Pd-catalyzed intramolecular C(sp^2)−H amination of phenylalanine moieties in the dipeptides: synthesis of indoline-2-carboxylate-containing dipeptides

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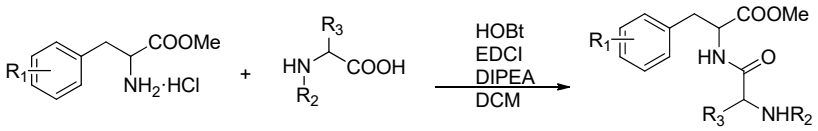
General information

All the reagents were used without further purification. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker NMR spectrometer with $CDCl_3$ as the solvent and TMS as an internal standard. HRESIMS was measured on an Agilent G6224A TOF spectrometer. HPLC was performed on Chiralcel OD-H column (30% to 50% *i*-PrOH in hexanes, 1 mL/min), λ = 254 nm. TLC was performed on pre-coated silica gel GF254 plates (Qingdao Marine Chemical Factory). Column chromatography was performed on silica gel (200−300 mesh, Qingdao Marine Chemical Factory). Visualization was carried out with UV or PMA staining by heating.

General procedures for preparation of compounds 1a−1l, 3a-3i:



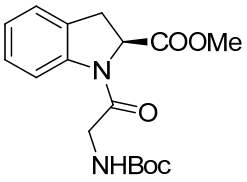
R_2 = Boc, Cbz, Fmoc, Ac

To a solution of protected-amino acid (1equiv) and phenylalanine methyl ester hydrochloride (1 equiv) in dry DCM (0.2 M) was added DIPEA (2 equiv), HOBt (1.1 equiv), and EDCI·HCl (1.2 equiv) at 0°C. After 1 h, the mixture was warmed to rt and stirred overnight. Water was added and the mixture was extracted with DCM. The combined organic layer was washed with 10% HCl, sat. $NaHCO_3$, and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel flash chromatography (Hexane/EA) to give the desired products. **3j** and **3k** were prepared by the similar methods.

General procedure for C−H amiantion：

A mixture of peptide (0.3 mmol), $PhI(OAc)_2$ (0.6 mmol), $Pd(OAc)_2$ (5 % mol), and toluene (2 mL) in sealed tube was heated at 120 °C for 20 h. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by silica gel flash chromatography (Hexane/EA) to give the products.

Characterization of compounds



2a

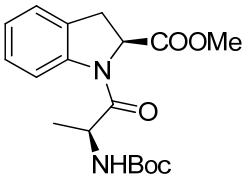
According to the general experimental procedure, compound **2a** was obtained as yellow oil. Two amide rotamers (1.6:1) exist in NMR spectra.

Major amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.9 Hz, 1H), 7.28 – 7.15 (m, 2H), 7.07 (t, *J* = 7.4 Hz, 1H), 5.58 (brs, 1H), 4.96 (d, *J* = 10.2 Hz, 1H), 4.20 – 4.07 (m, 1H), 3.90 – 3.79 (m, 1H), 3.78(s, 3H), 3.70 – 3.61 (m, 1H), 3.33 (d, *J* = 16.4 Hz, 1H), 1.47 (s, 9H).

Minor amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.15 (m, 3H), 7.07 (t, *J* = 7.4 Hz, 1H), 5.56 (brs, 1H), 5.23 (d, *J* = 8.9 Hz, 1H), 4.49 – 4.30 (m, 2H), 3.76 (s, 3 H), 3.60 – 3.49 (m, 1H), 3.16 (d, *J* = 16.9 Hz, 1H), 1.45 (s, 9H).

Mixture of amide rotamers: ^{13}C NMR (101 MHz, $CDCl_3$) δ 171. 4, 171.3, 167.3, 155.8, 142.2, 139.9, 130.7, 128.4, 128.1, 125.8, 124.6, 124.4, 124.1, 117.4, 114.1, 79.9, 60.2, 59.7, 53.2, 52.6, 45.1, 43.5, 33.7, 31.5, 28.4.

HRMS (ESI) Calcd for $C_{17}H_{22}N_2O_5Na$ [M+Na^+]: 357.1421, Found: 357.1416.



2b

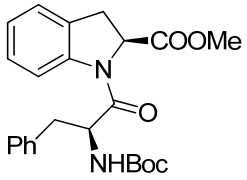
According to the general experimental procedure, compound **2b** was obtained as yellow oil. Two amide rotamers (1.3:1) exist in NMR spectra.

Major amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.1 Hz, 1H), 7.35 – 7.16 (m, 2H), 7.15 – 7.00 (m, 1H), 5.27 (d, *J* = 11.1, 3.5 Hz, 1H), 4.97 (d, *J* = 9.2 Hz, 1H), 4.55 – 4.40 (m, 1H), 3.77 (s, 3H), 3.63 (dd, *J* = 16.4, 10.6 Hz, 1 H), 3.36 (d, *J* = 16.4 Hz, 1H), 1.45 (s, 9H), , 1.41 (d, *J* = 6.8 Hz, 3H).

Minior amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.16 (m, 3H), 7.15 – 7.00 (m, 1H), 5.52 (d, *J* = 7.5 Hz, 1H), 5.48 (d, *J* = 8.3 Hz, 1H), 5.10 – 5.02 (m, 1H), 3.75 (s, 3H), 3.57 – 3.45 (m, 1H), 3.13 (dd, *J* = 16.6, 3.4 Hz, 1H), 1.55 (d, *J* = 6.9 Hz, 3 H), 1.44 (s, 9 H),

Mixture of amide rotamers: ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 171.7, 171.5, 171.4, 155.2, 154.8, 142.3, 139.9, 131.1, 128.7, 128.3, 128.1, 125.9, 124.6, 124.4, 124.1, 117.5, 114.1, 79.8, 79.6, 60.4, 60.2, 53.3, 52.5, 48.6, 48.4, 33.5, 31.3, 28.4, 19.9, 18.8.

HRMS (ESI) Calcd for $C_{18}H_{24}N_2O_5Na$ [M+Na^+]: 371.1577, Found: 371.1586.



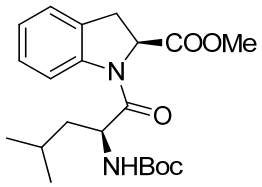
2c

According to the general experimental procedure, compound **2c** was obtained as yellow solid. Two amide rotamers (4:1) exist in NMR spectra.

Mixture of amide rotamers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.1 Hz, 1H), 7.39 – 7.17 (m, 9H), 7.15 – 7.01 (m, 2.6H), 5.59 (d, *J* = 8.7 Hz, 1H), 5.42 – 5.24 (m, 0.7H), 4.62 (td, *J* = 9.4, 5.2 Hz, 1H), 4.14 (d, *J* = 9.0 Hz, 1H), 3.78 (s, 0.7 H), 3.69 (s, 3H), 3.21 – 2.98 (m, 3.7H), 2.83 (dd, *J* = 16.2, 10.5 Hz, 1H), 1.46 (s, 9H), 1.37 (s, 2.1H).

Mixture of amide rotamers: ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 170.8, 154.7, 141.5, 136.2, 129.7, 129.4, 129.1, 128.7, 128.4, 127.8, 127.1, 124.6, 124.3, 117.6, 79.7, 77.4, 60.5, 60.4, 54.6, 53.1, 52.6, 41.6, 38.2, 32.8, 31.4, 28.4.

HRMS (ESI) Calcd for $C_{24}H_{28}N_2O_5Na$ [M+Na^+]: 447.1890, Found: 447.1884.



2d

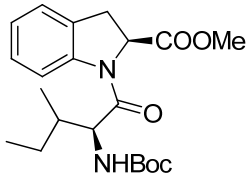
According to the general experimental procedure, compound **2d** was obtained as yellow solid. Two amide rotamers (1.7:1) exist in NMR spectra.

Major amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.1 Hz, 1H), 7.40 – 7.21 (m, 2H), 5.36 – 5.33 (m, 1H), 4.98 (dd, *J* = 10.6, 1.9 Hz, 1H), 4.47 (td, *J* = 9.8, 3.6 Hz, 1H), 3.77 (s, 3H), 3.71 – 3.57 (m, 1H), 3.35 (d, *J* = 15.5 Hz, 1H), 1.73-1.68 (m, 2H), 1.62 – 1.56 (m, 1H), 1.43 (s, 9H), 1.03 (d, *J* = 6.5 Hz, 3H), 0.96 (d, *J* = 6.7 Hz, 3H).

Minor amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.21 (m, 3H), 7.06 (m, 1H), 5.36 – 5.33 (m, 1H), 5.22 (dd, *J* = 11.1, 4.2 Hz, 1H), 5.17 – 5.14 (m, 1H), 3.74 (s, 3H), 3.56 – 3.42 (m, 1H), 3.12 (dd, *J* = 16.6, 4.0 Hz, 1H), 1.73-1.68 (m, 2H), 1.62 – 1.56 (m, 1H), 1.42 (s, 9H), 1.16 (d, *J* = 6.5 Hz, 3H), 1.00 (d, *J* = 6.7 Hz, 3H)

Mixture of amide rotamers: ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.2, 172.1, 171.5, 171.4, 155.7, 155.2, 142.4, 140.1, 131.0, 128.7, 128.5, 128.1, 128.0, 125.9, 124.5, 124.4, 124.0, 117.4, 114.0, 79.7, 79.4, 60.5, 60.4, 53.3, 52.4, 51.3, 51.2, 43.7, 41.2, 33.6, 31.2, 28.3, 24.9, 24.6, 23.6, 23.4, 21.9, 21.7.

HRMS (ESI) Calcd for $C_{21}H_{30}N_2O_5Na$ [M+Na^+]: 413.2047, Found: 413.2046.



2e

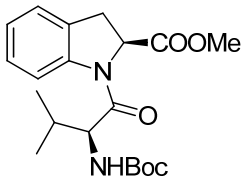
According to the general experimental procedure, compound **2e** was obtained as yellow solid. Two amide rotamers (1.3:1) exist in NMR spectra.

Major amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.1 Hz, 1H), 7.27 – 7.18 (m, 2H), 7.12 – 7.05 (m, 1H), 5.34 (d, *J* = 9.4 Hz, 1H), 5.09 (d, *J* = 9.1 Hz, 1H), 4.32 – 4.21 (m, 1H), 3.76 (s, 3H), 3.62 (dt, *J* = 19.0, 9.5 Hz, 1H), 3.36 (d, *J* = 16.4 Hz, 1H), 1.76 (td, *J* = 9.9, 4.8 Hz, 1H), 1.72 – 1.57 (m, 2H), 1.45 (s, 9H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.93 (t, *J* = 7.9 Hz, 3H).

Minor amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.18 (m, 3H), 7.12 – 7.05 (m, 1H), 5.40 (d, *J* = 9.0 Hz, 1H), 5.26 (dd, *J* = 11.2, 4.6 Hz, 1H), 5.03 (dd, *J* = 9.2, 3.3 Hz, 1H), 3.74 (s, 3H), 3.50 (dd, *J* = 16.6, 11.3 Hz, 1H), 3.15 (dd, *J* = 16.6, 4.5 Hz, 1H), 1.76 (td, *J* = 9.9, 4.8 Hz, 1H), 1.72 – 1.57 (m, 2H), 1.18 (d, *J* = 6.8 Hz, 3H), 0.92 (t, *J* = 7.9 Hz, 3H).

Mixture of amide rotamers: ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 171.3, 171.0, 155.4, 142.3, 131.1, 128.9, 128.3, 128.0, 125.9, 124.6, 124.5, 124.0, 117.5, 114.0, 79.7, 79.4, 60.7, 60.5, 57.1, 56.8, 53.3, 52.4, 39.4, 37.3, 33.4, 31.2, 29.7, 28.3, 24.2, 22.6, 15.8, 15.5, 11.7, 11.4.

HRMS (ESI) Calcd for $C_{21}H_{30}N_2O_5Na$ [M+Na^+]: 413.2047, Found: 413.2044.



2f

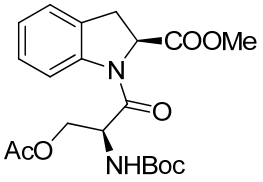
According to the general experimental procedure, compound **2f** was obtained as yellow solid. Two amide rotamers (1.3:1) exist in NMR spectra.

Major amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.1 Hz, 1H), 7.35 – 7.16 (m, 2H), 7.09 – 7.05 (m, 1H), 5.37 (d, *J* = 9.4 Hz, 1H), 5.08 (dd, *J* = 10.6, 1.8 Hz, 1 H), 4.25 (dd, *J* = 9.3, 6.6 Hz, 1H), 3.77 (s, 3H), 3.61 (dt, *J* = 15.9, 7.9 Hz, 1H), 3.38 – 3.34 (m, 1H), 2.10 – 1.96 (m, 1H), 1.46 (s, 9H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.98 (d, *J* = 6.7 Hz, 3H).

Minor amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ7.35 – 7.16 (m, 3H), 7.09 – 7.05 (m, 1H), 5.45 (d, *J* = 9.0 Hz, 1H), 5.25 (dd, *J* = 11.2, 4.7 Hz, 1H), 5.03 (dd, *J* = 9.1, 2.9 Hz, 1 H), 3.74 (s, 3H), 3.49 (dd, *J* = 16.6, 11.3 Hz, 1H), 3.14 (dd, *J* = 16.6, 4.6 Hz, 1H), 2.48 – 2.37 (m, 1H), 1.46 (s, 9H), 1.18 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 3H).

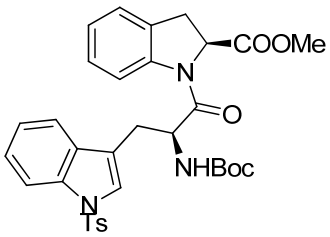
Mixture of amide rotamers: ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.59, 171.44, 171.31, 170.86, 156.06, 155.44, 142.27, 140.08, 131.04, 128.81, 128.28, 128.02, 125.90,

124.53, 124.45, 123.99, 117.48, 113.90, 79.65, 79.40, 60.67, 60.38, 57.66, 56.62, 53.25, 52.42, 33.39, 32.70, 31.17, 30.37, 28.33, 19.70, 19.44, 17.53, 15.63.
HRMS (ESI) Calcd for $C_{20}H_{28}N_2O_5Na$ [M+Na^+]: 399.1890, Found: 399.1891.



2g

According to the general experimental procedure, compound **2g** was obtained as white powder. Two amide rotamers (3:1) exist in NMR spectra.
Major amide rotamer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.1 Hz, 1H), 7.33 – 7.18 (m, 2H), 7.12 – 7.08 (m, 1H), 5.46 (d, *J* = 8.8 Hz, 1H), 5.29 (dd, *J* = 10.4, 1.6 Hz, 1H), 4.81 (dd, *J* = 14.6, 7.3 Hz, 1H), 4.35 (dd, *J* = 11.1, 5.7 Hz, 1H), 4.12 – 4.03 (m, 1H), 3.75 (s, 3H), 3.61 (dd, *J* = 16.3, 10.5 Hz, 1H), 3.40 (d, *J* = 16.3 Hz, 1H), 2.05 (s, 3H), 1.45 (s, 9H).
Minor amide rotamer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.1 Hz, 1H), 7.30 – 7.23 (m, 2H), 7.10 – 7.07 (m, 1H), 5.54 (d, *J* = 8.4 Hz, 1H), 5.42 (d, *J* = 4.7 Hz, 1H), 5.27 – 5.22 (m, 1H), 4.53 (dd, *J* = 11.3, 4.6 Hz, 1H), 4.25 (dd, *J* = 11.2, 7.9 Hz, 1H), 3.72 (s, 3H), 3.50 (dd, *J* = 16.4, 11.3 Hz, 1H), 3.14 (dd, *J* = 16.7, 3.2 Hz, 1H), 2.08 (s, 3H), 1.43 (s, 9H).
Mixture of amide rotamers: ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.27, 171.13, 170.83, 170.78, 168.17, 167.77, 155.26, 154.96, 141.89, 129.10, 128.53, 128.06, 125.89, 124.98, 124.58, 117.61, 114.47, 80.20, 80.09, 65.14, 63.85, 60.63, 60.53, 53.33, 52.66, 51.73, 51.58, 33.32, 31.34, 28.27, 20.77.
HRMS (ESI) Calcd for $C_{20}H_{26}N_2O_7Na$ [M+Na^+]: 429.1632, Found: 429.1623.



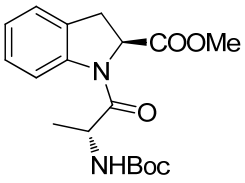
2h

According to the general experimental procedure, compound **2h** was obtained as yellow solid. Two amide rotamers (3:1) exist in NMR spectra.
Major amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.1 Hz, 1H), 7.93 (d, *J* = 8.3 Hz, 1H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.49 (s, 1H), 7.24 (t, *J* = 7.7 Hz, 2H), 7.18 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 3H), 7.02 (m, 4H), 5.59 (d, *J* = 8.6 Hz, 1H), 4.71 (dd, *J* = 14.8, 8.1 Hz, 1H), 4.14 (d, *J* = 9.5 Hz, 1H), 3.70 (s, 3H), 3.25 – 3.15 (m, 2H), 2.81 (d, *J* = 14.3 Hz, 1H), 2.33 (s, 3H), 2.27 – 2.20 (m, 1H), 1.47 (s, 9H).
Minor amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ8.10 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.69 – 7.66 (m, 1H), 7.60 (dd, *J* = 13.7, 5.5

Hz, 2H), 7.48 (s, 1H), 7.24 (t, *J* = 7.7 Hz, 3H), 7.18 (d, *J* = 8.1 Hz, 2H), 5.46 – 5.37 (m, 2H), 5.29 (dd, *J* = 11.1, 4.0 Hz, 1H), 3.82 (s, 3H), 3.16 – 3.10 (m, 3H), 2.24 – 2.20 (m, 1H), 2.19 (s, 3H), 1.40 (s, 9H).

Mixture of amide rotamers: ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.76, 170.91, 170.61, 155.16, 154.79, 144.89, 144.64, 143.53, 141.53, 135.02, 134.94, 134.70, 130.36, 129.90, 129.76, 129.04, 129.00, 128.27, 127.84, 127.14, 126.88, 126.73, 125.96, 125.41, 125.31, 124.95, 124.78, 124.70, 124.62, 124.23, 123.35, 123.16, 120.35, 119.68, 119.55, 117.65, 117.26, 116.47, 114.05, 113.61, 113.50, 109.36, 104.93, 80.03, 76.81, 60.52, 60.30, 53.30, 53.15, 52.82, 51.96, 32.28, 31.35, 30.56, 29.73, 28.36, 28.31, 21.61.

HRMS (ESI) Calcd for $C_{33}H_{35}N_3O_7SNa$ [M+Na$^+$]: 640.2088, Found: 640.2087.



2i

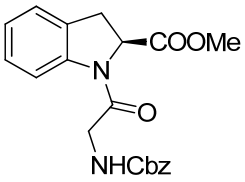
According to the general experimental procedure, compound **2i** was obtained as yellow oil. Two amide rotamers (3:1) exist in NMR spectra.

Major amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.0 Hz, 1H), 7.28 – 7.12 (m, 2 H), 7.10 – 6.99 (t, *J* = 7.4 Hz, 1H), 5.68 (d, *J* = 10.2 Hz, 1 H), 5.30 (d, *J* = 8.3 Hz, 1 H), 4.47 – 4.34 (m, 1H), 3.75 (s, 3H), 3.61 (dd, *J* = 16.2, 10.9 Hz, 1 H), 3.32 (d, *J* = 16.3 Hz, 1 H), 1.41 (m, 3 H), 1.40 (s, 9H).

Minor amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.35 (m, 1H), 7.28 – 7.12 (m, 2 H), 7.10 – 6.99 (t, *J* = 7.4 Hz, 1H), 5.68 – 5.67 (m, 1 H), 5.20 – 5.17 (m, 2 H), 3.73 (s, 3H), 3.50 (d, *J* = 8.3 Hz, 1 H), 3.13 (d, *J* = 15.6 Hz, 1H), 1.44 (m, 3H), 1.38 (s, 9H)

Mixture of amide rotamers: ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 172.1, 171.5, 155.4, 142.3, 131.0, 129.5, 128.3, 127.8, 125.8, 124.5, 124.4, 124.1, 117.9, 114.5, 79.9, 77.5, 77.2, 76.8, 61.1, 60.5, 52.9, 52.5, 49.0, 48.1, 33.3, 31.4, 29.7, 28.3, 18.7, 18.2.

HRMS (ESI) Calcd for $C_{18}H_{24}N_2O_5Na$ [M+Na$^+$]: 371.1577, Found: 371.1590.



