Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information for

A *De Novo* Synthesis of Bisindole Alkaloid Geissolosimine: Collective Synthesis of Geissoschizoline, Akuammicine, (16*S*)-deshydroxymethylstemmadenine and Aspidospermatan Alkaloids

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1. General Information

All commercially available reagents were used without further purification unless otherwise noted. All solvents were dried and distilled as follow: THF and Et_2O were distilled from sodium; CH_2Cl_2 and toluene ware distilled from calcium hydride; $CHCl_3$ was distilled from P_2O_5, anhydrous ethyl acetate, acetonitrile, 2-Methylfuran, 1,2-dichloroethane, 1,4-dioxane and other solvents were commercially available. Reactions were monitored by thin layer chromatography (TLC) carried out on 0.2 mm commercial silica gel plates. TLC plates were visualized by exposure to ultraviolet light (UV, 254 nm) and/or exposure to an aqueous solution of ceric ammonium molybdate (CAM), an aqueous solution of potassium permanganate ($KMnO_4$), or an ethanolic solution of 4-anisaldehyde followed by heating with a heat gun. Column chromatography was carried out by normal 200-400 mesh silica gel.

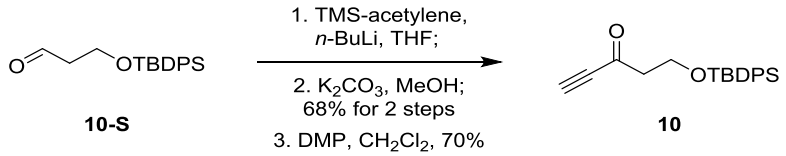
NMR spectra were obtained in Chloroform-*d*, DMSO-d_6 or Methanol-d_4 (*Sigma-Aldrich, Inc.*) at ambient temperature using Bruker Avance Neo 400 (400 MHz, ^{1}H at 400 MHz, ^{13}C at 101 MHz) or Bruker Avance III 500 (500 MHz, ^{1}H at 500 MHz, ^{13}C at 126 MHz) NMR spectrometer. Chemical shifts were reported in parts per million relatives (ppm, δ) to the internal solvent peak ($CDCl_3$, δ 7.26 for ^{1}H; δ 77.16 for ^{13}C. $(CD_3)_2SO$, δ 2.50 for ^{1}H; δ 39.52 for ^{13}C. CD_3OD, δ 3.31 for ^{1}H; δ 49.00 for ^{13}C). All ^{13}C NMR spectra were recorded with complete proton decoupling.

Melting points were recorded on a SGW X-4 apparatus. Optical rotations were measured on Anton Paar MCP 300 polarimeter. HRMS were obtained from IonSpec 4.7 Tesla FTMS (MALDI-TOF) and Bruker APEX III 7.0 Tesla FTMS (ESI-Quadrupole). Chiral HPLC analyses were performed on Waters 2487 Series using Daicel Chiralpak (AD-H, OD-H and IC) column with hexane, *i*-PrOH, or MeOH as the eluent.

2. Synthetic procedures of (+)-geissoschizoline

2.1 Experimental Procedures and Data

2.2.1 Preparation of compound 10



n-BuLi (2.5 M in THF; 84 mL, 210 mmol, 1.05 equiv.) was added dropwise to a solution of trimethylsilylacetylene (29.7 mL, 210 mmol, 1.05 equiv.) in 300 mL THF at -78 ºC. The mixture was stirred for 0.5 h, then aldehyde **10-S** (62.5 g, 200 mmol, 1.0 equiv.) in 100 mL THF was added dropwise to the reaction. The mixture was stirred at -78 ℃ for 2 h. The solvent was removed in vacuo and the residue was diluted with EtOAc (300 mL), washed with saturated NH_4Cl solution (150 mL). The aqueous phase was extracted with EtOAc (100 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4. The filtrate was concentrated under reduced pressure to give the crude product which was used directly in the next step without further purification.

The above residue was redissolved in MeOH (800 mL). To the stirred solution was added K_2CO_3 (33.2 g, 240 mmol, 1.2 equiv.) in one portion and the mixture was stirred at room temperature for 2 h. Upon the complete consumption of the starting material as indicated by TLC, the mixture was filtrated through Celite pad and MeOH was removed in vacuo. The residue was diluted with EtOAc (300 mL), washed with water (150 mL). The aqueous phase was extracted with EtOAc (100 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether/EtOAc = 70:1) to afford the pure product (46.0 mg, 136 mmol, 68% for 2 steps) as a colorless oil.

$NaHCO_3$ (54.6 g, 650 mmol, 5.0 equiv.), Dess-Martin periodinane (66.2 g, 156 mmol, 1.2 equiv.) ware added to a solution of previous product (44.0 g, 130 mmol, 1.0 equiv.) in 520 mL CH_2Cl_2 at 0 ºC. Then the mixture was stirred at room temperature for 3 h. Upon the complete consumption of the starting material as indicated by TLC, the mixture was filtrated through Celite pad and washed with water (200 mL). The aqueous phase was extracted with CH_2Cl_2 (150 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether/EtOAc = 150:1) to afford the pure product **10** (30.6 mg, 91 mmol, 70%).

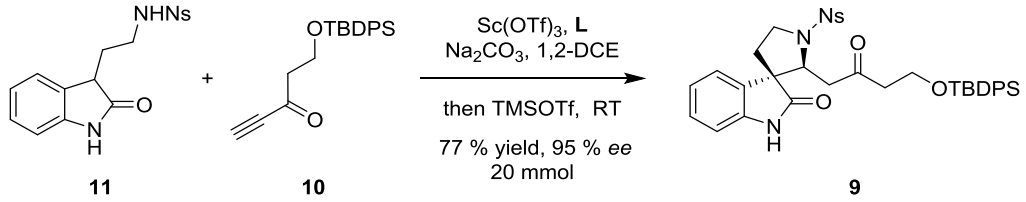
R_f = 0.6 (petroleum ether/EtOAc = 20:1, v/v), colorless oil.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 7.1 Hz, 4H), 7.46 – 7.38 (m, 6H), 4.05 (t, *J* = 6.1 Hz, 2H), 3.21 (s, 1H), 2.82 (t, *J* = 6.0 Hz, 2H), 1.06 (s, 9H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 185.8, 135.7, 133.4, 129.9, 127.8, 81.5, 78.9, 59.2, 48.3, 26.9, 19.3.

The spectroscopic data for this product match the literature data.[1]

2.2.2 Preparation of compound 9



N, N'-dioxide ligand **L** (678 mg, 1.2 mmol, 0.06 equiv.), Scandium triflate (492 mg, 1.0 mmol, 0.05 equiv.), and 4Å molecular sieves (2.00 g) were stirred in 50 mL CH_2Cl_2 at room temperature for 2 hours [2]. After that the solvent was removed in vacuo, 200 mL 1,2-DCE was added. Then oxindole **11** (7.2 g, 20.0 mmol, 1.0 equiv.), alkynone **10** (7.4 g, 22.0 mmol, 1.1 equiv.), Na_2CO_3 (424 mg, 4.0 mmol, 0.2 equiv.) were added to the suspension, and the mixture was stirred at 30 ℃ in oil bath for 48 h until the **11** was consumed. The resulting mixture was filtrated through Celite pad and diluted with CH_2Cl_2 (150 mL), washed with water (100 mL). The aqueous phase was extracted with CH_2Cl_2 (100 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4. The filtrate was concentrated under reduced pressure to give the crude product which was used directly in the next step without further purification.

The above residue was redissolved in 1,2-DCE (200 mL). To the stirred solution was added TMSOTf (362 μL, 2.0 mmol, 0.1 equiv.) slowly in 2 h at room temperature and the mixture was stirred for an additional 1 h. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (100 mL) and extracted with CH_2Cl_2 (100 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether/EtOAc = 3.8:1) to afford the pure product **9** (10.8 g, 15.4 mmol, 77%) and its isomer **9a** with 10:1 *dr*.

R_f = 0.4 (petroleum ether/EtOAc = 2:1, v/v), white crystalline solid.

M.p.: 83.3-85.4 ºC.

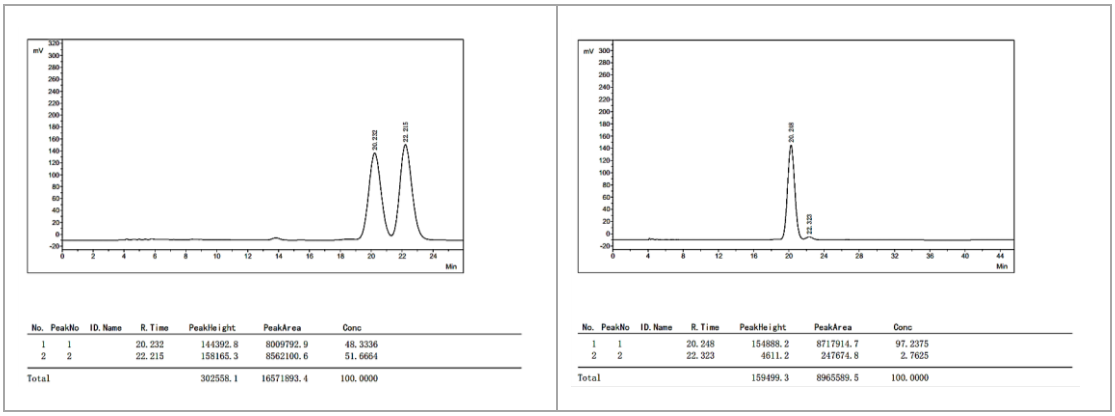
$[\alpha]_D^{20.0}$ = -36.2 (*c* = 0.61 in $CHCl_3$).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.15 (s, 1H), 8.01 (d, *J* = 7.4 Hz, 1H), 7.73 (t, *J* = 7.7 Hz, 1H), 7.67 – 7.60 (m, 6H), 7.43 – 7.33 (m, 6H), 7.07 (t, *J* = 7.7 Hz, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.67 (t, *J* = 7.6 Hz, 1H), 6.54 (d, *J* = 7.5 Hz, 1H), 4.61 (dd, *J* = 10.1, 3.4 Hz, 1H), 3.98 – 3.85 (m, 4H), 3.44 (dd, *J* = 18.2, 10.2 Hz, 1H), 3.15 (dd, *J* = 18.2, 3.4 Hz, 1H), 2.74 – 2.66 (m, 1H), 2.64 – 2.56 (m, 1H), 2.52 – 2.42 (m, 1H), 2.03 – 1.95 (m, 1H), 1.01 (s, 9H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 207.8, 177.4, 148.5, 139.6, 135.6, 134.0, 133.7, 133.6, 132.8, 131.8, 131.1, 129.8, 128.6, 127.81, 127.79, 124.0, 122.7, 122.4, 110.1, 63.1, 59.3, 55.0, 47.3, 45.8, 45.6, 34.9, 26.9, 19.2.

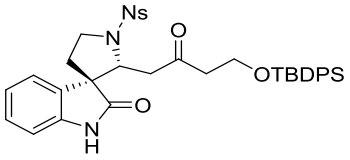
HRMS-ESI (*m/z*): [M + H]$^+$ calculated for $C_{37}H_{40}N_3O_7SSi$ 698.2351, found 698.2350.

HPLC: Enantiomeric excess was found to be 95% by chiral HPLC (ChiralPak AD-H column, *n*-hexane/*i*-PrOH = 8:2, 214 nm, 0.7 mL/min, t_{major} = 20.25 min, t_{minor} = 22.32 min).



No.	PeakNo	ID. Name	R. Time	PeakHeight	PeakArea	Conc
1	1		20.232	144392.8	8009792.9	48.3336
2	2		22.215	158165.3	8562100.6	51.6664
Total				302558.1	16571893.4	100.0000

No.	PeakNo	ID. Name	R. Time	PeakHeight	PeakArea	Conc
1	1		20.248	154888.2	8717914.7	97.2375
2	2		22.323	4611.2	247674.8	2.7625
Total				159499.3	8965589.5	100.0000



9a

R_f = 0.45 (petroleum ether/EtOAc = 20:1, v/v), white crystalline solid.

M.p.: 86.0-87.3 ºC.

$[\alpha]_D^{20.0}$ = +8.8 (*c* = 0.17 in $CHCl_3$).

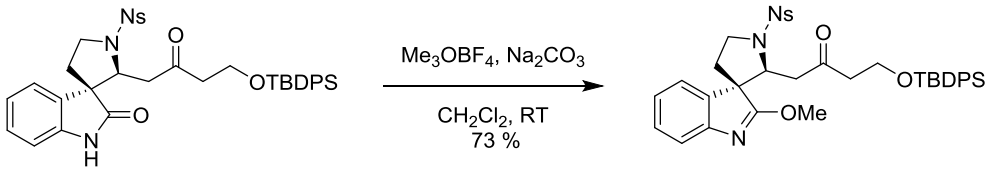
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.36 (s, 1H), 8.13 – 8.08 (m, 1H), 7.73 – 7.69 (m, 2H), 7.61 – 7.57 (m, 5H), 7.44 – 7.33 (m, 7H), 7.17 (d, *J* = 7.4 Hz, 1H), 7.11 (t, *J* = 7.8 Hz, 1H), 6.93 (t, *J* = 7.6 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 4.70 (dd, *J* = 9.5, 4.4 Hz, 1H), 4.06 – 4.00 (m, 1H), 3.82 – 3.74 (m, 1H), 3.69 – 3.62 (m, 1H), 3.55 – 3.48 (m, 1H), 3.27 (dd, *J* = 18.3, 4.4 Hz, 1H), 2.84 (dd, *J* = 18.4, 9.6 Hz, 1H), 2.36 – 2.28 (m, 1H), 2.20 – 2.06 (m, 2H), 1.99 – 1.93 (m, 1H), 0.99 (s, 9H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 206.3, 179.2, 149.0, 141.1, 135.59, 135.58, 134.2,

133.5, 133.4, 131.7, 131.2, 130.4, 129.82, 129.81, 129.1, 129.0, 127.8, 124.4, 123.9, 122.4, 110.6, 61.8, 59.1, 57.1, 48.5, 46.7, 45.6, 36.1, 26.9, 19.2.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{37}H_{40}N_3O_7SSi$ 698.2351, found 698.2347.

2.2.3 Preparation of compound 12-S1



9 **12-S1**

Me_3OBF_4 (3.4 g, 23.0 mmol, 1.5 equiv.), Na_2CO_3(2.4 g, 23.0 mmol, 1.5 equiv.) and 4Å molecular sieves (3.0 g) were added to a solution of **9** (10.7 g, 15.3 mmol, 1.0 equiv.) in 150 mL CH_2Cl_2 and the mixture was stirred at room temperature overnight. Upon the complete consumption of the starting material as indicated by TLC, the mixture was filtrated through Celite pad and washed with water (100 mL). The aqueous phase was extracted with CH_2Cl_2 (100 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (CH_2Cl_2/EtOAc = 100:1) to afford the pure product **12-S1** (8.0 g, 11.2 mmol, 73%).

$\mathbf{R}_f$ = 0.5 (CH_2Cl_2/EtOAc = 20:1, v/v), white crystalline solid.

M.p.: 59.4-60.9 ºC.

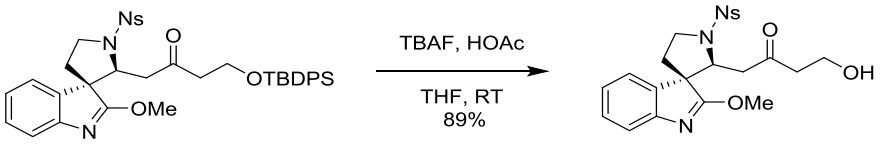
$\mathbf{[\alpha]_D^{20.0}}$ = -44.3 (*c* = 0.13 in $CHCl_3$).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.01 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.77 – 7.70 (m, 1H), 7.69 – 7.59 (m, 6H), 7.45 – 7.34 (m, 6H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 7.0 Hz, 1H), 6.83 (t, *J* = 8.1 Hz, 1H), 6.67 (d, *J* = 8.7 Hz, 1H), 4.58 (dd, *J* = 7.4, 4.9 Hz, 1H), 4.03 – 3.80 (m, 7H), 3.21 (dd, *J* = 18.0, 4.9 Hz, 1H), 2.70 – 2.62 (m, 2H), 2.61 – 2.51 (m, 1H), 2.36 – 2.27 (m, 1H), 2.07 – 1.95 (m, 1H), 1.00 (s, 9H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 205.9, 179.3, 151.7, 148.6, 137.6, 135.6, 134.0, 133.52, 133.45, 131.8, 131.5, 131.2, 129.81, 129.79, 129.0, 127.83, 127.80, 124.1, 123.9, 121.2, 119.0, 61.2, 59.9, 59.2, 56.7, 47.5, 45.7, 45.6, 32.8, 26.9, 19.2.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{38}H_{42}N_3O_7SSi$ 712.2507, found 712.2500.

2.2.4 Preparation of compound 12-S2



12-S1 **12-S2**

HOAc (13.5 mL, 224 mmol, 20 equiv.), TBAF (1.0 M; 33.6 mL, 33.6 mmol, 3.0 equiv.) were added to a solution of **12-S1** (8.0 g, 11.2 mmol, 1.0 equiv.) in 112 mL THF, then the mixture was stirred at room temperature overnight. Upon the complete consumption of the starting material as indicated by TLC, the solvent was removed in vacuo and the residue was diluted with EtOAc (100 mL), washed with saturated NH_4Cl solution (100 mL), and basified with saturated $NaHCO_3$ solution. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (CH_2Cl_2/MeOH = 100:1) to afford the pure product **12-S2** (4.72 g, 10.0 mmol, 89%).

R_f = 0.2 (CH_2Cl_2/MeOH = 15:1, v/v), white amorphous solid.

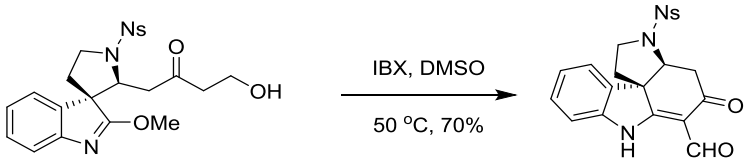
$[\alpha]_D^{20.0}$ = -55.5 (*c* = 0.22 in $CHCl_3$).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.12 (dd, *J* = 7.9, 1.4 Hz, 1H), 8.06 (dd, *J* = 7.9, 1.4 Hz, 1H), 8.00 (td, *J* = 7.7, 1.4 Hz, 1H), 7.94 (td, *J* = 7.6, 1.4 Hz, 1H), 7.27 – 7.16 (m, 2H), 6.77 (td, *J* = 7.4, 1.4 Hz, 1H), 6.49 (d, *J* = 7.4 Hz, 1H), 4.54 (s, 1H), 4.42 (dd, *J* = 9.4, 3.8 Hz, 1H), 3.88 (s, 3H), 3.85 – 3.74 (m, 2H), 3.58 (s, 2H), 3.05 (dd, *J* = 18.4, 9.5 Hz, 1H), 2.93 (dd, *J* = 18.4, 3.9 Hz, 1H), 2.56 (dt, *J* = 16.5, 6.3 Hz, 1H), 2.51 – 2.43 (m, 2H), 2.01 – 1.92 (m, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 206.3, 178.3, 151.4, 147.7, 139.2, 135.1, 132.6, 130.1, 130.0, 128.4, 124.4, 123.4, 120.8, 118.3, 61.0, 58.4, 56.6, 55.9, 46.6, 45.2, 45.1, 31.9.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{22}H_{24}N_3O_7S$ 474.1329, found 474.1327.

2.2.5 Preparation of compound 12



12-S2 **12**

IBX (7.0 g, 24.9 mmol, 2.5 equiv.) was added to a solution of **12-S2** (4.72 g, 10.0 mmol, 1.0 equiv.) in 130 mL DMSO, and the mixture was stirred at 50 ºC in oil bath overnight. The resulting solution was diluted with EtOAc (150 mL), washed with water (150 mL). The aqueous phase was extracted with EtOAc (100 mL×5). The combined organic layers were

washed with brine (80 mL×2), dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel chromatography (CH_2Cl_2/MeOH = 100:1) to afford the pure product **12** (3.0 mg, 6.9 mmol, 70%).

R_f = 0.3 (petroleum ether/EtOAc = 1:1, v/v), yellow amorphous solid.

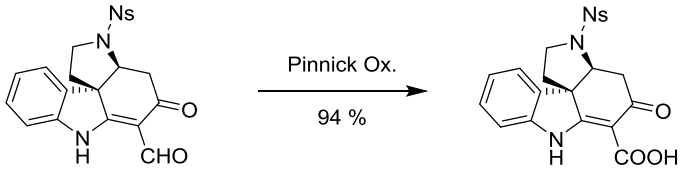
$[\alpha]_D^{20.0}$ = -153.5 (*c* = 0.19 in $CHCl_3$).

^{1}H NMR (500 MHz, DMSO-d_6) δ 12.20 (s, 1H), 9.85 (s, 1H), 8.21 (dd, *J* = 7.9, 1.4 Hz, 1H), 8.07 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.98 (td, *J* = 7.7, 1.4 Hz, 1H), 7.92 (td, *J* = 7.7, 1.3 Hz, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.32 (t, *J* = 7.1 Hz, 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 7.5 Hz, 1H), 4.68 (t, *J* = 7.8 Hz, 1H), 3.95 (t, *J* = 9.9 Hz, 1H), 3.84 – 3.76 (m, 1H), 2.85 (dd, *J* = 18.3, 8.0 Hz, 1H), 2.66 – 2.56 (m, 2H), 2.08 (dd, *J* = 12.7, 7.4 Hz, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 191.4, 187.1, 171.7, 147.3, 142.5, 135.0, 134.3, 132.7, 131.6, 130.1, 128.8, 124.2, 123.7, 121.4, 113.6, 107.4, 59.2, 55.3, 44.9, 40.8, 40.1.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{21}H_{18}N_3O_6S$ 440.0911, found 440.0906.

2.2.6 Preparation of compound 8-S1



12 **8-S1**

$NaH_2PO_4 \cdot 2H_2O$ (10.8 g, 69.0 mmol, 10 equiv.), $NaClO_2$ (3.12 g, 34.5 mmol, 5 equiv.), 2-Methyl-2-butene (7.3 mL, 69.0 mmol, 10 equiv.) were added to a solution of **12** (3.0 g, 6.9 mmol, 1.0 equiv.) in 100 mL THF, 20 mL *t*-BuOH and 20 mL H_2O. The reaction was stirred 4 h at room temperature. The solvent was removed in vacuo and the residue was diluted with CH_2Cl_2 (100 mL), washed with water (100 mL). The aqueous phase was extracted with CH_2Cl_2 (100 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (CH_2Cl_2/MeOH = 150:1) to afford the pure product **8-S1** (2.95 g, 6.5 mmol, 94%).

R_f = 0.3 (CH_2Cl_2/MeOH = 20:1, v/v), white crystalline solid.

M.p.: 63.5-65.0 ºC.

$[\alpha]_D^{20.0}$ = -131.0 (*c* = 0.10 in THF).

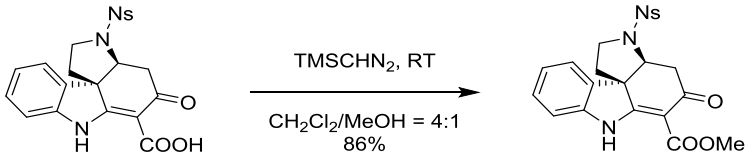
^{1}H NMR (500 MHz, DMSO-d_6) δ 14.15 (s, 1H), 12.15 (s, 1H), 8.20 (dd, *J* = 7.8, 1.4 Hz, 1H), 8.07 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.98 (td, *J* = 7.7, 1.4 Hz, 1H), 7.92 (td, *J* = 7.7, 1.4 Hz, 1H),

7.53 (d, *J* = 7.8 Hz, 1H), 7.34 (t, *J* = 8.3 Hz, 1H), 6.99 (t, *J* = 7.0 Hz, 1H), 6.90 (d, *J* = 6.5 Hz, 1H), 4.76 (t, *J* = 7.8 Hz, 1H), 3.95 (t, *J* = 9.2 Hz, 1H), 3.85 – 3.75 (m, 1H), 2.96 (dd, *J* = 18.6, 7.9 Hz, 1H), 2.85 (dd, *J* = 18.6, 7.9 Hz, 1H), 2.75 – 2.65 (m, 1H), 2.08 (dd, *J* = 12.7, 7.5 Hz, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 195.3, 175.6, 166.2, 147.2, 142.2, 135.1, 134.8, 132.8, 131.6, 130.1, 128.9, 124.3, 124.0, 121.2, 114.0, 96.7, 59.4, 56.0, 54.9, 44.9, 40.1.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{21}H_{18}N_3O_7S$ 456.0860, found 456.0858.

2.2.7 Preparation of compound 8-S2



8-S1 **8-S2**

$TMSCHN_2$ (2.0 M in hexanes; 9.8 mL, 19.5 mmol, 3.0 equiv.,) was added dropwise to a solution of **8-S1** (2.96 g, 6.5 mmol, 1.0 equiv.) in 120 mL CH_2Cl_2 and 30 mL MeOH. The reaction was stirred at room temperature overnight. Upon the complete consumption of the starting material as indicated by TLC, HOAc was added until the bubble disappeared. The solvent was removed in vacuo and the residue was diluted with CH_2Cl_2 (100 mL), washed with saturated $NaHCO_3$ solution (100 mL). The aqueous phase was extracted with CH_2Cl_2 (80 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (CH_2Cl_2/MeOH = 50:1) to afford the pure product **8-S2** (2.62 g, 5.6 mmol, 86%).

