Supporting Information

Divergent Synthesis of Okaramines C, J, L, and S-U

Xiao-Wan Li,[‡a,c] Tong-Xu Si,[‡b] Ya-Ping Liu,[b] Ming-Zhong Wang,*[a,b] and Albert S. C. Chan[c]

[a]School of Pharmaceutical Science, Shenzhen Technology University, Shenzhen 518118, China.

[b]State Key Laboratory of Photochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650201, P. R. China.

[c]School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou 510006, P. R. China.

*Corresponding Authors: mzwang2000@163.com, Tel.: +86-(0)755-23256206.

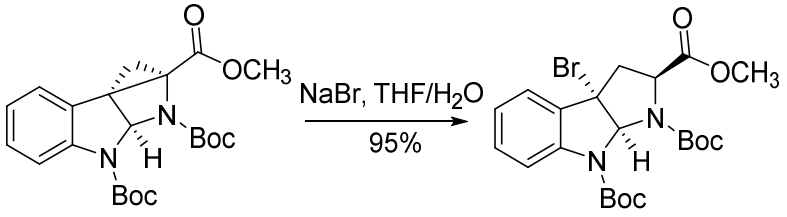
‡These authors contributed equally.

Table of Contents

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, tetrahydrofuran, and toluene were distilled from Na/benzophenone, DMF, dichloromethane, 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, 0.2 mm) 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.

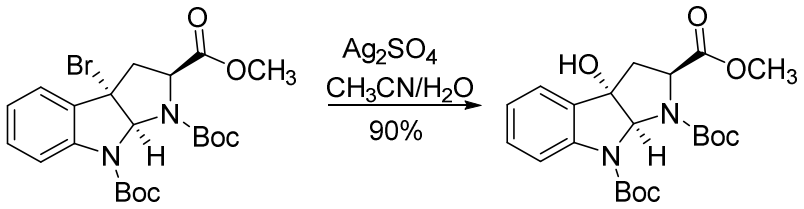
*(2S,3aS,8aS)-1,8-Di-tert-butyl 2-methyl 3a-bromo-3,3a-dihydropyrrolo[2,3-b]indole-1,2,8(2H,8aH)-tricarboxylate (**11**).*



12 **11**

NaBr aqueous solution (2.0 g, in 20.0 mL water) was added to a solution of cyclopropylazetoindoline **12**[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 *vacuo*. The residue was purified by flash chromatography (EtOAc: hexanes = 1:14) to produce **11** (2.0 g, 95% yield) as a colorless oil. $[\alpha]_D^{20}$ = +42.0 (c 1.3, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (brs, 1H), 7.33 – 7.26 (m, 2H), 7.04 (dd, J = 7.5, 1.5 Hz, 1H), 6.45 (s, 1H), 4.54 (d, J = 9.0 Hz, 1H), 3.27 (d, J = 13.0 Hz, 1H), 3.13 (s, 3H), 3.07 (dd, J = 13.0, 9.5 Hz, 1H), 1.60 (s, 9H), 1.47 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 152.1 (2C), 142.5, 132.5, 130.6, 123.9 (2C), 118.1, 84.4, 82.1, 81.4, 60.4, 59.7, 52.0, 43.5, 28.3 (3C), 28.2 (3C); HRESIMS *m/z* 519.1095 $[M+Na]^+$, calcd for $C_{22}H_{29}BrN_2O_6Na$, 519.1101.

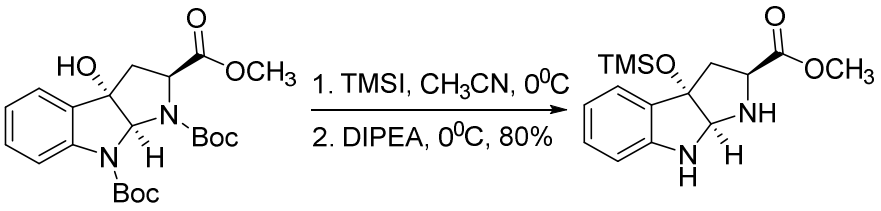
*1,8-Di-tert-butyl 2-methyl (2S,3aS,8aS)-3a-hydroxy-2,3,3a,8a-tetrahydropyrrolo[2,3-b]indole-1,2,8-tricarboxylate (**13**).*



11 **13**

To a solution of **11** (3.6 g, 7.2 mmol) in a mixture solvent of CH_3CN (30.0 mL) and H_2O (10.0 mL) was added Ag_2SO_4 (4.5 g, 14.5 mmol), the mixture was stirred for 6 hours, and filtered through a short plug of silica gel. The filtrate was concentrated and extracted with EtOAc/H_2O (200.0 mL, 1:1). The residue was purified by column chromatography (EtOAc: hexanes = 1:3) to produce **13** as a colorless oil (2.8 g, 90%). $[\alpha]_D^{20}$ = +70.0 (c 0.1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (brs, 1H), 7.32 – 7.26 (m, 2H), 7.03 (dd, J = 10.0, 10.0 Hz, 1H), 6.01 (s, 1H), 4.60 (t, J = 5.5 Hz, 1H), 3.36 (s, 1H), 3.17 (s, 3H), 2.73 (d, J = 7.0 Hz, 2H), 1.55 (s, 9H), 1.46 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 152.6 (2C), 143.3, 132.0, 130.5, 123.6, 123.4, 117.3, 84.4, 81.9, 81.7, 60.5, 59.5, 51.9, 39.6, 28.4 (3C), 28.3 (3C); HRESIMS *m/z* 435.2123 $[M+H]^+$, calcd for $C_{22}H_{31}N_2O_7$, 435.2126.

*Methyl (2S,3aS,8aS)-3a-((trimethylsilyl)oxy)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carboxylate (**14**).*

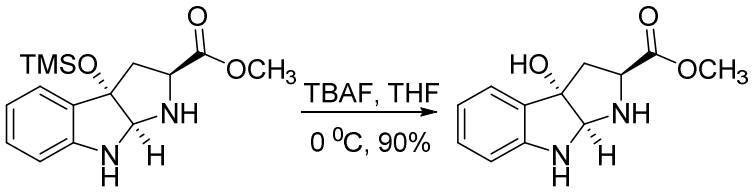


13 **14**

Iodotrimethylsilane (4.5 mL, 31.5 mmol) was added dropwise to a solution of **13** (3.6 g, 8.3 mmol) in acetonitrile (40.0 mL) at 0 ºC under an argon atmosphere. After the addition, the mixture was stirred for 2 hours at 0 ºC. When the starting material was consumed, which was monitored by TLC, *N*, *N*-Diisopropylethylamine (11.0 mL, 63.3 mmol) was introduced *via* a syringe at 0 ºC. The cooling bath was removed and the reaction mixture was stirred for another 1 hour. Volatiles were removed in *vacuo*, 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 *vacuo*. The residue was purified by flash chromatography (EtOAc: hexanes = 1:1) to give the **14** as a white solid (2.0 g, 80%). $[\alpha]_D^{20}$ = +81.3 (c 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, J = 7.0 Hz, 1H), 7.12 (dd, J = 7.0, 2.0 Hz, 1H), 6.80 – 6.72 (m, 1H), 6.60 (d, J = 8.0 Hz, 1H), 4.88 (s, 1H), 4.01 (dd, J = 7.6, 4.8 Hz, 1H), 3.41 (s, 3H), 2.68 (dd, J = 13.2 , 5.6 Hz, 1H), 2.55 (dd, J = 13.2, 5.6 Hz, 1H), -0.06 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 148.1, 128.9, 128.5, 123.9, 117.5, 108.9, 89.0, 82.8, 58.0, 50.4, 43.1, 0.00 (3C); HRESIMS *m/z* 307.1472 $[M+H]^+$, calcd for $C_{15}H_{23}N_2O_3Si$, 307.1472.

Methyl (2S,3aS,8aS)-3a-hydroxy-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-

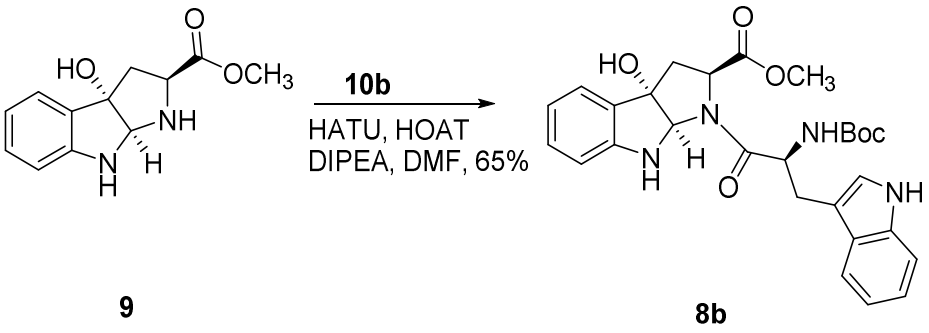
*b]indole-2-carboxylate (**9**)*.



14 **9**

To a solution of **14** (2.3 g, 7.5 mmol) in 40.0 mL anhydrous THF under an argon atmosphere was added TBAF (1.0 mol/L, 11.0 mL) at 0 ºC. After the addition, the mixture was kept stirred for 40 minutes at 0 ºC and the reaction was then quenched by the addition of saturated ammonium chloride. 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 = 1:1) to give **9** (1.6 g, 90%) as a colorless oil. $[\alpha]_D^{20}$ = -103.6 (c 1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, J = 8.0 Hz, 1H), 7.13 (dd, J = 8.0, 1.5 Hz, 1H), 6.79 (dd, J = 7.5, 1.5 Hz, 1H), 6.59 (d, J = 8.0 Hz, 1H), 4.84 (s, 1H), 4.55 (s, 2H), 4.02 (dd, J = 7.5, 5.5 Hz, 1H), 3.46 (s, 3H), 2.60 (dd, J = 13.0, 7.5 Hz, 1H), 2.50 (dd, J = 13.0, 5.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 149.1, 130.8, 130.2, 123.9, 119.5, 110.6, 88.9, 85.4, 59.7, 52.1, 42.4; HRESIMS *m/z* 235.1072 $[M+H]^+$, calcd for $C_{12}H_{15}N_2O_3$, 235.1077.

Methyl (2S,3aS,8aR)-1-((tert-butoxycarbonyl)-L-tryptophyl)-3a-hydroxy-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carboxylate (***8b***).

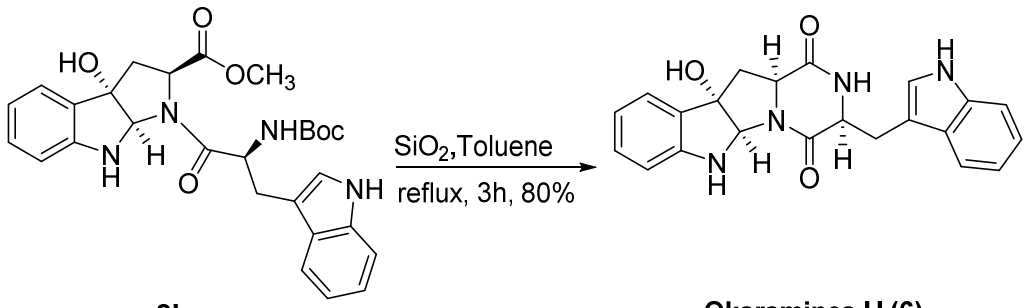


9 **8b**

To a solution of the mixture of **9** (100.0 mg, 0.43 mmol) and **10b** (130.0 mg, 0.43 mmol) in 5.0 mL DMF was added HATU (246.0 mg, 0.65 mmol), HOAT (6.0 mg, 0.04 mmol) and DIPEA (0.45 mL, 2.6 mmol) at 0 °C. The cooling bath was removed, and the mixture was further stirred at 25 °C overnight. The reaction was quenched by the addition of H_2O (20.0 mL), and the aqueous layer was extracted with EtOAc (20.0 mL x 3). The combined organic layer was washed with brine and dried with Na_2SO_4, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc: hexanes = 1:1) to afford **8b** as a light yellow oil (144.0 mg, 65%) $[\alpha]_D^{20}$ = +48.5 (c 1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$, major rotamer) δ 8.56 (s, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.21 (dd, J = 8.0, 2.0 Hz, 1H), 7.17 – 7.10 (m, 1H), 7.07-7.01 (m, 3H), 6.69 – 6.59 (m, 1H), 6.49 (d, J = 8.0 Hz, 1H), 5.60 (d, J = 8.4 Hz, 1H), 5.20 (s, 1H), 4.97 (s, 1H), 4.57 – 4.38 (m, 1H), 3.56 (d, J = 8.4 Hz, 1H), 3.35 – 3.21 (m, 1H), 3.19 (s, 1H), 3.04 (s, 3H), 2.31 (d, J = 12.4 Hz, 1H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 170.0, 154.7, 150.1, 136.1, 130.9, 127.5, 127.3, 124.4, 123.3, 122.6, 120.0, 119.2, 118.8, 111.5, 110.4, 109.9, 84.7, 81.1, 79.7, 59.1, 52.7, 52.4, 52.0, 37.7,

28.4 (3C); HRESIMS *m/z* 543.2208 $[M+Na]^+$, calcd for $C_{28}H_{32}N_4O_6Na$, 543.2214.

*(3S,5aR,10bS,11aS)-3-((1H-indol-3-yl)methyl)-10b-Hydroxy-2,3,6,10b,11,11a-hexahydro-4H-pyrazino[1',2':1,5]pyrrolo[2,3-b]indole-1,4(5aH)-dione (**6**)*.

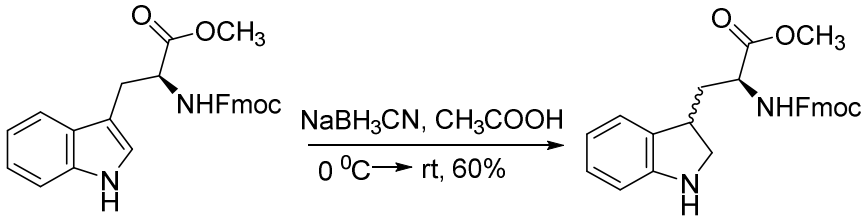


8b **Okaramines U (6)**

To a solution of **8b** (130.0 mg, 0.25 mmol) in anhydrous toluene (15.0 mL) was added SiO_2 (2.0 g), and the reaction mixture was heated with stirring at 110 °C for 5 hours. The reaction was filtered through a pad of Celite, which was washed with a mixture of CH_2Cl_2/MeOH (20.0 mL, 1:1). The solvents of the filtrate were evaporated. The residue was purified by column chromatography (EtOAc: hexanes = 3:2) to afford **6** (78.0 mg, 80%) as a colorless oil. $[\alpha]_D^{25}$ = +34.9 (c 0.2, MeOH) (Literature[2], $[\alpha]_D^{25}$ = +16.6 (c 0.25, MeOH)); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.87 (s, 1H), 7.74 (s, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.25 (s, 1H), 7.18 (dd, J = 7.6, 1.2 Hz, 1H), 7.06 (dd, J = 7.6, 1.2 Hz, 2H), 7.00 (dd, J = 7.6, 1.2 Hz, 1H), 6.73 – 6.63 (m, 2H), 6.55 (d, J = 7.8 Hz, 1H), 6.05 (s, 1H), 5.33 (d, J = 4.0 Hz, 1H), 4.66 (dd, J = 11.2, 6.8 Hz, 1H), 4.47 (t, J = 5.6 Hz, 1H), 3.35 (s, 1H), 3.06 (dd, J = 15.2, 6.4 Hz, 1H), 2.43 (dd, J = 13.2, 6.4

Hz, 1H), 1.82 (dd, J = 13.2, 11.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.2, 168.1, 148.8, 136.4, 131.5, 129.4, 127.8, 124.6, 122.9, 121.4, 118.9, 118.7, 118.2, 111.7, 110.2, 110.0, 86.3, 84.4, 59.1, 55.5, 41.7, 25.1; HRESIMS *m/z* 389.1602 $[M+H]^+$, calcd for $C_{22}H_{21}N_4O_3$, 389.1608.

1,8-Di-tert-butyl 2-methyl (2S,3aS,8aS)-3a-bromo-2,3,3a,8a-tetrahydropyrrolo[2,3-b]indole-1,2,8-tricarboxylate (***16***).



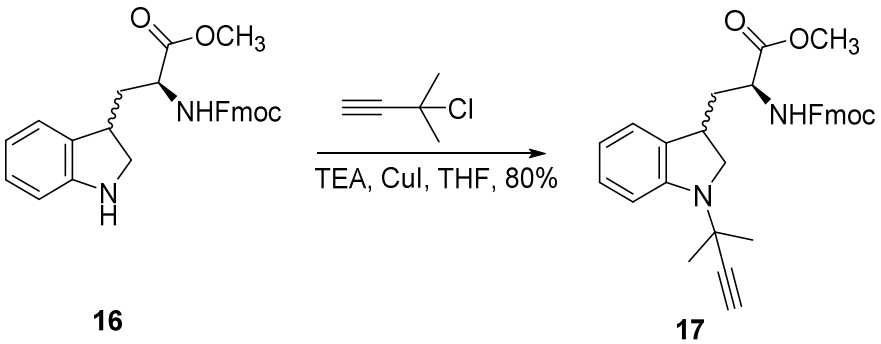
15 **16**

To a solution of **15** (6.7 g, 15.2 mmol) in AcOH (100.0 mL), $NaBH_3CN$ (9.6 g, 0.15 mol) was added at 0 °C. Then, the mixture was stirred for 12 hours at 25°C, and the crude material was diluted with water/CH_2Cl_2 (1:1, 600.0 mL). Using 1 *N* aq. NaOH, the pH value of the mixture was adjusted to 12. The organic layer was separated and washed with brine (300.0 mL), and concentrated in *vacuo*. Purification by flash column chromatography (EtOAc: hexanes = 1:3) yield a mixture of **16a** and **16b** (1:1, 4.0 g, 60%). **16a**: $[\alpha]_D^{20}$ = +12.7 (c 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, J = 7.6, 4.8 Hz, 2H), 7.62 (dd, J = 7.6, 5.2 Hz, 2H), 7.46 – 7.35 (m, 2H), 7.33 (dd, J = 7.2, 4.0 Hz, 2H), 7.06 (dd, J = 7.2, 1.2 Hz, 2H), 6.74 (dd, J = 7.6, 1.2 Hz, 1H), 6.65 (d, J = 7.6 Hz, 1H), 5.49 (d, J = 8.8 Hz, 1H), 4.49-4.45 (m, 3H), 4.24 (t, J = 6.8 Hz, 1H), 3.75 (s, 3H), 3.71 (d, J = 8.0 Hz, 1H), 3.38 – 3.20 (m, 2H), 2.27 – 1.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 173.0, 156.1, 151.3, 143.9, 143.7, 141.4, 131.6, 127.9, 127.8 (2C), 127.1 (3C), 125.1 (2C), 123.7, 120.1, 120.0, 118.8, 109.7, 66.9, 53.0, 52.6, 52.5, 47.2, 38.7, 37.4; HRESIMS *m/z* 443.1967 $[M+H]^+$, calcd for $C_{27}H_{27}N_2O_4$, 443.1965.

16b: $[\alpha]_D^{20}$ = -38.8 (c 0.1, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 7.2 Hz, 2H), 7.62 (dd, J = 6.4, 1.2 Hz, 2H), 7.41 (dd, J = 7.2, 1.2 Hz, 2H), 7.36 – 7.29 (m, 2H), 7.17 (d, J = 7.2 Hz, 1H), 7.06 (dd, J = 7.6, 2.0 Hz, 1H), 6.76 (dd, J = 7.6, 2.0 Hz, 1H), 6.67 (d, J = 7.6 Hz, 1H), 5.56 (d, J = 8.8 Hz, 1H), 4.60 – 4.47 (m, 1H), 4.45 (d, J = 7.2 Hz, 2H), 4.24 (t, J = 7.2 Hz, 1H), 3.72 (s, 3H), 3.68 (d, J = 8.8 Hz, 1H), 3.39 – 3.30 (m, 1H), 3.26 – 3.13 (m, 1H), 2.33 (dd, J = 13.6, 6.0 Hz, 1H), 1.97 – 1.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 156.0, 151.0, 143.9, 143.7, 141.4, 131.4, 128.0, 127.8 (2C), 127.1 (3C), 125.1 (2C), 124.3, 120.0 (2C), 119.0, 109.9, 67.0, 53.6, 52.7, 52.5, 47.2, 38.8, 37.3; HRESIMS *m/z* 443.1965 $[M+H]^+$, calcd for $C_{27}H_{27}N_2O_4$, 443.1965.

*Methyl (2S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(1-(2-methylbut-3-yn-2-yl)indolin-3-yl)propanoate (**17**).*



16 **17**

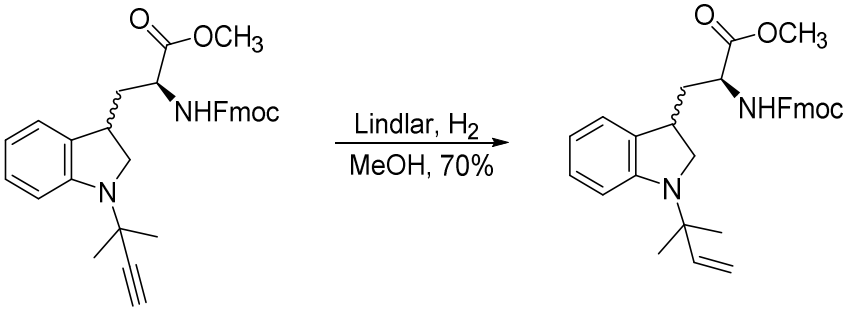
To a 100.0 mL round bottom flask containing **16** (6.5 g, 14.7 mmol), 3-

chloro-3-methylbut-1-yne (3.3 mL, 29.4 mmol), and CuI (28.0 mg, 1.5 mmol) in anhydrous THF (60.0 mL) under an argon atmosphere, was added Et_3N (2.6 mL, 18.6 mmol) dropwise at 0 °C. After the addition, the mixture was stirred at 0 °C for 15 minutes. Then, the reaction was extracted with EtOAc/H_2O (1:1, 200.0 mL), and the organic layer was concentrated under reduced pressure. The residue was purified by column chromatography (EtOAc: hexanes = 1:5) to give **17** (6.0 g, 80%) as a yellow oil. **17a**: $[\alpha]_D^{20}$ = +10.6 (c 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, J = 7.6, 4.4 Hz, 2H), 7.65 – 7.58 (m, 2H), 7.40 (dd, J = 7.6, 4.4 Hz, 2H), 7.35 – 7.29 (m, 2H), 7.21 (d, J = 8.0 Hz, 1H), 7.14 – 7.06 (m, 1H), 7.03 (d, J = 7.2 Hz, 1H), 6.74 (dd, J = 7.2, 7.2 Hz, 1H), 5.37 (d, J = 8.8 Hz, 1H), 4.51 – 4.42 (m, 3H), 4.24 (t, J = 6.8 Hz, 1H), 3.75 (s, 3H), 3.62 (t, J = 8.0 Hz, 1H), 3.21 (t, J = 7.2 Hz, 1H), 3.11 (t, J = 8.0 Hz, 1H), 2.39 (s, 1H), 2.08 (t, J = 4.0 Hz, 2H), 1.62 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 156.2, 149.7, 143.9, 143.7, 141.4, 133.7, 127.8, 127.4 (2C), 127.1 (3C), 125.0 (2C), 123.2, 120.0 (2C), 118.4, 111.8, 87.3, 70.9, 67.1, 54.9, 52.6, 52.5, 50.9, 47.2, 37.1, 36.4, 27.7, 26.7; HRESIMS *m/z* 509.2434 $[M+H]^+$, calcd for $C_{32}H_{33}N_2O_4$, 509.2435.

17b: $[\alpha]_D^{20}$ = -26.1 (c 0.15, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 7.6 Hz, 2H), 7.62 (dd, J = 6.4, 4.0 Hz, 2H), 7.40 (dd, J = 7.6, 4.0 Hz, 2H), 7.33 (dd, J = 7.6, 4.0 Hz, 2H), 7.22 (d, J = 8.0 Hz, 1H), 7.12 (dd, J = 8.0, 4.0 Hz, 2H), 6.77 (dd, J = 8.0, 7.6 Hz, 1H), 5.58 (d, J = 8.8 Hz, 1H),

4.53 (d, J = 7.6 Hz, 1H), 4.46 (d, J = 7.2 Hz, 2H), 4.25 (t, J = 7.2 Hz, 1H), 3.72 (s, 3H), 3.57 (t, J = 8.4 Hz, 1H), 3.23 (t, J = 7.2 Hz, 1H), 3.09 (t, J = 7.2 Hz, 1H), 2.39 (s, 1H), 2.36 – 2.26 (m, 1H), 2.00 – 1.86 (m, 1H), 1.59 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 156.0, 149.5, 143.9, 143.7, 141.3, 133.4, 127.8 (2C), 127.5, 127.1 (3C), 125.1 (2C), 123.9, 120.0 (2C), 118.7, 111.9, 87.1, 71.0, 67.1, 55.5, 52.7, 52.5, 51.0, 47.2, 36.9, 36.6, 27.2, 27.1; HRESIMS *m/z* 509.2435 $[M+H]^+$, calcd for $C_{32}H_{33}N_2O_4$, 509.2435.

*Methyl (2S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(1-(2-methylbut-3-en-2-yl)indolin-3-yl)propanoate (**18**).*



17 **18**

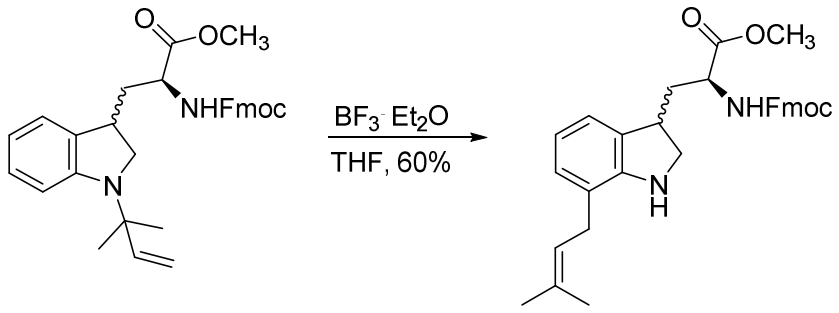
To a solution of **17** (1.5 g, 3.0 mmol) in MeOH (80.0 mL) was added Lindlar catalyst (450.0 mg, wt 30%). The mixture was stirred under an atmosphere of H_2 until the starting material disappeared, the reaction mixture was filtered through a short plug of silica gel and concentrated under reduced pressure. The residue was purified by column chromatography (EtOAc: hexanes = 1:5) to yield the title compound **18** (1.1 g, 70.0%) as a yellow oil. **18a**: $[\alpha]_D^{20}$ = +11.6 (c 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, J = 7.6, 3.6 Hz, 2H), 7.63 (dd, J = 6.4, 1.2 Hz, 2H), 7.42 (dd, J = 7.6, 3.6 Hz, 2H), 7.37 – 7.28 (m, 2H), 7.07 – 6.94

(m, 2H), 6.81 (d, J = 8.0 Hz, 1H), 6.67 (dd, J = 8.0, 7.2 Hz, 1H), 6.13 (dd, J = 17.6, 10.8 Hz, 1H), 5.46 (d, J = 8.8 Hz, 1H), 5.30 – 5.11 (m, 2H), 4.52 (dd, J = 9.2, 6.0 Hz, 1H), 4.47 (d, J = 6.8 Hz, 2H), 4.26 (t, J = 7.2 Hz, 1H), 3.77 (s, 3H), 3.71 – 3.57 (m, 1H), 3.19 (p, J = 7.6, 6.8 Hz, 2H), 2.18 – 2.05 (m, 2H), 1.36 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.1, 156.2, 150.4, 146.7, 143.9, 143.6, 141.3, 133.4, 127.8 (2C), 127.2, 127.1 (3C), 125.1 (2C), 123.1, 120.0 (2C), 117.3, 112.3, 111.4, 67.1, 57.2, 54.7, 52.6, 52.5, 47.2, 37.4, 36.4, 25.1, 23.2; HRESIMS *m/z* 511.2591 $[M+H]^+$, calcd for $C_{32}H_{35}N_2O_4$, 511.2591.

18b: $[\alpha]_D^{20}$ = -26.1 (c 0.1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, J = 7.5 Hz, 2H), 7.62 (dd, J = 7.5, 2.5 Hz, 2H), 7.49 – 7.38 (m, 2H), 7.36 – 7.29 (m, 2H), 7.09 (d, J = 7.5 Hz, 1H), 7.00 (dd, J = 8.0, 7.5 Hz, 1H), 6.82 (d, J = 8.0 Hz, 1H), 6.68 (dd J = 7.5, 2.5 Hz, 1H), 6.11 (dd, J = 17.5, 11.0 Hz, 1H), 5.66 (d, J = 8.0 Hz, 1H), 5.22 (d, J = 17.5 Hz, 1H), 5.13 (d, J = 11.0 Hz, 1H), 4.55 – 4.50 (m, 1H), 4.44 (t, J = 7.0 Hz, 2H), 4.25 (t, J = 7.0 Hz, 1H), 3.71 (s, 3H), 3.59 (t, J = 8.5 Hz, 1H), 3.23 (t, J = 7.0 Hz, 1H), 3.14 (s, 1H), 2.32 (dd, J = 13.5, 6.5 Hz, 1H), 2.05 – 1.92 (m, 1H), 1.32 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 156.0, 150.2, 146.6, 143.9, 143.7, 141.3, 133.1, 127.7 (2C), 127.3, 127.1 (3C), 125.1 (2C), 123.9, 120.0 (2C), 117.6, 112.3, 111.7, 67.1, 57.3, 55.2, 52.6, 52.5, 47.2, 37.1, 36.6, 24.6, 23.5; HRESIMS *m/z* 511.25891 $[M+H]^+$, calcd for $C_{32}H_{35}N_2O_4$, 511.2591.

Methyl (2S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(7-(3-

*methylbut-2-en-1-yl)indolin-3-yl)propanoate (**19**).*



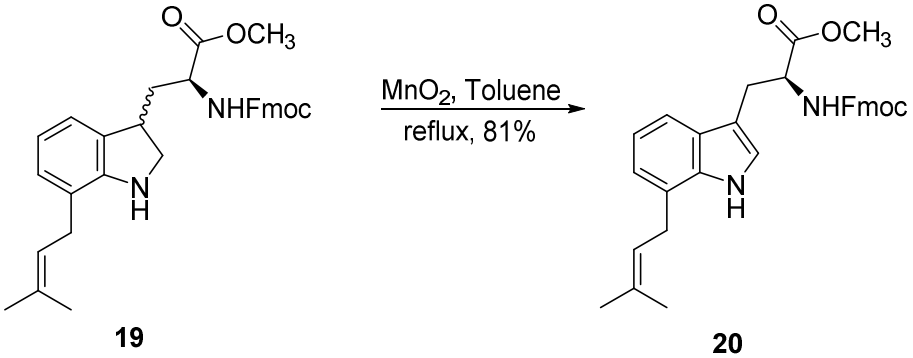
18 **19**

To a solution of **18** (1.0 g, 2.0 mmol) in a solvent of 50.0 mL anhydrous THF was added $BF_3{\cdot}Et_2O$ at 0 °C (2.5 mL, 20.0 mmol). After the addition, the cooling bath was removed and the mixture was stirred at room temperature for 40 hours. The reaction was quenched by addition of saturated sodium bicarbonate (30.0 mL), and the mixture was extracted with EtOAc (50.0 mL). The organic layers were concentrated in vacuum. The residue was purified by flash chromatography (EtOAc: Hexanes = 1:3) to produce **19** (0.60 g, 60.0%) as a colourless oil. **19a**: $[\alpha]_D^{20}$ = +11.8 (c 0.1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, J = 7.0, 7.0 Hz, 2H), 7.62 (dd, J = 7.0, 7.0 Hz, 2H), 7.40 (dd, J = 7.5, 7.0 Hz, 2H), 7.32 (dd, J = 7.0, 7.0 Hz, 2H), 6.95 (d, J = 7.5 Hz, 1H), 6.91 (d, J = 7.5 Hz, 1H), 6.71 (dd, J = 7.5, 2.5 Hz, 1H), 5.39 (d, J = 8.5 Hz, 1H), 5.26 (t, J = 7.5 Hz, 1H), 4.49 – 4.44 (m, 3H), 4.24 (t, J = 7.0 Hz, 1H), 3.75 (s, 3H), 3.75 – 3.69 (m, 1H), 3.35 – 3.26 (m, 2H), 3.19 (d, J = 7.0 Hz, 2H), 2.10 (td, J = 8.5, 4.5 Hz, 2H), 1.77 (s, 3H), 1.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.1, 156.1, 149.6, 143.9, 143.7, 141.4, 133.3, 131.4, 127.8 (2C), 127.1 (3C), 125.1 (2C), 123.0, 121.7, 121.4, 120.0 (3C), 119.0, 67.0, 53.0, 52.6, 47.2, 38.9,

37.6, 30.4, 25.8 (2C), 17.9; HRESIMS *m/z* 511.2591 $[M+H]^+$, calcd for $C_{32}H_{35}N_2O_4$, 511.2591.

