Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Total synthesis and absolute configuration reassignment of mollenines A and B

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General Experimental

General information. Unless otherwise noted, commercially available reagents were used without further purification. All reactions were conducted in oven-dried or flame-dried glassware under a N_2 atmosphere, and at ambient temperature unless otherwise stated. All solvents were distilled prior to use: Benzene, THF, and toluene were distilled from Na/benzophenone, DMF, DCM, and triethylamine were distilled from CaH_2. All non-aqueous reactions were performed under an atmosphere of argon or nitrogen using oven-dried glassware and standard syringe in septa techniques. Concentration and evaporation under reduced pressure were performed at 10 - 400 mbar. Melting points were measured with a Stanford research system (OptiMelt-100). ^{1}H NMR spectra were recorded in $CDCl_3$ (unless stated otherwise) on a Bruker Avance 400 at 400 MHz (^{13}C NMR spectra at 100 MHz). Chemical shifts are reported as δ values referenced to either a tetramethylsilane internal standard. Data for ^{1}H NMR are reported as follows: chemical shift (ppm), multiplicity (s = singlet, brs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, coupling constant (Hz). Mass spectra were measured on an ABI Q-star Elite. The reaction progress was checked on pre-coated TLC plates. TLC was carried out using pre-coated sheets (Qingdao silica gel 60-G254, 0.2mm) which, after development, were visualized under UV light at 254 nm. Flash column chromatography was performed using the indicated solvents on Qingdao silica gel 60 (200-300 mesh ASTM). Yields refer to chromatographically purified compounds, unless otherwise stated.

*(2R,3aR,8aR)-1,8-Di-tert-butyl 2-methyl 3a-bromo-3,3a-dihydropyrrolo[2,3-b]indole-1,2,8(2H,8aH)-tricarboxylate (***7***)*. Method a: N-Bromosuccinimide (106.0 mg, 0.6 mmol) and AIBN (33.0 mg, 0.2 mmol) were added to a degassed solution of hexahydropyrroloindole **8**[1] (240.0 mg, 0.57 mmol) in carbon tetrachloride (50.0 mL), and the reaction mixture was heated to reflux. After 1 hour, the reaction mixture was allowed to cool to room temperature. The volatiles were removed under reduced pressure and the residue was purified by column chromatography (EtOAc: hexanes = 1:14) to afford **7** (50.0 mg, 18%) as a colorless oil.

Method b: NaBr aqueous solution (2.0 g, in 10 mL water) was added to a solution of cyclopropylazetoindoline **17**[1] (1.8 g, 4.0 mmol) in THF (20.0 mL) at 0 °C. The reaction mixture was allowed to warm up to 25 °C within 1 hour and stirred for 10 hours. Volatiles were removed in *vacuo*, the residue was extracted with CH_2Cl_2/H_2O (100.0 mL, 1:1). The organic phase was concentrated in vacuum. The residue was purified by flash chromatography (EtOAc: hexanes = 1:14) to produce **7** (2.0 g, 95% yield) as a colorless oil. $[\alpha]_D^{20}$ = -41.0 (c 1.4, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.28 (dd, J = 7.6, 3.6 Hz, 2H), 7.05 (t, J = 7.6 Hz, 1H), 6.45 (s, 1H), 4.54 (d, J = 8.4 Hz, 1H), 3.28 (d, J = 13.2 Hz, 1H), 3.18 – 3.02 (m, 1H), 3.13 (s, 3H) 1.60 (s, 9H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 170.7, 152.1, 142.5, 132.5, 130.6, 123.9, 118.1, 84.3, 82.1, 81.2, 60.3, 59.6, 52.0, 43.1, 28.3, 28.2; HRESIMS *m/z* 519.1093 $[M+Na]^+$, calcd for $C_{22}H_{29}BrN_2O_6Na$, 519.1101.

*(2R,3aS,8aR)-1,8-Di-tert-butyl 2-methyl 3a-allyl-3,3a-dihydropyrrolo[2,3-b]indole-1,2,8(2H,8aH)-tricarboxylate (**18**).* Method a: Allylzinc (II) bromide[2] (20.0 mL, 3.0 mmol, 0.15 M in THF) was added to a solution of cyclopropylazetoindoline **17** (1.0 g, 2.4 mmol) in THF (20.0 mL) at -30 °C. The reaction mixture was allowed to warm up to 0 °C within 1 hour and quenched with ice water (20.0 mL). Volatiles were removed in vacuum, the residue was extracted with CH_2Cl_2 (50.0 mL). The organic phase was concentrated in vacuum. The residue was purified by column chromatography (EtOAc: hexanes = 1:15) to produce **18** (0.16 g, 15% yield) and **7** (0.12 g, 10% yield) as colorless oil.

Method b: Allyltributyltin (1.5 g, 4.5 mmol) and AIBN (118 mg, 0.72 mmol) were added to a degassed solution of **7** (1.8 g, 3.6 mmol) in toluene (60.0 mL), and the mixture was heated at 90 ^{0}C for 10 hours, and then cooled to room temperature. The volatiles were removed under reduced pressure and the residue was purified by column chromatography (EtOAc: hexanes = 1:10) to afford **18** (1.4 g, 85%). $[\alpha]_D^{20}$ = -20.0 (*c* 0.7, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.52 (s, 1H), 7.23 – 7.14 (m, 1H), 7.04 (d, J = 6.7 Hz, 1H), 6.99 – 6.91 (m, 1H), 6.03 (s, 1H), 5.54 (td, J = 17.2, 7.6 Hz, 1H), 5.02 (t, J = 12.0 Hz, 2H), 4.54 (d, J = 8.8 Hz, 1H), 3.09 (d, J = 17.2

Hz, 3H), 2.61 (d, J = 12.0 Hz, 1H), 2.45 – 2.30 (m, 3H), 1.56 (s, 9H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 152.3, 143.2, 134.2, 132.5, 128.4, 123.1, 122.9, 118.9, 117.4, 81.1, 80.5, 59.5, 55.5, 51.7, 42.2, 38.3, 28.3, 28.2; HR-ESIMS *m/z*: calculated for $C_{25}H_{34}N_2O_6Na$ $[M+Na]^+$: 481.2314, found 481.2309.

*(2R,3aS,8aR)-1,8-Di-tert-butyl 2-((R)-1-methoxy-4-methyl-1-oxopentan-2-yl) 3a-allyl-3,3a-dihydropyrrolo[2,3-b]indole-1,2,8(2H,8aH)-tricarboxylate (**4**).*

To a solution of **18** (1.3 g, 2.8 mmoL) in a mixture solvent of CH_3OH and THF (40 mL, 1:1), LiOH (0.5 g, 20.0 mmoL, dissolved in 20 mL water) was added at 0 ^{0}C. The mixture was stirred for 12 hours at 25 ^{0}C. Removal the organic solvent under vacuum, the residue was extracted with H_2O/CH_2Cl_2 (200 mL, 1:1). The aqueous layer was acidified with $NaHSO_4$ (pH < 3) and extracted with EtOAc (50.0 mL x 3). The organic layer were combined and concentrated to give **5** (1.2 g, 95%) as a colorless foam, which was used directly in the next step without purification.

A solution of **5** (1.0 g, 2.2 mmol), N, N-diisopropylethylamine (0.52 g, 4.0 mmol), and 2,4,6-trichlorobenzoyl chloride (0.73 g, 3.0 mmol) in dry THF (50.0 mL) were stirred for 1 hour at 0 °C. DMAP (60.0 mg, 0.5 mmol) and (*R*)-methyl 2-hydroxy-4-methylpentanoate (**6**, 0.32 g, 2.2 mmol) were dissolved in dry THF (10.0 mL) and added to the above reaction. The mixture was stirred at 25 °C for 10 hours, and then concentrated in vacuum.

The resulting mixture was extracted with EtOAc and water (200.0 mL, 1:1). After separation, the organic phase was concentrated in vacuum. The residue was purified by column chromatography (EtOAc: hexanes = 1:10) to afford **4** (0.81 g, 65%) as a colorless oil. $[\alpha]_D^{20}$ = -25.6 (*c* 6, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (brs, 1H), 7.23 – 7.15 (m, 1H), 7.06 (t, J = 9.2 Hz, 1H), 6.99 – 6.90 (m, 1H), 6.05 (s, 1H), 5.56 (td, J = 17.2, 7.6 Hz, 1H), 5.18 – 4.94 (m, 2H), 4.60 (t, J = 7.6 Hz, 1H), 4.46 – 4.40 (m, 1H), 3.65 (s, 3H), 2.70 (dd, J = 17.2, 9.2 Hz, 1H), 2.50 – 2.36 (m, 3H), 1.57 (brs, 9H), 1.57 – 1.47 (m, 3H), 1.47 (brs, 9H), 0.86 (d, J = 6.4 Hz, 3H), 0.83 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 170.6, 152.3, 142.8, 132.5, 128.4, 123.6, 122.9, 119.0, 117.0, 81.2, 80.6, 71.4, 69.1, 59.4, 51.8, 42.4, 39.7, 28.2, 24.2, 22.8, 22.3; HRESIMS *m/z* 595.2995 $[M+Na]^+$, calcd for $C_{31}H_{44}N_2O_8Na$, 595.2990.

*(2R,3aS,8aR)-(R)-1-Methoxy-4-methyl-1-oxopentan-2-yl 3a-allyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carboxylate (**19**)*. To a solution of **4** (0.5 g, 0.87 mmol) in CH_2Cl_2 (20.0 mL) was added DIPEA (0.66 mL, 4.0 mmol) at 0 °C, followed by dropwise addition of TMSOTf (0.36 mL, 2.0 mmol) at 0 °C, stirred for 20 min. The cooling bath was removed and the mixture was stirred at room temperature for 12 hours. The reaction was quenched by addition of ice water (50.0 mL). Layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (50.0 mL). The combined organic layers were concentrated in vacuum. The residue

was purified by flash chromatography (EtOAc: Hexane = 1:5) to produce the **19** (0.29 g, 90%) as a colorless oil. $[\alpha]_D^{20}$ = -20.5 (*c* 1, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.10 – 6.97 (m, 2H), 6.71 (t, J = 7.6 Hz, 1H), 6.54 (d, J = 7.6 Hz, 1H), 5.83 – 5.56 (m, 1H), 5.18 – 5.01 (m, 2H), 4.87 (s, 1H), 4.83 (dd, J = 8.4, 4.4 Hz, 1H), 3.98 (dd, J = 7.6, 4.4 Hz, 1H), 3.64 (s, 3H), 2.57 – 2.38 (m, 4H), 1.73 – 1.53 (m, 3H), 0.91 (d, J = 6.4 Hz, 3H), 0.88 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 170.8, 148.9, 134.1, 133.4, 128.1, 123.9, 119.1, 118.1, 109.6, 82.8, 71.2, 59.4, 57.2, 52.1, 43.0, 41.6, 39.8, 24.4, 22.8, 21.7; HRESIMS *m/z* 373.2125 $[M+H]^+$, calcd for $C_{21}H_{29}N_2O_4$, 373.2122.

*(2R,3aS,8aR)-Methyl 3a-allyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carboxylate (**20**)*. Iodotrimethylsilane (1.0 mL, 7.0 mmol) was added dropwise to a solution of **18** (1.0 g, 2.2 mmol) in acetonitrile (40.0 mL) at 0 ºC. The resulting yellow solution was stirred at 0 ºC. When starting material was consumed, which was monitored by TLC. N,N-Diisopropylethylamine (1.6 mL, 10.0 mmol) was introduced via a syringe at 0 ºC. The cooling bath was removed and the reaction mixture was stirred for 20 min. Volatiles were removed in vacuum, and ice water (50.0 mL) was added to the residue. The aqueous solution was then extracted with EtOAc (50.0 mL x 3). The combined organic layers were concentrated in vacuum. The residue was purified by flash chromatography (EtOAc: Hexane = 1:1) to give **20** (0.51 g, 90%) as a colorless oil. $[\alpha]_D^{20}$ = -88.0 (*c*

1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (dd, J = 20.0, 15.2 Hz, 2H), 6.70 (t, J = 7.6 Hz, 1H), 6.55 (d, J = 8.0 Hz, 1H), 5.71 (td, J = 15.2, 7.6 Hz, 1H), 5.13 – 5.01 (m, 2H), 4.85 (s, 1H), 3.88 (dd, J = 7.6, 3.2 Hz, 1H), 3.33 (s, 3H), 2.55 – 2.31 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 149.6, 134.1, 132.8, 128.2, 123.8, 118.7, 118.1, 109.4, 82.3, 59.9, 57.0, 51.8, 42.8, 41.4. HRESIMS *m/z* 259.1433 [M+H]$^+$, calcd for $C_{15}H_{19}N_2O_2$, 259.1441.

(2R,3aS,8aS)-Methyl 3a-allyl-1-((R)-2-hydroxy-4-methylpentanoyl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carboxylate (**22**). 2,4,6-Collidine (0.65 mL, 5.0 mmol) was added to a solution of **21** (0.3 g, 2.2 mmol) and BOPCl (0.76 g, 3.0 mmol) in THF (30.0 mL) at 25 °C. The mixture was stirred for 10 hours at 25 °C, and **20** (0.5 g, 1.9 mmol) was added and stirred for 10 hours at 25 °C, and the reaction was then quenched by the addition of ice H_2O (50.0 mL). Removal of THF under vacuum, the aqueous residue was extracted with EtOAc (50.0 mL x 3). The combined organic layers were concentrated in *vacuo*. The residue was purified by column chromatography on silica gel (EtOAc: hexanes = 1:8) to give **22** (0.47 g, 67%) as a colorless oil. $[\alpha]_D^{20}$ = -86.6 (*c* 0.9, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) main peaks of rotamers δ 7.07 – 6.97 (m, 2H), 6.69 (t, J = 7.6 Hz, 1H), 6.58 (d, J = 7.6 Hz, 1H), 5.71 (qd, J = 16.4, 7.6 Hz, 1H), 5.32 (s, 1H), 5.17 – 5.04 (m, 2H), 4.40 (t, J = 8.4 Hz, 1H), 4.26 (4.00) (dd, J = 8.4, 4.4 Hz, 1H), 3.17 (s, 3H), 2.80 (d, J = 13.2 Hz, 1H), 2.53 – 2.43 (m, 2H), 1.97 – 1.85 (m, 1H), 1.70 – 1.58 (1.55-1.51) (m, 2H), 1.28 – 1.18

(1.08 – 1.02) (m, 1H), 0.99 – 0.88 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) main peaks of rotamers δ 175.7, 170.6, 149.8, 132.9, 129.4, 129.0, 123.8, 118.9, 118.6, 109.2, 81.4, 67.9, 59.2, 52.7, 43.2, 41.9, 39.5, 24.4, 23.5, 23.2, 21.4; HRESIMS *m/z* 373.2126 $[M+H]^+$, calcd for $C_{21}H_{29}N_2O_4$, 373.2122.

*(3R,5aS,10bS,11aR)-10b-Allyl-3-isobutyl-5a,6,11,11a-tetrahydro-[1,4]oxazino[4',3':1,5]pyrrolo[2,3-b]indole-1,4(3H,10bH)-dione (**3**).* PTSA (0.17 g, 1.0 mmol) was added to a solution of **22** (0.4 g, 1.0 mmol) in toluene (20.0 mL). The mixture was heated and stirred for 20 min at 110 ^{0}C, cooled, and quenched by the addition of saturated aqueous $NaHCO_3$ (50.0 mL). The aqueous residue was extracted with EtOAc (50.0 mL x 3). The combined organic layers were concentrated in vacuum. The residue was purified by column chromatography on silica gel (EtOAc: hexanes = 1:19) to give **3** (180.0 mg, 52%) as a colorless oil. $[\alpha]_D^{20}$ = -131.0 (*c* 1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (dd, J = 15.2, 7.6 Hz, 2H), 6.78 (t, J = 7.6 Hz, 1H), 6.59 (d, J = 7.6 Hz, 1H), 5.71 (tt, J = 15.2, 7.6 Hz, 1H), 5.45 (s, 1H), 5.20 – 5.12 (m, 2H), 4.75 (dd, J = 9.6, 2.4 Hz, 1H), 4.42 (t, J = 8.0 Hz, 1H), 2.70 (dd, J = 9.6, 7.6 Hz, 1H), 2.64 – 2.42 (m, 3H), 1.98 – 1.85 (m, 2H), 1.83 – 1.69 (m, 1H), 0.96 (d, J = 5.6 Hz, 3H), 0.93 (d, J = 5.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 166.8, 147.2, 132.7, 131.2, 128.8, 123.2, 119.6, 119.5, 109.8, 81.1, 77.2, 56.9, 55.5, 41.3, 38.2, 37.6, 23.9, 23.2, 21.3; HRESIMS *m/z* 341.1861 $[M+H]^+$, calcd for $C_{20}H_{25}N_2O_3$, 341.1860.