R_f = 0.1 (petroleum ether/EtOAc = 1:1, v/v), white crystalline solid.

M.p.: 48.6-49.9 ºC.

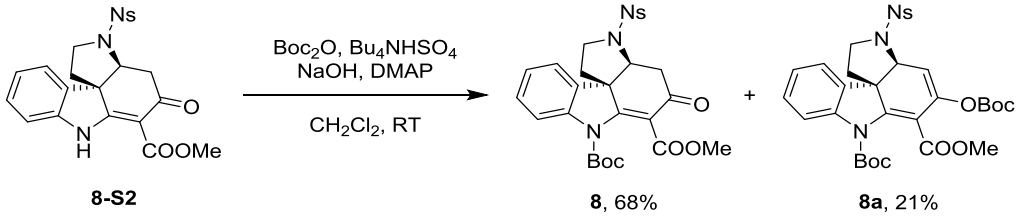
$[\alpha]_D^{20.0}$ = -56.8 (*c* = 0.08 in $CHCl_3$).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 10.70 (s, 1H), 8.10 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.82 – 7.71 (m, 2H), 7.69 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.32 (td, *J* = 7.7, 1.1 Hz, 1H), 7.25 (d, *J* = 8.9 Hz, 1H), 7.08 (d, *J* = 7.9 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 4.67 (t, *J* = 7.9 Hz, 1H), 4.03 – 3.95 (m, 2H), 3.88 (s, 3H), 3.11 (dd, *J* = 18.7, 8.7 Hz, 1H), 2.54 – 2.44 (m, 2H), 2.23 (dd, *J* = 12.6, 5.5 Hz, 1H).

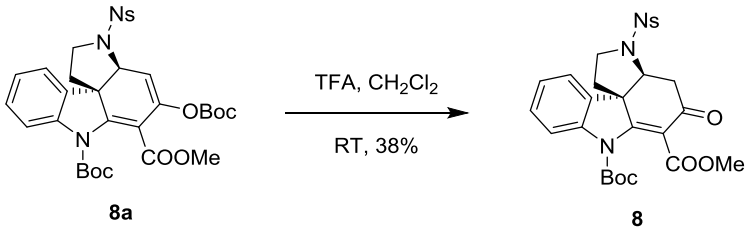
^{13}C NMR (126 MHz, DMSO-d_6) δ 187.7, 172.9, 165.6, 147.3, 142.5, 135.0, 134.2, 132.7, 131.3, 130.2, 128.8, 124.2, 122.7, 121.1, 112.6, 98.6, 58.0, 55.3, 54.9, 50.8, 44.9, 42.5, 41.3.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{22}H_{20}N_3O_7S$ 470.1016, found 470.1019.

2.2.8 Preparation of compound 8



NaOH (448 mg, 11.2 mmol, 2.0 equiv.), Bu_4NHSO_4 (190 mg, 0.56 mmol, 0.1 equiv.), DMAP (68 mg, 0.56 mmol, 0.1 equiv.) and Boc_2O (2.44 g, 11.2 mmol, 2.0 equiv.) were added to a solution of **8-S2** (2.62 g, 5.6 mmol, 1.0 equiv.) in 112 mL CH_2Cl_2. The reaction was stirred at room temperature for 3 h. After the starting material disappeared, the reaction was quenched with a saturated aqueous solution of NH_4Cl (100 mL) and extracted with CH_2Cl_2 (100 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether/EtOAc = 3:1) to afford the pure products **8** (2.17 g, 3.8 mmol, 68%) and **8a** (788 mg, 1.2 mmol, 21%) as white solid.



TFA (99 μL, 1.3 mmol, 1.1 equiv.) was added to a solution of **8a** (788 mg, 1.2 mmol, 1.0 equiv.) in 12 mL CH_2Cl_2. The reaction was stirred at room temperature for 4 h. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (5 mL) and extracted with CH_2Cl_2 (10 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether/EtOAc = 3:1) to afford the pure products **8** (253 mg, 0.44 mmol, 38%) and starting material **8a** (251 mg, 0.37 mmol, 32%).

Compound 8

R_f = 0.2 (petroleum ether/EtOAc = 1:1, v/v), white crystalline solid.

M.p.: 99.3-101.0 ºC.

$[\alpha]_D^{20.0}$ = -89.1 (*c* = 0.08 in $CHCl_3$).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.11 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.81 – 7.73 (m, 2H),

7.69 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.29 (td, *J* = 7.9, 1.3 Hz, 1H), 7.14 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.00 (td, *J* = 7.6, 1.0 Hz, 1H), 4.69 (dd, *J* = 10.2, 6.9 Hz, 1H), 3.99 (t, *J* = 9.7 Hz, 1H), 3.90 – 3.84 (m, 1H), 3.82 (s, 3H), 3.03 (dd, *J* = 17.1, 6.9 Hz, 1H), 2.73 (dd, *J* = 22.7, 10.0 Hz, 1H), 2.59 (dd, *J* = 17.1, 10.2 Hz, 1H), 2.23 (dd, *J* = 12.7, 7.2 Hz, 1H), 1.62 (s, 9H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 190.4, 164.5, 160.3, 149.7, 148.2, 139.9, 134.4, 133.4, 132.9, 132.3, 130.6, 129.3, 125.1, 124.4, 122.0, 117.6, 115.9, 85.9, 60.6, 52.9, 52.7, 45.7, 42.0, 39.2, 28.3.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{27}H_{28}N_3O_9S$ 570.1540, found 570.1544.

Compound 8a

R_f = 0.6 (petroleum ether/EtOAc = 1:1, v/v), white crystalline solid.

M.p.: 113.2-114.8 ºC.

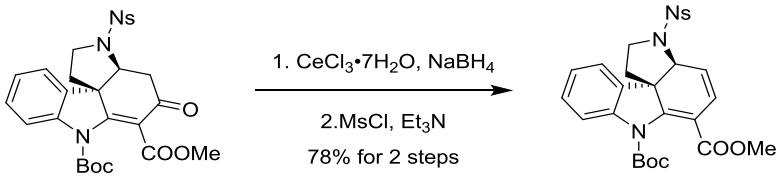
$[\alpha]_D^{20.0}$ = -130.1 (*c* = 0.09 in $CHCl_3$).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.10 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.80 – 7.72 (m, 2H), 7.70 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.61 (d, *J* = 8.1 Hz, 1H), 7.22 (td, *J* = 7.9, 1.3 Hz, 1H), 6.83 (t, *J* = 7.0 Hz, 1H), 6.73 (d, *J* = 7.6 Hz, 1H), 5.41 (d, *J* = 2.2 Hz, 1H), 5.19 (d, *J* = 2.2 Hz, 1H), 3.75 (s, 3H), 3.72 – 3.62 (m, 2H), 2.97 – 2.89 (m, 1H), 2.04 – 1.99 (m, 1H), 1.57 (s, 9H), 1.54 (s, 9H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 163.6, 151.3, 150.0, 148.2, 147.5, 142.8, 141.6, 134.1, 133.1, 132.9, 132.1, 130.6, 128.9, 124.3, 121.5, 116.3, 110.8, 107.5, 84.4, 83.7, 62.7, 53.5, 52.1, 43.6, 37.2, 28.2, 27.8.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{32}H_{36}N_3O_{11}S$ 670.2065, found 670.2062.

2.2.9 Preparation of compound 13



$CeCl_3 \cdot 7H_2O$ (3.13 g, 8.4 mmol, 2.0 equiv.) was added to a solution of **8** (2.39 g, 4.2 mmol, 1.0 equiv.) in 21 mL MeOH and 21 mL THF. The mixture was stirred at 0 ºC for 10 min and then $NaBH_4$ (238 mg, 6.3 mmol, 1.5 equiv.) was slowly added. The mixture was stirred for 30 min at 0 ºC. Upon the complete consumption of the starting material as

indicated by TLC, the solvent was removed in vacuo and the residue was diluted with CH_2Cl_2 (50 mL), washed with saturated $NaHCO_3$ solution (50 mL). The aqueous phase was extracted with CH_2Cl_2 (50 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give the crude product which was used directly in the next step without further purification.

Et_3N (1.8 mL, 12.6 mmol, 3.0 equiv.) was added to a solution of the precious crude product in 42 mL CH_2Cl_2. The mixture was stirred at 0 ºC for 10 min and then MsCl (0.5 mL, 6.3 mmol, 1.5 equiv.) was added dropwise. The mixture was stirred at room temperature for 1 h. The reaction was diluted with CH_2Cl_2 (30 mL), washed with water (50 mL). The aqueous phase was extracted with CH_2Cl_2 (50 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether/EtOAc = 4:1) to afford the pure product **13** (1.81 g, 3.3 mmol, 78% for 2 steps).

R_f = 0.7 (petroleum ether/EtOAc = 2:1, v/v), white crystalline solid.

M.p.: 105.0-107.1 ºC.

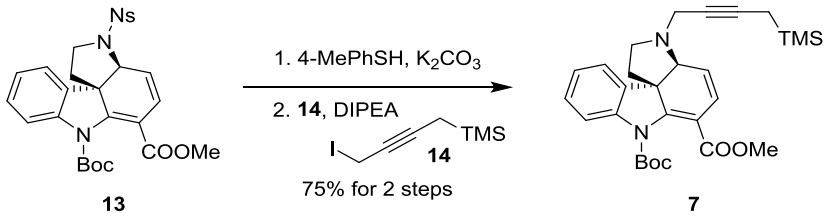
$[\alpha]_D^{20.0}$ = -162.7 (*c* = 0.30 in $CHCl_3$).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 7.8 Hz, 1H), 7.82 – 7.73 (m, 2H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.22 (t, *J* = 7.8 Hz, 1H), 6.81 (t, *J* = 7.5 Hz, 1H), 6.66 (d, *J* = 7.4 Hz, 1H), 6.27 (d, *J* = 10.0 Hz, 1H), 5.62 (d, *J* = 10.1 Hz, 1H), 5.06 (s, 1H), 3.77 (s, 3H), 3.67 – 3.53 (m, 2H), 2.74 – 2.63 (m, 1H), 1.99 – 1.90 (m, 1H), 1.56 (s, 9H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 166.3, 150.3, 148.2, 147.0, 141.9, 134.1, 133.4, 133.1, 132.0, 130.6, 128.8, 124.24, 124.16, 122.8, 121.5, 116.3, 108.5, 83.9, 63.1, 53.3, 51.9, 43.4, 36.9, 31.7, 28.2.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{27}H_{28}N_3O_8S$ 554.1592, found 554.1597.

2.2.10 Preparation of compound 7



K_2CO_3 (1.37 g, 9.9 mmol, 3.0 equiv.), 4-MePhSH (820 mg, 6.6 mmol, 2.0 equiv.) was added to a solution of **13** (1.81 g, 3.3 mmol, 1.0 equiv.) in 33 mL *N,N*-Dimethylformamide. The reaction was stirred at room temperature overnight. The resulting solution was diluted

with EtOAc (50 mL), washed with water (50 mL). The aqueous phase was extracted with EtOAc (50 mL×5). The combined organic layers were washed with brine (30 mL×2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give the crude product which was used directly in the next step without further purification.

The above residue was redissolved in 33 mL CH_3CN. To the stirred solution was added **14** (1.25 g, 5.0 mmol, 1.5 equiv.) and DIPEA (1.7 mL, 9.9 mmol, 3.0 equiv.) in one portion. The resulting reaction mixture was stirred at room temperature for 5 h. The solvent was removed in vacuo and the residue was diluted with CH_2Cl_2 (50 mL), washed with saturated NH_4Cl solution (50 mL). The aqueous phase was extracted with CH_2Cl_2 (50 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether/EtOAc = 10:1) to afford the pure product **7** (1.22 g, 2.5 mmol, 75% for 2 steps).

R_f = 0.3 (petroleum ether/EtOAc = 20:1, v/v), yellow crystalline solid.

M.p.: 102.7-104.5 ºC.

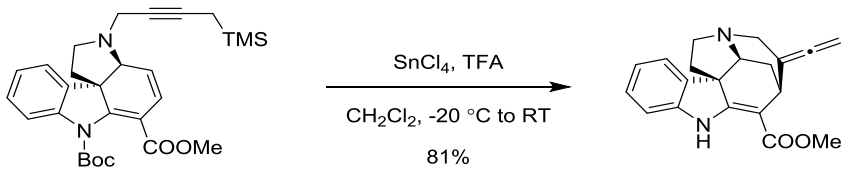
$[\alpha]_D^{20.0}$ = -112.6 (*c* = 0.14 in $CHCl_3$).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.65 – 7.57 (m, 2H), 7.22 (t, *J* = 8.6 Hz, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.31 (dd, *J* = 10.1, 2.1 Hz, 1H), 5.83 (dd, *J* = 10.1, 2.1 Hz, 1H), 4.14 (s, 1H), 3.77 (s, 3H), 3.70 (t, *J* = 2.5 Hz, 2H), 3.03 (q, *J* = 7.7 Hz, 1H), 2.61 (td, *J* = 8.8, 3.8 Hz, 1H), 2.48 – 2.39 (m, 1H), 1.95 – 1.88 (m, 1H), 1.57 (s, 9H), 1.50 (t, *J* = 2.5 Hz, 2H), 0.10 (s, 9H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 166.9, 150.7, 149.5, 141.8, 137.6, 127.7, 124.0, 123.1, 123.0, 121.3, 115.5, 108.3, 83.1, 82.1, 75.6, 64.3, 53.1, 51.7, 48.0, 40.8, 40.6, 28.3, 7.2, -1.8.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{28}H_{37}N_2O_4Si$ 493.2517, found 493.2515.

2.2.11 Preparation of compound 6



7 **6**

$SnCl_4$ (1.0 M in CH_2Cl_2; 4.9 mL, 4.9 mmol, 2.0 equiv.) was added dropwise to a solution of **7** (1.22 g, 2.5 mmol, 1.0 equiv.) in 25 mL anhydrous CH_2Cl_2 at -20 ºC under argon atmosphere. The mixture was stirred at -20 ºC for 1 h. Then TFA (0.95 mL, 12.4 mmol, 5.0 equiv.) was added dropwise to the reaction. After it was stirred at -20 ºC for 1 h, the reaction was moved to room temperature for final 5 h. The resulting solution was diluted with CH_2Cl_2

(25 mL), washed with saturated $NaHCO_3$ solution (25 mL). The aqueous phase was extracted with CH_2Cl_2 (25 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (CH_2Cl_2/MeOH/$NH_3 \cdot H_2O$= 100:1:0.1) to afford the pure product **6** (641 mg, 2.0 mmol, 81%).

R_f = 0.5 (CH_2Cl_2/MeOH = 10:1, v/v), yellow crystalline solid.

M.p.: 133.0-133.9 ºC.

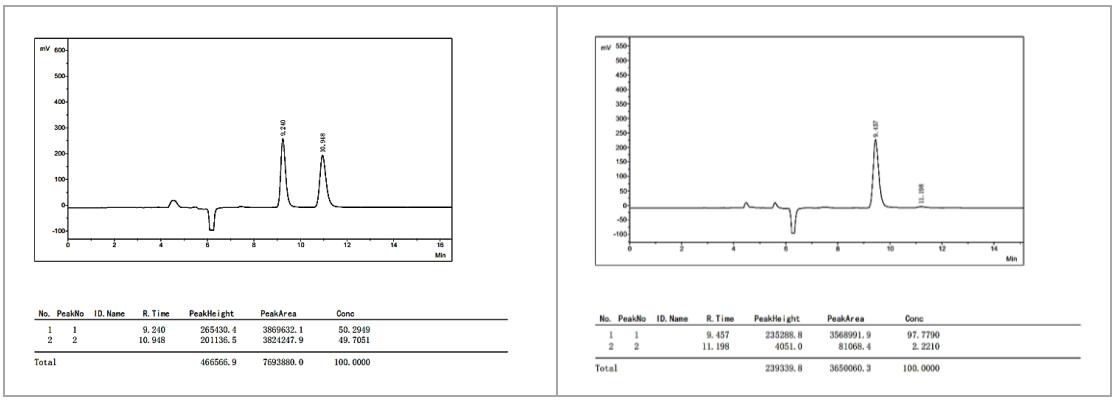
$[\alpha]_D^{20.0}$ = -375.3 (*c* = 0.06 in $CHCl_3$).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.82 (s, 1H), 7.21 (d, *J* = 7.4 Hz, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 6.88 (t, *J* = 7.0 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 4.62 (t, *J* = 4.4 Hz, 2H), 4.07 (s, 1H), 4.01 (dt, *J* = 15.1, 4.7 Hz, 1H), 3.96 (s, 1H), 3.75 (s, 3H), 3.28 – 3.21 (m, 1H), 3.08 (d, *J* = 15.2 Hz, 1H), 3.03 (ddd, *J* = 12.1, 6.6, 2.7 Hz, 1H), 2.49 (ddd, *J* = 12.3, 11.2, 6.6 Hz, 1H), 2.39 – 2.32 (m, 1H), 1.88 (ddd, *J* = 12.4, 5.8, 2.7 Hz, 1H), 1.30 – 1.24 (m, 1H).

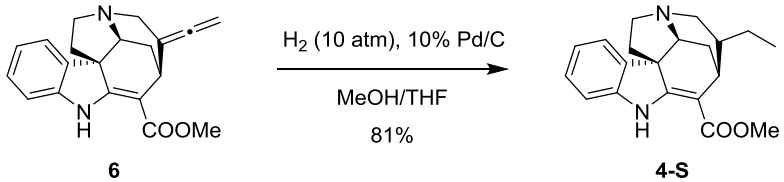
^{13}C NMR (126 MHz, Chloroform-*d*) δ 204.6, 168.1, 166.9, 143.8, 136.2, 128.0, 121.0, 120.9, 109.6, 102.1, 100.0, 75.4, 60.1, 58.1, 55.5, 51.7, 51.1, 46.4, 29.0, 28.8.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{20}H_{21}N_2O_2$ 321.1598, found 321.1601.

HPLC: Enantiomeric excess was found to be 96% by chiral HPLC (ChiralPak IC column, *n*-hexane/*i*-PrOH/ diethylamine = 75:25:0.1, 214 nm, 0.7 mL/min, t_{major} = 9.46 min, t_{minor} = 11.20 min).



2.2.12 Preparation of compound 4-S



6 **4-S**

To a solution of compound **6** (641 mg, 2.0 mmol, 1.0 equiv.) in 20 mL MeOH/THF (v/v=1:1) was added 10% Pd/C (wet, 640 mg, 10 weight% palladium). Hydrogenate the mixture at 10 atm of hydrogen atmosphere at room temperature for 12 h. The mixture was filtrated through Celite pad and the solvent was removed in vacuo. The residue was purified by silica gel chromatography (CH_2Cl_2/MeOH/$NH_3 \cdot H_2O$= 80:1:0.1) to afford the pure product **4-S** (526 mg, 1.62 mmol, 81%).

R_f = 0.4 (CH_2Cl_2/MeOH = 10:1, v/v), white amorphous solid.

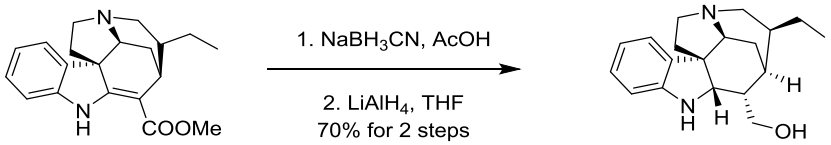
$[\alpha]_D^{25.0}$ = -428.4 (*c* = 0.08 in MeOH); {lit.[3] $[\alpha]_D^{23}$ = -508 (*c* = 0.55 in MeOH)}.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.02 (s, 1H), 7.15 (d, *J* = 7.3 Hz, 1H), 7.11 (t, *J* = 7.8 Hz, 1H), 6.87 (t, *J* = 7.3 Hz, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 3.86 (s, 1H), 3.74 (s, 3H), 3.14 (d, *J* = 3.4 Hz, 1H), 3.08 – 3.00 (m, 1H), 2.96 (dd, *J* = 12.8, 6.8 Hz, 1H), 2.91 – 2.86 (m, 1H), 2.82 (dd, *J* = 11.0, 6.7 Hz, 1H), 2.04 – 1.97 (m, 2H), 1.82 (dd, *J* = 12.8, 6.3 Hz, 1H), 1.71 – 1.63 (m, 1H), 1.42 – 1.32 (m, 2H), 1.07 – 0.99 (m, 1H), 0.99 – 0.94 (m, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.7, 168.8, 144.5, 134.7, 128.1, 121.4, 119.9, 110.0, 98.8, 61.2, 55.7, 53.7, 51.3, 51.2, 42.2, 39.0, 31.1, 30.5, 26.0, 11.7.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{20}H_{25}N_2O_2$ 325.1911, found 325.1918.

2.2.12 Preparation of geissoshcizoline (4)



4-S geissoshcizoline (**4**)

$NaCNBH_3$ (509 mg, 8.1 mmol, 5.0 equiv.) was added to a solution of **4-S** (526 mg, 1.62 mmol, 1.0 equiv.) in 54 mL AcOH over 20 min at 0 ºC. After being stirred at room temperature for 10 min, the reaction was quenched with a cold saturated aqueous solution of $NaHCO_3$ (100 mL) and extracted with CH_2Cl_2 (100 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4. The filtrate was concentrated under reduced pressure to give the crude product which was used directly in the next step without further purification.

The above residue was redissolved in 54 mL anhydrous THF. To the stirred solution was added $LiAlH_4$ (123 mg, 3.2 mmol, 5.0 equiv.) was added at 0 ºC. The reaction solution was stirred at 0 °C for 1 h, and then warmed to 10 °C and stirred for an additional 6 h. The reaction was diluted with EtOAc (50 mL), quenched by slow addition of H_2O (10 mL) and 15% aq. NaOH (10 mL) at 0 °C. The aqueous phase was extracted with EtOAc (50 mL×3).

The combined organic layers were washed saturated $NaHCO_3$ solution (50 mL) and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (CH_2Cl_2/MeOH/$NH_3 \cdot H_2O$= 20:1:0.1) to afford the pure product **4** (338 mg, 1.13 mmol, 70% for 2 steps).

$\mathbf{R_f}$ = 0.2 (CH_2Cl_2/MeOH = 10:1, v/v), white amorphous solid.

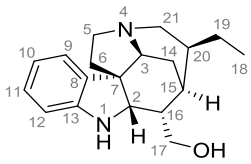
$\mathbf{[\alpha]_D^{25.0}}$ = +32.0 (*c* = 0.03 in MeOH); {lit.[3] $[\alpha]_D^{23}$ = +18.3 (*c* = 1.34 in MeOH)}.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.03 (dd, *J* = 15.3, 7.2 Hz, 2H), 6.76 (t, *J* = 7.1 Hz, 1H), 6.60 (d, *J* = 7.7 Hz, 1H), 4.13 (brs, 1H), 4.00 (d, *J* = 5.6 Hz, 1H), 3.76 (t, *J* = 10.2 Hz, 1H), 3.69 (dd, *J* = 10.2, 5.6 Hz, 1H), 3.15 – 3.02 (m, 1H), 3.00 – 2.91 (m, 1H), 2.91 (brs, 1H), 2.85 (dd, *J* = 11.6, 4.7 Hz, 1H), 2.34 – 2.24 (m, 3H), 2.18 (ddd, *J* = 13.3, 4.3, 2.5 Hz, 1H), 1.92 – 1.84 (m, 1H), 1.67 – 1.61 (m, 1H), 1.60 – 1.53 (m, 1H), 1.43 (brs, 1H), 1.27 – 1.16 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 149.7, 137.9, 127.7, 122.5, 119.5, 109.8, 67.5, 66.4, 65.2, 55.6, 53.4, 50.4, 42.5, 39.8, 34.4, 28.8, 26.3, 24.3, 11.8.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{19}H_{27}N_2O$ 299.2118, found 299.2124.

