Electronic Supplementary Information

Enantioselective Total Syntheses of Marine Natural Products (+)-Cylindricines C, D, E and Their 2-*epi*-Diastereomers

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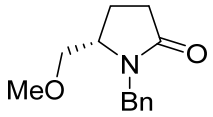
1. General Information

Infrared spectra were measured with a Nicolet Avatar 360 FT-IR spectrometer using film KBr pellet techniques. Optical rotations were measured on a Perkin-Elmer 341 automatic polarimeter or an Anton Paar MCP 500 polarimeter. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker spectrometer at either 400, 500 or 600 MHz. Chemical shifts (δ) were reported in ppm and respectively referenced to either the internal standard Me_4Si or solvent signals ($CDCl_3$ at 7.26 ppm for ^{1}H NMR and $CDCl_3$ at 77.0 ppm for ^{13}C NMR). HRMS spectra were obtained using a Bruker microFlex MALDI TOF MS/MS high-resolution mass spectrometer equipped with Fourier Transform Ion Cyclotron Resonance-Mass Spectrometry (FTICR-MS). Silica gel (200-300 mesh) was used for flash column chromatography, eluting (unless otherwise stated) with *n*-hexane/EtOAc mixture. All reactions were performed in oven-dried glassware fitted with rubber septa under a positive pressure of dry nitrogen or argon. Toluene and THF were distilled over sodium benzophenone ketyl under N_2. Dichloromethane was distilled over calcium hydride under N_2. Trifluoromethanesulfonic anhydride (Tf_2O) was distilled over phosphorous pentoxide and was stored for no more than a week before redistilling. All other commercially available compounds were used as received. All the Grignard reagents were titrated immediately before use.

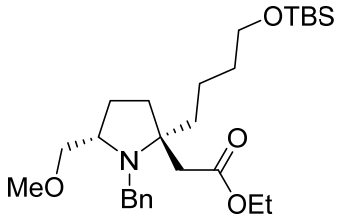
2. Synthesis and Characterization of Compounds

(*S*)-1-Benzyl-5-(methoxymethyl)pyrrolidin-2-one (9)



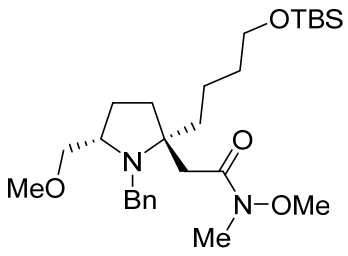
To a cooled suspension (0 °C) of NaH (600 mg, 60% dispersion in mineral oil, 15.0 mmol, 1.5 equiv) in THF (20 mL) was added dropwise a solution of (*S*)-*N*-benzyl-pyroglutaminol [(*S*)-**11**, 2.05 g, 10.0 mmol] in THF (10 mL). After being stirred for 30 min, MeI (2.12 g, 15.0 mmol, 1.5 equiv) was added dropwise, then the mixture was warmed to room temperature gradually. The mixture was stirred for 2 h before being quenched with a saturated aqueous solution of NH_4Cl (10 mL) and extracted with EtOAc (10 mL x 3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:2) to give methyl ether (*S*)-**9** (1.97 g, yield: 90%) as a colorless oil. $[\alpha]_D^{25}$ +66.6 (*c* 1.0, MeOH), lit.[1] $[\alpha]_D$ +65.3 (*c* 0.33, MeOH); IR (film) ν_{max}: 2924, 1686, 1449, 1361, 1258, 1120, 947, 800, 703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.32–7.20 (m, 5H), 4.87 (d, *J* = 15.0 Hz, 1H), 4.18 (d, *J* = 15.0 Hz, 1H), 3.59 (dd, *J* = 8.6, 4.2 Hz, 1H), 3.36 (dd, *J* = 10.0, 3.8 Hz, 1H), 3.30 (dd, *J* = 10.0, 4.8 Hz, 1H), 3.22 (s, 3H), 2.50 (ddd, *J* = 17.1, 10.0, 7.6 Hz, 1H), 2.34 (ddd, *J* = 17.1, 10.0, 5.4 Hz, 1H), 2.11–1.97 (m, 1H), 1.81 (ddd, *J* = 17.9, 10.0, 5.0 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 175.1, 136.9, 128.2 (2C), 127.7 (2C), 127.0, 73.4, 58.7, 56.7, 44.5, 29.9, 21.4 ppm; HRMS (ESI) calcd for $[C_{13}H_{17}NNaO_2]^+$ ($M+Na^+$): 242.1152; found: 242.1157.

Ethyl 2-(2*S*,5*S*)-1-benzyl-2-{4-[(*tert*-butyldimethylsilyl)oxy]butyl}-5-(methoxymethyl)pyrrolidin-2-ylacetate (8)



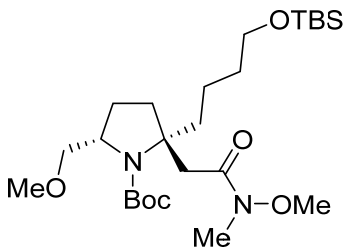
Tf_2O (Trifluoromethylsulfonic anhydride, 37 μL, 0.22 mmol, 1.1 equiv) was added dropwise to a cooled solution (−78 °C) of lactam (*S*)-**9** (43.8 mg, 0.20 mmol, 1.0 equiv) and TTBP (2,4,6-tri-*tert*-butylpyrimidine, 59.2 mg, 0.24 mmol, 1.2 equiv) in CH_2Cl_2 (15 mL) and stirred at −78 °C for 45 min. A solution of Grignard reagent **10** (0.65 mL, 0.20 mmol, 1.0 equiv, 0.31 M) in THF was added dropwise to the resultant mixture, the mixture was stirred at −78 °C for 1 h. Then enolate (0.30 mmol, 1.5 equiv), prepared by dropwise addition of NaHMDS (2.0 M in THF, 0.6 mL, 1.2 mmol) to a THF solution (2 mL) of ethyl acetate (97 μL, 1.0 mmol) at −78 °C under argon, and stirred for 30 min at the same temperature, was added dropwise. After being stirred for 3 h, the reaction was quenched with a saturated aqueous NH_4Cl (10 mL), and the mixture was extracted with CH_2Cl_2 (3 ×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane= 1:20) to give pyrrolidine **8** (73.6 mg, yield: 75%, dr = 7: 1) as a colorless oil. $[\alpha]_D^{20}$ −14.1 (*c* 0.15, $CHCl_3$); IR (film) ν_{max}: 2923, 2850, 1731, 1384, 1096, 875, 775, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (data of the major diastereomer read from the spectrum) 7.34–7.17 (m, 5H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.95 (d, *J* = 14.2 Hz, 1H), 3.58 (t, *J* = 6.8 Hz, 2H), 3.52 (d, *J* = 14.2 Hz, 1H), 3.04 (s, 3H), 3.02–2.97 (m, 1H), 2.83 (dd, *J* = 9.2, 7.9 Hz, 1H), 2.74 (dd, *J* = 9.2, 4.0 Hz, 1H), 2.49 (d, *J* = 12.9 Hz, 1H), 2.39 (d, *J* = 12.9 Hz, 1H), 2.05–1.84 (m, 2H), 1.83–1.68 (m, 2H), 1.68–1.46 (m, 3H), 1.46–1.33 (m, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 0.90 (s, 9H), 0.05 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (data of the major diastereomer read from the spectrum) 172.7, 141.9, 128.3 (2C), 128.0 (2C), 126.6, 76.5, 67.3, 63.2, 63.1, 60.2, 58.6, 52.3, 39.4, 37.5, 33.4, 31.4, 26.2, 26.0 (3C), 20.1, 18.3, 14.2, −5.3 (2C) ppm; HRMS-ESI calcd for $[C_{27}H_{47}NaNO_4Si]^+$ ($M+Na^+$): 500.3167; found: 500.3166.

2-(2*S*,5*S*)-1-Benzyl-2-{4-[(*tert*-butyldimethylsilyl)oxy]butyl}-5-(methoxymethyl)pyrrolidin-2-yl-*N*-methoxy-*N*-methylacetamide (7)



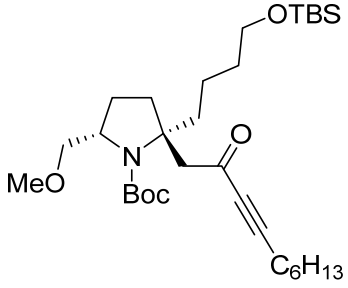
A solution of ester **8** (477.0 mg, 1.0 mmol, 1.0 equiv) and *N*,*O*-dimethylhydroxylamine hydrochloride (145.5 mg, 1.5 mmol, 1.5 equiv) in THF (10 mL) at –20 °C under argon, *i*-PrMgCl (2.0 M in THF, 1.5 mL, 3.0 mmol, 3.0 equiv) was added dropwise. After being stirred for 40 min at the same temperature, the reaction was quenched with a saturated aqueous NH_4Cl (10 mL) and warmed to room temperature, the mixture was extracted with EtOAc (3 ×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:2) to give Weinreb amide **7** (472.0 mg, yield: 96%) as a colorless oil. $[\alpha]_D^{25}$ –4.7 (*c* 0.25, $CHCl_3$); IR (film) ν_{max}: 2927, 2854, 1654, 1456, 1383, 1256, 1180, 1099, 839 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.35–7.30 (m, 2H), 7.29–7.25 (m, 2H), 7.22–7.18 (m, 1H), 3.99 (d, *J* = 14.2 Hz, 1H), 3.69 (s, 3H), 3.58 (dd, *J* = 6.6, 3.1 Hz, 2H), 3.55 (d, *J* = 14.2 Hz, 1H), 3.18 (s, 3H), 3.04 (s, 3H), 3.04–3.01 (m, 1H), 2.84 (dd, *J* = 9.1, 8.1 Hz, 1H), 2.75 (dd, *J* = 9.1, 4.0 Hz, 1H), 2.62 (d, *J* = 13.5 Hz, 1H), 2.52 (d, *J* = 13.5 Hz, 1H), 2.06–1.91 (m, 2H), 1.81–1.70 (m, 2H), 1.65–1.49 (m, 2H), 1.49–1.37 (m, 3H), 1.34–1.22 (m, 1H), 0.90 (s, 9H), 0.05 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 173.4, 142.1, 128.3 (2C), 127.9 (2C), 126.5, 76.7, 67.9, 63.4, 63.2, 61.0, 58.6, 52.3, 37.0, 34.5, 33.5, 32.0, 31.3, 26.4, 25.9 (3C), 20.0, 18.3, –5.3 (2C) ppm; HRMS-ESI calcd for $[C_{27}H_{49}N_2O_4Si]^+$ ($M+H^+$): 493.3456; found: 493.3447.

***tert*-Butyl (2*S*,5*S*)-2-{4-[(*tert*-butyldimethylsilyl)oxy]butyl}-2-{2-[methoxy(methyl)amino]-2-oxoethyl}-5-(methoxymethyl)pyrrolidine-1-carboxylate (6)**



To a solution of compound **7** (246.0 mg, 0.5 mmol, 1.0 equiv), Boc_2O (327.0 mg, 1.5 mmol, 3.0 equiv) in EtOH (20 mL) was added 20% $Pd(OH)_2/C$ (49.2 mg, 20% Pd on C). The mixture was stirred for 18 hours under H_2 atmosphere (1 atm, balloon) at room temperature. The mixture was filtered off, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:2) to give compound **6** (233.4 mg, yield: 93%) as a colorless oil. $[\alpha]_D^{25}$ –31.2 (*c* 0.5, $CHCl_3$); IR (film) ν_{max}: 2929, 2856, 1691, 1462, 1384, 1254, 1170, 1097, 840, 756 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.08–3.81 (m, 1H), 3.62 (s, 3H), 3.59–3.38 (m, 3H), 3.29 (s, 3H), 3.19–3.03 (m, 4H), 2.95–2.56 (m, 1H), 2.30–2.04 (m, 1H), 2.00–1.64 (m, 5H), 1.52–1.34 (m, 11H), 1.28–1.05 (m, 3H), 0.84 (s, 9H), –0.01 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 172.3 (171.8), 153.8 (153.2), 79.7 (78.8), 73.6 (72.4), 70.6 (70.5), 65.8 (65.3), 63.2 (63.1), 61.1 (61.0), 58.7 (58.6), 58.3 (57.9), 38.2 (37.5), 33.1 (32.9), 32.3 (32.0), 31.8 (31.7), 29.6 (29.5), 25.9 (3C), 24.6 (23.8), 20.3 (20.0), 19.3, 18.3 (18.2), 13.8, –5.4 (2C) ppm; HRMS-ESI calcd for $[C_{25}H_{50}N_2NaO_6Si]^+$ ($M+Na^+$): 525.3330; found: 525.3338.

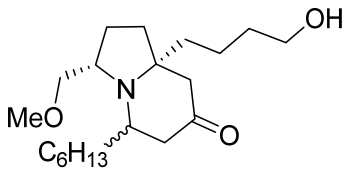
***tert*-Butyl (2*S*,5*S*)-2-{4-[(*tert*-butyldimethylsilyl)oxy]butyl}-5-(methoxymethyl)-2-(2-oxodec-3-yn-1-yl)pyrrolidine-1-carboxylate (5)**



n-BuLi (2.4 M in hexane, 250 μL, 0.6 mmol, 3.0 equiv) was added dropwise to a solution of 1-octyne (89 μL, 0.6 mmol, 3.0 equiv) in THF (3mL) at –78 °C under argon and stirred for 1 h. Then Weinreb amide **6** (100.4 mg, 0.2 mmol, 1.0 equiv) in THF (3

mL) was added dropwise at –78 °C. After being stirred for 30 min, the mixture was allowed to warm to 0 °C. The reaction was quenched with a saturated aqueous NH_4Cl (6 mL) and warmed to room temperature. The resulting mixture was extracted with EtOAc (3 ×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:10) to give compound **5** (103.3 mg, yield: 94%) as a colorless oil. $[\alpha]_D^{25}$ –47.2 (*c* 0.5, $CHCl_3$); IR (film) ν_{max}: 2926, 2856, 2210, 1693, 1663, 1460, 1384, 1256, 1180, 1096, 834, 776 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ4.04–3.85 (m, 1H), 3.61–3.35 (m, 3H), 3.28 (s, 3H), 3.22–3.03 (m, 2H), 2.96–2.60 (m, 1H), 2.36–2.22 (m, 2H), 2.05–1.65 (m, 5H), 1.57–1.37 (m, 13H), 1.37–1.05 (m, 9H), 0.84 (s, 12H), –0.01 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 186.9 (186.8), 153.5 (153.1), 95.2 (93.9), 82.2 (81.8), 79.8 (79.1), 73.6 (72.5), 66.0 (65.3), 63.0, 58.9 (58.7), 58.6 (58.2), 53.3, 51.0, 38.6 (37.7), 33.3 (33.0), 32.8 (32.1), 31.1, 28.5, 28.4, 27.6 (27.5) 25.9 (3 C), 24.7, 23.9, 22.3, 20.2 (19.9), 19.0, 18.2, 13.9, –5.4 (2 C) ppm; HRMS-ESI calcd for $[C_{31}H_{57}NNaO_5Si]^+$ (M+Na^+): 574.3898; found: 574.3900.

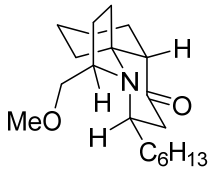
(3*S*,5*R*/*S*,8a*S*)-5-Hexyl-8a-(4-hydroxybutyl)-3-(methoxymethyl) hexahydroindolizin-7(1*H*)-one (18)



A round-bottom flask was charged with 30% Lindlar's catalyst (Aldrich, 5 % Pd on $CaCO_3$ poisoned with Pb, 33 mg) in toluene (10 mL)/1-hexene (1 mL) and purged with argon, the compound **5** (110.2 mg, 0.20 mmol, 1.0 equiv) was added. The flask was evacuated and refilled with H_2 four times, fitted with a H_2 balloon, and stirred at room temperature under H_2 for 12 h, and filtered. The filtrate was concentrated under reduced pressure to give crude product **17**. The crude product **17** was dissolved in CH_2Cl_2 (5.0 mL) at 0 °C, then TFA (0.3 mL) was added dropwise. The reaction mixture was stirred

for 1 h and was removed *in vacuo*. The mixture was then taken up in MeOH (5 mL), then K_2CO_3 (50.0 mg) was added. The reaction was stirred for 8 h at 60 °C. After being cooled to room temperature, H_2O (5 mL) was added, the resulting mixture was extracted with EtOAc (3 ×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:2) to give indolizidinone-ol **18** (56.2 mg, yield form **5**, 83%) as an inseparable mixture of two diastereomers (*dr* at C_2 = 1:1, the diastereomeric ratio was determined by integrating the peaks at 3.37 and 3.35 ppm of the ^{1}H NMR spectrum of the mixture). Colorless oil. IR (film) ν_{max}: 3395, 2959, 2933, 2859, 1786, 1739, 1684, 1200, 1178, 1127 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, data of the two diastereomers) δ 3.65–3.59 (m, 2H), 3.37 (s, 1.5H), 3.35 (s, 1.5H), 3.33–3.21 (m, 2H), 3.20–3.15 (m, 1H), 3.06–2.99 (m, 1H), 2.63–2.40 (m, 1H), 2.33–2.10 (m, 3H), 2.06–1.80 (m, 3H), 1.75–1.44 (m, 5H), 1.41–1.15 (m, 13H), 0.97–0.81 (m, 3H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, data of the two diastereomers) δ 211.8, 211.4, 77.8, 77.6, 68.7, 67.4, 64.6 (2C), 62.7,62.6, 59.7, 59.0, 55.4, 55.3, 49.1, 47.6, 42.4, 42.0, 37.8 (2C), 36.8, 36.6, 35.1, 34.6, 33.0 (2C), 31.8, 30.1, 29.6, 29.2, 27.0 (2C), 26.4, 26.2, 25.6, 22.6, 22.6, 20.8, 20.0, 14.1, 14.0 ppm; HRMS-ESI calcd for $[C_{20}H_{37}NNaO_3]^+$ (M+Na$^+$): 362.2666; found: 362.2662.

(+)-Cylindricine D (**1d**)

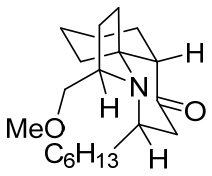


To a cooled solution (0 °C) of indolizidinone-ol **18** (40.0 mg, 0.12 mmol, 1.0 equiv) and Et_3N (77 μL, 0.54 mmol, 4.5 equiv) in CH_2Cl_2 (5 mL) was added MsCl (27 μL, 0.36 mmol, 3.0 equiv). After being stirred at room temperature for 2 h, the reaction was quenched with a saturated aqueous $NaHCO_3$ (5 mL). The mixture was extracted with CH_2Cl_2 (3 ×10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude

mesylate (48 mg) as a colorless oil, which was used in the next step without further purification. To a cooled solution (0 °C) of the above mentioned crude mesylate (48 mg) in THF (5 mL) was added *t*-BuOK (16 mg, 0.14 mmol, 1.2 equiv). After being stirred for 10 min, the reaction mixture was warmed to room temperature and stirred until the completion of the reaction (monitored by TLC). The reaction was quenched with a saturated aqueous NH_4Cl (5 mL). The resulting mixture was extracted with EtOAc (4 ×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:20) to give (+)-cylindricine D (**1d,** 15.4 mg, yield: 40%) and (+)-2-*epi*-cylindricine D (2-*epi*-**1d**, 15.4 mg, yield: 40%).