19b: $[\alpha]_D^{20}$ = -41.7 (c 0.1, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 7.6 Hz, 2H), 7.66 – 7.52 (m, 2H), 7.47 – 7.36 (m, 2H), 7.31 (dd, J = 7.6, 7.2 Hz, 2H), 7.03 (d, J = 7.2 Hz, 1H), 6.91 (d, J = 7.6 Hz, 1H), 6.72 (dd, J = 7.6, 7.2 Hz, 1H), 5.44 (d, J = 8.8 Hz, 1H), 5.25 (dd, J = 7.6, 7.2 Hz, 1H), 4.53 (t, J = 7.6 Hz, 1H), 4.44 (d, J = 7.2 Hz, 2H), 4.24 (t, J = 7.2 Hz, 1H), 3.73 (s, 3H), 3.73 – 3.68 (m, 1H), 3.38 (t, J = 7.6 Hz, 1H), 3.26 (d, J = 8.0 Hz, 1H), 3.19 (d, J = 7.2 Hz, 2H), 2.33 (dd, J = 13.2, 7.2 Hz, 1H), 1.93 (dt, J = 13.2, 7.8 Hz, 1H), 1.76 (s, 3H), 1.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 155.9, 149.4, 143.9, 143.7, 141.3, 133.3, 131.1, 127.8, 127.7 (2C), 127.1 (3C), 125.1 (2C), 123.0, 121.9, 121.6, 120.0 (2C), 119.1, 67.0, 53.6, 52.7, 52.5, 47.2, 39.0, 37.5, 30.5, 25.8, 17.9; HRESIMS *m/z* 511.2582 $[M+H]^+$, calcd for $C_{32}H_{35}N_2O_4$, 511.2591.

*Methyl (S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(7-(3-methylbut-2-en-1-yl)-1H-indol-3-yl)propanoate (**20**).*

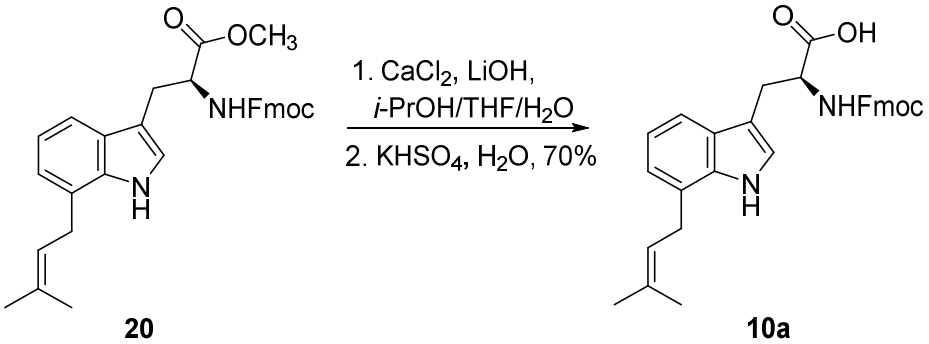


19 **20**

To a solution of **19** (2.1 g, 4.1 mmol) in anhydrous toluene (30.0 mL) was added activated manganese (IV) oxide (3.6 g, 41.0 mmol). The mixture

was kept refluxing for 4 hours, allowed to cool, and filtered through a short plug of silica gel. Concentration of the filtrate under reduced pressure was followed by column chromatography (EtOAc: hexanes = 1:3) to produce **20** as a light-yellow oil (1.7 g, 81.0%). $[\alpha]_D^{20}$ = +13.0 (c 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.77 (d, J = 7.6 Hz, 2H), 7.56 (dd, J = 10.4, 7.6 Hz, 2H), 7.45 – 7.38 (m, 3H), 7.35 – 7.27 (m, 2H), 7.08 (dd, J = 10.4, 7.6 Hz, 1H), 7.02 (d, J = 7.2 Hz, 1H), 6.94 (d, J = 2.4 Hz, 1H), 5.39 (dd, J = 10.4, 5.2 Hz, 2H), 4.75 (dt, J = 8.0, 5.2 Hz, 1H), 4.39 (qd, J = 10.4, 7.2 Hz, 2H), 4.21 (t, J = 7.2 Hz, 1H), 3.72 (s, 3H), 3.56 (d, J = 7.2 Hz, 2H), 3.34 (d, J = 5.2 Hz, 2H), 1.83 (s, 3H), 1.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 155.8, 143.9, 143.8, 141.3, 135.4, 133.4, 127.7 (2C), 127.6, 127.1 (3C), 125.2, 124.2, 122.6, 122.1, 121.9, 120.0 (3C), 116.6, 110.3, 100.0, 67.0, 54.6, 52.4, 47.2, 30.7, 28.0, 25.8, 18.0; HRESIMS *m/z* 509.2432 $[M+H]^+$, calcd for $C_{32}H_{33}N_2O_4$, 509.2435.

*(S)-2-((((9H-Fluoren-9-yl)methoxy)carbonyl)amino)-3-(7-(3-methylbut-2-en-1-yl)-1H-indol-3-yl)propanoic acid (**10a**)*.

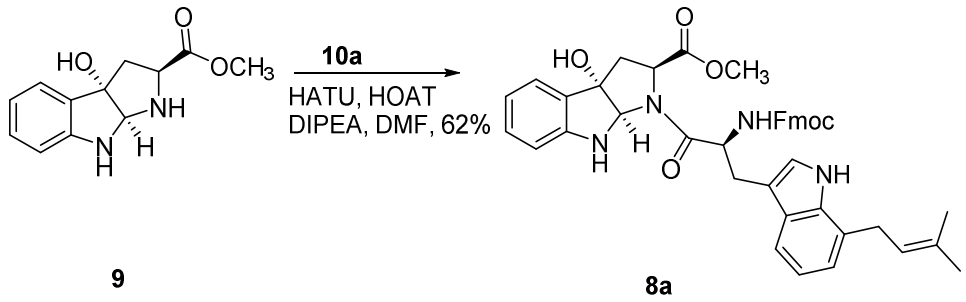


20 **10a**

To a solution of **20** (130.0 mg, 0.26 mmol) in a mixture solvent of *i*-PrOH (6.0 mL), THF (2.0 mL) and H_2O (2.0 mL) was added LiOH (28.0 mg, 1.2

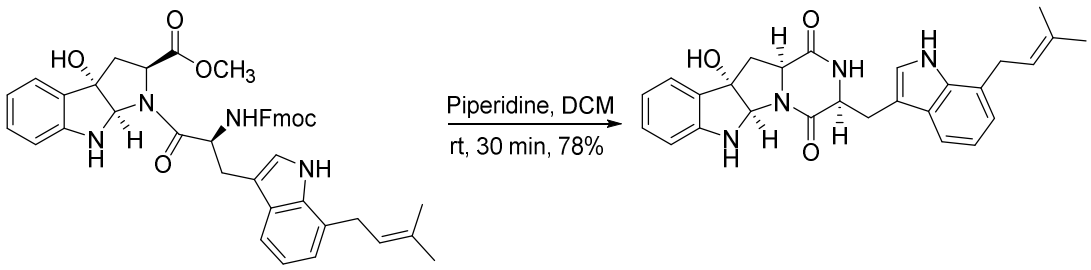
mmol) and $CaCl_2$ (450.0 mg, 4.0 mmol). After the addition, the mixture was stirred for 10 hours at 25 °C. Removal of the organic solvent under vacuum, the residue was extracted with H_2O/CH_2Cl_2 (200 mL, 1:1), and the aqueous layer was acidified with $KHSO_4$ (pH < 2) and extracted with EtOAc (50.0 mL x 3). The organic layer was combined and concentrated to give **10a** (88.0 mg, 70.0%) as a light-yellow oil, which was used directly in next step without further purification. $[\alpha]_D^{20}$ = +76.2 (c 0.1, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.75 (d, J = 7.5 Hz, 2H), 7.61 – 7.46 (m, 3H), 7.42 – 7.33 (m, 2H), 7.32 – 7.22 (m, 1H), 7.07 (d, J = 7.5 Hz, 1H), 7.02 (d, J = 7.0 Hz, 1H), 6.95 (d, J = 2.5 Hz, 1H), 5.38 (d, J = 8.5 Hz, 2H), 4.86 – 4.70 (m, 1H), 4.48 – 4.29 (m, 2H), 4.18 (t, J = 7.0 Hz, 1H), 3.53 (d, J = 7.0 Hz, 2H), 3.36 (s, 2H), 1.80 (s, 3H), 1.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.2, 156.1, 143.8, 143.7, 141.3 (2C), 135.4, 133.5, 127.7 (2C), 127.6, 127.1 (3C), 125.2, 124.3, 122.9, 122.0, 121.9, 120.1, 120.0 (2C), 116.6, 109.9, 67.2, 54.6, 47.1, 30.6, 27.7, 25.7, 18.0; HRESIMS *m/z* 495.2271 $[M+H]^+$, calcd for $C_{31}H_{31}N_2O_4$, 495.2278.

*Methyl (2S,3aS,8aR)-1-((S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(7-(3-methylbut-2-en-1-yl)-1H-indol-3-yl)propanoyl)-3a-hydroxy-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carboxylate (**8a**)*.



Compounds **8a** (colorless oil, 188.0 mg, 62%) was prepared from **10a** (210.0 mg, 0.43 mmol) with **9** (100.0 mg, 0.43 mmol) under the same procedure as for **8b**. $[\alpha]_D^{20}$ = +30.0 (c 0.1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, major rotamer) δ 8.21 (s, 1H), 7.77 (d, J = 7.5 Hz, 2H), 7.75-7.50 (m, 3H), 7.40 (dd, J = 8.0, 7.5 Hz, 2H), 7.32 (dd, J = 8.0, 7.5 Hz, 2H), 7.25-7.07 (m, 5H), 6.64 (dd, J = 8.0, 7.5 Hz, 1H), 6.52 (d, J = 8.0 Hz, 1H), 5.86 (d, J = 8.0 Hz, 1H), 5.46 – 5.35 (m, 1H), 5.02 (s, 1H), 4.51 (brs, 1H), 4.46 – 4.38 (m, 1H), 4.32 (t, J = 9.0 Hz, 1H), 4.21 (t, J = 8.5 Hz, 1H), 3.67 – 3.51 (m, 3H), 3.42 – 3.27 (m, 1H), 3.17 (s, 1H), 3.02 (s, 3H), 2.61 – 2.53 (m, 1H), 2.33 (d, J = 12.6 Hz, 1H), 1.83 (s, 3H), 1.80 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.9, 169.9, 155.3, 149.0, 143.8 (2C), 141.3 (2C), 135.3, 133.7, 130.5, 127.7 (3C), 127.1 (2C), 125.1 (2C), 124.5, 124.3, 123.0, 122.3, 121.9, 120.3, 120.0 (3C), 119.4, 116.8, 110.1, 109.5, 84.8, 81.2, 66.9, 59.0, 53.2, 52.5, 47.2, 38.8, 30.7, 25.8 (2C), 18.1; HRESIMS *m/z* 711.3183 $[M+H]^+$, calcd for $C_{43}H_{43}N_4O_6$, 711.3177.

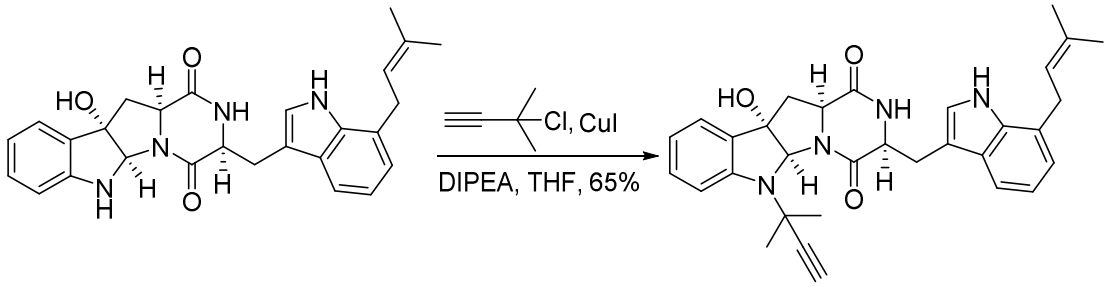
*(3S,5aR,10bS,11aS)-10b-Hydroxy-3-((7-(3-methylbut-2-en-1-yl)-1H-indol-3-yl)methyl)-2,3,6,10b,11,11a-hexahydro-4H-pyrazino[1',2':1,5]pyrrolo[2,3-b]indole-1,4(5aH)-dione (**5**).*



8a **Okaramines T (5)**

To a solution of **8a** (100.0 mg, 0.14 mmol) in 10.0 mL anhydrous DCM was added piperidine (1.0 ml, 11.0 mmol). After the addition, the mixture was kept stirred for 40 minutes at 25 °C, and the organic solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc: hexanes = 1:1) to give **5** (50.0 mg, 78.0%) as a light-yellow oil. $[\alpha]_D^{25}$= +36.7 (c 0.2, MeOH) (Literature[2], $[\alpha]_D^{25}$ = +16.7 (c 0.25, MeOH)); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.82 (brs, 1H), 7.72 (s, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.25 (s, 1H), 7.19 (d, J = 7.5 Hz, 1H), 7.05 (dd, J = 8.0, 7.5 Hz, 1H), 6.97 – 6.88 (m, 1H), 6.85 (d, J = 7.0 Hz, 1H), 6.75-6.66 (m, 2H), 6.55 (d, J = 8.0 Hz, 1H), 6.06 (s, 1H), 5.43 (d, J = 7.5 Hz, 1H), 5.34 (d, J = 4.0 Hz, 1H), 4.67 (dd, J = 11.5, 6.5 Hz, 1H), 4.46 (s, 1H), 3.51 (d, J = 7.5 Hz, 2H), 3.05 (dd, J = 15.5, 6.5 Hz, 1H), 2.44 (dd, J = 13.0, 6.5 Hz, 1H), 1.84 (t, J = 13.0 Hz, 1H), 1.72 (s, 6H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.3, 168.2, 148.9, 135.3, 132.4, 131.6, 129.4, 127.8, 124.7, 124.4, 122.9, 122.7, 120.5, 119.1, 118.2, 116.6, 110.5, 110.3, 86.3, 84.4, 59.1, 55.5, 41.7, 29.5, 26.0, 25.2, 18.2; HRESIMS *m/z* 457.2238 $[M+H]^+$, calcd for $C_{27}H_{29}N_4O_3$, 457.2234.

*(3S,5aR,10bS,11aS)-10b-Hydroxy-3-((7-(3-methylbut-2-en-1-yl)-1H-indol-3-yl)methyl)-6-(2-methylbut-3-yn-2-yl)-2,3,6,10b,11,11a-hexahydro-4H-pyrazino[1',2':1,5]pyrrolo[2,3-b]indole-1,4(5aH)-dione (**21**)*.

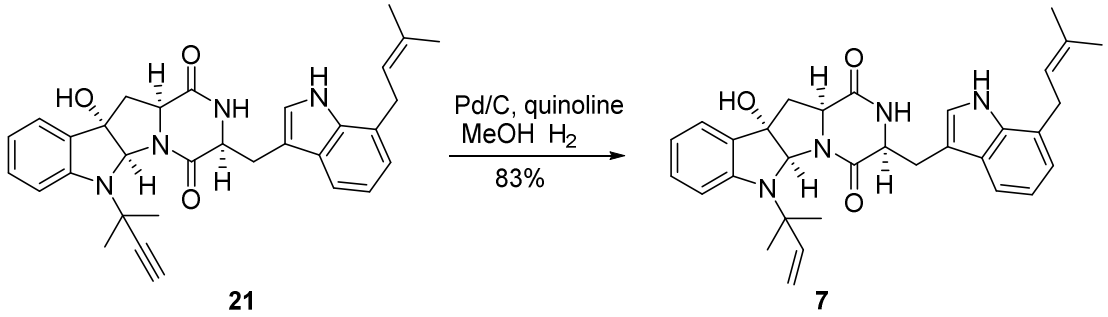


Okaramine T (5) **21**

To a 100 mL round bottomed flask containing **5** (100.0 mg, 0.22 mmol), 3-chloro-3-methylbut-1-yne (0.10 mL, 0.6 mmol), and CuI (40.0 mg, 0.2 mmol) in anhydrous THF (15.0 mL) under an argon atmosphere was added DIPEA (0.4 mL, 3.0 mmol) dropwise at 0 °C. After the addition, the cooling bath was removed and the mixture was stirred at 25 °C for 3 days. The reaction was extracted with EtOAc/H_2O (60.0 mL, 1:1), and the organic layer was concentrated under reduced pressure. The crude material was purified by column chromatography (EtOAc: hexanes = 1:1) to give **21** (74.0 mg, 65.0%) as a light-yellow oil. $[\alpha]_D^{20}$ = +58.2 (c 1, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.37 (dd, J = 7.5, 4.5 Hz, 2H), 7.25 (d, J = 13.5 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H), 7.03 (dd, J = 13.5, 7.0 Hz, 2H), 6.96 (d, J = 7.5 Hz, 1H), 6.93 (d, J = 2.5 Hz, 1H), 5.50 (s, 1H), 5.46 (s, 1H), 5.37 (t, J = 7.0 Hz, 1H), 4.25 (dd, J = 10.5, 5.0 Hz, 1H), 4.18 (dd, J = 10.5, 3.5 Hz, 1H), 3.65 (dd, J = 13.5, 4.0 Hz, 1H), 3.53 (d, J = 7.0

Hz, 2H), 3.08 (dd, J = 13.5, 4.0 Hz, 1H), 2.88 – 2.77 (m, 1H), 2.62-2.58 (m, 2H), 2.38 (s, 1H), 1.94 (s, 3H), 1.89 (s, 3H), 1.80 (s, 3H), 1.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.9, 167.8, 147.8, 135.8, 134.3, 133.6, 129.8, 126.6, 124.5, 124.2, 123.0, 122.3, 122.2, 122.0, 120.2, 117.4, 116.4, 110.1, 89.3, 85.4, 84.2, 71.3, 57.5, 55.0, 54.2, 33.3, 30.7, 30.6, 30.0, 26.3, 25.7, 18.0; HRESIMS *m/z* 523.2700 $[M+H]^+$, calcd for $C_{32}H_{35}N_4O_3$, 523.2704.

(3S,5aR,10bS,11aS)-10b-Hydroxy-3-((7-(3-methylbut-2-en-1-yl)-1H-indol-3-yl)methyl)-6-(2-methylbut-3-en-2-yl)-2,3,6,10b,11,11a-hexahydro-4H-pyrazino[1',2':1,5]pyrrolo[2,3-b]indole-1,4(5aH)-dione (7).

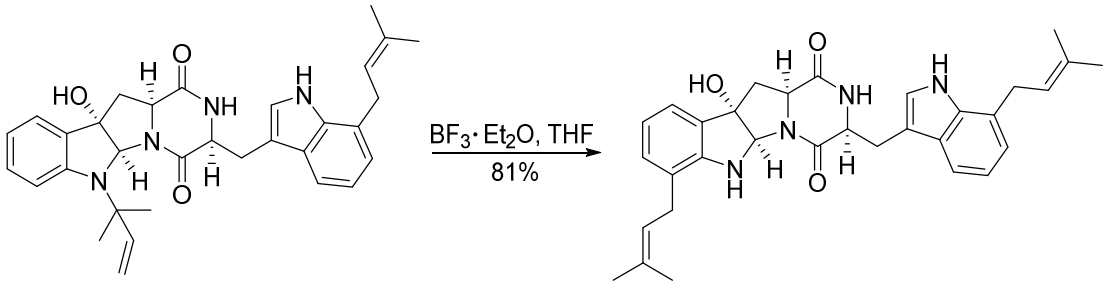


21 **7**

To a solution of **21** (50.0 mg, 0.09 mmol) in a mixture solvent of (CH_3OH/quinoline 10:1, 10.0 mL) was added 10% Pd/C catalysis (10.0 mg). After the addition, the reaction mixture was kept stirring under an atmosphere of H_2 until the starting material disappeared, then the mixture was filtered through a short plug of silica gel purified by column chromatography (EtOAc: hexanes = 1:1) to afford the compound **7** (41.0 mg, 83.0%) as a colorless oil. $[\alpha]_D^{20}$ = +12.0 (c 0.1, CH_2Cl_2); ^{1}H NMR (400

MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.39 (d, J = 7.2 Hz, 1H), 7.28 (d, J = 7.2 Hz, 1H), 7.16 (dd, J = 7.8, 7.2 Hz, 1H), 7.10 – 6.98 (m, 3H), 6.92 (d, J = 2.0 Hz, 1H), 6.82 (dd, J = 7.6, 2.0 Hz, 1H), 6.43 (dd, J = 17.6, 10.6 Hz, 1H), 5.49 (s, 1H), 5.41 (s, 1H), 5.39 – 5.31 (m, 1H), 5.25 – 5.07 (m, 2H), 4.21 (ddd, J = 14.4, 10.4, 4.0 Hz, 2H), 3.64 (dd, 1H), 3.53 (d, J = 7.2 Hz, 2H), 3.13 (dd, J = 13.6, 4.4 Hz, 1H), 2.85 (dd, J = 14.4, 10.4 Hz, 1H), 2.56 (dd, J = 13.6, 10.4 Hz, 1H), 2.07 (s, 1H), 1.81 (s, 3H), 1.78 (s, 3H), 1.71 (s, 3H), 1.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 167.7, 148.8, 147.1, 135.8, 133.5, 132.9, 130.0, 126.6, 124.5, 123.8, 122.9, 122.3, 122.0, 120.2, 120.2, 116.4, 115.4, 111.9, 110.1, 84.8, 83.7, 59.4, 57.2, 55.0, 32.8, 30.7, 27.7, 26.4, 25.9, 25.7, 18.0; HRESIMS *m/z* 525.2851 $[M+H]^+$, calcd for $C_{32}H_{37}N_4O_3$, 525.2860.

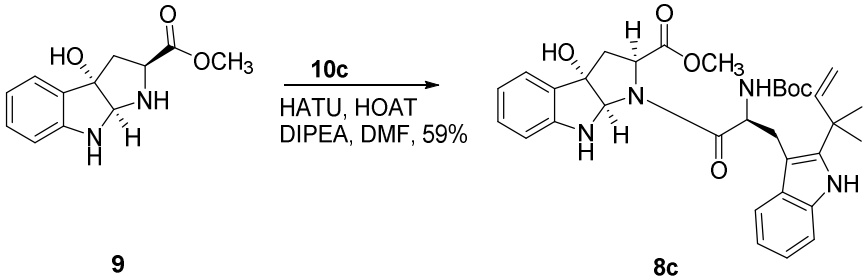
*(3S,5aR,10bS,11aS)-10b-Hydroxy-7-(3-methylbut-2-en-1-yl)-3-((7-(3-methylbut-2-en-1-yl)-1H-indol-3-yl)methyl)-2,3,6,10b,11,11a-hexahydro-4H-pyrazino[1',2':1,5]pyrrolo[2,3-b]indole-1,4(5aH)-dione (**4**)*.



7 **Okaramine S (4)**

To a solution of **7** (23.0 mg, 0.04 mmol) in a solvent of 10.0 mL anhydrous THF was added $BF_3{\cdot}Et_2O$ (0.1 mL, 0.4 mmol) at 0 °C. The reaction solution was kept stirring for 3 hours at 0 °C. When the starting material disappeared, the reaction was quenched by addition of saturated sodium bicarbonate (20.0 mL), and the mixture was extracted with EtOAc (30.0 mL). The organic layer was concentrated in vacuum, and the residue was purified by flash chromatography (EtOAc: hexanes = 1:1) to produce **4** (18.0 mg, 81%) as a colorless oil. $[\alpha]_D^{25}$ = -5.0 (c 0.1, MeOH) (Literature[2], $[\alpha]_D^{25}$ = -3.0 (c 0.25, MeOH)); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.78 (brs, 1H), 7.68 (s, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.25 (s, 1H), 7.04 (d, J = 7.5 Hz, 1H), 6.91 (t, J = 7.5 Hz, 1H), 6.86 (dd, J = 7.5, 1.0 Hz, 1H), 6.83 (dd, J = 7.0 Hz, 1H), 6.66 (t, J = 7.5 Hz, 1H), 6.04 (d, J = 4.5 Hz, 1H), 6.00 (s, 1H), 5.44 – 5.37 (m, 1H), 5.34 (d, J = 4.5 Hz, 1H), 5.27 – 5.19 (m, 1H), 4.64 (dd, J = 11.0, 6.5 Hz, 1H), 4.43 (t, J = 6.5 Hz, 1H), 3.49 (d, J = 7.5 Hz, 2H), 3.37 (d, J = 4.5 Hz, 1H), 3.21 (dd, J = 16.0, 7.5 Hz, 1H), 3.06 (td, J = 16.0, 7.0 Hz, 2H), 2.41 (dd, J = 13.0, 7.0 Hz, 1H), 1.82 (t, J = 13.0 Hz, 1H), 1.71 (s, 3H), 1.70 (s, 6H), 1.65 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.3, 168.5, 146.7, 135.4, 132.8, 132.5, 131.7, 128.7, 127.9, 124.8, 124.6, 123.4, 122.8, 122.3, 120.7, 120.6, 119.2 (2C), 116.8, 110.5, 86.5, 84.4, 59.1, 55.6, 41.8, 29.6, 29.0, 26.1 (2C), 25.3, 18.3, 18.2; HRESIMS *m/z* 525.2854 $[M+H]^+$, calcd for $C_{32}H_{37}N_4O_3$, 525.2860.

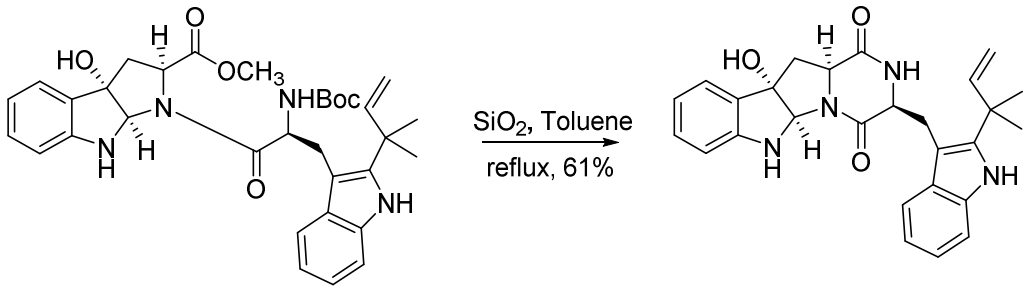
*Methyl (2S,3aS,8aR)-1-((S)-2-((tert-butoxycarbonyl)amino)-3-(2-(2-methylbut-3-en-2-yl)-1H-indol-3-yl)propanoyl)-3a-hydroxy 1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carboxylate (**8c**).*



9 **8c**

Compound **8c** (colorless oil, 280.0 mg, 59%) was prepared from **10c**[3] (302.0 mg, 0.8 mmol) with **9** (190.0 mg, 0.8 mmol) under the same procedure as **8b**. $[\alpha]_D^{20}$ = +180.9 (c 1, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.55 (d, J = 7.6 Hz, 1H), 7.33 (d, J = 7.6 Hz, 1H), 7.20 (dd, J = 8.0, 7.6 Hz, 1H), 7.14 (dd, J = 8.0, 7.6 Hz, 1H), 7.05 (dd, J = 8.0, 7.6 Hz, 1H), 6.98 (d, J = 7.6 Hz, 1H), 6.63 (dd, J = 7.6, 7.2 Hz, 1H), 6.53 (d, J = 8.0 Hz, 1H), 6.13 (dd, J = 17.2, 10.4 Hz, 1H), 5.62 (d, J = 8.4 Hz, 1H), 5.25-5.16 (m, 3H), 4.91 (s, 1H), 4.47 (td, J = 8.4, 4.4 Hz, 1H), 3.46 (d, J = 8.4 Hz, 1H), 3.39 (dd, J = 14.0, 4.0 Hz, 1H), 3.18 (dd, J = 14.0, 11.6 Hz, 1H), 3.06 (s, 3H), 2.21 (d, J = 11.6 Hz, 1H), 1.60 (s, 3H), 1.58 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 170.0, 154.3, 150.2, 145.2, 140.9, 133.9, 130.9, 129.6, 127.4, 124.2, 122.1, 119.8, 119.2, 118.7, 112.8, 110.6, 109.9, 105.7, 84.6, 81.2, 79.3, 58.7, 52.3, 52.2, 39.1, 38.8, 31.1, 28.4 (3C), 27.8, 27.2; HRESIMS *m/z* 611.2837 $[M+Na]^+$, calcd for $C_{33}H_{40}N_4O_6Na$, 611.2840.

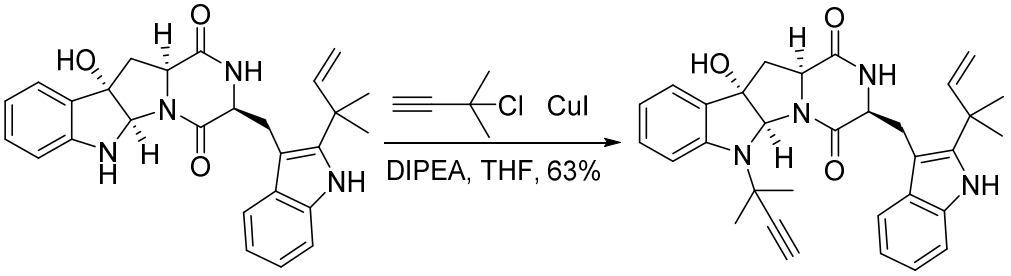
*(3S,5aR,10bS,11aS)-10b-Hydroxy-3-((2-(2-methylbut-3-en-2-yl)-1H-indol-3-yl)methyl)-2,3,6,10b,11,11a-hexahydro-4H-pyrazino[1',2':1,5]pyrrolo[2,3-b]indole-1,4(5aH)-dione (**3a**).*



8c **3a**

Compound **3a** (colorless oil, 236.0 mg, 61%) was prepared from **8c** (500.0 mg, 0.85 mmol) with SiO_2 (4.0 g) under the same procedure as **6**. $[\alpha]_D^{20}$ = +14.4 (c 0.1, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.48 (d, J = 7.9 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.28 (s, 1H), 7.22 – 7.15 (m, 2H), 7.11 (dd, J = 8.0, 7.5 Hz, 1H), 6.81 (dd, J = 8.0, 7.5 Hz, 1H), 6.65 (d, J = 7.9 Hz, 1H), 6.12 (dd, J = 17.5, 10.5 Hz, 1H), 5.67 (s, 1H), 5.50 (d, J = 4.0 Hz, 1H), 5.21 (d, J = 4.0 Hz, 1H), 5.18 (d, J = 4.5 Hz, 1H), 5.15 (d, J = 2.5 Hz, 1H), 4.55 (dd, J = 11.1, 6.6 Hz, 1H), 4.46 (dd, J = 11.5, 4.0 Hz, 1H), 3.75 (dd, J = 15.0, 4.0 Hz, 1H), 3.18 (dd, J = 15.0, 11.5 Hz, 1H), 2.83 (s, 1H), 2.72 (dd, J = 13.5, 6.5 Hz, 1H), 2.35 (dd, J = 13.5, 11.0 Hz, 1H), 1.55 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 167.5, 147.5, 145.5, 141.5, 134.3, 130.4, 129.4, 129.0, 123.0, 122.3, 120.2, 119.8, 117.8, 112.9, 110.9, 110.4, 104.3, 87.0, 85.0, 59.0, 55.0, 40.9, 39.0, 28.0, 27.9, 26.0; HRESIMS *m/z* 457.2227 $[M+H]^+$, calcd for $C_{27}H_{29}N_4O_3$, 457.2234.

