Electronic Supplementary Information for

Stereodivergentand Enantioselective Total Syntheses of Isochaetominines A–C and EightDiastereomers: A Six-Step Approach

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General Procedure for the Step 2 (General Procedure 2)

To a stirring solution of **14** (5.09 mmol) in THF (20 mL) at −20 °C were added successively *N*-methylmorpholine (0.84 mL, 7.63 mmol) and ^{i}BuOCOC1 (0.74 mL, 5.60 mmol). After being stirred at −20 °C under N_2 for 15 min, the resulting suspension was added slowly to a solution of an amino acid benzyl ester *p*-toluenesulfonic acid salt (10.18 mmol) and *N*-methylmorpholine (1.68 mL, 15.28 mmol) in THF (36 mL) at −78 °C. The mixture was stirred for 12 h at −20 °C before quenching with a saturated aqueous solution of NH_4Cl (20 mL). The mixture was diluted with water (100 mL) and the phases separated. The aqueous phase was extracted with EtOAc (3 × 20 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent: EtOAc: PE = 3:2) to give the dipeptide derivative.

Benzyl (*S*)-2-((*R*)-3-(1*H*-indol-3-yl)-2-(2-nitrobenzamido)propanamido)propanoate (15a).

Following the general procedure 2, the coupling of (*R*)-**14** (1.80 g, 5.09 mmol) with L-alanine benzyl ester *p*-toluenesulfonic acid salt (3.57 g, 10.18 mmol) gave compound **15a** (2.38 g, yield: 91%) as a yellow solid. Mp 129–131 °C; $[\alpha]_D^{20}$ –36.9 (*c* 1.1, $CHCl_3$); IR (film) ν_{max}: 3415, 1738, 1646, 1529, 1455, 1349, 1198, 1140 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.00–7.96 (m, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.56–7.46 (m, 2H), 7.36–7.26 (m, 6H), 7.20–7.13 (m, 2H), 7.12–7.04 (m, 2H), 6.60 (d, *J* = 8.0 Hz, 1H), 6.56 (d, *J* = 8.0 Hz, 1H), 5.12 (d, *J* = 12.0 Hz, 1H), 5.07 (d, *J* = 12.0 Hz, 1H), 5.00 (dd, *J* = 14.8, 7.2 Hz, 1H), 4.52 (dq, *J* = 7.2, 7.3 Hz, 1H), 3.49 (dd, *J* = 14.8, 6.0 Hz, 1H), 3.30 (dd, *J* = 14.8, 7.2 Hz, 1H), 1.23 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 170.3, 166.3, 146.3, 136.1, 135.4, 133.7, 132.4, 130.6, 128.6 (2C), 128.5, 128.3, 128.1 (2C), 127.7, 124.6, 123.3, 122.3, 119.8, 118.6, 111.3, 110.3, 67.0, 54.3, 48.4, 27.2, 17.5; MS (ESI) *m/z* 537 ($M+Na^+$, 100%); HRMS (ESI, *m/z*) calcd for $C_{28}H_{26}N_4O_6Na$ $[M+Na]^+$: 537.1745, found: 537.1750.

Benzyl (*S*)-2-((*R*)-3-(1*H*-indol-3-yl)-2-(2-nitrobenzamido)propanamido)butanoate (15b).

Following the general procedure 2, the coupling of (*R*)-**14** (1.80 g, 5.09 mmol) with L-2-aminobutyricbenzyl ester *p*-toluenesulfonic acid salt (3.72 g, 10.18 mmol) gave compound **15b** (2.45 g, yield: 91%) as a yellow solid. Mp 142−144 °C (EtOAc); $[\alpha]_D^{20}$ –35.9 (*c* 0.5, $CHCl_3$); IR (film) ν_{max}: 3421, 1734, 1642, 1530, 1457, 1349, 1196, 1139 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 8.02–7.97 (m, 1H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.56–7.47 (m, 2H), 7.37–7.26 (m, 6H), 7.20–7.14 (m, 2H), 7.13–7.06 (m, 2H), 6.57 (d, *J* = 7.7 Hz, 1H), 6.52 (d, *J* = 7.7 Hz, 1H), 5.13 (d, *J* = 12.5 Hz, 1H), 5.07 (d, *J* = 12.5 Hz, 1H), 5.07–5.01 (m, 1H), 4.55–4.45 (m, 1H), 3.50 (dd, *J* = 14.8, 6.0 Hz, 1H), 3.32 (dd, *J* = 14.8, 7.2 Hz, 1H), 1.77–1.56 (m, 2H), 0.73 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 170.5, 166.3, 146.4, 136.2, 135.5, 133.7, 132.4, 130.6, 128.6, 128.6 (2C), 128.4, 128.2 (2C), 127.6, 124.6, 123.2, 122.4, 119.9, 118.6, 111.3, 110.3, 67.0, 54.3, 53.8, 27.3, 25.2, 9.5; MS (ESI) *m/z* 551 ($M+Na^+$, 100%); HRMS (ESI, *m/z*) calcd for $C_{29}H_{28}N_4O_6Na$ $[M+Na]^+$: 551.1901, found: 551.1908.

Benzyl (*S*)-2-((*R*)-3-(1*H*-indol-3-yl)-2-(2-nitrobenzamido)propanamido)-3-methyl –butanoate (15c).

Following the general procedure 2, the coupling of (*R*)-**14** (1.80 g, 5.09 mmol) with benzyl L-valinate *p*-toluenesulfonic acid salt (3.86 g, 10.18 mmol) gave compound **15c** (2.57 g, yield: 93%) as a yellow solid. Mp 148–150 °C (EtOAc); $[\alpha]_D^{20}$ –25.6 (*c* 1.0, $CHCl_3$); IR (film) ν_{max}: 3420, 1733, 1643, 1530, 1459,1349, 1195, 1143 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.97–7.91 (m, 1H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.50–7.42 (m, 2H), 7.34–7.24 (m, 6H), 7.18–7.10 (m, 2H), 7.10–7.02 (m, 2H), 6.69 (d, *J* = 8.4 Hz, 1H), 6.66 (d, *J* = 8.4 Hz, 1H), 5.14–5.02 (m, 3H), 4.44 (dd, *J* = 8.4, 5.3 Hz, 1H), 3.44 (dd, *J* = 14.9, 6.4 Hz, 1H), 3.26 (dd, *J* = 14.9, 6.4 Hz, 1H), 2.07–1.95 (m, 1H), 0.74 (d, *J* = 6.8 Hz, 3H), 0.71 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 170.8, 166.5, 146.2, 136.2, 135.3, 133.7, 132.2, 130.5, 128.6, 128.5 (2C), 128.3, 128.3 (2C), 127.5, 124.4, 123.2, 122.2, 119.7, 118.6, 111.3, 110.2, 66.9, 57.8, 54.2, 30.8, 27.5, 18.6, 17.7; MS (ESI) *m/z* 565 ($M+Na^+$, 100%); HRMS (ESI, *m/z*) calcd for $C_{30}H_{30}N_4O_6Na$ $[M+Na]^+$: 565.2058, found: 565.2063.

Benzyl (*S*)-2-((*S*)-3-(1*H*-indol-3-yl)-2-(2-nitrobenzamido)propanamido)-3-methyl

–butanoate (18).

Following the general procedure 2, the coupling of compound (*S*)-**14** (1.80 g, 5.09 mmol) with benzyl L-valinate *p*-toluenesulfonic acid salt (3.86 g, 10.18 mmol) gave compound **18** (2.51 g, yield: 91%) as a yellow solid. Mp 83–85 °C (EtOAc); $[\alpha]_D^{20}$ +11.4 (*c* 1.0, $CHCl_3$); IR (film) ν_{max}: 3420, 1736, 1652, 1527, 1351, 1191, 1140, 1079 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.97 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.56–7.45 (m, 2H), 7.39–7.26 (m, 7H), 7.15 (ddd, *J* = 7.2, 7.2, 1.0 Hz, 1H), 7.10–7.02 (m, 2H), 6.93 (d, *J* = 7.7 Hz, 1H), 6.40 (d, *J* = 7.7 Hz, 1H), 5.08 (d, *J* = 12.2 Hz, 1H), 5.04 (d, *J* = 12.2 Hz, 1H), 4.98 (m, 1H), 4.40 (dd, *J* = 8.3, 5.3 Hz, 1H), 3.46 (dd, *J* = 14.9, 5.8 Hz, 1H), 3.23 (dd, *J* = 14.9, 8.1 Hz, 1H), 2.10–2.00 (m, 1H), 0.80 (d, *J* = 6.9 Hz, 3H), 0.74 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.9, 166.2, 146.2, 136.2, 135.4, 133.6, 132.3, 130.5, 128.7, 128.6 (2C), 128.4, 128.3 (2C), 127.4, 124.4, 123.5, 122.1, 119.7, 118.8, 111.2, 110.2, 66.9, 57.7, 54.4, 31.0, 28.0, 18.7, 17.7; MS (ESI) *m/z* 565 ($M+Na^+$, 100%); HRMS (ESI, *m/z*) calcd for $C_{30}H_{30}N_4O_6Na$ $[M+Na]^+$: 565.2058, found: 565.2059.

Benzyl (*R*)-2-((*S*)-3-(1*H*-indol-3-yl)-2-(2-nitrobenzamido)propanamido)-3-methyl –butanoate (21).

Following the general procedure 2, the coupling of compound (*S*)-**14** (1.80 g, 5.09 mmol) with D-valinate *p*-toluenesulfonic acid salt (3.86 g, 10.18 mmol) gave compound **21** (2.57 g, yield: 93%) as a yellow solid. Mp 148–150 °C (EtOAc); $[\alpha]_D^{20}$ +25.6 (*c* 1.0, $CHCl_3$); IR (film) ν_{max}: 3414, 1736, 1640, 1534, 1454, 1354, 1194, 1143 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.97–7.91 (m, 1H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.50–7.42 (m, 2H), 7.34–7.24 (m, 6H), 7.18–7.10 (m, 2H), 7.10–7.02 (m, 2H), 6.69 (d, *J* = 8.4Hz, 1H), 6.66 (d, *J* = 8.4 Hz, 1H), 5.14–5.02 (m, 3H), 4.44 (dd, *J* = 8.4, 5.3 Hz, 1H), 3.44 (dd, *J* = 14.9, 6.4 Hz, 1H), 3.26 (dd, *J* = 14.9, 6.4 Hz, 1H), 2.07–1.95 (m, 1H), 0.74 (d, *J* = 6.8 Hz, 3H), 0.71 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 170.8, 166.5, 146.2, 136.2, 135.3, 133.7, 132.2, 130.5, 128.6, 128.5 (2C), 128.3, 128.3 (2C), 127.5, 124.4, 123.2, 122.2, 119.7, 118.6, 111.3, 110.2, 66.9, 57.8, 54.2, 30.8, 27.5, 18.6, 17.7; MS (ESI) *m/z* 565 ($M+Na^+$, 100%); HRMS (ESI, *m/z*) calcd for $C_{30}H_{30}N_4O_6Na$ $[M+Na]^+$: 565.2058, found: 565.2056.

Benzyl (*R*)-2-((*R*)-3-(1*H*-indol-3-yl)-2-(2-nitrobenzamido)propanamido)-3-methyl –butanoate (24).

Following the general procedure for the step 2, the coupling of compound (*R*)-**14** (1.80 g, 5.09 mmol) with D-valinate *p*-toluenesulfonic acid salt (3.86 g, 10.18 mmol) gave compound **24** (2.51 g, yield: 91%) as a yellow solid. Mp 83–85 °C (EtOAc); $[\alpha]_D^{20}$ –11.4 (*c* 1.0, $CHCl_3$); IR (film) ν_{max}: 3420, 1736, 1652, 1527, 1351, 1191, 1140, 1079 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.97 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.56–7.45 (m, 2H), 7.39–7.26 (m, 7H), 7.15 (ddd, *J* = 7.2, 7.2, 1.0 Hz, 1H), 7.10–7.02 (m, 2H), 6.93 (d, *J* = 7.7 Hz, 1H), 6.40 (d, *J* = 7.7 Hz, 1H), 5.08 (d, *J* = 12.2 Hz, 1H), 5.04 (d, *J* = 12.2 Hz, 1H), 4.98 (m, 1H), 4.40 (dd, *J* = 8.3, 5.3 Hz, 1H), 3.46 (dd, *J* = 14.9, 5.8 Hz, 1H), 3.23 (dd, *J* = 14.9, 8.1 Hz, 1H), 2.10–2.00 (m, 1H), 0.80 (d, *J* = 6.9 Hz, 3H), 0.74 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.9, 166.2, 146.2, 136.2, 135.4, 133.6, 132.3, 130.5, 128.7, 128.6 (2C), 128.4, 128.3 (2C), 127.4, 124.4, 123.5, 122.1, 119.7, 118.8, 111.2, 110.2, 66.9, 57.7, 54.4, 31.0, 28.0, 18.7, 17.7; MS (ESI) *m/z* 565 ($M+Na^+$, 100%); HRMS (ESI, *m/z*) calcd for $C_{30}H_{30}N_4O_6Na$ $[M+Na]^+$: 565.2058, found: 565.2062.

General Procedure for the Step 3 (General Procedure 3)

To a mixture of zinc powder (776 mg, 11.94 mmol) and THF (50 mL) was added $TiCl_4$ (0.66 mL, 5.98 mmol). The resulting mixture were stirred for 1 h at 50 °C. After cooling to 0 °C, a THF (10 mL) solution of a tryptophan-derived dipeptide (1.50 mmol) and trimethylorthoformate (0.66 mL, 5.98 mmol) were added. The resulting mixture was stirred for 24 h at 0 °C. To the reaction mixture was added brine (10 mL) and the resulting mixture was stirred for 2 h. After separating the phases, the aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent: EtOAc: PE = 1:3 to DCM: MeOH = 40:1) to give the corresponding quinazolino-dipeptide derivative.

Benzyl (*S*)-2-((*R*)-3-(1*H*-indol-3-yl)-2-(4-oxoquinazolin-3(4*H*)-yl)propanamido)-propanoate (12a).

Following the general procedure 3, the reaction of compound **15a** (771 mg, 1.50

mmol) gave compound **12a** (704 mg, yield: 95%) as a white solid. Mp 161−163 °C (EtOAc); $[\alpha]_D^{20}$ +58.6 (*c* 1.0, $CHCl_3$); IR (film) ν_{max}: 3318, 2928, 1741, 1662, 1607, 1455, 1327, 1196, 1153 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.22–8.16 (m, 2H), 7.74–7.60 (m, 3H), 7.42 (ddd, *J* = 8.1, 6.8, 1.4 Hz, 1H), 7.31–7.24 (m, 4H), 7.22–7.18 (m, 2H), 7.15 (ddd, *J* = 8.0, 7.2, 1.1 Hz, 1H), 7.07 (ddd, *J* = 8.0, 7.9, 1.1 Hz, 1H), 6.99 (d, *J* = 2.4 Hz, 1H), 6.93 (d, *J* = 7.2 Hz, 1H), 5.83 (dd, *J* = 8.5, 7.2 Hz, 1H), 5.05 (d, *J* = 12.3 Hz, 1H), 5.01 (d, *J* = 12.3 Hz, 1H), 4.51 (dq, *J* = 7.3, 7.2 Hz, 1H), 3.72 (dd, *J* = 14.5, 8.7 Hz, 1H), 3.41 (dd, *J* = 14.5, 7.1 Hz, 1H), 1.20 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 168.4, 161.1, 147.5, 144.2, 136.2, 135.2, 134.4, 128.5 (2C), 128.3, 128.0 (2C), 127.5, 127.2, 126.9, 126.9, 123.2, 122.4, 121.4, 119.9, 118.4, 111.3, 109.7, 67.1, 56.5, 48.5, 27.2, 17.6; MS (ESI) *m/z* 517 ($M+Na^+$, 100%), HRMS (ESI, *m/z*) calcd for $C_{29}H_{26}N_4O_4Na$ $[M+Na]^+$: 517.1846, found: 517.1850.

Benzyl (*S*)-2-((*R*)-3-(1*H*-indol-3-yl)-2-(4-oxoquinazolin-3(4*H*)-yl)propanamido)-butaneate (12b).

Following the general procedure 3, the reaction of compound **15b** (792 mg, 1.50 mmol) gave compound **12b** (724 mg, yield: 95%) as a white solid. Mp 185–187 °C (EtOAc); $[\alpha]_D^{20}$ +47.6 (*c* 1.0, $CHCl_3$); IR (film) ν_{max}: 3422, 2968, 1738, 1659, 1610, 1477, 1328, 1195, 1140 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.24 (br. s, 1H), 8.20 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.72–7.61 (m, 3H), 7.41 (ddd, *J* = 8.1, 6.8, 1.4 Hz, 1H), 7.30–7.26 (m, 4H), 7.21–7.17 (m, 2H), 7.14 (ddd, *J* = 7.9, 6.8, 0.9 Hz, 1H), 7.06 (ddd, *J* = 7.9, 7.8, 0.8 Hz, 1H), 6.99 (d, *J* = 2.2 Hz, 1H), 6.91 (d, *J* = 8.1 Hz, 1H), 5.88 (dd, *J* = 8.5, 7.2 Hz, 1H), 5.04 (d, *J* = 12.2 Hz, 1H), 4.99 (d, *J* = 12.2 Hz, 1H), 4.51–4.44 (m, 1H), 3.73 (dd, *J* = 14.5, 8.7 Hz, 1H), 3.41 (dd, *J* = 14.5, 7.1 Hz, 1H), 1.76–1.63 (m, 1H), 1.61–1.49 (m, 1H), 0.61 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 168.7, 161.2, 147.5, 144.3, 136.2, 135.2, 134.4, 128.5 (2C), 128.3, 128.1 (2C), 127.5, 127.2, 126.9, 126.9, 123.2, 122.4, 121.5, 119.8, 118.4, 111.3, 109.6, 67.0, 56.6, 53.8, 27.3, 25.0, 9.2; MS (ESI) *m/z* 531 ($M+Na^+$, 100%); HRMS (ESI, *m/z*) calcd for $C_{30}H_{28}N_4O_4Na$ $[M+Na]^+$: 531.2003, found: 531.2000.

Benzyl (*S*)-2-((*R*)-3-(1*H*-indol-3-yl)-2-(4-oxoquinazolin-3(4*H*)-yl)propanamido)-3

-methylbutanoate (12c).

Following the general procedure 3, the reaction of compound **15c** (813 mg, 1.50 mmol) gave compound **12c** (744 mg, yield: 95%) as a white solid. Mp 165–167 °C (EtOAc); $[\alpha]_D^{20}$ +55.6 (*c* 1.0, $CHCl_3$); IR (film) ν_{max}: 3417, 2965, 1738, 1659, 1610, 1477, 1328, 1195, 1143 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.30 (s, 1H), 8.22 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.72–7.62 (m, 3H), 7.41 (ddd, *J* = 8.1, 6.8, 1.5 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 1H), 7.26–7.17 (m, 5H),7.14 (ddd, *J* = 7.9, 6.8, 0.9 Hz, 1H), 7.07 (ddd, *J* = 7.9, 7.9, 0.9 Hz, 1H), 7.00 (d, *J* = 2.3 Hz, 1H), 6.94 (d, *J* = 8.1 Hz, 1H), 5.94 (dd, *J* = 7.6, 7.6 Hz, 1H), 5.03 (d, *J* = 12.2 Hz, 1H), 4.98 (d, *J* = 12.2 Hz, 1H), 4.46 (dd, *J* = 8.5, 5.0 Hz, 1H), 3.74 (dd, *J* = 14.5, 8.7 Hz, 1H), 3.44 (dd, *J* = 14.5, 7.1 Hz, 1H), 2.04–1.96 (m, 1H), 0.68 (d, *J* = 6.8 Hz, 3H), 0.64 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 168.8, 161.2, 147.5, 144.3, 136.2, 135.1, 134.4, 128.4 (2C), 128.3, 128.2 (2C), 127.4, 127.1, 126.9, 126.8, 123.2, 122.3, 121.4, 119.8, 118.4, 111.3, 109.4, 66.9, 57.7, 56.6, 30.8, 27.4, 18.6, 17.5; MS (ESI) *m/z* 545 ($M+Na^+$, 100%); HRMS (ESI, *m/z*) calcd for $C_{31}H_{30}N_4O_4Na$ $[M+Na]^+$: 545.2159, found: 545.2161.

Benzyl (*S*)-2-((*S*)-3-(1*H*-indol-3-yl)-2-(4-oxoquinazolin-3(4*H*)-yl)propanamido)-3 -methylbutanoate (19).

Following the general procedure 3, the reaction of compound **18** (813 mg, 1.50 mmol) gave compound **19** (752 mg, yield: 96%) as a white solid. Mp 81–83 °C (EtOAc); $[\alpha]_D^{20}$ –31.5 (*c* 1.0, $CHCl_3$); IR (film) ν_{max}: 3440, 2965, 1729, 1656, 1607, 1556, 1457, 1194, 1137 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.44 (s, 1H), 8.21 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.12 (s, 1H), 7.75–7.66 (m, 2H), 7.50 (d, *J* = 8.1 Hz, 1H), 7.43 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.38–7.30 (m, 5H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.13 (d, *J* = 8.6 Hz, 1H), 6.93 (ddd, *J* = 8.1, 6.8, 0.9 Hz, 1H), 6.90 (d, *J* = 2.3 Hz, 1H), 5.96 (dd, *J* = 7.9, 7.9 Hz, 1H), 5.13 (d, *J* = 12.2 Hz, 1H), 5.07 (d, *J* = 12.2 Hz, 1H), 4.52 (dd, *J* = 8.6, 5.1 Hz, 1H), 3.67 (dd, *J* = 14.9, 8.0 Hz, 1H), 3.40 (dd, *J* = 14.9, 7.9 Hz, 1H), 2.12–2.04 (m, 1H), 0.75 (d, *J* = 6.9 Hz, 3H), 0.71 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 169.3, 161.3, 147.4, 144.5, 136.1, 135.3, 134.5, 128.6 (2C), 128.4, 128.3 (2C), 127.4, 127.2, 127.0, 126.7, 123.2, 122.2, 121.3, 119.6, 118.2, 111.3, 109.3, 67.0,

57.6, 56.5, 31.0, 27.2, 18.8, 17.6; MS (ESI) *m/z* 545 ($M+Na^+$, 100%); HRMS (ESI, *m/z*) calcd for $C_{31}H_{30}N_4O_4Na$ $[M+Na]^+$: 545.2159, found: 545.2151.