(+)-Cylindricine D (**1d**): colorless oil. $[\alpha]_D^{25}$ +22.4 (*c* 0.2, $CHCl_3$), lit.[2] $[\alpha]_D^{23}$ +21.3 (*c* 0.1, $CHCl_3$), lit.[3] $[\alpha]_D^{25}$ +21.5 (*c* 0.08, CH_2Cl_2); IR (film) ν_{max}: 2925, 2854, 1711, 1647, 1456, 1379, 1260, 1116, 1021, 775 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 3.47–3.38 (m, 2H), 3.37 (s, 3H), 3.26–3.17 (m, 1H), 3.06 (dd, *J* = 9.0, 9.0 Hz, 1H), 2.32–2.15 (m, 3H), 2.13–2.00 (m, 2H), 1.91–1.82 (m, 1H), 1.76–1.59 (m, 5H), 1.50–1.39 (m, 2H), 1.38–1.17 (m, 12H), 0.89 (t, *J* = 6.7 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 211.3, 78.2, 70.0, 59.1, 55.5, 55.4, 50.9, 42.9, 35.9, 35.2, 34.9, 31.8, 29.3, 27.1, 26.7, 24.4, 22.9, 22.6, 21.9, 14.1 ppm; HRMS-ESI calcd for $[C_{20}H_{36}NO_2]^+$ ($M+H^+$): 322.2741; found: 322.2745.

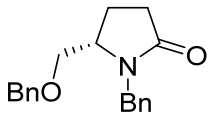
(+)-2-*epi*-Cylindricine D (2-*epi*-**1d**)



(+)-2-*epi*-Cylindricine D (2-*epi*-**1d**): colorless oil. $[\alpha]_D^{25}$ +7.4 (*c* 0.1, $CHCl_3$); IR (film) ν_{max}: 2961, 2921, 2855, 1747, 1661, 1489, 1385, 1261, 1192, 1020, 797 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 3.36 (s, 3H), 3.36–3.31 (m, 2H), 3.28–3.21 (m, 1H), 3.16 (t, *J* = 8.8 Hz, 1H), 2.60 (dd, *J* = 15.3, 5.4 Hz, 1H), 2.46 (s, 1H), 2.29–2.21 (m, 2H), 2.15 (dd, *J* = 15.3, 6.4 Hz, 1H), 2.08–1.97 (m, 2H), 1.83–1.71 (m, 4H), 1.50–1.43 (m, 2H), 1.35–

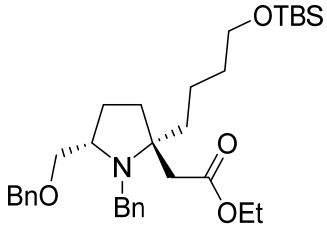
1.28 (m, 12H), 0.88 (t, J = 6.9 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ212.4, 77.9, 68.2, 63.9, 59.0, 58.8, 50.9, 43.1, 40.4, 37.0, 36.4, 31.9, 29.3, 26.2, 26.2, 24.4, 23.1, 22.6, 21.7, 14.1 ppm; HRMS-ESI calcd for $[C_{20}H_{35}NNaO_2]^+$ ($M+Na^+$): 344.2560; found: 344.2566.

(*S*)-1-Benzyl-5-(benzyloxymethyl)pyrrolidin-2-one (12)



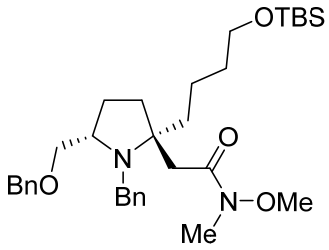
To a cooled suspension (0 °C) of NaH (2.40 g, 60% dispersion in mineral oil, 60.0 mmol, 1.5 equiv) in THF (100 mL) was added dropwise a solution of (*S*)-*N*-benzyl-pyroglutaminol [(*S*)-**11**, 8.20 g, 40.0 mmol] in THF (100 mL). After being stirred for 30 min, BnBr (10.26 g, 60.0 mmol) was added dropwise, then the mixture was warmed to room temperature gradually. The mixture was stirred for 2 h before being quenched with a saturated aqueous solution of NH_4Cl (10 mL) and extracted with EtOAc (10 mL x 3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:2) to give benzyl ether (*S*)-**12** (11.12 g, yield: 94%) as a colorless oil. $[\alpha]_D^{25}$ +14.5 (*c* 1.0, MeOH), lit.[1] $[\alpha]_D$ +14.8 (*c* 0.33, MeOH); IR (film) ν_{max}: 2922, 2853, 1685, 1454, 1375, 1260, 1101, 806, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.37–7.31 (m, 2H), 7.30–7.23 (m, 5H), 7.23–7.17 (m, 3H), 4.89 (d, J = 15.0 Hz, 1H), 4.40 (d, J = 12.0 Hz, 1H), 4.37 (d, J = 12.0 Hz, 1H), 4.09 (d, J = 15.0 Hz, 1H), 3.60 (dd, J = 8.4, 4.2 Hz, 1H), 3.45 (dd, J = 9.9, 3.8 Hz, 1H), 3.38 (dd, J = 9.9, 4.5 Hz, 1H), 2.54 (ddd, J = 17.1, 9.5, 7.5 Hz, 1H), 2.35 (ddd, J = 17.1, 10.1, 5.1 Hz, 1H), 2.11–1.97 (m, 1H), 1.91–1.80 (m, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 175.3, 137.6, 136.9, 128.3 (2C), 128.2 (2C), 127.8 (2C), 127.6, 127.4 (2C), 127.1, 73.0, 70.6, 56.8, 44.6, 30.1, 21.6 ppm; HRMS (ESI) calcd for $[C_{19}H_{21}NNaO_2]^+$ ($M+Na^+$): 318.1465; found: 318.1472.

Ethyl 2-(2*S*,5*S*)-1-benzyl-5-(benzyloxy)methyl-2-{4-[(*tert*-butyldimethylsilyl) oxy]butyl}pyrrolidin-2-yl acetate (13)



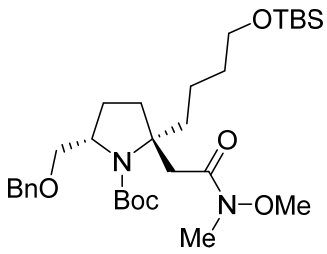
Tf_2O (Trifluoromethylsulfonic anhydride, 37 μL, 0.22 mmol, 1.1 equiv) was added dropwise to a cooled solution (−78 °C) of lactam (*S*)-**12** (59.0 mg, 0.2 mmol, 1.0 equiv) and TTBP (2,4,6-tri-*tert*-butylpyrimidine, 59.2 mg, 0.24 mmol, 1.2 equiv) in CH_2Cl_2 (15 mL) and stirred at −78 °C for 45 min. A solution of Grignard reagent **10** (0.67 mL, 0.2 mmol, 1.0 equiv, 0.30 M) in THF was added dropwise to the resultant mixture, the mixture was stirred at −78 °C for 1 h. Then enolate (0.30 mmol, 1.5 equiv) was added dropwise. After being stirred for 3 h, the reaction was quenched with a saturated aqueous NH_4Cl (10 mL), the mixture was extracted with CH_2Cl_2 (3 ×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane= 1:20) to give pyrrolidine **13** (88.4 mg, yield: 80%, dr ≥ 20: 1) as a colorless oil. $[\alpha]_D^{25}$ −3.2 (*c* 1.0, $CHCl_3$); IR (film) ν_{max}:2923, 2852, 1730, 1661, 1564, 1453, 1029, 803 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.27–7.09 (m, 10H), 4.15 (s, 2H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.89 (d, *J* = 14.1 Hz, 1H), 3.53 (t, *J* = 6.5 Hz, 2H), 3.48 (d, *J* = 14.1 Hz, 1H), 3.07–2.98 (m, 1H), 2.83 (dd, *J* = 9.2, 7.9 Hz, 1H), 2.83 (dd, *J* = 9.2, 4.1 Hz, 1H), 2.45 (d, *J* = 12.9 Hz, 1H), 2.35 (d, *J* = 12.9 Hz, 1H), 2.02–1.92 (m, 1H), 1.89–1.81 (m, 1H), 1.78–1.70 (m, 1H), 1.68–1.60 (m, 2H), 1.54–1.44 (m, 1H), 1.43–1.34 (m, 3H), 1.33–1.29 (m, 1H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.85 (s, 9H), 0.00 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 172.7, 141.8, 138.6, 128.4 (2C), 128.2 (2C), 128.0 (2C), 127.4 (2C), 127.3, 126.6, 74.2, 72.9, 67.3, 63.3, 63.2, 60.2, 52.3, 39.5, 37.4, 33.4, 31.4, 26.3, 26.0 (3C), 20.1, 18.3, 14.2, −5.3 (2C) ppm; HRMS-ESI calcd for $[C_{33}H_{51}NNaO_4Si]^+$ ($M+H^+$): 576.3480; found: 576.3488.

2-(2*S*,5*S*)-1-Benzyl-5-(benzyloxy)methyl-2-{4-[(*tert*-butyldimethylsilyl)oxy] butyl}pyrrolidin-2-yl-*N*-methoxy-*N*-methylacetamide (14)



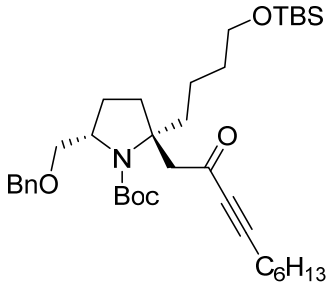
A solution of ester **13** (1.11 g, 2.0 mmol, 1.0 equiv) and *N*,*O*-dimethylhydroxylamine hydrochloride (291 mg, 3.0 mmol, 1.5 equiv) in THF (20 mL) at –20 °C under argon, *i*-PrMgCl (2 M in THF, 3.0 mL, 6.0 mmol, 3.0 equiv) was added dropwise. After being stirred for 40 min at the same temperature, the reaction was quenched with a saturated aqueous NH_4Cl (10 mL) and warmed to room temperature, the mixture was extracted with EtOAc (3 ×10 mL).The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:2) to give Weinreb amide **14** (1.09 g, yield: 96%) as a colorless oil. $[\alpha]_D^{25}$ –0.7 (*c* 1.0, $CHCl_3$); IR (film) ν_{max}: 2926, 2854, 1662, 1453, 1377, 1254, 1100, 1028, 837, 777, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.45–7.04 (m, 10H), 4.15 (s, 2H), 3.94 (d, J = 14.1 Hz, 1H), 3.64 (s, 3H), 3.56–3.49 (m, 3H), 3.13 (s, 3H), 3.09–3.01 (m, 1H), 2.89 (t, J = 8.4 Hz, 1H), 2.85 (dd, J = 9.1, 4.2 Hz, 1H), 2.58 (d, J = 13.5 Hz, 1H), 2.48 (d, J = 13.5 Hz, 1H), 2.07–1.95 (m, 1H), 1.95–1.89 (m, 1H), 1.79–1.68 (m, 2H), 1.66–1.59 (m, 1H), 1.54–1.47 (m, 1H), 1.44–1.35 (m, 3H), 1.30–1.22 (m, 1H), 0.85 (s, 9H), 0.00 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 142.1, 138.6, 128.4 (2C), 128.1 (2C), 128.0 (2C), 127.4 (2C), 127.2, 126.5, 74.4, 72.9, 67.9, 63.4, 63.3, 61.0, 52.4, 37.0, 34.7, 33.5, 32.1, 31.3, 26.5, 26.0 (3C), 20.0, 18.3, –5.2 (2C) ppm; HRMS-ESI calcd for $[C_{33}H_{53}N_2O_4Si]^+$ ($M+H^+$): 569.3769; found: 569.3769.

***tert*-Butyl (2*S*,5*S*)-5-(benzyloxy)methyl-2-{4-[(*tert*-butyldimethylsilyl)oxy]butyl}-2-{2-[methoxy(methyl)amino]-2-oxoethyl}pyrrolidine-1-carboxylate (15)**



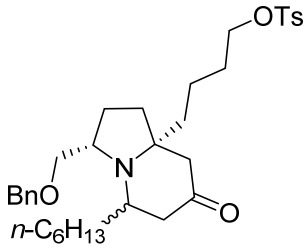
To a solution of compound **14** (113.6 mg, 0.2 mmol, 1.0 equiv), Boc_2O (65.4 mg, 0.3 mmol, 3.0 equiv) in EtOH (5 mL) was added 20% $Pd(OH)_2/C$ (22.7 mg, 20% Pd on C). The mixture was stirred for 18 hours under H_2 atmosphere (1 atm, balloon) at room temperature. The mixture was filtered off, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane= 1:2) to give compound **15** (109.8 mg, yield: 95%) as a colorless oil. $[\alpha]_D^{25}$ –5.8 (*c* 1.0, $CHCl_3$); IR (film) ν_{max}: 2928, 2856, 1691, 1454, 1380, 1254, 1174, 1101, 836, 775, 698 cm^{-1}, ^1H NMR (600 MHz, $CDCl_3$) δ 7.37–7.25 (m, 5H), 4.63–4.44 (m, 2H), 4.18–3.94 (m, 1H), 3.74–3.69 (m, 1H), 3.68 (s, 3H), 3.64–3.41 (m, 3H), 3.36–3.22 (m, 1H), 3.20–3.15 (m, 3H), 3.05–2.63 (m, 2H), 2.48–2.14 (m, 1H), 2.04–1.76 (m, 5H), 1.50 (s, 3H), 1.41 (s, 9H), 0.90 (s, 9H), 0.04 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 172.4 (171.9), 153.9 (153.2), 138.6 (138.4), 128.3, 128.2, 127.5 (127.5), 127.4, 127.3, 79.7 (78.9), 73.0, 71.3, 70.5, 65.9 (65.5), 63.2 (63.2), 61.0, 58.5 (58.2), 38.2 (37.6), 37.1 (36.9), 33.2 (33.0), 32.4 (32.2), 31.9 (31.8), 28.6 (28.4), 25.9 (3C), 24.8, 24.0, 20.4 (20.0), 18.3 (18.3), –5.3 (2C) ppm; HRMS-ESI calcd for $[C_{31}H_{54}N_2NaO_6Si]^+$ ($M+Na^+$): 601.3643; found: 601.3651.

tert-Butyl (2*S*,5*S*)-5-(benzyloxy)methyl-2-{4-[(_tert_-butyldimethylsilyl)oxy]butyl}-2-(2-oxodec-3-yn-1-yl)pyrrolidine-1-carboxylate (16)



n-BuLi (2.4 M in hexane, 250 μL, 0.6 mmol, 3.0 equiv) was added dropwise to a solution of 1-octyne (89 μL, 0.6 mmol, 3.0 equiv) in THF (3mL) at –78 °C under argon and stirred for 1 h. Then Weinreb amide **15** (115.6 mg, 0.2 mmol, 1.0 equiv) in THF (3 mL) was added dropwise at –78 °C. After being stirred for 30 min, the mixture was allowed to warm to 0 °C, the reaction was quenched with a saturated aqueous NH_4Cl (6 mL) and warmed to room temperature. The resulting mixture was extracted with EtOAc (3 ×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane= 1:10) to give compound **16** (110.3 mg, yield: 88%) as a colorless oil. $[\alpha]_D^{25}$ –10.1 (*c* 1.0, $CHCl_3$); IR (film) ν_{max}: 2928, 2856, 2211, 1693, 1455, 1383, 1255, 1172, 1100, 835, 775 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40–7.15 (m, 5H), 4.58–4.37 (m, 2H), 4.19–3.84 (m, 1H), 3.69–3.48 (m, 3H), 3.34–3.20 (m, 1H), 3.20–3.07 (m, 1H), 2.96–2.63 (m, 1H), 2.38–2.25 (m, 2H), 2.09–1.72 (m, 6H), 1.60–1.30 (m, 16H), 1.30–1.16 (m, 5H), 0.85 (s, 12H), 0.00 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 186.9 (186.8), 153.5 (153.1), 138.5 (138.3), 128.3, 128.2, 127.5, 127.4, 127.3, 95.2 (93.9), 82.2 (81.9), 79.8 (79.1), 73.0, 71.2 (70.6), 66.1 (65.5), 63.0, 59.1 (58.5), 53.3, 50.9, 38.8 (37.9), 33.5 (33.0), 32.9 (32.3), 31.1, 28.5, 28.5 (28.4), 27.6 (27.5), 25.9 (3C), 24.9, 24.1, 22.3, 20.3, 19.9 (19.0), 18.2, 13.9, –5.4 (2C) ppm; HRMS-ESI calcd for $[C_{37}H_{61}NaNO_5Si]^+$ ($M+Na^+$): 650.4211; found: 650.4227.

4-(3*S*,5*R*/*S*,8a*S*)-3-[(Benzyloxy)methyl-5-hexyl-7-oxohexahydroindolizin-8a(1*H*)-yl]butyl 4-methylbenzenesulfonate (21)

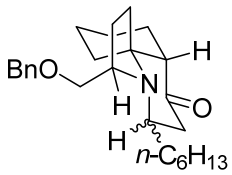


A round-bottom flask was charged with 30% Lindlar's catalyst (Aldrich, 5 % Pd on $CaCO_3$ poisoned with Pb, 30 mg) in toluene (10 mL)/1-hexene (1 mL) and purged with

argon, the compound **16** (100 mg, 0.16 mmol, 1.0 equiv) was added. The flask was evacuated and refilled with H_2 four times, fitted with a H_2 balloon, and stirred at room temperature under H_2 for 12 h, and filtered. The filtrate was concentrated under reduced pressure to give crude product **19**. The crude product **19** was dissolved in CH_2Cl_2 (5.0 mL) at 0 °C, then TFA (0.3 mL) was added dropwise, the reaction mixture was stirred for 1 h and was removed *in vacuo*. The mixture was then taken up in MeOH (5 mL), then K_2CO_3 (50.0 mg) was added. The reaction was stirred for 8 h at 60 °C. After being cooled to room temperature, H_2O (5 mL) was added, the resulting mixture was extracted with EtOAc (3 ×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give indolizidinone **20**, which was used in the next step without further purification. The indolizidinone **20** and Et_3N (33 μL, 0.24 mmol, 1.5 equiv) in DCM (5 mL) at room temperature. then the solution was added dropwise *p*-TsCl (45.6 mg, 0.24 mmol, 1.5 equiv). After being stirred for 2 h at this temperature, the reaction was quenched with a saturated aqueous NH_4Cl (5 mL). The resulting mixture was extracted with EtOAc (3 ×5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:5) to give **21** (70.1 mg, yield: 77% from **16**, two steps) as an inseparable mixture of two diastereomers (*dr* at C_2 = 1.1:1, the diastereomeric ratio was determined by integrating the peaks at 3.27 and 3.08 ppm of the ^{1}H NMR spectrum of the mixture). Colorless oil. IR (film) ν_{max}: 2921, 2851, 1689, 1384, 1256, 1098, 1029, 776 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$ data of the two diastereomers) δ 7.77 (d, J = 8.2 Hz, 2H), 7.41–7.25 (m, 7H), 4.59–4.45 (m, 2H), 4.04–3.94 (m, 2H), 3.46–3.28 (m, 2H), 3.27 (t, J = 8.5 Hz, 0.51H), 3.23–3.17 (m, 1H), 3.08 (t, J = 9.1 Hz, 0.57H), 2.5–2.35 (m, 1H), 2.44 (s, 3H), 2.27–2.02 (m, 4H), 2.00–1.78 (m, 3H), 1.76–1.36 (m, 9H), 1.35–1.24 (m, 7H), 0.92–0.82 (m, 3H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 211.3, 211.0, 144.6 (2C), 138.4 (2C), 133.2 (2C), 129.8 (4C), 128.4 (2C), 128.3 (2C), 127.8 (4C), 127.6 (2C), 127.6 (4C), 75.0 (2C), 73.3, 73.1, 70.3 (2C), 68.5 (2C), 67.2 (2C), 64.9 (2C), 59.6 (2C), 55.6, 55.4, 49.1 (2C), 42.2, 42.0, 37.3, 36.8, 35.0, 34.6, 31.8, 31.7, 29.2,

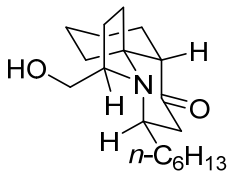
29.2, 26.9 (2C), 26.4, 26.3, 22.6 (2C), 21.6 (2C), 20.6, 19.8, 14.0, 14.0 ppm; HRMS-ESI calcd for $[C_{33}H_{47}NNaO_5S]^+$ ($M+Na^+$): 592.3067; found: 592.3079.