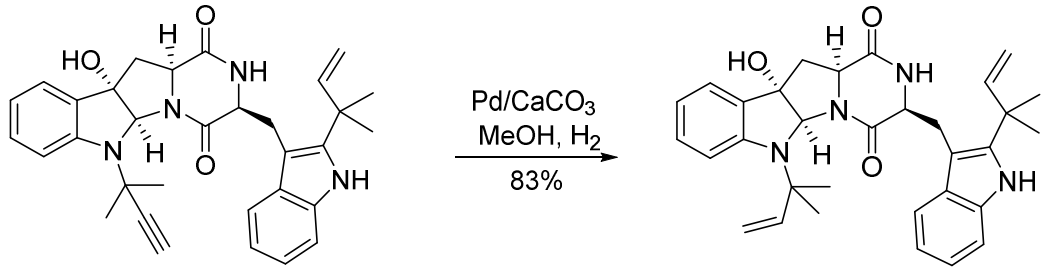
*(3S,5aR,10bS,11aS)-10b-Hydroxy-3-((2-(2-methylbut-3-en-2-yl)-1H-indol-3-yl)methyl)-6-(2-methylbut-3-yn-2-yl)-2,3,6,10b,11,11a-hexahydro-4H-pyrazino[1',2':1,5]pyrrolo[2,3-b]indole-1,4(5aH)-dione (**22**)*.



3a **22**

Compound **22** (colorless oil, 80.0 mg, 63%) was prepared from **3a** (110 mg, 0.24 mmol) under the same procedure as **21**. $[\alpha]_D^{20}$ = +14.9 (c 0.1, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.38 (dd, J = 7.5, 2.5 Hz, 2H), 7.27 (dd, J = 7.5, 2.5 Hz, 2H), 7.21 (d, J = 8.0 Hz, 1H), 7.13 (dd, J = 7.5, 2.5 Hz, 1H), 7.05 (dd, J = 7.5, 2.5 Hz, 1H), 6.99 (dd, J = 7.5, 2.5 Hz, 1H), 6.01 (dd, J = 17.5, 10.5 Hz, 1H), 5.47 (s, 1H), 5.41 (s, 1H), 5.16 – 4.90 (m, 2H), 4.24 (dd, J = 11.0, 4.5 Hz, 2H), 3.64 (dd, J = 15.5, 4.5 Hz, 1H), 3.14 (dd, J = 14.0, 4.5 Hz, 1H), 3.06 (dd, J = 15.5, 11.0 Hz, 1H), 2.62 (dd, J = 14.0, 10.5 Hz, 1H), 2.61 (brs, 1H), 2.39 (s, 1H), 1.95 (s, 3H), 1.91 (s, 3H), 1.45 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.8, 168.4, 147.7, 145.5, 141.4, 134.4, 134.3, 129.8, 129.0, 124.2, 122.4, 122.1, 120.1, 117.8, 117.6, 112.7, 110.8, 104.5, 89.4, 85.4, 84.2, 71.3, 57.5, 55.2, 54.2, 38.9, 33.3, 30.7, 30.0, 27.8, 27.7, 25.5; HRESIMS *m/z* 545.2524 $[M+Na]^+$, calcd for $C_{32}H_{34}N_4O_3Na$, 545.2523.

*(3S,5aR,10bS,11aS)-10b-Hydroxy-6-(2-methylbut-3-en-2-yl)-3-((2-(2-methylbut-3-en-2-yl)-1H-indol-3-yl)methyl)-2,3,6,10b,11,11a-hexahydro-4H-pyrazino[1',2':1,5]pyrrolo[2,3-b]indole-1,4(5aH)-dione (**1**).*

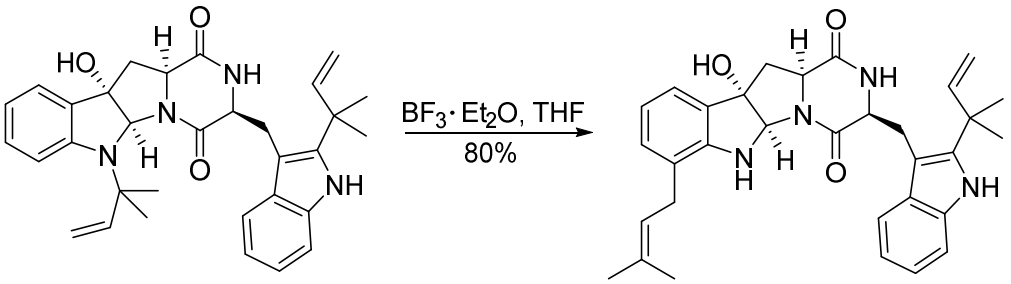


22 **Okaramine C (1)**

To a solution of **22** (20.0 mg, 0.038 mmol) in 10.0 mL MeOH was added 5% $Pd/CaCO_3$ (6.0 mg). After the addition, the reaction mixture was kept stirring under an atmosphere of H_2 until the starting material disappeared, then the reaction mixture was filtered through a short plug of silica gel and purified by column chromatography (EtOAc: hexanes = 1:1) to afford compound **1** (17.0 mg, 83%) as a white solid. $[\alpha]_D^{25}$ = +14.5 (c 0.1, MeOH) (Literature[4], $[\alpha]_D^{25}$ = +19.0 (c 0.2, MeOH)); ^{1}H NMR (500 MHz, Acetone-d_6) δ 9.84 (s, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.19 (d, J = 8.0 Hz, 1H), 7.09 (dd, J = 7.5, 1.5 Hz, 1H), 6.93 (m, 2H), 6.87 – 6.82 (m, 1H), 6.81 (d, J = 8.0 Hz, 1H), 6.60 (t, J = 7.5 Hz, 1H), 6.34 (dd, J = 17.5, 10.5 Hz, 1H), 6.03 (dd, J = 17.5, 10.5 Hz, 1H), 5.35 (s, 1H), 5.31 (s, 1H), 5.06 (dd, J = 17.5, 1.5 Hz, 1H), 4.97 – 4.88 (m, 2H), 4.84 (dd, J = 10.5, 1.0 Hz, 1H), 4.56 (s, 1H), 4.35 (dd, J = 10.0, 5.5 Hz, 1H), 4.24 (dd, J = 10.5, 4.5 Hz, 1H), 3.51 (dd, J = 13.5, 4.5 Hz, 1H), 2.94 – 2.83 (m, 2H), 2.35 (dd, J = 13.5, 10.0 Hz, 1H), 1.58 (s, 3H), 1.39 (s, 6H), 1.37 (s, 3H); ^{13}C NMR (125 MHz, Acetone-

d$_6$) δ 170.0, 169.8, 149.7, 149.3, 147.2, 142.6, 136.2, 134.8, 130.1, 129.7, 124.5, 122.1, 120.1, 120.0, 118.5, 115.3, 112.1, 112.0, 111.6, 105.7, 85.7, 84.6, 59.8, 58.3, 56.6, 39.9, 35.0, 28.4, 28.3, 28.2, 26.4, 25.6; HRESIMS *m/z* 525.2861 $[M+H]^+$, calcd for $C_{32}H_{37}N_4O_3$, 525.2860.

*(3S,10bS,11aS)-10b-Hydroxy-7-(3-methylbut-2-en-1-yl)-3-((2-(2-methylbut-3-en-2-yl)-1H-indol-3-yl)methyl)-2,3,6,10b,11,11a-hexahydro-4H-pyrazino[1',2':1,5]pyrrolo[2,3-b]indole-1,4(5aH)-dione (**2**)*.

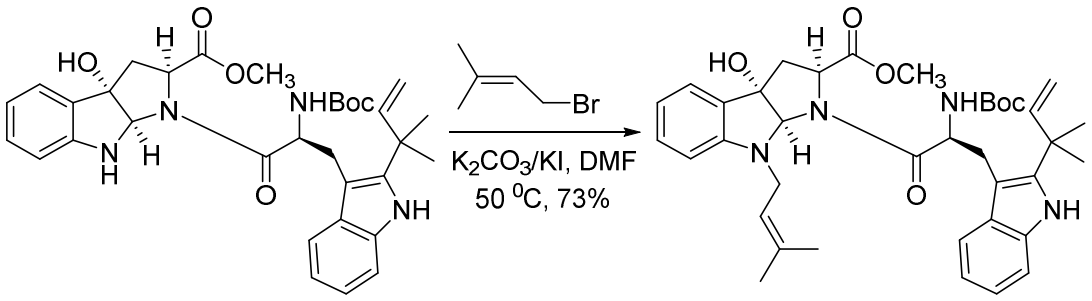


Okaramine C (**1**) **Okaramine J** (**2**)

Compound **2** (white solid, 8.0 mg, 80%) was prepared from **1** (10.0 mg, 0.02 mmol) with $BF_3{\cdot}Et_2O$ under the same procedure as **4**. $[\alpha]_D^{20}$ = +18.0 (c 0.1, MeOH) (Literature[5], $[\alpha]_D^{20}$ = +31.0 (c 0.33, MeOH)); ^{1}H NMR (500 MHz, Acetone-*d*$_6$) δ 10.00 (brs, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.08 (d, J = 7.5 Hz, 1H), 7.05 – 6.99 (m, 1H), 6.98 – 6.93 (m, 1H), 6.91 (d, J = 7.5 Hz, 1H), 6.65 (t, J = 7.5 Hz, 1H), 6.19 (dd, J = 17.5, 10.5, 1.5 Hz, 1H), 5.67 (d, J = 6.0 Hz, 1H), 5.53 (d, J = 4.5 Hz, 1H), 5.40 (dd, J = 4.5, 1.5 Hz, 1H), 5.27 – 5.20 (m, 1H), 5.08 (d, J = 17.5 Hz, 2H), 5.02 (d, J = 10.5, 1.0 Hz, 1H), 4.63 (dd, J = 11.0, 7.0, 1.5 Hz, 1H), 4.53 (dd, J = 11.0, 4.0 Hz, 1H), 3.67 (dd, J = 15.0, 4.0 Hz, 1H), 3.24 – 3.12 (m, 2H), 3.07 (dd, J = 15.0, 11.0 Hz, 1H), 2.53 (dd, J = 13.5, 7.0 Hz, 1H), 2.07 (dd,

J = 13.5, 11.0 Hz, 1H), 1.70 (s, 3H), 1.69 (s, 3H), 1.54 (s, 3H), 1.53 (d, J = 1.5 Hz, 3H); ^{13}C NMR (125 MHz, Acetone-d_6) δ 169.8, 168.5, 147.2 (2C), 142.5, 136.1, 133.5, 131.6, 130.0, 129.6, 123.8, 122.5, 122.0, 121.2, 120.0, 119.9, 118.4, 112.1, 111.9, 105.4, 87.3, 85.4, 59.5, 56.1, 42.3, 39.8, 30.0 28.3, 28.3, 26.5, 25.8, 17.8. HRESIMS *m/z* 547.2683 $[M+Na]^+$, calcd for $C_{32}H_{36}N_4O_3Na$, 547.2680.

Methyl (2S,3aS,8aR)-1-((S)-2-((tert-butoxycarbonyl)amino)-3-(2-(2-methylbut-3-en-2-yl)-1H-indol-3-yl)propanoyl)-3a-hydroxy-8-(3-methylbut-2-en-1-yl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carboxylate (***23***).

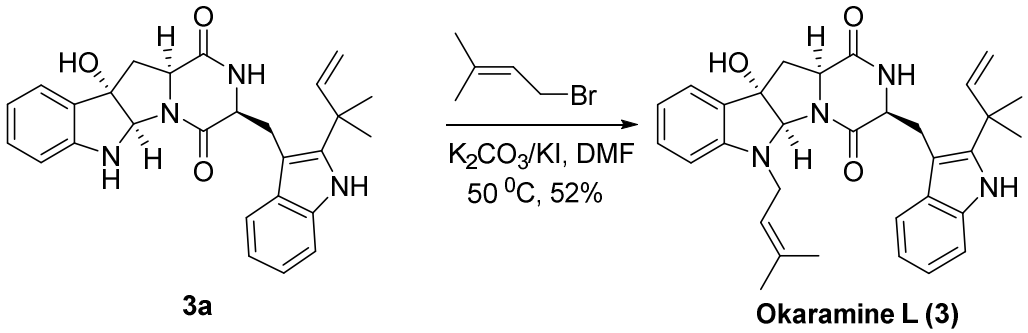


8c **23**

To a solution of **8c** (30.0 mg, 0.05 mmol), KI (17.0 mg, 0.1 mmol) and K_2CO_3 (14.0 mg, 0.1 mmol) in 6.0 mL DMF was added 1-bromo-3-methylbut-2-ene (15.0 mg, 0.1 mmol). After the addition, the reaction mixture was heated at 50 ^{0}C for 5 h until the starting material disappeared, The reaction mixture was cooled and extracted with EtOAc/H_2O (1:1, 100.0 mL). The organic layers were concentrated in vacuum. The residue was purified by flash chromatography (EtOAc: Hexanes = 1:3) to produce **23** (24.0 mg, 73.0%) as a colorless oil. $[\alpha]_D^{25}$ = +80.9 (c 1, MeOH); ^{1}H

NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.21 (dd, J = 8.0, 7.6 Hz, 1H), 7.14 (dd, J = 8.0, 7.6 Hz, 1H), 7.08 (dd, J = 8.0, 7.6 Hz, 1H), 6.96 (d, J = 7.6 Hz, 1H), 6.59 (dd, J = 8.0, 7.6 Hz, 1H), 6.35 (d, J = 8.0 Hz, 1H), 6.18 (dd, J = 17.2, 10.4 Hz, 1H), 5.63 (d, J = 8.4 Hz, 1H), 5.31 – 5.09 (m, 4H), 4.74 – 4.57 (m, 1H), 4.23 – 4.09 (m, 1H), 4.05 (dd, J = 16.0, 5.6 Hz, 1H), 3.81 (d, J = 8.8 Hz, 1H), 3.44 (dd, J = 14.0, 4.0 Hz, 1H), 3.35 – 3.24 (m, 1H), 3.23 (s, 3H), 2.21 (d, J = 12.8 Hz, 1H), 1.82 (s, 3H), 1.73 (s, 3H), 1.63 (s, 6H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 170.0, 154.5, 150.2, 145.2, 141.2, 134.0, 130.5, 129.6, 128.6, 128.6, 123.4, 122.0, 121.1, 119.6, 118.9, 117.8, 112.8, 110.7, 107.4, 105.7, 85.9, 85.1, 79.2, 58.9, 52.3, 44.7, 40.3, 39.1, 30.9, 28.4 (3C), 27.7, 27.2, 25.8 (2C), 18.1; HRESIMS *m/z* 679.3470 $[M+Na]^+$, calcd for $C_{38}H_{48}N_4O_6Na$, 679.3472.

*(3S,5aR,10bS,11aS)-10b-Hydroxy-6-(3-methylbut-2-en-1-yl)-3-((2-(2-methylbut-3-en-2-yl)-1H-indol-3-yl)methyl)-2,3,6,10b,11,11a-hexahydro-4H-pyrazino[1',2':1,5]pyrrolo[2,3-b]indole-1,4(5aH)-dione (**3**).*



3a **Okaramine L (3)**

To a solution of **3a** (25.0 mg, 0.05 mmol), KI (17.0 mg, 0.1 mmol) and K_2CO_3 (14.0 mg, 0.1 mmol) in 5.0 mL DMF was added 1-bromo-3-

methylbut-2-ene (15.0 mg, 0.1 mmol). After the addition, the reaction mixture was heated at 50 ^{0}C for 6 h until the starting material disappeared, The reaction mixture was cooled and extracted with EtOAc/H_2O (1:1, 100.0 mL). The organic layers were concentrated in vacuum. The residue was purified by flash chromatography (EtOAc: Hexanes = 1:4) to produce **3** (15.0 mg, 52.0%) as a white solid. $[\alpha]_D^{20}$ = +78.0 (c 0.1, MeOH) (Literature[5], $[\alpha]_D^{20}$ = +69.0 (c 0.03, MeOH)); ^{1}H NMR (500 MHz, Acetone-d_6) δ 10.04 (s, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.24 (d, J = 8.0 Hz, 1H), 7.16 (dd, J = 8.0, 1.0 Hz, 1H), 7.09 (dd, J = 8.0, 1.0 Hz, 1H), 7.04 (dd, J = 8.0, 1.0 Hz, 1H), 6.74 (dd, J = 8.0, 1.0 Hz, 1H), 6.58 (dd, J = 8.0, 3.5 Hz, 1H), 6.33 – 6.23 (m, 1H), 5.75 (s, 1H), 5.50 (d, J = 3.5 Hz, 1H), 5.28 – 5.22 (m, 1H), 5.17 (s, 1H), 5.17-5.12 (m, 2H), 4.71 (dd, J = 12.0, 6.5 Hz, 1H), 4.61 (dd, J = 11.0, 4.5 Hz, 1H), 4.32 (dd, J = 16.0, 7.5 Hz, 1H), 4.25 – 4.18 (m, 1H), 3.77 (dd, J = 15.0, 4.0 Hz, 1H), 3.33 – 3.11 (m, 1H), 2.50 (dd, J = 13.0, 6.5 Hz, 1H), 2.01 (dd, J = 13.0, 6.5 Hz, 1H), 1.83 (s, 3H), 1.70 (s, 3H), 1.62 (s, 3H), 1.61 (s, 3H); ^{13}C NMR (125 MHz, Acetone-d_6) δ 170.5, 170.3, 149.8, 147.4, 142.6, 136.2, 135.2, 132.7, 130.3, 130.2, 122.9, 122.2, 121.4, 120.2, 119.3, 118.6, 112.3, 112.1, 109.9, 105.6, 89.7, 86.7, 60.4, 56.7, 47.1, 41.8, 40.0, 28.5, 28.4, 26.6, 26.1, 18.5; HRESIMS *m/z* 525.2863 $[M+H]^+$, calcd for $C_{32}H_{37}N_4O_3$, 525.2860.

References

1. Espejo, V. R.; Li, X. B.; Rainier, J. D. Cyclopropylazetoindolines as precursors to C(3)-quaternary-substituted indolines. *J. Am. Chem. Soc*. **2010**, *132*, 8282-8284.

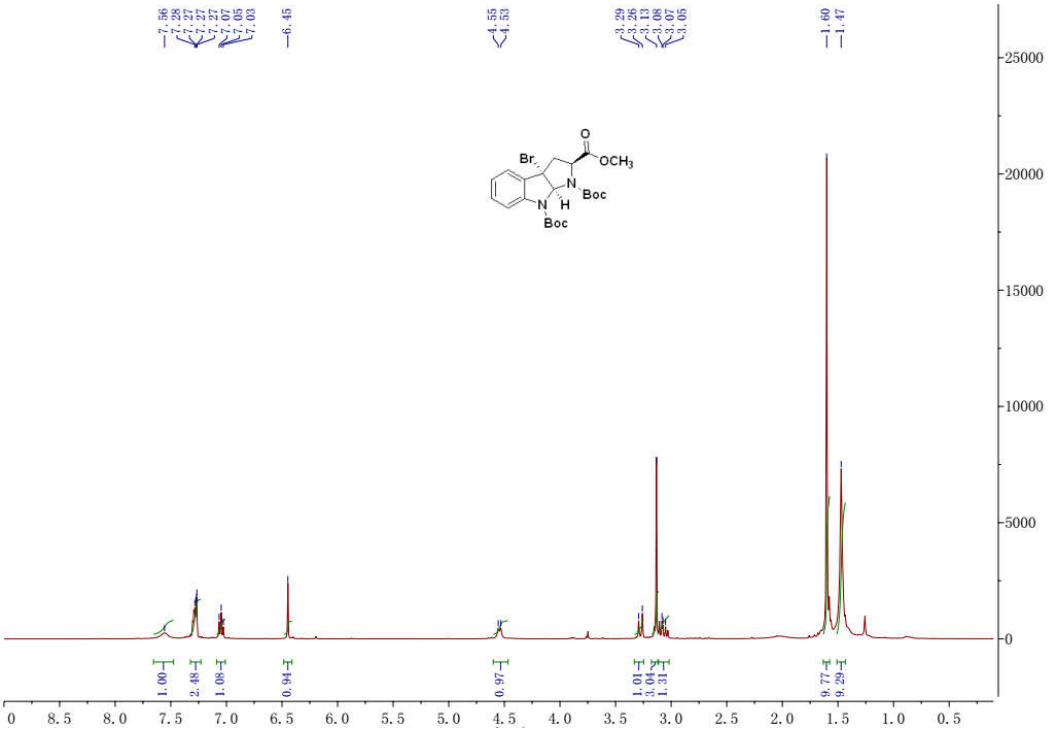
2. Cai, S. X.; Sun, S. W.; Peng, J. X.; Kong, X. L.; Zhou, H. N.; Zhu, T. J.; Gu, Q. Q.; Li, D. H. Okaramines S-U, three new indole diketopiperazine alkaloids from *Aspergillus taichungensis* ZHN-7-07. *Tetrahedron* **2015**, *71*, 3715-3719.

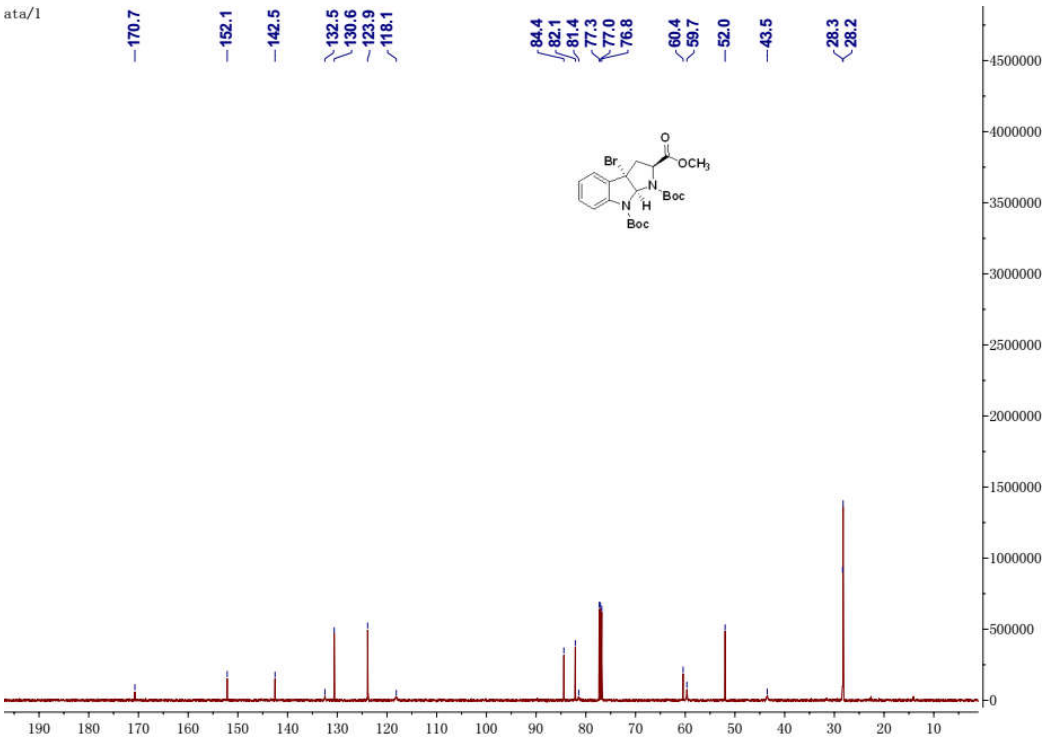
3. Zhao, L.; May, J. P.; Huang, J.; Perrin, D. M. Stereoselective synthesis of brevianamide E. *Org. Lett*. **2012**, *14*, 90-93.

4. Hayashi, H.; Fujiwara, T.; Murao, S.; Arai, M. Okaramine C, a new insecticidal indole alkaloid from *Penicillium simplicissimum*. *Agri. Biol. Chem*. **1991**, *55*, 3143-3145.

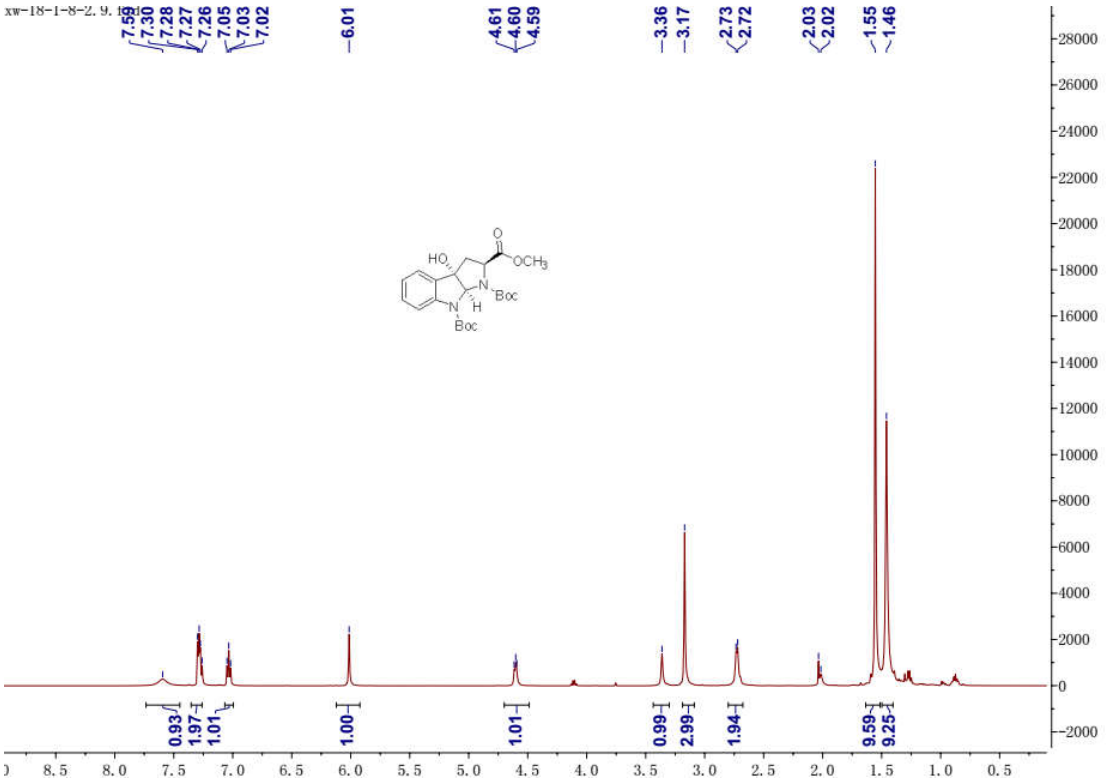
5. Shiono, Y.; Akiyama, K.; Hayashi, H. Okamines J, K, L, M and related compounds, from *Penicillium simplicissimum* ATCC 90288. *Biosci. Biotechnol. Biochem*. **1999**, *63*, 1910-1920.

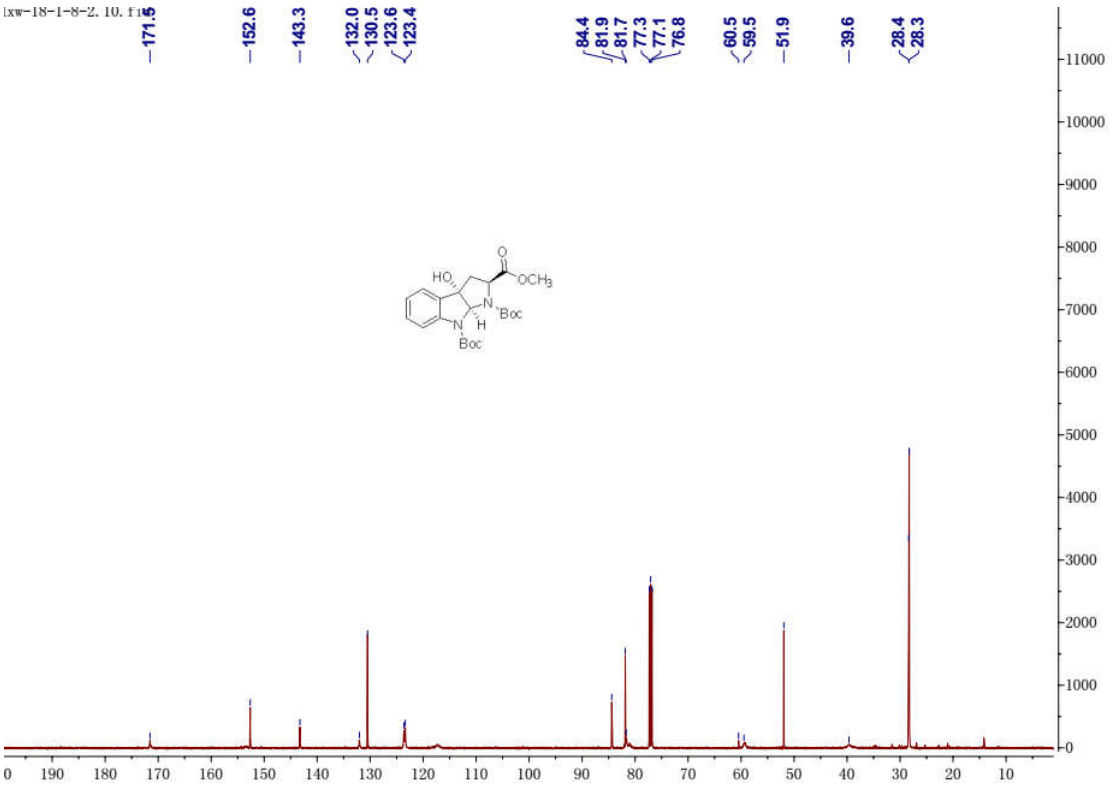
^{1}H NMR and ^{13}C NMR spectrum of **11** ($CDCl_3$)