Benzyl (*R*)-2-((*S*)-3-(1*H*-indol-3-yl)-2-(4-oxoquinazolin-3(4*H*)-yl)propanamido)-3-methylbutanoate (22).

Following the general procedure 3, the reaction of compound **21** (813 mg, 1.50 mmol) gave compound **22** (744 mg, yield: 95%) as a white solid. Mp 165–167 °C (EtOAc); $[\alpha]_D^{20}$ –55.6 (*c* 1.0, $CHCl_3$); IR (film) ν_{max}: 3417, 2965, 1738, 1659, 1610, 1477, 1328, 1195, 1143 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.30 (s, 1H), 8.22 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.72–7.62 (m, 3H), 7.41 (ddd, *J* = 8.1, 6.8, 1.5 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 1H), 7.26–7.17 (m, 5H), 7.14 (ddd, *J* = 7.9, 6.8, 0.9 Hz, 1H), 7.07 (ddd, *J* = 7.9, 7.9, 0.9 Hz, 1H), 7.00 (d, *J* = 2.3 Hz, 1H), 6.94 (d, *J* = 8.1 Hz, 1H), 5.94 (dd, *J* = 7.6, 7.6 Hz, 1H), 5.03 (d, *J* = 12.2 Hz, 1H), 4.98 (d, *J* = 12.2 Hz, 1H), 4.46 (dd, *J* = 8.5, 5.0 Hz, 1H), 3.74 (dd, *J* = 14.5, 8.7 Hz, 1H), 3.44 (dd, *J* = 14.5, 7.1 Hz, 1H), 2.04–1.96 (m, 1H), 0.68 (d, *J* = 6.8 Hz, 3H), 0.64 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 168.8, 161.2, 147.5, 144.3, 136.2, 135.1, 134.4, 128.4 (2C), 128.3, 128.2 (2C), 127.4, 127.1, 126.9, 126.8, 123.2, 122.3, 121.4, 119.8, 118.4, 111.3, 109.4, 66.9, 57.7, 56.6, 30.8, 27.4, 18.6, 17.5; MS (ESI) *m/z* 545 ($M+Na^+$, 100%); HRMS (ESI, *m/z*) calcd for $C_{31}H_{30}N_4O_4Na$ $[M+Na]^+$: 545.2159, found: 545.2161.

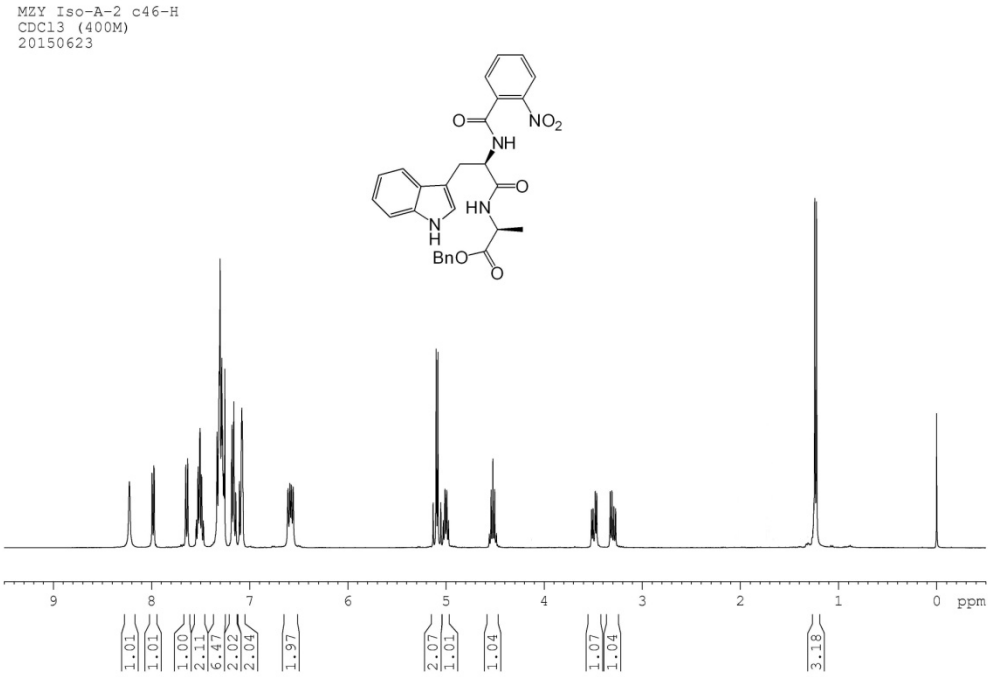
Benzyl (*R*)-2-((*R*)-3-(1*H*-indol-3-yl)-2-(4-oxoquinazolin-3(4*H*)-yl)propanamido)-3-methylbutanoate (25).

Following the general procedure 3, the reaction of compound **24** (813 mg, 1.50 mmol) gave compound **25** (752 mg, yield: 96%) as a white solid. Mp 81–83 °C (EtOAc); $[\alpha]_D^{20}$ +31.5 (*c* 1.0, $CHCl_3$); IR (film) ν_{max}: 3440, 2965, 1729, 1656, 1607, 1556, 1457, 1194, 1137 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.44 (s, 1H), 8.21 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.12 (s, 1H), 7.75–7.66 (m, 2H), 7.50 (d, *J* = 8.1 Hz, 1H), 7.43 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.38–7.30 (m, 5H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.13 (d, *J* = 8.6 Hz, 1H), 6.93 (ddd, *J* = 8.1, 6.8, 0.9 Hz, 1H), 6.90 (d, *J* = 2.3 Hz, 1H), 5.96 (dd, *J* = 7.9, 7.9 Hz, 1H), 5.13 (d, *J* = 12.2 Hz, 1H), 5.07 (d, *J* = 12.2 Hz, 1H), 4.52 (dd, *J* = 8.6, 5.1 Hz, 1H), 3.67 (dd, *J* = 14.9, 8.0 Hz, 1H), 3.40 (dd, *J* = 14.9, 7.9 Hz, 1H), 2.12–2.04 (m, 1H), 0.75 (d, *J* = 6.9 Hz, 3H), 0.71 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$)

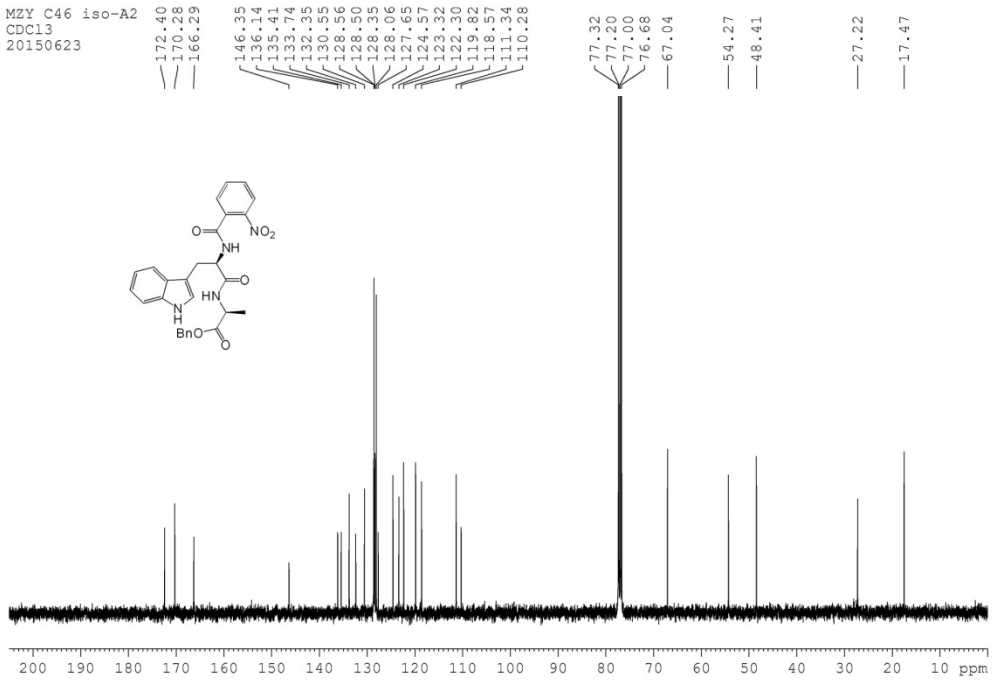
δ 171.1, 169.3, 161.3, 147.4, 144.5, 136.1, 135.3, 134.5, 128.6 (2C), 128.4, 128.3 (2C), 127.4, 127.2, 127.0, 126.7, 123.2, 122.2, 121.3, 119.6, 118.2, 111.3, 109.3, 67.0, 57.6, 56.5, 31.0, 27.2, 18.8, 17.6; MS (ESI) *m/z* 545 ($M+Na^+$, 100%); HRMS (ESI, *m/z*) calcd for $C_{31}H_{30}N_4O_4Na$ $[M+Na]^+$: 545.2159, found: 545.2156.

^{1}H NMR and ^{13}C NMR spectra of new products

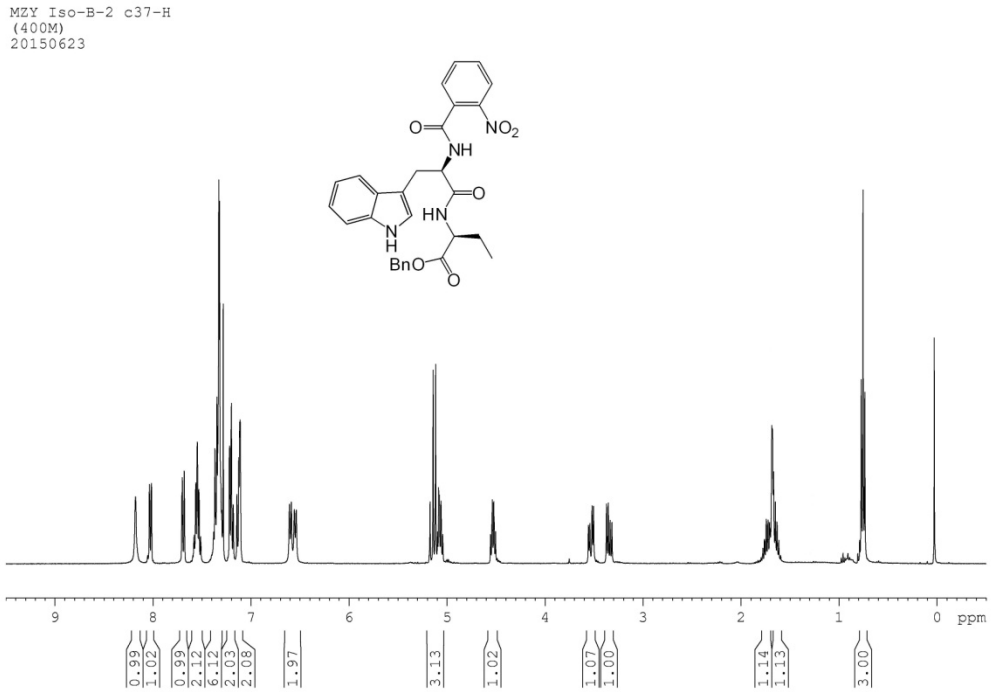
^{1}H NMR spectrum of **15a** ($CDCl_3$)



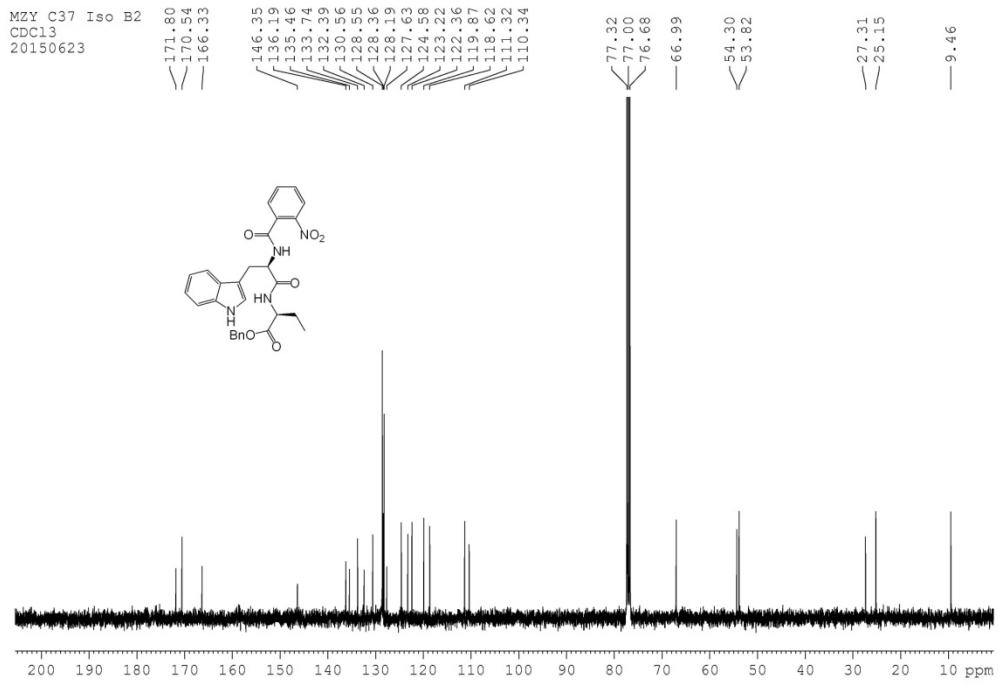
^{13}C NMR spectrum of **15a** ($CDCl_3$)



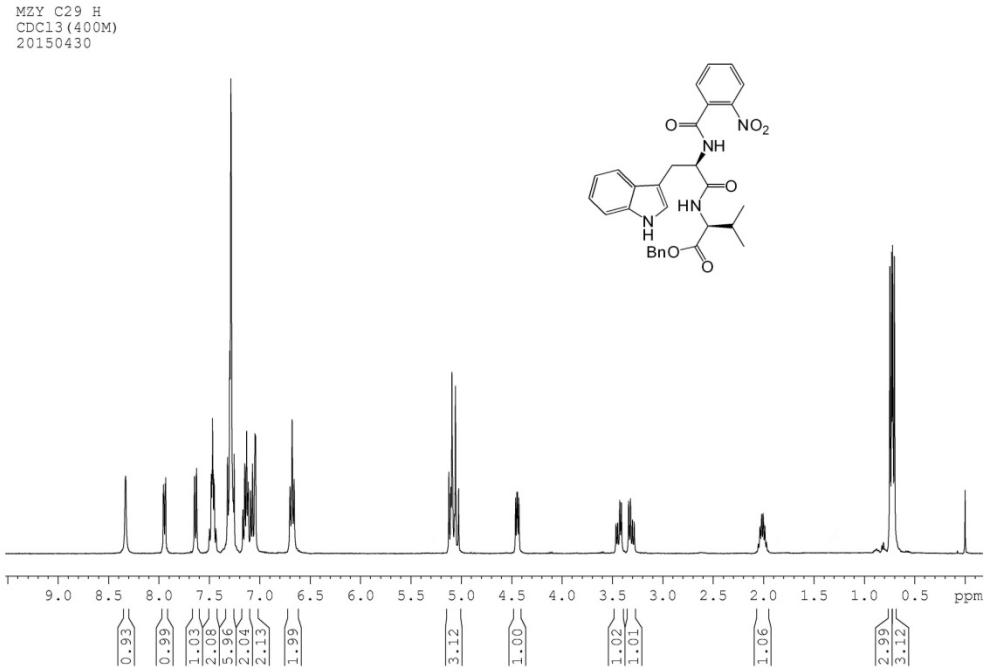
^{1}H NMR spectrum of **15b** ($CDCl_3$)



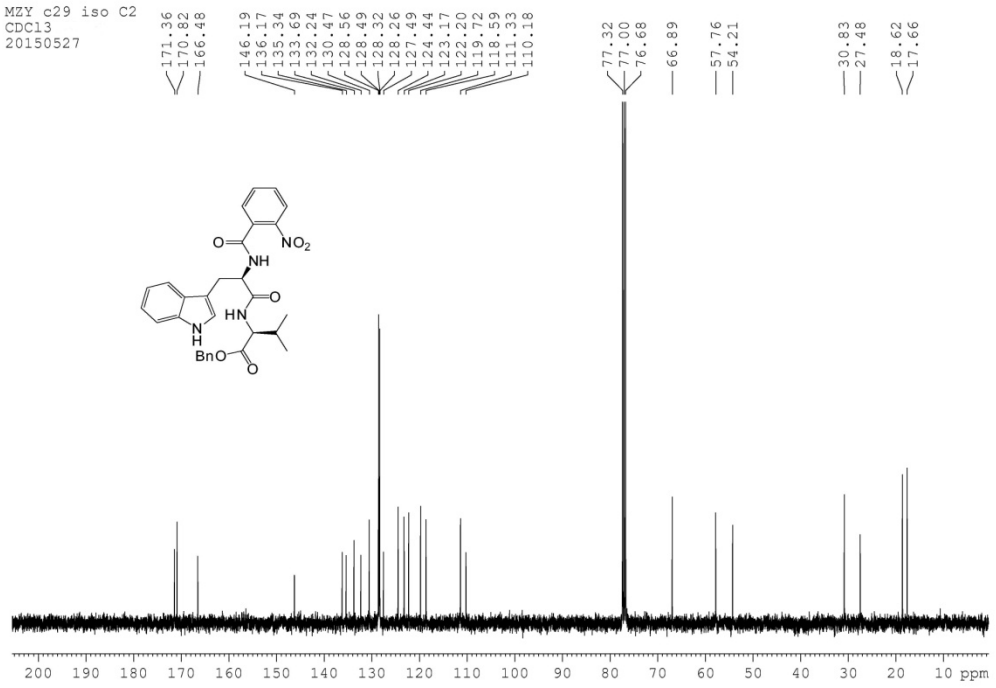
^{13}C NMR spectrum of **15b** ($CDCl_3$)



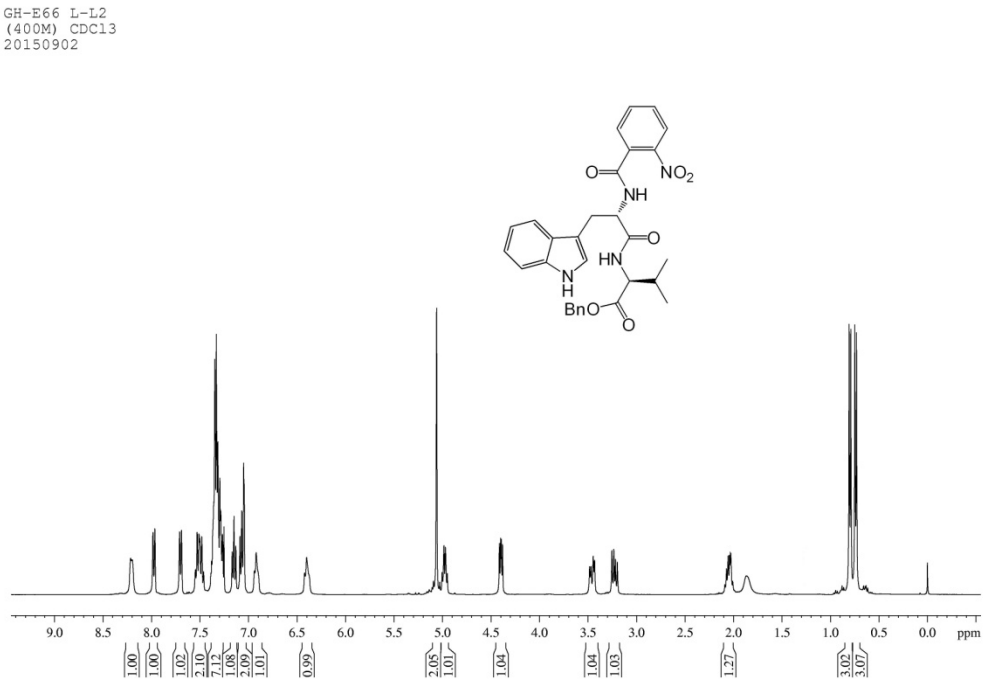
^{1}H NMR spectrum of **15c** ($CDCl_3$)



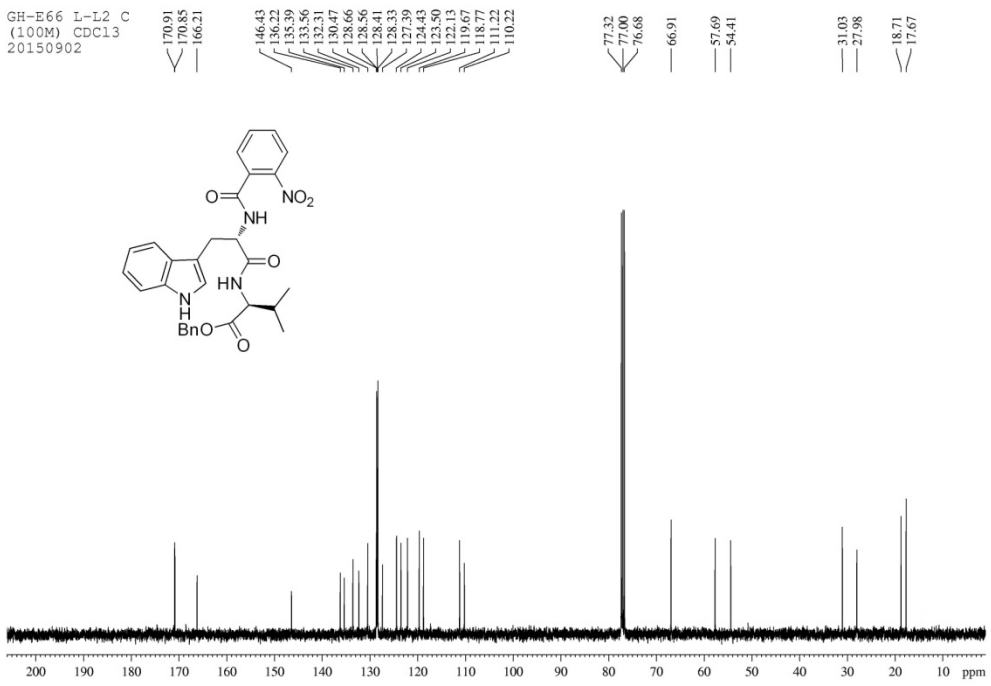
^{13}C NMR spectrum of **15c** ($CDCl_3$)



