An expedient modeling construction of the BCDEF pentacyclic ring system analog of aconitine and racemulosine

Suyan Cao,[a] Hailian Li,[a] Jie Zhao,[a] Yuxuan Tang,[a] and Liang Xu*[a]

Key Laboratory of Drug Targeting and Drug Delivery Systems of the Ministry of Education, Department of Chemistry of Medicinal Natural Products, West China School of Pharmacy, and State Key Laboratory of Biotherapy, West China Hospital, Sichuan University, Chengdu 610041, China

E-mail: Liangxu@scu.edu.cn

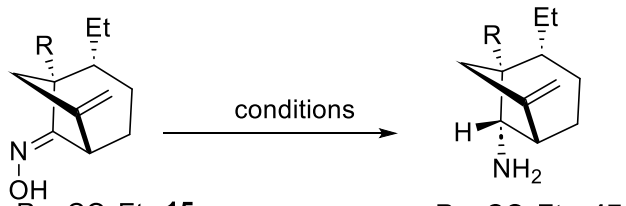
Table of Contents

1. General information

All reactions that require anhydrous conditions were performed in flame-dried glassware under Ar atmosphere and all reagents were purchased from commercial suppliers. Dry toluene was obtained according to Purification of Laboratory Chemicals (Peerrin, D. D.; Armarego, W. L. and Perrins, D. R., Pergamon Press: Oxford, 1980). Other dry solvents were purchased from Energy Chemical. Reactions were monitored by thin layer chromatography (TLC) supplied by Yantai Chemicals (China). Visualization was accomplished with UV light, exposure to iodine, stained with ethanolic solution of phosphomolybdic acid or basic solution of $KMnO_4$. The reaction products were purified by column chromatography on silica gel (200–300 meshes) from the Anhui Liangchen Silicon Material Company (China). ^1H NMR and ^{13}C NMR spectra were recorded on Varian INOVA-400/54 and Agilent DD2-600/54 instruments and calibrated by using residual undeuterated chloroform (δ, ^1H NMR = 7.26, ^{13}C NMR = 77.0). The following abbreviations are used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet, and coupling constants (J) are reported in Hertz (Hz). Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum Two FT-IR spectrometer. High-resolution mass spectra (HRMS) were recorded on Bruker Apex IV FTMS or Thermo Scientific LTQ Orbitrap XL ESI mass spectrometers. LC-MS analysis was performed on HP Agilent 6420 Triple Quad LC/MS. The specific optical rotation was obtained from Rudolph Research Analytical Autopol VI automatic polarimeter.

2. Evolution of the Key Reaction

Section 2.1 Attempts to reduce 15/16 by using some single electron donor reductants.

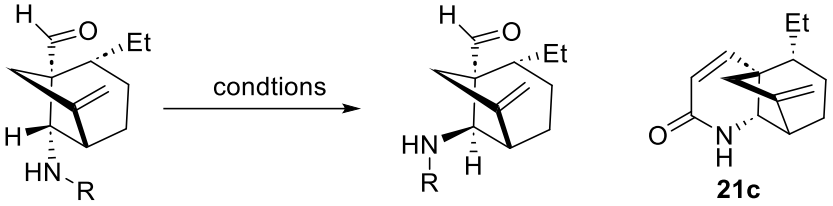


R = CO_2Et **15**
R = CH_2OH **16**

R = CO_2Et **17**
R = CH_2OH **18**

Entry	Substrates	Conditions	Results (yield)
1		Li, $NH_3(l)$, THF, -78 °C	decomposed
2		SmI_2, HMPA, THF, 0 °C to rt	**17**, 40%
3	**15**	SmI_2, HMPA, PhSH, THF, 0 °C to rt	SM recovered
4		SmI_2, MeOH, THF, 0 °C to rt	**17**, 71%
5		SmI_2, H_2O, THF, 0 °C to rt	**17**, 30%
6		Li, $NH_3(l)$, THF, -78 °C	decomposed
7		SmI_2, HMPA, THF, 0 °C to rt	**18**, 80%
8	**16**	SmI_2, HMPA, PhSH, THF, 0 °C to rt	**18**, 78%
9		SmI_2, H_2O, THF, 0 °C to rt	SM recovered
10		SmI_2, MeOH, THF, 0 °C to rt	**18**, 82%

Section 2.2 Optimization of the retro-Mannich/Mannich reaction of aldehyde substrates



20 R = Ns
20a R = Ts
20b R = Et
20c R = Ac
20d R = Boc

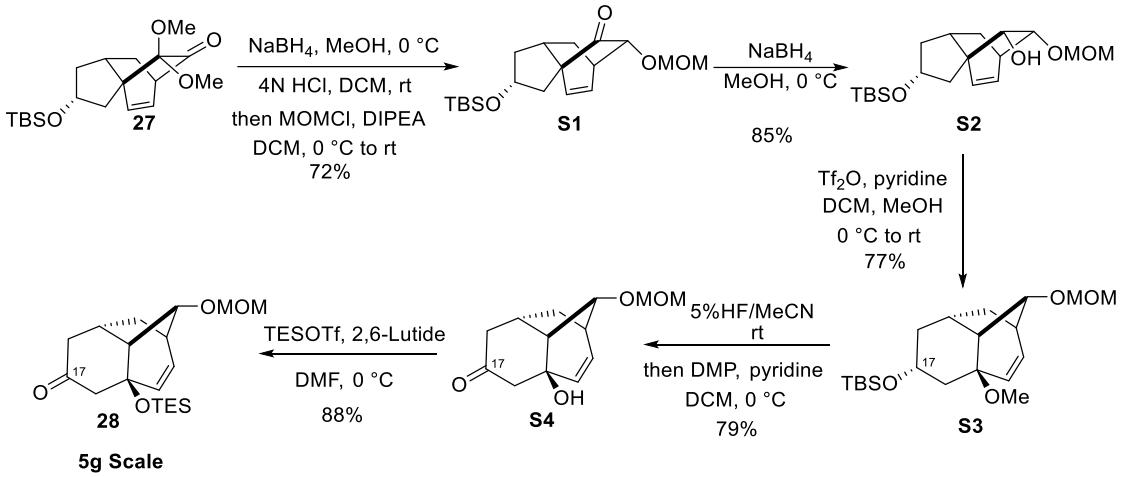
21 R = Ns
21a R = Ts
21b R = Et

21c

Entry	Substrates	Conditions	Results (yield)[a]
1		TFA, DCE, 0 °C to rt	decomposed
2		TsOH, DCE, 0 °C to rt	decomposed
3		BF_3•Et_2O, DCM, 0 °C to rt	decomposed
4	**20**	TMSOTf, MeCN, rt	SM recovered
5		LDA, DIPEA, THF, -78 °C	decomposed
6		NaH, THF, rt to reflux	decomposed
7		Cs_2CO_3, MeOH, rt to reflux	**21** (85%)
8	**20a**	Cs_2CO_3, MeOH, rt to reflux	**21a** (63%)
9	**20b**	Cs_2CO_3, MeOH, rt to reflux	**21b** (50%)
10		LiHMDS, THF, 0 °C to reflux	SM recovered
11		NaH, THF, 0 °C to reflux	SM recovered
12		*t*-BuOK, THF, 0 °C to reflux	SM recovered
13	**20c**	Cs_2CO_3, MeOH, 0 °C to reflux	SM recovered
14		Cs_2CO_3, EtOH, 0 °C to reflux	**21c** (78%)
15		$NaOCH_3$, MeOH, 0 °C to reflux	SM recovered
16		$NaOCH_3$, THF, 0 °C to reflux	SM recovered
17		LiHMDS, THF, 0 °C to reflux	SM recovered
18		NaH, THF, 0 °C to reflux	SM recovered
19		*t*-BuOK, THF, 0 °C to reflux	SM recovered
20	**20d**	Cs_2CO_3, MeOH, 0 °C to reflux	SM recovered
21		DBU, THF, 0 °C to reflux	SM recovered
22		LDA, THF, 0 °C to reflux	SM recovered
23		$NaOCH_3$, MeOH, 0 °C to reflux	SM recovered

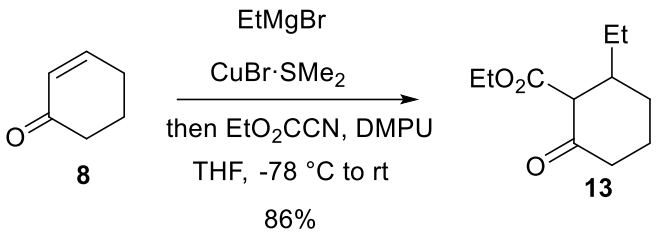
[a] separated yield

3. Gram-scale synthesis of 28 from 27 (ref. 15c).



4. Experimental Procedures and Characterization Data

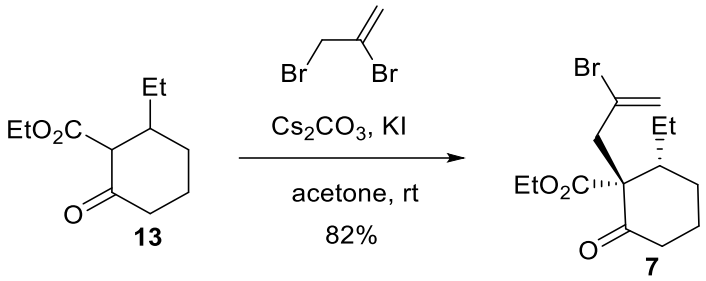
Preparation of Compound 13



In a 2 L flask, $CuBr{\cdot}SMe_2$ (5.1 g, 25 mmol.) was suspended in THF (620 mL) and cooled to -50 °C. Ethylmagnesium bromide solution (3.0 M in THF, 45.8 mL, 137 mmol) was added to the reaction via addition funnel over 30 minutes. After 30 minutes, the reaction flask was cooled to -78 °C. Cyclohexenone (12 g, 125 mmol) was added after 10 minutes. After 2 hours of stirring, freshly distilled DMPU (48.0 g, 45.3 mL, 374 mmol) was added, followed by ethyl cyanoformate (14.9 g, 13.9 mL, 150 mmol) was added. The reaction mixture was allowed to slowly warm to room temperature, and was quenched after 12 hours by addition of H_2O (300 mL). The aqueous layer was extracted with EtOAc (300 mL × 3) and the combined organic layers were washed with brine (500 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure by rotary evaporation. Purification of the residue by flash column chromatography (petroleum ether / ethyl acetate = 16:1 to 8:1) furnished **13** as a colorless oil (21.3 g, 86%). The characterization data are consistent with those reported in the literature.

TLC (petroleum ether / ethyl acetate, 6:1 v/v): R_f = 0.42; **IR** (neat) ν_{max}: 3340, 3027, 2994, 2965, 2922, 2855,1732, 1715, 1658, 1622, 1480, 1362, 1235, 1085 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 12.39 (s, 1H), 4.27 – 4.18 (m, 4H), 3.12 (dd, *J* = 10.8, 1.2 Hz, 1H), 2.51 – 2.45 (m, 1H), 2.43 – 2.36 (m, 1H), 2.33 – 2.22 (m, 3H), 2.21 – 2.11 (m, 1H), 2.07 – 2.05 (m, 3H), 1.76 – 1.63 (m, 4H), 1.50 – 1.35 (m, 5H), 1.32 – 1.26 (m, 6H), 0.95 – 0.88 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 206.6, 173.0, 172.5, 170.1, 103.0, 63.6, 61.0, 60.2, 42.6, 41.3, 33.4, 29.3, 28.5, 27.6, 27.3, 25.0, 24.8, 17.3, 14.4, 14.3, 12.6, 11.0; **HRMS (ESI)**: *m/z* calcd. for $C_{11}H_{18}O_3$ $[M+H]^+$ 199.1328, found 199.1325.

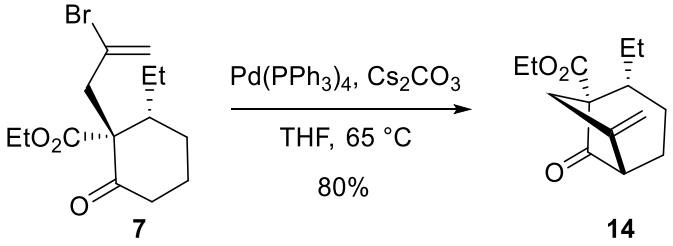
Preparation of Compound 7



To a three necked flask were added ketonester **13** (15.7 g, 75.7 mmol). The flask was evacuated and refilled with argon. Acetone (137 mL) was added to the flask under argon atmosphere, then Cs_2CO_3 (90.4 g, 277 mmol), 2,3-dibromopropene (19.0g, 9.8 mL, 94.8 mmol), KI (26.3 g, 158 mmol) were successively added at rt. After being stirred for 8 h at 23 °C, the reaction was quenched by saturated NH_4Cl solution (200 mL) and extracted with EtOAc (3 × 200 mL). The organic layer and extracts were combined, dried, and evaporated to dryness. Purification of the residue by flash column chromatography (petroleum ether / ethyl acetate = 20:1 to 10:1) furnished **7** as a colorless oil (20.4 g, 82%).

TLC (petroleum ether / ethyl acetate, 10:1 v/v): R_f = 0.52; **IR** (neat) ν_{max}: 3050, 2925, 2822, 1711, 1652, 1450, 1362, 1185, 562 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.83 – 5.81 (m, 1H), 5.64 (d, *J* = 2.0 Hz, 1H), 4.24 – 4.21 (m, 2H), 3.12 (dd, *J* = 10.8, 1.2 Hz, 1H), 2.78 – 2.75 (m, 1H), 2.71 – 2.61 (m, 1H), 2.52 – 2.46 (m, 1H), 2.33 – 2.12 (m, 4H), 2.09 – 1.97 (m, 3H), 1.28 (s, 3H), 0.93 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 206.6, 170.1, 127.7, 121.5, 63.6, 61.0, 43.0, 42.6, 41.3, 28.5, 27.6, 24.8, 14.3, 10.9; **HRMS (ESI)**: *m/z* calcd. for $C_{14}H_{21}BrO_3$ $[M+H]^+$ 317.0746, found 317.0749.

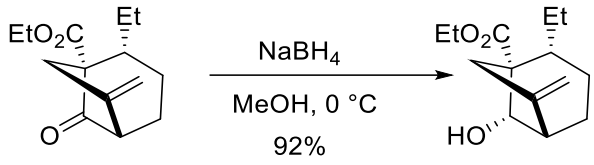
Preparation of Compound 14



A solution of **7** (16.7 g, 52.2 mmol) in anhydrous THF (522 mL) at 23 °C under argon, Cs_2CO_3 (51.6 g, 158.4 mmol), $Pd(PPh_3)_4$ (12.2 g, 10.5 mmol) were added. The reaction mixture was then stirred at 65 °C for 4 h. The resulting mixture was filtered through Celite, and the filter cake was rinsed with ethyl acetate. Afterwards, the filtrate was concentrated. Purification of the residue by flash column chromatography on silica gel (petroleum ether / ethyl acetate = 20:1 to 10:1) gave **14** as a colorless oil (10.0 g, 80%).

TLC (petroleum ether / ethyl acetate, 10:1 v/v): R_f = 0.43; **IR** (neat) ν_{max}: 3042, 2912, 2843, 1716, 1642, 1451, 1376, 1171 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.03 (dt, *J* = 9.6, 2.4 Hz, 2H), 4.26 – 4.15 (m, 3H), 3.02 – 2.84 (m, 1H), 2.92 – 2.82 (m, 2H), 2.41 – 2.32 (m, 1H), 2.27 – 2.16 (m, 1H), 1.93 – 1.81 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 4H), 1.09 – 1.05 (m, 1H), 0.91 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 210.6, 171.4, 142.7, 108.4, 62.2, 61.0, 55.5, 50.2, 40.3, 36.1, 22.5, 20.0, 14.3, 13.1; **HRMS (ESI)**: *m/z* calcd. for $C_{14}H_{20}O_3$ $[M+H]^+$ 237.1484, found 237.1488.

Preparation of Compound 14a



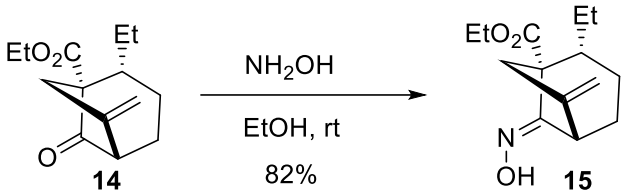
14 **14a**

To a solution of ketone **14** (1.0 g, 4.2 mmol) in MeOH (42 mL) was added $NaBH_4$ (320 mg, 8.5 mmol) at 0 °C. After being stirred at 0 °C for 10 min, the reaction mixture was then quenched by addition of saturated solution of NH_4Cl (30 mL). The organic layer was separated and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layers were washed with brine (15 mL) and dried over Na_2SO_4, filtered, and evaporated to dryness. Purification of the residue by flash column chromatography (petroleum ether / ethyl acetate = 20:1 to 10:1) furnished **14a** as a colorless oil (928 mg, 92%).

TLC (petroleum ether / ethyl acetate, 10:1 v/v): R_f = 0.32; **IR** (neat) ν_{max}: 3487, 3006, 2985, 2841, 1742, 1672, 1245, 1158, 1022cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.95

(td, J = 2.4, 1.6 Hz, 1H), 4.87 – 4.86 (m, 1H), 4.28 – 4.19 (m, 2H), 4.14 (dd, J = 10.8, 7.2Hz, 1H), 2.70 – 2.65 (m, 1H), 2.54 (d, J = 2.4 Hz, 1H), 2.44 (t, J = 2.4 Hz, 2H), 2.13 – 2.08 (m, 1H), 1.82 – 1.76 (m, 2H), 1.54 – 1.46 (m, 1H), 1.29 – 1.24 (m, 5H), 0.83 (d, J = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 177.1, 147.8, 107.2, 74.5, 60.6, 53.9, 45.9, 44.4, 40.1, 25.0, 21.9, 20.3, 14.4, 14.3; **HRMS (ESI)**: *m/z* calcd. for $C_{14}H_{22}O_3$ $[M+H]^+$ 239.1642, found 239.1640.

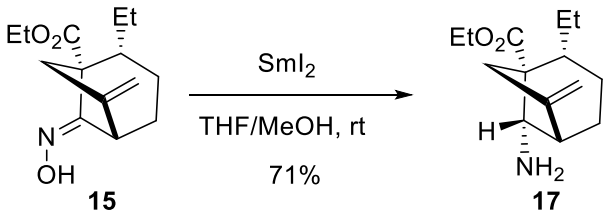
Preparation of Compound 15



A solution of **14** (1.0 g, 4.2 mmol) in anhydrous EtOH (42 mL) at 23 °C under argon, NH_2OH (50% in H_2O, 4.2 mL) were added. After being stirred for 8 h at 23 °C, the reaction was quenched by saturated NH_4Cl solution (20 mL) and extracted with EtOAc (3 × 20 mL). The organic layer and extracts were combined, dried, and evaporated to dryness. Purification of the residue by flash column chromatography (petroleum ether / ethyl acetate = 4:1 to 2:1) furnished **15** as a white solid (872 mg, 82%).

TLC (petroleum ether / ethyl acetate, 2:1 v/v): R_f = 0.52; **IR** (neat) ν_{max}: 3341, 3042, 2931, 2841, 1733, 1671, 1634, 1454, 1187, 1078 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.01 (s, 1H), 4.96 (d, J = 2.8 Hz, 1H), 4.91 (d, J = 2.4 Hz, 1H), 4.28 – 4.20 (m, 1H), 4.19 – 4.11 (m, 1H), 3.98 – 3.93 (m, 1H), 2.81 (dt, J = 16.8, 2.4 Hz, 1H), 2.72 (dt, J = 17.2, 2.4 Hz, 1H), 2.21 – 2.14 (m, 1H), 2.01 – 1.91 (m, 1H), 1.80 (s, 1H), 1.68 – 1.48 (m, 4H), 1.26 (d, J = 7.2 Hz, 3H), 0.88 (t, J = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.2, 162.0, 146.3, 107.2, 60.9, 57.1, 48.2, 43.5, 41.9, 31.8, 22.9, 20.3, 14.3, 13.0; **HRMS (ESI)**: *m/z* calcd. for $C_{14}H_{21}NO_3$ $[M+H]^+$ 252.1593, found 252.1598.

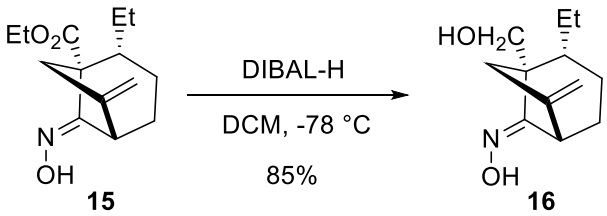
Preparation of Compound 17



To a solution of oxime **15** (100mg, 0.4 mmol) in THF / MeOH (0.4 mL / 0.04 mL) under Ar atmosphere (deoxygenated by sparging with argon) was added a solution of SmI_2 in THF (0.1 M) dropwise at room temperature until the dark blue color of the reaction mixture did not fade. The resulting mixture was stirred for 1h at room temperature when a saturated aqueous solution of Rochelle's salt (3 mL) was added. The mixture was extracted with EtOAc (3 × 5 mL) and the combined organic phase was dried with Na_2SO_4, and evaporated to dryness. Purification of the residue by flash column chromatography (dichloromethane / methanol = 40:1 to 20:1) furnished **17** as a colorless oil (67 mg, 71%).

TLC (dichloromethane / methanol, 20:1 v/v): R_f = 0.55; **IR** (neat) ν_{max}: 3381, 3045, 2933, 2845, 1743, 1651, 1436, 1180, 1071 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.38 (d, *J* = 8.8 Hz, 2H), 8.09 (d, *J* = 8.8 Hz, 2H), 5.40 (d, *J* = 2.0 Hz, 1H), 4.97 (t, *J* = 2.4 Hz, 1H), 4.87 (t, *J* = 2.4 Hz, 1H), 4.19 – 4.11 (m, 1H), 4.10 – 3.96 (m, 1H), 3.10 (dd, *J* = 5.2, 2,0 Hz, 1H), 3.03 – 2.96 (m, 1H), 2.45 – 2.32 (m, 2H), 2.20 – 2.12 (m, 1H), 1.76 (d, *J* = 3.1 Hz, 3H), 1.19 (t, *J* = 7.2 Hz, 3H), 0.88 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 176.5, 149.6, 106.0, 60.3, 56.9, 54.3, 47.1, 43.9, 42.8, 26.7, 21.8, 20.9, 14.8, 14.4; **HRMS (ESI)**: *m/z* calcd. for $C_{14}H_{23}NO_2$ $[M+H]^+$ 238.1801, found. 238.1807.