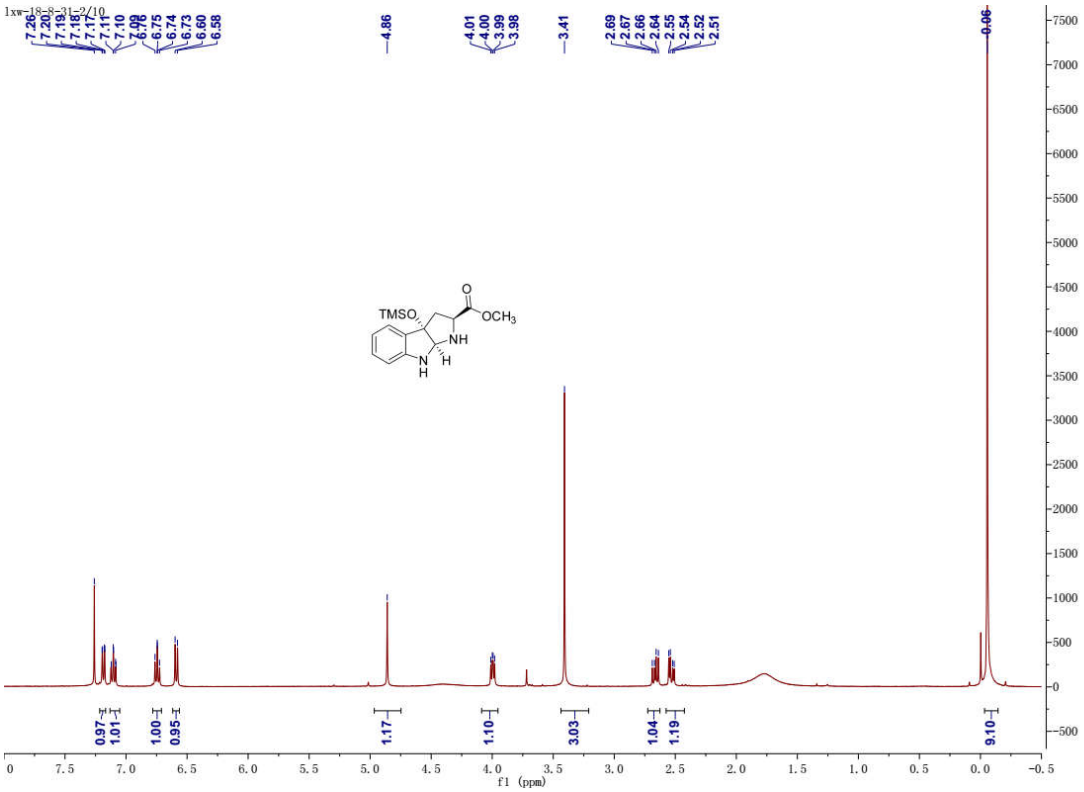


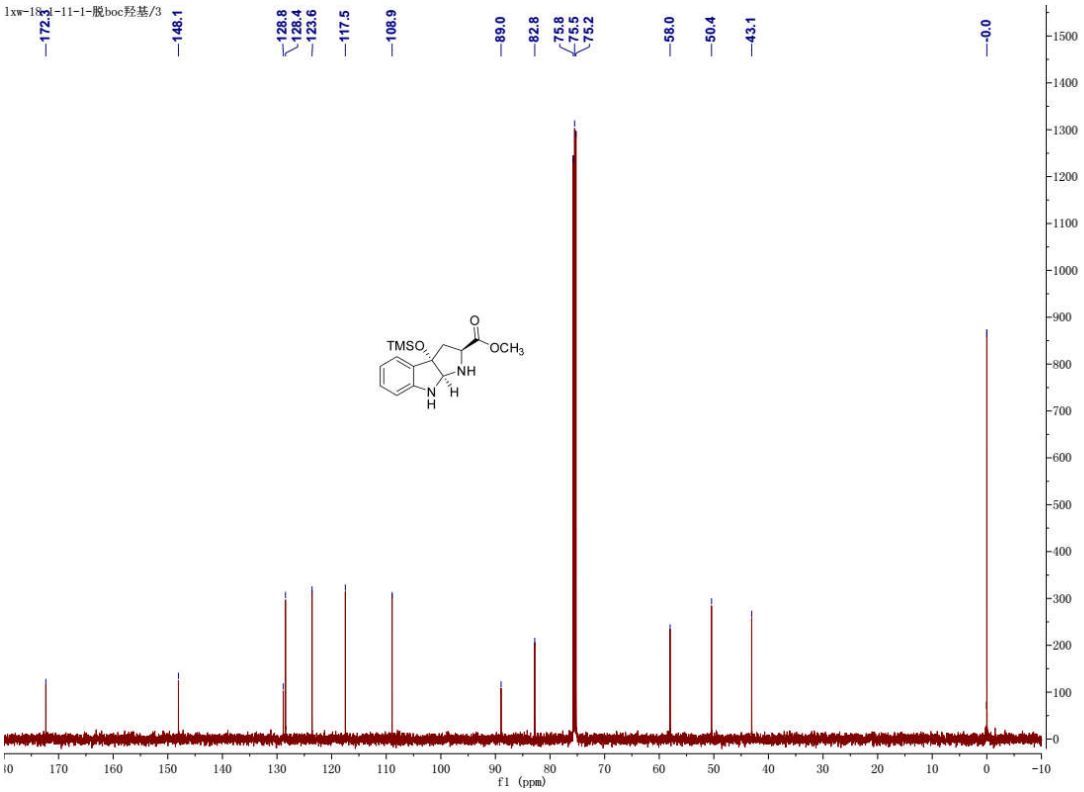
^{1}H NMR and ^{13}C NMR spectrum of **13** ($CDCl_3$)



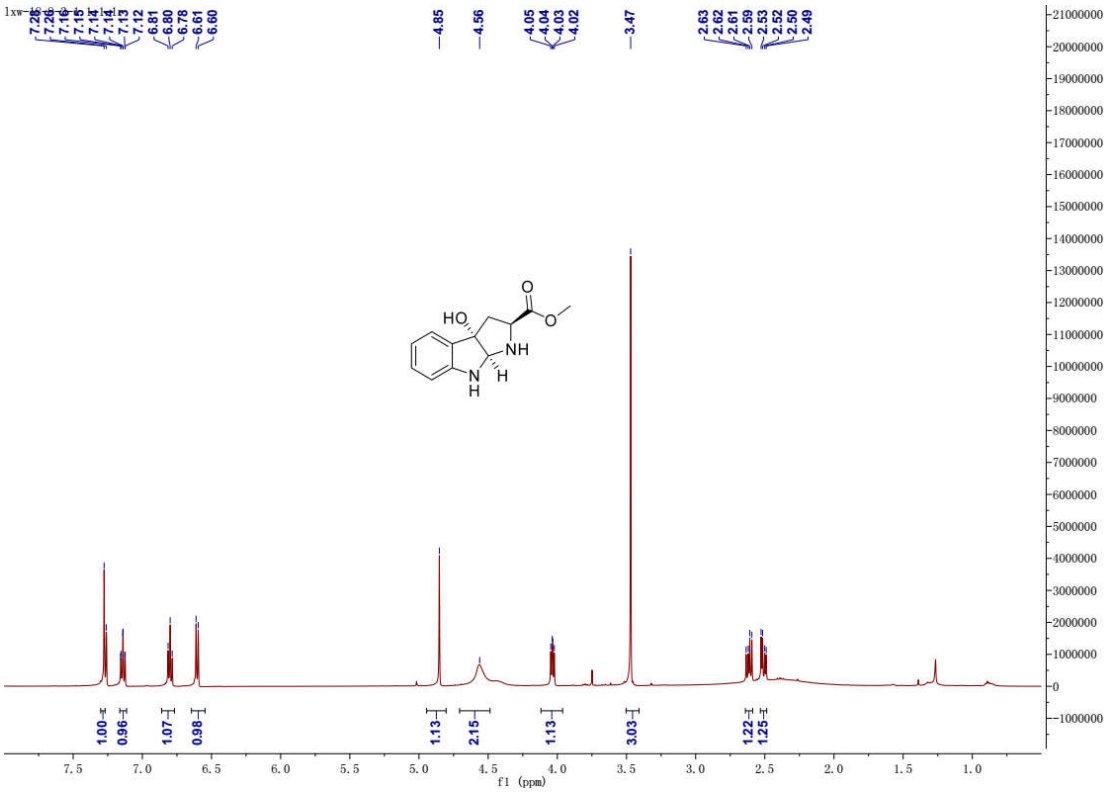


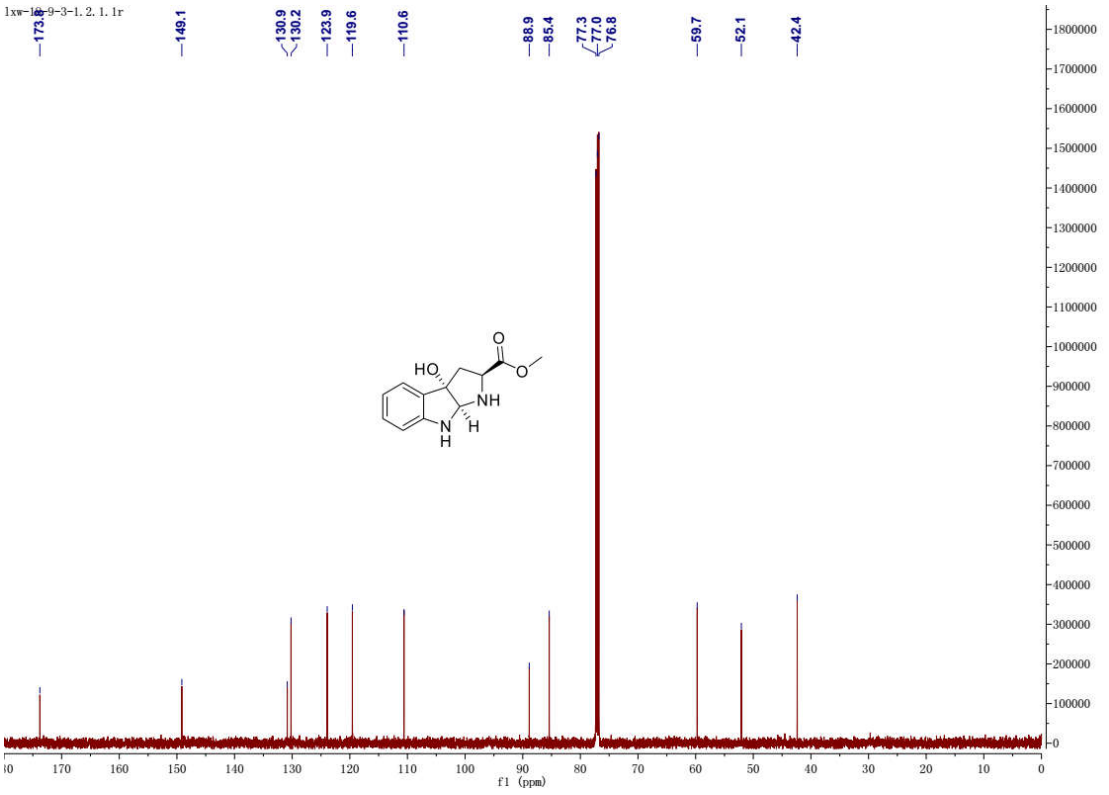
^{1}H NMR and ^{13}C NMR spectrum of **14** ($CDCl_3$)



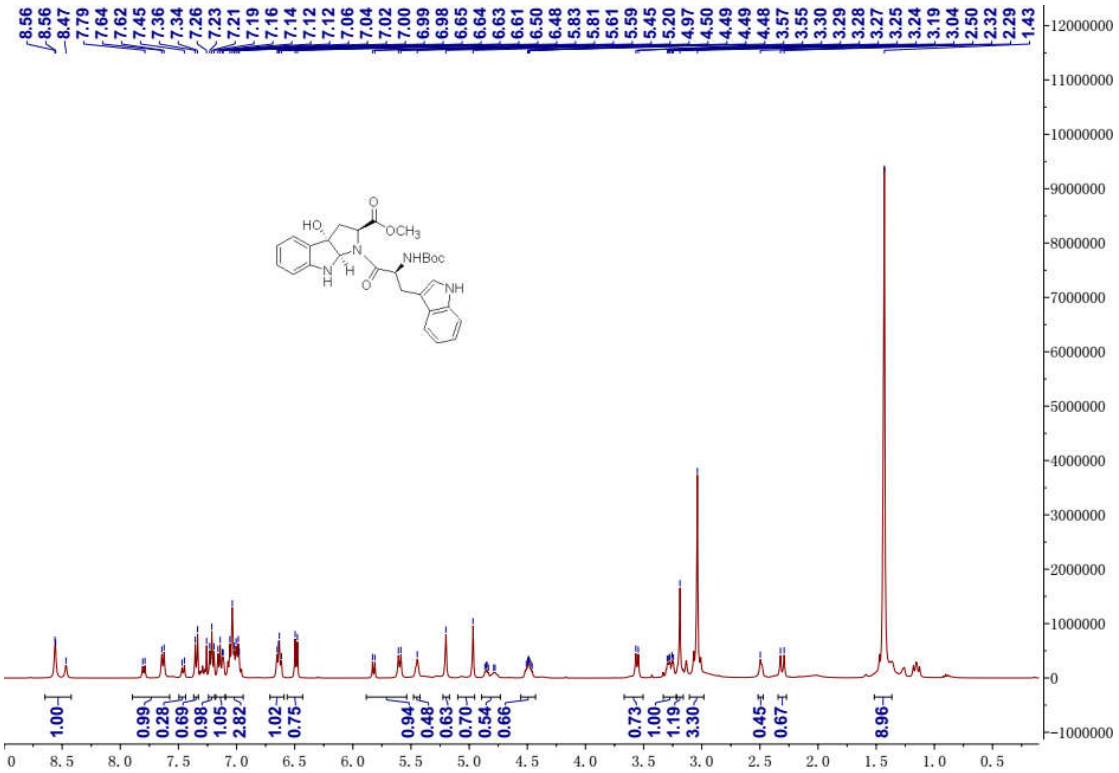


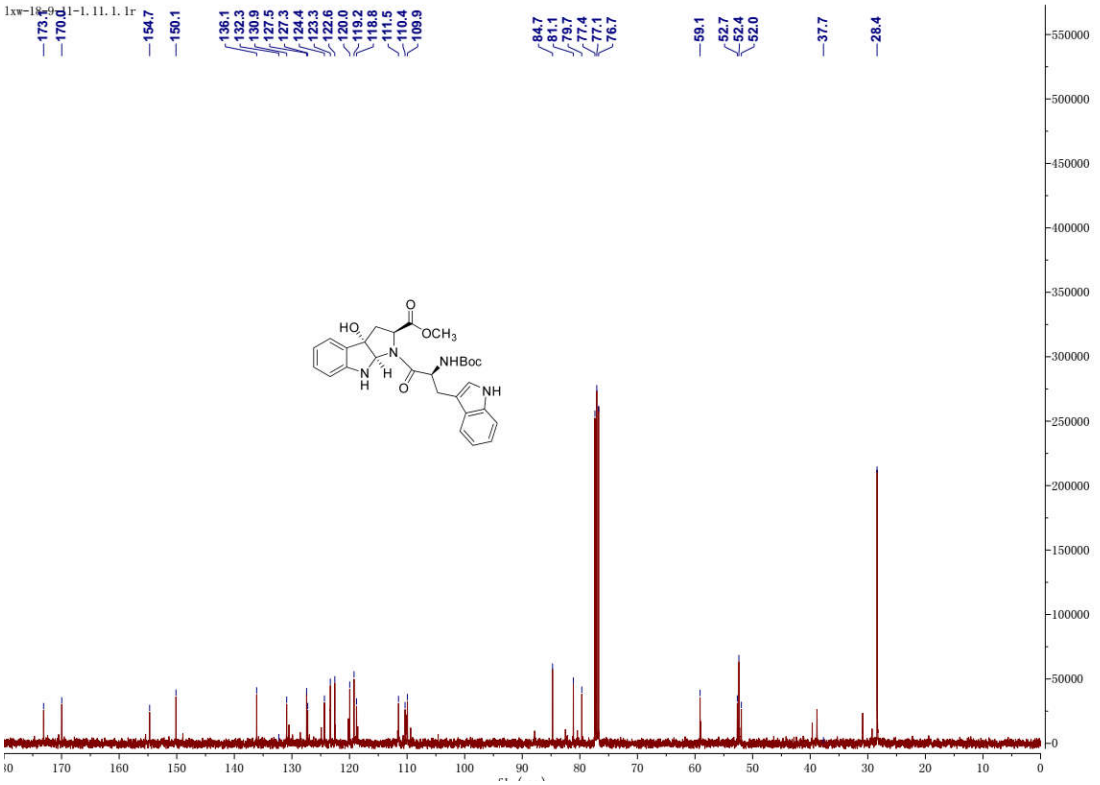
^{1}H NMR and ^{13}C NMR spectrum of **9** ($CDCl_3$)



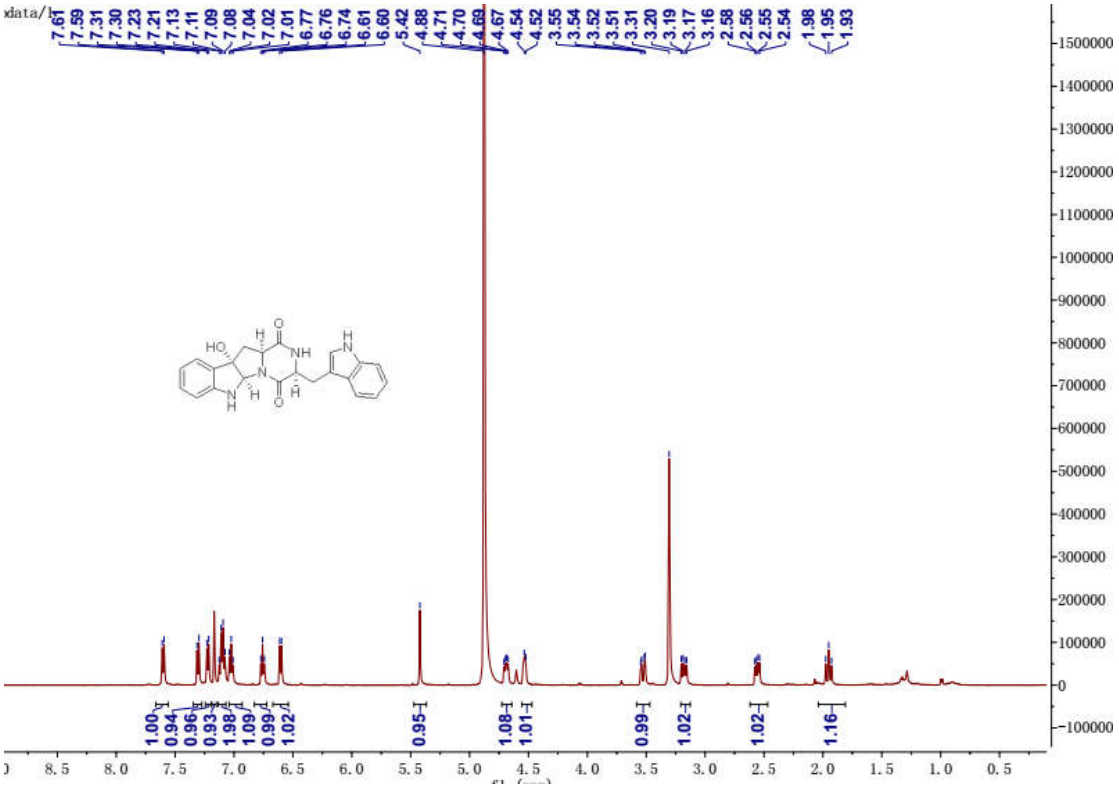


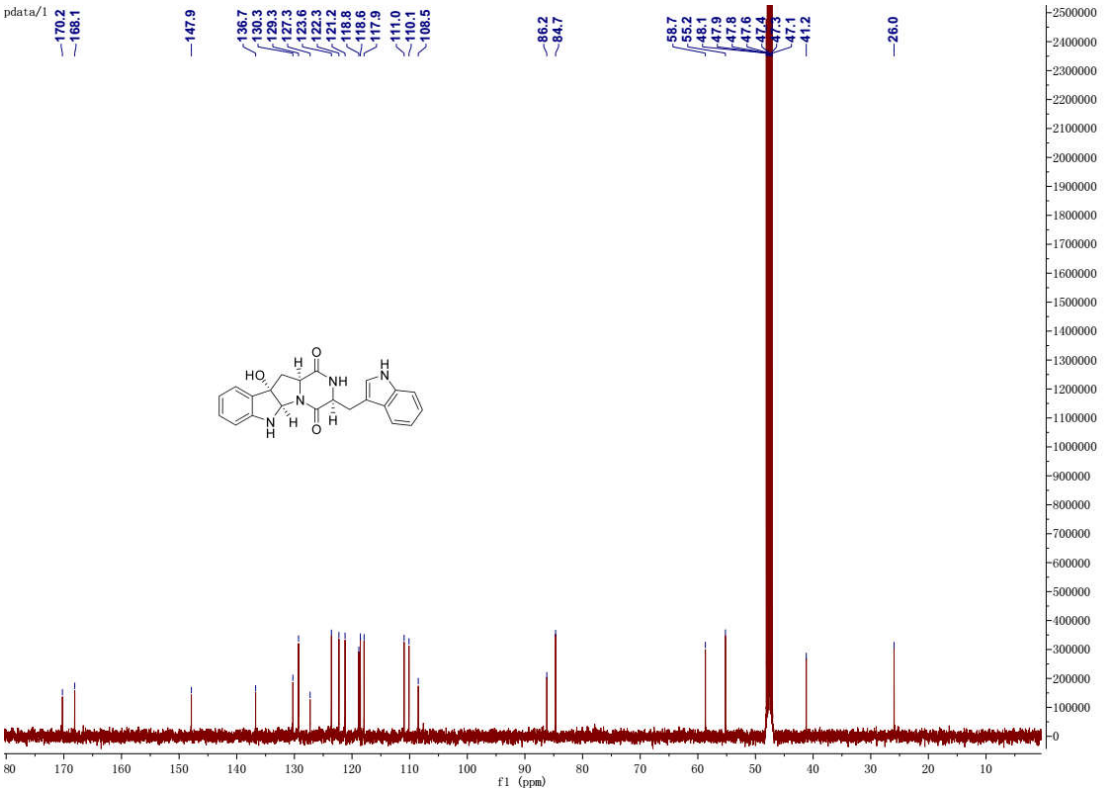
^{1}H NMR and ^{13}C NMR spectrum of **8b** ($CDCl_3$)



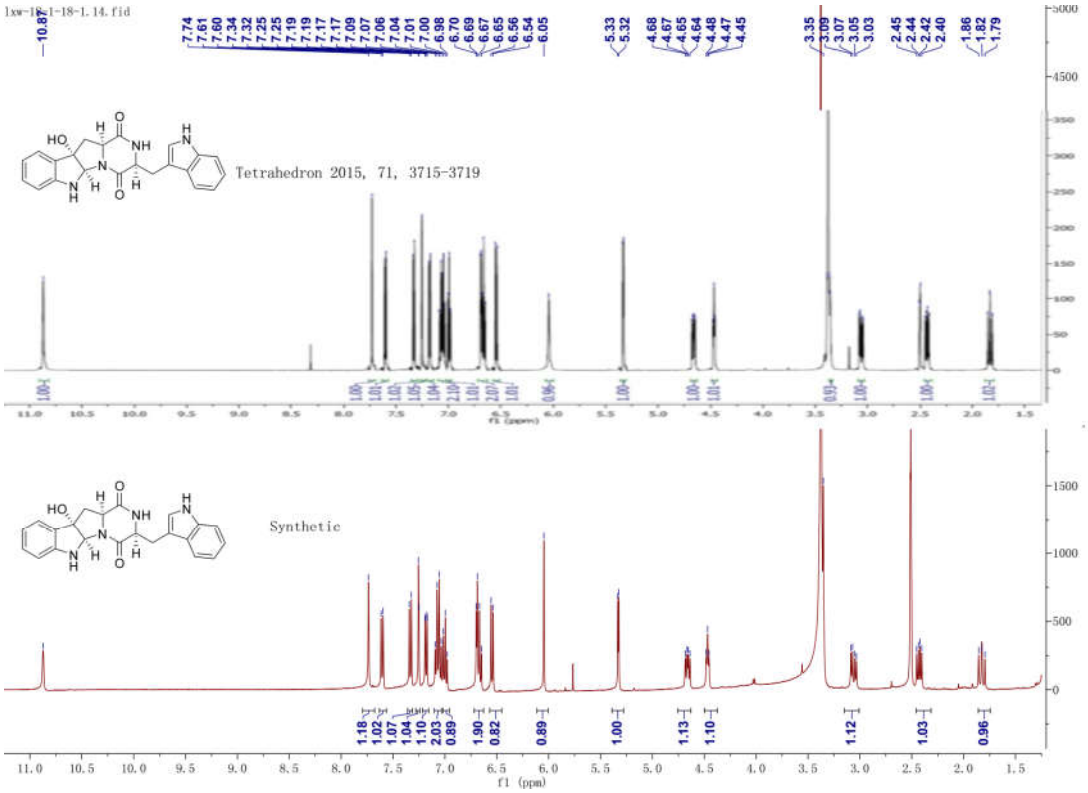


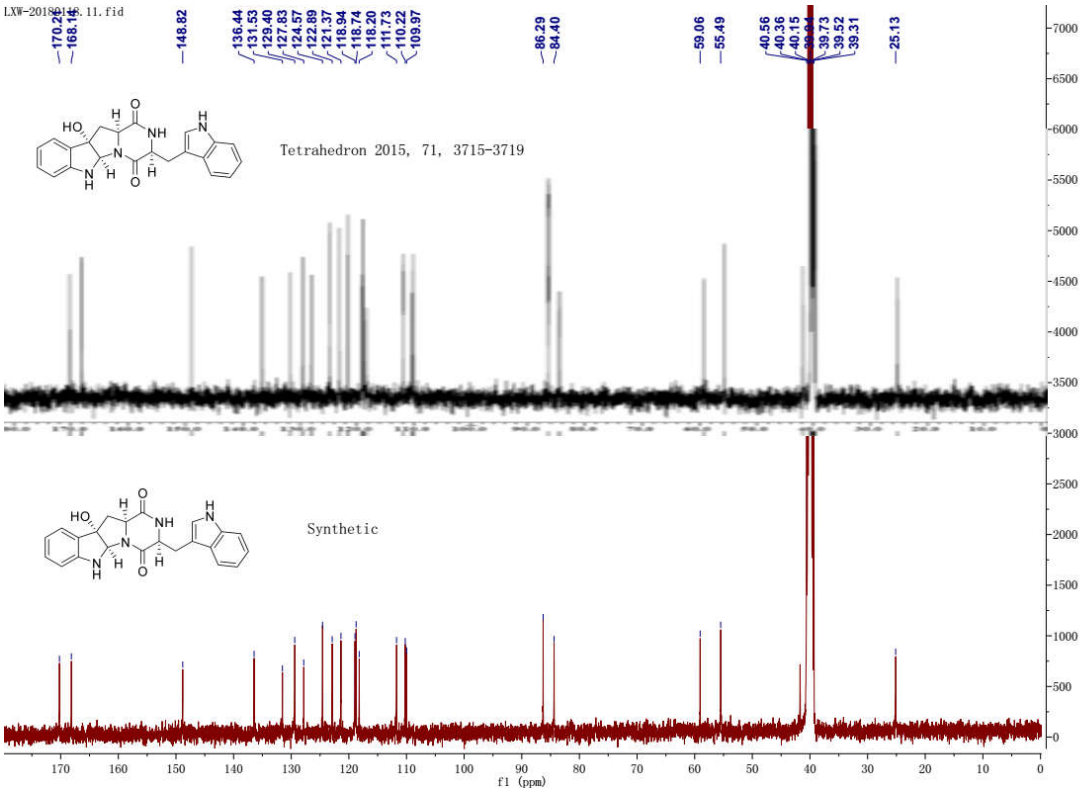
^{1}H NMR and ^{13}C NMR spectrum of **6** (MeOH-d_4)



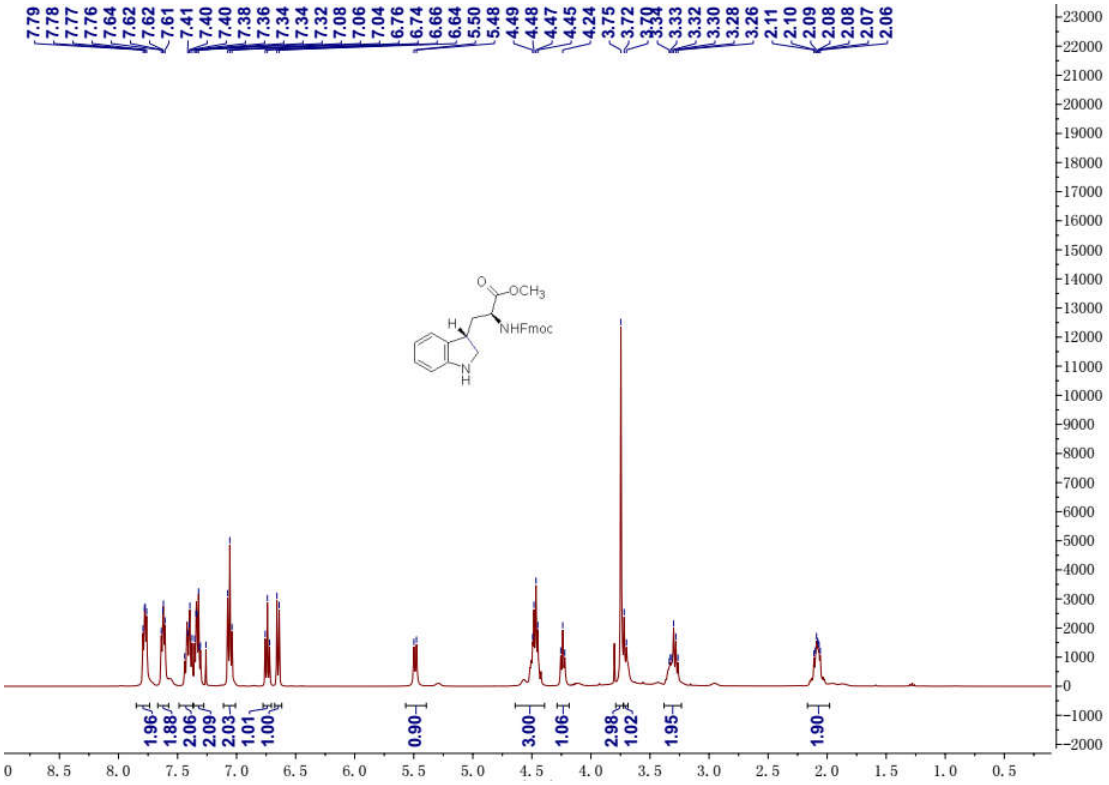


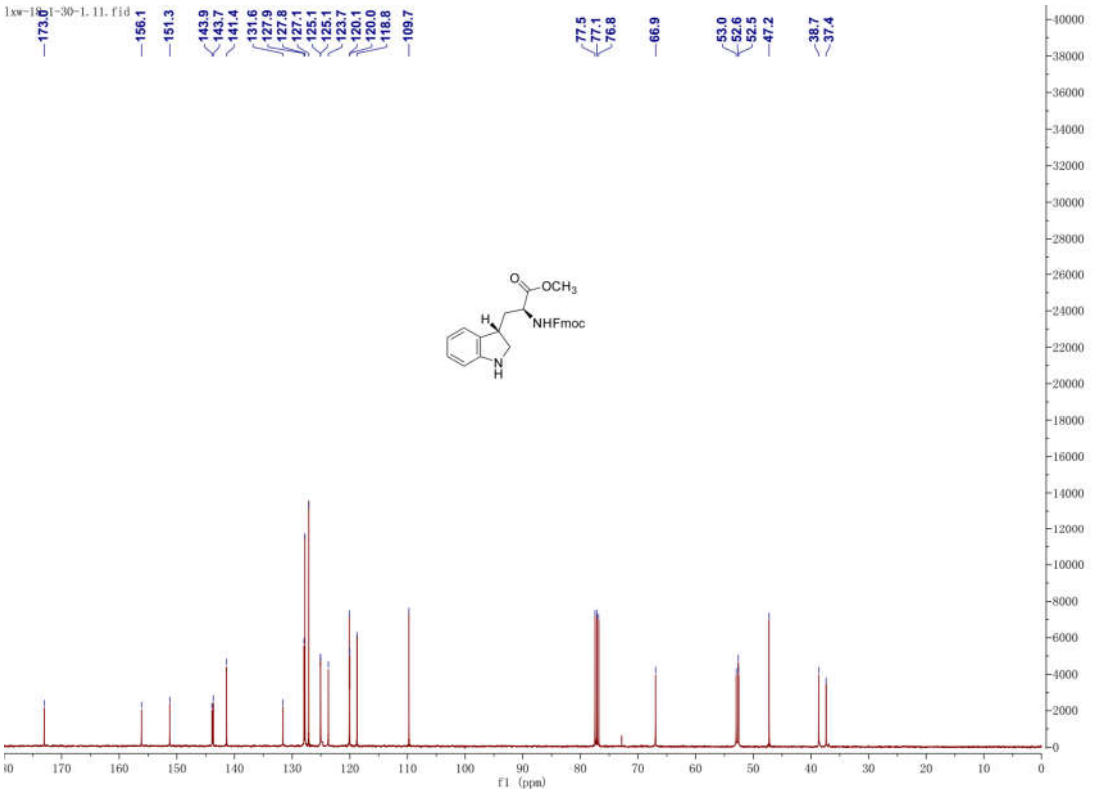
^{1}H and ^{13}C NMR spectrum of okaramines U (DMSO-d_6, provided) and **6** (DMSO-d_6)