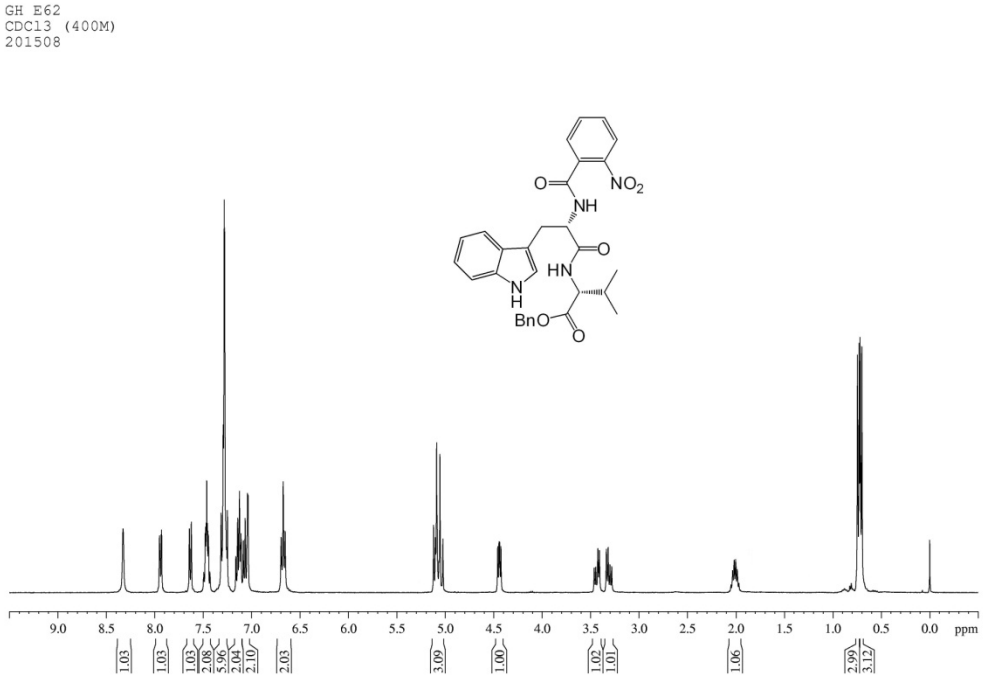
^{1}H NMR spectrum of **18** ($CDCl_3$)



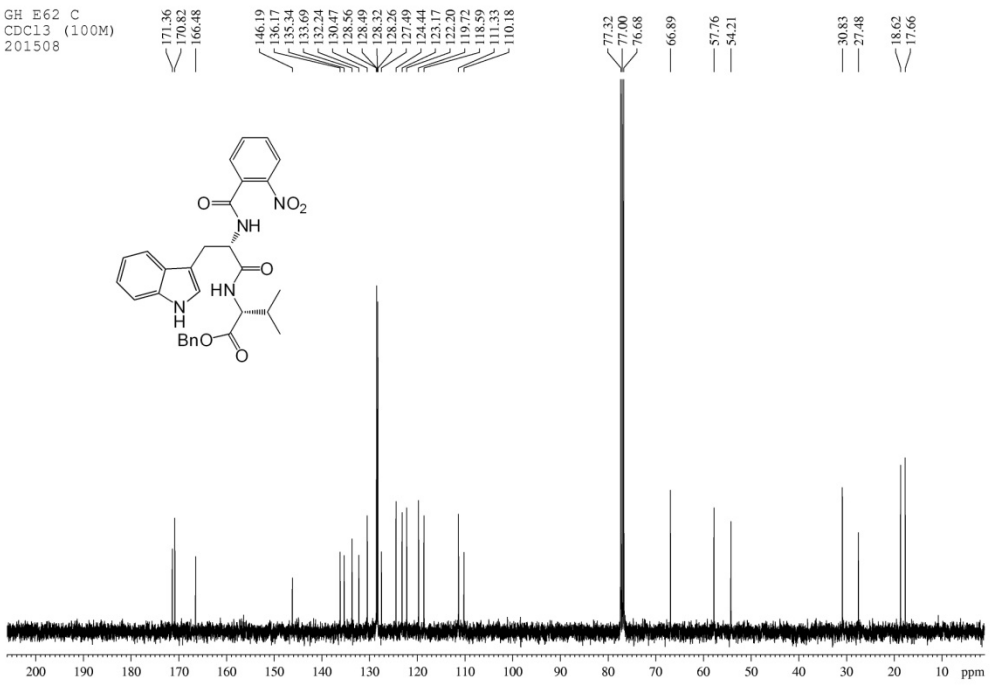
^{13}C NMR spectrum of **18** ($CDCl_3$)



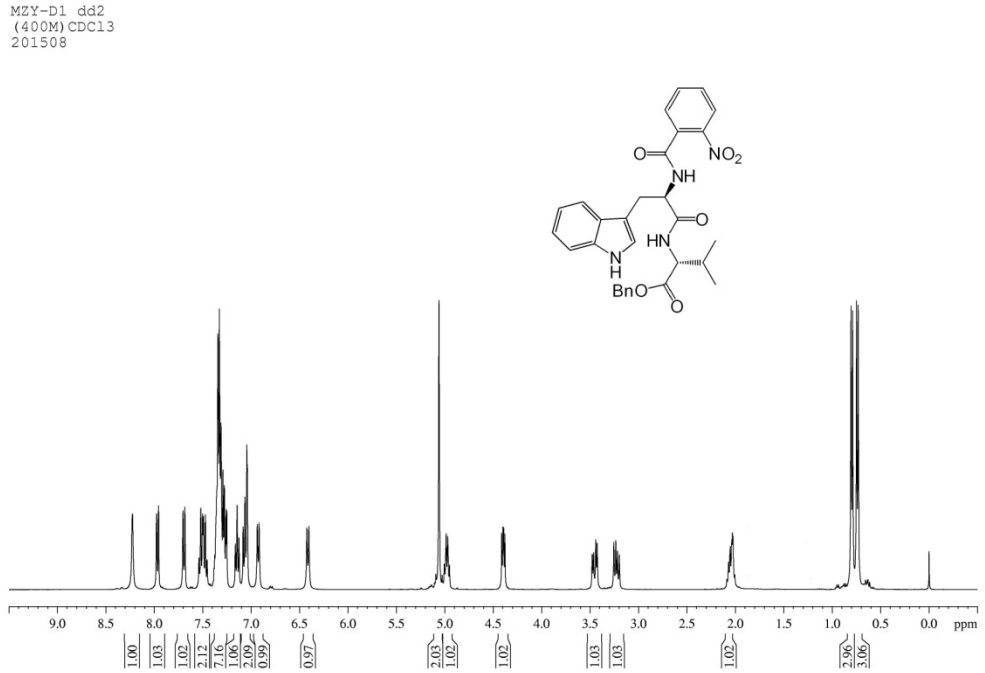
^{1}H NMR spectrum of **21** ($CDCl_3$)



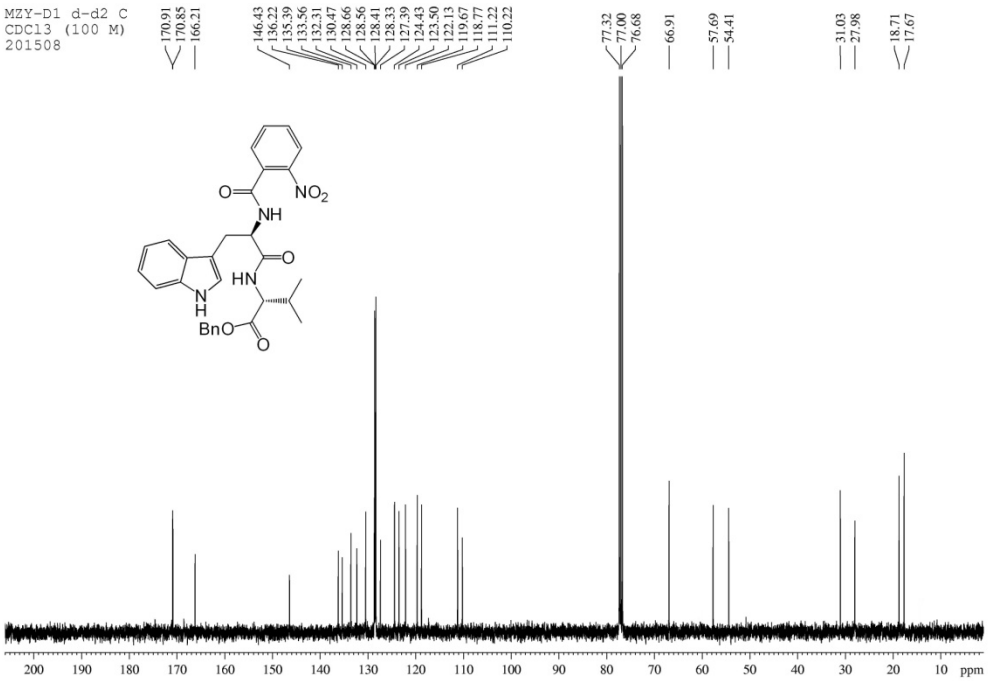
^{13}C NMR spectrum of **21** ($CDCl_3$)



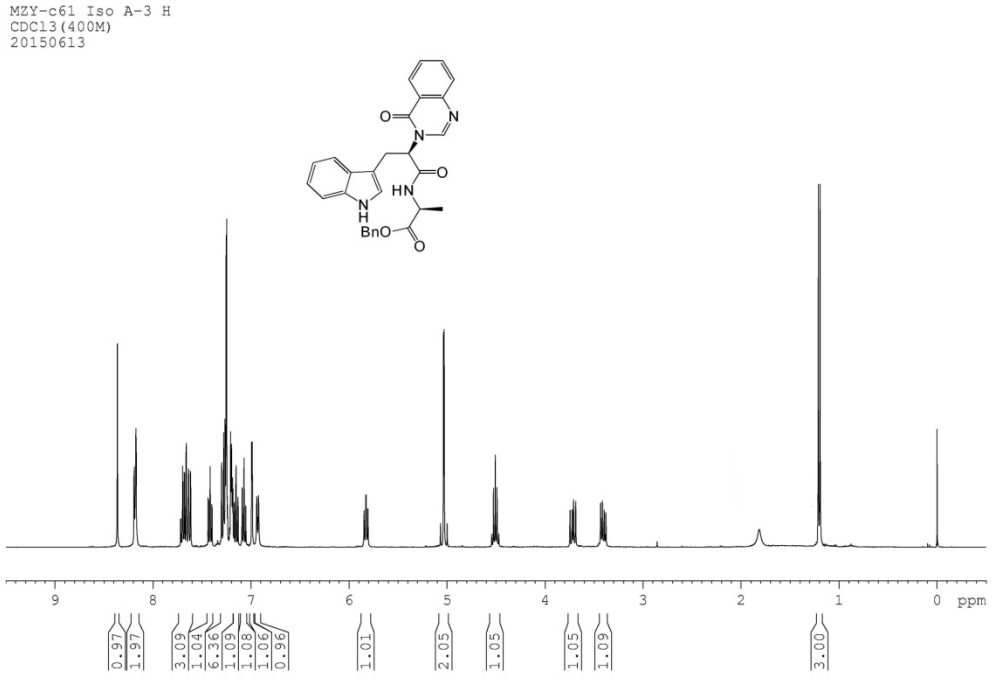
^{1}H NMR spectrum of **24** ($CDCl_3$)



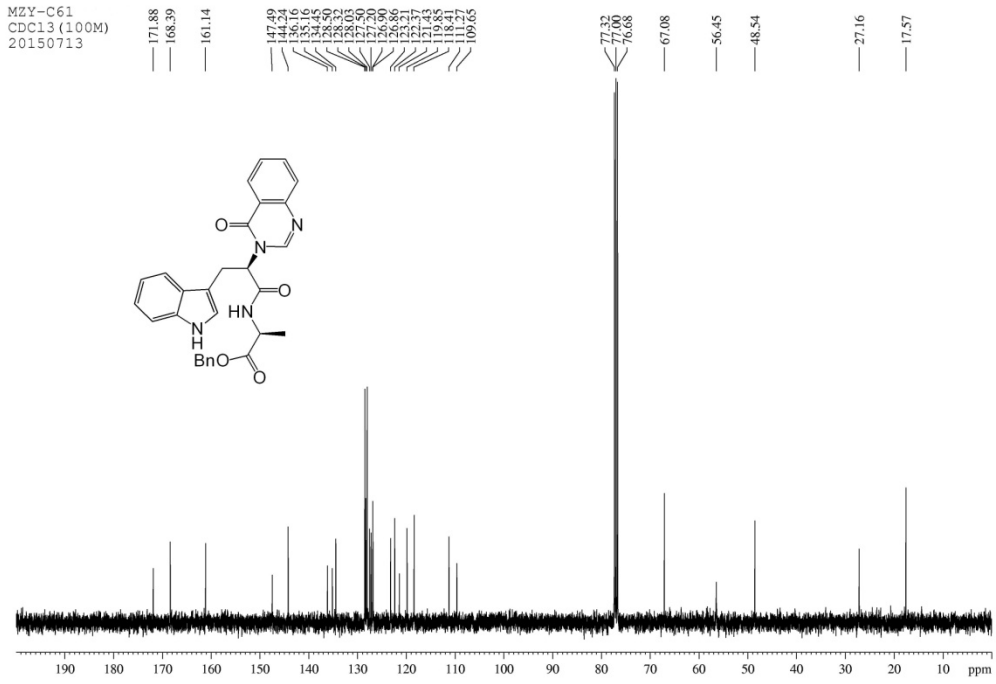
^{13}C NMR spectrum of **24** ($CDCl_3$)



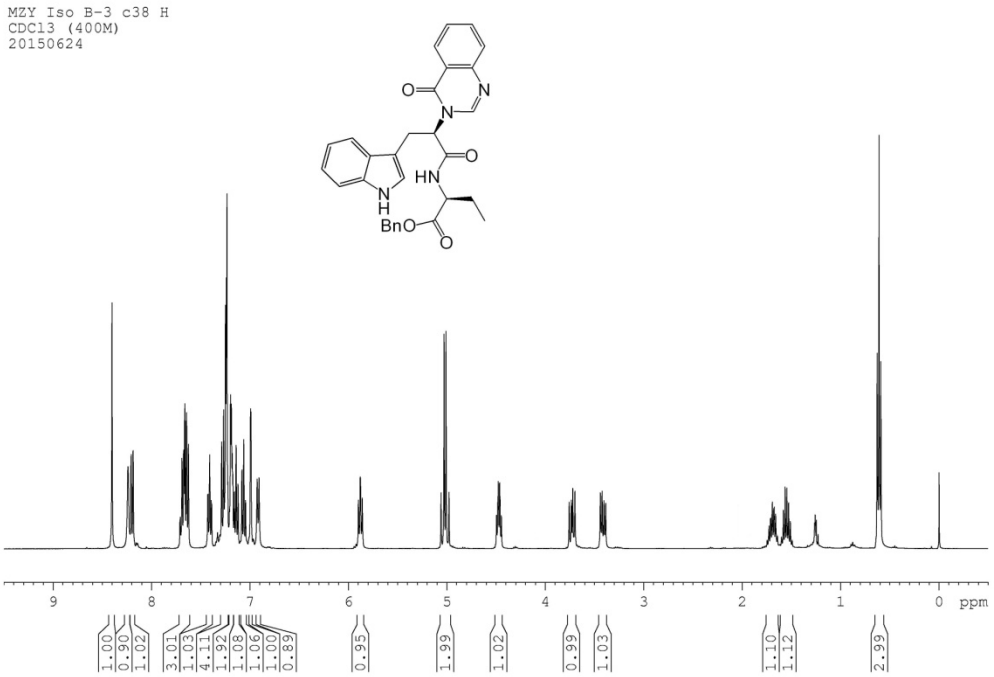
^{1}H NMR spectrum of **12a** ($CDCl_3$)



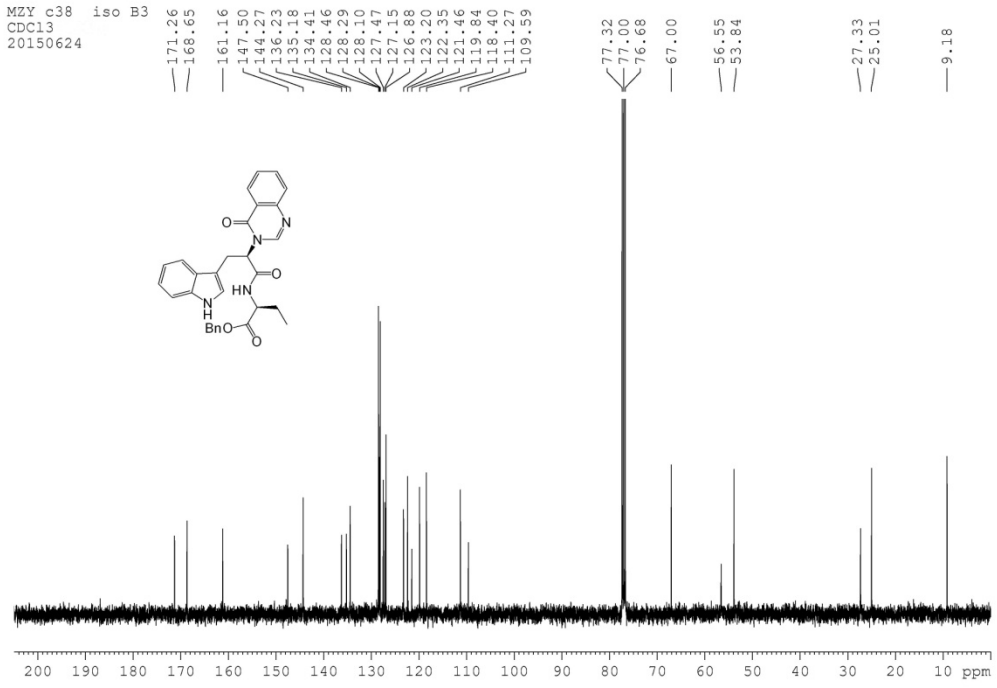
^{13}C NMR spectrum of **12a** ($CDCl_3$)



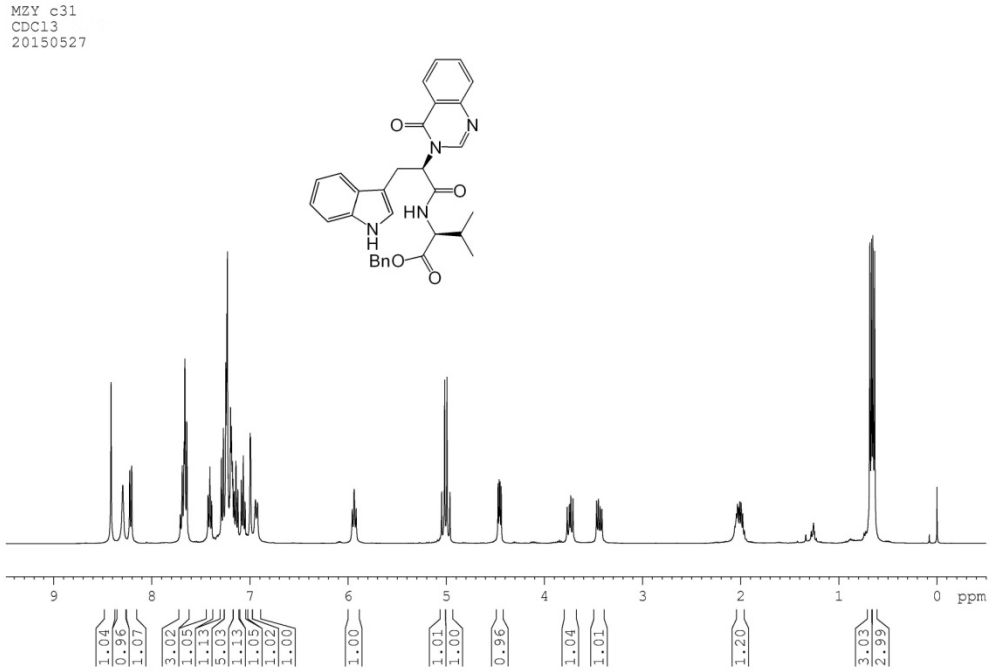
^{1}H NMR spectrum of **12b** ($CDCl_3$)



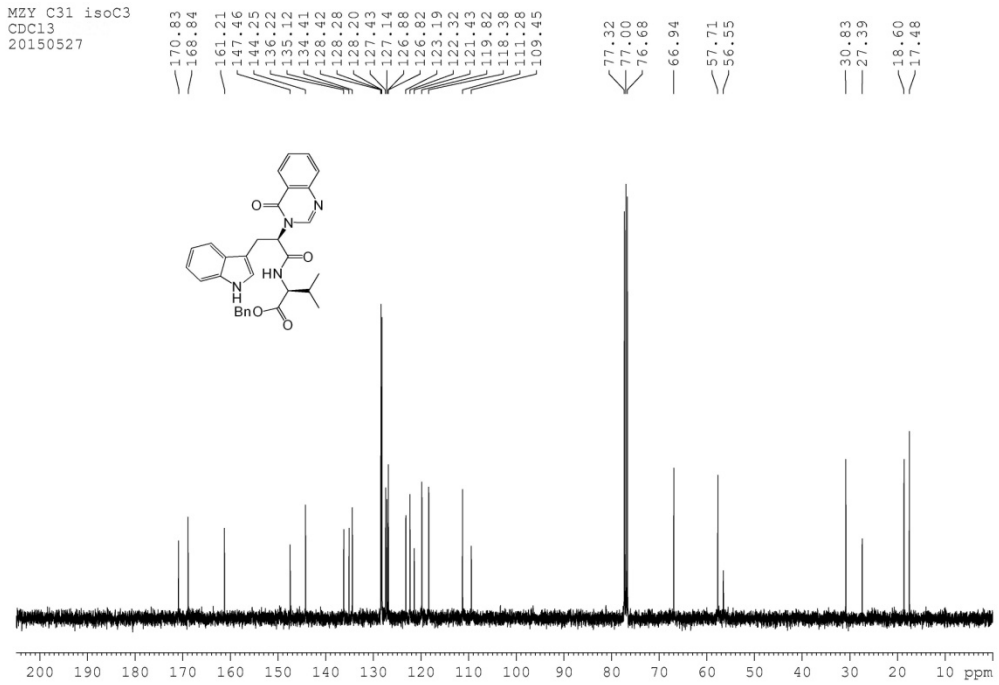
^{13}C NMR spectrum of **12b** ($CDCl_3$)