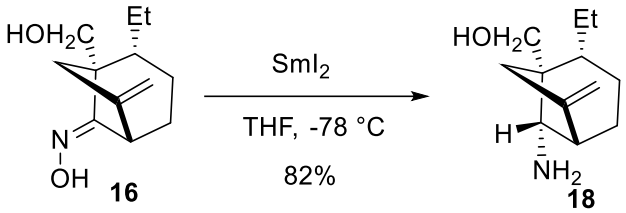
Preparation of Compound 16



To a stirred solution of esters **15** (1 g, 4.0 mmol) in CH_2Cl_2 (40 mL) were slowly added DIBAL-H (1.5 M in PhMe, 5.6 mL, 8.4 mmol) under Ar atmosphere at -78 °C. The reaction mixture was kept stirring for 0.5 h and quenched with saturated aqueous Rochelle's salt (50 mL) at 0 °C. After being warmed to ambient temperature and stirred for 0.5 h, the mixture was filtered through diatomite and extracted with CH_2Cl_2 (3 × 30 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. Purification of the residue via flash chromatography on silica gel (petroleum ether / ethyl acetate = 2:1 to 1:1) furnished **16** as a colorless oil (708 mg, 85%).

TLC (dichloromethane / methanol, 20:1 v/v): R_f = 0.82; **IR** (neat) ν_{max}: 3478, 3294, 2978, 1783, 1643, 1468, 1225, 1152, 856 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 4.8 Hz, 1H), 4.94 (t, *J* = 2.4 Hz, 1H), 4.91 (d, *J* = 2.4 Hz, 1H),3.99 (dd, *J* = 11.6, 2.4 Hz, 1H), 3.85 – 3.82 (m, 1H), 3.47 (dd, *J* = 12.4, 8.0 Hz, 1H), 2.85 (dt, *J* = 16.8, 2.8 Hz, 1H), 2.39 (dq, *J* = 16.8, 1.6 Hz, 1H), 2.25 (d, *J* = 7.2 Hz, 1H), 1.95 – 1.76 (m, 2H), 1.69 – 1.60 (m, 2H), 1.57 – 1.48 (m, 2H), 1.12 – 1.08 (m, 1H), 0.86 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR**(100 MHz, $CDCl_3$): δ 166.5, 147.7, 106.7, 62.6, 52.8, 47.6, 43.9, 38.8, 31.8, 20.9, 20.7, 13.1; **HRMS (ESI)**: m/z calcd. for $C_{12}H_{19}NO_2$ $[M+H]^+$ 210.1488, found 210.1483.

Preparation of Compound 18

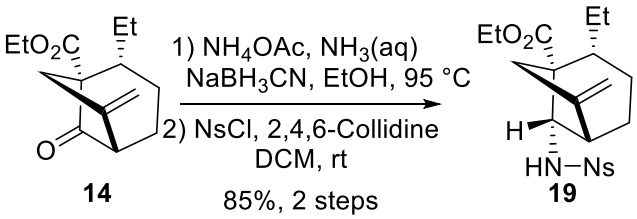


To a solution of oxime **16** (100 mg, 0.5 mmol) in THF / MeOH (0.5 mL / 0.05 mL) under Ar atmosphere (deoxygenated by sparging with argon) was added a solution of SmI_2 in THF (0.1 M) dropwise at room temperature until the dark blue color of the reaction mixture did not fade. The resulting mixture was stirred for 1h at room temperature when a saturated aqueous solution of Rochelle's salt (3 mL) was added. The mixture was extracted with EtOAc (3 × 5 mL) and the combined organic phase was

dried with Na_2SO_4, and evaporated to dryness. Purification of the residue via flash chromatography on silica gel (dichloromethane / methanol = 20:1 to 10:1) furnished **18** as a colorless oil (77 mg, 82%).

TLC (dichloromethane / methanol, 10:1 v/v): R_f = 0.52; **IR** (neat) ν_{max}: 3631, 3459, 3189, 3027, 2988, 1565, 1021 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.97 (s, 1H), 4.89 (s, 1H), 4.52 (s, 2H), 4.01 (d, *J* = 11.6 Hz, 1H), 3.58 (d, *J* = 11.6 Hz, 1H), 3.44 (d, *J* = 4.8 Hz, 1H), 2.90 (d, *J* = 4.8 Hz, 1H), 2.52 – 2.44 (m, 1H), 2.12 (d, *J* = 17.2 Hz, 1H), 2.02 – 1.75 (m, 3H), 1.51 – 1.49 (m, 2H), 1.43 – 1.27 (m, 3H), 0.93 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR**(100 MHz, $CDCl_3$): δ 148.1, 107.3, 65.9, 55.6, 46.9, 45.2, 44.6, 41.0, 24.5, 23.1, 21.6, 15.1; **HRMS (ESI)**: *m/z* calcd. for $C_{12}H_{21}NO$ $[M+H]^+$ 196.1695, found 196.1690.

Preparation of Compound 19



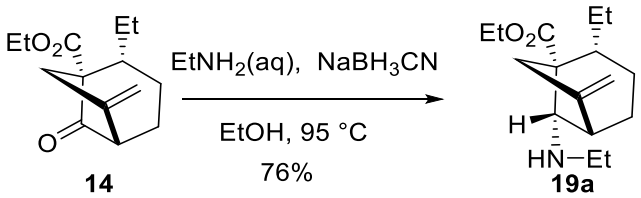
To a solution of **14** (9.6 g, 40.6 mmol) in a saturated solution of NH_4OAc in EtOH (200 mL) were added $NaCNBH_3$ (2.6 g, 40.6 mmol) and 30% aq NH_3 (200 mL). The mixture was stirred at reflux for 3 h, cooled to room temperature, and concentrated under reduced pressure. The residue was redissolved in H_2O, and the resultant mixture was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated to afford a crude product, which was directly used in the following step without purification.

To a mixture of the above crude product in CH_2Cl_2 (400 mL, anhydrous) were added NsCl (9.0 g, 40.6 mmol) and 2,4,6-Collidine (10.4 g, 11.4 mL, 86.0 mmol). After stirring for 0.5 h at 23 °C, the reaction was quenched by H_2O (200 mL) and the resultant mixture was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. Purification of the residue via flash

chromatography on silica gel (petroleum ether / ethyl acetate = 8:1 to 4:1) yielded **19** as a white solid (10.3 g, 85%).

TLC (petroleum ether / ethyl acetate, 4:1 v/v): R_f = 0.52; **IR** (neat) ν_{max}: 3452, 3078, 2875, 1741, 1542, 1521, 1443, 1376, 1260, 1161, 1072, 768 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.38 (d, *J* = 8.8 Hz, 2H), 8.09 (d, *J* = 8.8 Hz, 2H), 5.40 (d, *J* = 2.0 Hz, 1H), 4.97 (d, *J* = 2.4 Hz, 1H), 4.87 (t, *J* = 2.4 Hz, 1H), 4.15 (dd, *J* = 10.8, 7.2 Hz, 1H), 4.00 (dd, *J* = 10.8, 7.2 Hz, 1H), 3.10 (dd, *J* = 5.2, 2.0 Hz, 1H), 2.99 (s, 1H), 2.43 (dt, *J* = 17.2, 2.4 Hz, 1H), 2.35 (dt, *J* = 17.2, 2.4 Hz, 1H), 2.20 – 2.12 (m, 1H), 1.80 – 1.69 (m, 3H), 1.58 (s, 1H), 1.50 (s, 1H), 1.37 – 1.30 (m, 1H), 1.19 (t, *J* = 7.2 Hz, 3H), 0.88 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 175.6, 150.3, 146.8, 144.3, 129.1 (× 2), 124.5 (× 2), 108.2, 61.1, 57.9, 54.1, 44.8, 44.2, 40.9, 25.6, 22.2, 20.2, 14.3, 14.3; **HRMS (ESI)**: *m/z* calcd. for $C_{20}H_{26}N_2O_6S$ $[M+H]^+$ 423.1584, found 423.1581.

Preparation of Compound 19a



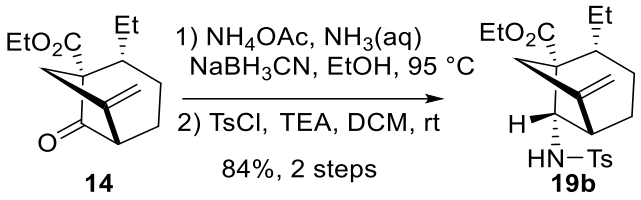
14 **19a**

To a solution of **14** (1 g, 4.2 mmol) in EtOH (21 mL) were added $NaCNBH_3$ (279 mg, 4.4 mmol) and 70% aq $EtNH_2$ (21 mL). The mixture was stirred at reflux for 3 h, cooled to room temperature, and concentrated under reduced pressure. The residue was redissolved in H_2O, and the resultant mixture was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. Purification of the residue via flash chromatography on silica gel (petroleum ether / ethyl acetate = 6:1 to 3:1) furnished **19a** as a colorless oil (854 mg, 76%).

TLC (petroleum ether / ethyl acetate, 3:1 v/v): R_f = 0.32; **IR** (neat) ν_{max}: 3045, 2975, 2893, 1748, 1723, 1674, 1334, 1189, 1077 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.91 (td, *J* = 2.4, 1.2 Hz, 1H), 4.83 (td, *J* = 2.4, 1.2 Hz, 1H), 4.19 (dd, *J* = 10.8, 7.2 Hz, 1H), 4.11 (dd, *J* = 10.8, 7.2 Hz, 1H), 3.17 (d, *J* = 4.8 Hz, 1H), 2.68 – 2.64 (m, 1H), 2.61 – 2.52 (m, 2H), 2.51 – 2.39 (m, 3H), 2.08 – 2.07 (m, 1H), 1.92 – 1.88 (m, 1H), 1.80 –

1.71 (m, 3H), 1.48 – 1.41 (m, 1H), 1.25 (t, J = 7.2 Hz, 3H), 1.20 – 1.14 (m, 1H), 1.09 (t, J = 7.2 Hz, 3H), 0.82 (t, J = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 176.7, 150.3, 105.9, 63.4, 60.1, 54.4, 44.6, 44.2, 43.2, 43.0, 25.8, 21.9, 20.7, 15.7, 14.2, 14.2; **HRMS (ESI)**: *m/z* calcd. for $C_{16}H_{27}NO_2$ $[M+H]^+$ 266.2114, found 266.2110.

Preparation of Compound 19b



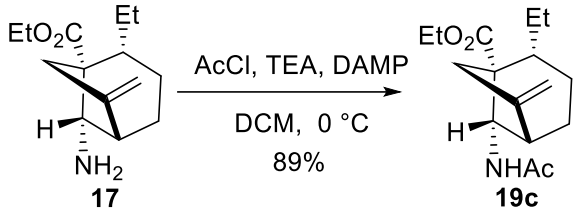
To a solution of **14** (1 g, 4.2 mmol) in a saturated solution of NH_4OAc in EtOH (21 mL) were added $NaCNBH_3$ (266 mg, 4.2 mmol) and 30% aq NH_3 (21 mL). The mixture was stirred at reflux for 3 h, cooled to room temperature, and concentrated under reduced pressure. The residue was redissolved in H_2O, and the resultant mixture was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated to afford a crude product, which was directly used in the following step without purification.

To a mixture of the above crude product in CH_2Cl_2 (42 mL, anhydrous) were added TsCl (969 mg, 5.1 mmol) and TEA (1.3 g, 1.8 mL, 12.7 mmol). After stirring for 0.5 h at 23 °C, the reaction was quenched by H_2O (20 mL) and the resultant mixture was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. Purification of the residue via flash chromatography on silica gel (petroleum ether / ethyl acetate = 8:1 to 4:1) yielded **19b** as a white solid (1.4 g, 84%).

TLC (petroleum ether / ethyl acetate, 4:1 v/v): R_f = 0.42; **IR** (neat) ν_{max}: 3455, 2892, 1745, 1656, 1505, 1333, 1201, 1187 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.75 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 5.22 (d, J = 2.0 Hz, 1H), 4.93 (t, J = 2.4 Hz, 1H), 4.82 (t, J = 2.4 Hz, 1H), 4.19 – 4.09 (m, 2H), 4.03 – 3.94 (m, 1H), 3.12 – 3.07 (m, 1H), 2.99 – 2.94 (m, 1H), 2.44 – 2.33 (m, 5H), 2.25 – 2.16 (m, 2H), 1.74 (q, J = 4.8, 4.0 Hz, 3H), 1.48 (dd, J = 13.6, 5.6 Hz, 1H), 1.17 (t, J = 7.2 Hz, 3H), 0.84 (d, J = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 175.5, 147.7, 143.6, 135.5, 129.8 (× 2), 127.6 (× 2), 107.5, 60.8, 57.7, 54.3, 44.7, 44.3, 41.2, 25.6, 22.2, 21.6, 20.3, 14.2, 14.2; **HRMS (ESI)**: *m/z* calcd. for $C_{21}H_{29}NO_4S$ $[M+H]^+$ 392.1889 , found 392.1883.

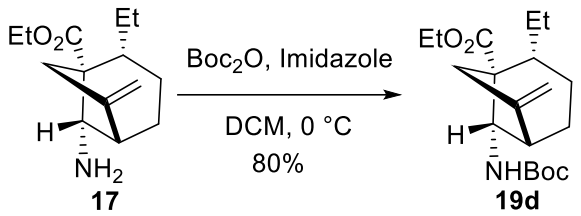
Preparation of Compound 19c



To a solution of **17** (1 g, 4.2 mmol) in CH_2Cl_2 (42 mL, anhydrous) were added AcCl (0.45 mL, 496 mg, 6.3 mmol), TEA (1.3 g, 1.8 mL, 12.6 mmol) and DMAP (155 mg, 1.3 mmol). After stirring for 0.5 h at 0 °C, the reaction was quenched by saturated aqueous NH_4Cl (20 mL) and the resultant mixture was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. Purification of the residue via flash chromatography on silica gel (petroleum ether / ethyl acetate = 8:1 to 4:1) yielded **19c** as a white solid (1.0 g, 89%).

TLC (petroleum ether / ethyl acetate, 5:1 v/v): R_f = 0.52; **IR** (neat) ν_{max}: 3340, 2987, 2876, 1745, 1689, 1675, 1423, 1550 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.91 (d, *J* = 5.6 Hz, 1H), 4.96 – 4.93 (m, 1H), 4.89 – 4.86 (m, 1H), 4.23 (dd, *J* = 8.0, 3.2Hz, 1H), 4.21 – 4.10 (m, 3H), 3.02 (t, *J* = 4.8 Hz, 1H), 2.64 (d, *J* = 9.2 Hz, 1H), 2.56 (dt, *J* = 16.8, 2.8 Hz, 1H), 2.46 – 2.39 (m, 1H), 1.99 (s, 3H), 1.90 – 1.85 (m, 1H), 1.83 – 1.76 (m, 1H), 1.45 – 1.40 (m, 2H), 1.36 – 1.33 (m, 1H), 1.24 (t, *J* = 7.2 Hz, 3H), 0.94 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 175.1, 169.9, 147.9, 107.3, 60.7, 54.8, 53.3, 44.3, 43.8, 42.0, 26.3, 24.0, 22.6, 20.9, 14.8, 14.3; **HRMS (ESI)**: *m/z* calcd. for $C_{16}H_{25}NO_3$ $[M+H]^+$ 280.1906, found 280.1902.

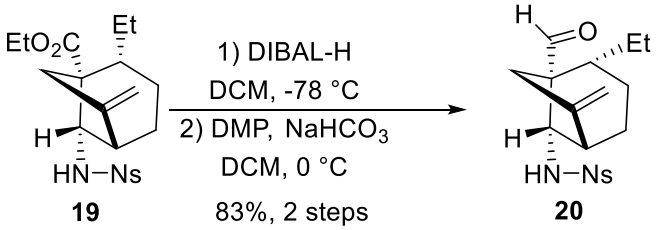
Preparation of Compound 19d



To a solution of **17** (1 g, 4.2 mmol) in CH_2Cl_2 (42 mL, anhydrous) were added Boc_2O (1.8 g, 8.4 mmol) and Imidazole (1.1 g, 16.8 mmol). After stirring for 0.5 h at 0 °C, the reaction was quenched by saturated aqueous NH_4Cl (20 mL) and the resultant mixture was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. Purification of the residue via flash chromatography on silica gel (petroleum ether / ethyl acetate = 16:1 to 8:1) yielded **19d** as a white solid (1.1 g, 80%).

TLC (petroleum ether / ethyl acetate, 8:1 v/v): R_f = 0.55; **IR** (neat) ν_{max}: 3450, 2897, 2850, 1745, 1650, 1387, 899 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.92 (s, 1H), 4.87 (s, 1H), 4.79 (d, *J* = 1.2 Hz, 1H), 4.13 – 4.07 (m, 2H), 3.97 (t, *J* = 5.6 Hz, 1H), 2.88 (s, 1H), 2.52 – 2.45 (m, 1H), 2.38 – 2.31 (m, 1H), 1.82 – 1.76 (m, 1H), 1.73 (d, *J* = 8.8 Hz, 1H), 1.46 (s, 1H), 1.38 (s, 10H), 1.35 – 1.23 (m, 3H), 1.18 (t, *J* = 7.2 Hz, 3H), 0.86 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 175.2, 155.7, 148.2, 107.0, 79.3, 60.6, 53.4, 44.8, 43.7, 42.2, 28.5 (× 3), 27.5, 26.1, 22.5, 20.9, 14.7, 14.3; **HRMS (ESI)**: *m/z* calcd. for $C_{19}H_{31}NO_4$ $[M+H]^+$ 338.2325, found 338.2321.

Preparation of Compound 20



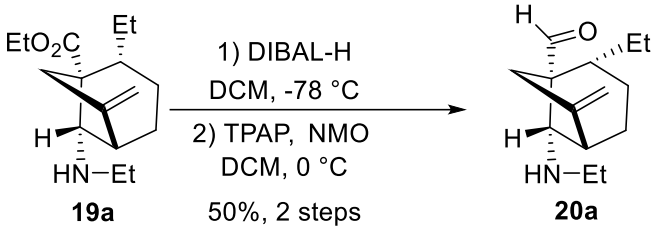
To a stirred solution of esters **19** (6.8 g, 16.1 mmol) in CH_2Cl_2 (160 mL) were slowly added DIBAL-H (1.5 M in PhMe, 32.2 mL, 48.3 mmol) under Ar atmosphere at -78 °C. The reaction mixture was kept stirring for 0.5 h and quenched with saturated aqueous Rochelle's salt (200 mL) at 0 °C. After being warmed to ambient temperature

and stirred for 0.5 h, the mixture was filtered through diatomite and extracted with CH_2Cl_2 (3 × 300 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated to afford a crude product, which was directly used in the following step without purification.

To a mixture of the above crude product in CH_2Cl_2 (160 mL) was added Dess-Martin periodinane (10.2 g, 24.1 mmol) and $NaHCO_3$ (4.0 g, 47.2 mmol) at 0 °C. After stirring for 0.5 h, the reaction was quenched by saturated aqueous $Na_2S_2O_3$ (100 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. Purification of the residue via flash chromatography on silica gel (petroleum ether / ethyl acetate = 8:1 to 4:1) yielded **20** as a white solid (5.1 g, 83%).

TLC (petroleum ether / ethyl acetate, 4:1 v/v): R_f = 0.51; **IR** (neat) ν_{max}: 3450, 3102, 2983, 2883, 2734, 1724, 1682, 1566, 1375, 1105 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.41 (d, *J* = 0.8 Hz, 1H), 8.39 (d, *J* = 8.8 Hz, 2H), 8.09 (d, *J* = 8.8 Hz, 2H), 5.01 (q, *J* = 2.4 Hz, 2H), 4.92 (d, *J* = 2.4 Hz, 1H), 3.35 (t, *J* = 4.8 Hz, 1H), 2.90 – 2.85 (m, 1H), 2.29 (q, *J* = 2.4 Hz, 2H), 2.07 – 1.96 (m, 1H), 1.83 – 1.76 (m, 3H), 1.46 – 1.40 (m, 1H), 1.37 – 1.29 (m, 2H), 0.95 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.7, 150.4, 145.6, 144.8, 128.9 (× 2), 124.6 (× 2), 108.9, 58.4, 56.5, 45.2, 41.7, 38.6, 25.6, 22.8, 20.5, 14.5; **HRMS (ESI)**: *m/z* calcd. for $C_{18}H_{22}N_2O_5S$ $[M+H]^+$ 379.1321 , found 379.1325.

Preparation of Compound 20a



19a **20a**

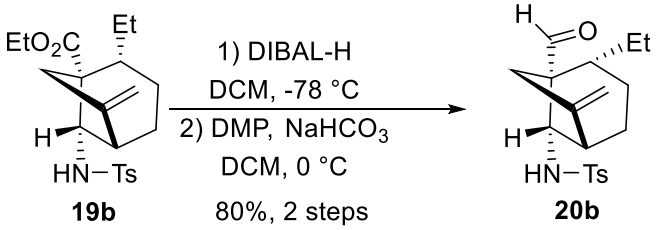
To a stirred solution of esters **19a** (400 mg, 1.5 mmol) in CH_2Cl_2 (15 mL, anhydrous) were slowly added DIBAL-H (1.5 M in PhMe, 3.0 mL, 4.5 mmol) under Ar atmosphere at -78 °C. The reaction mixture was kept stirring for 0.5 h and quenched with saturated aqueous Rochelle's salt (5 mL) at -78 °C. After being warmed to ambient

temperature and stirred for 0.5 h, the mixture was filtered through diatomite and extracted with CH_2Cl_2 (3 × 3 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The crude product was used in the following step without purification.

To a solution of the crude product in DCM (15 mL, anhydrous) was added TPAP (159 mg, 0.45 mmol), NMO (530 mg, 4.5 mmol) at 0 °C. After stirring for 0.5 h at 0 °C, the resulting mixture was filtered. The filter cake was rinsed with ethyl acetate repeatedly. After concentration of the filtrate, the residue was purified by flash column chromatography on silica gel (petroleum ether / ethyl acetate = 4:1 to 2:1) to give **20a** as a white solid (167 mg, 50%).