2j

According to the general experimental procedure, compound **2j** was obtained as yellow solid. Two amide rotamers (1.5:1) exist in NMR spectra.

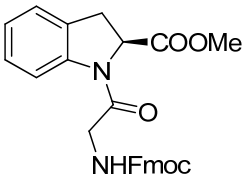
Major amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 7.7 Hz, 1H), 7.43 – 7.15 (m, 7H), 7.08 (t, *J* = 7.4 Hz, 2H), 5.90 (br s, 1H), 5.17 (s, 2H), 4.96 (d, *J* = 9.9

Hz, 1H), 4.15 (d, *J* = 13.1 Hz, 1H), 3.95 (d, *J* = 16.3 Hz, 1H), 3.79 (s, 3H), 3.70 – 3.61 (m, 1H), 3.34 (d, *J* = 16.5 Hz, 1H),

Minor amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.15 (m, 10H), 5.79 (br s, 1H), 5.28 – 5.20 (m, 1H), 5.15 (s, 2H), 4.55 – 4.37 (m, 2H), 3.76 (s, 3H), 3.59 – 3.52 (m, 1H), 3.16 (d, *J* = 16.4 Hz, 1H).

Mixture of amide rotamers: ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.3, 167.0, 156.4, 142.1, 139.8, 136.4, 130.8, 129.4, 128.5, 128.4, 128.1, 128.1, 125.9, 124.7, 124.4, 124.2, 117.4, 114.1, 67.0, 60.3, 59.8, 53.2, 52.7, 45.4, 43.9, 33.6, 31.5.

HRMS (ESI) Calcd for $C_{20}H_{20}N_2O_5Na$ [M+Na^+]: 391.1264, Found: 391.1265.



2k

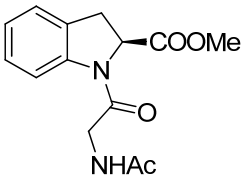
According to the general experimental procedure, compound **2k** was obtained as white solid. Two amide rotamers (1.1:1) exist in NMR spectra.

Major amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 7.8 Hz, 1H), 7.79 (d, *J* = 7.5 Hz, 2H), 7.65 (d, *J* = 7.4 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.32 – 7.18 (m, 2H), 7.11 (t, *J* = 7.4 Hz, 1H), 5.91 (brs, 1H), 4.98 (d, *J* = 10.3 Hz, 1H), 4.58 – 4.48 (m, 1H), 4.42 (d, *J* = 6.5 Hz, 2H), 4.27 (t, *J* = 7.2 Hz, 1H), 4.18 – 4.24 (m, 1H), 3.78 (s, 3H), 3.71 – 3.60 (m, 1H), 3.37 (d, *J* = 16.3 Hz, 1H),.

Minor amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.5 Hz, 2H), 7.65 (d, *J* = 7.4 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.32 – 7.18 (m, 3H), 7.11 (t, *J* = 7.4 Hz, 1H), 5.89 (brs, 1H), 5.26 (d, *J* = 9.2 Hz, 1H), 4.60 – 4.56 (m, 1H), 4.42 (d, *J* = 6.5 Hz, 2H), 4.27 (t, *J* = 7.2 Hz, 1H), 3.97 (d, *J* = 15.0 Hz, 1H), 3.78 (s, 3H), 3.59 – 3.47 (m, 1H), 3.28 – 3.12 (m, 1H).

Mixture of amide rotamers: ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 166.9, 156.3, 143.9, 142.1, 141.3, 139.8, 129.4, 128.2, 127.7, 127.1, 126.0, 125.2, 124.8, 124.5, 120.0, 117.4, 114.0, 67.3, 60.3, 59.8, 53.3, 52.7, 47.1, 45.4, 43.9, 33.7, 31.5, 29.7.

HRMS (ESI) Calcd for $C_{27}H_{24}N_2O_5Na$ [M+Na^+]: 479.1577, Found: 479.1579.

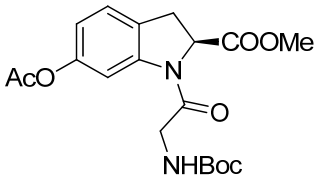


2l

According to the general experimental procedure, compound **2l** was obtained as white solid. Two amide rotamers (1.4:1) exist in NMR spectra.

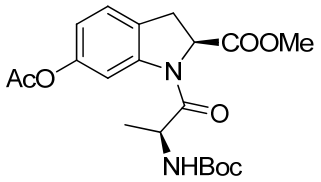
Major amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.0 Hz, 1H), 7.39 – 7.26 (m, 2H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.62 (s, 1H), 4.98 (d, *J* = 10.5 Hz, 1H), 4.28

(dd, *J* = 17.2, 4.4 Hz, 1H), 3.94 (d, *J* = 17.2 Hz, 1H), 3.79 (s, 3H), 3.71 – 3.60 (m, 1H), 3.37 (d, *J* = 16.6 Hz, 1H), 2.09 (s, 3H).
Minor amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.26 (m, 3H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.62 (s, 1H), 5.23 (d, *J* = 8.1 Hz, 1H), 4.52 – 4.48 (m, 2H), 3.77 (s, 3H), 3.59 – 3.48 (m, 1H), 3.19 (d, *J* = 16.4 Hz, 1H), 2.09 (s, 3H).
Mixture of amide rotamers: ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 170.2, 166.9, 142.0, 128.4, 128.1, 125.9, 124.8, 124.45, 124.4, 117.3, 114.1, 60.3, 59.8, 53.3, 52.7, 44.1, 42.6, 33.6, 31.5, 23.0.
HRMS (ESI) Calcd for $C_{14}H_{16}N_2O_4Na$ [M+Na$^+$]: 299.1002, Found: 299.1002.



4a

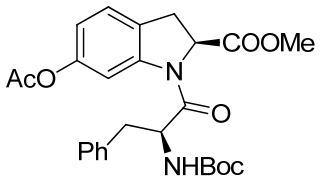
According to the general experimental procedure, compound **4a** was obtained as yellow oil. Two amide rotamers (2:1) exist in NMR spectra.
Major amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 6.77 (d, *J* = 7.9 Hz, 1H), 5.51 (br s, 1H), 4.99 (d, *J* = 9.9 Hz, 1H), 4.07 (d, *J* = 13.2 Hz, 1H), 3.81 (d, *J* = 17.4 Hz, 1H), 3.72 (s, 3H), 3.59 – 3.39 (m, 1H), 3.28 (d, *J* = 16.5 Hz, 1H), 2.27 (s, 3H), 1.46 (s, 9H).
Minor amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.06 (m, 2H), 6.85 (s, 1H), 5.58 (br s, 1H), 5.20 (d, *J* = 8.4 Hz, 1H), 4.40 – 4.18 (m, 2H), 3.71 (s, 3H), 3.59 – 3.39 (m, 1H), 3.19 – 3.03 (m, 1H), 2.27 (s, 3H), 1.46 (s, 9H)
Mixture of amide rotamers: ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 169.5, 167.6, 167.2, 155.8, 150.4, 143.1, 128.1, 126.0, 125.9, 124.5, 121.6, 117.7, 117.4, 111.4, 108.2, 79.9, 61.0, 60.4, 53.2, 52.7, 45.0, 43.5, 33.2, 31.0, 29.7, 28.3, 21.0.
HRMS (ESI) Calcd for $C_{19}H_{24}N_2O_7Na$ [M+Na$^+$]: 415.1476, Found: 415.1470.



4b

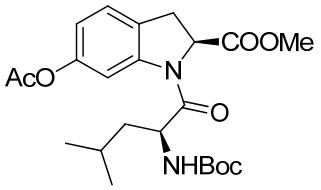
According to the general experimental procedure, compound **4b** was obtained as yellow solid. Two amide rotamers (2:1) exist in NMR spectra.
Major amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 1.6 Hz, 1H), 7.20 – 7.14 (m, 1H), 6.86 – 6.80 (m, 1H), 5.42 (d, *J* = 8.3 Hz, 1H), 5.00 (dd, *J* = 10.6, 1.7 Hz, 1H), 4.52 – 4.40 (m, 1H), 3.78 (s, 3H), 3.60 (dd, *J* = 16.4, 10.8 Hz, 1H), 3.36 (d, *J* = 16.3 Hz, 1H), 2.30 (s, 3H), 1.46 (s, 9H), 1.40 (d, *J* = 6.8 Hz, 3H).
Minor amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.19 (m, 1H), 6.93 (s, 1H), 6.86 – 6.80 (m, 1H),5.52 (d, *J* = 7.4 Hz, 1H), 5.28 (dd, *J* = 11.1, 3.8 Hz, 1H),

4.97 – 4.91 (m, 1H), 3.76 (s, 3H), 3.48 (dd, *J* = 16.5, 11.3 Hz, 1H), 3.12 (dd, *J* = 16.6, 3.5 Hz, 1H), 2.34 (s, 3H), 1.54 (d, *J* = 6.9 Hz, 3H), 1.46 (s, 9H).
Mixture of amide rotamers: ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.98, 171.56, 171.15, 169.56, 169.29, 155.14, 154.75, 150.70, 150.43, 143.26, 140.75, 128.31, 126.14, 125.97, 124.56, 117.79, 117.22, 111.66, 108.27, 79.86, 79.70, 61.06, 60.39, 53.33, 52.57, 48.61, 33.10, 31.58, 30.73, 29.70, 28.35, 22.65, 21.19, 21.03, 19.82, 18.64, 14.20, 14.11.
HRMS (ESI) Calcd for $C_{20}H_{26}N_2O_7Na$ [M+Na$^+$]: 429.1632, Found: 429.1631.



4c

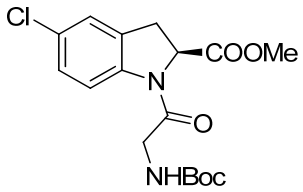
According to the general experimental procedure, compound **4c** was obtained as yellow solid. Two amide rotamers (>10:1) exist in NMR spectra.
Major amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 1.9 Hz, 1H), 7.28 – 7.17 (m, 5H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.84 – 6.75 (m, 1H), 5.53 (d, *J* = 8.7 Hz, 1H), 4.59 (td, *J* = 9.4, 5.2 Hz, 1H), 4.16 (d, *J* = 9.2 Hz, 1H), 3.70 (s, 3H), 3.20 – 2.94 (m, 3H), 2.81 (dd, *J* = 16.2, 10.5 Hz, 1H), 2.29 (s, 3H), 1.43 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 171.03, 170.95, 169.53, 154.69, 150.21, 142.43, 136.07, 129.40, 128.74, 127.15, 126.50, 124.40, 117.84, 111.67, 79.79, 61.01, 54.57, 53.21, 41.54, 32.38, 28.34, 21.06.
HRMS (ESI) Calcd for $C_{26}H_{30}N_2O_7Na$ [M+Na$^+$]: 505.1945, Found: 505.1948.



4d

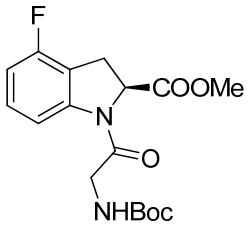
According to the general experimental procedure, compound **4d** was obtained as yellow solid. Two amide rotamers (3:1) exist in NMR spectra.
Major amide rotamer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, *J* = 1.6 Hz, 1H), 7.14 (t, *J* = 10.6 Hz, 1H), 6.79 (dd, *J* = 8.0, 2.1 Hz, 1H), 5.22 (dd, *J* = 13.8, 6.9 Hz, 1H), 5.03 – 4.94 (m, 1H), 4.43 (td, *J* = 9.8, 3.6 Hz, 1H), 3.77 (s, 3H), 3.66 – 3.55 (m, 1H), 3.32 (d, *J* = 16.4 Hz, 1H), 2.28 (s, 3H), 1.79 – 1.70 (m, 1H), 1.60 – 1.52 (m, 2H), 1.43 (s, 9H), 1.01 (d, *J* = 6.5 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 3H).
Minor amide rotamer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, *J* = 9.2 Hz, 1H), 7.03 (d, *J* = 20.4 Hz, 1H), 6.79 (dd, *J* = 8.0, 2.1 Hz, 1H), 5.29 (d, *J* = 8.7 Hz, 1H), 5.03 – 4.94 (m, 1H), 4.43 (td, *J* = 9.8, 3.6 Hz, 1H), 3.73 (s, 3H), 3.45 (dd, *J* = 16.5, 11.3 Hz, 1H), 3.17 – 3.05 (m, 1H), 2.28 (s, 3H), 1.90 (m, 1H), 1.59 (m, 1H), 1.43 (s, 9H), 1.39 (m, 1H), 1.12 (d, *J* = 6.5 Hz, 3H), 0.98 (d, *J* = 6.7 Hz, 3H).

Mixture of amide rotamers: ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.33, 171.90, 171.26, 171.14, 169.54, 169.21, 155.65, 155.15, 150.68, 150.42, 143.34, 140.91, 128.28, 126.14, 125.94, 124.53, 117.69, 117.04, 111.56, 108.40, 79.76, 79.52, 61.26, 61.05, 53.35, 52.51, 51.45, 51.18, 43.62, 40.93, 33.16, 31.58, 30.74, 29.69, 28.31, 24.80, 24.64, 23.57, 23.40, 22.64, 21.90, 21.35, 21.01, 14.11.
HRMS (ESI) Calcd for $C_{23}H_{32}N_2O_7Na$ [M+Na^+]: 471.2102, Found: 471.2120.



4e

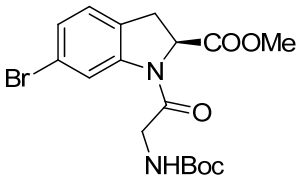
According to the general experimental procedure, compound **4e** was obtained as yellow oil. Two amide rotamers (2:1) exist in NMR spectra.
Major amide rotamer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.4 Hz, 1H), 7.25 – 7.13 (m, 2H), 5.46 (s, 1H), 4.97 (d, *J* = 10.0 Hz, 1H), 4.19 – 4.06 (m, 1H), 3.81 (d, *J* = 18.8 Hz, 1H), 3.78 (s, 3H), 3.68 – 3.55 (m, 1H), 3.30 (d, *J* = 16.5 Hz, 1H), 1.46 (s, 9H).
Minor amide rotamer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 (s, 1H), 7.25 – 7.13 (m, 2H), 5.53 (s, 1H), 5.21 (s, 1H), 4.43 – 4.25 (m, 2H), 3.75 (s, 3H), 3.50 (d, *J* = 14.1 Hz, 1H), 3.13 (d, *J* = 15.5 Hz, 1H), 1.46 (s, 9H).
Mixture of amide rotamers: ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 167.4, 155.8, 140.9, 130.4, 129.4, 128.0, 126.0, 124.6, 118.1, 114.8, 79.9, 77.1, 60.7, 59.9, 53.3, 52.7, 45.0, 43.4, 33.4, 31.3, 29.7, 28.3.
HRMS (ESI) Calcd for $C_{17}H_{21}ClN_2O_5Na$ [M+Na^+]: 391.1031, Found: 391.1027.



4f

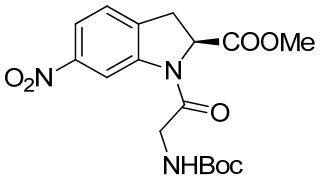
According to the general experimental procedure, compound **4f** was obtained as yellow solid. Two amide rotamers (1.4:1) exist in NMR spectra.
Major amide rotamer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 6.6 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 5.46 (br s, 1H), 5.01 (d, *J* = 8.5 Hz, 1H), 4.11 (d, *J* = 14.1 Hz, 1H), 3.85 – 3.80 (m, 1H), 3.79 (s, 3H), 3.70 – 3.54 (m, 1H), 3.41 (d, *J* = 16.4 Hz, 1H), 1.46 (s, 9H).
Minor amide rotamer: ^{1}H NMR (500 MHz, $CDCl_3$) δ7.22 (d, *J* = 8.1 Hz, 1H), 6.98 (d, *J* = 27.8 Hz, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 5.50 (d, *J* = 16.0 Hz, 1H), 5.24 (s, 1H), 4.37 (d, *J* = 24.2 Hz, 2H), 3.76 (s, 3H), 3.46 (d, *J* = 12.3 Hz, 1H), 3.28 – 3.11 (m, 1H), 1.46 (s, 9H).

Mixture of amide rotamers: ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 167.4, 159.8, 157.4, 155.8, 144.5, 142.3, 130.1, 128.9, 117.4, 114.8, 113.2, 111.5, 111.3, 109.8, 80.0, 60.7, 60.1, 53.3, 52.7, 45.1, 43.6, 30.1, 29.7, 28.3, 28.1, 27.8.
HRMS (ESI) Calcd for $C_{17}H_{21}FN_2O_5Na$ [M+Na^+]: 375.1327, Found: 375.1325.



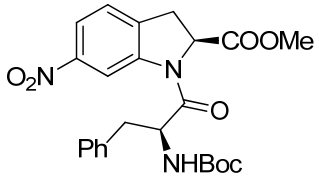
4g

According to the general experimental procedure, compound **4g** was obtained as yellow solid. Two amide rotamers (3:1) exist in NMR spectra.
Major amide rtamer: ^1H NMR (500 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.19 – 7.16 (m, 1H), 7.03 (d, *J* = 7.4 Hz, 1H), 5.45 (br s, 1H), 4.97 (d, *J* = 9.9 Hz, 1H), 4.19 – 4.06 (m, 1H), 3.81 (d, *J* = 12.5 Hz, 1H), 3.78 (s, 3H), 3.57 (dd, *J* = 33.9, 17.9 Hz, 1H), 3.27 (d, *J* = 16.3 Hz, 1H), 1.46 (s, 9H).
Minor amide rotamer: ^1H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.20 (m, 2H), 7.06 (s, 1H), 5.48 (br s, 1H), 5.21 (s, 1H), 4.34 – 4.26 (m, 2H), 3.74 (s, 3H), 3.46 – 3.43 (m, 1H), 3.08 (d, *J* = 14.0 Hz, 1H), 1.47 (s, 9H).
Mixture of amide rotamers: ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 167.6, 155.8, 143.4, 127.5, 127.4, 127.1, 126.9, 125.5, 121.4, 120.4, 80.0, 77.5, 60.7, 60.1, 53.3, 52.7, 45.0, 43.5, 33.3, 31.1, 29.7, 28.3.
HRMS (ESI) Calcd for $C_{17}H_{21}BrN_2O_5Na$ [M+Na^+]: 435.0526, Found: 435.0529.



4h

According to the general experimental procedure, compound **4h** was obtained as yellow solid. Two amide rotamers (>20:1) exist in NMR spectra.
Major amide rotamer: ^1H NMR (400 MHz, $CDCl_3$) δ 8.95 (s, 1H), 7.93 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.41 – 7.26 (m, 2H), 5.51 (s, 1H), 5.14 (d, *J* = 9.7 Hz, 1H), 4.25 – 4.10 (m, 1H), 3.80 (s, 3H), 3.72 (m, 2H), 3.41 (d, *J* = 17.6 Hz, 1H), 1.46 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 168.1, 155.9, 148.1, 143.1, 135.8, 124.6, 120.0, 112.3, 80.2, 60.26, 53.4, 43.5, 33.6, 28.3.
HRMS (ESI) Calcd for $C_{17}H_{21}N_3O_7Na$ [M+Na^+]: 402.1272, Found: 402.1277.



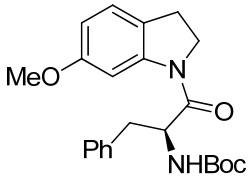
4i

According to the general experimental procedure, compound **4i** was obtained as yellow solid. **4i** contains two amide rotamers (>20:1).

Major amide rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (d, *J* = 2.0 Hz, 1H), 7.96 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.27 – 7.16 (m, 6H), 5.54 (d, *J* = 8.8 Hz, 1H), 4.65 (td, *J* = 9.7, 5.2 Hz, 1H), 4.20 (d, *J* = 9.3 Hz, 1H), 3.71 (s, 3H), 3.19 – 2.97 (m, 3H), 2.83 (dd, *J* = 17.1, 10.7 Hz, 1H), 1.47 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.48, 170.39, 154.70, 148.15, 142.40, 136.27, 135.96, 129.42, 128.78, 127.29, 124.43, 120.18, 112.66, 80.02, 60.79, 54.53, 53.37, 41.55, 32.72, 28.33.

HRMS (ESI) Calcd for $C_{24}H_{27}N_3O_7Na$ [M+Na^+]: 492.1741, Found: 492.1752.