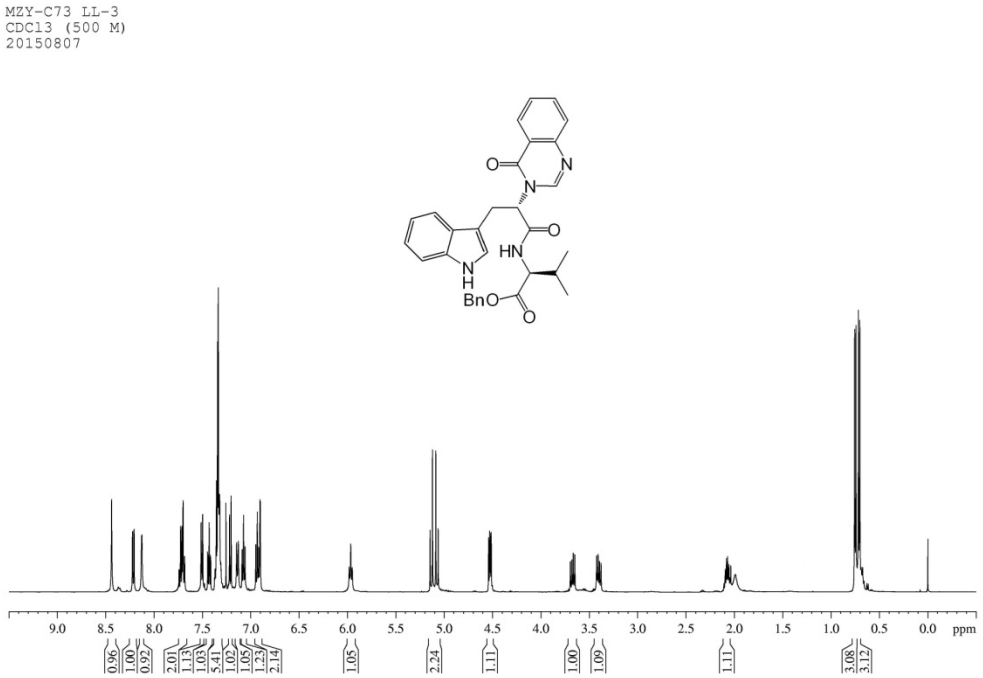
^{1}H NMR spectrum of **12c** ($CDCl_3$)



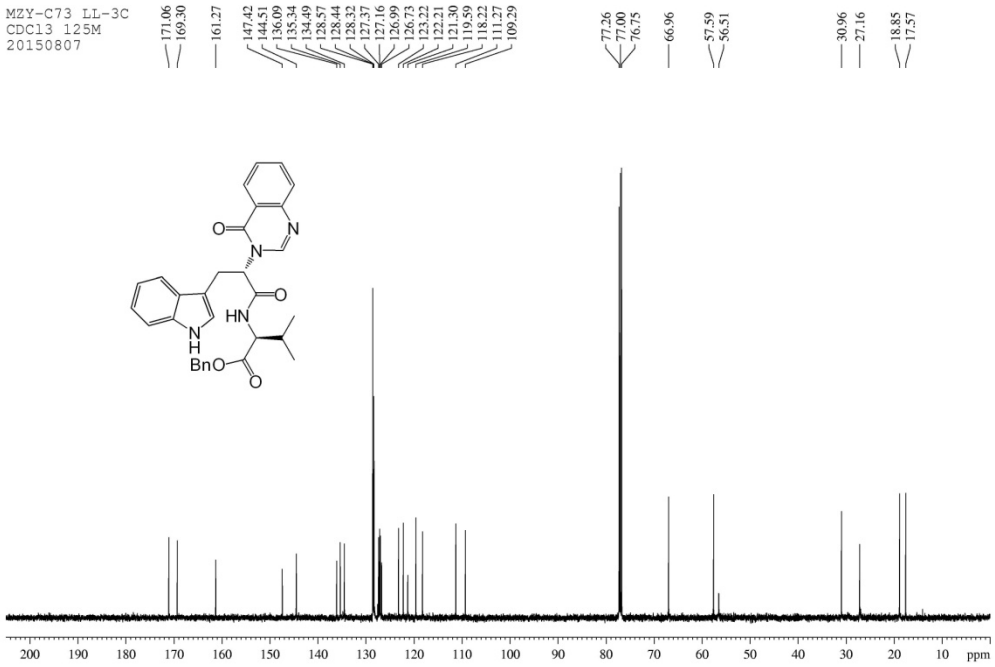
^{13}C NMR spectrum of **12c** ($CDCl_3$)



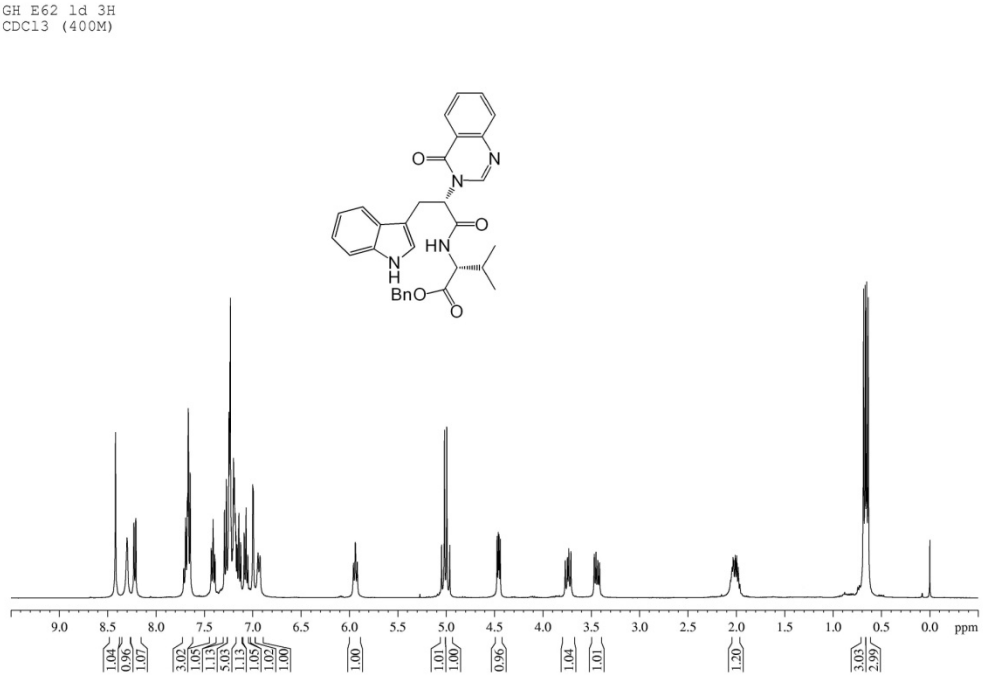
^{1}H NMR spectrum of **19** ($CDCl_3$)



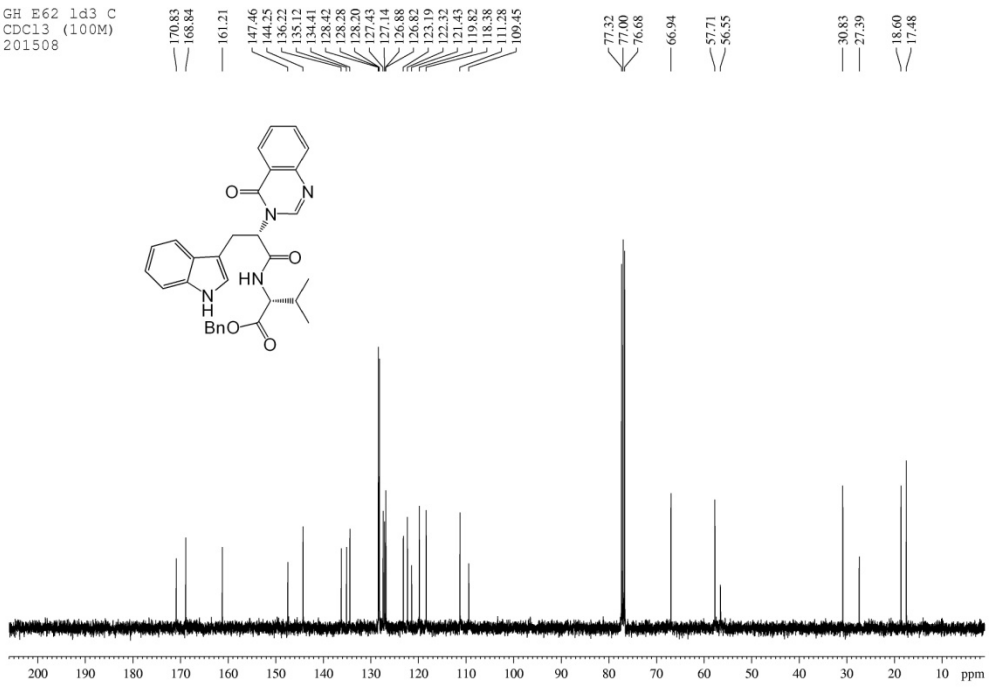
^{13}C NMR spectrum of **19** ($CDCl_3$)



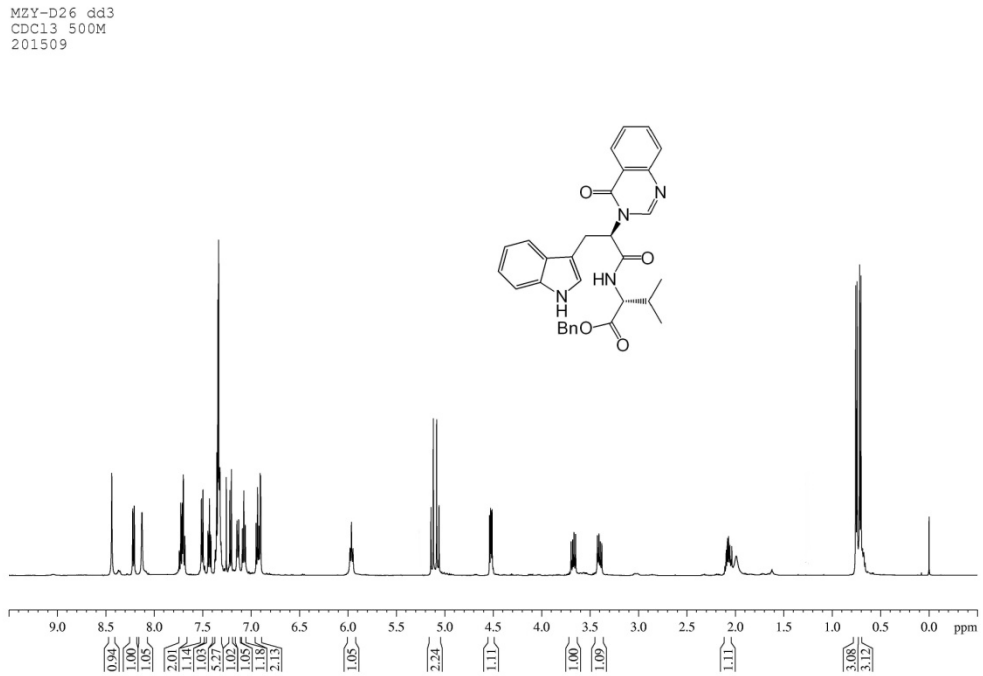
^{1}H NMR spectrum of **22** ($CDCl_3$)



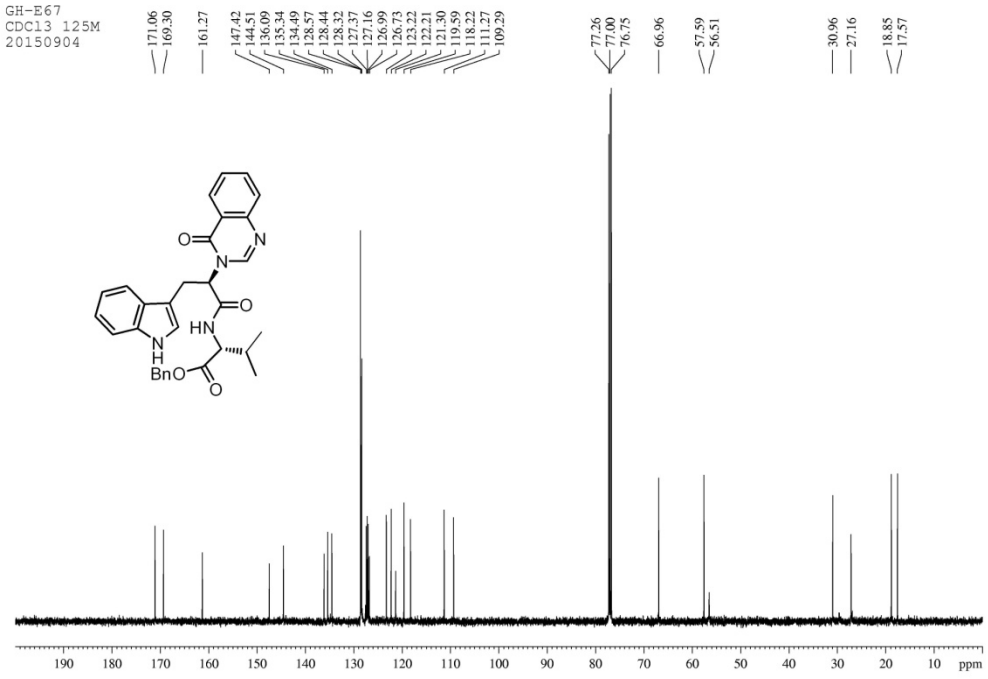
^{13}C NMR spectrum of **22** ($CDCl_3$)



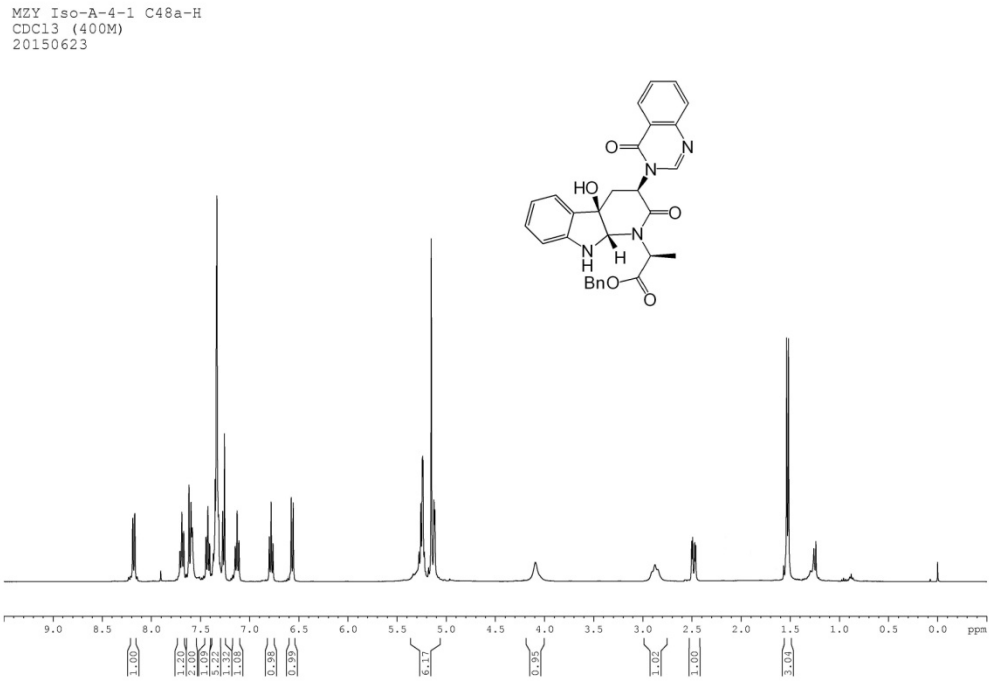
^{1}H NMR spectrum of **25** ($CDCl_3$)



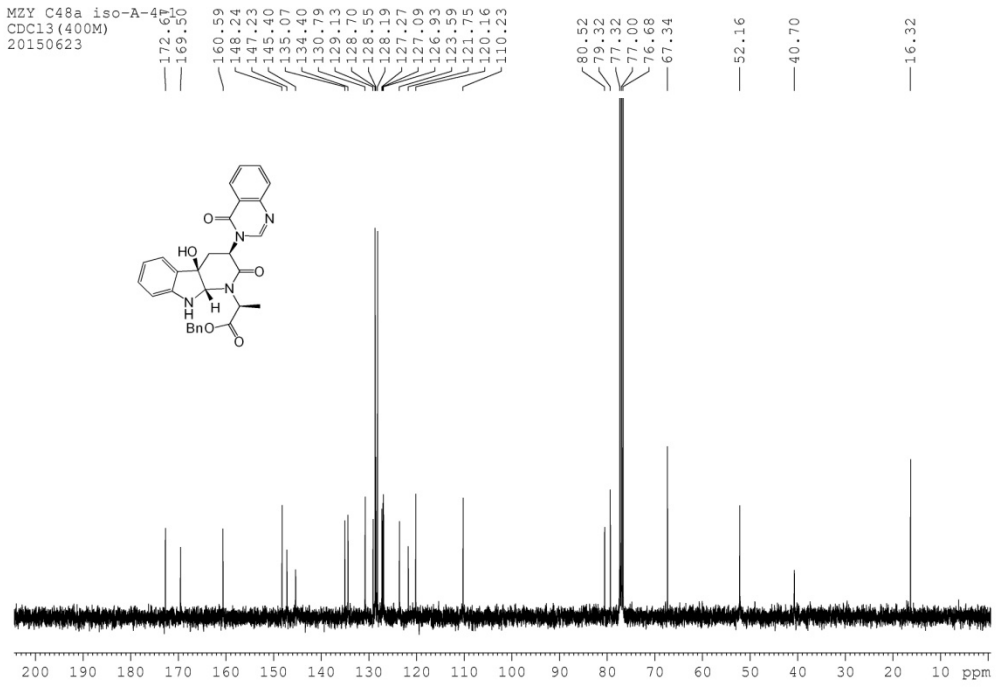
^{13}C NMR spectrum of **25** ($CDCl_3$)



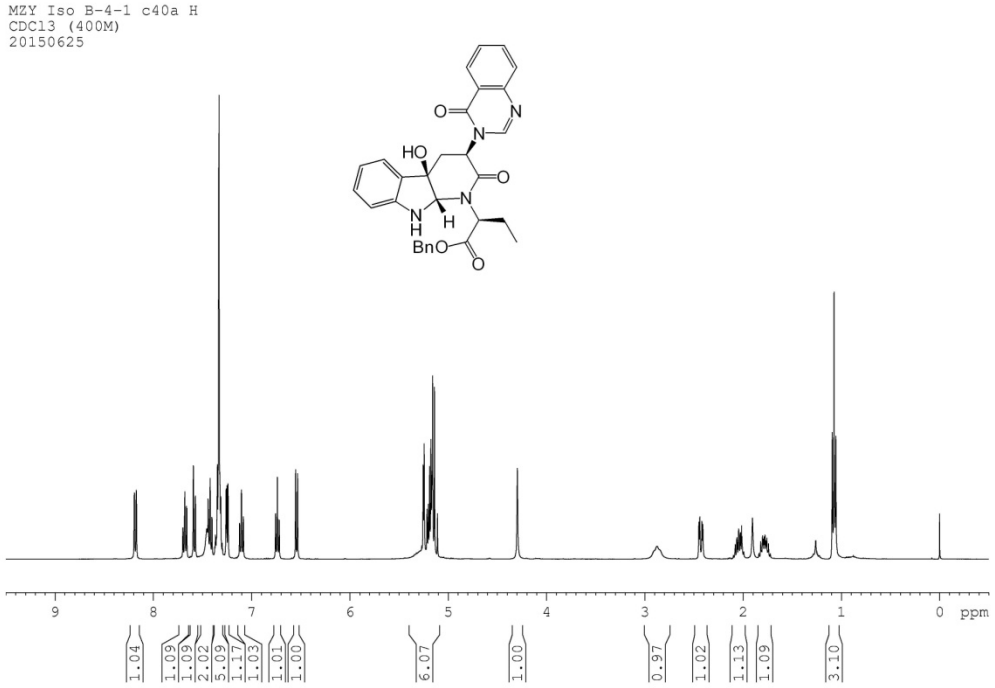
^{1}H NMR spectrum of **11a** ($CDCl_3$)