*(3R,5aS,10bS,11aR)-3-Isobutyl-10b-(3-methylbut-2-en-1-yl)-5a,6,11,11a-tetrahydro-[1,4]oxazino[4',3':1,5]pyrrolo[2,3-b]indole-1,4(3H,10bH)-dione (**1**)*. To a 25 mL flame-dried flask was added diketomorpholine **3** (160 mg, 0.47 mmol), Hoveyda-Grubbs II catalyst (32.0 mg, 0.05 mmol) was added, followed by 2-methyl-2-butene (4.0 mL) and CH_2Cl_2 (15.0 mL). The flask was equipped with a condenser and heated to 38 °C for 10 hours. The reaction mixture was filtered through a silica gel plug, eluting with 50% EtOAc in hexanes. The filtrate was concentrated in *vacuo*. The residue was purified by column chromatography on silica gel (CH_2Cl_2: hexanes = 1:3) to afford **1** (107 mg, 62%) as a colorless oil. $[\alpha]_D^{20}$ = -123.5 (*c* 1.4, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (dt, J = 13.5, 7.0 Hz, 2H), 6.77 (t, J = 7.0 Hz, 1H), 6.59 (d, J = 7.5 Hz, 1H), 5.38 (s, 1H), 5.30 (s, 1H), 5.12 (t, J = 7.5 Hz, 1H), 4.74 (dd, J = 9.0, 2.0 Hz, 1H), 4.40 (t, J = 7.5 Hz, 1H), 2.69 (dd, J = 13.5, 7.0 Hz, 1H), 2.58 (dd, J = 13.5, 8.5 Hz, 1H), 2.48 (dd, J = 13.5, 8.5 Hz, 1H), 2.44 – 2.36 (m, 1H), 1.97 – 1.89 (m, 2H), 1.81 – 1.75 (m, 1H), 1.71 (s, 3H), 1.59 (s, 3H), 0.96 (d, J = 6.0 Hz, 3H), 0.92 (d, J = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 166.8, 147.1, 136.1, 131.7, 128.7, 123.2, 119.5, 118.3, 109.7, 81.2, 77.2, 57.0, 56.2, 37.7, 37.6, 35.0, 26.0, 23.9, 23.2, 21.2, 18.1; HRESIMS *m*/*z* 369.2170 $[M+H]^+$, calcd for $C_{22}H_{29}N_2O_3$, 369.2173.

*(2S,3aS,8aR)-1,8-Di-tert-butyl 2-methyl 3a-allyl-3,3a-dihydropyrrolo[2,3-b]indole-1,2,8(2H,8aH)-tricarboxylate (**23**)*. Allyltributyltin (1.7 g, 5.0

mmol) and AIBN (130 mg, 0.8 mmol) were added to a degassed solution of **16** (2.0 g, 4.0 mmol) in toluene (50 mL), and the mixture was heated at 90 ^{0}C for 10 hours, and the reaction was cooled to room temperature. The volatiles were removed under reduced pressure and the residue was purified by column chromatography (EtOAc: hexanes = 1:10) to afford **23** (1.5 g, 84%) as a colorless oil. $[\alpha]_D^{20}$ = -59.6 (*c* 3, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (brs, 1H), 7.23 (t, J = 7.0 Hz, 1H), 7.13 (d, J = 7.0 Hz, 1H), 7.06 (d, J = 6.5 Hz, 1H), 6.03 (s, 1H), 5.52 (d, J = 7.5 Hz, 1H), 5.02 (d, J = 16.5 Hz, 2H), 3.89 (dd, J = 16.5, 9.0 Hz, 1H), 3.72 (s, 3H), 2.55 (dd, J = 12.0, 6.0 Hz, 1H), 2.44 – 2.33 (m, 2H), 2.12 (t, J = 12.0 Hz, 1H), 1.56 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9, 152.3, 142.2, 134.7, 132.2, 128.4, 123.5, 122.7, 119.0, 81.3, 80.3, 59.3, 55.4, 52.0, 41.9, 37.7, 28.3; HRESIMS *m/z* 481.2316 $[M+Na]^+$, calcd for $C_{25}H_{34}N_2O_6Na$, 481.2309.

*(2S,3aS,8aR)-Methyl 3a-allyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carboxylate (**24**)*. Compounds **24** (colorless oil, 0.5 g, 90%) was prepared from **23** (1.0 g, 2.2 mmol) with iodotrimethylsilane (1.0 mL, 7.0 mmol) under the same procedure as for **20**. $[\alpha]_D^{20}$ = -98.5 (*c* 1.4, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 – 6.96 (m, 2H), 6.73 (t, J = 7.0 Hz, 1H), 6.56 (t, J = 10.5 Hz, 1H), 5.75 – 5.60 (m, 1H), 5.11 – 4.97 (m, 3H), 3.90 (brs, 2H), 3.76 – 3.72 (m, 1H), 3.69 (s, 3H), 2.60-2.50 (m, 1H), 2.49 – 2.35 (m, 2H), 2.08 – 1.97 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 150.0,

134.1, 132.2, 128.3, 123.6, 118.8, 118.3, 109.1, 82.0, 59.2, 58.1, 52.2, 44.1, 43.1; HRESIMS *m/z* 259.1436 $[M+H]^+$, calcd for $C_{15}H_{19}N_2O_2$, 259.1441.

*(2S,3aS,8aS)-Methyl 3a-allyl-1-((R)-2-hydroxy-4-methylpentanoyl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carboxylate (**25**).* Compounds **25** (colorless oil, 0.39 g, 68%) was prepared from **24** (0.4 g, 1.5 mmol) with (*R*)-2-hydroxy-4-methylpentanoic acid (**21**) (0.2 g, 1.5 mmol) under the same procedure as for **22**. $[\alpha]_D^{20}$ = -60.8 (*c* 1.2, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (dd, J = 12.0, 4.0 Hz, 2H), 6.82 – 6.74 (m, 1H), 6.62 (d, J = 7.6 Hz, 1H), 5.74 – 5.60 (m, 1H), 5.27 (s, 1H), 5.09 (t, J = 12.0 Hz, 2H), 4.11 – 4.03 (m, 1H), 3.89 (dd, J = 12.0, 6.0 Hz, 1H), 3.74 (s, 3H), 2.60 (dd, J = 13.6, 6.4 Hz, 1H), 2.50 (dt, J = 13.6, 6.8 Hz, 2H), 2.23 (dd, J = 21.6, 9.6 Hz, 1H), 1.93 – 1.81 (m, 1H), 1.60-1.42 (m, 2H), 0.94 (d, J = 2.4 Hz, 3H), 0.93 (d, J = 2.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.5, 171.4, 149.3, 133.3, 131.0, 128.8, 123.3, 119.2, 118.9, 109.2, 81.9, 69.7, 58.4, 57.8, 52.6, 43.8, 42.5, 42.5, 24.6, 23.4, 21.4; HRESIMS *m/z* 373.2120 $[M+H]^+$, calcd for $C_{21}H_{29}N_2O_4$, 373.2122.

*(3S,5aS,10bS,11aS)-10b-Allyl-3-isobutyl-5a,6,11,11a-tetrahydro-[1,4]oxazino[4',3':1,5]pyrrolo[2,3-b]indole-1,4(3H,10bH)-dione (**29**).* 2,4,6-Collidine (6.5 mL, 5.0 mmol) was added to a solution of (*S*)-2-hydroxy-4-methylpentanoic acid (**27**, 0.2 g, 1.5 mmol) and BOPCl (0.76 g, 3.0 mmol) in THF (30.0 mL) at 25 °C. The mixture was stirred for 10 hours at 25 °C, and **24** (0.4 g, 1.5 mmol) was added and stirred for another 10

hours at 25 °C, and then quenched by the addition of ice H_2O (50.0 mL). After removal of THF under vacuum, the aqueous residue was extracted with EtOAc (100.0 mL). The organic layers were concentrated in *vacuo*. The residue was used directly in the next step without purification. PTSA (0.25 g, 1.5 mmol) was added to a solution of above residue in toluene (20.0 mL). The mixture was stirred at 110 ^{0}C for 20 min, cooled, and quenched by the addition of saturated aqueous $NaHCO_3$ (50.0 mL). The aqueous residue was extracted with EtOAc (50.0 mL). The organic layers were concentrated in vacuum. The residue was purified by column chromatography on silica gel (EtOAc: hexanes = 1:15) to give **29** (0.18 g, 35%, 2 steps) as a colorless oil. $[\alpha]_D^{20}$ = -375 (*c* 1.4, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (t, J = 8.0 Hz, 2H), 6.73 (t, J = 7.5 Hz, 1H), 6.55 (d, J = 7.5 Hz, 1H), 5.72 – 5.58 (m, 1H), 5.26 (s, 1H), 5.05 (dd, J = 21.0, 11.5 Hz, 2H), 4.66 – 4.59 (m, 1H), 4.11 – 4.04 (m, 1H), 2.65 (dt, J = 15.5, 7.5 Hz, 1H), 2.44 – 2.39 (m, 2H), 2.36 (dd, J = 19.0, 9.5 Hz, 1H), 1.92 – 1.82 (m, 2H), 1.71 (dd, J = 19.0, 9.5 Hz, 1H), 0.91 (d, J = 6.0 Hz, 3H), 0.84 (d, J = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 166.0, 148.5, 132.5, 130.1, 129.1, 123.4, 119.5, 119.4, 109.7, 79.5, 77.5, 57.4, 55.3, 41.6, 38.4, 37.7, 24.0, 23.2, 21.2; HRESIMS *m/z* 341.1855 $[M+H]^+$, calcd for $C_{20}H_{25}N_2O_3$, 341.1860.

(3S,5aS,10bS,11aS)-3-Isobutyl-10b-(3-methylbut-2-en-1-yl)-5a,6,11,11a-tetrahydro-[1,4]oxazino[4',3':1,5]pyrrolo[2,3-b]indole-1,4(3H,10bH)-

*dione (**30**)*. Compounds **30** (colorless oil, 99.0 mg, 61%) was prepared from **29** (150 mg, 0.44 mmol) with 2-methyl-2-butene (3.0 mL) under the same procedure as for **1**. $[\alpha]_D^{20}$ = -322 (*c* 6, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.17 – 7.09 (m, 2H), 6.81 (td, J = 7.6, 0.8 Hz, 1H), 6.64 (dd, J = 5.6, 2.4 Hz, 1H), 5.31 (s, 1H), 5.17 (dd, J = 14.0, 6.8 Hz, 1H), 5.13 (s, 1H), 4.72 (dd, J = 9.6, 2.8 Hz, 1H), 4.21 – 4.11 (m, 1H), 2.72 (dt, J = 12.8, 6.4 Hz, 1H), 2.45 (dt, J = 12.8, 9.6 Hz, 3H), 2.02 – 1.93 (m, 2H), 1.82 (t, J = 9.6 Hz, 1H), 1.74 (s, 3H), 1.56 (s, 3H), 1.00 (d, J = 6.4 Hz, 3H), 0.94 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 166.0, 148.4, 136.2, 130.8, 128.9, 123.2, 119.5, 118.0, 109.7, 79.4, 77.5, 57.5, 56.0, 37.8, 37.7, 35.0, 25.9, 24.0, 23.2, 21.2, 17.9; HRESIMS *m*/*z* 369.2175 $[M+H]^+$, calcd for $C_{22}H_{29}N_2O_3$, 369.2173.

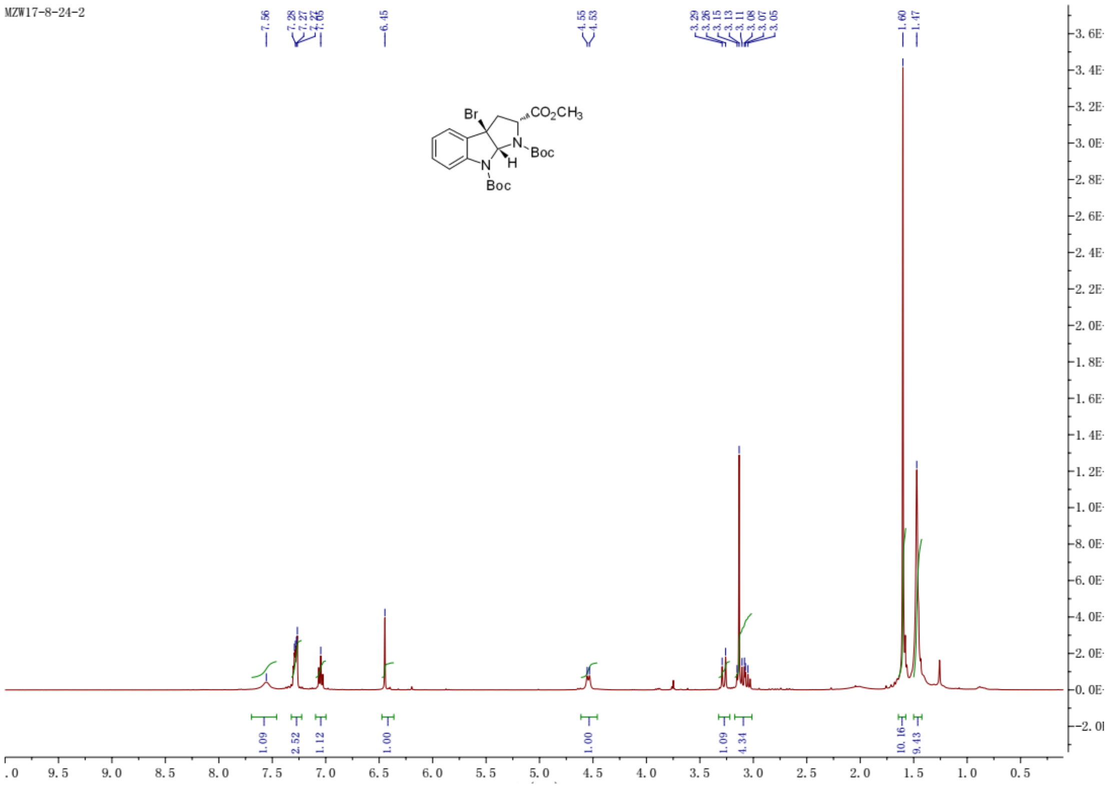
*(3S,5aS,10bS,11aS)-3-Isobutyl-10b-(3-methylbut-2-en-1-yl)-1,4-dioxo-1,3,4,10b,11,11a-hexahydro-[1,4]oxazino[4',3':1,5]pyrrolo[2,3-b]indole-6(5aH)-carbaldehyde (**31**)*. To a solution of **30** (50.0 mg, 0.14 mmol) in dry THF (5.0 mL), formic acid (0.5 mL) was added and stirred for 10 hours. After removal of the solvent and excess formic acid under vacuum, saturated aqueous $NaHCO_3$ (20.0 mL) was added to the above residue. The aqueous residue was extracted with EtOAc (50.0 mL). The organic layer was concentrated in vacuum. The residue was purified by column chromatography on silica gel (EtOAc: hexanes = 1:10) to give **31** (44 mg, 82%) as a colorless oil. $[\alpha]_D^{20}$ = -250 (*c* 1, CH_2Cl_2); ^1H NMR (500 MHz,