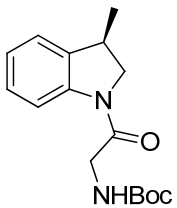
4j

According to the general experimental procedure, compound **4j** was obtained as yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 2.2 Hz, 1H), 7.28 – 7.20 (m, 5H), 7.02 (d, *J* = 8.2 Hz, 1H), 6.61 (dd, *J* = 8.2, 2.4 Hz, 1H), 5.45 (d, *J* = 8.8 Hz, 1H), 4.76 (dd, *J* = 14.8, 8.4 Hz, 1H), 4.21 – 4.09 (m, 1H), 3.86 (s, 3H), 3.42 (td, *J* = 10.2, 6.3 Hz, 1H), 3.19 – 2.94 (m, 3H), 2.86 – 2.72 (m, 1H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 159.3, 155.2, 143.4, 136.2, 129.4, 128.5, 127.0, 124.7, 123.6, 110.7, 103.4, 79.9, 55.6, 54.2, 48.7, 40.0, 28.3, 27.2.

HRMS (ESI) Calcd for $C_{23}H_{28}N_2O_4Na$ [M+Na^+]: 419.1941, Found: 419.1938.

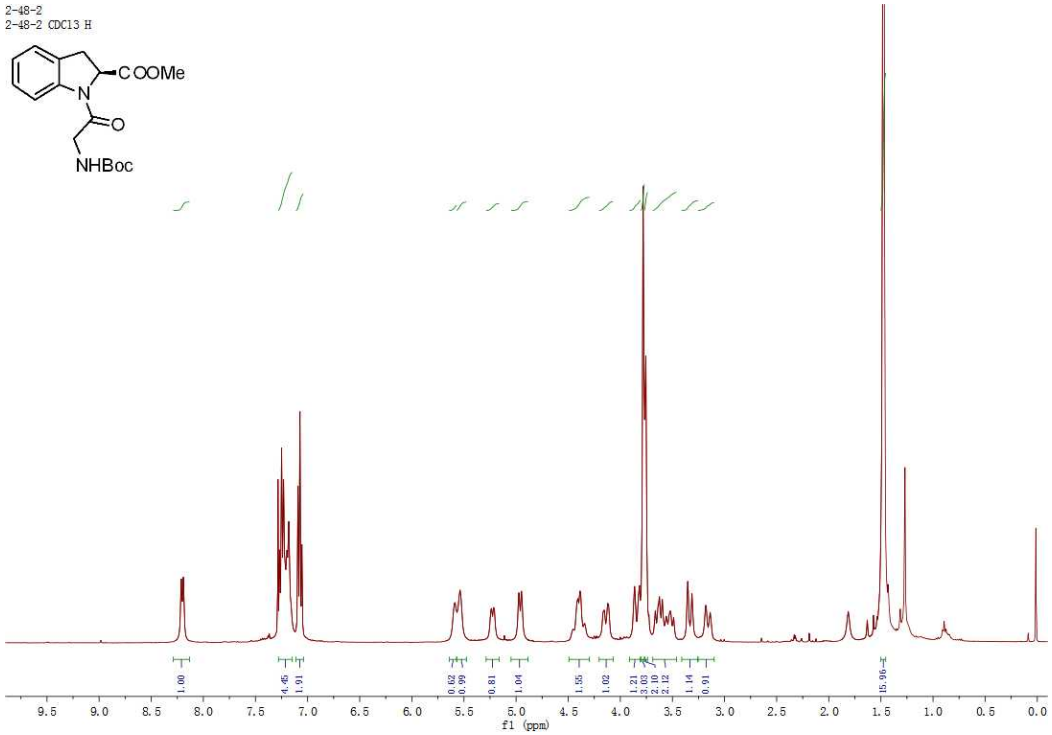


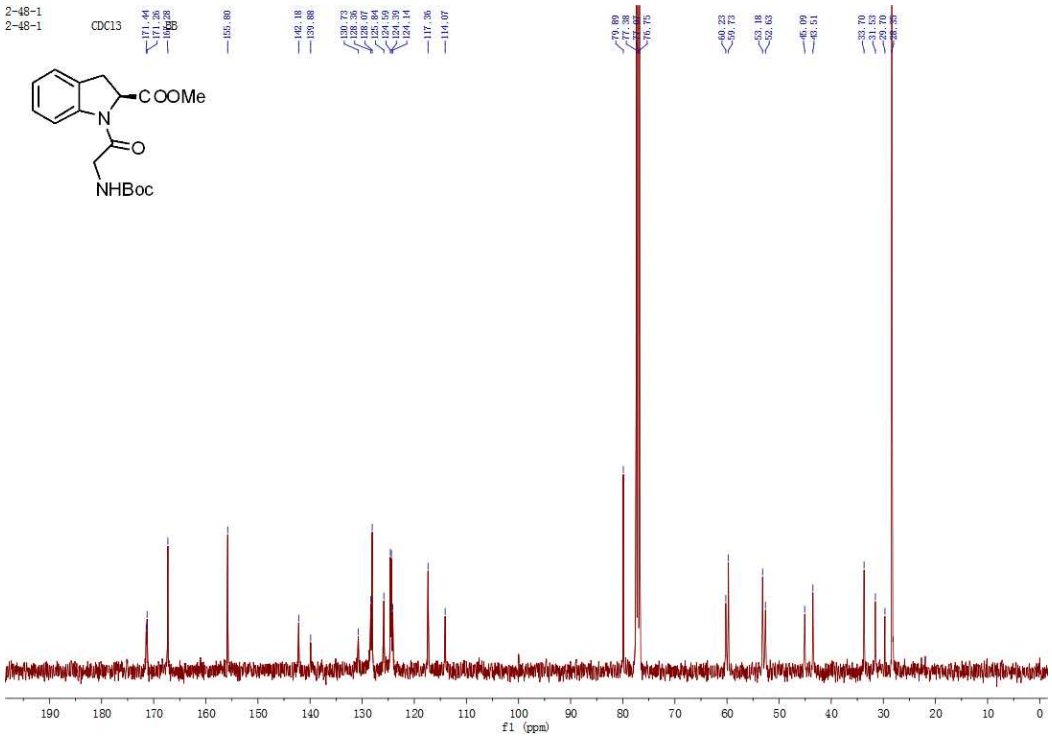
4k

According to the general experimental procedure, compound **4k** was obtained as yellow oil.

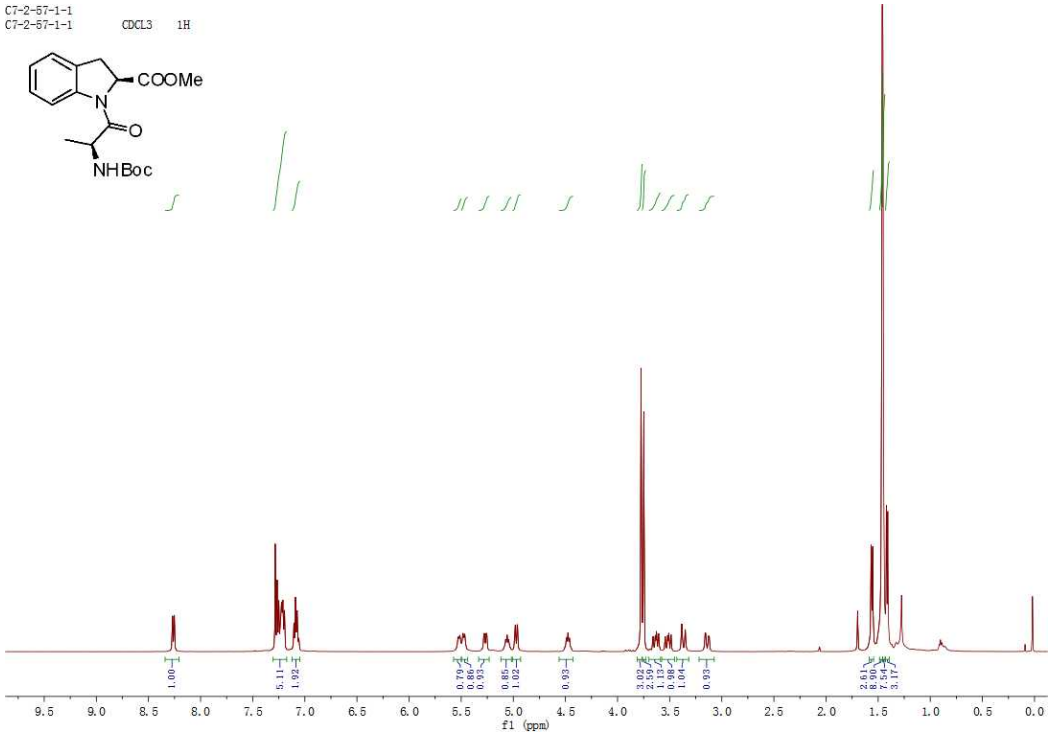
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.0 Hz, 1H), 7.26 – 7.17 (m, 2H), 7.08 (t, *J* = 7.4 Hz, 1H), 5.59 (s, 1H), 4.24 – 4.10 (m, 1H), 4.04 (d, *J* = 4.3 Hz, 2H), 3.62 – 3.47 (m, 2H), 1.48 (s, 9H), 1.36 (d, *J* = 6.4 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 155.9, 142.0, 136.2, 127.8, 124.3, 123.5, 116.8, 79.8, 54.6, 43.9, 35.0, 28.4, 20.3.
HRMS (ESI) Calcd for $C_{16}H_{22}N_2O_3Na$ [$M+Na^+$]: 313.1523, Found: 313.1518.

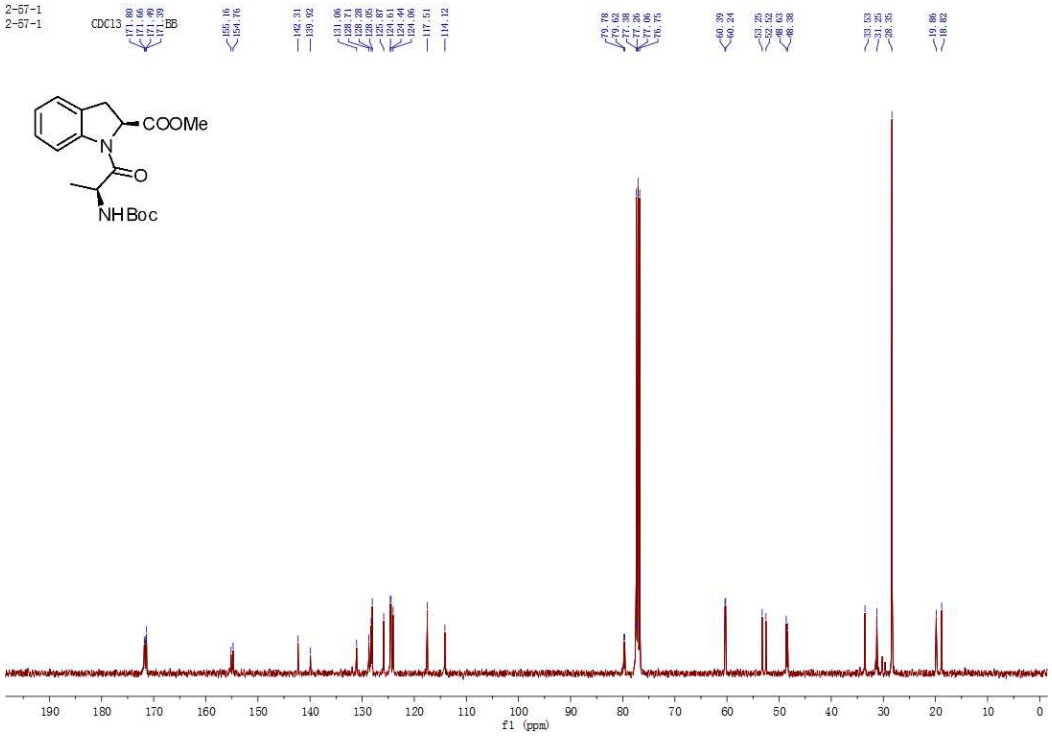
^{1}H and ^{13}C NMR spectra of **2a** (two amide rotamers, 1.6:1)



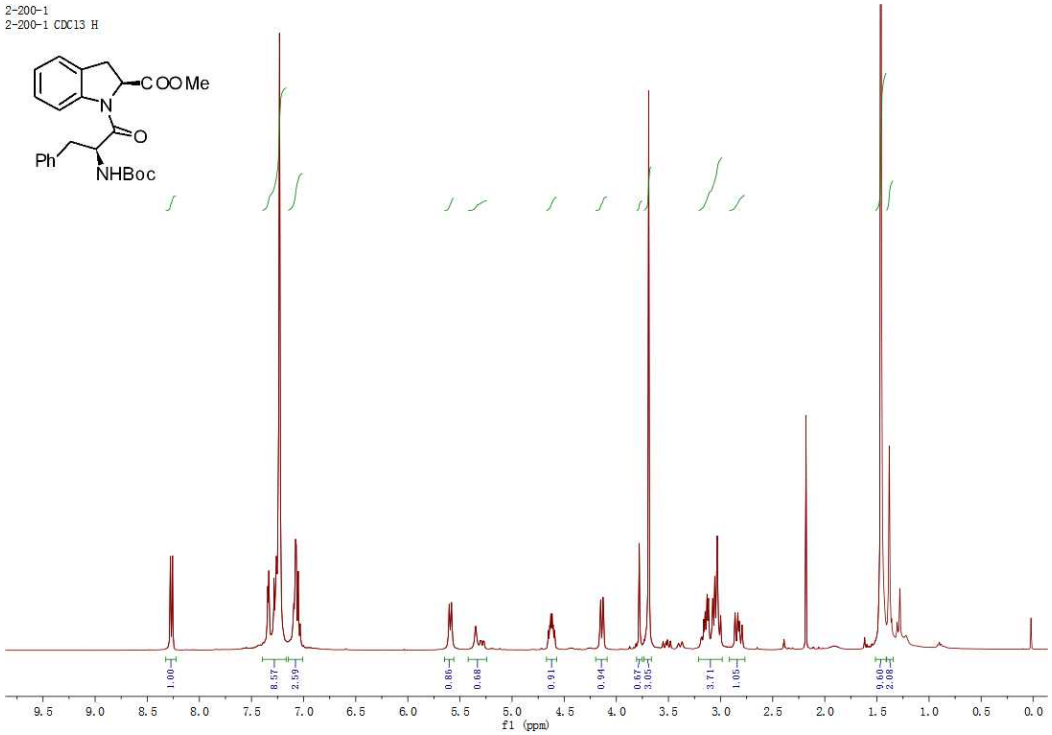


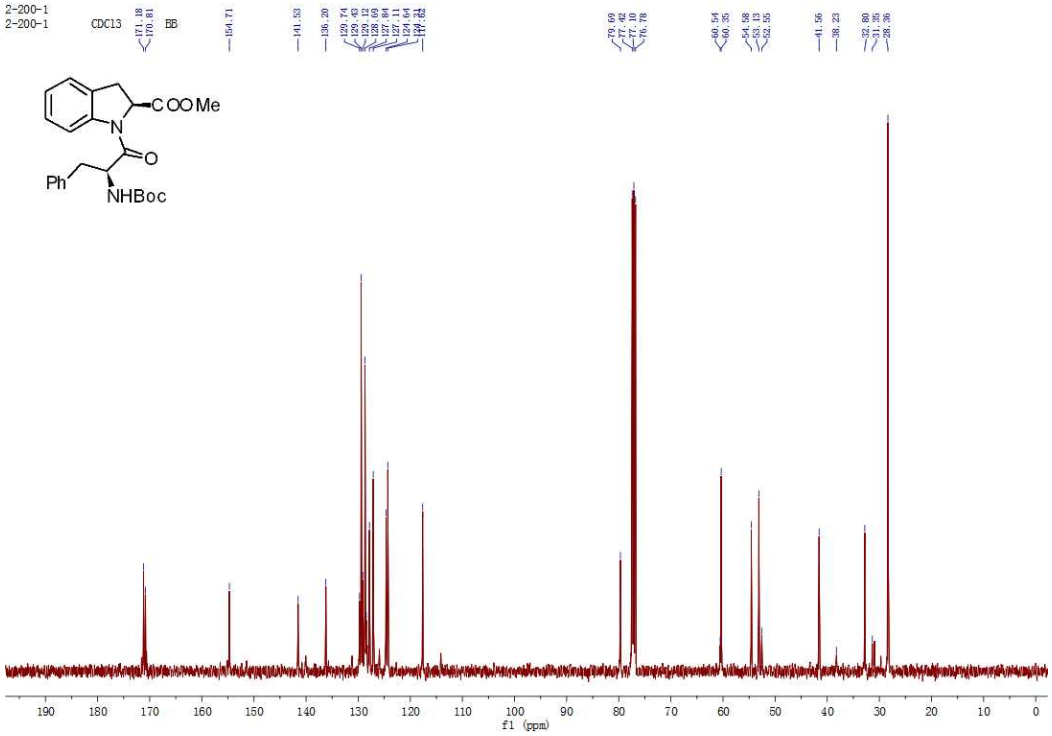
^{1}H and ^{13}C NMR spectra of **2b** (two amide rotamers, 1.3:1)



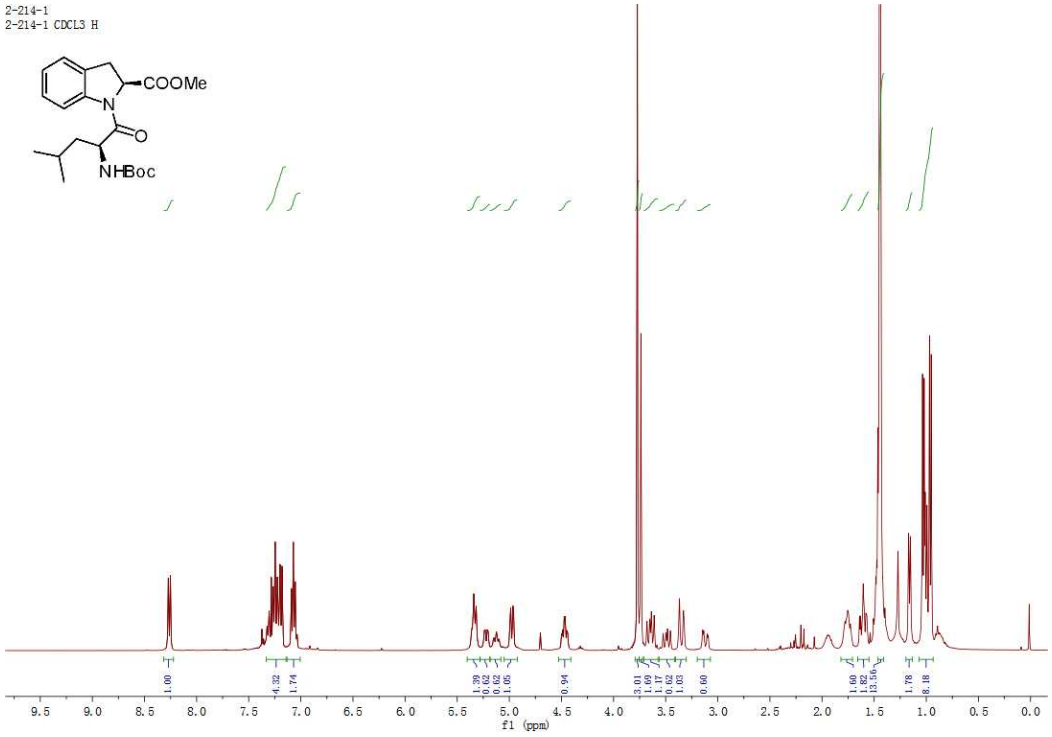


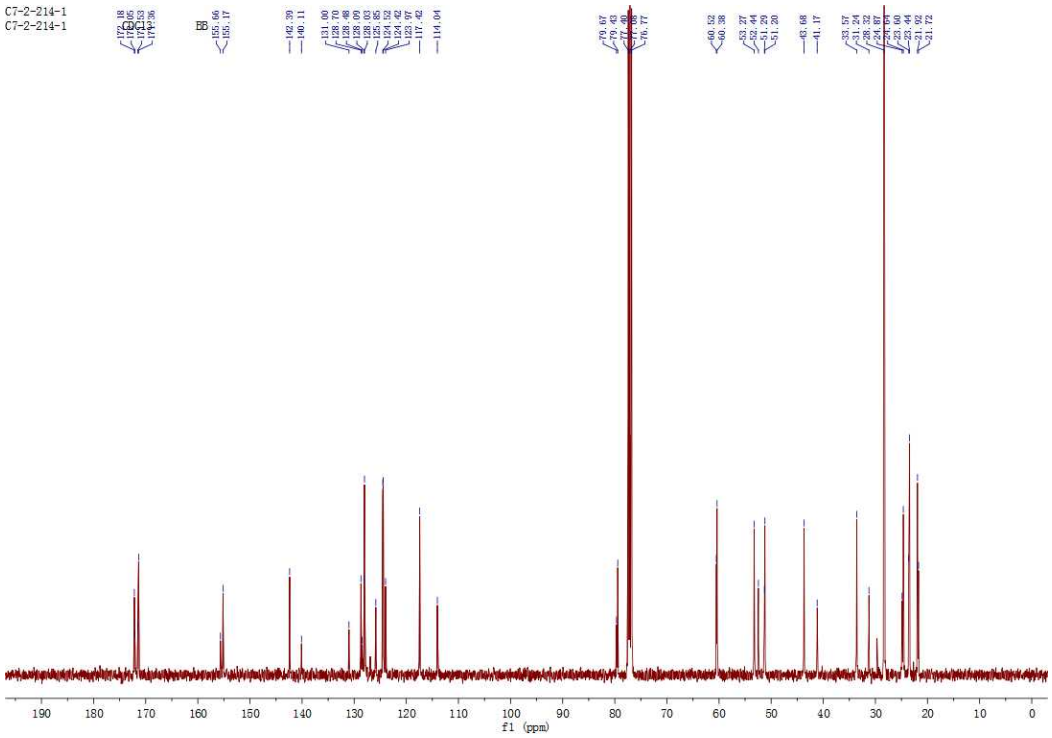
^{1}H and ^{13}C NMR spectra of **2c** (two amide rotamers, 4.5:1)