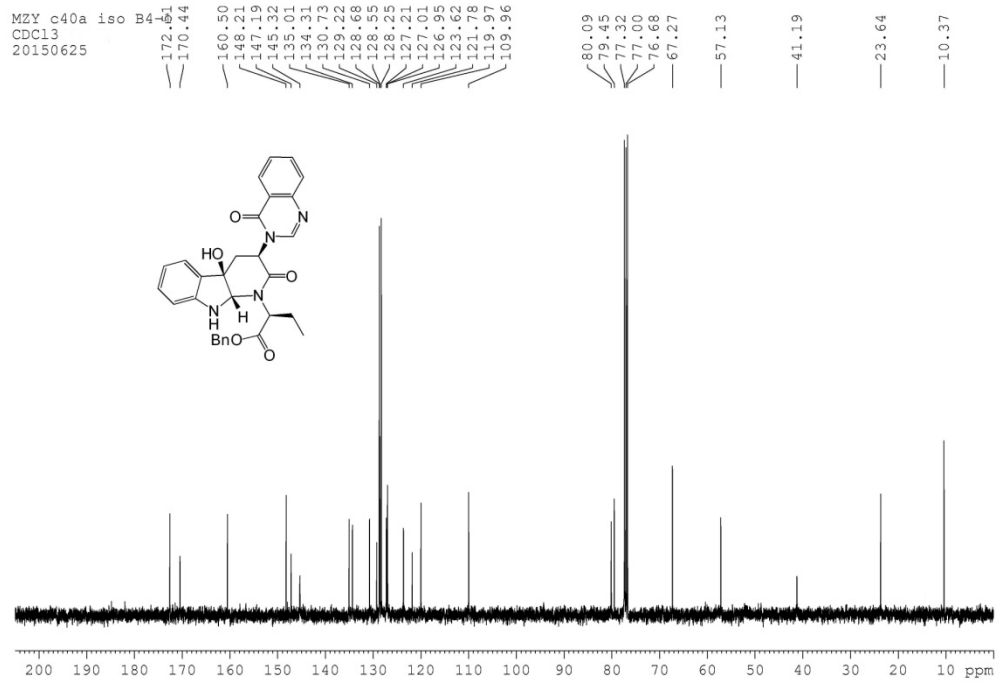
^{13}C NMR spectrum of **11a** ($CDCl_3$)



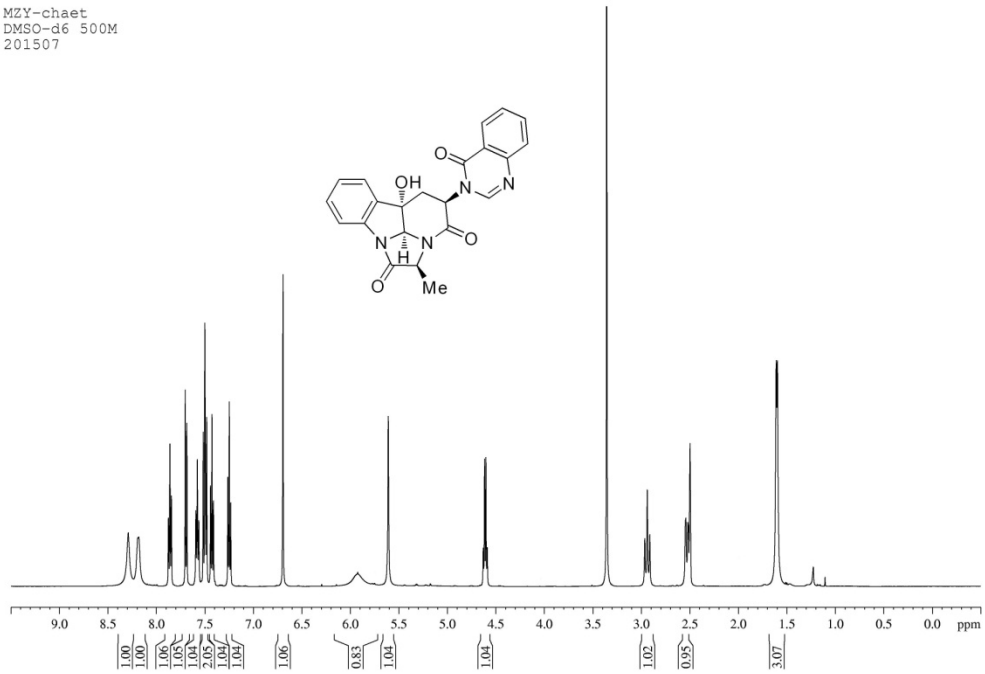
^{1}H NMR spectrum of **11b** ($CDCl_3$)



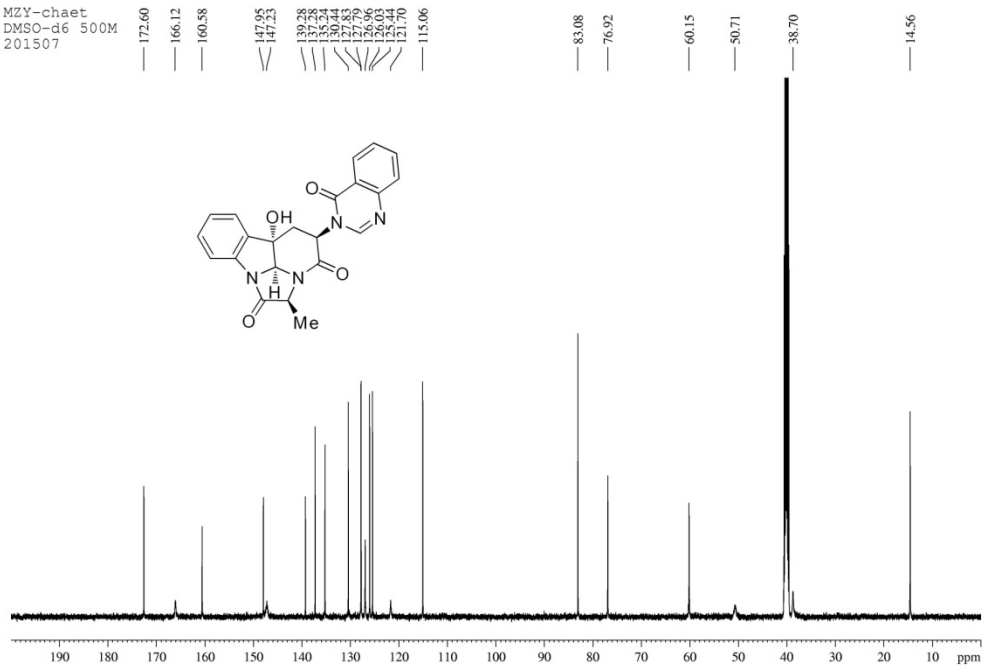
^{13}C NMR spectrum of **11b** ($CDCl_3$)



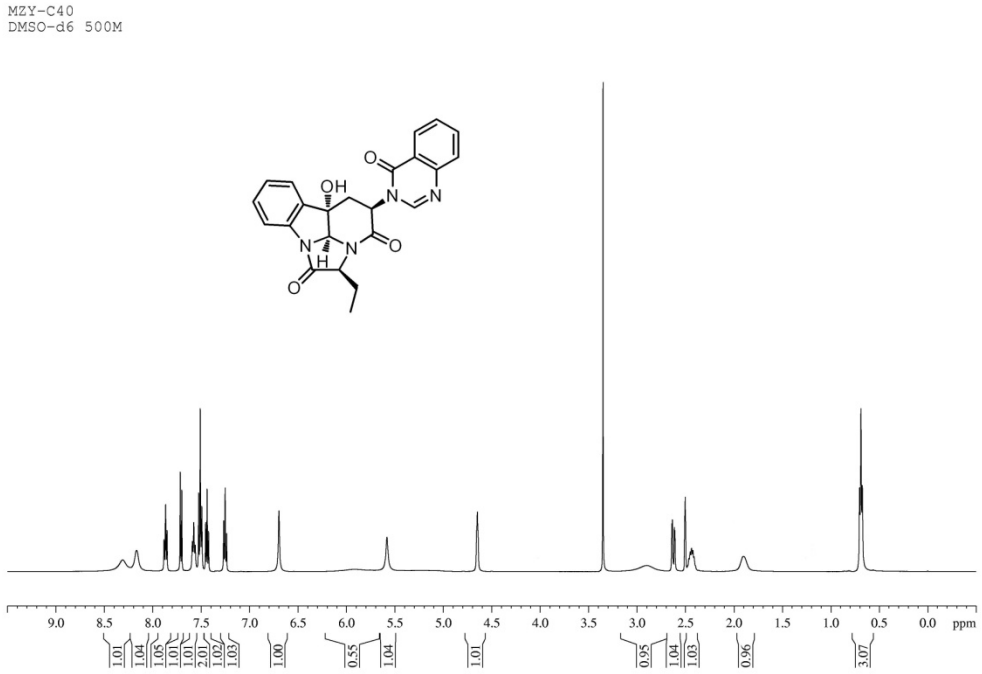
^{1}H NMR spectrum of **1** (DMSO-d_6)



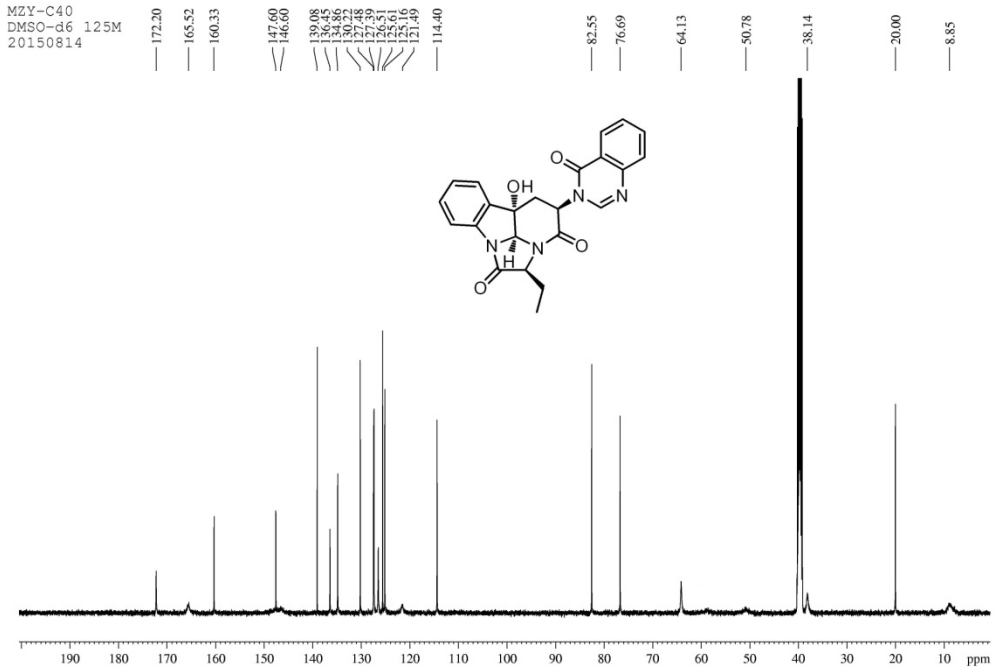
^{13}C NMR spectrum of **1** (DMSO-d_6)



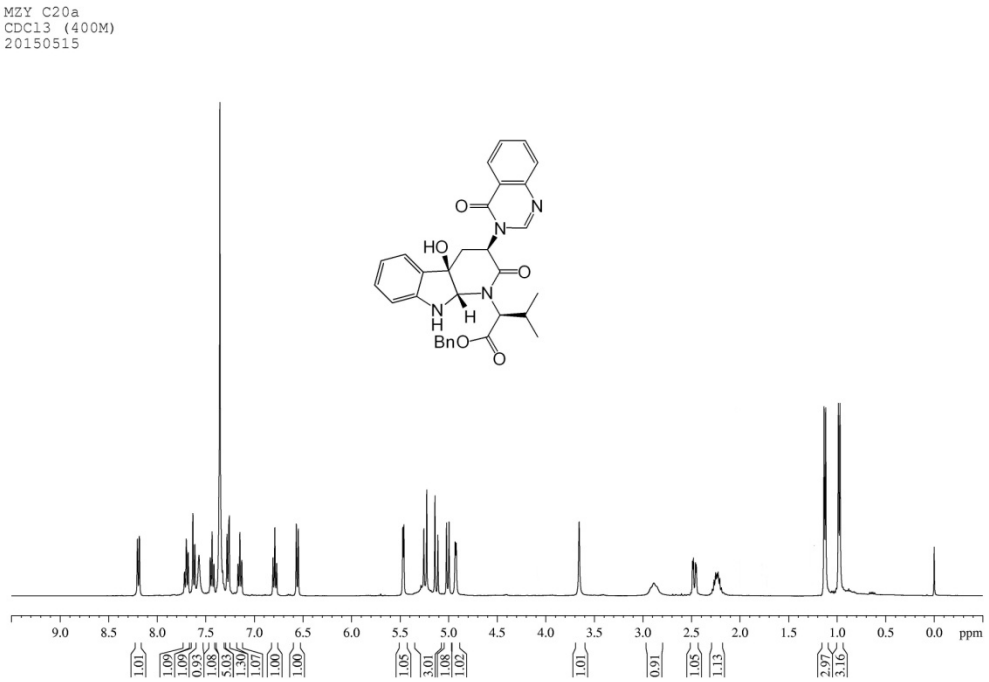
^{1}H NMR spectrum of **17** (DMSO-d_6)



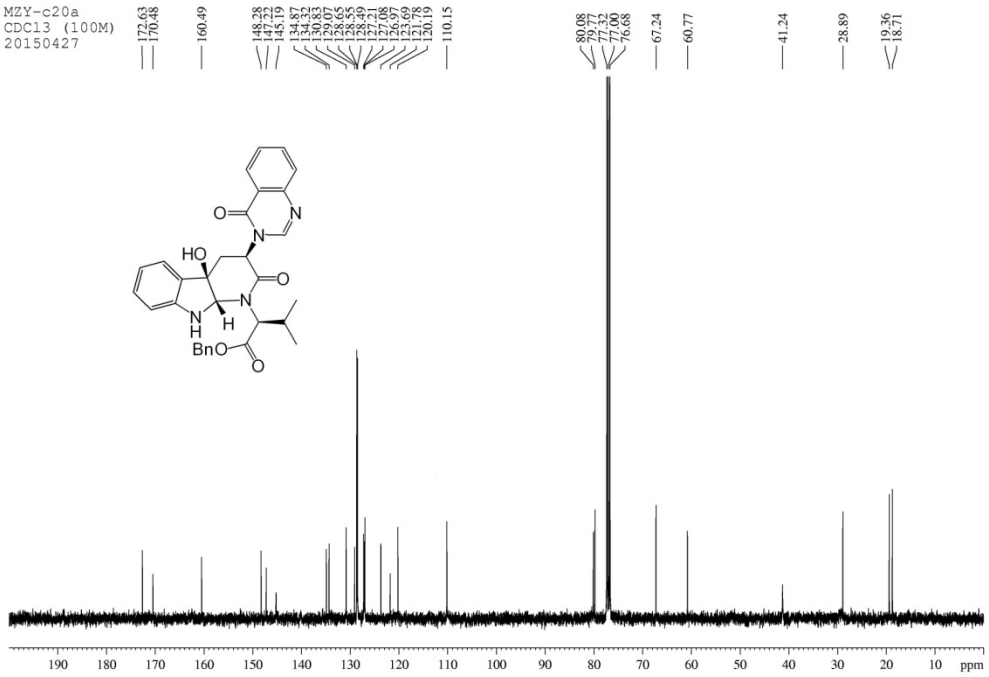
^{13}C NMR spectrum of **17** (DMSO-d_6)



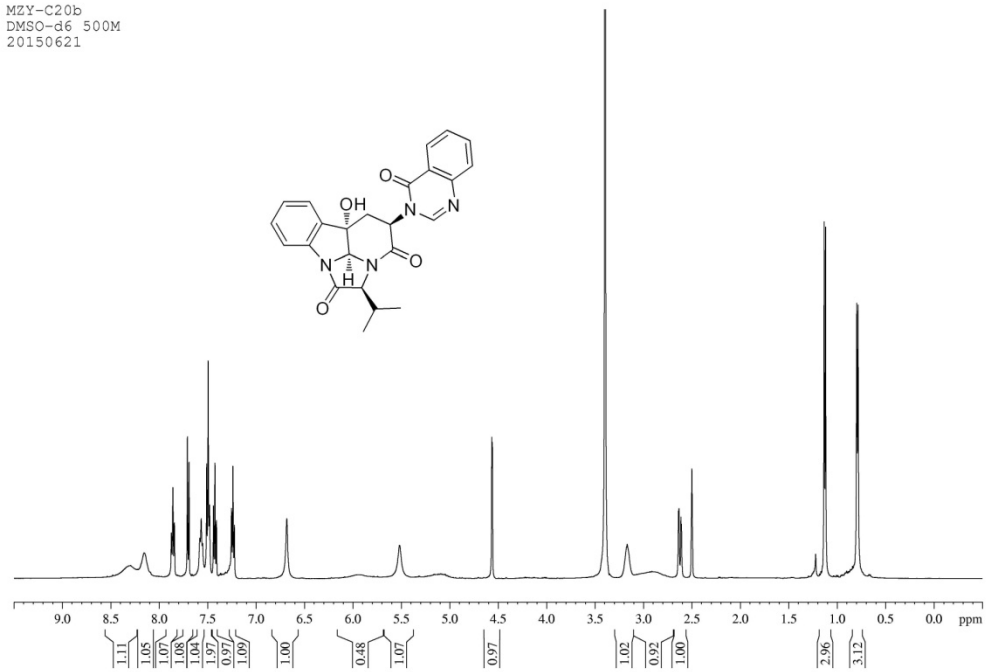
^{1}H NMR spectrum of **11c** ($CDCl_3$)



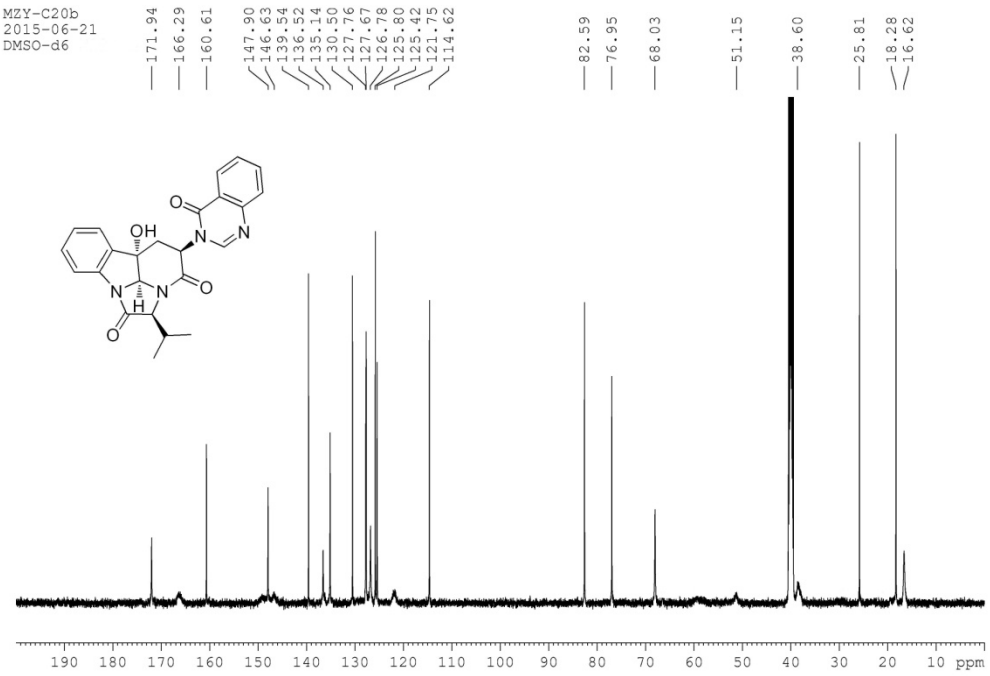
^{13}C NMR spectrum of **11c** ($CDCl_3$)



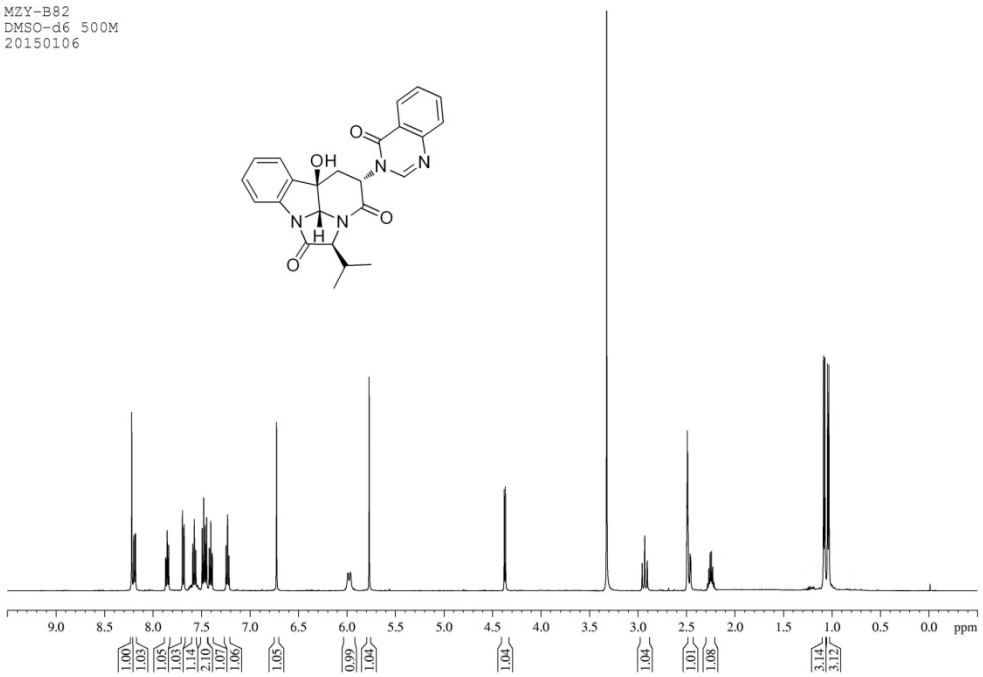
^{1}H NMR spectrum of **3** (DMSO-d_6)