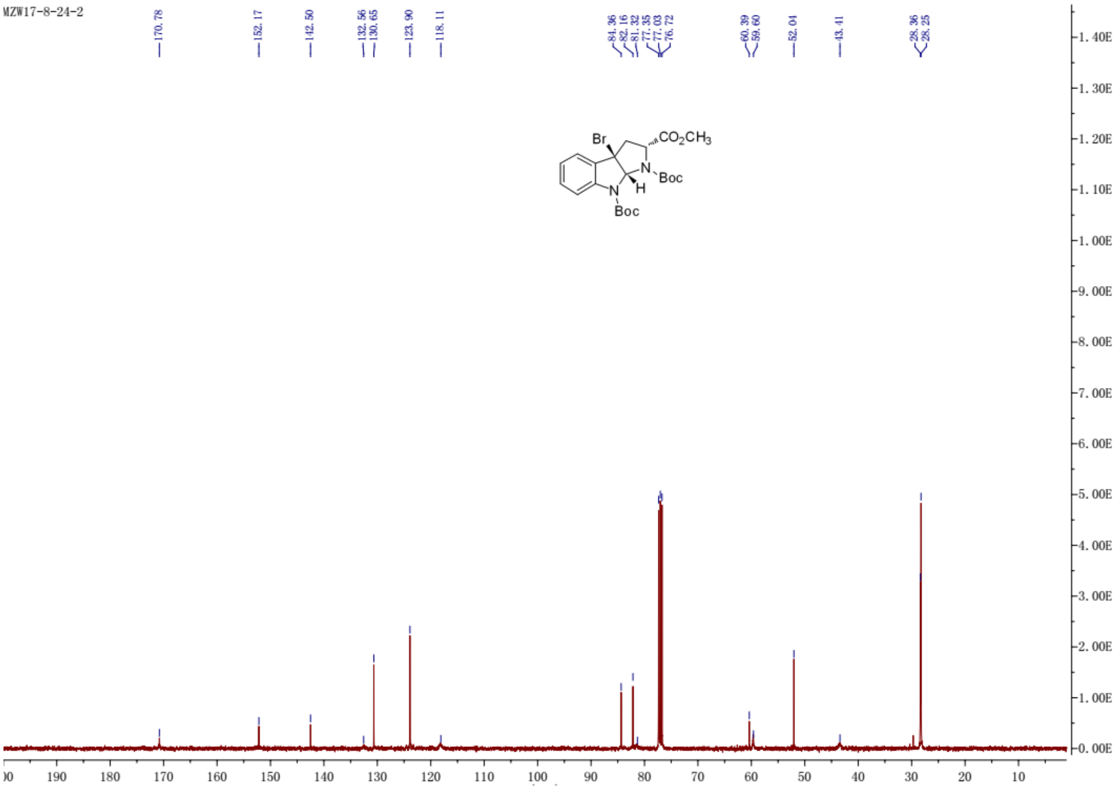
$CDCl_3$) δ 9.03 (s, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.32 (t, J = 7.5 Hz, 1H), 7.24 (d, J = 7.5 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 5.81 (s, 1H), 5.03 (t, J = 7.0 Hz, 1H), 4.80 – 4.73 (m, 1H), 4.18 (dd, J = 10.5, 6.5 Hz, 1H), 2.80 (dd, J = 13.5, 6.5 Hz, 1H), 2.52 – 2.36 (m, 3H), 2.01 – 1.88 (m, 2H), 1.81 (t, J = 10.5 Hz, 1H), 1.70 (s, 3H), 1.52 (s, 3H), 0.98 (d, J = 6.0 Hz, 3H), 0.92 (d, J = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.0, 165.5, 161.7, 140.1, 137.4, 133.9, 129.4, 125.4, 123.1, 117.3, 116.9, 78.4, 77.4, 57.4, 54.9, 38.8, 37.6, 35.8, 25.9, 23.9, 23.2, 21.2, 18.0; HRESIMS *m*/*z* 397.2123 $[M+H]^+$, calcd for $C_{23}H_{29}N_2O_4$, 397.2122.

Reference

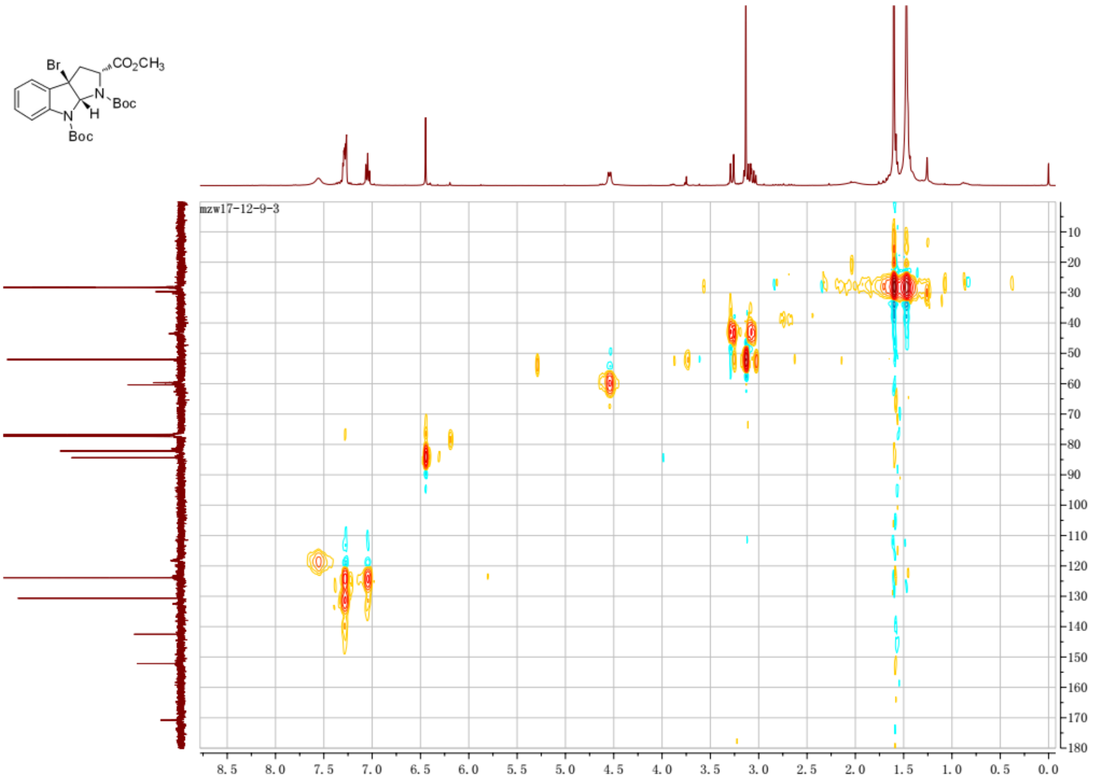
1. V. R. Espejo, X. B. Li, and J. D. Rainier, *J. Am. Chem. Soc.*, 2010, **132**, 8282.
2. E. Negishi, L. D. Boardman, H. Sawada, V. Bagheri, A. T. Stoll, J. M. Tour, and C. L. Rand, *J. Am. Chem. Soc.*, 1988, **110**, 5383.

^{1}H NMR and ^{13}C NMR spectrum of **7** ($CDCl_3$)

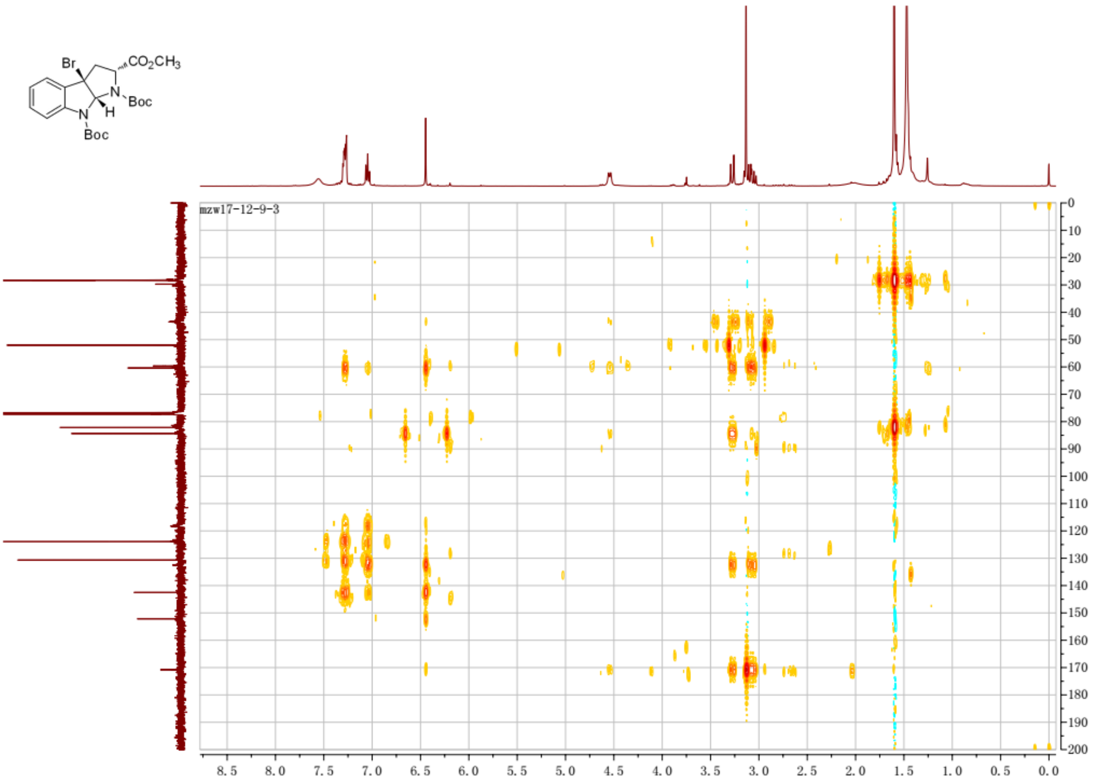




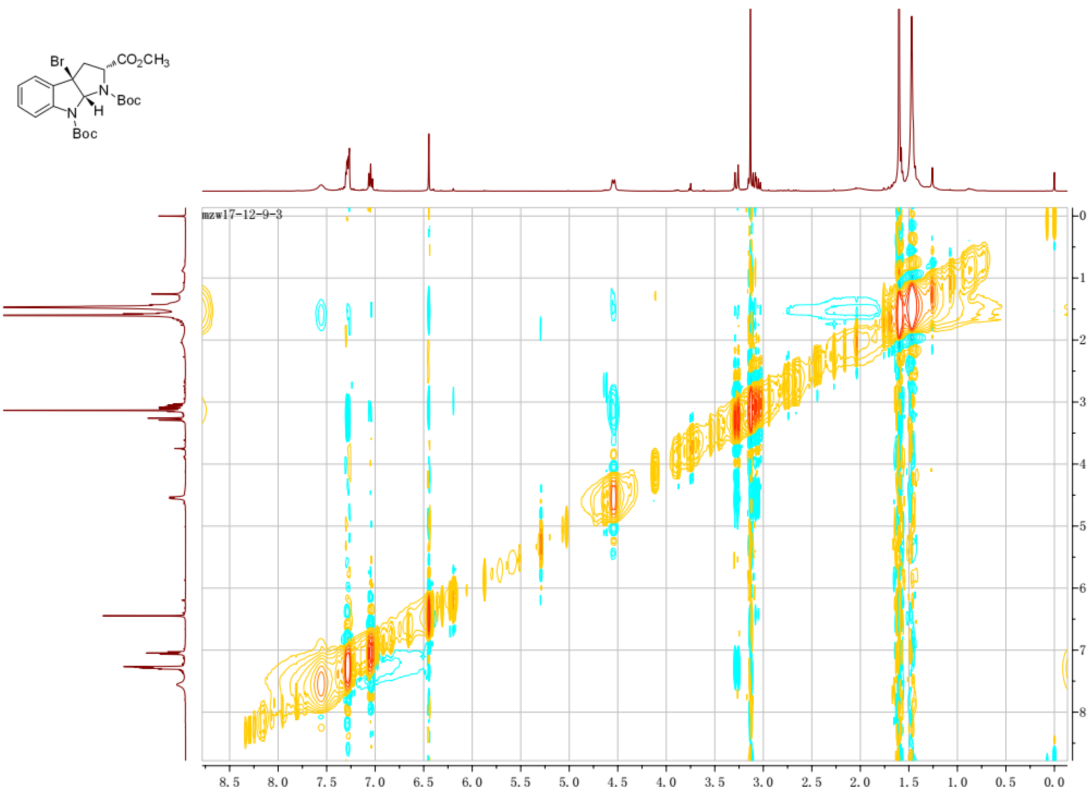
HSQC spectrum of **7** ($CDCl_3$)



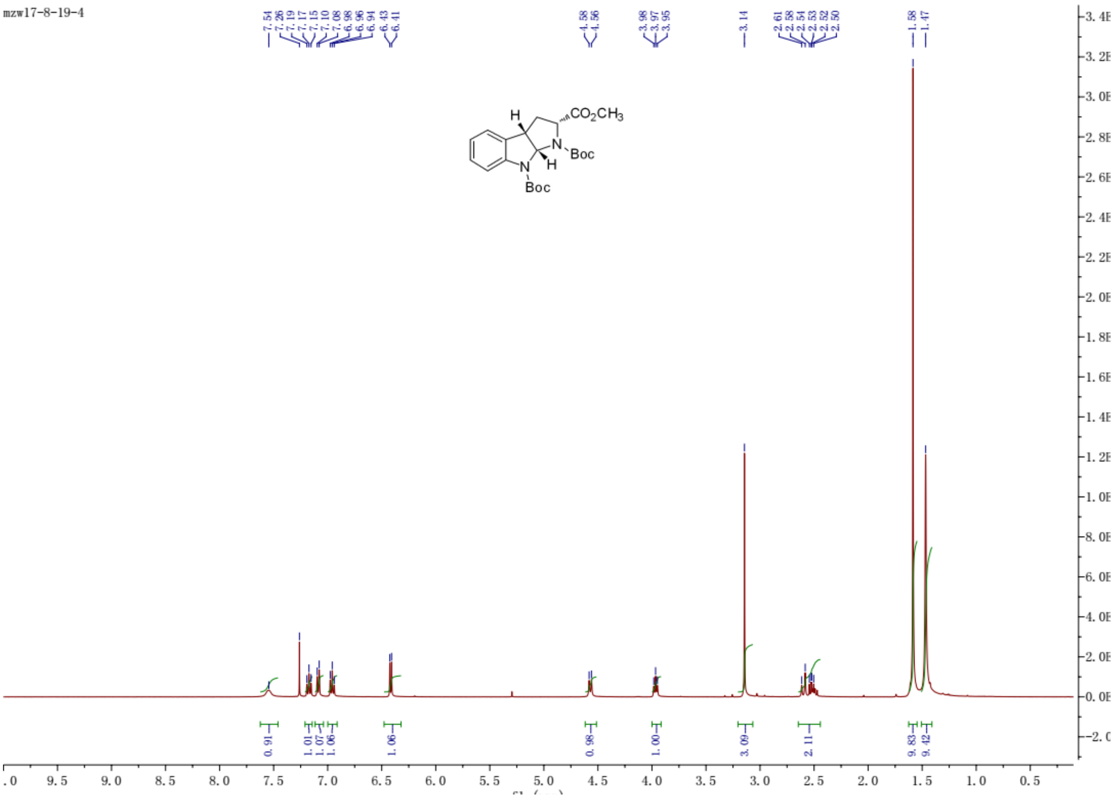
HMBC spectrum of **7** ($CDCl_3$)