(3*S*,7a*S*,11a*S*)-3-(Benzyloxy)methyl-5-hexyloctahydro-1*H*-pyrrolo[2,1-*j*]quinolin-7(7a*H*)-one (22)



To a cooled solution (–78 °C) of compound **21** (123.3 mg, 0.25 mmol, 1.0 equiv) in THF (5 mL) was added KHMDS (0.38 mL, 1 M in THF, 0.38 mmol, 1.5 equiv). After being stirred for 10 min the mixture was warmed to room temperature and stirred until no start material remained (by TLC), the reaction was quenched with a saturated aqueous NH_4Cl (3 mL) and warmed to room temperature, the mixture was extracted with DCM (4 ×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:10) to give **22** (93.2 mg, yield: 94%) as a colorless oil. IR (film) ν_{max}: 2918, 2850, 1689, 1384, 1256, 1098, 1028, 772, 608 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38–7.27 (m, 5H), 4.60–4.46 (m, 2H), 3.50–3.41 (m, 1.5H), 3.32–3.15 (m, 2H), 3.14–3.08 (m, 0.5H), 2.63–2.43 (m, 1H), 2.31–2.01 (m, 5H), 1.96–1.77 (m, 1H), 1.70–1.53 (m, 5H), 1.50–1.40 (m, 2H), 1.39–1.22 (m, 11H), 0.94–0.87 (m, 3H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ212.3, 211.2, 138.5, 138.5, 128.4 (2C), 128.3 (2C), 127.6, 127.6, 127.6 (2C), 127.5 (2C), 75.4, 75.4, 73.3, 73.2, 69.9, 68.1, 64.1 (2C), 58.8 (2C), 55.7, 55.4, 51.0, 50.9, 43.1, 43.0, 40.5 (2C), 37.0, 36.4, 35.9, 35.1, 31.8, 31.7, 29.3, 29.2, 27.1, 26.8, 26.3, 26.1, 24.4 (2C), 22.6, 22.6, 21.9, 21.7, 14.1, 14.0ppm; HRMS-ESI calcd for $[C_{26}H_{40}NO_2]^+$ ($M+H^+$): 398.3054; found: 398.3059.

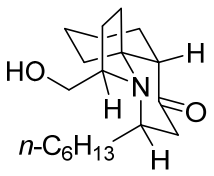
(+)-Cylindricine C (1c)



A suspension of compound **22** (21.8 mg, 0.055 mmol, 1.0 equiv) and 30% Pd/C (6.6 mg, Aldrich, 10% Pd on C) in MeOH/H_2O/AcOH (3/0.3/0.05 mL) was stirred under a hydrogen atmosphere (1 atm, balloon) at room temperature for 24 h. After the mixture was filtered off, the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:2) to give (+)-cylindricine C (**1c**, 6.9 mg, yield: 41%) and (+)-2-*epi*-cylindricine C (2-*epi*-**1c**, 6.9 mg, yield: 41%).

(+)-Cylindricine C (**1c**): colorless oil. $[\alpha]_D^{25}$ +56.9 (*c* 0.25, $CHCl_3$), lit.[2] $[\alpha]_D^{22}$ +60.2 (*c* 0.5, $CHCl_3$), lit.[3] $[\alpha]_D^{25}$ +60.82 (*c* 0.4, CH_2Cl_2), lit.[4] $[\alpha]_D^{23}$ +59.8 (*c* 1.72, $CHCl_3$); IR (film) ν_{max}: 3458, 2928, 1626, 1384, 1255, 1098, 798, 655 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 3.64–3.49 (m, 2H), 3.42 (d, J = 10.2 Hz, 1H), 3.30–3.22 (m, 1H), 3.00 (br, 1H), 2.32–2.26 (m, 2H), 2.24–2.16 (m, 3H), 2.10 (dd, J = 12.4, 7.8 Hz, 1H), 1.84–1.76 (m, 1H), 1.70–1.60 (m, 4H), 1.51–1.44 (m, 1H), 1.40–1.30 (m, 4H), 1.30–1.18 (m, 9H), 0.86 (t, J = 6.9 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 210.5, 70.7, 66.3, 56.6, 55.4, 50.2, 42.4, 36.4, 35.8, 35.1, 31.7, 29.2, 28.6, 27.1, 24.2, 22.7, 22.5, 21.8, 14.0 ppm; HRMS-ESI calcd for $[C_{19}H_{34}NO_2]^+$ ($M+H^+$): 308.2584; found: 308.2588.

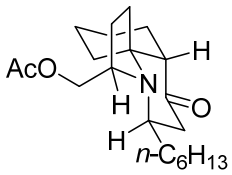
(+)-2-*epi*-Cylindricine C (2-*epi*-**1c)**



(+)-2-*epi*-Cylindricine C (2-*epi*-**1c**): colorless oil. $[\alpha]_D^{25}$ +46.2 (*c* 1.0, $CHCl_3$), lit.[5] $[\alpha]_D^{25}$ –39 (*c* 0.5, CH_2Cl_2), lit.[6] $[\alpha]_D^{25}$ –12.4 (*c* 0.15, $CHCl_3$); IR (film) ν_{max}: 3459, 2921, 2850, 1662, 1385, 1260, 1106, 1028, 773 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 3.60–3.52 (m, 1H), 3.42–3.36 (m, 1H), 3.34–3.30 (m, 1H), 3.26–3.19 (m, 1H), 2.66 (dd, J =

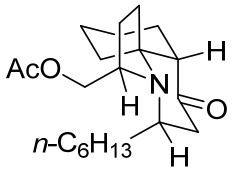
15.5, 5.5 Hz, 1H), 2.53 (brs, 1H), 2.26 (d, J = 12.2 Hz, 1H), 2.21–2.14 (m, 1H), 2.09–1.99 (m, 2H), 1.87–1.76 (m, 2H), 1.72–1.64 (m, 1H), 1.62–1.50 (m, 3H), 1.48–1.44 (m, 1H), 1.43–1.34 (m, 3H), 1.33–1.22 (m, 10H), 0.87 (t, J = 6.9 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 211.4, 68.8, 64.7, 60.6, 54.2, 50.8, 42.7, 39.3, 36.9, 36.6, 31.7, 29.2, 26.6, 26.1, 24.2, 22.8, 22.5, 21.4, 14.0 ppm; HRMS-ESI calcd for $[C_{19}H_{34}NO_2]^+$ ($M+H^+$): 308.2584; found: 308.2588

(+)-Cylindricine E (1e)



To a cooled solution (0 °C) of (+)-cylindricine C (**1c**, 10.0 mg, 0.033 mmol) in DCM (1.0 mL) was added Et_3N (4 μL, 0.033 mmol, 1.0 equiv), DMAP (3.7 mg, 0.033 mmol, 1.0 equiv) and acetic anhydride (7 μL, 0.066 mmol, 2.0 equiv). The solution was then warmed to room temperature and stirred for 1 h. The reaction was quenched with a saturated aqueous NH_4Cl (3 mL) and extracted with DCM (3 ×5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:5) to give (+)-cylindricine E (**1e**, 11.1 mg, yield: 97%) as a colorless oil. $[\alpha]_D^{25}$ +27.5 (*c* 0.25, $CHCl_3$), lit.[2] $[\alpha]_D^{22}$ +28.3 (*c* 0.15, $CHCl_3$), lit.[3] $[\alpha]_D^{25}$ 28.67 (*c* 0.13, CH_2Cl_2); IR (film) ν_{max}: 2925, 2855, 1743, 1631, 1456, 1383, 1226, 1142, 1031, 775 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.11 (dd, J = 10.8, 3.1 Hz, 1H), 3.71–3.63 (m, 1H), 3.53–3.45 (m, 1H), 3.25–3.17 (m, 1H), 2.24–2.18 (m, 3H), 2.06 (s, 3H), 1.85–1.26 (m, 22H), 0.87 (t, J = 6.6 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 211.0, 171.0, 70.0, 68.6, 55.2, 54.5, 51.0, 42.9, 36.0, 34.9 (2C), 31.7, 29.2, 27.1, 26.4, 24.4, 22.9, 22.5, 21.9, 21.0, 14.0 ppm; HRMS-ESI calcd for $[C_{21}H_{36}NO_3]^+$ ($M+H^+$): 350.2690; found: 350.2690.

(+)-2-*epi*-Cylindricine E (2-*epi*-**1e)**



To a cooled solution (0 °C) of (+)-2-*epi*-cylindricine C (2-*epi*-**1c**, 30.7 mg, 0.10 mmol) in DCM (2.0 mL) was added Et_3N (14 μL, 0.10 mmol, 1.0 equiv), DMAP (11.2 mg, 0.10 mmol, 1.0 equiv) and acetic anhydride (20 μL, 0.20 mmol). The solution was then warmed to room temperature and stirred for 1 h. The reaction was quenched with a saturated aqueous NH_4Cl (3 mL) and extracted with DCM (3 ×5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:5) to give (+)-2-*epi*-cylindricine E (2-*epi*-**1e**, 33.1 mg, yield: 95%) as a colorless oil. $[\alpha]_D^{25}$ +29.1 (*c* 1.0, $CHCl_3$), IR (film) ν_{max}: 2925, 2855, 1744, 1646, 1453, 1383, 1228, 1181, 1031, 800 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.97 (dd, J = 10.8, 4.6 Hz, 1H), 3.78–3.71 (m, 1H), 3.28–3.20 (m, 1H), 3.19–3.13 (m, 1H), 2.51 (dd, J = 15.5, 5.2 Hz, 1H), 2.38 (s, 1H), 2.22–2.17 (m, 1H), 2.11 (dd, J = 15.5, 6.9 Hz, 1H), 2.00 (s, 3H), 1.79–1.71 (m, 1H), 1.65–1.59 (m, 1H), 1.57–1.48 (m, 2H), 1.45–1.37 (m, 3H), 1.32–1.15 (m, 14H), 0.81 (t, J = 6.8 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 212.1, 171.0, 68.2, 68.0, 63.0, 58.7, 51.0, 43.1, 40.5, 36.9, 36.3, 31.8, 29.3, 26.1, 26.0, 24.4, 23.2, 22.6, 21.6, 21.0, 14.0 ppm; HRMS-ESI calcd for $[C_{21}H_{36}NO_3]^+$ ($M+H^+$): 350.2690; found: 350.2688.

3. Comparison of ^{1}H and ^{13}C NMR Data of our Synthetic Products with Those Reported

3.1. (+)-Cylindricine C

^{1}H NMR ($CDCl_3$)		^{13}C NMR ($CDCl_3$)	
This work (600 MHz)	Janakiram's work[2] (600 MHz)	This work (151 MHz)	Janakiram's Work[2] (201 MHz)
3.64–3.49 (m, 2H)	3.52 (q, *J* = 8.4, 6.0 Hz, 2H)	14.0	14.05
3.42 (d, *J* = 10.2 Hz, 1H)	3.41 (d, *J* = 9.8 Hz, 1H)	21.8	21.87
3.30–3.22 (m, 1H)	3.30–3.22 (m, 1H)	22.5	22.58
3.00 (s, 1H)	2.89 (s, 1H)	22.7	22.74
2.32–2.26 (m, 2H)	2.32–2.26 (m, 2H)	24.2	24.28
2.24–2.16 (m, 3H)	2.24–2.16 (m, 3H)	27.1	27.12
2.10 (dd, *J* = 12.4, 7.8 Hz, 1H)	2.10 (dd, *J* = 12.4, 7.9 Hz, 1H)	28.6	28.71
1.84–1.76 (m, 1H)	1.81 (dd, *J* = 13.3, 8.3 Hz, 1H)	29.2	29.30
1.70–1.60 (m, 4H)	1.70–1.59 (m, 4H)	31.7	31.71
1.51–1.44 (m, 1H)	1.47 (dd, *J* = 12.7, 7.8 Hz, 1H)	35.1	35.21
1.40–1.30 (m, 4H)	1.34 (td, *J* = 12.3, 11.1, 6.6 Hz, 4H)	35.8	35.91
1.30–1.18 (m, 9H)	1.30–1.21 (m, 7H)	36.4	36.42
0.86 (t, *J* = 6.9 Hz, 3H)	0.86 (t, *J* = 7.0 Hz, 3H).	42.4	42.53
		50.2	50.26
		55.4	55.44
		56.6	56.54
		66.3	66.39
		70.7	70.70
		210.5	210.56

3.2. (+)-2-*epi*-Cylindricine C

^{1}H NMR ($CDCl_3$)		^{13}C NMR ($CDCl_3$)		
This work (600 MHz)	Shibasaki's work[7] (500 MHz)	This work (126 MHz)	Ciufolini's work[5] (75 MHz)	Hsung's work[6] (75 MHz)
3.60–3.52 (m, 1H)	3.56 (dd, *J* = 10.5, 4.1 Hz, 1H)	14.0	14.1	13.9
3.42–3.36 (m, 1H)	3.34 (dd, *J* = 10.7, 2.8 Hz, 1H)	21.4	-	21.3
3.34–3.30 (m, 1H)	3.31 (m, 1H)	22.5	22.6	22.4
3.26–3.19 (m, 1H)	3.22 (m, 1H)	22.8	22.6	22.7
2.66 (dd, *J* = 15.5, 5.5 Hz, 1H)	2.80 (m, 1H)	24.2	24.3	24.1
2.53 (s, 1H)	2.66 (dd, *J* = 15.4, 5.6 Hz, 1H)	26.1	26.2	26.1
2.26 (d, *J* = 12.2 Hz, 1H)	2.52 (m, 1H)	26.6	26.6	26.5
2.21–2.14 (m, 1H)	2.26 (m, 1H)	29.2	29.2	29.1
2.09–1.99 (m, 2H)	2.16 (dd, *J* = 15.6, 6.1 Hz, 1H),	-	29.7	29.5
1.87–1.76 (m, 2H)	2.07–2.02 (m, 2H)	31.7	31.7	31.6
1.72–1.64 (m, 1H)	1.83–1.25 (m, 19H)	36.6	36.7	36.5,
1.62–1.50 (m, 3H)		36.9	36.9	36.8
1.48–1.44 (m, 1H)		39.3	39.4	39.1
1.43–1.34 (m, 3H)		42.7	42.7	42.6,
1.33–1.22 (m, 10H)		50.8	50.9	50.7
0.87 (t, *J* = 6.9 Hz, 3H)	0.87 (t, *J* = 6.9 Hz, 3H)	57.9	57.9	57.8
		63.6	63.7	63.5
		64.7	64.6	64.6
		68.8	68.9	-
		211.4	211.5	211.4

3.3. (+)-Cylindricine D

^{1}H NMR ($CDCl_3$)		^{13}C NMR ($CDCl_3$)	
This work (600 MHz)	Hsung's work[4] (500 MHz)	This work (151 MHz)	Hsung's work[4] (75 MHz)
3.47–3.38 (m, 2H)	3.42 (m, 1H)	14.1	14.1
	3.38 (m, 1H)	21.9	21.9
3.37 (s, 3H)	3.37 (s, 3H)	22.6	22.6
3.26–3.17 (m, 1H)	3.21 (m, 1H)	22.9	23.0
3.06 (dd, J = 9.0, 9.0 Hz, 1H)	3.05 (dd, J = 9.0, 9.0 Hz, 1H)	24.4	24.5
2.32–2.15 (m, 3H)	2.28–2.17 (m, 3H)	26.7	26.7
2.13–2.00 (m, 2H)	2.12–2.02 (m, 2H)	27.1	27.1
1.91–1.82 (m, 1H)	1.86 (m, 1H)	29.3	29.3
1.76–1.59 (m, 5H)	1.74–1.56 (m, 5H)	31.8	31.8
1.50–1.39 (m, 2H)	1.49–1.39 (m, 2H)	34.9	35.0
1.38–1.27 (m, 12H)	1.36–1.25 (m, 12H)	35.2	35.2
0.89 (t, J = 6.9 Hz, 3H)	0.89 (t, J = 7.0 Hz, 3H)	35.9	35.9
		42.9	42.9
		50.9	50.9
		55.4	55.5
		55.5	55.5
		59.1	59.1
		70.0	70.1
		78.2	78.2
		211.3	211.3

3.4. (+)-Cylindricine E

^{1}H NMR ($CDCl_3$)		^{13}C NMR ($CDCl_3$)	
This work (500 MHz)	Snider's work[8] (300 MHz)	This work (126 MHz)	Snider's work[8] (75 MHz)
4.11 (dd, *J* = 10.8, 3.1 Hz, 1H)	4.12 (dd, *J* =10.5, 3.4，1H)	14.0	14.0
3.71–3.63 (m, 1H)	3.68 (dd, *J* = 10.5, 8.7, 1H)	21.0	21.0
3.55–3.45 (m, 1H)	3.55–3.45 (m, 1H)	21.9	21.9
3.28–3.16 (m, 1H)	3.28–3.16 (m, 1H)	22.5	22.6
2.28–2.14 (m, 3H)	2.28–2.14 (m. 3H)	22.9	22.9
2.06 (s, 3H)	2.07 (s, 3H)	24.4	24.4
1.85–1.04 (m, 22H)	1.84–1.04 (m, 22H)	26.4	26.4
0.87 (t, *J* = 6.6 Hz, 3H)	0.88 (t, *J* = 6.0, 3H)	27.1	27.1
		29.3	29.3
		31.8	31.8
		34.9 (2C)	34.9 (2C)
		36.0	36.0
		42.9	42.9
		51.0	51.1
		54.5	54.5
		55.2	55.2
		68.6	68.6
		70.0	70.0
		171.0	171.0
		211.0	211.0