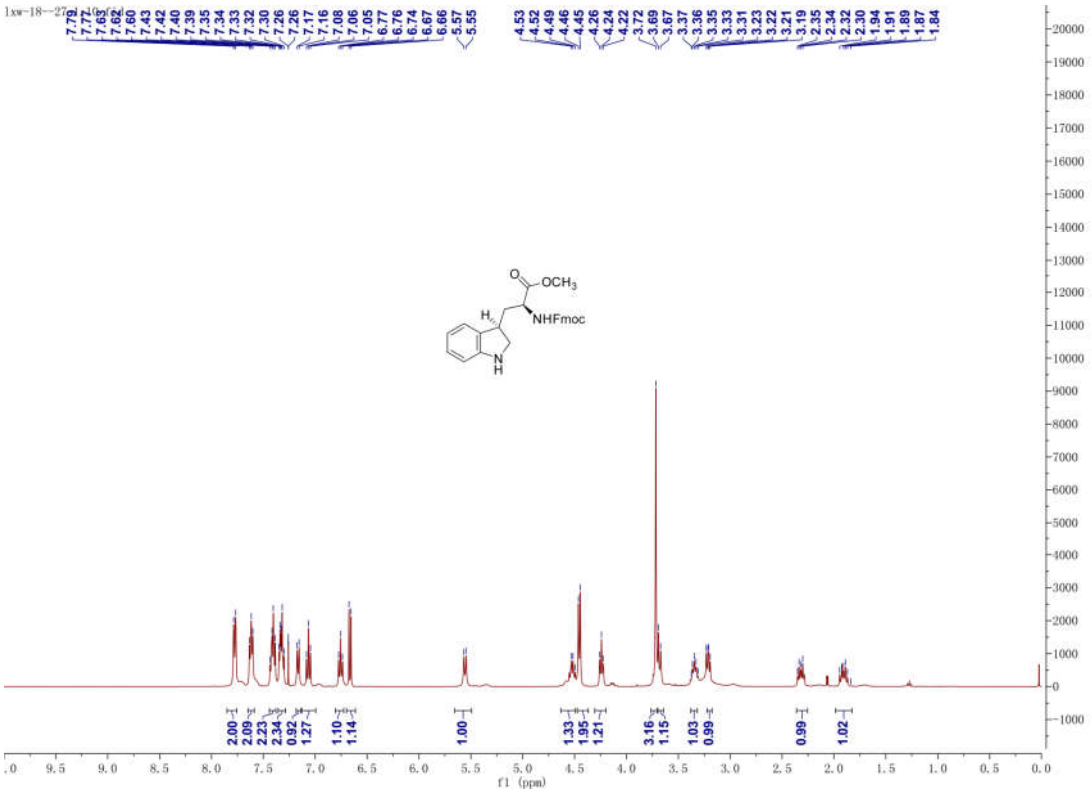


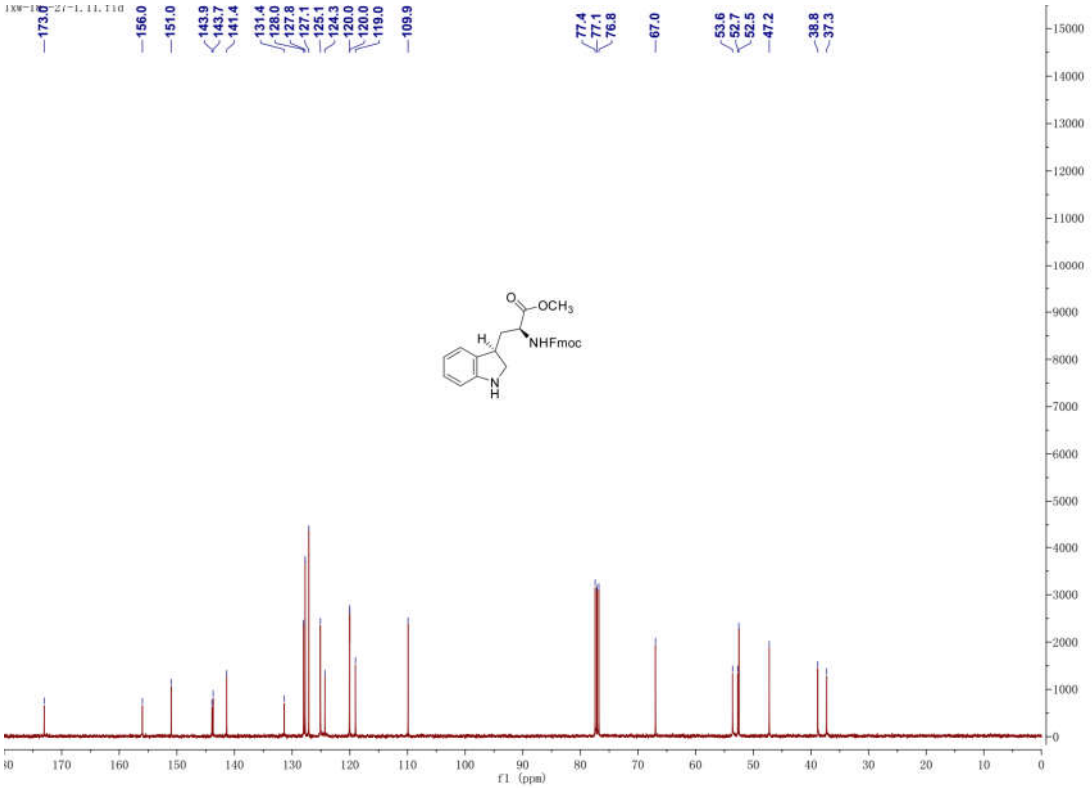
^{1}H NMR and ^{13}C NMR spectrum of **16a** ($CDCl_3$)



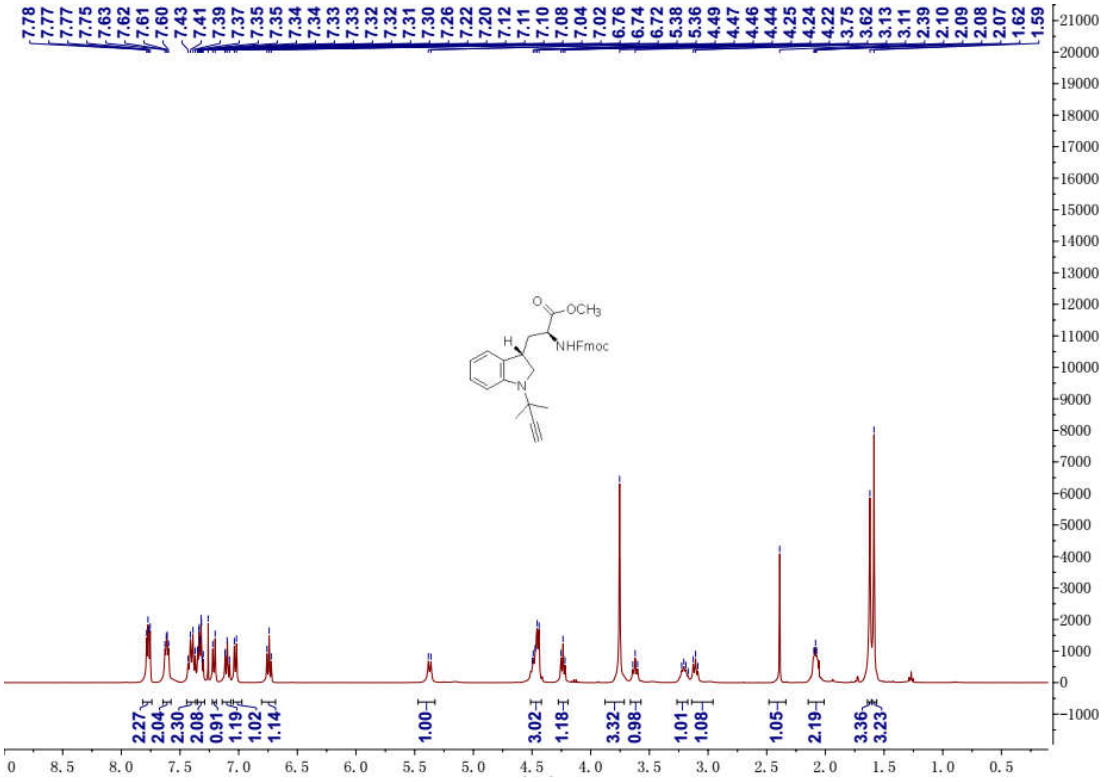


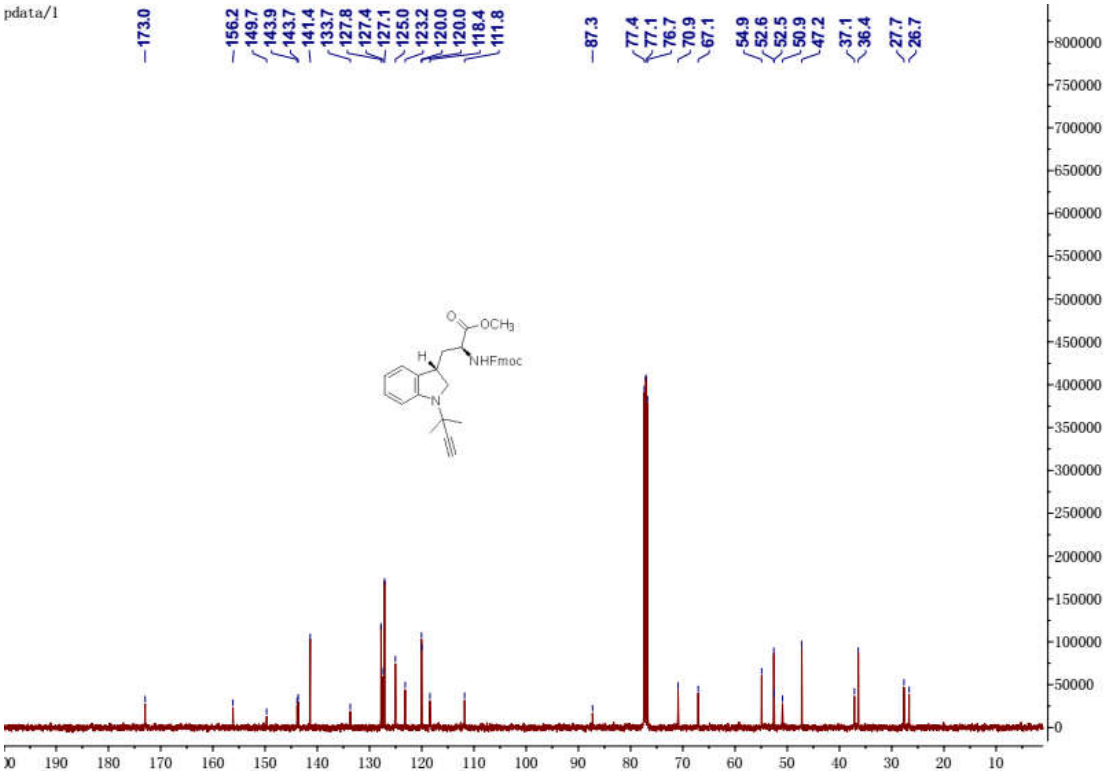
^{1}H NMR and ^{13}C NMR spectrum of **16b** ($CDCl_3$)



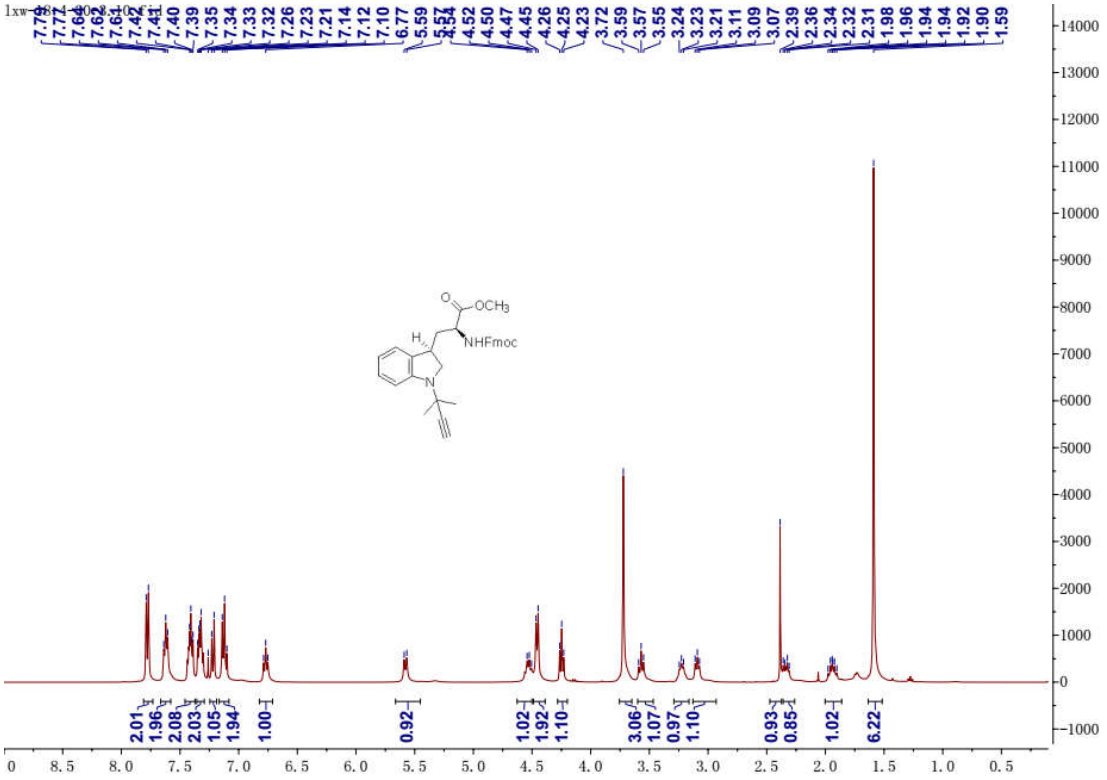


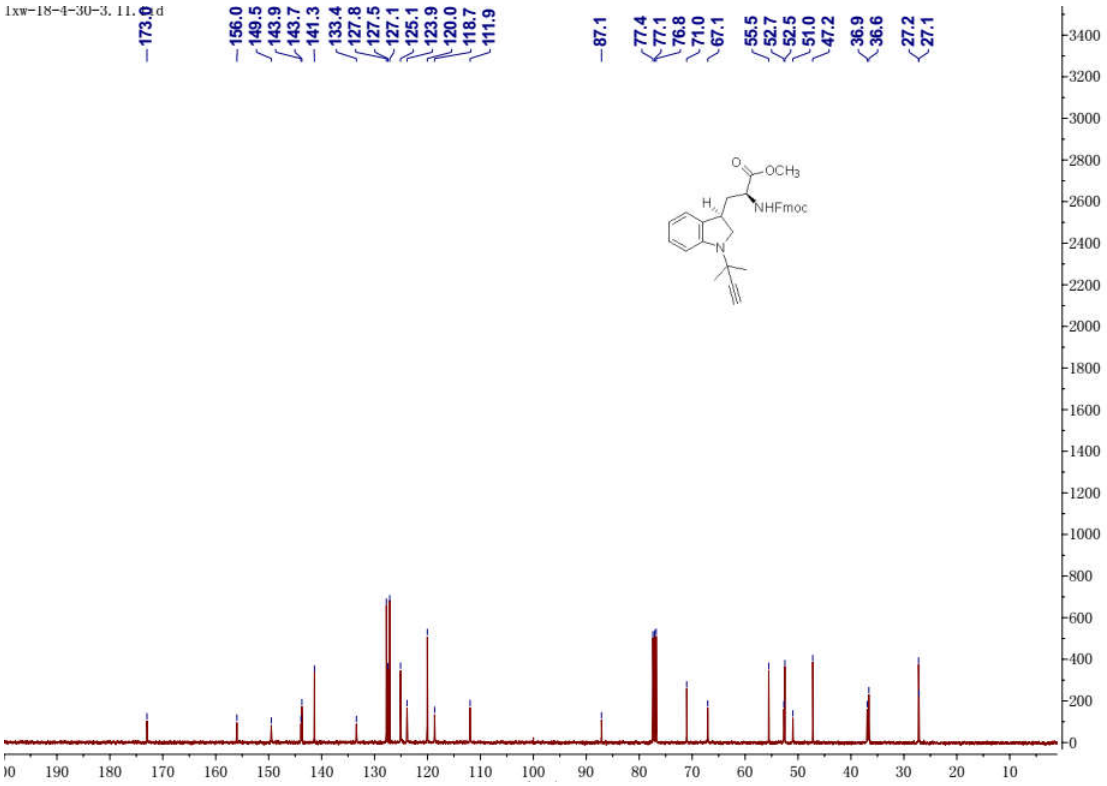
^{1}H NMR and ^{13}C NMR spectrum of **17a** ($CDCl_3$)



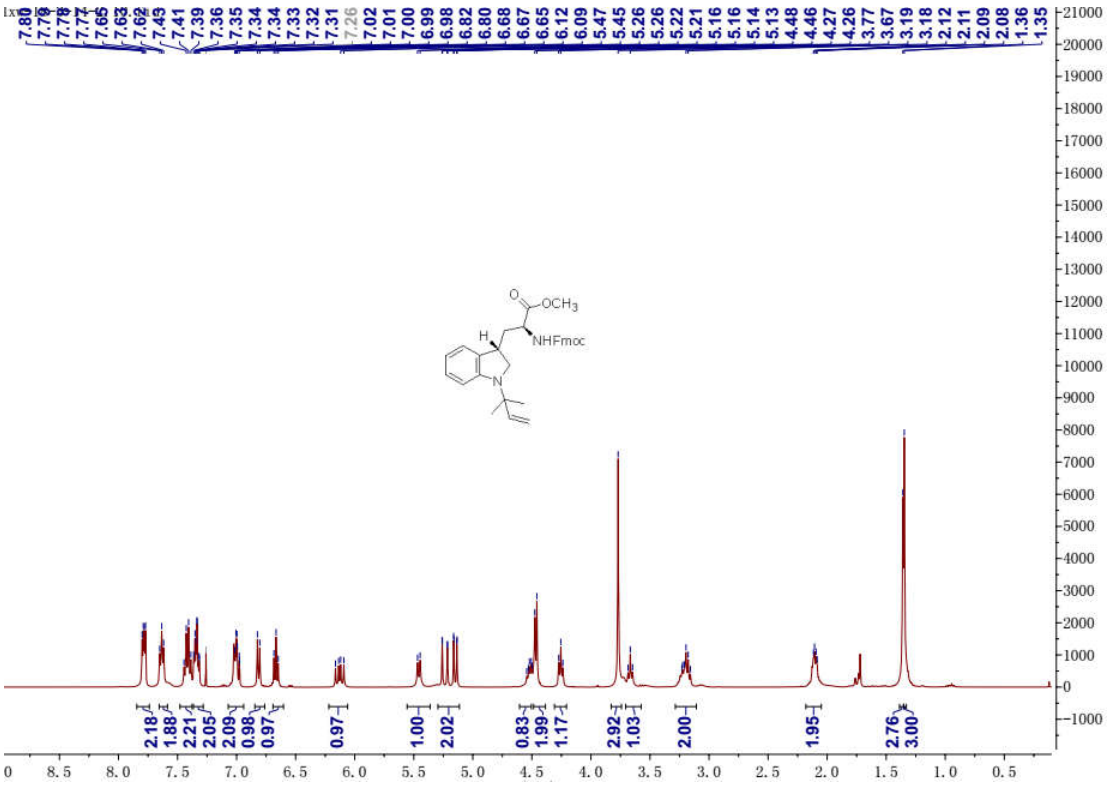


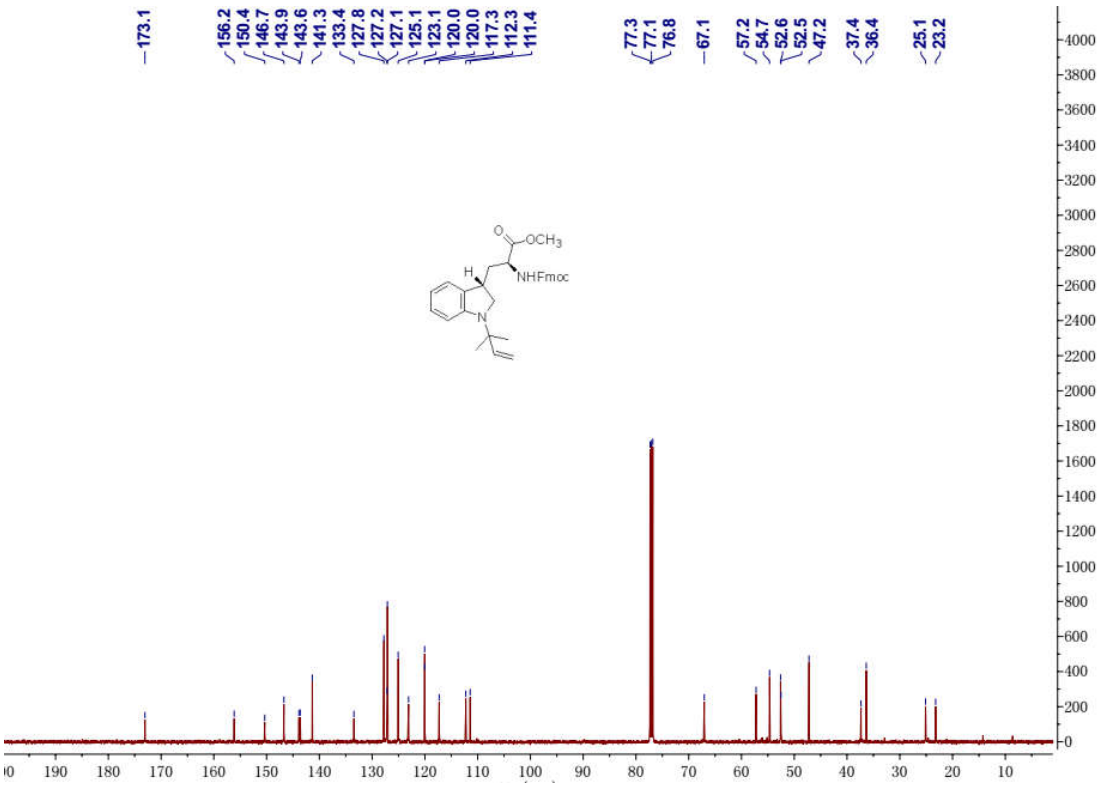
^{1}H NMR and ^{13}C NMR spectrum of **17b** ($CDCl_3$)



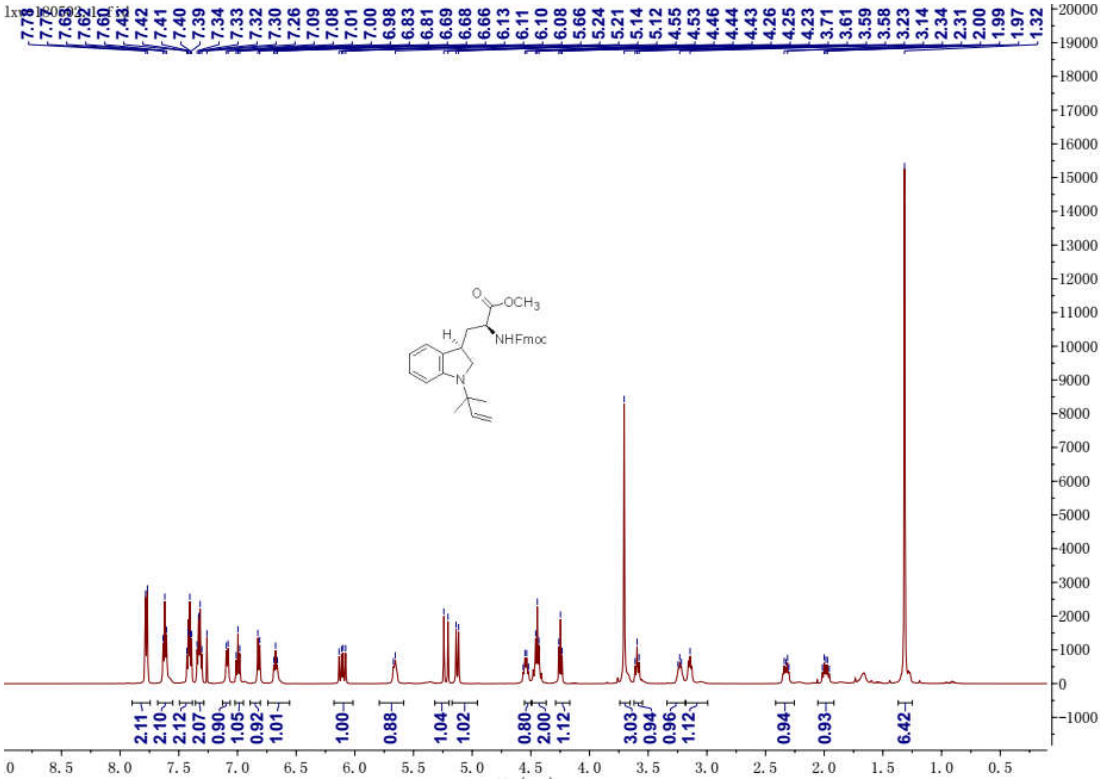


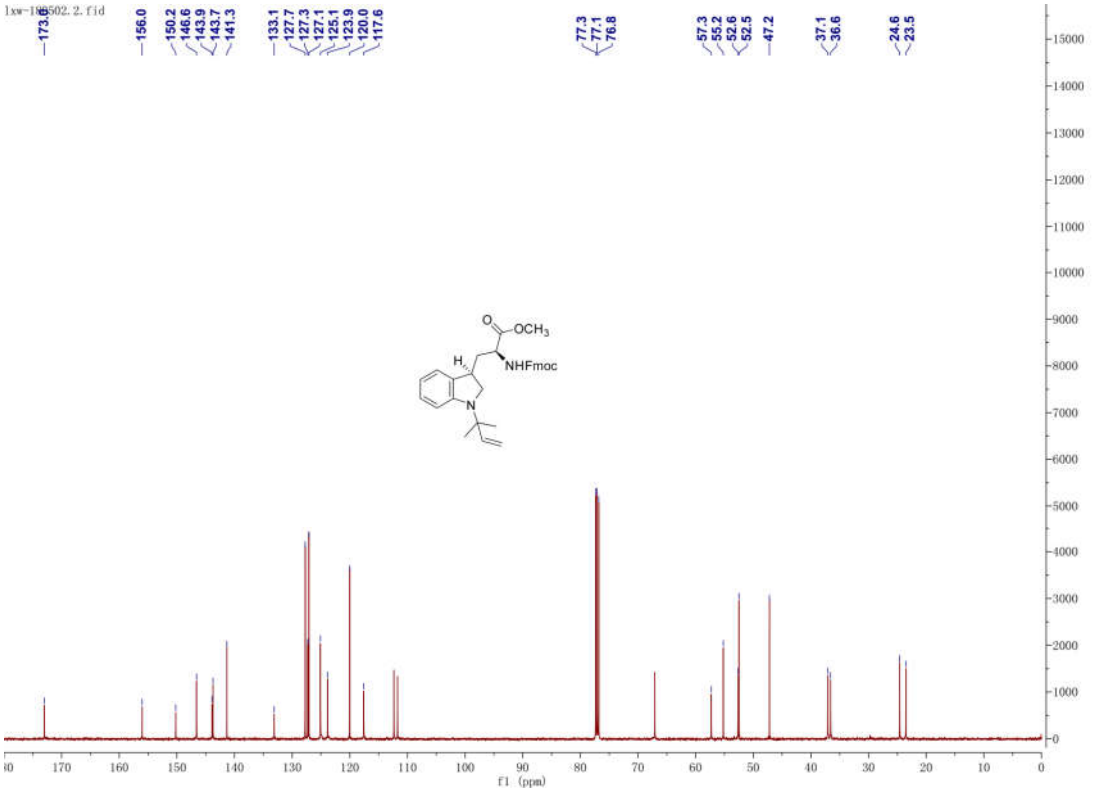
^{1}H NMR and ^{13}C NMR spectrum of **18a** ($CDCl_3$)



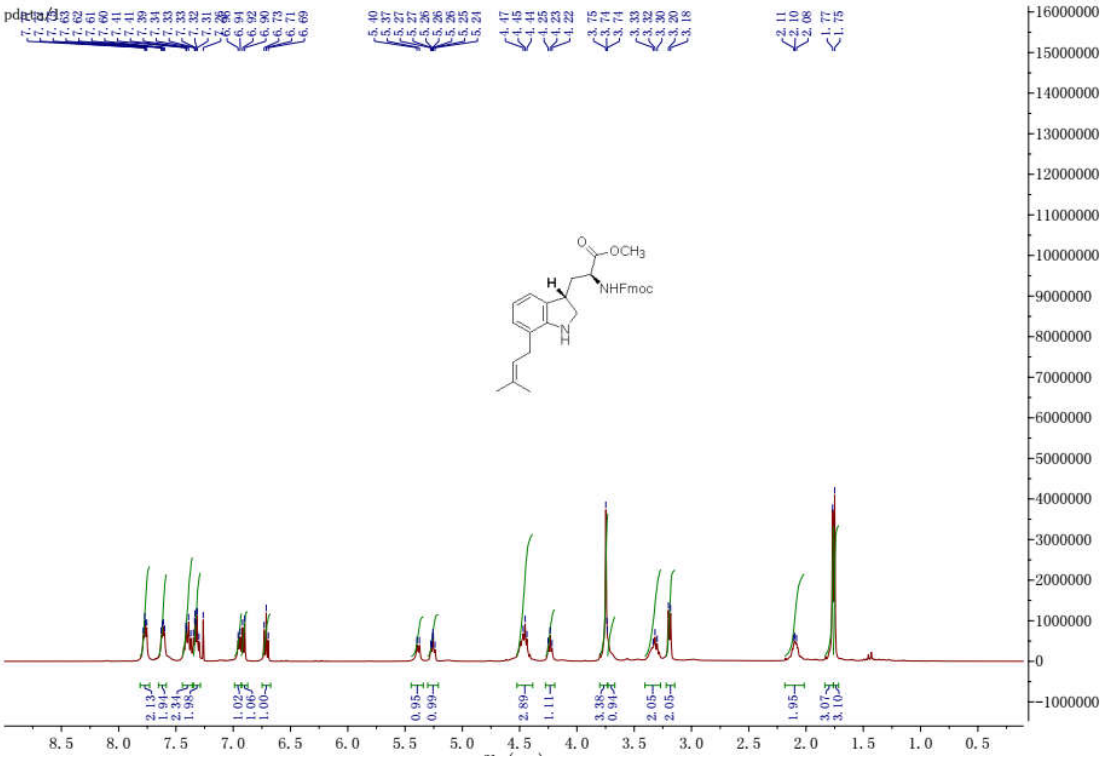


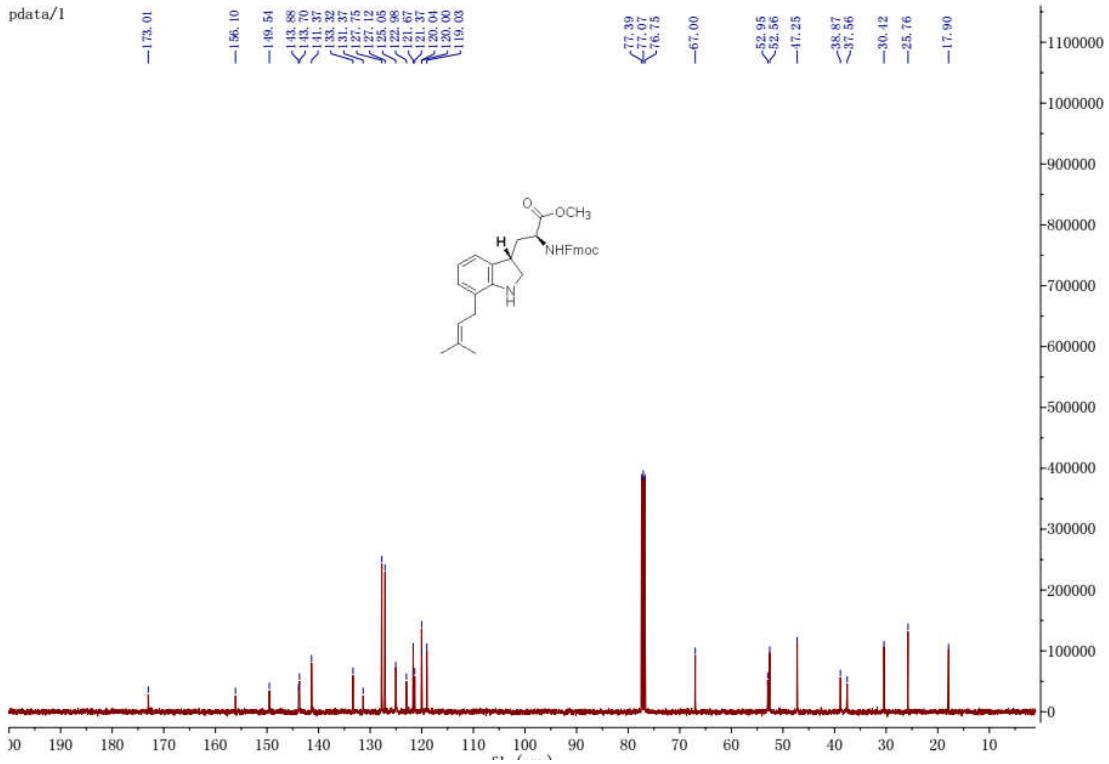
^{1}H NMR and ^{13}C NMR spectrum of **18b** ($CDCl_3$)