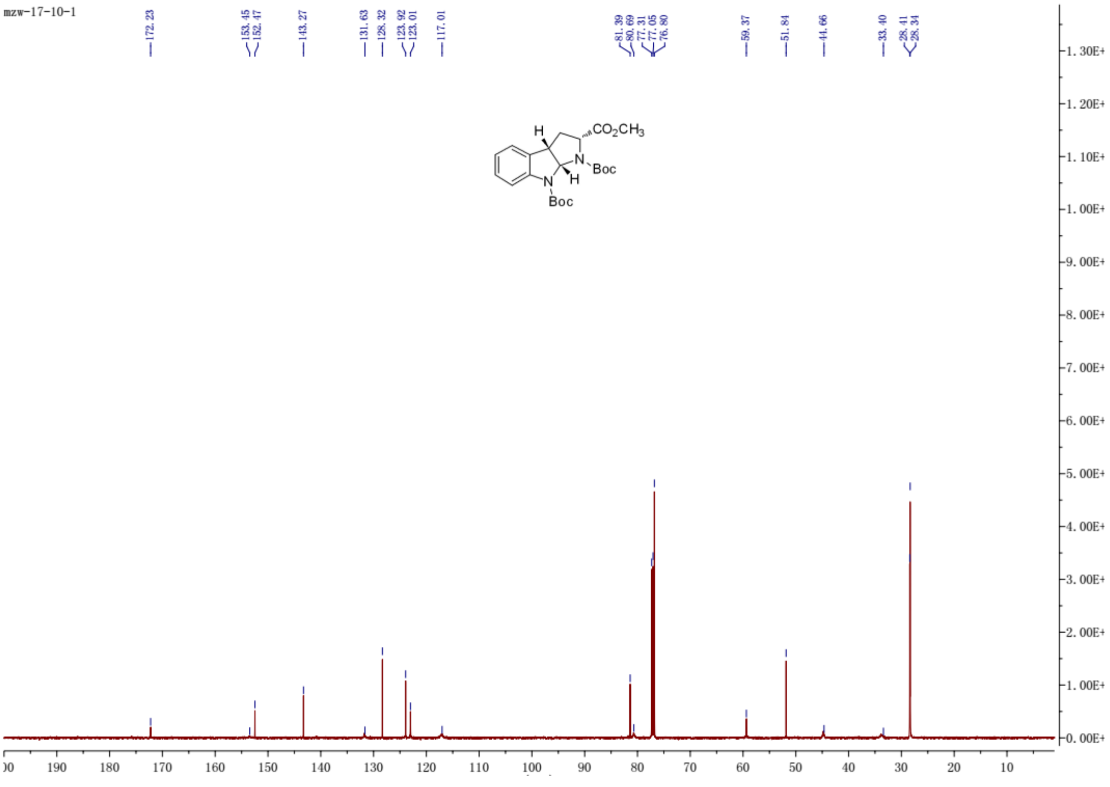


NOESY spectrum of **7** ($CDCl_3$)

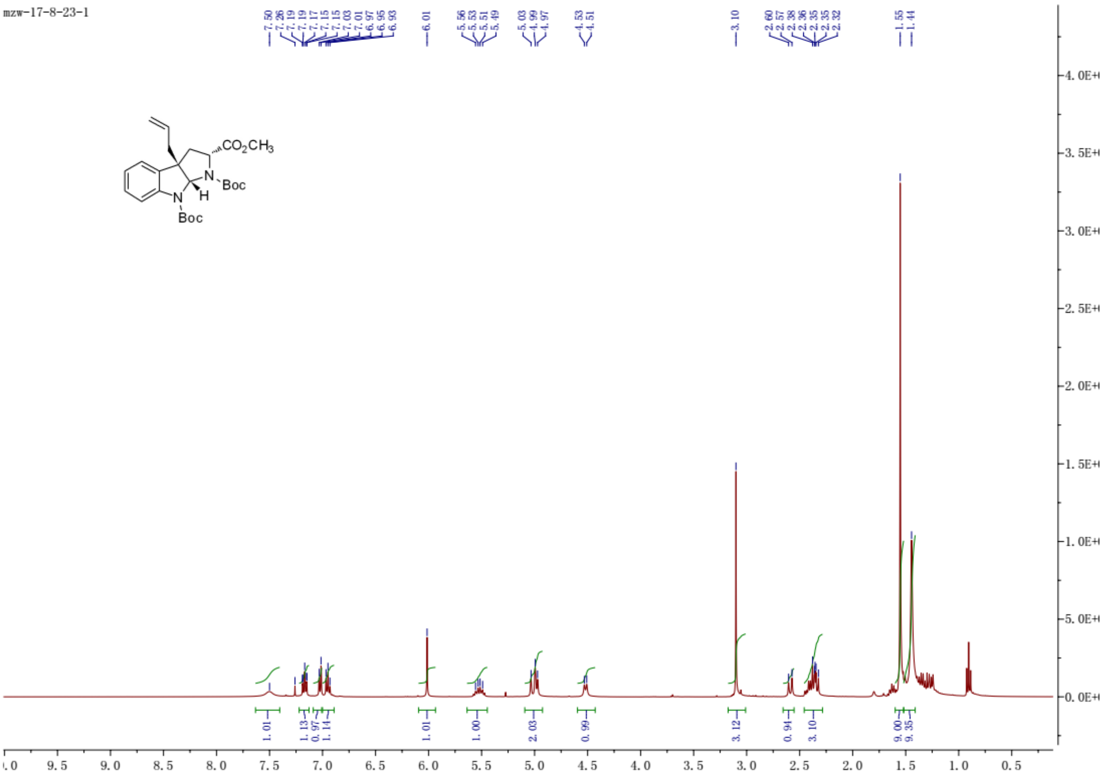


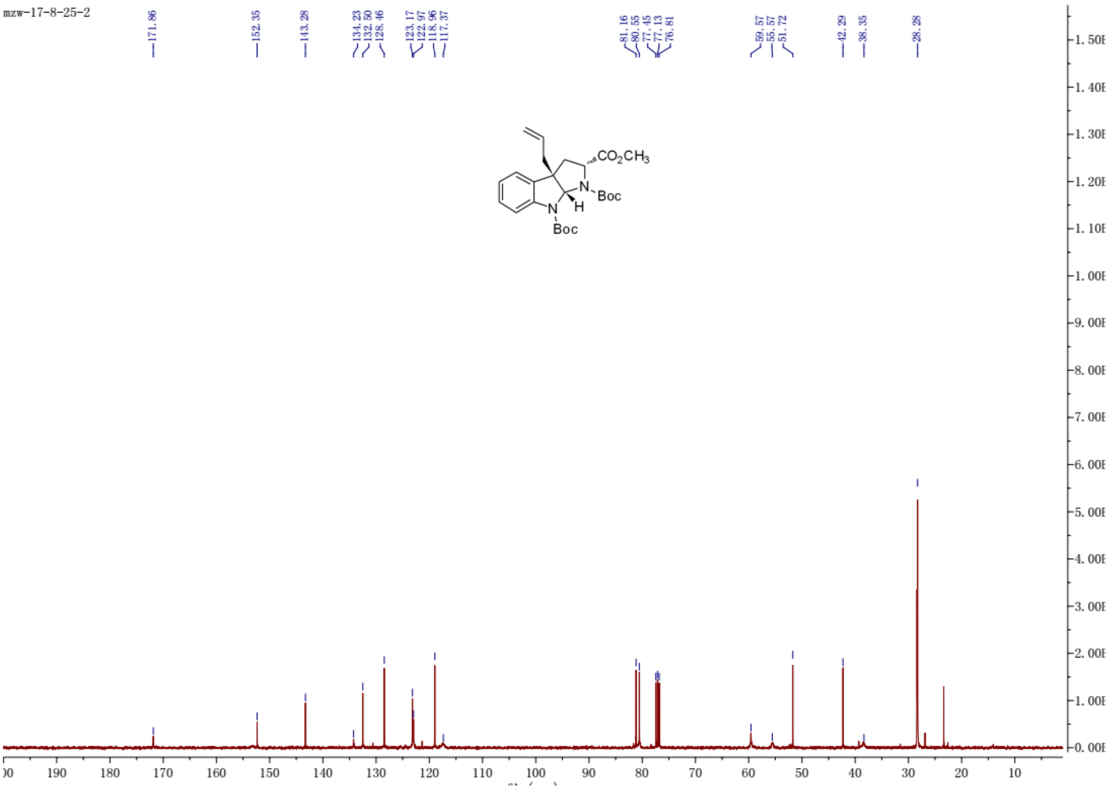
^{1}H NMR and ^{13}C NMR spectrum of **8** (CDCl$_3$)



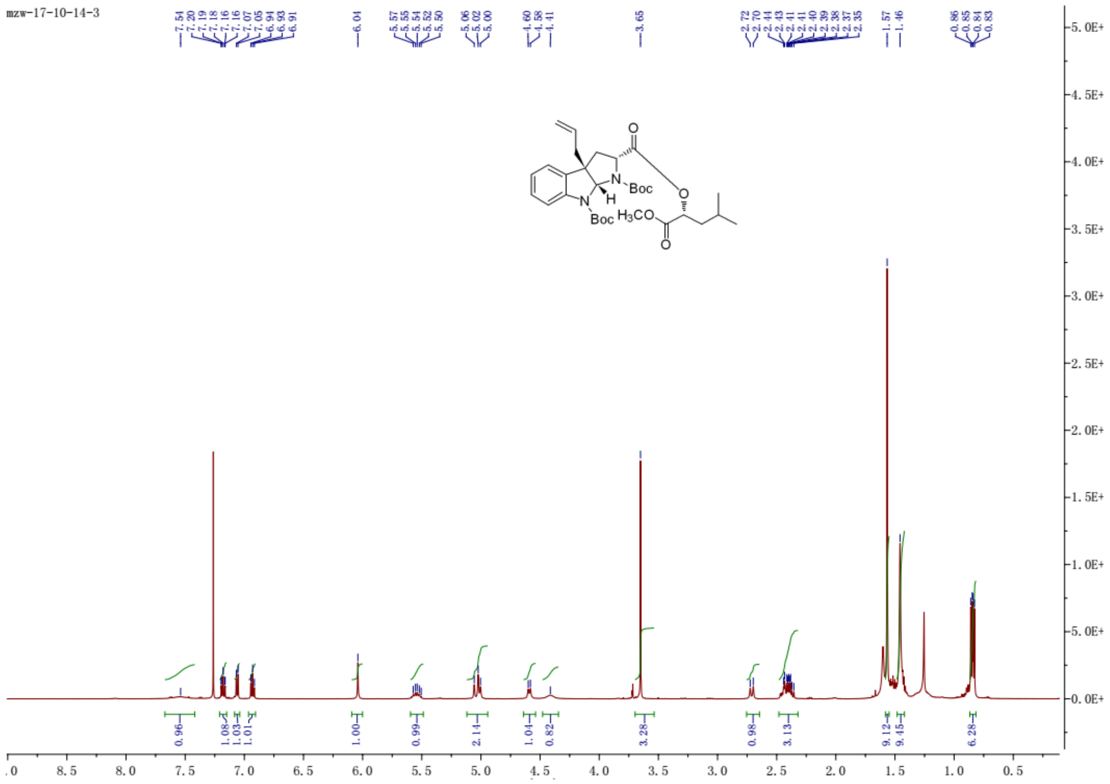


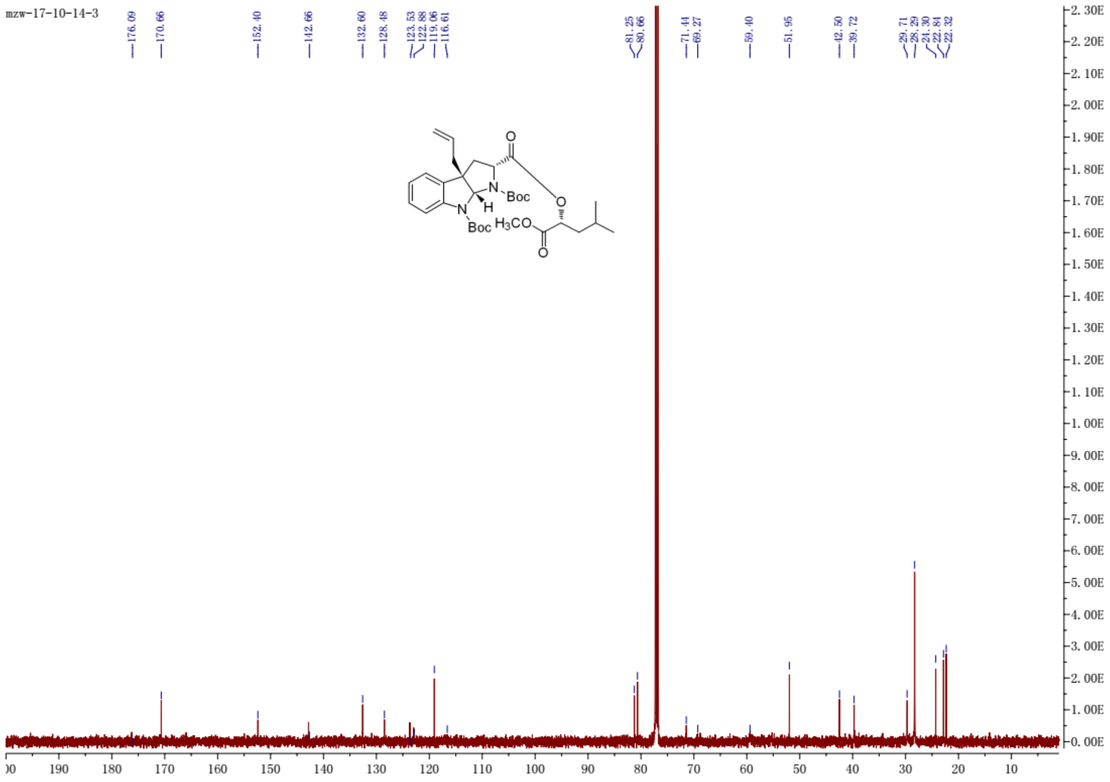
^{1}H NMR and ^{13}C NMR spectrum of **18** ($CDCl_3$)



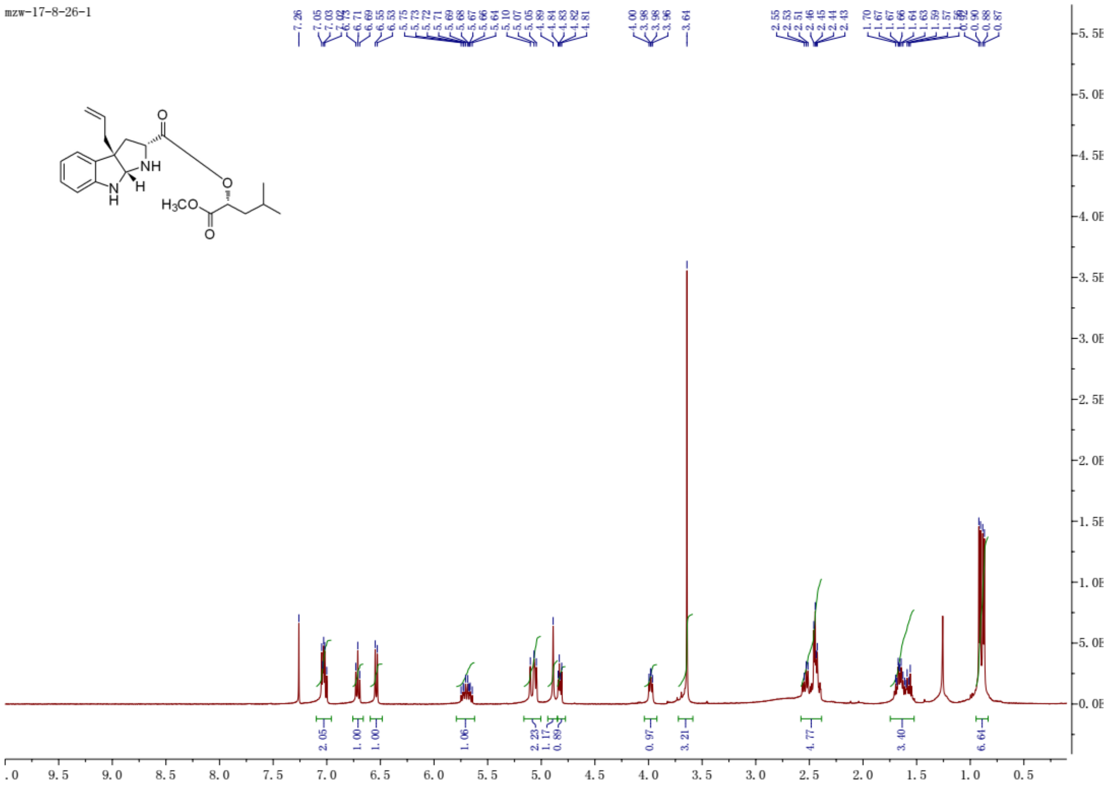


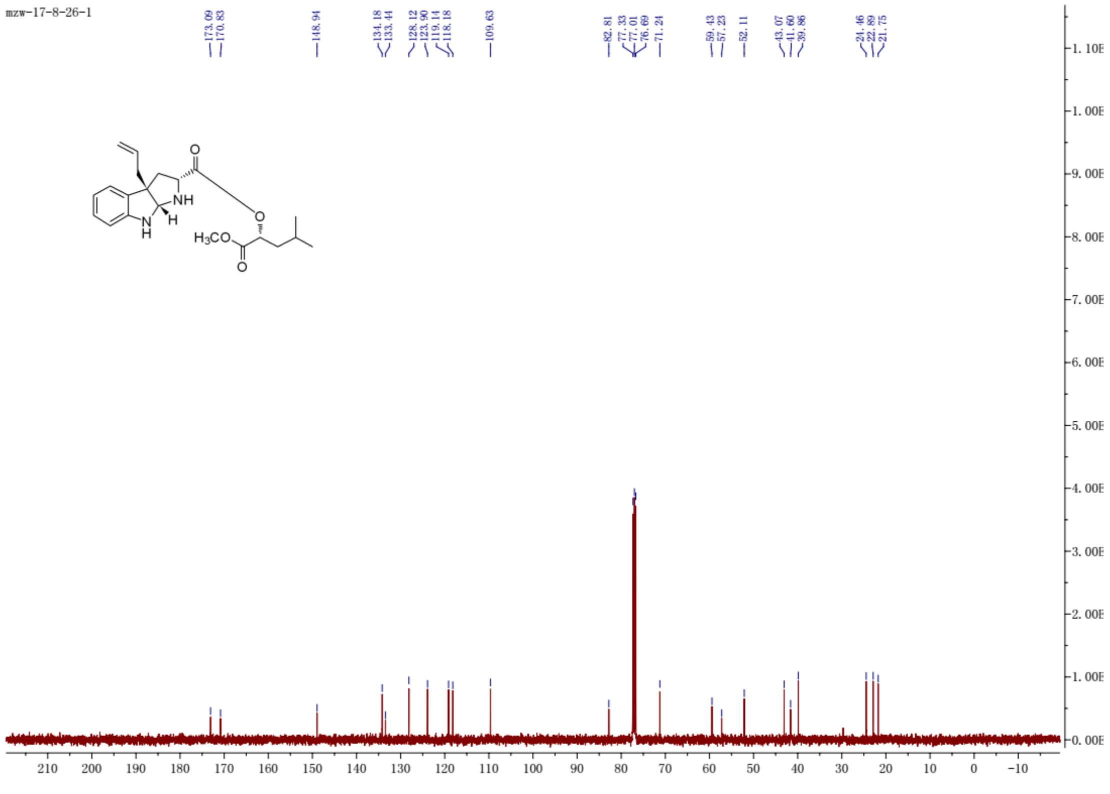
^{1}H NMR and ^{13}C NMR spectrum of **4** (CDCl$_3$)