4. References

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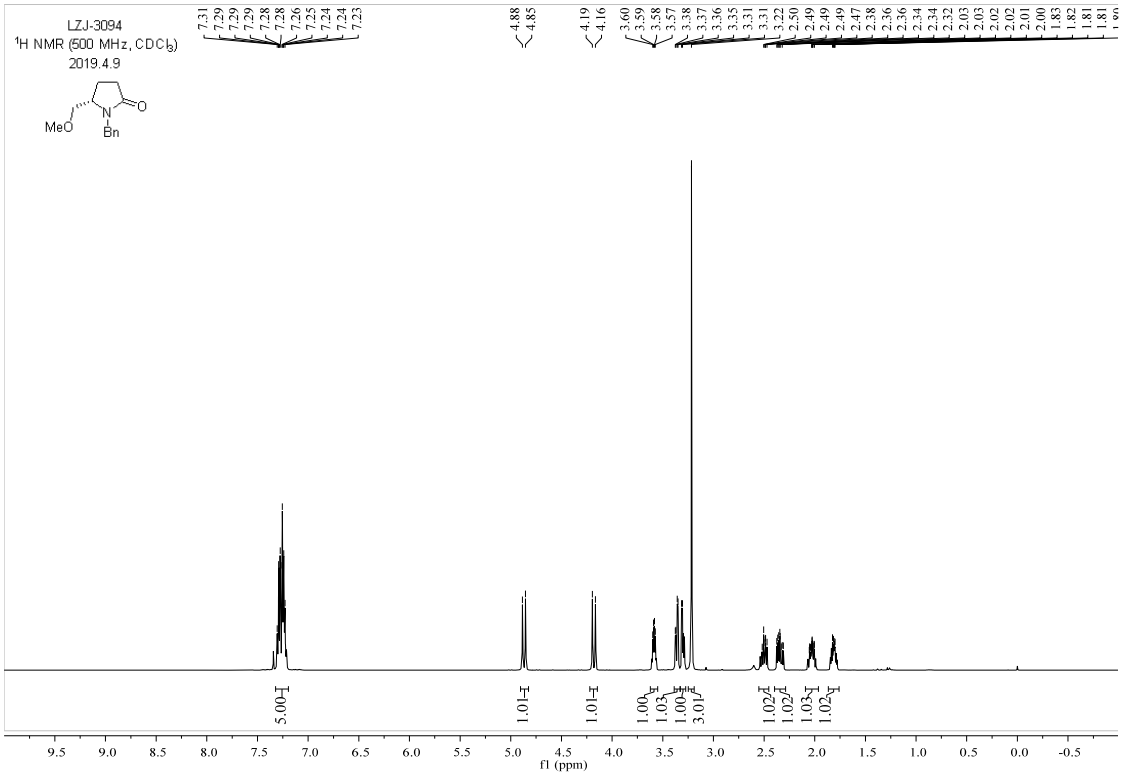
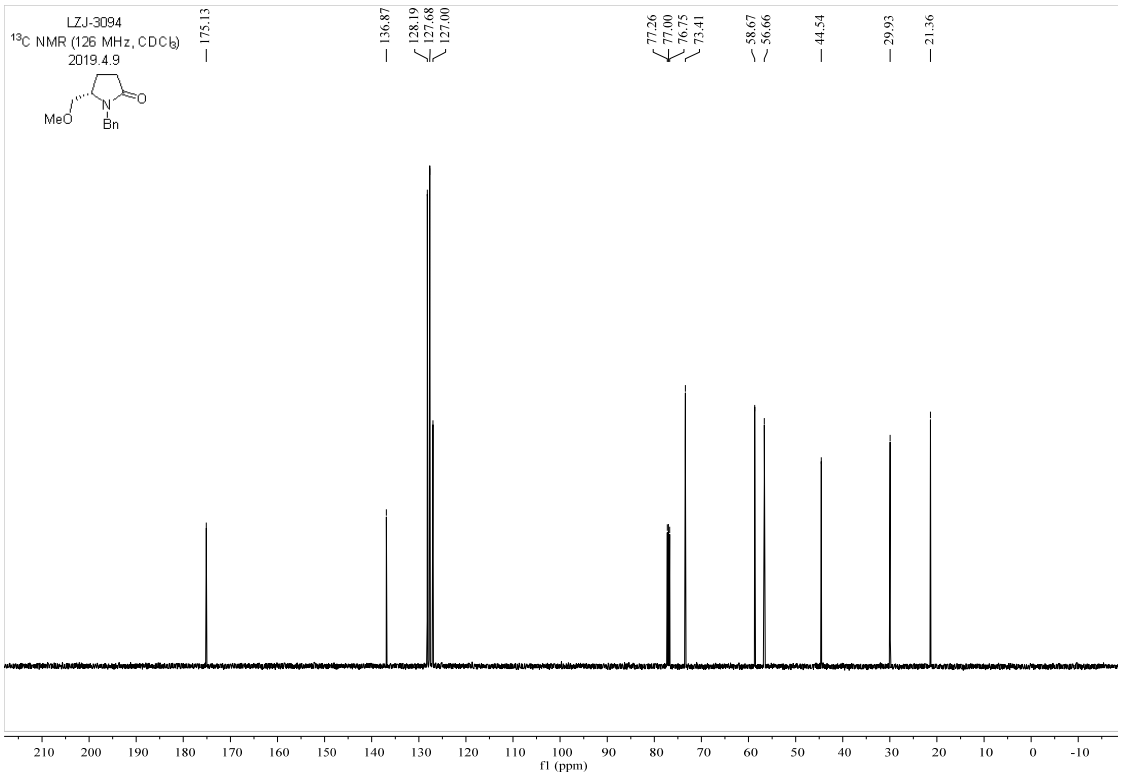
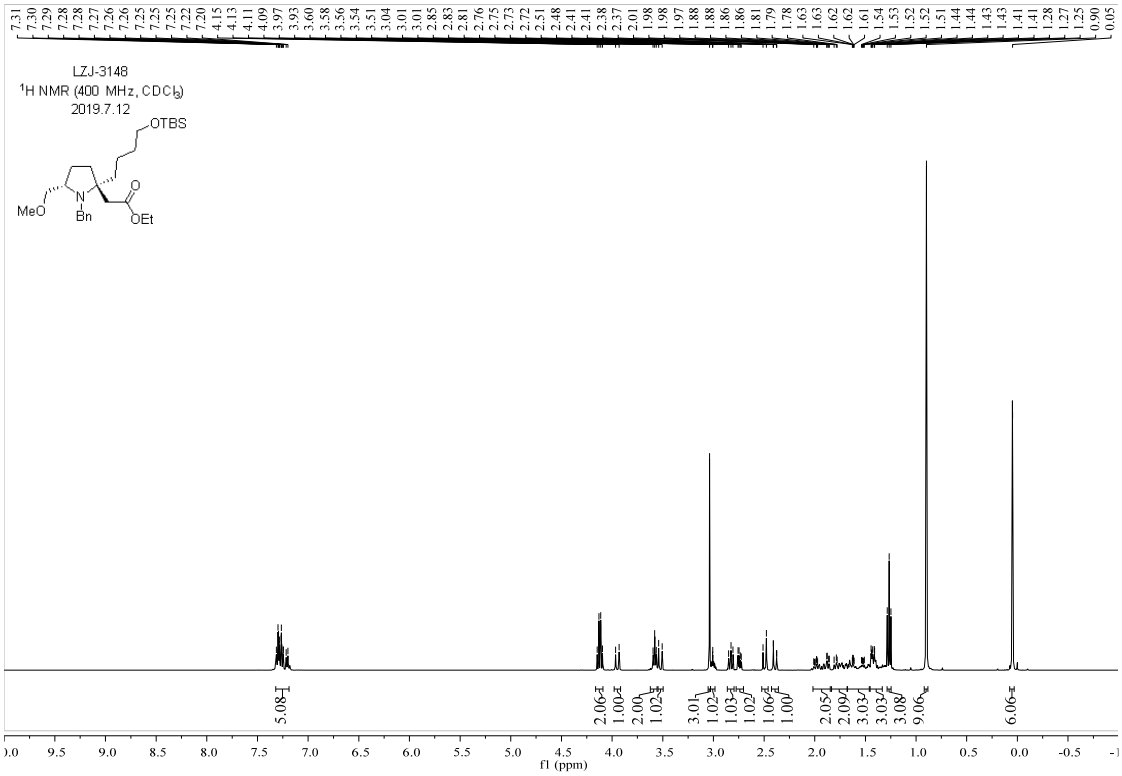
5. NMR Spectra.

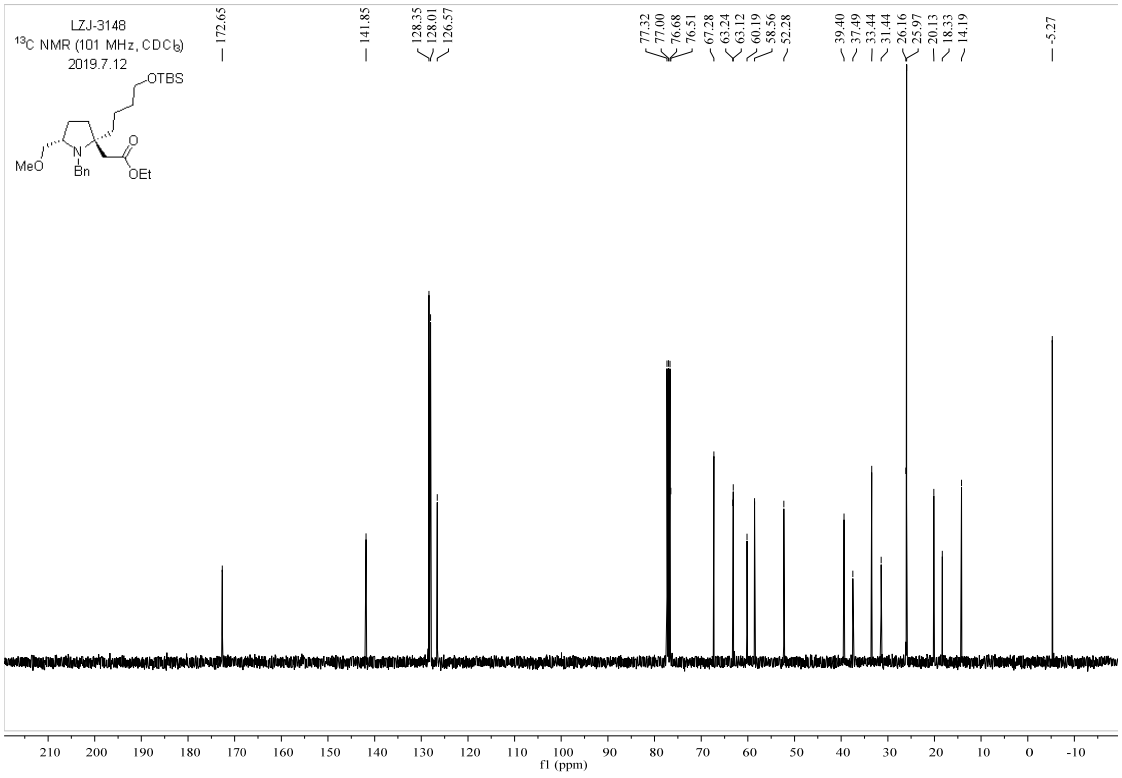
^{1}H NMR and ^{13}C NMR spectra of compound **9**



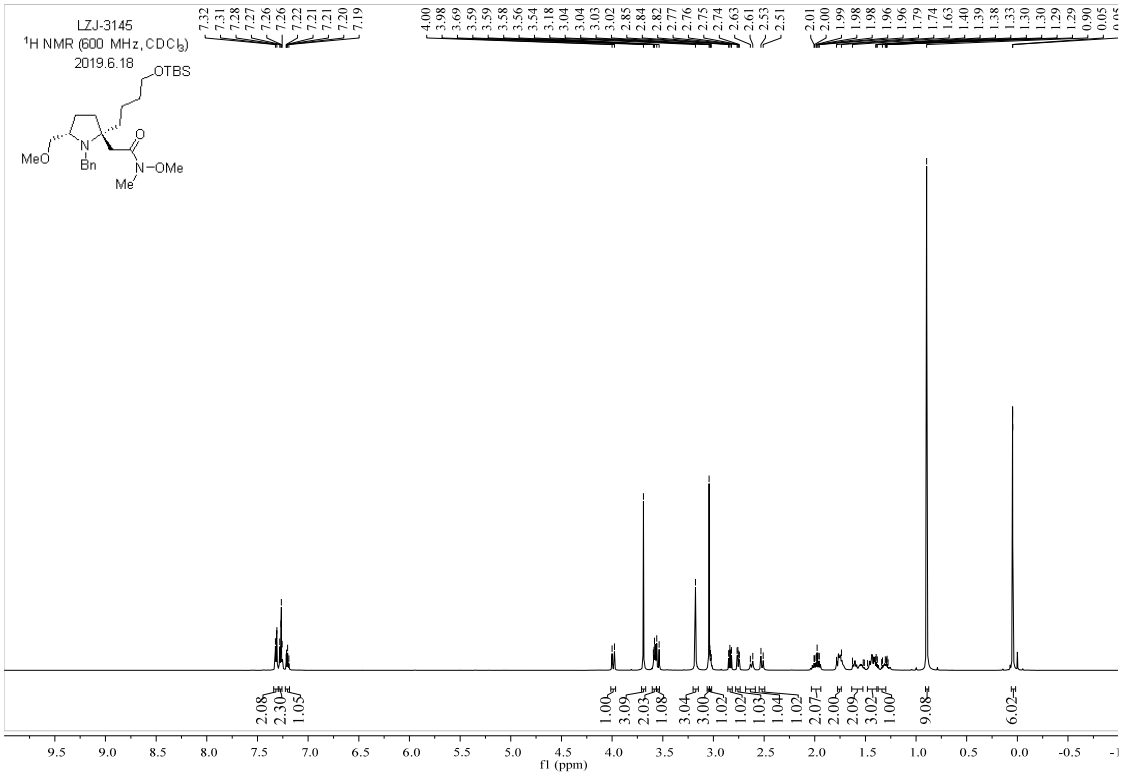


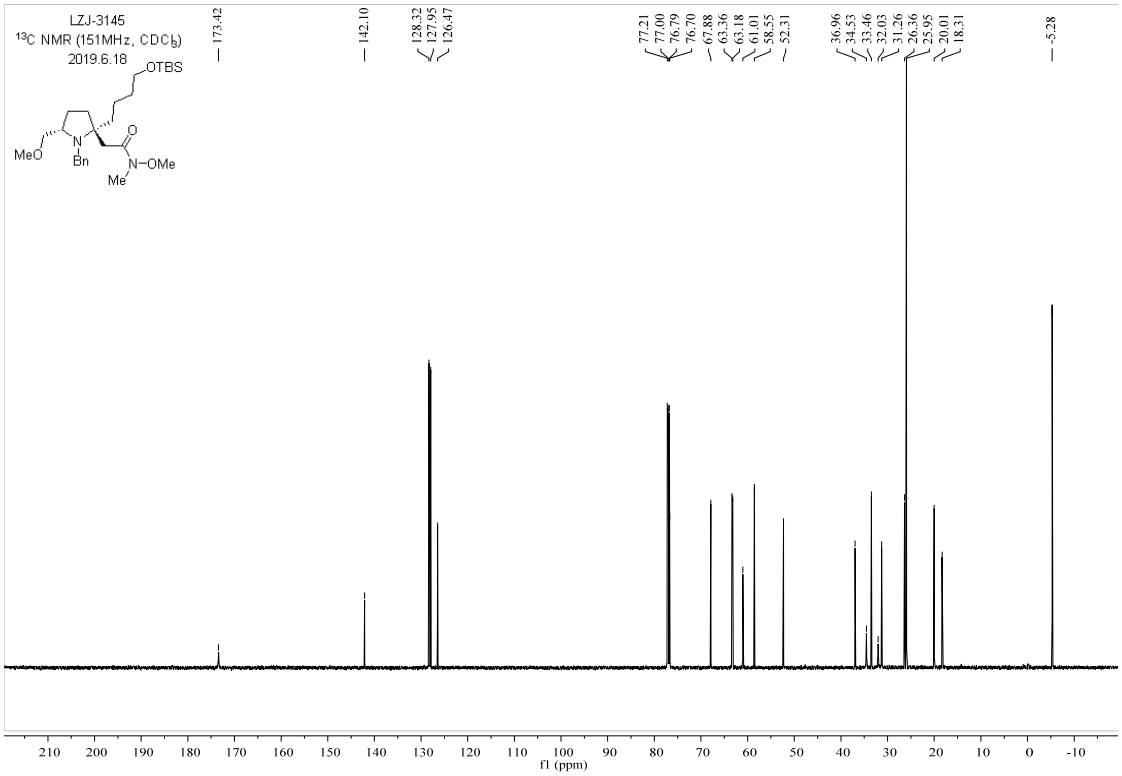
^{1}H NMR and ^{13}C NMR spectra of compound **8**



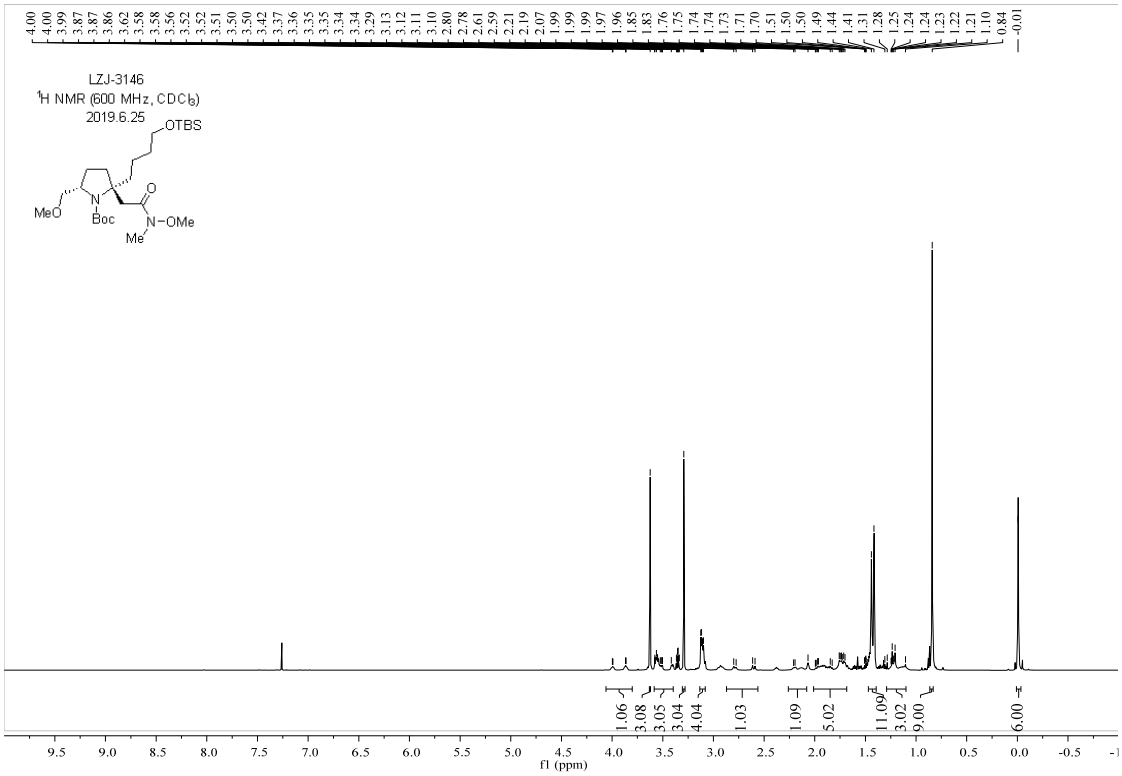


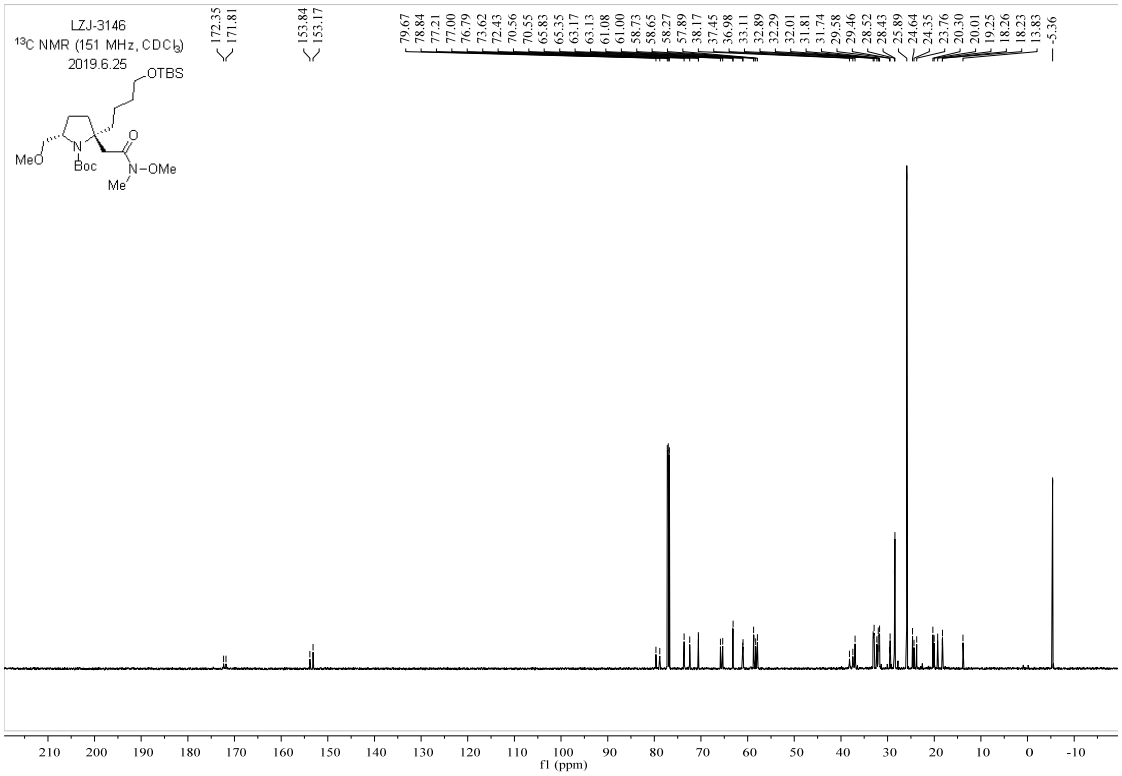
^{1}H NMR and ^{13}C NMR spectra of compound **7**