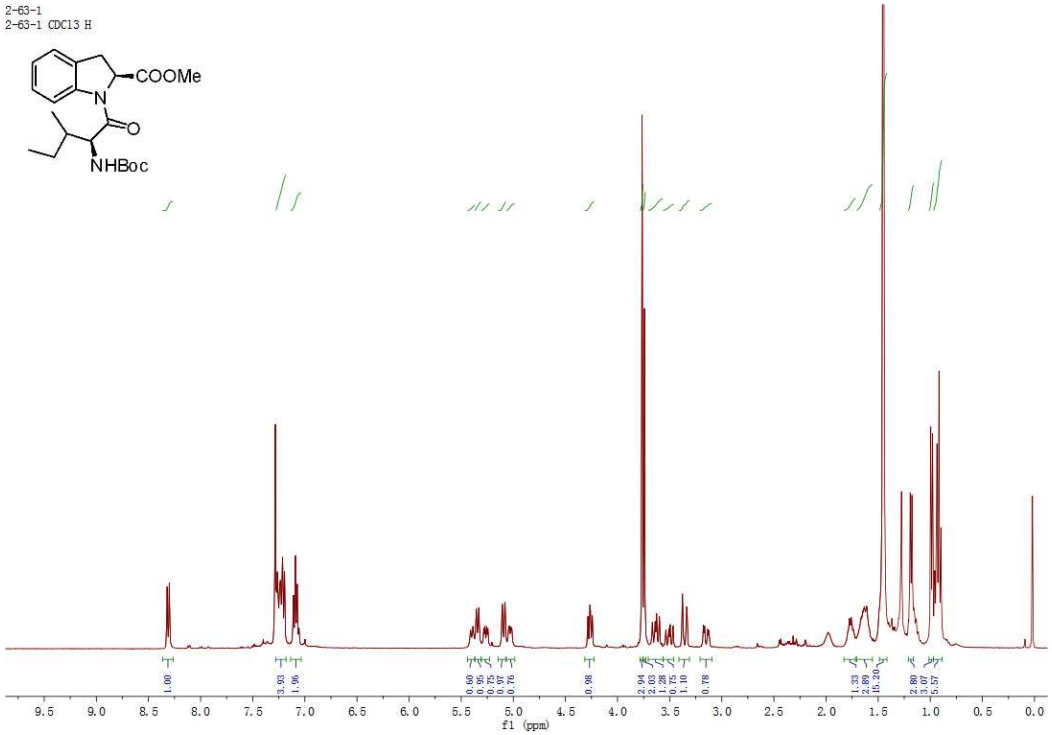


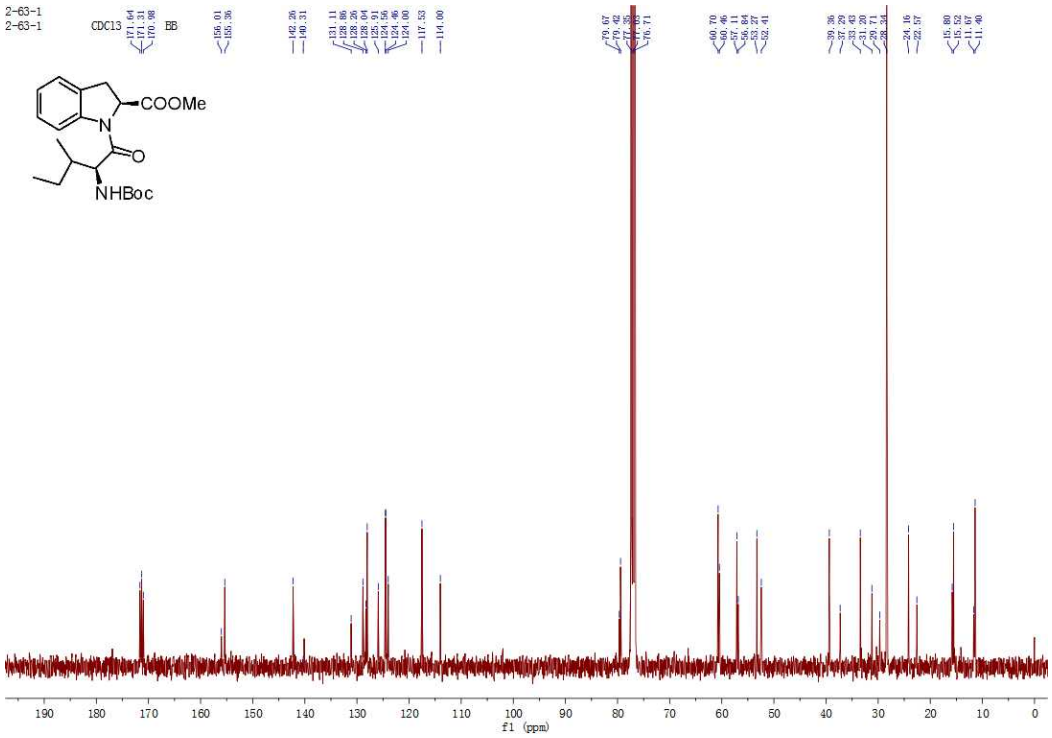
^{1}H and ^{13}C NMR spectra of **2d** (two amide rotamers, 1.7:1)



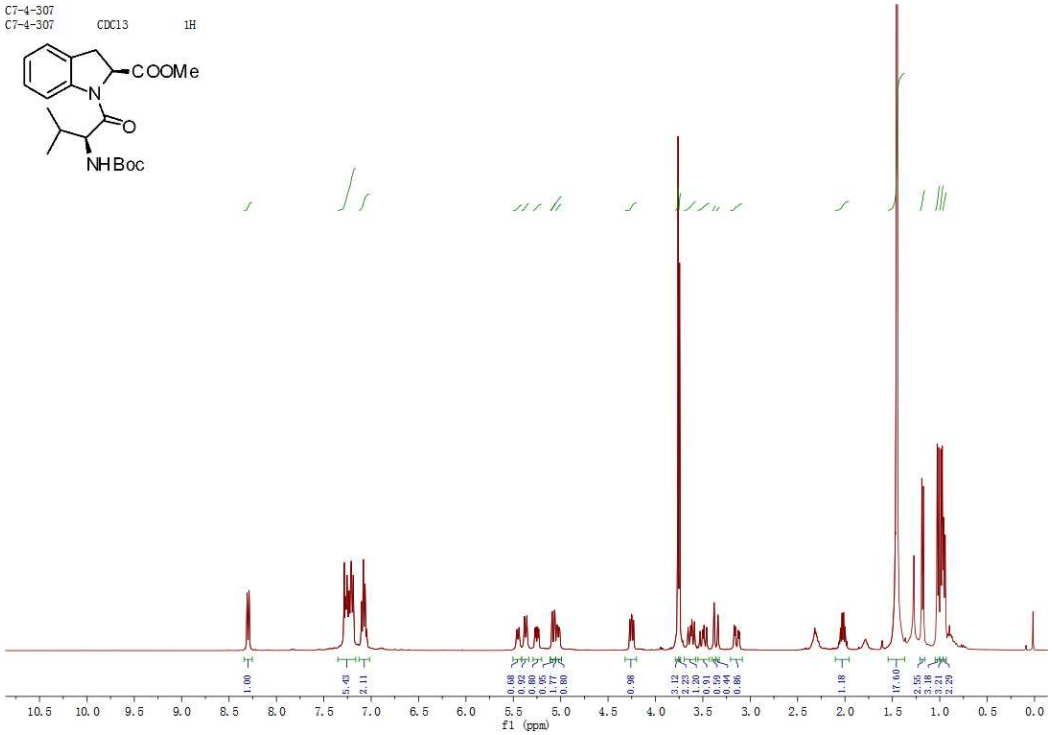


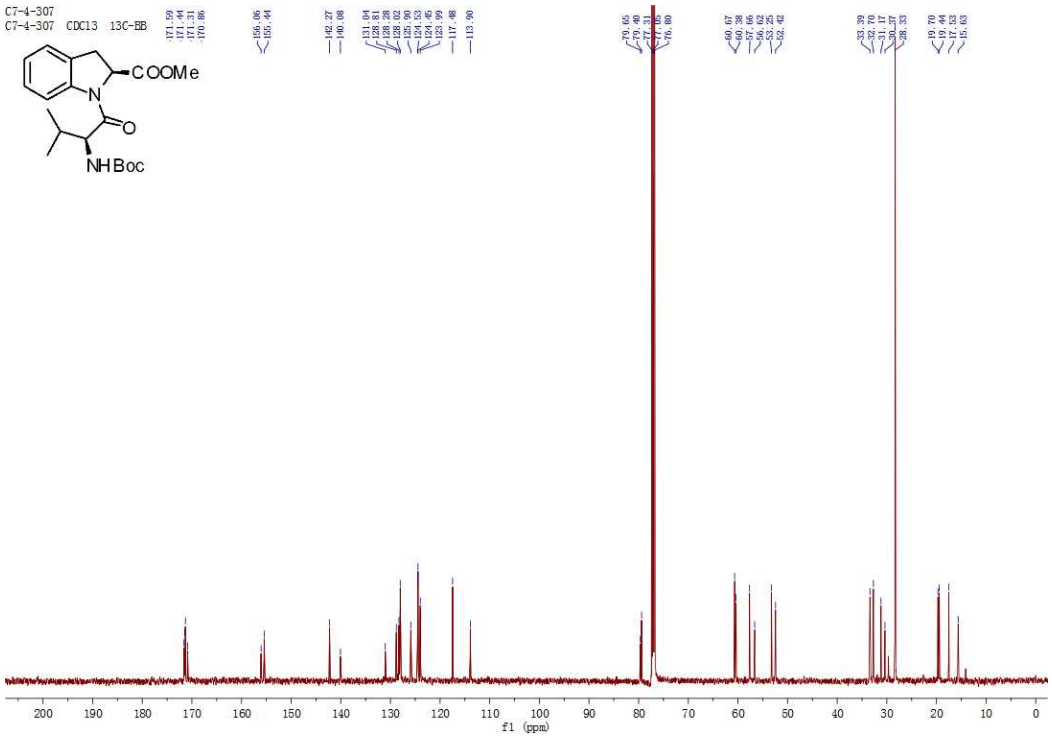
^{1}H and ^{13}C NMR spectra of **2e** (two amide rotamers, 1.3:1)



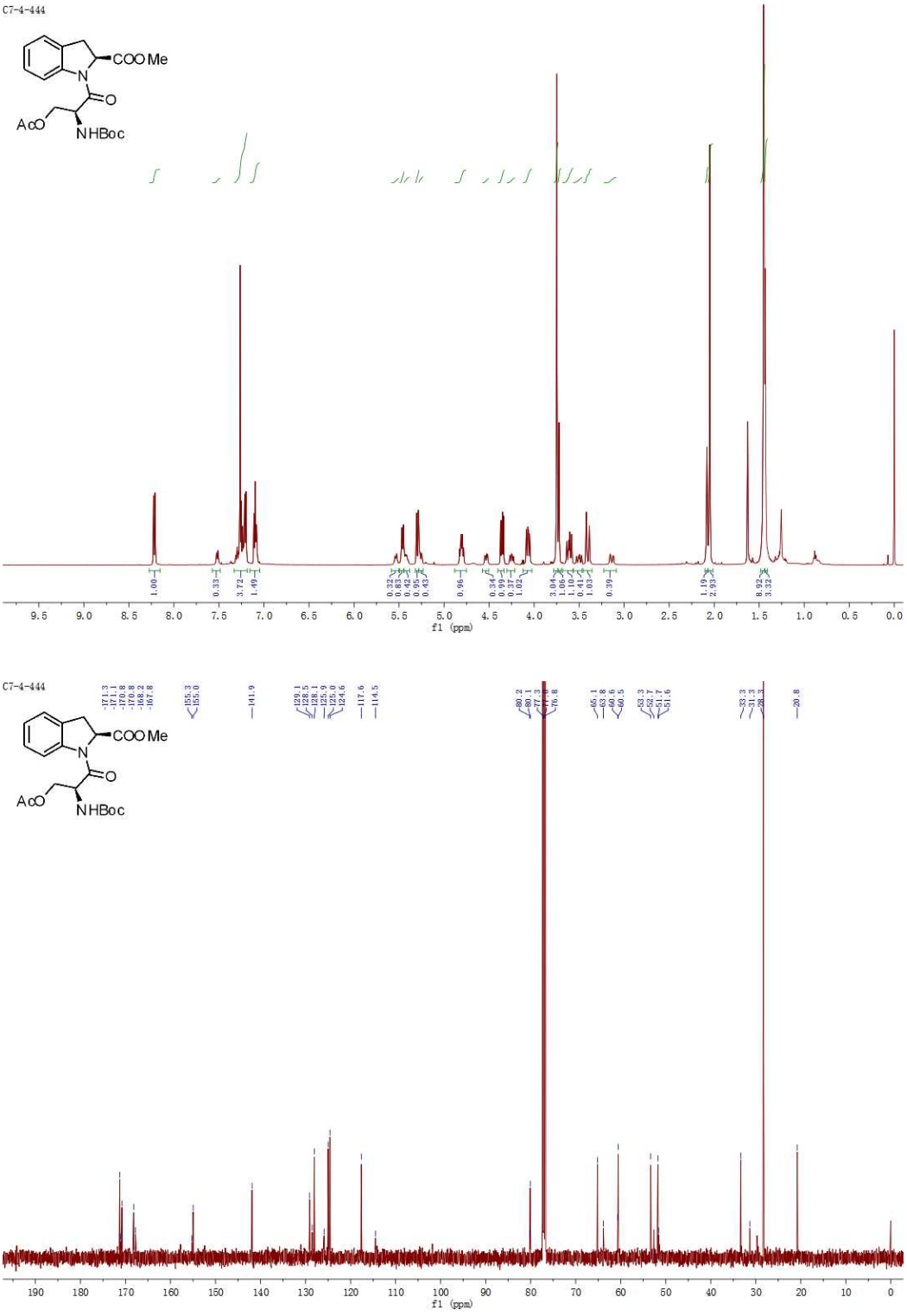


^{1}H and ^{13}C NMR spectra of **2f** (two amide rotamers, 1.3:1)

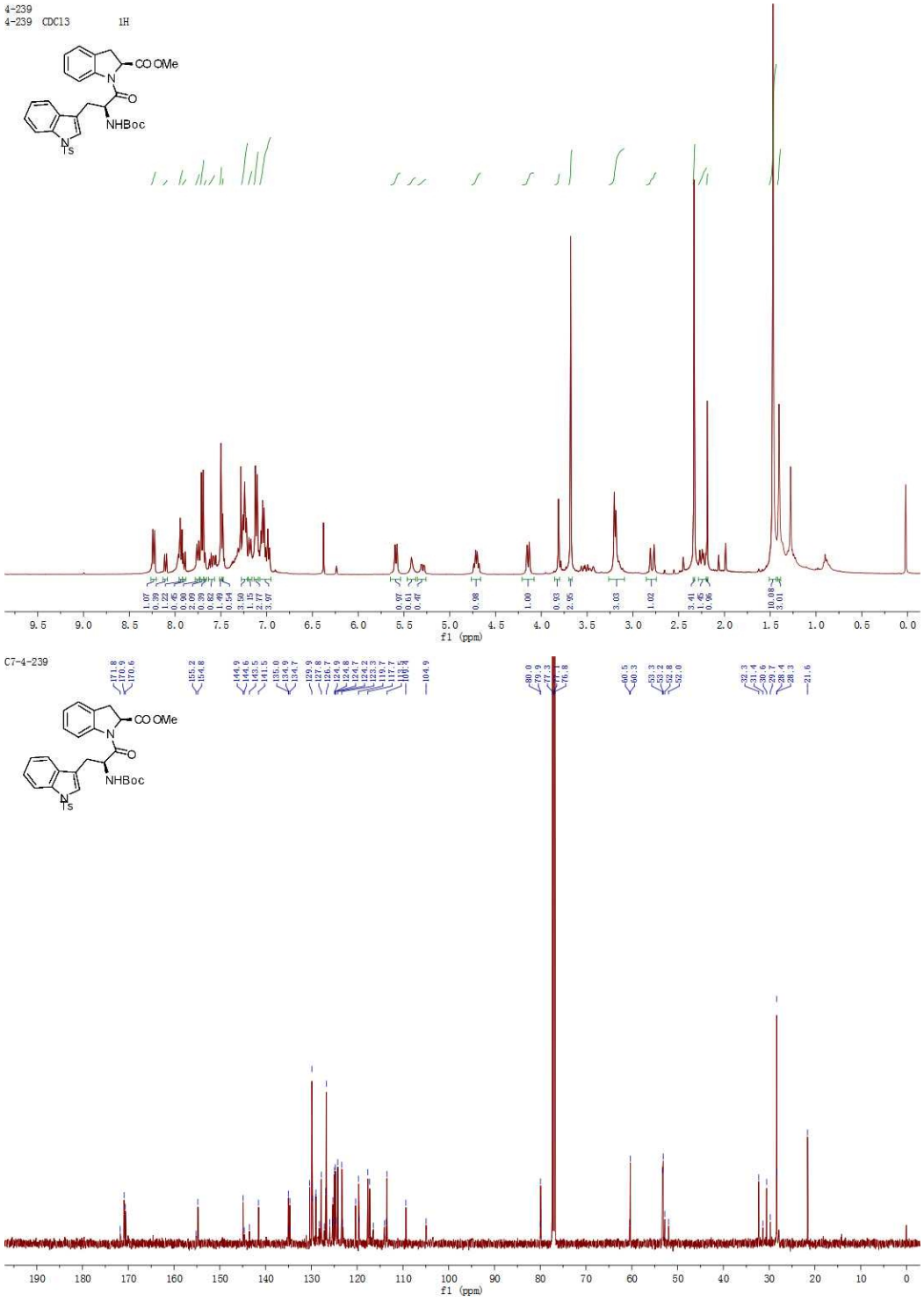




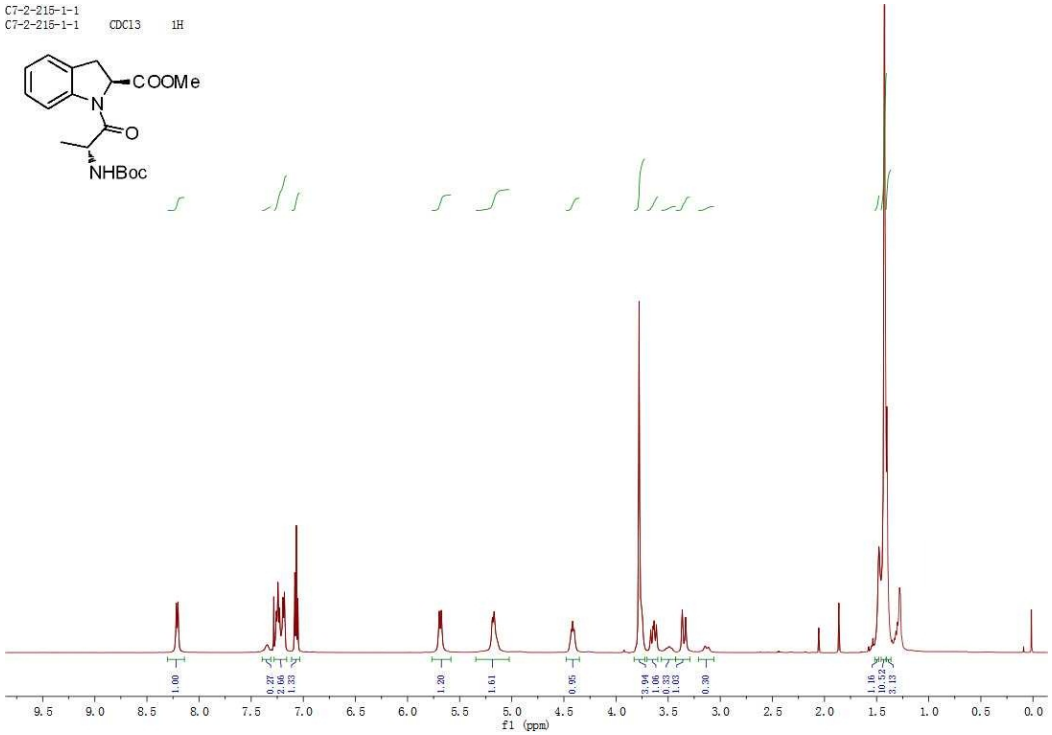
^{1}H and ^{13}C NMR spectra of **2g** (two amide rotamers, 3:1)