TLC (petroleum ether / ethyl acetate, 1:1 v/v): R_f = 0.32; **IR** (neat) ν_{max}: 3356, 2894, 2825, 2710, 1745, 1663, 1556, 1376,1073 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.57 (s, 1H), 4.96 (dd, *J* = 3.2, 2.0 Hz, 1H), 4.88 – 4.86 (m, 1H), 3.20 (d, *J* = 4.8 Hz, 1H), 2.74 (t, *J* = 4.8 Hz, 1H), 2.59 (dd, *J* = 11.2, 7.2 Hz, 1H), 2.50 (dd, *J* = 11.2, 7.2 Hz, 1H), 2.40 (dt, *J* = 11.2, 2.4 Hz, 1H), 2.22 (dt, *J* = 11.2, 3.2 Hz, 1H), 2.00 – 1.96 (m, 1H), 1.79 – 1.63 (m, 3H), 1.52 – 1.43 (m, 4H), 1.07 (t, *J* = 7.2 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 205.7, 149.4, 106.6, 63.6, 58.9, 45.3, 43.4, 41.9, 39.8, 25.2, 22.8, 21.2, 15.8, 14.6; **HRMS (ESI)**: *m/z* calcd. for $C_{14}H_{23}NO$ $[M+H]^+$ 222.1852, found 222.1850.

Preparation of Compound 20b



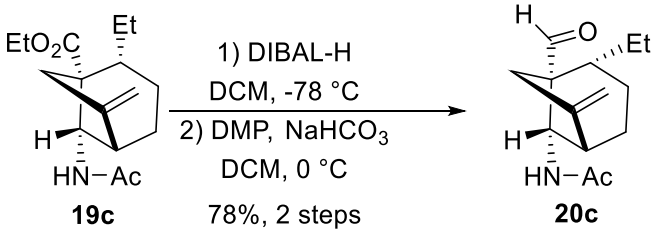
To a stirred solution of esters **19b** (500 mg, 1.3 mmol) in CH_2Cl_2 (13 mL) were slowly added DIBAL-H (1.5 M in PhMe, 2.6 mL, 3.9 mmol) under Ar atmosphere at -78 °C. The reaction mixture was kept stirring for 0.5 h and quenched with saturated aqueous Rochelle's salt (5 mL) at 0 °C. After being warmed to ambient temperature and stirred for 0.5 h, the mixture was filtered through diatomite and extracted with CH_2Cl_2

(3 × 3 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated to afford a crude product, which was directly used in the following step without purification.

To a mixture of the above crude product in CH_2Cl_2 (13 mL) was added Dess-Martin periodinane (813 mg, 1.9 mmol) and $NaHCO_3$ (319 mg, 3.8 mmol) at 0 °C. After stirring for 0.5 h, the reaction was quenched by saturated aqueous $Na_2S_2O_3$ (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. Purification of the residue via flash chromatography on silica gel (petroleum ether / ethyl acetate = 8:1 to 4:1) yielded **20b** as a white solid (444 mg, 80%).

TLC (petroleum ether / ethyl acetate, 4:1 v/v): R_f = 0.40; **IR** (neat) ν_{max}: 3320, 3008, 2876, 2812, 2733, 1725, 1678, 1623, 1556, 1357 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.34 (s, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 4.99 (t, *J* = 2.4 Hz, 1H), 4.89 – 4.87 (m, 2H), 3.36 (t, *J* = 5.2 Hz, 1H), 2.79 (t, *J* = 5.2 Hz, 1H), 2.44 (s, 3H), 2.35 – 2.27 (m, 1H), 2.26 – 2.18 (m, 1H), 2.07 – 1.95 (m, 1H), 1.82 – 1.69 (m, 2H), 1.54 – 1.48 (m, 2H), 1.45 – 1.34 (m, 2H), 0.92 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.8, 146.5, 143.9, 136.1, 129.9 (× 2), 127.5 (× 2), 108.1, 58.4, 56.8, 45.1, 41.5, 38.5, 25.4, 22.9, 21.7, 20.7, 14.5; **HRMS (ESI)**: *m/z* calcd. for $C_{19}H_{25}NO_3S$ $[M+H]^+$ 348. 1627, found 348. 1622.

Preparation of Compound 20c



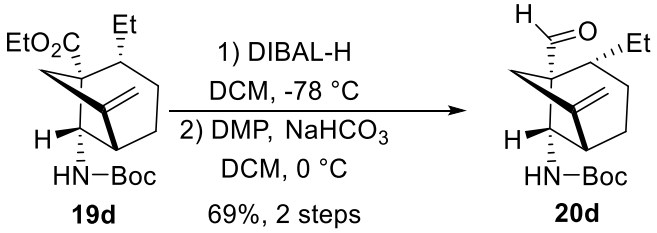
To a stirred solution of esters **19c** (500 mg, 1.8 mmol) in CH_2Cl_2 (18 mL) were slowly added DIBAL-H (1.5 M in PhMe, 3.6 mL, 5.4 mmol) under Ar atmosphere at -78 °C. The reaction mixture was kept stirring for 0.5 h and quenched with saturated aqueous Rochelle's salt (10 mL) at 0 °C. After being warmed to ambient temperature and stirred for 0.5 h, the mixture was filtered through diatomite and extracted with

CH_2Cl_2 (3 × 10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated to afford a crude product, which was directly used in the following step without purification.

To a mixture of the above crude product in CH_2Cl_2 (18 mL) was added Dess-Martin periodinane (1.5 g, 3.6 mmol) and $NaHCO_3$ (602 mg, 7.2 mmol) at 0 °C. After stirring for 0.5 h, the reaction was quenched by saturated aqueous $Na_2S_2O_3$ (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. Purification of the residue via flash chromatography on silica gel (petroleum ether / ethyl acetate = 10:1 to 5:1) yielded **20c** as a white solid (324 mg, 78%).

TLC (petroleum ether / ethyl acetate, 5:1 v/v): R_f = 0.45; **IR** (neat) ν_{max}: 3452, 2985, 2780, 2734, 1746, 1724, 1655, 1245, 1120, 890 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.57 (s, 1H), 5.85 – 5.77 (m, 1H), 5.02 (t, *J* = 2.4, 1H), 4.93 (t, *J* = 2.4 Hz, 1H), 4.27 (dd, *J* = 7.6, 5.2 Hz, 1H), 2.79 (t, *J* = 4.8 Hz, 1H), 2.57 (dt, *J* = 16.8, 2.4 Hz, 1H), 2.26 (s, 1H), 2.14 (dt, *J* = 16.8, 2.4 Hz, 1H), 1.97 (s, 3H), 1.83 – 1.73 (m, 3H), 1.64 – 1.56 (m, 1H), 1.52 – 1.46 (m, 2H), 0.95 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.0, 170.3, 147.1, 107.6, 58.3, 54.2, 45.0, 40.6, 38.6, 25.2, 23.7, 23.6, 21.3, 14.8; **HRMS (ESI)**: *m/z* calcd. for $C_{14}H_{21}NO_2$ $[M+H]^+$ 236.1645, found 236.1649.

Preparation of Compound 20d



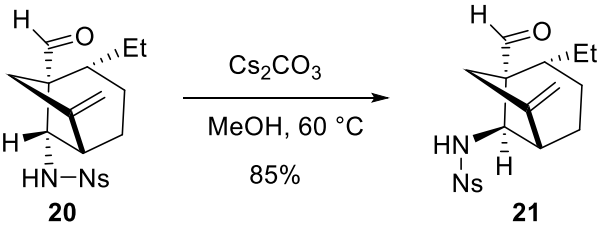
To a stirred solution of esters **19d** (500 mg, 1.5 mmol) in CH_2Cl_2 (15 mL) were slowly added DIBAL-H (1.5 M in PhMe, 3.0 mL, 4.5 mmol) under Ar atmosphere at -78 °C. The reaction mixture was kept stirring for 0.5 h and quenched with saturated aqueous Rochelle's salt (10 mL) at 0 °C. After being warmed to ambient temperature and stirred for 0.5 h, the mixture was filtered through diatomite and extracted with

CH_2Cl_2 (3 × 10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated to afford a crude product, which was directly used in the following step without purification.

To a mixture of the above crude product in CH_2Cl_2 (15 mL) was added Dess-Martin periodinane (1.3 g, 3.0 mmol) and $NaHCO_3$ (498 mg, 6.0 mmol) at 0 °C. After stirring for 0.5 h, the reaction was quenched by saturated aqueous $Na_2S_2O_3$ (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. Purification of the residue via flash chromatography on silica gel (petroleum ether / ethyl acetate = 16:1 to 8:1) yielded **20d** as a white solid (300 mg, 69%).

TLC (petroleum ether / ethyl acetate, 8:1 v/v): R_f = 0.35; **IR** (neat) ν_{max}: 3362, 2890, 2822, 2712, 1756, 1723, 1675, 1122 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.58 (s, 1H), 5.00 (t, *J* = 2.4 Hz, 1H), 4.91 (t, *J* = 2.4 Hz, 1H), 4.81 (d, *J* = 6.8 Hz, 1H), 4.04 (t, *J* = 6.0Hz, 1H), 2.77 (s, 1H), 2.55 (dt, *J* = 17.2, 2.4 Hz, 1H), 2.12 (dt, *J* = 17.2, 2.4 Hz, 1H), , 1.80 – 1.74 (m, 2H), 1.65 – 1.55 (m, 2H), 1.48 – 1.40 (m, 11H), 0.94 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.3, 155.6, 147.4, 107.4, 80.0, 58.2, 55.3, 45.4, 40.6, 38.6, 28.5 (× 3), 24.9, 23.6, 21.2, 14.9; **HRMS (ESI)**: *m/z* calcd. for $C_{17}H_{27}NO_3$ $[M+H]^+$ 294.2063, found 294.2060.

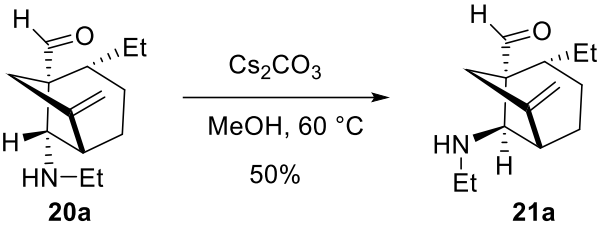
Preparation of Compound 21



To a solution of aldehyde **20** (3.0 g, 7.9 mmol) in MeOH (80 mL, anhydrous) was added Cs_2CO_3 (10.3 g, 31.7 mmol) under Ar atmosphere at rt. After being stirring for 3 h at 60 °C, Then the mixture was evaporated to dryness. Purification of the residue by flash column chromatography (petroleum ether / ethyl acetate = 6:1 to 3:1) furnished **21** as a white solid (2.6 g, 85%).

TLC (petroleum ether / ethyl acetate, 3:1 v/v): R_f = 0.52; **IR** (neat) ν_{max}: 3082, 3001, 2850, 2821, 2720, 1722, 1622, 1390, 920, 821cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.69 (s, 1H), 8.37 (d, *J* = 8.8 Hz, 2H), 8.05 (d, *J* = 8.8 Hz, 2H), 5.39 (d, *J* = 5.6 Hz, 1H), 4.98 (t, *J* = 2.4 Hz, 1H), 4.87 (t, *J* = 2.4 Hz, 1H), 3.71 (d, *J* = 5.6 Hz, 1H), 2.58 (dt, *J* = 17.2, 2.4 Hz, 2H), 2.34 (d, *J* = 17.2 Hz, 1H), 1.84 (d, *J* = 6.0 Hz, 1H), 1.70 – 1.60 (m, 1H), 1.53 – 1.42 (m, 3H), 1.36 – 1.24 (m, 3H), 0.89 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 205.5, 150.2, 147.4, 146.6, 128.5 (× 2), 124.5 (× 2), 110.1, 60.4, 60.1, 50.0, 44.0, 36.9, 28.9, 22.7, 20.0, 13.3; **HRMS (ESI)**: *m/z* calcd. for $C_{18}H_{22}N_2O_5S$ $[M+H]^+$ 379.1321, found 379.1325.

Preparation of Compound 21a

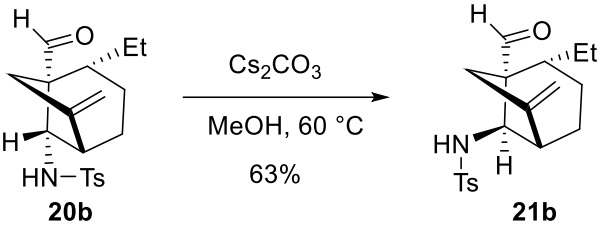


20a **21a**

To a solution of aldehyde **20a** (100 mg, 0.45 mmol) in MeOH (5 mL, anhydrous) was added Cs_2CO_3 (588 mg, 1.81 mmol) under Ar atmosphere at rt. After being stirring for 3 h at 60 °C, Then the mixture was evaporated to dryness. Purification of the residue by flash column chromatography (petroleum ether / ethyl acetate = 2:1 to 1:1) furnished **21a** as a white solid (50 mg, 50%).

TLC (petroleum ether / ethyl acetate, 1:1 v/v): R_f = 0.20; **IR** (neat) ν_{max}: 3346, 2876, 2812, 2731, 1720, 1632, 1566, 1380 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.88 (s, 1H), 4.98 (d, *J* = 5.6 Hz, 2H), 3.48 (s, 1H), 3.08 (s, 1H), 2.74 – 2.67 (m, 3H), 2.48 – 2.45 (m, 1H), 2.20 (d, *J* = 11.6 Hz, 1H), 1.73 – 1.66 (m, 2H), 1.60 – 1.49 (m, 3H), 1.45 – 1.43 (m, 2H), 1.41 – 1.34 (m, 1H), 1.04 (t, *J* = 7.2 Hz, 3H), 0.89 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 207.2, 151.0, 108.1, 63.6, 61.8, 48.6, 44.2, 42.2, 36.8, 29.4, 22.5, 20.8, 15.7, 13.5; **HRMS (ESI)**: *m/z* calcd. for $C_{14}H_{23}NO$ $[M+H]^+$ 222.1852, found 222.1856.

Preparation of Compound 21b

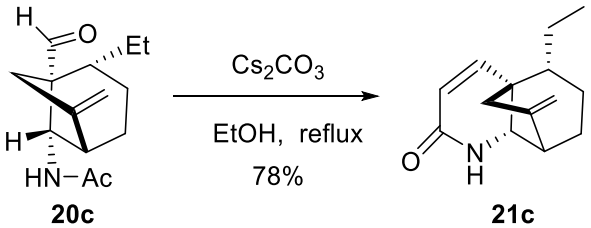


20b **21b**

To a solution of aldehyde **20b** (100 mg, 0.29 mmol) in MeOH (3 mL, anhydrous) was added Cs_2CO_3 (375 mg, 1.15 mmol) under Ar atmosphere at rt. After being stirring for 3 h at 60 °C, Then the mixture was evaporated to dryness. Purification of the residue by flash column chromatography (petroleum ether / ethyl acetate = 6:1 to 3:1) furnished **21b** as a white solid (63 mg, 63%).

TLC (petroleum ether / ethyl acetate, 3:1 v/v): R_f = 0.50; **IR** (neat) ν_{max}: 3345, 2894, 2820, 2734, 1735, 1647, 1556, 1347, 1193, 1156 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.76 (s, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 5.00 (t, *J* = 2.4 Hz, 1H), 4.94 (t, *J* = 2.4 Hz, 1H) 4.76 (d, *J* = 7.2 Hz, 1H), 3.69 (d, *J* = 7.2 Hz, 1H), 2.55 (dt, *J* = 17.6 Hz, 1H), 2.44 (s, 4H), 2.26 (dt, *J* = 17.6 Hz, 1H), 1.84 – 1.76 (m, 1H), 1.48 – 1.46 (m, 3H), 1.41 – 1.25 (m, 3H), 0.88 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 205.9, 148.0, 143.8, 137.6, 129.9 (× 2), 127.2 (× 2), 110.1, 60.5, 59.6, 50.1, 44.4, 36.7, 29.3, 22.5, 21.7, 20.2, 13.4; **HRMS (ESI)**: *m/z* calcd. for $C_{19}H_{25}NO_3S$ $[M+H]^+$ 348. 1627, found 348. 1621.

Preparation of Compound 21c



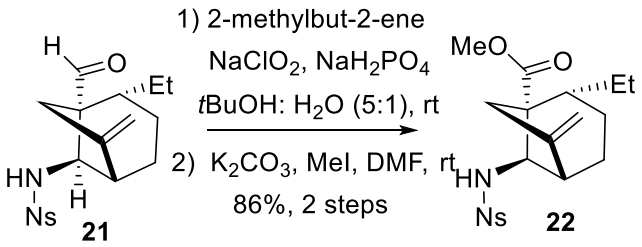
20c **21c**

To a solution of aldehyde **20c** (100 mg, 0.43 mmol) in EtOH (4.3 mL, anhydrous) was added Cs_2CO_3 (554 mg, 1.7 mmol) under Ar atmosphere at rt. After being stirring for 2 h at 90 °C, Then the mixture was evaporated to dryness. Purification of the residue

by flash column chromatography (petroleum ether / ethyl acetate = 6:1 to 3:1) furnished **21c** as a white solid (72 mg, 78%).

TLC (petroleum ether / ethyl acetate, 5:1 v/v): R_f = 0.55; **IR** (neat) ν_{max}: 3302, 2980, 1689, 1628, 1565, 1553, 1437, 1059 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.60 (d, *J* = 9.6 Hz, 1H), 6.05 (dd, *J* = 9.6, 2.0 Hz, 1H), 5.93 (s, 1H), 5.02(t, *J* = 2.4 Hz, 1H), 4.97 (t, *J* = 2.4 Hz, 1H), 3.45 (d, *J* = 4.8 Hz, 1H), 2.75 (t, *J* = 4.8 Hz, 1H), 2.36 – 2.34 (m, 2H), 1.81 – 1.77 (m, 2H), 1.64 (s, 1H), 1.61 – 1.50 (m, 2H), 1.49 – 1.38 (m, 2H), 0.77 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 169.5, 150.0, 148.2, 127.0, 108.2, 59.2, 45.9, 43.9, 43.7, 40.3, 22.6, 22.0, 19.9, 14.3; **HRMS (ESI)**: *m/z* calcd. for $C_{14}H_{19}NO$ $[M+H]^+$ 218.1539, found 218.1536.

Preparation of Compound 22

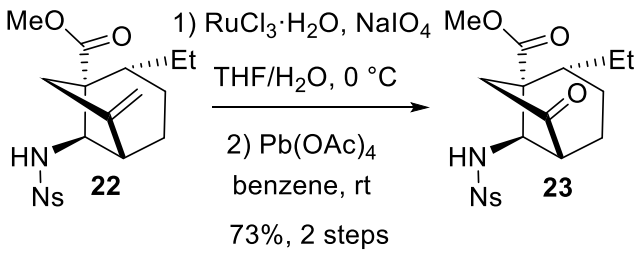


To a solution of aldehyde **21** (2.0 g, 5.3 mmol) in *t*BuOH (45 mL) was added 2-methyl-2-butene (3.7 g, 5.6 mL, 52.9 mmol) in one portion at rt. Then a freshly prepared mixture of 8 mL of aqueous solution of $NaClO_2$ (957 mg, 10.6 mmol) and NaH_2PO_4(3.7 g, 26.4 mmol) was added. The reaction was continued for 1 h at room temperature. Then the mixture was quenched with ammonium chloride (30 mL) and extracted with EtOAc (3 × 20 mL). dried over anhydrous $MgSO_4$, filtered, and concentrated to afford a crude product, which was directly used in the following step without purification.

To a mixture of the above crude product in DMF (50 mL) was added K_2CO_3 (2.2 g, 15.9 mmol) and MeI (912 mg, 0.4 mL, 6.3 mmol) at rt. After stirring for 0.5 h, the reaction was quenched by saturated aqueous NH_4Cl (30 mL) and extracted with EtOAc (3 × 30 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. Purification of the residue via flash chromatography on silica gel (petroleum ether / ethyl acetate = 8:1 to 4:1) yielded **22** as a white solid (1.9 g, 86%).

TLC (petroleum ether / ethyl acetate, 4:1 v/v): R_f = 0.54; **IR** (neat) ν_{max}: 3360, 2950, 1743, 1659, 1345, 1245, 1230, 1160 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.34 (d, *J* = 8.8 Hz, 2H), 8.07 (d, *J* = 8.8 Hz, 2H), 5.99 (d, *J* = 2.4 Hz, 1H), 4.87 (d, *J* = 2.4 Hz, 1H), 4.71 (s, 1H), 3.65 (s, 3H), 3.53 (t, *J* = 2.4 Hz, 1H), 2.91 (d, *J* = 4.8 Hz, 1H), 2.67 (dt, *J* = 17.2, 2.8 Hz, 1H), 2.48 (d, *J* = 17.2 Hz, 1H), 1.89 – 1.80 (m, 1H), 1.64 – 1.58 (m, 4H), 1.45 – 1.38 (m, 2H), 0.81 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 175.7, 150.1, 148.5, 146.7, 128.7 (× 2), 124.2 (× 2), 108.7, 60.7, 57.4, 52.3, 48.3, 45.5, 39.4, 28.5, 23.0, 20.0, 13.2; **HRMS (ESI)**: *m/z* calcd. for $C_{19}H_{24}N_2O_6S$ $[M+H]^+$ 409.1427, found 409.1421.

Preparation of Compound 23

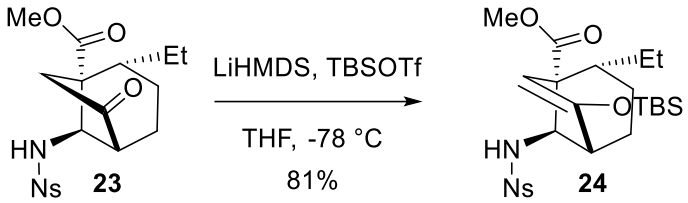


To an ice-cooled stirred solution of **22** (1.9 g, 4.7 mmol) in THF / H_2O (2: 1, 48 mL), $RuCl_3·H_2O$ (202 mg, 0.8 mmol) and $NaIO_4$ (5.0 g, 23.2 mmol) was added. The mixture was kept stirring for 0.5 h at 0 °C before it was quenched with saturated aqueous $NaHCO_3$ (20 mL) and saturated aqueous $Na_2S_2O_3$(10 mL), extracted with EtOAc (3 × 40 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness. The crude product was used in the following step without purification.