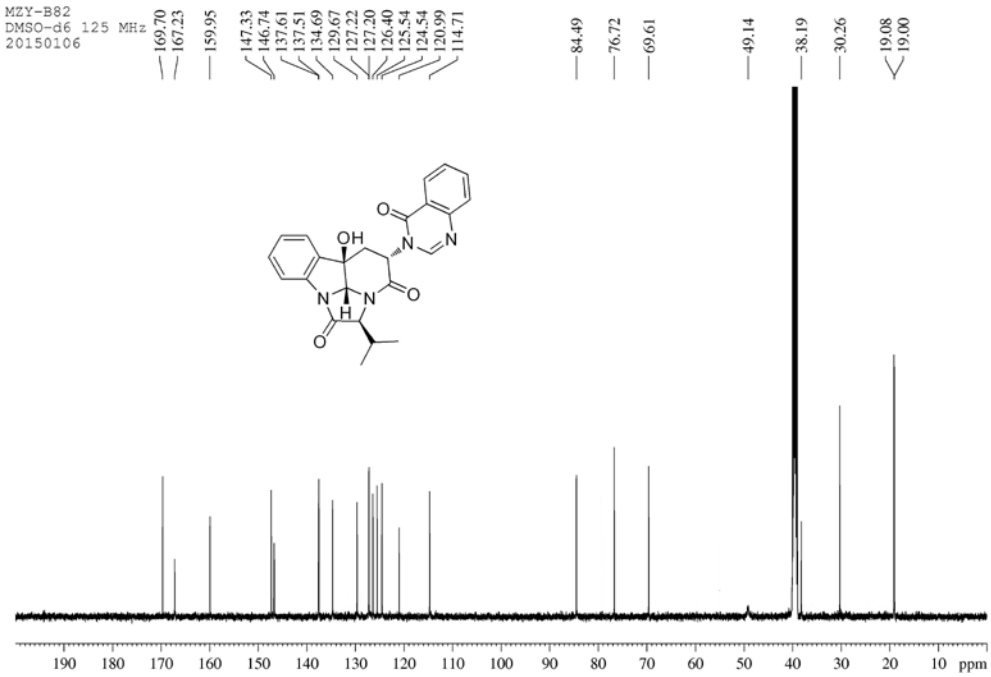
^{13}C NMR spectrum of **3** (DMSO-d_6)



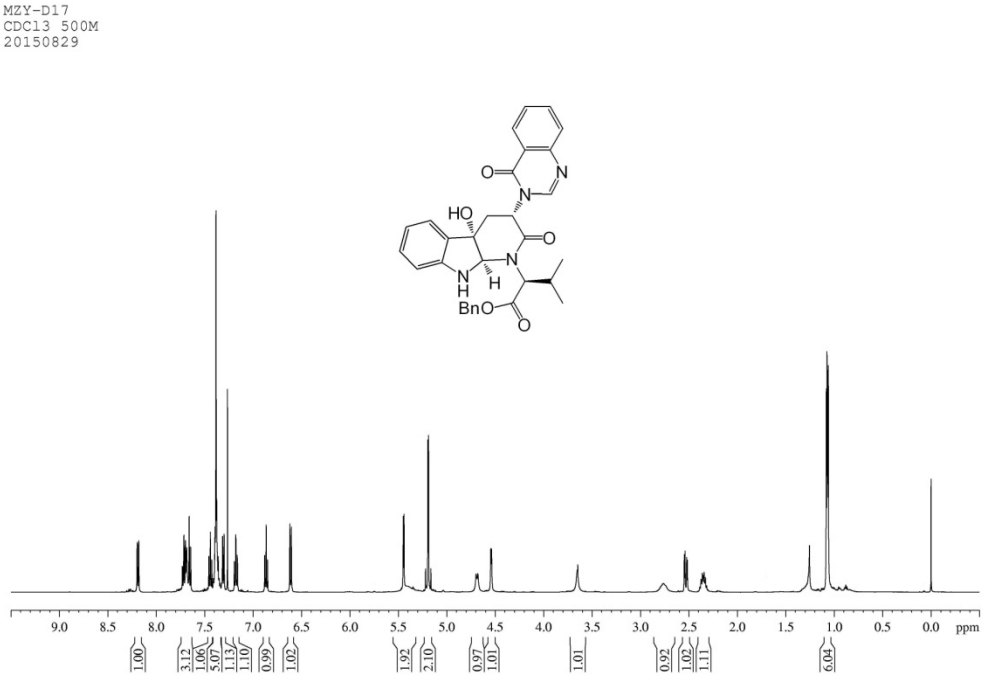
^{1}H NMR spectrum of **7** (DMSO-d_6)



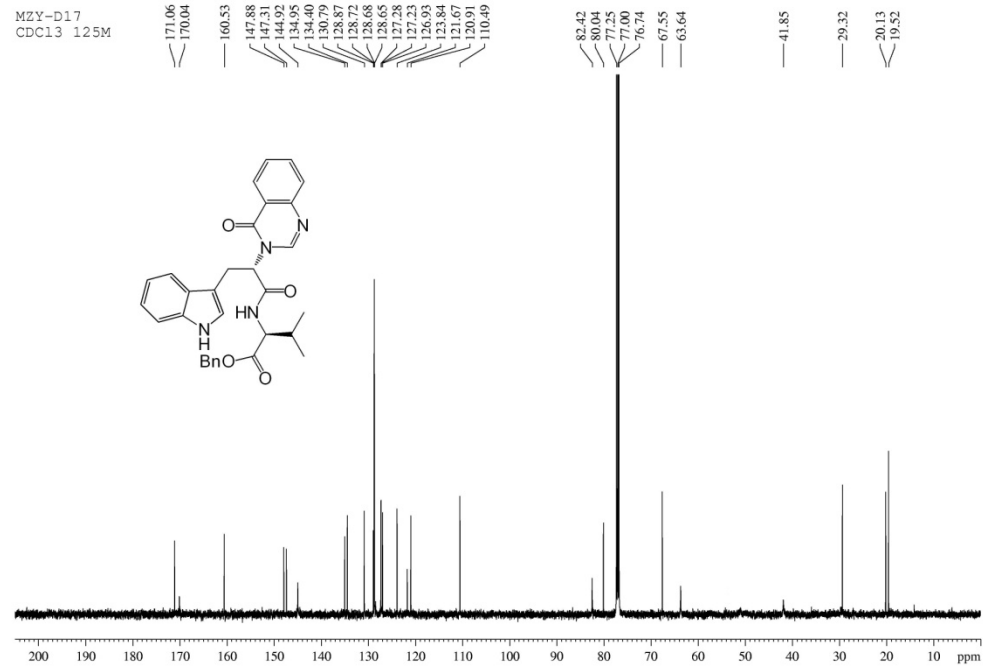
^{13}C NMR spectrum of **7** (DMSO-d_6)



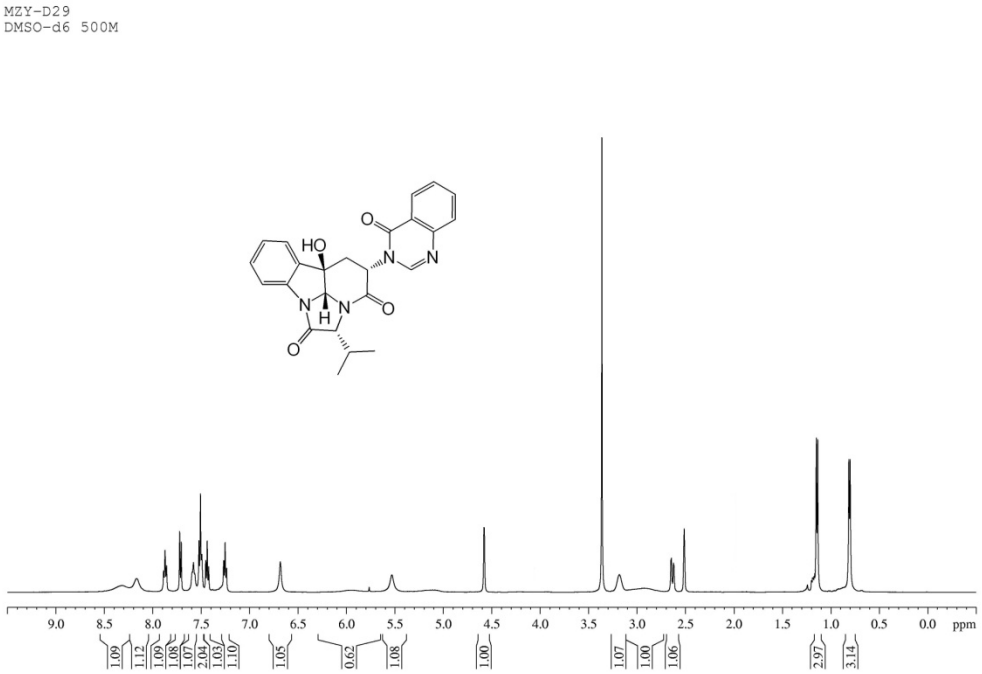
^{1}H NMR spectrum of **20** ($CDCl_3$)



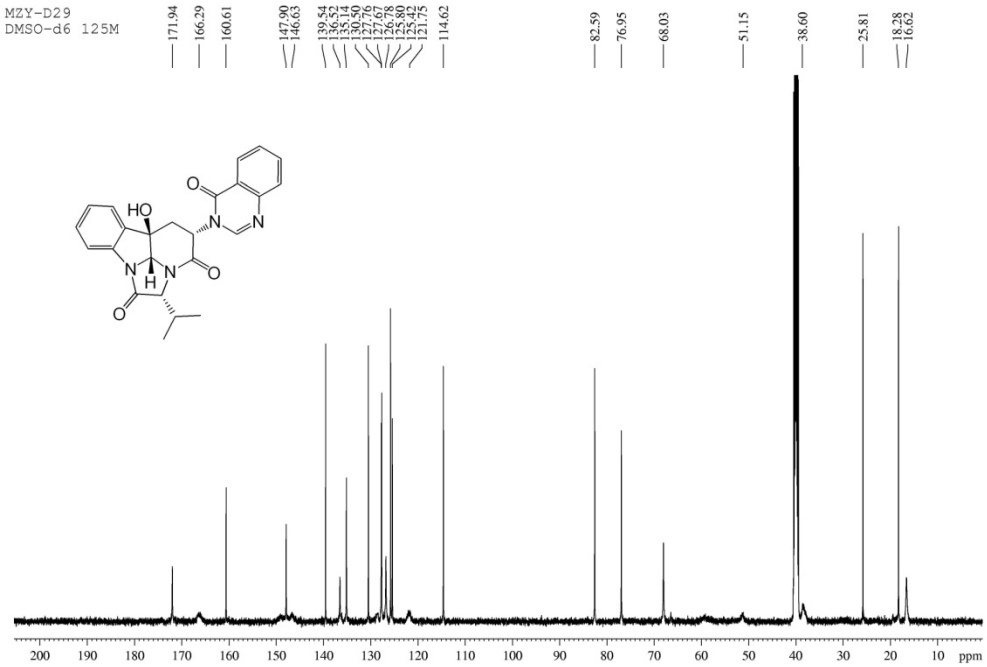
^{13}C NMR spectrum of **20** ($CDCl_3$)



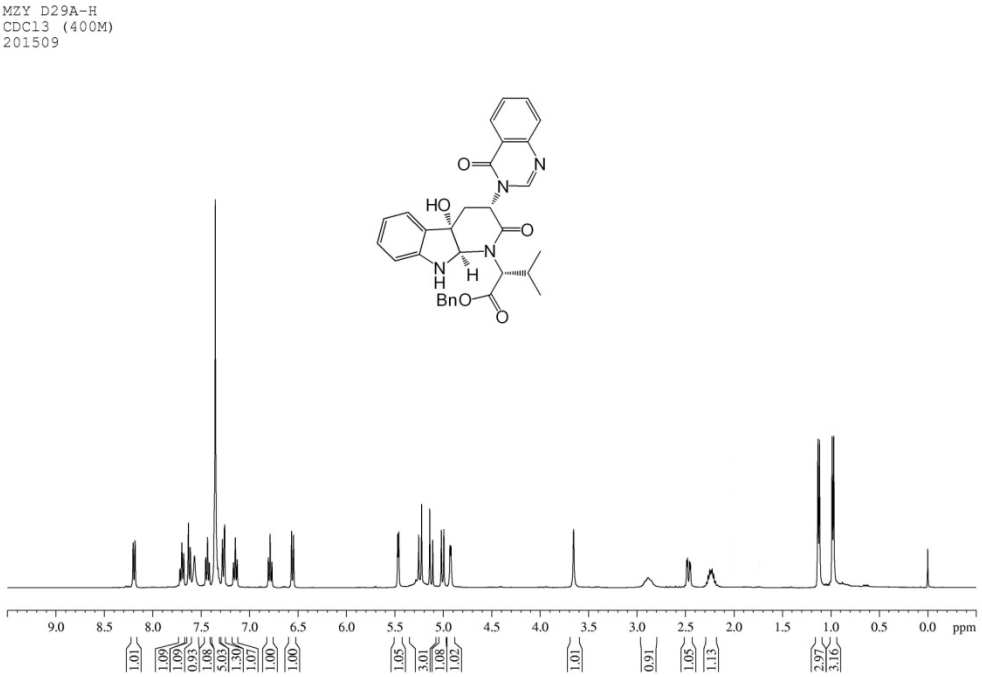
^{1}H NMR spectrum of ***ent*-3** (DMSO-d_6)



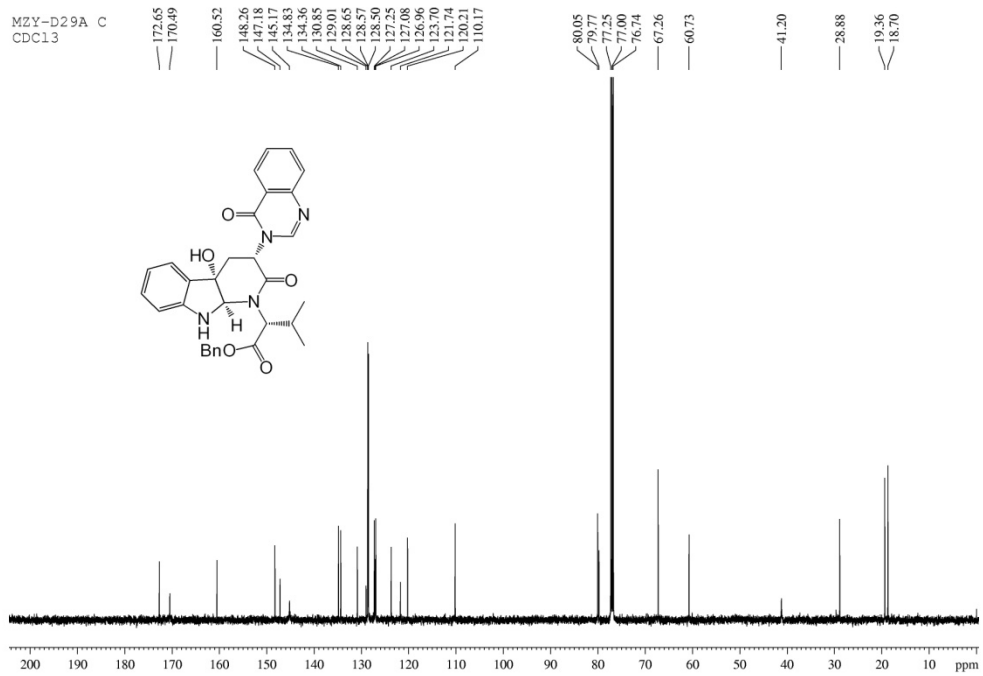
^{13}C NMR spectrum of ***ent*-3** (DMSO-d_6)



^{1}H NMR spectrum of **23** ($CDCl_3$)

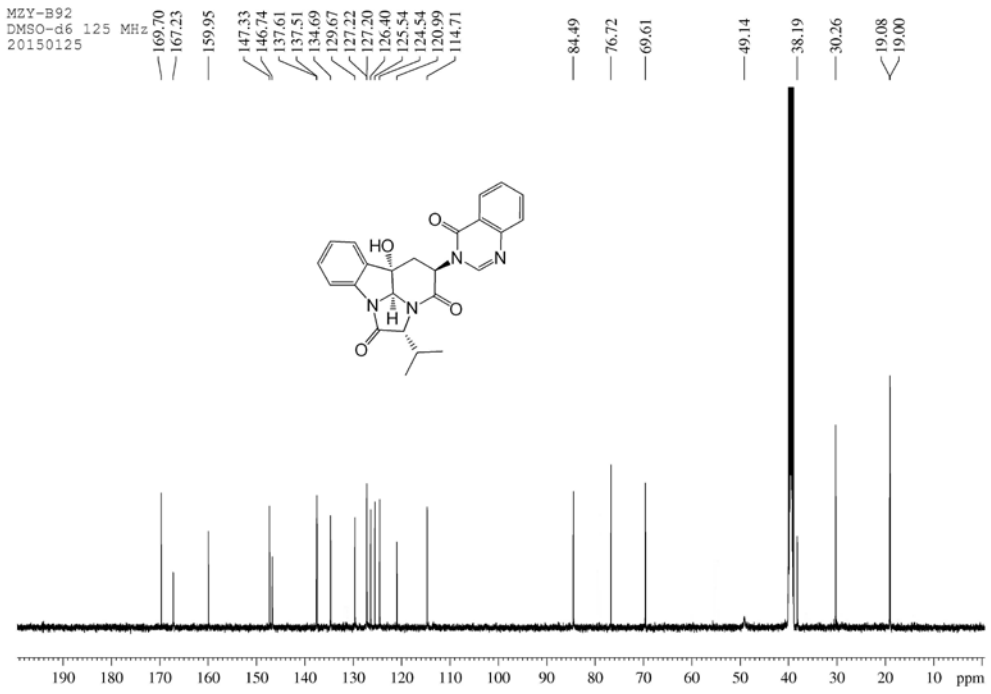


^{13}C NMR spectrum of **23** ($CDCl_3$)

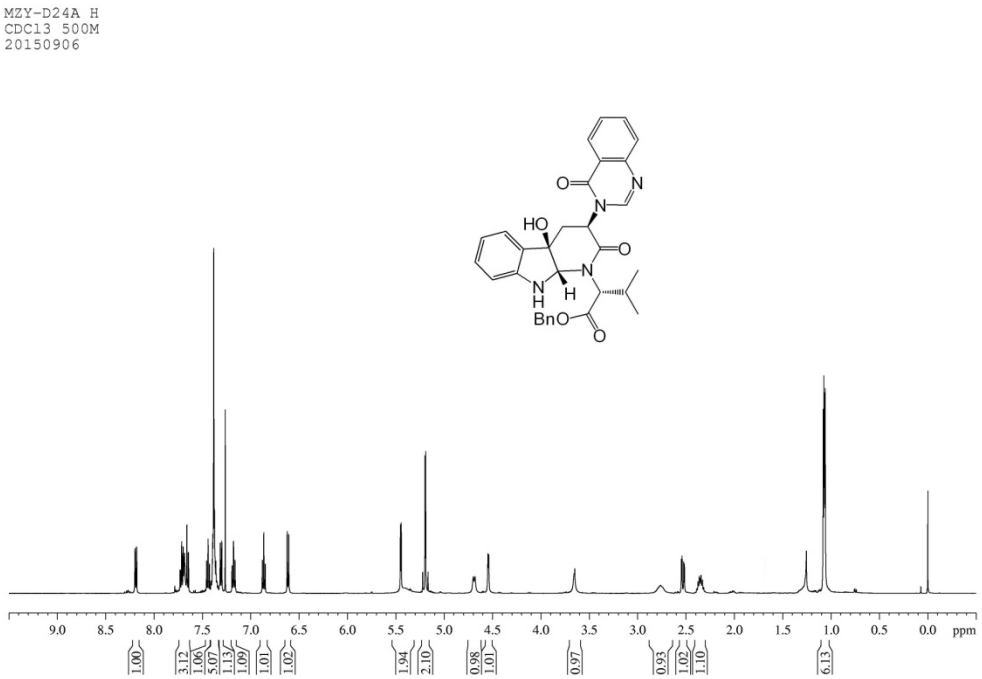


^{1}H NMR spectrum of ***ent*-7** (DMSO-d_6)

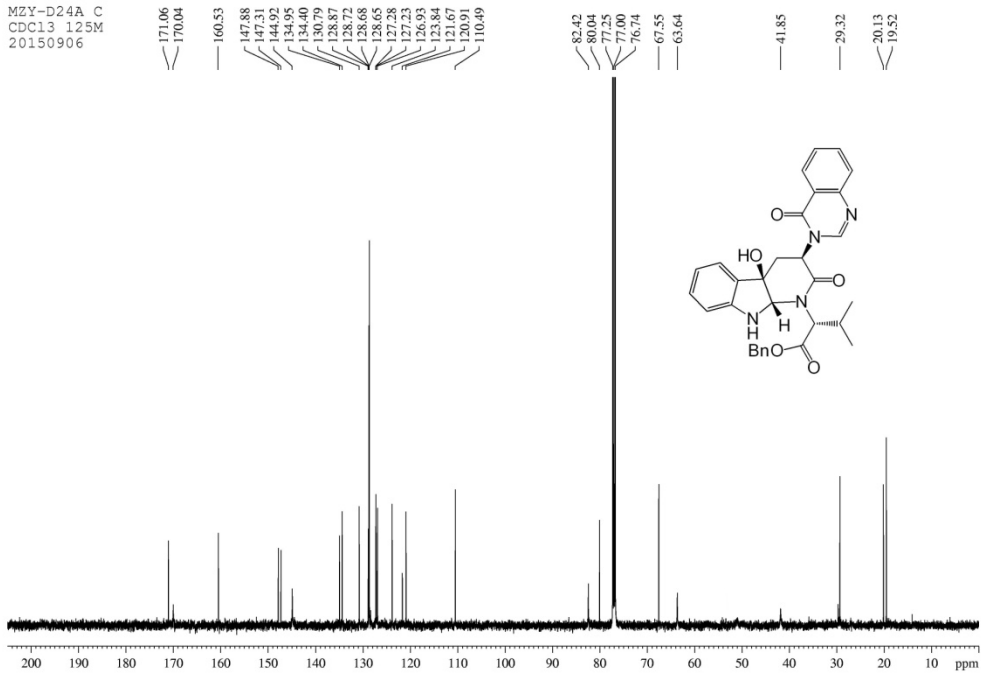
^{13}C NMR spectrum of ***ent*-7** (DMSO-d_6)