2.2 Comparison of Spectroscopic Data of (+)-geissoschizoline



geissoshcizoline (**4**)

Table S1. ^{1}H NMR spectroscopic data comparison [3,4]

Position of hydrogens	δ_H of natural (+)-geissoschizoline (500 MHz, $CDCl_3$) [4]	δ_H of Andrade′s synthetic (+)-geissoschizoline (400 MHz, $CDCl_3$) [3]	δ_H of our synthetic (+)-geissoschizoline (400 MHz, $CDCl_3$)	$\Delta\delta_H$ (δ_{ours} vs $\delta_{Andrade's}$)
9	7.04 (d, *J* = 7.6 Hz,1H)	7.04 (dd, *J* = 14.9, 7.4 Hz, 2H)	7.03 (dd, *J* = 15.3, 7.2 Hz, 2H)	-0.01
11	7.02 (td, *J* = 7.6, 0.9 Hz, 1H)			
10	6.76 (td, *J* = 7.6, 0.9 Hz, 1H)	6.76 (t, *J* = 7.4 Hz, 1H)	6.76 (t, *J* = 7.1 Hz, 1H)	0
12	6.59 (d, *J* = 7.6 Hz,1H)	6.60 (d, *J* = 7.7 Hz, 1H)	6.60 (d, *J* = 7.7 Hz, 1H)	0
OH	nr	4.14 (brd, *J* = 3.2 Hz, 1H)	4.13 (brs, 1H)	-0.01
2	4.00 (d, *J* = 5.5 Hz, 1H)	4.00 (t, *J* = 4.4 Hz, 1H)	4.00 (d, *J* = 5.6 Hz, 1H)	0
17a	3.74 (t, *J* = 10.4 Hz, 1H)	3.76 (t, *J* = 10.2 Hz, 1H)	3.76 (t, *J* = 10.2 Hz, 1H)	0
17b	3.67 (dd, *J* = 10.4, 5.5 Hz, 1H)	3.68 (dd, *J* = 10.1, 5.6 Hz, 1H)	3.69 (dd, *J* = 10.2, 5.6 Hz, 1H)	+0.01
NH	nr	3.36 (brs, 1H)	nr	-
5a	3.09 (m, 1H)	3.08 (dd, *J* = 20.6, 10.2 Hz, 1H)	3.15 – 3.02 (m, 1H)	-
5b	2.95 (m, 1H)	2.99 – 2.93 (m, 1H)	3.00 – 2.91 (m, 1H)	-
3	2.93 (brs, 1H)	2.91 (brs, 1H)	2.91 (brs, 1H)	-
21a	2.86 (dd, *J* = 11.6, 4.6 Hz, 1H)	2.84 (dd, *J* = 11.6, 4.5 Hz, 1H)	2.85 (dd, *J* = 11.6, 4.7 Hz, 1H)	+0.01
21b	2.31 (m, 1H)	2.31 – 2.23 (m, 3H)	2.34 – 2.24 (m, 3H)	-
6	2.27 (m, 2H)			
14a	2.20 (ddd, *J* =13.4, 4.0, 2.4 Hz, 1H)	2.18 (brd, *J* = 13.2 Hz, 1H)	2.18 (ddd, *J* = 13.3, 4.3, 2.5 Hz, 1H)	0
16	1.87 (m, 1H)	1.93 – 1.83 (m, 1H)	1.92 – 1.84 (m, 1H)	-
14b	1.63 (m, 1H)	1.67 – 1.61 (m, 1H)	1.67 – 1.61 (m, 1H)	-
20	1.57 (m, 1H)	1.60 – 1.53 (m, 1H)	1.60 – 1.53 (m, 1H)	-
15	1.40 (brs, 1H)	1.42 (brs, 1H)	1.43 (brs, 1H)	+0.01
19	1.21 (m, 2H)	1.31 – 1.09 (m, 2H)	1.27 – 1.16 (m, 2H)	-
18	0.92 (t, *J* = 7.4 Hz 3H)	0.91 (t, *J* = 7.4 Hz, 3H)	0.91 (t, *J* = 7.4 Hz, 3H)	0

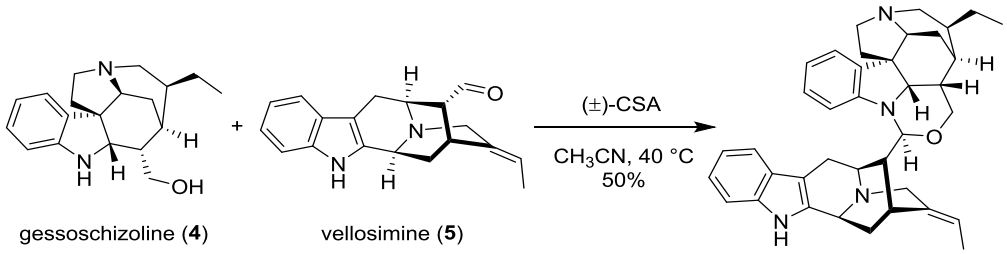
Table S2. ^{13}C NMR spectroscopic data comparison[3,4]

Position of carbons	δ_C of natural (+)-geissoschizoline (125 MHz, $CDCl_3$) [4]	δ_C of Andrade′s synthetic (+)-geissoschizoline (100 MHz, $CDCl_3$) [3]	δ_C of our synthetic (+)-geissoschizoline (100 MHz, $CDCl_3$)	$\Delta\delta_C$ (δ_{ours} vs $\delta_{Andrade's}$)
13	149.9	149.7	149.7	0
8	137.7	137.9	137.9	0
11	128.0	127.7	127.7	0
9	122.5	122.5	122.5	0
10	120.0	119.6	119.5	-0.1
12	109.8	109.8	109.8	0
3	67.7	67.5	67.5	0
17	66.2	66.4	66.4	0
2	65.7	65.2	65.2	0
5	55.8	55.7	55.6	-0.1
7	53.3	53.4	53.4	0
21	50.2	50.5	50.4	-0.1
20	42.3	42.5	42.5	0
6	39.9	39.8	39.8	0
16	34.5	34.4	34.4	0
15	28.6	28.8	28.8	0
14	26.2	26.4	26.3	-0.1
19	24.3	24.4	24.3	-0.1
18	11.6	11.9	11.8	-0.1

3. Synthetic procedures of (+)-geissolosimine

3.1 Experimental Procedures and Data

Preparation of (+)-geissolosimine



gessoschizoline (**4**) vellosimine (**5**) geissolosimine (**1**)

DL-Camphorsulfonic acid (2.0 mg, 8.6 μmol, 2.5 equiv.) was added to a solution of **4** (1.0 mg, 3.4 μmol, 1.0 equiv.) and **5** (1.0 mg, 3.4 μmol, 1.0 equiv.) in 1.0 mL anhydrous CH_3CN at room temperature. The resulting reaction mixture was stirred at 40 ^oC under argon atmosphere for 5 h. Upon the complete consumption of the starting material as indicated by TLC, the reaction was cooled to 0 ^oC and treated with a saturated aqueous solution of $NaHCO_3$ (1 mL). The resulting mixture was extracted with CH_2Cl_2 (2 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (CH_2Cl_2/MeOH/$NH_3 \cdot H_2O$= 20:1:0.1) to afford the pure product **1** (1.0 mg, 1.7 μmol, 50%).

R_f = 0.3 (CH_2Cl_2/MeOH, 10:1), white crystalline solid.

M.p.: 99.6-100.2 ºC.

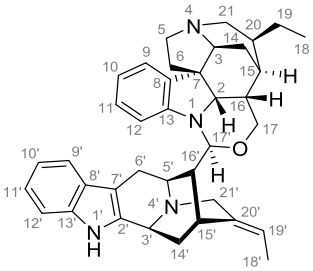
$[\alpha]_D^{25.0}$ = +74.0 (*c* = 0.04 in MeOH); {lit.[5] $[\alpha]_D^{25}$ = +84.0 (*c* = 0.16 in MeOH)}.

^{1}H NMR (400 MHz, Methanol-d_4) δ 7.35 (d, *J* = 7.7 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.12 (d, *J* = 7.3 Hz, 1H), 7.10 (t, *J* = 7.3 Hz, 1H), 7.06 (t, *J* = 7.8 Hz, 1H), 7.00 (t, *J* = 7.3 Hz, 1H), 6.72 (t, *J* = 7.4 Hz, 1H), 6.51 (d, *J* = 7.8 Hz, 1H), 5.56 (q, *J* = 6.7 Hz, 1H), 5.16 (d, *J* = 9.8 Hz, 1H), 4.20 (d, *J* = 9.7 Hz, 1H), 3.78 (d, *J* = 9.2 Hz, 1H), 3.63 – 3.57 (m, 2H), 3.26 – 3.21 (m, 2H), 3.17 (d, *J* = 3.4 Hz, 1H), 3.12 (brs, 1H), 2.95 (t, *J* = 10.8 Hz, 1H), 2.88 – 2.80 (m, 2H), 2.66 (d, *J* = 14.4 Hz, 1H), 2.52 – 2.44 (m, 1H), 2.23 (t, *J* = 11.7 Hz, 1H), 2.17 – 2.11 (m, 2H), 2.02 – 1.97 (m, 1H), 1.84 – 1.74 (m, 2H), 1.69 (d, *J* = 6.6 Hz, 3H), 1.67 – 1.63 (m, 1H), 1.52 – 1.45 (m, 2H), 1.32 – 1.31 (m, 1H), 0.98 (q, *J* = 7.1 Hz, 2H), 0.73 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (101 MHz, Methanol-d_4) δ 151.9, 139.5, 138.4, 136.0, 135.4, 129.5, 128.6, 123.7, 122.2, 120.0, 119.7, 118.7, 118.2, 112.2, 106.7, 104.5, 84.5, 68.3, 65.6, 65.1, 56.7, 55.6, 55.0, 54.9, 52.9, 52.0, 47.5, 46.3, 42.9, 37.6, 34.4, 31.1, 28.3, 27.3, 25.8, 25.4, 13.3, 11.8.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{38}H_{45}N_4O$ 573.3588, found 573.3591.

3.2 **Comparison of Spectroscopic Data of (+)-geissolosimine**



geissolosimine (**1**)

Table S3. ^{1}H NMR spectroscopic data comparison [6]

Position of hydrogens	δ_H of natural (+)-geissolosimine (600 MHz, MeOD) [6]	δ_H of our synthetic (+)-geissolosimine (400 MHz, MeOD)	$\Delta\delta_H$ (δ_{ours} vs $\delta_{natural}$)
9'	7.34 (d, *J* = 8.7 Hz, 1H)	7.35 (d, *J* = 7.7 Hz, 1H)	+0.01
12'	7.32 (d, *J* = 7.8 Hz, 1H)	7.32 (d, *J* = 8.0 Hz, 1H)	0
9	7.12 (d, *J* = 7.8 Hz, 1H)	7.12 (d, *J* = 7.3 Hz, 1H)	0
11	7.09 (t, *J* = 7.5 Hz, 1H)	7.10 (t, *J* = 7.3 Hz, 1H)	+0.01
10'	7.06 (t, *J* = 7.5 Hz, 1H)	7.06 (t, *J* = 7.8 Hz, 1H)	0
11'	6.99 (t, *J* = 7.5 Hz, 1H)	7.00 (t, *J* = 7.3 Hz, 1H)	+0.01
10	6.71 (t, *J* = 7.5 Hz, 1H)	6.72 (t, *J* = 7.4 Hz, 1H)	+0.01
12	6.49 (d, *J* = 7.8 Hz, 1H)	6.51 (d, *J* = 7.8 Hz, 1H)	+0.02
19'	5.54 (q, *J* = 6.5 Hz, 1H)	5.56 (q, *J* = 6.7 Hz, 1H)	+0.02
17'	5.16 (d, *J* = 9.8 Hz, 1H)	5.16 (d, *J* = 9.8 Hz, 1H)	0
3'	4.19 (d, *J* = 8.8 Hz, 1H)	4.20 (d, *J* = 9.7 Hz, 1H)	+0.01
2	3.77 (d, *J* = 9.5 Hz, 1H)	3.78 (d, *J* = 9.2 Hz, 1H)	+0.01
21'	3.59 (m, 2H)	3.63 – 3.57 (m, 2H)	-
3	3.26 (m, 1H)	3.26 – 3.21 (m, 2H)	-
5a	3.21 (d, *J* = 11.0 Hz, 1H)		
17	3.15 (dd, *J* = 11.0, 4.0 Hz, 1H)	3.17 (d, *J* = 3.4 Hz, 1H)	+0.02
15'	3.12 (br s, 1H)	3.12 (brs, 1H)	0
5b	2.94 (t, *J* = 11.0 Hz, 1H)	2.95 (t, *J* = 10.8 Hz, 1H)	+0.01
5'	2.85 (m, 1H)	2.88 – 2.80 (m, 2H)	-
6'a	2.84 (m, 1H)		
6'b	2.65 (d, *J* = 15.0 Hz, 1H)	2.66 (d, *J* = 14.4 Hz, 1H)	+0.01
6a	2.48 (m, 1H)	2.52 – 2.44 (m, 1H)	-

6b	2.23 (t, *J* = 11.6 Hz, 1H)	2.23 (t, *J* = 11.7 Hz, 1H)	0
14'a	2.13 (m, 1H)	2.17 – 2.11 (m, 2H)	-
16'	2.11 (m, 1H)		
16	1.98 (m, 1H)	2.02 – 1.97 (m, 1H)	-
14'b	1.79 (m, 1H)	1.84 – 1.74 (m, 2H)	-
21	1.75 (m, 1H)		
18'	1.69 (d, *J* = 6.5 Hz, 3H)	1.69 (d, *J* = 6.6 Hz, 3H)	0
14a	1.66 (d, *J* = 6.9 Hz, 1H)	1.67 – 1.63 (m, 1H)	-
20	1.51 (m, 1H)	1.52 – 1.45 (m, 2H)	-
14b	1.45 (dt, *J* = 13.8, 3.0 Hz, 1H)		
15	1.29 (m, 1H)	1.32 – 1.31 (m, 1H)	-
19	0.96 (m, 2H)	0.98 (q, *J* = 7.1 Hz, 2H)	+0.02
18	0.71 (t, *J* = 7.5 Hz, 3H)	0.73 (t, *J* = 7.6 Hz, 3H)	+0.02

Table S4. ^{13}C NMR spectroscopic data comparison [6]

Position of carbons	δ_C of natural (+)-geissolosimine (150 MHz, MeOD) [6]	δ_C of our synthetic (+)-geissolosimine (100 MHz, MeOD)	$\Delta\delta_C$ (δours vs δnatural)
13	152.0	151.9	-0.1
2'	139.5	139.5	0
13'	138.5	138.4	-0.1
20'	136.3	136.1	-0.2
8	135.3	135.4	+0.1
11	129.7	129.5	-0.2
8'	128.7	128.6	-0.1
9	123.8	123.7	-0.1
11'	122.3	122.2	-0.1
10'	120.1	120.0	-0.1
10	119.8	119.7	-0.1
19'	118.8	118.7	-0.1
9'	118.3	118.2	-0.1
12'	112.3	112.2	-0.1
12	106.8	106.7	-0.1
7'	104.5	104.5	0
17'	84.6	84.5	-0.1
2	68.3	68.3	0
17	65.6	65.6	0

3	65.2	65.1	-0.1
21'	56.8	56.7	-0.1
5'	55.8	55.6	-0.2
5	55.1	55.0	-0.1
21	55.0	54.9	-0.1
7	52.9	52.9	0
3'	52.1	52.0	-0.1
6	47.4	47.5	+0.1
16'	46.3	46.3	0
20	43.0	42.9	-0.1
16	37.7	37.6	-0.1
14'	34.4	34.4	0
15	31.2	31.1	-0.1
15'	28.4	28.3	-0.1
6'	27.4	27.3	-0.1
14	25.9	25.8	-0.1
19	25.5	25.4	-0.1
18'	13.4	13.3	-0.1
18	11.9	11.8	-0.1

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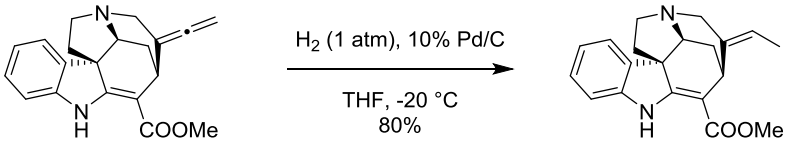
4. Synthetic procedures of akuammicine, condylocarpine and isocondylocarpine.

4.1 Experimental Procedures and Data

4.1.1 Preparation of akuammicine



6 **akuammicine**

To a solution of compound **6** (200 mg, 0.62 mmol, 1.0 equiv.) in 20 mL THF was added 10% Pd/C (wet, 200 mg, 10 weight% palladium). The solution was placed under a hydrogen atmosphere at -20 ℃ for 2 h. After filtration through Celite pad and removal of the solvent, the residue was purified by silica gel chromatography (CH_2Cl_2/MeOH/$NH_3 \cdot H_2O$ = 100:1:0.1) to afford the pure product **akuammicine (17)** (160 mg, 0.50 mmol, 80%).

R_f = 0.4 (CH_2Cl_2/MeOH = 15:1, v/v), yellow amorphous solid.

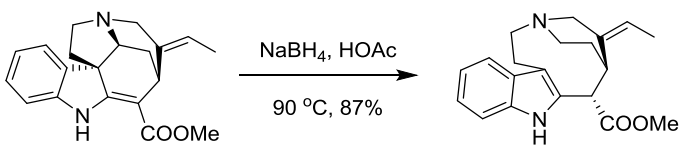
$[\alpha]_D^{20.0}$ = -709.2 (*c* = 0.20 in $CHCl_3$); {lit.[7] $[\alpha]_D^{23}$ = -731 (*c* = 0.34 in $CHCl_3$)}.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.99 (s, 1H), 7.23 (d, *J* = 7.4 Hz, 1H), 7.17 – 7.10 (m, 1H), 6.88 (td, *J* = 7.5, 1.1 Hz, 1H), 6.81 (d, *J* = 7.7 Hz, 1H), 5.36 (q, *J* = 7.0 Hz, 1H), 4.10 – 4.06 (m, 1H), 3.96 – 3.88 (m, 2H), 3.80 (s, 3H), 3.35 – 3.26 (m, 1H), 3.03 (dd, *J* = 12.4, 6.7 Hz, 1H), 2.97 (d, *J* = 15.0 Hz, 1H), 2.51 (td, *J* = 12.6, 6.8 Hz, 1H), 2.42 (ddd, *J* = 13.6, 4.0, 2.3 Hz, 1H), 1.83 (dd, *J* = 12.3, 5.8 Hz, 1H), 1.60 (d, *J* = 7.0 Hz, 3H), 1.30 (dt, *J* = 13.6, 2.8 Hz, 1H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.0, 167.7, 143.5, 138.6, 136.8, 128.0, 121.5, 121.1, 120.9, 109.6, 101.4, 62.0, 57.5, 56.9, 56.2, 51.1, 46.1, 30.9, 29.8, 13.0.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{20}H_{23}N_2O_2$ 323.1754; found 323.1756.

4.1.2 Preparation of compound 18



akuammicine (17) **18**

$NaBH_4$ (167 mg, 4.7 mmol, 10 equiv.) was added slowly to a solution of **17** (150 mg, 0.47 mmol, 1.0 equiv.) in 15 mL HOAc at 90 ℃ in oil bath. The reaction was stirred for 1 h. After cooled to room temperature, the mixture was diluted with 50 mL CH_2Cl_2 and basified

with $NH_3 \cdot H_2O$. The aqueous phase was extracted with CH_2Cl_2 (50 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (CH_2Cl_2/MeOH/$NH_3 \cdot H_2O$ = 100:1:0.1) to afford the pure product **18** (131 mg, 0.40 mmol, 87%).

R_f = 0.4 (CH_2Cl_2/MeOH = 15:1, v/v), yellow amorphous solid.

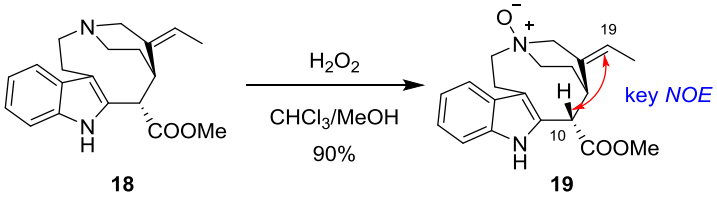
$[\alpha]_D^{20.0}$ = -89.1 (*c* = 0.18 in $CHCl_3$).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.22 (s, 1H), 7.44 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 7.11 (t, *J* = 7.7 Hz, 1H), 5.73 (d, *J* = 7.7 Hz, 1H), 4.32 (s, 1H), 3.91 – 3.86 (m, 3H), 3.83 – 3.77 (m, 1H), 3.49 – 3.40 (m, 2H), 3.33 – 3.19 (m, 3H), 3.07 (t, *J* = 11.1 Hz, 1H), 2.97 (d, *J* = 13.7 Hz, 1H), 1.83 (d, *J* = 7.0 Hz, 3H), 1.64 – 1.58 (m, 1H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 174.6, 135.4, 129.7, 126.7, 122.4, 120.0, 118.2, 111.5, 57.0, 53.6, 53.2, 52.8, 47.4, 44.4, 37.2, 29.8, 22.8, 21.9, 13.7.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{20}H_{25}N_2O_2$ 325.1911; found 325.1914.

4.1.3 Preparation of compound 19



30% H_2O_2 (70 μL, 0.62 mmol, 2.0 equiv.) was added to a solution of **18** (100 mg, 0.31 mmol, 1.0 equiv.) in 6 mL $CHCl_3$ and 6 mL MeOH. The mixture was stirred at room temperature overnight. The residue was diluted with CH_2Cl_2 (20 mL), washed with saturated $Na_2S_2O_3$ solution (10 mL). The aqueous phase was extracted with CH_2Cl_2 (20 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (CH_2Cl_2/MeOH/$NH_3 \cdot H_2O$ = 20:1:0.1) to afford the pure product **19** (94 mg, 0.28 mmol, 90%).

R_f = 0.5 (CH_2Cl_2/MeOH = 10:1, v/v), white amorphous solid.

$[\alpha]_D^{20.0}$ = -21.4 (*c* = 0.13 in $CHCl_3$).

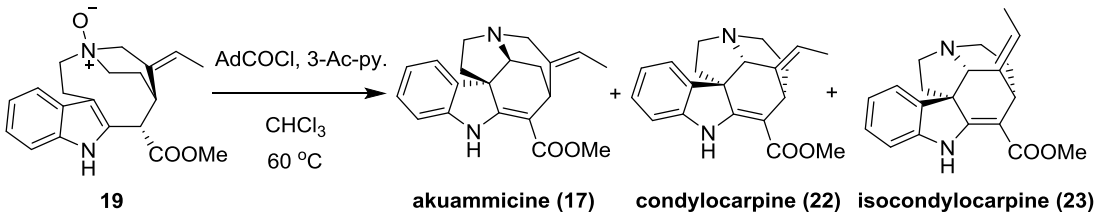
^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.47 (s, 1H), 7.41 (d, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.18 (t, *J* = 7.0 Hz, 1H), 7.11 (d, *J* = 7.6 Hz, 1H), 5.91 (t, *J* = 7.6 Hz, 1H), 4.29 (s, 1H), 4.25 (d, *J* = 15.7 Hz, 1H), 4.03 (d, *J* = 15.2 Hz, 1H), 3.90 (s, 3H), 3.80 – 3.65 (m, 2H),

3.54 – 3.47 (m, 2H), 3.42 - 3.34 (m, 2H), 3.13 (d, *J* = 16.1 Hz, 1H), 3.83 - 2.72 (m, 1H), 2.31 - 2.21 (m, 1H), 1.92 - 1.83 (m, 4H).

^{13}C NMR (126 MHz, Methanol-d_4) δ 186.3 , 172.6 , 154.9 , 138.6 , 135.1 , 131.9 , 128.9 , 127.2 , 124.5 , 122.6 , 101.3 , 84.0 , 74.7 , 70.4 , 68.4 , 53.1 , 32.6 , 32.0 , 22.6 , 14.0 .

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{20}H_{25}N_2O_2$ 341.1860; found 341.1856.

4.1.4 Preparation of condylocarpine and isocondylocarpine



3-acetyl pyridine (80 μL, 0.7 mmol, 10 equiv.) was added to a solution of 1-adamantanecarbonyl chloride (58 mg, 0.28 mmol, 4.0 equiv.) in 2 mL $CHCl_3$ under argon atmosphere. The mixture was stirred for 1 h at room temperature. Then **19** (24 mg, 0.07 mmol, 1.0 equiv.) in 1 mL $CHCl_3$ was added and the reaction was stirred at 60 ℃ in oil bath overnight. The resulting mixture was diluted with CH_2Cl_2 (3 mL), washed with saturated $NaHCO_3$ solution (3 mL). The aqueous phase was extracted with CH_2Cl_2 (5 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (CH_2Cl_2/MeOH/$NH_3{\cdot}H_2O$ = 100:1:0.1) to afford the mixture (17 mg, 0.05 mmol, 75%). The ratio of products was determined by ^{1}H NMR spectroscopy. Then the mixture was separated by normal HPLC (ChiralPak IC column, *n*-hexane/*i*-PrOH/diethylamine = 90:10:0.1, 256 nm, 0.7 mL/min, $t_{\text{isocondylocarpine}}$ = 12.89 min (40%), $t_{\text{condylocarpine}}$ = 13.87 min (15%), $t_{\text{akuammicine}}$ = 25.46 min (15%)).

Condylocarpine (22)

R_f = 0.4 (CH_2Cl_2/MeOH = 15:1, v/v), white amorphous solid.

$[\alpha]_D^{20.0}$ = +550.3 (*c* = 0.13 in EtOH); {lit.[8] $[\alpha]_D^{23}$ = +631 (*c* = 0.59 in EtOH)}.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.67 (s, 1H), 7.19 (d, *J* = 7.3 Hz, 1H), 7.11 (t, *J* = 7.7 Hz, 1H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.77 (d, *J* = 7.7 Hz, 1H), 5.33 (q, *J* = 6.9 Hz, 1H), 4.16 (s, 1H), 3.91 (t, *J* = 4.7 Hz, 1H), 3.79 (s, 3H), 3.12 (q, *J* = 10.2 Hz, 1H), 3.07 – 3.01 (m, 1H), 3.00 – 2.94 (m, 1H), 2.79 – 2.72 (m, 1H), 2.67 (dt, *J* = 12.9, 6.3 Hz, 1H), 2.01 – 1.95 (m, 1H), 1.94 – 1.82 (m, 2H), 1.59 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.3, 168.2, 144.6, 137.3, 135.4, 127.8, 121.2, 120.4, 117.8, 109.8, 101.7, 68.8, 60.1, 53.1, 51.4, 46.1, 45.2, 29.0, 28.4, 13.2.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{20}H_{23}N_2O_2$ 323.1754; found 323.1754.