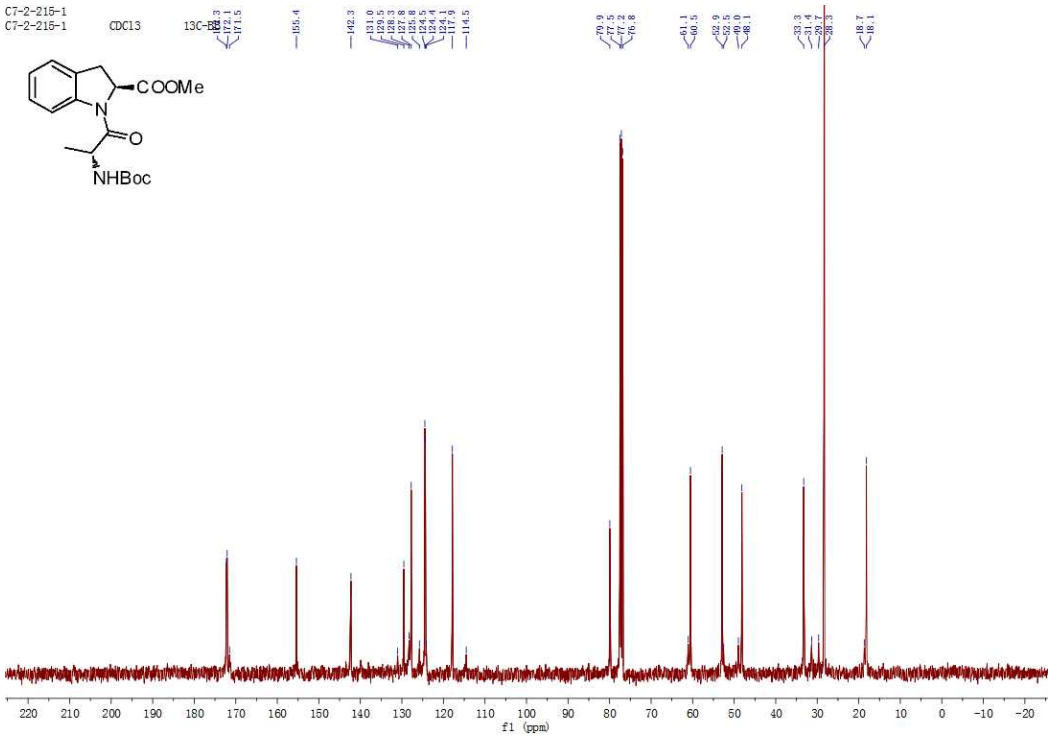


^{1}H and ^{13}C NMR spectra of **2h** (two amide rotamers, 3:1)

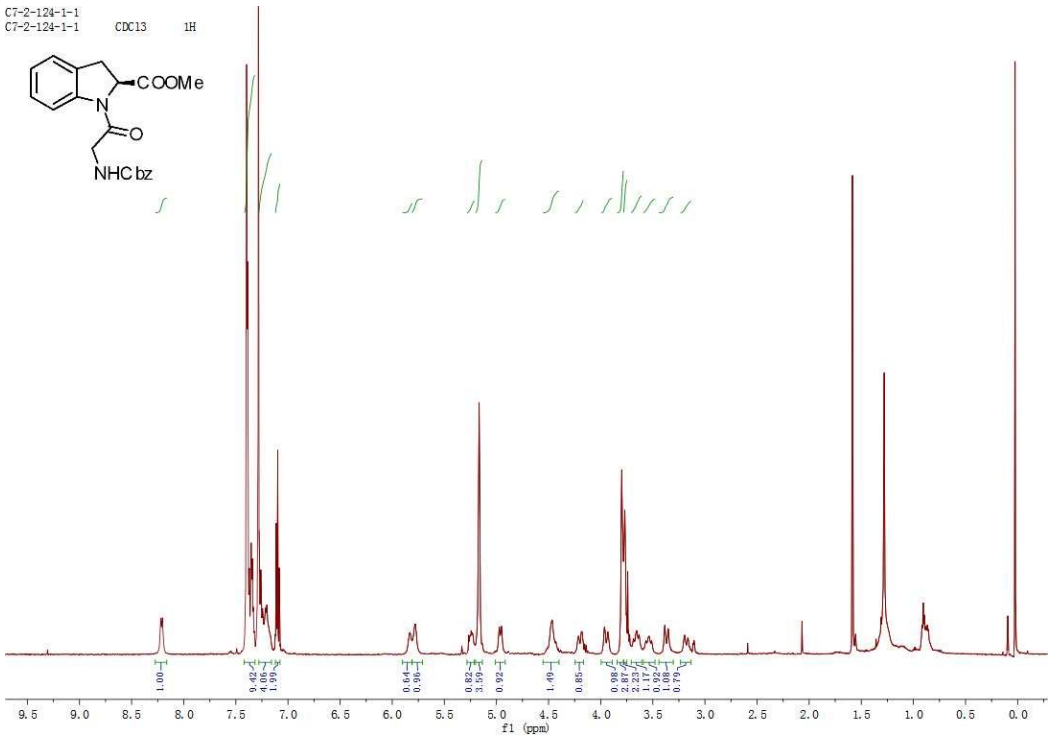


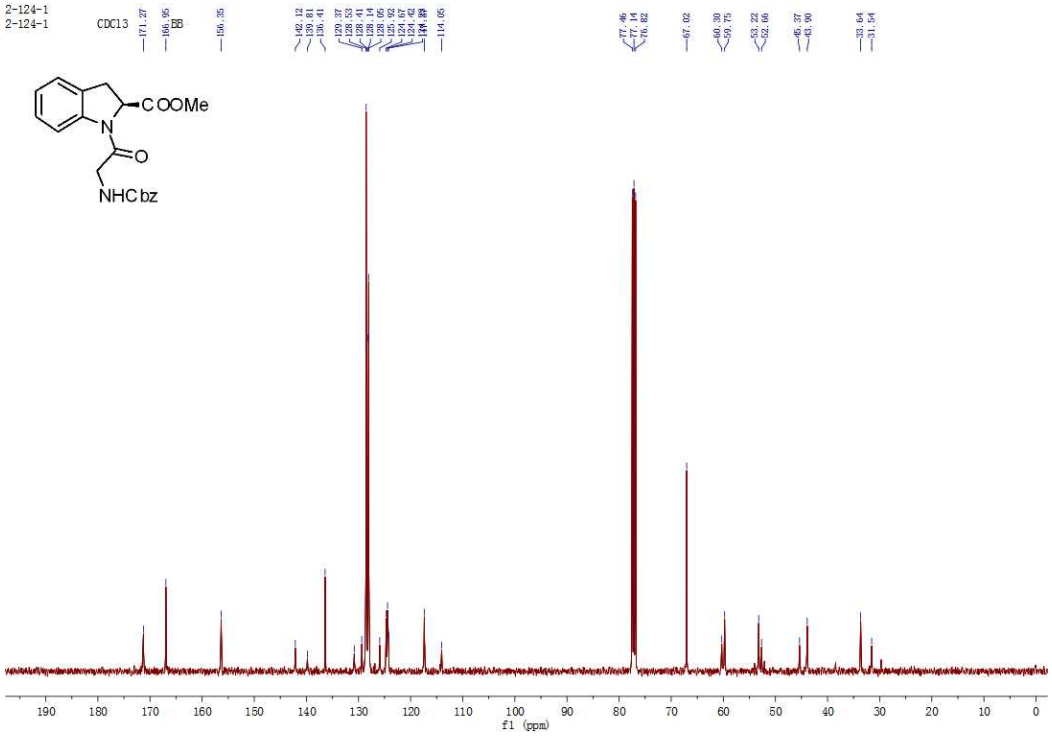
^{1}H and ^{13}C NMR spectra of **2i** (two amide rotamers, 3:1)



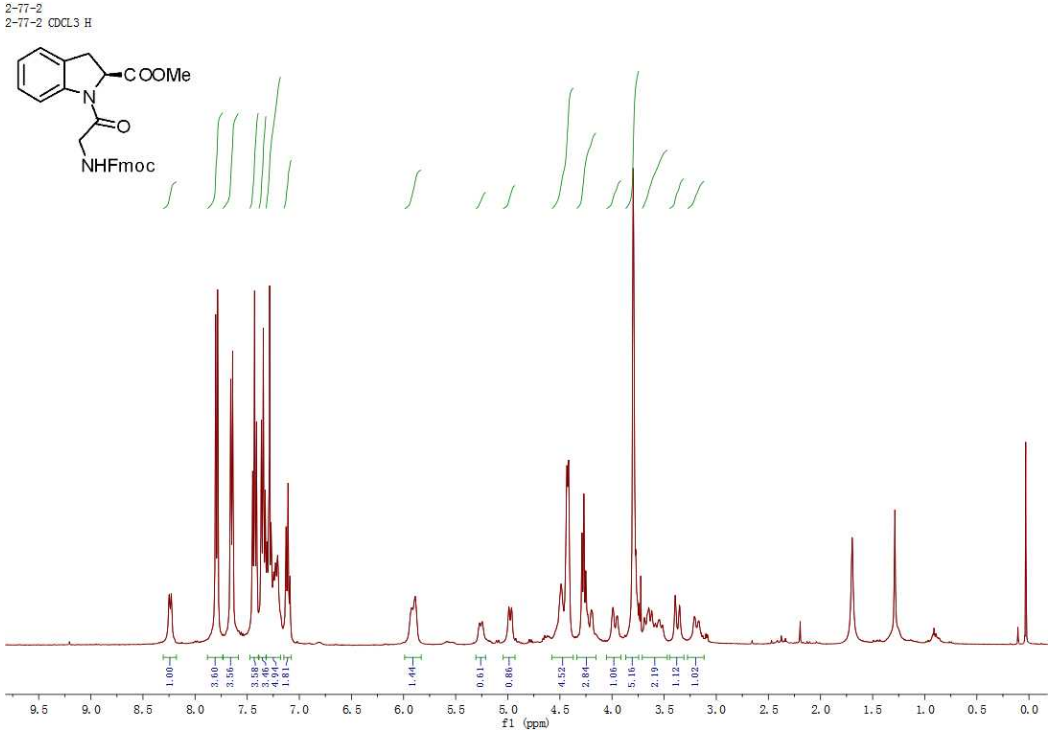


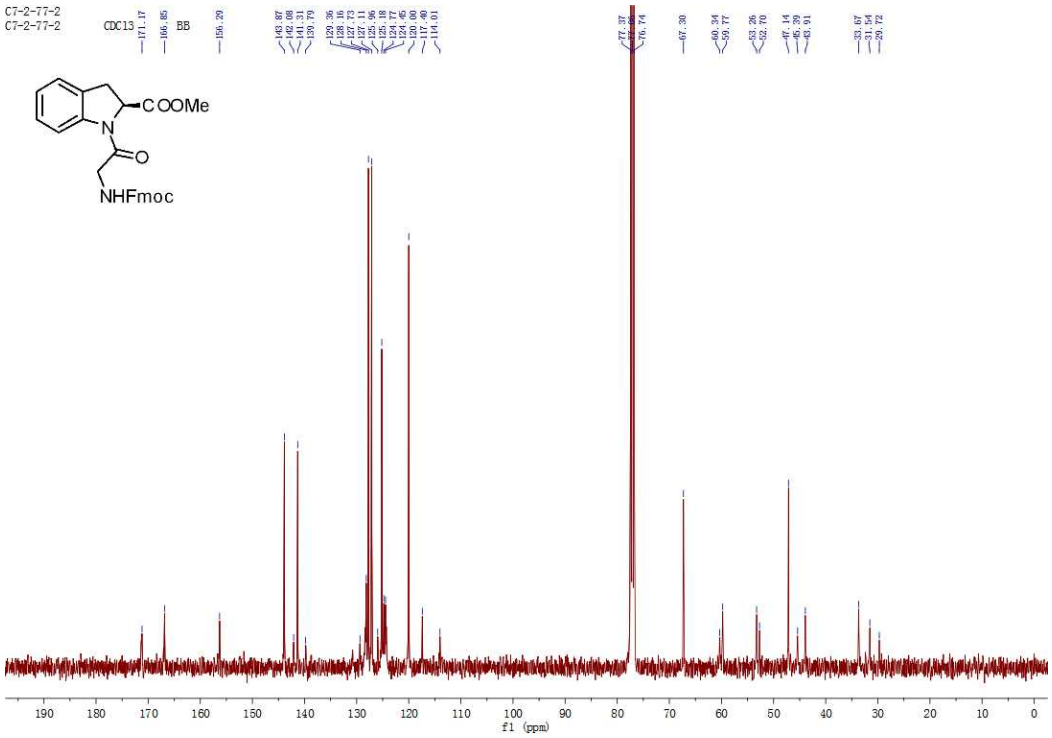
^{1}H and ^{13}C NMR spectra of **2j** (two amide rotamers, 1.5:1)



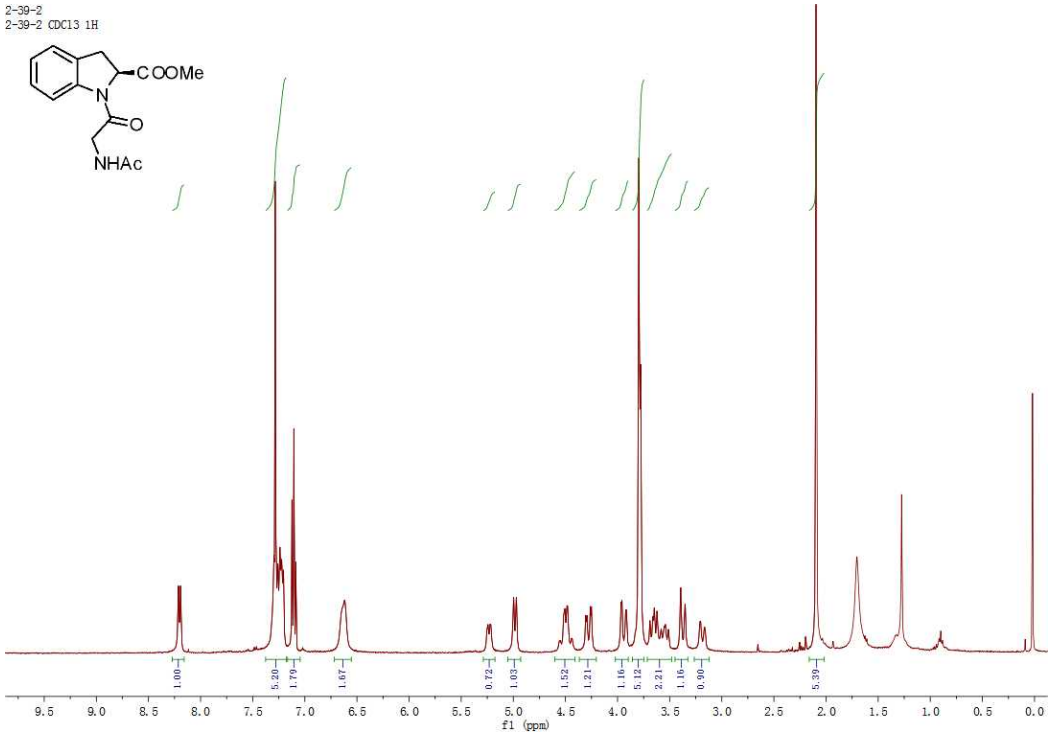


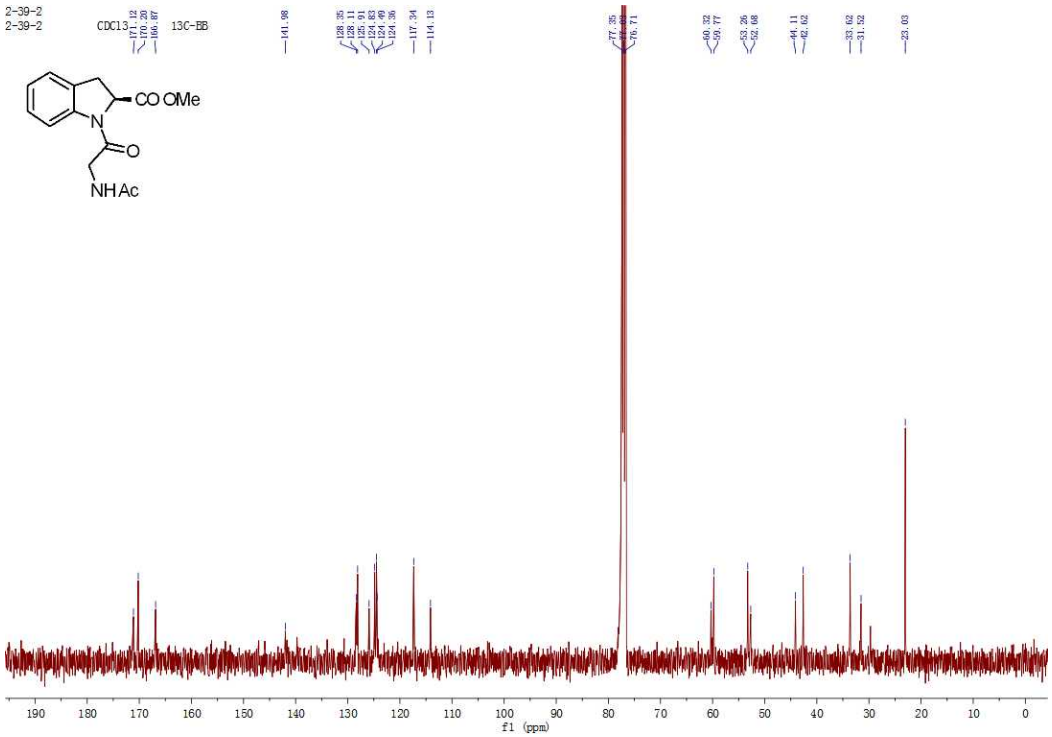
^{1}H and ^{13}C NMR spectra of **2k** (two amide rotamers, 1.1:1)