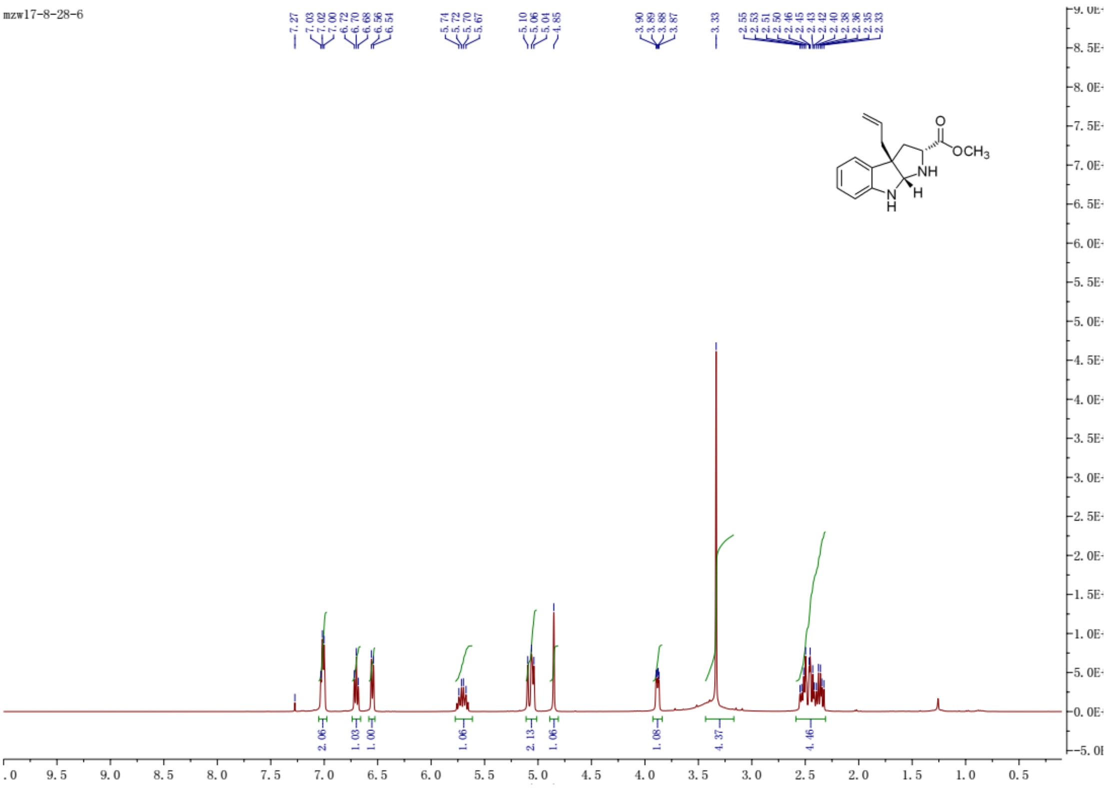


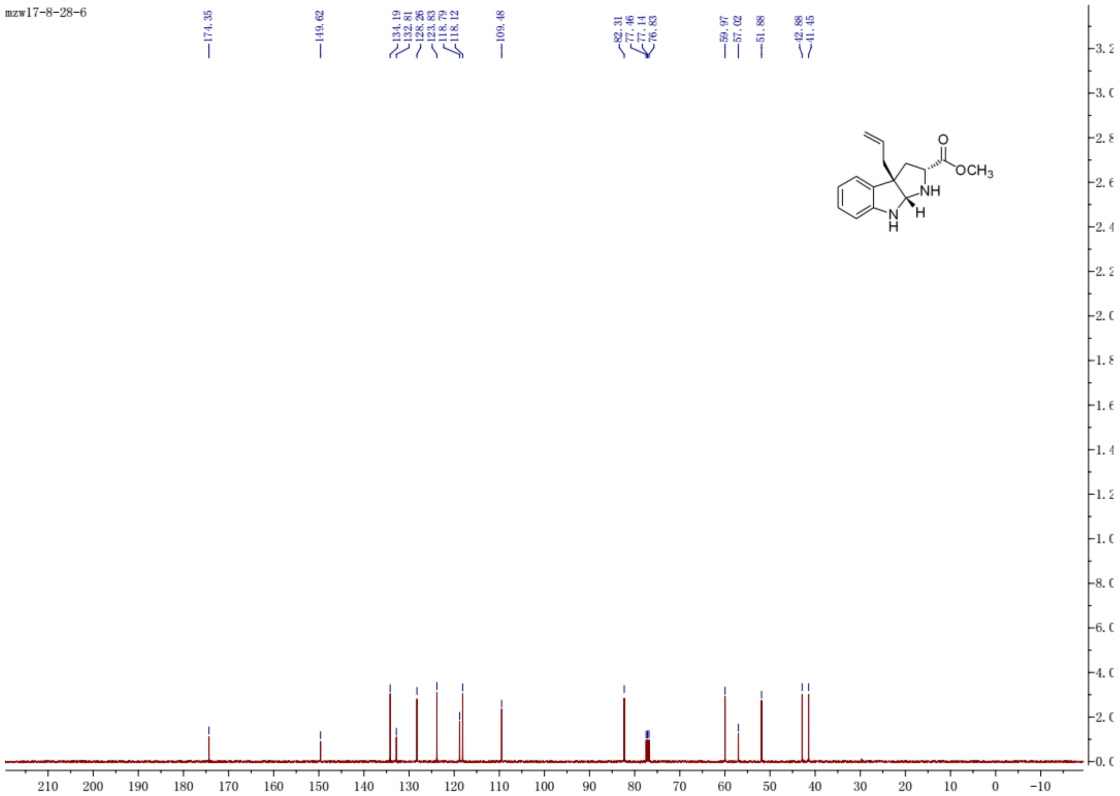
^{1}H NMR and ^{13}C NMR spectrum of **19** (CDCl$_3$)



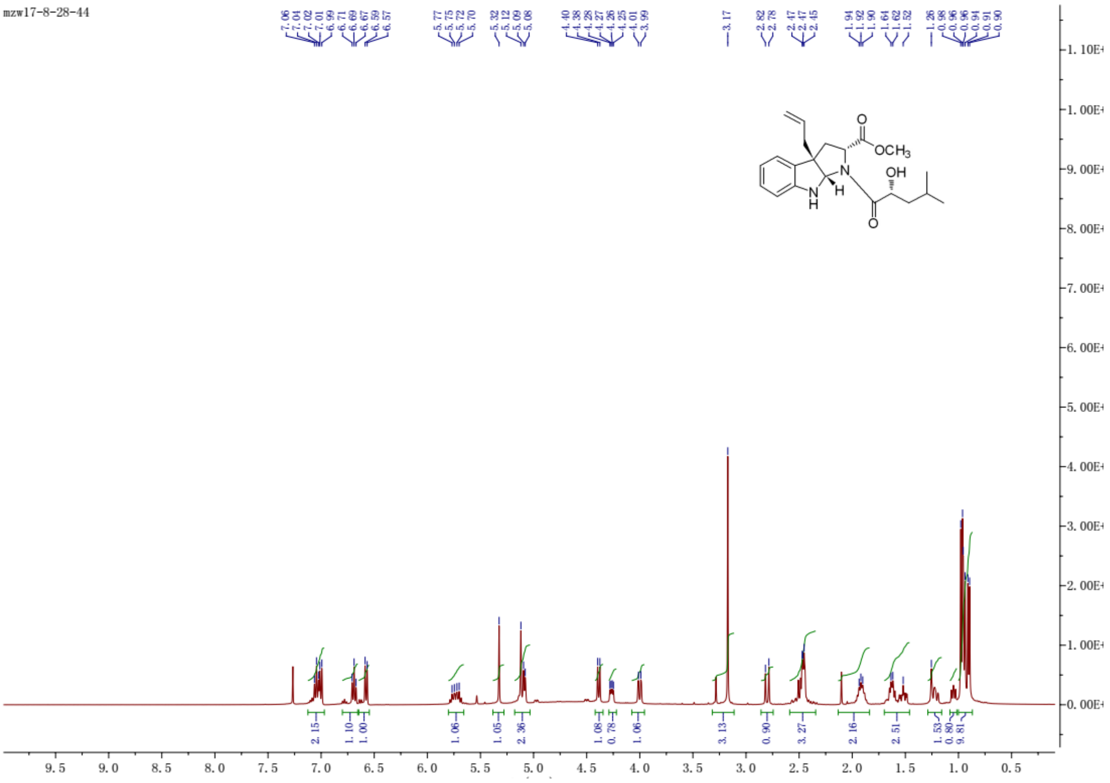


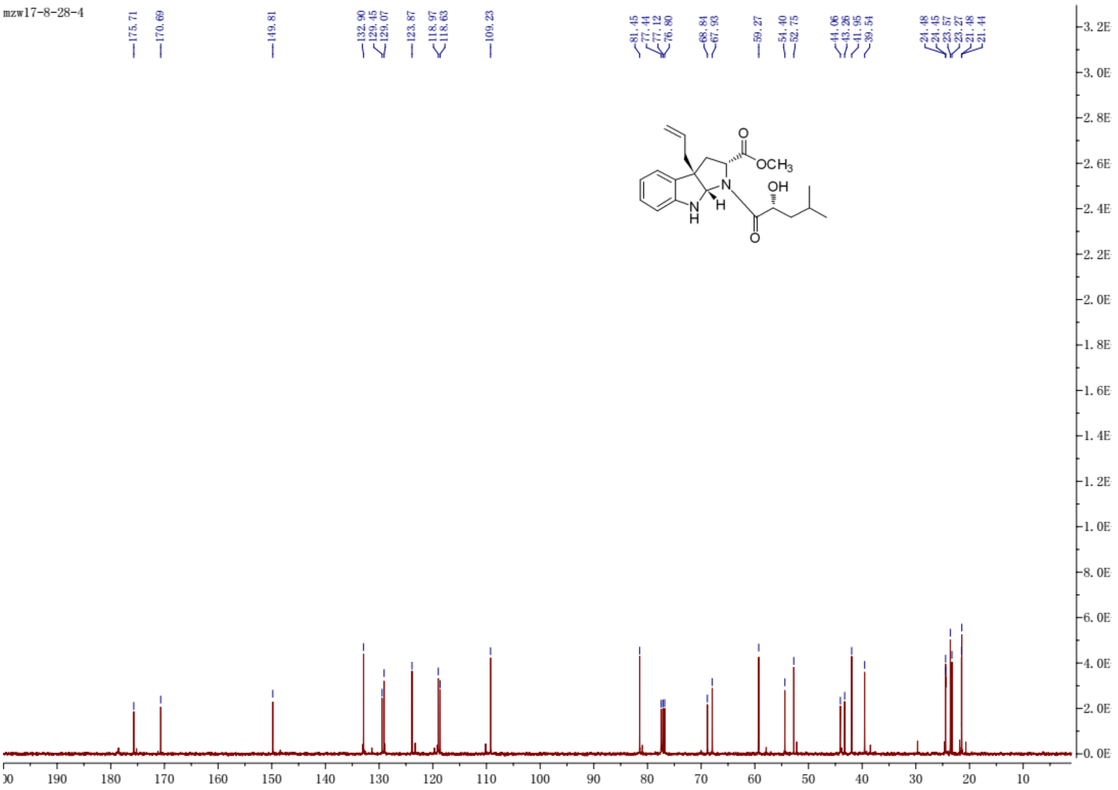
^{1}H NMR and ^{13}C NMR spectrum of **20** ($CDCl_3$)