Isocondylocarpine (23)

$\mathbf{R_f}$ = 0.4 (CH_2Cl_2/MeOH = 15:1, v/v), white amorphous solid.

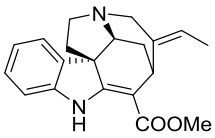
$\mathbf{[\alpha]_D^{20.0}}$ = +490.6 (*c* = 0.09 in EtOH); {lit.[8] $[\alpha]_D^{23}$ = +560 (*c* = 0.22 in EtOH)}.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.66 (s, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 7.7 Hz, 1H), 6.89 (t, *J* = 7.4 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 5.43 (q, *J* = 6.8 Hz, 1H), 4.71 (s, 1H), 3.77 (s, 3H), 3.44 (s, 1H), 3.19 – 3.11 (m, 1H), 3.08 – 2.98 (m, 2H), 2.82 – 2.74 (m, 1H), 2.70 – 2.64 (m, 1H), 2.04 – 1.98 (m, 1H), 1.95 – 1.88 (m, 2H), 1.60 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.8, 168.1, 144.7, 136.8, 135.1, 127.9, 121.3, 120.2, 118.5, 109.9, 102.3, 60.3, 59.9, 53.2, 51.3, 46.1, 45.0, 37.3, 28.8, 13.1.

HRMS-ESI (*m/z*): $[M + H]^+$ calculated for $C_{20}H_{23}N_2O_2$ 323.1754; found 323.1751.

4.2 Comparison of Spectroscopic Data of akuammicine



akuammicine (**17**)

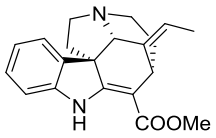
Table S5. ^{1}H NMR spectroscopic data comparison [7]

δ_H of our synthetic akuammicine (500 MHz, $CDCl_3$)			δ_H of MacMillan's synthetic akuammicine (500 MHz, $CDCl_3$) [7]			$\Delta\delta_H$ (δ_{ours} vs $\delta_{MacMillan's}$)
δ (ppm)	Integration	Multiplicity	δ (ppm)	Integration	Multiplicity	Δδ (ppm)
8.99	1H	s	9.01	1H	s	-0.02
7.23	1H	d, *J* = 7.4 Hz	7.24	1H	d, *J* = 7.3 Hz	-0.01
7.17-7.10	1H	m	7.15	1H	td, *J* = 7.6, 0.9 Hz	-
6.88	1H	td, *J* = 7.5, 1.1 Hz	6.90	1H	t, *J* = 7.5 Hz	-0.02
6.81	1H	d, *J* = 7.7 Hz	6.83	1H	d, *J* = 7.8 Hz	-0.02
5.36	1H	q, *J* = 7.0 Hz	5.34	1H	q, *J* = 6.7 Hz	0.02
4.10-4.06	1H	m	4.04-4.02	1H	m	-
3.96-3.88	2H	m	3.95-3.92	1H	m	-
			3.89	1H	d, *J* = 15.0 Hz	
3.80	3H	s	3.81	3H	s	-0.01
3.35 – 3.26	1H	m	3.27	1H	ddd, *J* = 12.6, 12.6, 5.6 Hz	-
3.03	1H	dd, *J* = 12.4, 6.7 Hz	3.03	1H	dd, *J* = 12.4, 6.7 Hz	0
2.97	1H	d, *J* = 15.0 Hz	2.95	1H	d, *J* = 15.1 Hz	0.02
2.51	1H	td, *J* = 12.6, 6.8 Hz	2.51	1H	ddd, *J* = 12.6, 12.6, 6.7 Hz	0
2.42	1H	ddd, *J* = 13.6, 4.0, 2.3 Hz	2.43	1H	ddd, *J* = 13.4, 3.9, 2.2 Hz	-0.01
1.83	1H	dd, *J* = 12.3, 5.8 Hz	1.82	1H	dd. *J* = 12.3, 5.5 Hz	0.01
1.60	3H	d, *J* = 7.0 Hz	1.61	3H	d, *J* = 6.9 Hz	-0.01
1.30	1H	dt, *J* = 13.6, 2.8 Hz	1.30	1H	ddd, *J* = 13.1, 2.8, 2.8 Hz	0

Table S6. ^{13}C NMR spectroscopic data comparison [7]

δ_C of our synthetic akuammicine (126 MHz, $CDCl_3$)	δ_C of MacMillan′s synthetic akuammicine (125 MHz, $CDCl_3$) [7]	$\Delta\delta_C$ (δ_{ours} vs $\delta_{MacMillan's}$)
168.0	168.2	-0.2
167.7	168.1	-0.4
143.5	143.4	0.1
138.6	139.4	0.2
136.8	137.0	-0.2
128.0	127.7	0.3
121.5	120.9	0.6
121.1	120.8	0.3
120.9	120.6	0.3
109.6	109.4	0.2
101.4	101.2	0.2
62.0	62.0	0
57.5	57.6	-0.1
56.9	57.0	-0.1
56.2	56.4	-0.2
51.1	51.0	0.1
46.1	46.4	-0.3
30.9	30.9	0
29.8	29.8	0
13.0	12.9	0.1

4.3 Comparison of Spectroscopic Data of condylocarpine



condylocarpine (**22**)

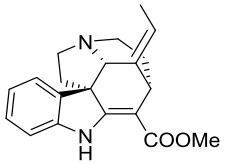
Table S7. ^{1}H NMR spectroscopic data comparison [8]

δ_H of our synthetic condylocarpine (500 MHz, $CDCl_3$)			δ_H of Overman′s synthetic condylocarpine (500 MHz, $CDCl_3$) [8]			$\Delta\delta_H$ (δ_{ours} vs $\delta_{Overman's}$)
δ (ppm)	Integration	Multiplicity	δ (ppm)	Integration	Multiplicity	Δδ (ppm)
8.67	1H	s	8.68	1H	s	-0.01
7.19	1H	d, *J* = 7.3 Hz	7.18	1H	d, *J* = 7.3 Hz	0.01
7.11	1H	t, *J* = 7.7 Hz	7.12	1H	t, *J* = 7.7 Hz	-0.01
6.89	1H	t, *J* = 7.5 Hz	6.89	1H	t, *J* = 7.4 Hz	0
6.77	1H	d, *J* = 7.7 Hz	6.78	1H	d, *J* = 7.7 Hz	-0.01
5.33	1H	q, *J* = 6.9 Hz	5.32	1H	q, *J* = 6.7 Hz	0.01
4.16	1H	s	4.12	1H	s	0.04
3.91	1H	t, *J* = 4.7 Hz	3.89	1H	m	0.02
3.79	3H	s	3.80	3H	s	-0.01
3.12	1H	q, *J* = 10.2 Hz	3.08	1H	ddd, *J* = 11.3, 10.0, 6.8 Hz	0.04
3.07-3.01	1H	m	3.03	1H	ddd, *J* = 13.0, 7.0, 6.1 Hz	-
3.00-2.94	1H	m	2.98	1H	ddd, *J* = 11.3, 6.9, 3.3 Hz	-
2.79-2.72	1H	m	2.78	1H	ddd, *J* = 13.0, 9.6, 7.1 Hz	-
2.67	1H	dt, *J* = 12.9, 6.3 Hz	2.66	1H	ddd, *J*= 12.8, 7.6, 5.2 Hz	0.01
2.01-1.95	1H	m	1.96	1H	ddd, *J* = 12.9, 6.7, 3.3 Hz	-
1.94-1.82	2H	m	1.94-1.89	1H	m	-
			1.89-1.83	1H	m	
1.59	3H	d, *J* = 6.8 Hz	1.59	3H	d, *J* = 6.8 Hz	0

Table S8. ^{13}C NMR spectroscopic data comparison [8]

δ_C of our synthetic condylocarpine (126 MHz, $CDCl_3$)	δ_C of Overman′s synthetic condylocarpine (125 MHz, $CDCl_3$) [8]	$\Delta\delta_C$ (δ_{ours} vs $\delta_{Overman's}$)
169.3	169.7	-0.4
168.2	168.3	-0.1
144.6	144.7	-0.1
137.3	137.8	-0.5
135.4	135.7	-0.3
127.8	127.8	0
121.2	121.2	0
120.4	120.4	0
117.8	117.4	0.4
109.8	109.9	-0.1
101.7	101.6	0.1
68.8	69.1	-0.3
60.1	60.2	-0.1
53.1	53.4	-0.3
51.4	51.4	0
46.1	46.3	-0.2
45.2	45.5	-0.3
29.0	29.2	-0.2
28.4	28.6	-0.2
13.2	13.3	-0.1

4.4 Comparison of Spectroscopic Data of isocondylocarpine



isocondylocarpine (**23**)

Table S9. ^{1}H NMR spectroscopic data comparison [8]

δ_H of our synthetic isocondylocarpine (500 MHz, $CDCl_3$)			δ_H of Overman′s synthetic isocondylocarpine (500 MHz, $CDCl_3$) [8]			$\Delta\delta_H$ (δ_{ours} vs $\delta_{Overman's}$)
δ (ppm)	Integration	Multiplicity	δ (ppm)	Integration	Multiplicity	Δδ (ppm)
8.66	1H	s	8.67	1H	s	-0.01
7.23	1H	d, *J* = 7.5 Hz	7.22	1H	d, *J* = 7.3 Hz	0.01
7.11	1H	t, *J* = 7.7 Hz	7.12	1H	t, *J* = 7.7 Hz	-0.01
6.89	1H	t, *J* = 7.4 Hz	6.89	1H	t, *J* = 7.4 Hz	0
6.78	1H	d, *J* = 7.8 Hz	6.78	1H	d, *J* = 7.8 Hz	0
5.43	1H	q, *J* = 6.8 Hz	5.41	1H	q, *J* = 6.7 Hz	0.02
4.71	1H	s	4.65	1H	s	0.06
3.77	3H	s	3.80	3H	s	-0.03
3.44	1H	s	3.43	1H	t, *J* = 4.2 Hz	0.01
3.19-3.11	1H	m	3.11	1H	ddd, *J* = 11.2, 9.7, 6.9 Hz	-
3.08-2.98	2H	m	3.03	1H	ddd, *J* = 12.4, 6.4, 6.1 Hz	-
			2.99	1H	ddd, *J* = 11.3, 7.0, 3.4 Hz	
2.82-2.74	1H	m	2.80	1H	ddd, *J* = 12.9, 9.6, 7.1 Hz	-
2.70-2.64	1H	m	2.65	1H	ddd, *J* = 13.2, 6.6, 6. 3 Hz	-
2.04-1.98	1H	m	1.98	1H	ddd, *J* = 12.9, 6.8, 3.2 Hz	-
1.95-1.88	2H	m	1.91	2H	q, *J* = 5.8 Hz	-
1.60	3H	d, *J* = 6.6 Hz	1.60	3H	d, *J* = 6.8 Hz	0

Table S10. ^{13}C NMR spectroscopic data comparison [8]

δ_C of our synthetic isocondylocarpine (126 MHz, $CDCl_3$)	δ_C of Overman′s synthetic isocondylocarpine (125 MHz, $CDCl_3$) [8]	$\Delta\delta_C$ (δ_{ours} vs $\delta_{Overman's}$)
168.8	169.2	-0.4
168.1	168.2	-0.1
144.7	144.8	-0.1
136.8	137.6	-0.2
135.1	135.6	-0.5
127.9	127.8	0.1
121.3	121.2	0.1
120.2	120.2	0
118.5	117.9	0.6
109.9	109.9	0
102.3	102.3	0
60.3	60.5	-0.2
59.9	60.1	-0.2
53.2	53.6	-0.4
51.3	51.4	-0.1
46.1	46.2	-0.1
45.0	45.3	-0.3
37.3	37.7	-0.4
28.8	29.1	-0.3
13.1	13.1	0

5. References

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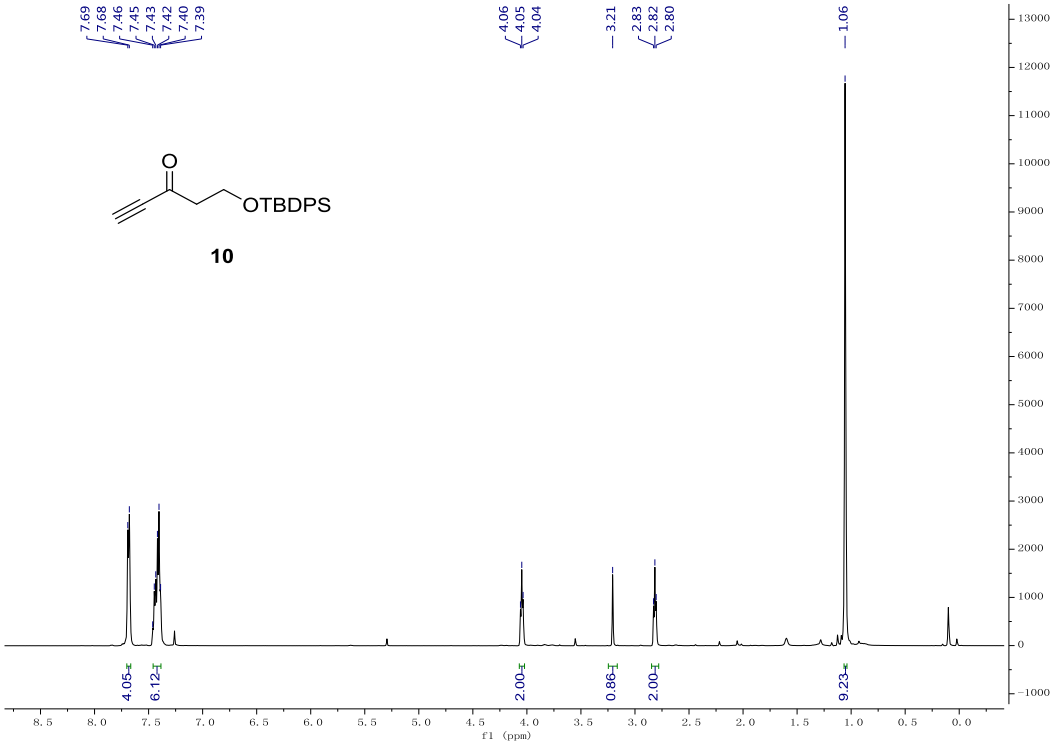
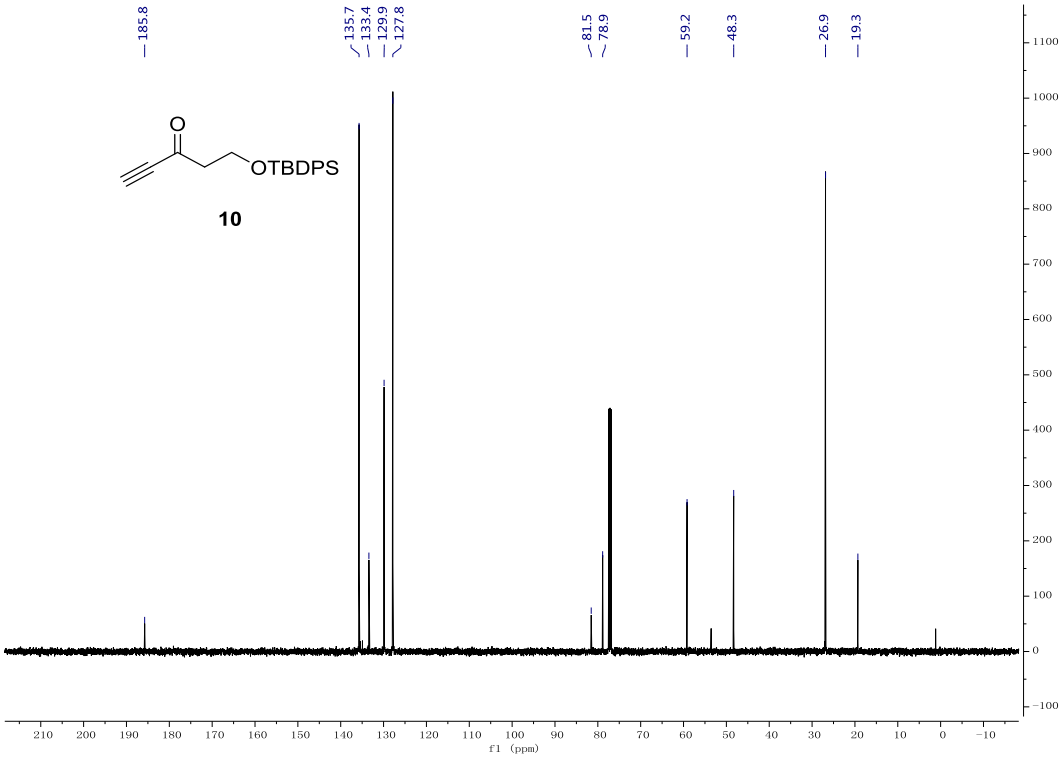
6. NMR Spectra

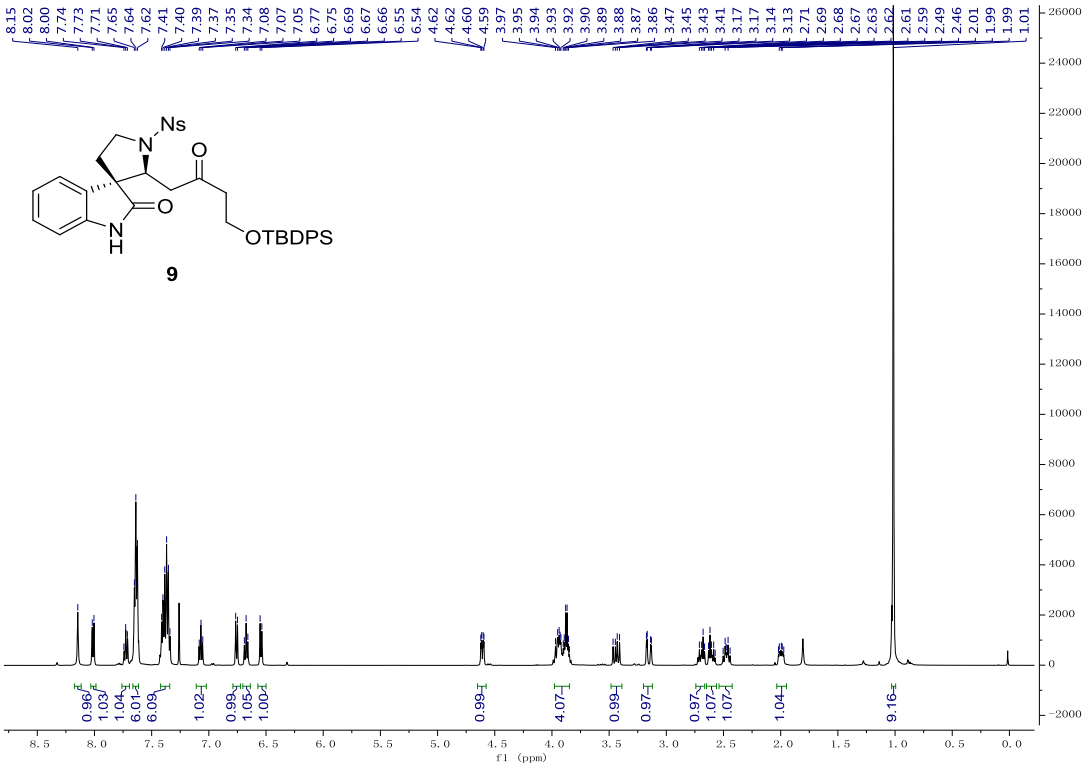
^{1}H NMR spectrum of compound **10** (500 MHz, Chloroform-*d*)



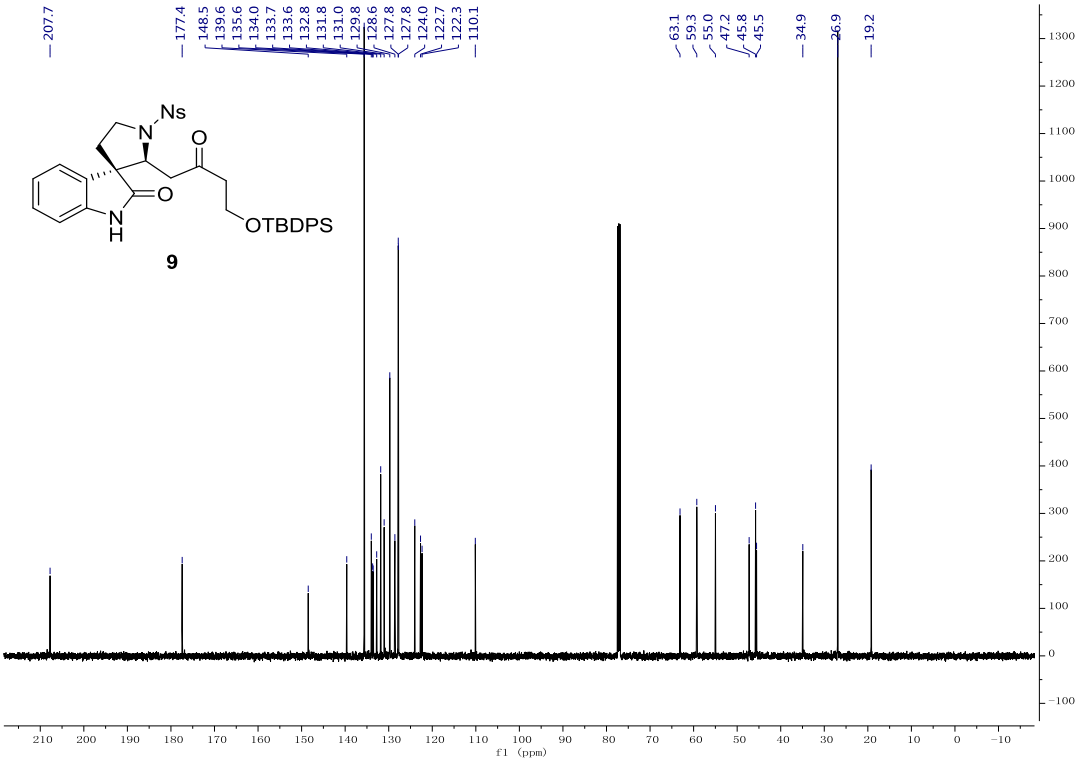
^{13}C NMR spectrum of compound **10** (126 MHz, Chloroform-*d*)



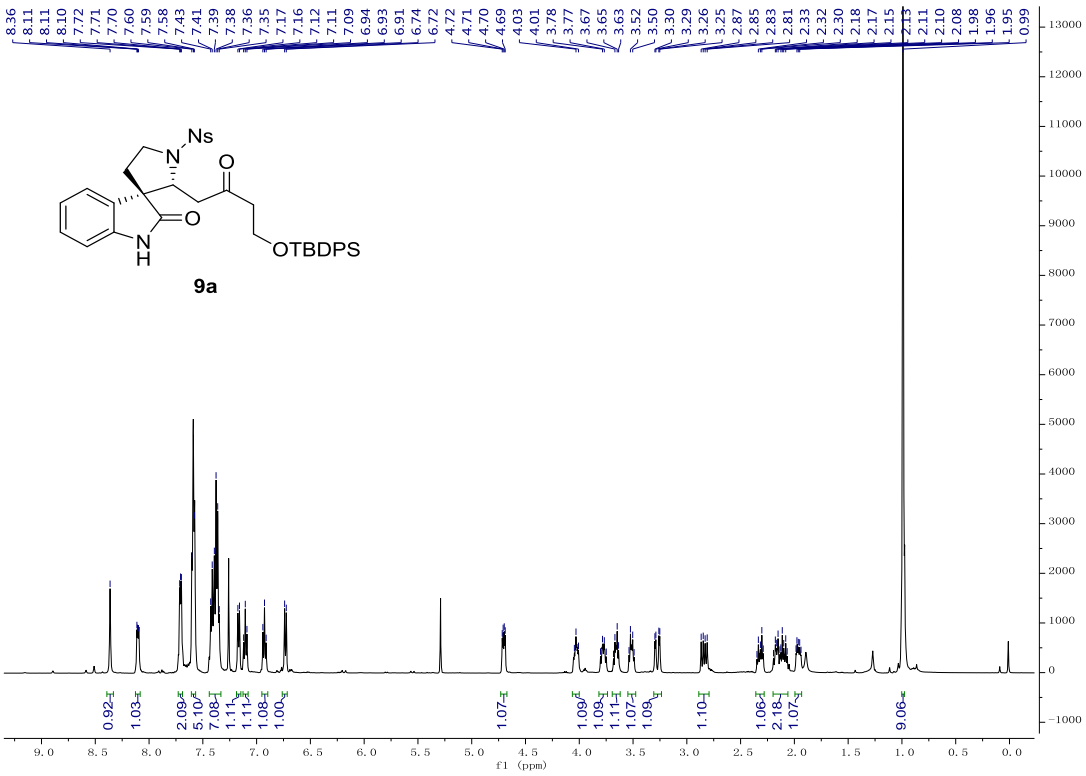
^{1}H NMR spectrum of compound **9** (500 MHz, Chloroform-*d*)