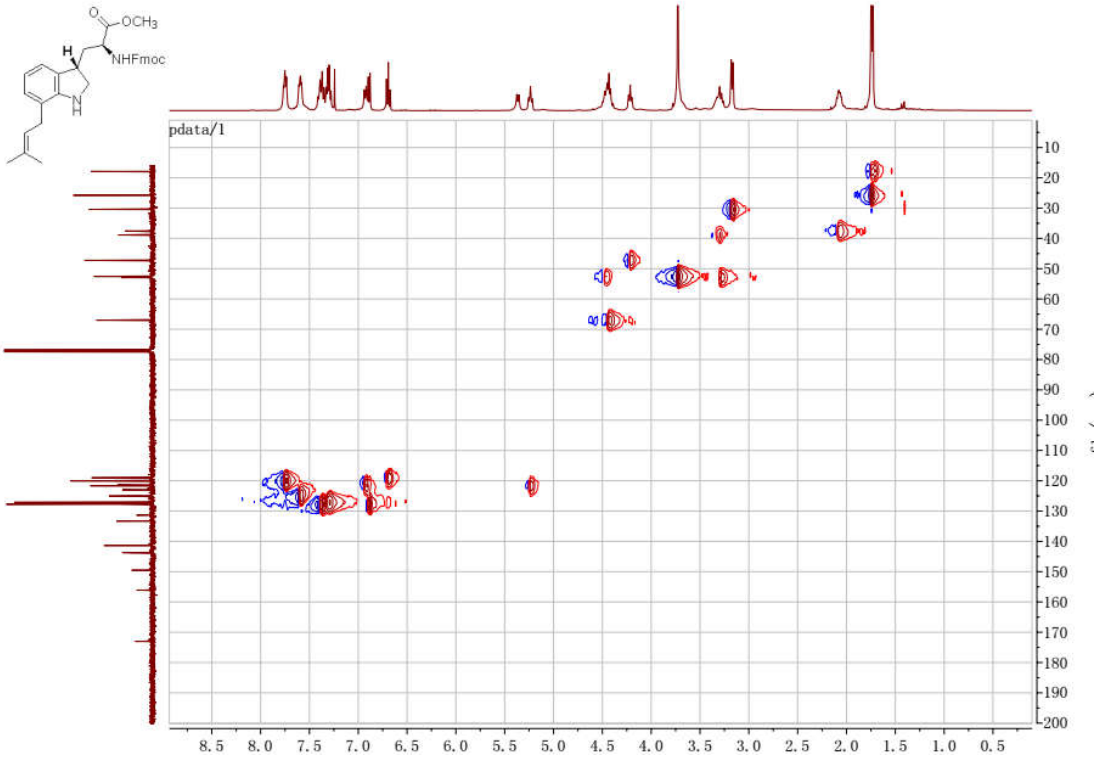


^{1}H NMR and ^{13}C NMR spectrum of **19a** ($CDCl_3$)

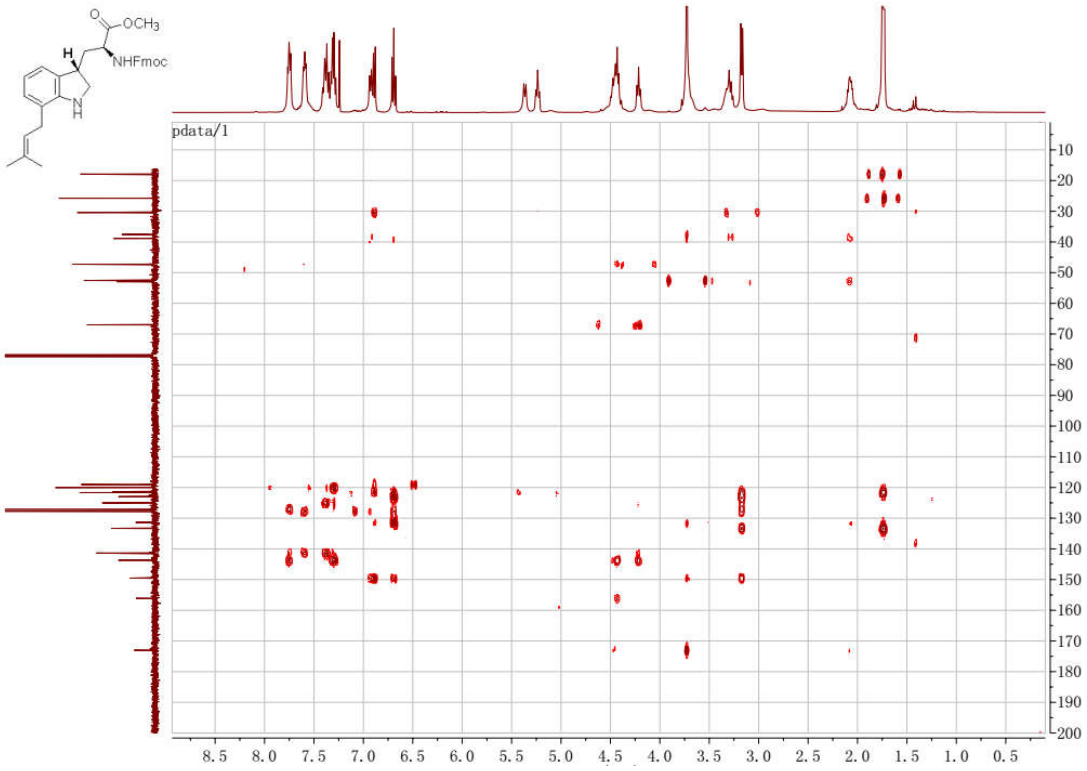




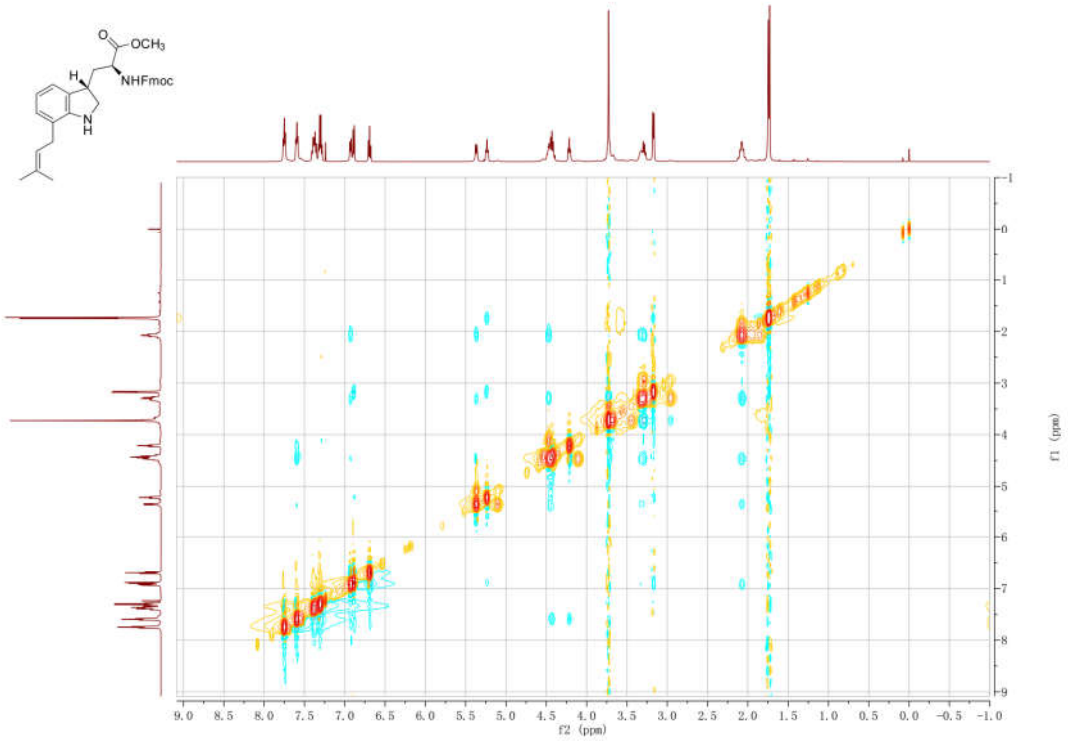
HSQC spectrum of **19a** ($CDCl_3$)



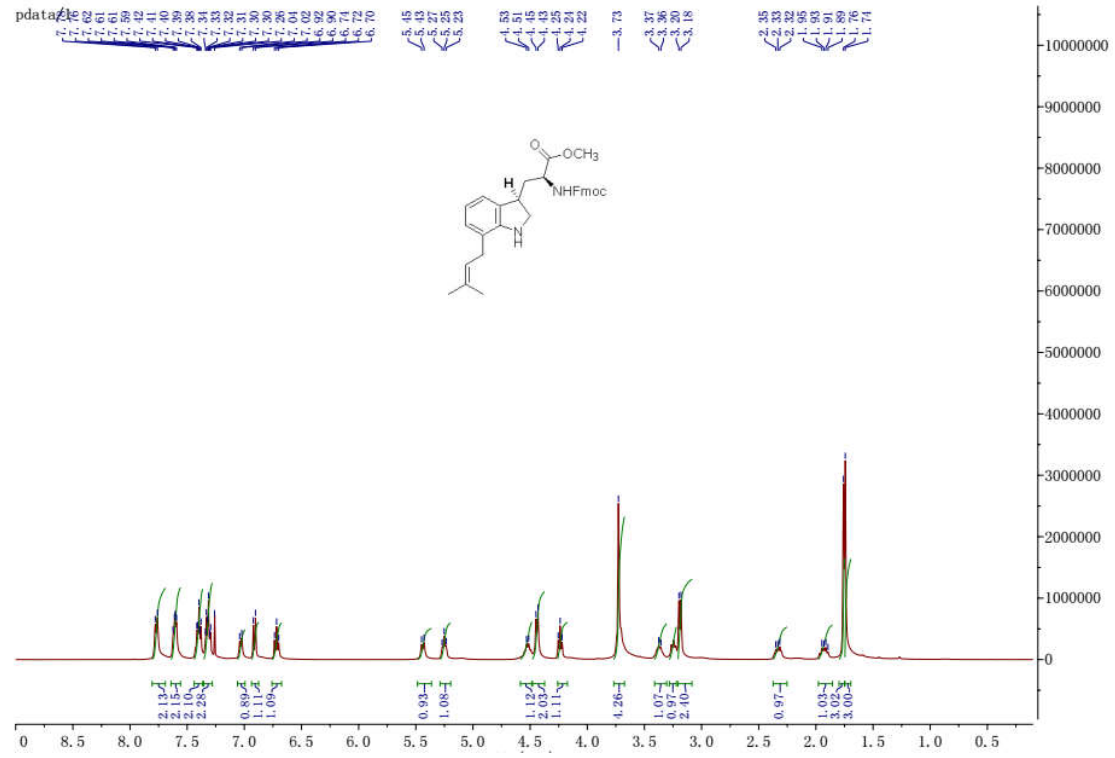
HMBC spectrum of **19a** ($CDCl_3$)

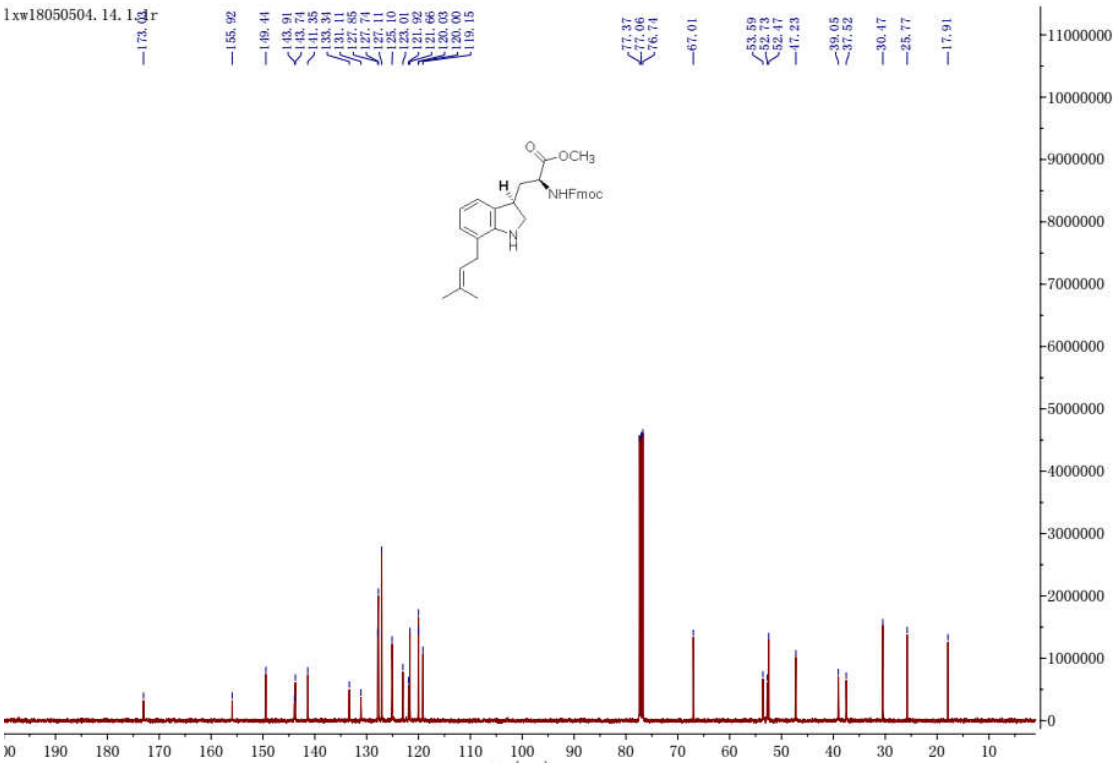


NOESY spectrum of **19a** ($CDCl_3$)

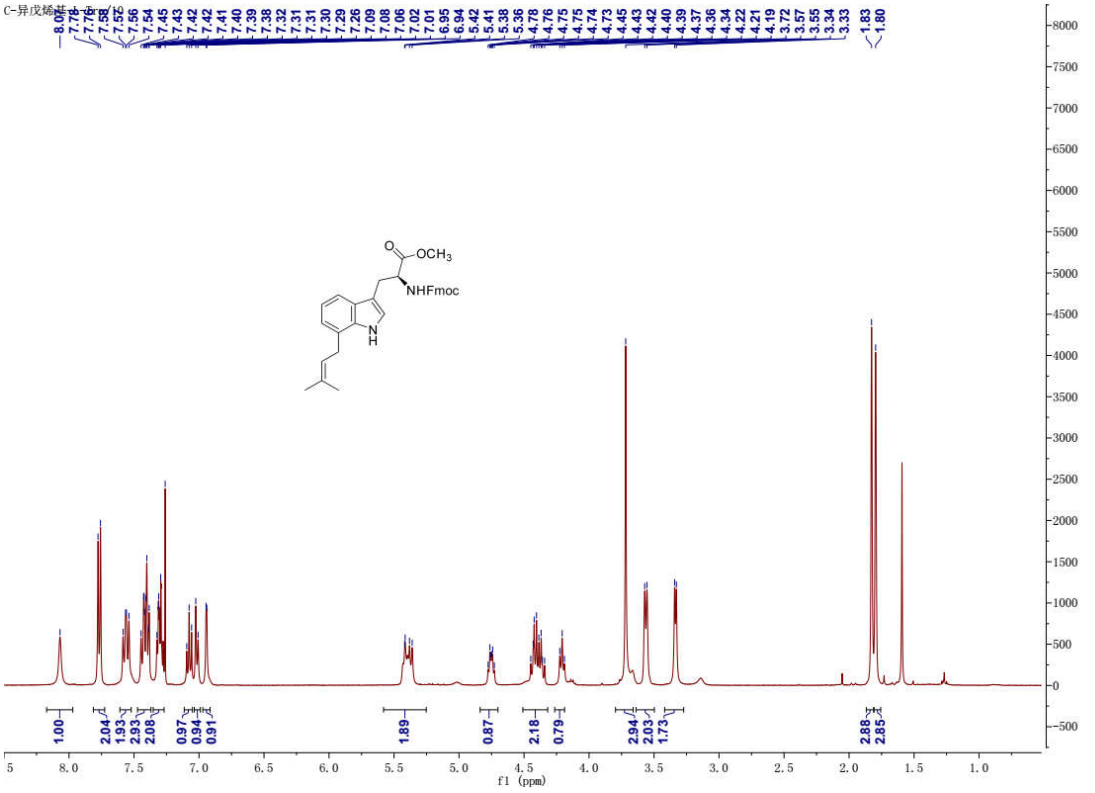


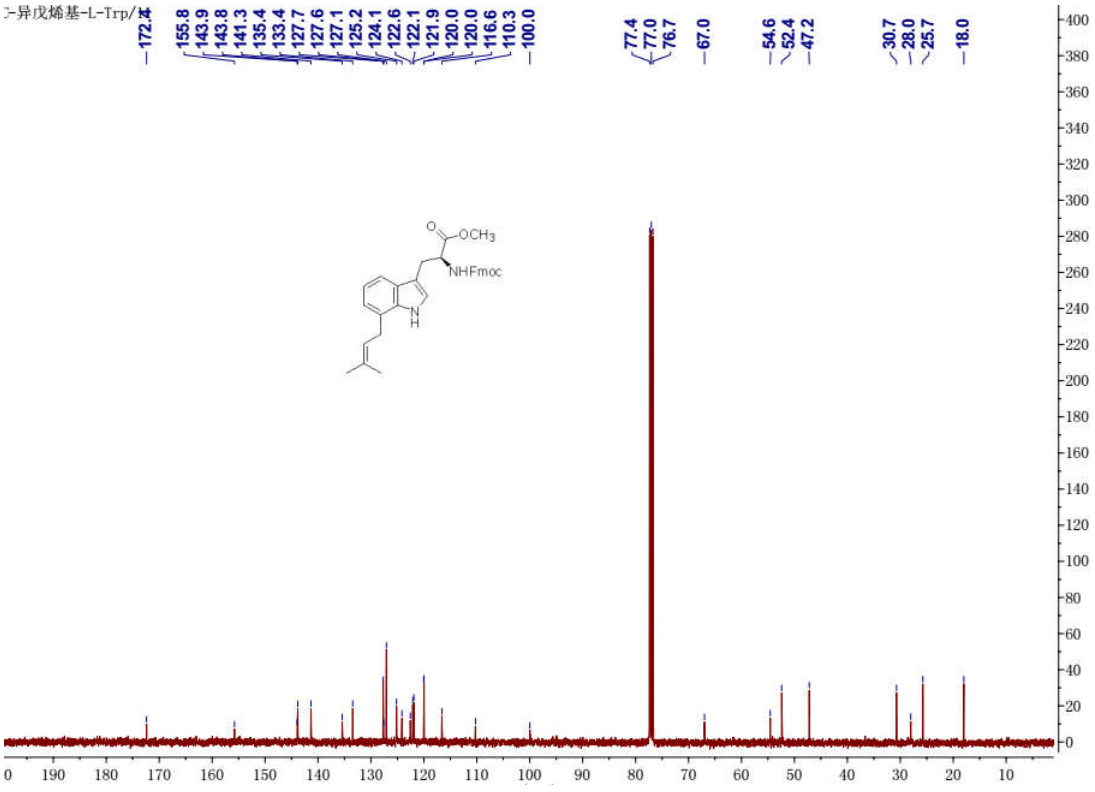
^{1}H NMR and ^{13}C NMR spectrum of **19b** ($CDCl_3$)



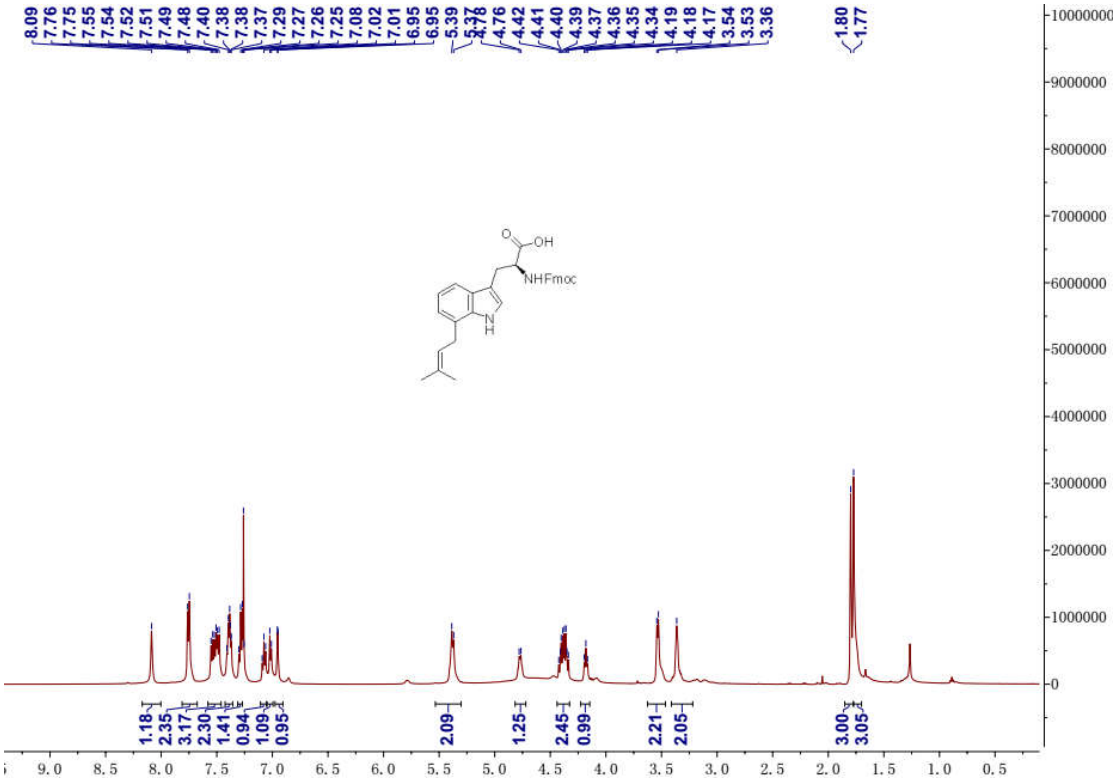


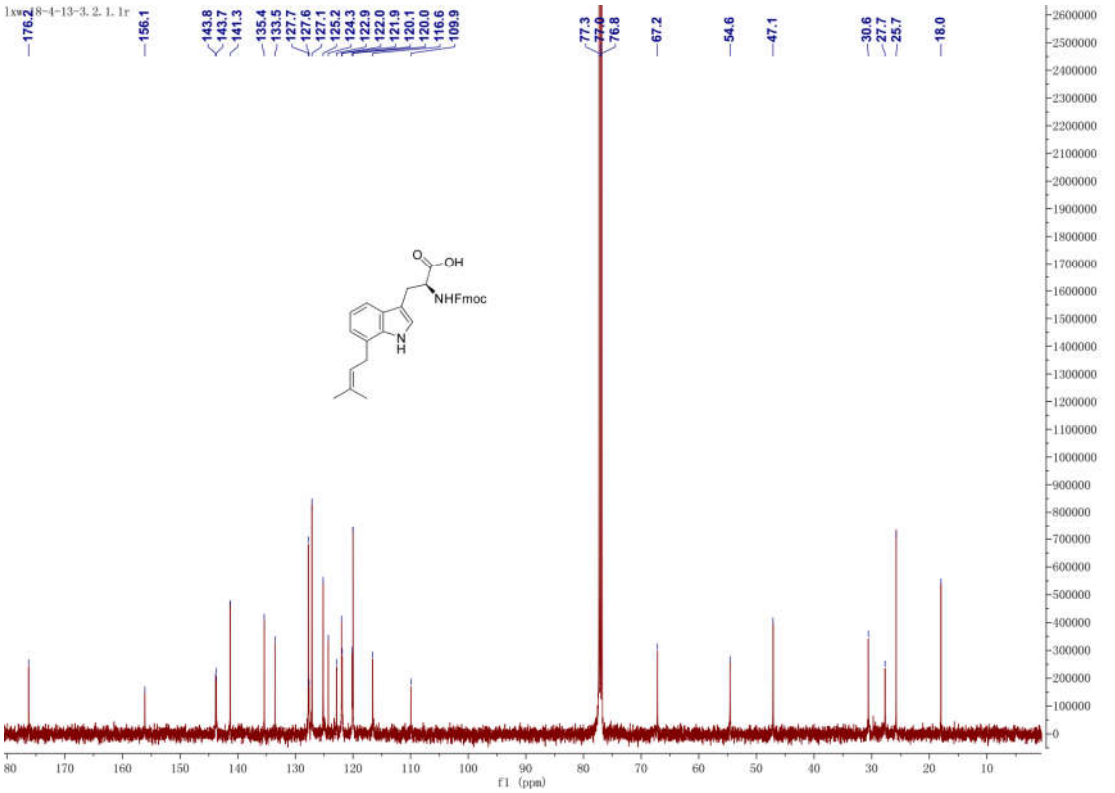
^{1}H NMR and ^{13}C NMR spectrum of **20** ($CDCl_3$)



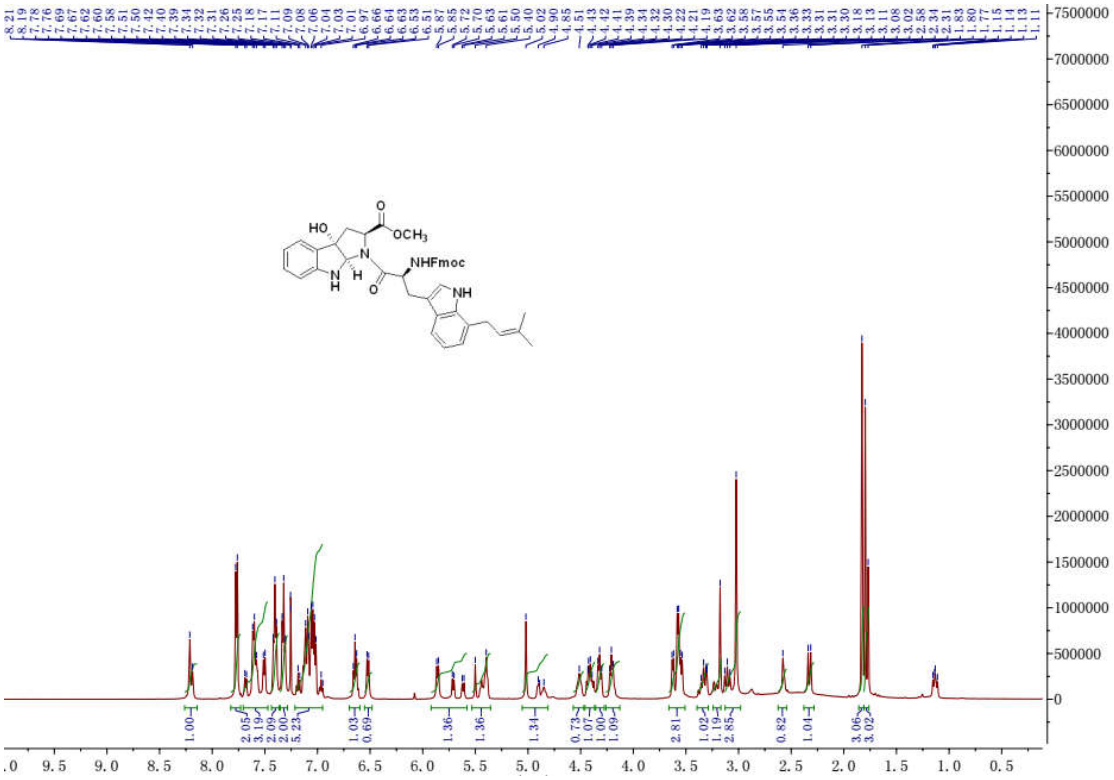


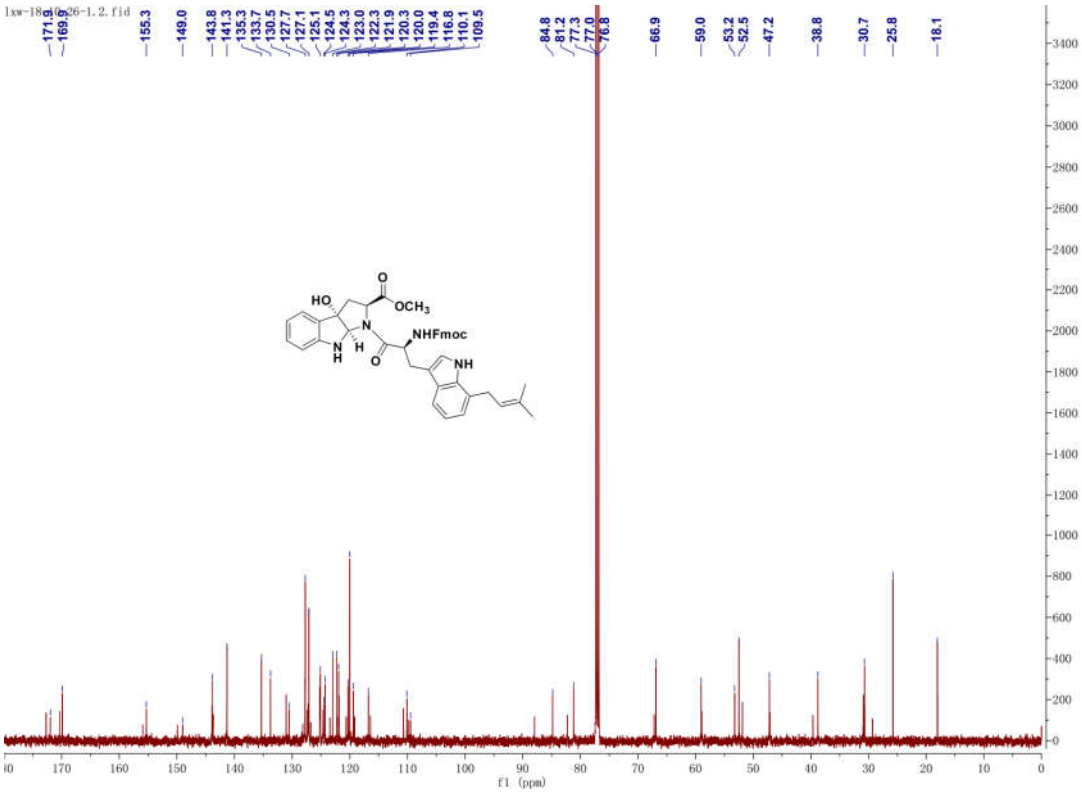
^{1}H NMR and ^{13}C NMR spectrum of **10a** ($CDCl_3$)