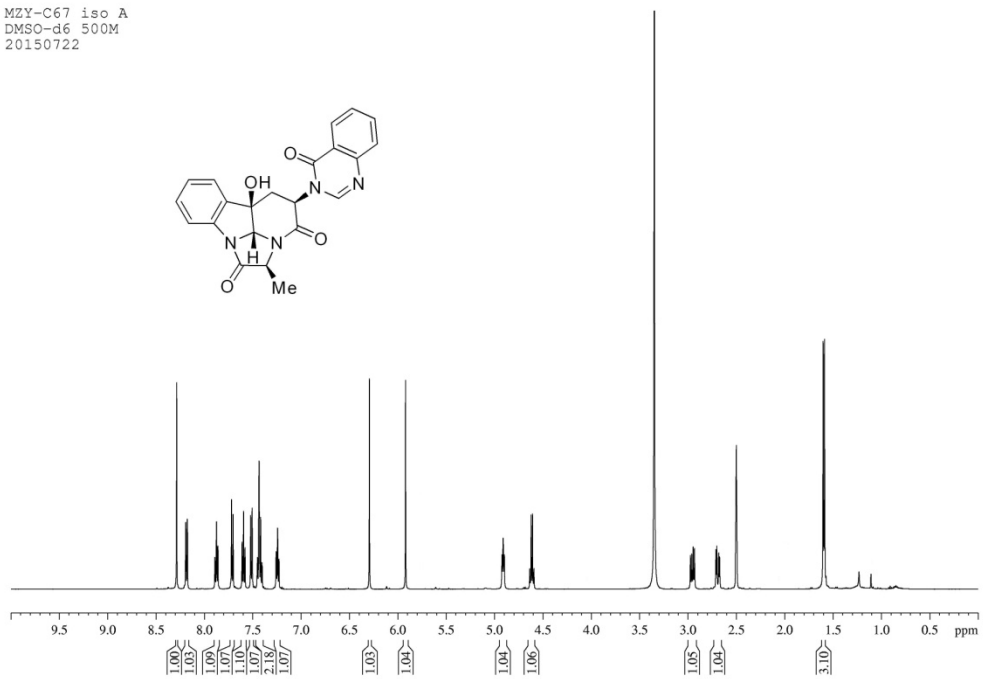
^{1}H NMR spectrum of **26** ($CDCl_3$)



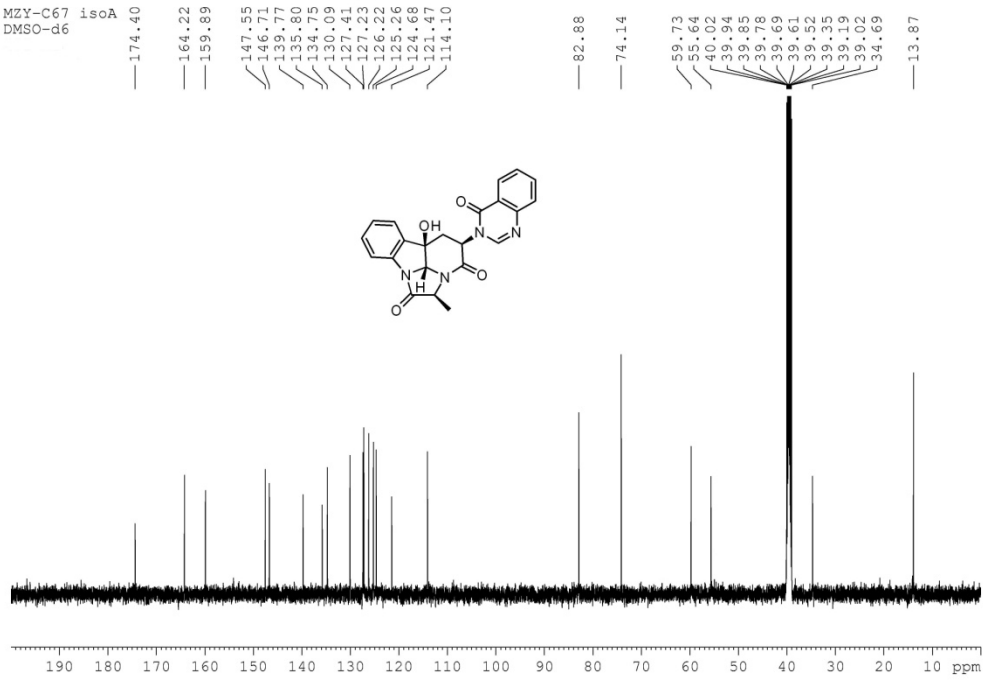
^{13}C NMR spectrum of **26** ($CDCl_3$)



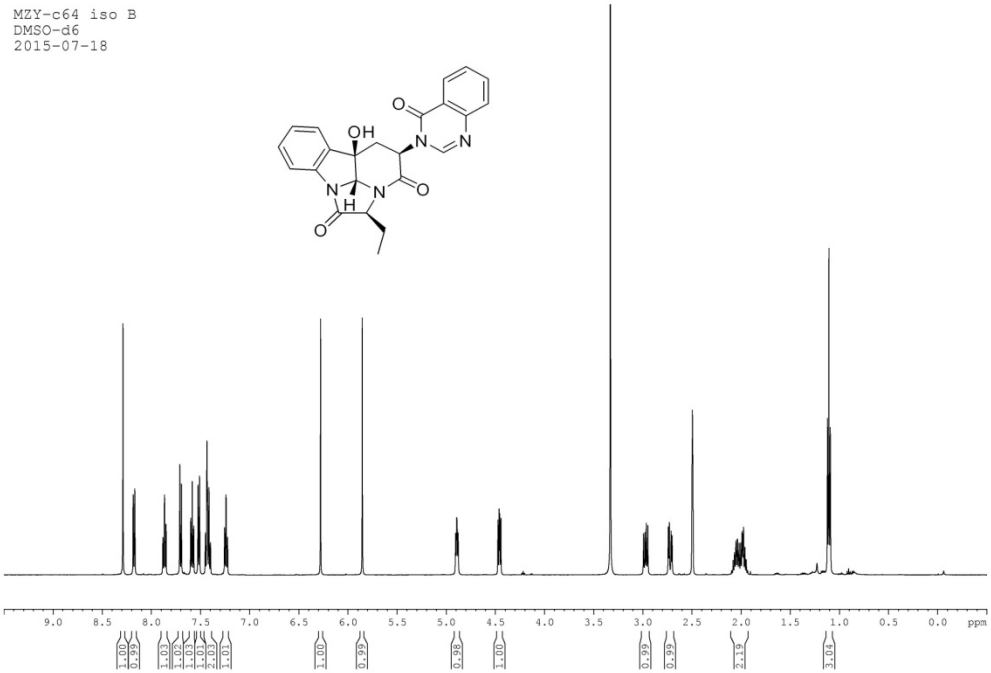
^{1}H NMR spectrum of **4** (DMSO-d_6)



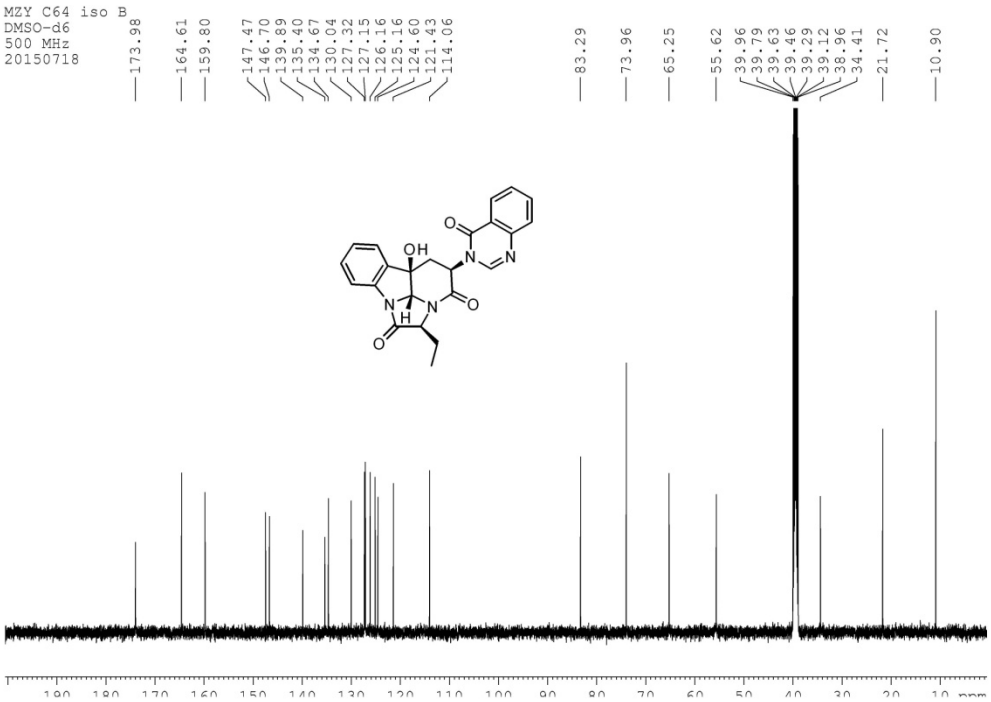
^{13}C NMR spectrum of **4** (DMSO-d_6)



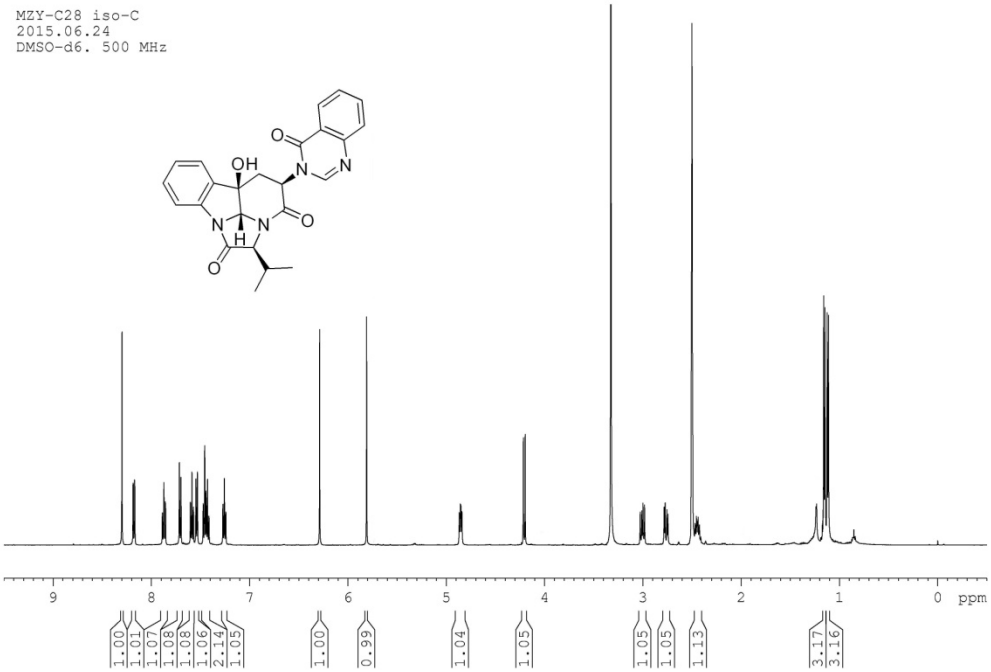
^{1}H NMR spectrum of **5** (DMSO-d_6)



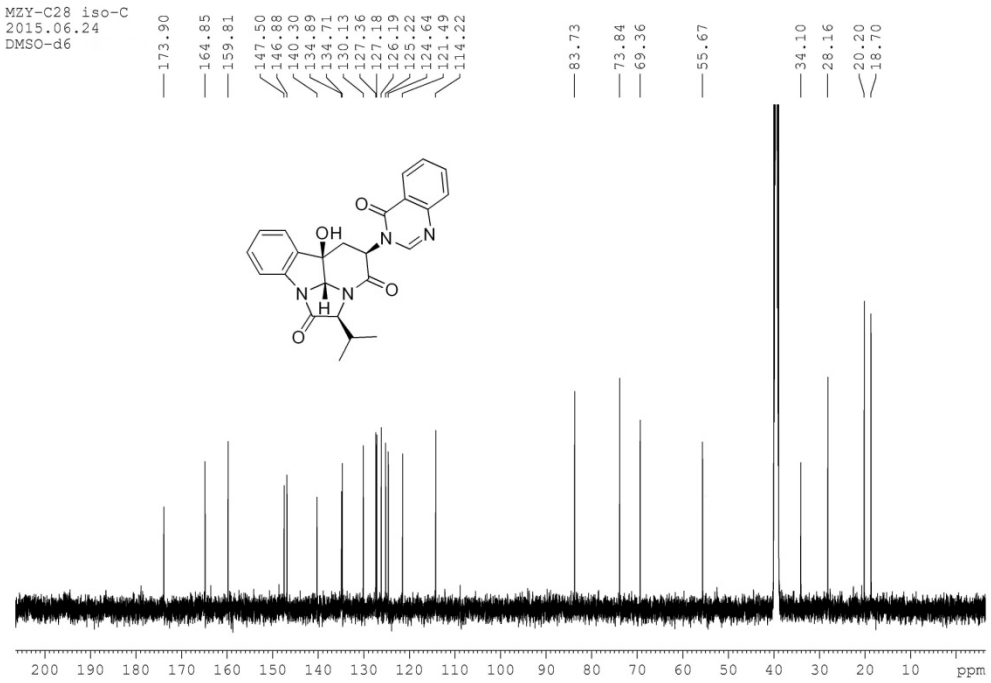
^{13}C NMR spectrum of **5** (DMSO-d_6)



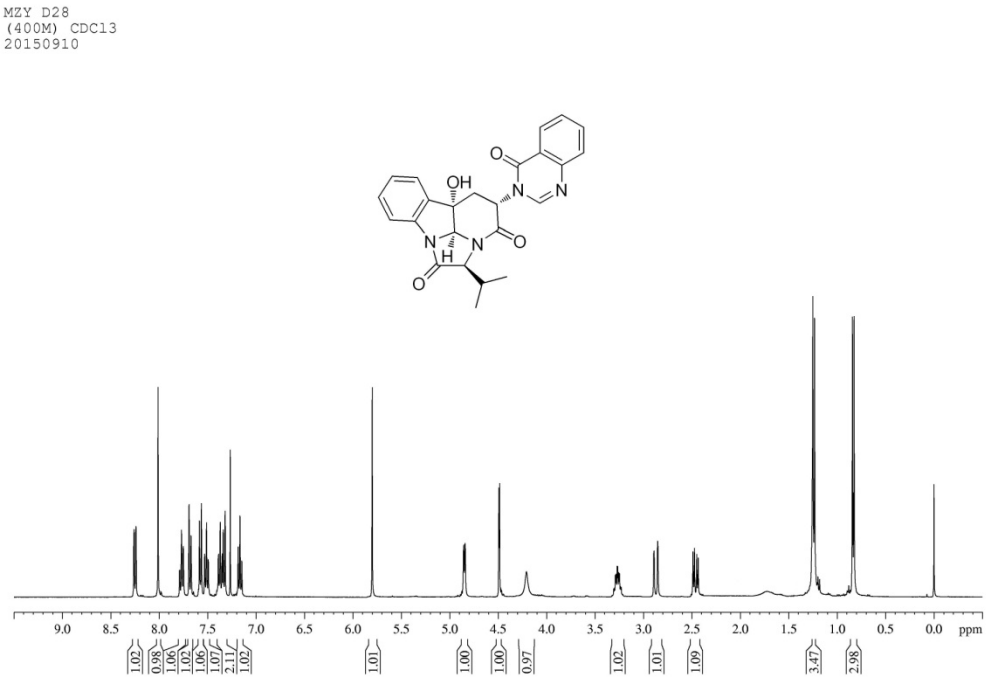
^{1}H NMR spectrum of **6** (DMSO-d_6)



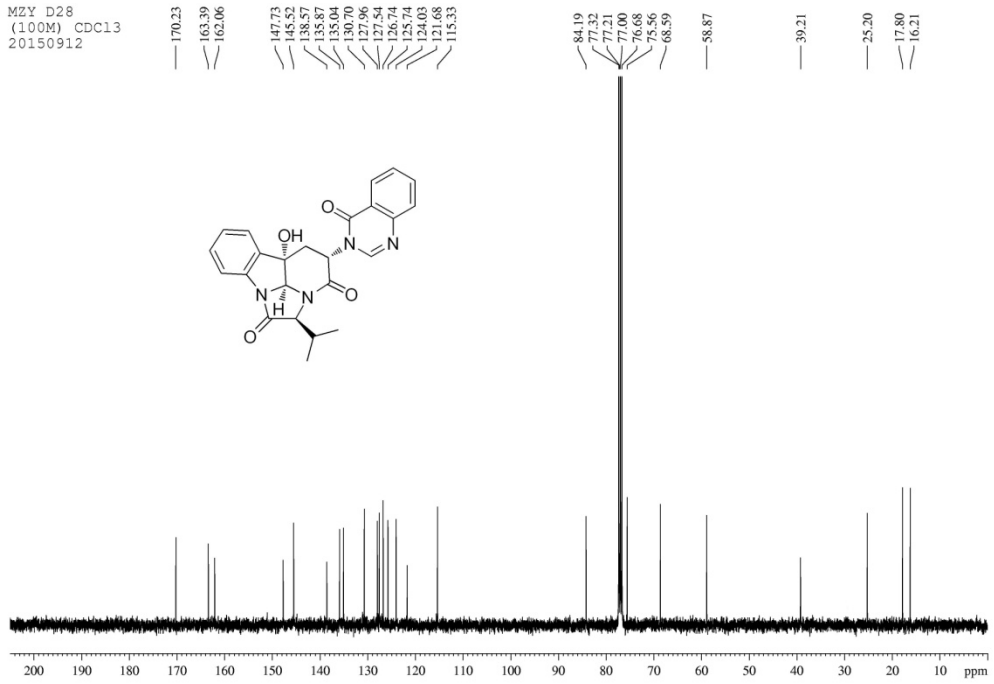
^{13}C NMR spectrum of **6** (DMSO-d_6)



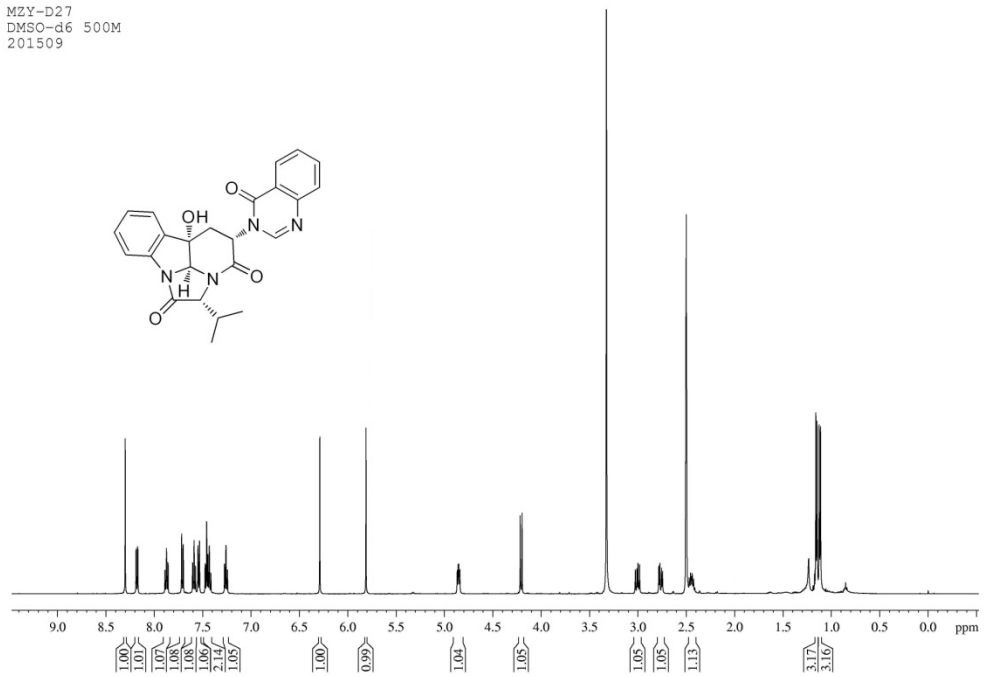
^{1}H NMR spectrum of ***ent*-8** ($CDCl_3$)



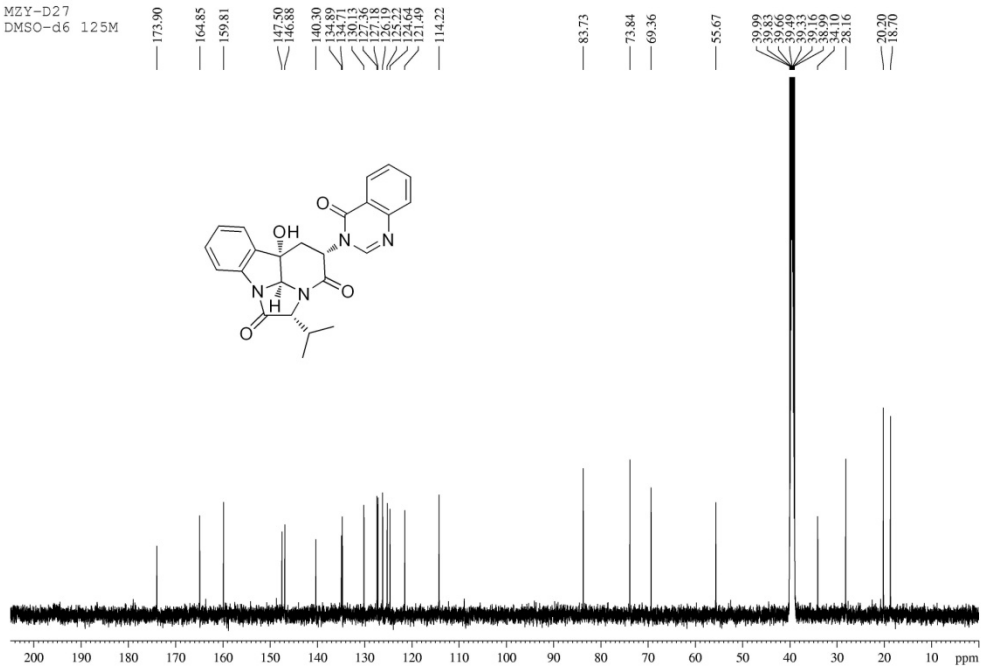
^{13}C NMR spectrum of ***ent*-8** ($CDCl_3$)