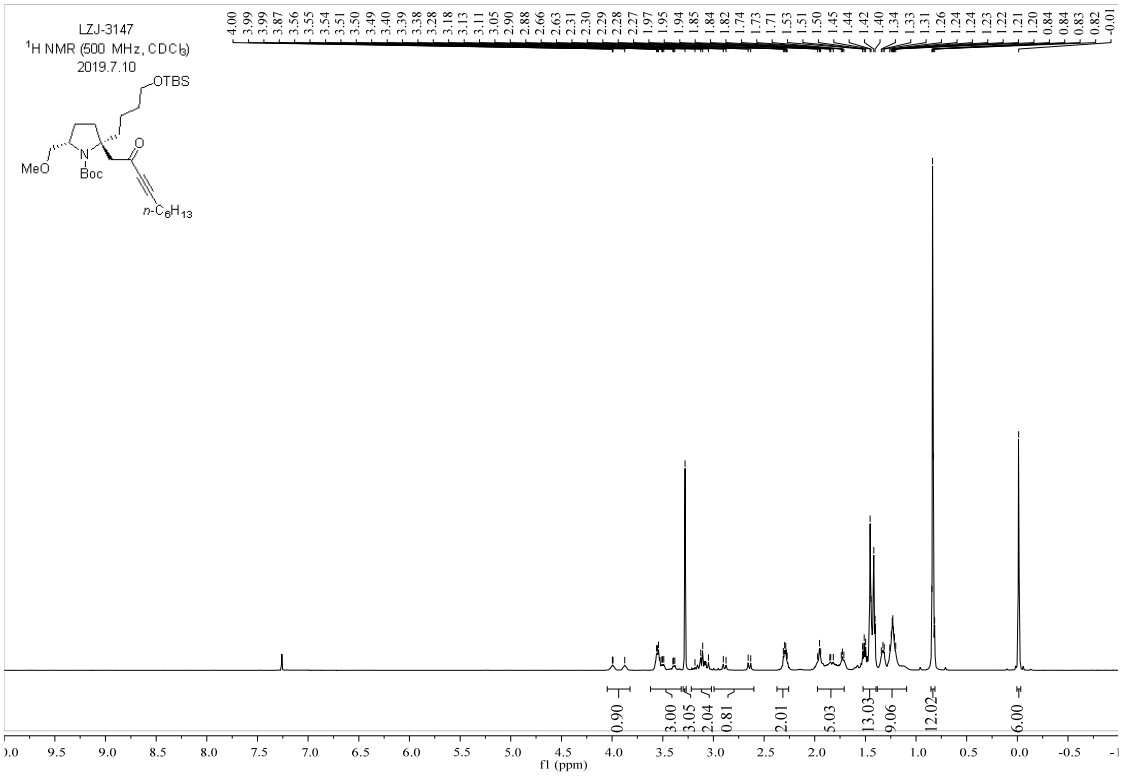


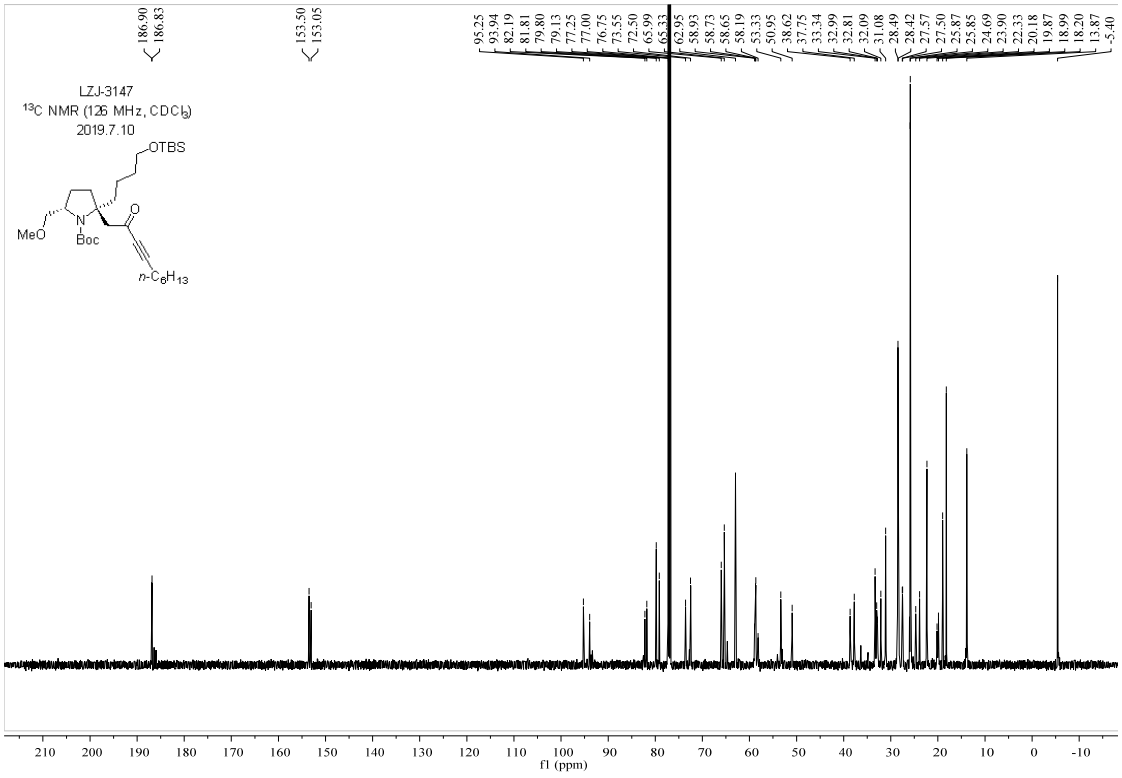
^{1}H NMR and ^{13}C NMR spectra of compound **6**



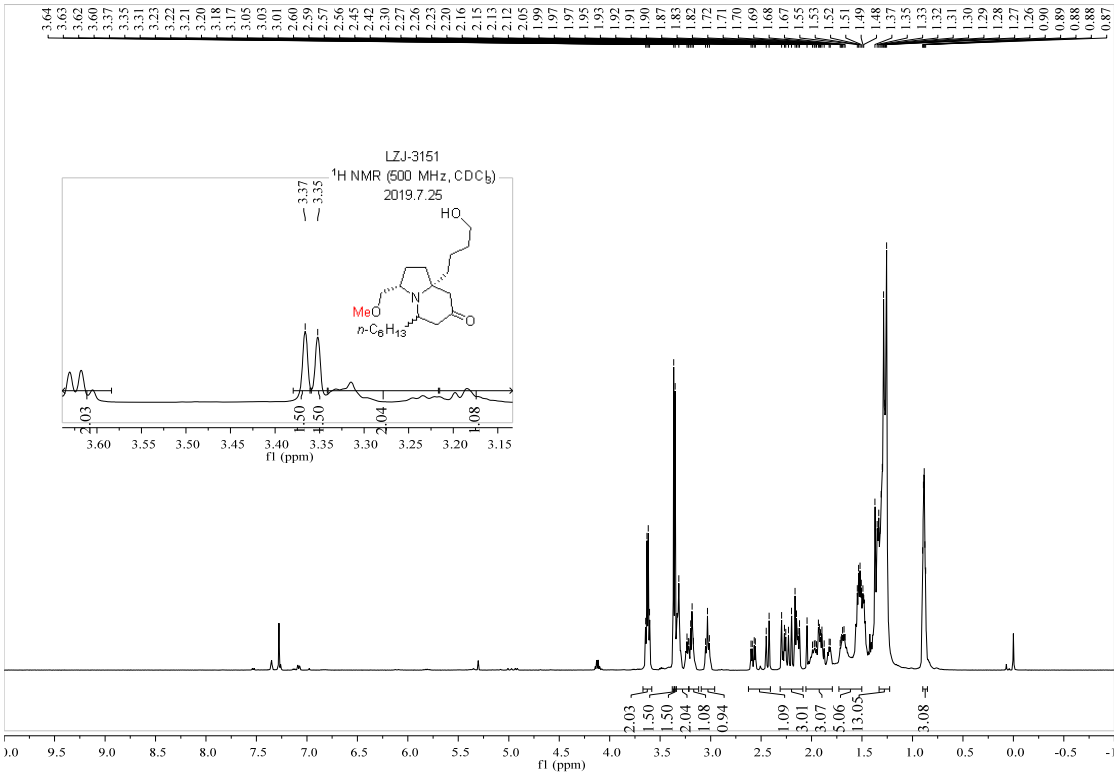


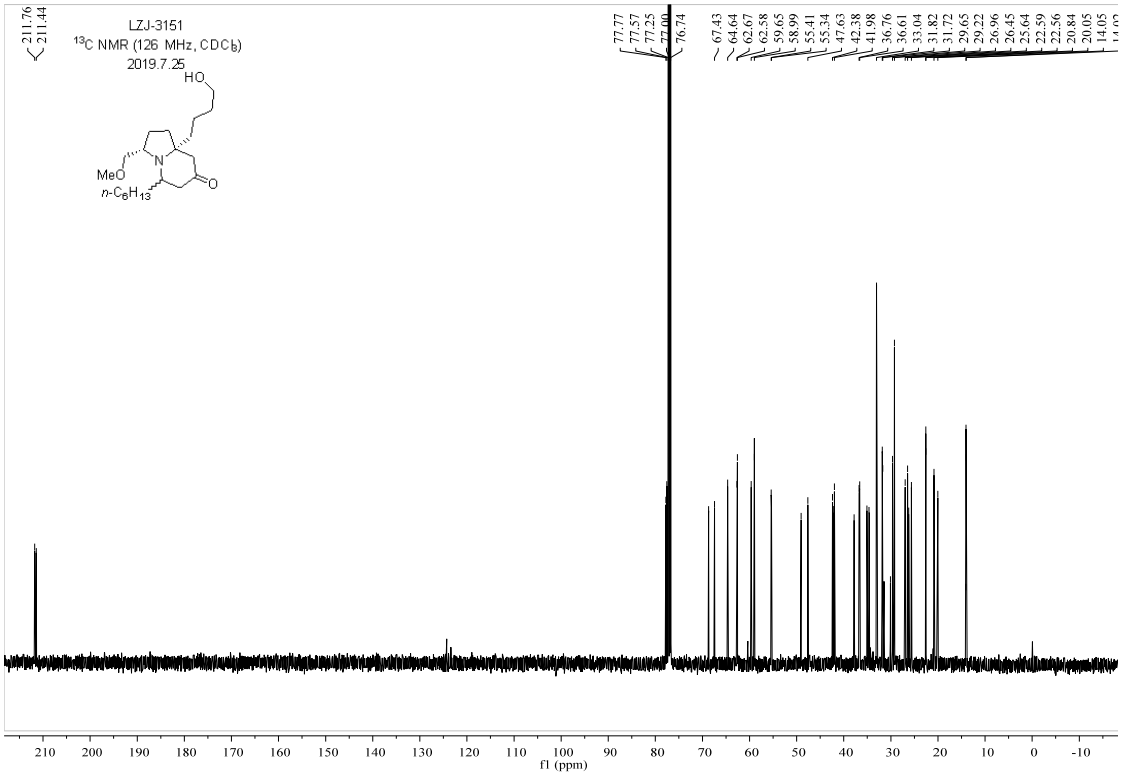
^{1}H NMR and ^{13}C NMR spectra of compound **5**



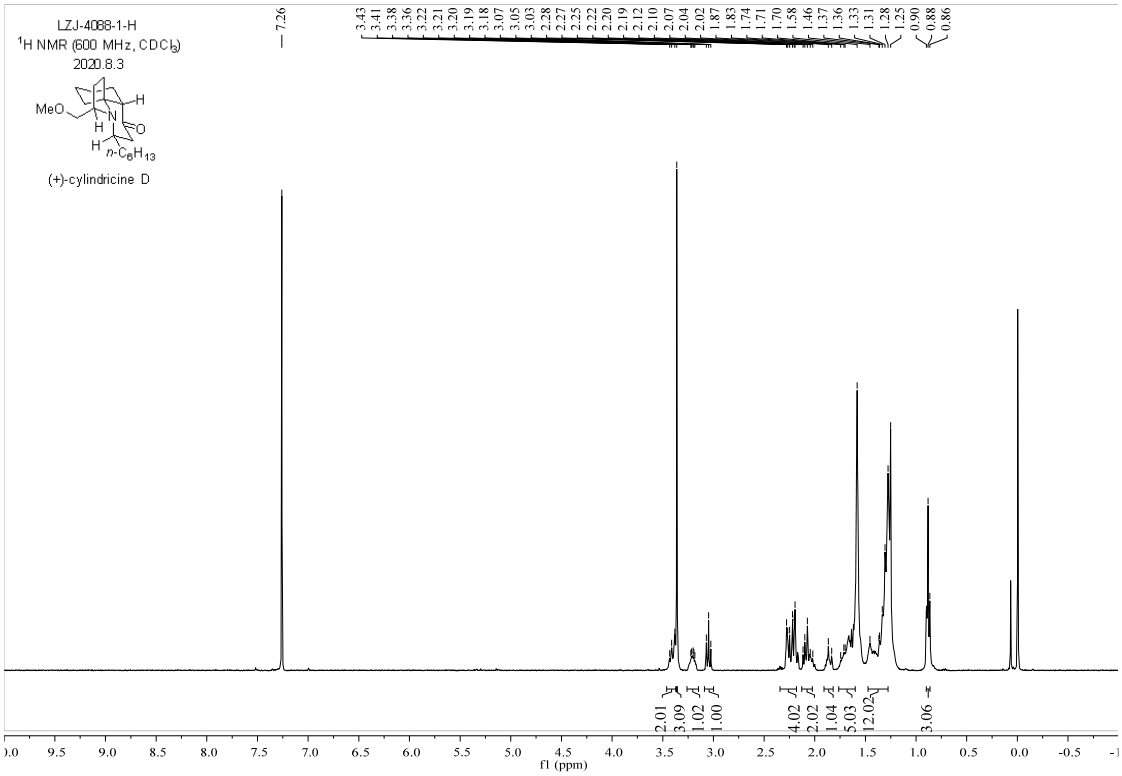


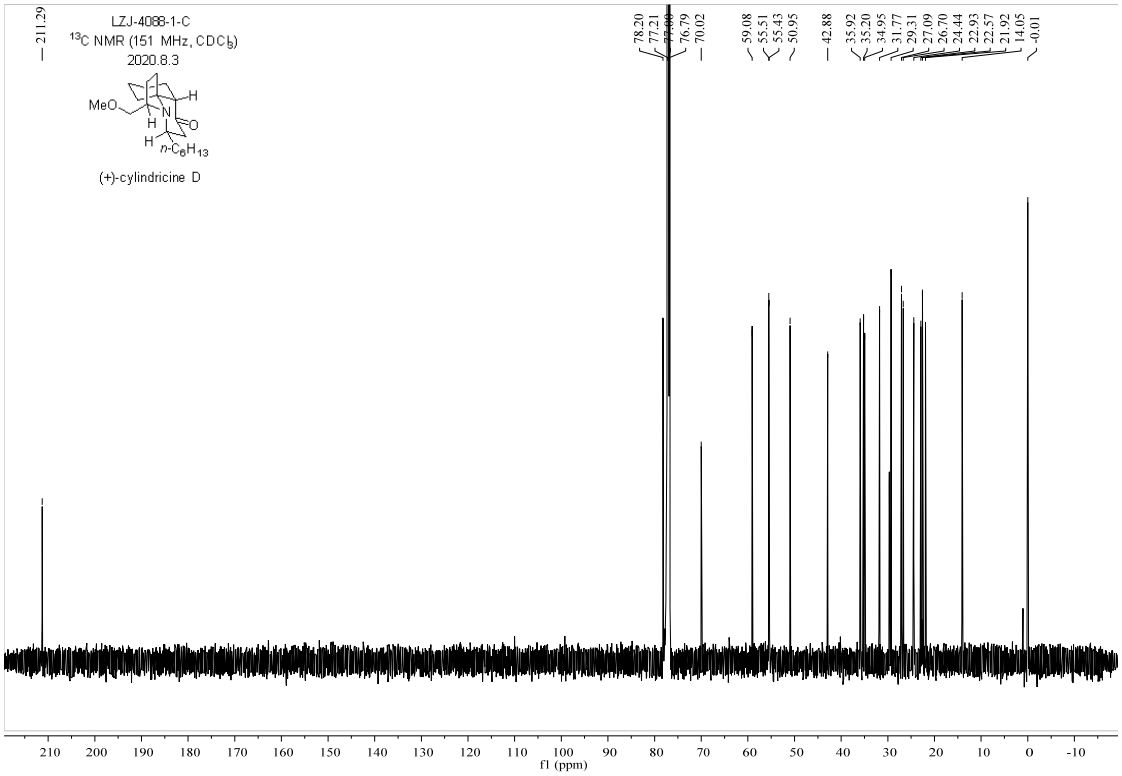
^{1}H NMR and ^{13}C NMR spectra of compound **18**



