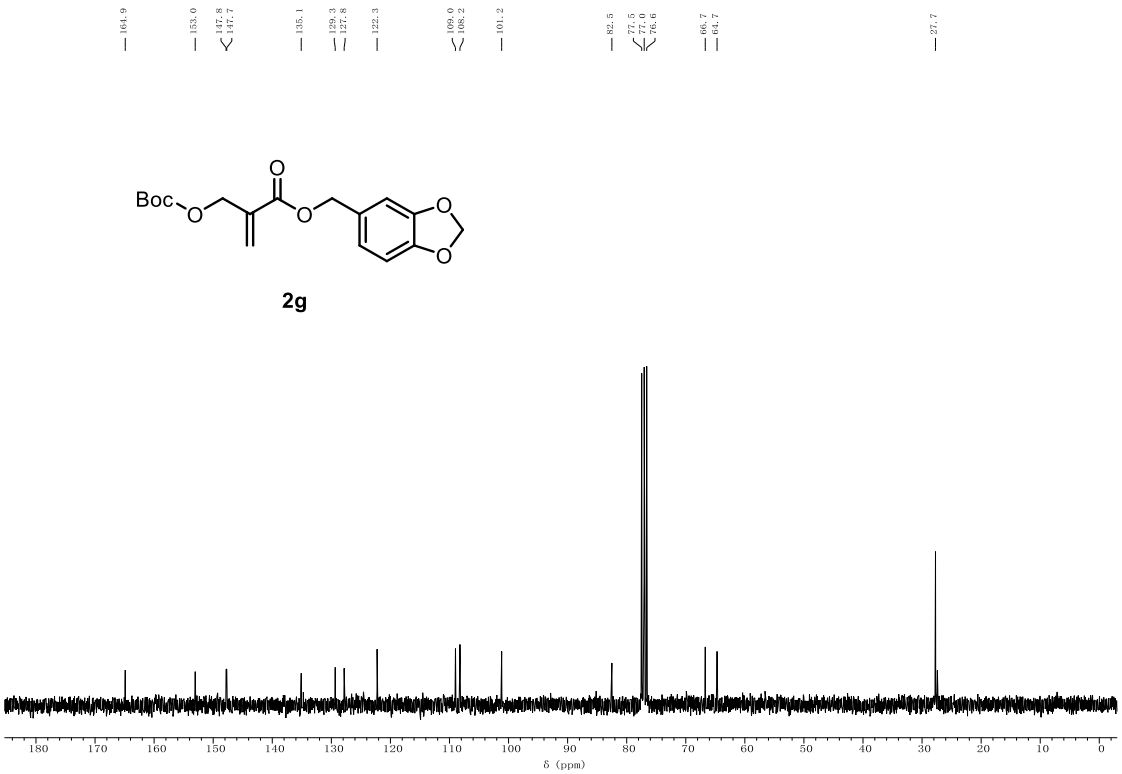


^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2f**



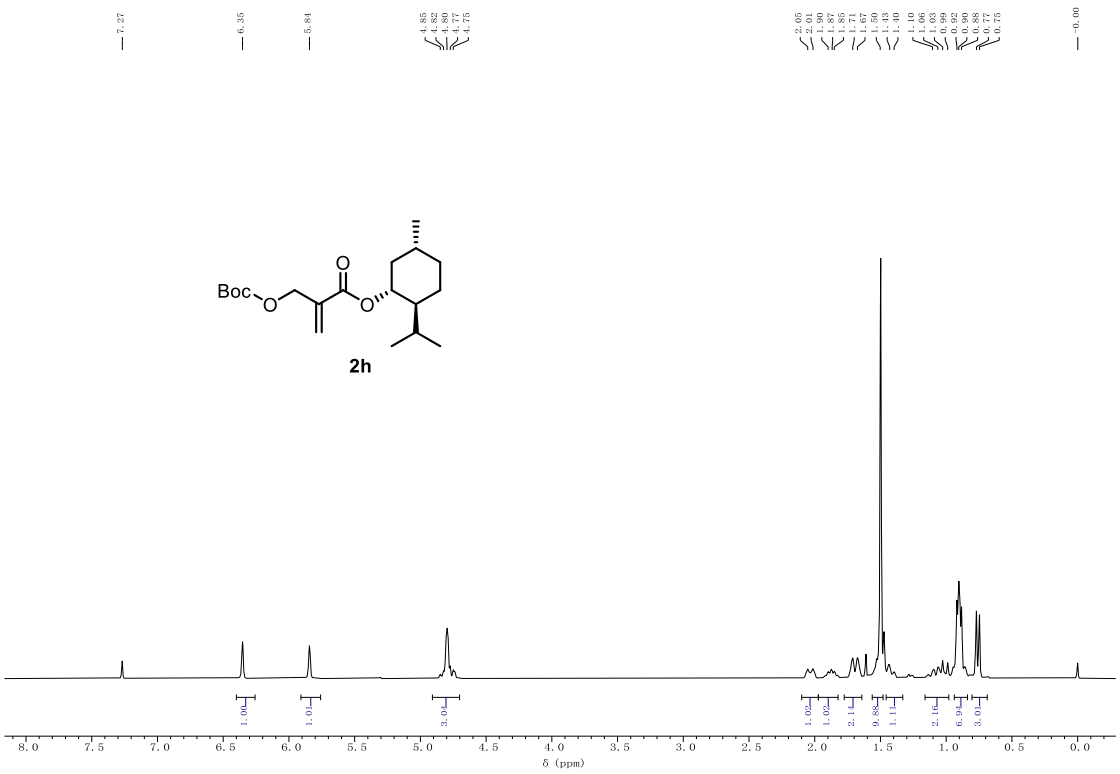
2g

^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2g**

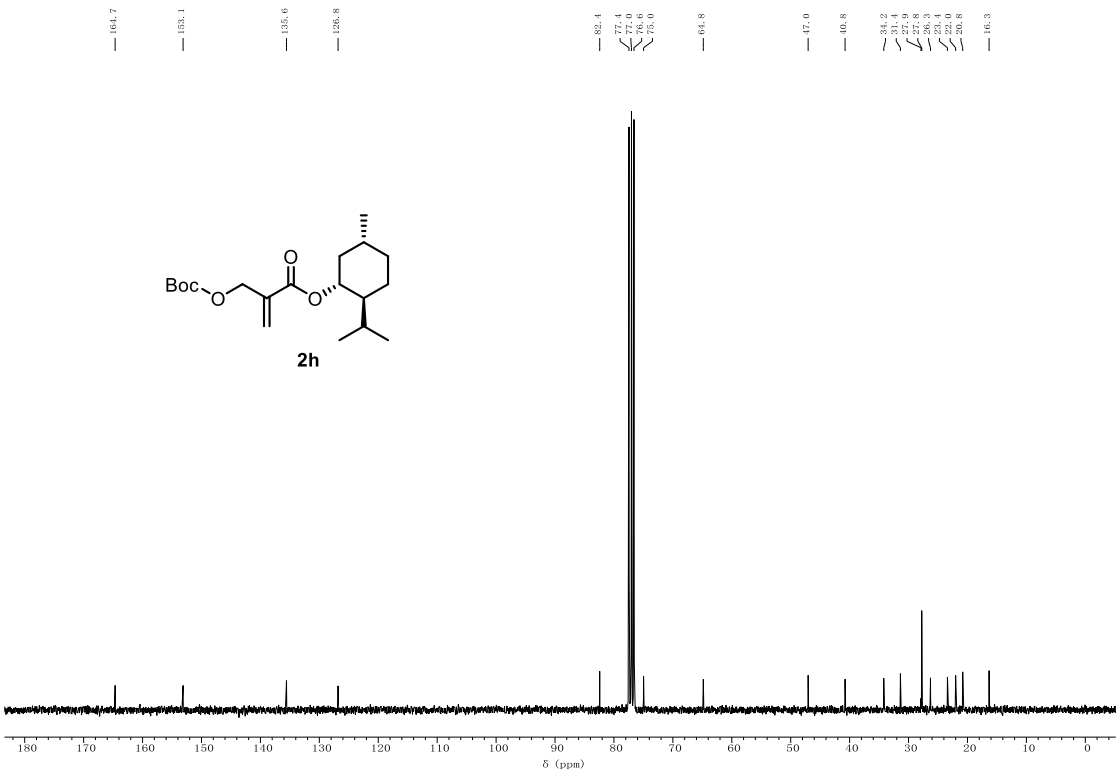


2g

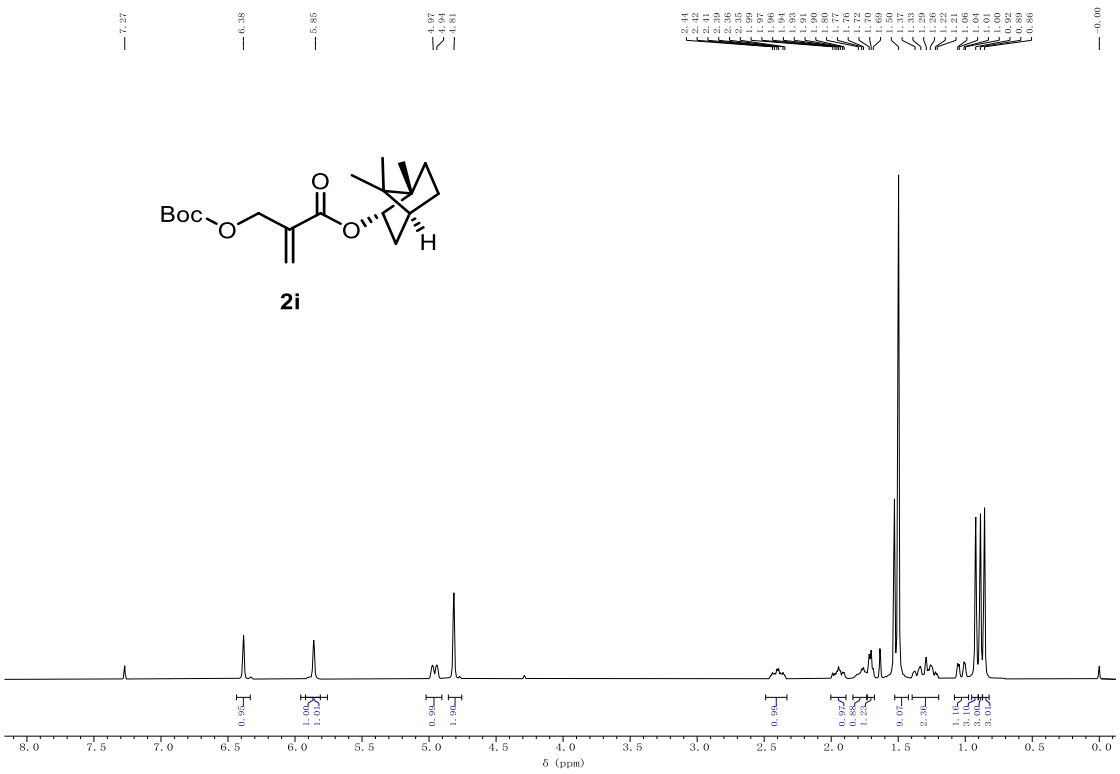
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2g**



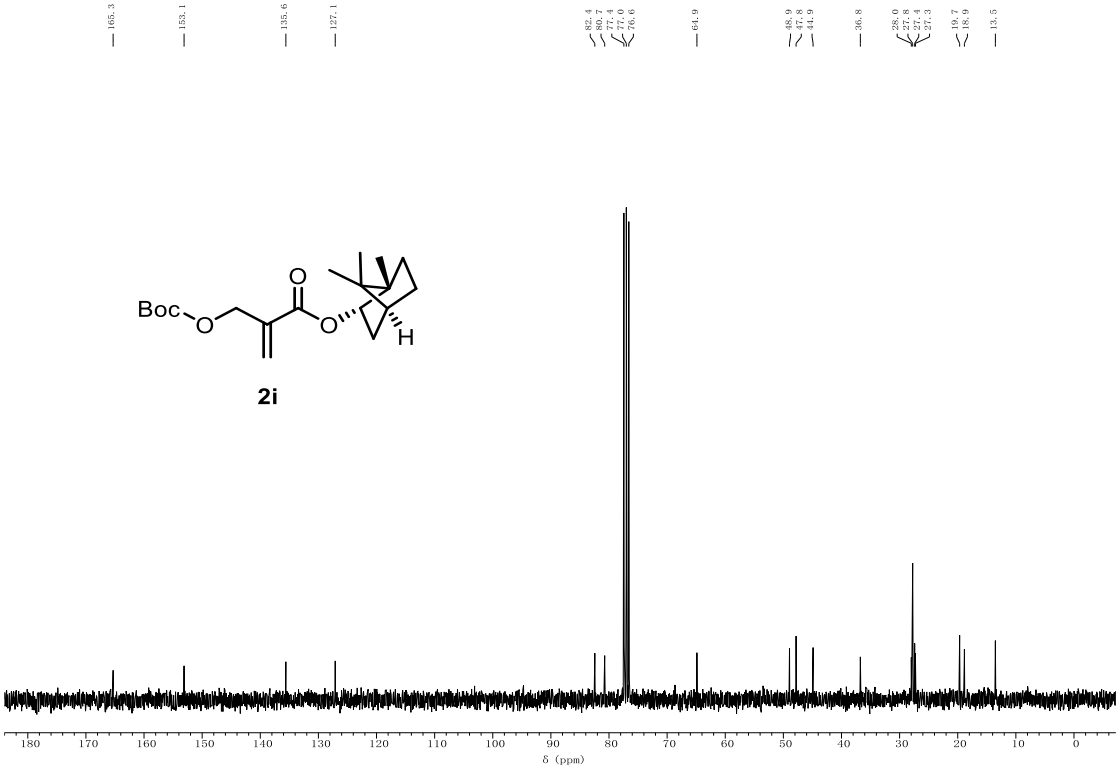
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2h**



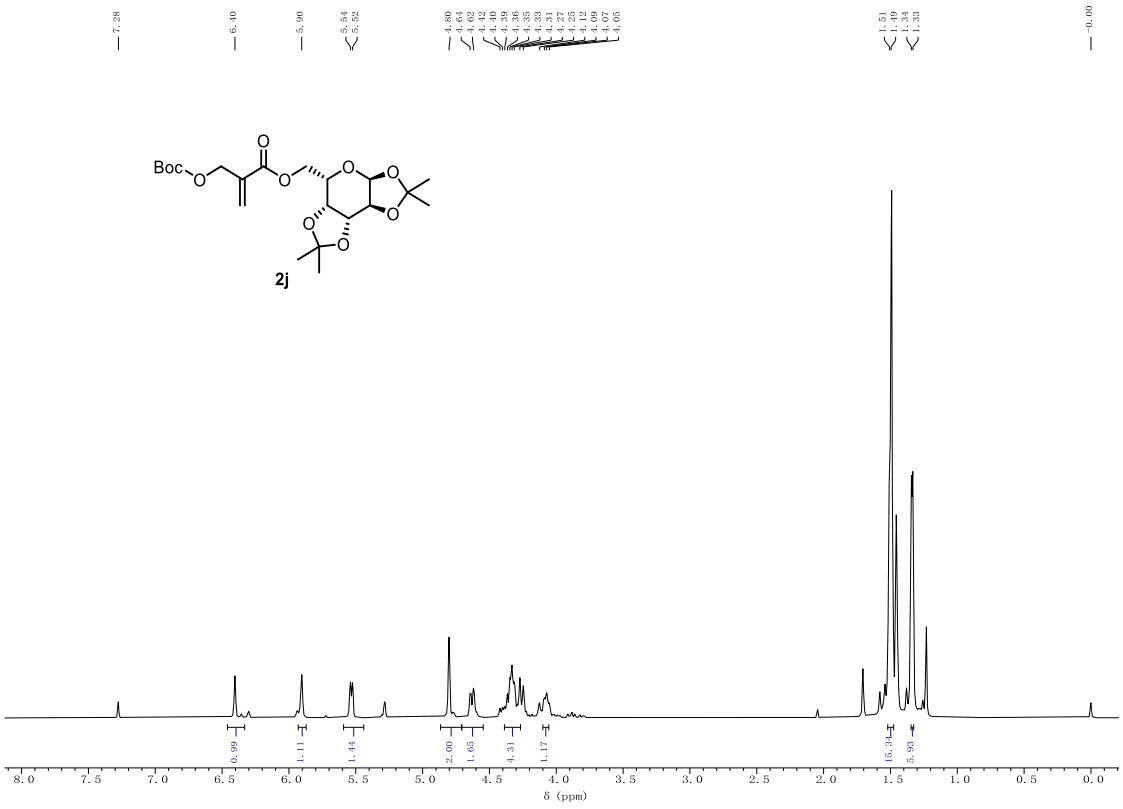
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2h**



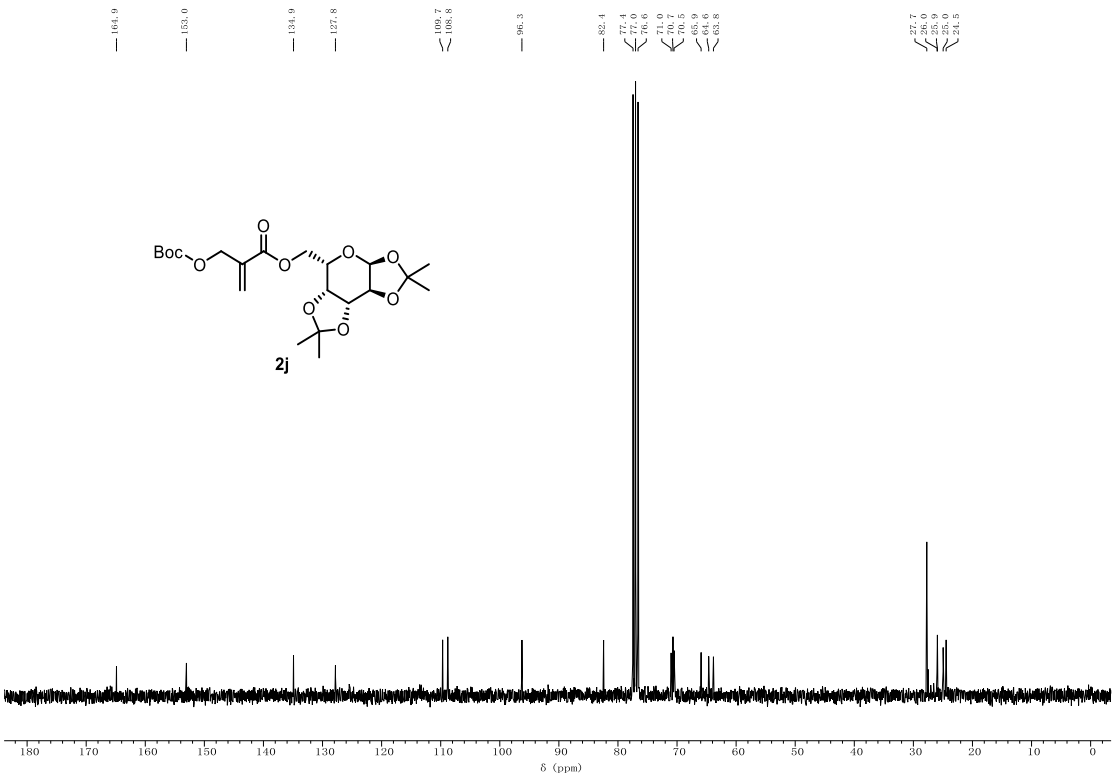
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2i**



^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2i**

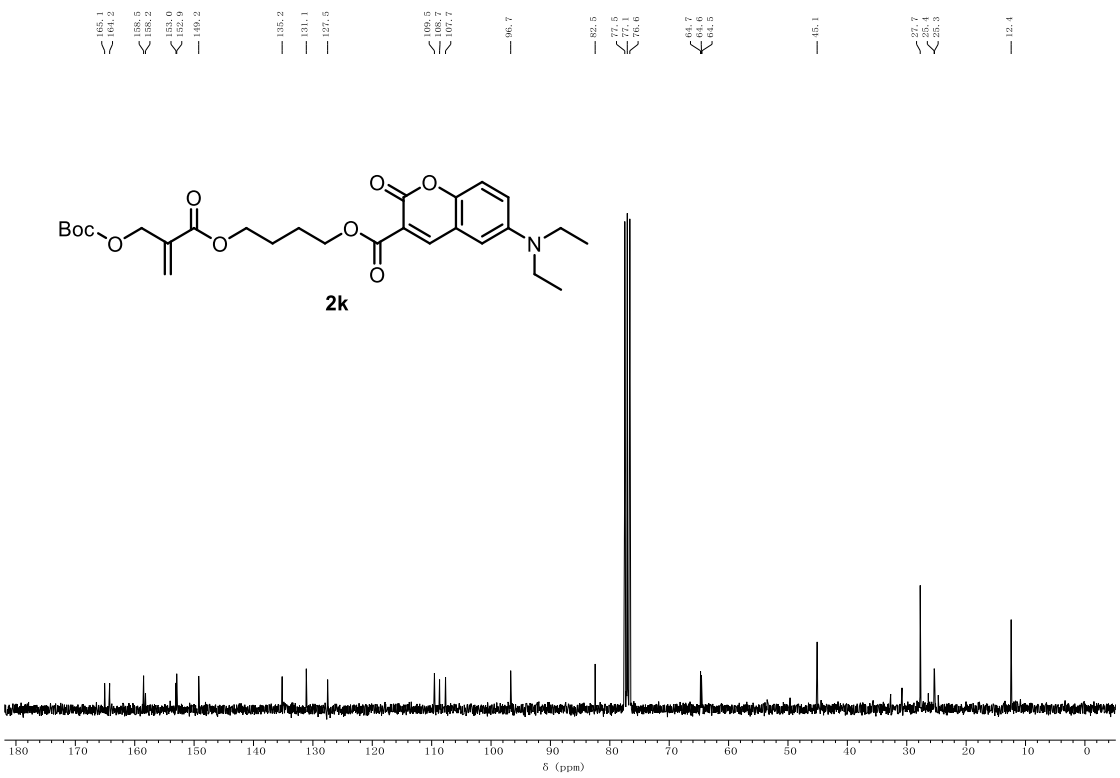


^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2j**

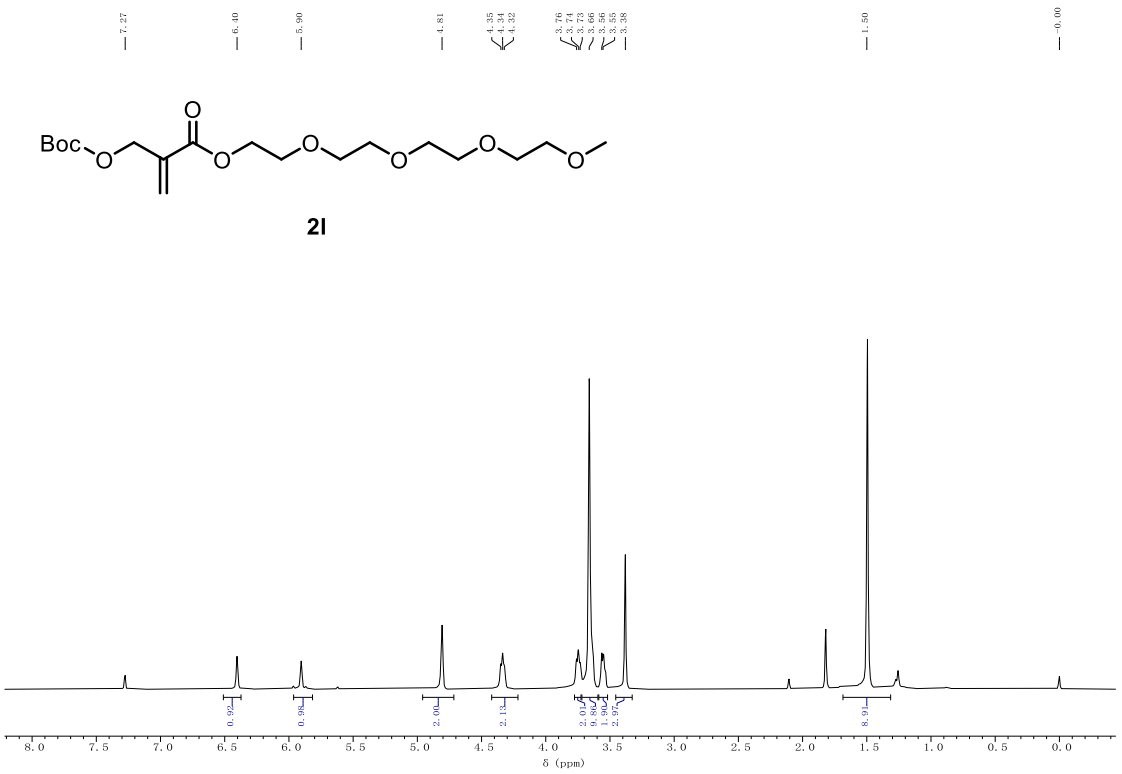


^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2j**

^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2k**

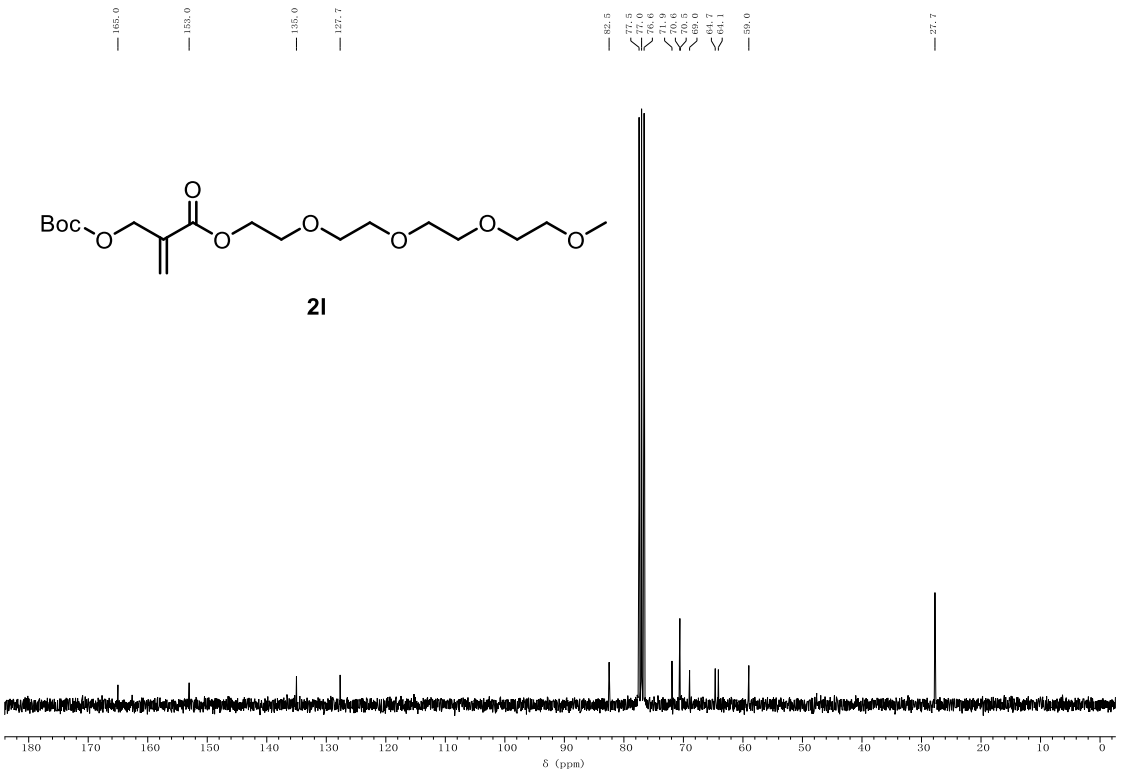


^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2k**



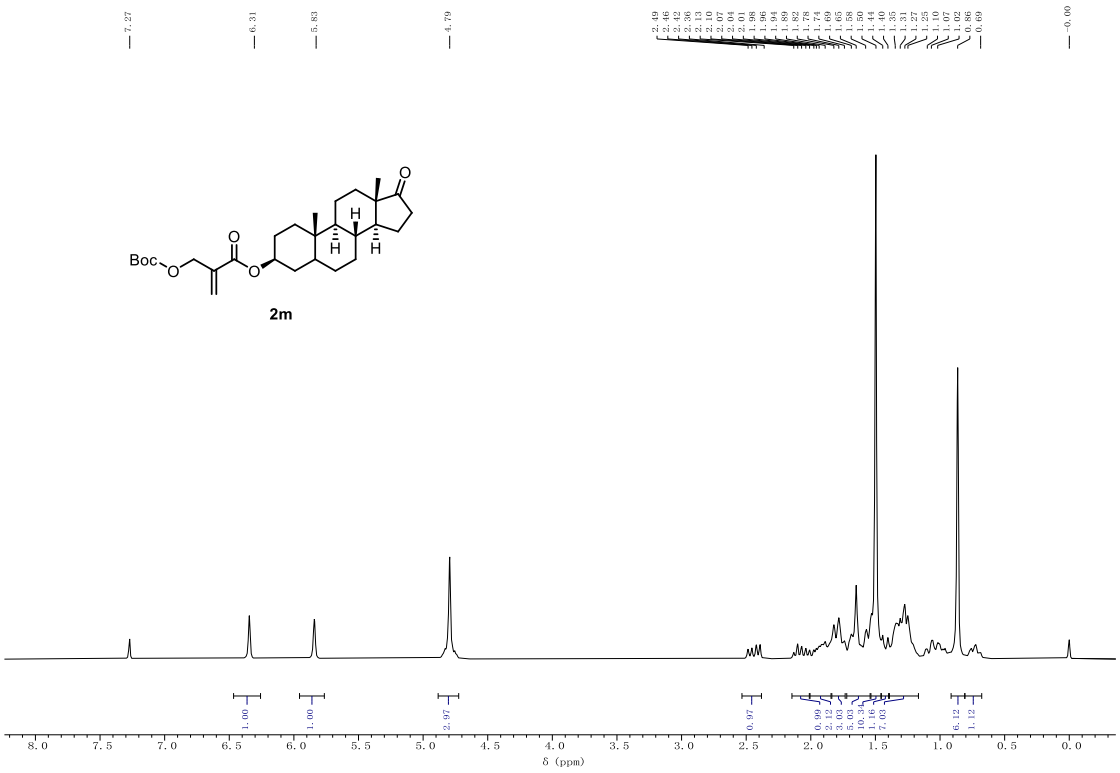
2l

^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2l**

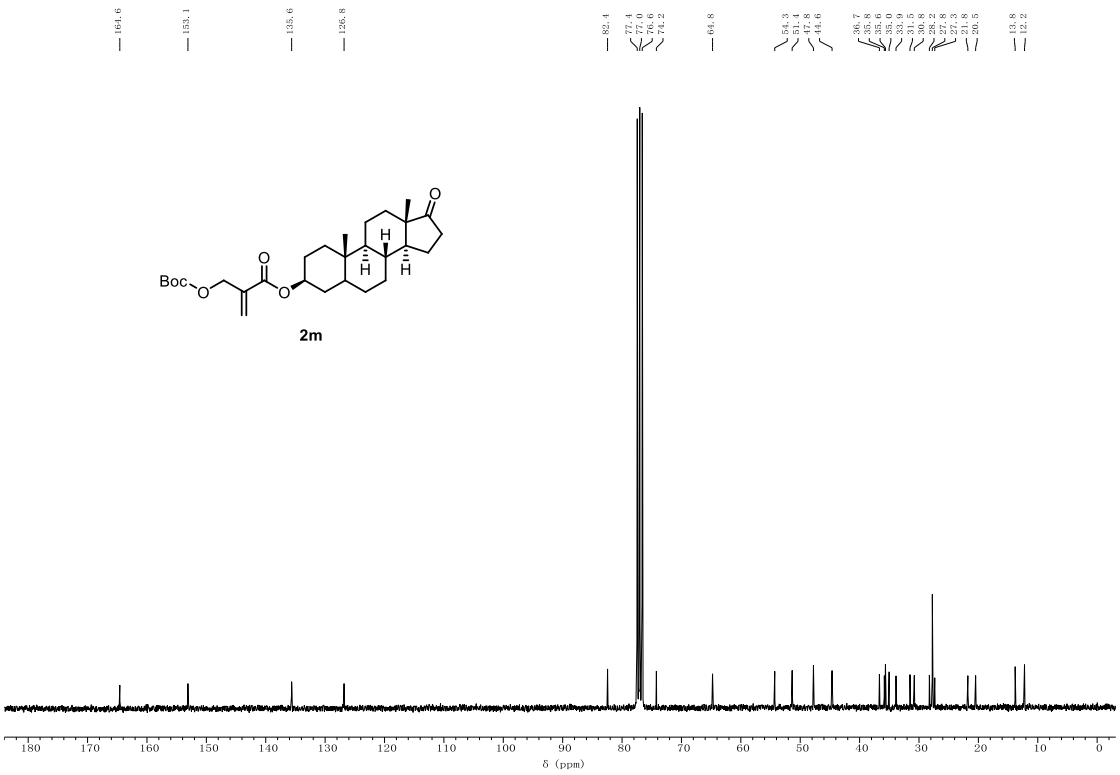


2l

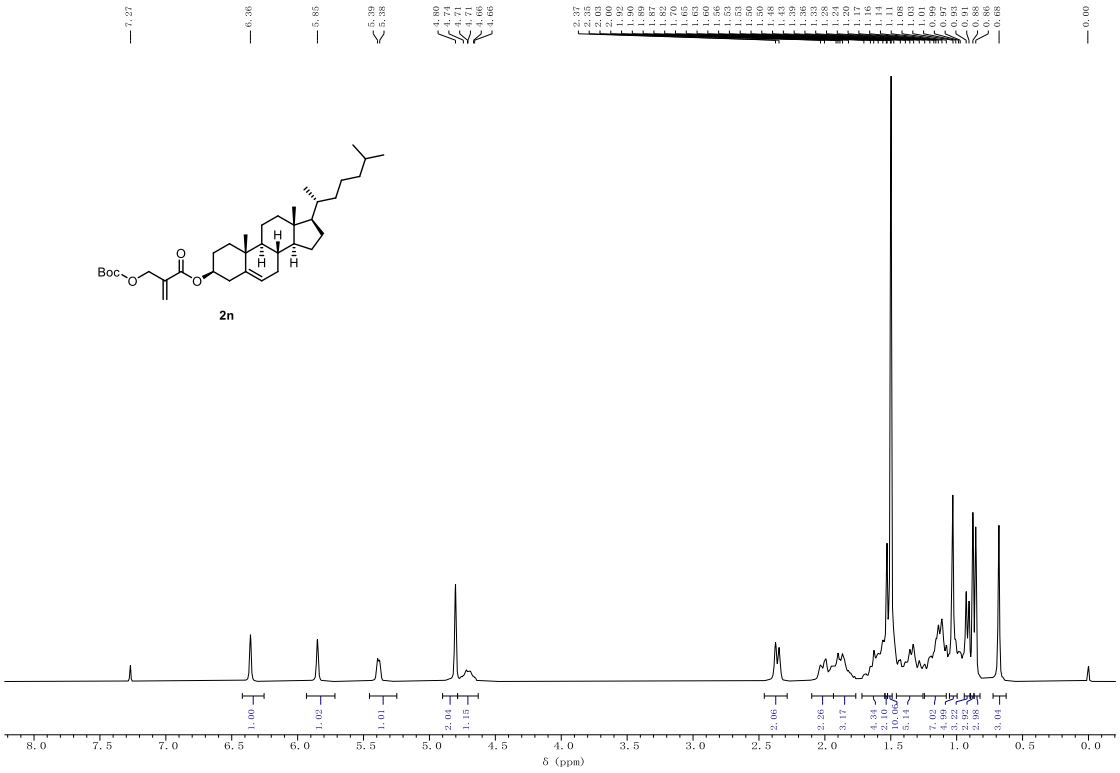
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2l**



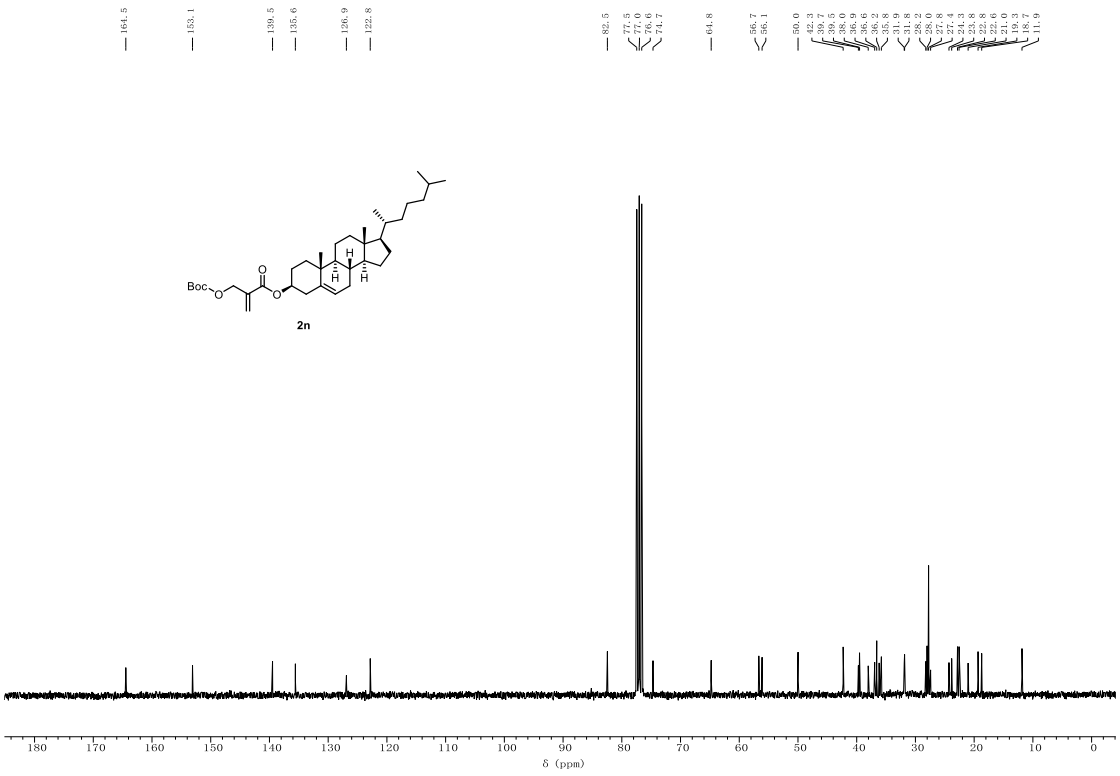
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2m**



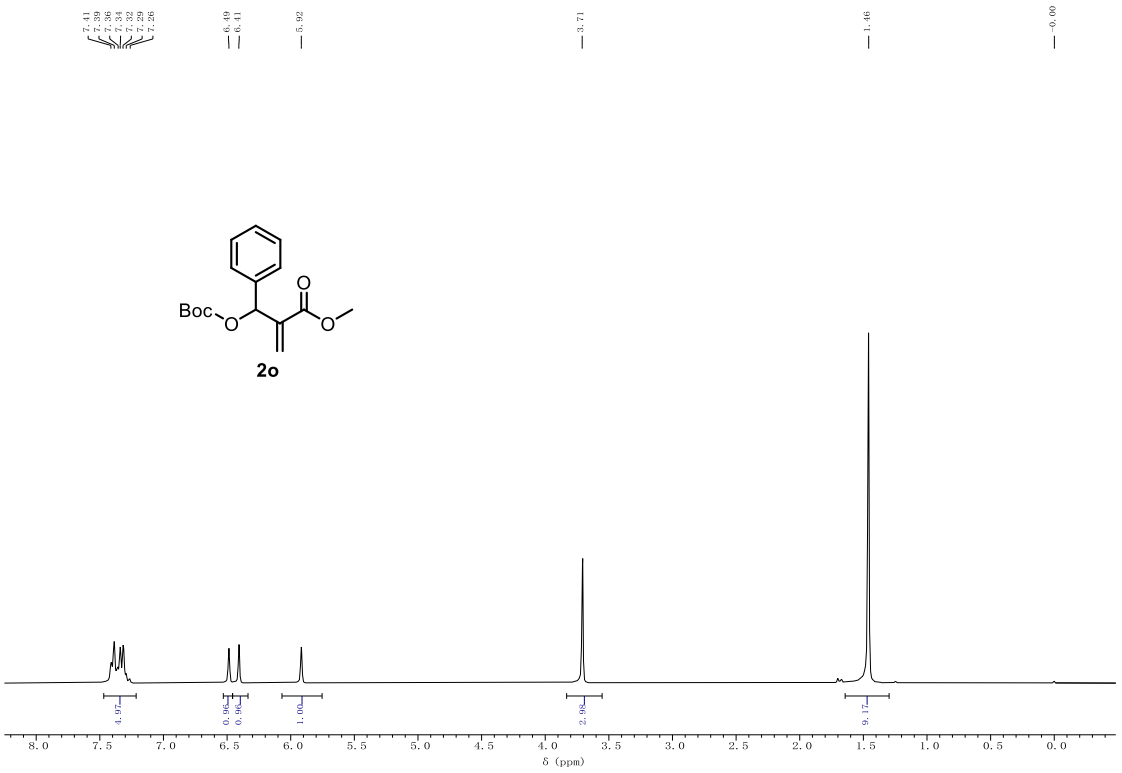
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2m**



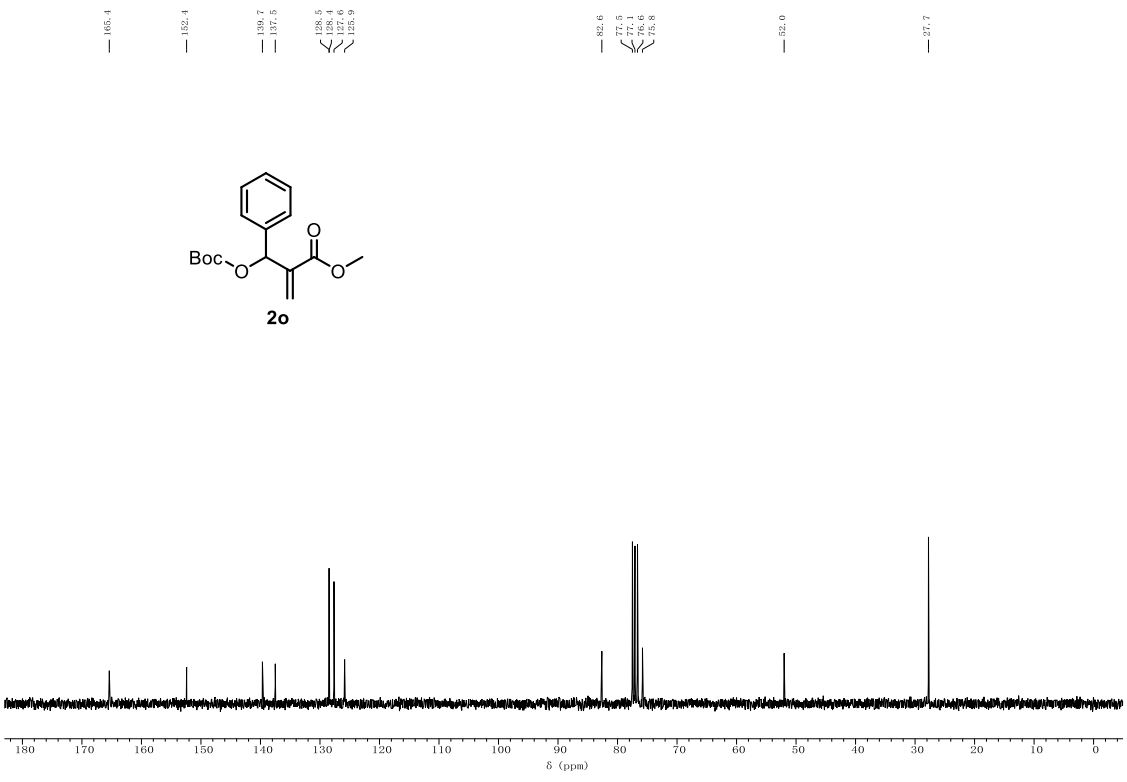
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2n**



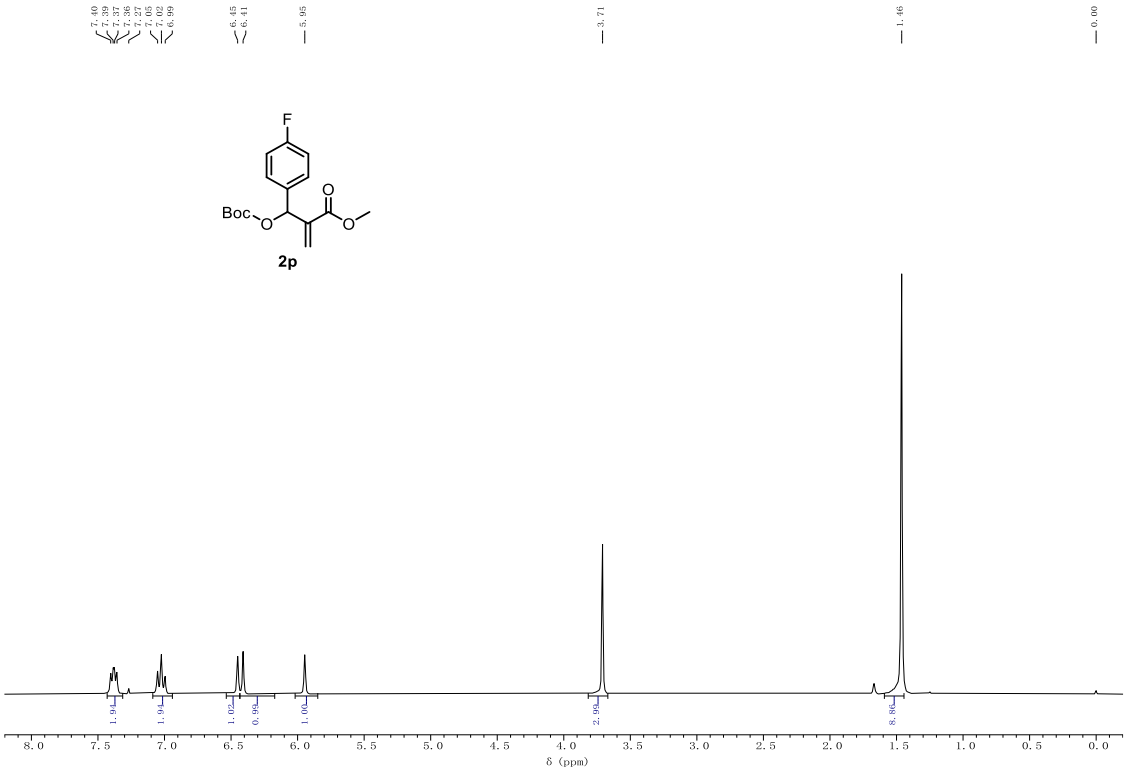
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2n**



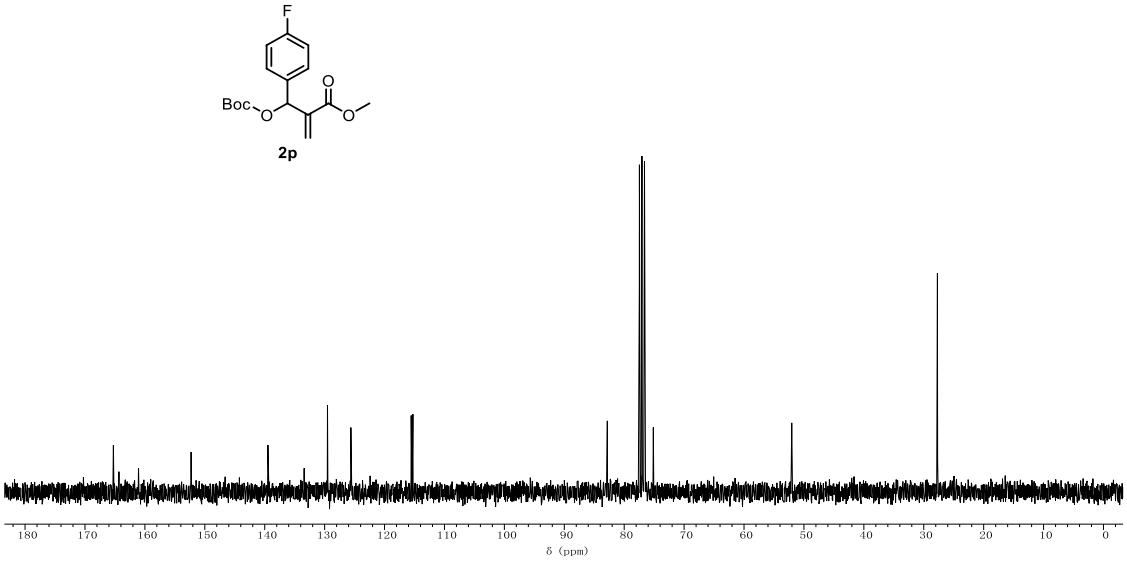
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2o**