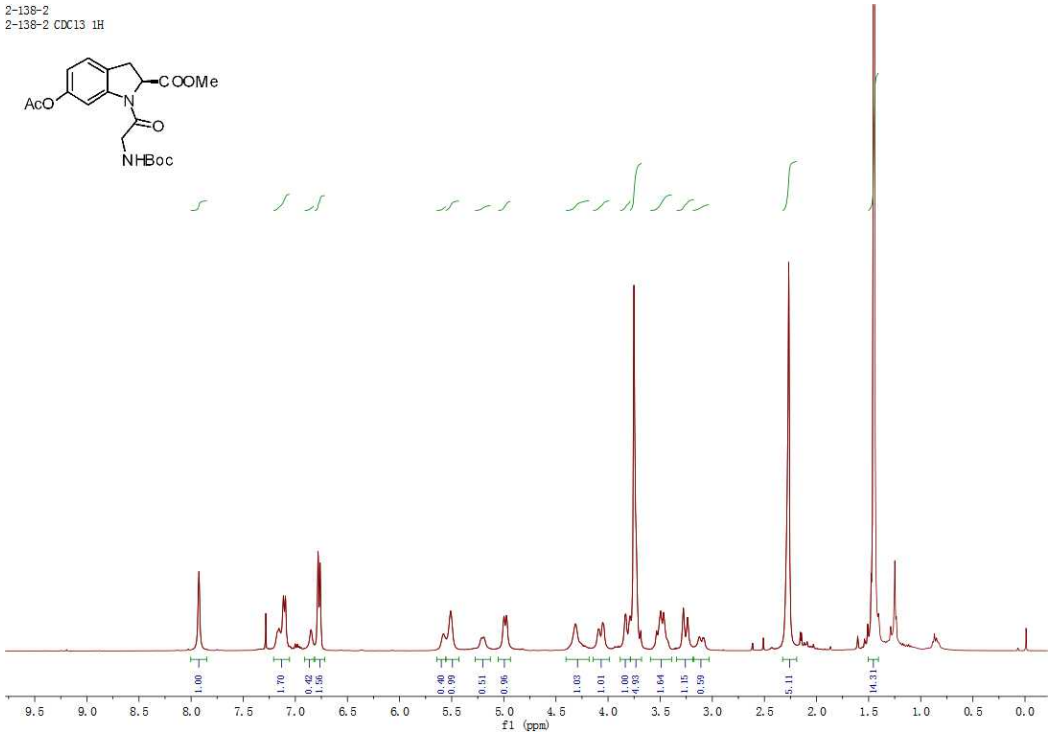


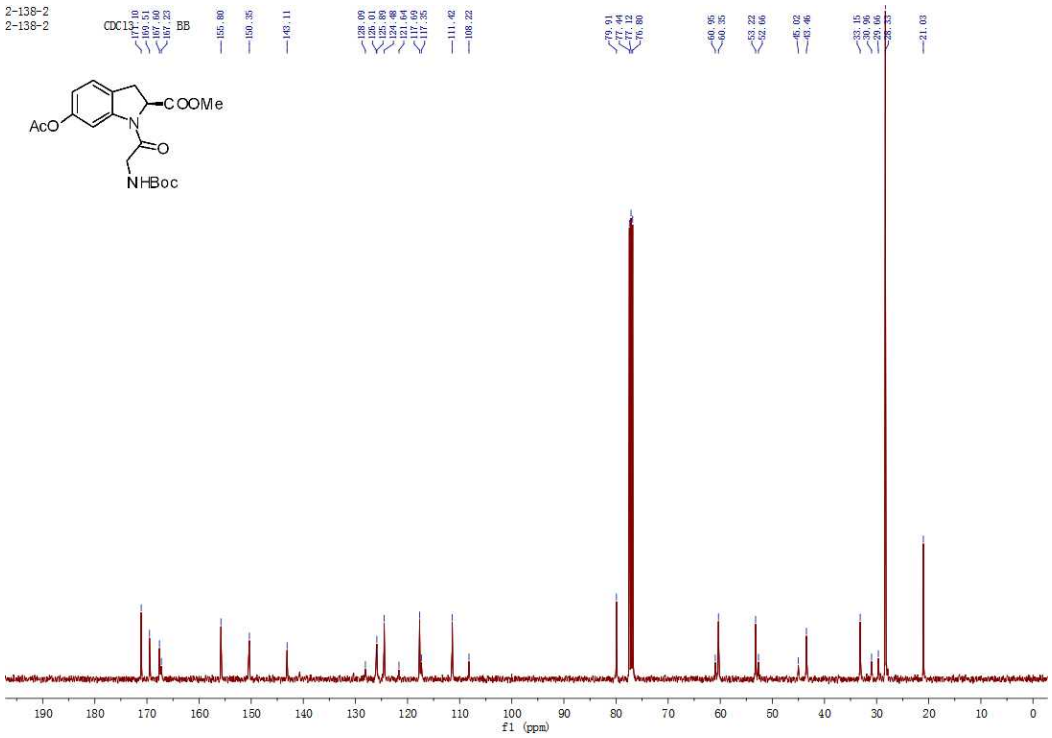
^{1}H and ^{13}C NMR spectra of **2l** (two amide rotamers, 1.4:1)



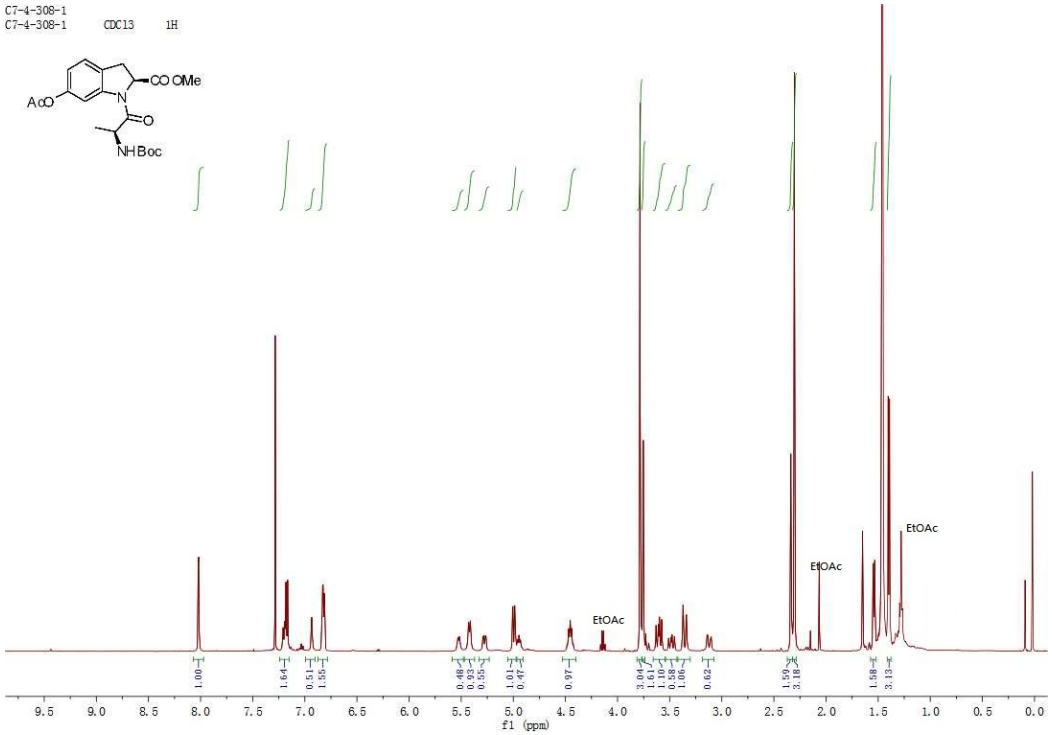


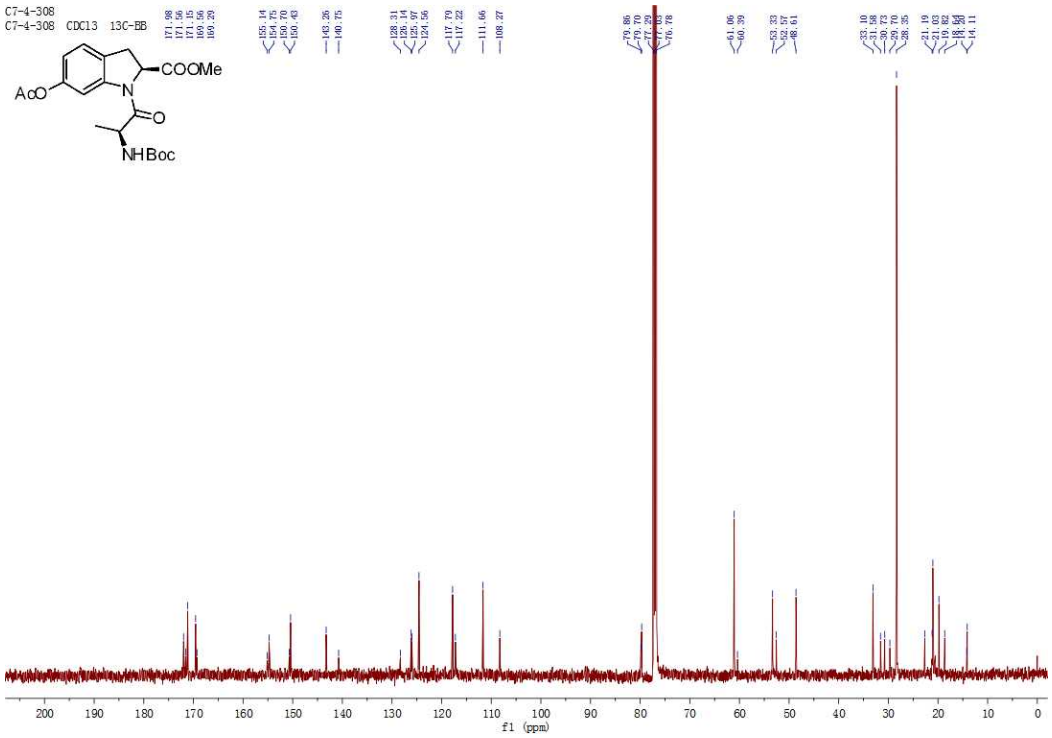
^{1}H and ^{13}C NMR spectra of **4a** (two amide rotamers, 2:1)



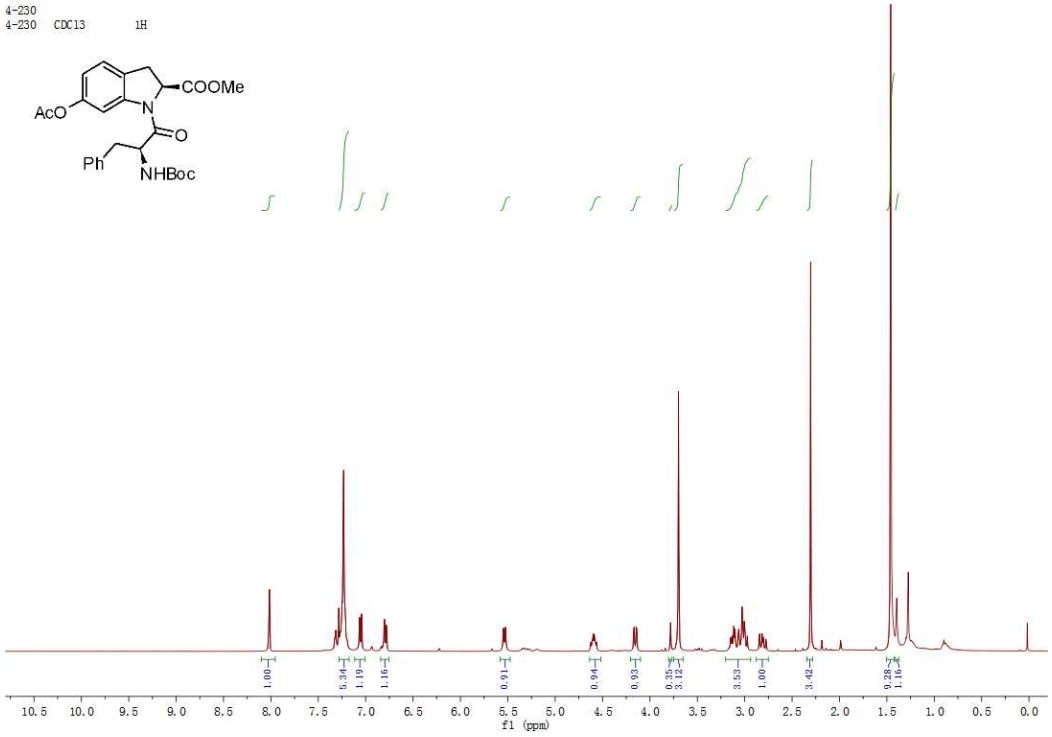


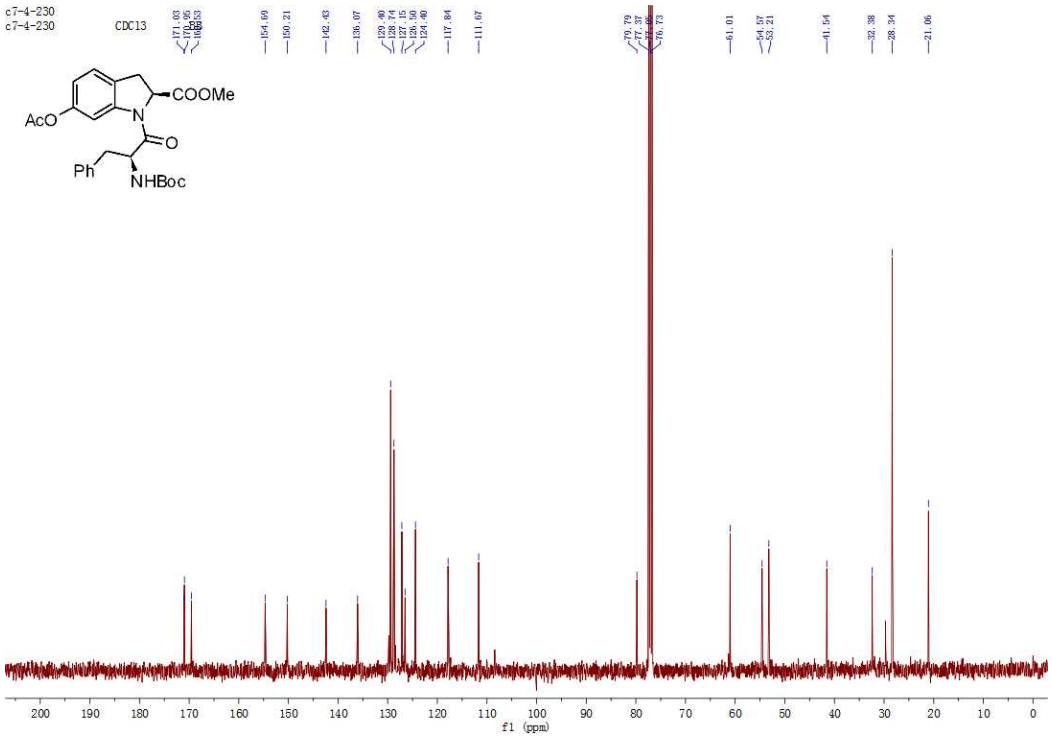
^{1}H and ^{13}C NMR spectra of **4b** (two amide rotamers, 1.9:1)



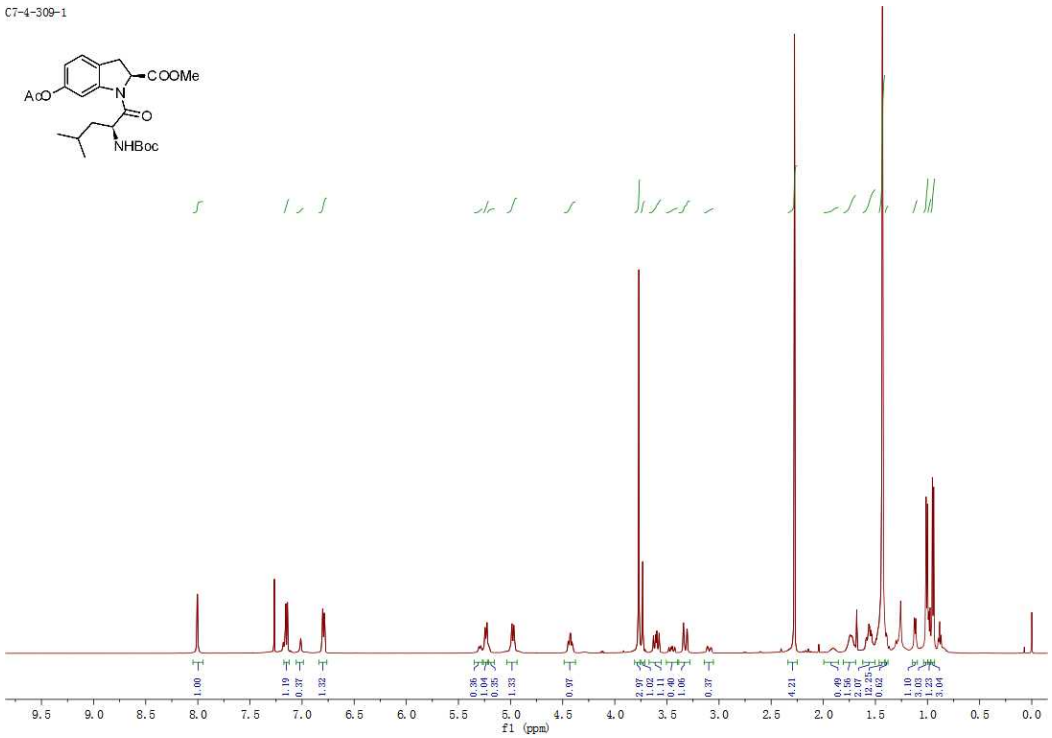


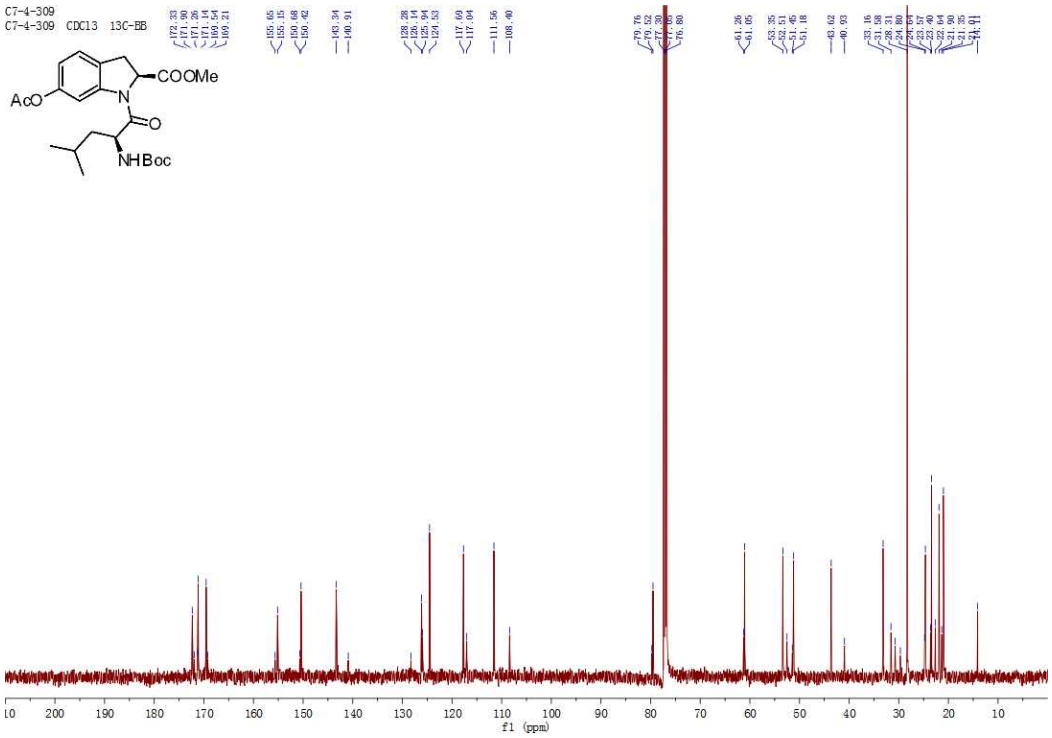
^{1}H and ^{13}C NMR spectra of **4c** (two amide rotamers, 10:1)