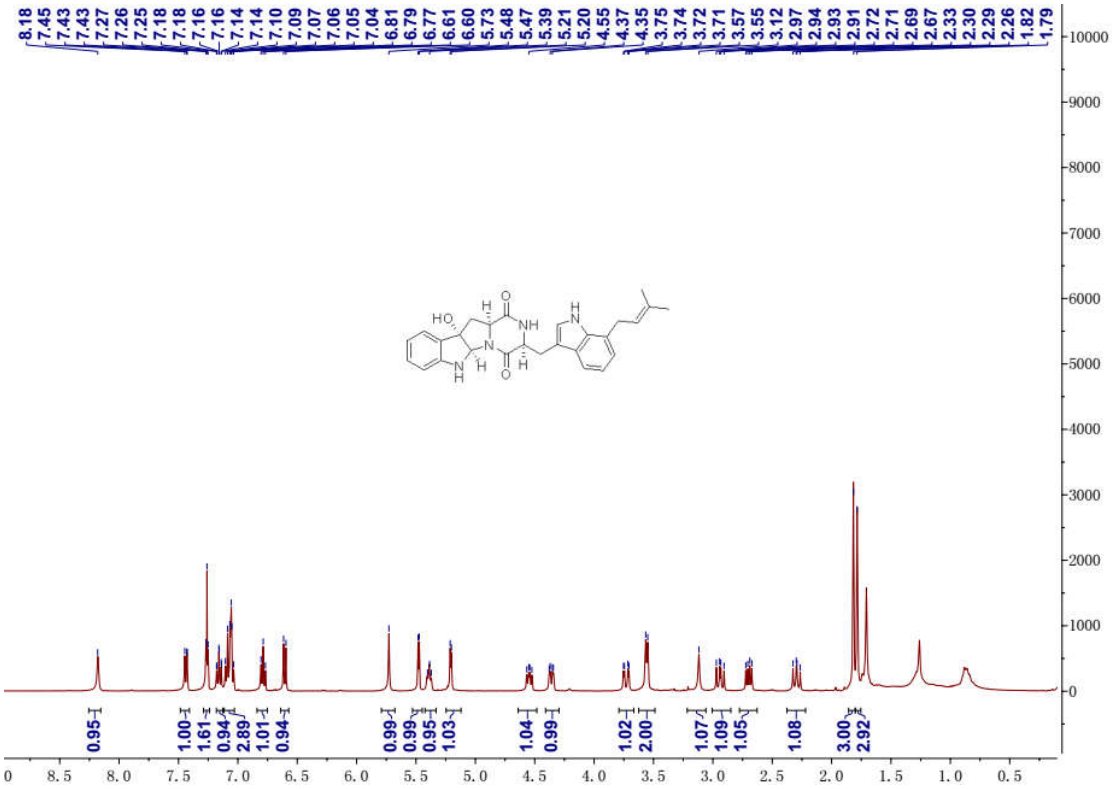


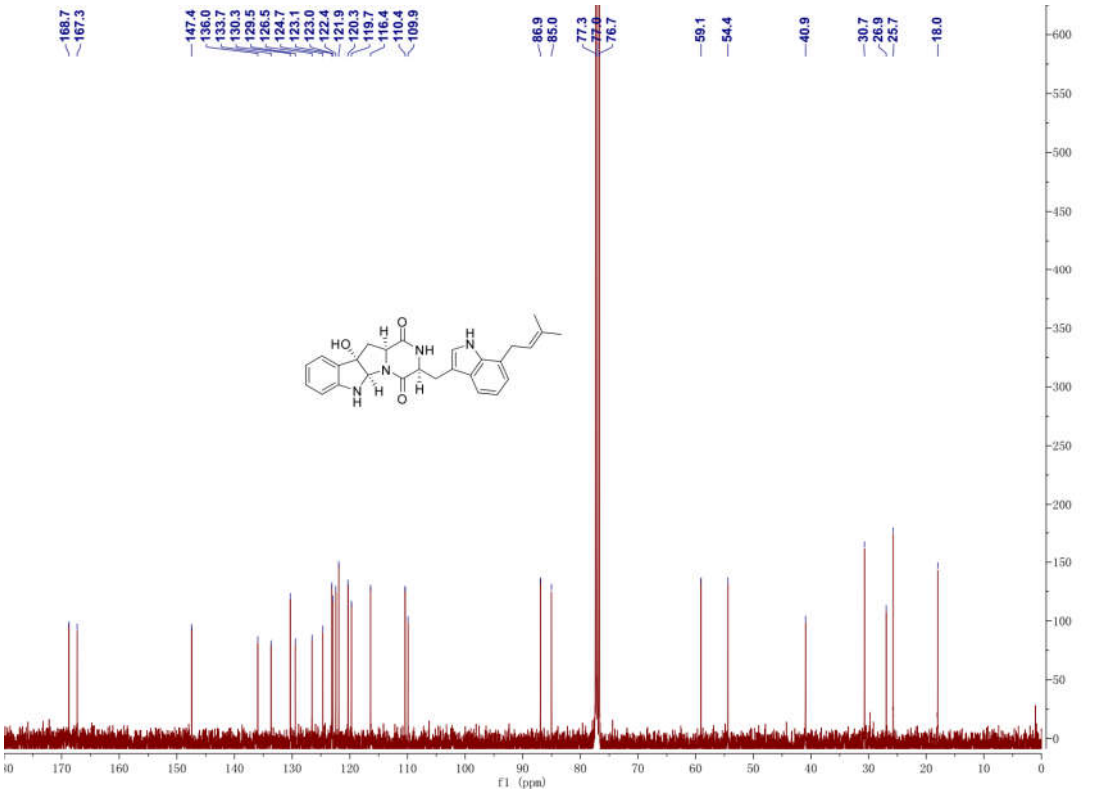
^{1}H NMR and ^{13}C NMR spectrum of **8a** ($CDCl_3$)



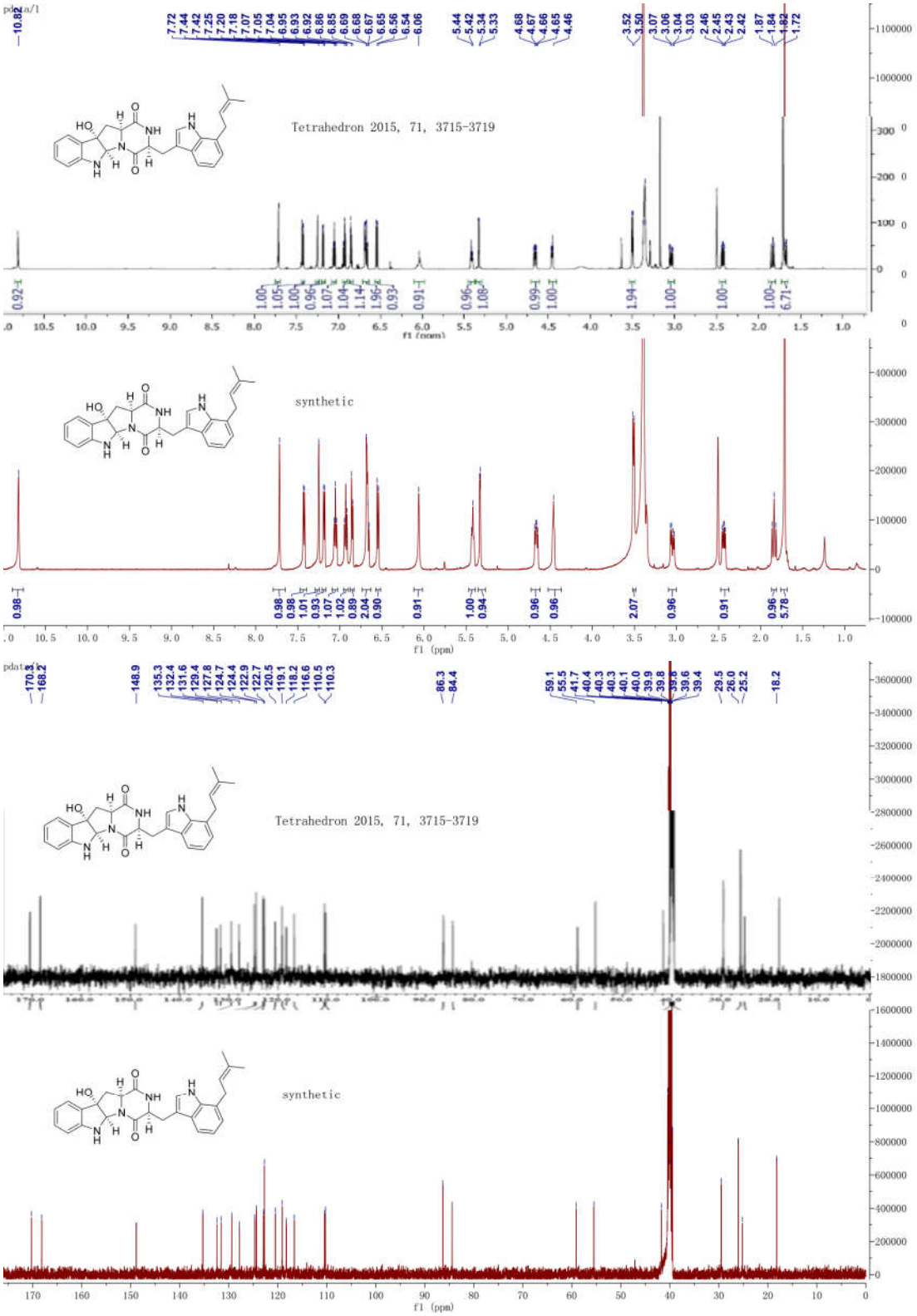


^{1}H NMR and ^{13}C NMR spectrum of **5** ($CDCl_3$)

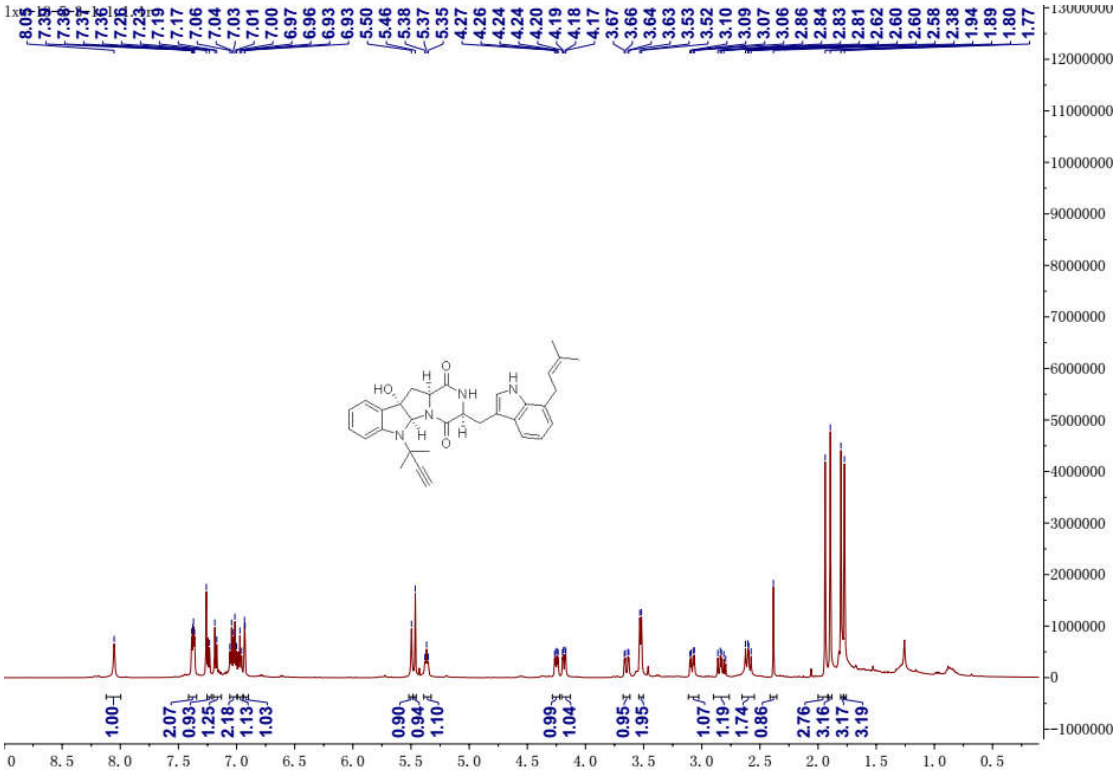


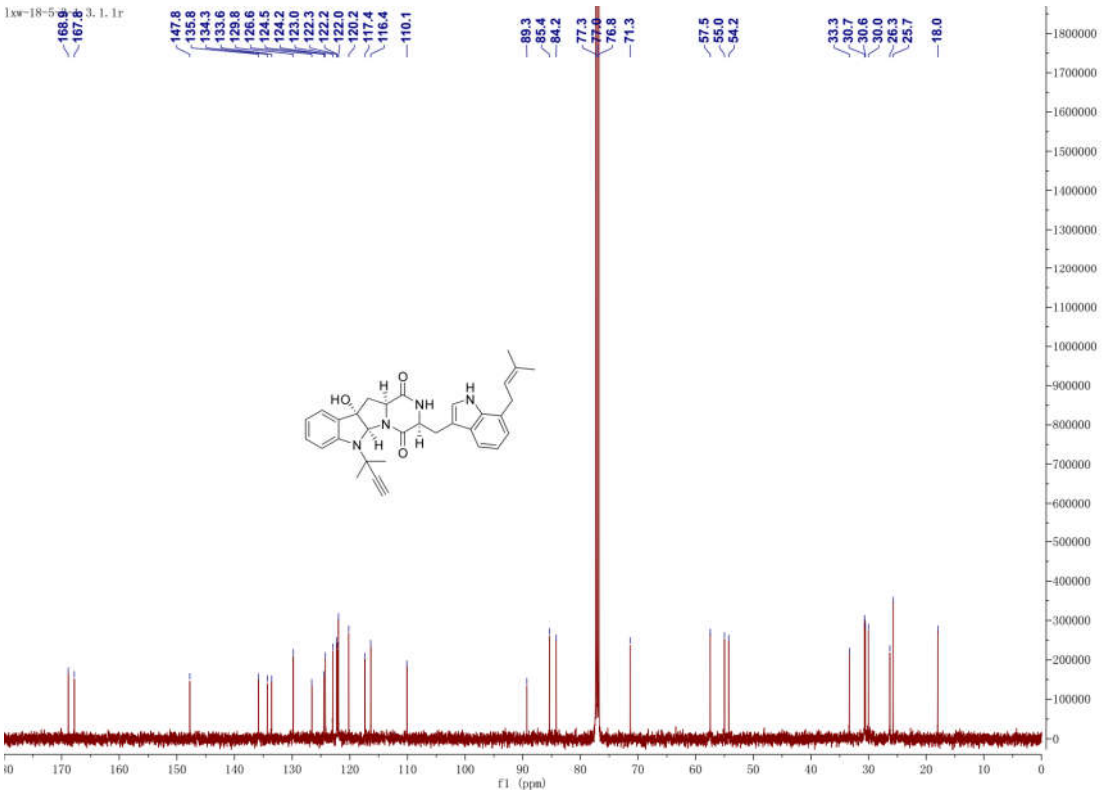


[1]H and [13] C NMR spectrum of okaramines T (DMSO-d_6, provided) and **5** (DMSO-d_6)

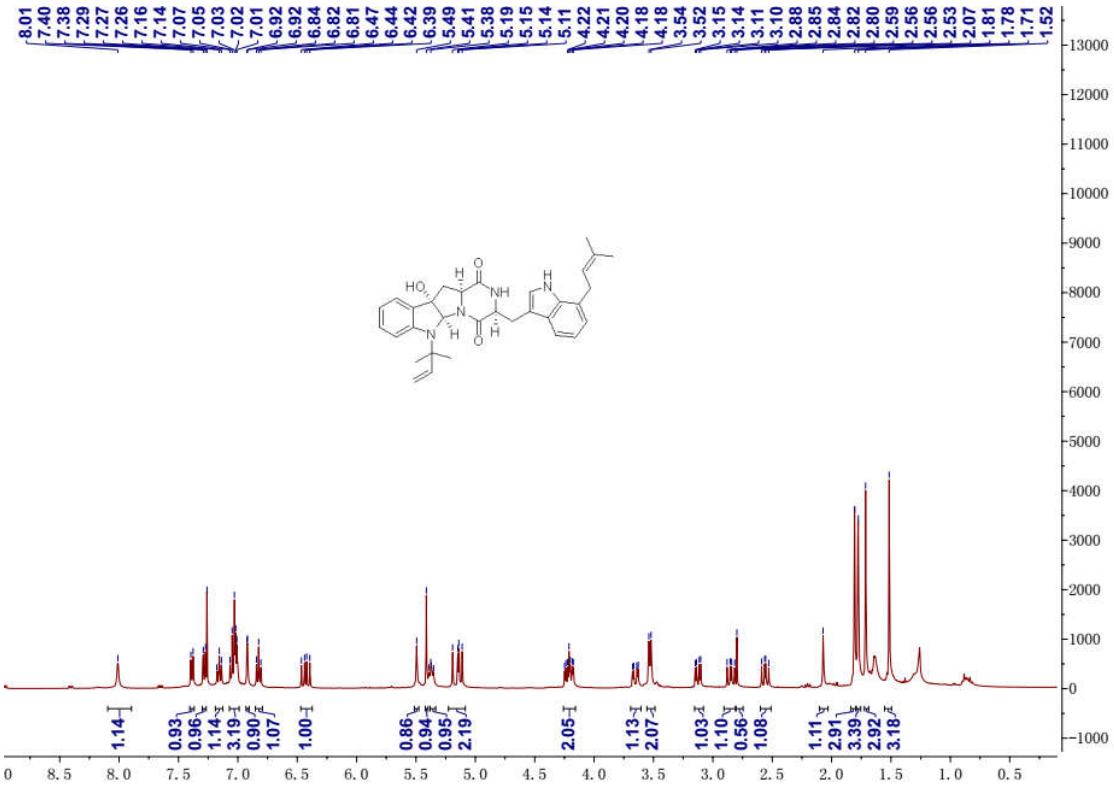


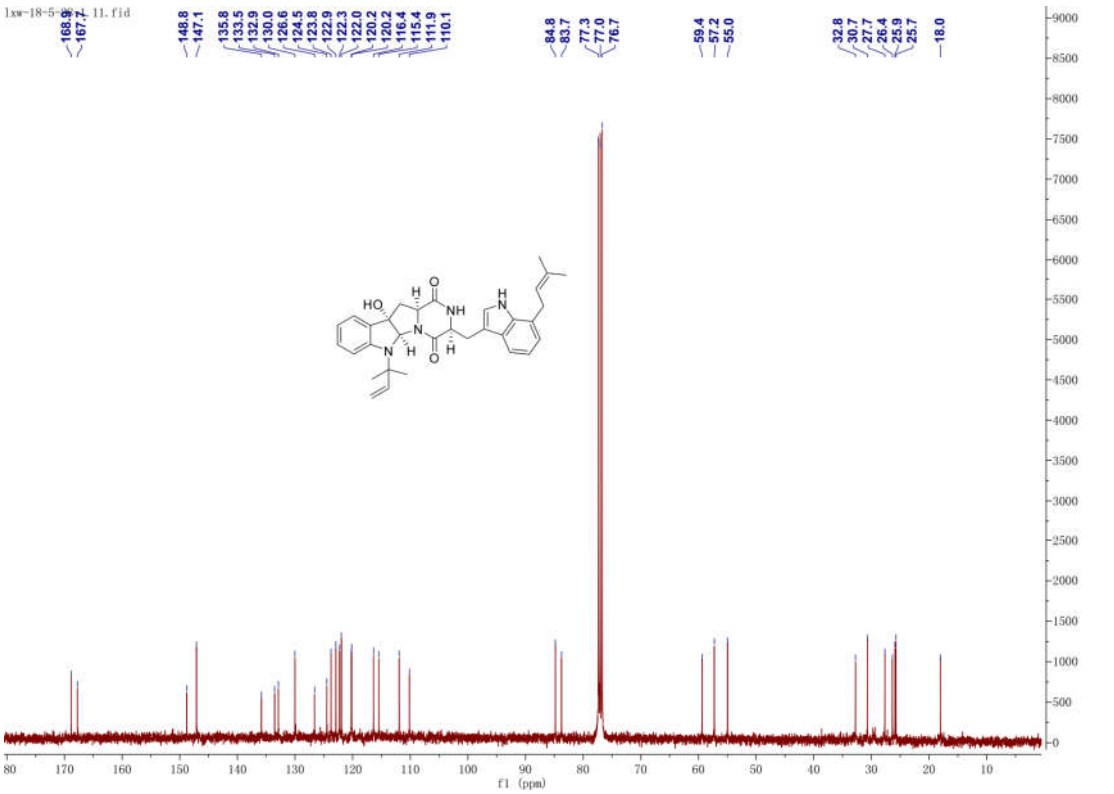
^{1}H NMR and ^{13}C NMR spectrum of **21** ($CDCl_3$)



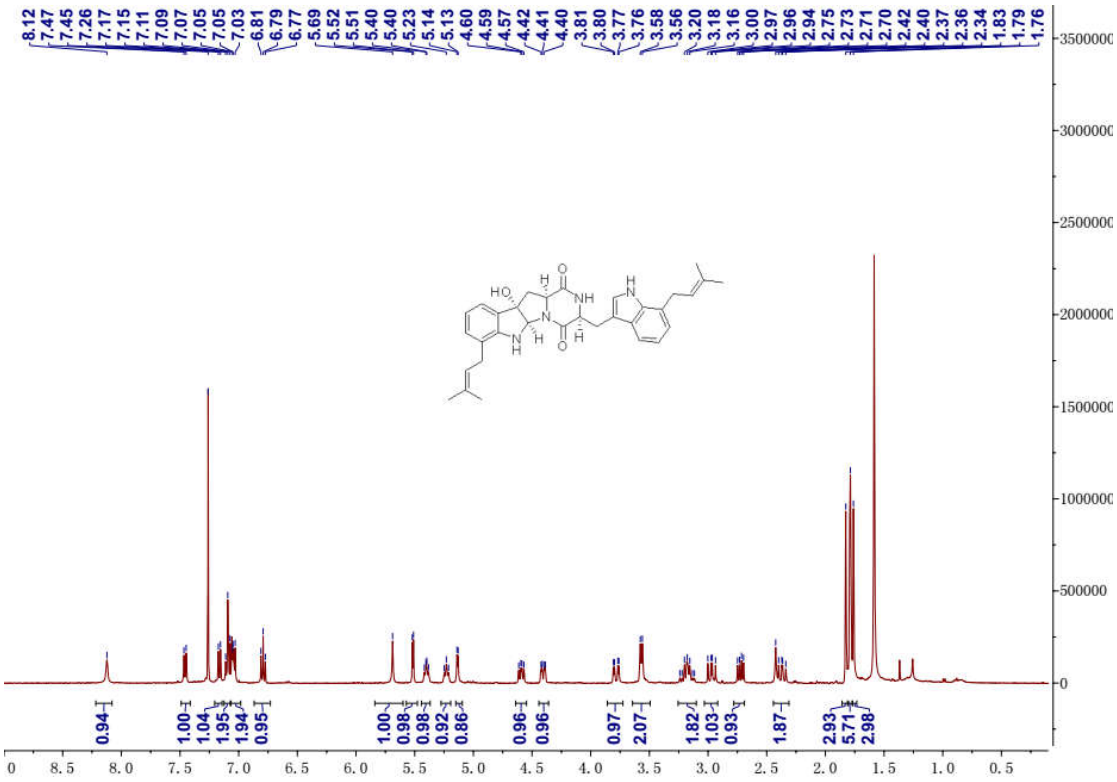


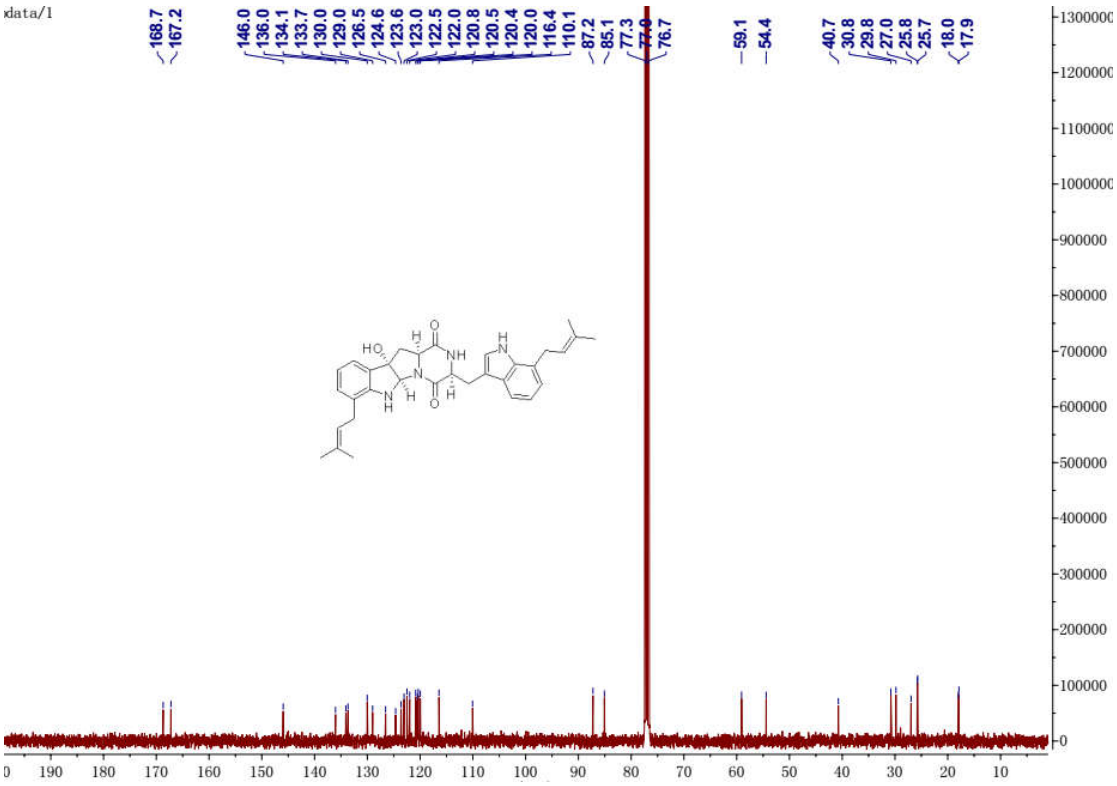
^{1}H NMR and ^{13}C NMR spectrum of **7** ($CDCl_3$)



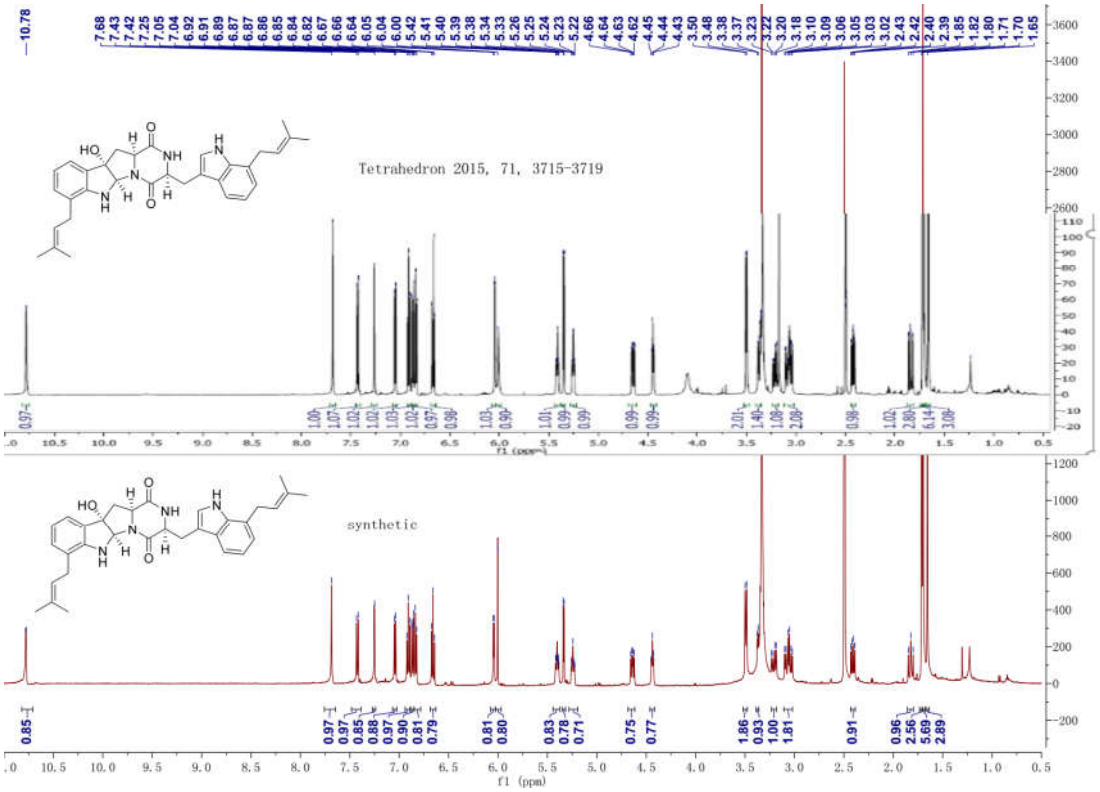


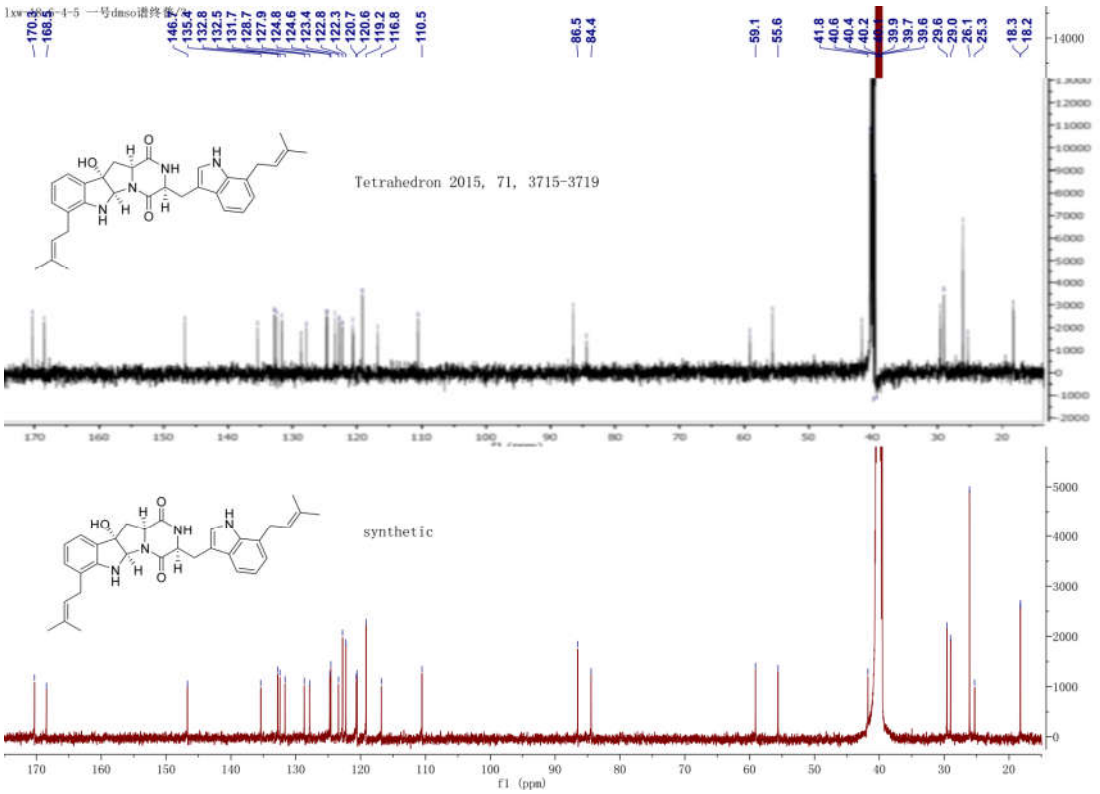
^{1}H NMR and ^{13}C NMR spectrum of **4** ($CDCl_3$)