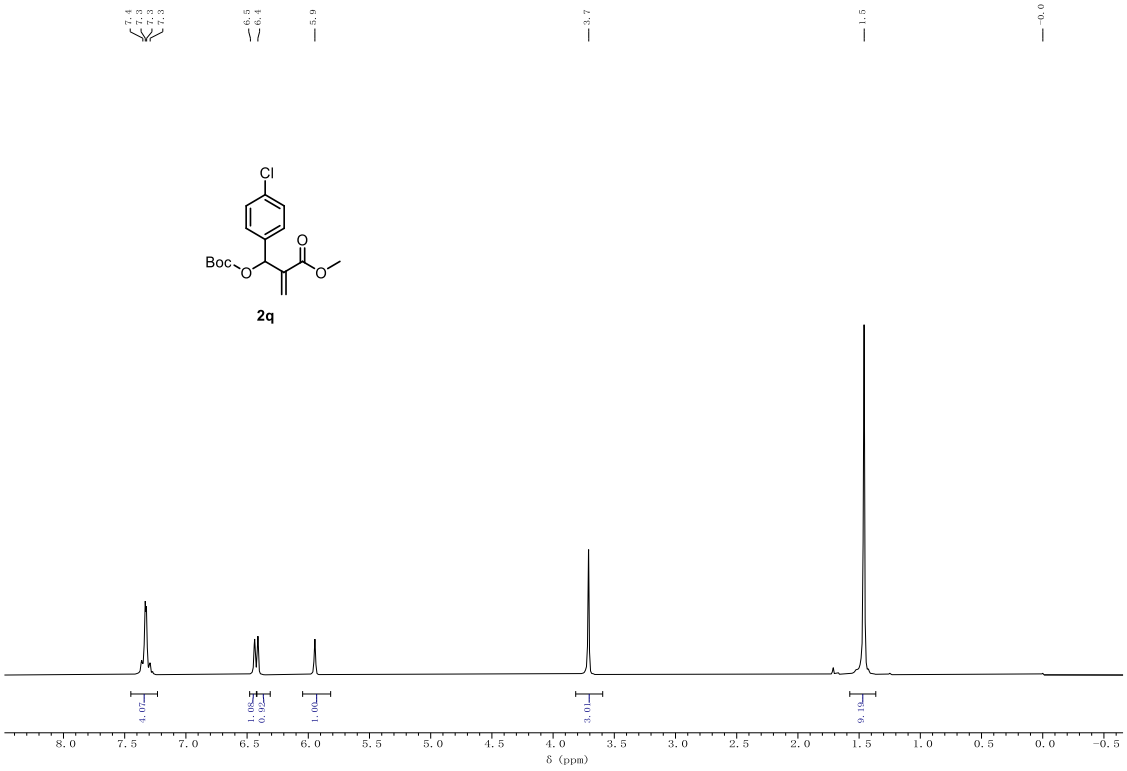
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2o**



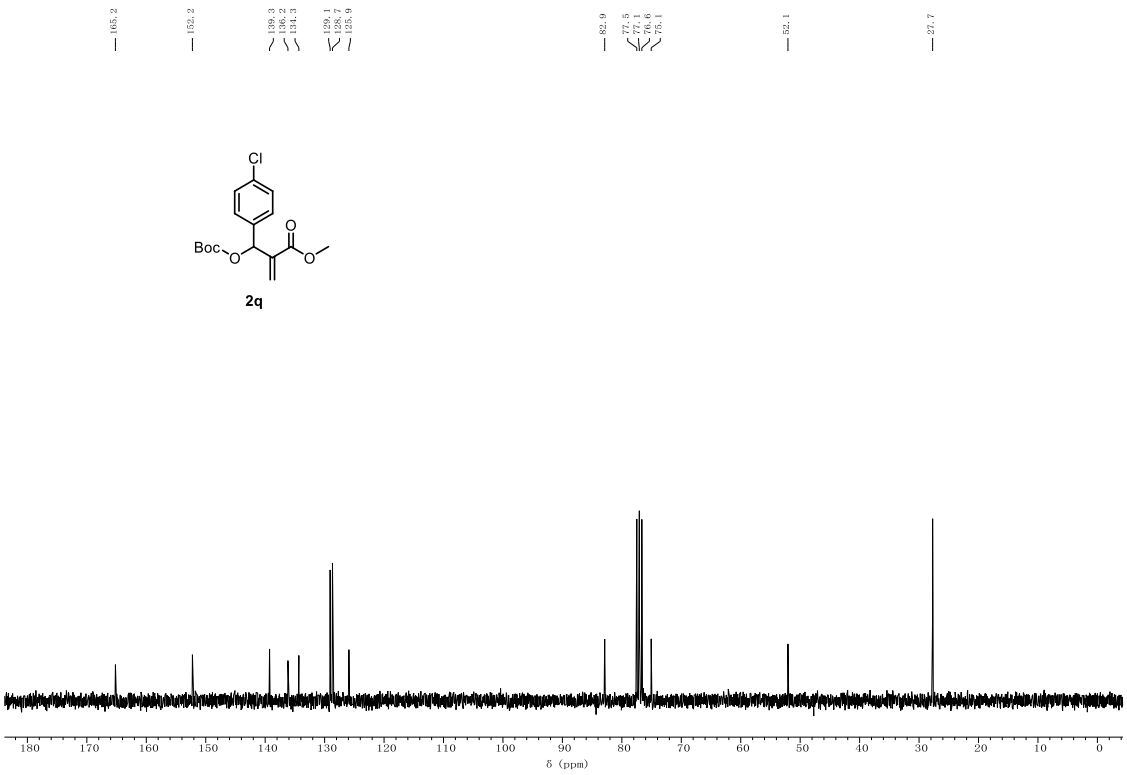
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2p**



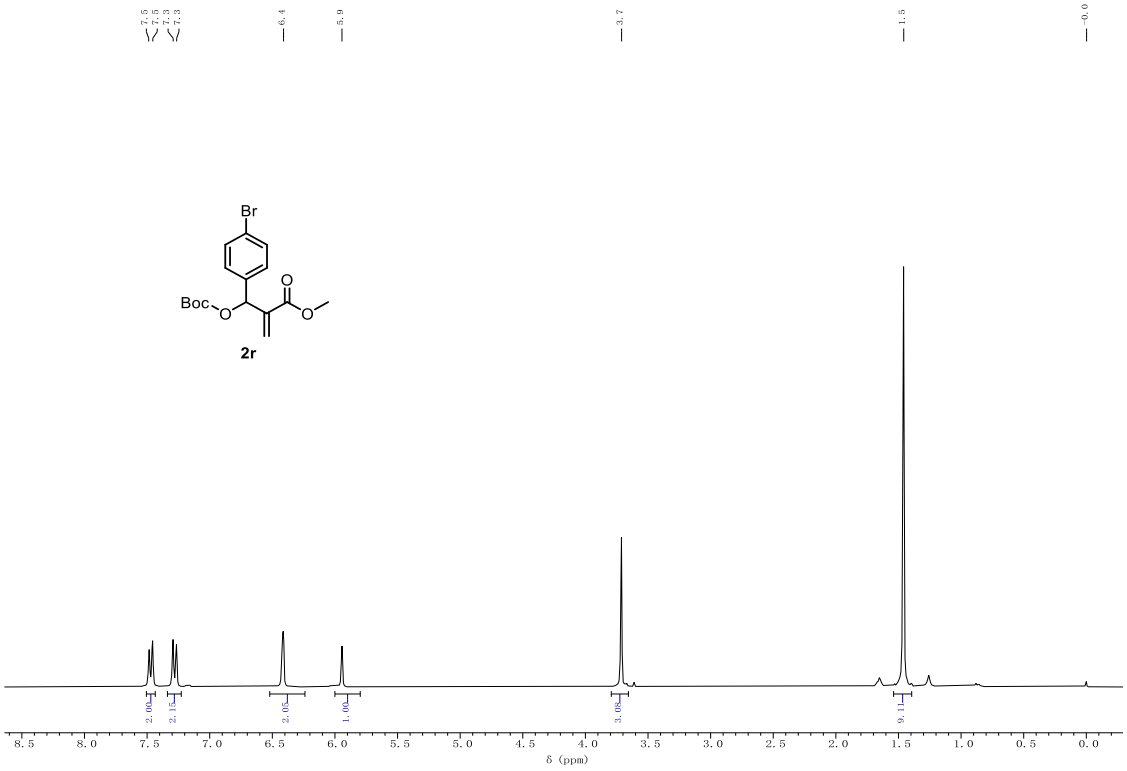
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2p**



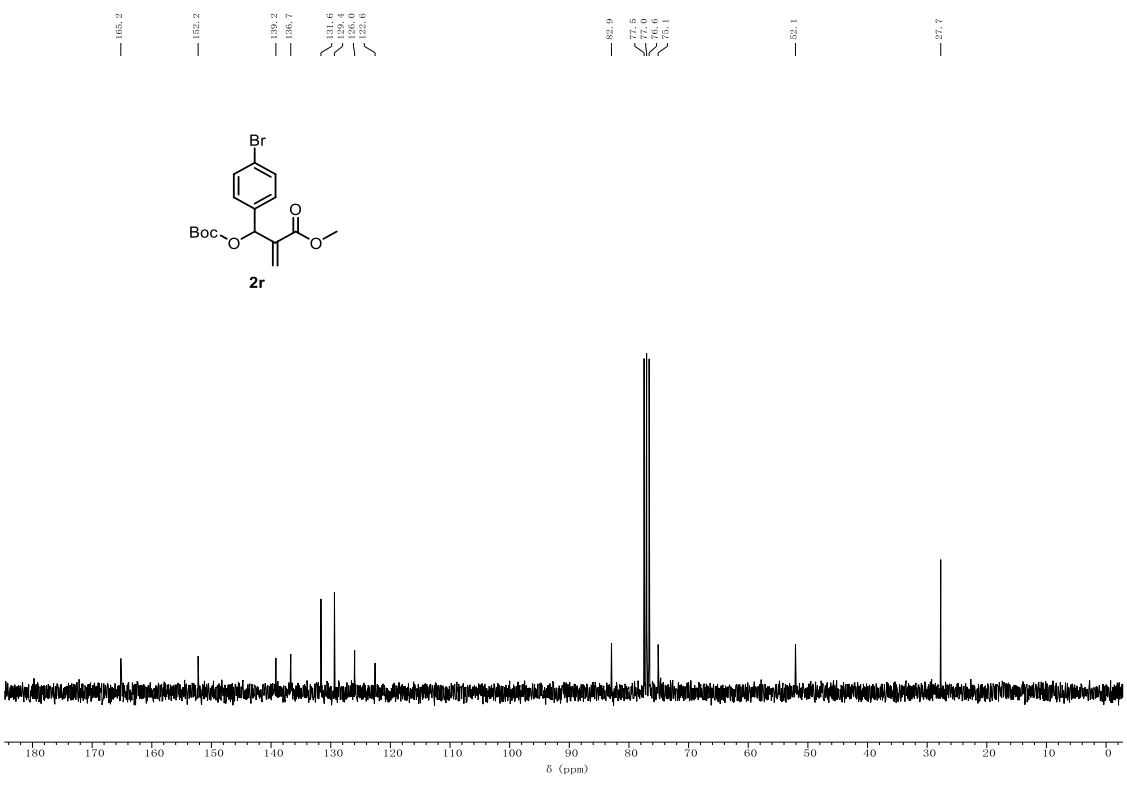
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2q**



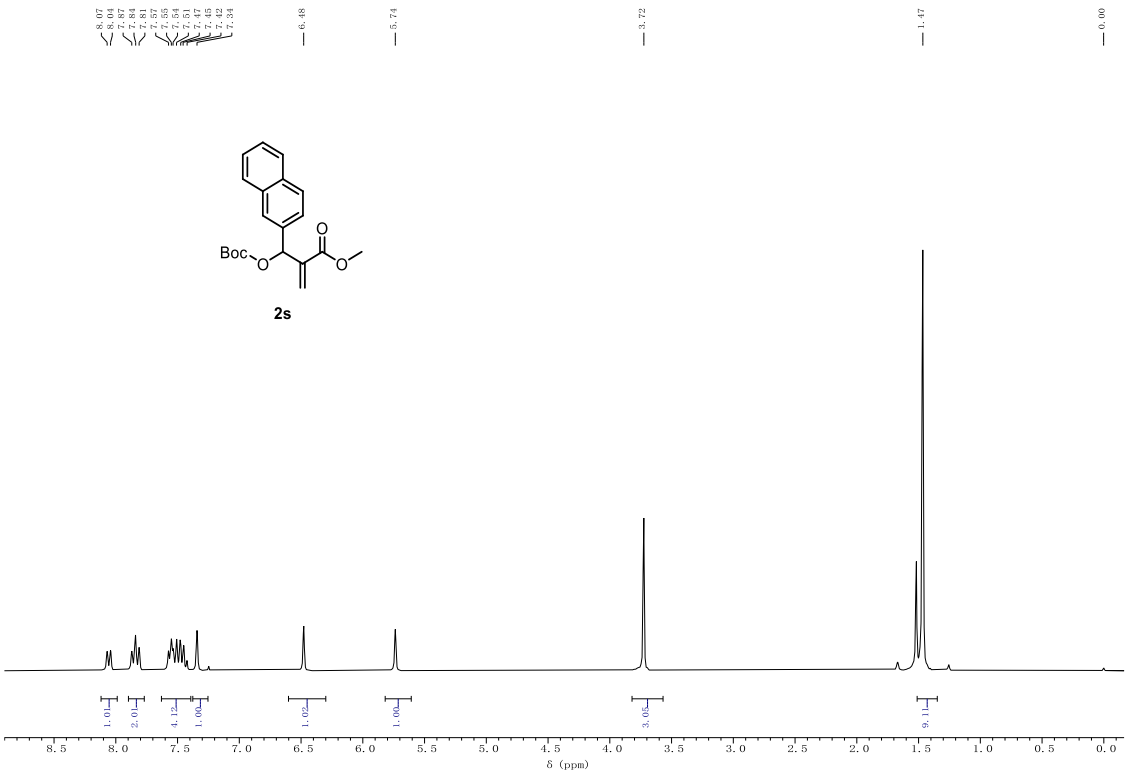
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2q**



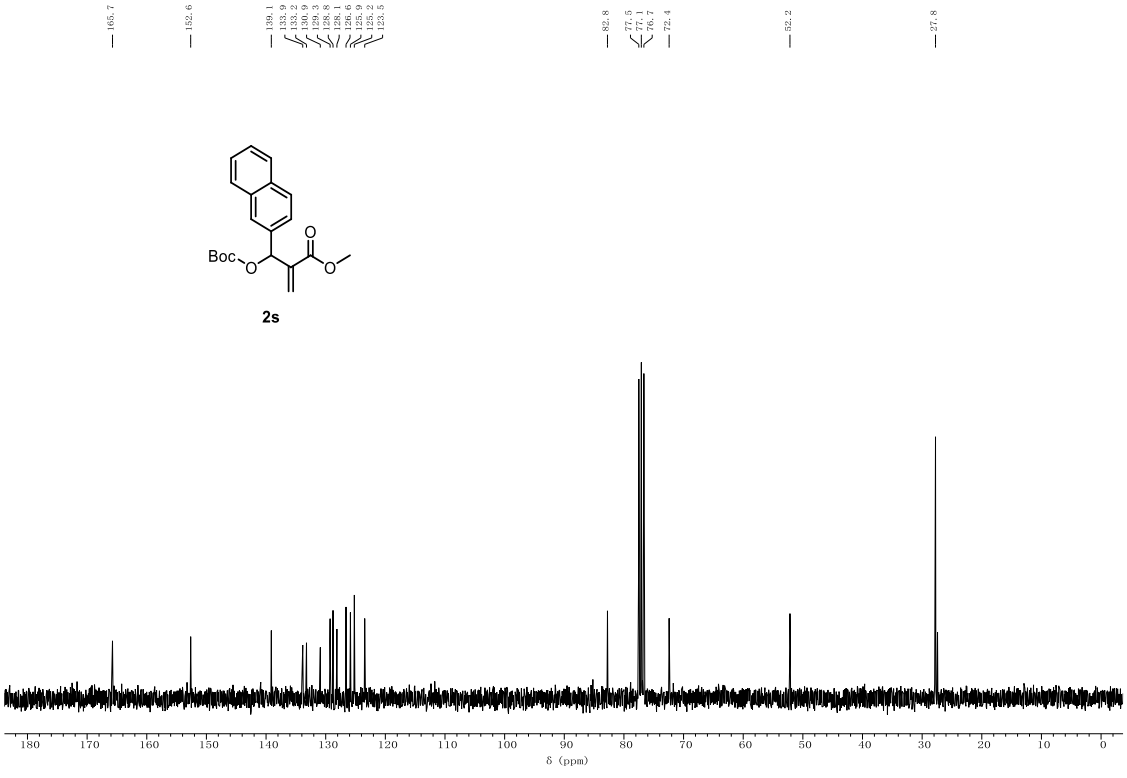
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2r**



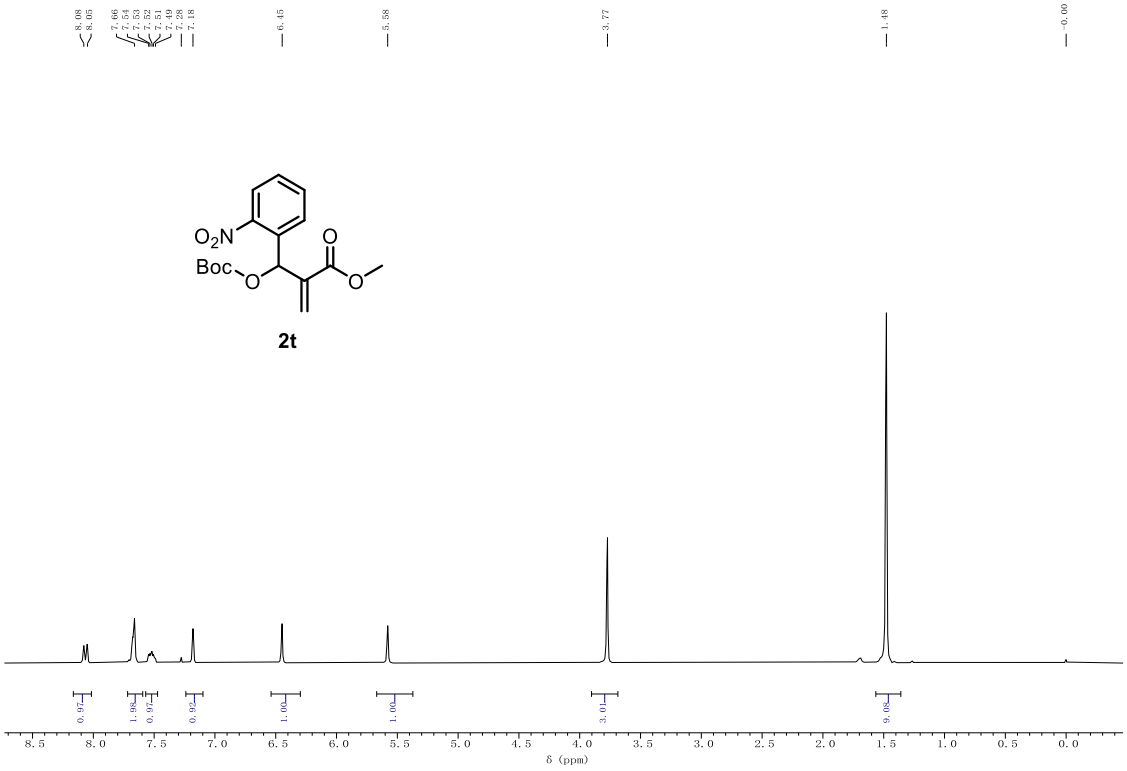
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2r**



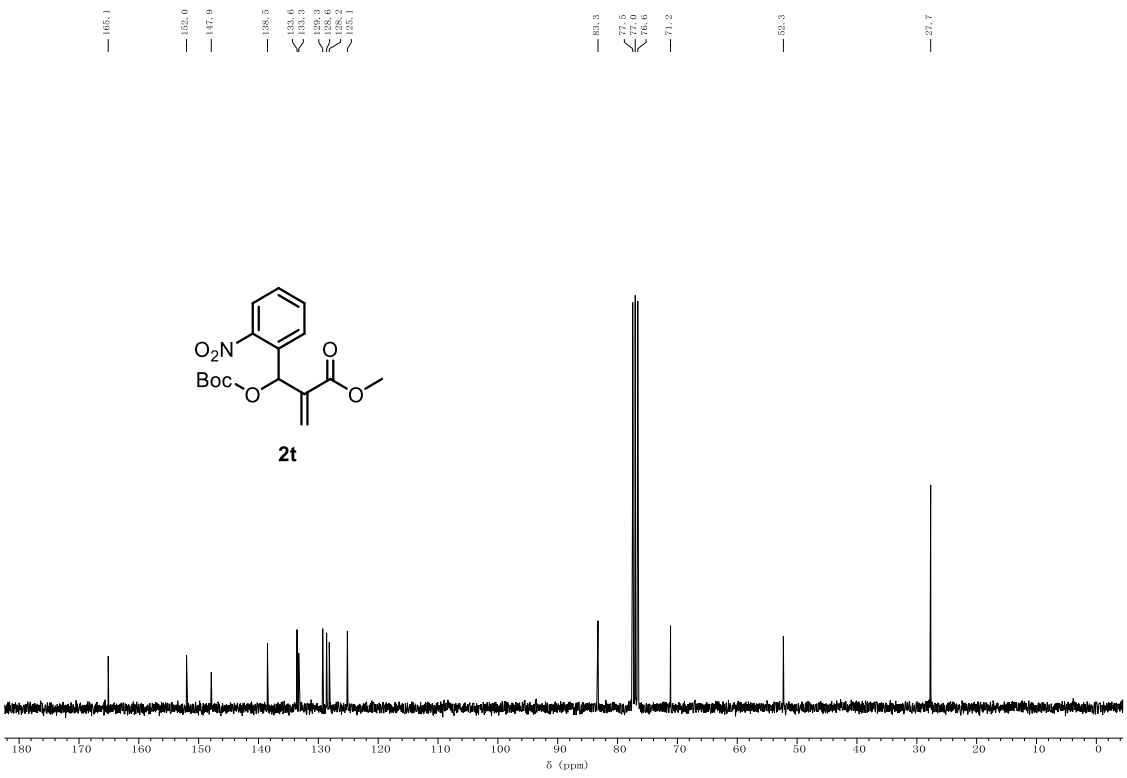
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2s**



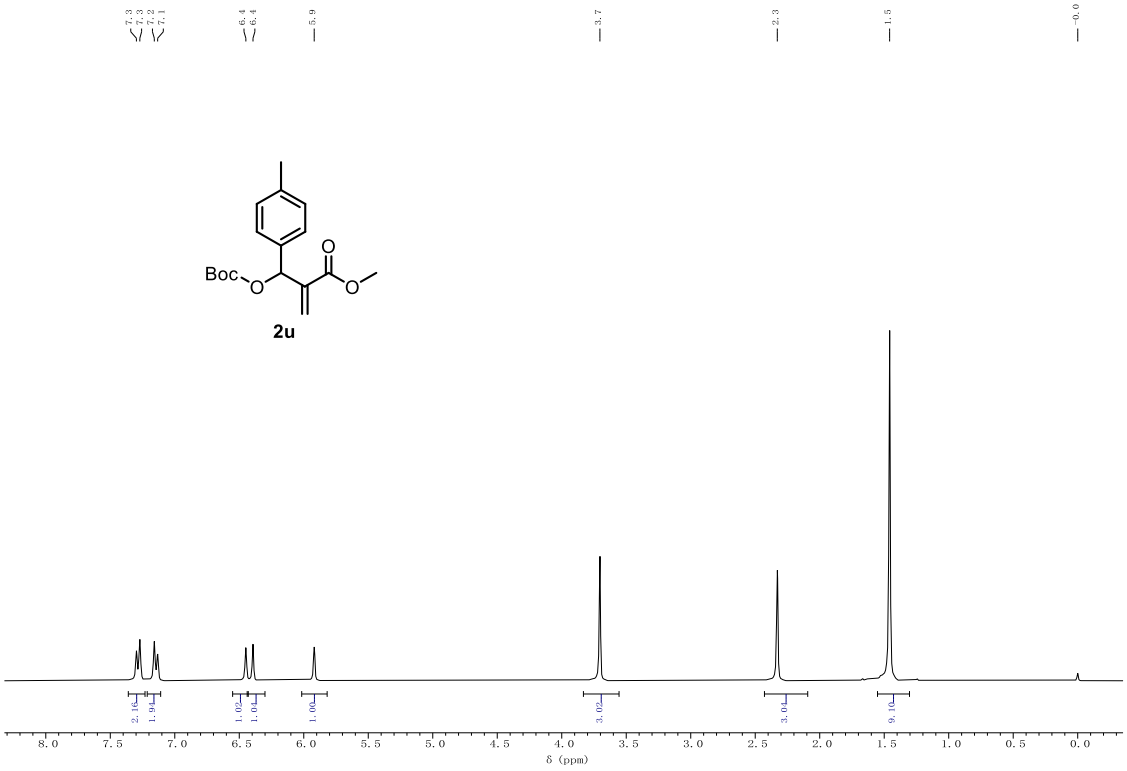
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2s**



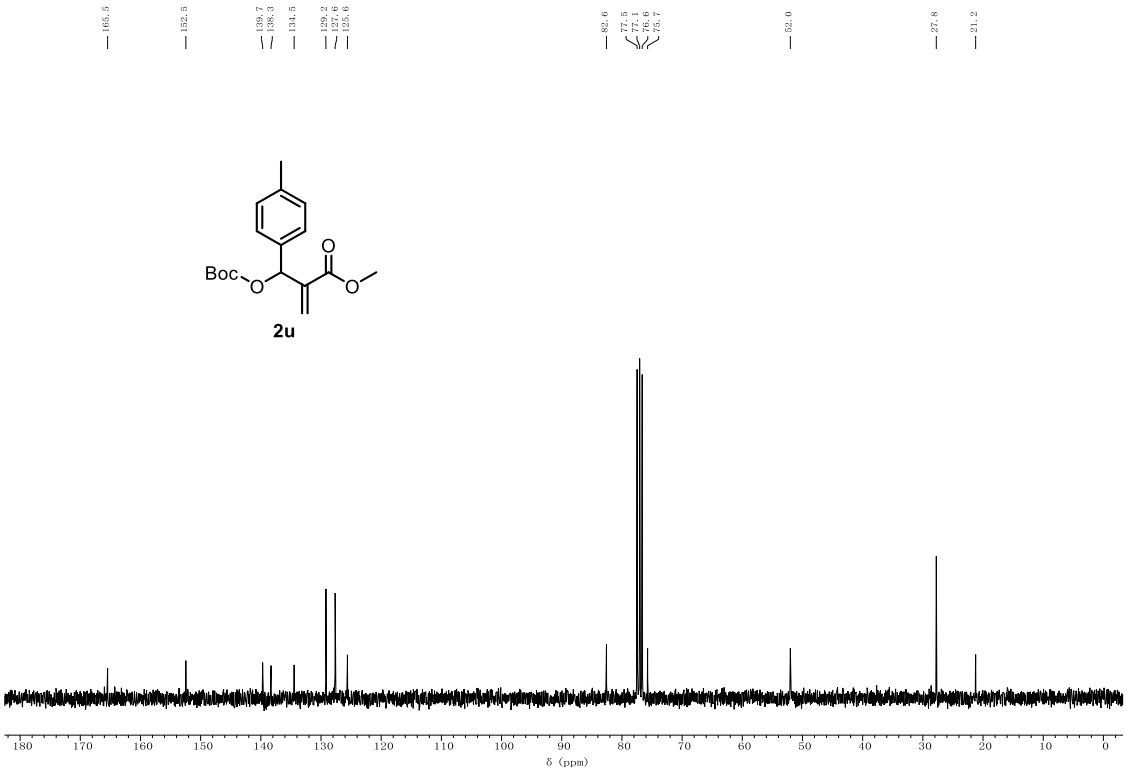
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2t**



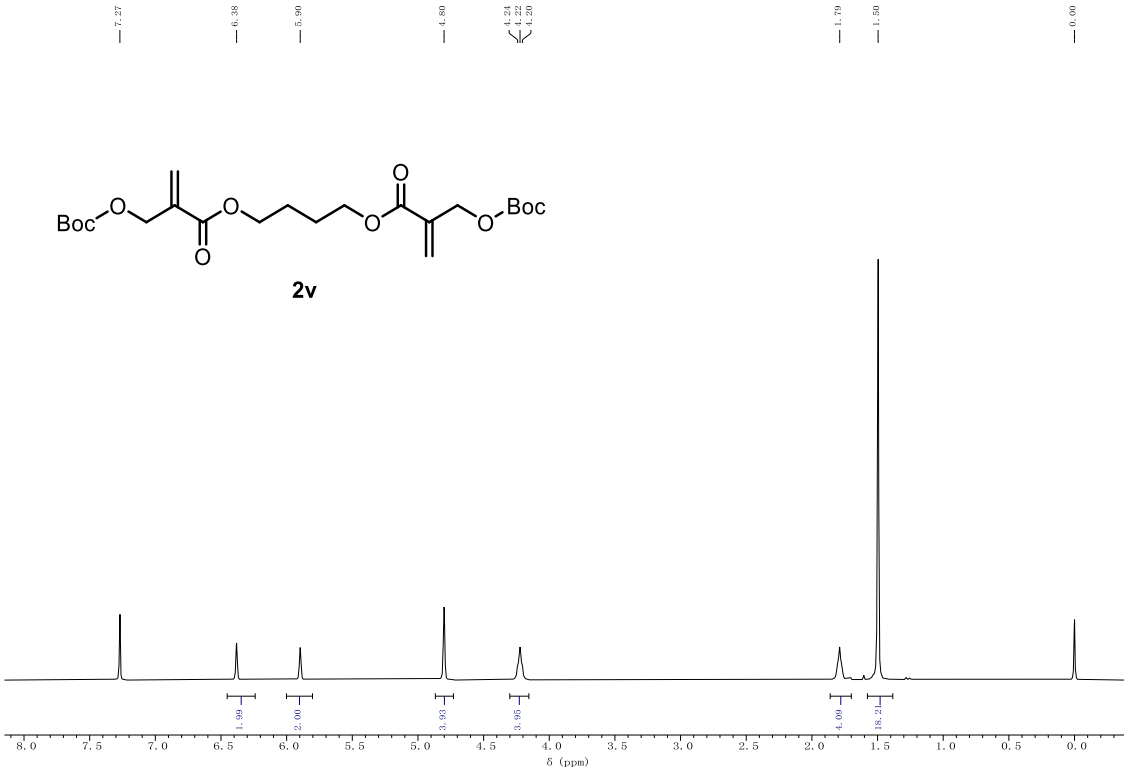
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2t**



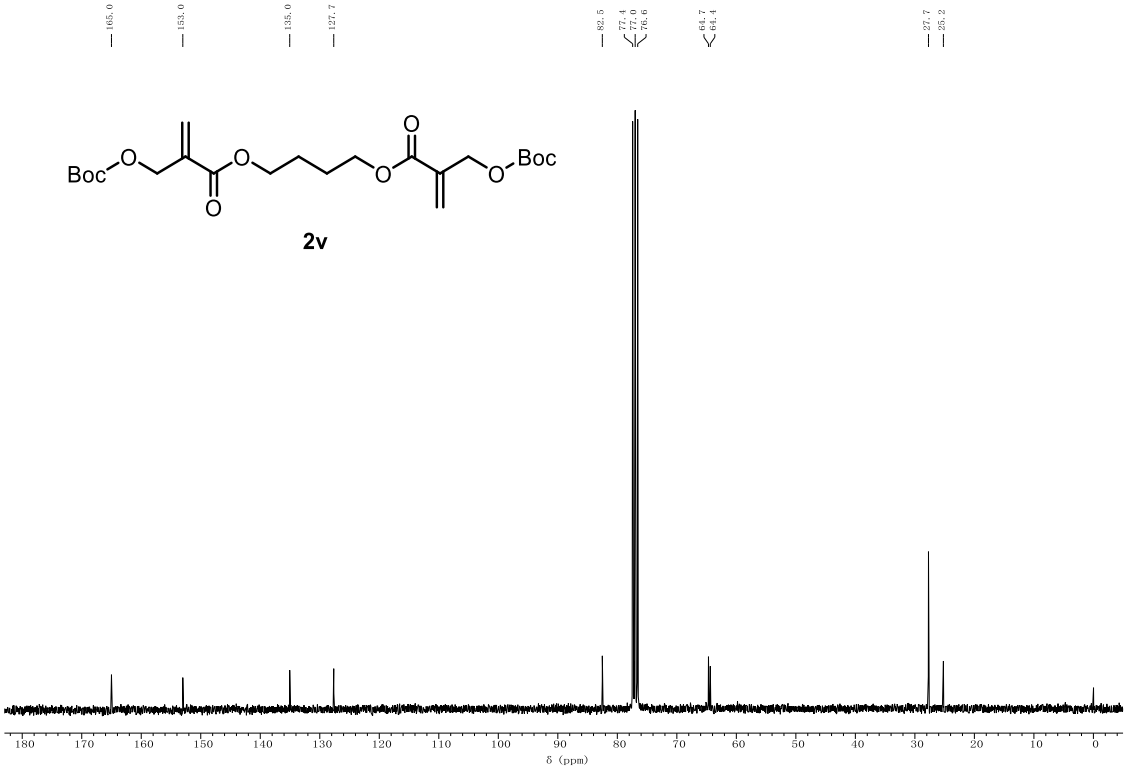
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2u**



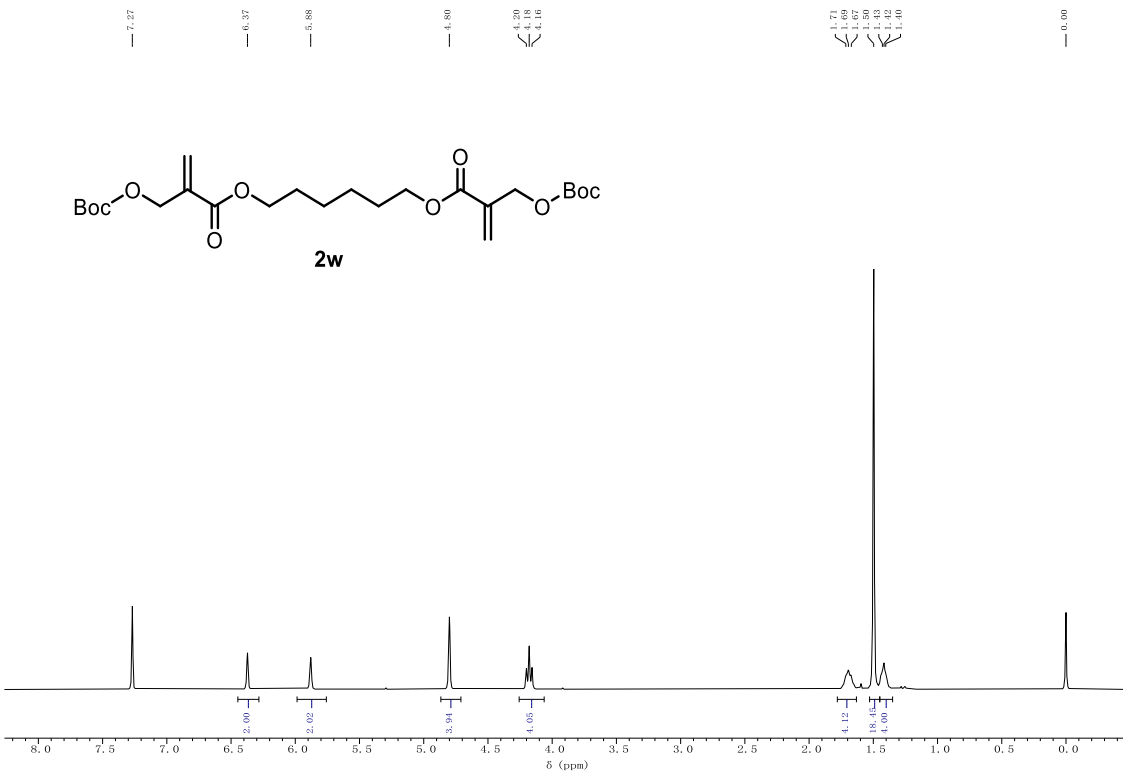
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2u**



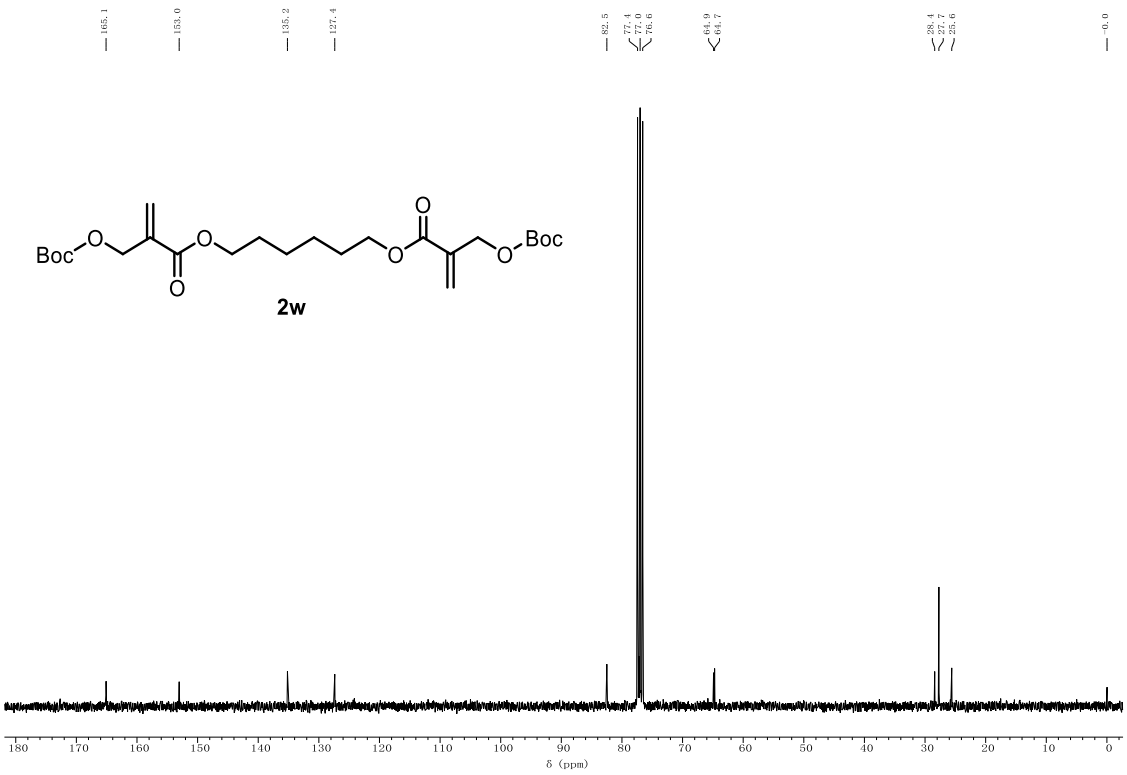
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2v**



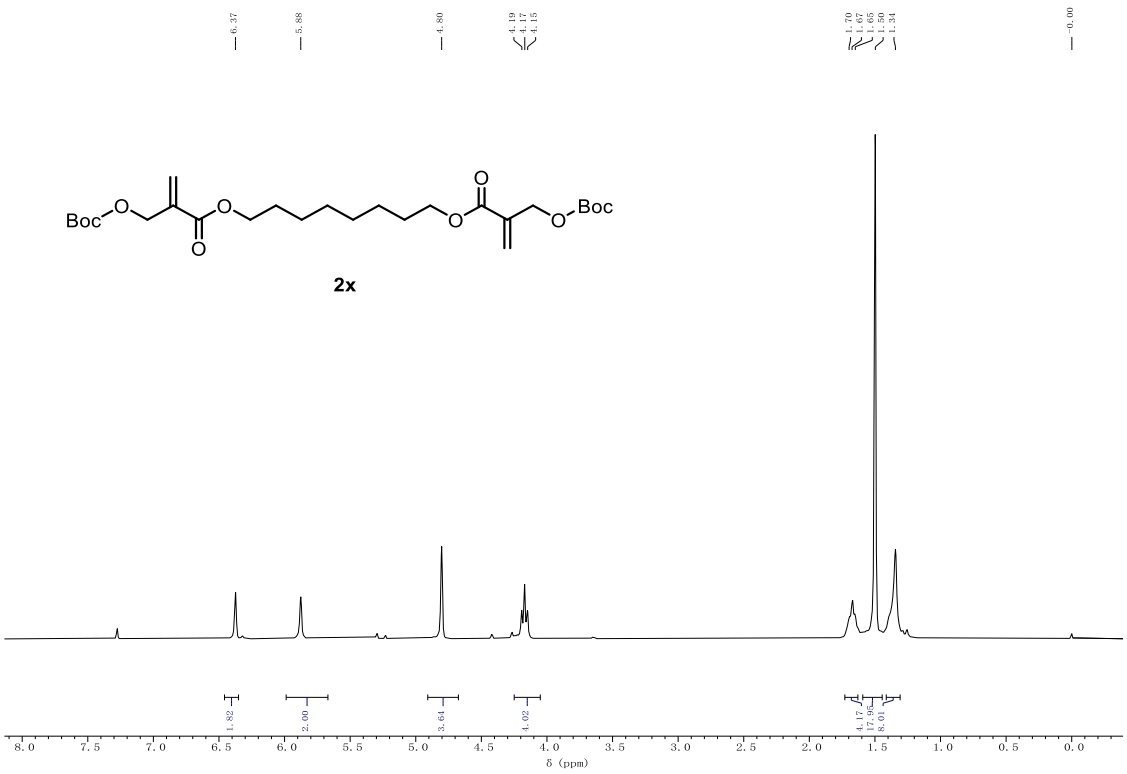
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2v**



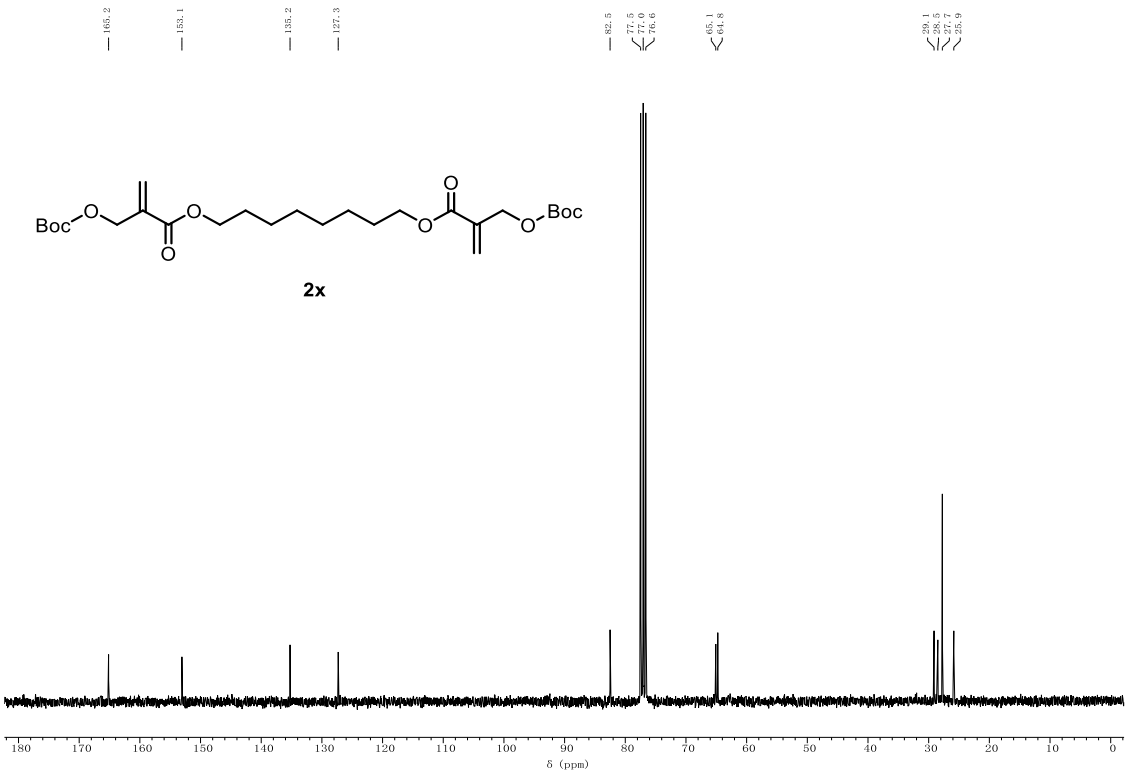
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2w**



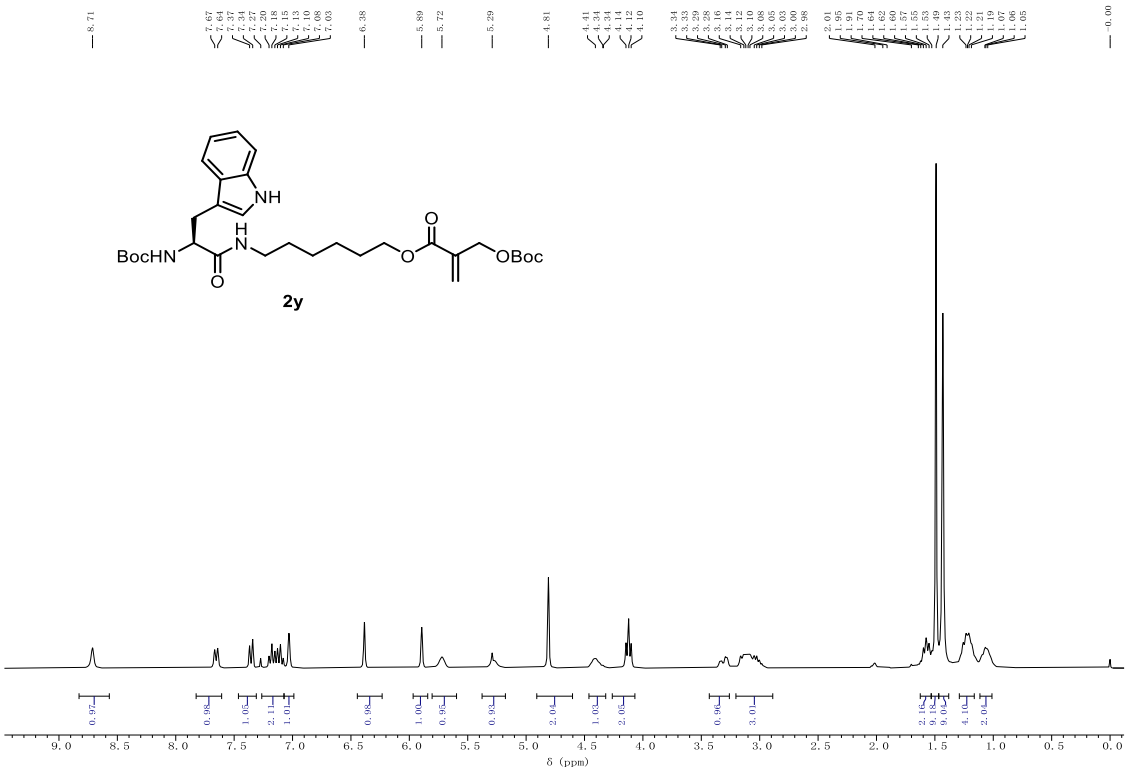
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2w**