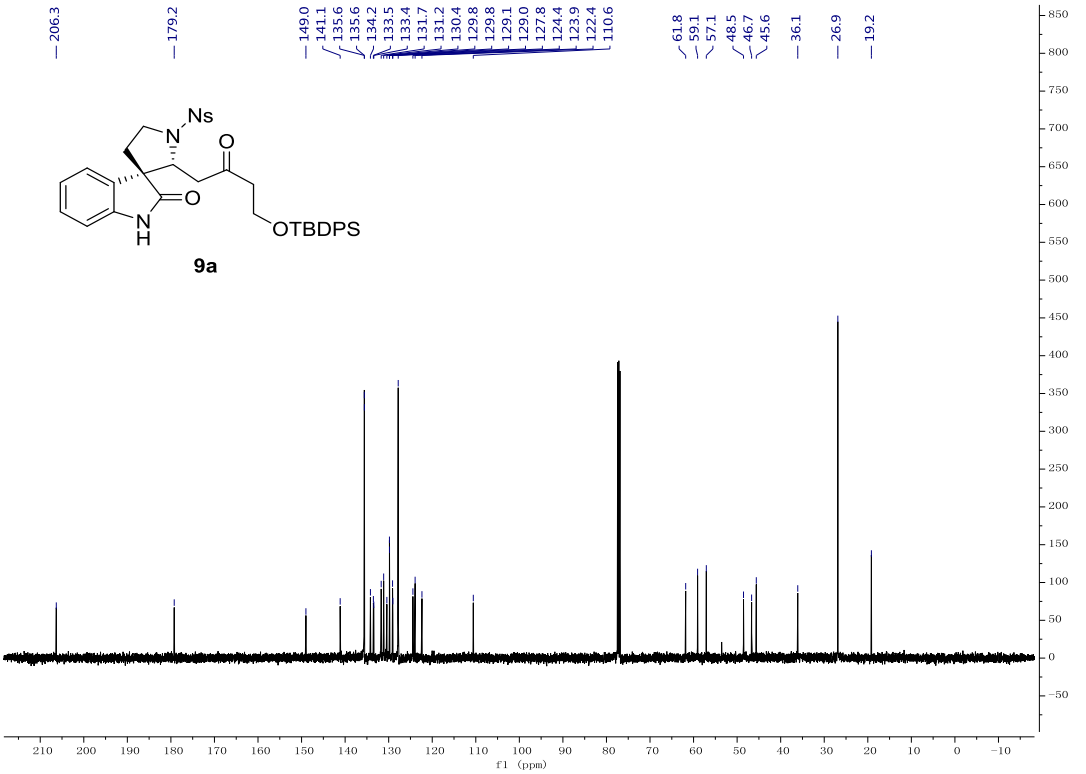
^{13}C NMR spectrum of compound **9** (126 MHz, Chloroform-*d*)



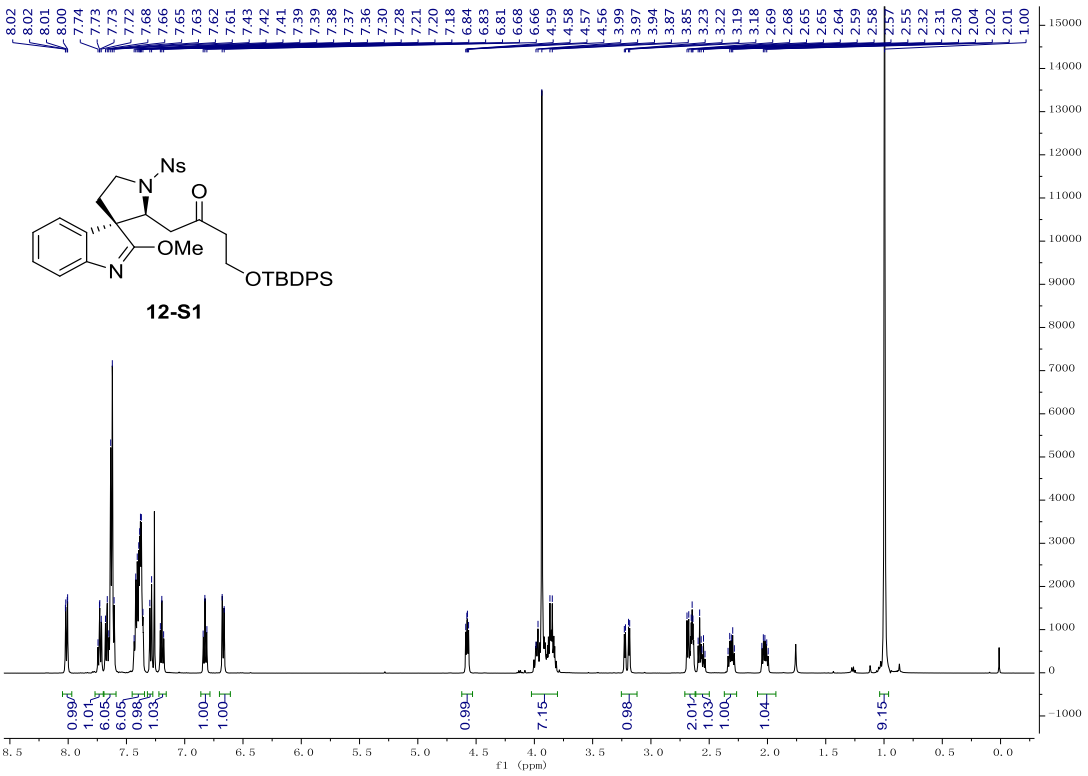
^{1}H NMR spectrum of compound **9a** (500 MHz, Chloroform-*d*)



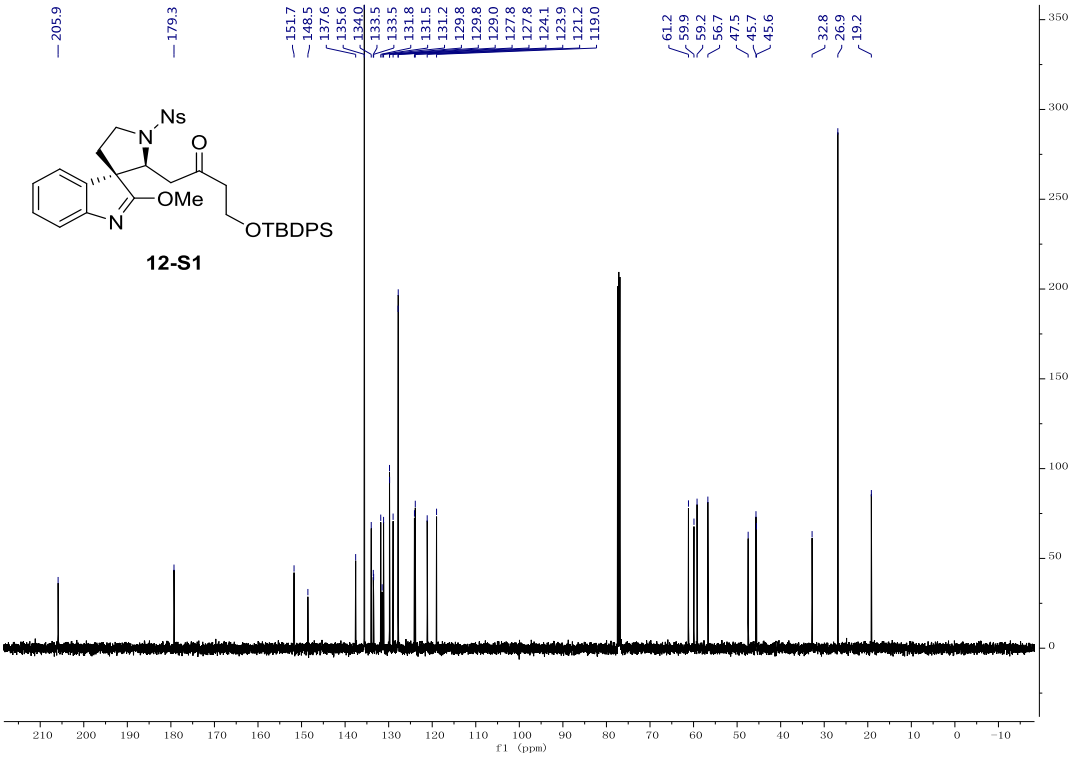
^{13}C NMR spectrum of compound **9a** (126 MHz, Chloroform-*d*)



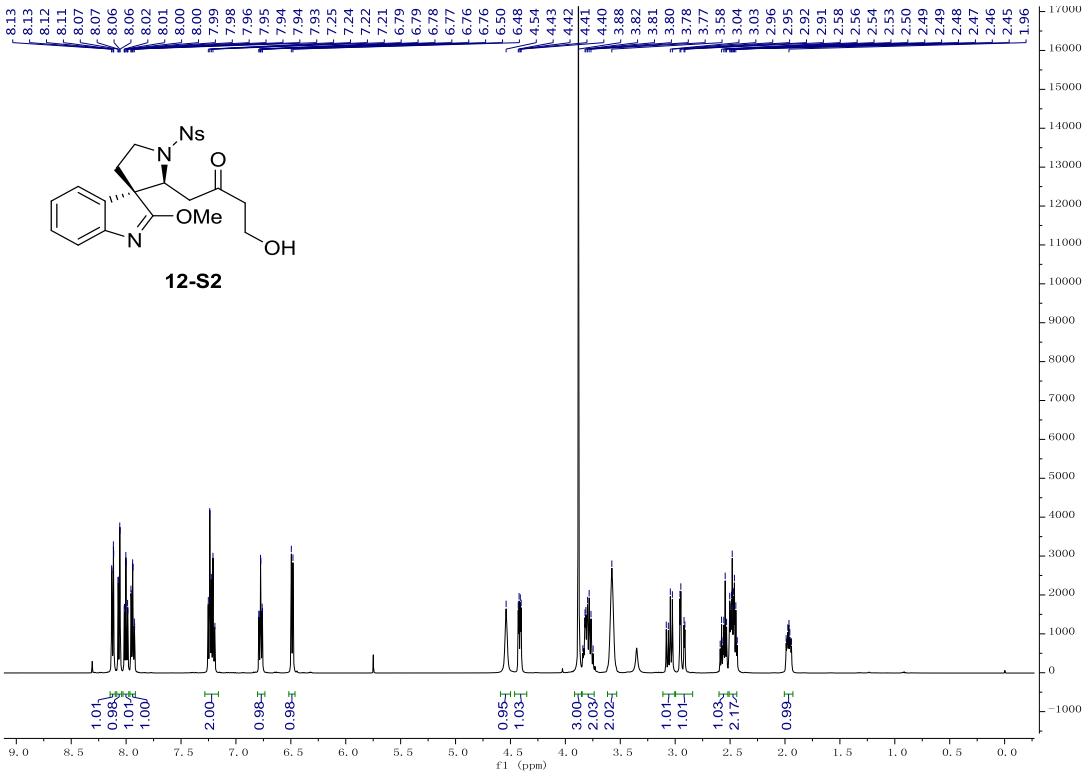
^{1}H NMR spectrum of compound **12-S1** (500 MHz, Chloroform-*d*)



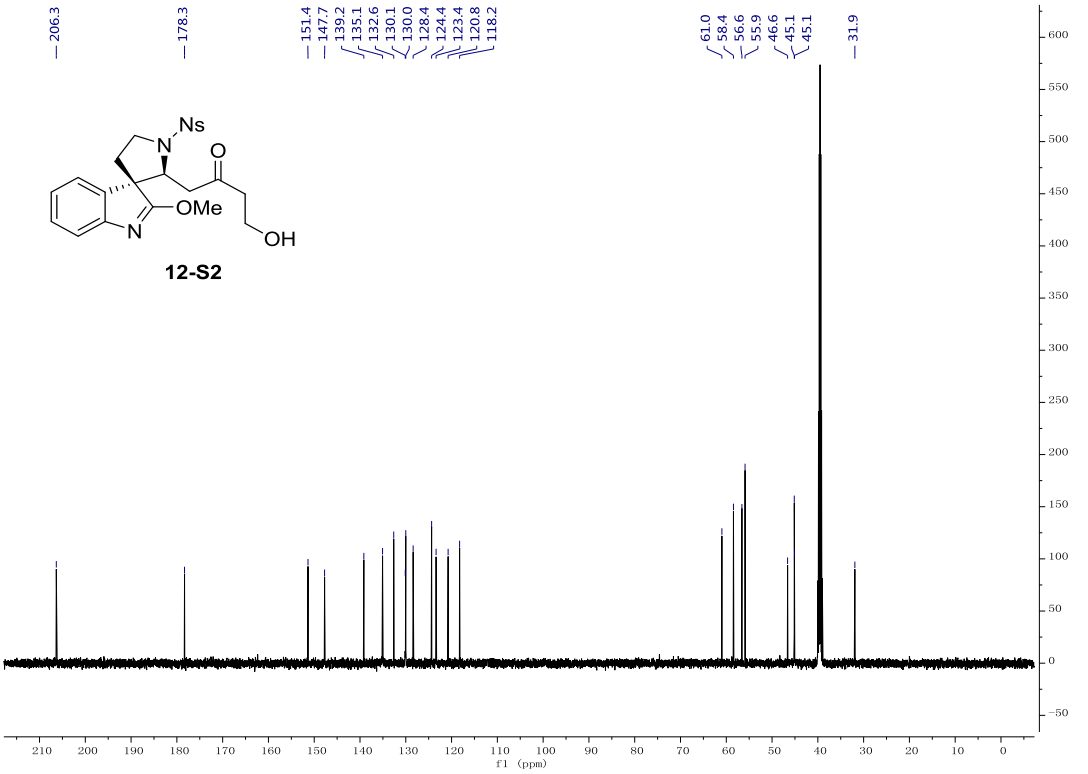
^{13}C NMR spectrum of compound **12-S1** (126 MHz, Chloroform-*d*)



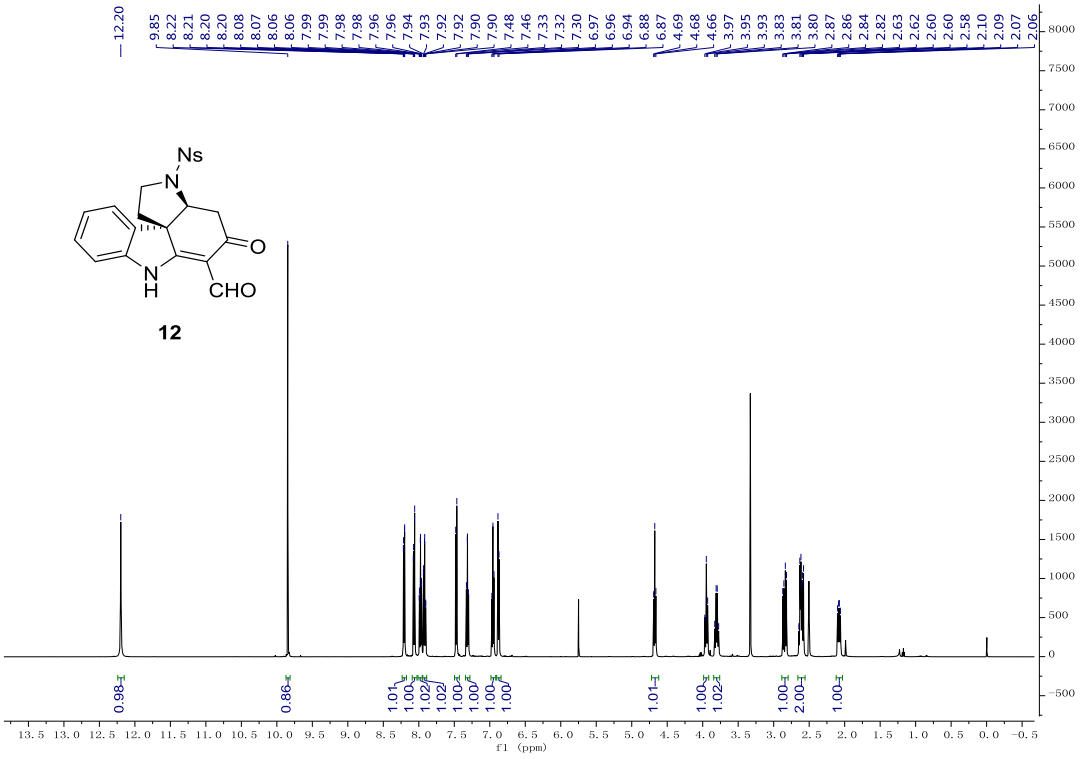
^{1}H NMR spectrum of compound **12-S2** (500 MHz, DMSO-d_6)



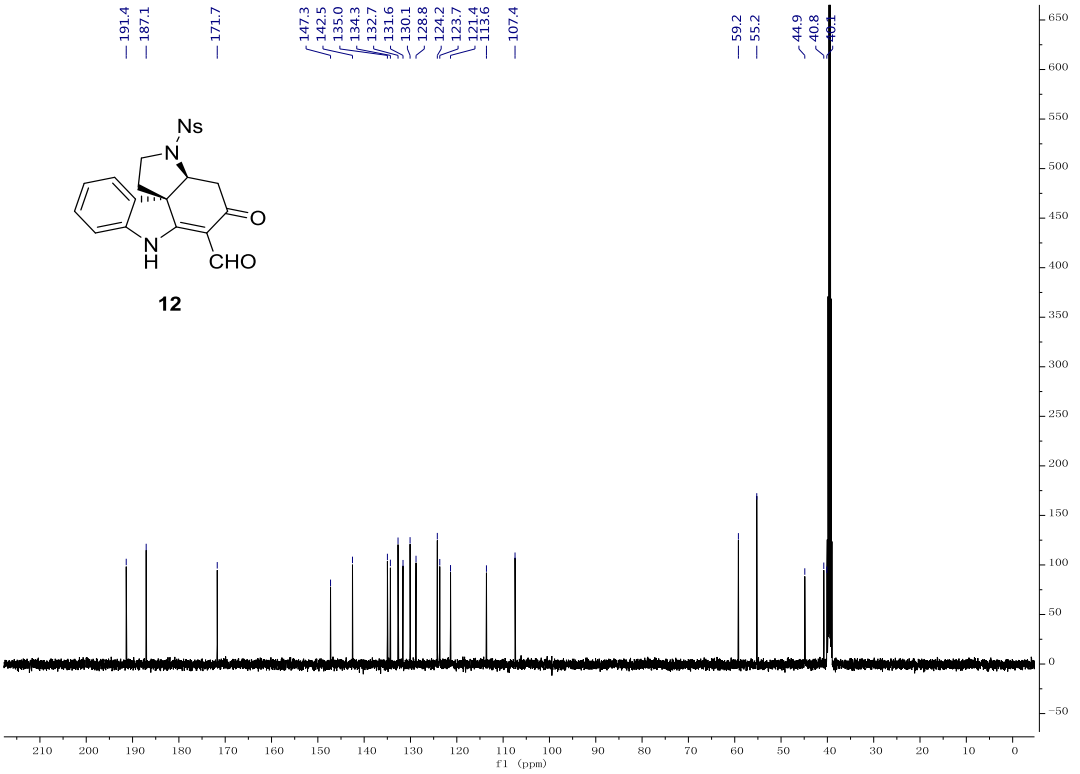
^{13}C NMR spectrum of compound **12-S2** (126 MHz, DMSO-d_6)



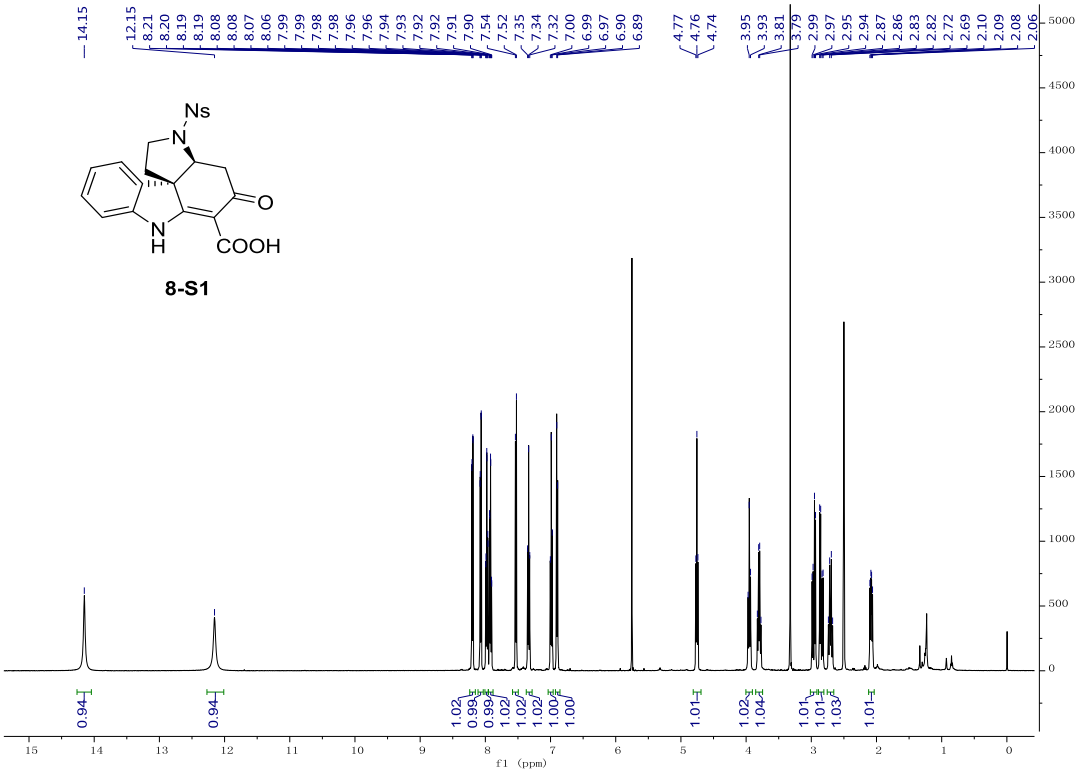
^{1}H NMR spectrum of compound **12** (500 MHz, DMSO-d_6)



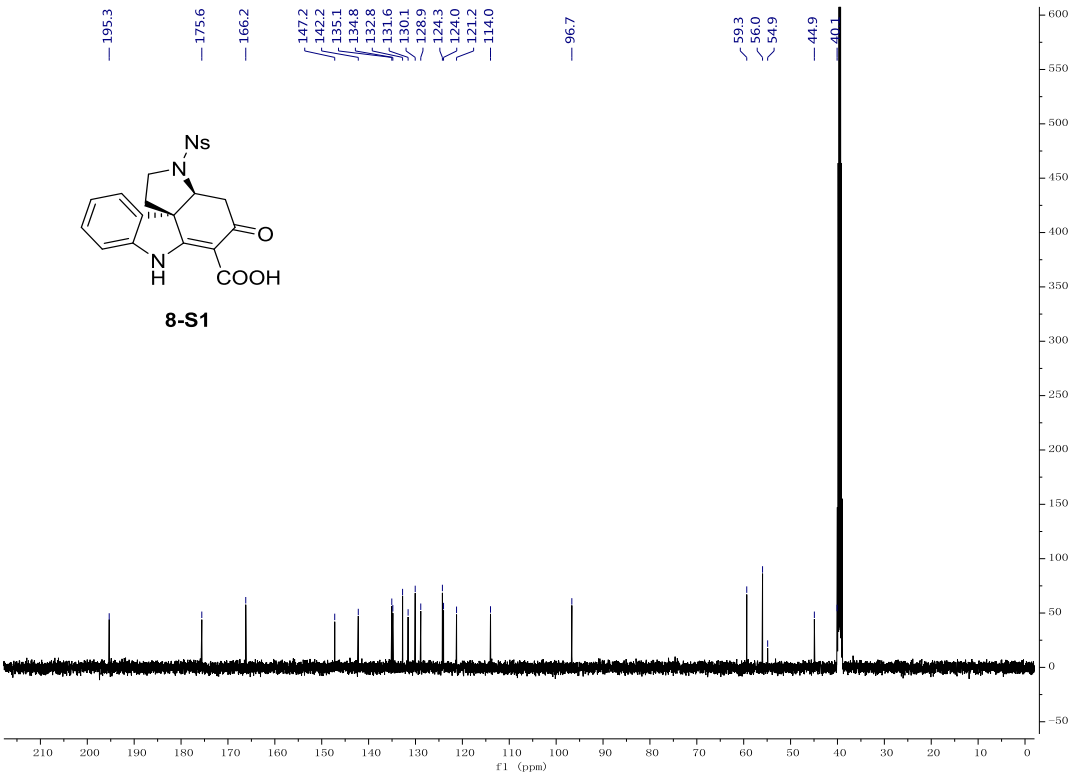
^{13}C NMR spectrum of compound **12** (126 MHz, DMSO-d_6)