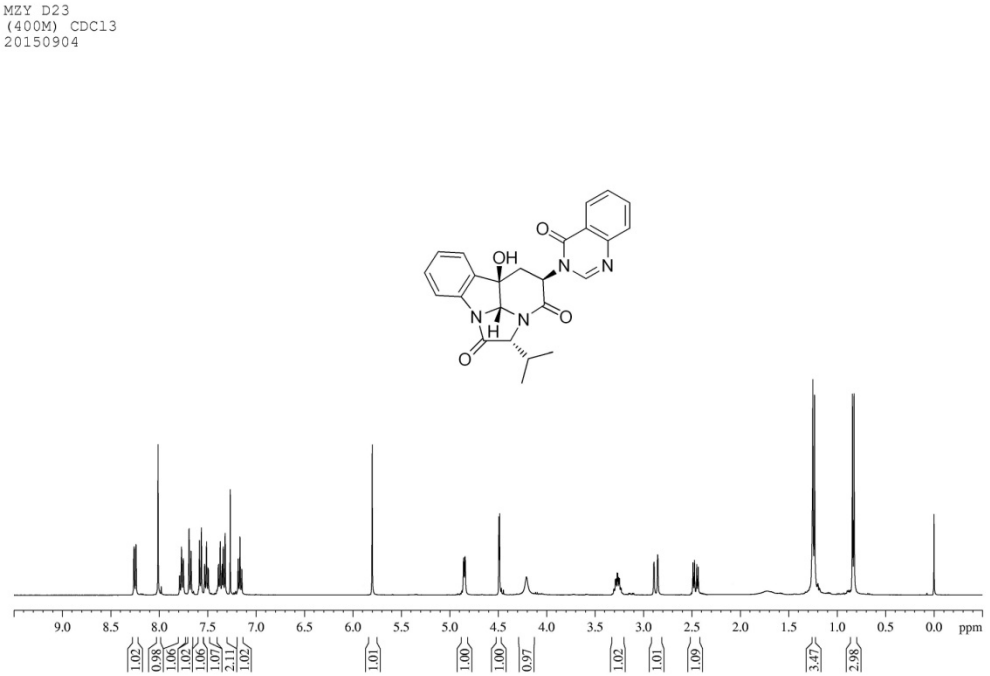
^{1}H NMR spectrum of ***ent*-6** (DMSO-d6)



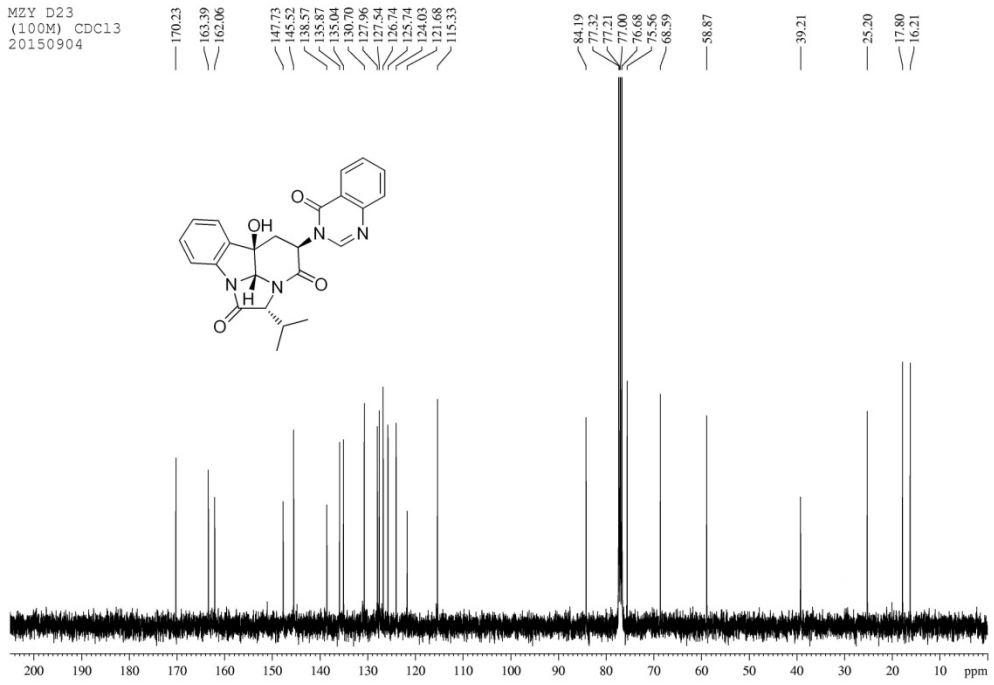
^{13}C NMR spectrum of ***ent*-6** (DMSO-d6)



^{1}H NMR spectrum of **8** ($CDCl_3$)

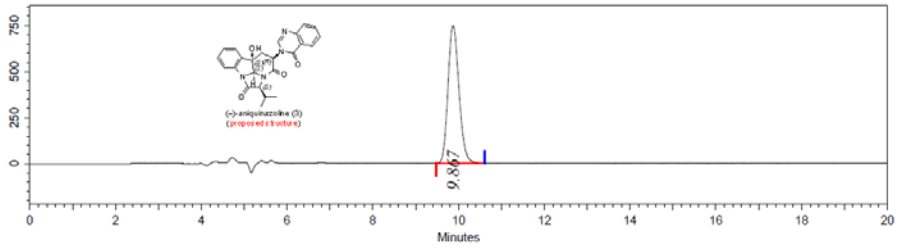


^{13}C NMR spectrum of **8** ($CDCl_3$)



HPLC analysis of compound **3** and *ent*-**3**

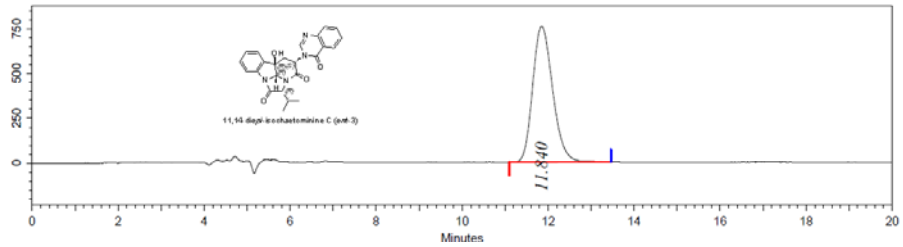
Shimadzu CLASS-VP V6.13 SP2 *Area % Report*
Column: Chirlapak AD-H
Mobile Phase: Hex/EtOH=30/70(v/v)
Flow Rate: 0.8mL/min
CT: 40℃ **Sample Name: 3**



Detector A-230 nm

Pk #	Retention Time	Area	Area Percent
1	9.867	13276112	100.00
Totals		13276112	100.00

Shimadzu CLASS-VP V6.13 SP2 *Area % Report*
Column: Chirlapak AD-H
Mobile Phase: Hex/EtOH=30/70(v/v)
Flow Rate: 0.8mL/min
CT: 40℃ **Sample Name: *ent*-3**

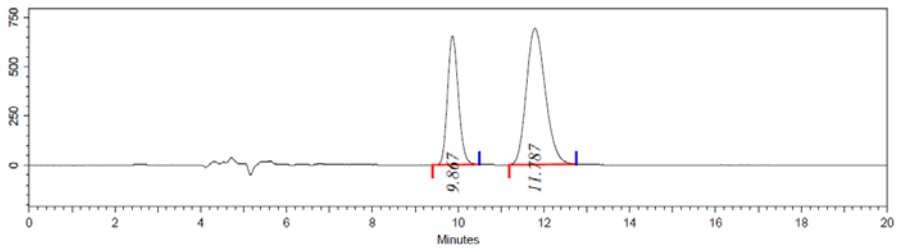


Detector A-230 nm

Pk #	Retention Time	Area	Area Percent
1	11.840	24538507	100.00
Totals		24538507	100.00

HPLC analysis of the mixture of compound **3** and *ent*-**3**

Shimadzu CLASS-VP V6.13 SP2 *Area % Report*
Column: Chirlapak AD-H
Mobile Phase: Hex/EtOH=30/70(v/v)
Flow Rate: 0.8mL/min
CT: 40℃ **Sample Name: 3 +*ent*-3**

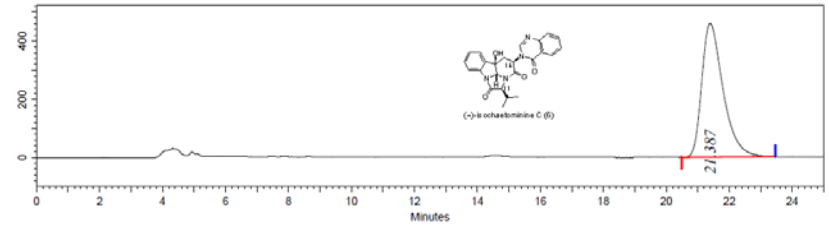


Detector A-230 nm

Pk #	Retention Time	Area	Area Percent
1	9.867	11448715	35.02
2	11.787	21239230	64.98
Totals		32687945	100.00

HPLC analysis of compound **6** and *ent*-**6**

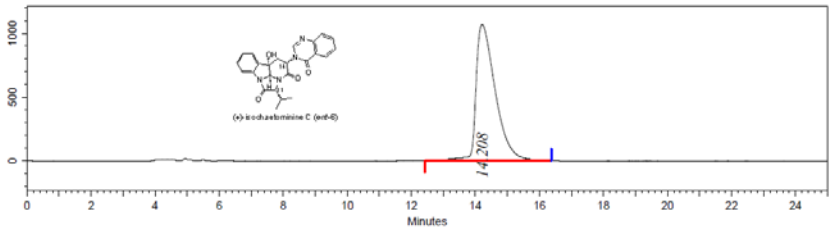
Shimadzu CLASS-VP V6.13 SP2 *Area % Report*
Column: Chirlapak AD-H
Mobile Phase: Hex/IPA=70/30(v/v)
Flow Rate: 0.8mL/min
CT: 30℃ **Sample Name: 6**



Detector A-230 nm

Pk #	Retention Time	Area	Area Percent
1	21.387	21587527	100.00
Totals		21587527	100.00

Shimadzu CLASS-VP V6.13 SP2 *Area % Report*
Column: Chirlapak AD-H
Mobile Phase: Hex/IPA=70/30(v/v)
Flow Rate: 0.8mL/min
CT: 30℃ **Sample Name: *ent*-6**

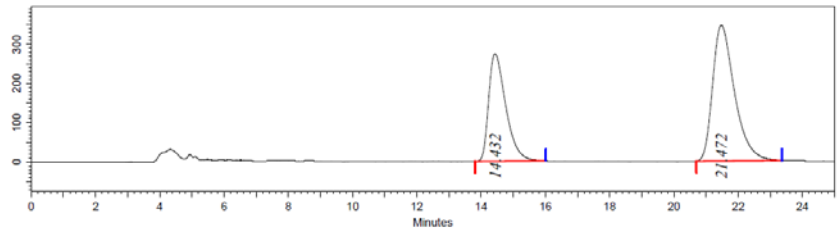


Detector A-230 nm

Pk #	Retention Time	Area	Area Percent
1	14.208	44695640	100.00
Totals		44695640	100.00

HPLC analysis of the mixture of compound **6** and *ent*-**6**

Shimadzu CLASS-VP V6.13 SP2 *Area % Report*
Column: Chirlapak AD-H
Mobile Phase: Hex/IPA=70/30(v/v)
Flow Rate: 0.8mL/min
CT: 30℃ **Sample Name: 6+ *ent*-6**

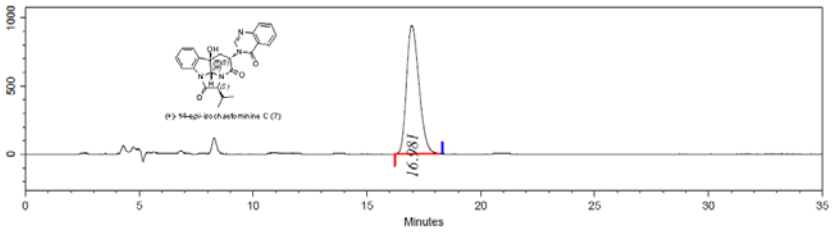


Detector A-230 nm

Pk #	Retention Time	Area	Area Percent
1	14.432	10145140	38.21
2	21.472	16402704	61.79
Totals		26547844	100.00

HPLC analysis of compound **7** and *ent*-**7**

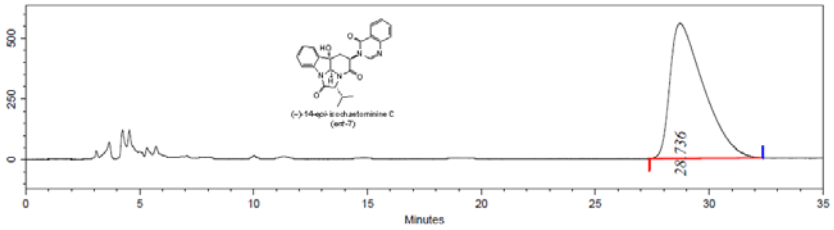
Shimadzu CLASS-VP V6.13 SP2 *Area % Report*
Column: Chirlapak AD-H
Mobile Phase: Hex/EtOH=30/70(v/v)
Flow Rate: 0.8mL/min
CT: 40℃ **Sample Name: (+)-14- *epi*-isochaetominine C (7)**



Detector A-230 nm

Pk #	Retention Time	Area	Area Percent
1	16.981	35841003	100.00
Totals		35841003	100.00

Shimadzu CLASS-VP V6.13 SP2 *Area % Report*
Column: Chirlapak AD-H
Mobile Phase: Hex/EtOH=30/70(v/v)
Flow Rate: 0.8mL/min
CT: 40℃ **Sample Name: (-)-14- *epi*-isochaetominine C (*ent*-7)**

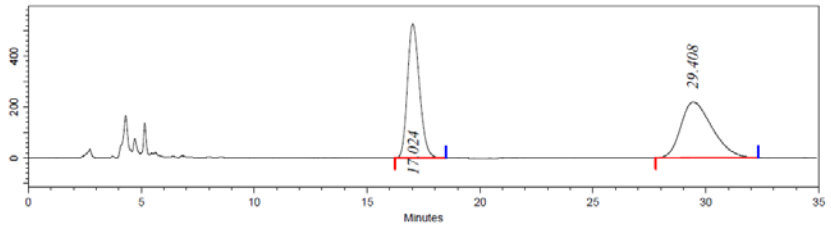


Detector A-230 nm

Pk #	Retention Time	Area	Area Percent
1	28.736	57425127	100.00
Totals		57425127	100.00

HPLC analysis of the mixture of compound **7** and *ent*-**7**

Shimadzu CLASS-VP V6.13 SP2 *Area % Report*
Column: Chirlapak AD-H
Mobile Phase: Hex/EtOH=30/70(v/v)
Flow Rate: 0.8mL/min
CT: 40℃ **Sample Name: 7 + *ent*-7**

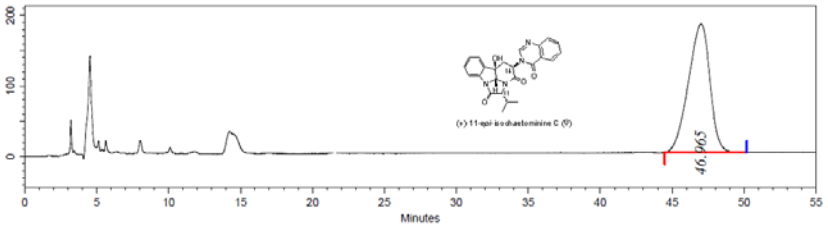


Detector A-230 nm

Pk #	Retention Time	Area	Area Percent
1	17.024	19419077	48.09
2	29.408	20959002	51.91
Totals		40378079	100.00

HPLC analysis of compound **8** and *ent*-**8**

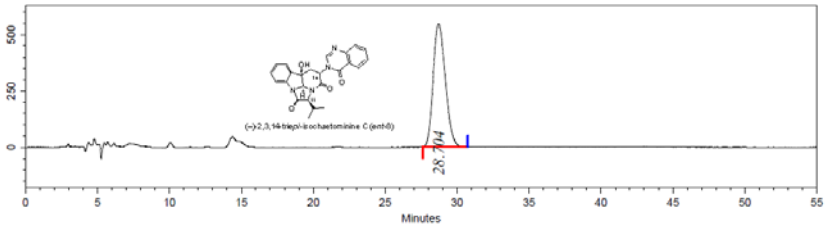
Shimadzu CLASS-VP V6.13 SP2 *Area % Report*
Column: Chirlapak AD-H
Mobile Phase: Hex/EtOH=30/70(v/v)
Flow Rate: 0.8mL/min
CT: 40℃ **Sample Name: 8**



Detector A-230 nm

Pk #	Retention Time	Area	Area Percent
1	46.965	19095447	100.00
Totals		19095447	100.00

Shimadzu CLASS-VP V6.13 SP2 *Area % Report*
Column: Chirlapak AD-H
Mobile Phase: Hex/EtOH=30/70(v/v)
Flow Rate: 0.8mL/min
CT: 40℃ **Sample Name: *ent*-8**

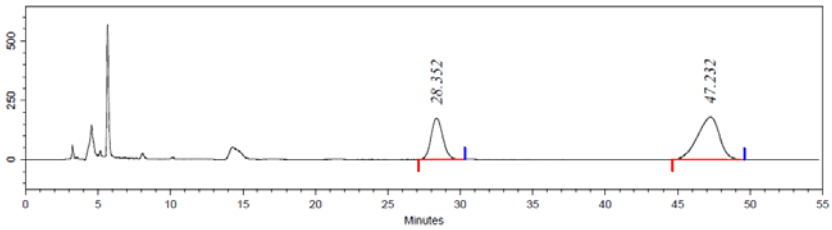


Detector A-230 nm

Pk #	Retention Time	Area	Area Percent
1	28.704	32190413	100.00
Totals		32190413	100.00

HPLC analysis of the mixture of compound **8** and *ent*-**8**

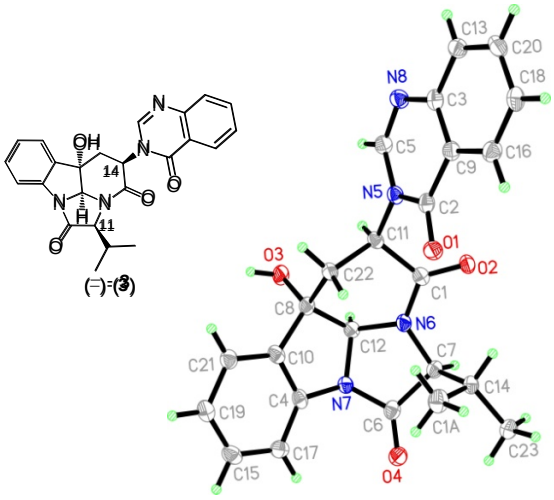
Shimadzu CLASS-VP V6.13 SP2 *Area % Report*
Column: Chirlapak AD-H
Mobile Phase: Hex/EtOH=30/70(v/v)
Flow Rate: 0.8mL/min
CT: 40℃ **Sample Name: 8+ent-8**



Detector A-230 nm

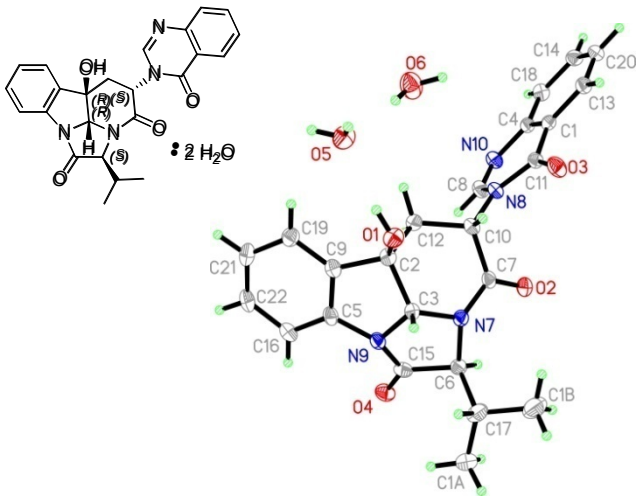
Pk #	Retention Time	Area	Area Percent
1	28.352	9705454	33.96
2	47.232	18869477	66.04
Totals		28574931	100.00

X-ray structure and crystal data for the proposed structure of (–)-aniquinazoline D (3)



Crystal Data [for (–)-**3]**. $C_{24}N_4O_4H_{22}$ (*M* =430.46 g/mol): orthorhombic, space group $P2_12_12_1$ (no.19), *a* =7.6889(2) Å, *b* =15.5382(5) Å, *c* =16.4272(6) Å, *V* =1962.58(11)Å^3, *Z* = 4,*T* = 99.8(5) K, μ(CuKα) = 0.832 mm^{-1}, *Dcalc* = 1.457 g/cm^3, 4748 reflections measured (7.84° ≤ 2θ ≤ 137.68°), 3186 unique (R_{int} = 0.0469, R_{sigma} = 0.0597) which were used in all calculations. The final R_1 was 0.0413 (>2sigma(I)) and wR_2 was 0.1026 (all data).

X-ray structure and crystal data of (+)-14-*epi*-isochaetominine C (7)·2H$_2$O



Crystal Data [for (+)-14-*epi*-isochaetominine C (**7**)·2H$_2$O**]**. $C_{24}N_4O_6H_{26}$ (*M* =466.50 g/mol): triclinic, space group P-1 (no. 2), *a* = 9.3200(6) Å, *b* = 10.5489(6) Å, *c* = 12.1772(7) Å, *α* = 95.818(5)°, *β* =90.490(5)°,*γ* = 111.805(6)°, *V* = 1104.43(12) Å^3, *Z* = 2, *T* = 173.00(14) K, μ(Cu Kα) = 0.849 mm^{-1}, *Dcalc* = 1.4027 g/cm^3, 5671 reflections measured (7.3° ≤ 2θ ≤ 120.36°), 3246 unique (R_{int} = 0.0442, R_{sigma} = 0.0662) which were used in all calculations. The final R_1 was 0.0380 (I>=2u(I)) and wR_2 was 0.0947 (all data).