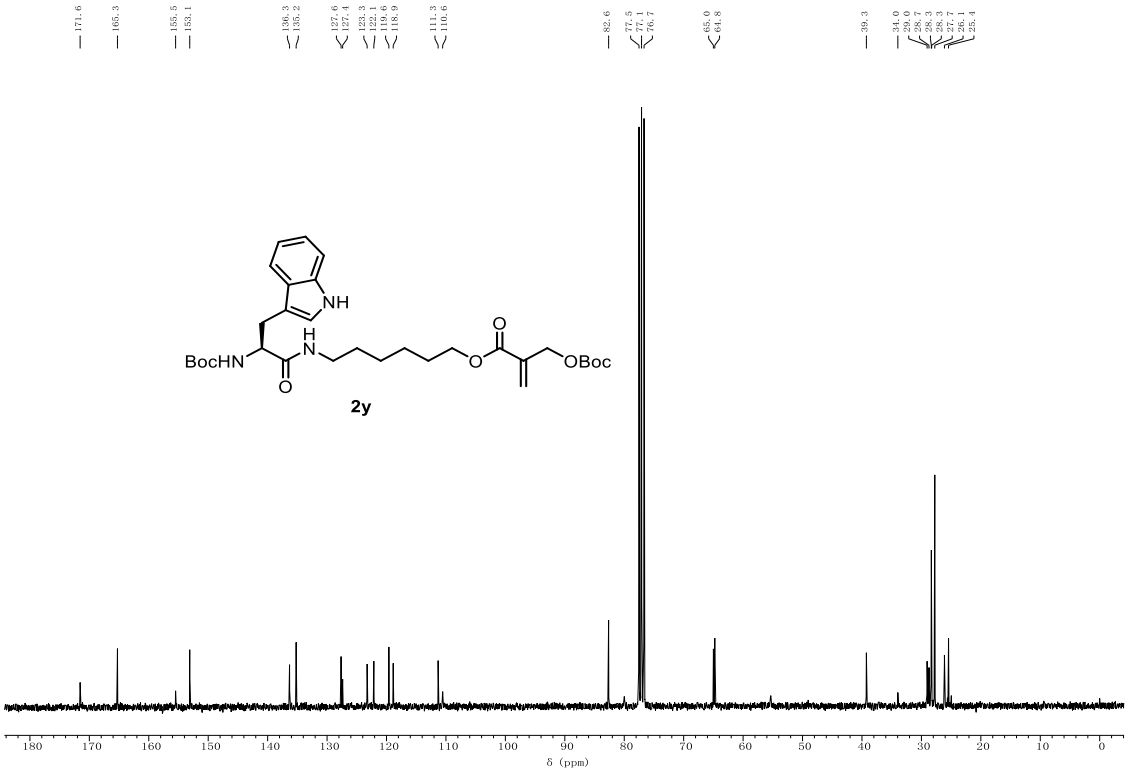
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2x**



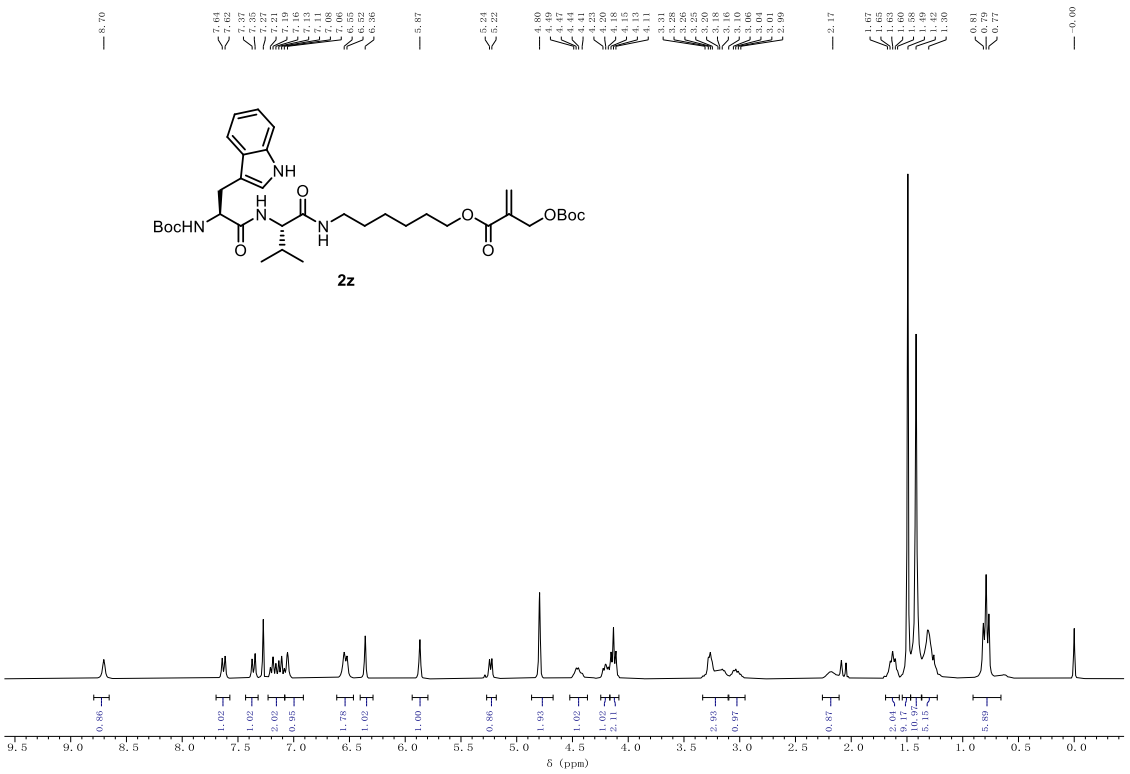
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2x**



^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2y**

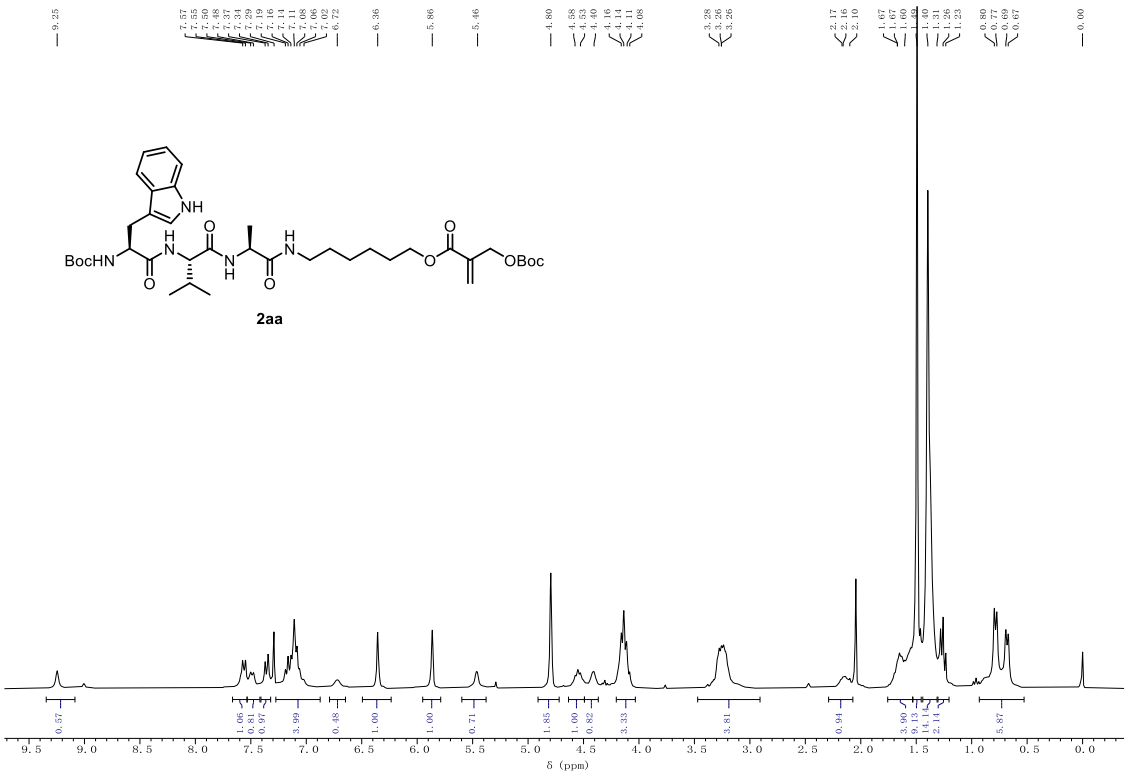


^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2y**

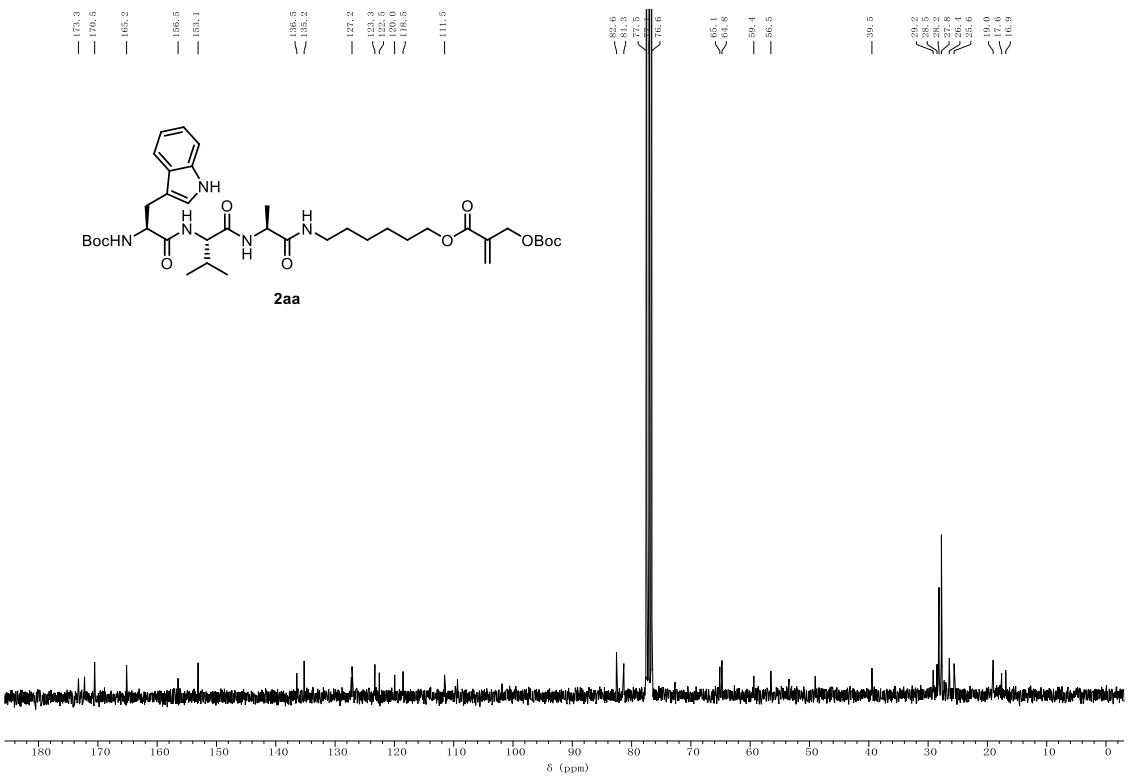


^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2z**

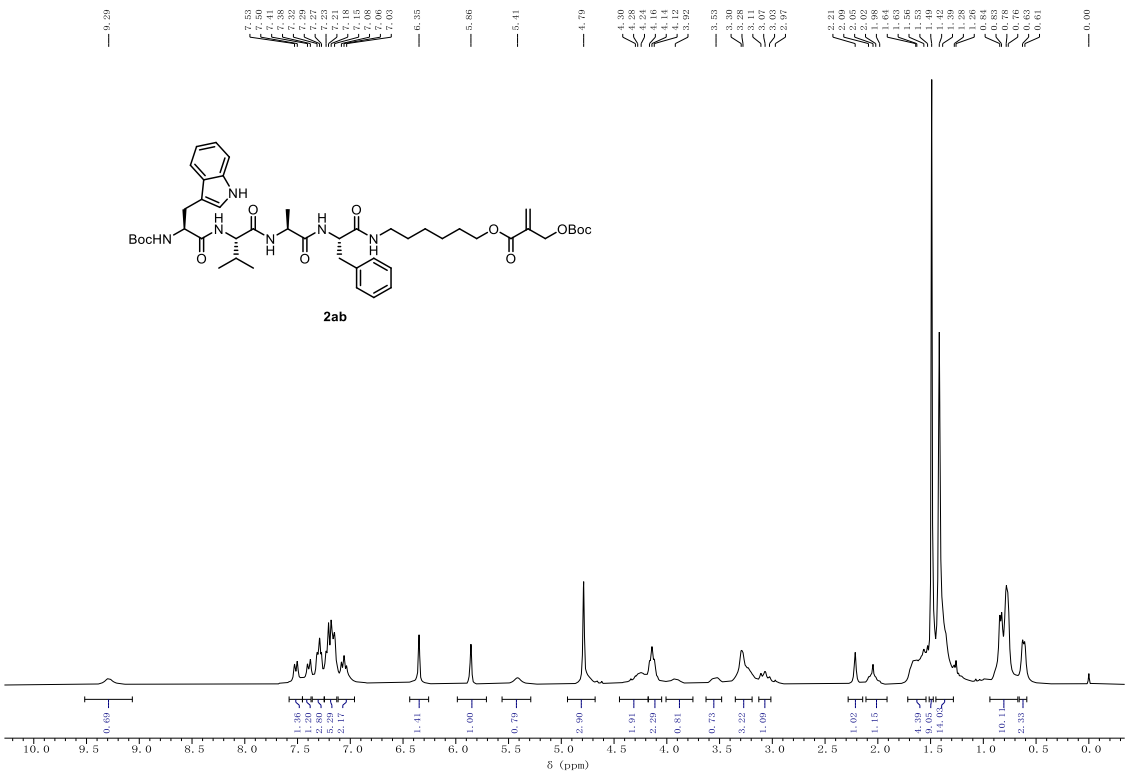
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2z**



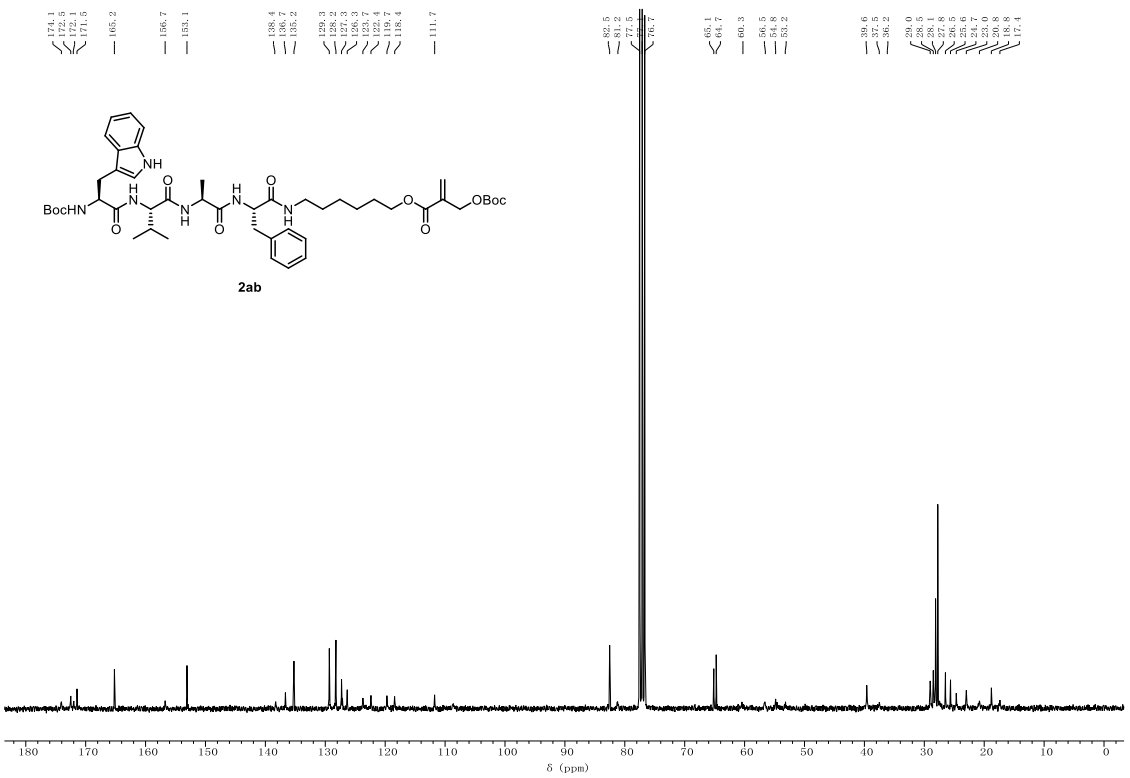
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2aa**



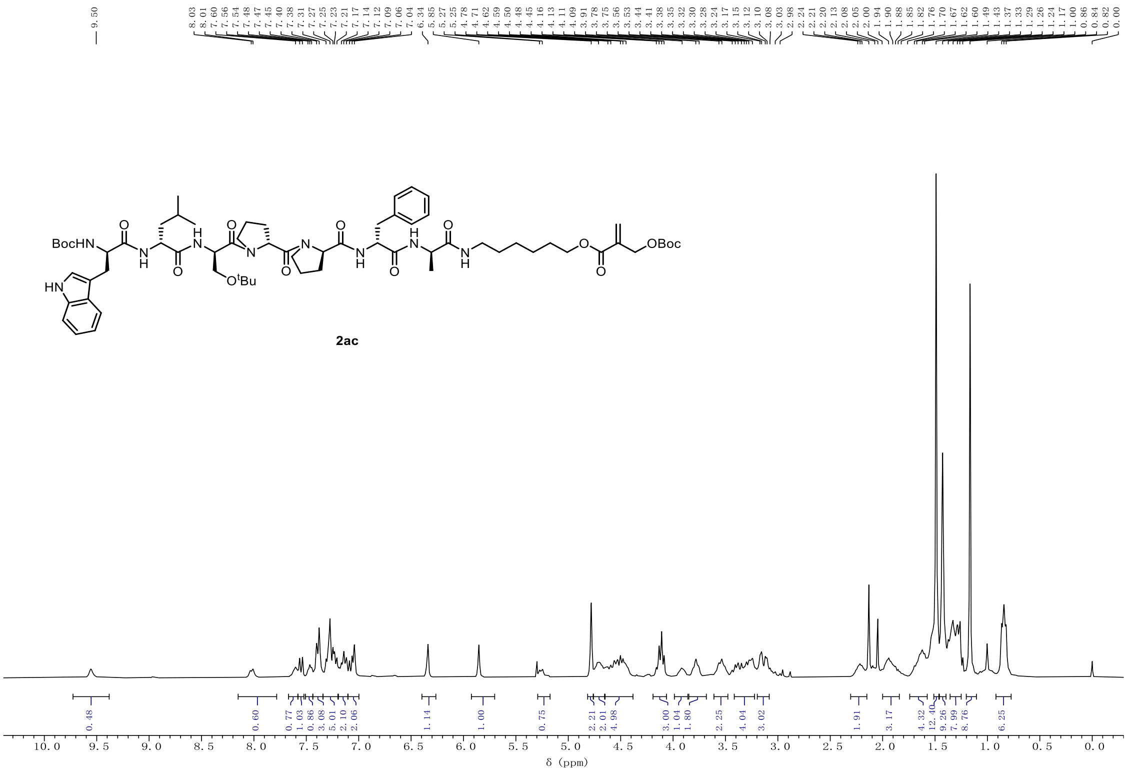
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2aa**



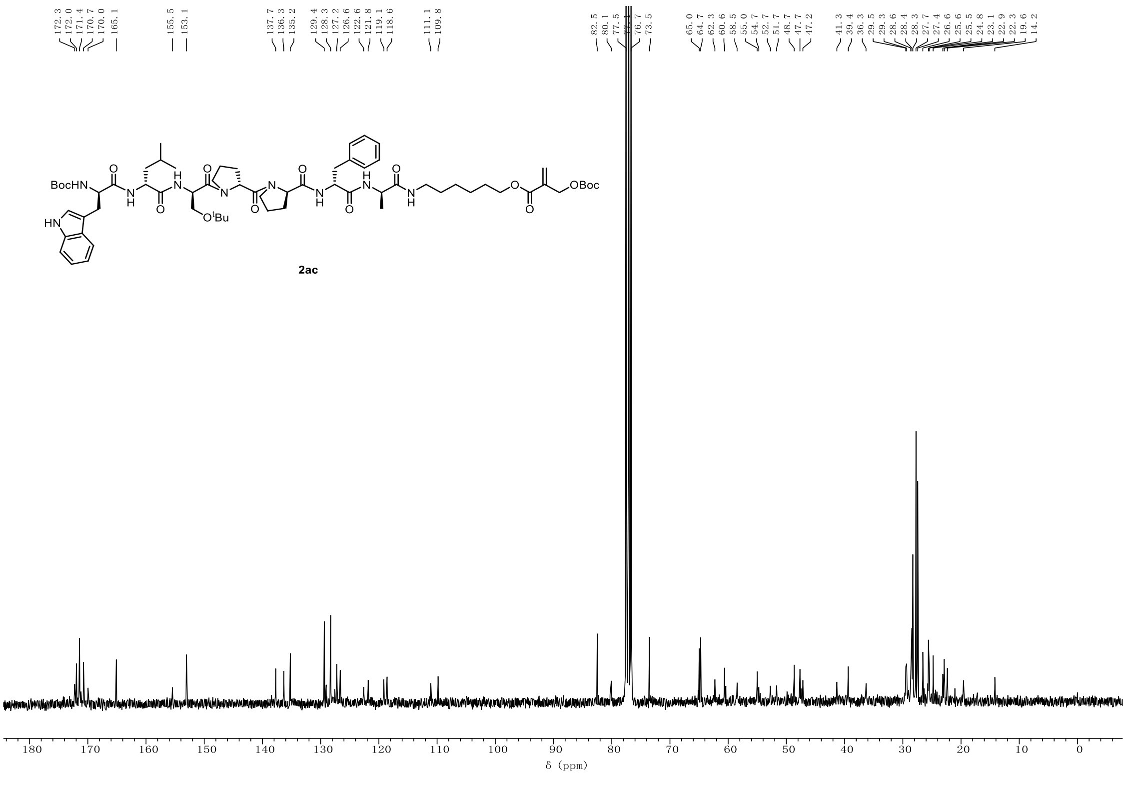
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2ab**



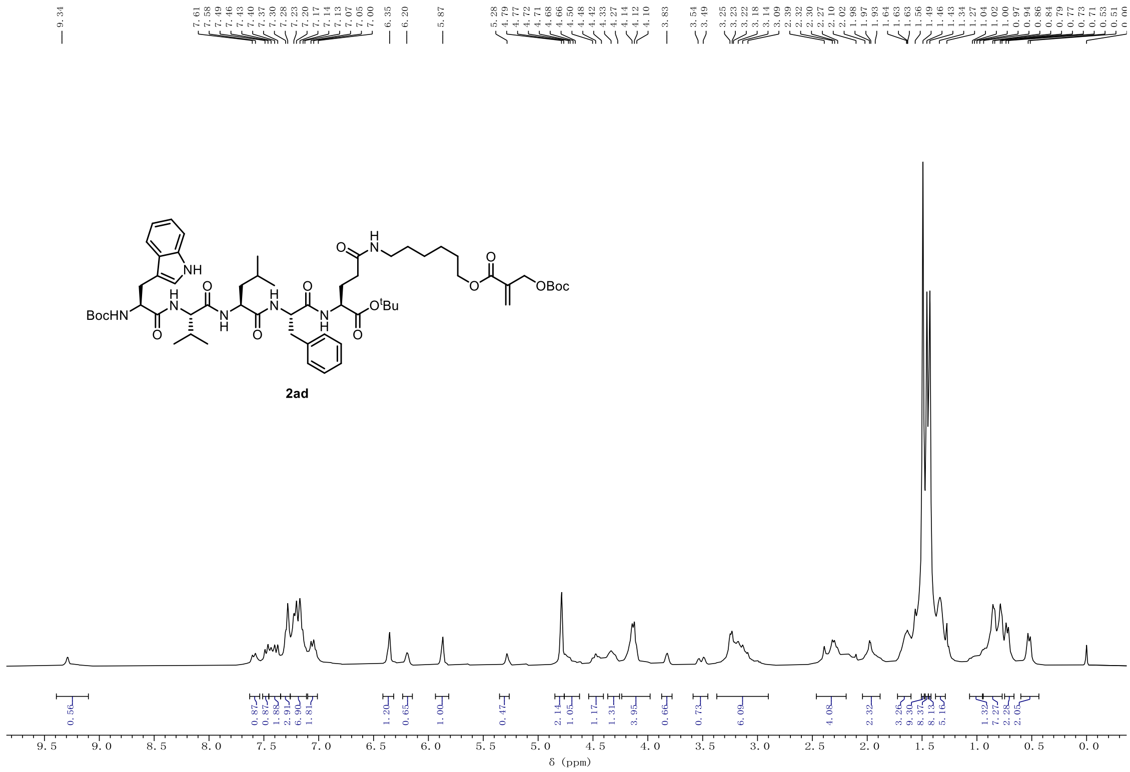
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2ab**



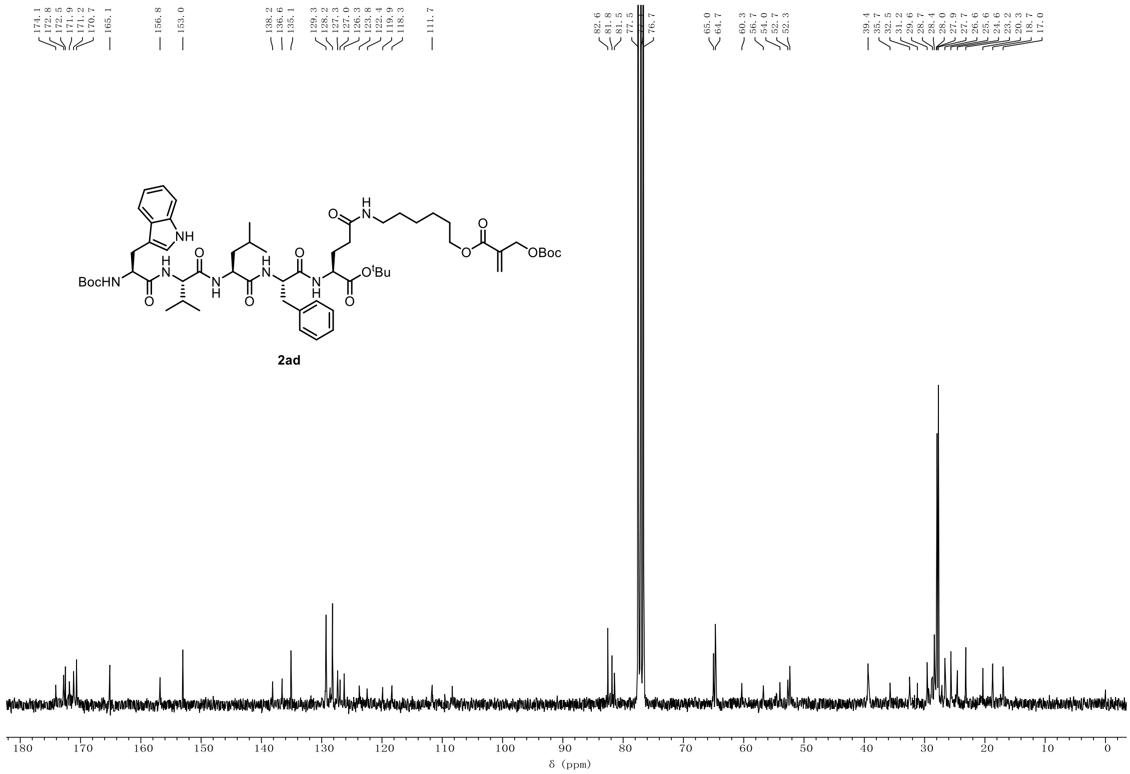
^{1}**H NMR** (300 MHz, $CDCl_3$) spectrum of **2ac**



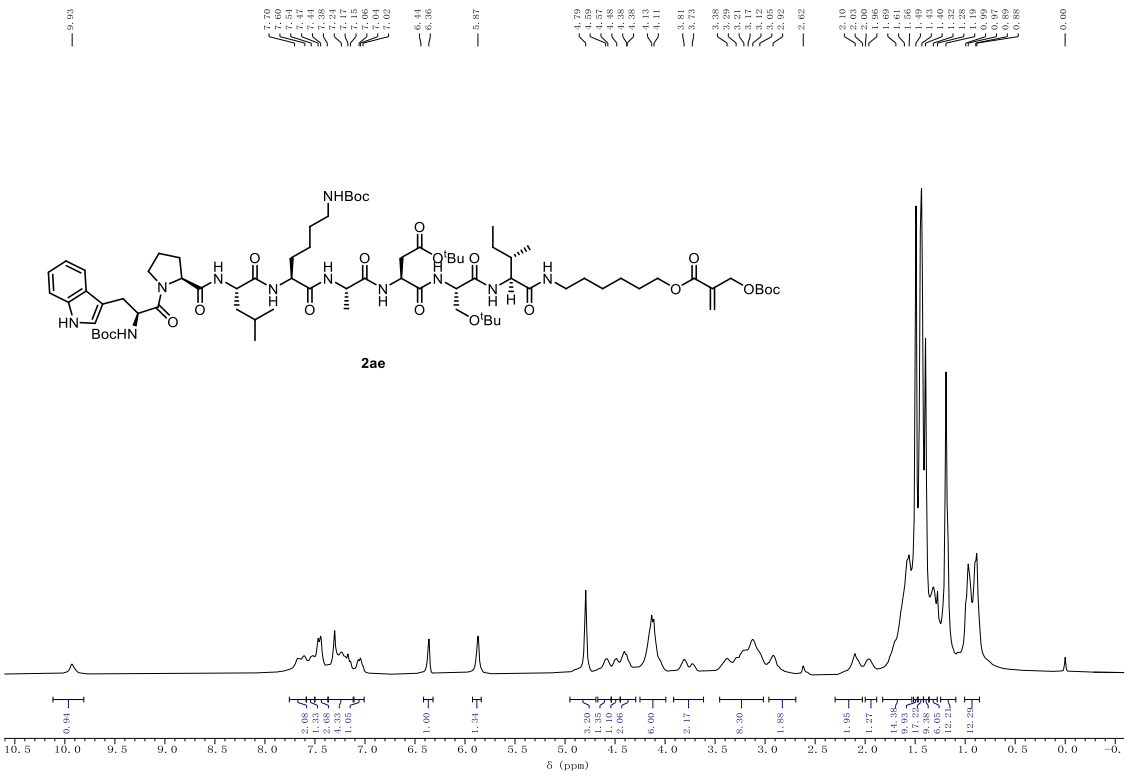
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2ac**



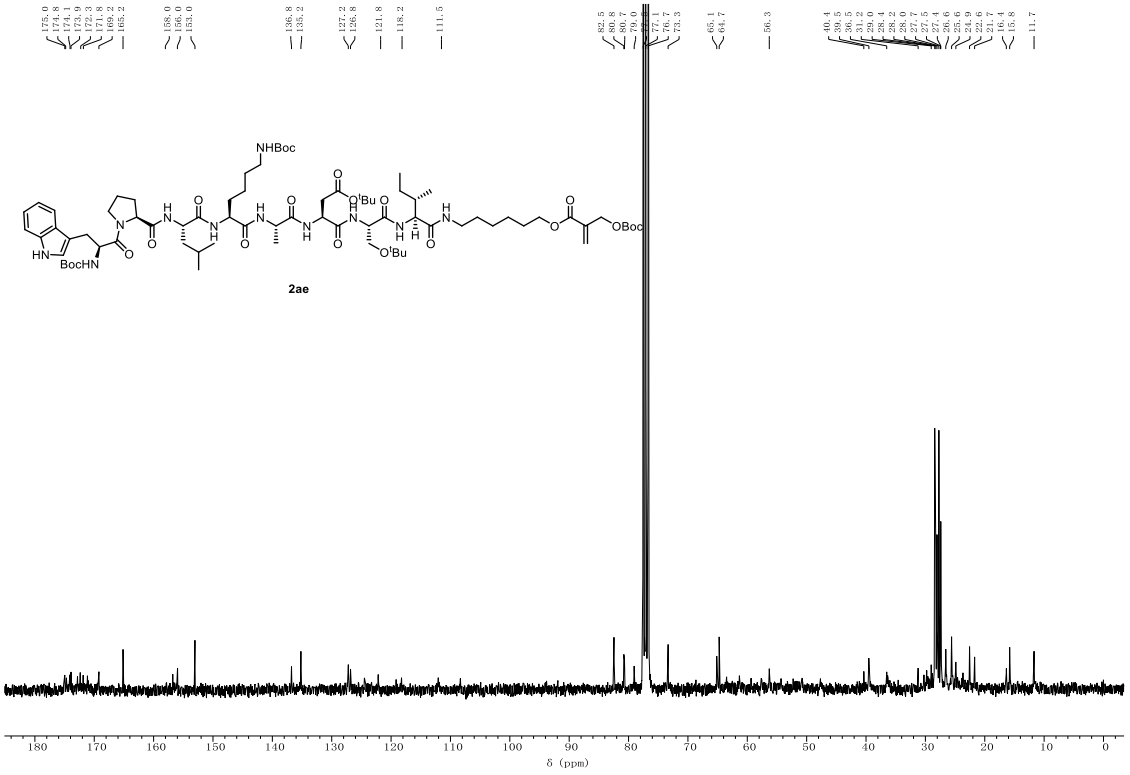
^{1}**H NMR** (300 MHz, $CDCl_3$) spectrum of **2ad**



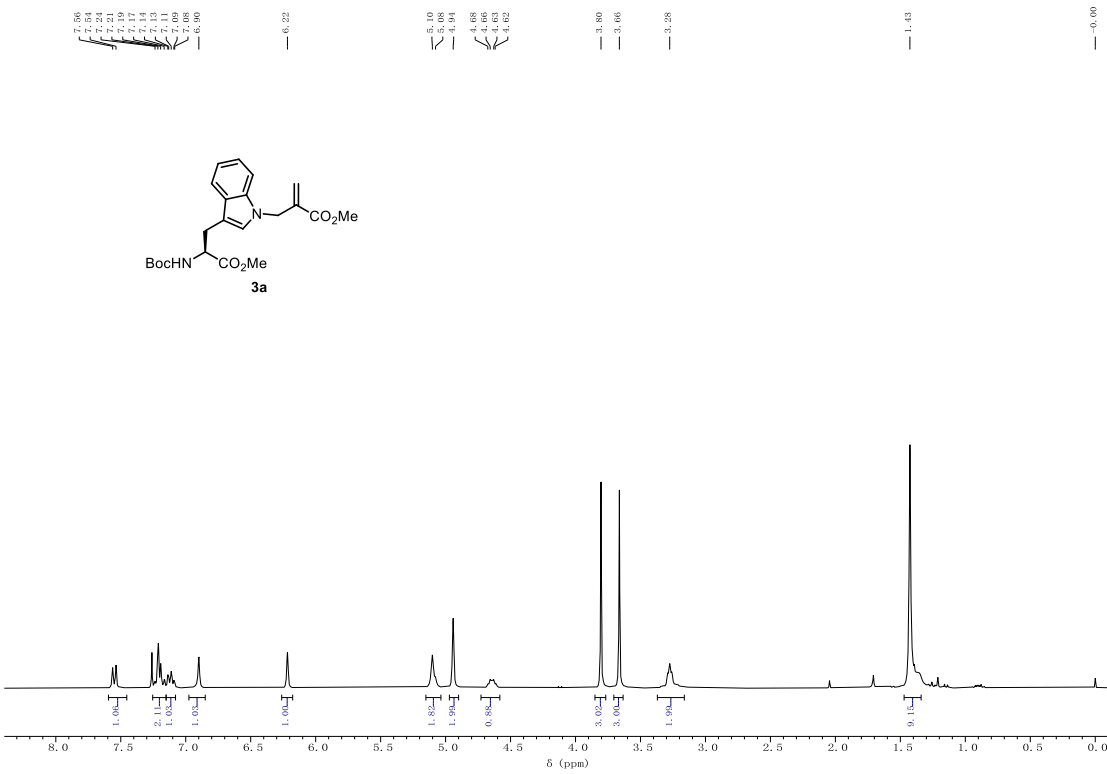
^{13}**C NMR** (75 MHz, $CDCl_3$) spectrum of **2ad**



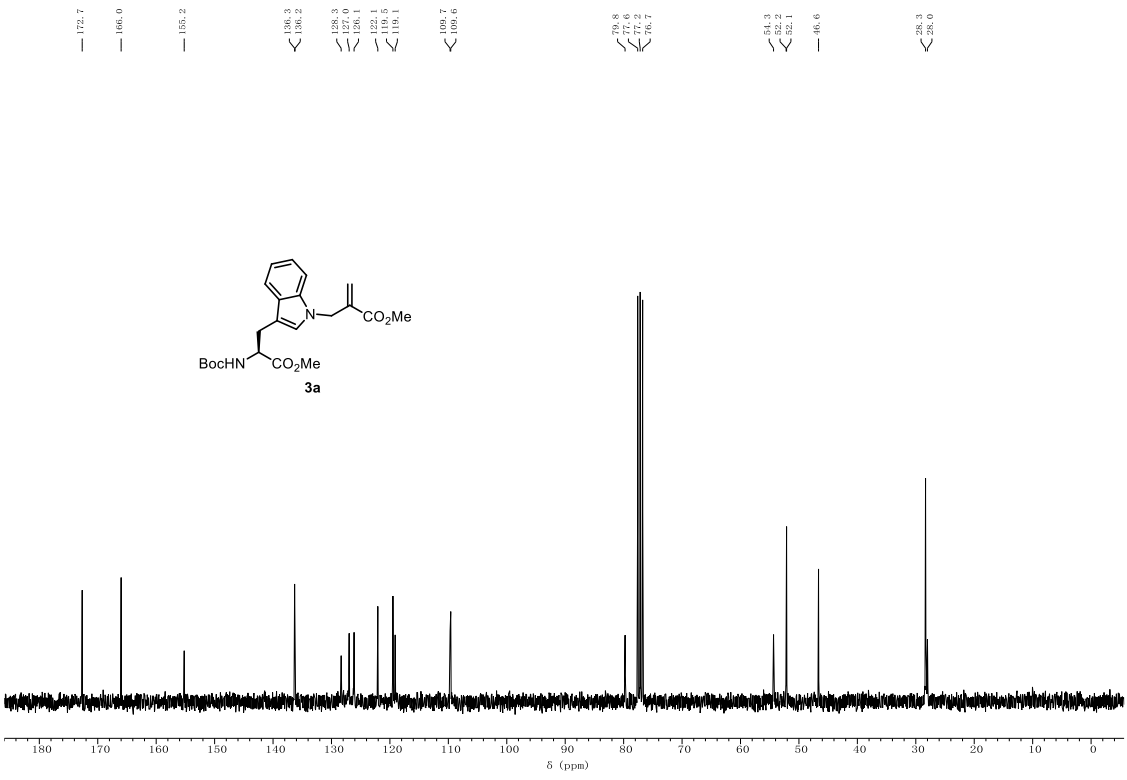
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **2ae**



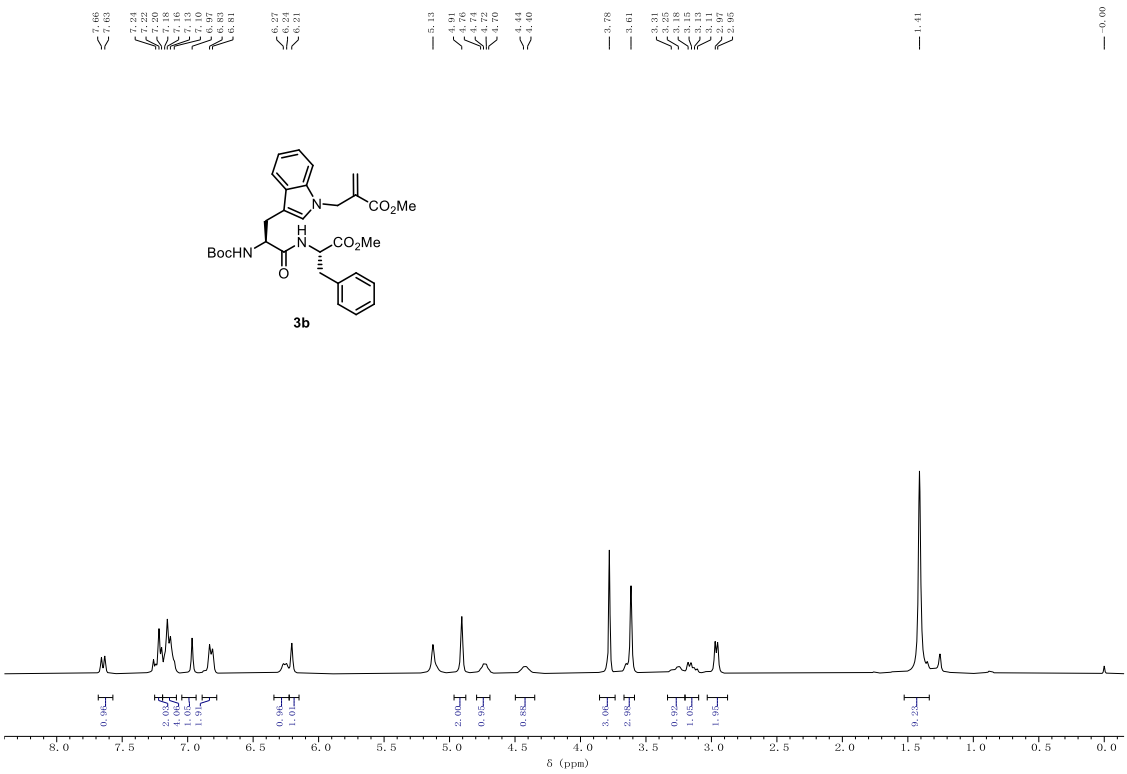
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **2ae**



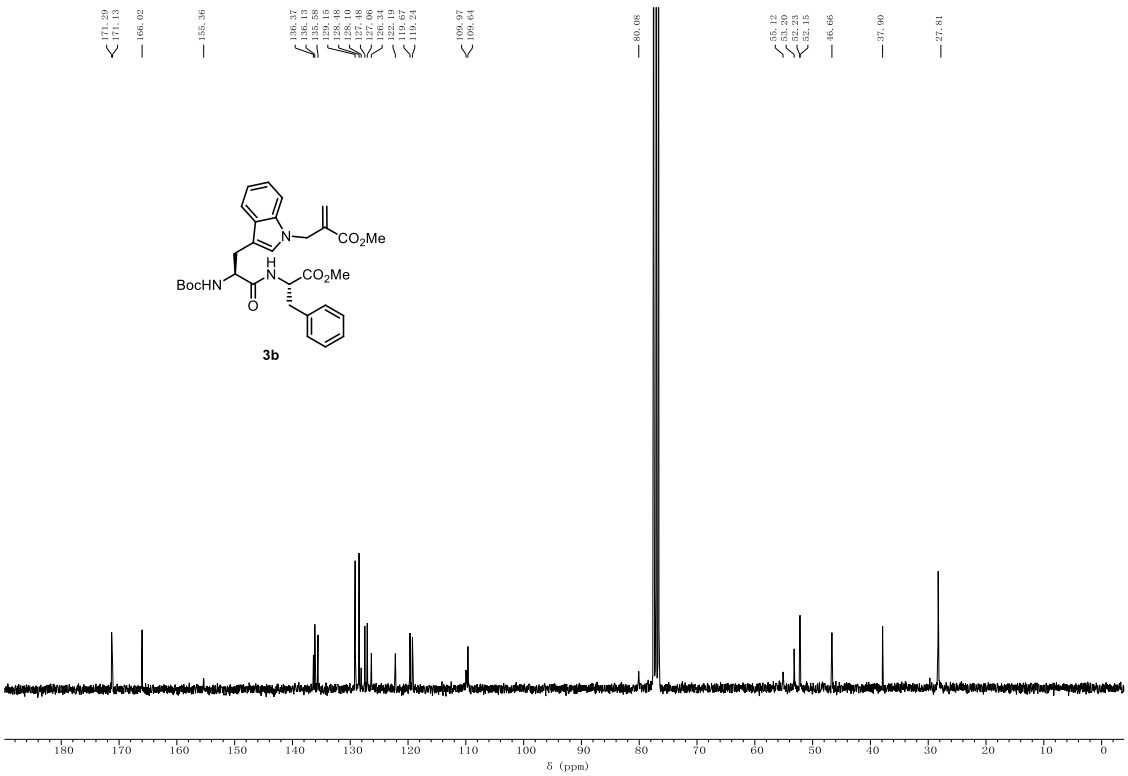
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **3a**



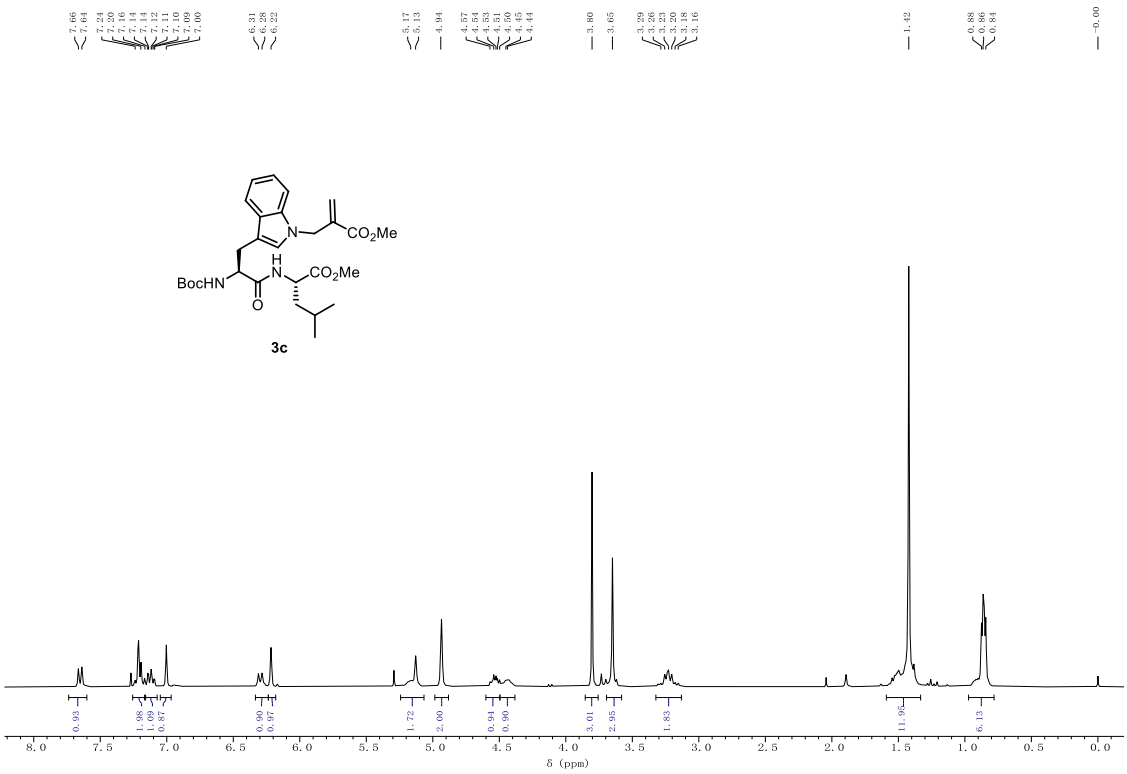
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **3a**