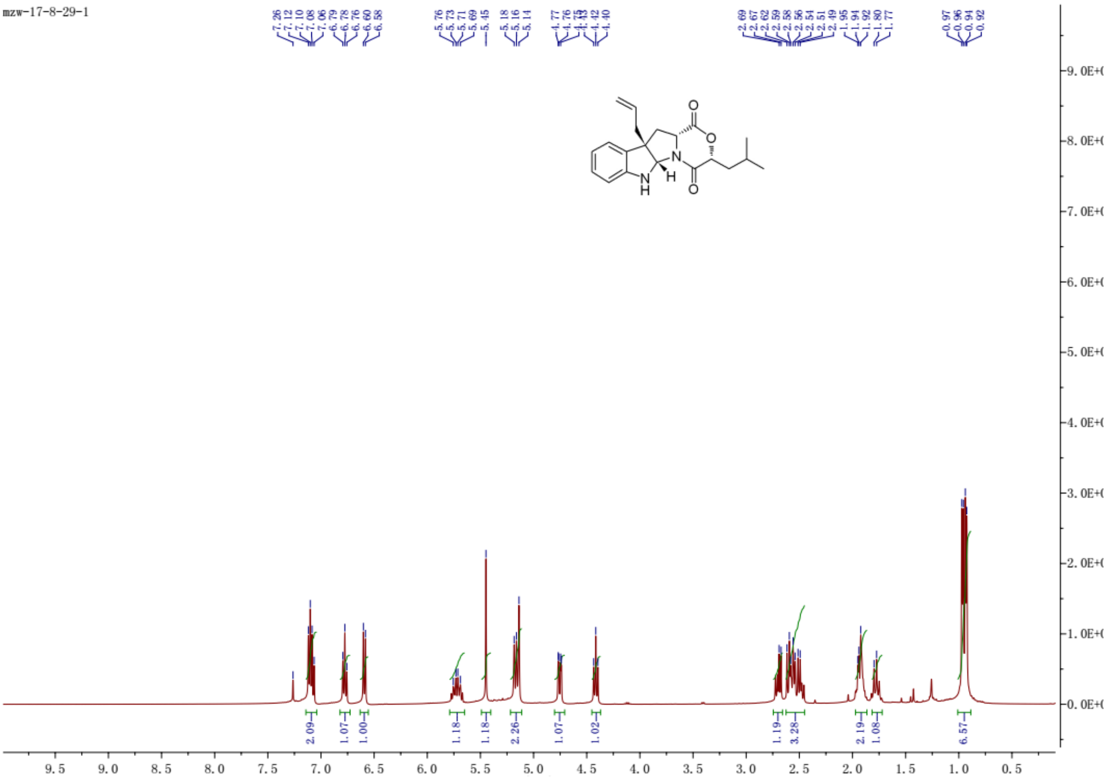


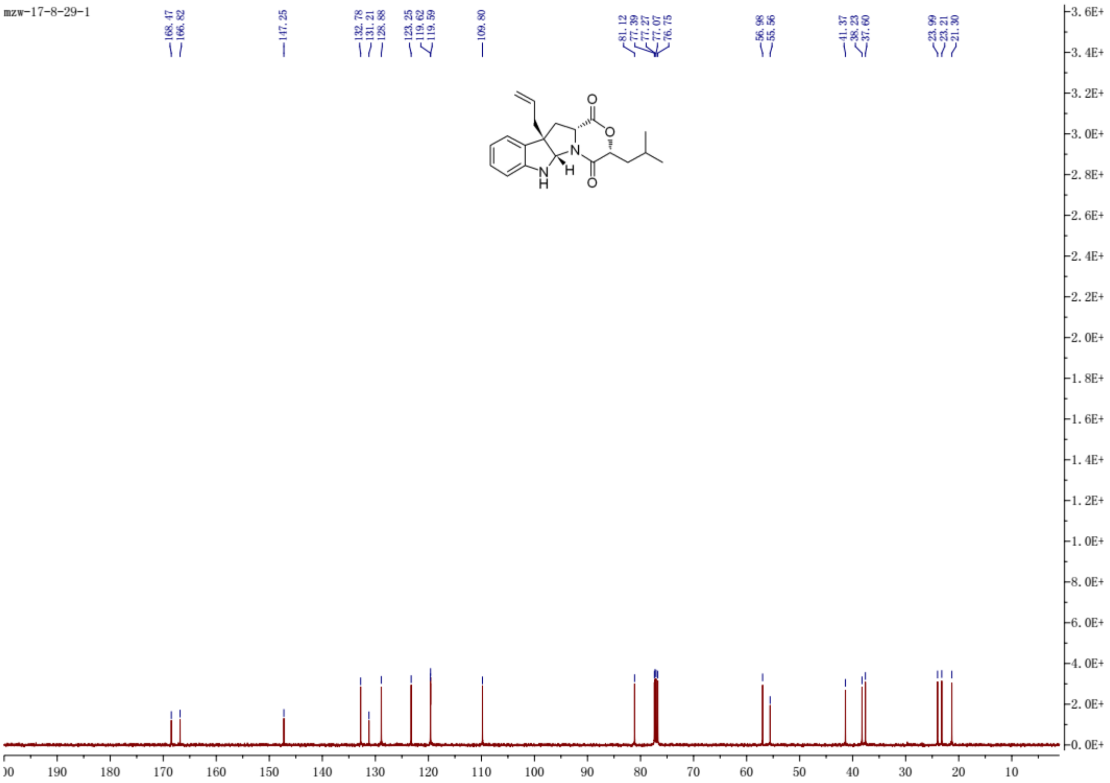
^{1}H NMR and ^{13}C NMR spectrum of **22** (CDCl$_3$)



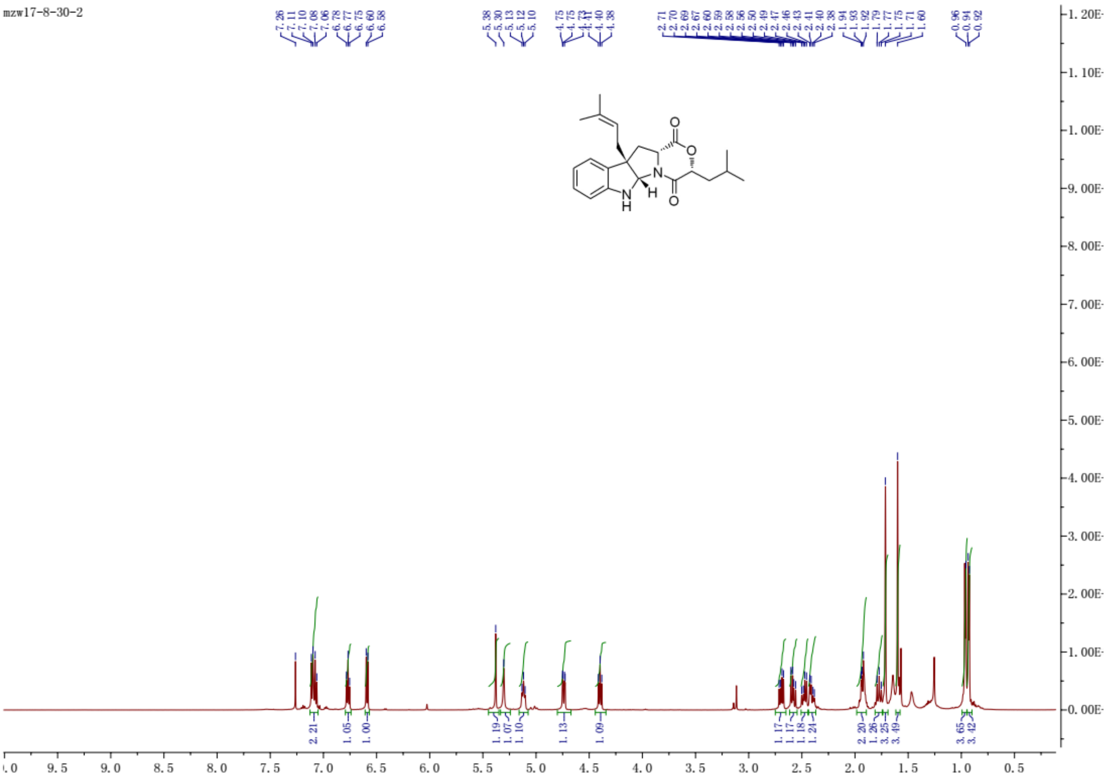


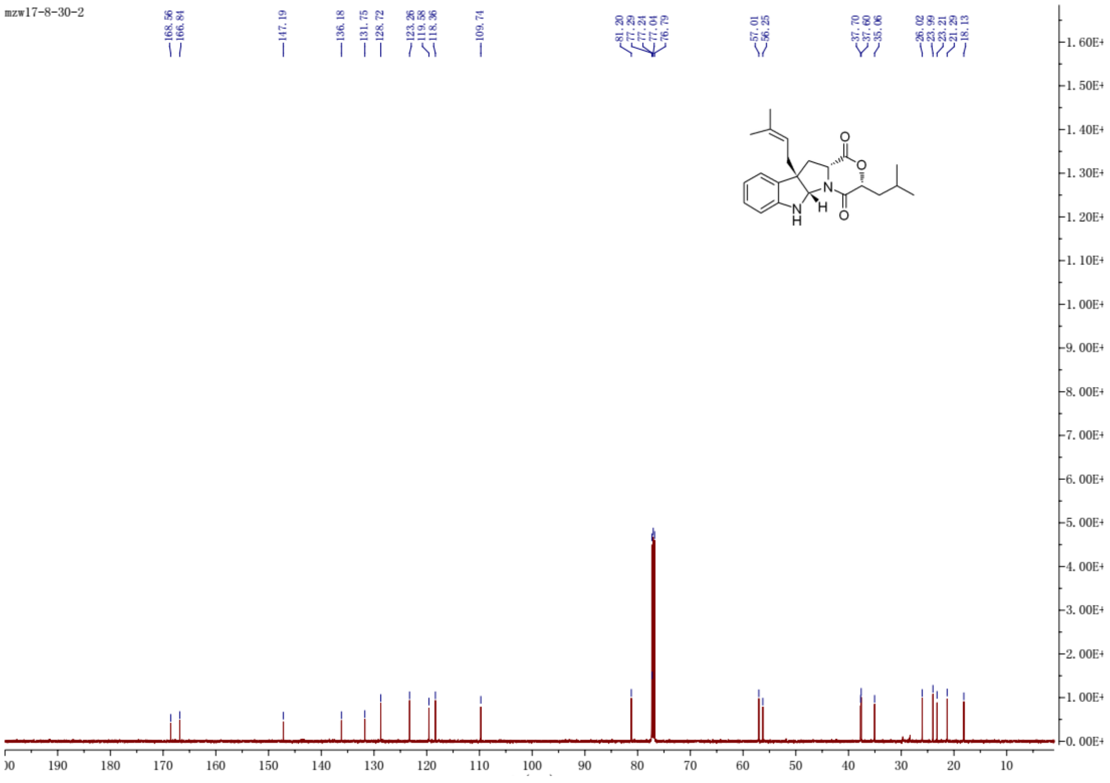
^{1}H NMR and ^{13}C NMR spectrum of **3** ($CDCl_3$)



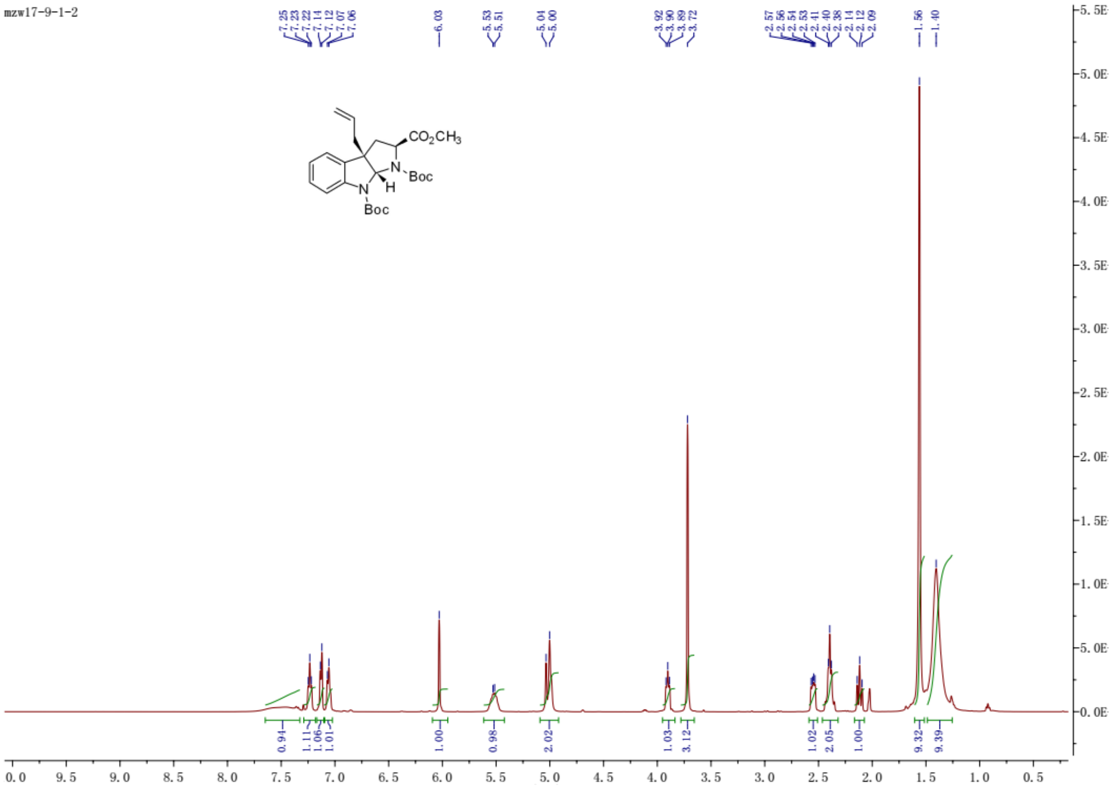


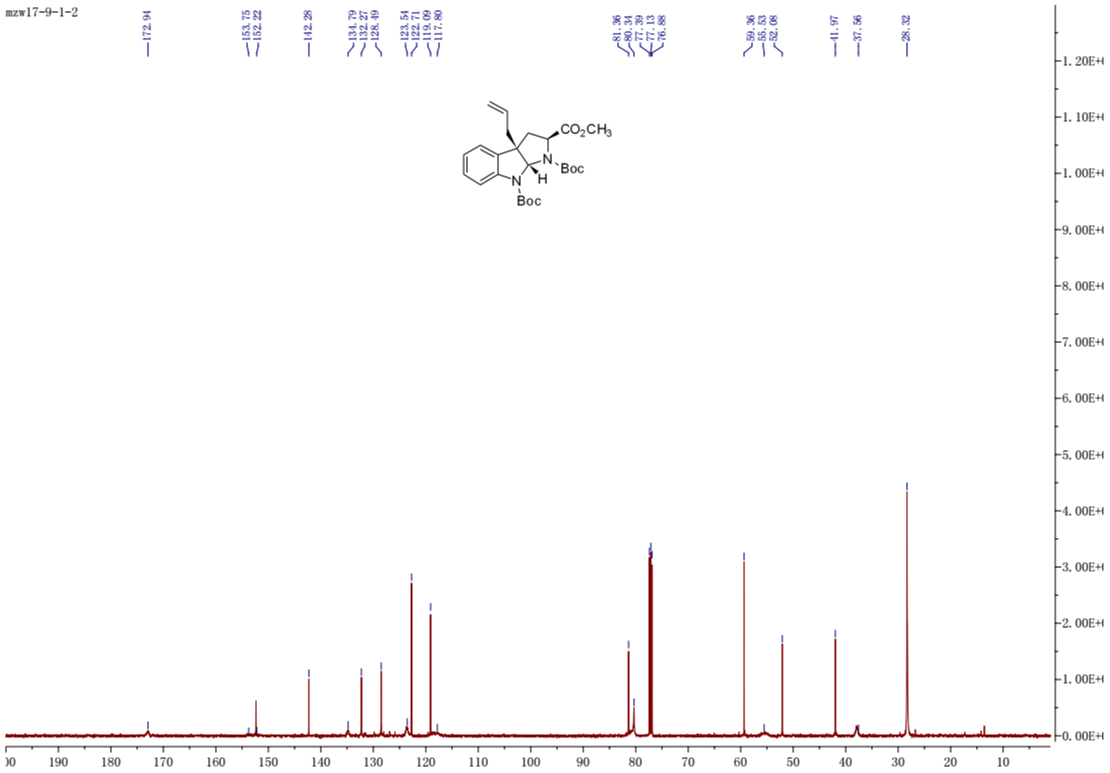
^{1}H NMR and ^{13}C NMR spectrum of **1** ($CDCl_3$)