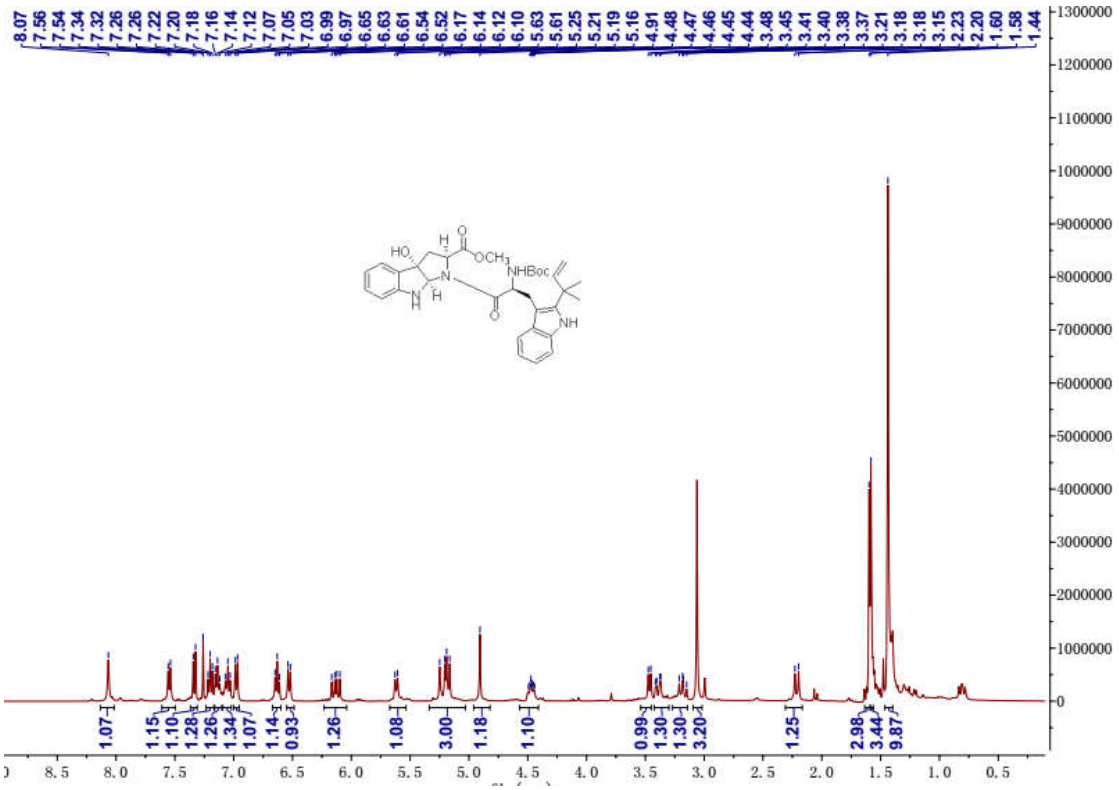


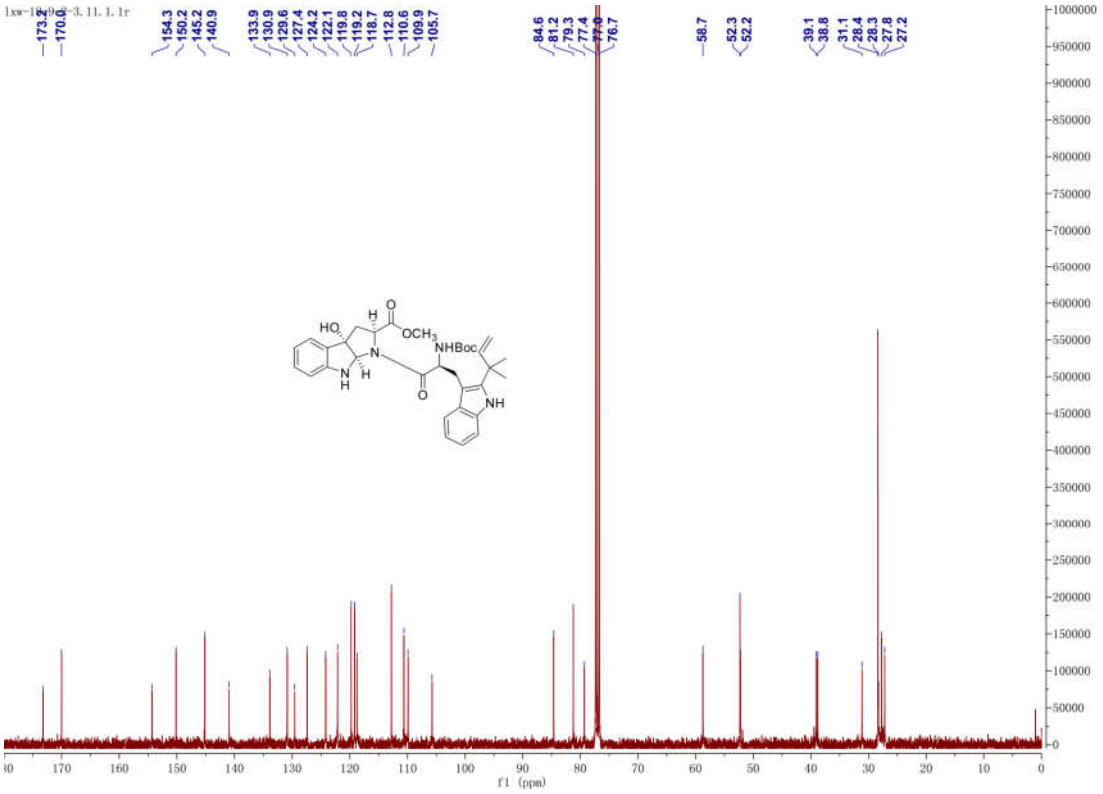
[1]H and [13] C NMR spectrum of okaramines S (DMSO-d_6, provided) and **4** (DMSO-d_6)



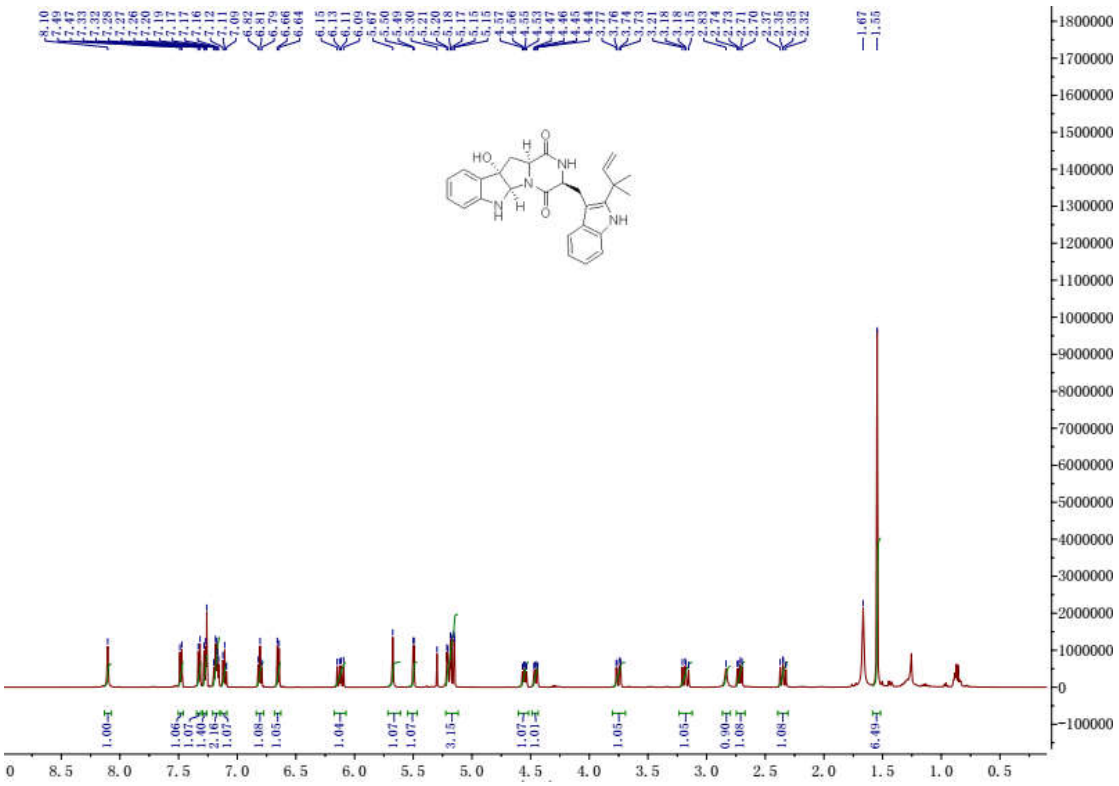


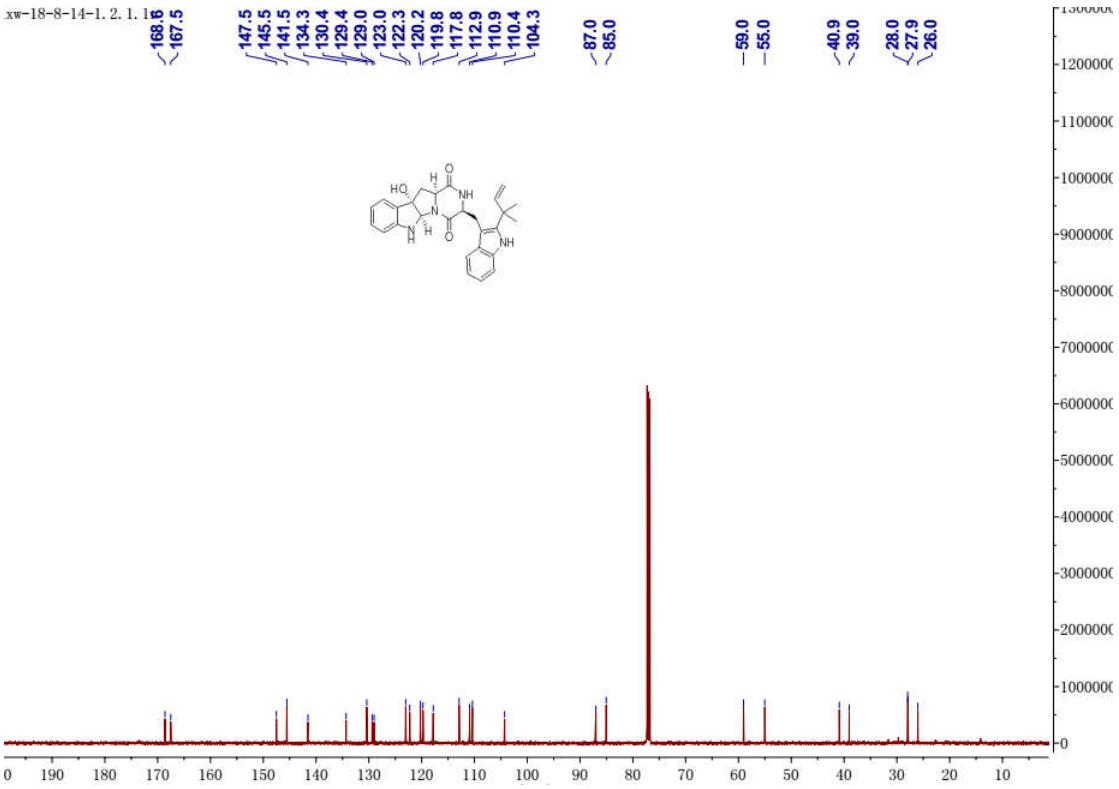
^{1}H NMR and ^{13}C NMR spectrum of **8c** ($CDCl_3$)



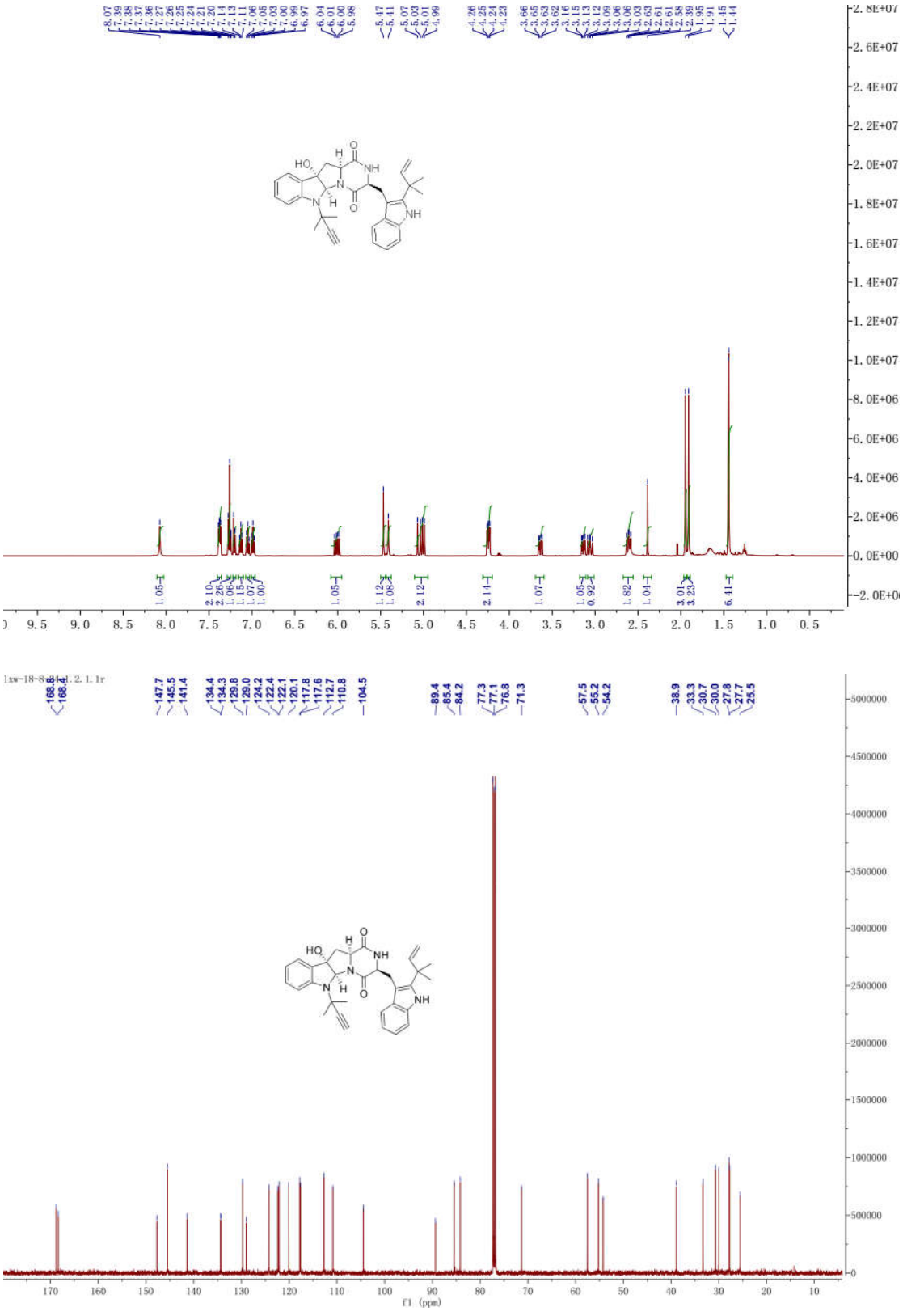


^{1}H NMR and ^{13}C NMR spectrum of **3a** ($CDCl_3$)

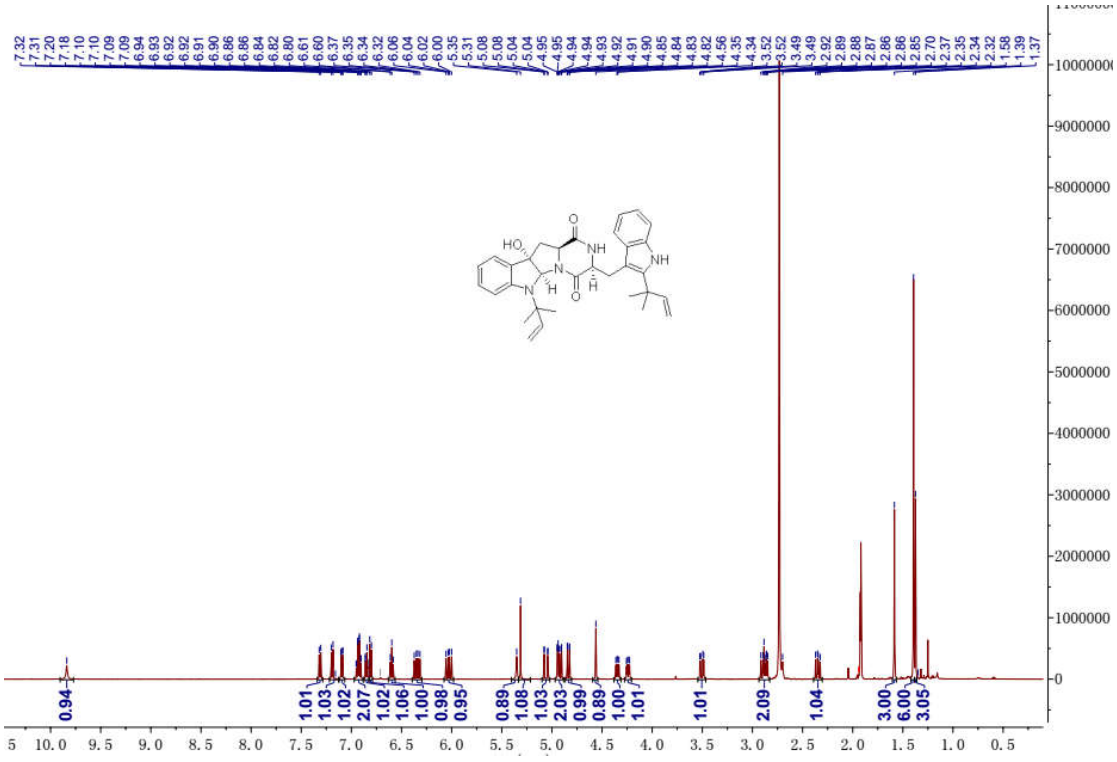


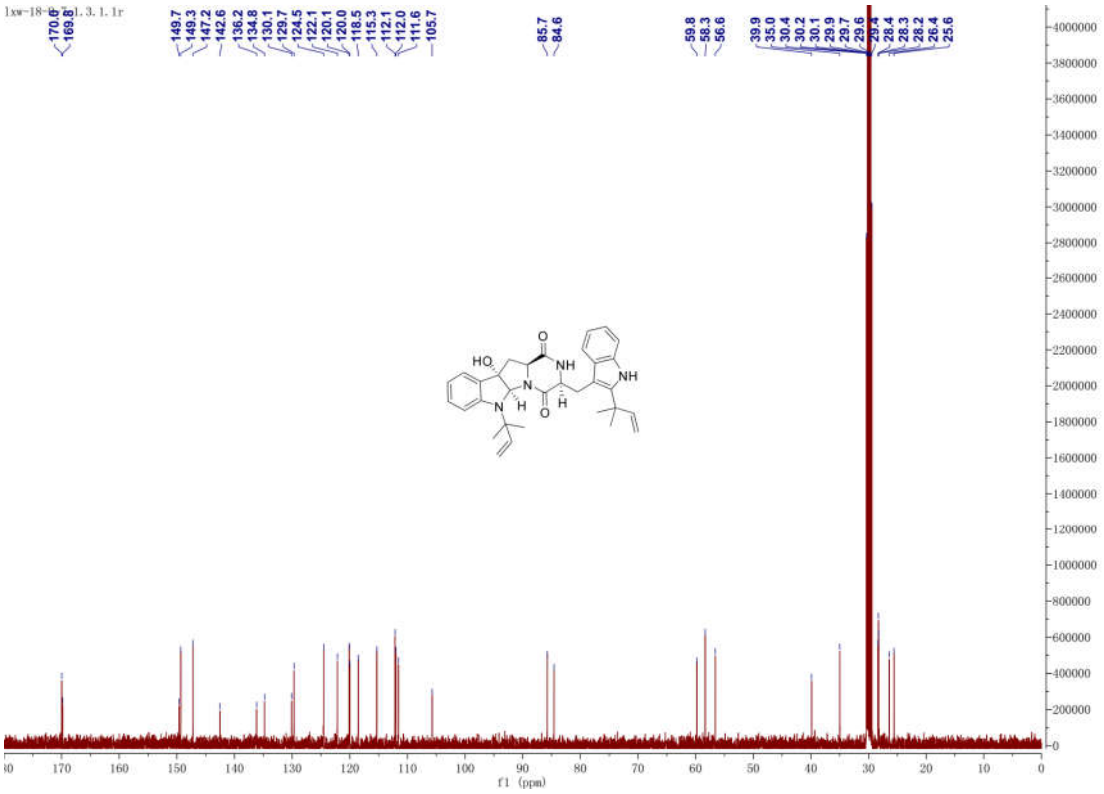


^{1}H NMR and ^{13}C NMR spectrum of **22** ($CDCl_3$)

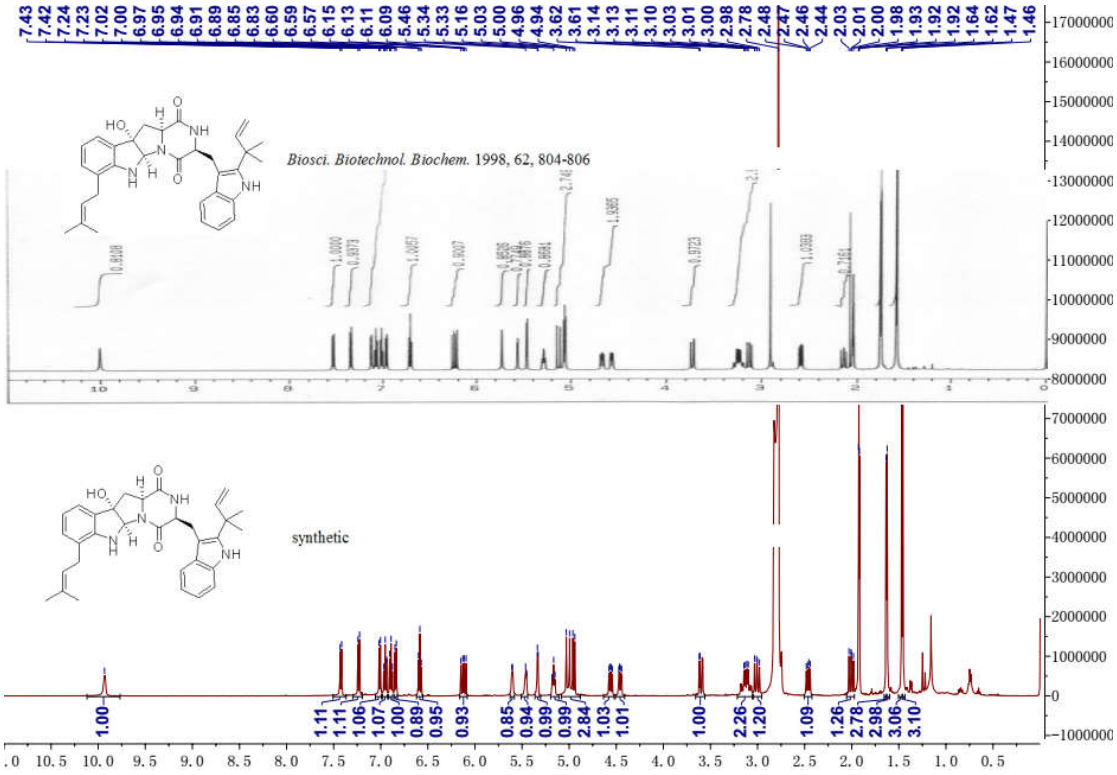


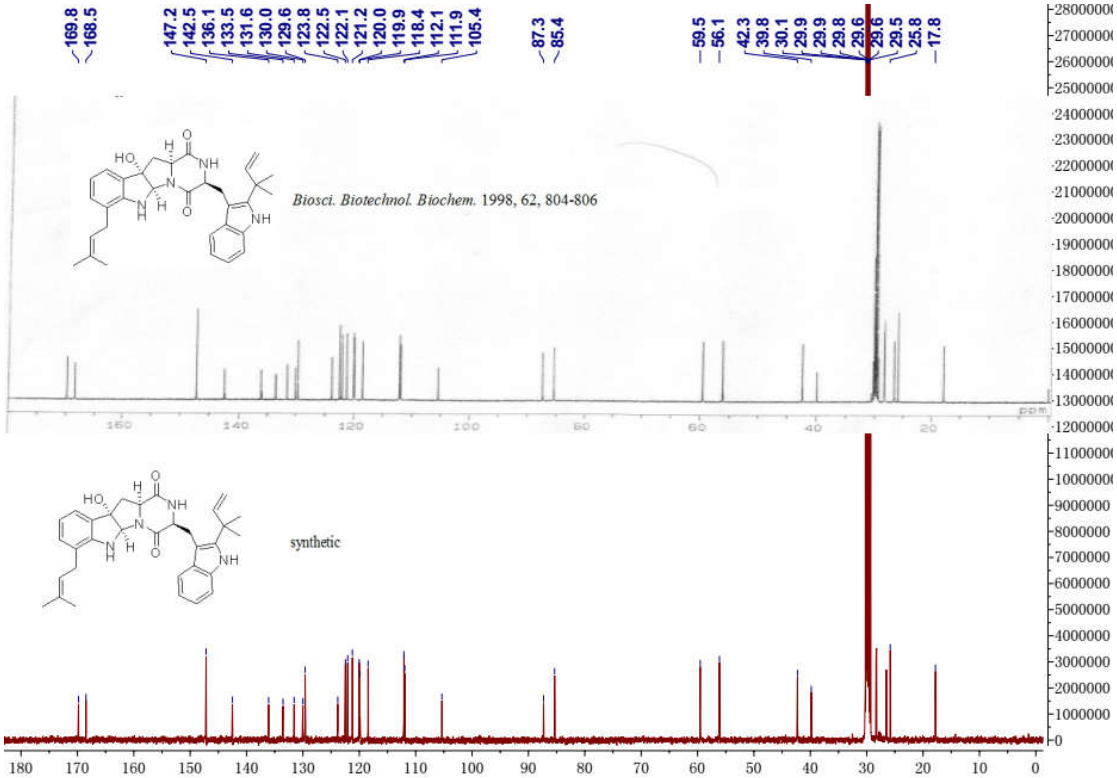
^{1}H NMR and ^{13}C NMR spectrum of **1** (Acetone-d_6)



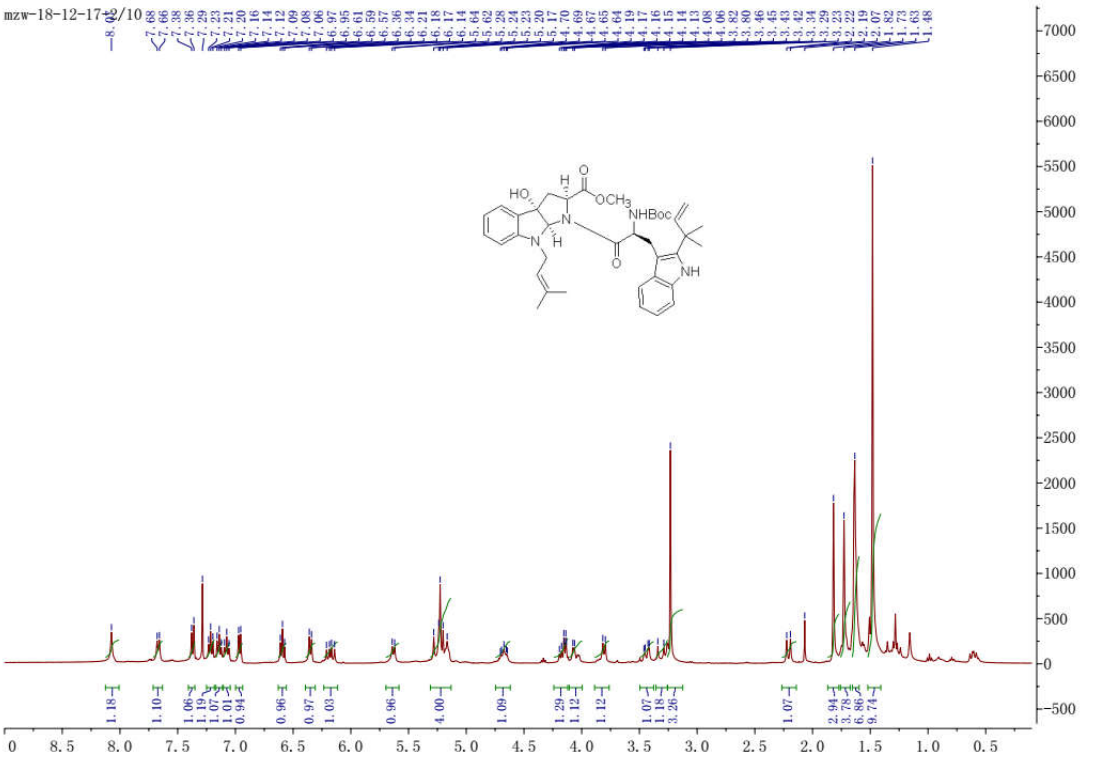


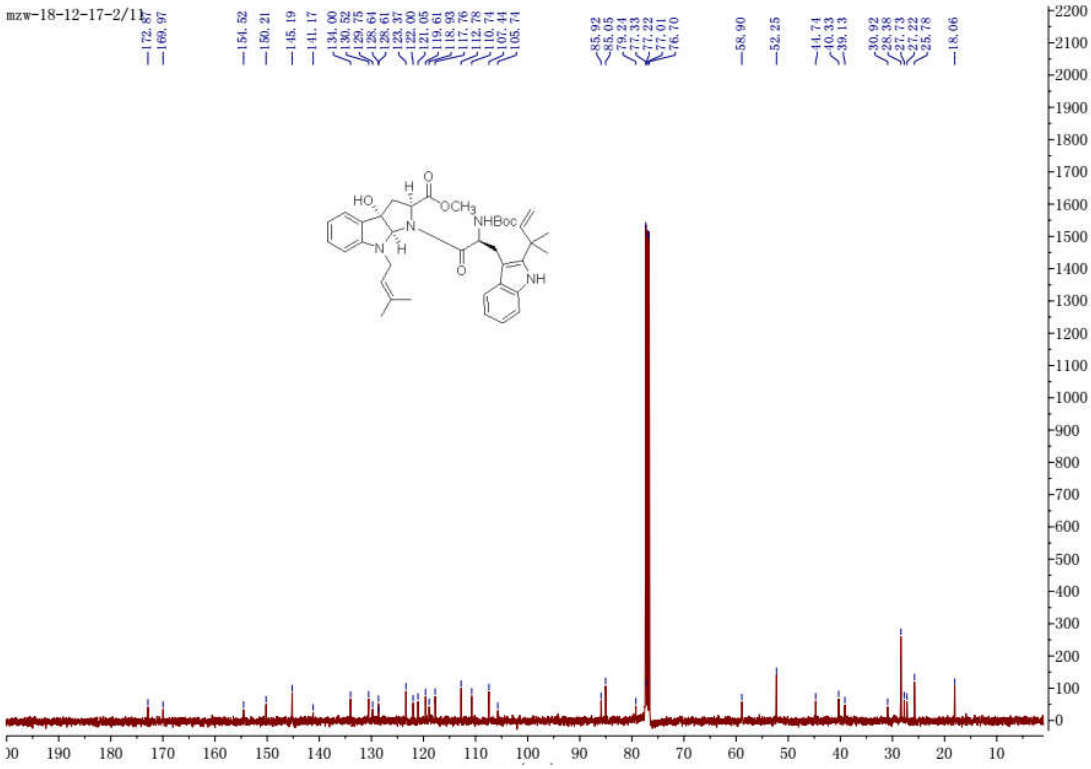
^{1}H and ^{13} C NMR spectrum of okaramine J (Acetone-d_6, provided) and **2** (Acetone-d_6)





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





^{1}H and ^{13} C NMR spectrum of **3** (Acetone-d_6)