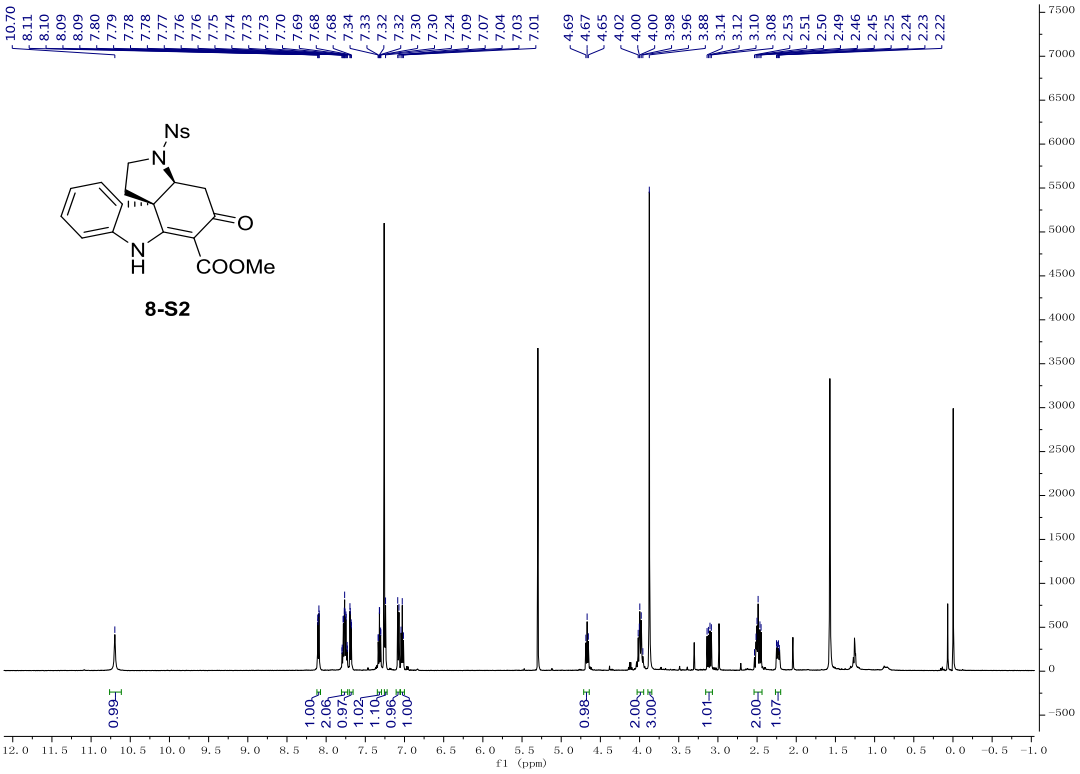
^{1}H NMR spectrum of compound **8-S1** (500 MHz, DMSO-d_6)



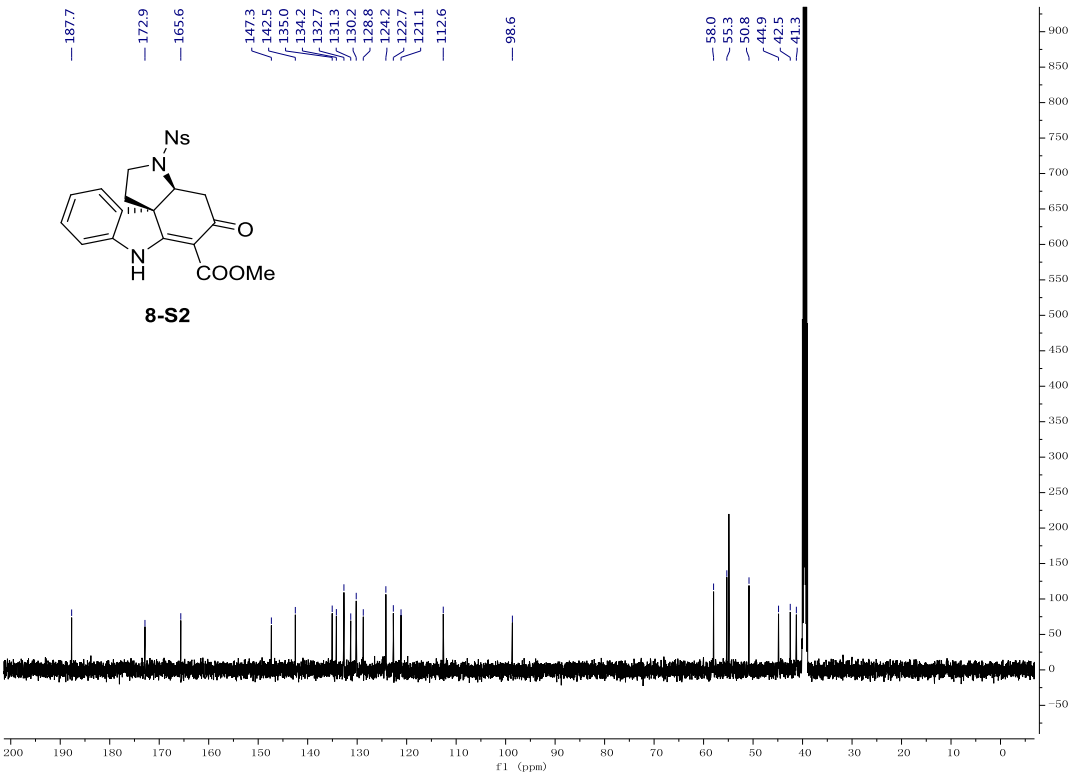
^{13}C NMR spectrum of compound **8-S1** (126 MHz, DMSO-d_6)



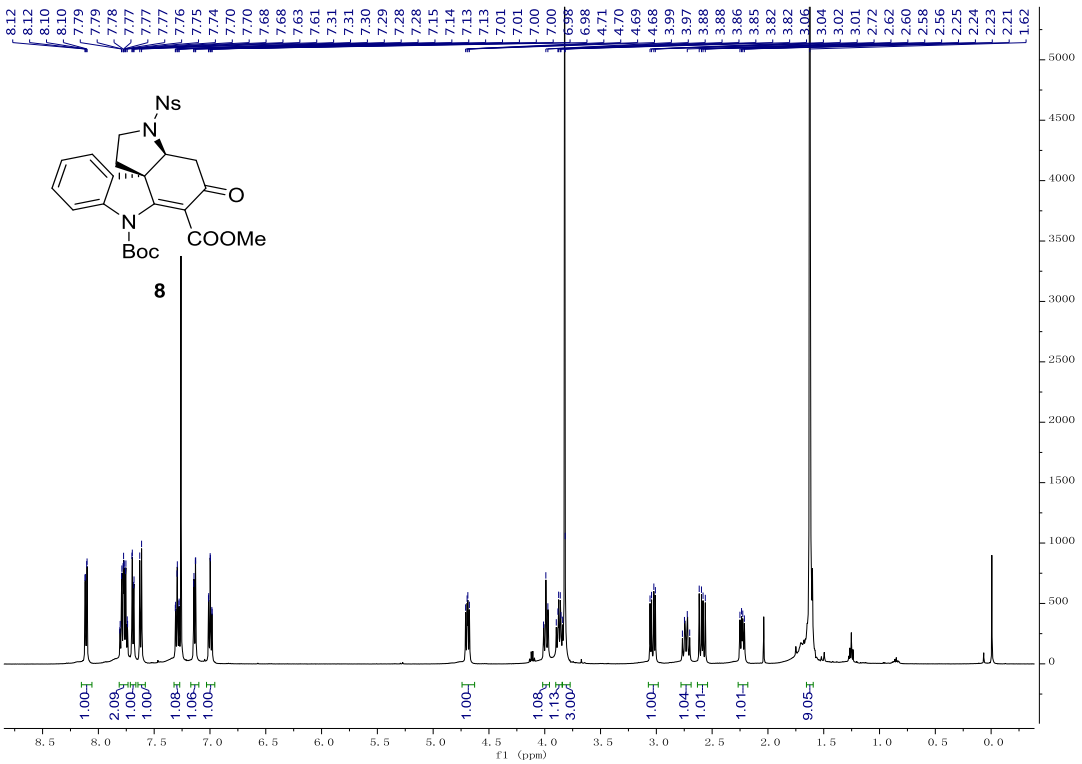
^{1}H NMR spectrum of compound **8-S2** (500 MHz, Chloroform-*d*)



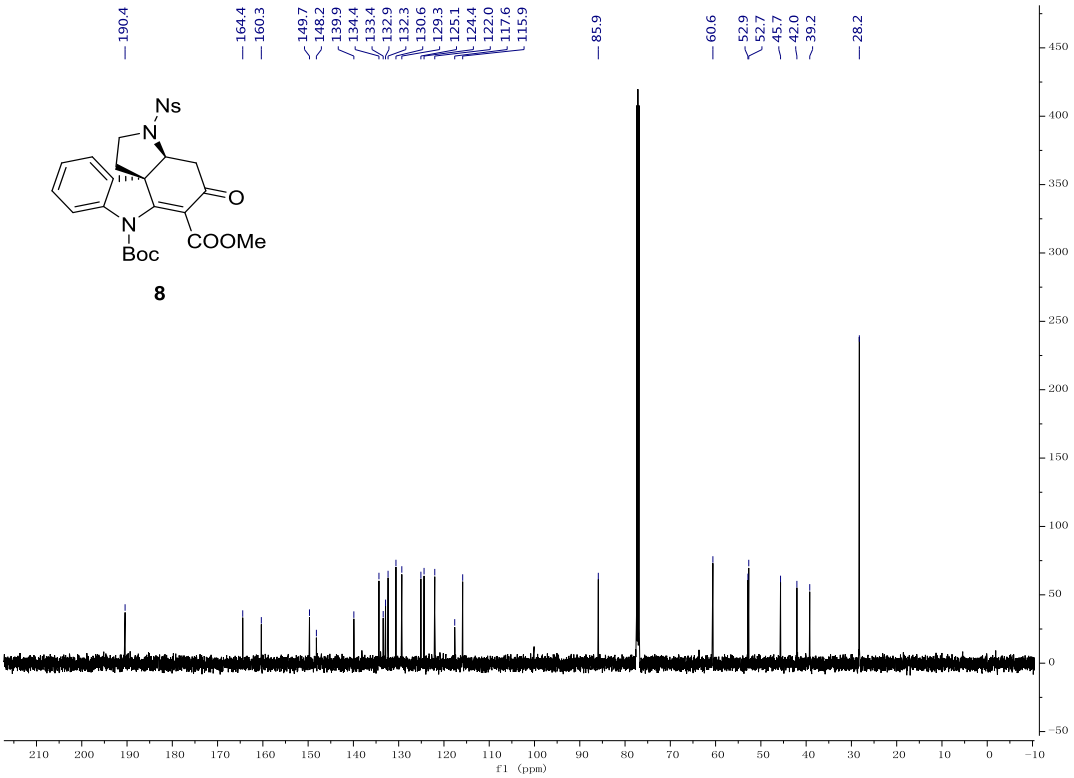
^{13}C NMR spectrum of compound **8-S2** (126 MHz, DMSO-d_6)



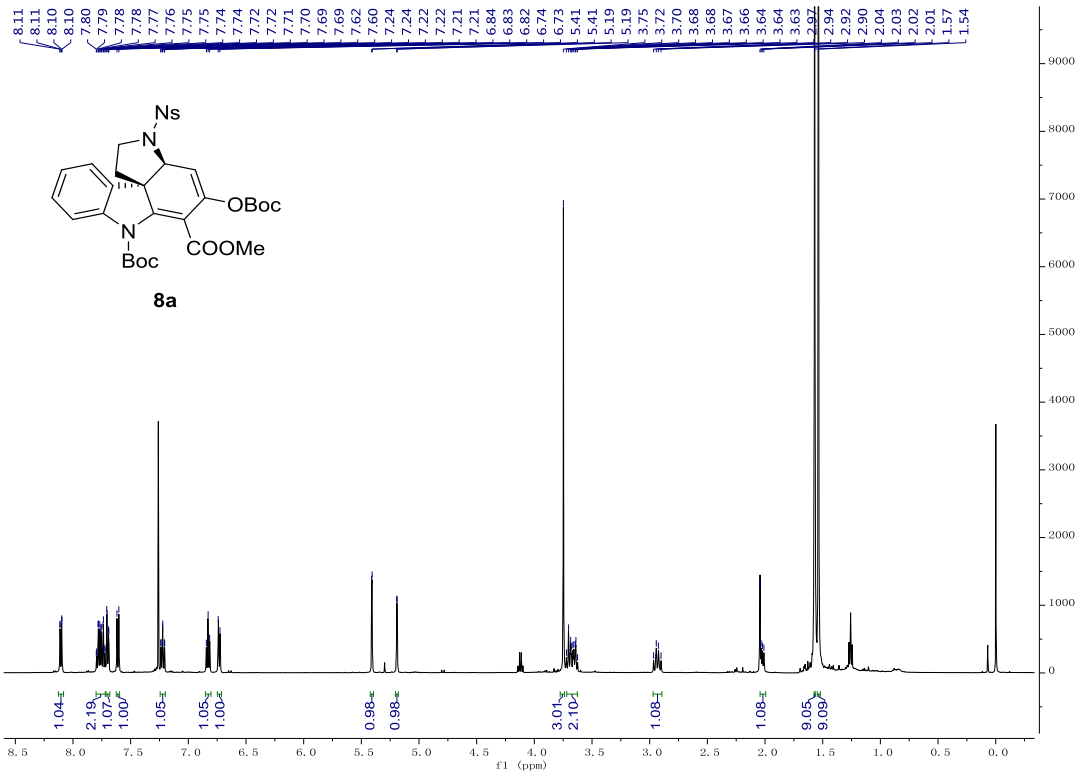
^{1}H NMR spectrum of compound **8** (500 MHz, Chloroform-*d*)



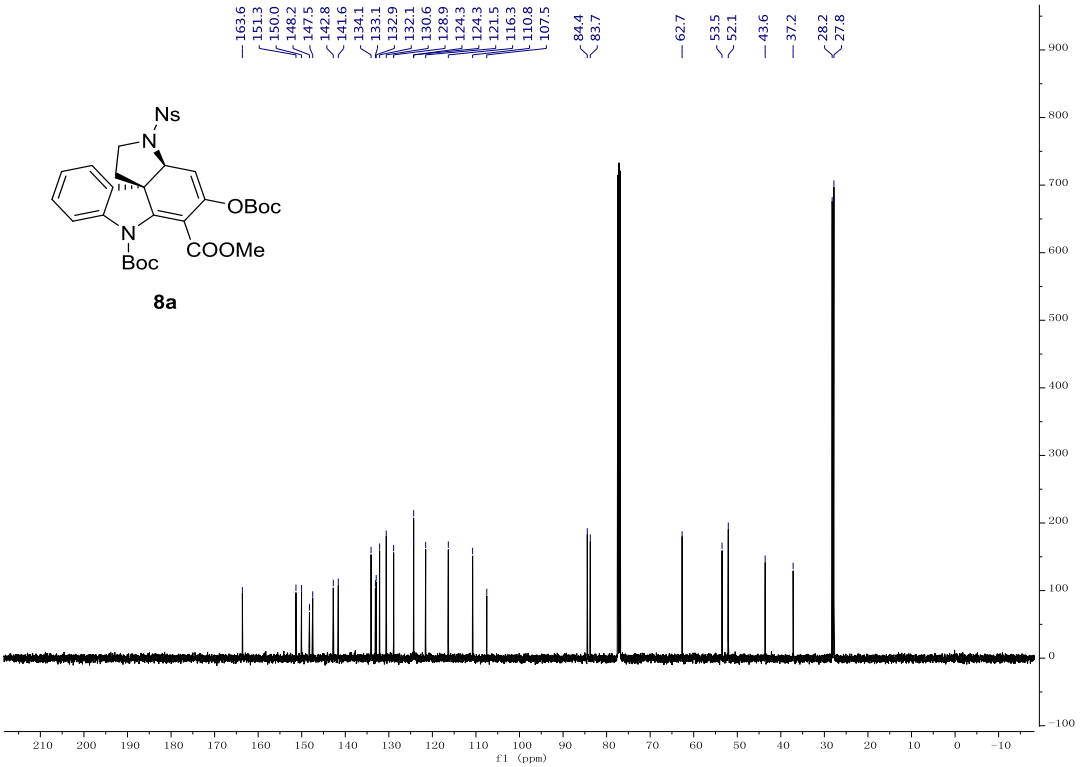
^{13}C NMR spectrum of compound **8** (126 MHz, Chloroform-*d*)



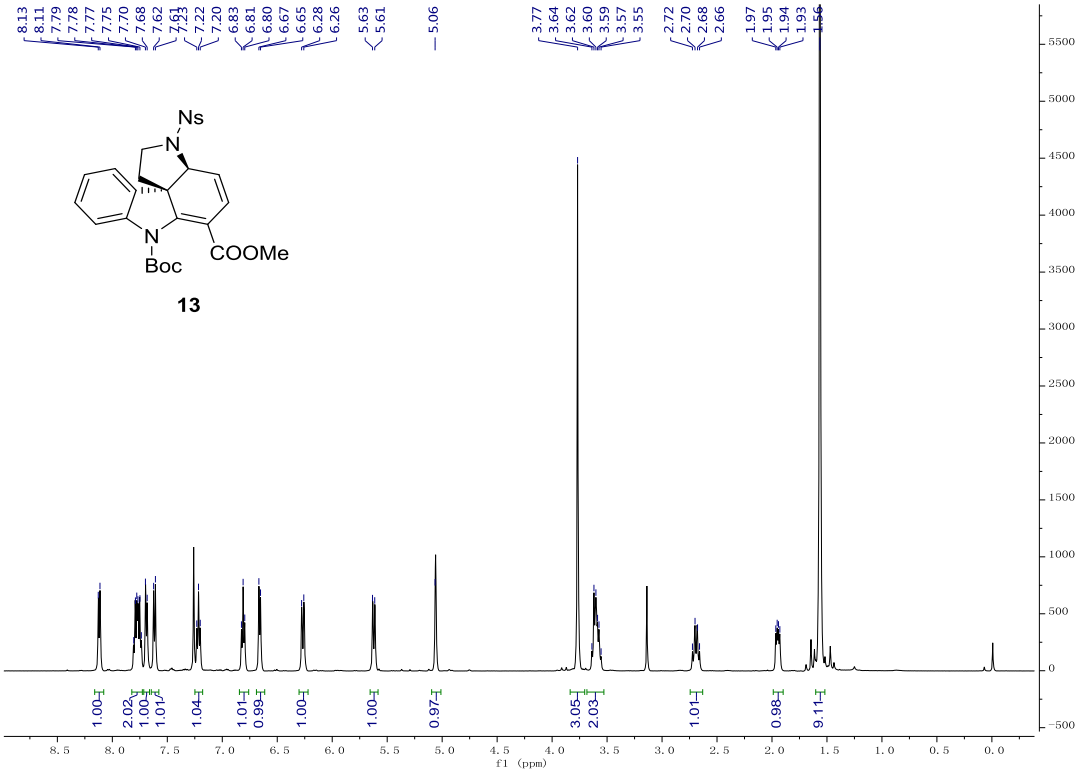
^{1}H NMR spectrum of compound **8a** (500 MHz, Chloroform-*d*)



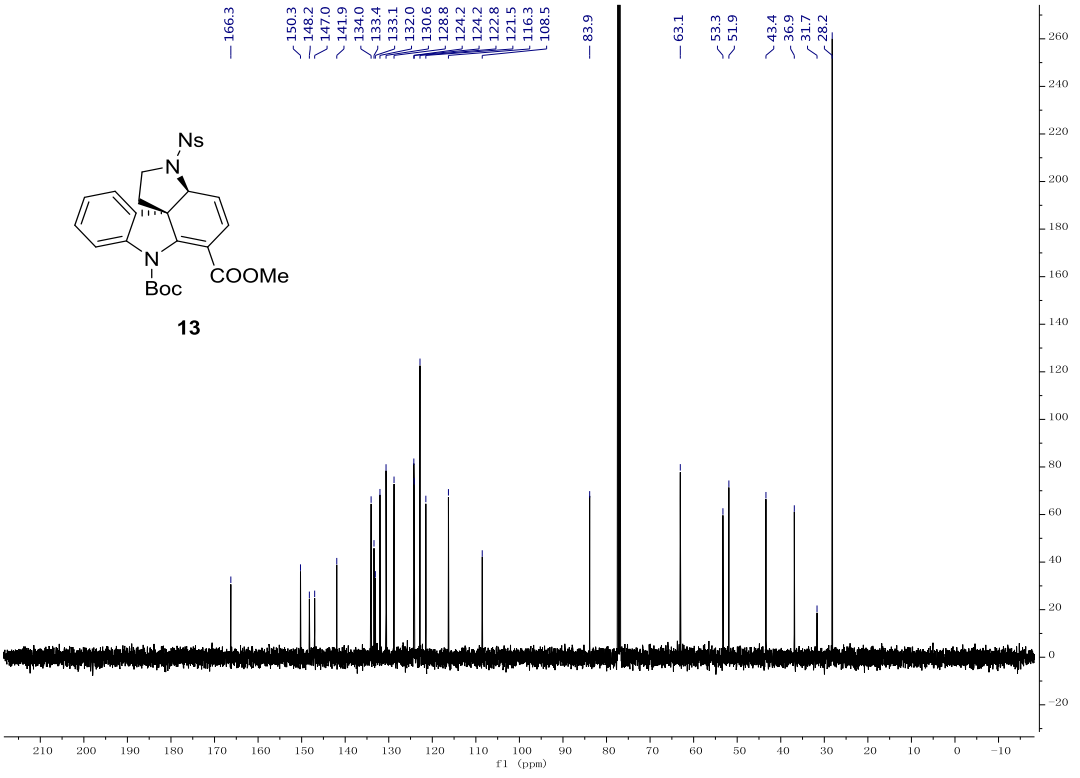
^{13}C NMR spectrum of compound **8a** (126 MHz, Chloroform-*d*)



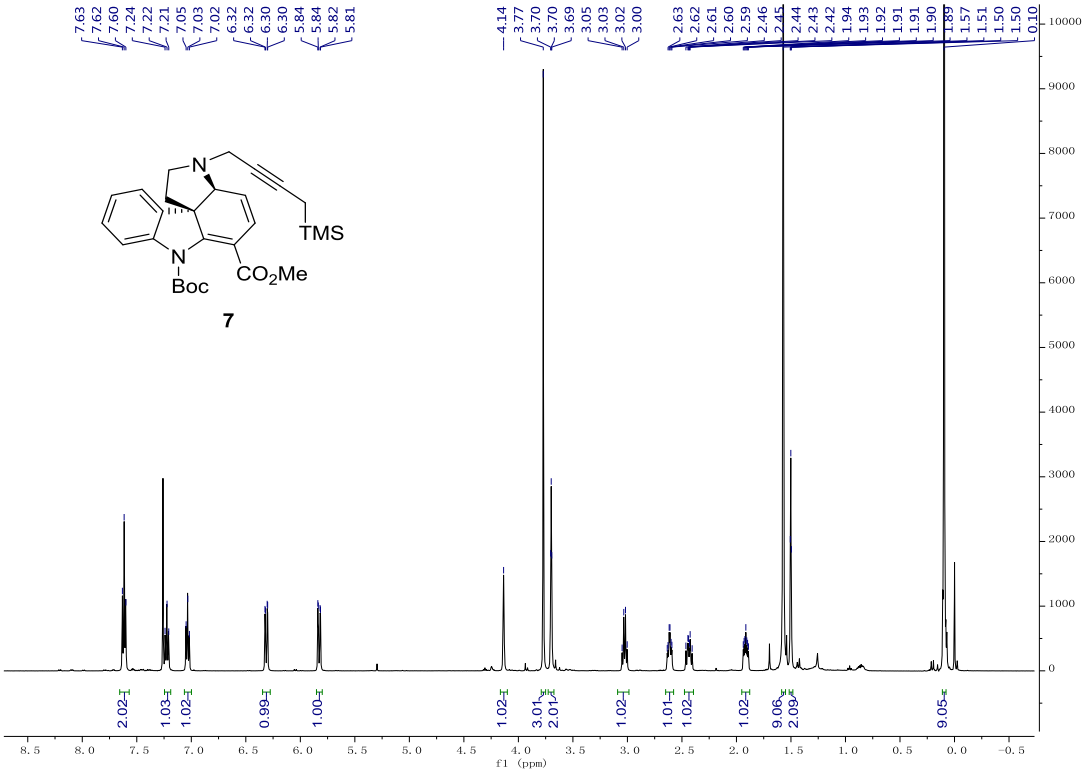
^{1}H NMR spectrum of compound **13** (500 MHz, Chloroform-*d*)



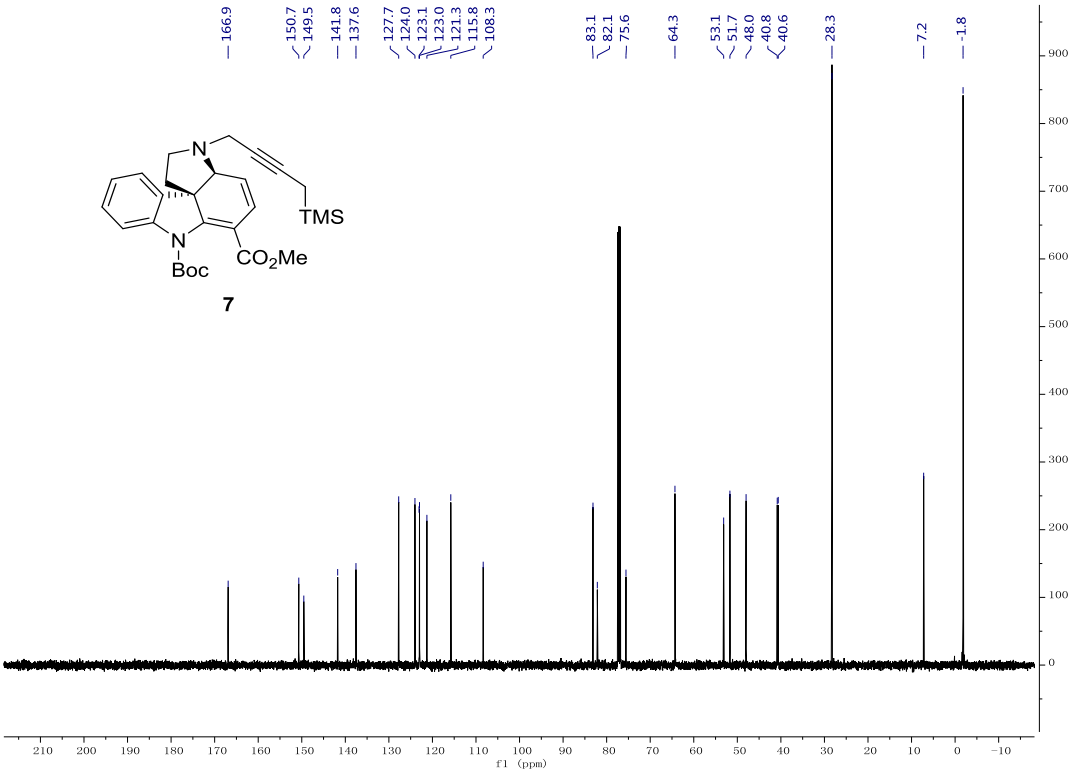
^{13}C NMR spectrum of compound **13** (126 MHz, Chloroform-*d*)