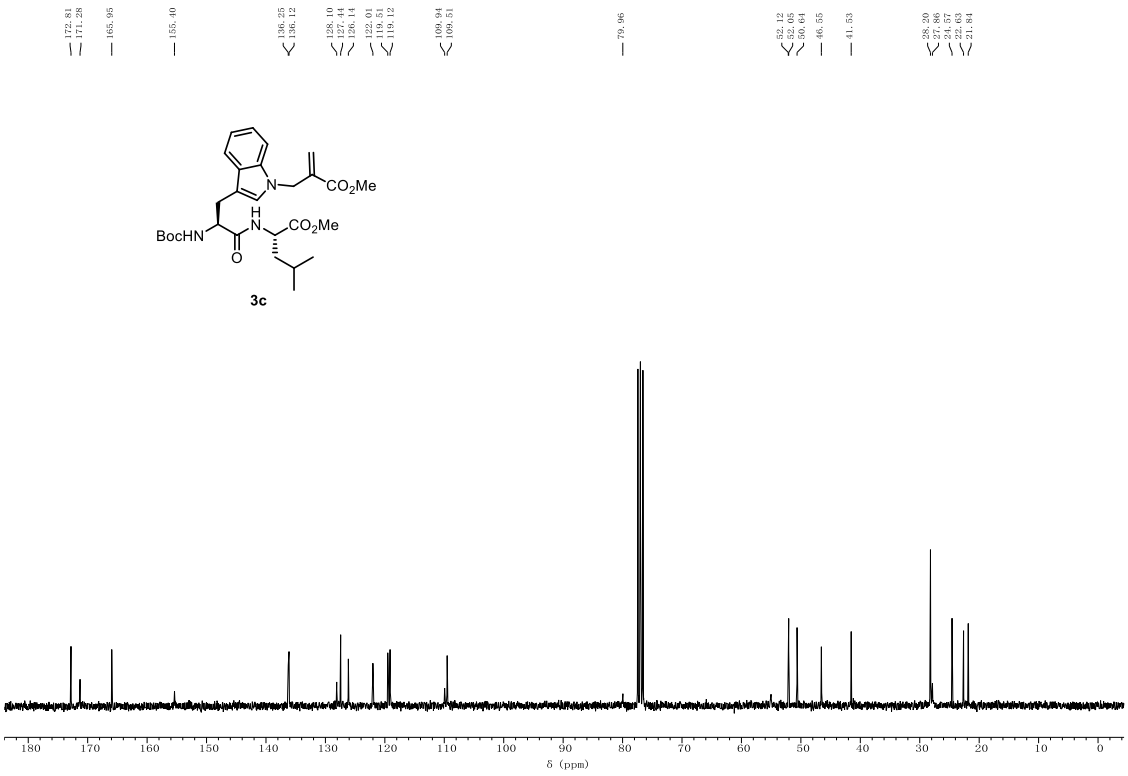
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **3b**



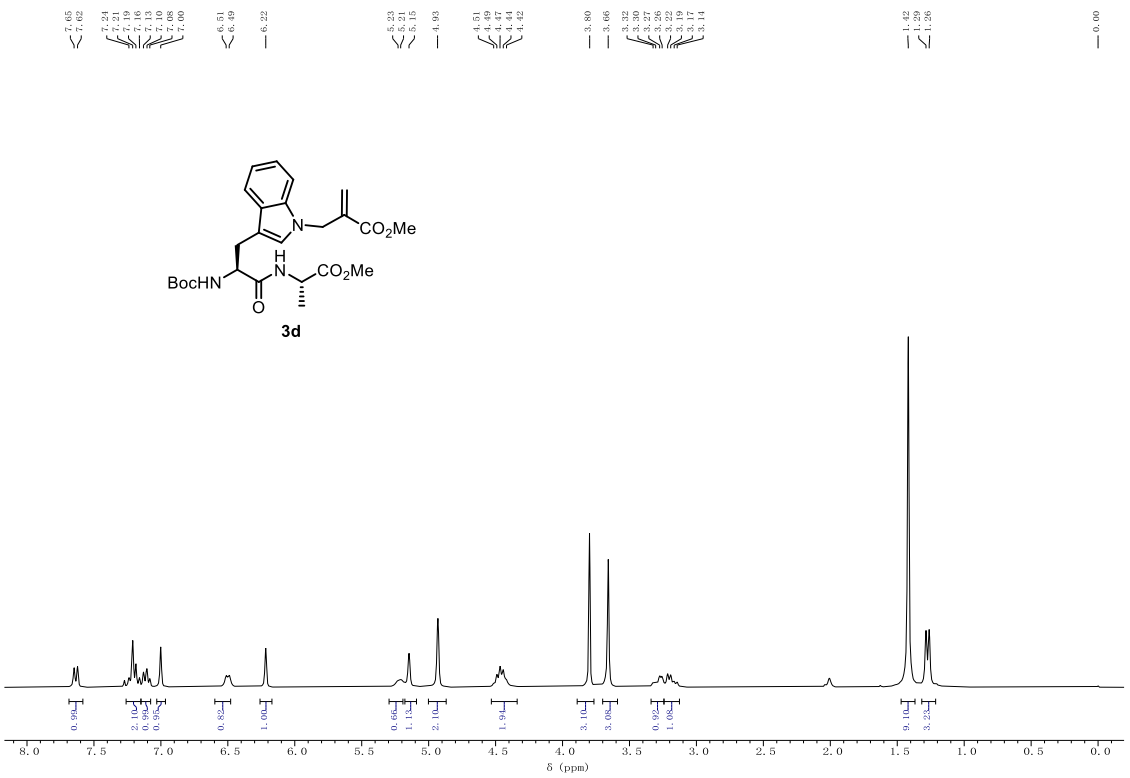
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **3b**



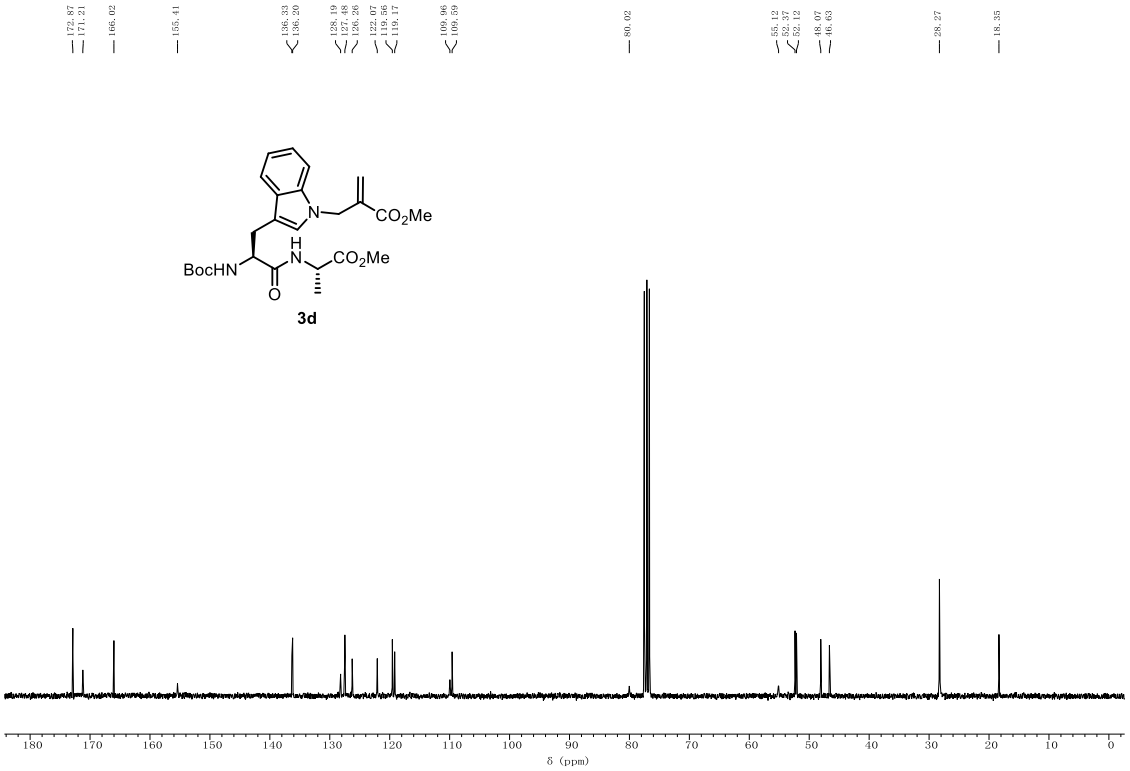
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **3c**



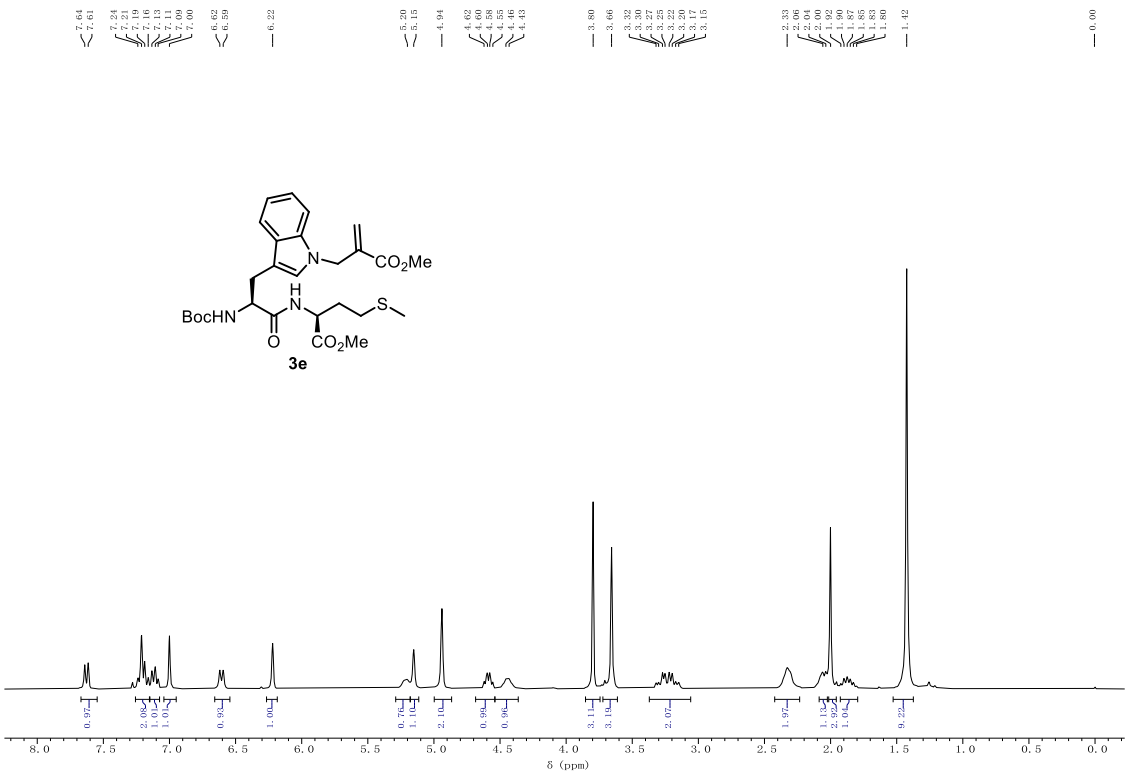
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **3c**



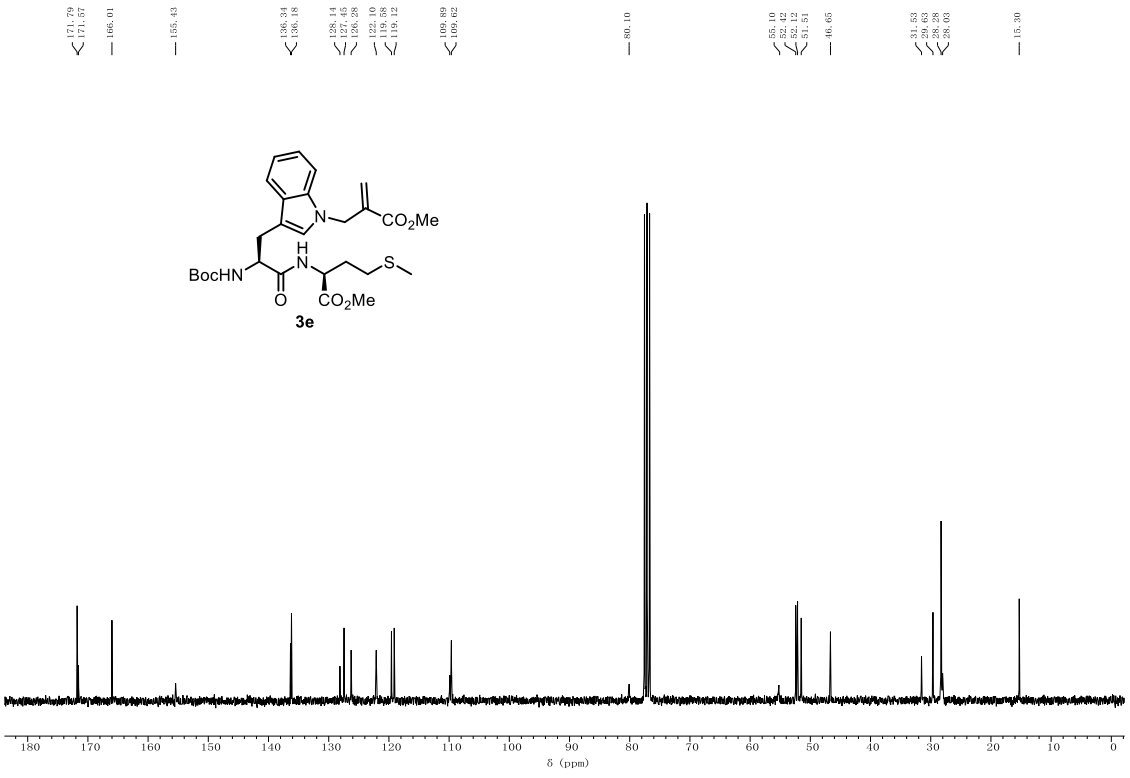
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **3d**



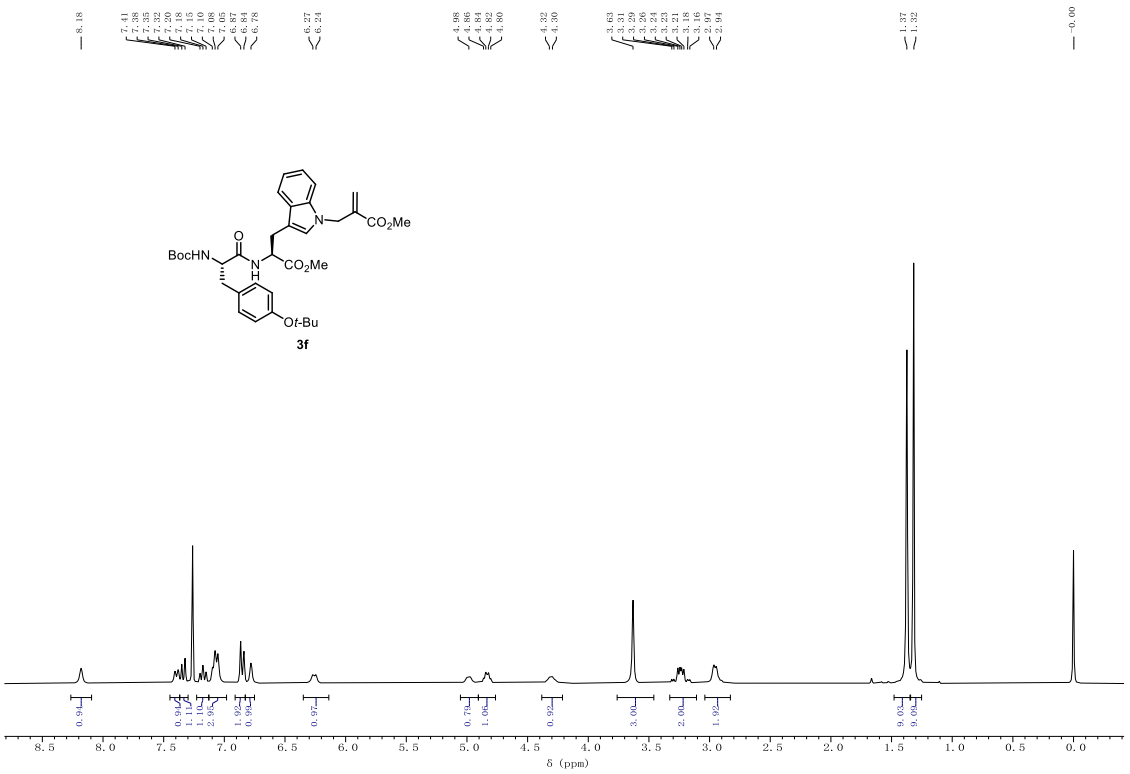
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **3d**



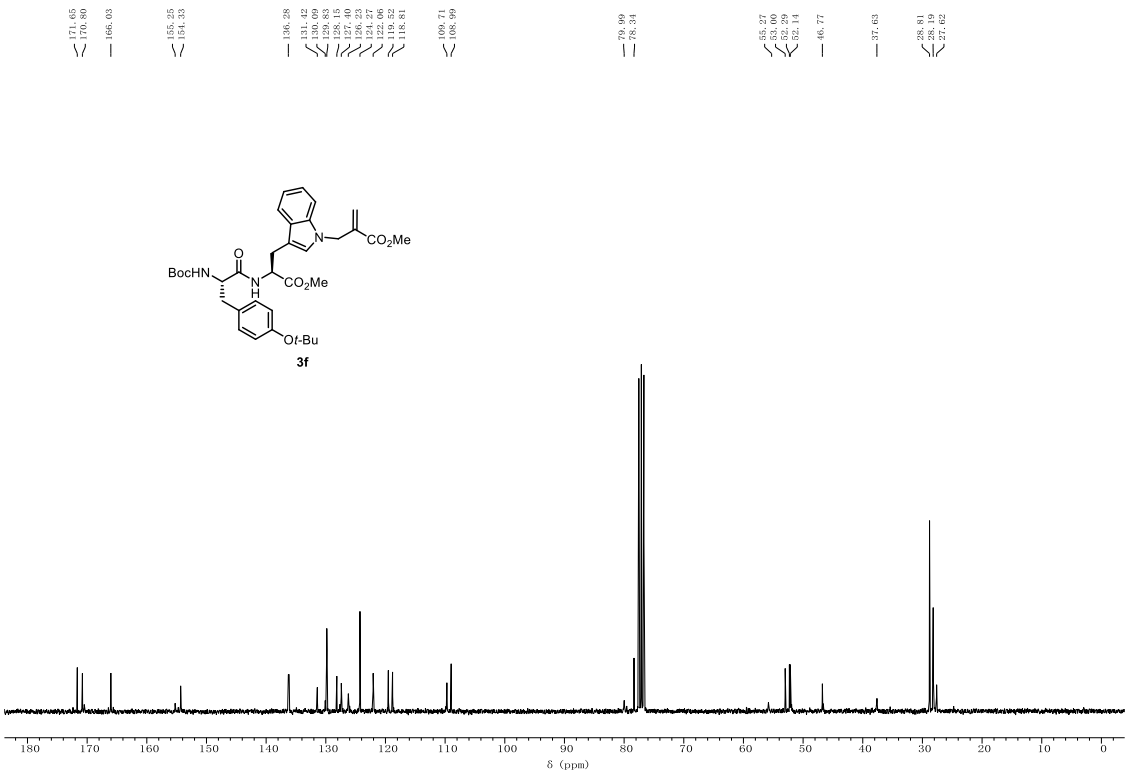
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **3e**



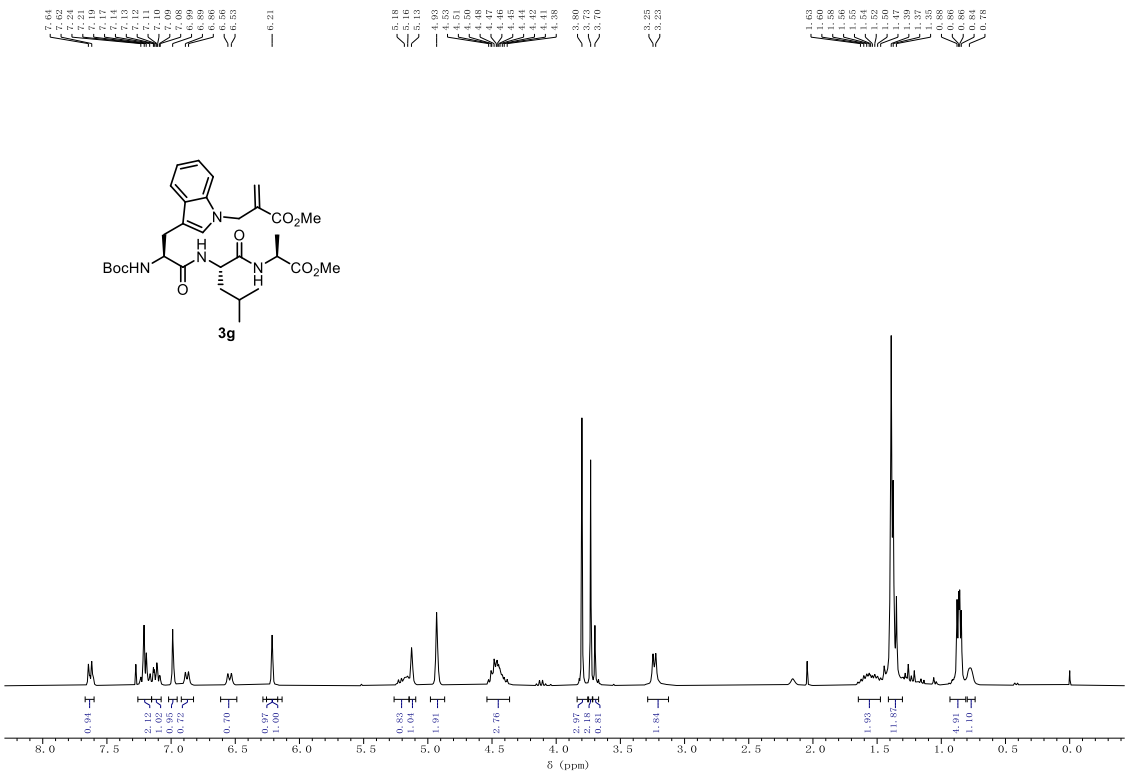
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **3e**



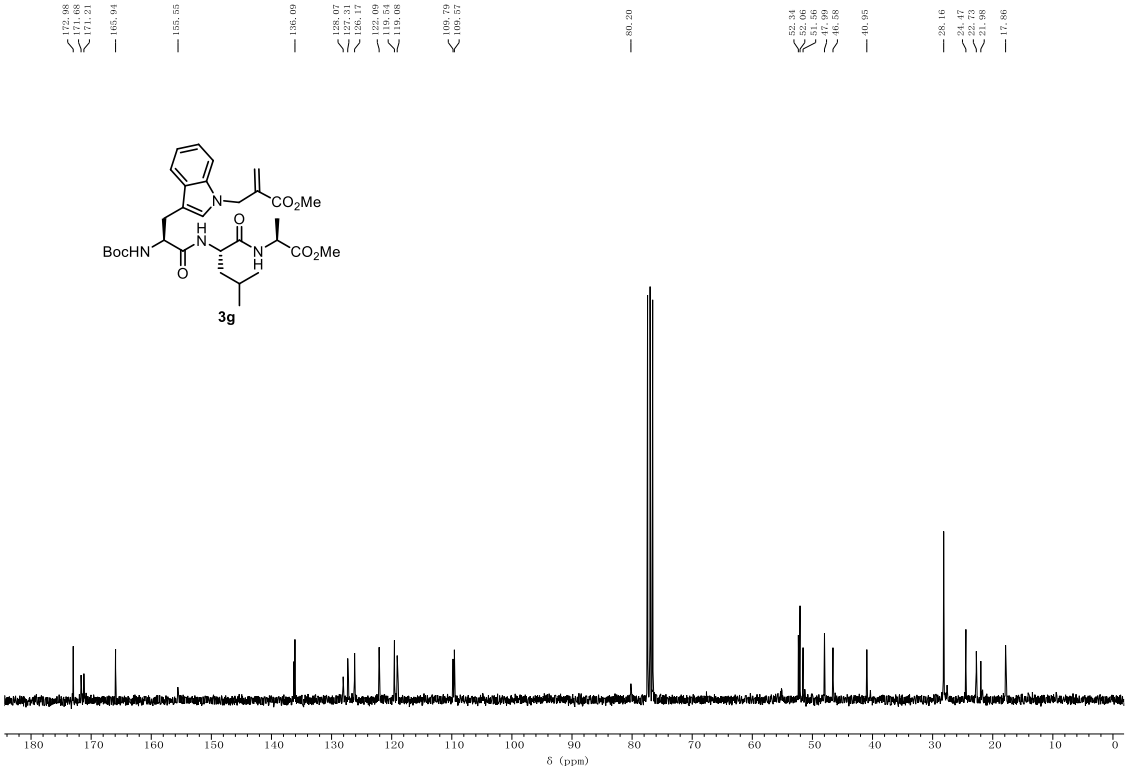
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **3f**



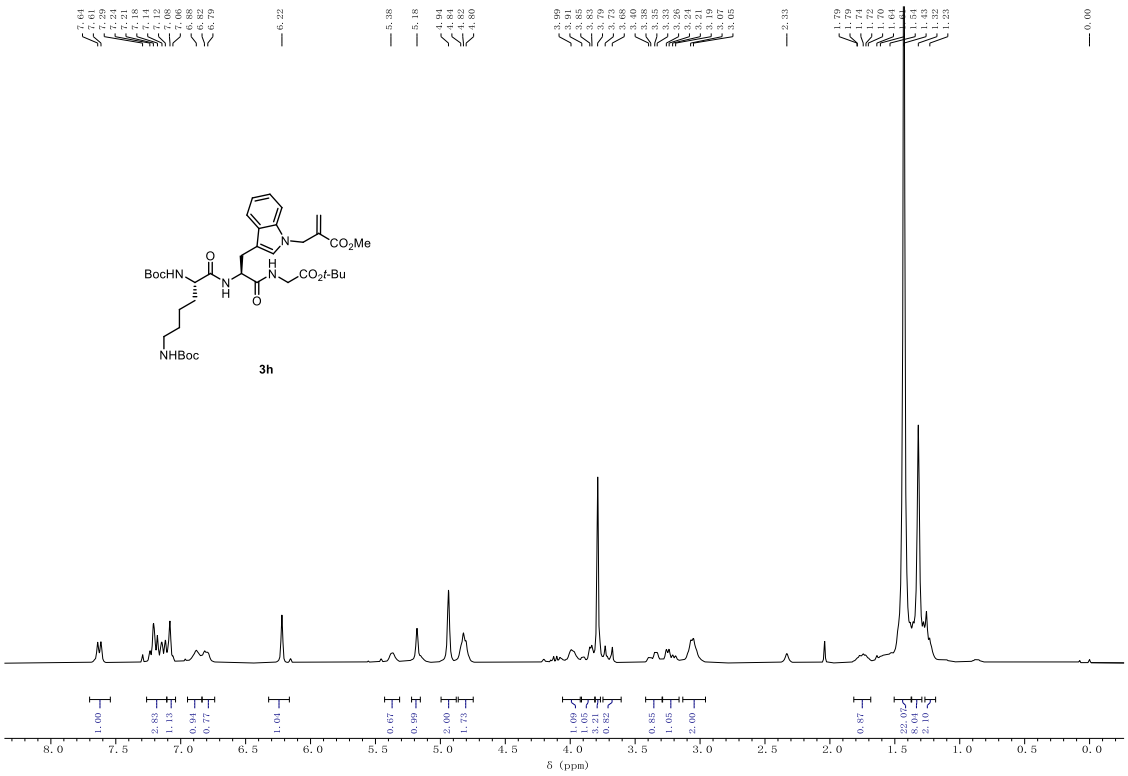
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **3f**



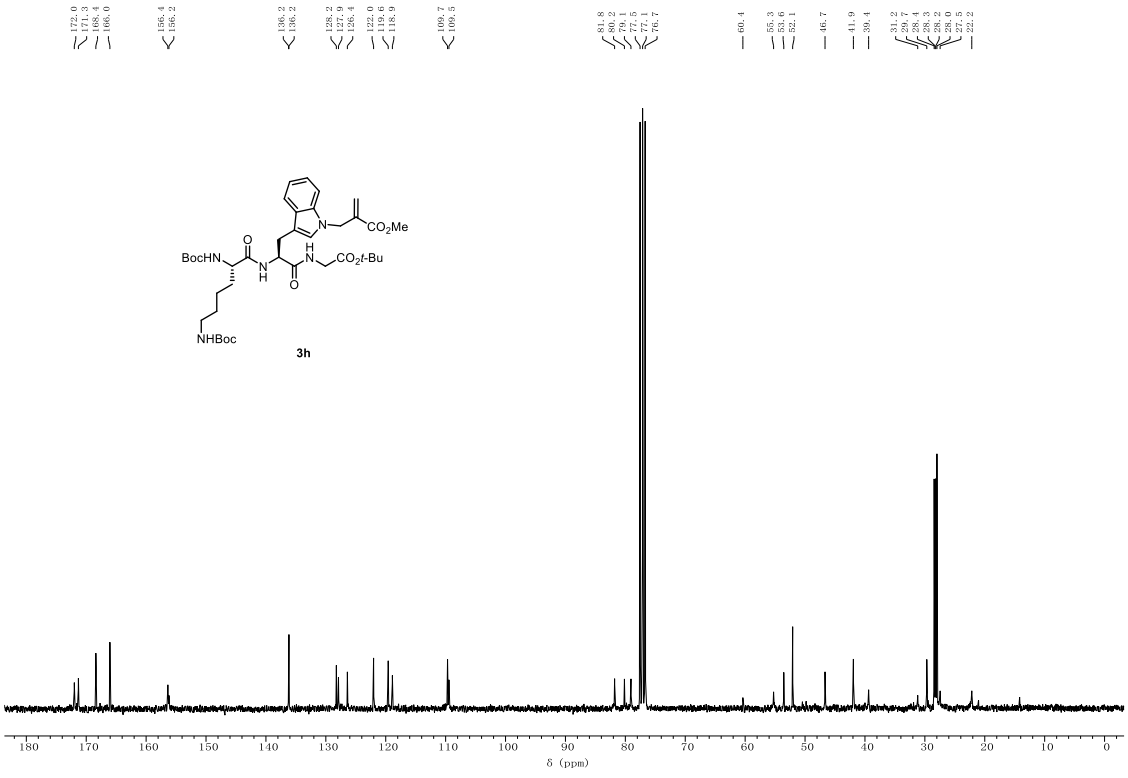
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **3g**



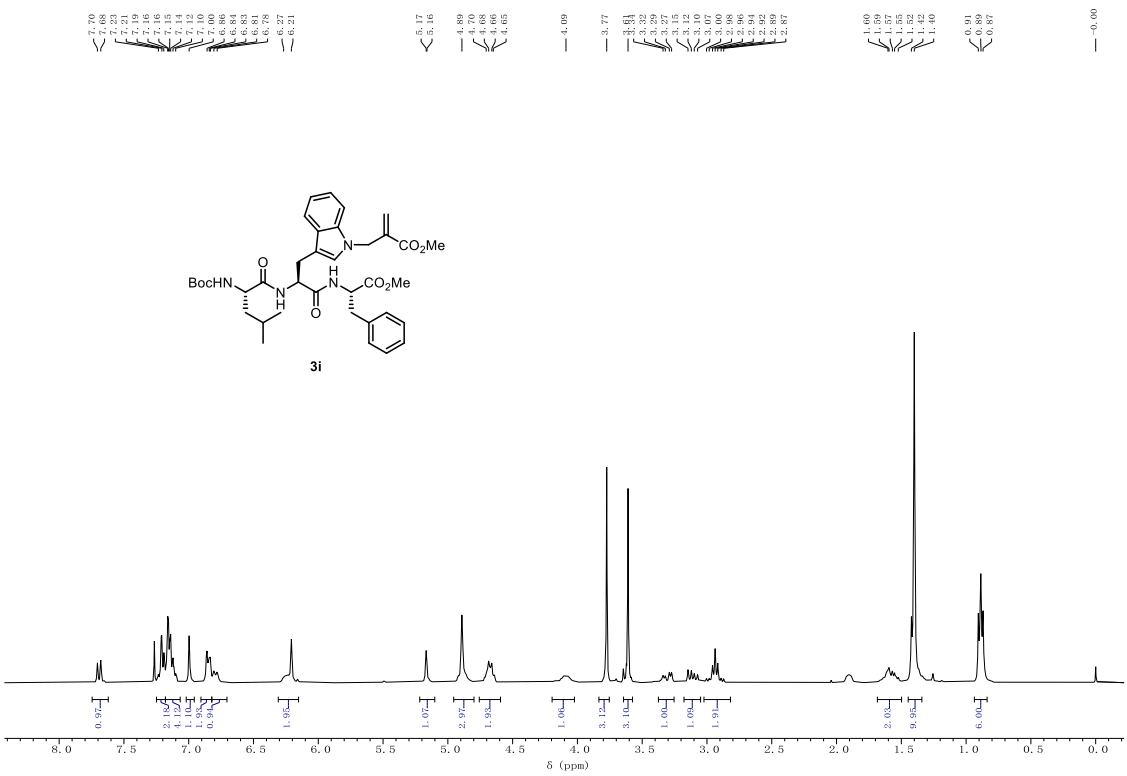
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **3g**



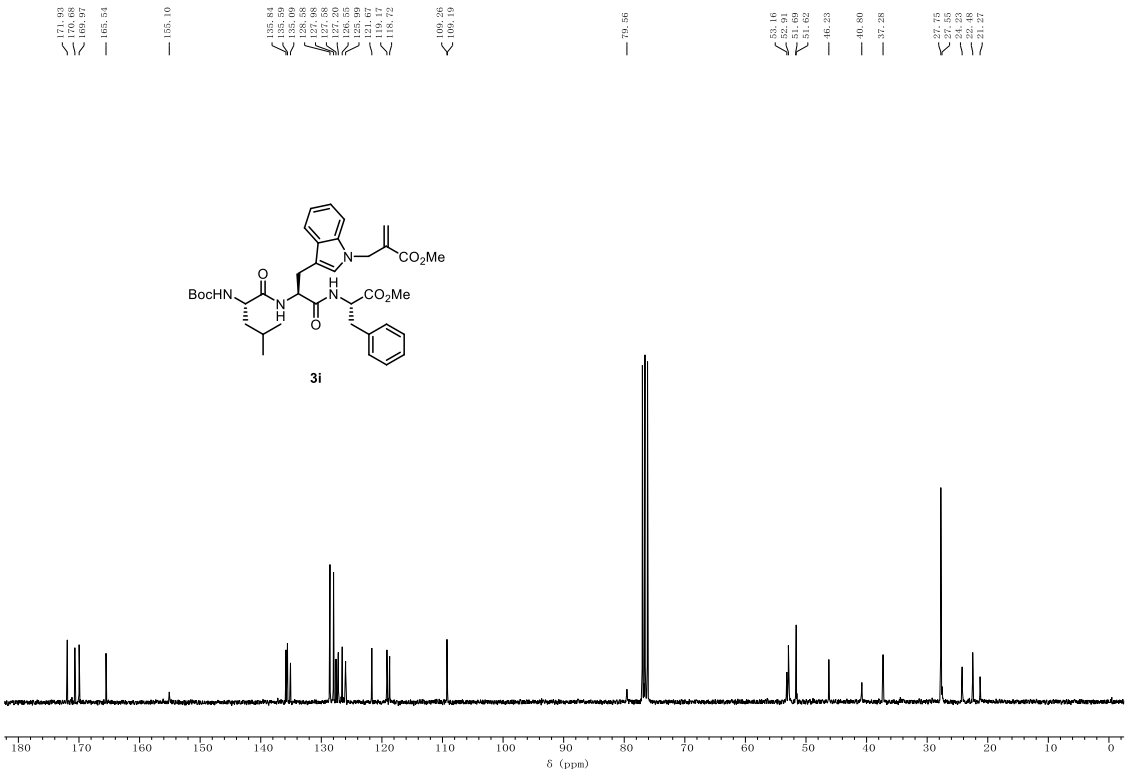
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **3h**



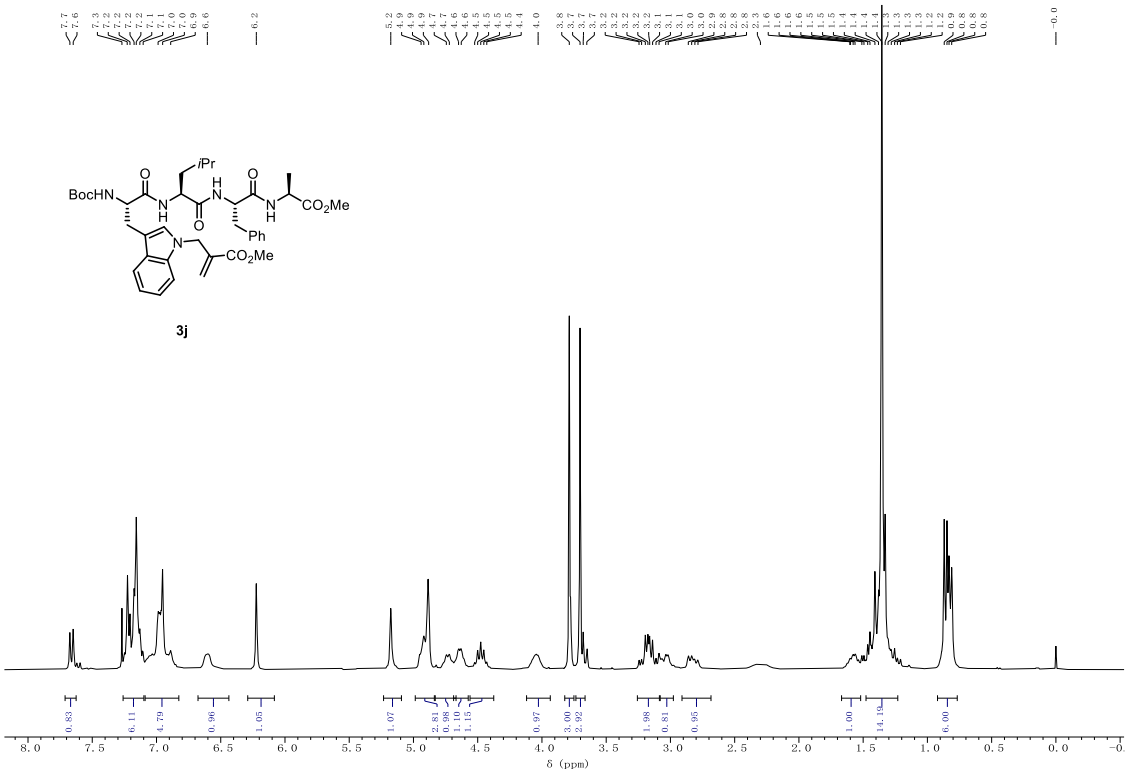
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **3h**



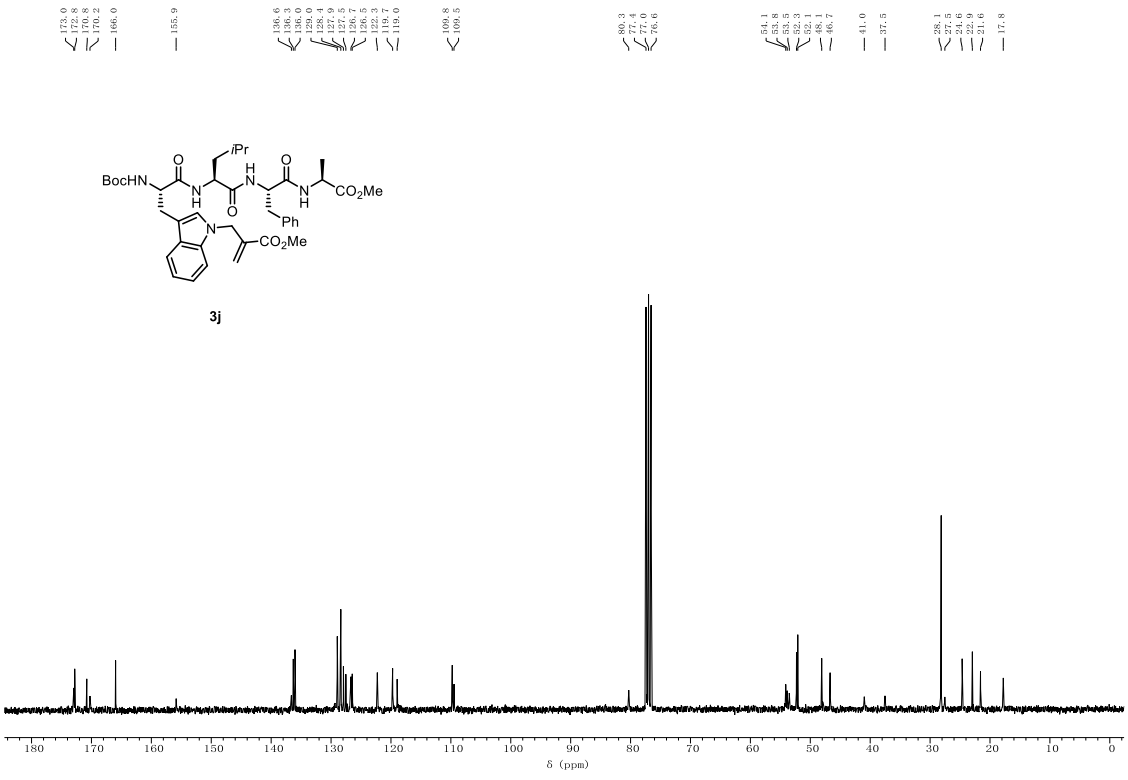
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **3i**



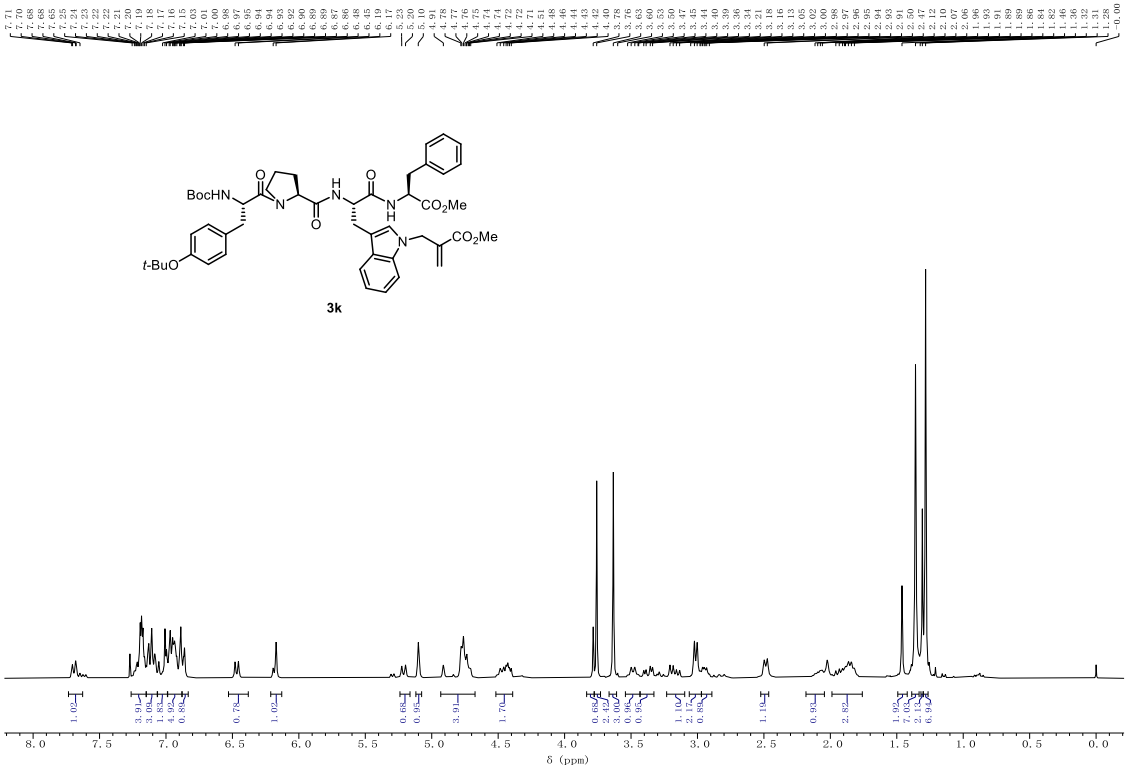
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **3i**



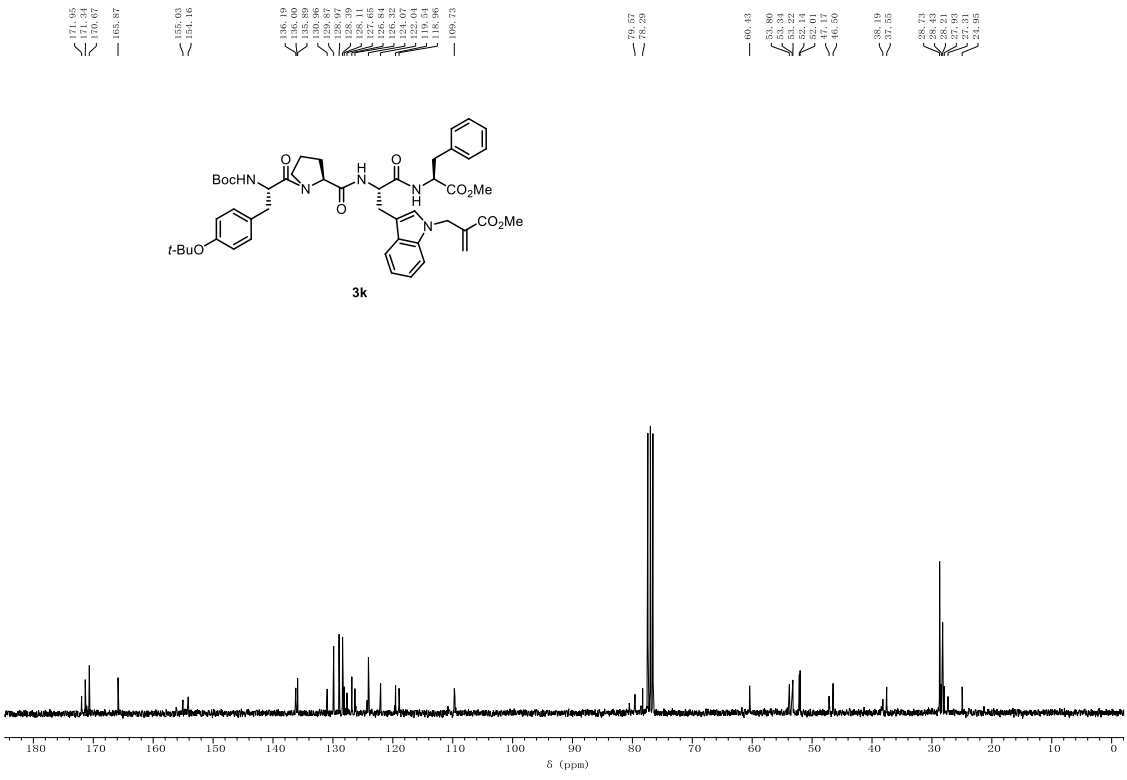
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **3j**