To a solution of the crude product in benzene (48 mL) was slowly added $Pb(OAc)_4$ (4.5 g, 14.0 mmol) under Ar atmosphere at 23 °C. The mixture was kept stirring for 0.5 h at 23 °C before it was quenched with saturated aqueous $NaHCO_3$ (20 mL) and saturated aqueous $Na_2S_2O_3$(10 mL), extracted with EtOAc (3 × 40 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was subjected to flash chromatography on silica gel (petroleum ether / ethyl acetate = 4:1 to 2:1) to give **23** as a white solid (1.4 g, 73%).

TLC (petroleum ether / ethyl acetate, 2:1 v/v): R_f = 0.55; **IR** (neat) ν_{max}: 3355, 2876, 1745, 1720, 1645, 1437,1334, 1235, 1156 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 8.8 Hz, 2H), 8.06 (d, *J* = 8.8 Hz, 2H), 6.38 (s, 1H), 3.74 (s, 3H), 3.70 (s, 1H), 2.93 (d, *J* = 4.4 Hz, 1H), 2.61 (d, *J* = 18.4 Hz, 1H), 2.32 (d, *J* = 18.4 Hz, 1H), 2.07 – 2.00 (m, 1H), 1.81 – 1.66 (m, 2H), 1.34 – 1.22 (m, 4H), 1.17 – 1.05 (m, 1H), 0.85 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 214.1, 174.9, 150.4, 145.6, 128.6 (× 2), 124.6 (× 2), 58.5, 54.6, 52.9, 52.0, 44.7, 44.6, 24.9, 22.7, 20.3, 13.2; **HRMS (ESI)**: *m/z* calcd. for $C_{18}H_{22}N_2O_7S$ $[M+H]^+$ 411.1499, found 411.1493.

Preparation of Compound 24

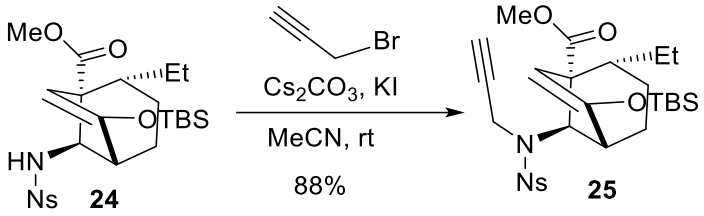


To a solution of **23** (1.0 g, 2.4 mmol) in THF (24 mL, anhydrous) was added LiHMDS (1 M in THF, 7.2 mL, 7.2 mmol) under Ar atmosphere at -78 °C. After stirring for 30 min at the same temperature, to the mixture was added TBSOTf (0.9 g, 0.8 mL, 3.6 mmol) at the same temperature. The reaction was stirred for 1 h before it was quenched with saturated NH_4Cl solution (20 mL). After warming to room temperature, the mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the crude product via flash column chromatography on silica gel (petroleum ether / ethyl acetate = 10:1 to 5:1) delivered **24** as a white solid (1.0 g, 81%).

TLC (petroleum ether / ethyl acetate, 5:1 v/v): R_f = 0.51; **IR** (neat) ν_{max}: 2967, 2857, 2151, 1742, 1724, 1372, 1352, 1178, 1078 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.35 (d, *J* = 8.8 Hz, 2H), 8.08 (d, *J* = 8.8 Hz, 2H), 5.75 (d, *J* = 5.6 Hz, 1H), 4.59 (d, *J* = 0.8 Hz, 1H), 3.57 (s, 3H), 3.51 (d, *J* = 5.6 Hz, 1H), 2.54 (t, *J* = 2.8 Hz, 1H), 1.69-1.65 (m, 2H), 1.53 – 1.40 (m, 5H), 0.89 (s, 9H), 0.83 (d, *J* = 7.2 Hz, 3H), 0.20 (d, *J* = 4.0 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 173.72, 155.8, 150.0, 147.0, 128.6 (× 2), 124.2

(× 2), 100.1, 62.2, 60.5, 52.0, 49.8, 41.1, 25.6 (× 3), 22.2, 21.1, 20.1, 18.1, 13.8, -4.36, -4.70; **HRMS (ESI)**: *m/z* calcd. for $C_{24}H_{36}N_2O_7S$ $[M+H]^+$ 525.2084, found 525.2080.

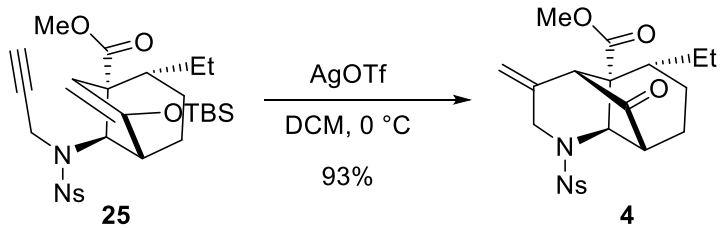
Preparation of Compound 25



To a mixture of **24** (780 mg, 1.5 mmol) and Cs_2CO_3 (1.5 g, 4.5 mmol) in MeCN (15 mL, anhydrous) was slowly added propargyl bromide (261.8 mg, 0.2 mL, 2.2 mmol) and KI (370 mg, 2.2 mmol) under argon atmosphere. After stirring for 6 h at 23 °C, the reaction was quenched by saturated NH_4Cl solution (10 mL) at 0 °C and the resultant mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the crude product via flash column chromatography on silica gel (petroleum ether / ethyl acetate = 10:1 to 5:1) delivered **25** as a white solid (738 mg, 88%).

TLC (petroleum ether / ethyl acetate, 5:1 v/v): R_f = 0.62; **IR** (neat) ν_{max}: 3082, 3002, 2980, 2801, 1745, 1720, 1455, 1375, 1360, 1353 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.34 (d, *J* = 8.8 Hz, 2H), 8.08 (d, *J* = 8.8 Hz, 2H), 4.70 (s, 1H), 4.38 (s, 1H), 4.30 (dd, *J* = 18.4, 2.4 Hz, 1H), 4.14 (dd, *J* = 18.4, 2.4 Hz, 1H), 3.61 (s, 3H), 2.32 (dd, *J* = 4.0, 2.0 Hz, 1H), 1.98 (t, *J* = 2.4 Hz, 1H), 1.74 – 1.62 (m, 3H), 1.54 – 1.36 (m, 3H), 0.89 (s, 13H), 0.21 (s, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.7, 154.3, 150.0, 147.0, 128.9 (× 2), 124.1 (× 2), 100.6, 72.5, 65.8, 60.3, 51.8, 48.3, 43.3, 35.1, 25.6, 25.6 (× 3), 22.5, 22.3, 21.9, 18.1, 14.1, -4.7, -4.9; **HRMS (ESI)**: *m/z* calcd. for $C_{27}H_{38}N_2O_7SSi$ $[M+H]^+$ 563.2241, found 563.2245.

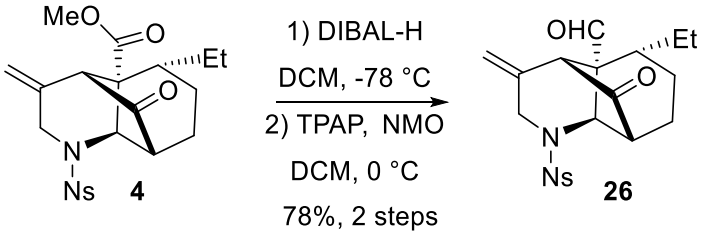
Preparation of Compound 4



To a solution of **25** (300 mg, 0.5 mmol) in DCM (5 mL, anhydrous) was slowly added AgOTf (68 mg, 0.3 mmol) under Ar atmosphere at 0 °C. After being stirred for 10 h at 0 °C, the mixture was evaporated to dryness. Purification of the residue by flash column chromatography (petroleum ether / ethyl acetate = 4:1 to 2:1) provided **4** as a white solid (220 mg, 93%).

TLC (petroleum ether / ethyl acetate, 2:1 v/v): R_f = 0.5; **IR** (neat) ν_{max}: 3102, 2879, 2806, 1741, 1720, 1662, 1455, 1384, 1372, 1204, 1189, 1030 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.38 (d, *J* = 8.8 Hz, 2H), 8.07 (d, *J* = 8.8 Hz, 2H), 5.02 (d, *J* = 1.6 Hz, 1H), 4.95 (t, *J* = 1.6 Hz, 1H), 4.69 (d, *J* = 2.0 Hz, 1H), 3.73 (dd, *J* = 4.0, 2.0 Hz, 2H), 3.55 (s, 3H), 3.19 (d, *J* = 2.0 Hz, 1H), 2.47 (t, *J* = 4.0 Hz, 1H), 2.04 – 2.01 (m, 1H), 1.94 – 1.90 (m, 2H), 1.65 (d, *J* = 14.4 Hz, 1H), 1.44 – 1.23 (m, 3H), 0.90 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 215.3, 171.2, 150.4, 145.1, 135.7, 129.1 (× 2), 124.5 (× 2), 114.7, 62.2, 59.9, 59.3, 52.5, 52.2, 46.1, 44.6, 26.4, 22.3, 20.6, 13.1**; HRMS (ESI)**: *m/z* calcd. for $C_{21}H_{24}N_2O_7S$ $[M+H]^+$ 449.1376, found 449.1373.

Preparation of Compound 26



To a stirred solution of esters **4** (380 mg, 0.7 mmol) in CH_2Cl_2 (16 mL, anhydrous) were slowly added DIBAL-H (1.5 M in PhMe, 1.3 mL, 2.0 mmol) under Ar atmosphere at -78 °C. The reaction mixture was kept stirring for 0.5 h and quenched with saturated aqueous Rochelle's salt (20 mL) at -78 °C. After being warmed to ambient temperature

and stirred for 0.5 h, the mixture was filtered through diatomite and extracted with CH_2Cl_2 (3 × 30mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The crude product was used in the following step without purification.

To a solution of the crude product in DCM (6 mL, anhydrous) was added TPAP (27 mg, 0.1 mmol), NMO (90 mg, 0.8 mmol) at 0 °C. After stirring for 0.5 h at 0 °C, the resulting mixture was filtered. The filter cake was rinsed with ethyl acetate repeatedly. After concentration of the filtrate, the residue was purified by flash column chromatography on silica gel (petroleum ether / ethyl acetate = 4:1 to 2:1) to give **26** as a white solid (277 mg, 78%).

TLC (petroleum ether / ethyl acetate, 4:1 v/v): R_f = 0.52; **IR** (neat) ν_{max}: 3034, 2987, 2876, 2745, 1742, 1705, 1642, 1630, 1452, 1380, 1323, 1156 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.66 (s, 1H), 8.41 (d, *J* = 8.8 Hz, 2H), 8.05 (d, *J* = 8.8 Hz, 2H), 5.04 (d, *J* = 2.0 Hz, 1H), 5.02 – 5.00 (m, 1H), 4.80 (d, *J* = 2.0 Hz, 1H), 3.97 (d, *J* = 14.4 Hz, 1H), 3.67 – 3.61 (m, 1H), 3.20 (d, *J* = 2.0 Hz, 1H), 2.30 (t, *J* = 4.0 Hz, 1H), 2.04 (s, 2H), 1.93 (dt, *J* = 11.6, 4.0 Hz, 2H), 1.66 (d, *J* = 14.6 Hz, 1H), 1.45 – 1.39 (m, 2H), 0.91 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 214.2, 201.7, 150.5, 144.4, 133.9, 128.8 (× 2), 124.7 (× 2), 115.5, 61.2, 60.6, 58.7, 51.2, 46.5, 42.7, 26.6, 21.7, 20.5, 12.9; **HRMS (ESI)**: *m/z* calcd. for $C_{20}H_{22}N_2O_6S$ $[M+H]^+$ 419.1271, found 419.1274.

Preparation of Compound S1

To a solution of ketone **27** (20.0 g, 56.8 mmol) in MeOH (570 mL) was added $NaBH_4$ (4.4 g, 113.4 mmol) at 0 °C. After being stirred at 0 °C for 10 min, the reaction mixture was then quenched by addition of saturated solution of NH_4Cl (300 mL). The aqueous layer was extracted with DCM (3 x 200 mL). The combined organic layers

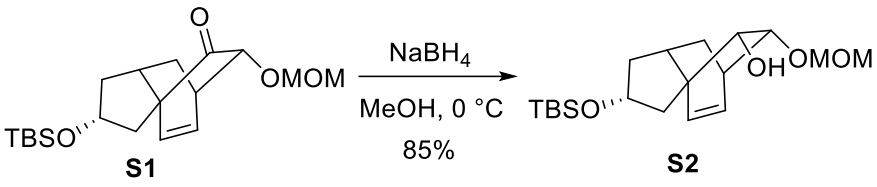
were washed with brine (300 mL) and dried over Na_2SO_4, filtered, and evaporated to dryness. The crude product was used in the following step without purification.

To a solution of the crude product in DCM (600 mL) was added 4 N HCl (2.8 mL, 11.4 mmol). The reaction mixture was stirred for 1 h and quenched with saturated aqueous $NaHCO_3$ (300 mL) at 0 °C. The organic layer was separated and the aqueous layer was extracted with DCM (3 x 200 mL). The combined organic layers were washed with brine (300 mL) and dried over Na_2SO_4, filtered, and evaporated to dryness. The crude product was used in the following step without purification.

To a solution of the crude product in DCM (1200 mL) was added DIPEA (139.8 g, 187.6 mL, 1134.6 mmol) and MOMCl (45.6 g, 43.0 mL, 567.2 mmol) at 0 °C. Following addition, the reaction mixture was allowed to warm to rt and stirred at that temperature for 12 h before being cooled to 0 °C and quenched by addition of saturated solution of $NaHCO_3$ (400 mL). The organic layer was separated and the aqueous layer was extracted with DCM (3 x 400 mL). The combined organic layers were washed with brine (200 mL) and dried over Na_2SO_4, filtered, and evaporated to dryness. Purification of the residue by flash column chromatography (petroleum ether / ethyl acetate = 8:1 to 4:1) furnished **S1** as a colorless oil (14.2 g, 72%).

TLC (petroleum ether / ethyl acetate, 4:1 v/v): R_f = 0.45; **IR** (neat) ν_{max}: 3008, 2966, 1734, 1668, 1354, 1135, 1008 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.48 (t, *J* = 7.2 Hz, 1H), 5.91 (dd, *J* = 7.2, 2.0 Hz, 1H), 4.87 (dd, *J* = 6.8, 1.6 Hz, 1H), 4.70 (dd, *J* = 6.8, 1.6 Hz, 1H), 4.36 – 4.28 (m, 1H), 3.76 – 3.73 (m, 1H), 3.40 (d, *J* = 1.4 Hz, 3H), 2.97 – 2.95 (m, 1H), 2.49 (dd, *J* = 14.4, 8.8 Hz, 1H), 2.21 (dt, *J* = 12.4, 6.8 Hz, 1H), 2.07 – 1.90 (m, 2H), 1.63 (dd, *J* = 14.4, 3.2 Hz, 1H), 1.32 – 1.15 (m, 2H), 0.86 (d, *J* = 1.2 Hz, 9H), 0.02 (dd, *J* = 7.2, 1.2 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 206.8, 135.0, 131.1, 96.7, 74.0, 73.0, 59.6, 55.7, 42.7, 39.0, 38.6, 37.5, 28.9, 26.0 (× 3), 18.2, -4.7 (× 2); **HRMS (ESI)**: *m/z* calcd. for $C_{19}H_{32}O_4Si$ $[M+H]^+$ 353.2142, found 353.2146.

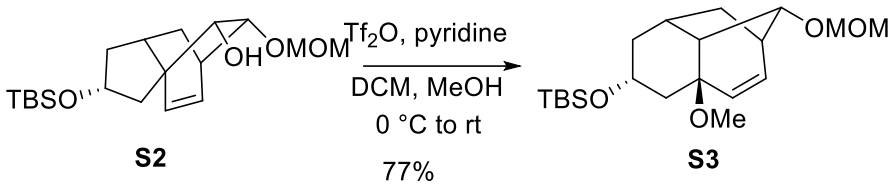
Preparation of Compound S2



To a solution of ketone **S1** (14.2 g, 40.8 mmol) in MeOH (400 mL) was added $NaBH_4$ (3.2 g, 81.6 mmol) at 0 °C. After being stirred at 0 °C for 10 min,the reaction mixture was then quenched by addition of saturated solution of NH_4Cl (200 mL). The aqueous layer was extracted with DCM (3 x 200 mL). The combined organic layers were washed with brine (150 mL) and dried over Na_2SO_4, filtered, and evaporated to dryness. Purification of the residue by flash column chromatography (petroleum ether / ethyl acetate = 6:1 to 3:1) furnished **S2** as a colorless oil (12.4 g, 85%).

TLC (petroleum ether / ethyl acetate, 3:1 v/v): R_f = 0.54; **IR** (neat) ν_{max}: 3602, 3076, 2876, 1673, 1348, 1145, 1003 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.33 – 6.27 (m, 1H), 6.05 (dd, *J* = 8.0, 1.2 Hz, 1H), 4.67 (s, 2H), 4.39 – 4.33 (m, 1H), 3.92 (dd, *J* = 2.4, 0.8 Hz, 1H), 3.58 (t, *J* = 6.8 Hz, 1H), 3.39 (s, 3H), 2.75 (d, *J* = 6.4 Hz, 1H), 2.71 – 2.66 (m, 1H), 2.11 (dt, *J* = 12.4, 6.8 Hz, 1H), 2.01 – 1.98 (m, 1H), 1.75 – 1.73 (m, 1H), 1.58 (d, *J* = 4.0 Hz, 1H), 1.48 – 1.42 (m, 1H), 1.07 – 0.97 (m, 2H), 0.87 (s, 9H), 0.02 (d, *J* = 9.6 Hz, 6H); **^{13}C NMR**(100 MHz, $CDCl_3$): δ 136.2, 131.8, 96.4, 76.8, 76.2, 73.9, 55.9, 51.2, 44.3, 43.3, 38.9, 37.7, 29.9, 26.0 (× 3), 18.2, -4.63 (× 2); **HRMS (ESI)**: *m/z* calcd. for $C_{19}H_{34}O_4Si$ $[M+H]^+$ 355.2299 , found 355.2291.

Preparation of Compound S3

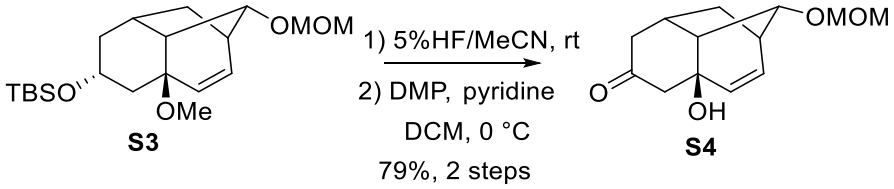


To a solution of alcohol **S2** (12.0 g, 33.8 mmol) in dry DCM (340 mL) was added pyridine (40.0 g, 40.8 mL, 507.9 mmol) and Tf_2O (47.8 g, 28.4 mL, 169.2 mmol) at 0 °C. The resulting mixture was stirred at 0 °C for 5 min, at which point TLC analysis indicated full consumption of starting material. Then the dry MeOH (170 mL) was added immediately and the reaction mixture was allowed to warm to rt. After being

stirred at rt for 3 h, the reaction mixture was then quenched by addition of saturated solution of $NaHCO_3$ (200 mL). The organic layer was separated and the aqueous layer was extracted with DCM (3 x 200 mL). The combined organic layers were washed with brine (200 mL) and dried over Na_2SO_4, filtered, and evaporated to dryness. The crude product was purified by silica gel chromatography (petroleum ether / ethyl acetate = 6:1 to 3:1) to give **S3** (9.6 g, 77 %) as a colourless oil

TLC (petroleum ether / ethyl acetate, 3:1 v/v): R_f = 0.54; **IR** (neat) ν_{max}: 3001, 2879, 1671, 1354, 1134, 1078, 1002 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.91 (ddd, *J* = 9.6, 6.8, 1.2 Hz, 1H), 5.75 (dd, *J* = 9.6, 2.0 Hz, 1H), 4.81 (d, *J* = 6.8 Hz, 1H), 4.62 (d, *J* = 6.8 Hz, 1H), 4.13 (t, *J* = 3.6 Hz, 1H), 3.94 (td, *J* = 4.4, 1.2 Hz, 1H), 3.37 (s, 3H), 3.24 (s, 3H), 2.53 (td, *J* = 6.4, 4.0 Hz, 1H), 2.37 – 2.28 (m, 1H), 2.25 – 2.21 (m, 1H), 2.08 – 2.02 (m, 1H), 1.93 – 1.84 (m, 1H), 1.80 – 1.74 (m, 1H), 1.65 (dd, *J* = 5.2, 3.2 Hz, 2H), 1.60 (d, *J* = 3.6 Hz, 1H), 0.86 (s, 9H), 0.02 (s, 3H), 0.00 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): 130.6, 130.1, 95.5, 78.9, 72.3, 68.2, 55.5, 49.3, 43.5, 41.9, 38.3, 34.3, 33.8, 31.2, 26.0 (× 3), 18.1, -4.8, -4.9; **HRMS (ESI)**: *m/z* calcd. for $C_{20}H_{36}O_4Si$ $[M+H]^+$ 369.2455 , found 369.2450.

Preparation of Compound S4

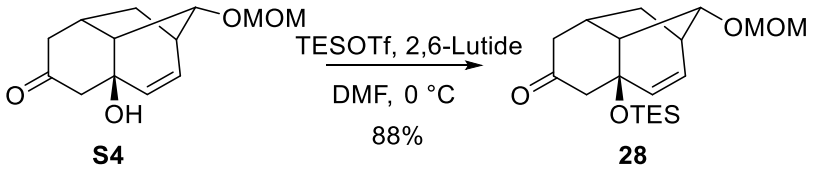


A suspension of compound **S3** (8.0 g, 21.8 mmol) in MeCN (220 ml) containing a drop of 5% HF was stirred for 30 min at rt. The reaction mixture was then quenched by addition of saturated solution of $NaHCO_3$ (200 mL). The aqueous layer was extracted with EtOAc (3 x 100 mL). The combined organic layers were washed with brine (100 mL) and dried over Na_2SO_4, filtered, and evaporated to dryness. The crude product was used in the following step without purification.To a solution of the crude product in DCM (220 mL) was added Dess-Martin periodinane (18.4 g, 43.4 mmol) and pyridine (6.8 g, 7.0 mL, 86.8 mmol) at rt. The reaction mixture was stirred at rt for 30 min and

then quenched with a saturated aqueous solution of $Na_2S_2O_3$ (100mL). The mixture was extracted with DCM (3 x 100 mL), and the organic layers were washed with brine (100 mL), dried over $MgSO_4$, filtered, and evaporated to dryness. The crude product was purified by silica gel chromatography (petroleum ether / ethyl acetate = 2:1 to 1:1) to give **S4** (4.0 g, 79 %) as a colourless oil.