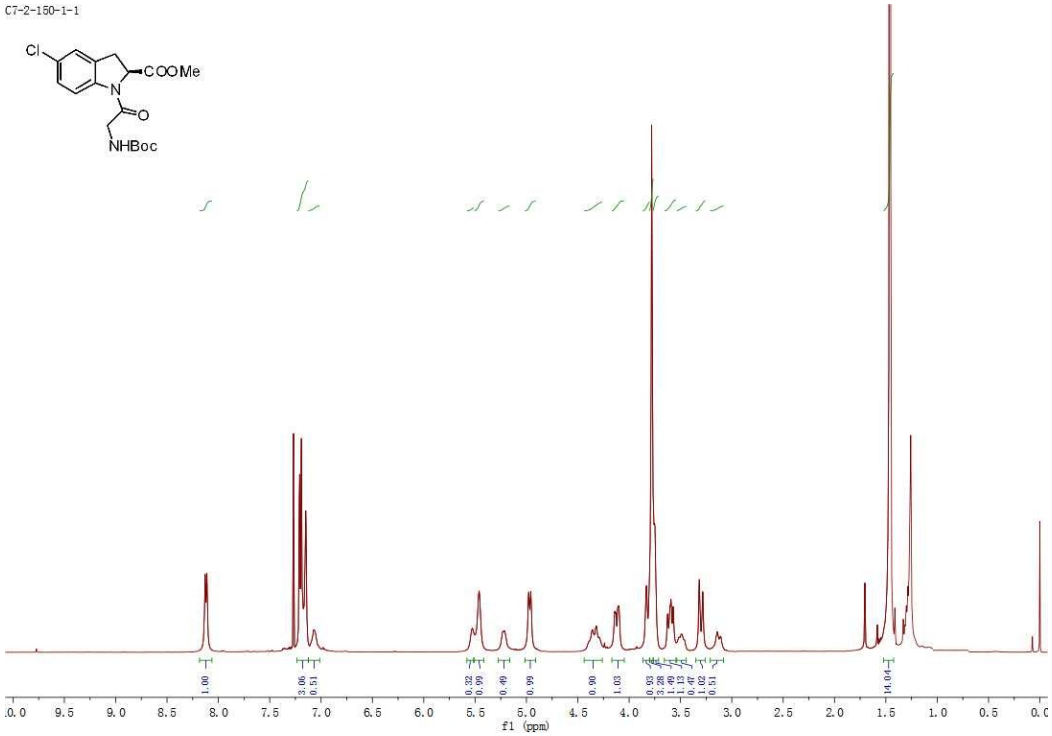


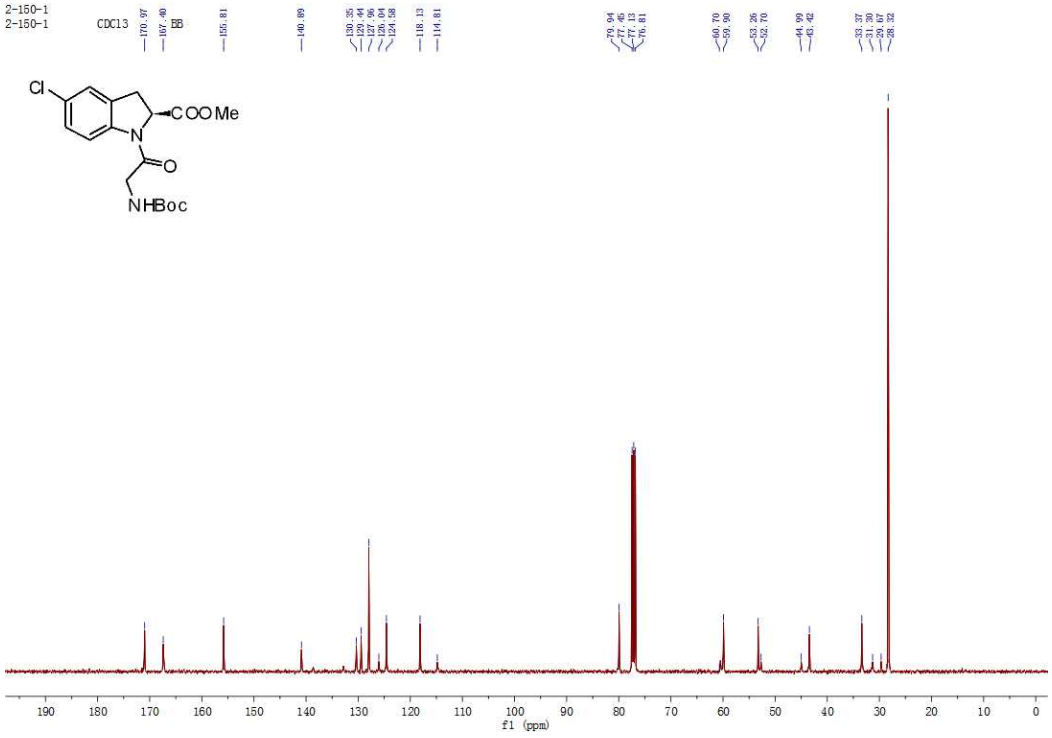
^{1}H and ^{13}C NMR spectra of **4d** (two amide rotamers, 3:1)



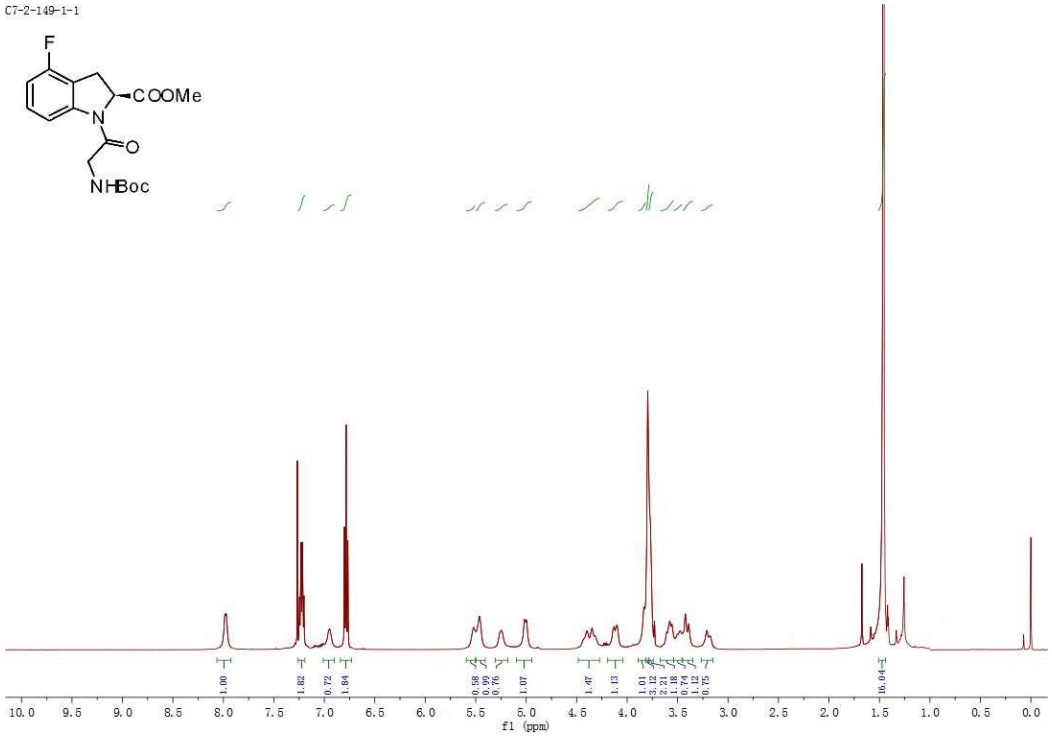


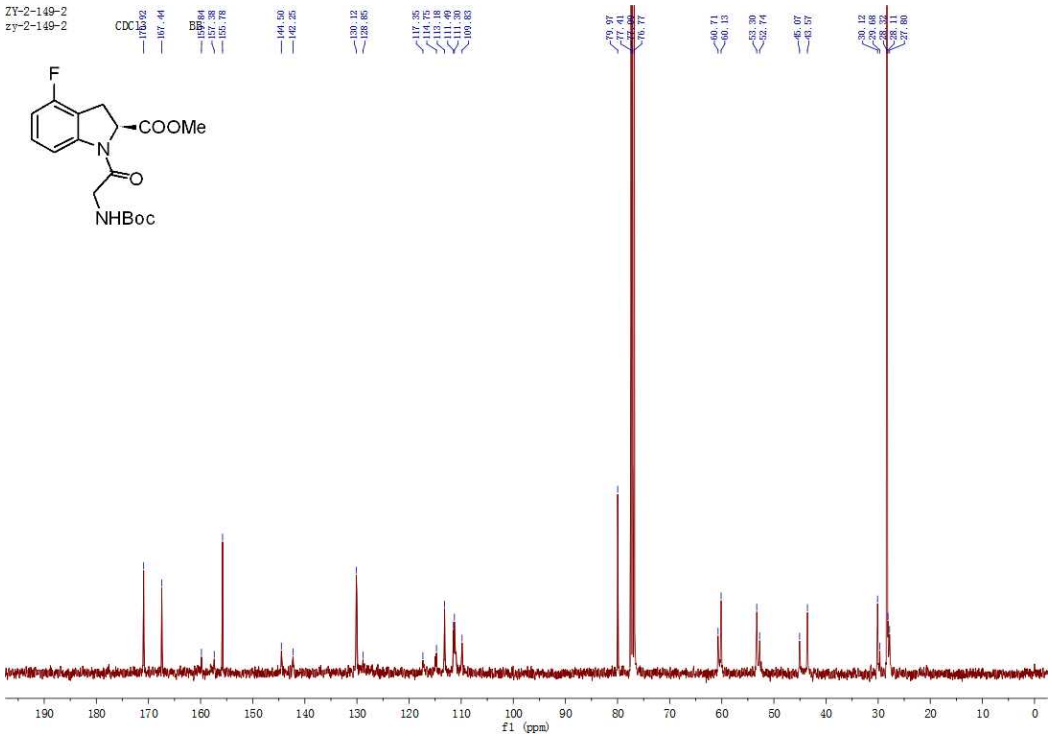
^{1}H and ^{13}C NMR spectra of **4e** (two amide rotamers, 2:1)



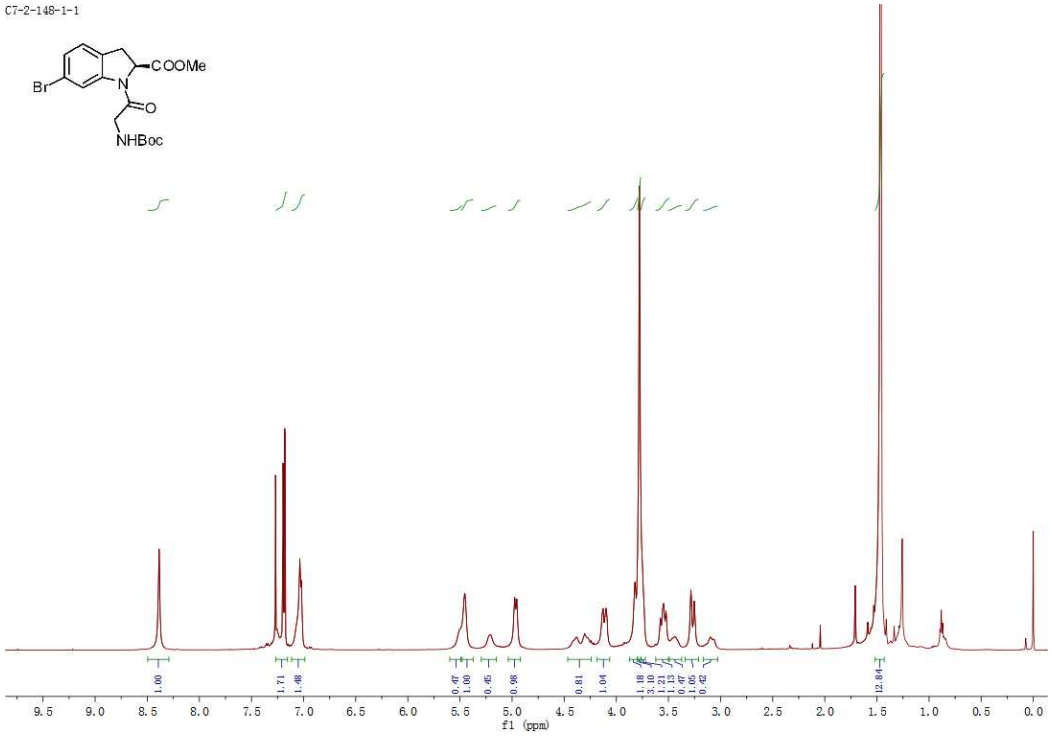


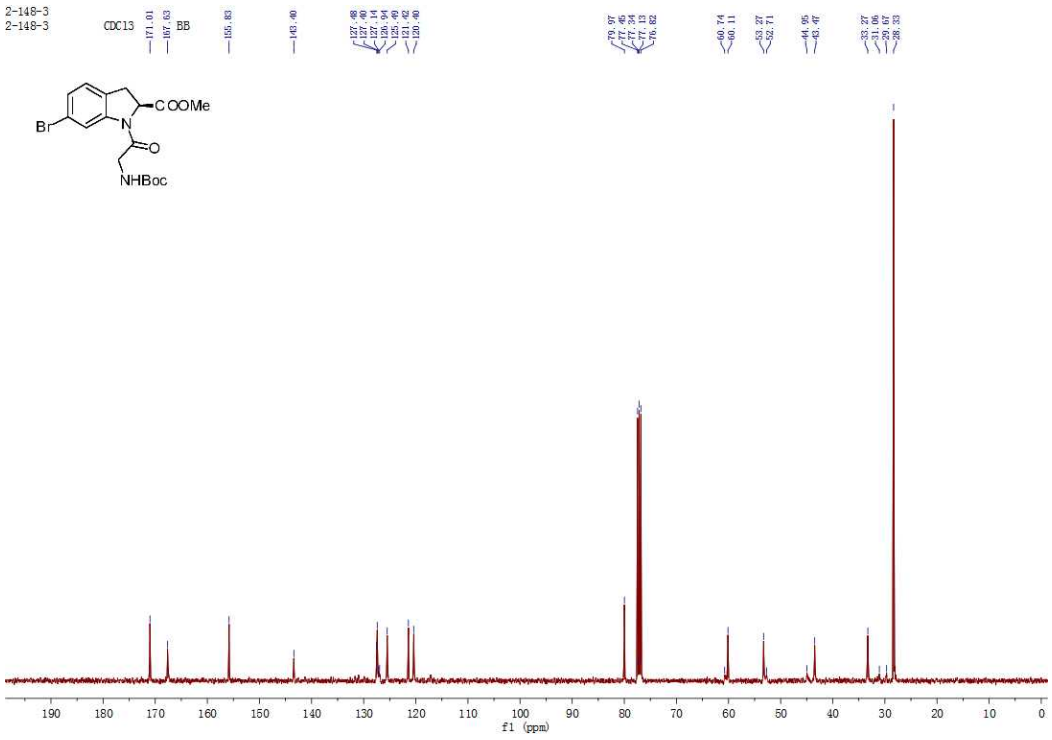
^{1}H and ^{13}C NMR spectra of **4f** (two amide rotamers, 1.4:1)



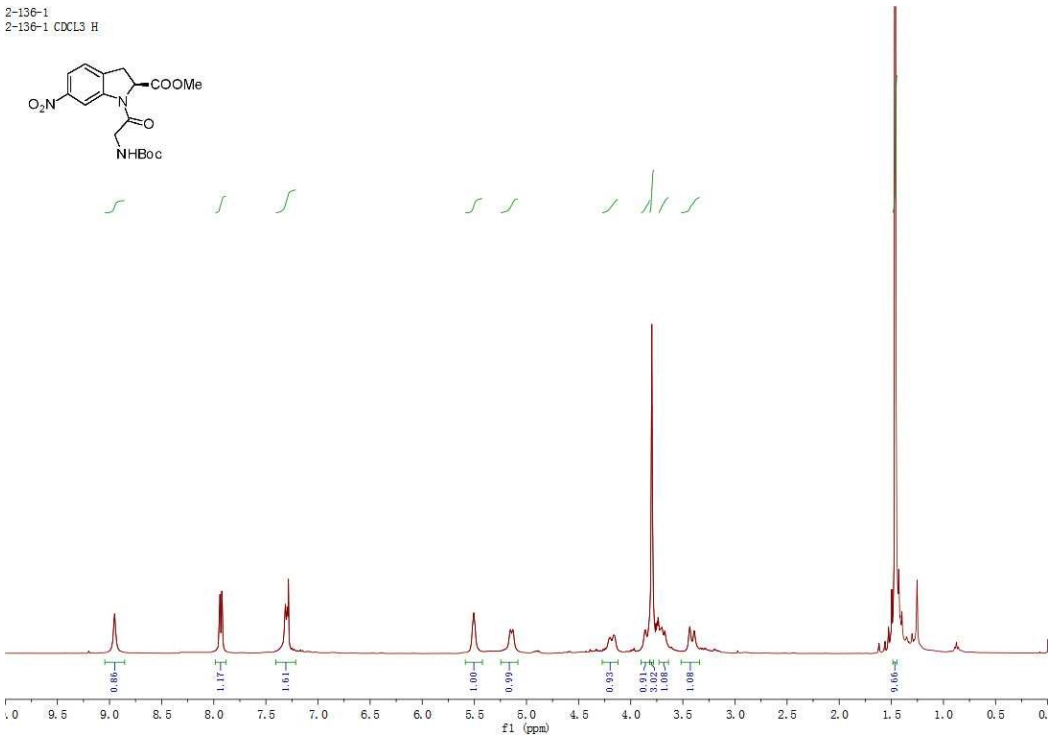


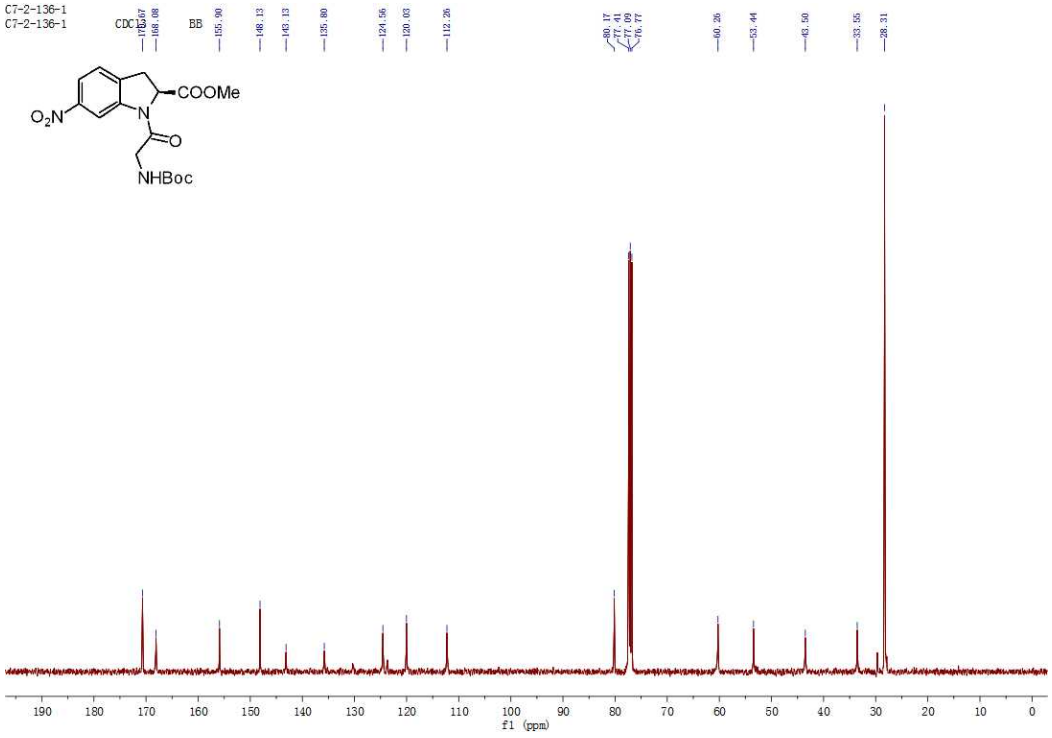
^{1}H and ^{13}C NMR spectra of **4g** (two amide rotamers, 3:1)