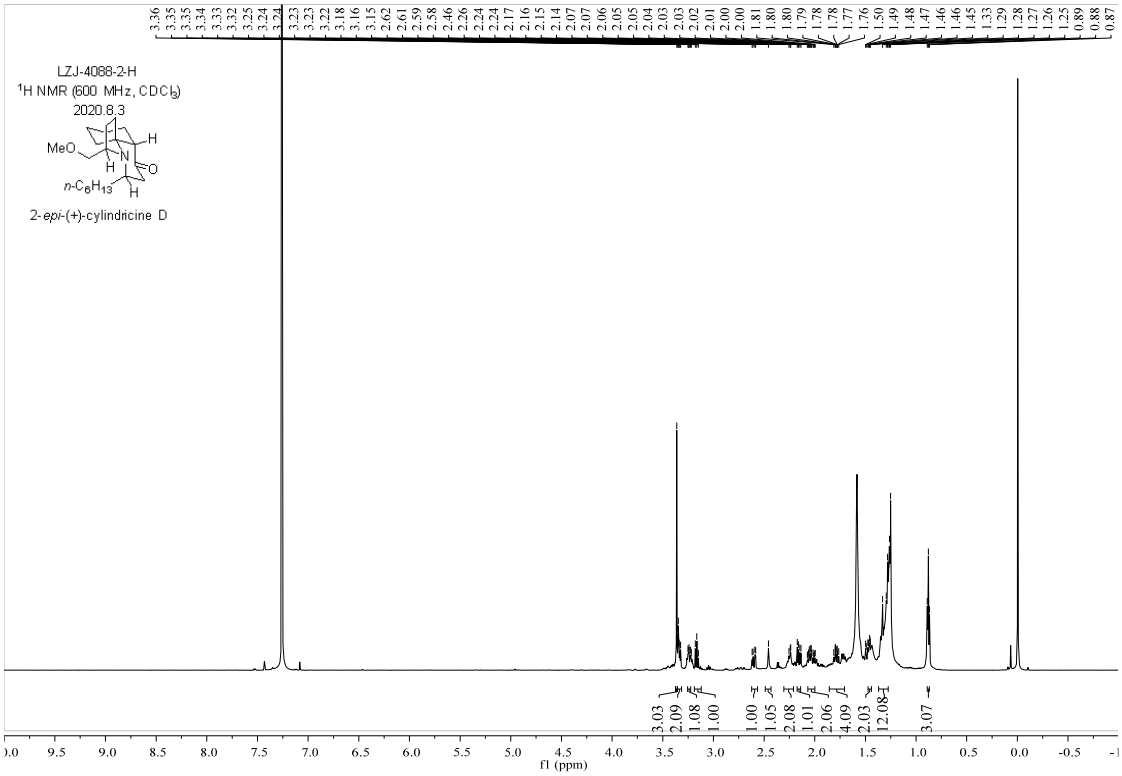


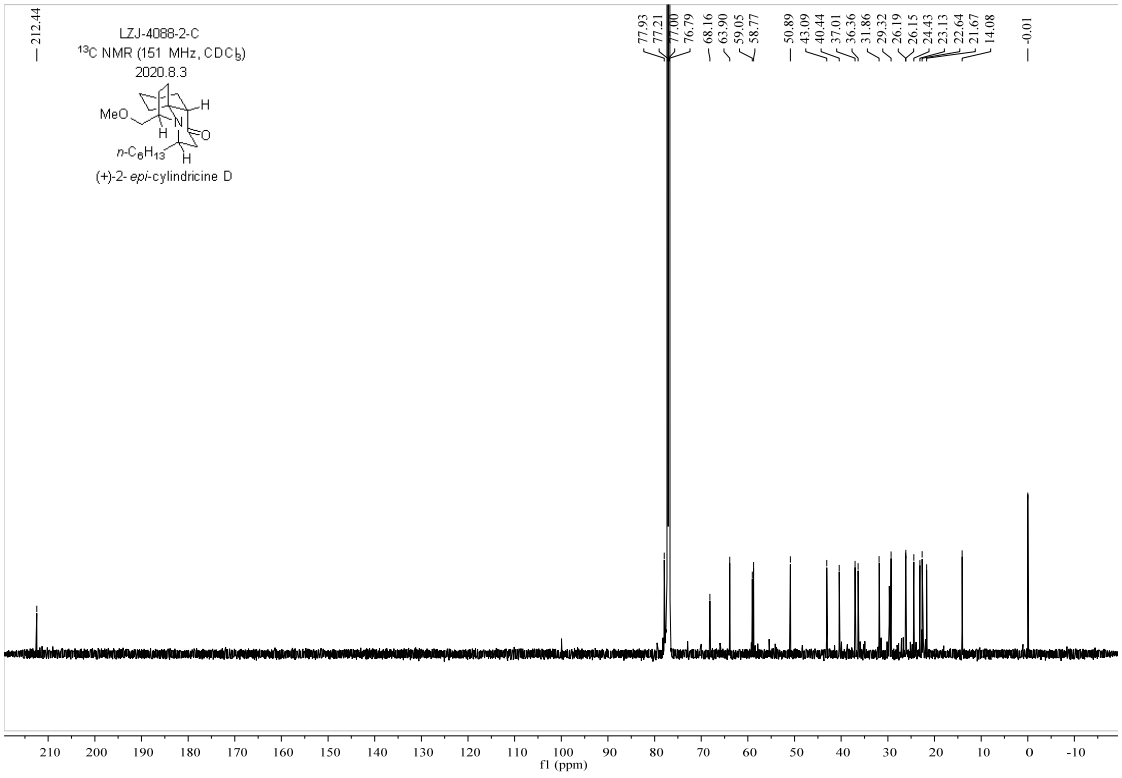
^{1}H NMR and ^{13}C NMR spectra of (+)-cylindricine D (**1d**)



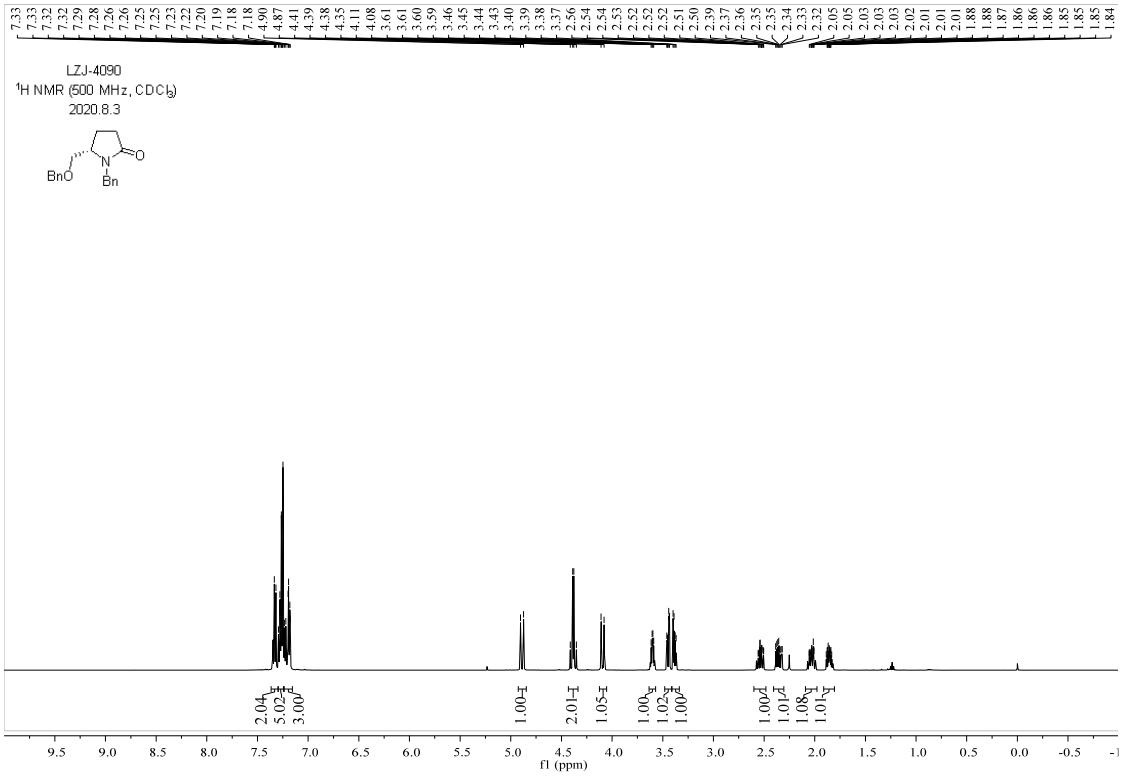


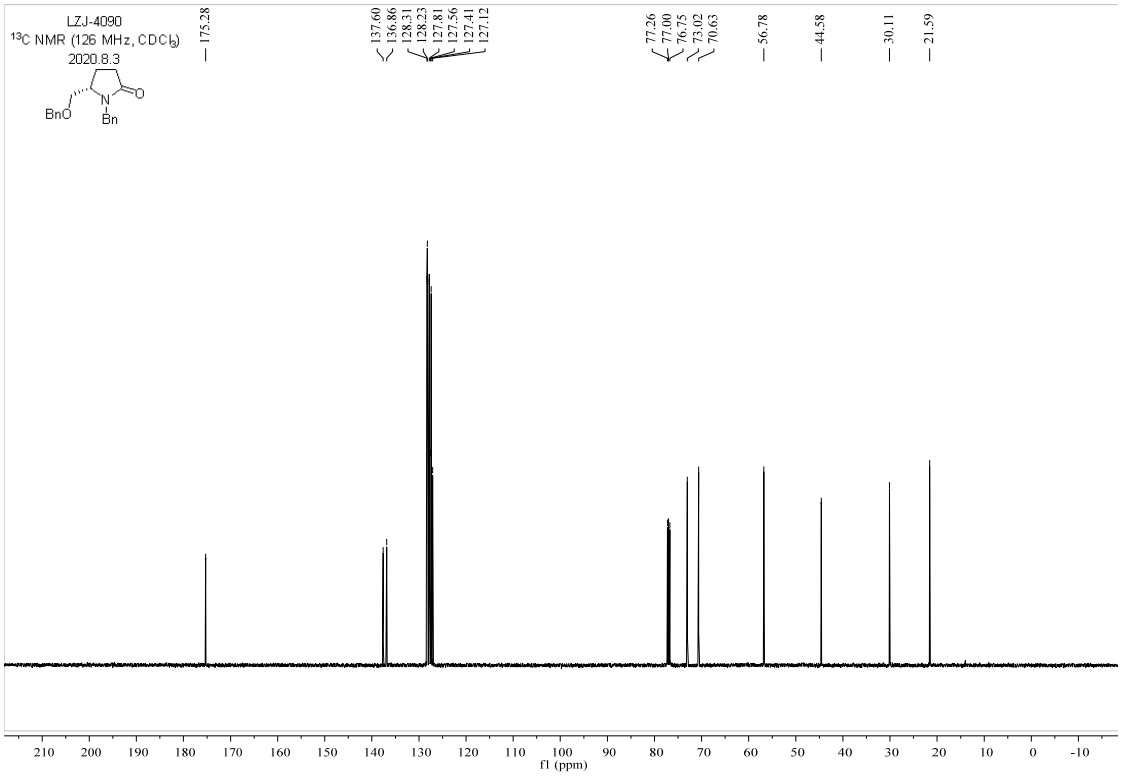
^{1}H NMR and ^{13}C NMR spectra of (+)-2-*epi*-cylindricine D (2-*epi*-**1d**)



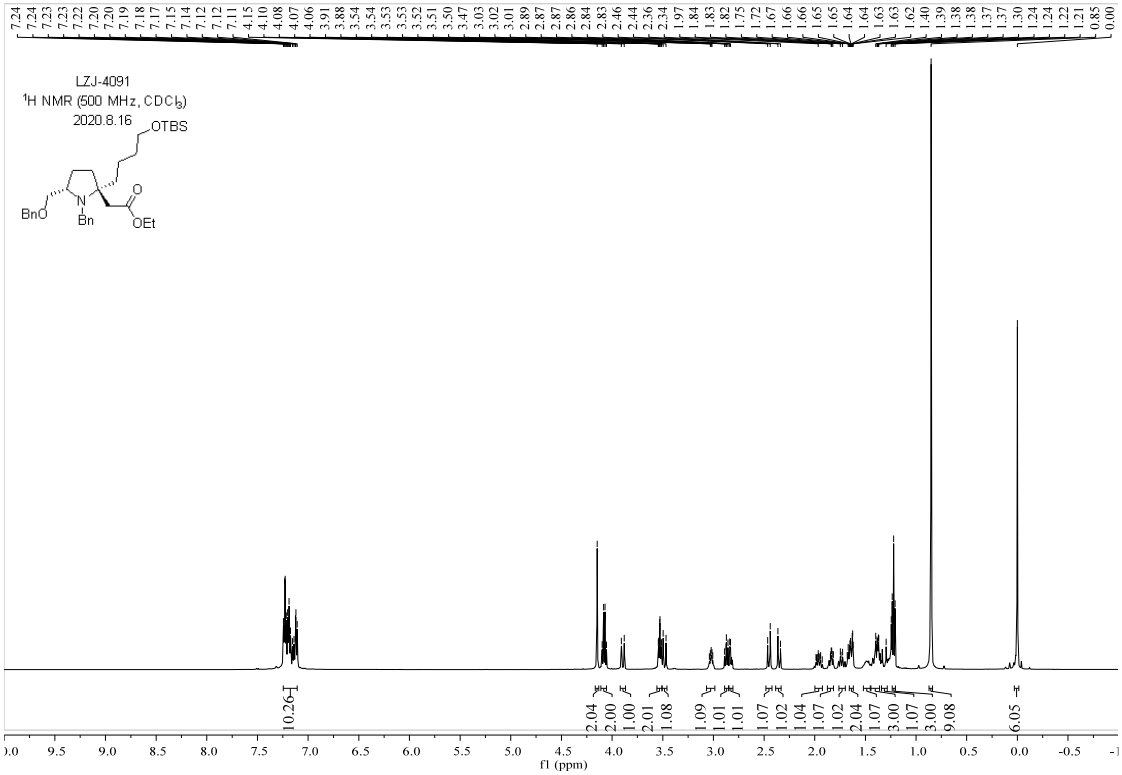


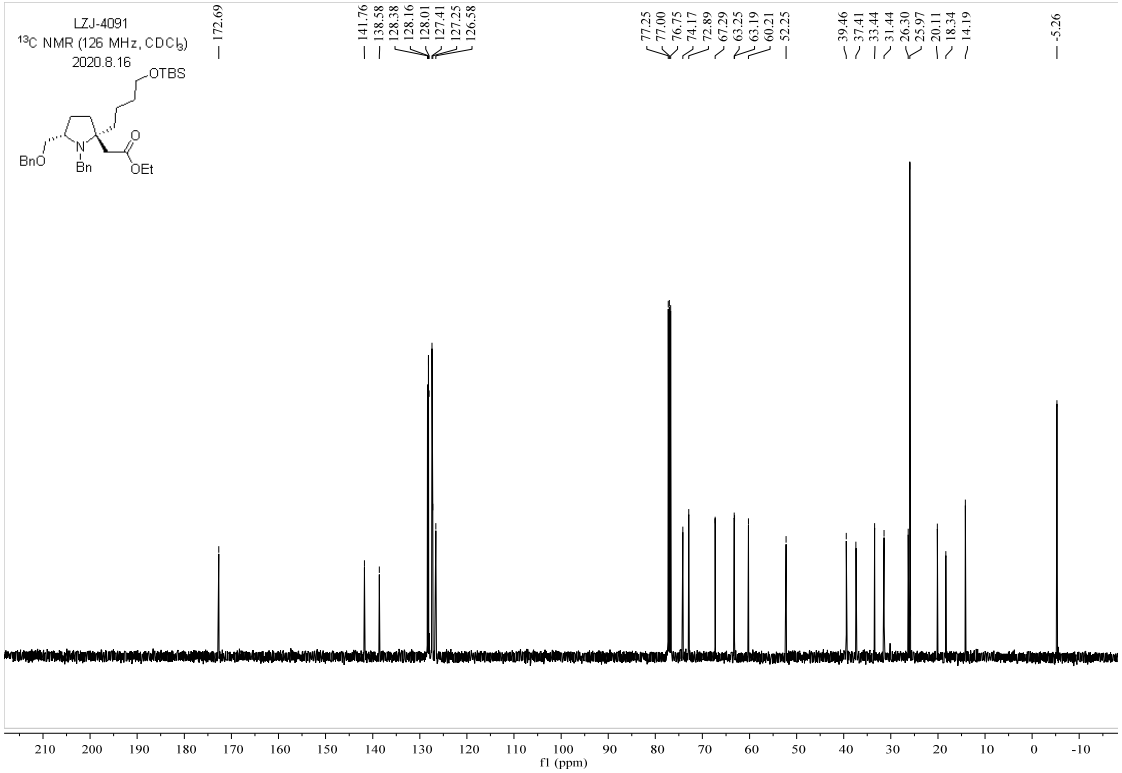
^{1}H NMR and ^{13}C NMR spectra of **12**



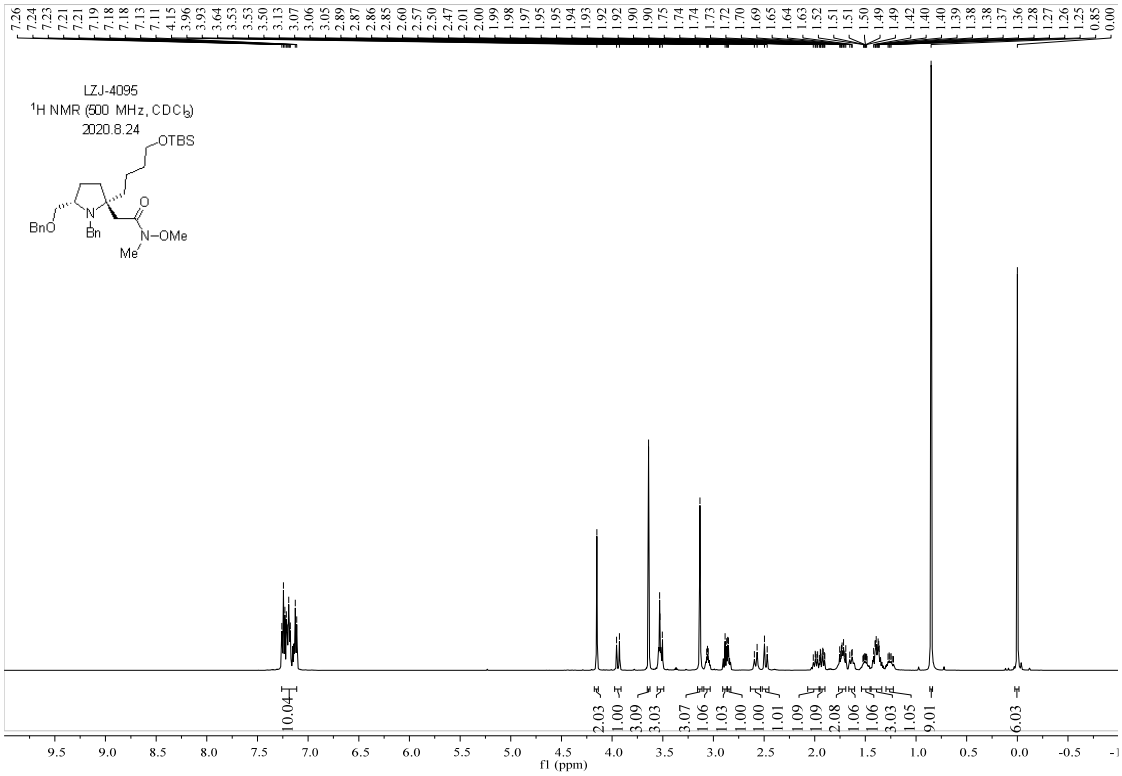


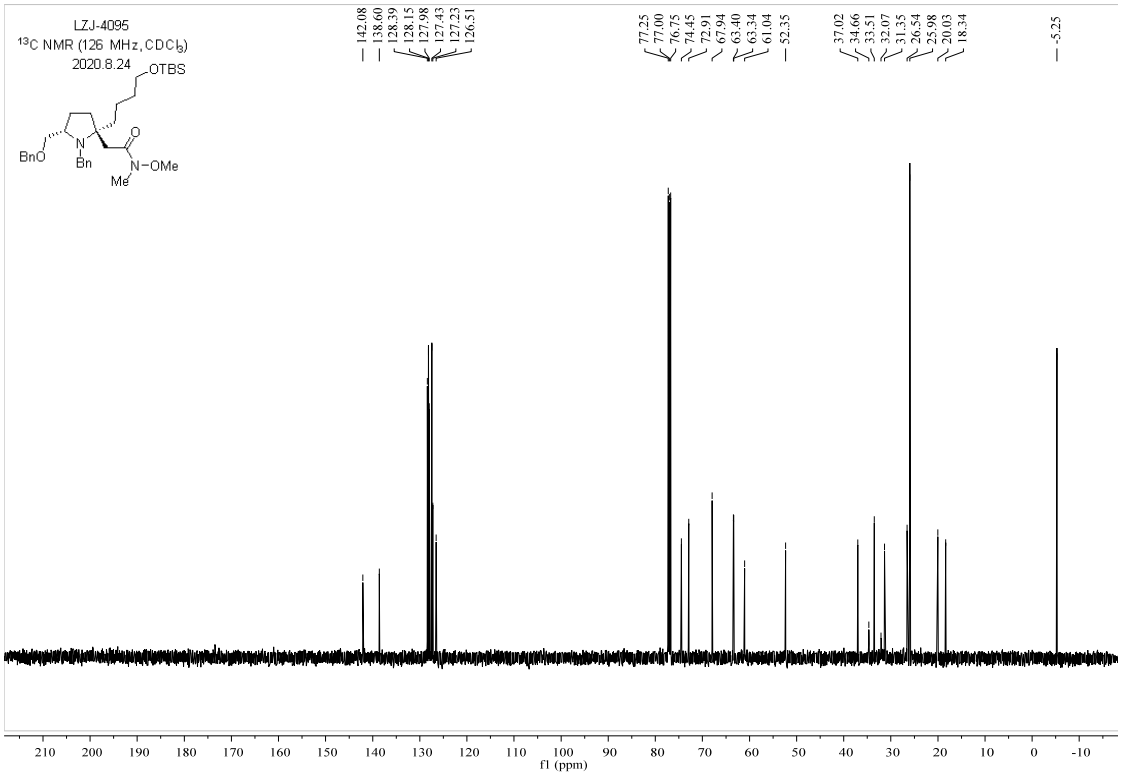
^{1}H NMR and ^{13}C NMR spectra of **13**