TLC (petroleum ether / ethyl acetate, 1:1 v/v): R_f = 0.44; **IR** (neat) ν_{max}: 3485, 3019, 2948, 1721, 1645, 1456, 1120 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.92 (ddd, *J* = 9.6, 6.8, 1.2 Hz, 1H), 5.55 (dd, *J* = 9.6, 2.0 Hz, 1H), 4.66 (q, *J* = 6.8 Hz, 2H), 4.15 – 4.12 (m, 1H), 3.83 (s, 1H), 3.37 (s, 3H), 2.76 – 2.67 (m, 1H), 2.66 – 2.47 (m, 5H), 2.23 – 2.17 (m, 1H), 2.12 – 2.06 (m, 1H), 1.15 (dd, *J* = 13.2, 5.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 208.4, 131.7, 130.7, 96.1, 80.5, 73.8, 56.0, 52.4, 47.3, 44.3, 37.1, 36.7, 31.1; **HRMS (ESI)**: *m/z* calcd. for $C_{13}H_{18}O_4$ $[M+H]^+$ 239.1277 , found 239.1279.

Preparation of Compound 28



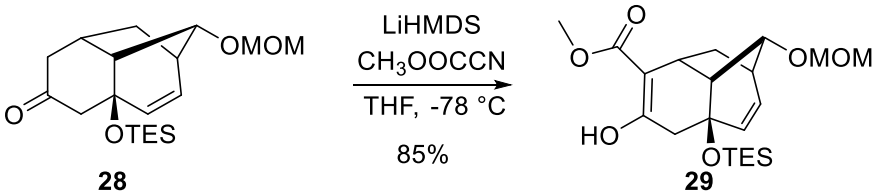
S4 **28**

To a solution of compound **S4** (4.0 g, 16.8 mmol) in DMF (168 mL) was added 2,6-Lutidine (9.0 g, 9.8 mL, 84.0 mmol) and TESOTf (13.8 g, 11.4 mL, 50.4 mmol) at 0 °C. After being stirred at 0 °C for 30 min, the reaction mixture was then quenched by addition of H_2O (100 mL). The aqueous layer was extracted with EtOAc (3 x 100 mL). The combined organic layers were washed with brine (100 mL) and dried over Na_2SO_4. The crude product was purified by silica gel chromatography (petroleum ether / ethyl acetate = 8:1 to 4:1) to give **28** (5.2 g, 88%) as a colourless oil.

TLC (petroleum ether / ethyl acetate, 4:1 v/v): R_f = 0.46; **IR** (neat) ν_{max}: 3012, 2938, 1756, 1701, 1654, 1367, 1114 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.95 (ddd, *J* = 9.6, 6.8, 1.2 Hz, 1H), 5.57 (dd, *J* = 9.6, 2.0 Hz, 1H), 4.85 (d, *J* = 6.8 Hz, 1H), 4.55 (d, *J* = 6.8 Hz, 1H), 4.11 (td, *J* = 4.0, 1.2 Hz, 1H), 3.37 (s, 3H), 2.71 – 2.49 (m, 6H), 2.16 – 2.01 (m, 2H), 0.94 (t, *J* = 8.0 Hz, 10H), 0.60 (q, *J* = 8.0 Hz, 6H); **^{13}C NMR** (100 MHz,

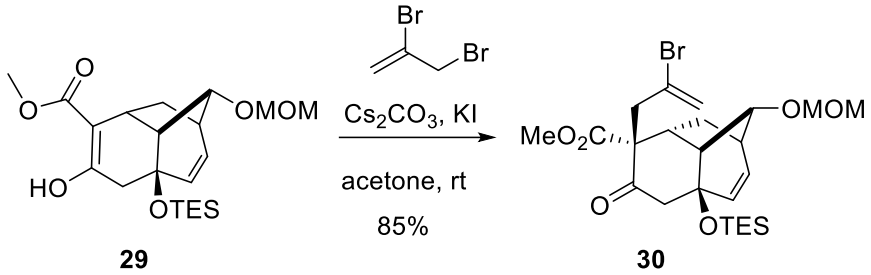
$CDCl_3$): δ 208.6, 132.5, 130.1, 95.2, 77.4, 76.1, 55.9, 55.5, 45.8, 44.3, 37.6, 35.8, 32.5, 7.2 (× 3), 6.9 (× 3); **HRMS (ESI)**: *m/z* calcd. for $C_{19}H_{32}O_4Si$ $[M+H]^+$ 353.2142, found 353.2140.

Preparation of Compound 29



To a solution of compound **28** (2.6 g, 7.4 mmol) in THF (30 mL) was added LiHMDS (22 mL, 22.1mmol, 1M in THF) and methyl cyanoformate (0.9 g, 0.9 mL, 11.1 mmol) at -78 °C. After being stirred at -78 °C for 10 min, the reaction mixture was then quenched by addition of H_2O (15 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (15 mL) and dried over Na_2SO_4. The crude product was purified by silica gel chromatography (petroleum ether / ethyl acetate = 16:1 to 8:1) to give **29** (2.6 g, 85%) as a white solid. **TLC** (petroleum ether / ethyl acetate, 8:1 v/v): R_f = 0.46**; IR** (neat) ν_{max}: 3450, 3021, 2892, 1736, 1347, 1278, 1128, 1098 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 11.91 (s, 1H), 5.90 (ddd, *J* = 9.6, 6.8, 1.2 Hz, 1H), 5.54 (dd, *J* = 9.6, 2.0 Hz, 1H), 4.86 (d, *J* = 6.8 Hz, 1H), 4.56 (d, *J* = 6.8 Hz, 1H), 4.07 (t, *J* = 4.4 Hz, 1H), 3.74 (s, 3H), 3.37 (s, 3H), 2.97 (ddd, *J* = 10.8, 7.2, 4.4 Hz, 1H), 2.62 – 2.56 (m, 1H), 2.52 (td, *J* = 6.0, 3.2 Hz, 1H), 2.47 – 2.40 (m, 2H), 2.12 – 2.05 (m, 2H), 0.95 (t, *J* = 8.0 Hz, 9H), 0.62 (q, *J* = 8.0 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.6, 167.8, 132.4, 130.0, 101.5, 95.3, 77.2, 71.6, 55.4, 51.6, 44.2, 43.3, 38.1, 36.4, 31.8, 7.3 (× 3), 7.0 (× 3); **HRMS (ESI)**: *m/z* calcd. for $C_{21}H_{34}O_6Si$ $[M+H]^+$ 411.2197, found 411.2193.

Preparation of Compound 30

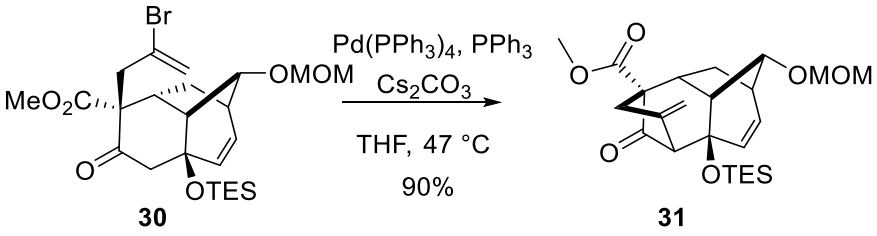


29 **30**

Compound **29** (2.0 g, 4.9 mmol) was dissolved in anhydrous acetone (49 mL), and Cs_2CO_3 (3.2 g, 9.8 mmol) was added sequentially with KI (1.6 g, 9.8 mmol) and 2,3-dibromo-1-propene (2.3 g, 1.2 mL, 7.3 mmol) at room temperature and stirred for 3 h. After the reaction was complete by TLC, the reaction was quenched by the addition of saturated $NaHCO_3$ aqueous solution (20 mL). The aqueous layer was extracted with EtOAc (3 × 20 mL), the organic layers were combined, washed with saturated brine (10 mL), dried with anhydrous Na_2SO_4. The crude product was purified by silica gel column chromatography (petroleum ether / ethyl acetate = 8:1 to 4:1) to afford colorless oily compounds **30** (2.2 g, 85%).

TLC (petroleum ether / ethyl acetate, 4:1 v/v): R_f = 0.52; **IR** (neat) ν_{max}: 3122, 2892, 1732, 1652, 1437, 1267, 1176, 1092, 902 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.99 (s, 1H), 5.65 (d, *J* = 2.0 Hz, 1H), 5.59 – 5.52 (m, 2H), 4.81 (dd, *J* = 6.8, 1.2 Hz, 1H), 4.54 (dd, *J* = 6.8, 1.2 Hz, 1H), 4.07 (s, 1H), 3.70 (d, *J* = 1.2 Hz, 3H), 3.36 (t, *J* = 2.8 Hz, 4H), 3.10 (d, *J* = 12.4 Hz, 1H), 2.90 – 2.87 (m, 1H), 2.84 – 2.76 (m, 1H), 2.56 – 2.45 (m, 2H), 2.15 – 2.07 (m, 1H), 1.63 – 1.60 (m, 1H), 1.17 – 1.12 (m, 1H), 0.94 (t, *J* = 8.0 Hz, 9H), 0.68 – 0.53 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 202.3, 170.0, 132.7, 130.5, 126.7, 121.7, 95.2, 76.3, 63.1, 55.6, 53.6, 53.0, 52.0, 47.7, 44.7, 41.1, 36.5, 33.1, 7.2 (× 3), 6.8 (× 3); **HRMS (ESI)**: *m/z* calcd. for $C_{24}H_{37}BrO_6Si$ $[M+H]^+$ 529.1615, found 529.1610.

Preparation of Compound 31

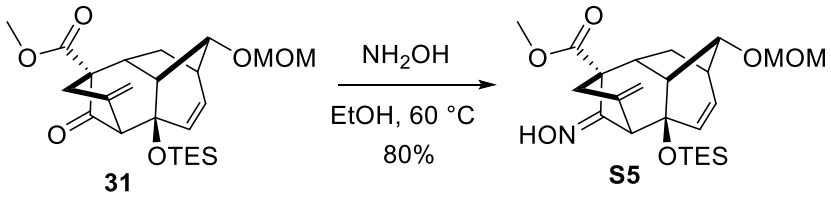


30 **31**

Compound **30** (2.2 g, 4.1 mmol) was dissolved in anhydrous THF (42 mL), and Cs_2CO_3 (6.8 g, 20.7 mmol) and PPh_3 (1.1 g, 4.1 mmol) and $Pd(PPh_3)_4$ (958.1 mg, 0.8 mmol) were added in turn at room temperature. The reaction system was purged with argon at 0 °C and then warmed up to 47 °C for 8 h. After the reaction was complete as detected by TLC, the reaction was diluted by addition of EtOAc (10 mL) and quenched by the addition of saturated aqueous solution of NH_4Cl (20 mL). The aqueous layer was extracted with EtOAc (3 × 15 mL), the organic layers were combined, washed with saturated brine (20 mL), dried with anhydrous Na_2SO_4, filtered. The crude product was purified by silica gel column chromatography (petroleum ether / ethyl acetate = 8:1 to 4:1) to afford colorless oily compound **31** (1.7 g, 90%).

TLC (petroleum ether / ethyl acetate, 4:1 v/v): R_f = 0.50; **IR** (neat) ν_{max}: 3429, 2890, 1742, 1712, 1656, 1375, 1267, 1158, 1034, 923 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.96 (ddd, *J* = 9.6, 6.8, 1.2 Hz, 1H), 5.72 (dd, *J* = 9.6, 2.0 Hz, 1H), 5.19 (s, 1H), 5.12 (s, 1H), 4.74 (d, *J* = 6.8 Hz, 1H), 4.52 (d, *J* = 6.8 Hz, 1H), 4.03 – 4.00 (m, 1H), 3.72 (s, 3H), 3.34 (s, 3H), 3.13 (dt, *J* = 16.8, 2.8 Hz, 1H), 2.80 (d, *J* = 1.2 Hz, 1H), 2.75 – 2.67 (m, 2H), 2.57 – 2.52 (m, 2H), 2.16 – 2.10 (m, 1H), 1.30 – 1.27 (m, 1H), 0.95 (t, *J* = 8.0 Hz, 9H), 0.68 – 0.62 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 205.4, 171.2, 136.4, 132.5, 129.7, 112.6, 95.1, 80.5, 76.2, 65.6, 61.3, 55.5, 52.4, 43.8, 43.7, 40.2, 37.2, 33.3, 7.4 (× 3), 6.9 (× 3); **HRMS (ESI)**: *m/z* calcd. for $C_{24}H_{36}BrO_6Si$ $[M+H]^+$ 449.2353, found 449.2350.

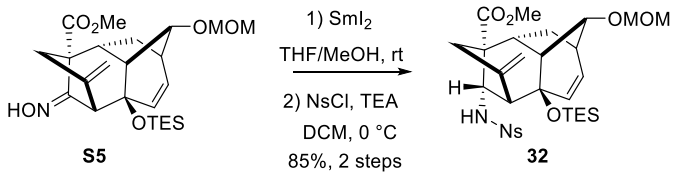
Preparation of Compound S5



To a solution of **31** (1.9 g, 4.2 mmol) in anhydrous EtOH (42 mL) at 23 °C under argonwas added NH_2OH (50% in H_2O, 4.2 mL). After being stirred for 8 h at 60 °C, the reaction was quenched by saturated NH_4Cl solution (20 mL) and extracted with EtOAc (3 ×20 mL). The organic layer and extracts were combined, dried, and

evaporated to dryness. Purification of the residue by flash column chromatography (petroleum ether / ethyl acetate = 4:1 to 2:1) furnished **S5** as a white solid (1.6 g, 80%). **TLC** (petroleum ether / ethyl acetate, 2:1 v/v): R_f = 0.42; **IR** (neat) ν_{max}: 3512, 3027, 2923, 1873, 1597, 1454, 1347, 1262, 1168, 1153, 1027, 803, 700 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.49 (s, 1H), 5.89 (ddd, *J* = 9.6, 6.8, 1.2 Hz, 1H), 5.82 (dd, *J* = 9.6, 2.0 Hz, 1H), 5.15 (d, *J* = 2.6 Hz, 1H), 5.04 (d, *J* = 2.0 Hz, 1H), 4.74 (d, *J* = 6.8 Hz, 1H), 4.50 (d, *J* = 6.8 Hz, 1H), 3.93 (t, *J* = 4.4 Hz, 1H), 3.83 (s, 1H), 3.69 (s, 3H), 3.33 (s, 3H), 2.98 (dt, *J* = 16.4, 2.8 Hz, 1H), 2.63 – 2.49 (m, 3H), 2.42 – 2.39 (m 1H), 2.02 – 2.06 (m, 1H), 1.39 (dd, *J* = 13.6, 5.6 Hz, 1H), 0.96 (t, *J* = 8.0 Hz, 9H), 0.68 (t, *J* = 8.0 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.1, 159.5, 140.0, 131.0, 130.2, 111.4, 95.1, 78.7, 76.1, 55.4, 55.1, 54.0, 52.1, 43.9, 43.3, 42.3, 37.2, 32.8, 7.5 (× 3), 7.0 (× 3); **HRMS (ESI)**: *m/z* calcd. for $C_{24}H_{37}NO_6Si$ $[M+H]^+$ 464.2462, found 464.2460.

Preparation of Compound 32



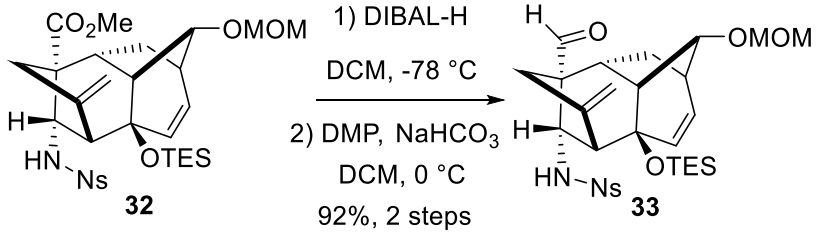
To a solution of oxime **S5** (100 mg, 0.2 mmol) in THF / MeOH (0.4 mL / 0.04 mL) under Ar atmosphere (deoxygenated by sparging with argon) was added a solution of SmI_2 in THF (0.1 M) dropwise at room temperature until the dark blue color of the reaction mixture did not fade. The resulting mixture was stirred for 1h at room temperature when a saturated aqueous solution of Rochelle's salt (3 mL) was added. The mixture was extracted with EtOAc (3 × 5 mL) and the combined organic phase was dried with Na_2SO_4, and evaporated to dryness. The crude product was used in the following step without purification.

To a solution of the crude product in CH_2Cl_2 (4 mL, anhydrous) were added NsCl (74.2 mg, 0.3 mmol) and TEA (67.7 mg, 93.0 μL, 0.7 mmol). After stirring for 0.5 h at 0 °C, the reaction was quenched by H_2O (2 mL) and the resultant mixture was extracted with CH_2Cl_2 (3 × 2 mL). The combined organic extracts were dried over $MgSO_4$,

filtered, and concentrated. Purification of the residue via flash chromatography on silica gel (petroleum ether / ethyl acetate = 6:1 to 3:1) yielded **32** as a white solid (116 mg, 85%).

TLC (petroleum ether / ethyl acetate, 3:1 v/v): R_f = 0.52; **IR** (neat) ν_{max}: 3470, 3035, 2890, 1735, 1559, 1546, 1475, 1387, 1266, 1168, 1102, 821, 745 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 8.8 Hz, 2H), 8.05 (d, *J* = 8.8 Hz, 2H), 6.38 (d, *J* = 11.2 Hz, 1H), 6.25 (ddd, *J* = 9.6, 6.8, 1.2 Hz, 1H), 5.89 (dd, *J* = 9.6, 2.0 Hz, 1H), 5.05 (d, *J* = 2.4 Hz, 1H), 4.97 (d, *J* = 2.4 Hz, 1H), 4.70 (d, *J* = 6.8 Hz, 1H), 4.49 (d, *J* = 6.8 Hz, 1H), 3.94 (ddd, *J* = 11.2, 4.8, 1.6 Hz, 1H), 3.90 (t, *J* = 4.0 Hz, 1H), 3.49 (s, 3H), 3.32 (s, 3H), 2.72 – 2.62 (m, 2H), 2.60 – 2.53 (m, 1H), 2.35 (d, *J* = 4.8 Hz, 1H), 2.32 – 2.26 (m, 2H), 2.17 – 2.15 (m, 1H), 1.74 (dd, *J* = 14.8, 6.0 Hz, 1H), 0.87 (t, *J* = 8.0 Hz, 9H), 0.55 – 0.46 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 173.5, 150.2, 146.8, 140.8, 135.5, 133.2, 128. 6 (× 2), 124.5 (× 2), 112.3, 95.1, 76.3, 73.1, 60.0, 55.5, 53.8, 52.1, 51.3, 43.0 (× 2), 39.6, 37.8, 32.6, 7.4 (× 3), 7.1 (× 3); **HRMS (ESI)**: *m/z* calcd. for $C_{30}H_{42}N_2O_9SSi$ $[M+H]^+$ 635.2452, found 635.2457.

Preparation of Compound 33

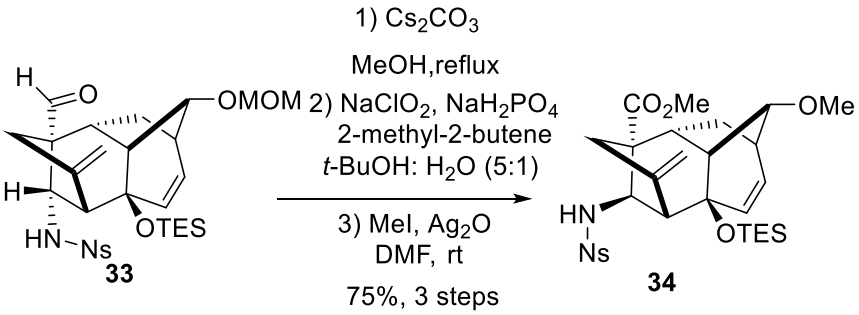


To a stirred solution of esters **32** (150 mg, 0.3 mmol) in CH_2Cl_2 (3 mL) were slowly added DIBAL-H (1.5 M in PhMe, 0.4 mL, 0.6 mmol) under Ar atmosphere at -78 °C. The reaction mixture was kept stirring for 0.5 h and quenched with saturated aqueous Rochelle's salt (2 mL) at 0 °C. After being warmed to ambient temperature and stirred for 0.5 h, the mixture was filtered through diatomite and extracted with CH_2Cl_2 (3 × 1.5 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated to afford a crude product, which was directly used in the following step without purification.

To a mixture of the above crude product in CH_2Cl_2 (3 mL) was added Dess-Martin periodinane (127.2 mg, 0.6 mmol) and $NaHCO_3$ (50.4 mg, 1.2 mmol) at 0 °C. After stirring for 0.5 h, the reaction was quenched by saturated aqueous $Na_2S_2O_3$ (5 mL) and extracted with CH_2Cl_2 (3 × 3 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. Purification of the residue via flash chromatography on silica gel (petroleum ether / ethyl acetate = 8:1 to 4:1) yielded **33** as a white solid (131 mg, 92%).