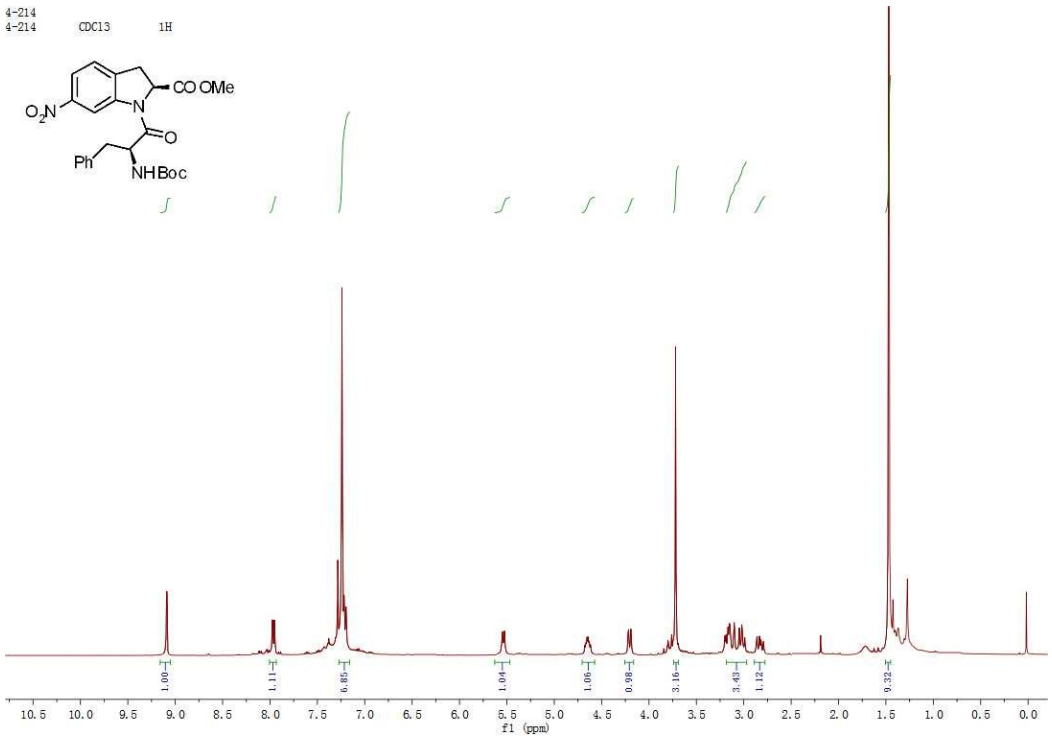


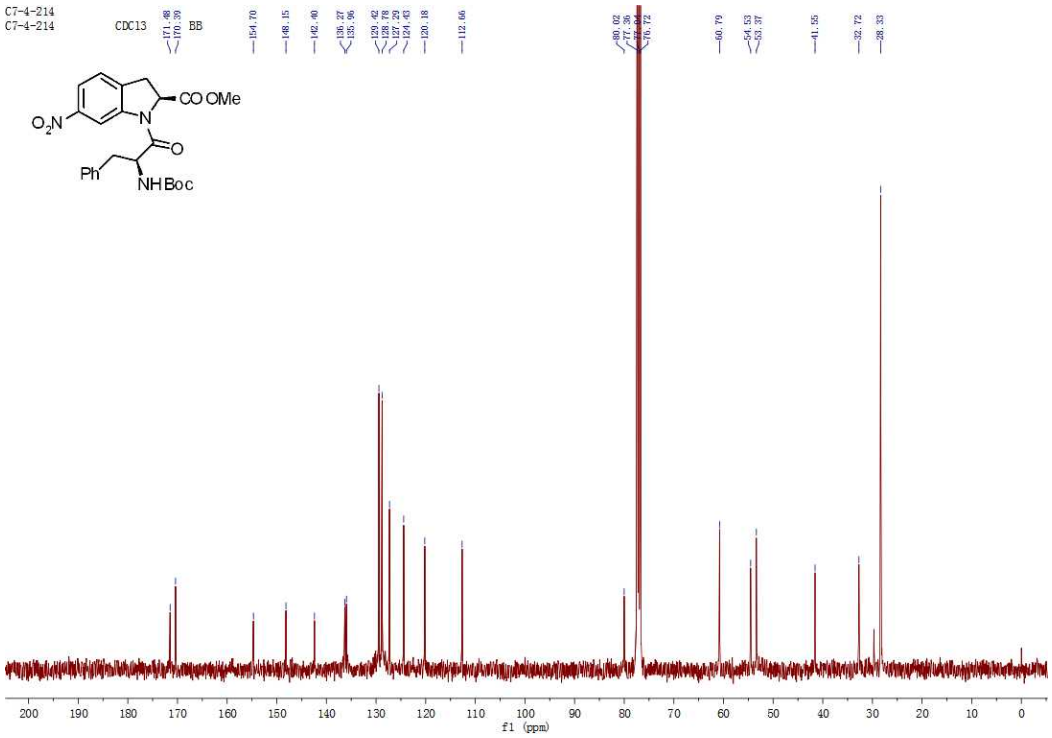
^{1}H and ^{13}C NMR spectra of **4h** (two amide rotamers, >20:1)



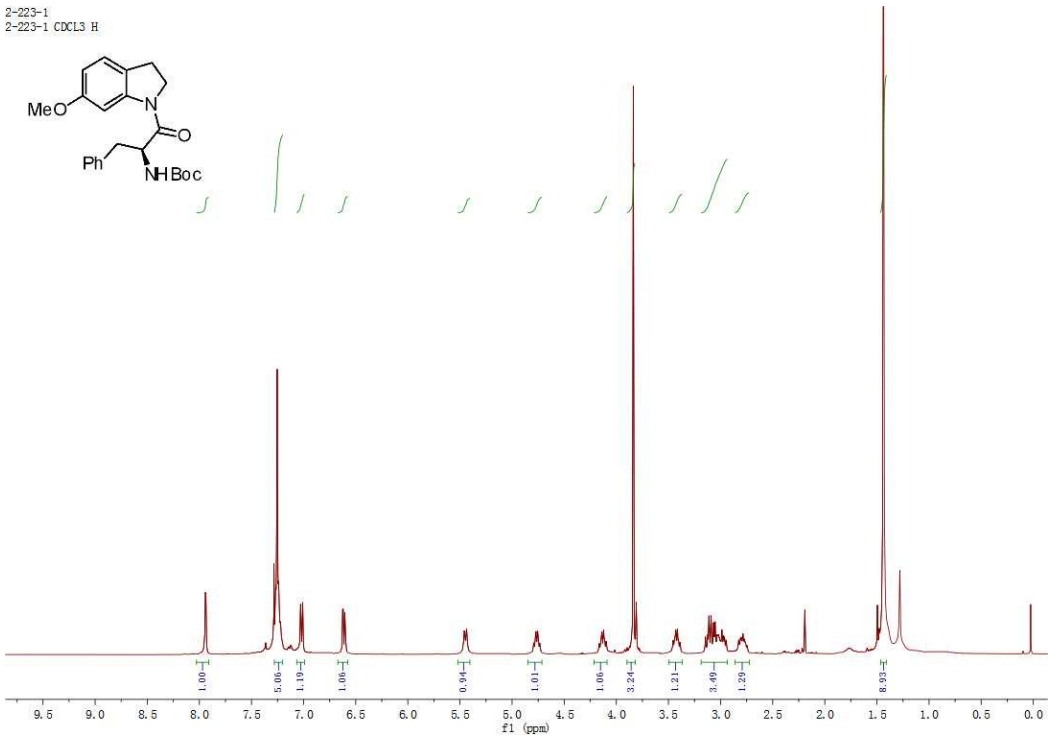


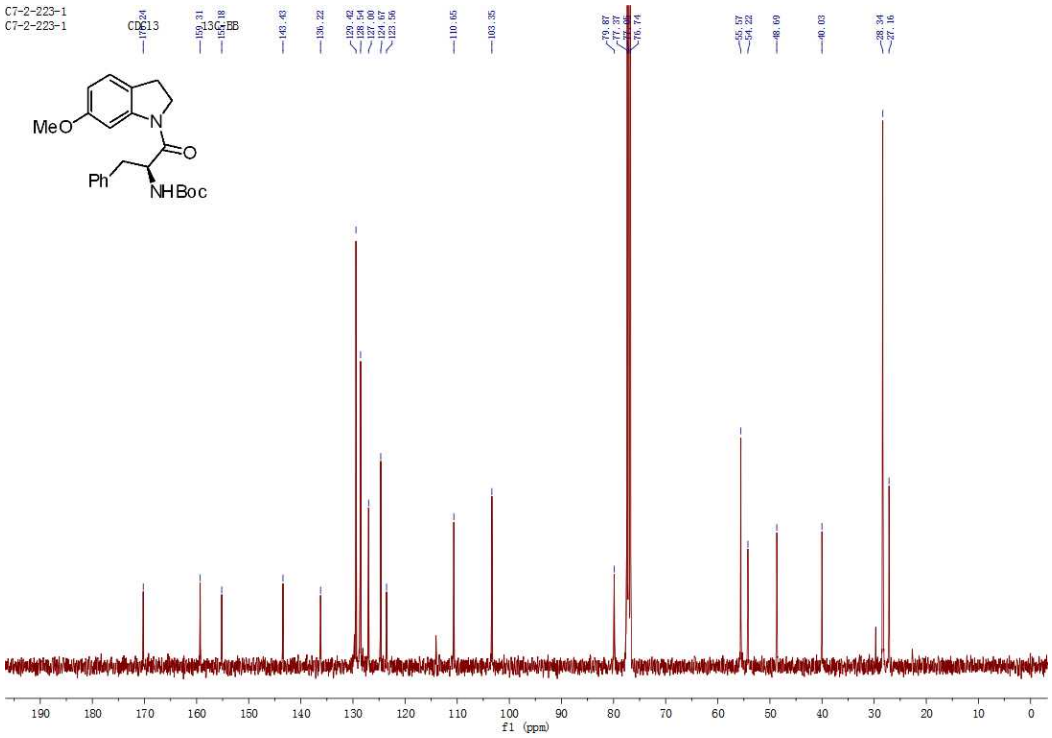
^{1}H and ^{13}C NMR spectra of **4i** (two amide rotamers, >20:1)



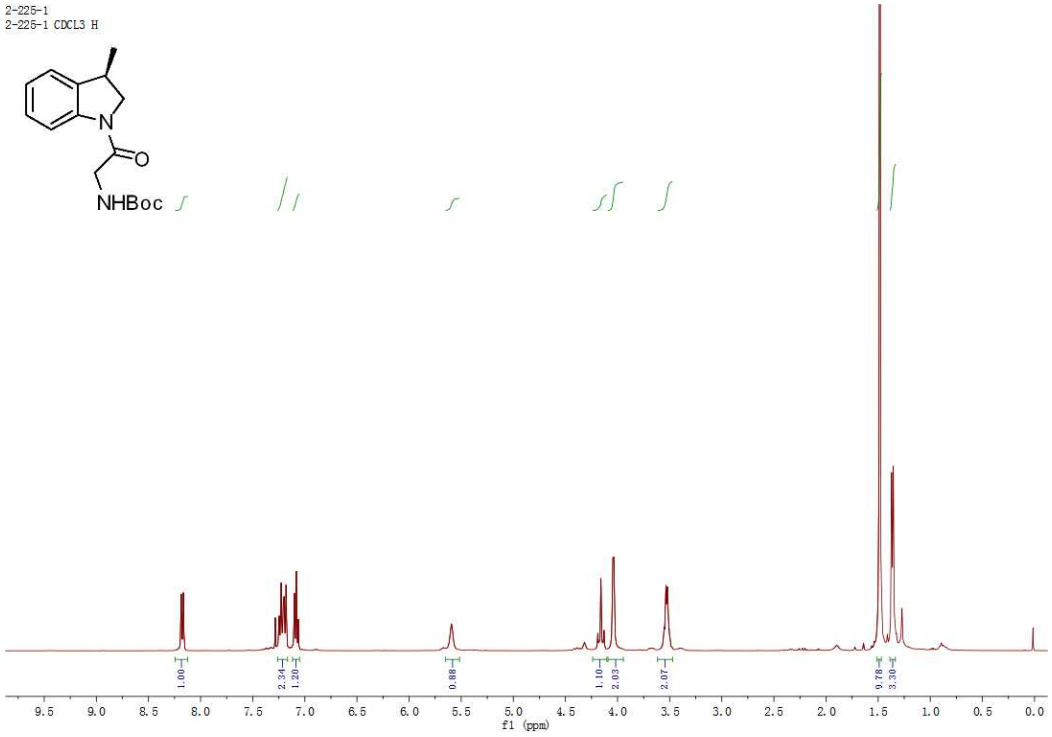


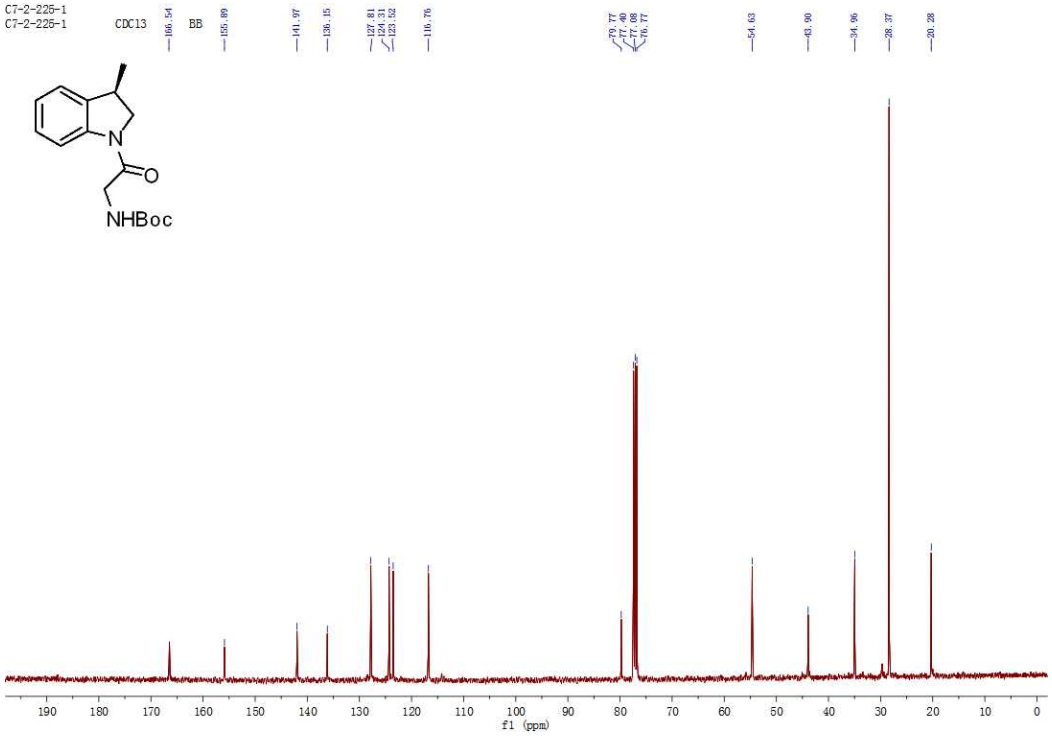
^{1}H and ^{13}C NMR spectra of **4j**



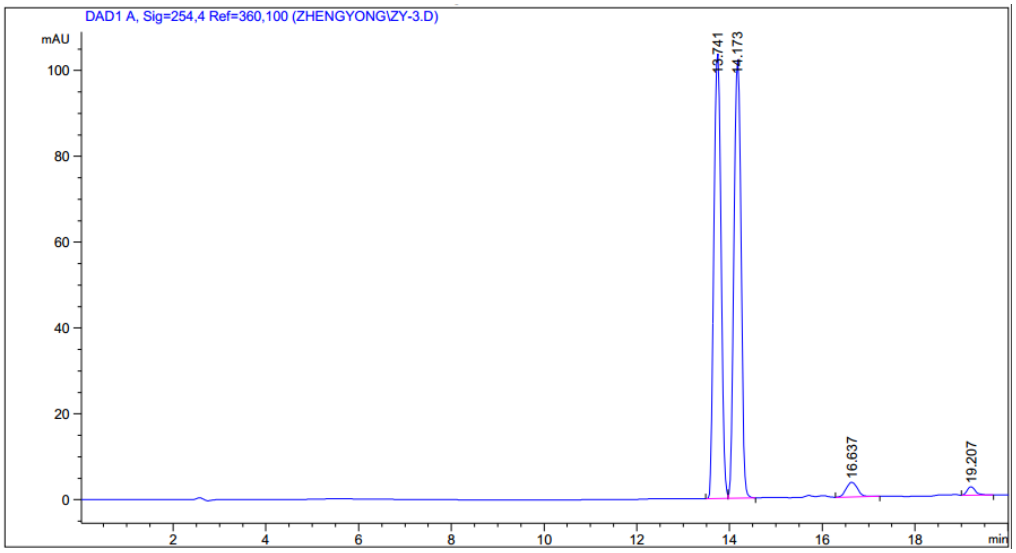


^{1}H and ^{13}C NMR spectra of **4k**



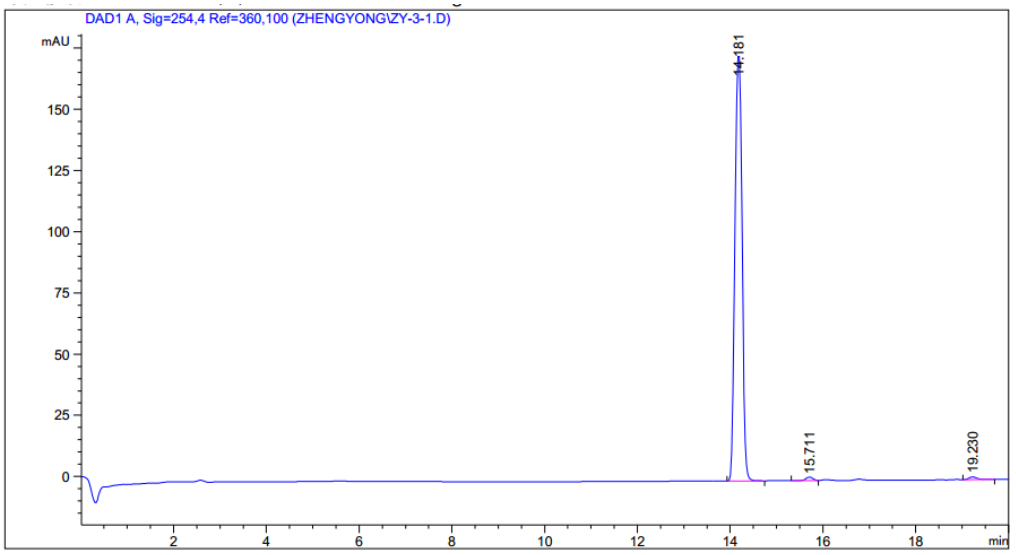


Chiral HPLC of racemic **2a**



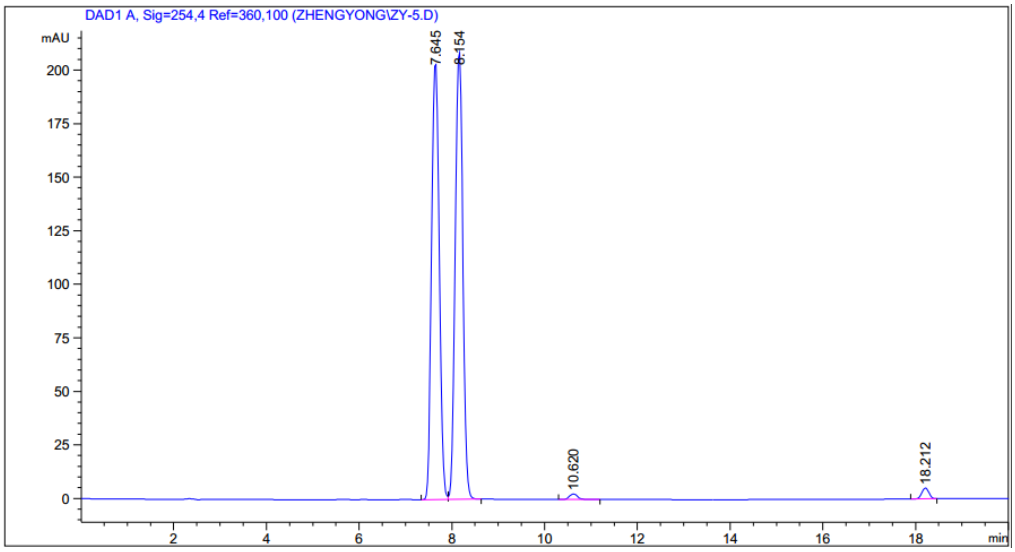
Time (min)	Area (%)
13. 74	48.57
14.17	47.78
16.64	2.57
19.21	1.08

Chiral HPLC of **2a**



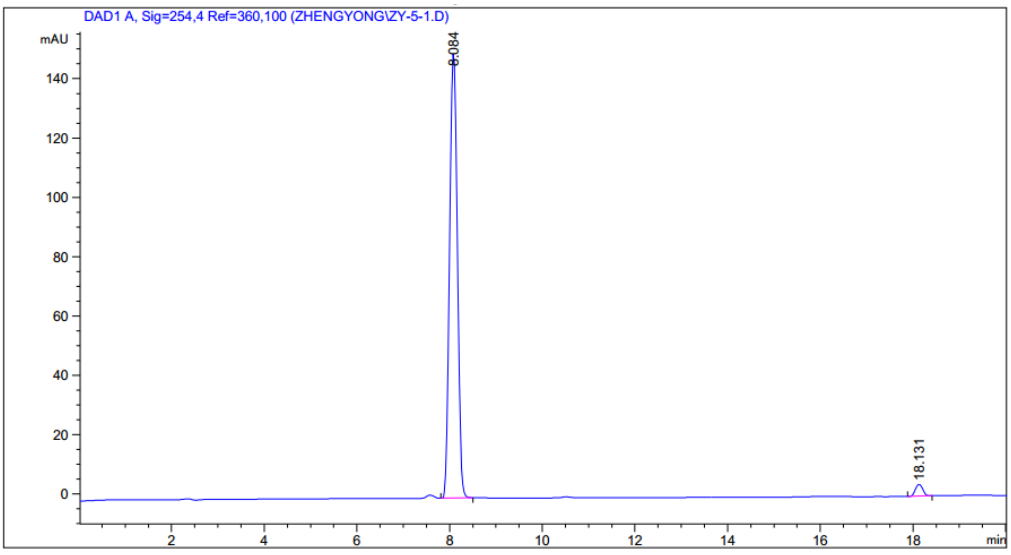
Time (min)	Area (%)
14.18	98.47
15.71	0.78
19.23	0.75

Chiral HPLC of racemic **2b**



Time (min)	Area (%)
7.65	48.37
8.15	49.80
10.62	0.69
18.21	1.14

Chiral HPLC of **2b**



Time (min)	Area (%)
8.08	97.49
18.13	2.51