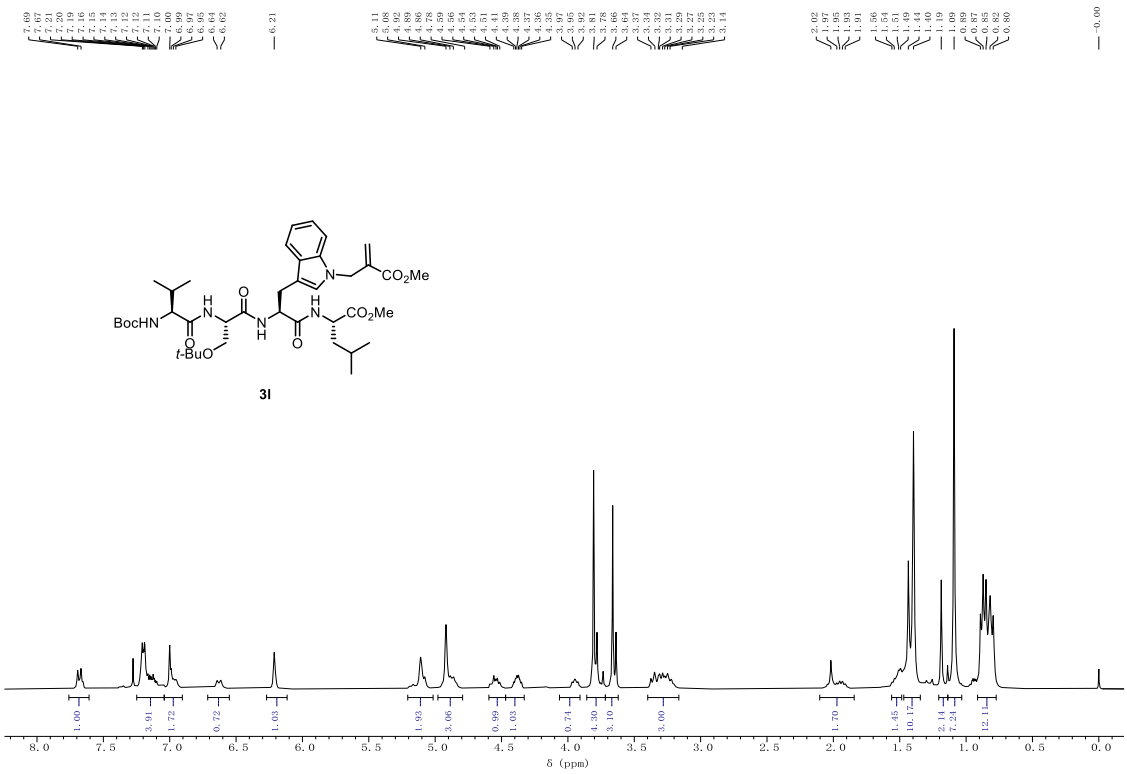
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **3j**



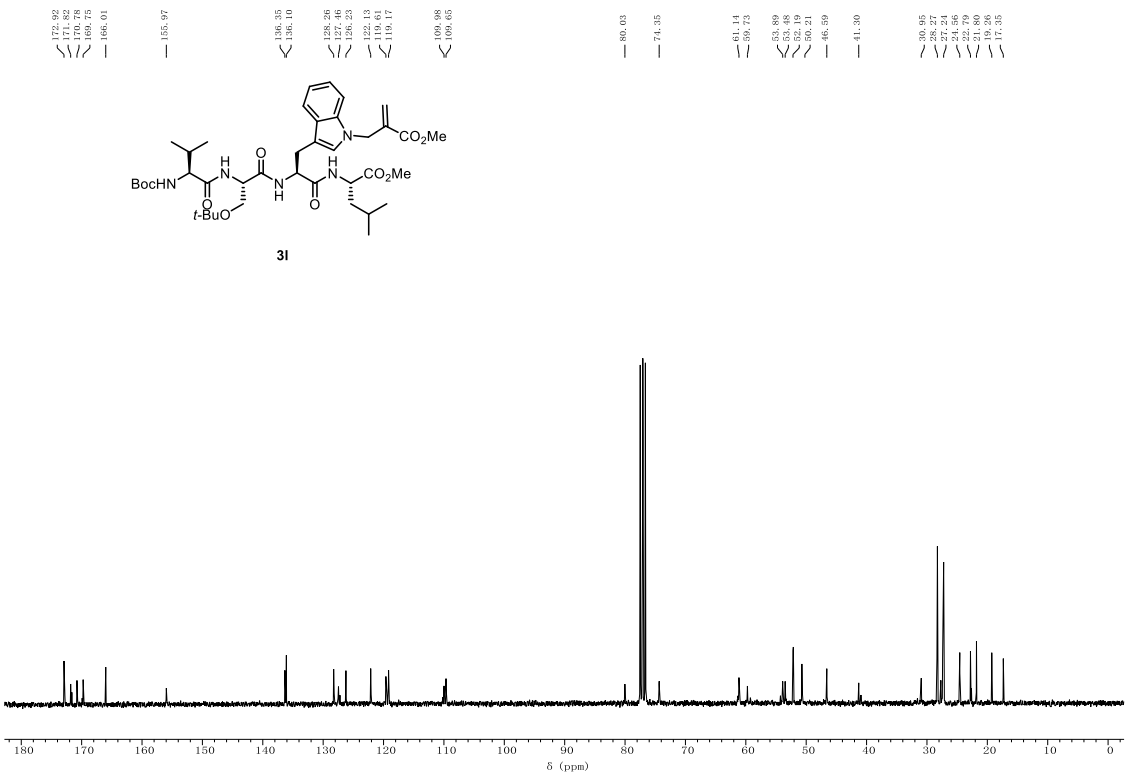
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **3k**



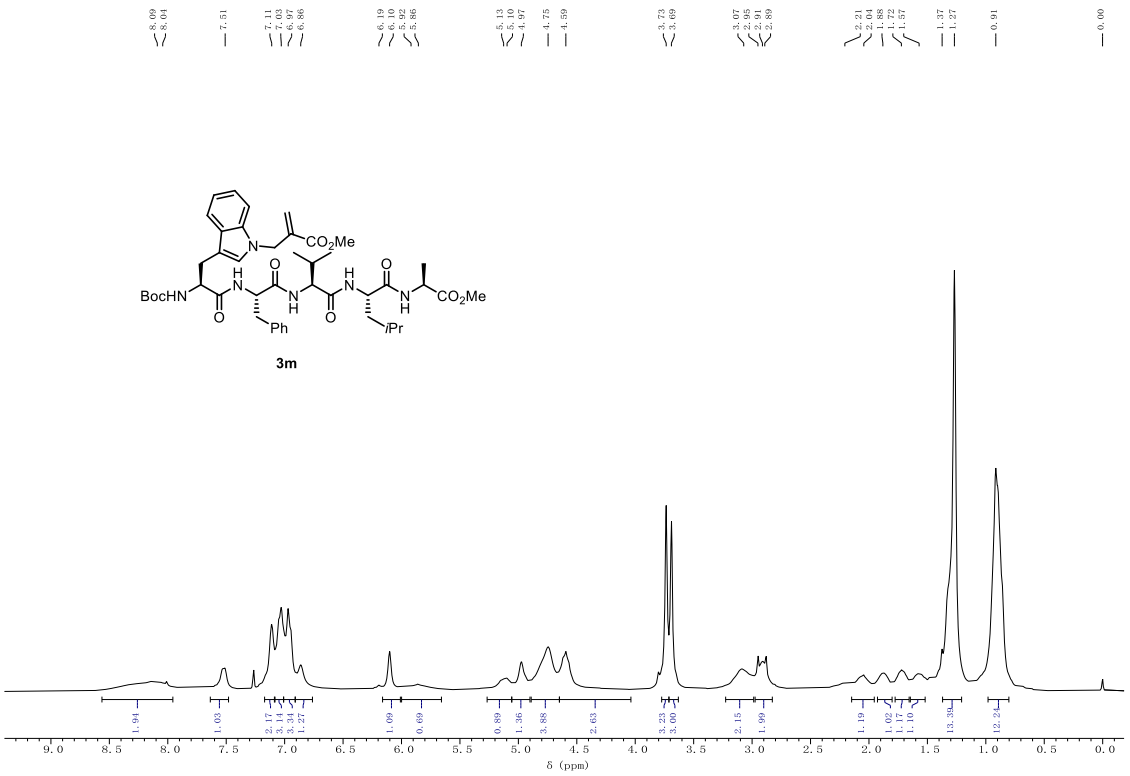
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **3k**



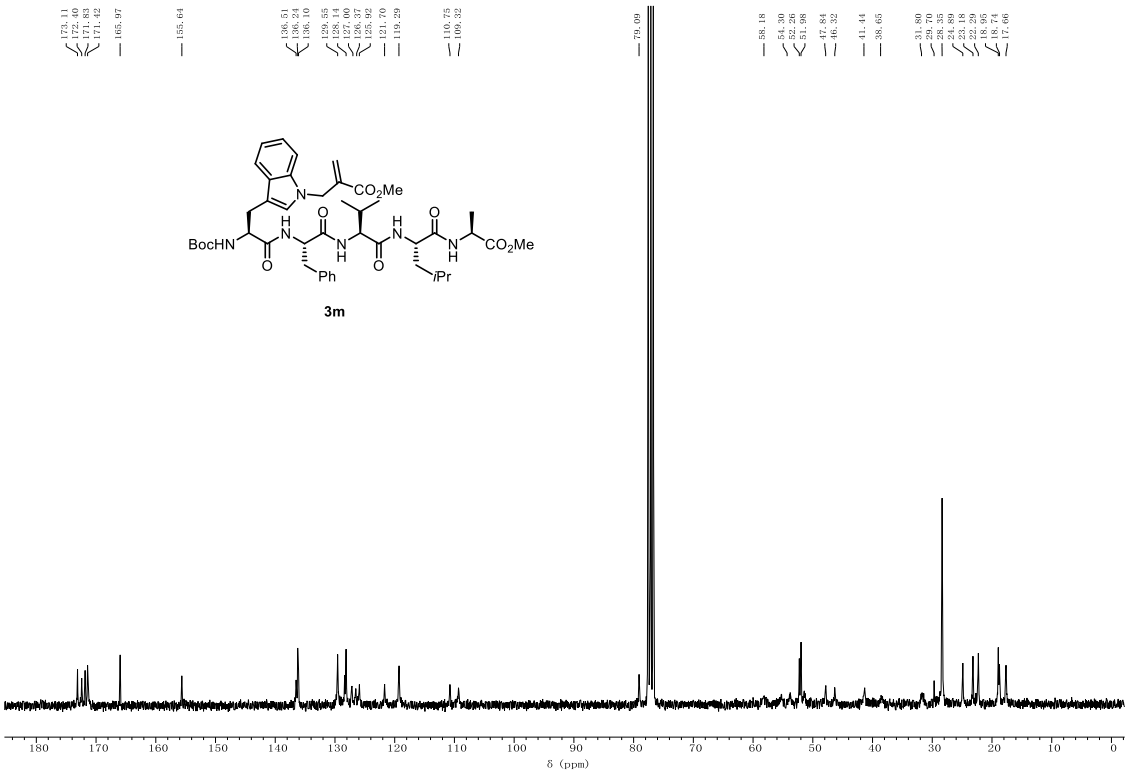
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **3l**



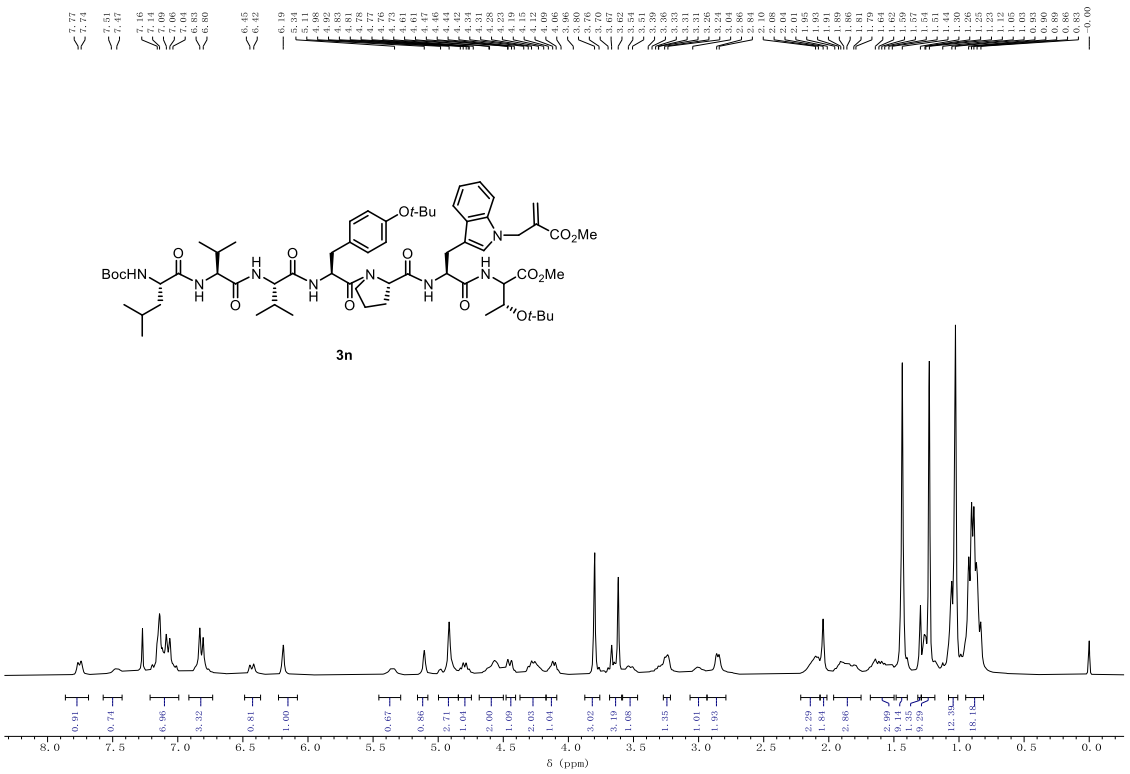
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **3l**



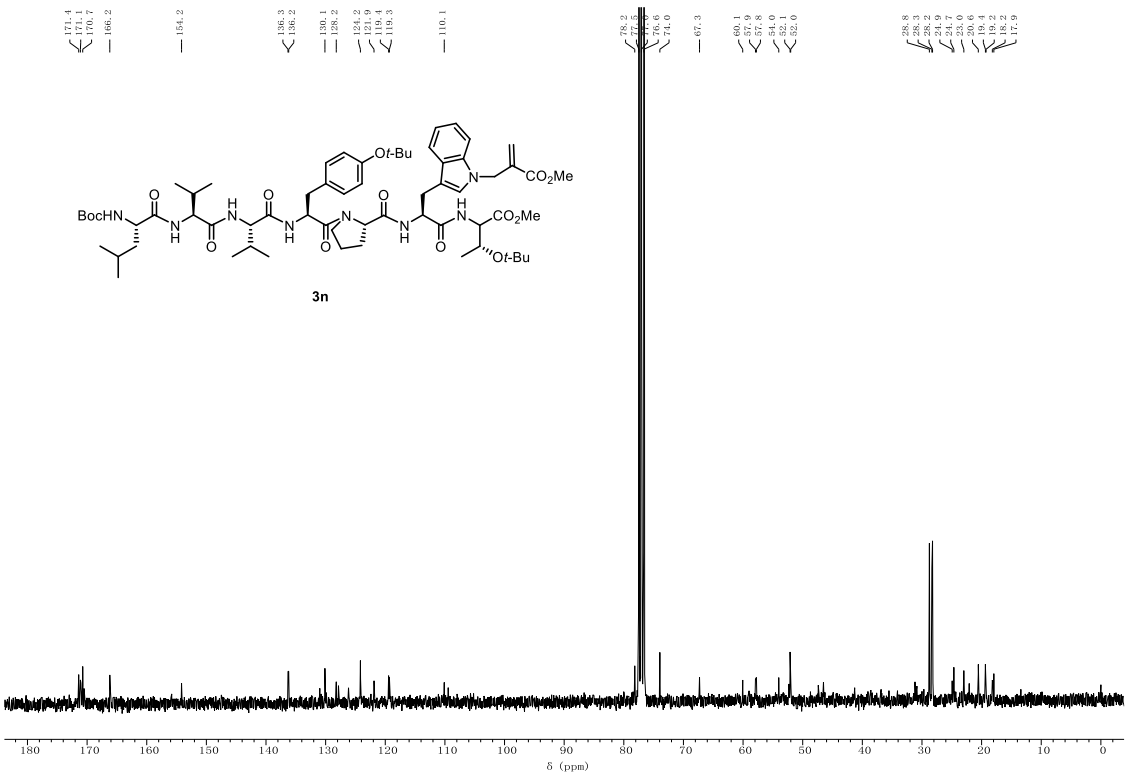
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **3m**



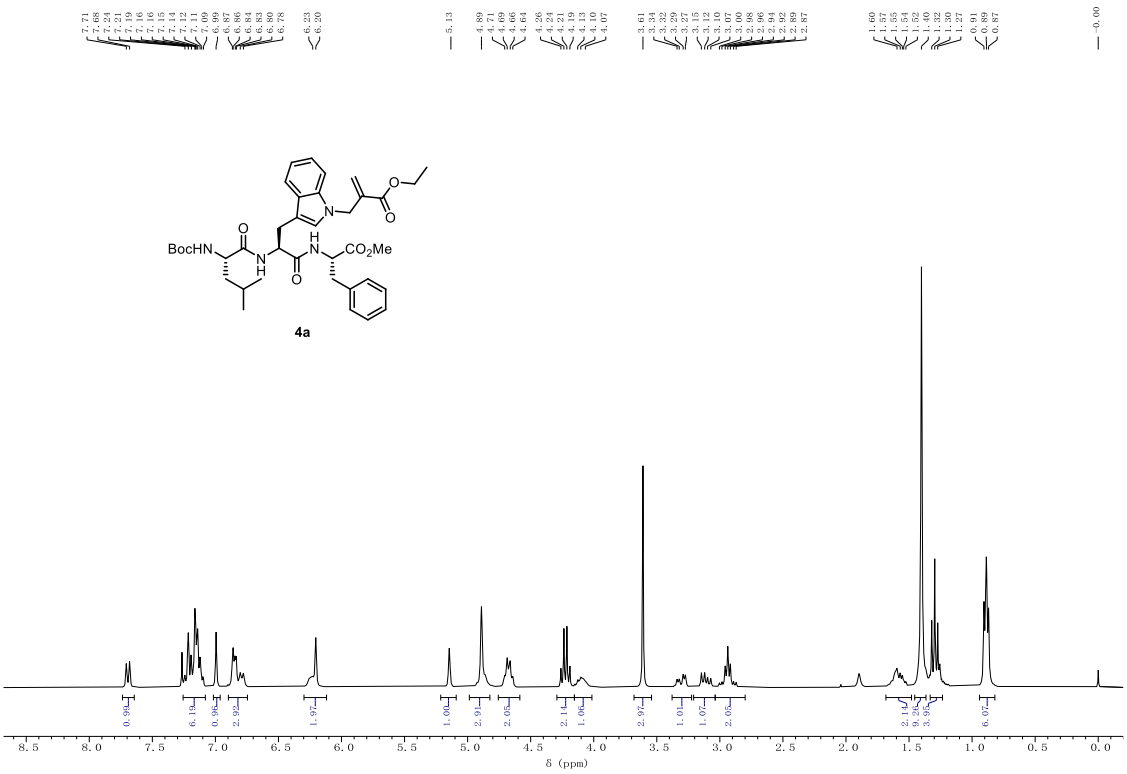
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **3m**



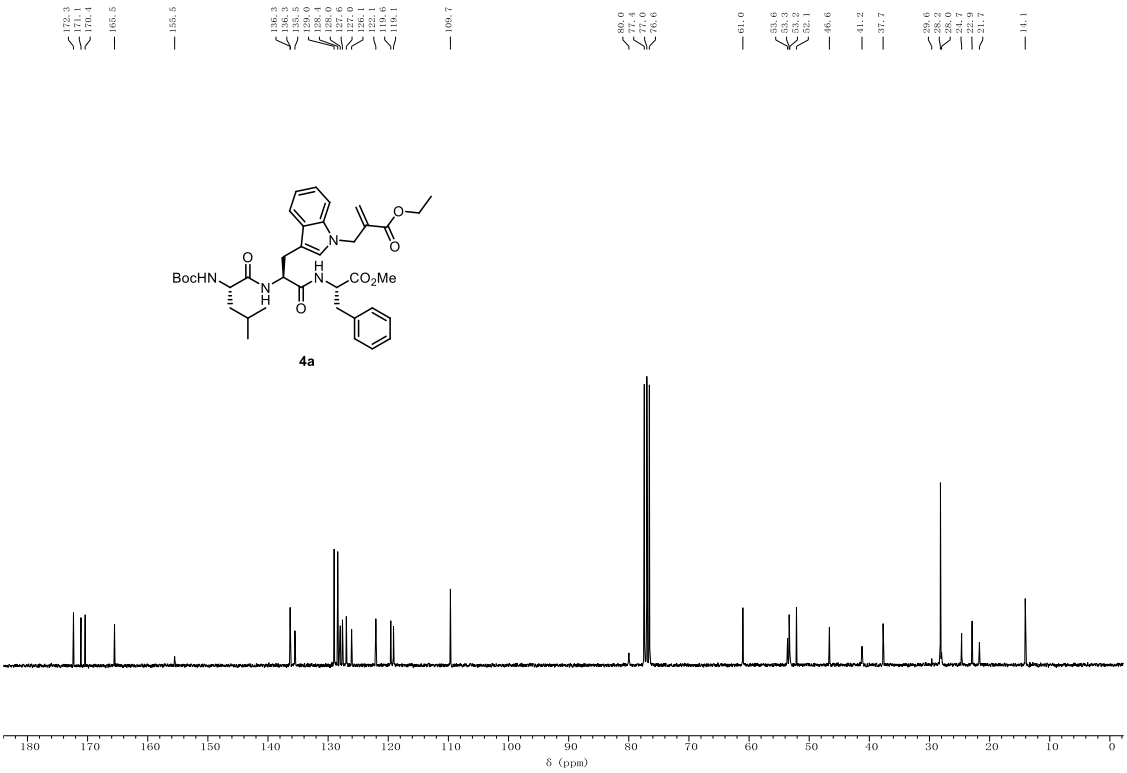
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **3n**



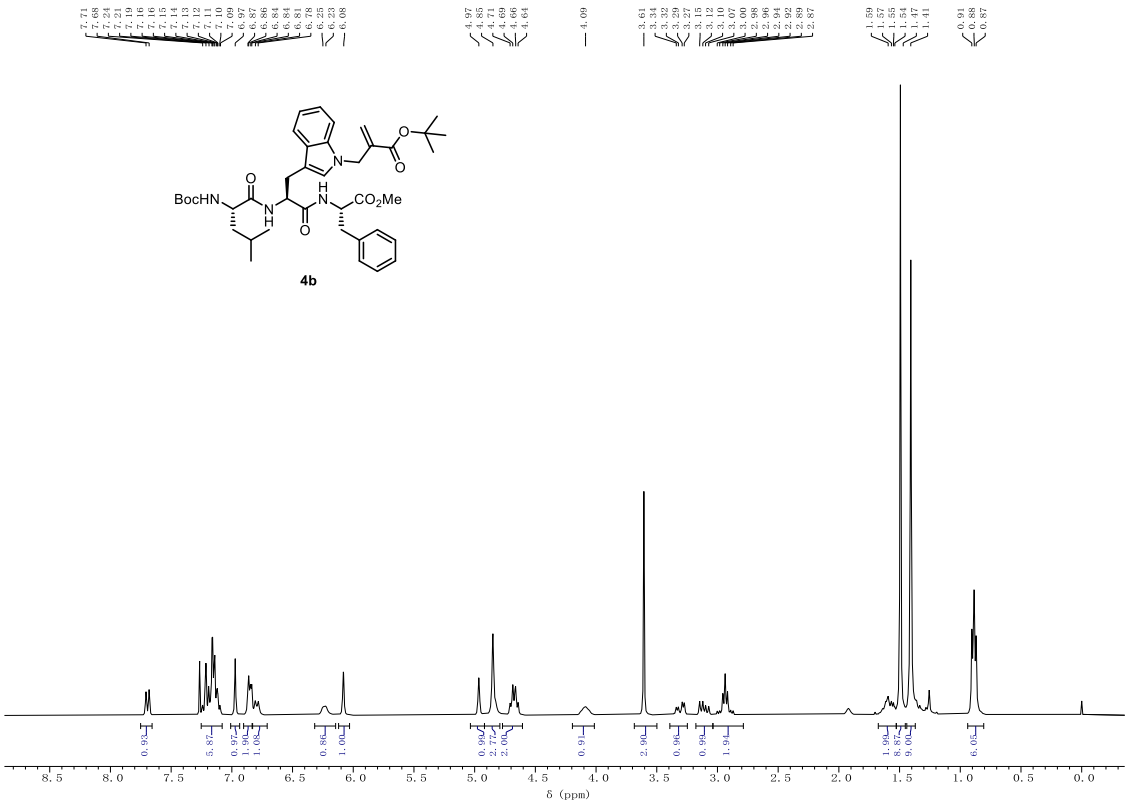
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **3n**



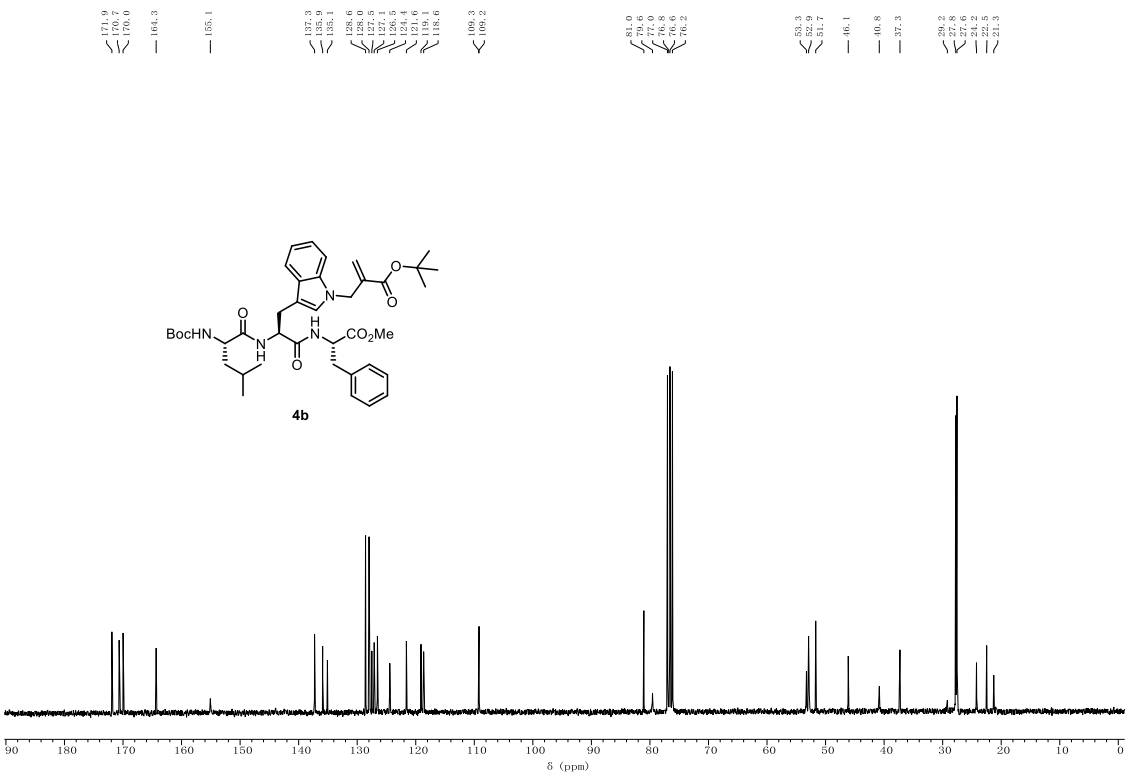
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4a**



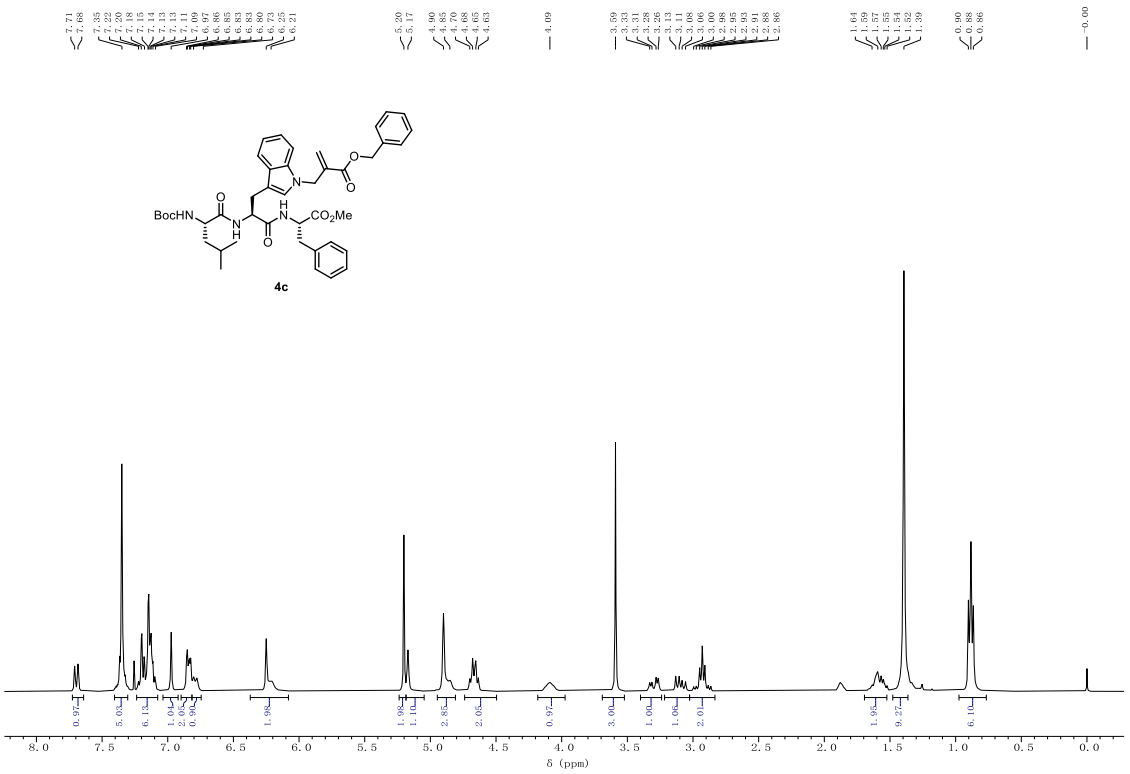
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4a**



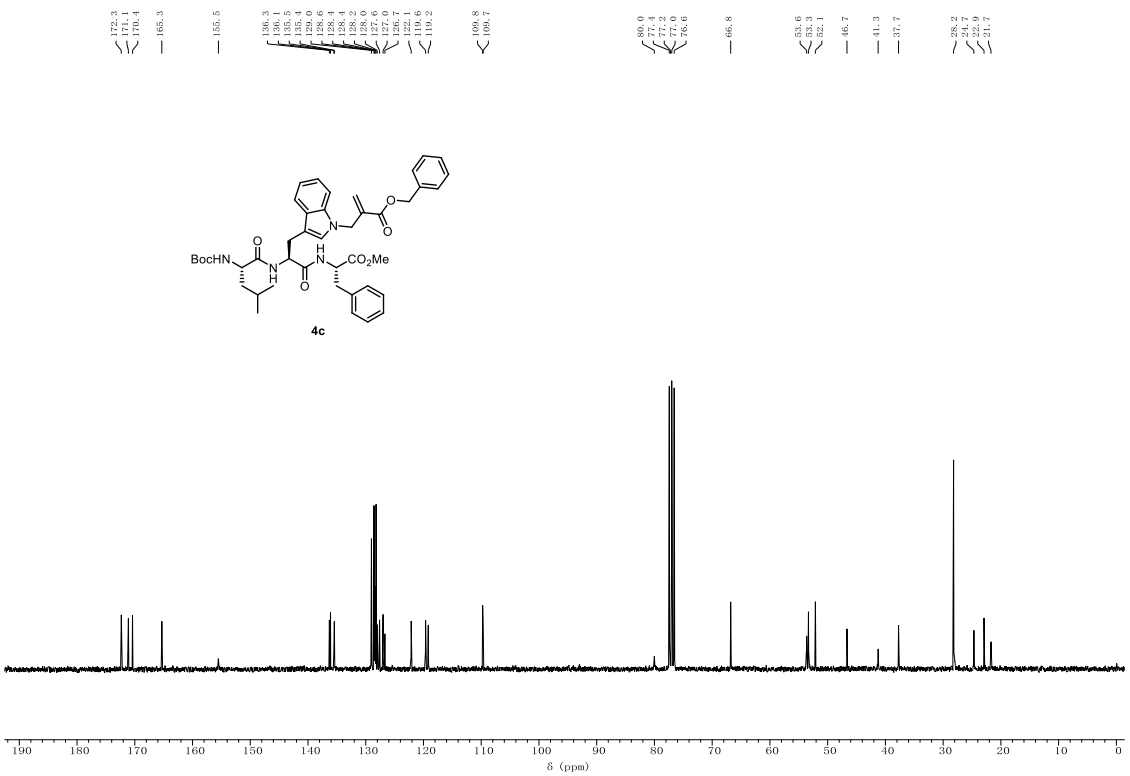
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4b**



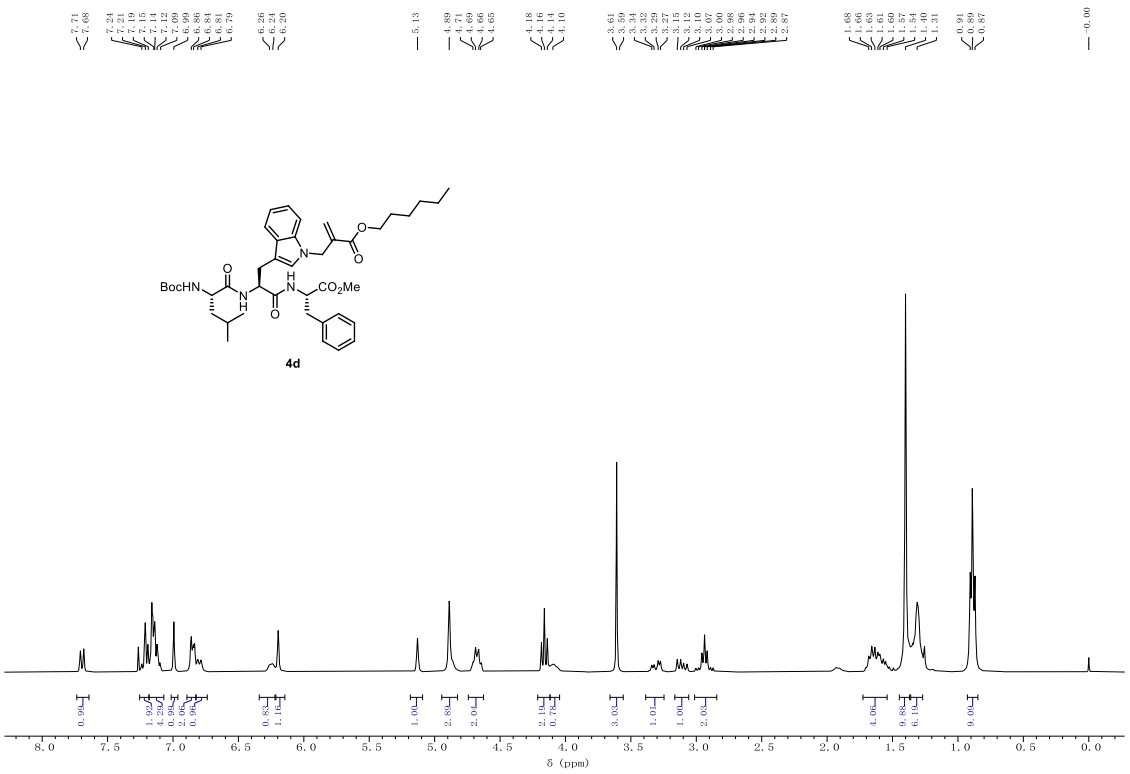
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4b**



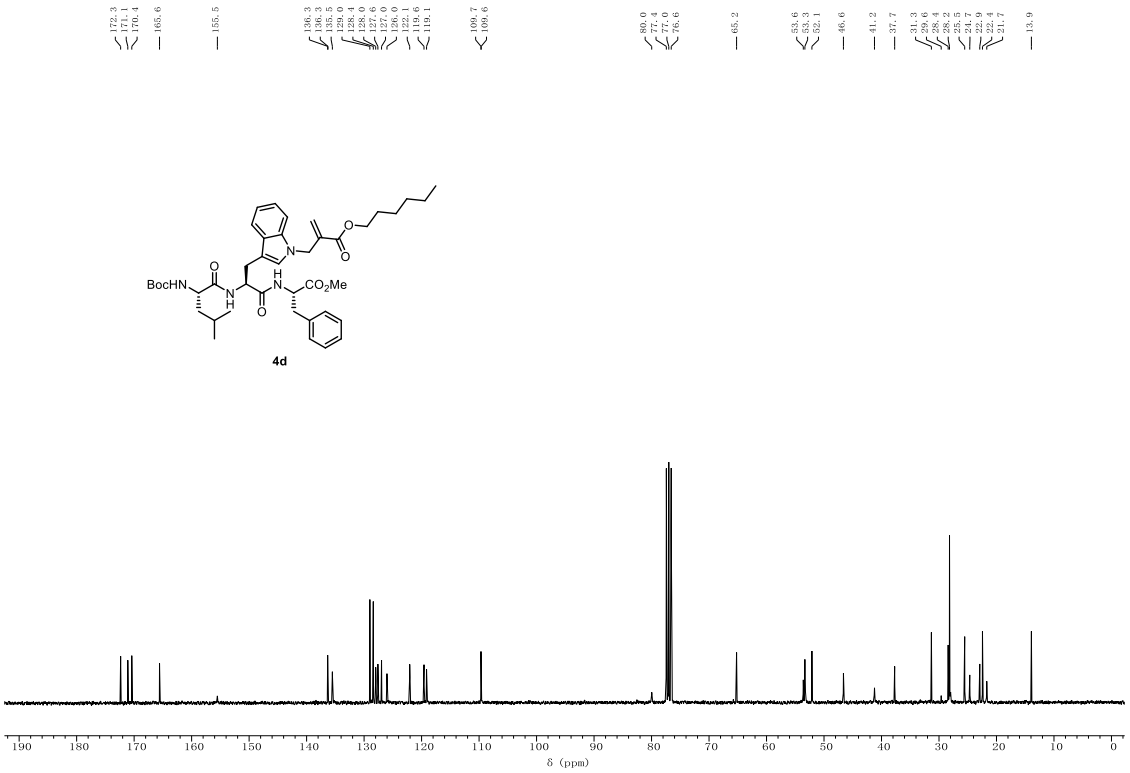
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4c**



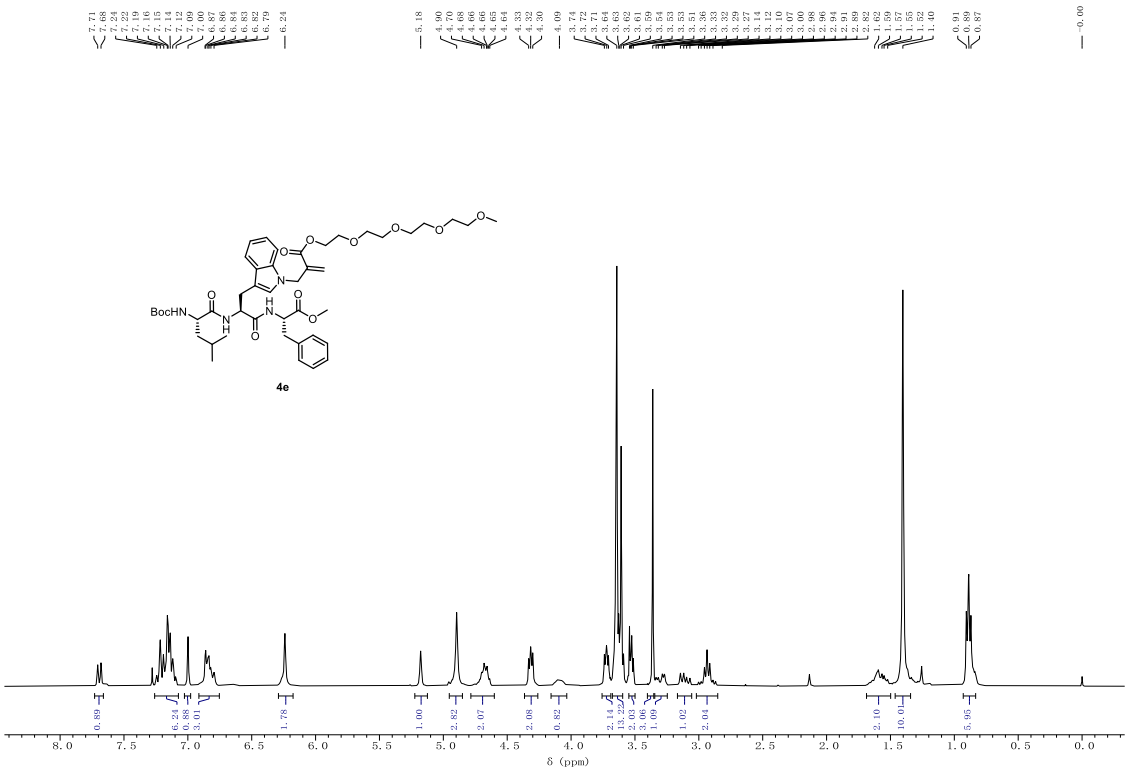
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4c**



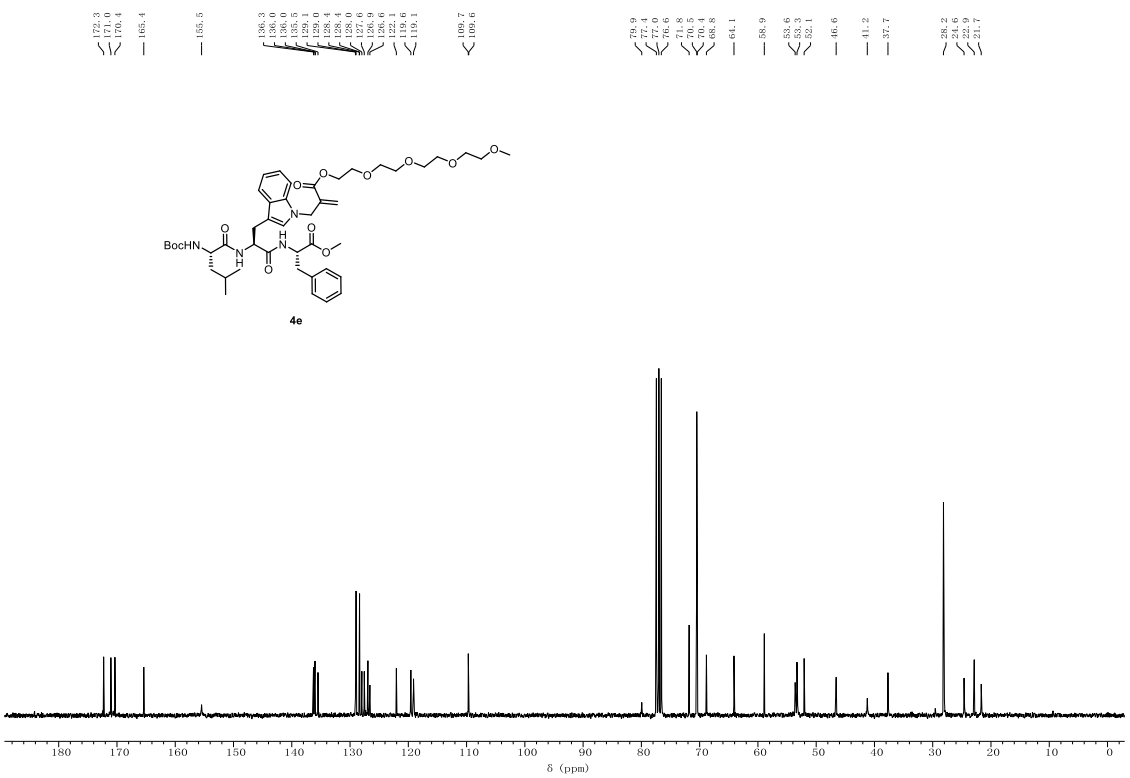
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4d**



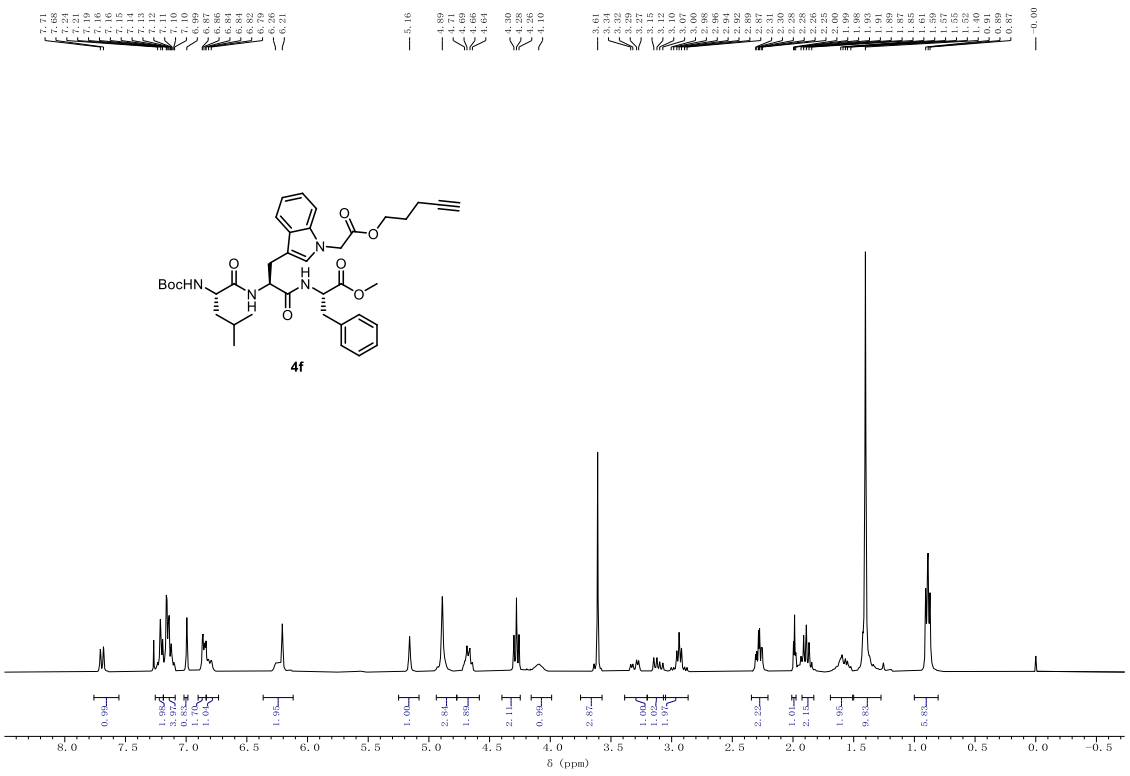
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4d**



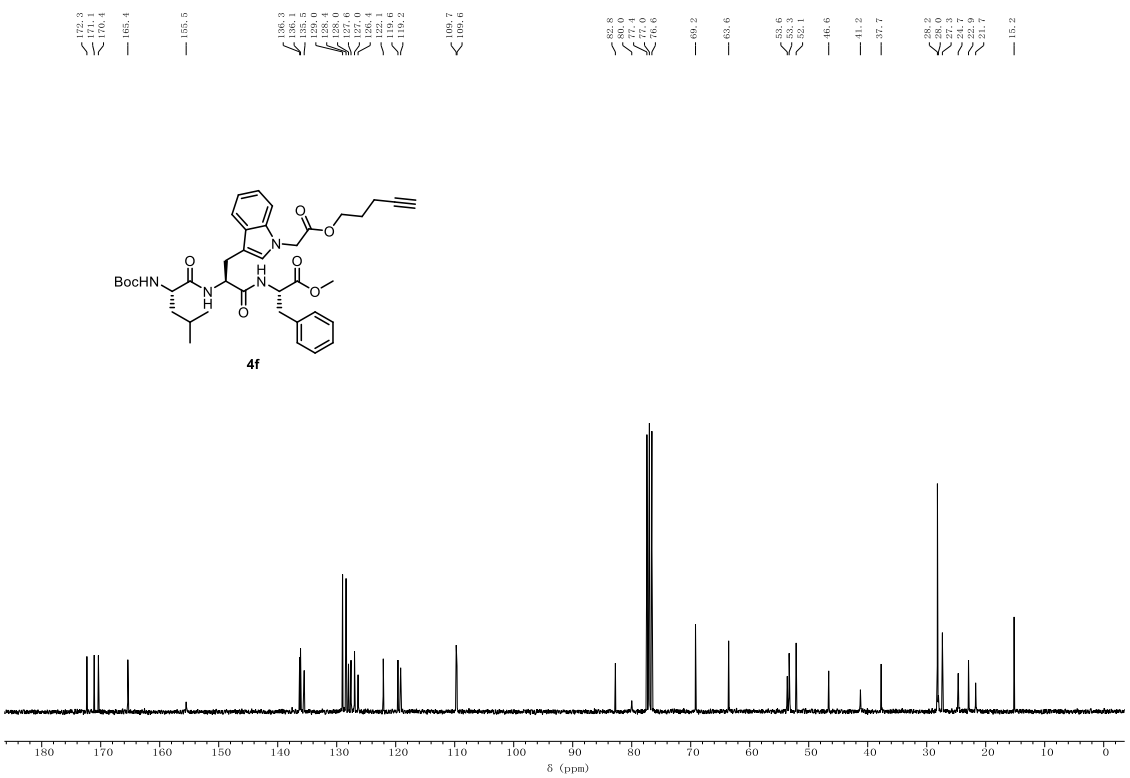
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4e**