TLC (petroleum ether / ethyl acetate, 3:1 v/v): R_f = 0.50; **IR** (neat) ν_{max}: 3340, 3023, 2898, 1734, 1558, 1536, 1423, 1378, 1265, 1178, 1034, 823, 712 cm^{-1}; **^{1}H NMR:**(400 MHz, $CDCl_3$) δ 9.43 (s, 1H), 8.41 (d, *J* = 8.8 Hz, 2H), 8.04 (d, *J* = 8.8 Hz, 2H), 6.44 (d, *J* = 11.2 Hz, 1H), 6.26 (ddd, *J* = 9.6, 6.8, 1.2 Hz, 1H), 5.81 (dd, *J* = 9.6, 2.0 Hz, 1H), 5.09 (d, *J* = 2.4 Hz, 1H), 5.02 (d, *J* = 2.4 Hz, 1H), 4.69 (d, *J* = 6.8 Hz, 1H), 4.48 (d, *J* = 6.8 Hz, 1H), 3.94 – 3.86 (m, 2H), 3.32 (s, 3H), 2.71 (t, *J* = 5.6 Hz, 1H), 2.58 (dt, *J* = 16.4, 2.8 Hz, 1H), 2.53 – 2.44 (m, 1H), 2.31 – 2.14 (m, 3H), 2.12 – 2.02 (m, 1H), 0.85 (t, *J* = 8.0 Hz, 10H), 0.52 – 0.44 (m, 6H); **^{13}C NMR**:(100 MHz, $CDCl_3$) δ 201.8, 150.4, 146.4, 140.2, 135.1, 133.9, 128.4 (× 2), 124.8 (× 2), 113.0, 95.2, 76.3, 73.7, 58.6, 56.0, 55.5, 53.7, 43.0, 38.9, 37.8, 37.5, 31.5, 7.4 (× 3), 7.1 (× 3); **HRMS (ESI)**: *m/z* calcd. for $C_{29}H_{40}N_2O_8SSi$ $[M+H]^+$ 605.2348 , found 605.2346.

Preparation of Compound 34

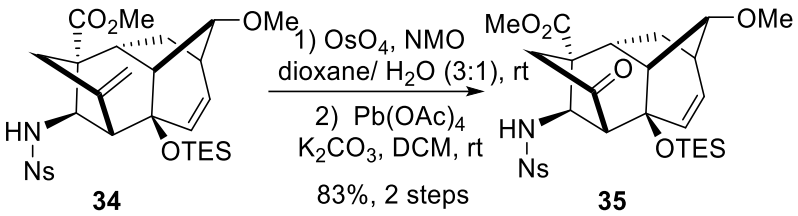


To a solution of aldehyde **33** (150 mg, 0.3 mmol) in MeOH (2.6 mL, anhydrous) was added Cs_2CO_3 (340.4 mg, 1.0 mmol) under Ar atmosphere at rt. After being stirred for 12 h at 60 °C, the mixture was evaporated to dryness. The crude product was used in the following step without purification.

To an ice-cooled stirred solution of the crude in *t*BuOH (2.5 mL) was added 2-methyl-2-butene (174 mg, 0.3 mL, 2.5 mmol) in one portion, a freshly prepared mixture of 0.5 mL of aqueous solution of $NaClO_2$ (37.8 mg, 0.4 mmol) and NaH_2PO_4 (125.4 mg, 1.0 mmol) was added. The reaction was continued for 0.5 h at room temperature. Then the mixture was quenched with ammonium chloride (3 mL) and extracted with EtOAc (3 × 2 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated to afford a crude product, which was directly used in the following step without purification.

To a mixture of the above crude product in DMF (4 mL) was added Ag_2O (46.3 mg, 0.2 mmol), MeI (85.2 mg, 39 μL, 0.6 mmol) at rt. After stirring for 0.5 h, the reaction was quenched by saturated aqueous NH_4Cl (3 mL) and extracted with EtOAc (3 × 2 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. Purification of the residue via flash chromatography on silica gel (petroleum ether / ethyl acetate = 8:1 to 4:1) yielded **34** as a white solid (112 mg, 75%). **TLC** (petroleum ether / ethyl acetate, 3:1 v/v): R_f = 0.55; **IR** (neat) ν_{max}: 3243, 3037, 2967, 1748, 1542, 1531, 1450, 1373, 1256, 1168, 1051, 830, 712 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.36 (d, *J* = 8.8 Hz, 2H), 8.05 (d, *J* = 8.8 Hz, 2H), 5.97 (ddd, *J* = 9.6, 6.8, 1.2 Hz, 1H), 5.61 (dd, *J* = 9.6, 2.0 Hz, 1H), 5.37 (d, *J* = 5.4 Hz, 1H), 5.09 (s, 1H), 5.01 (d, *J* = 2.4 Hz, 1H), 3.58 (s, 3H), 3.54 (d, *J* = 5.4 Hz, 1H), 3.44 (t, *J* = 4.4 Hz, 1H), 3.25 (s, 3H), 2.76 (dt, *J* = 17.2, 2.8 Hz, 1H), 2.56 (td, *J* = 10.4, 4.0 Hz, 1H), 2.46 (d, *J* = 17.2 Hz, 1H), 2.42 (s, 1H), 2.38 – 2.32 (m, 1H), 2.23 – 2.21 (m, 1H), 1.75 – 1.73 (m, 1H), 1.20 (dd, *J* = 14.0, 5.6 Hz, 1H), 0.89 (t, *J* = 8.0 Hz, 9H), 0.55 (qd, *J* = 8.0, 2.4 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 174.0, 150.2, 142.3, 131.2, 131.0, 128.7 (× 2), 124.2 (× 2), 113.8, 82.0, 75.4, 59.0, 58.9, 57.3, 54.0, 52.3, 42.8, 42.3, 39.4, 37.1, 31.7, 7.4 (× 3), 7.1 (× 3); **HRMS (ESI)**: *m/z* calcd. for $C_{28}H_{40}N_2O_8SSi$ $[M+H]^+$ 605.2348, found 605.2344.

Preparation of Compound 35



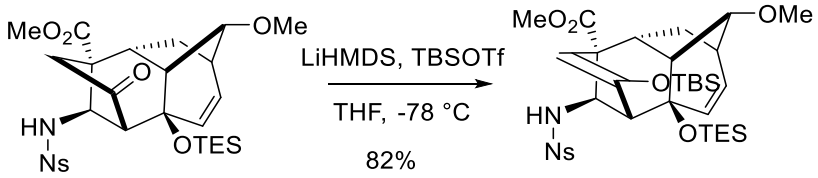
Compound **34** (120 mg, 0.2 mmol) was dissolved in a mixed solvent of 1,4-dioxane / water (3:1, 4 mL). NMO (116.3 mg, 1.0 mmol) and OsO_4 (25.4 mg, 0.1 mmol) were added sequentially at room temperature and stirred for 1 hour. After TLC indicated complete reaction, the mixture was diluted with EtOAc (2 mL), followed by the addition of saturated $Na_2S_2O_3$ solution (3 mL) to quench the reaction. The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 3 mL). The combined organic layers were washed with saturated brine (3 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude product.

The crude product was dissolved in DCM (2 mL), and $Pb(OAc)_4$ (352.2 mg, 0.8 mmol) and K_2CO_3 (137.2 mg, 1.0 mmol) were sequentially added at room temperature and stirred for 30 minutes. After TLC indicated complete reaction, the mixture was diluted with DCM (1 mL), followed by the addition of saturated $Na_2S_2O_3$ solution (2 mL) to quench the reaction. The organic layer was separated, and the aqueous layer was extracted with DCM (3 × 1 mL). The combined organic layers were washed with saturated brine (2 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude product. The crude product was purified by silica gel column chromatography (petroleum ether / ethyl acetate = 4:1 to 2:1) yielded **35** as a white solid (100 mg, 83%).

TLC (petroleum ether / ethyl acetate, 2:1 v/v): R_f = 0.52; **IR** (neat) ν_{max}: 3215, 3041, 2942, 1740, 1542, 1457, 1373, 1254, 1167, 1067, 841, 718 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 8.8 Hz, 2H), 8.04 (d, *J* = 8.8 Hz, 2H), 5.99 (ddd, *J* = 9.6, 6.8, 1.2 Hz, 1H), 5.93 (d, *J* = 2.4 Hz, 1H), 5.65 (dd, *J* = 9.6, 2.0 Hz, 1H), 3.67 (s, 4H), 3.50 (t, *J* = 4.0 Hz, 1H), 3.27 (s, 3H), 2.67 (d, *J* = 10.4 Hz, 1H), 2.61 – 2.56 (m, 3H), 2.41 – 2.32 (m, 2H), 1.86 – 1.78 (m, 1H), 1.11 (dd, *J* = 13.6, 5.6 Hz, 1H), 0.94 (t, *J* = 8.0 Hz,

9H), 0.61 (qd, J = 8.0, 4.0 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ. 208.9, 173.6, 150.4, 145.6, 131.5, 130.2, 128.8 (× 2), 124.4 (× 2), 81.5, 75.8, 62.1, 57.4, 57.3, 53.0, 51.1, 45.1, 43.1, 42.5, 37.23, 31.0, 7.1 (× 3), 6.8 (× 3); **HRMS (ESI)**: *m/z* calcd. for $C_{28}H_{38}N_2O_9SSi$ $[M+H]^+$ 607.2139, found 607.2133.

Preparation of Compound 36

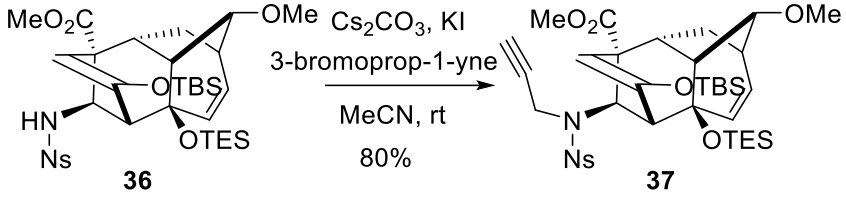


35 **36**

To a solution of **35** (100 mg, 0.2 mmol) in THF (2 mL, anhydrous) was added LiHMDS (1 M in THF, 1.0 mL, 1.0 mmol) under Ar atmosphere at -78 °C. After stirring for 30 min at the same temperature, to the mixture was added TBSOTf (238 mg, 0.2 mL, 0.9 mmol) at the same temperature. The reaction was stirred for 1 h before it was quenched with saturated NH_4Cl solution (2 mL). After warming to room temperature, the mixture was extracted with EtOAc (3 × 1 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the crude product via flash column chromatography on silica gel (petroleum ether / ethyl acetate = 8:1 to 4:1) delivered **36** as a white solid (97 mg, 82%).

TLC (petroleum ether / ethyl acetate, 4:1 v/v): R_f = 0.52; **IR** (neat) ν_{max}: 3332, 3014, 2890, 1749, 1541, 1530, 1452, 1372, 1271, 1160, 824, 712 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.37 (d, J = 8.8 Hz, 2H), 8.03 (d, J = 8.8 Hz, 2H), 6.00 (ddd, J = 9.6, 6.8, 1.2 Hz, 1H), 5.76 (dd, J = 9.6, 2.0 Hz, 1H), 5.29 (d, J = 8.4 Hz, 1H), 4.78 (s, 1H), 3.61 (d, J = 8.4 Hz, 1H), 3.55 (s, 1H), 3.50 (s, 3H), 3.28 (s, 3H), 2.63 (q, J = 5.6 Hz, 2H), 2.44 (dd, J = 5.6, 4.4 Hz, 3H), 2.23 (s, 1H), 0.96 (s, 9H), 0.87 (d, J = 8.0 Hz, 9H), 0.55 (dd, J = 8.0, 1.6 Hz, 6H), 0.25 (s, 3H), 0.22 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ. 172.8, 156.7, 150.1, 146.9, 133.01, 130.3, 128.6 (× 2), 124.3 (× 2), 102.3, 82.3, 72.7, 62.4, 60.1, 57.4, 57.3, 52.1, 44.9, 39.8, 38.7, 29.1, 26.2 (× 3), 18.6, 7.4 (× 3), 6.9 (× 3), -4.1, -4.4; **HRMS (ESI)**: *m/z* calcd. for $C_{34}H_{52}N_2O_9SSi_2$ $[M+H]^+$ 721.3004, found 721.3000.

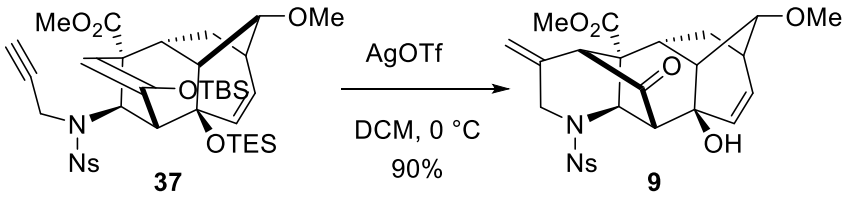
Preparation of Compound 37



To a mixture of **36** (110 mg, 0.15 mmol) and Cs_2CO_3 (149.3 mg, 0.46 mmol) in MeCN (1.5 mL, anhydrous) was slowly added propargyl bromide (27.4 mg, 20 μL, 0.23 mmol) and KI (38.0 mg, 0.22 mmol) under argon atmosphere. After stirring for 3 h at 23 °C, the reaction was quenched by saturated NH_4Cl solution (1 mL) at 0 °C and the resultant mixture was extracted with CH_2Cl_2 (3 × 1 mL). The combined organic extracts were washed with brine (2 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the crude product via flash column chromatography on silica gel (petroleum ether / ethyl acetate = 10:1 to 5:1) delivered **37** as a white solid (93 mg, 80%).

TLC (petroleum ether / ethyl acetate, 4:1 v/v): R_f = 0.62; **IR** (neat) ν_{max}: 3491, 3067, 2920, 2146, 1759, 1582, 1552, 1370, 1241, 1159, 1082, 781, 720 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.36 (d, *J* = 8.8 Hz, 2H), 8.14 (d, *J* = 8.8 Hz, 2H), 6.04 (dd, *J* = 9.6, 6.8 Hz, 1H), 5.51 (dd, *J* = 9.6, 2.0 Hz, 1H), 4.83 (s, 1H), 4.51 (t, *J* = 2.4 Hz, 2H), 4.27 (s, 1H), 3.62 (s, 3H), 3.59 (t, *J* = 4.4 Hz, 1H), 3.27 (s, 3H), 2.69 (q, *J* = 6.0 Hz, 2H), 2.47 – 2.38 (m, 4H), 2.07 (d, *J* = 2.4 Hz, 1H), 0.95 (s, 9H), 0.84 (t, *J* = 8.0 Hz, 9H), 0.50 (dd, *J* = 8.0, 3.6 Hz, 6H), 0.26 (s, 3H), 0.22 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ. 172.3, 155.8, 150.2, 146.6, 133.4, 130.8, 129.5 (× 2), 123.9 (× 2), 103.4, 82.6, 79.9, 74.3, 73.3, 65.8, 57.2 (× 2), 56.9, 52.1, 45.7, 41.0, 39.0, 34.7, 29.5, 26.2 (× 3), 18.6, 7.3 (× 3), 6.7 (× 3), -4.4, -4.9; **HRMS (ESI)**: *m/z* calcd. for $C_{37}H_{54}N_2O_9SSi_2$ $[M+H]^+$ 759.3161, found 759.3159.

Preparation of Compound 9



To a solution of **37** (50 mg, 0.07 mmol) in DCM (1.2 mL, anhydrous) was slowly added AgOTf (8.47 mg, 0.03 mmol) under Ar atmosphere at 0 °C. After being stirred for 30 min at 0 °C, the mixture was evaporated to dryness. Purification of the residue by flash column chromatography (petroleum ether / ethyl acetate = 2:1 to 1:1) provided **9** as a white solid (32 mg, 90%).

TLC (petroleum ether / ethyl acetate, 1:1 v/v): R_f = 0.22; **IR** (neat) ν_{max}: 3476, 3081, 2978, 1743, 1628, 1548,1436, 1371, 1347, 1234, 1162, 1088, 837, 712 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 8.4 Hz, 2H), 8.03 (d, *J* = 8.4 Hz, 2H), 6.16 (dd, *J* = 9.6, 6.8 Hz, 1H), 5.70 (dd, *J* = 9.6, 2.0 Hz, 1H), 5.07 (d, *J* = 2.0 Hz, 1H), 5.01 (d, *J* = 2.0 Hz, 1H), 4.69 (d, *J* = 2.4 Hz, 1H), 3.89 (d, *J* = 14.4 Hz, 1H), 3.68 (t, *J* = 4.4 Hz, 1H), 3.59 (s, 4H), 3.31 (s, 1H), 3.26 (d, *J* = 4.4 Hz, 4H), 2.74 – 2.70 (m, 1H), 2.65 – 2.56 (m, 1H), 2.30 (t, *J* = 5.6 Hz, 1H), 2.25 (s, 1H), 1.87 – 1.79 (m, 1H), 1.64 (dd, *J* = 14.0, 5.2 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ. 210.9, 170.1, 150.4, 144.6, 135.3, 130.7, 130.1, 128.9 (× 2), 124.6 (× 2), 115.3, 81.8,75.4, 62.0, 58.1, 58.1, 57.4, 56.4, 52.3, 46.0, 44.4, 40.7, 35.1, 31.4; **HRMS (ESI)**: *m/z* calcd. for $C_{25}H_{26}N_2O_9S$ $[M+H]^+$ 531.1431, found 531.1433.

5. X-ray Crystallographic Data

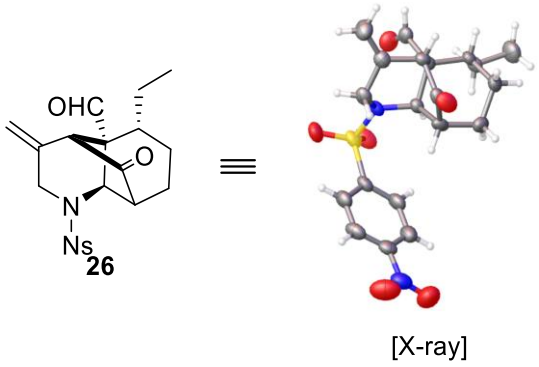


Figure S1:

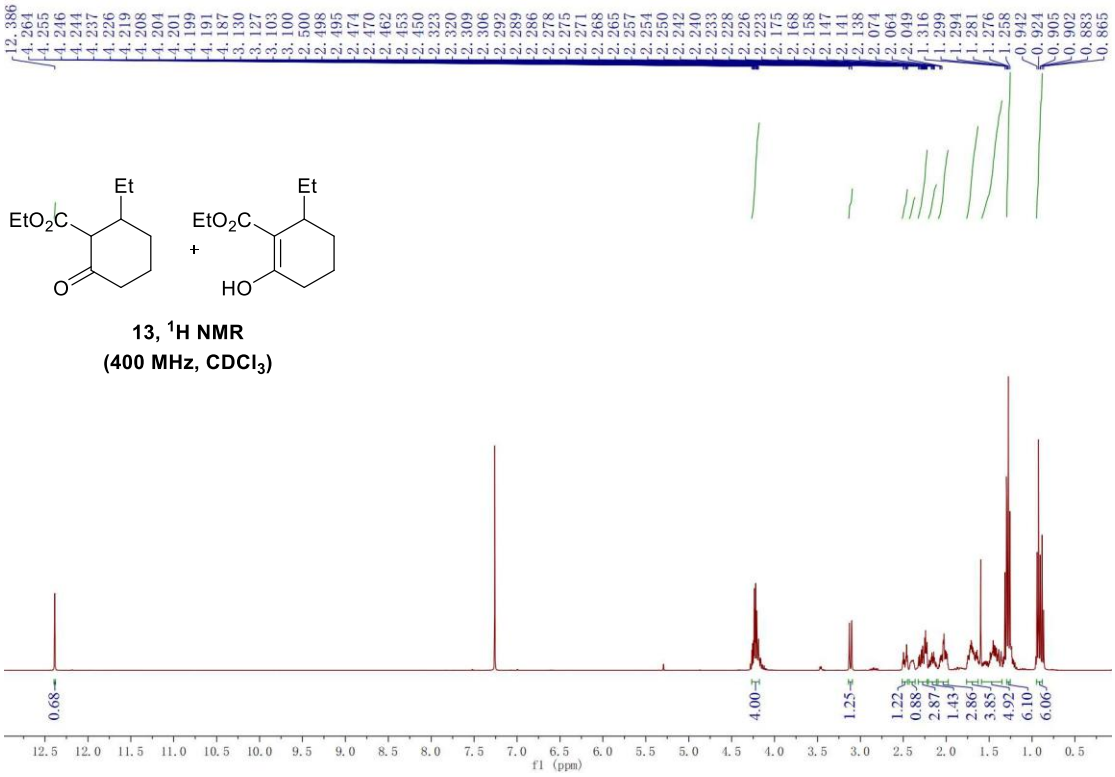
Sample preparation: crystals were obtained via slow evaporation of **26** with mixed solvent (dichloromethane / methanol = 4 / 1)

Table S1. Crystal data and structure refinement for compound 26.