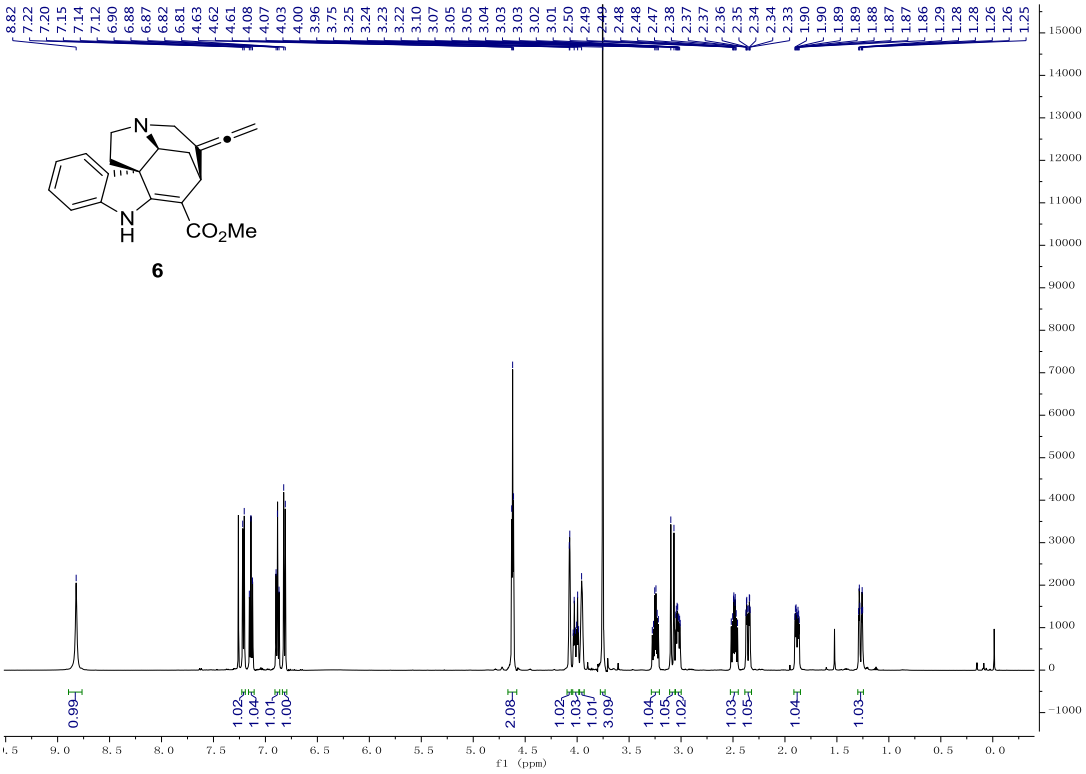
^{1}H NMR spectrum of compound **7** (500 MHz, Chloroform-*d*)



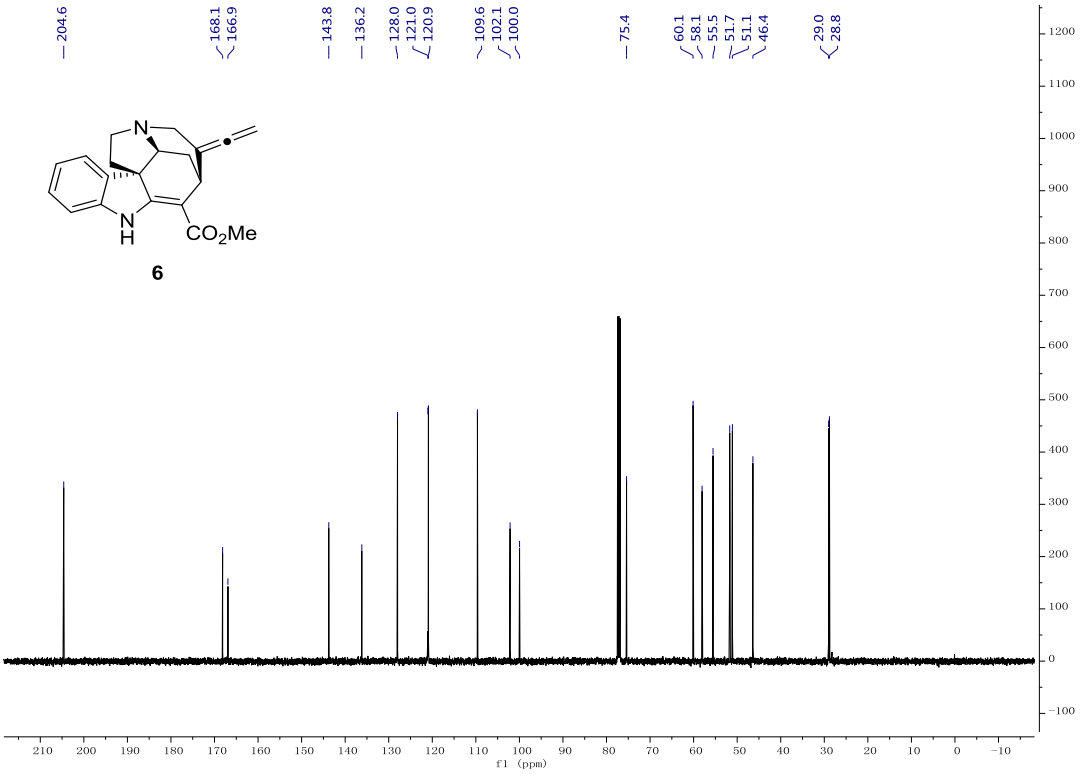
^{13}C NMR spectrum of compound **7** (126 MHz, Chloroform-*d*)



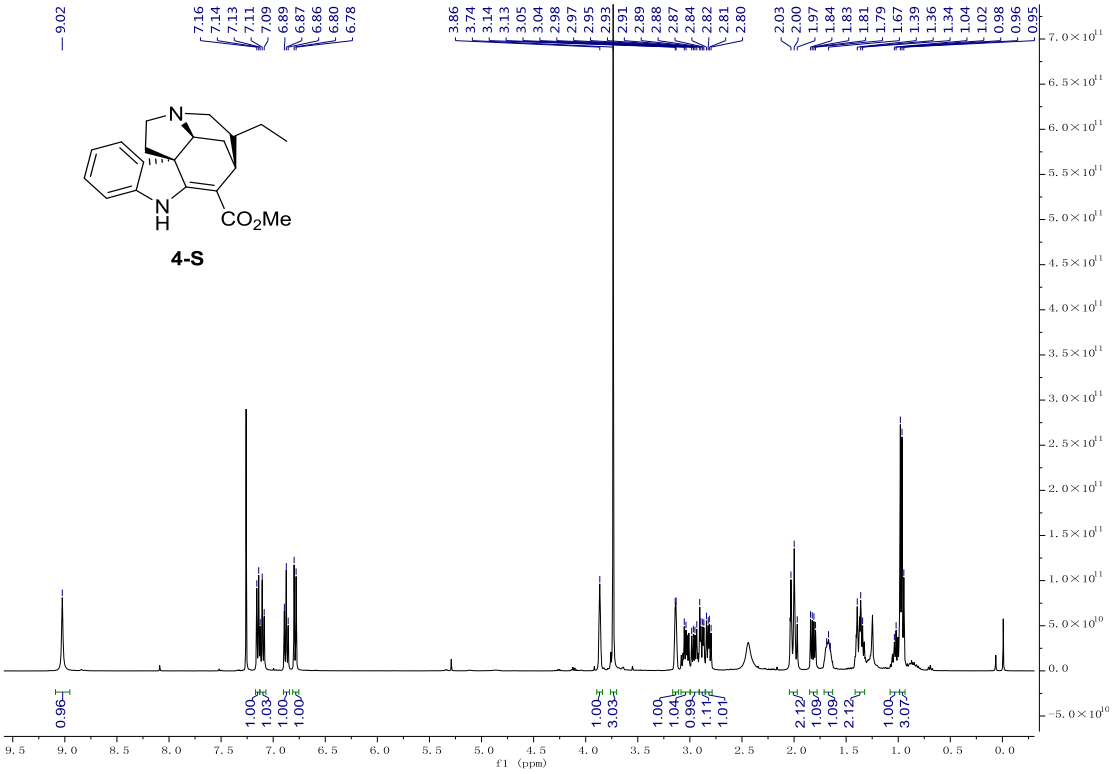
^{1}H NMR spectrum of compound **6** (500 MHz, Chloroform-*d*)



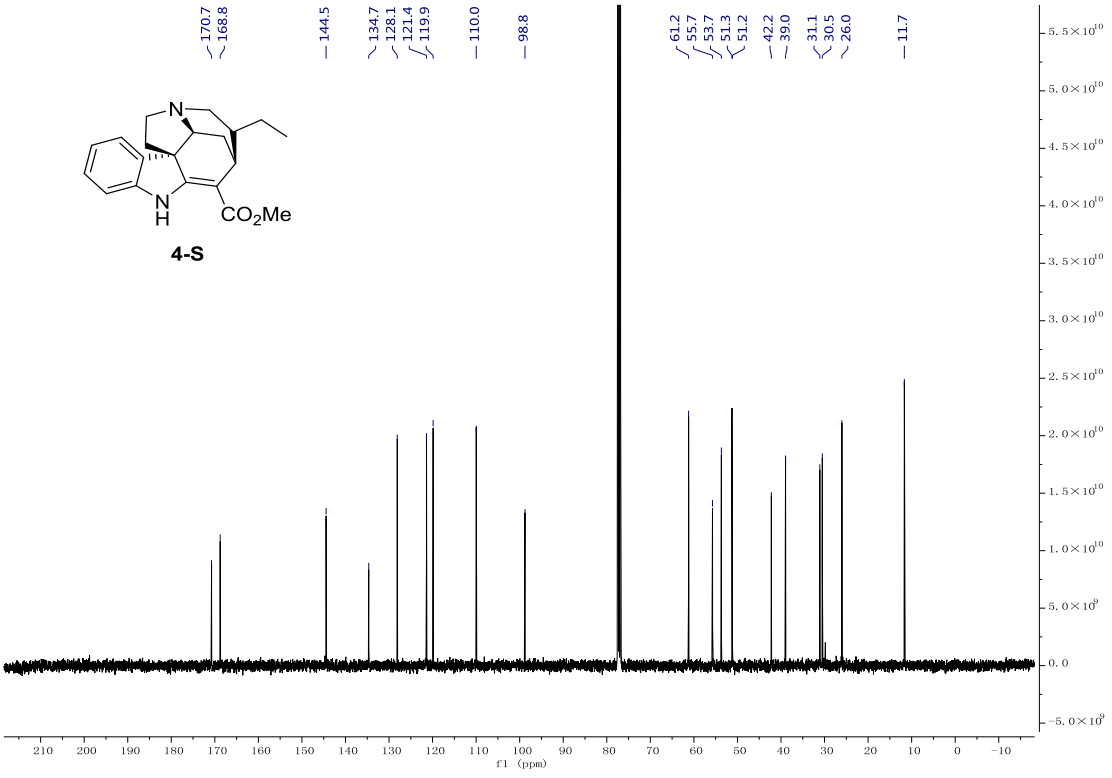
^{13}C NMR spectrum of compound **6** (126 MHz, Chloroform-*d*)



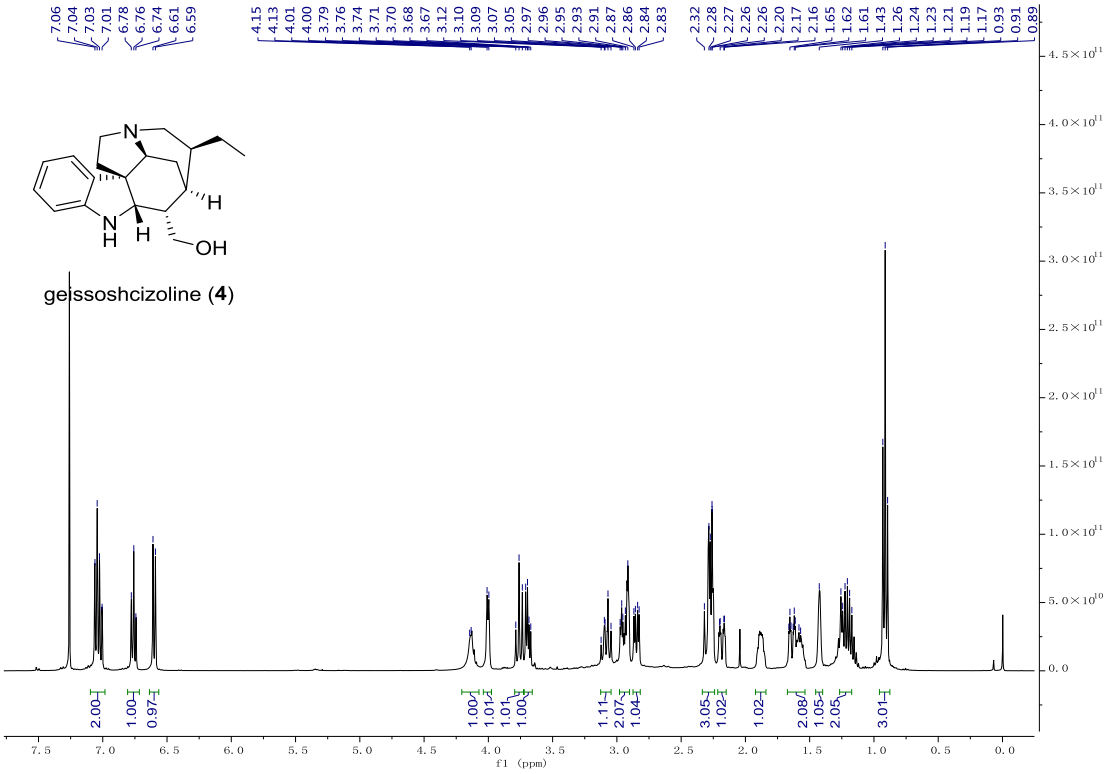
^{1}H NMR spectrum of compound **4-S** (400 MHz, Chloroform-*d*)



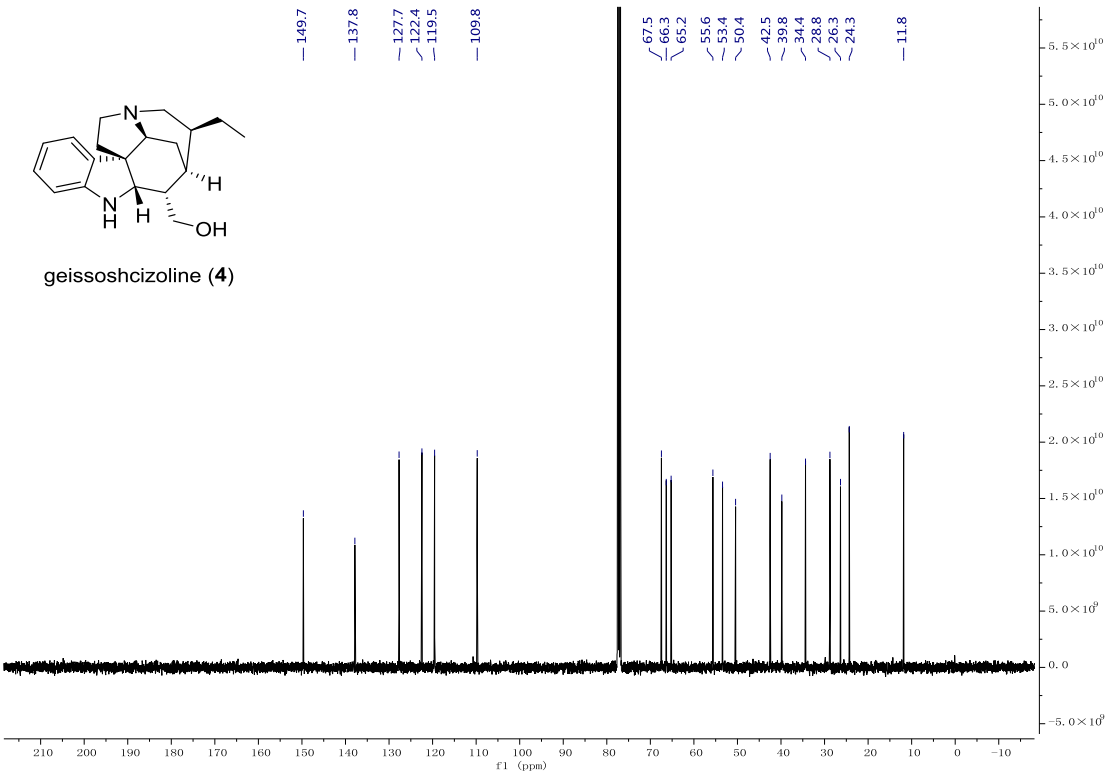
^{13}C NMR spectrum of compound **4-S** (101 MHz, Chloroform-*d*)



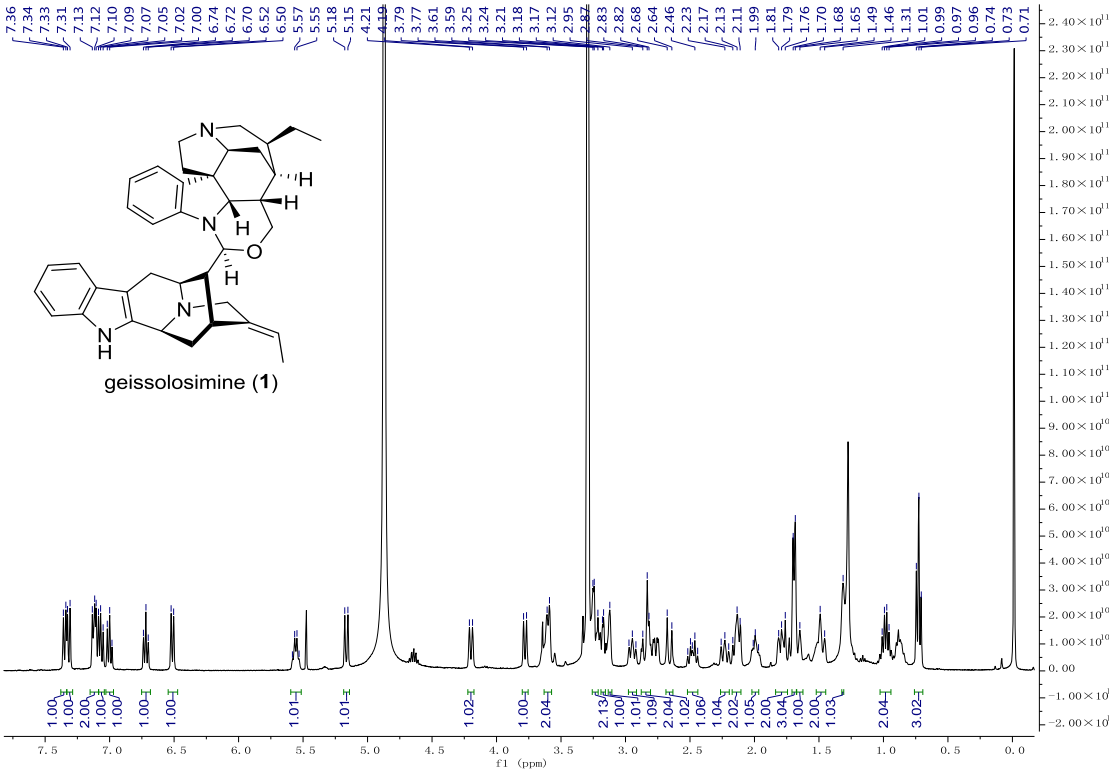
^{1}H NMR spectrum of compound **4** (400 MHz, Chloroform-*d*)



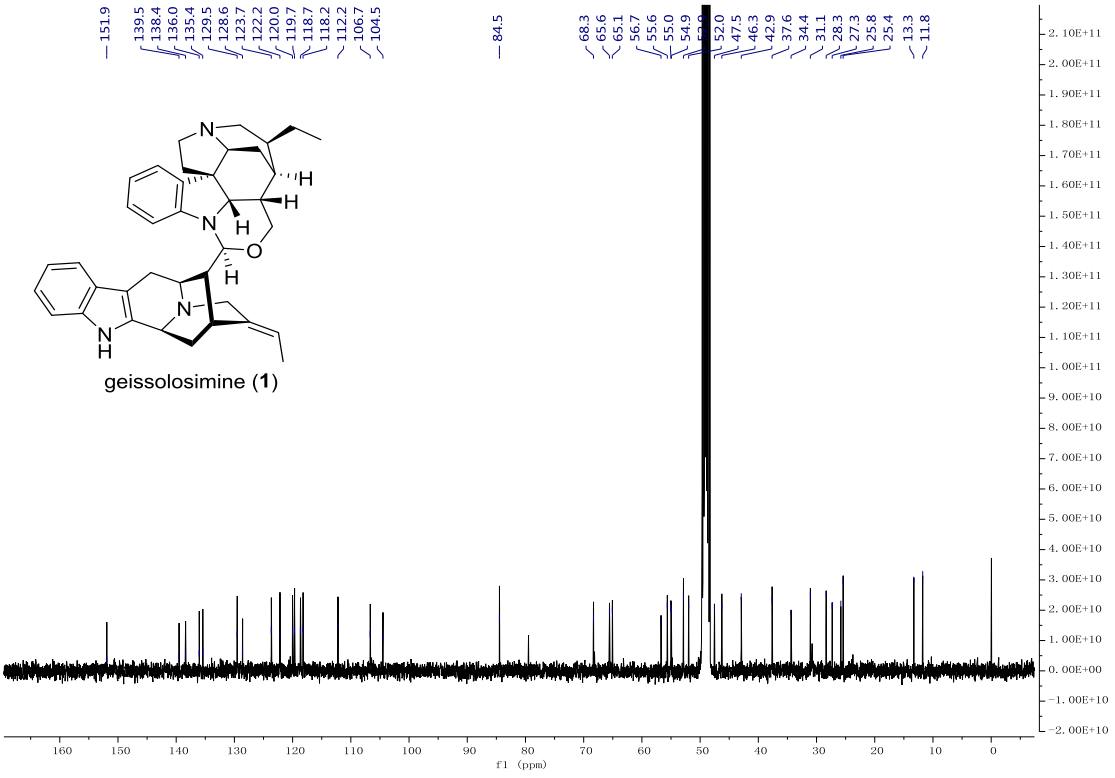
^{13}C NMR spectrum of compound **4** (101 MHz, Chloroform-*d*)



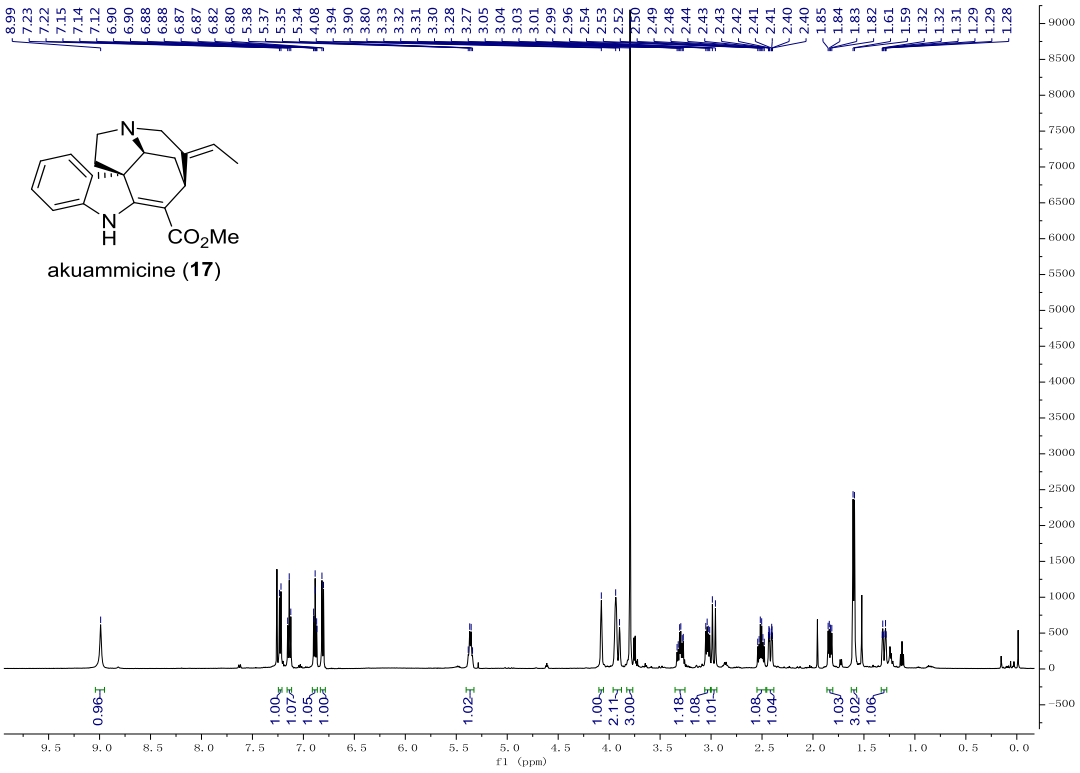
^{1}H NMR spectrum of compound **1** (400 MHz, Methanol-d_4)