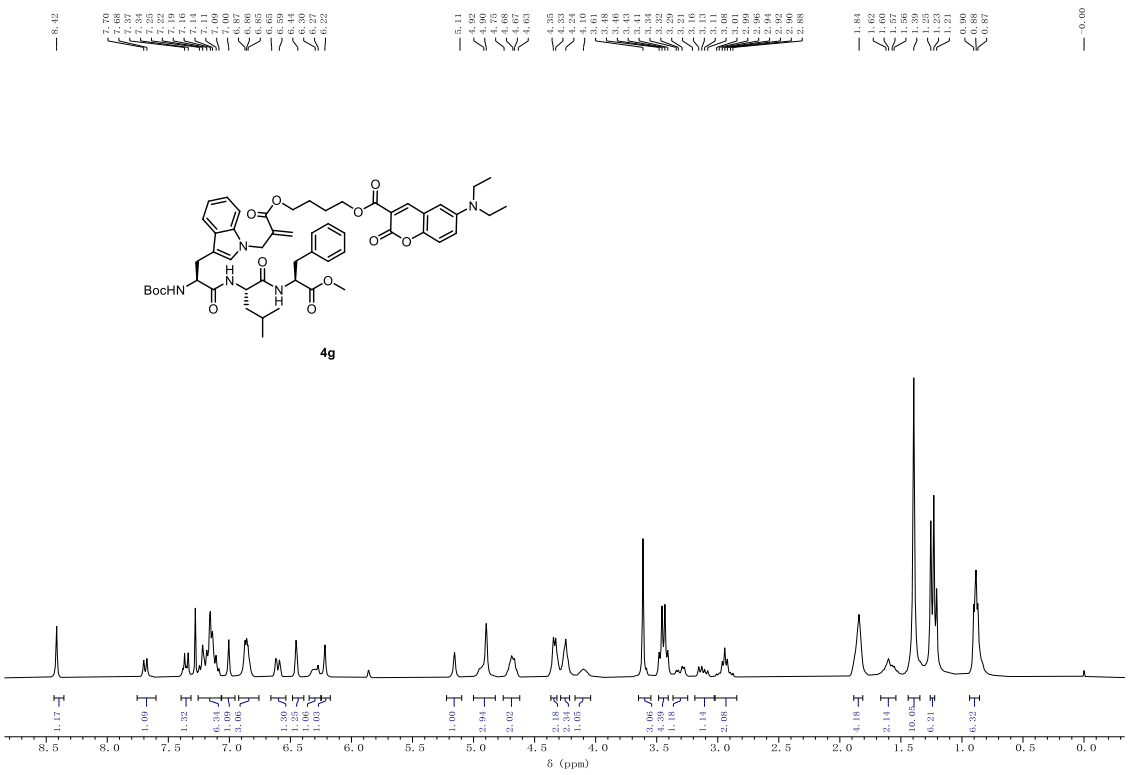
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4e**



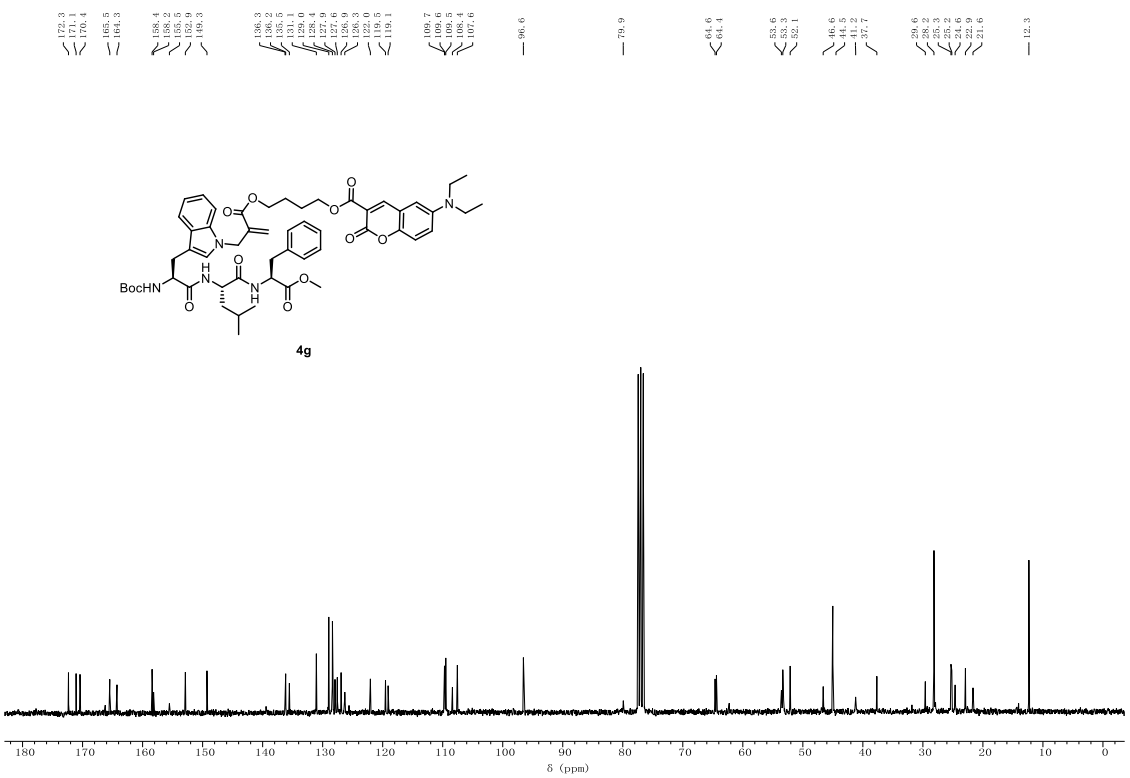
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4f**



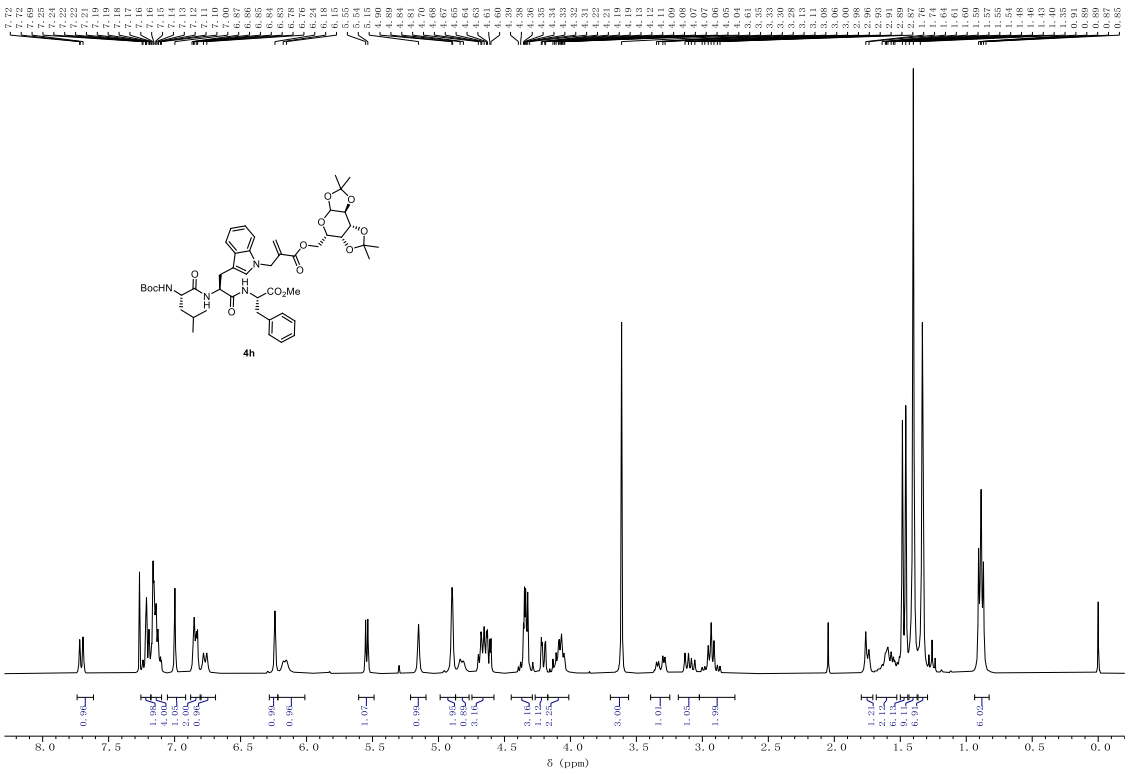
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4f**



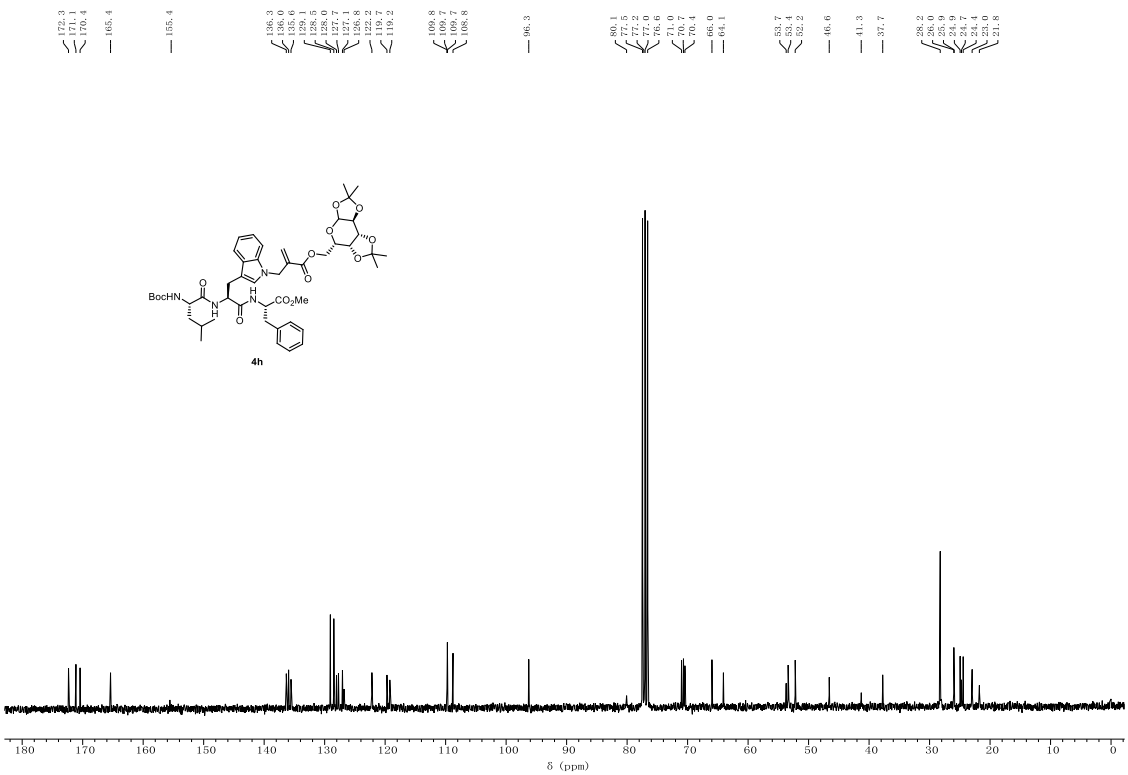
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4g**



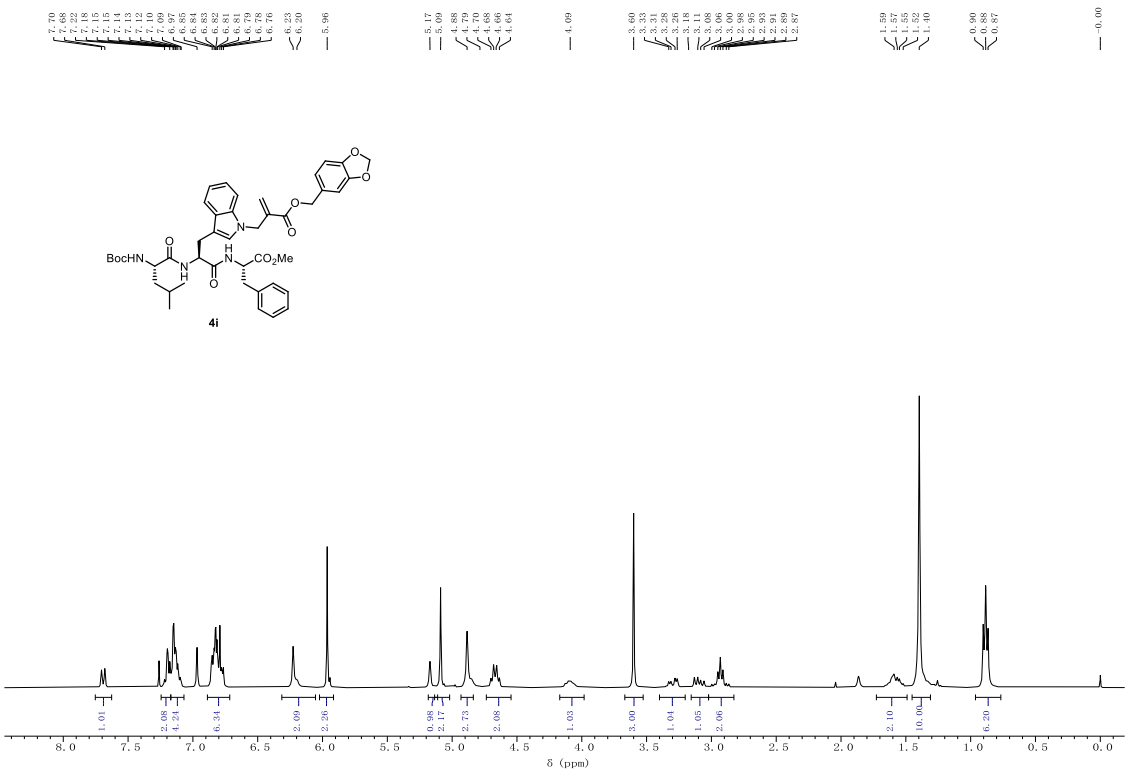
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4g**



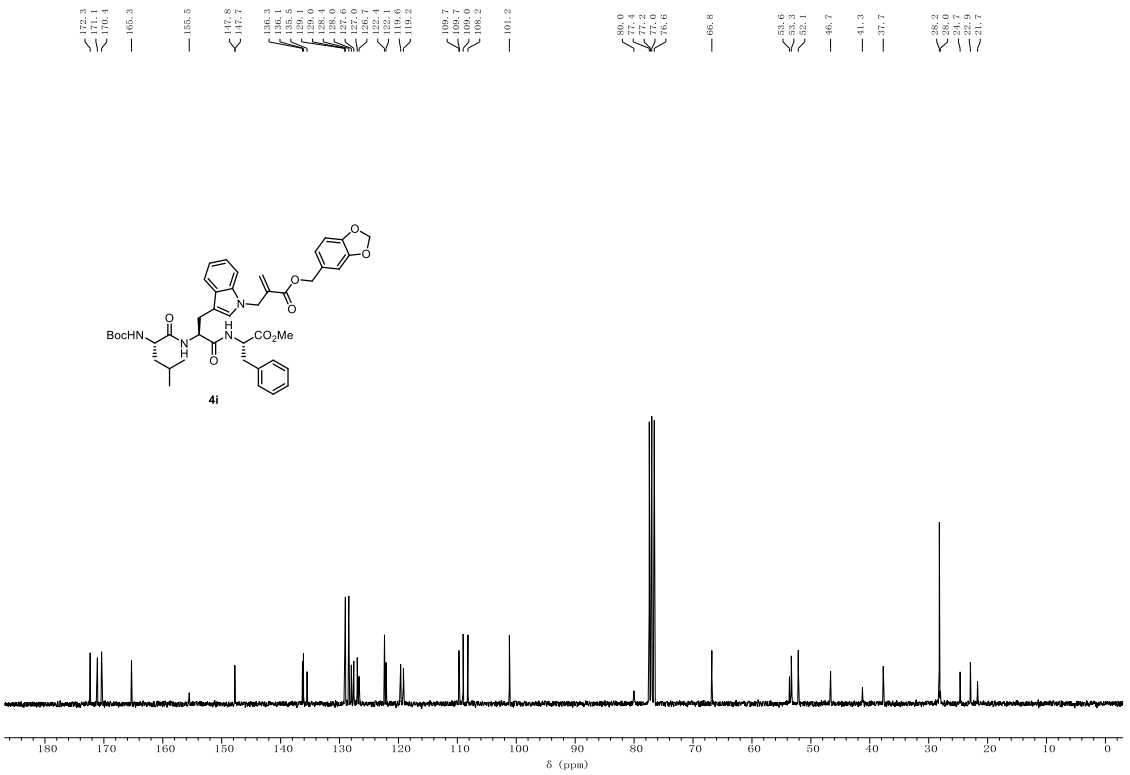
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4h**



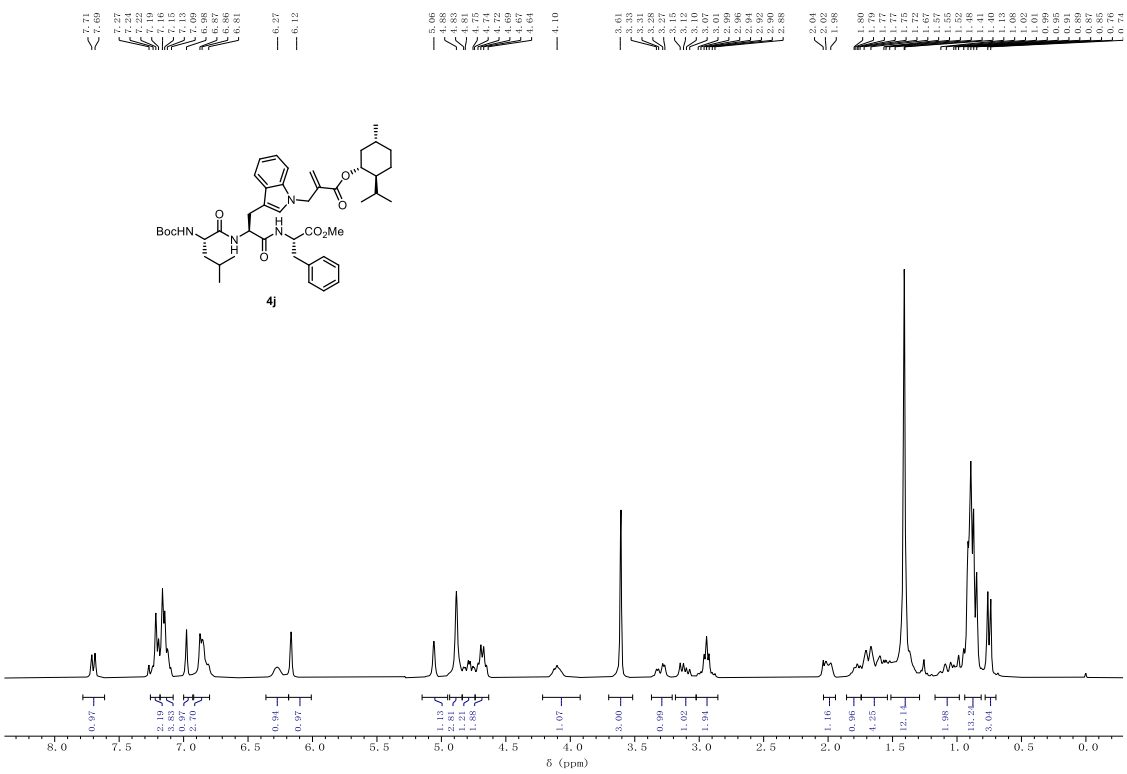
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4h**



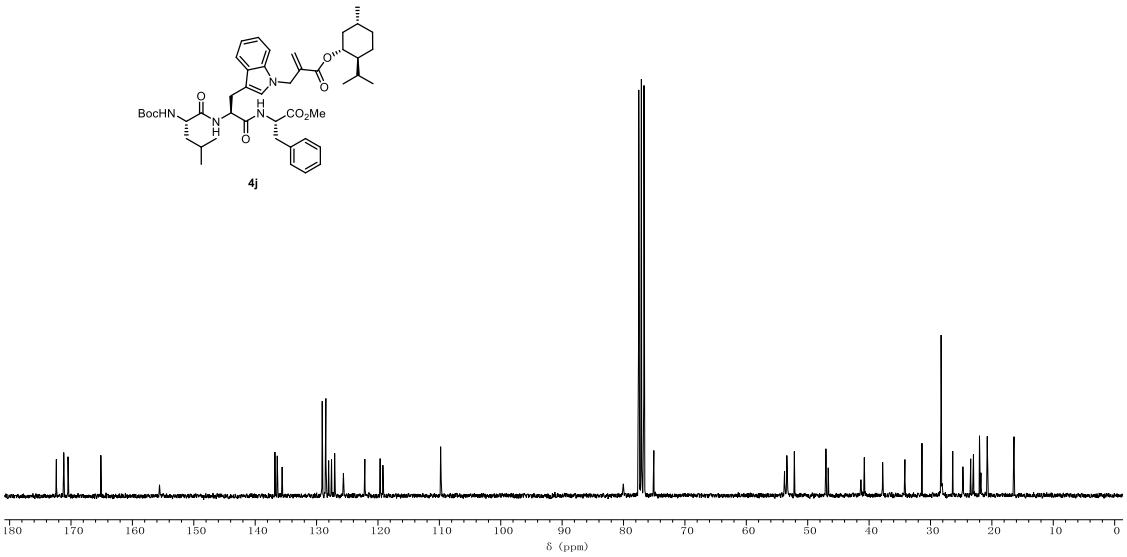
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4i**



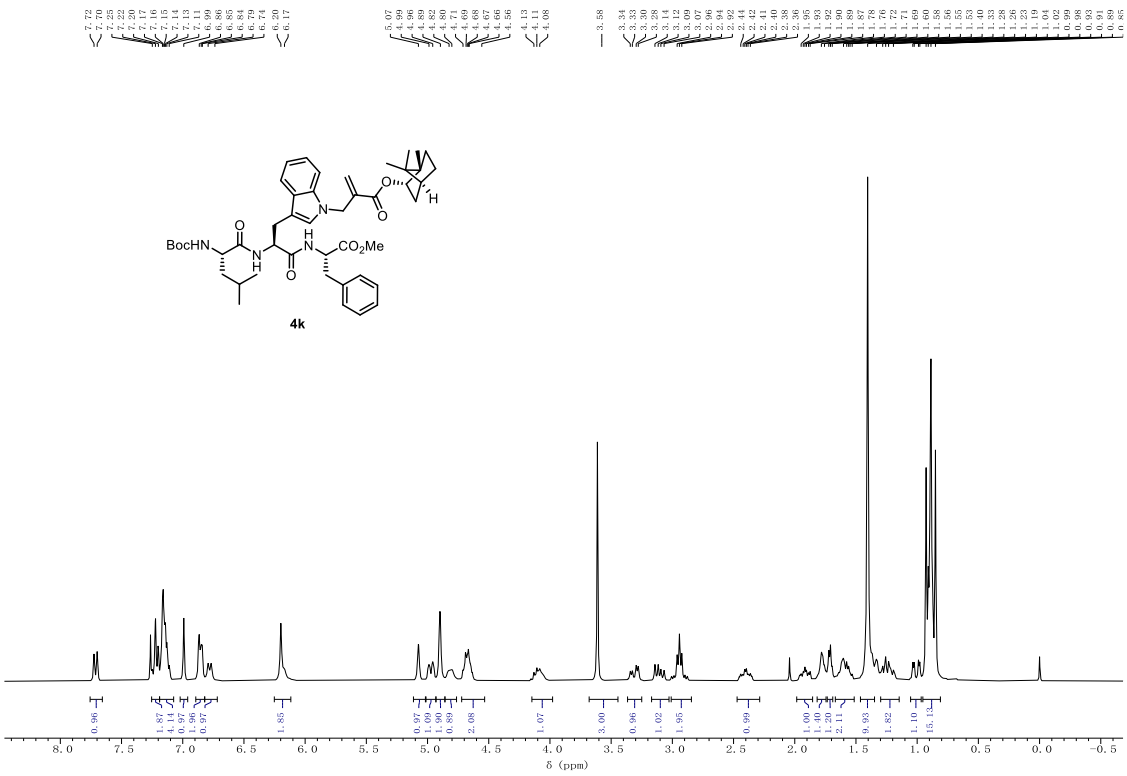
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4i**



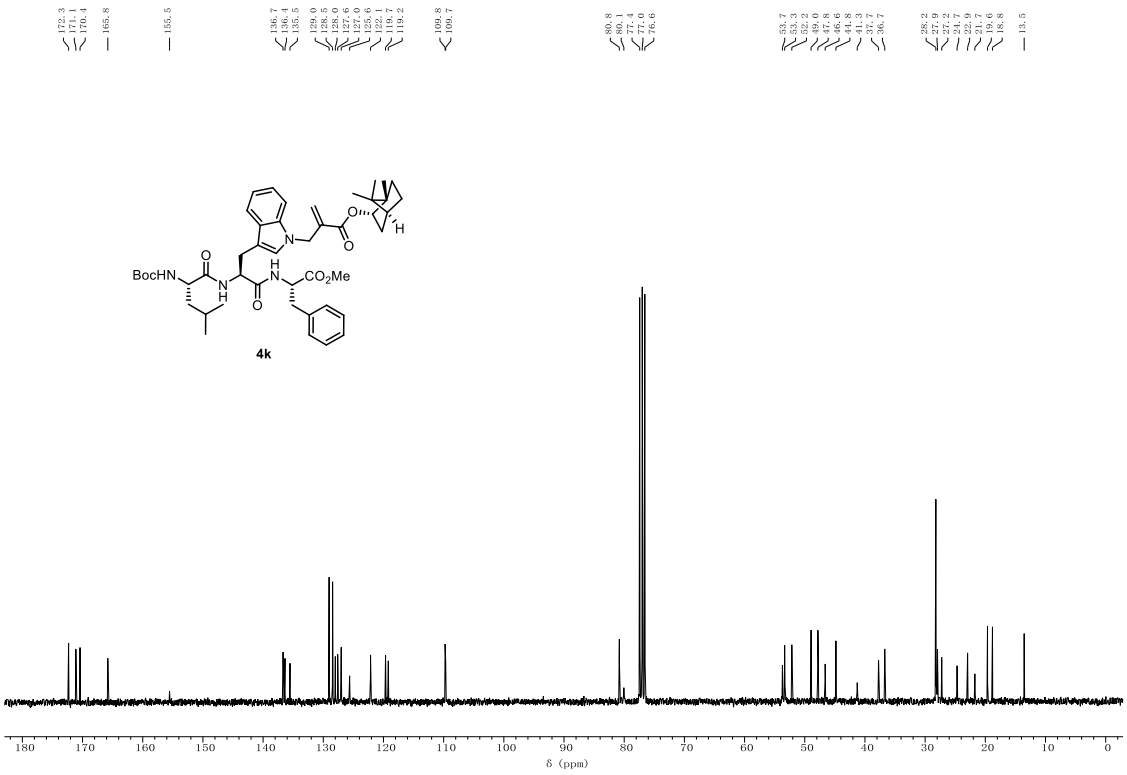
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4j**



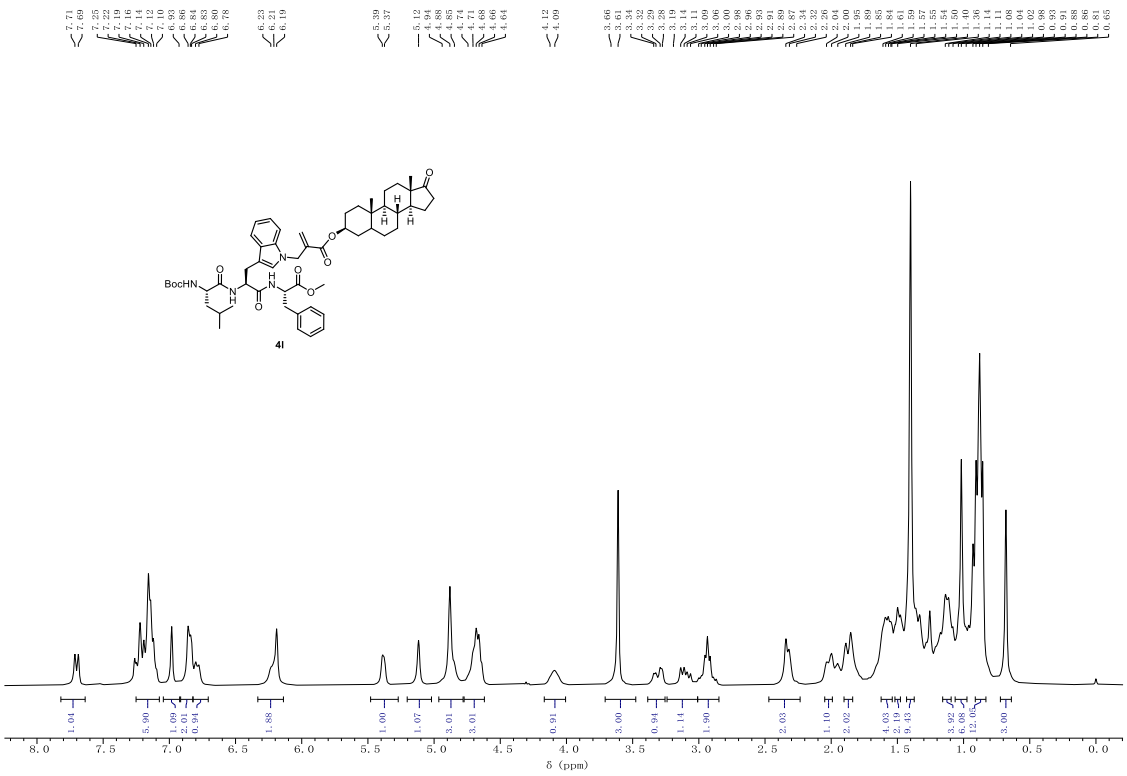
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4j**



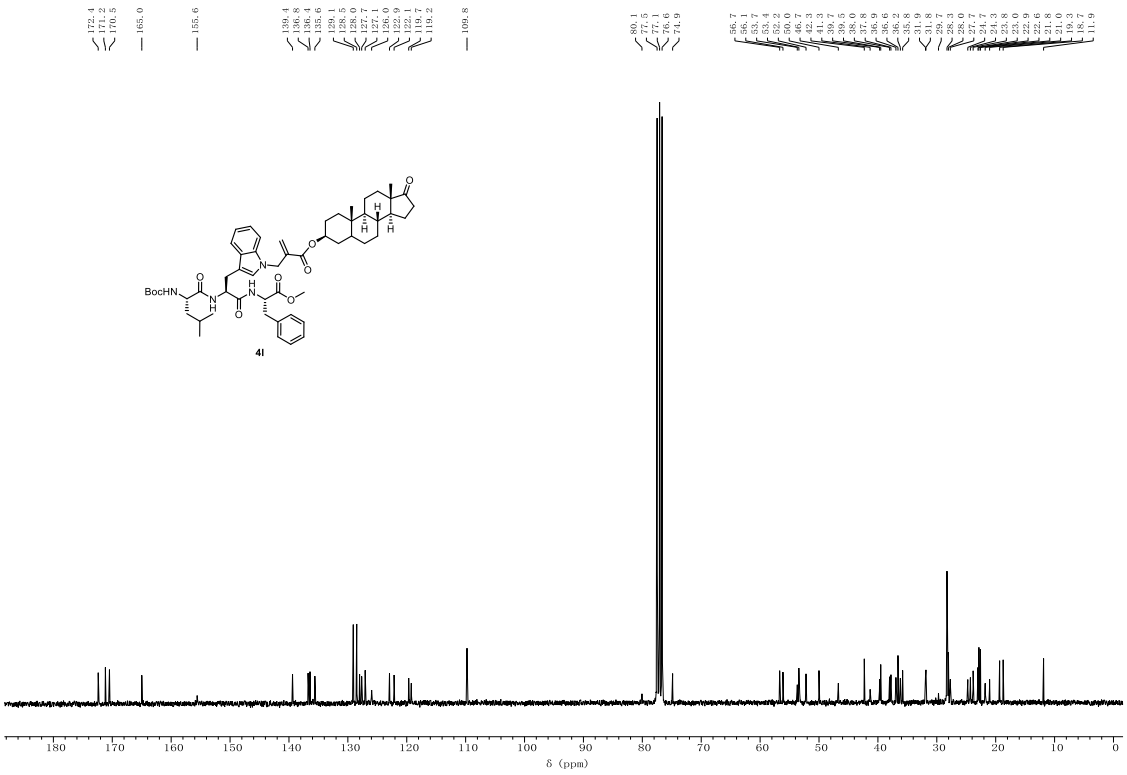
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4k**



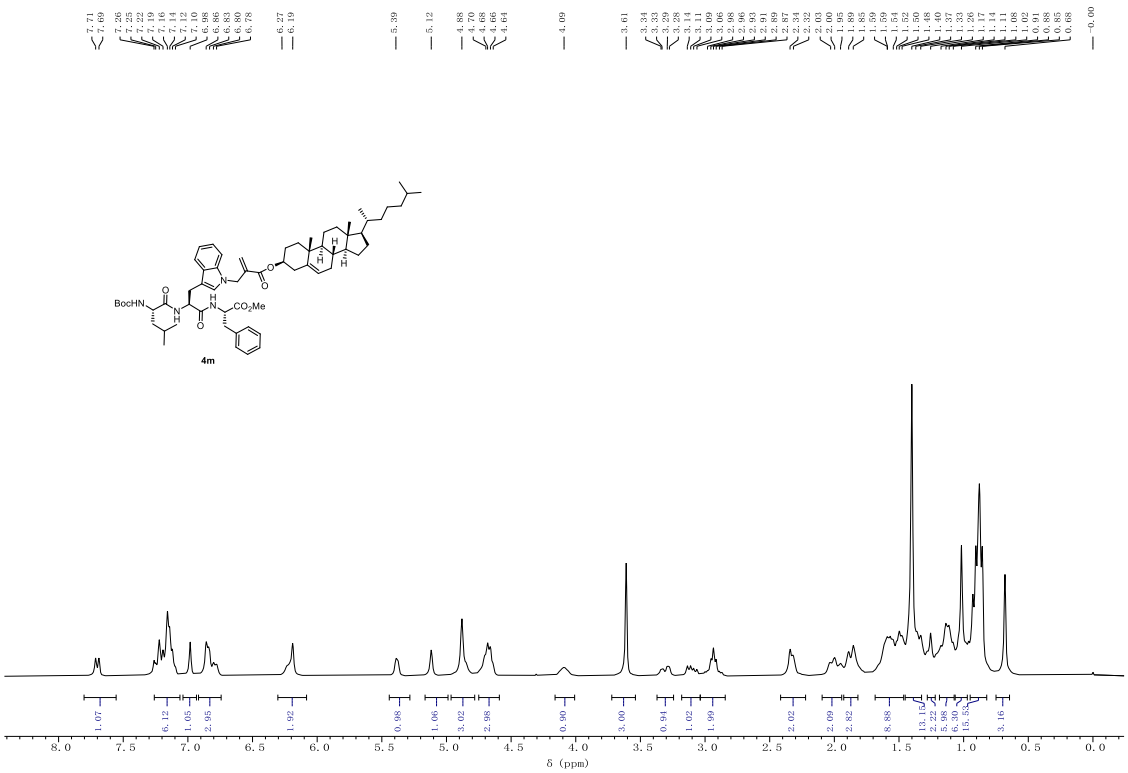
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4k**



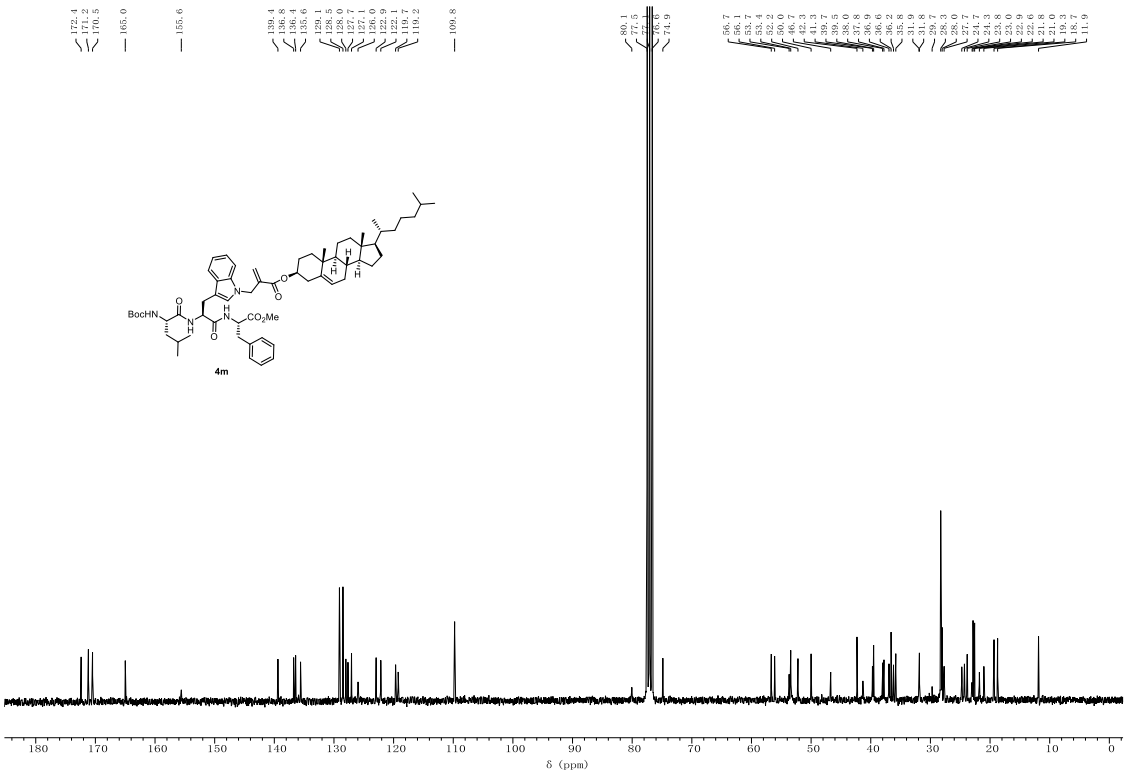
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4l**



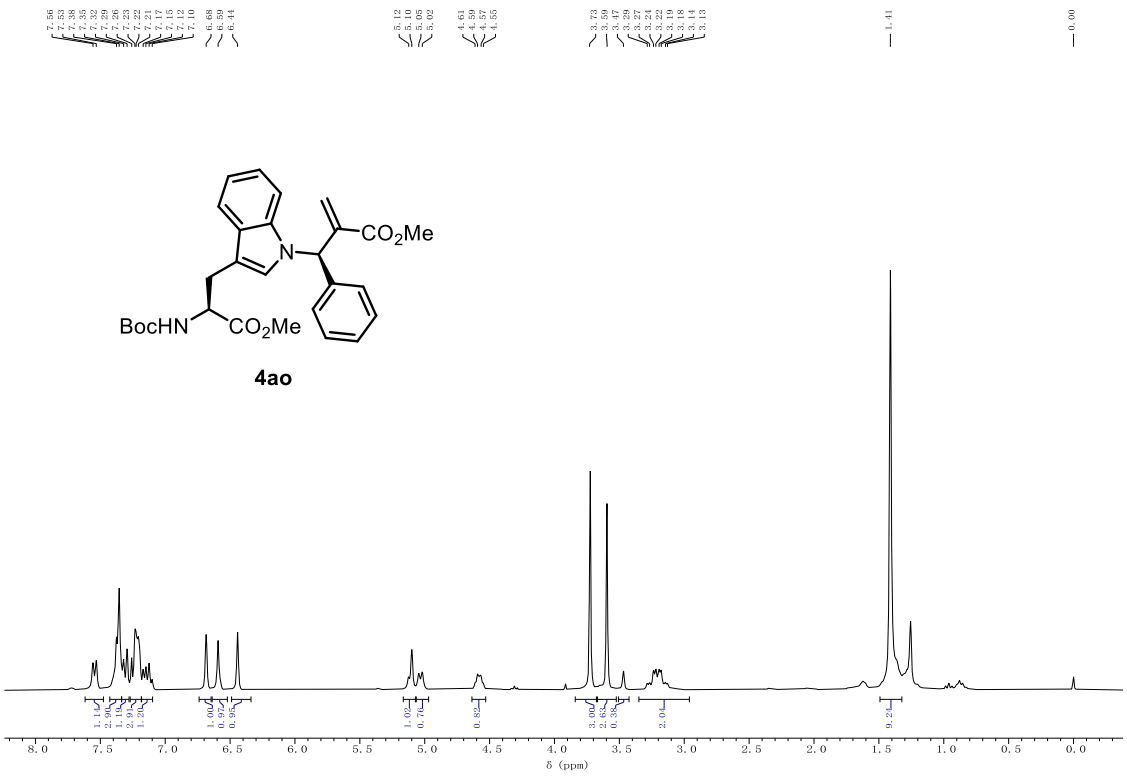
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4l**



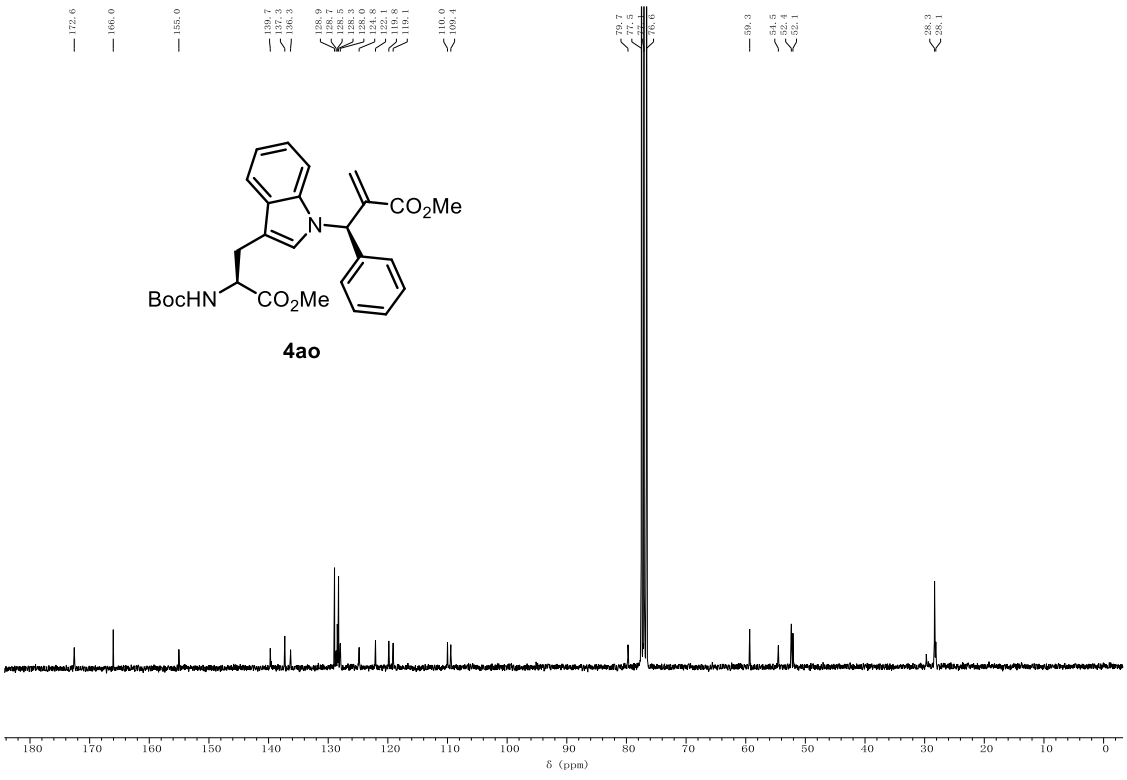
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4m**



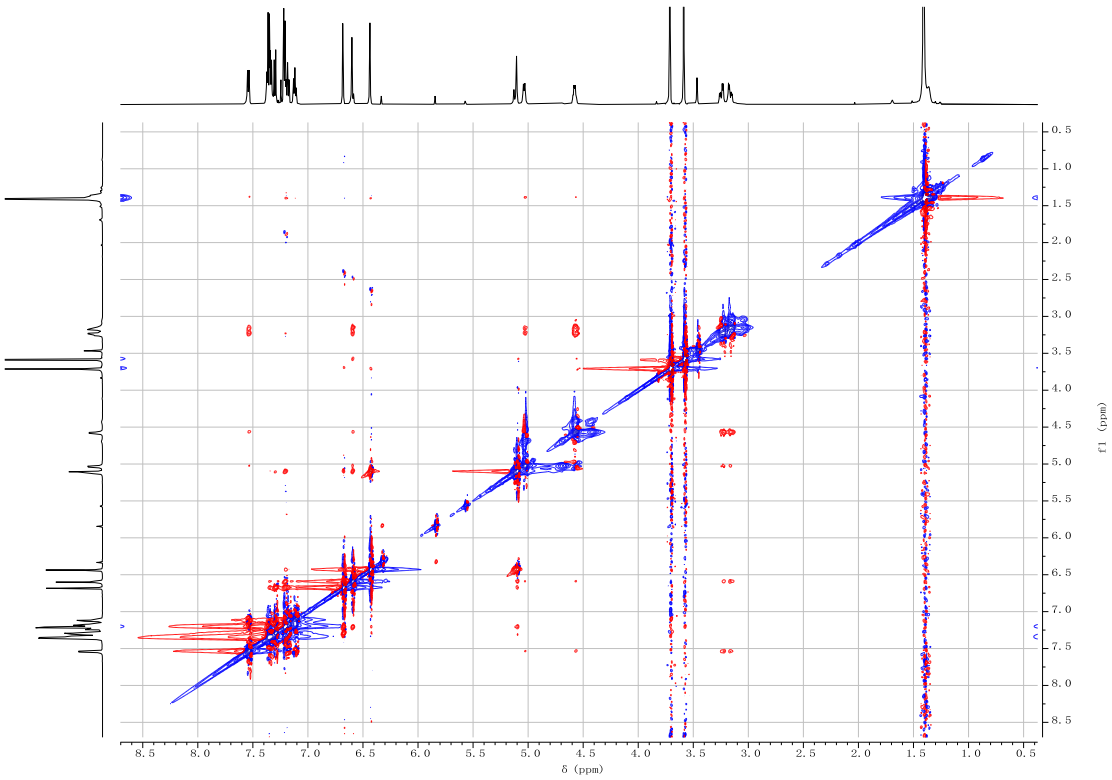
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4m**