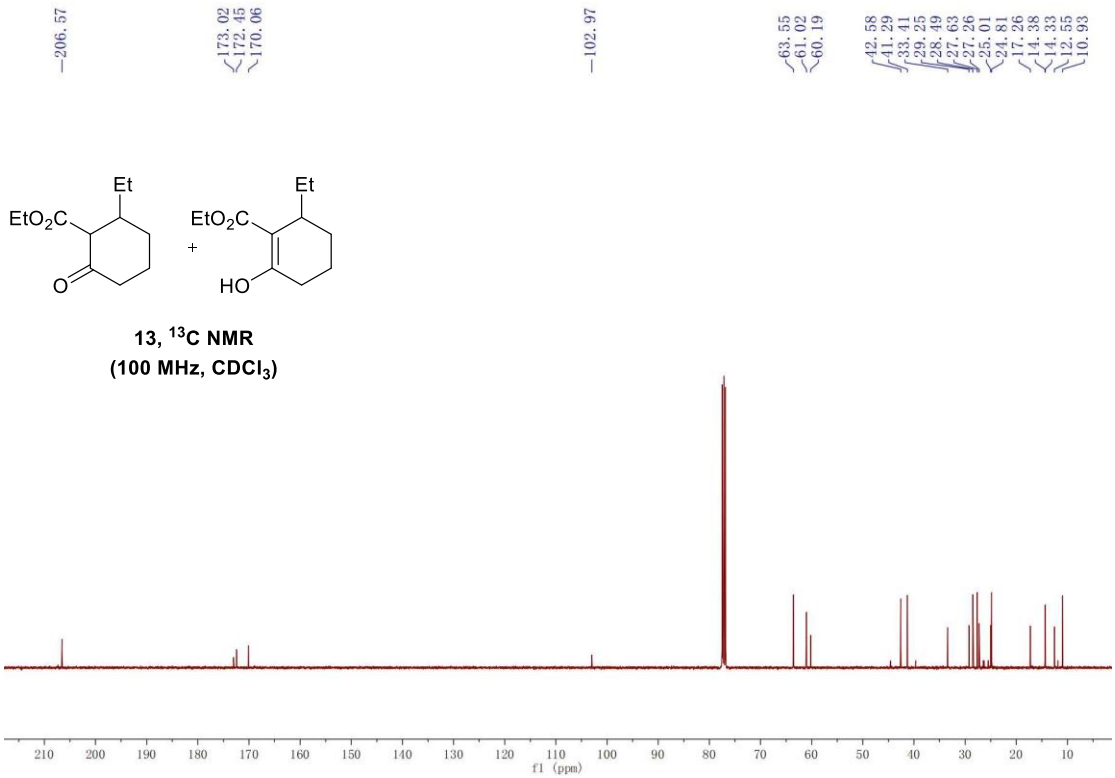
CCDC	2529297
Empirical formula	$C_{20}H_{22}N_2O_6S$
Formula weight	418.45
Temperature/K	292.0
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	11.1774(10)
b/Å	7.4574(7)
c/Å	23.2800(18)
α/°	90
β/°	92.084(3)
γ/°	90
Volume/Å^3	1939.2(3)
Z	4
ρ_{calc}g/cm^3	1.433
μ/mm^{-1}	0.208
F(000)	880.0
Crystal size/mm^3	0.5 × 0.29 × 0.03
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.964 to 49.976

Index ranges	$-13 \leq h \leq 13$, $-8 \leq k \leq 8$, $-27 \leq l \leq 27$
Reflections collected	15754
Independent reflections	3402 [R_{int} = 0.1297, R_{sigma} = 0.1094]
Data/restraints/parameters	3402/0/263
Goodness-of-fit on F^2	1.078
Final R indexes [I>=2σ (I)]	R1 = 0.0887, wR2 = 0.2139
Final R indexes [all data]	R1 = 0.1065, wR2 = 0.2301
Largest diff. peak/hole / e $Å^{-3}$	0.66/-0.41

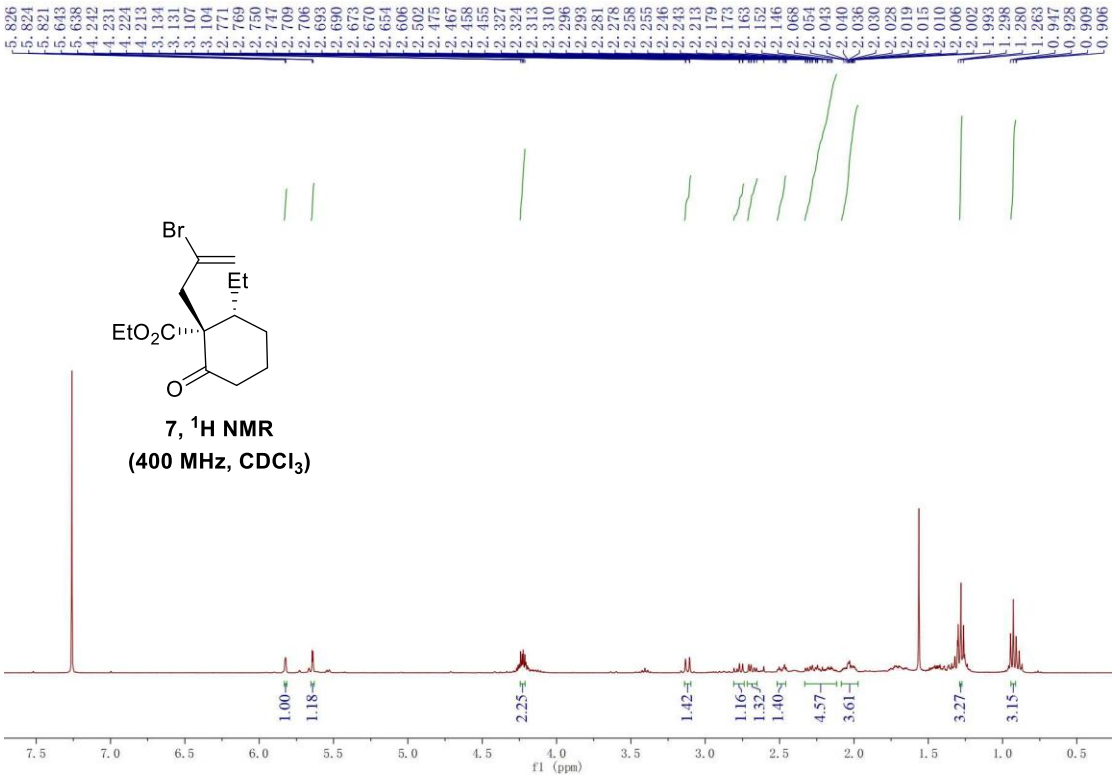
6. NMR Spectra

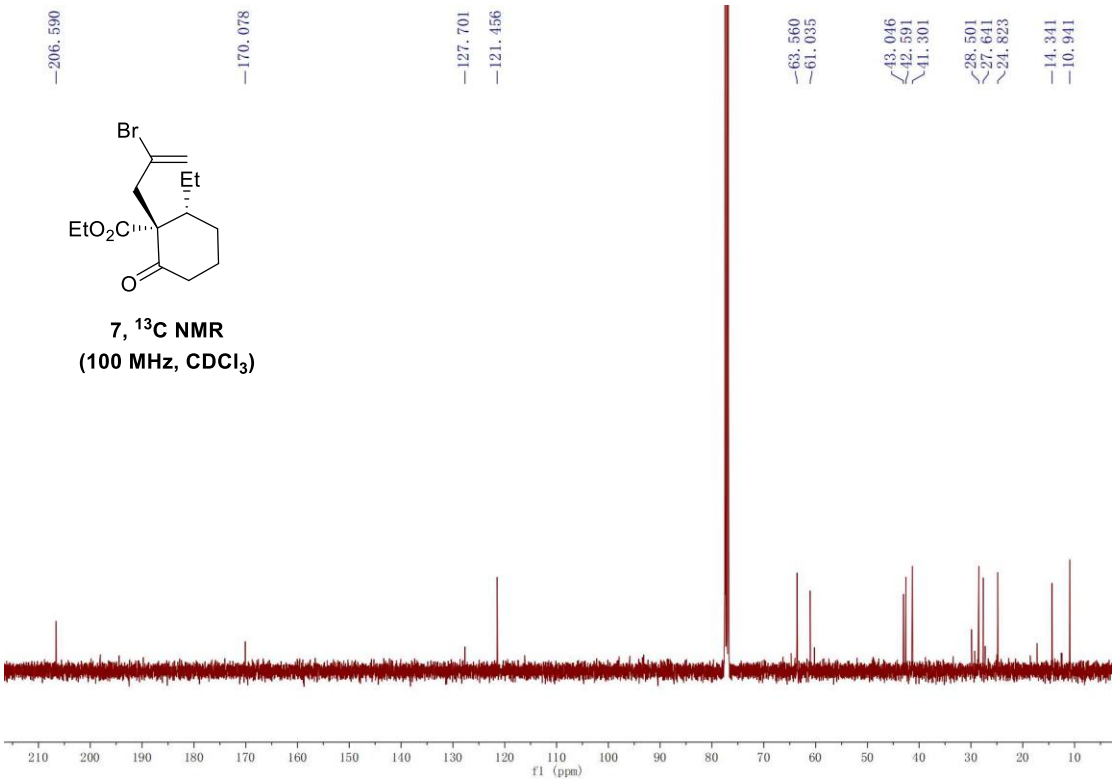


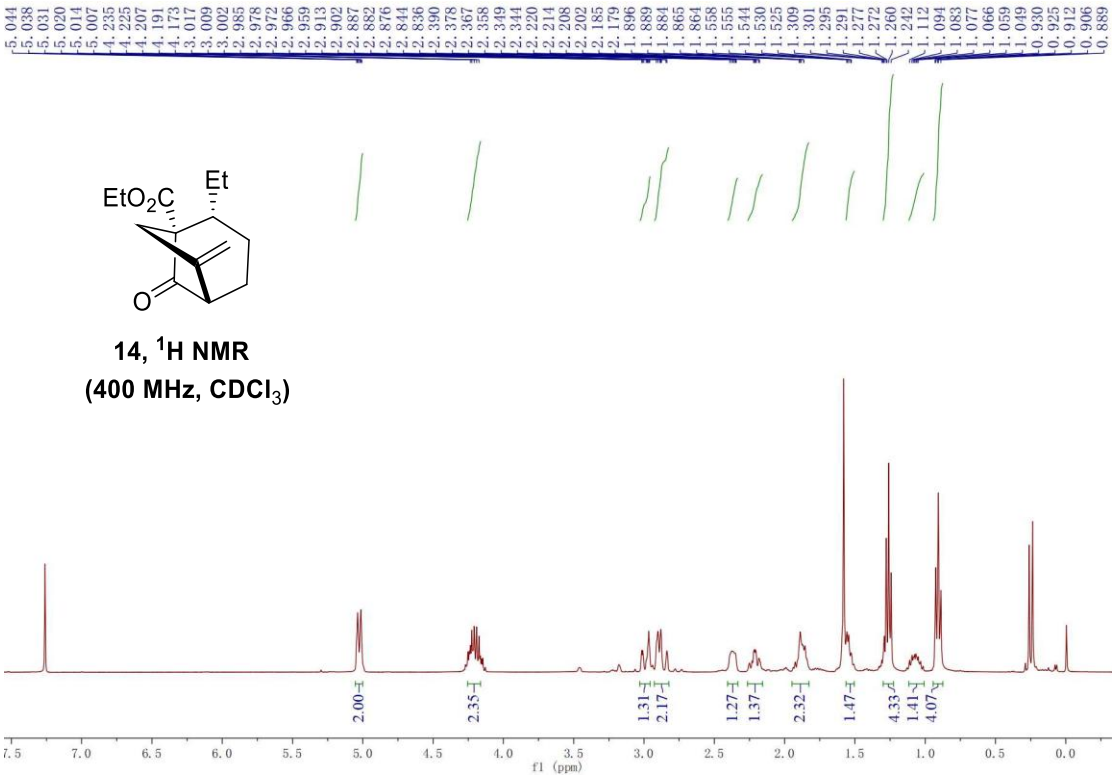
13, ^{1}H NMR
(400 MHz, $CDCl_3$)



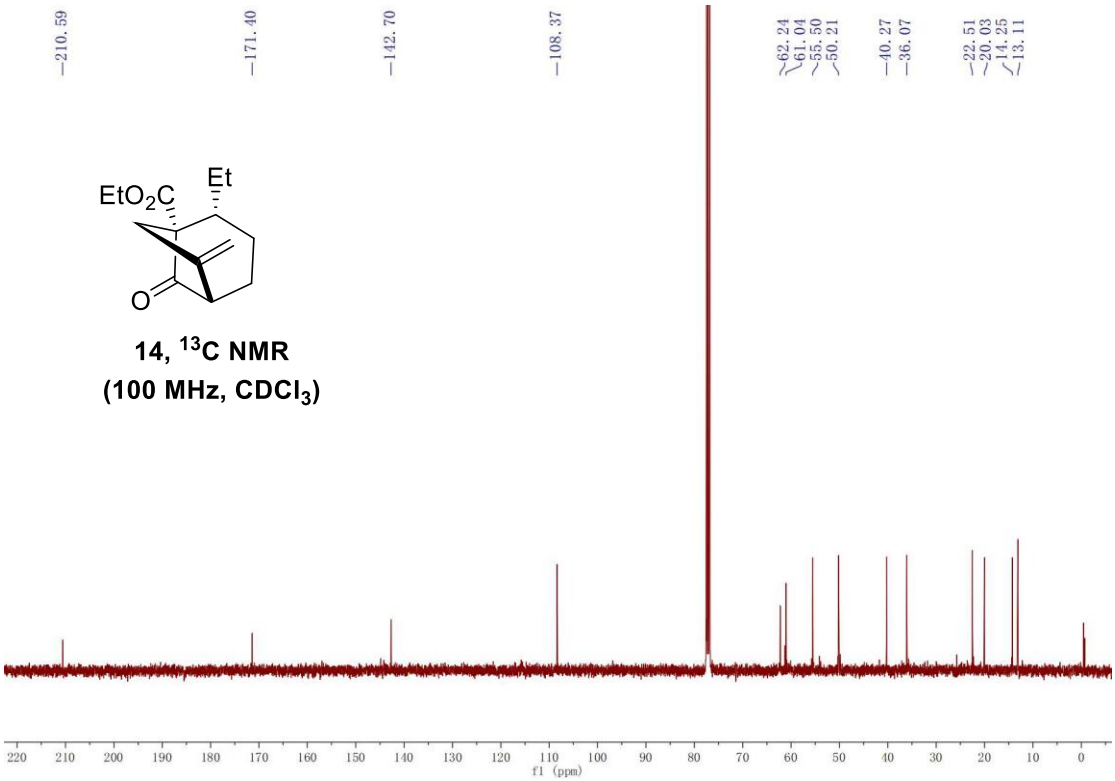
13, ^{13}C NMR
(100 MHz, $CDCl_3$)


Br
Et
EtO2C
O
7, 1H NMR
(400 MHz, CDCl3)
1.00
1.18
2.25
1.42
1.16
1.32
1.40
4.57
3.61
3.27
3.15
f1 (ppm)

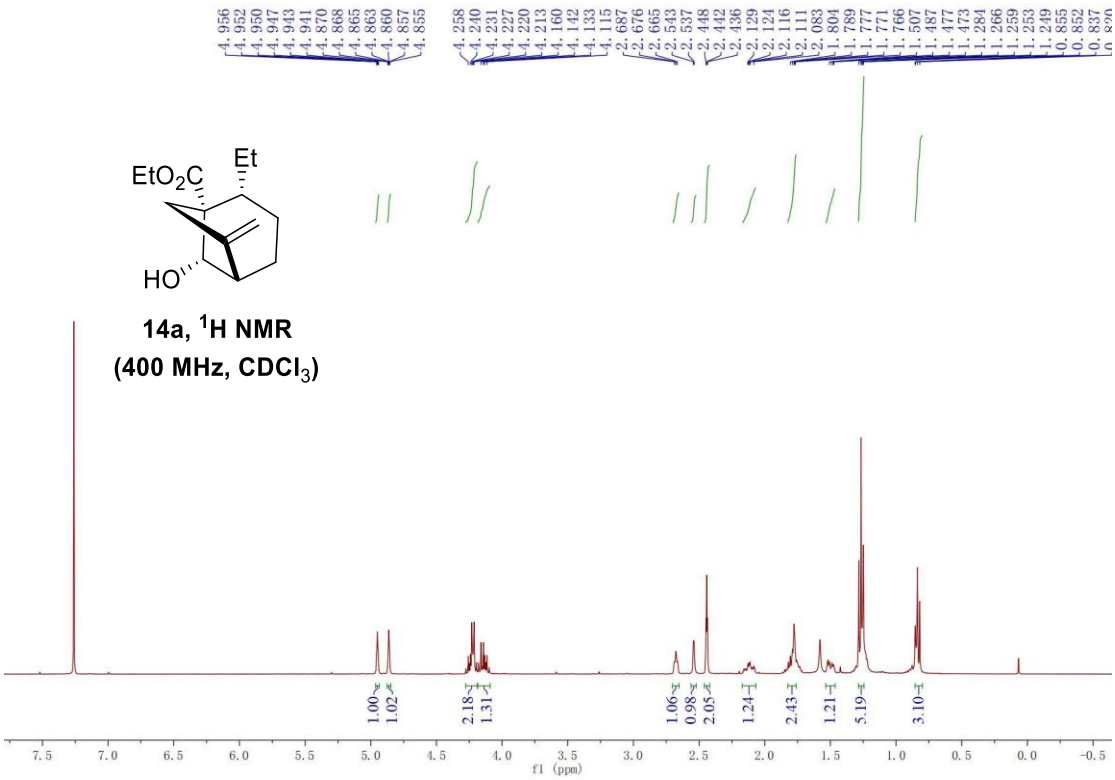

206.590
170.078
127.701
121.456
63.560
61.035
43.046
42.591
41.301
28.501
27.641
24.823
14.341
10.941
Br
Et
EtO2C
O
7, 13C NMR
(100 MHz, CDCl3)
f1 (ppm)



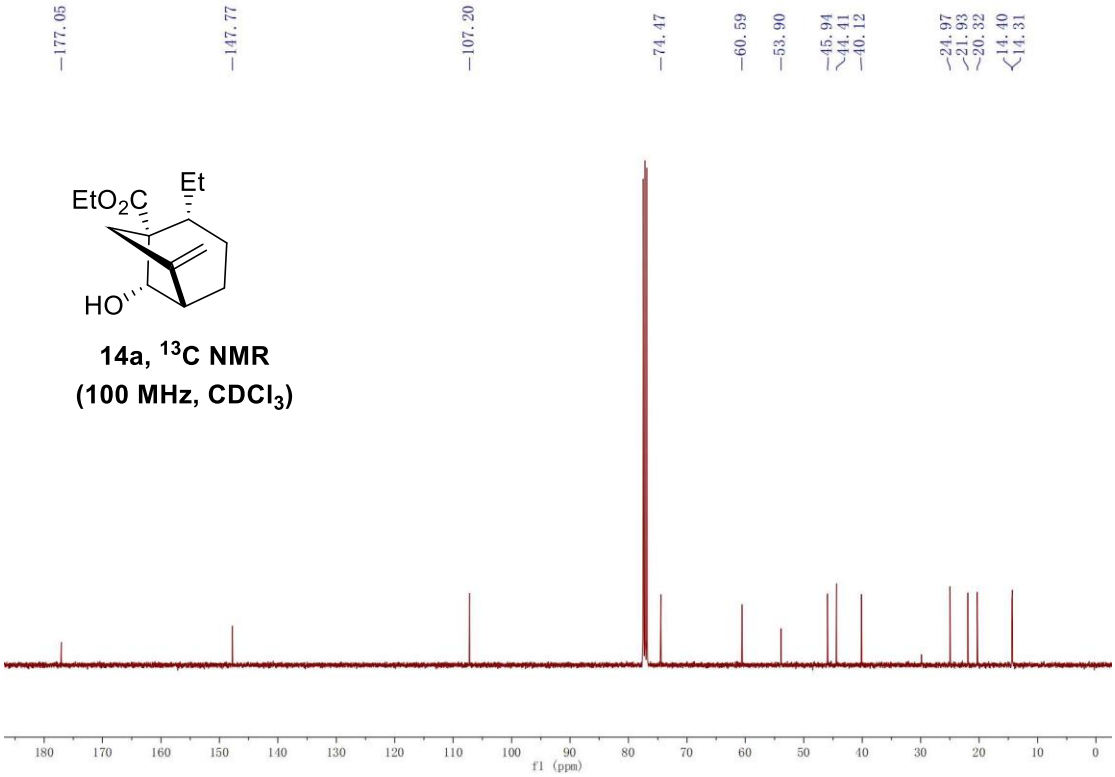
14, ^{1}H NMR
(400 MHz, $CDCl_3$)



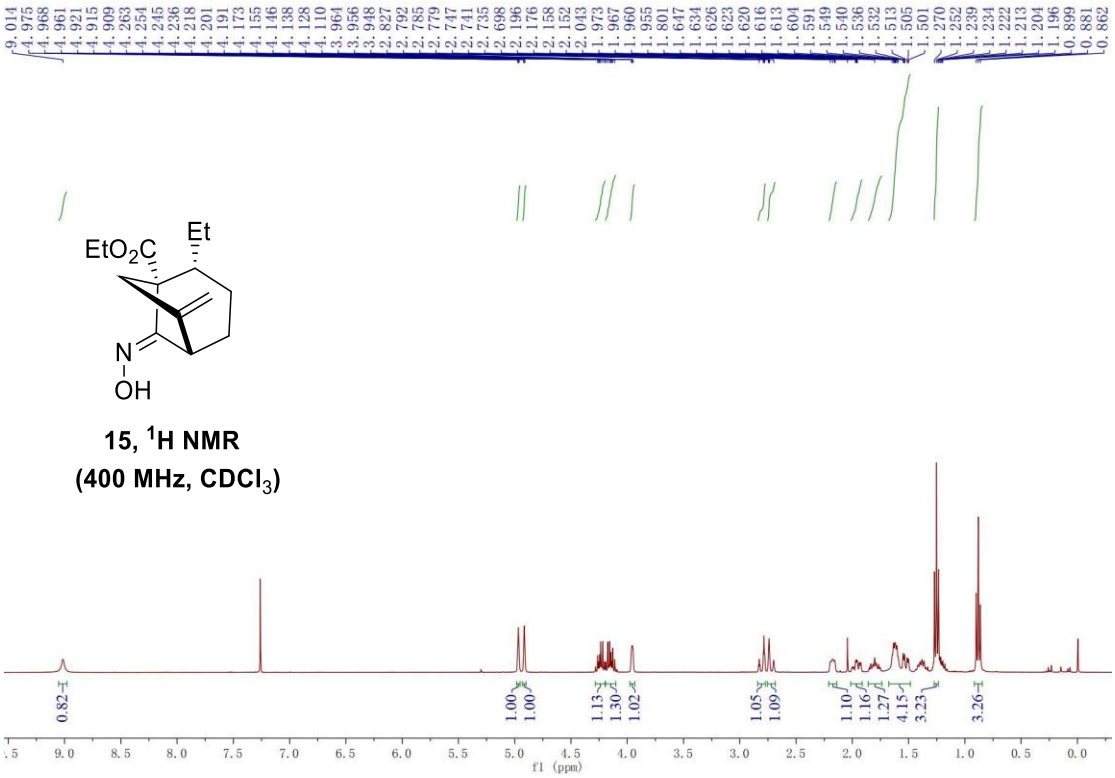
14, ^{13}C NMR
(100 MHz, $CDCl_3$)