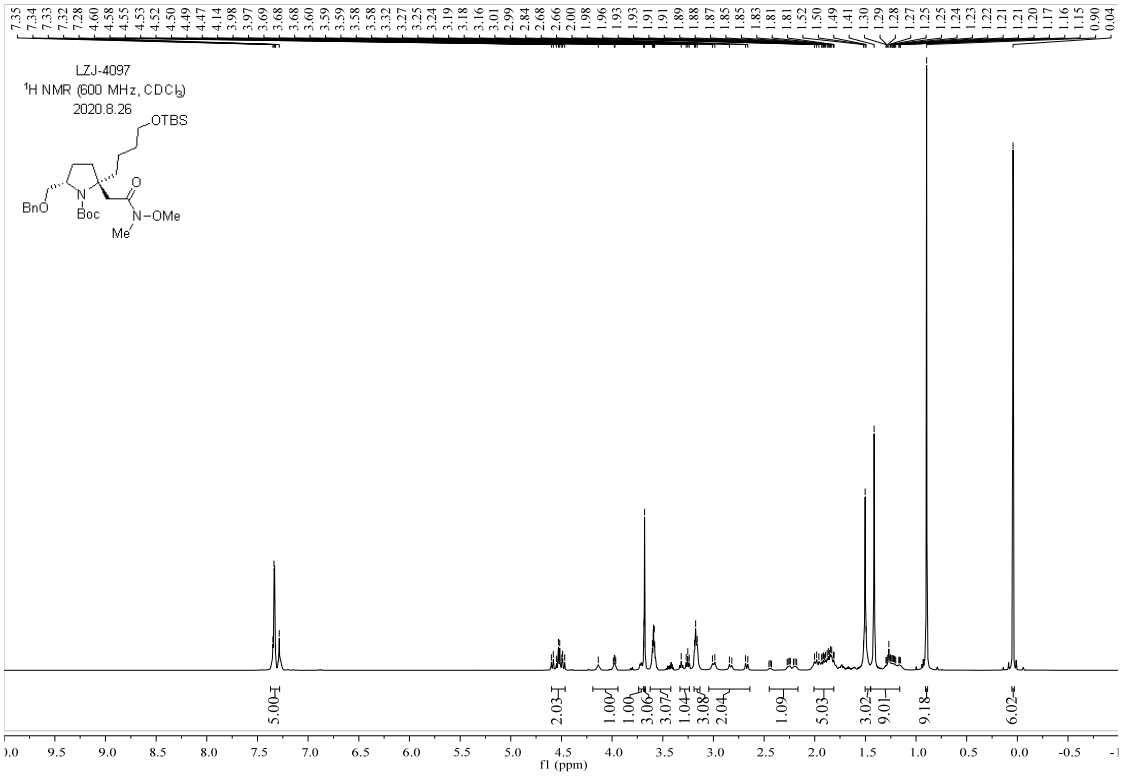


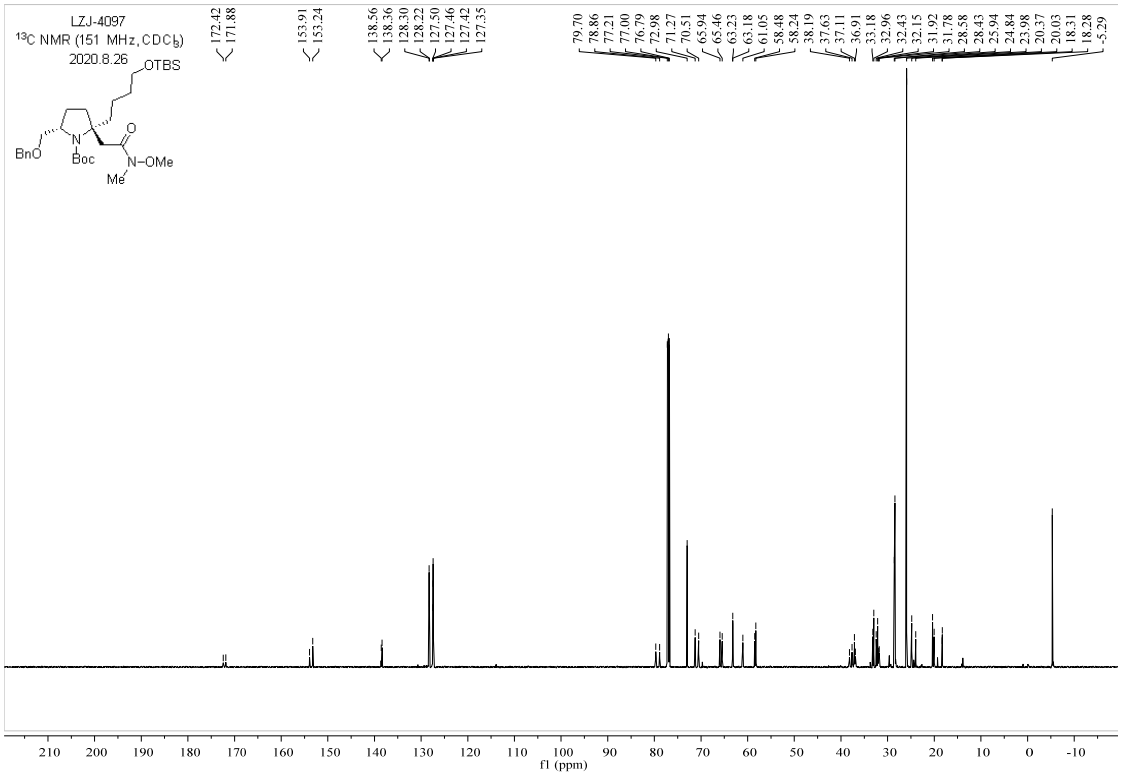
^{1}H NMR and ^{13}C NMR spectra of **14**



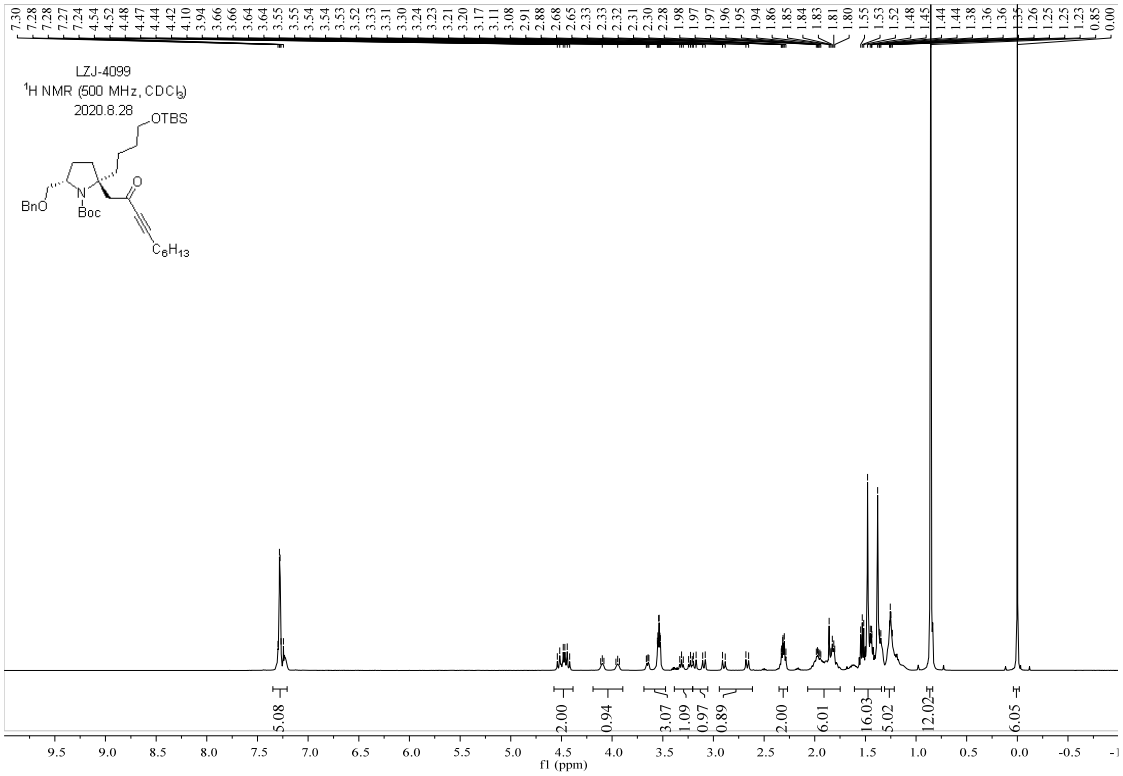


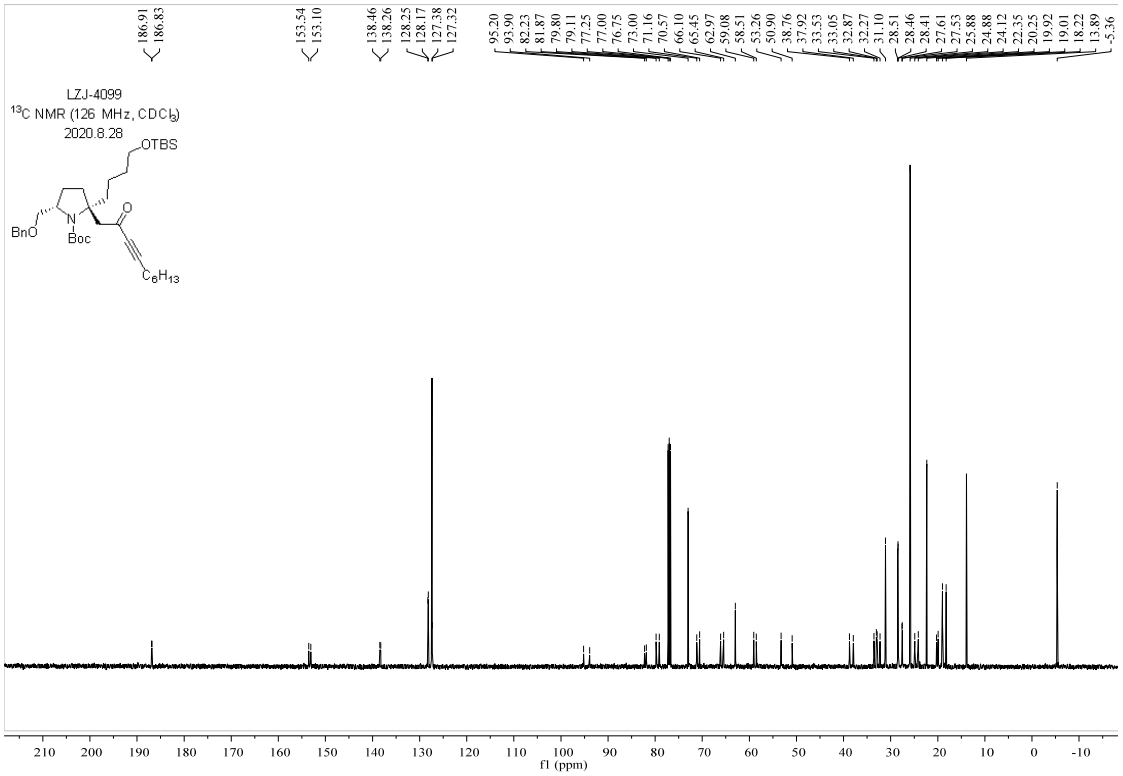
^{1}H NMR and ^{13}C NMR spectra of **15**



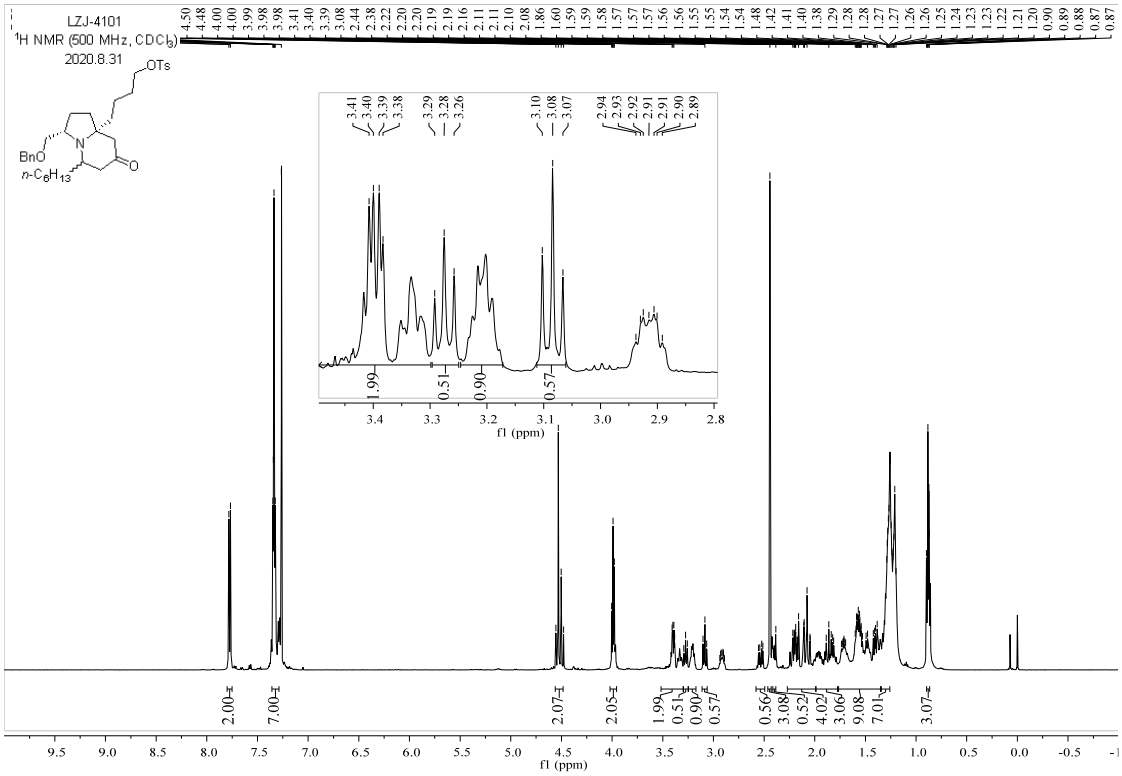


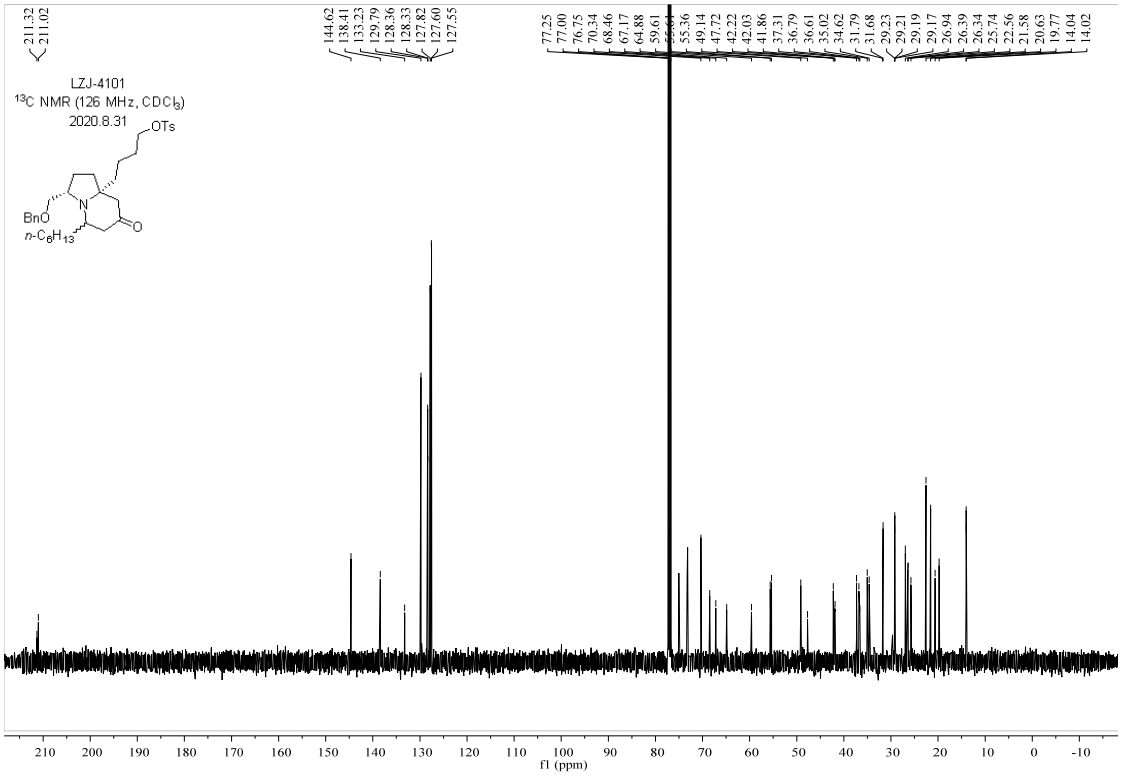
^{1}H NMR and ^{13}C NMR spectra of **16**



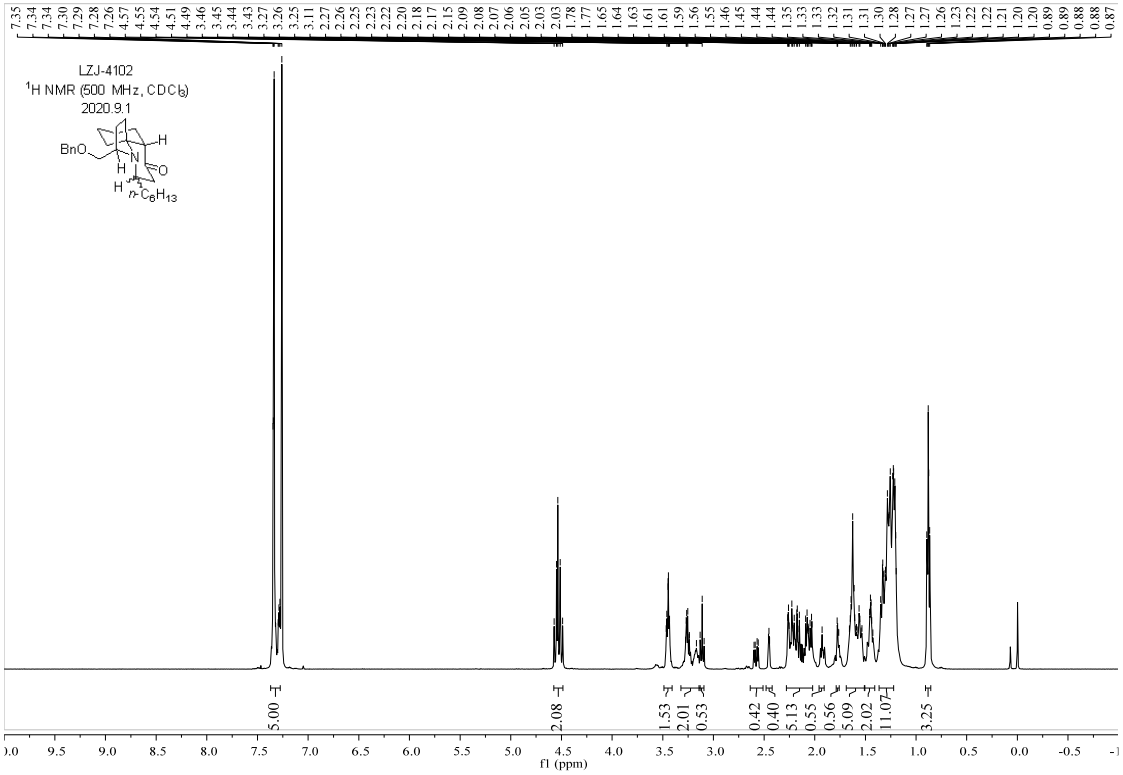


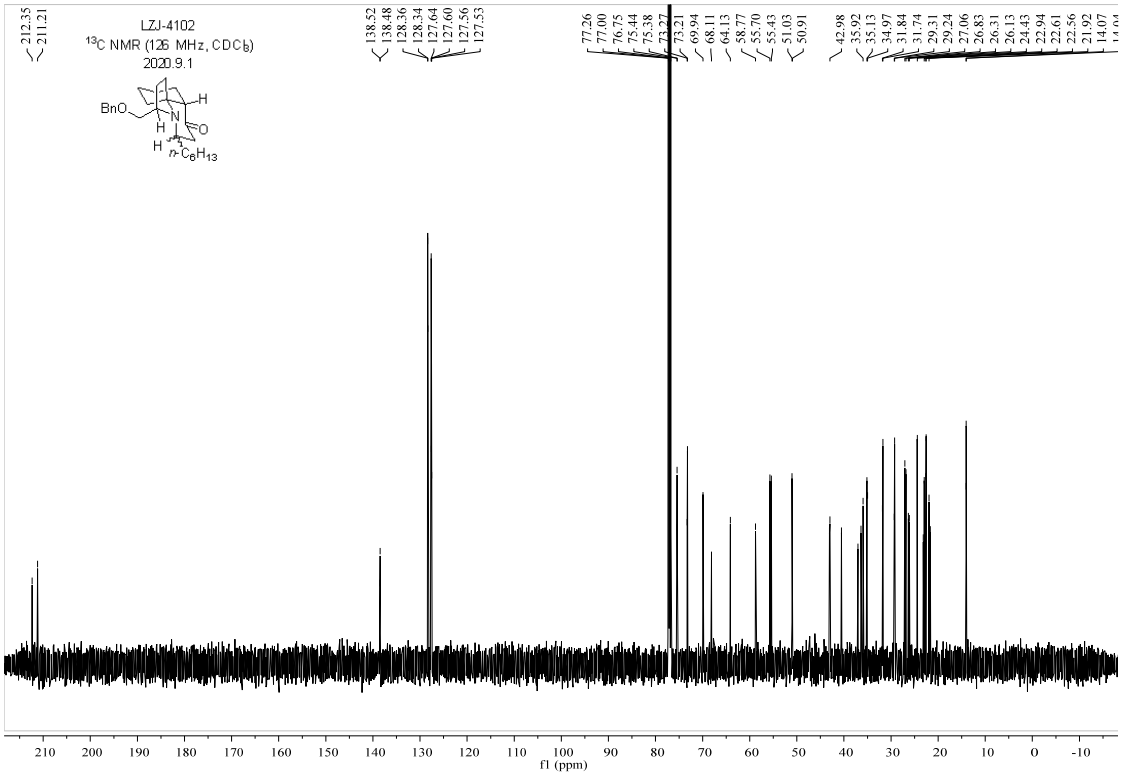
^{1}H NMR and ^{13}C NMR spectra of **21**