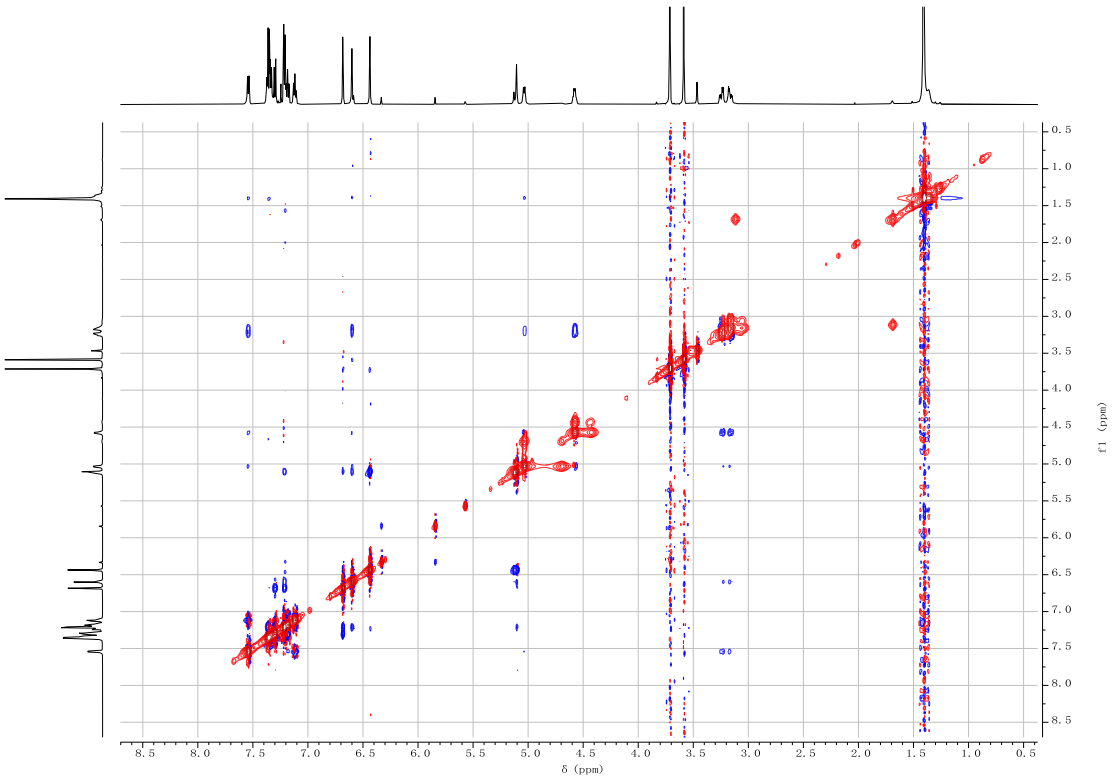
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4ao**



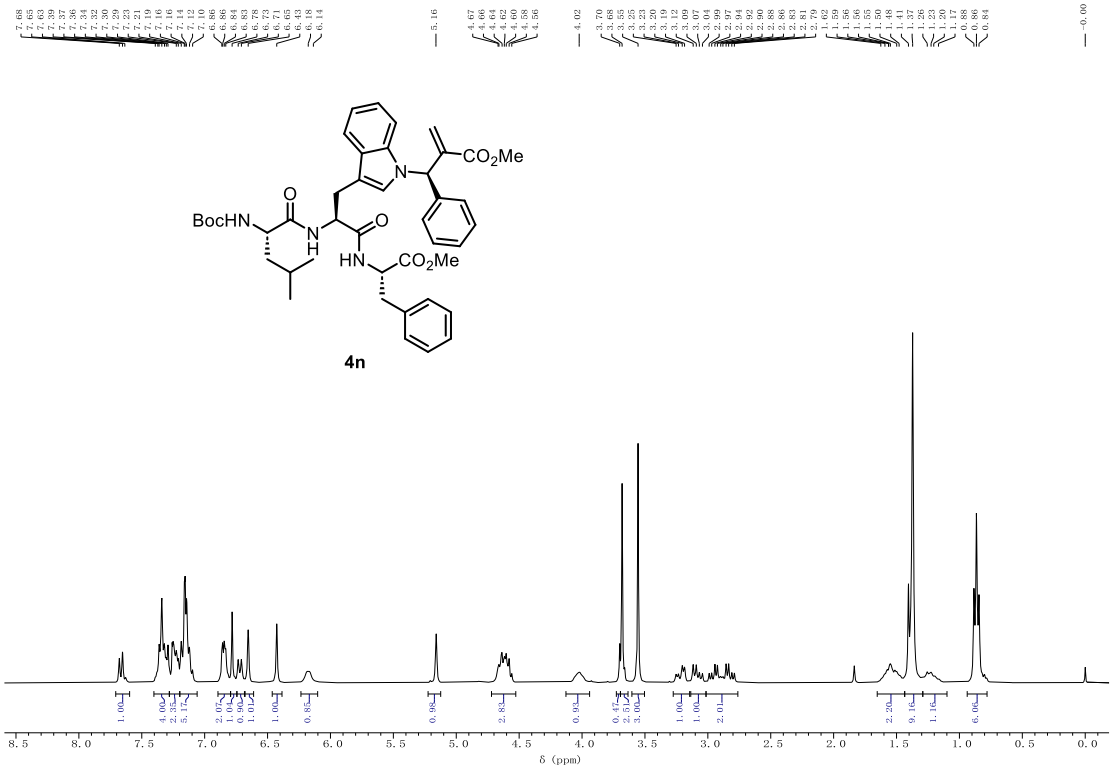
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4ao**



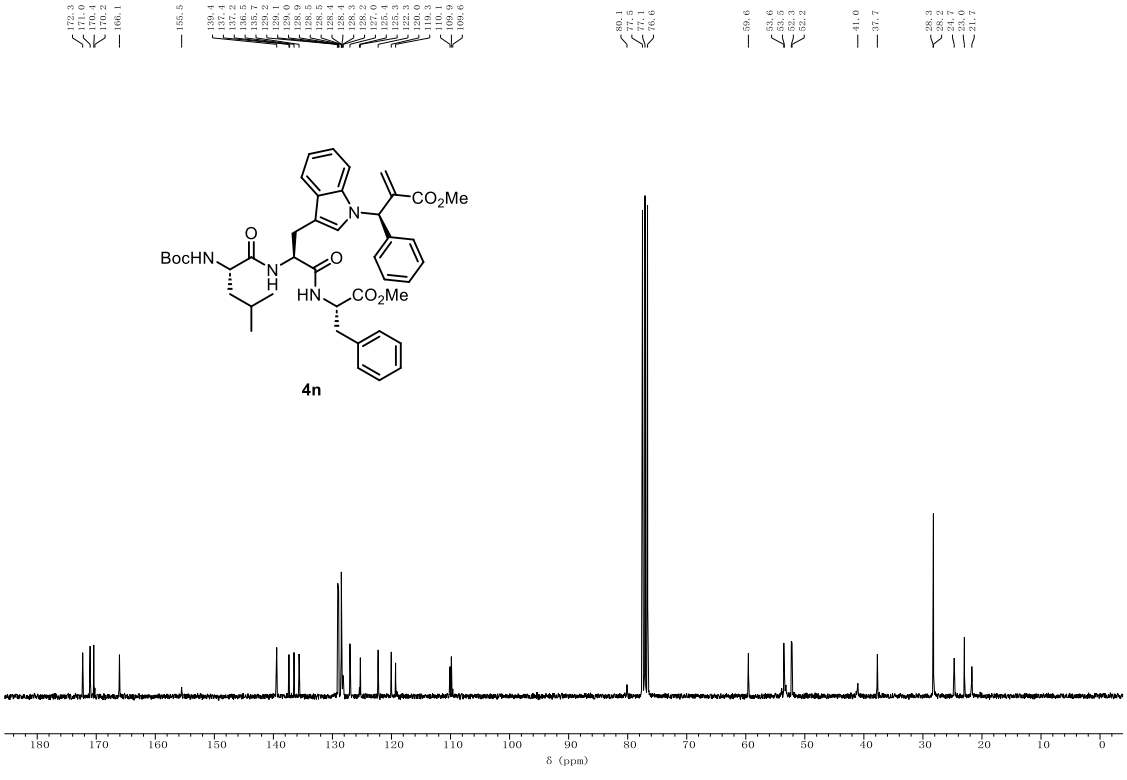
1H-1H ROESY spectrum of **4ao**



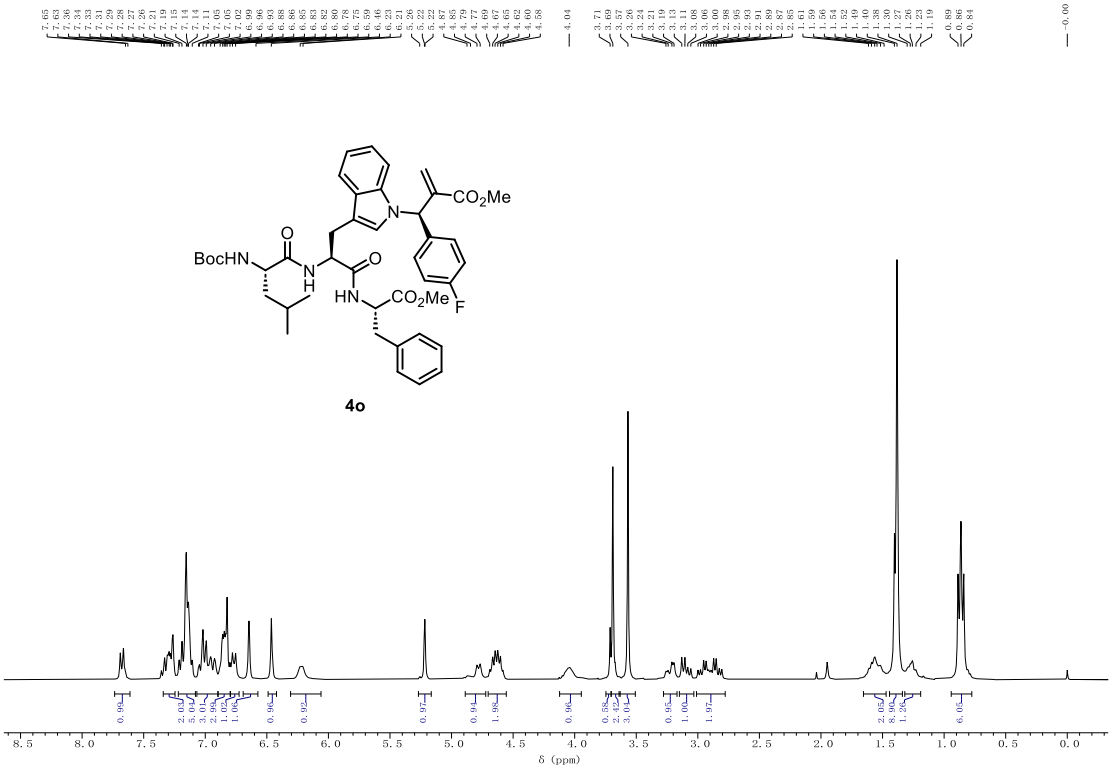
1H-1H NOESY spectrum of **4ao**



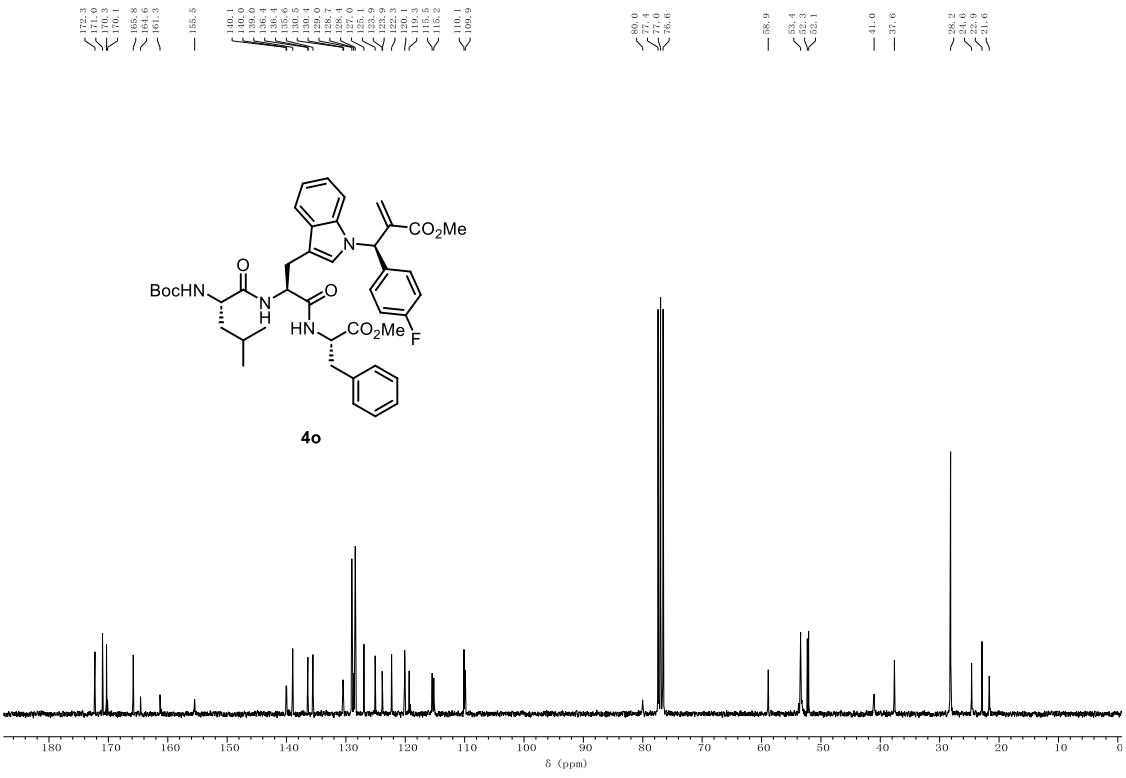
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4n**



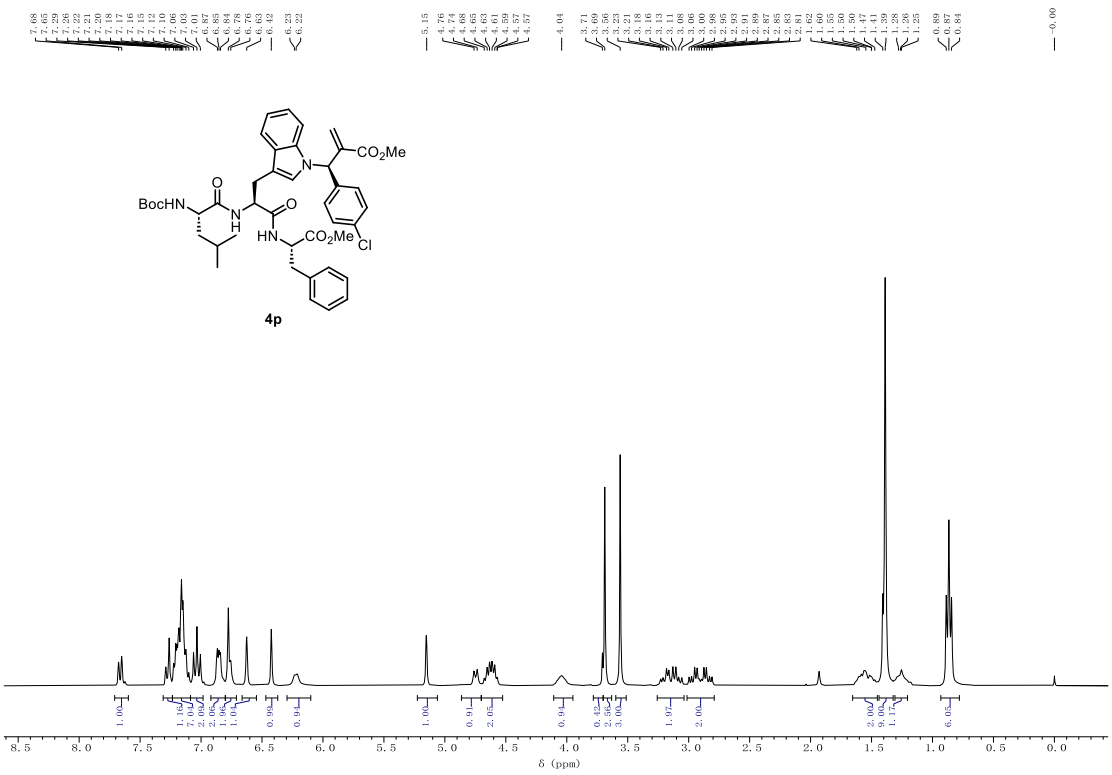
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4n**



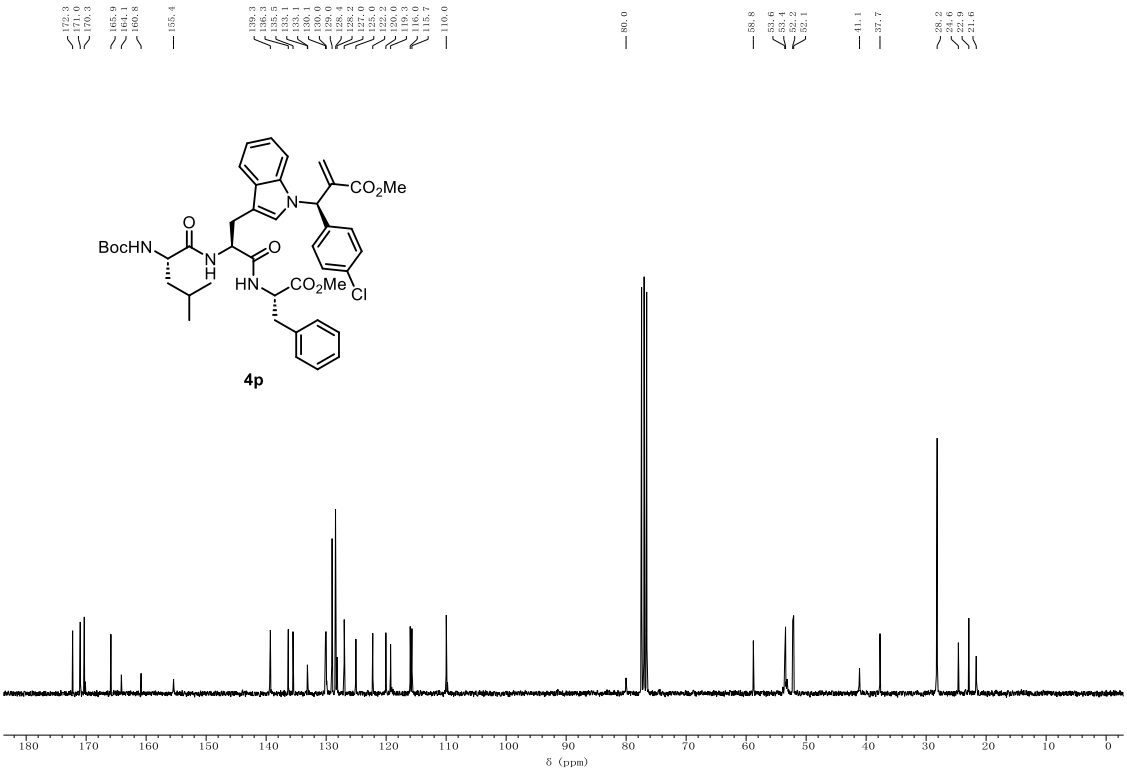
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4o**



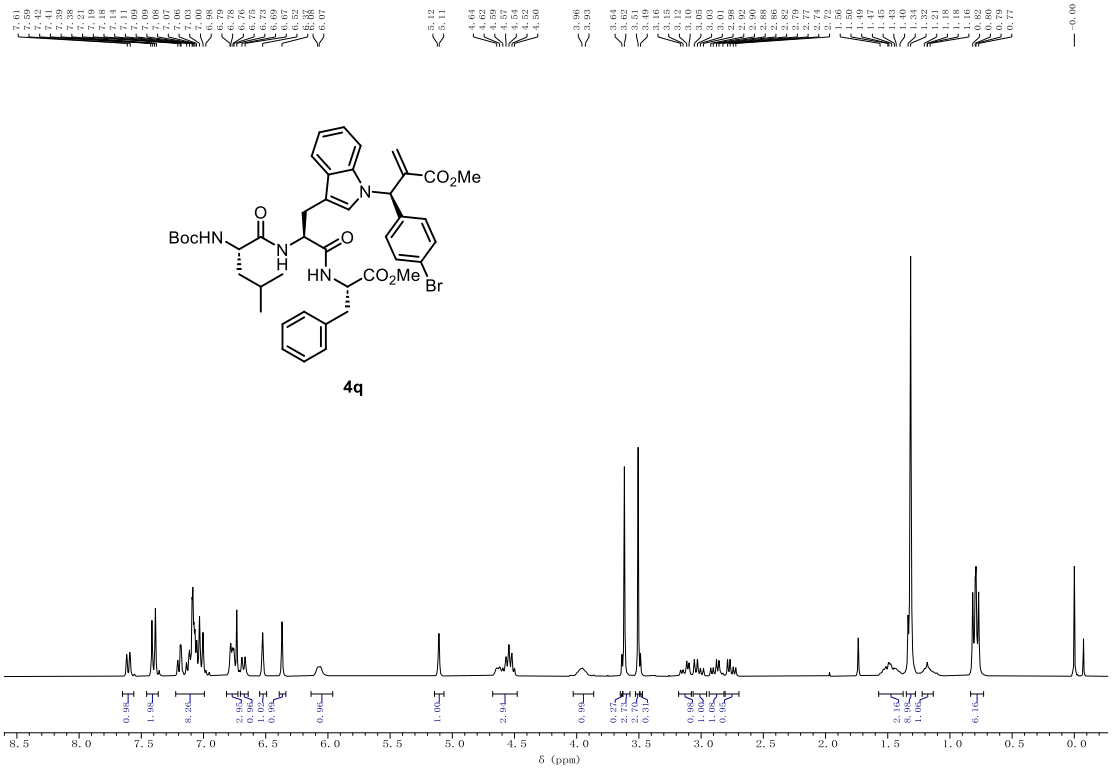
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4o**



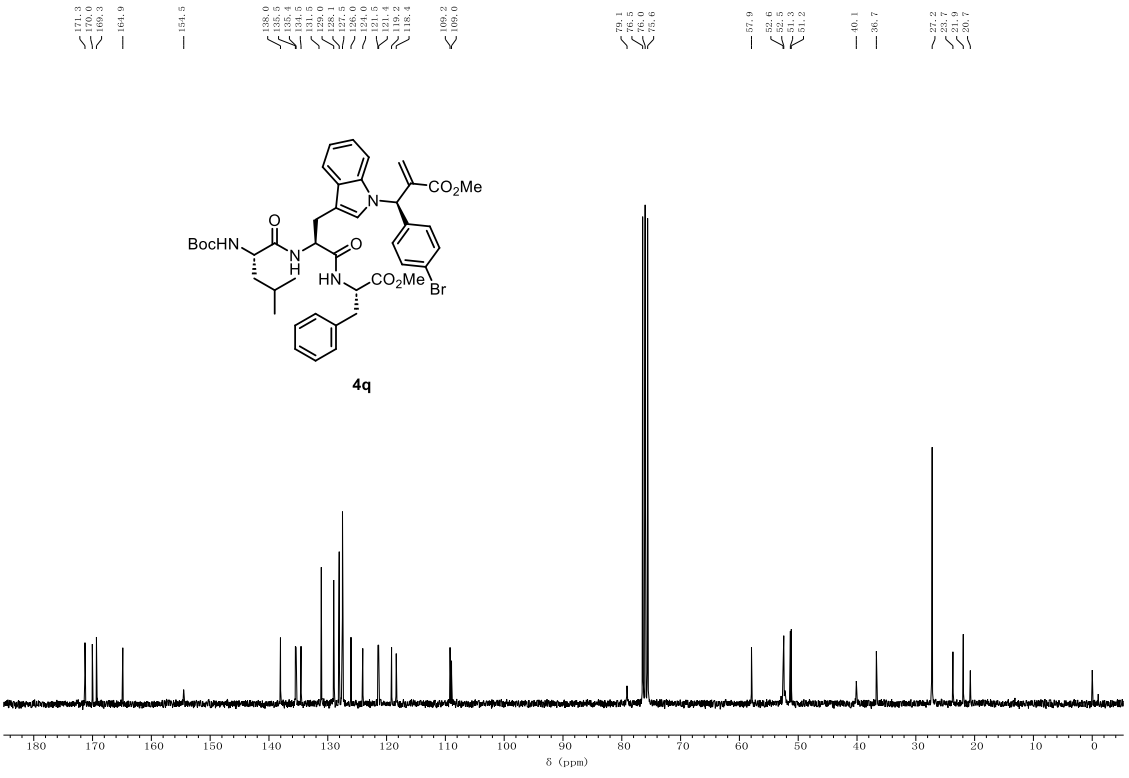
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4p**



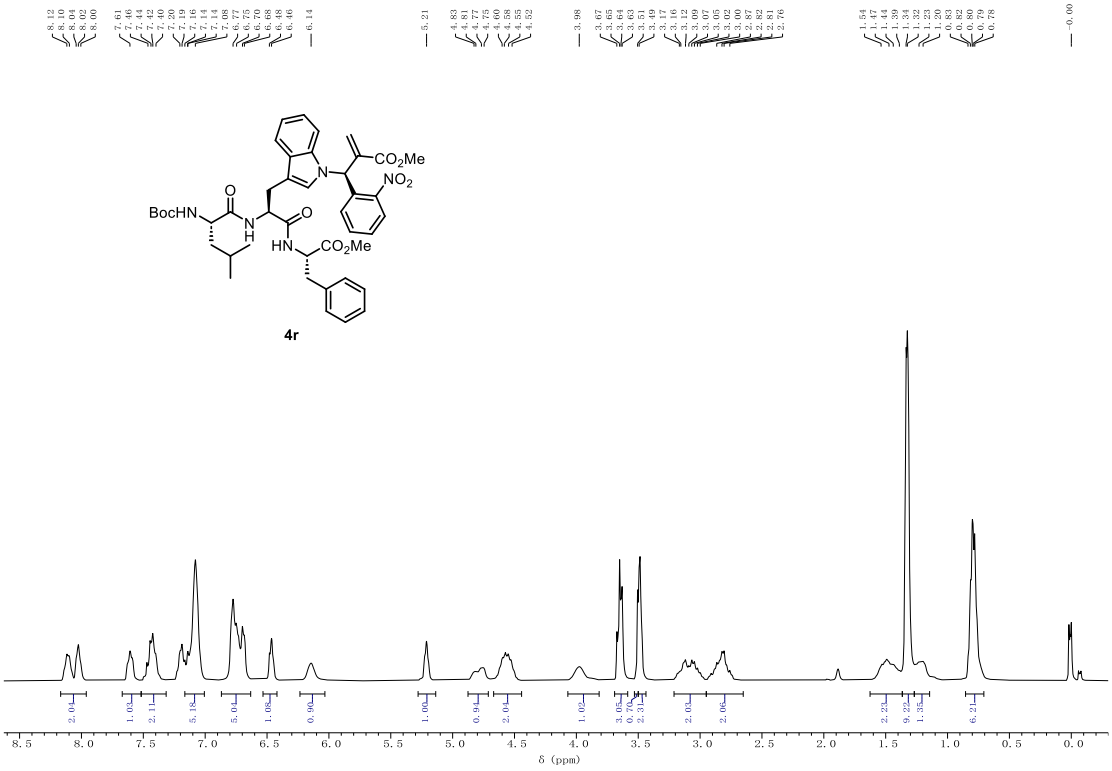
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4p**



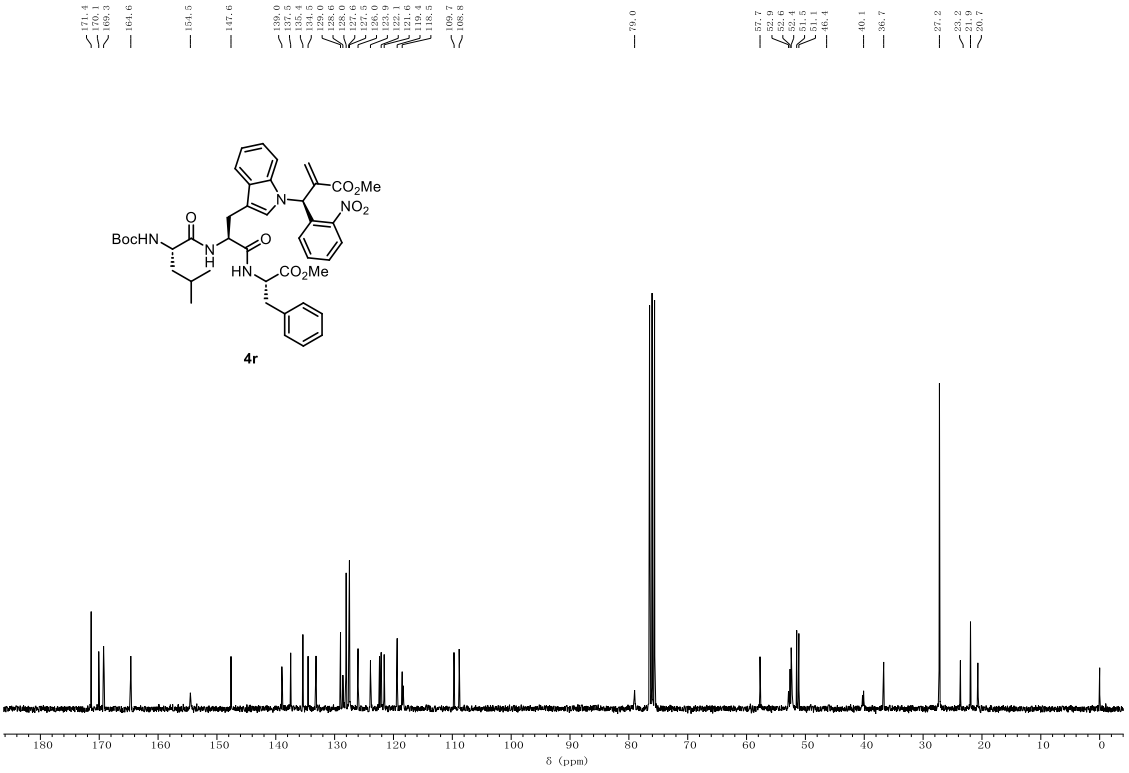
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4q**



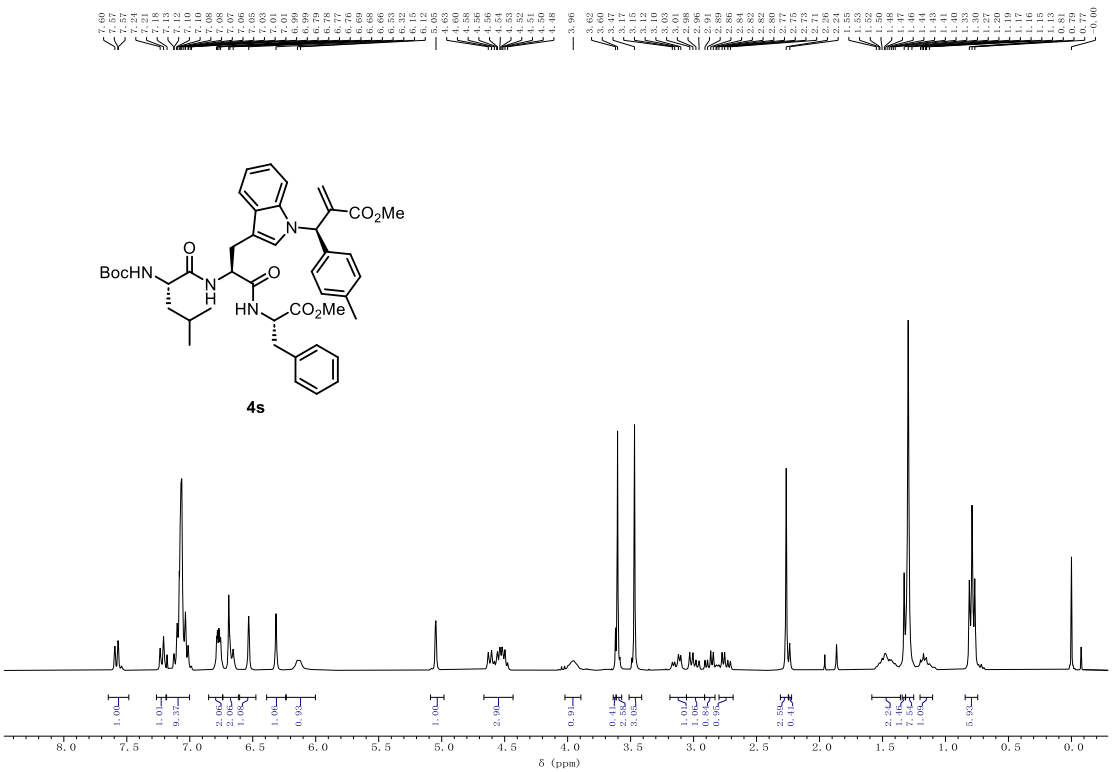
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4q**



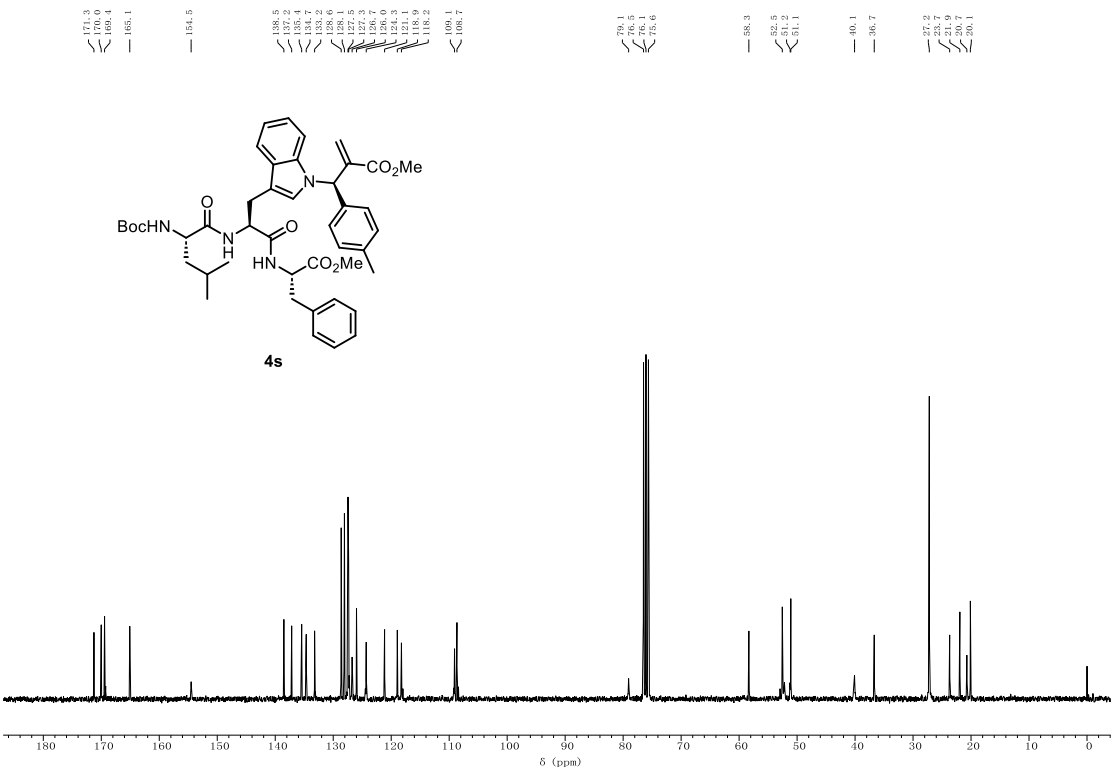
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4r**



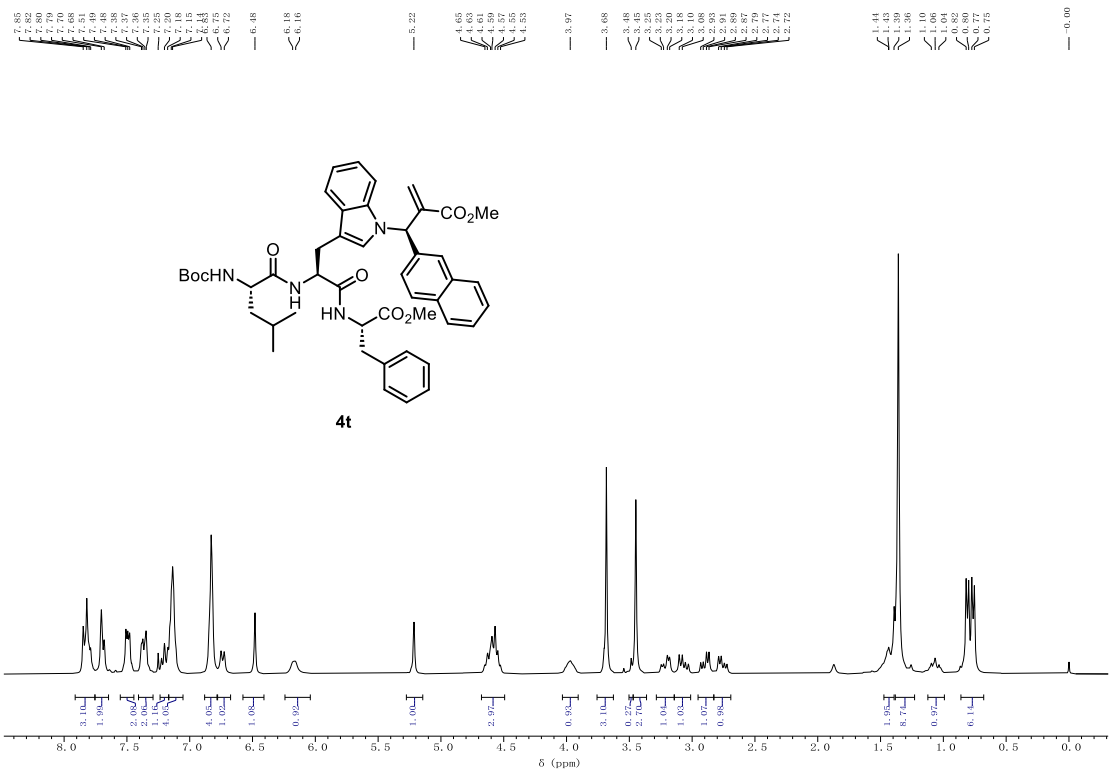
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4r**



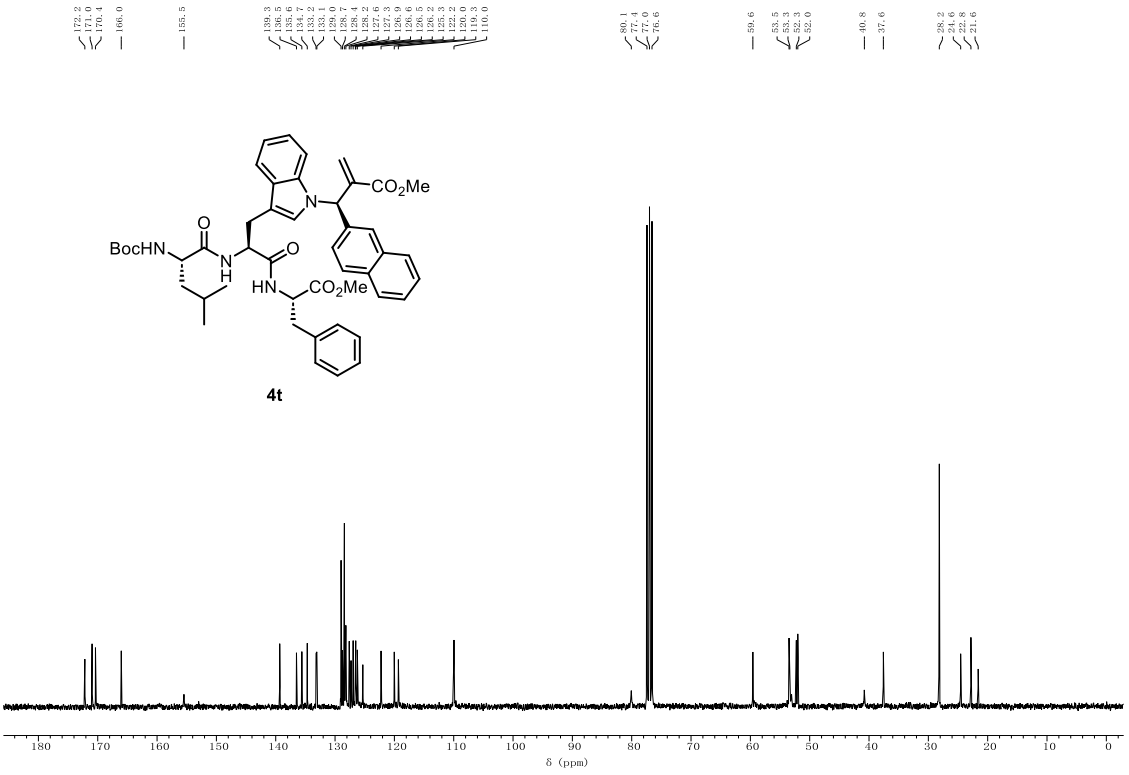
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4s**



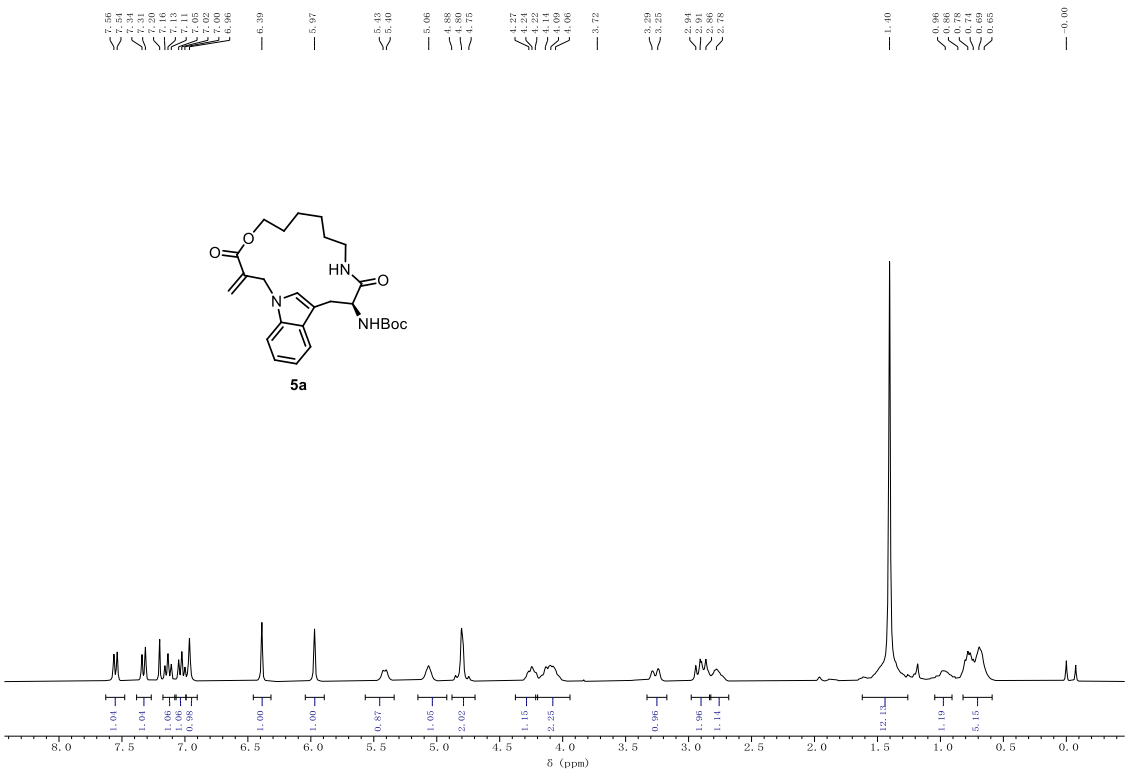
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4s**