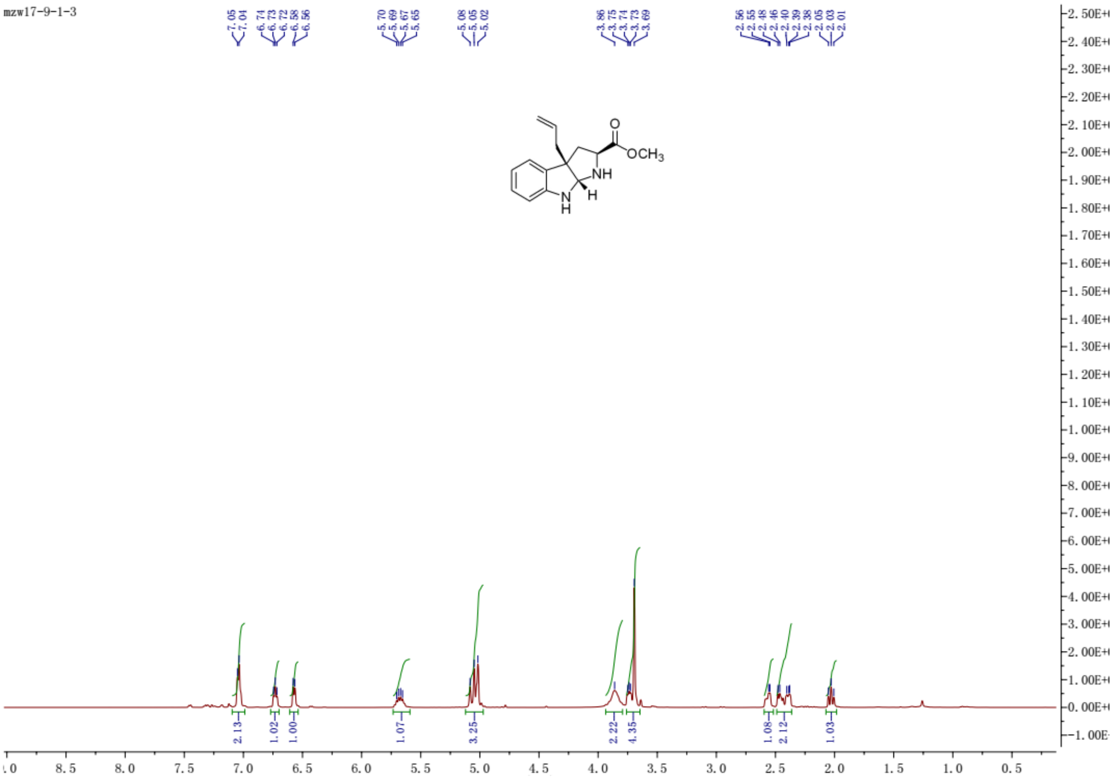


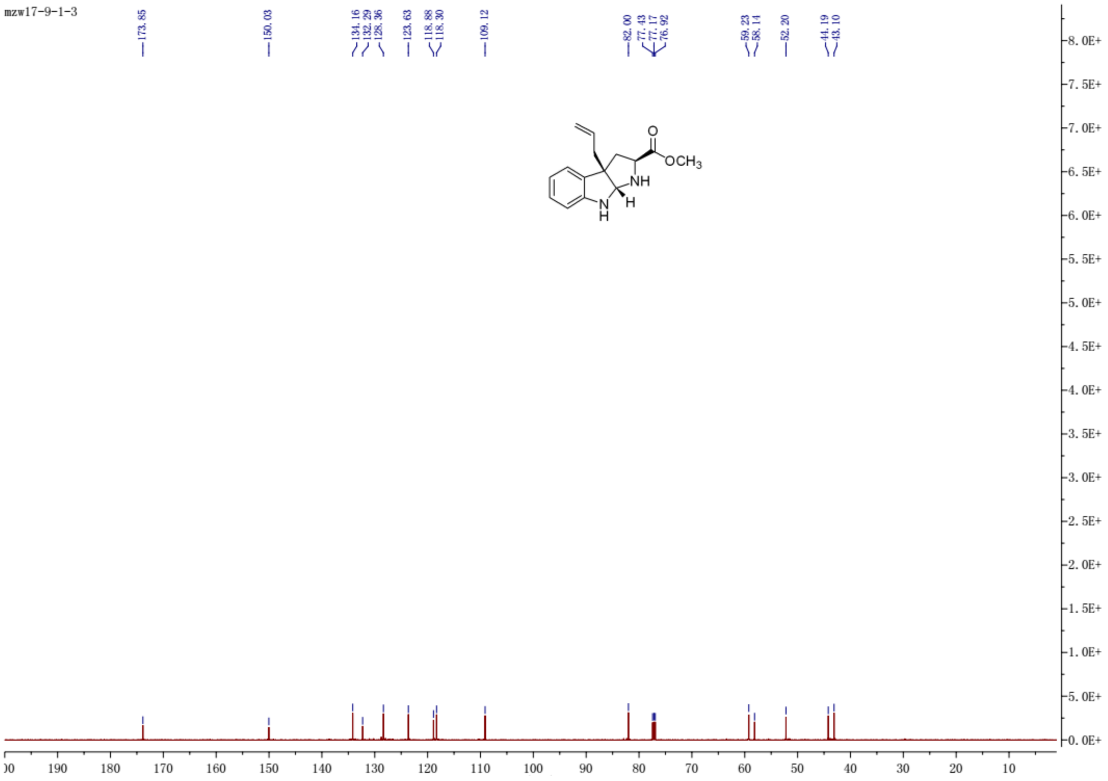
^{1}H NMR and ^{13}C NMR spectrum of **23** ($CDCl_3$)



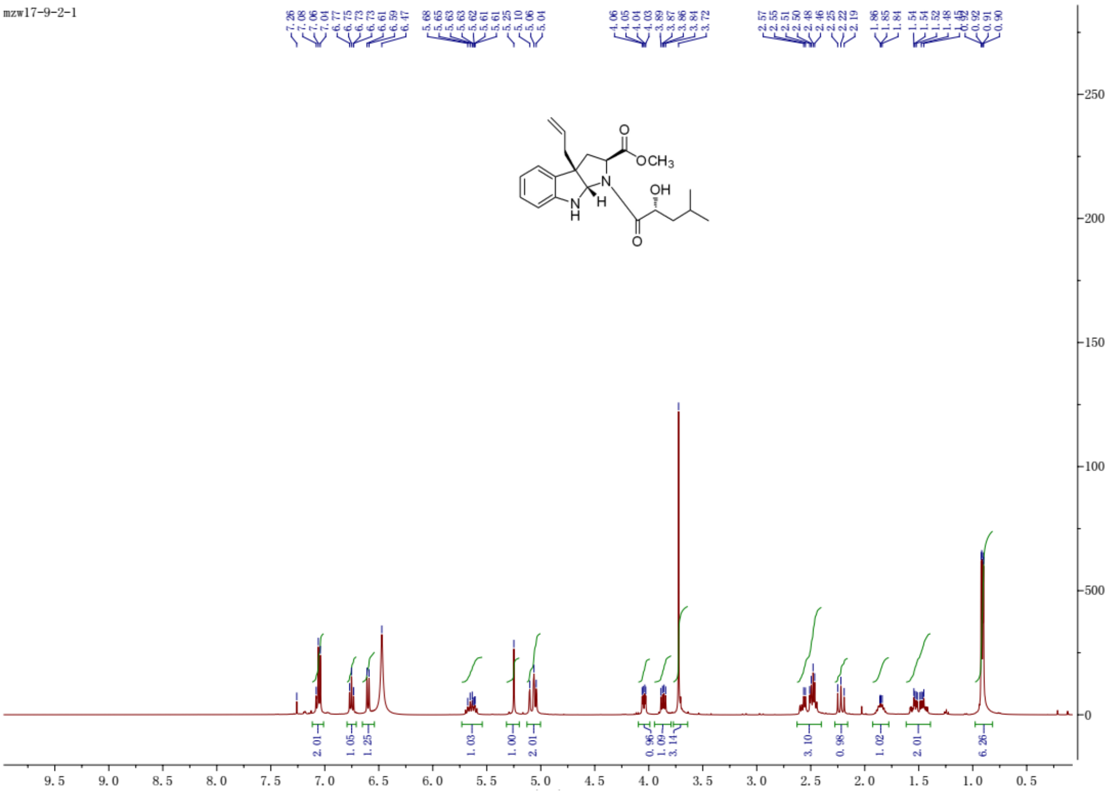


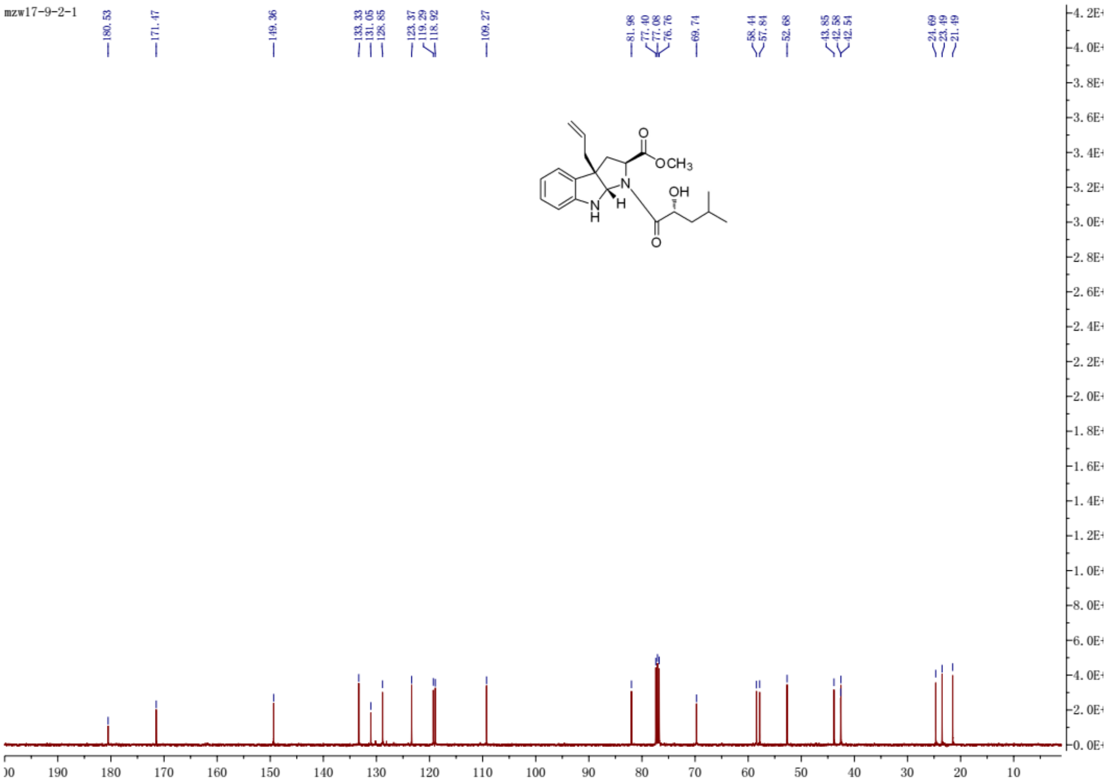
^1H NMR and ^{13}C NMR spectrum of **24** ($CDCl_3$)



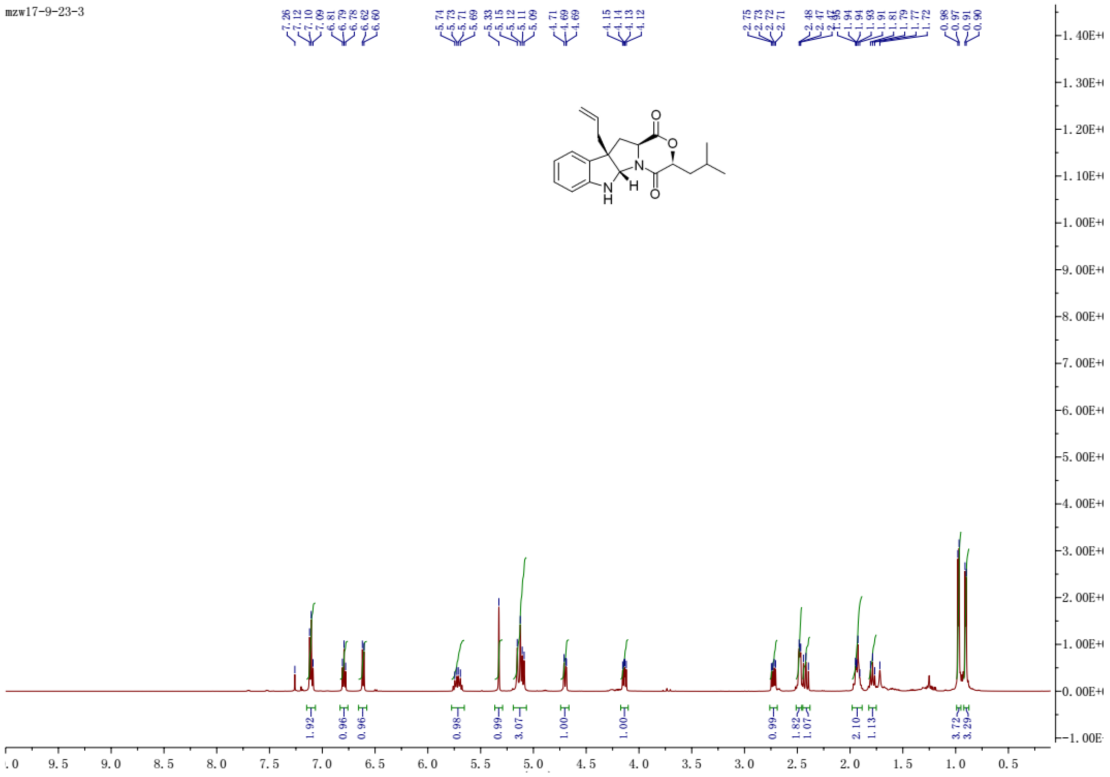


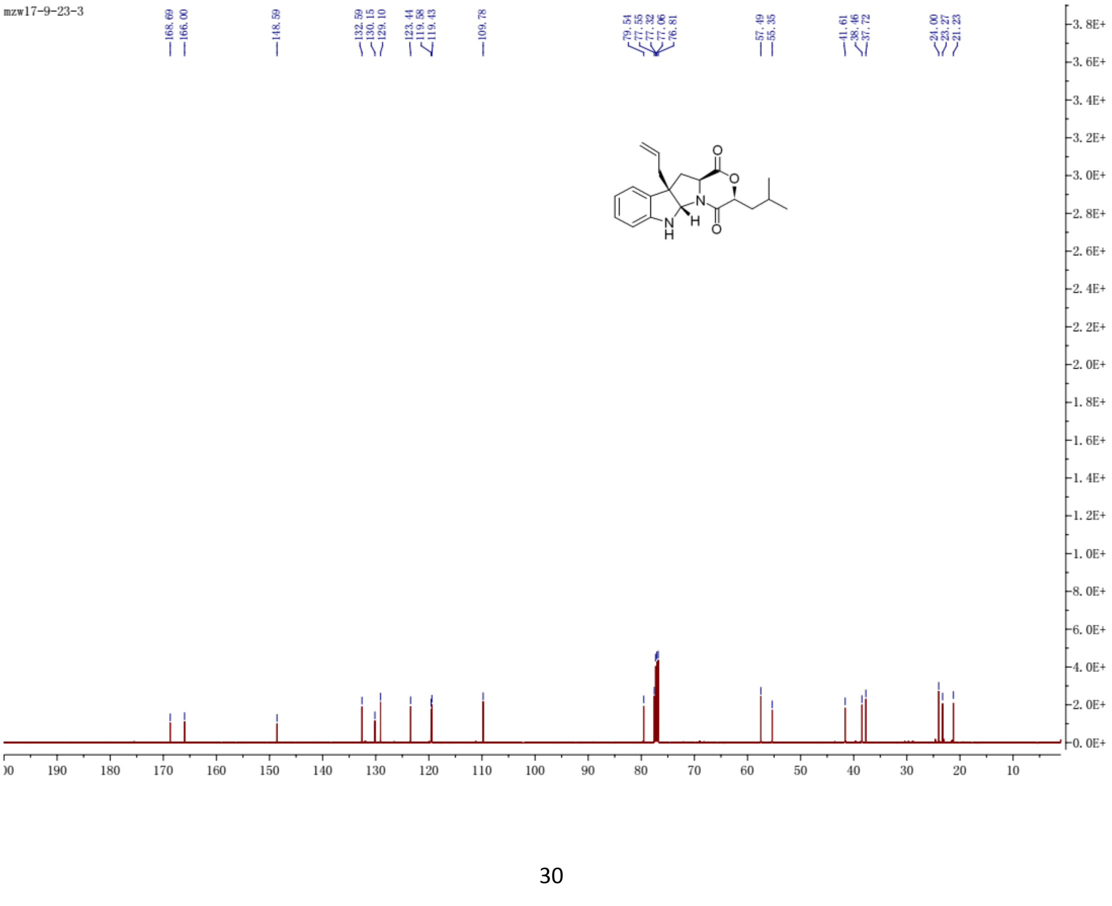
^{1}H NMR and ^{13}C NMR spectrum of **25** (CDCl$_3$)