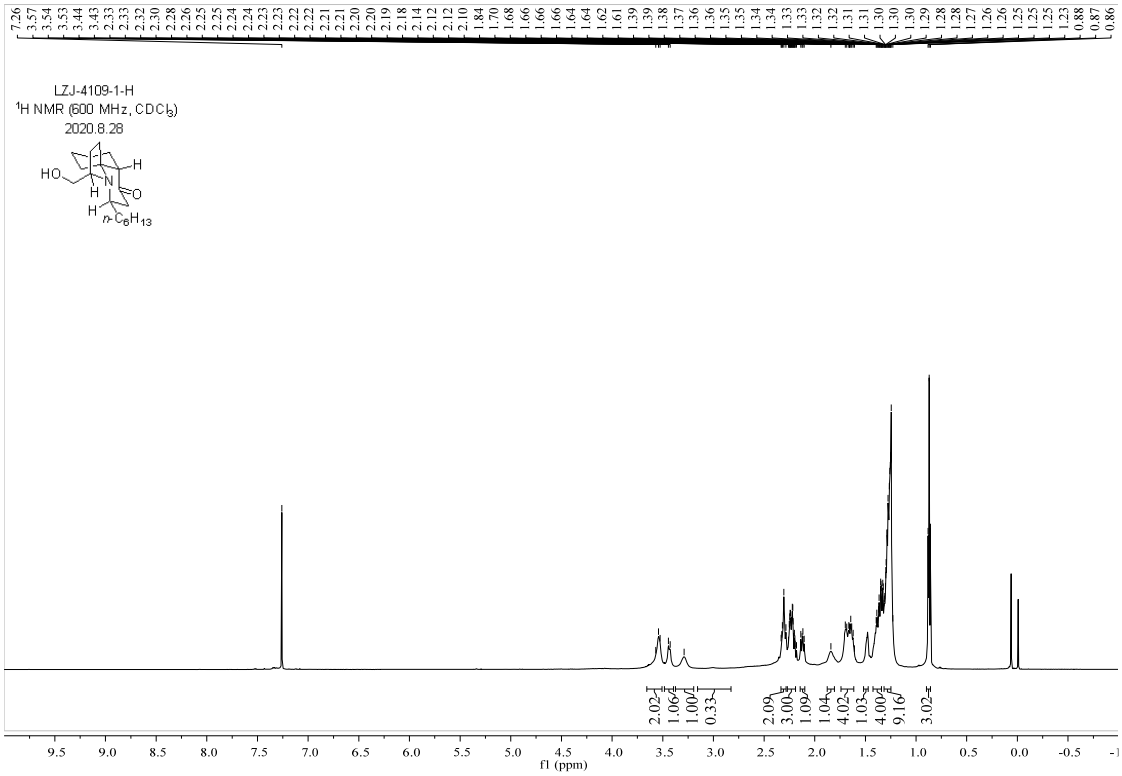


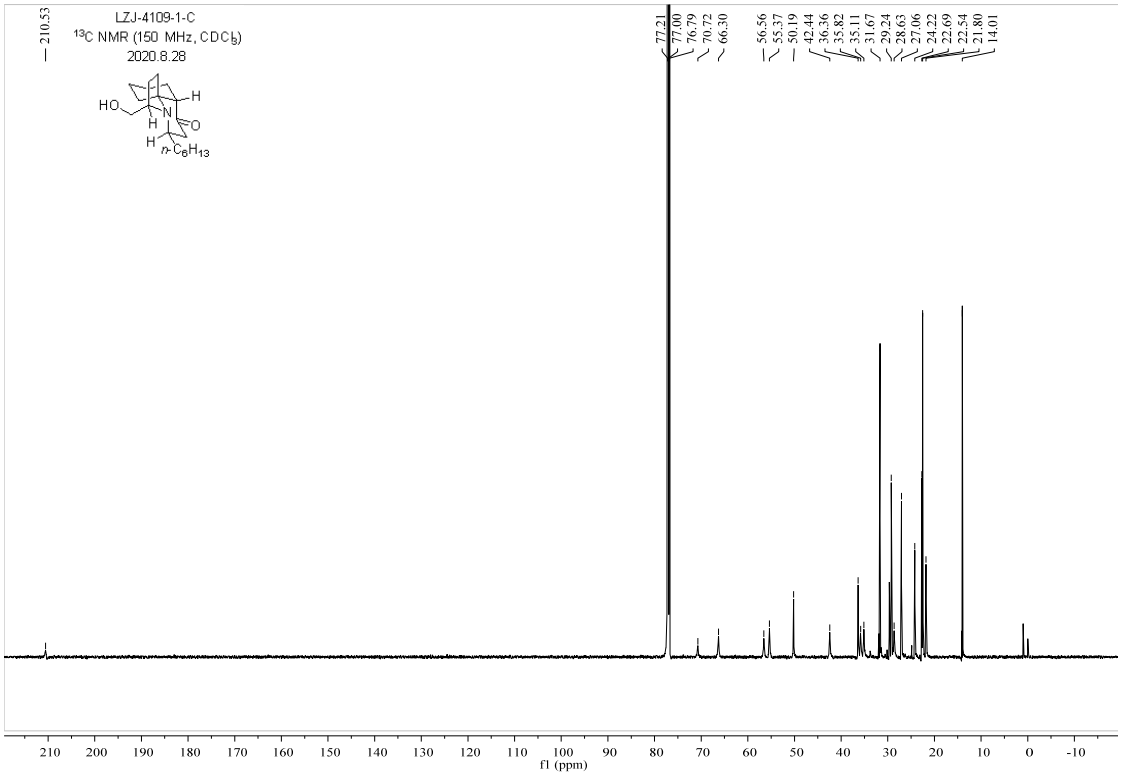
^{1}H NMR and ^{13}C NMR spectra of **22**



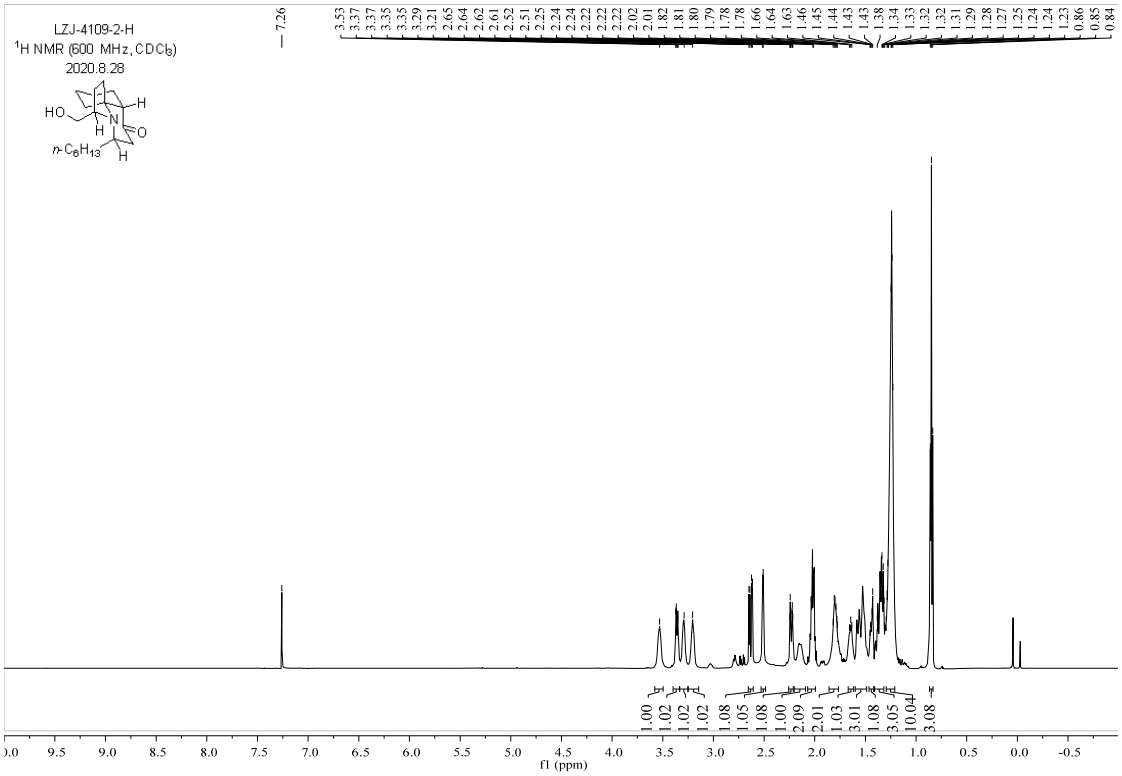


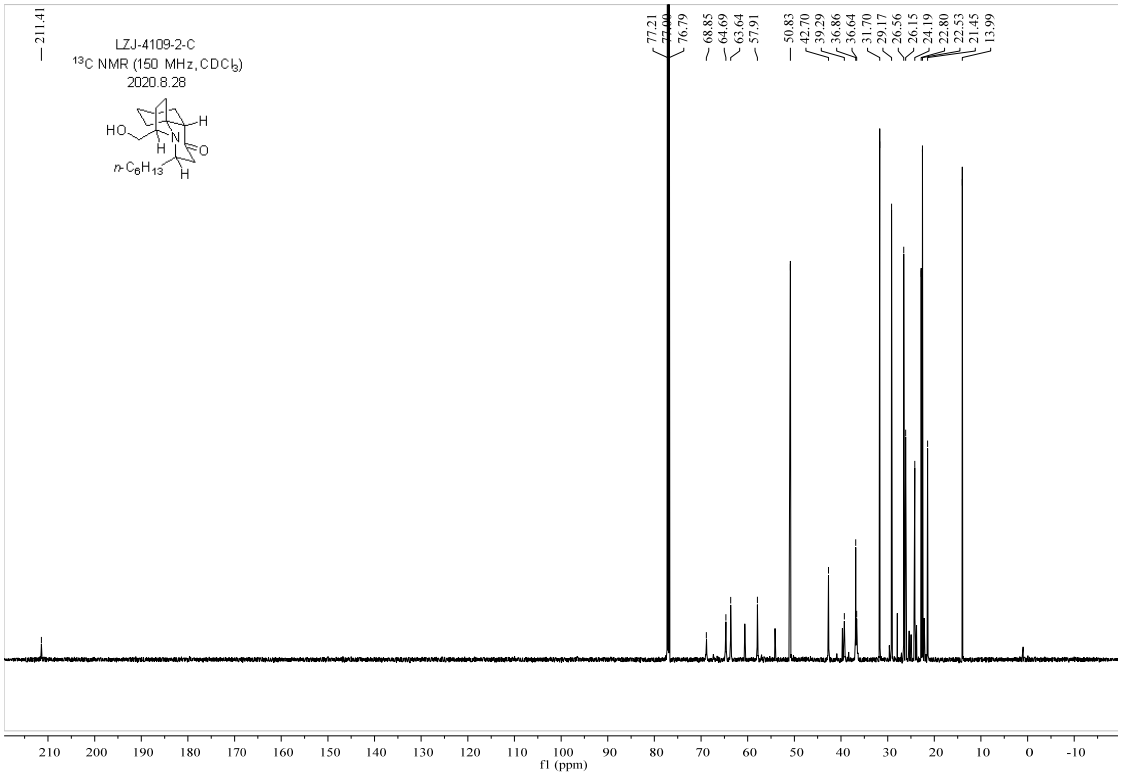
^{1}H NMR and ^{13}C NMR spectra of (+)-cylindricine C (**1c**)



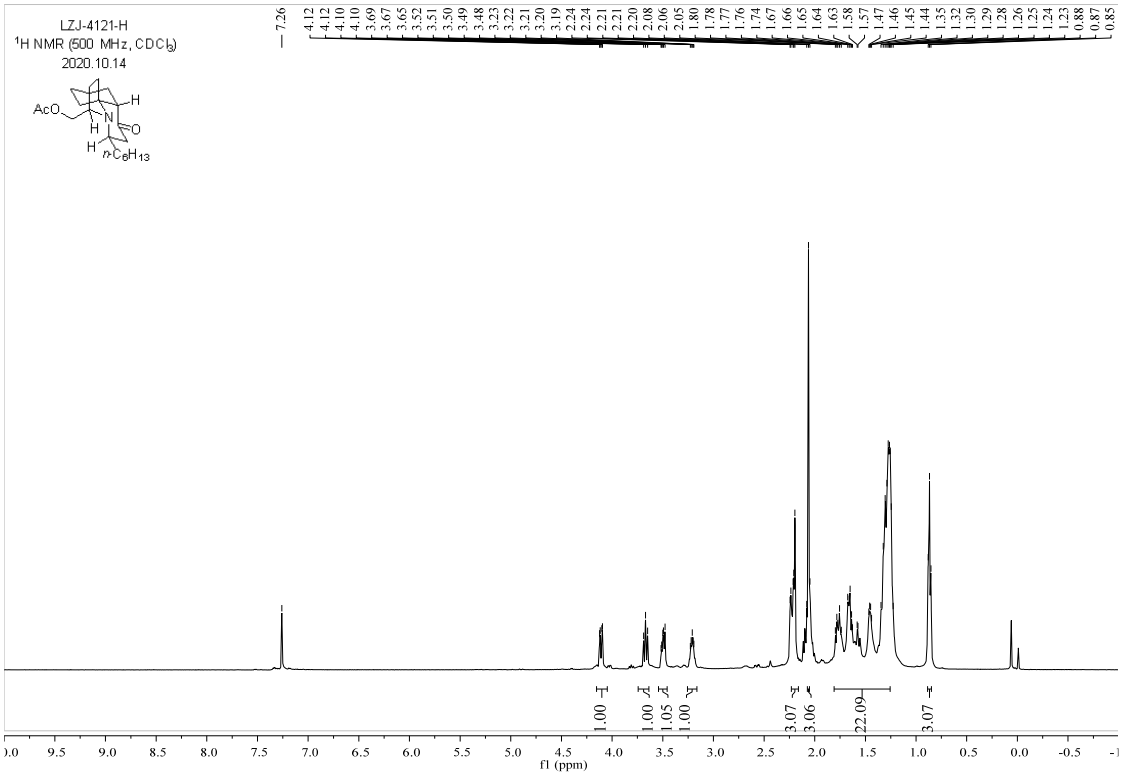


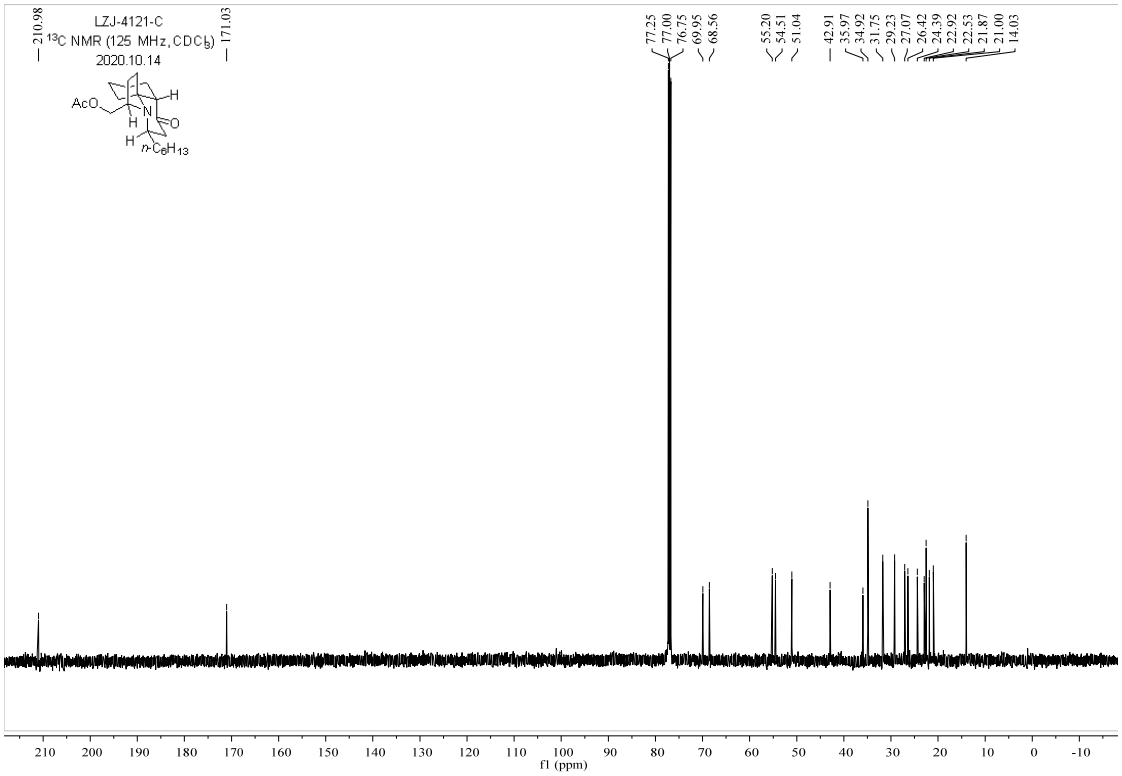
^{1}H NMR and ^{13}C NMR spectra of (+)-2-*epi*-cylindricine C (2-*epi*-**1c**)





^{1}H NMR and ^{13}C NMR spectra of (+)-cylindricine E (**1e**)





^{1}H NMR and ^{13}C NMR spectra of (+)-2-*epi*-cylindricine E (2-*epi*-**1e**)