^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **4t**

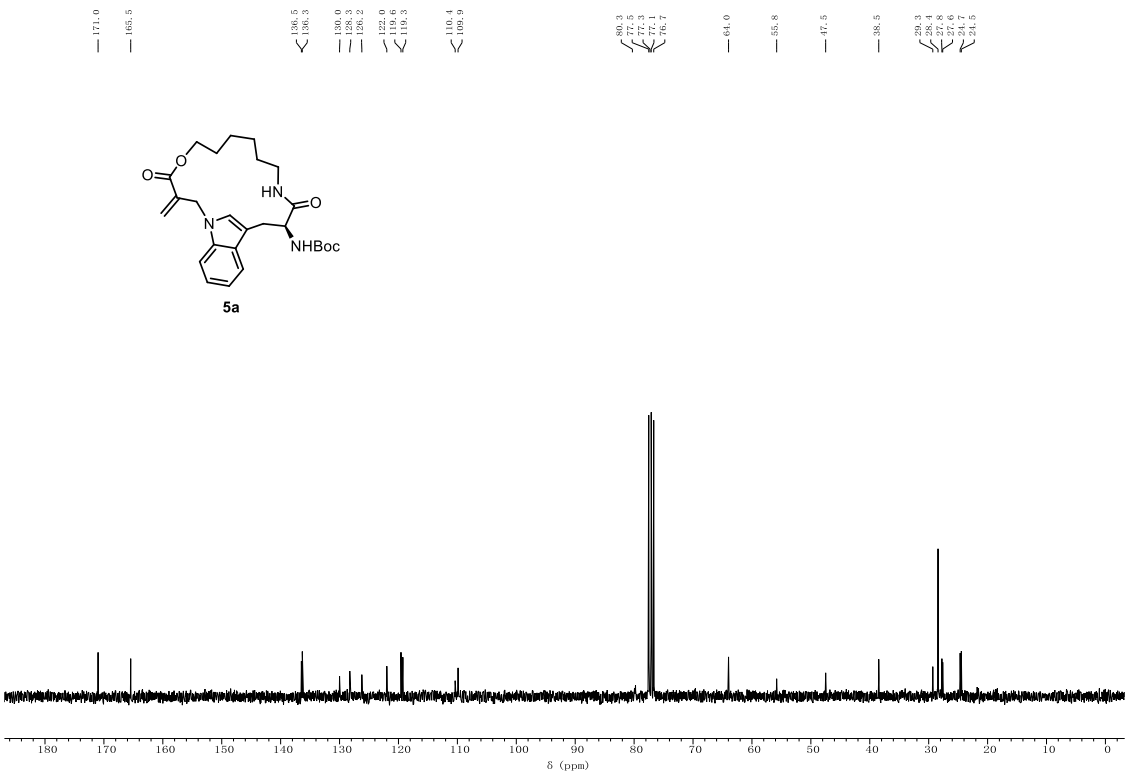


^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **4t**



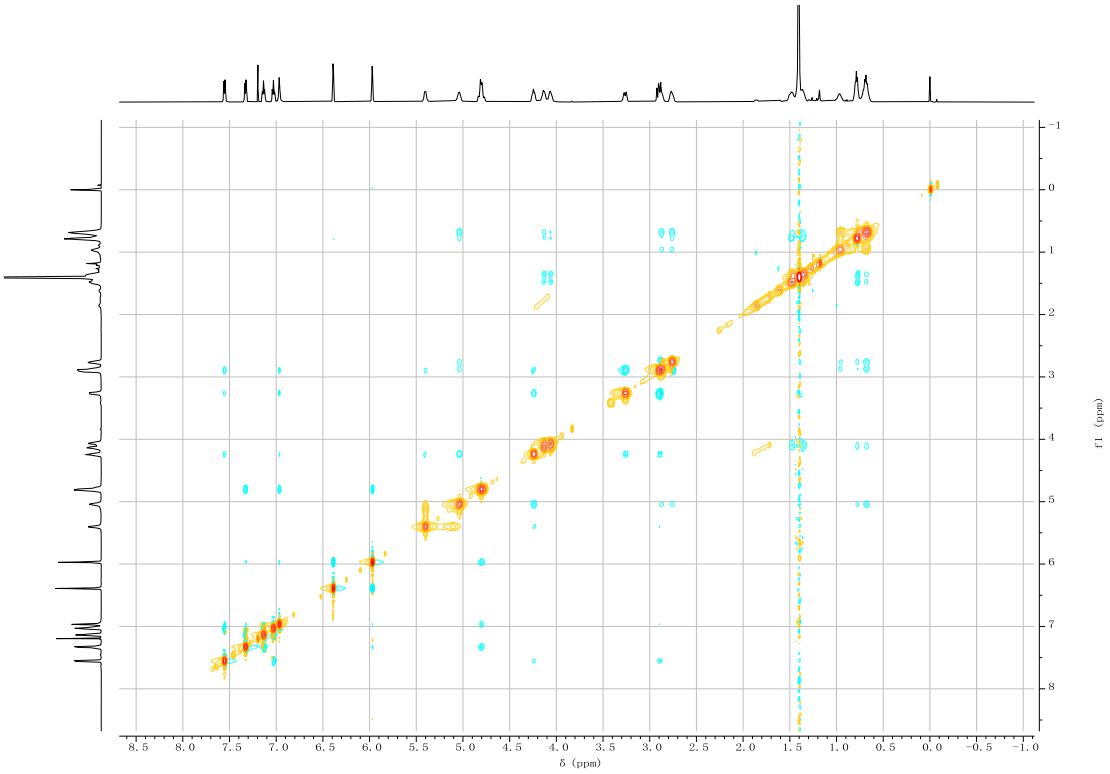
5a

^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **5a**

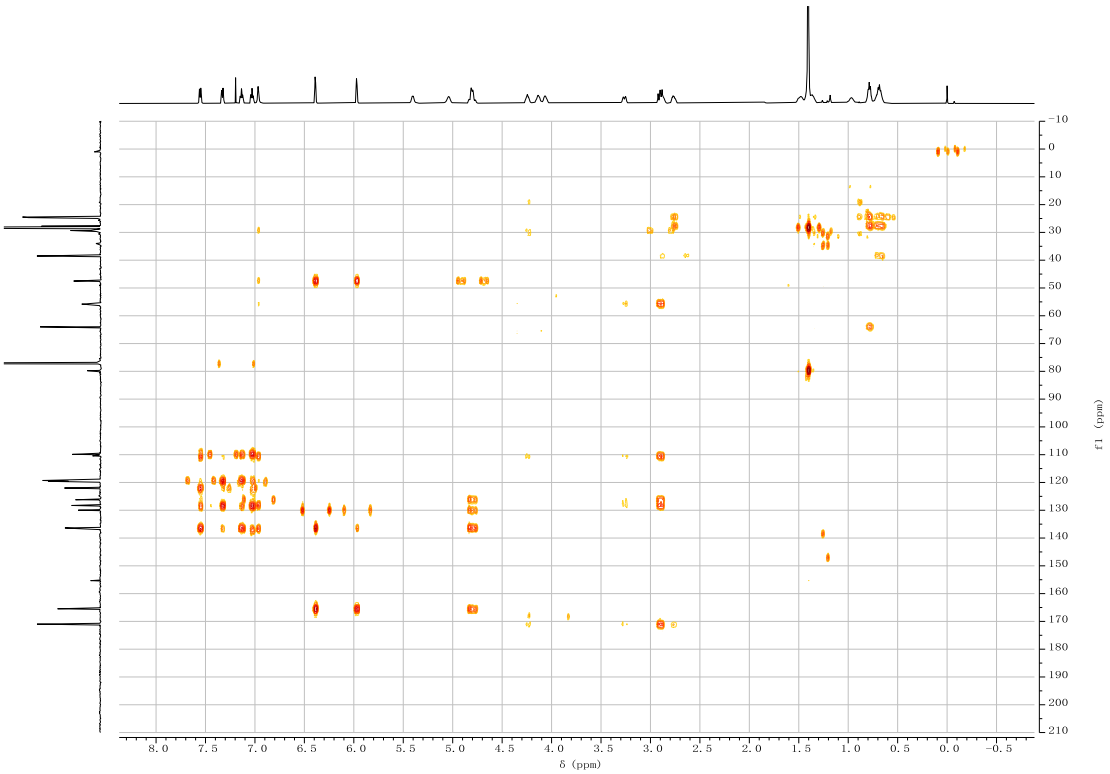


5a

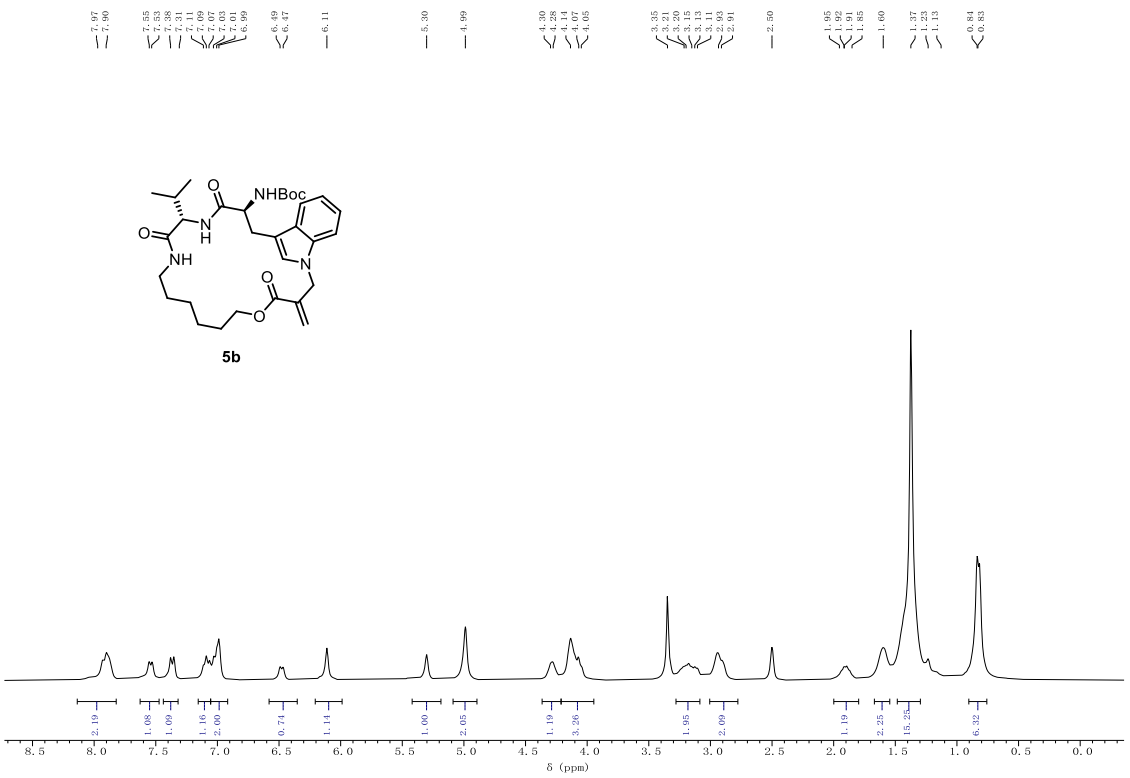
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **5a**



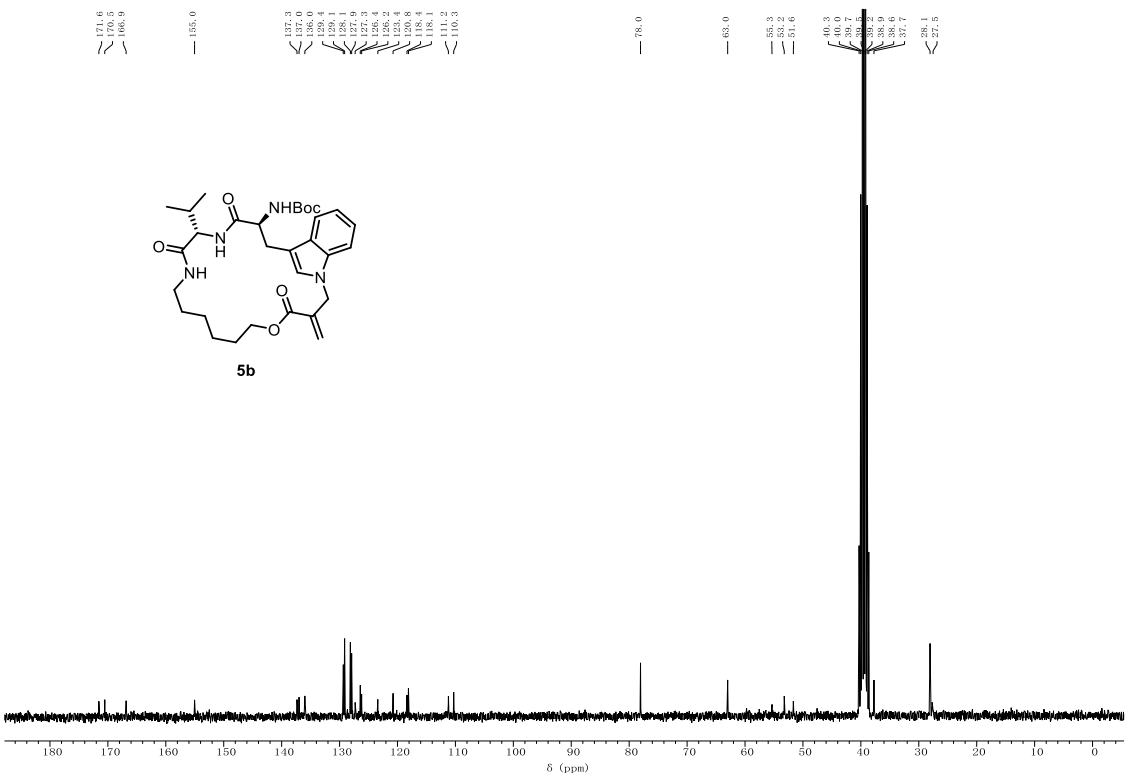
1H-1H NOESY spectrum of **5a**



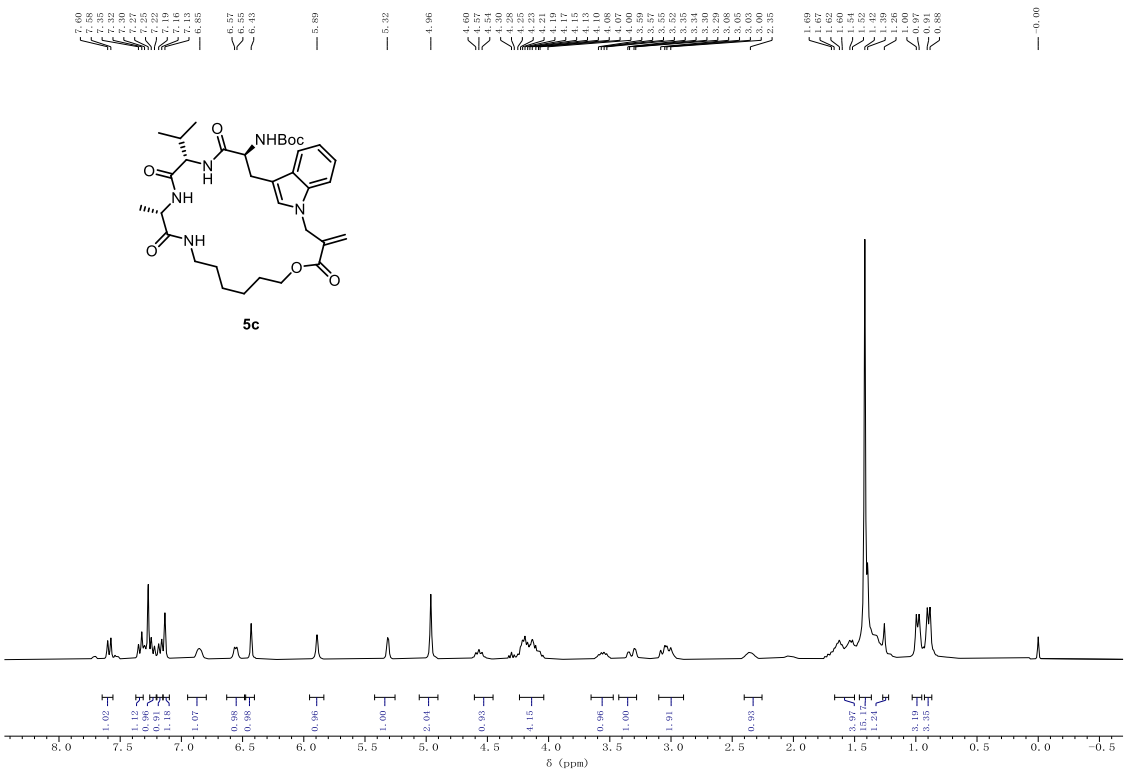
HMBC spectrum of **5a**



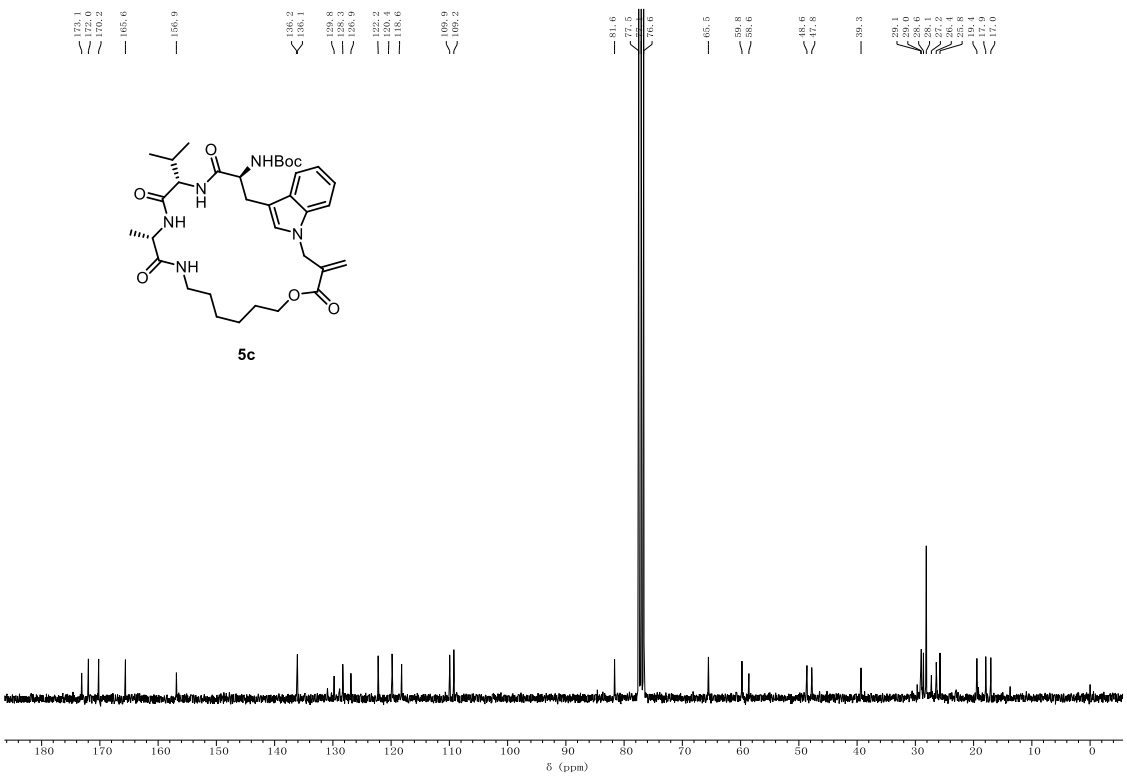
^{1}H NMR (300 MHz, DMSO-d_6) spectrum of **5b**



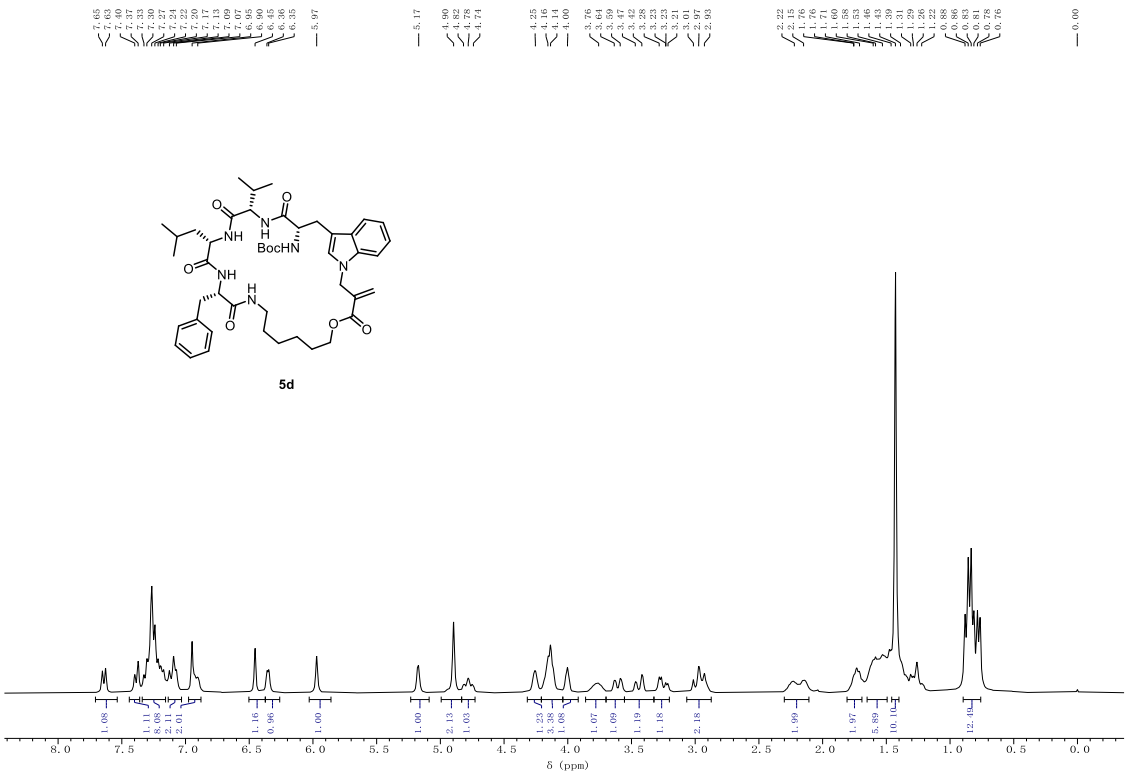
^{13}C NMR (75 MHz, DMSO-d_6) spectrum of **5b**



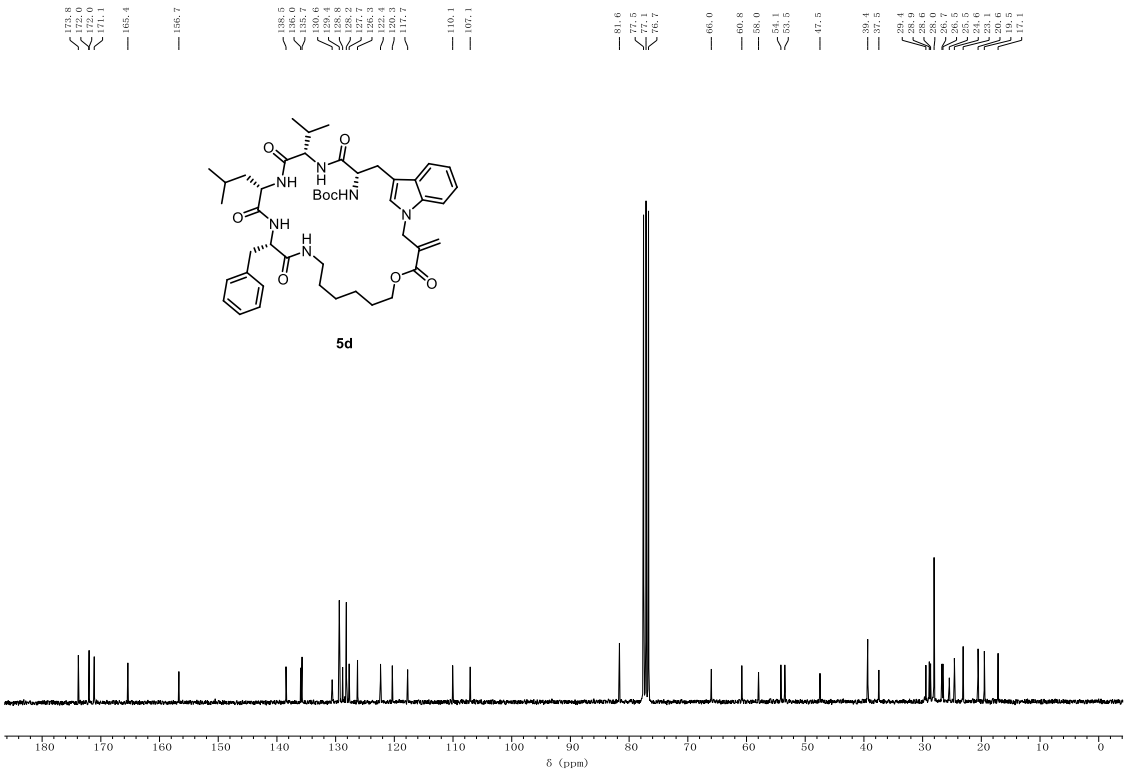
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **5c**



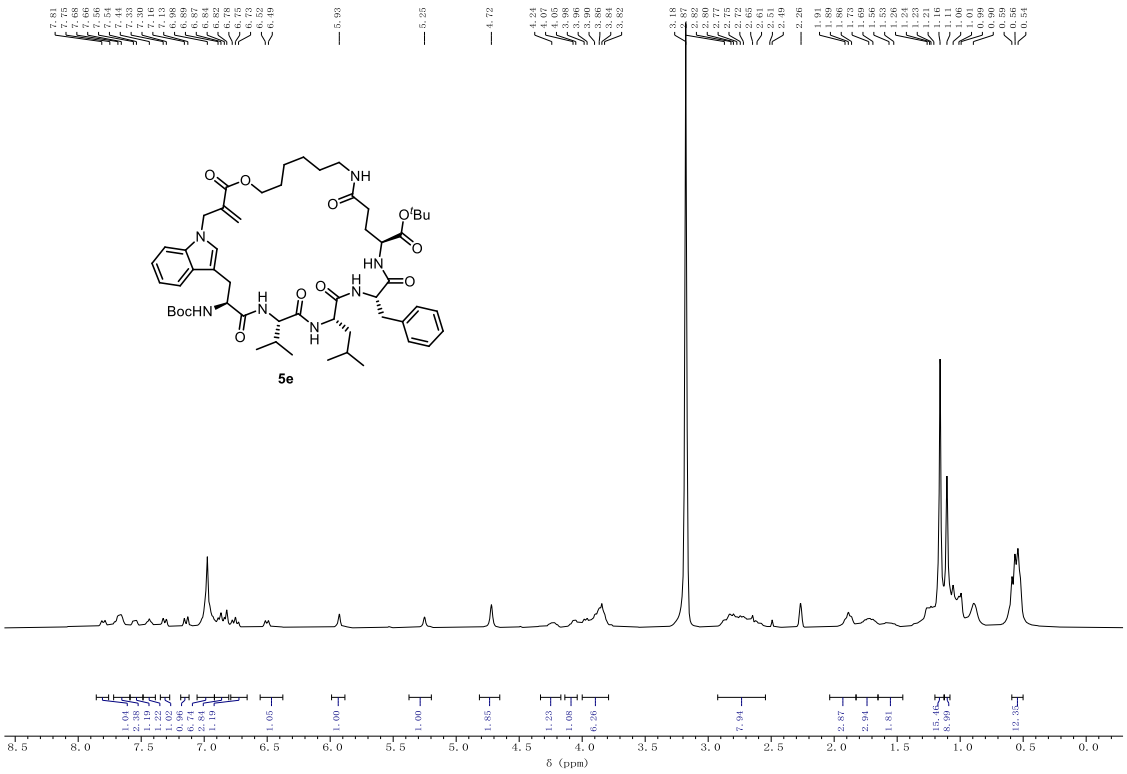
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **5c**



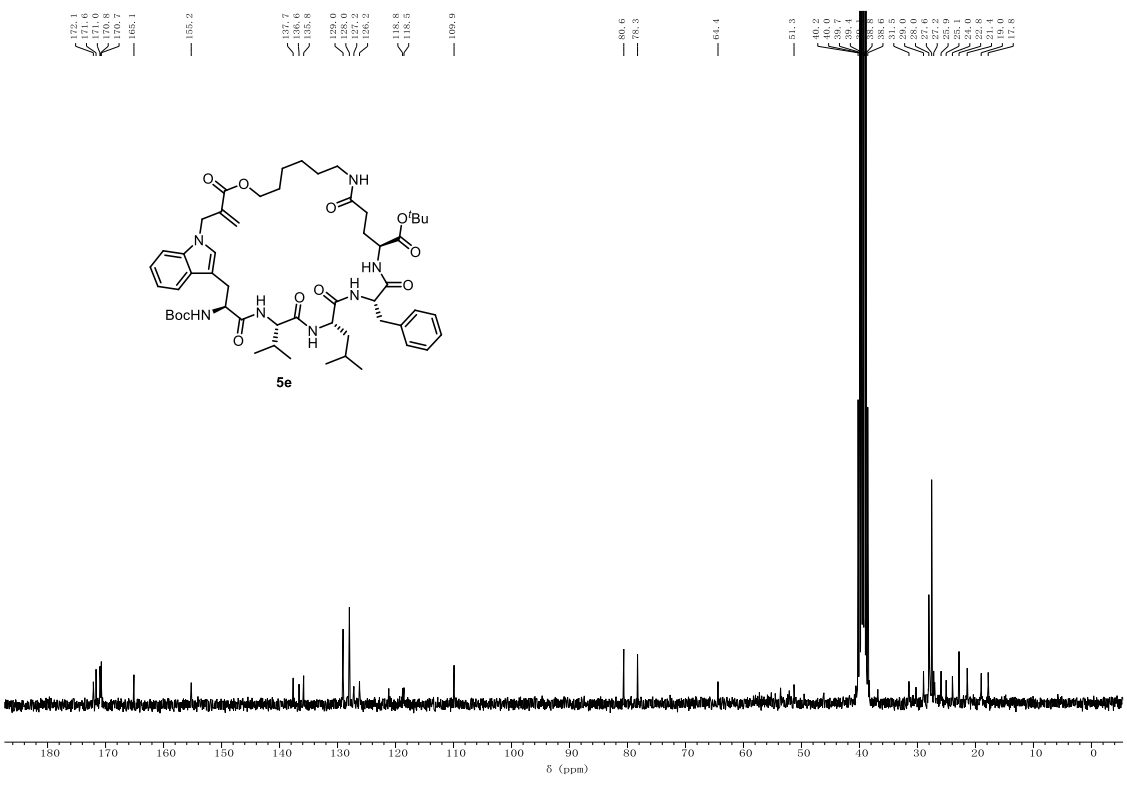
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **5d**



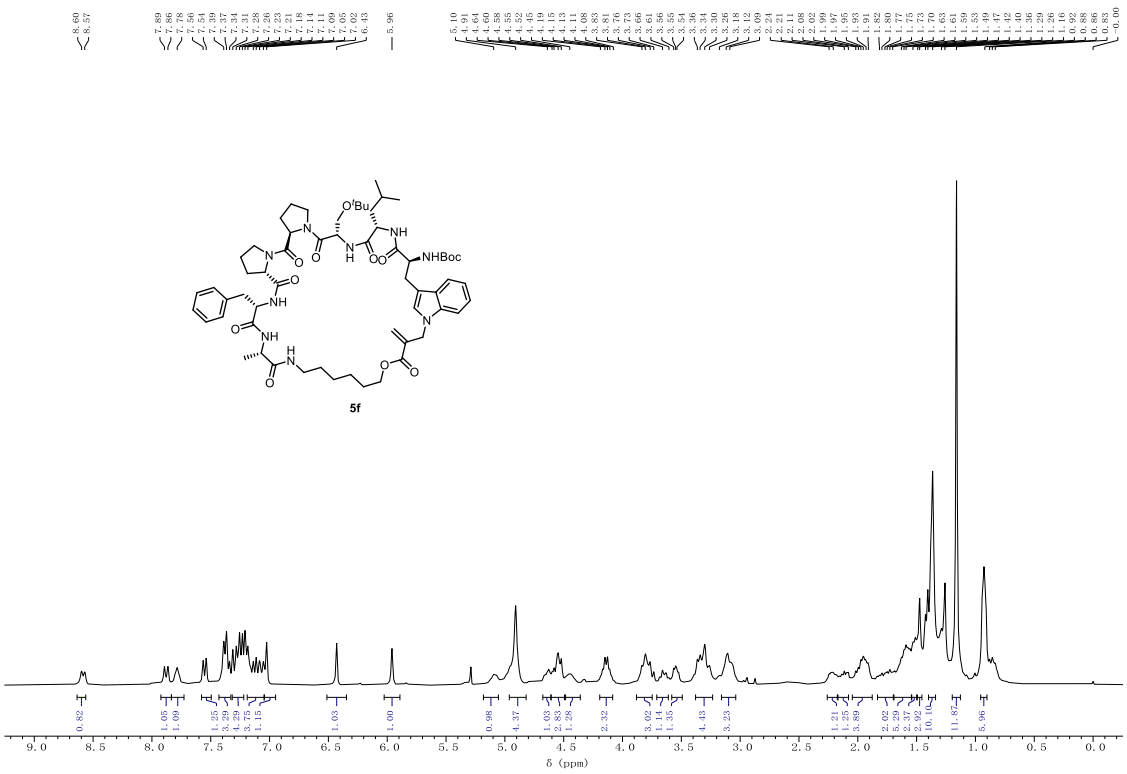
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **5d**



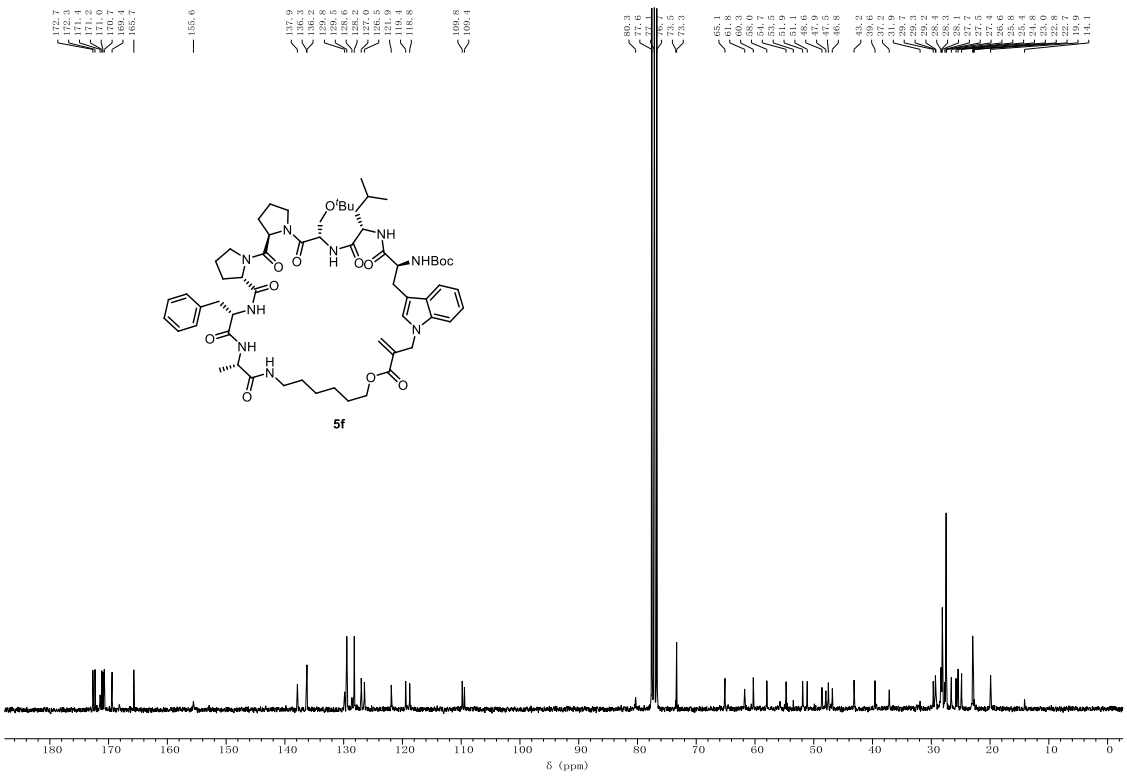
^{1}H NMR (300 MHz, DMSO-d_6) spectrum of **5e**



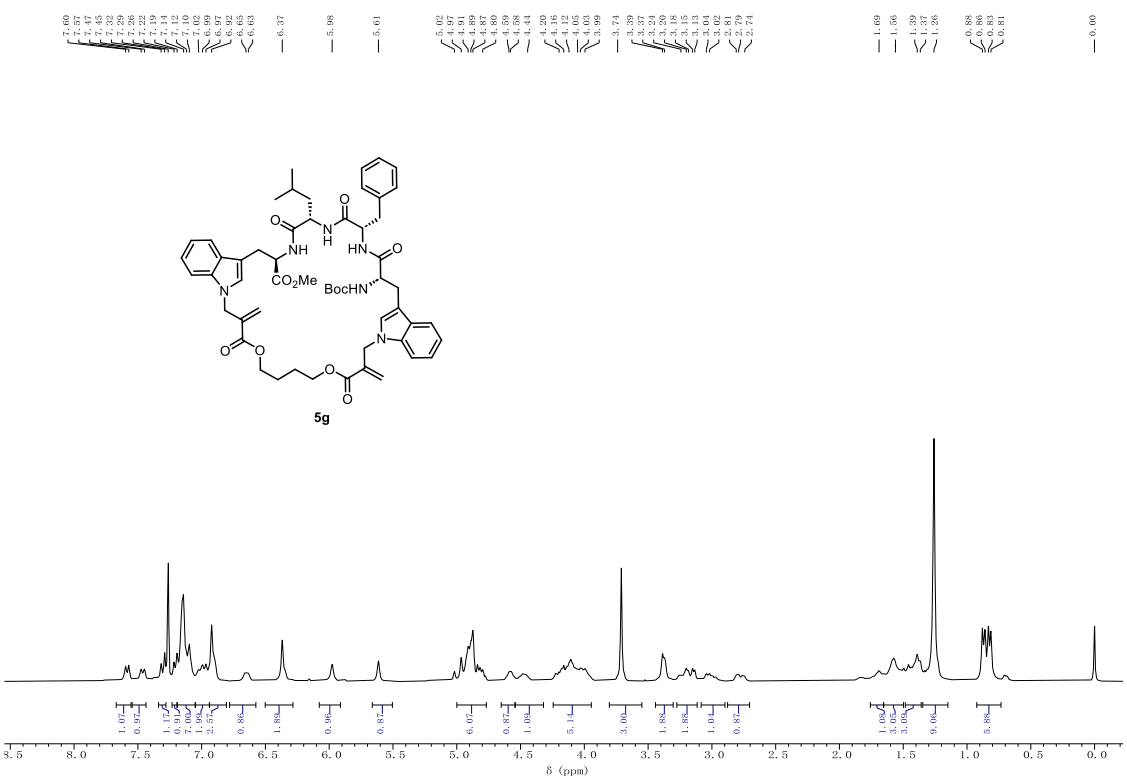
^{13}C NMR (75 MHz, DMSO-d_6) spectrum of **5e**



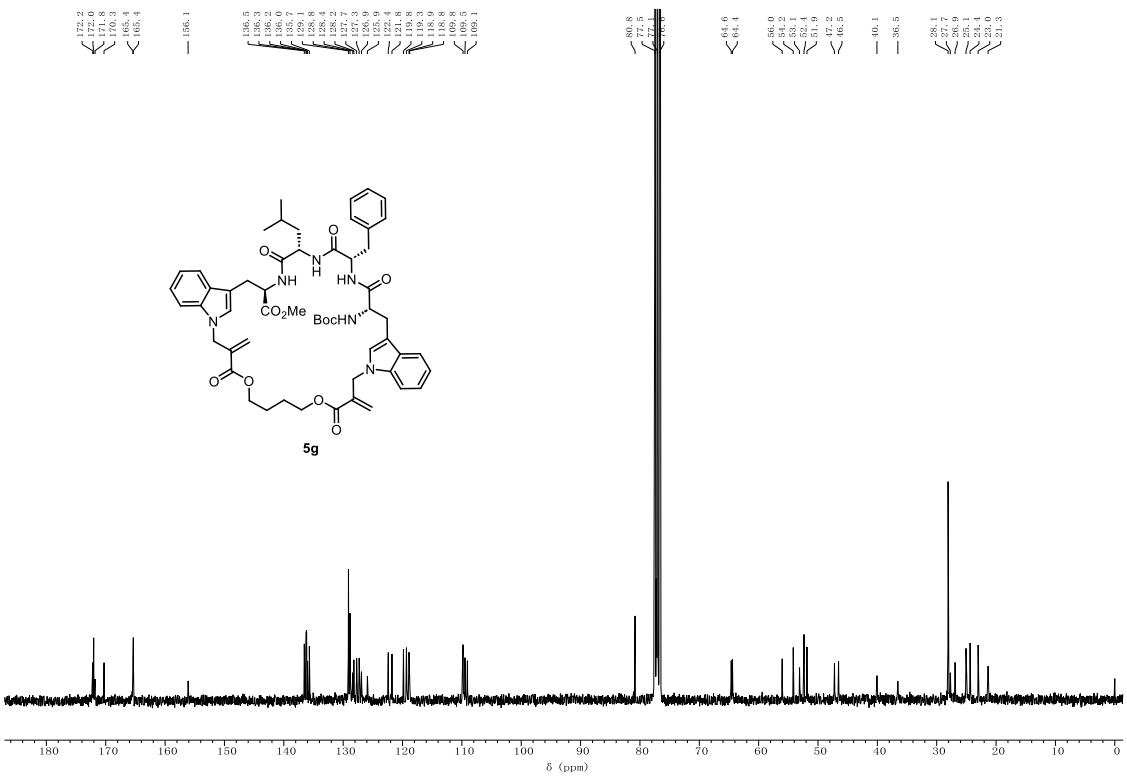
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **5f**



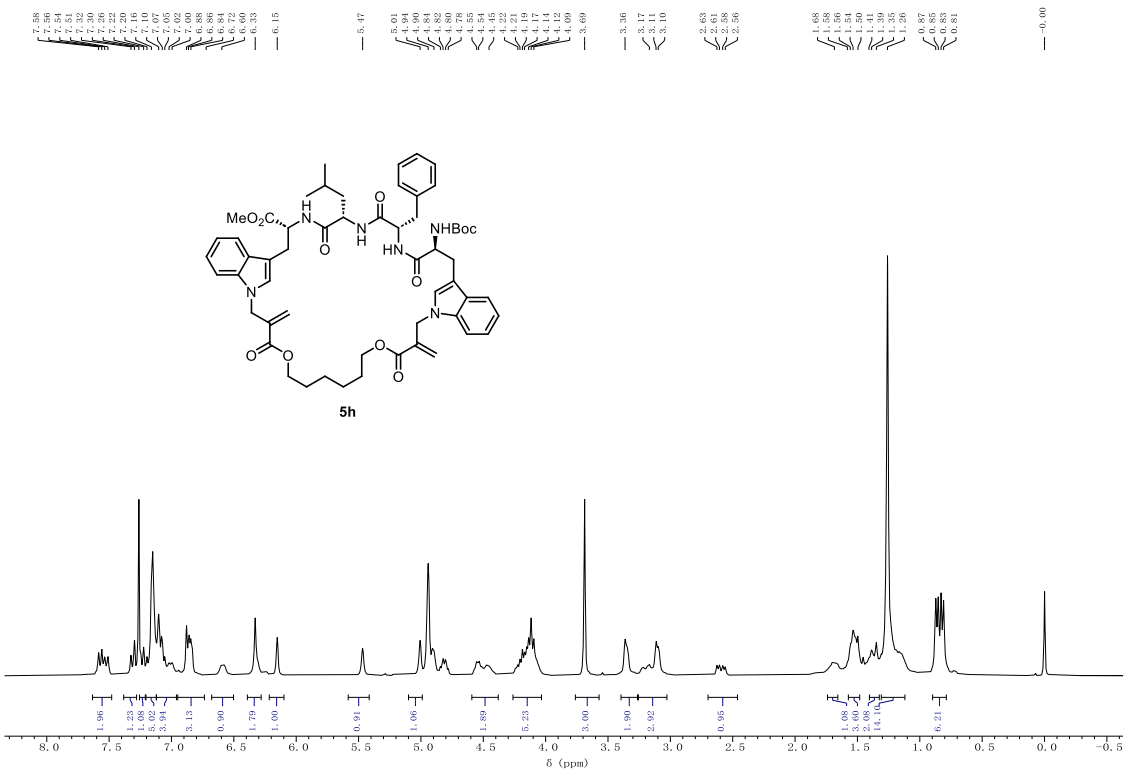
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **5f**



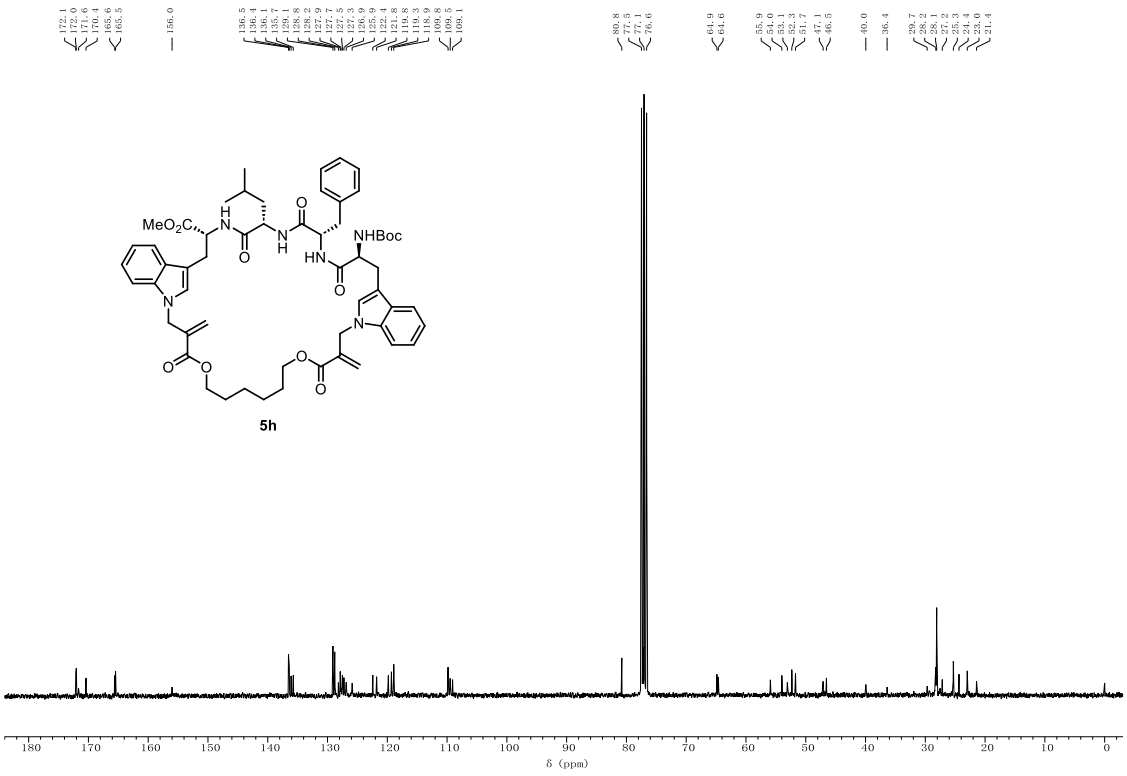
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **5g**



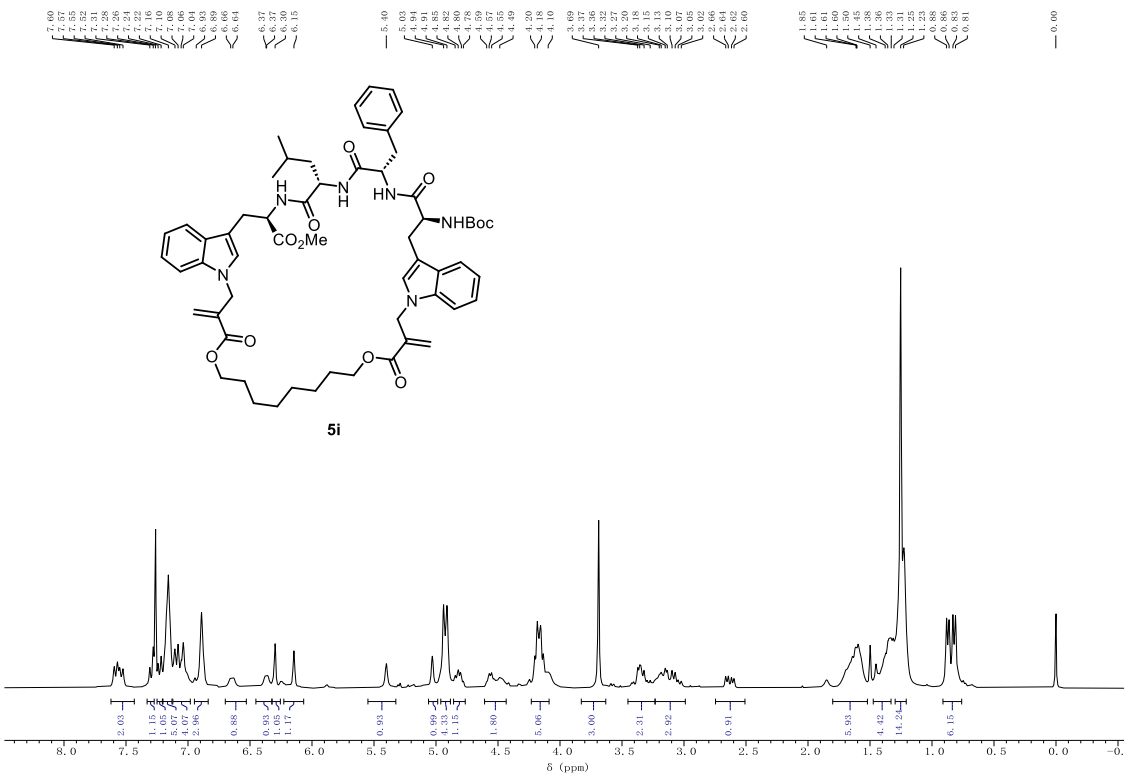
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **5g**



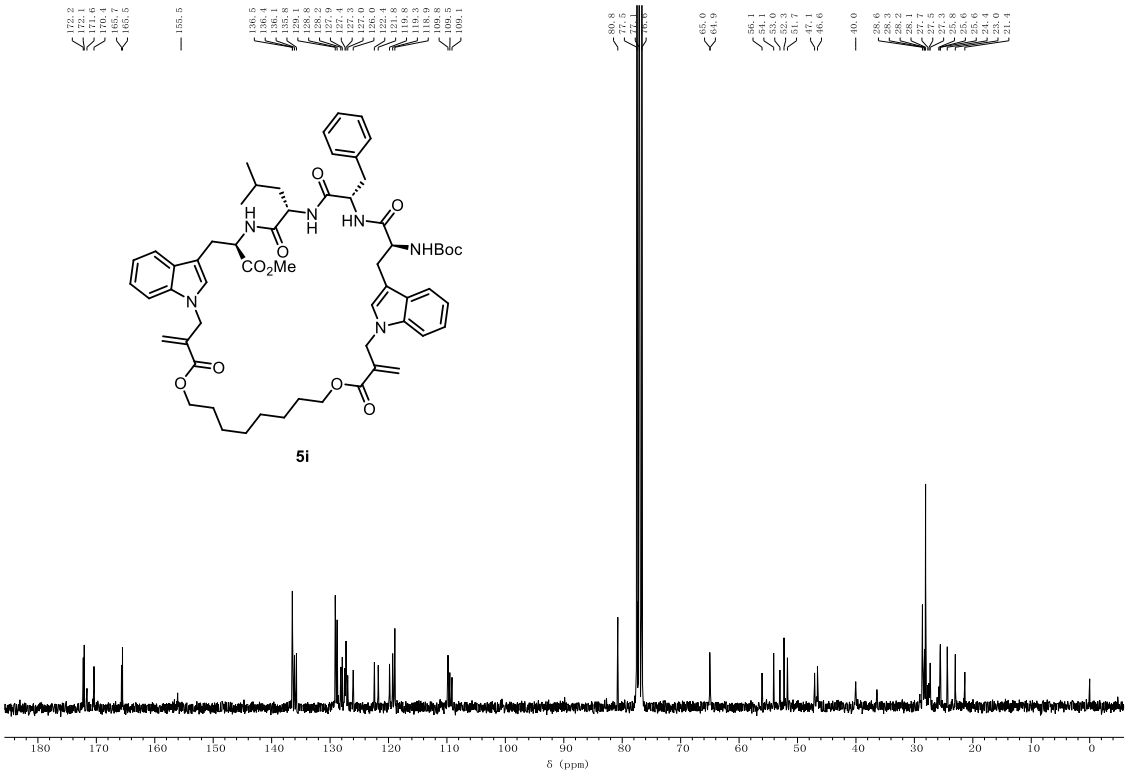
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **5h**



^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **5h**



^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **5i**



^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **5i**