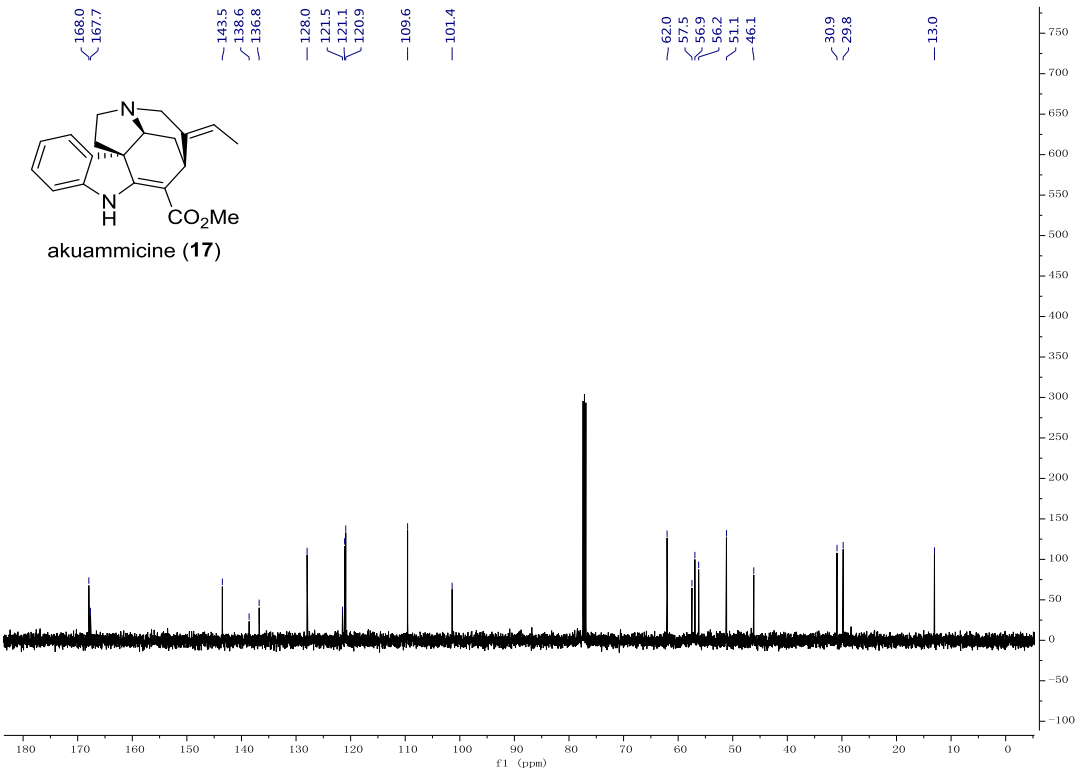
^{13}C NMR spectrum of compound **1** (101 MHz, Methanol-d_4)



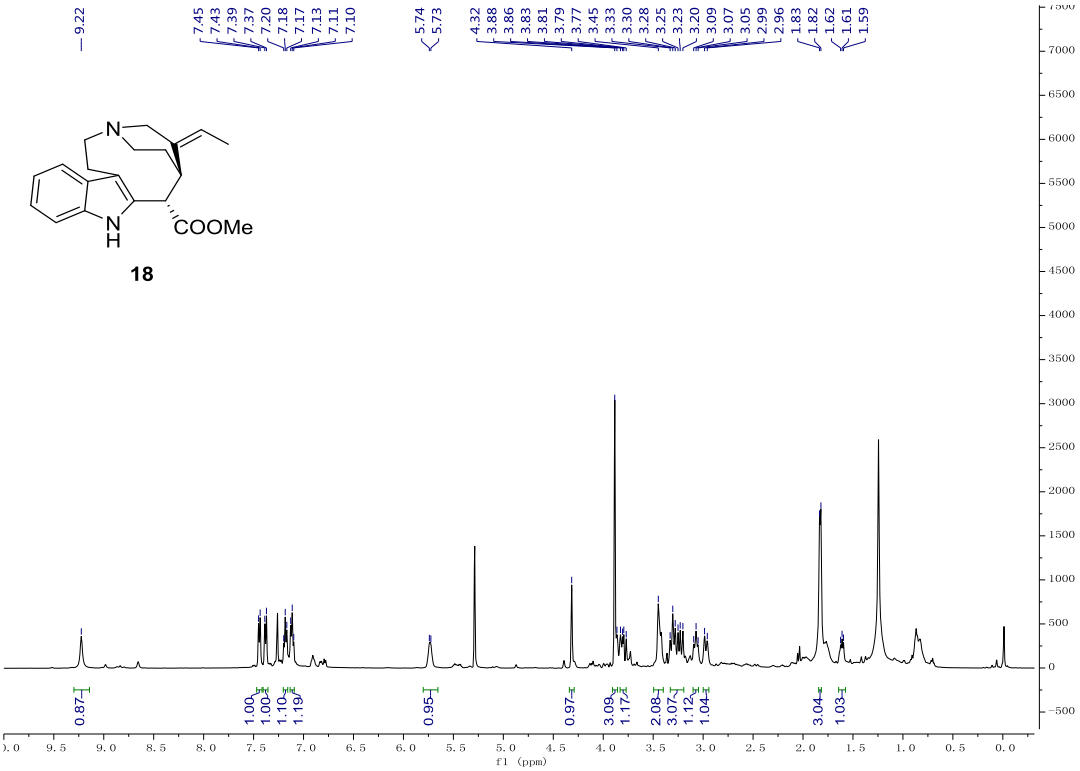
^{1}H NMR spectrum of compound **17** (500 MHz, Chloroform-*d*)



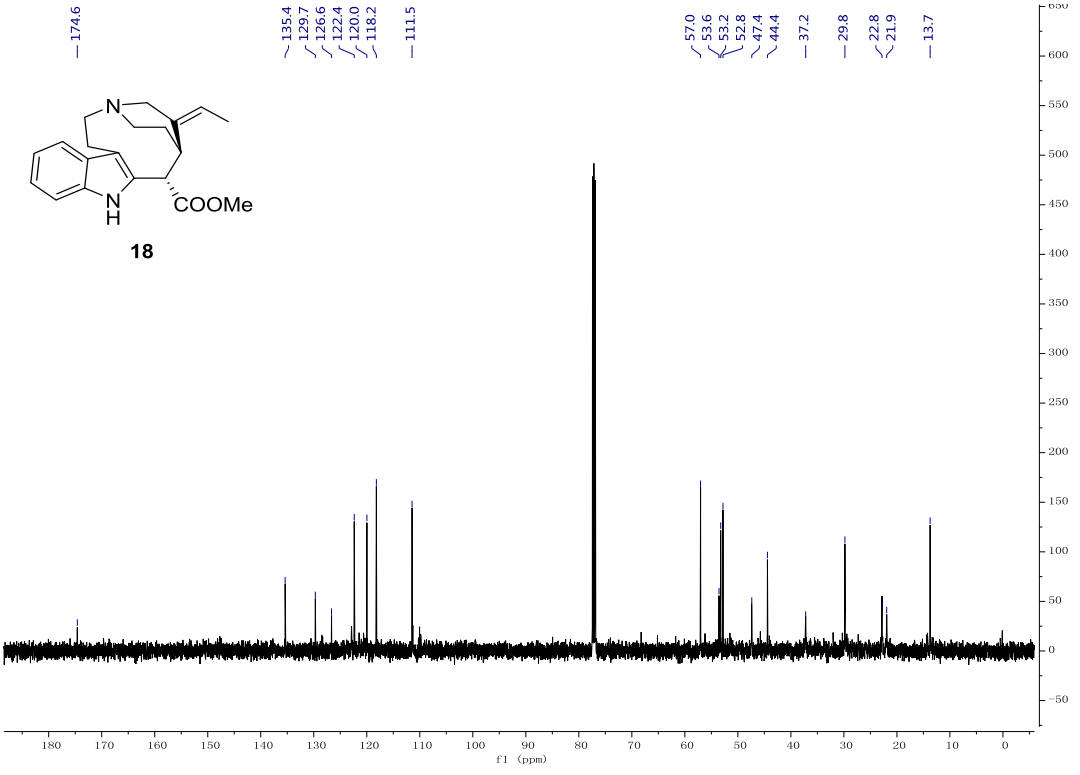
^{13}C NMR spectrum of compound **17** (126 MHz, Chloroform-*d*)



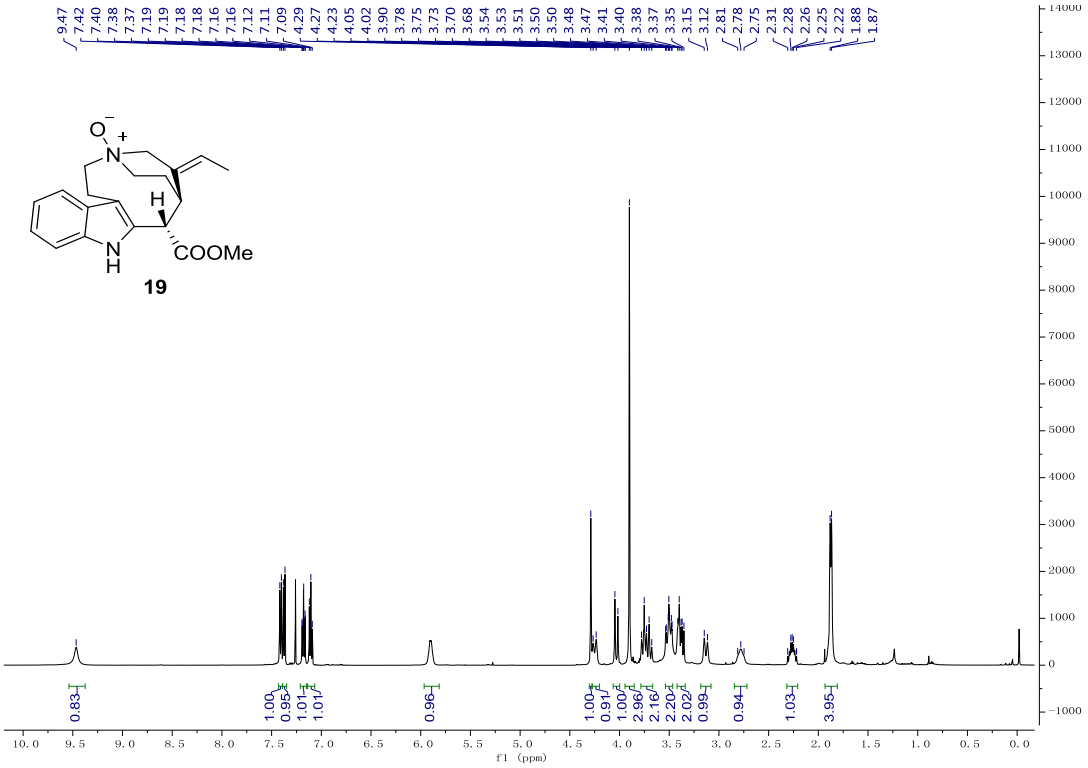
^{1}H NMR spectrum of compound **18** (500 MHz, Chloroform-*d*)



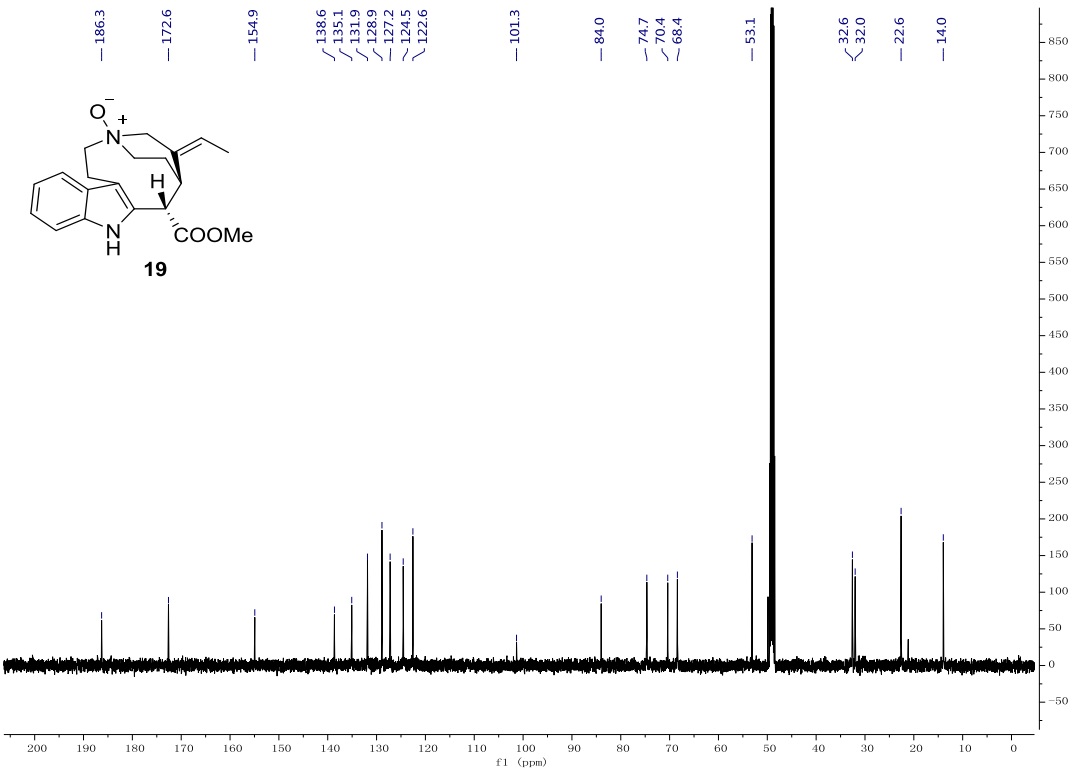
^{13}C NMR spectrum of compound **18** (126 MHz, Chloroform-*d*)



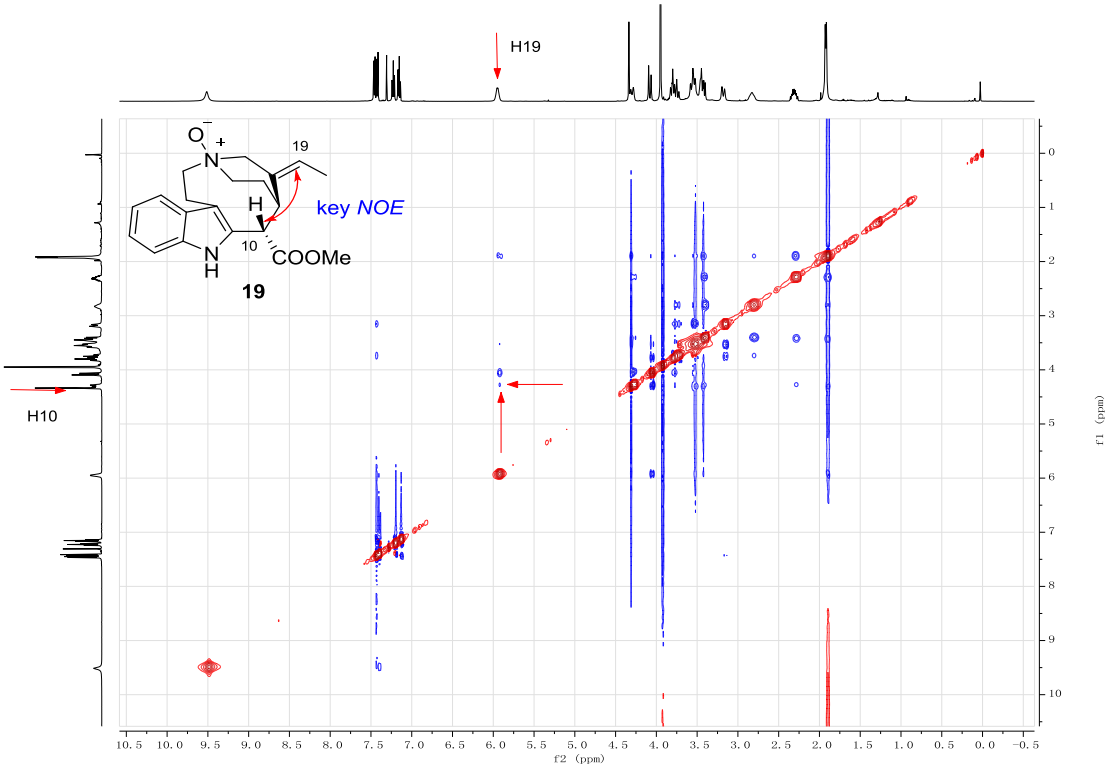
^{1}H NMR spectrum of compound **19** (500 MHz, Chloroform-*d*)



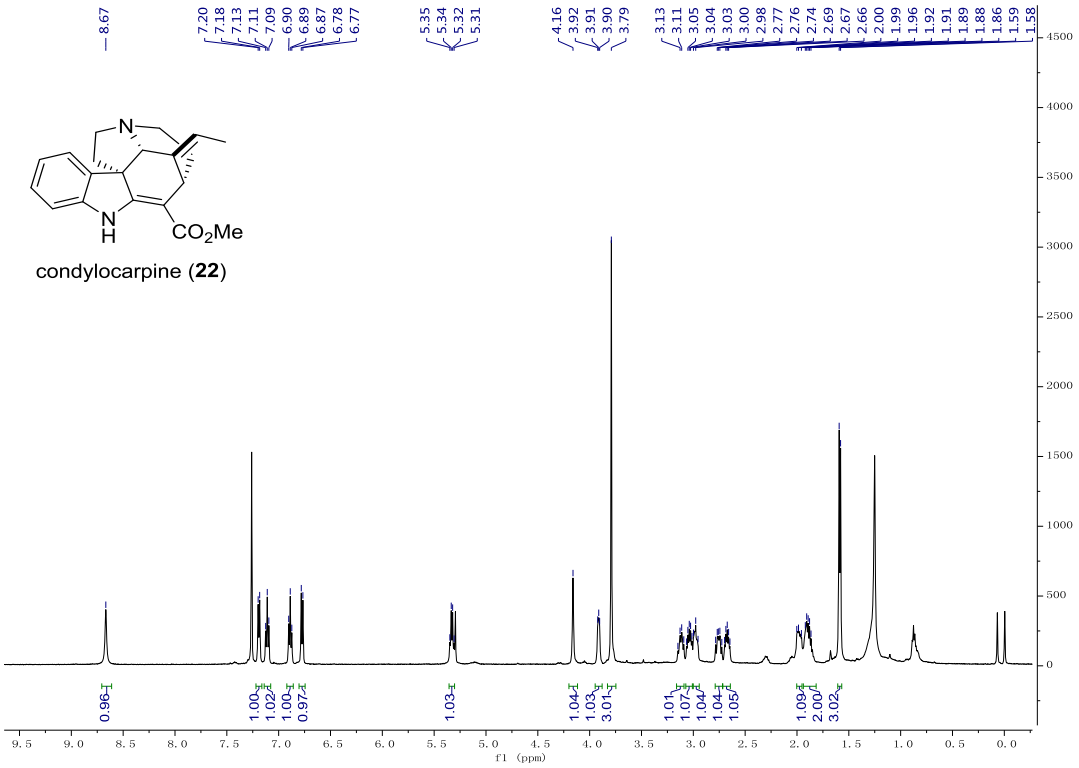
^{13}C NMR spectrum of compound **19** (126 MHz, Methanol-d_4)



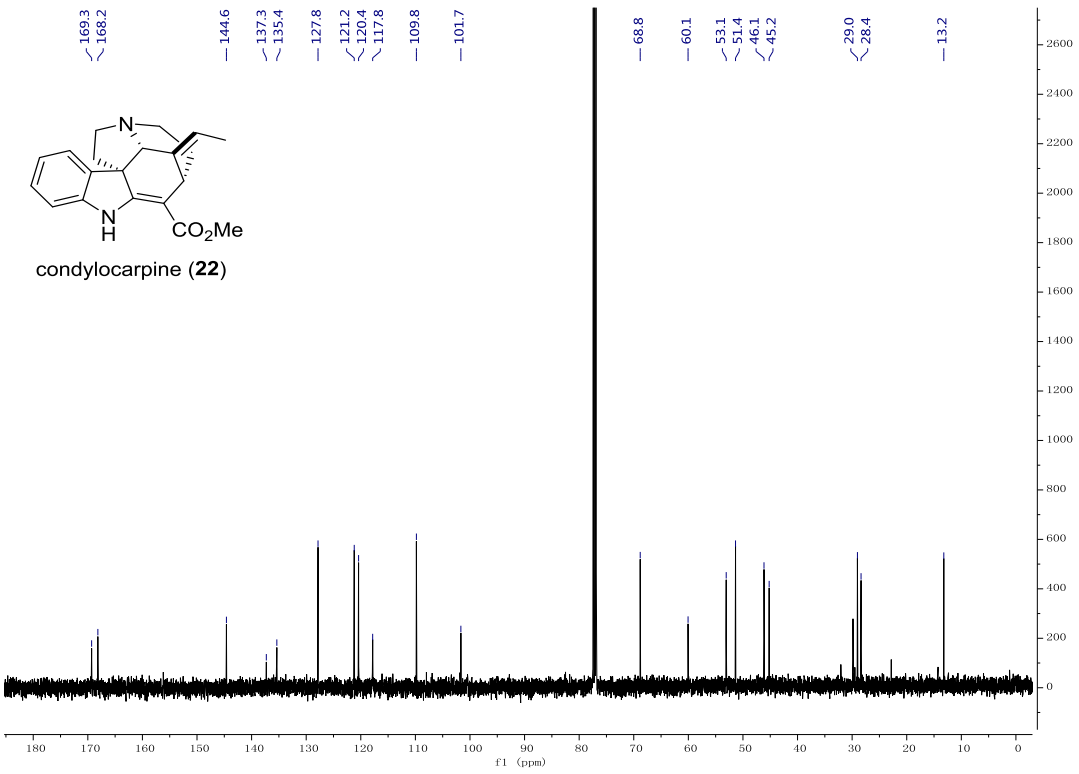
NOESY spectrum of compound **19** (Chloroform-*d*)



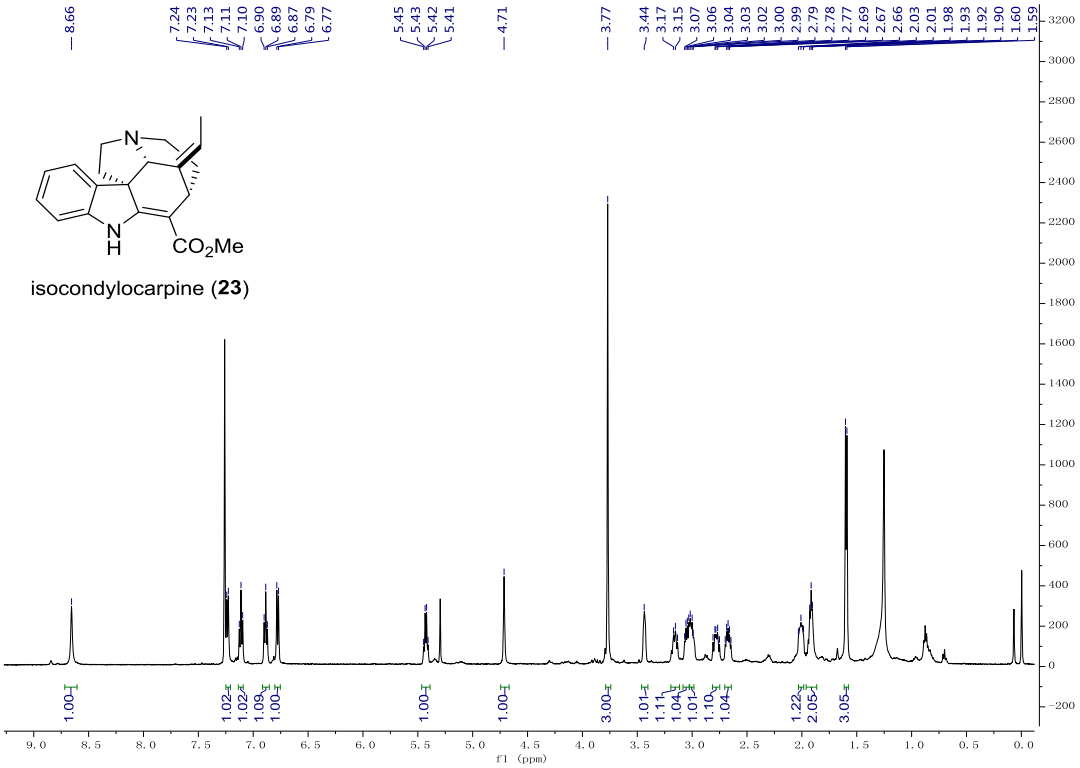
^{1}H NMR spectrum of compound **22** (500 MHz, Chloroform-*d*)



^{13}C NMR spectrum of compound **22** (126 MHz, Chloroform-*d*)



^{1}H NMR spectrum of compound **23** (500 MHz, Chloroform-*d*)



^{13}C NMR spectrum of compound **23** (126 MHz, Chloroform-*d*)