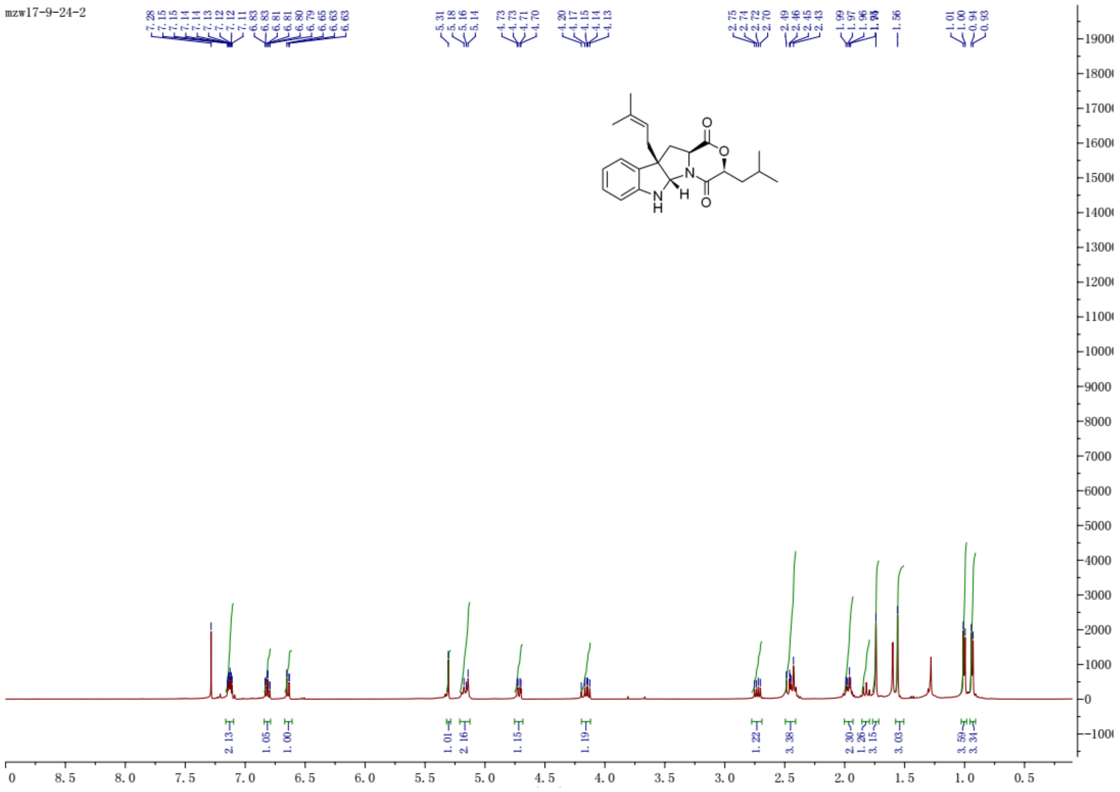


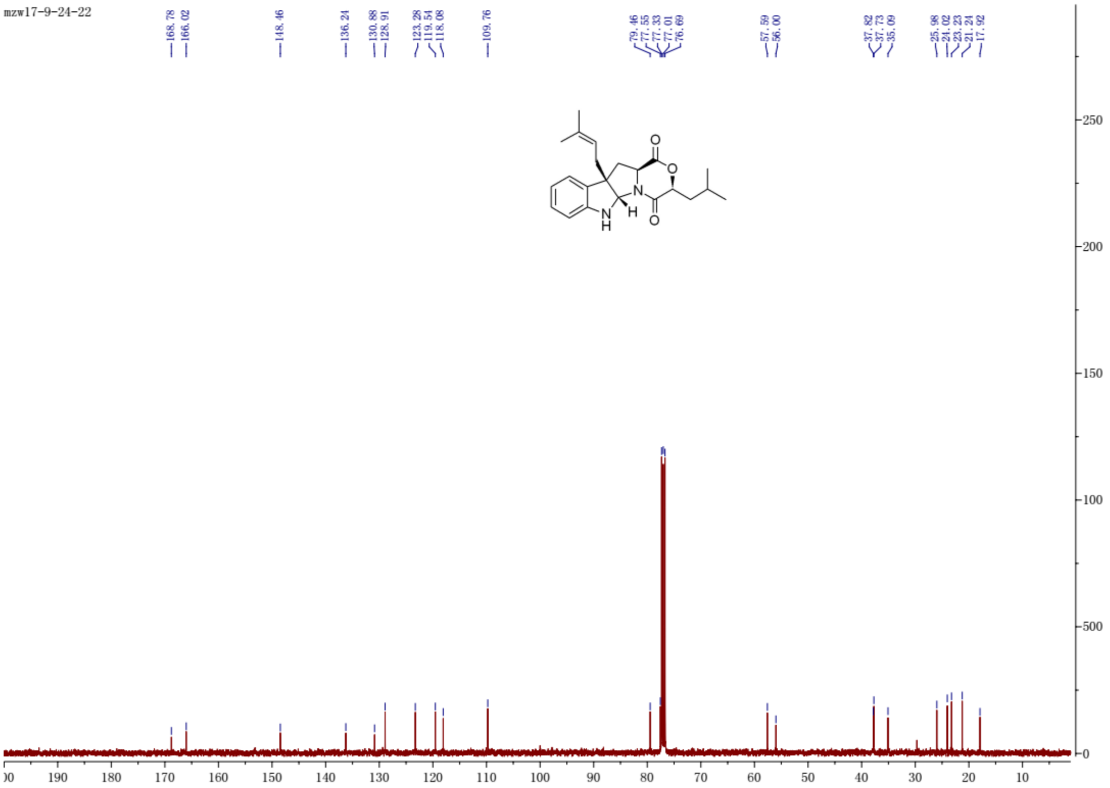
^{1}H NMR and ^{13}C NMR spectrum of **29** (CDCl$_3$)



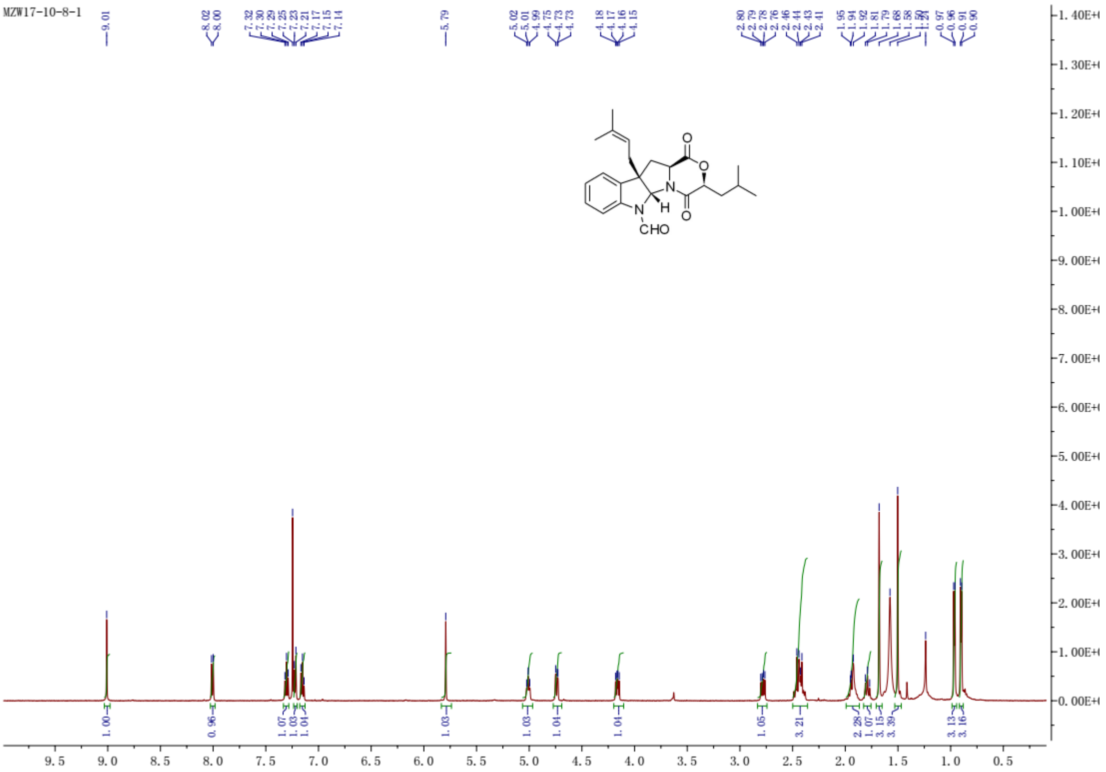


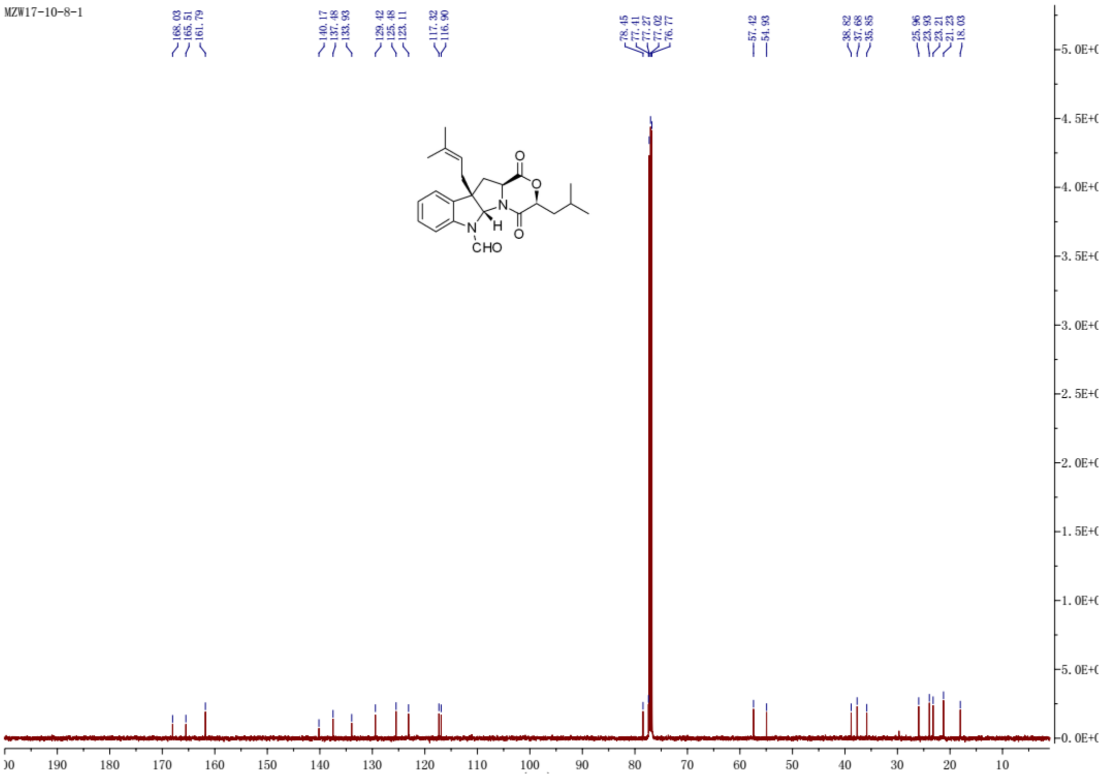
^{1}H NMR and ^{13}C NMR spectrum of **30** ($CDCl_3$)



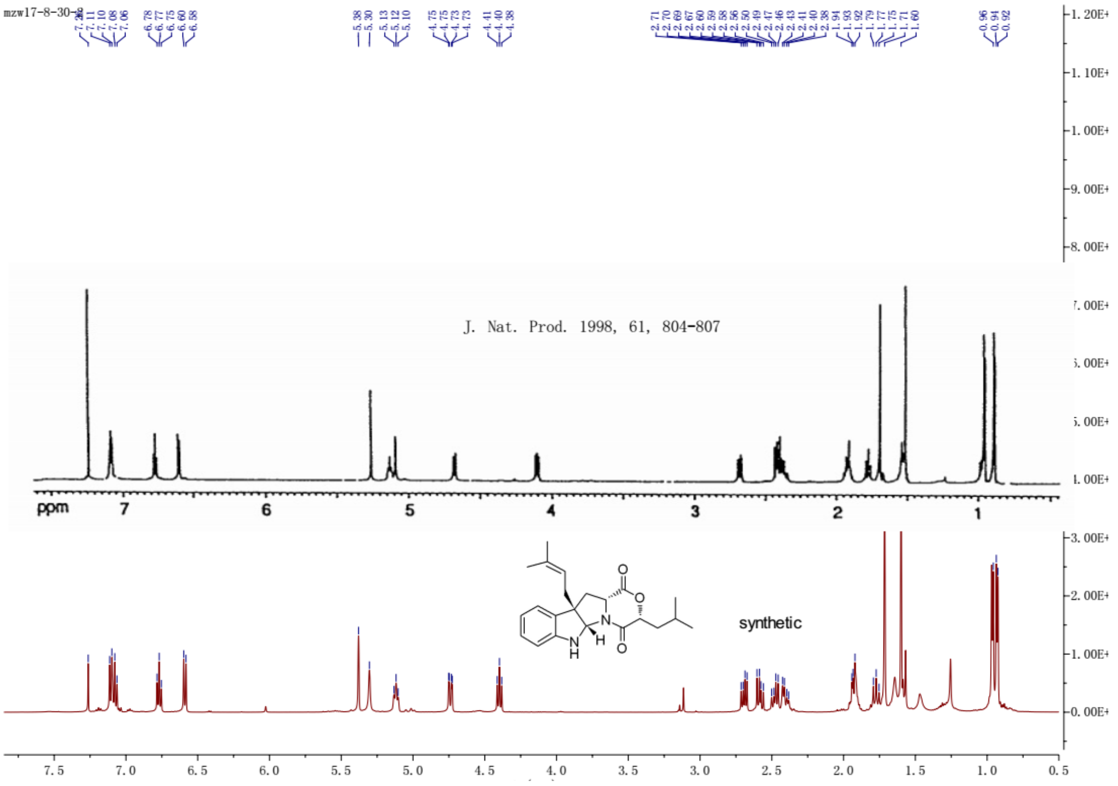


^{1}H NMR and ^{13}C NMR spectrum of **31**(CDCl$_3$)

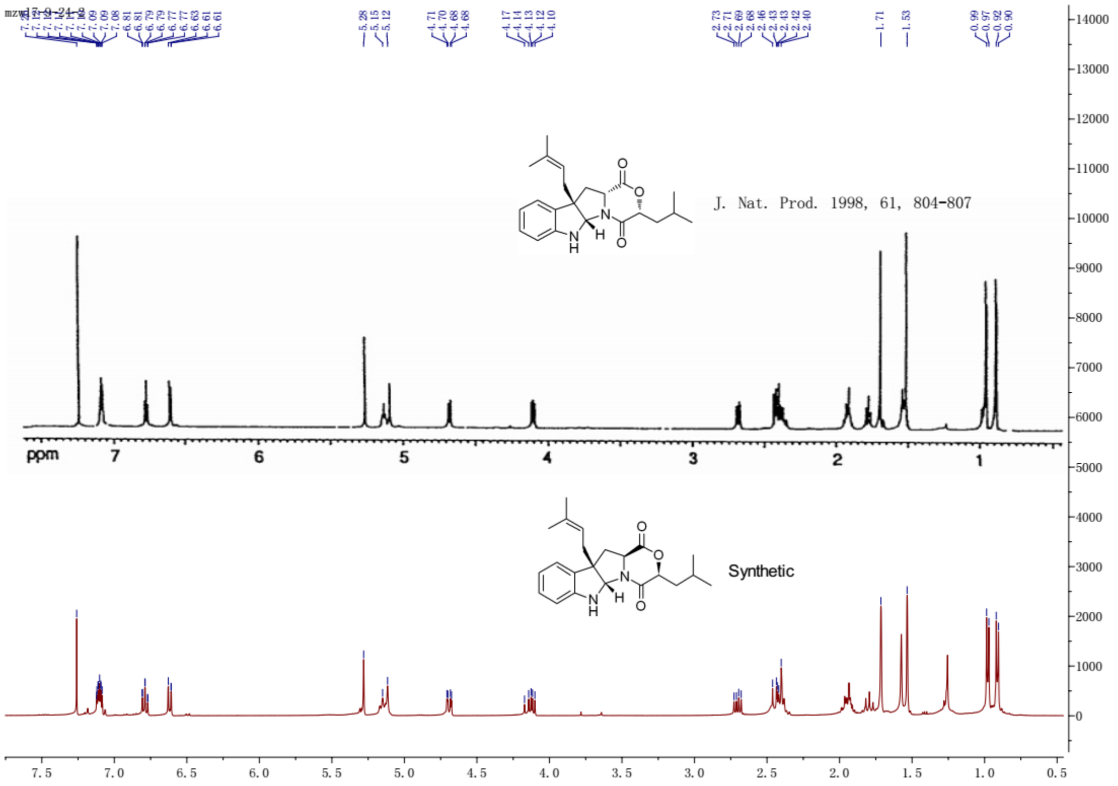




^{1}H NMR spectrum of mollenine A ($CDCl_3$, provided) and **1** ($CDCl_3$)



^{1}H NMR spectrum of mollenine A ($CDCl_3$, provided) and **30** ($CDCl_3$)



^{13}C NMR spectrum of mollenine A ($CDCl_3$, provided) and **30** ($CDCl_3$)