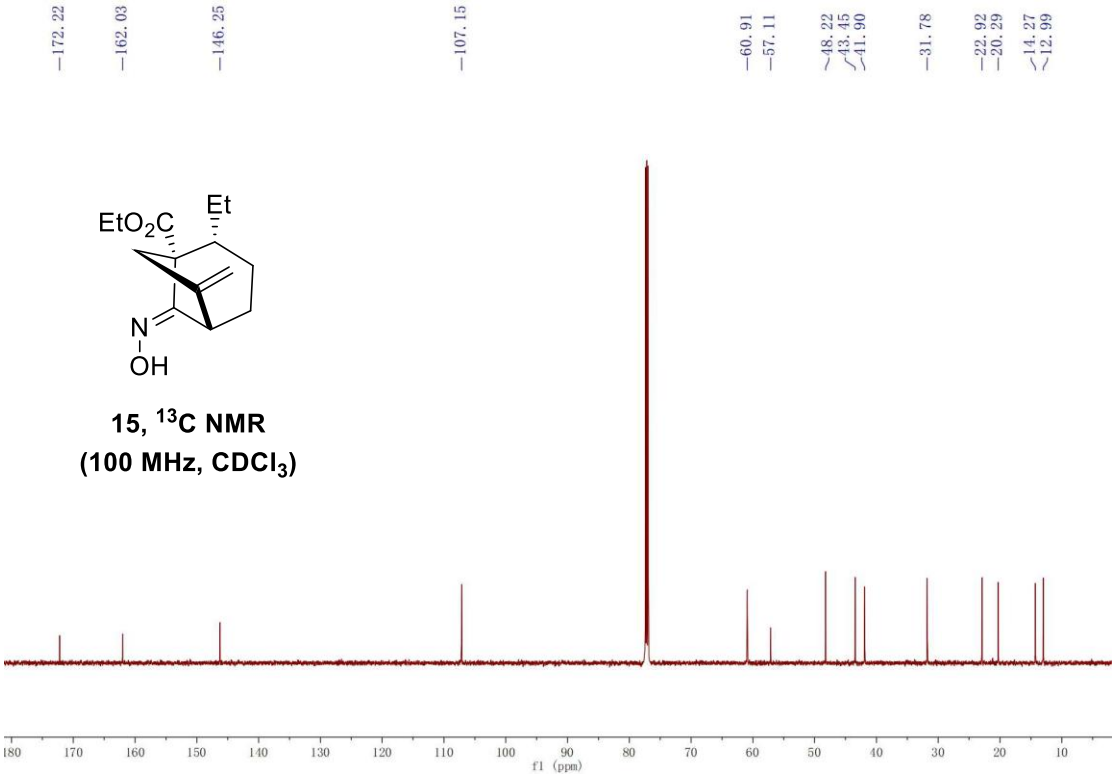


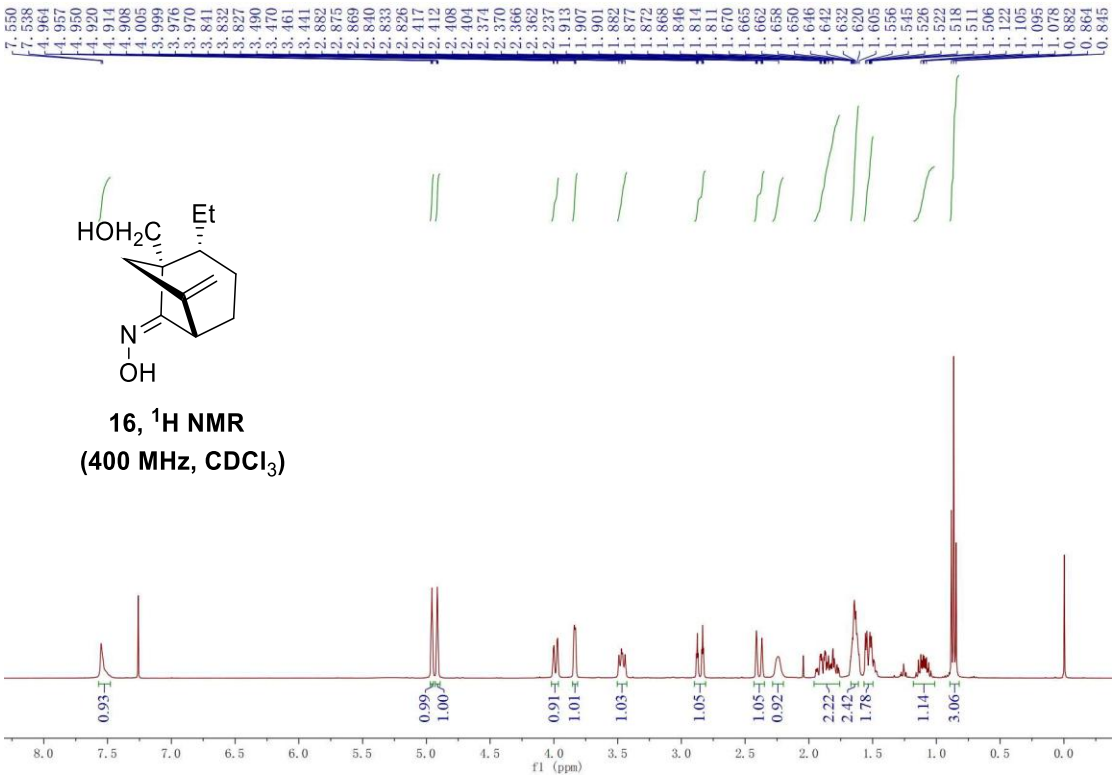
14a, ^{1}H NMR
(400 MHz, $CDCl_3$)



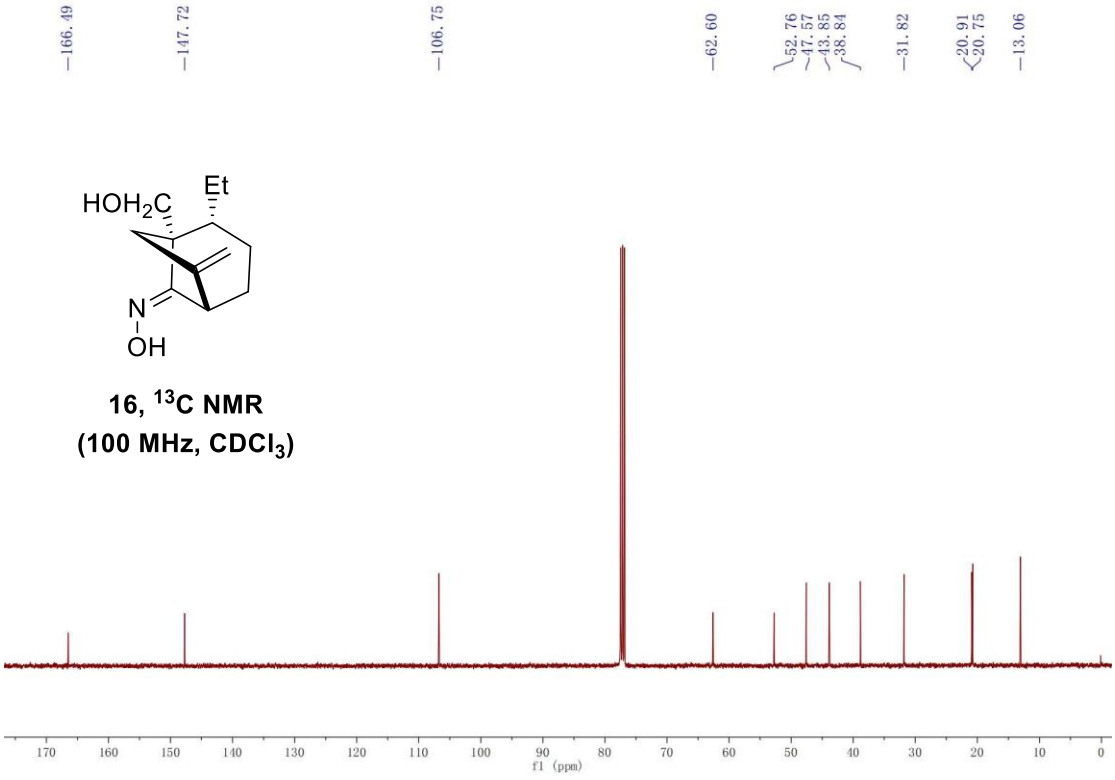
14a, ^{13}C NMR
(100 MHz, $CDCl_3$)


EtO2C
Et
N
OH
15, 1H NMR
(400 MHz, CDCl3)
f1 (ppm)

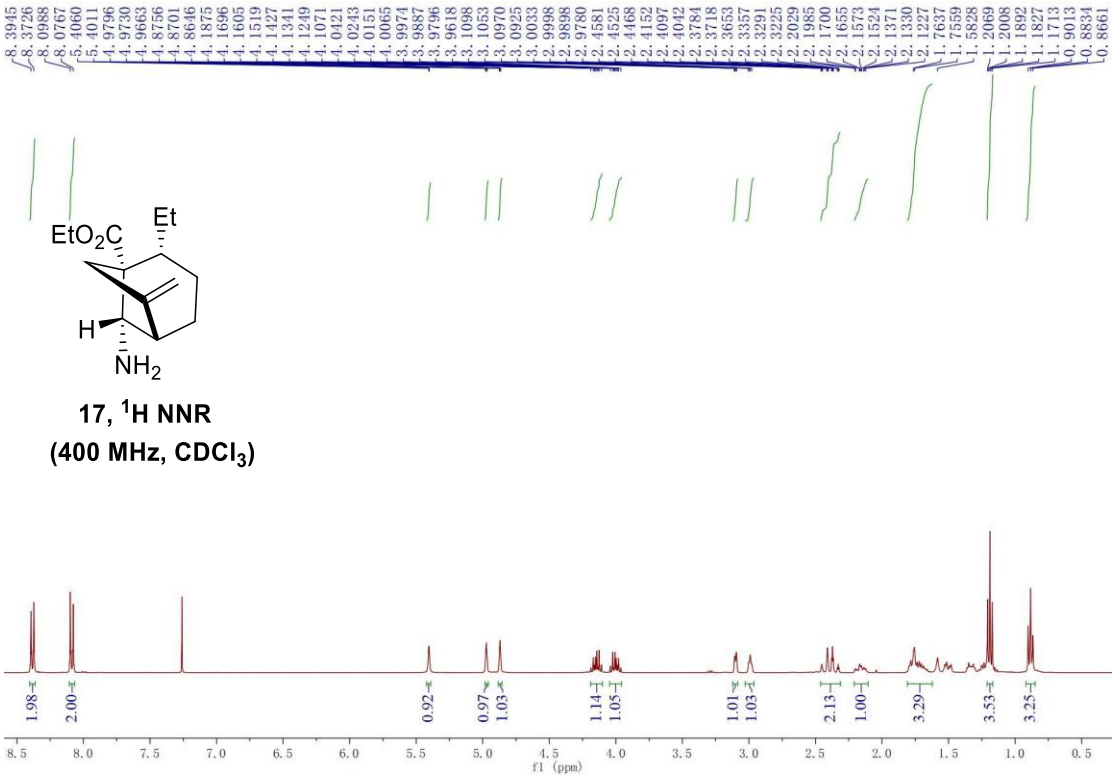

EtO2C
Et
N
OH
15, 13C NMR
(100 MHz, CDCl3)
f1 (ppm)



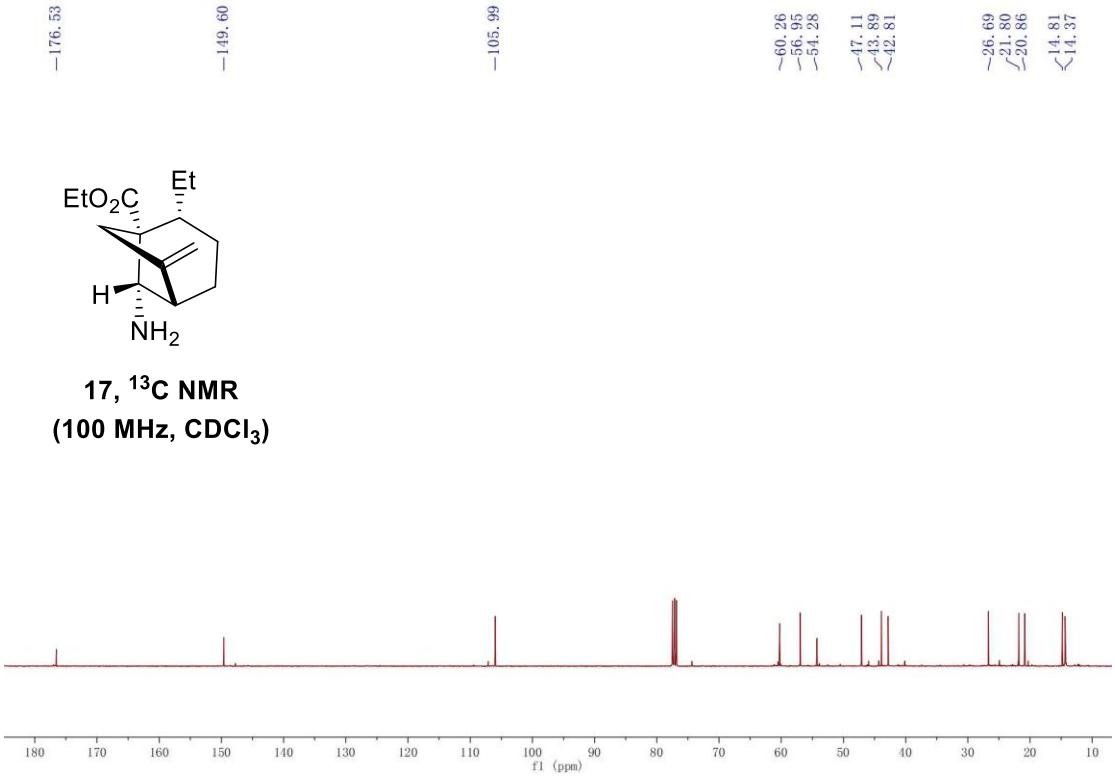
16, ^{1}H NMR
(400 MHz, $CDCl_3$)



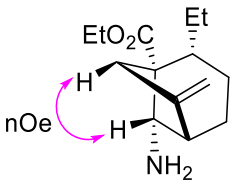
16, ^{13}C NMR
(100 MHz, $CDCl_3$)



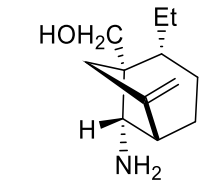
17, ^{1}H NNR
(400 MHz, $CDCl_3$)



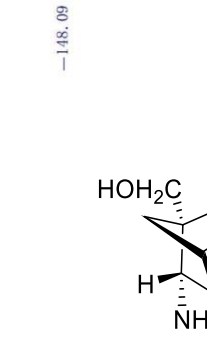
17, ^{13}C NMR
(100 MHz, $CDCl_3$)



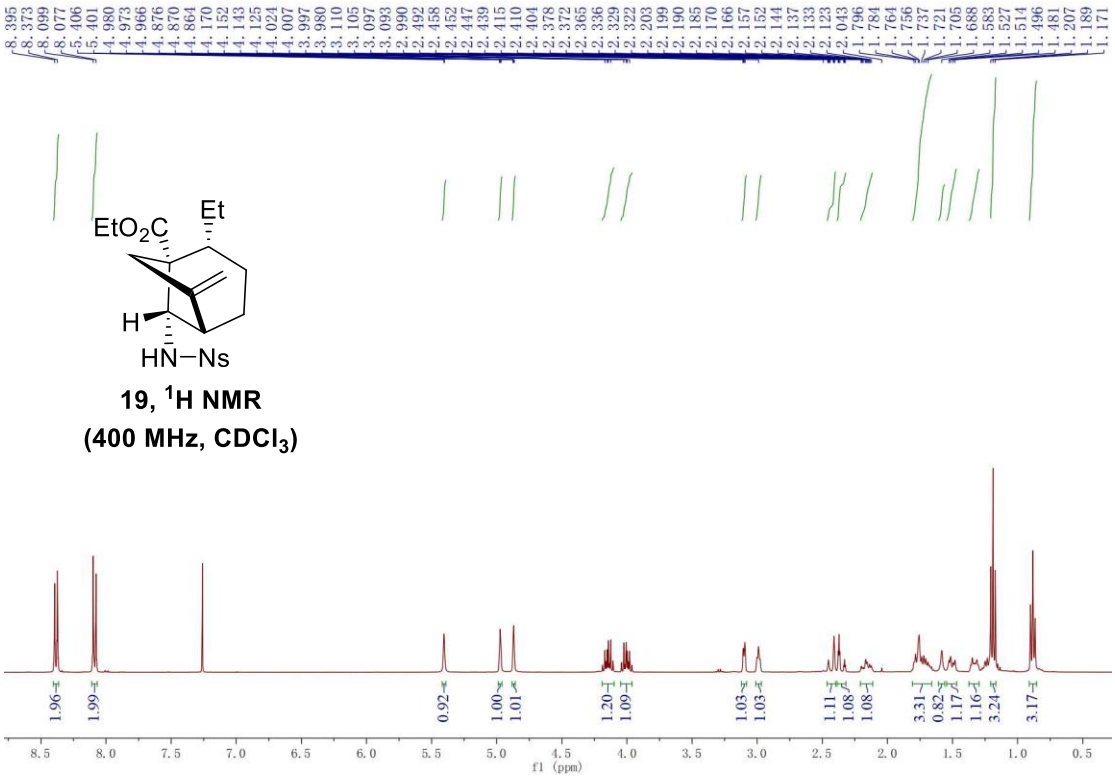
17, NOEDS
(400 MHz, $CDCl_3$)



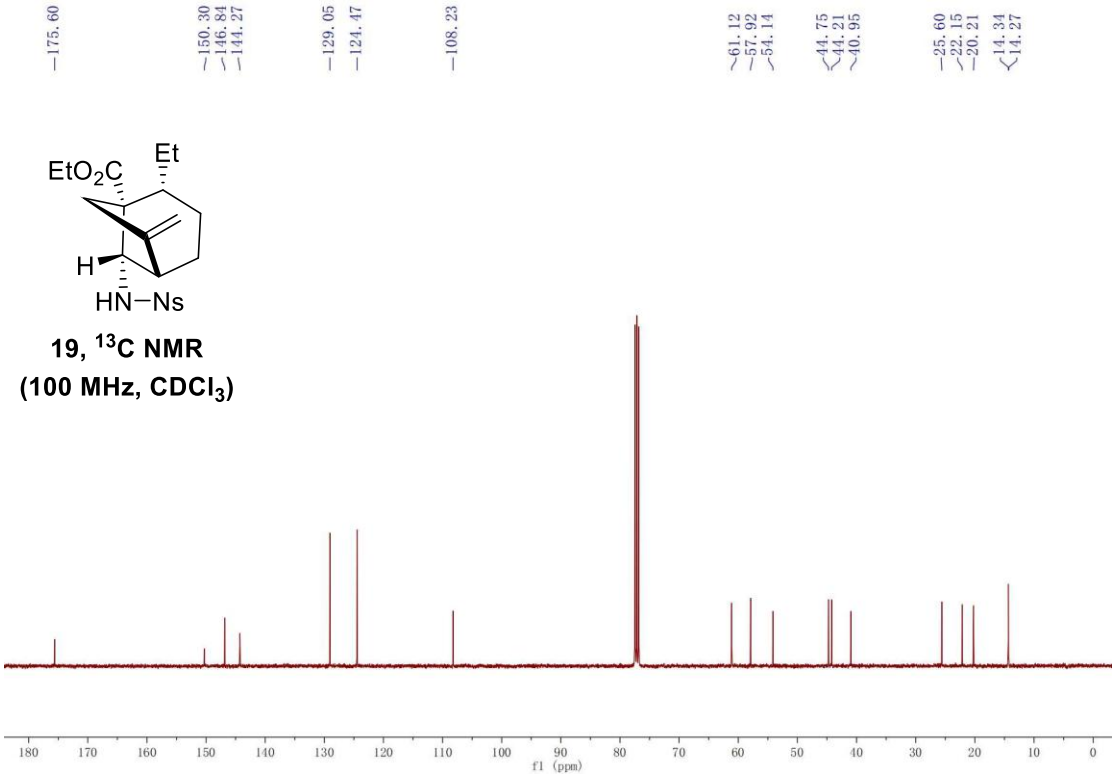
18, ^{1}H NMR
(400 MHz, $CDCl_3$)



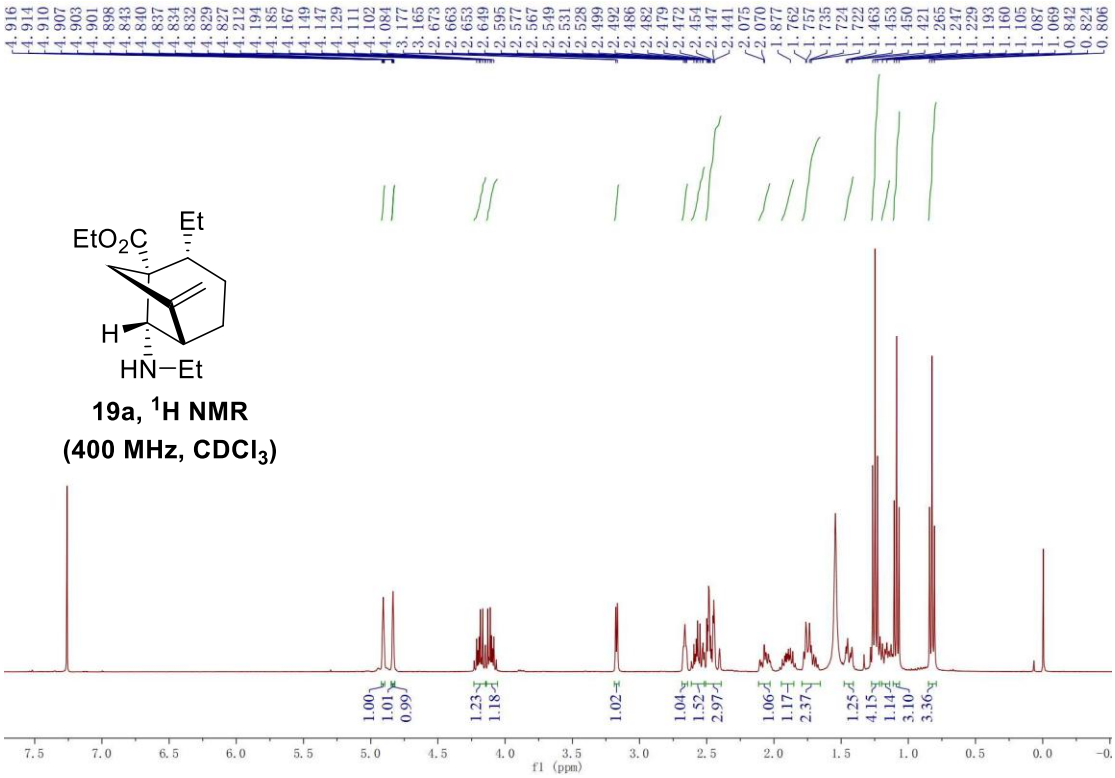
18, ^{13}C NMR
(100 MHz, $CDCl_3$)



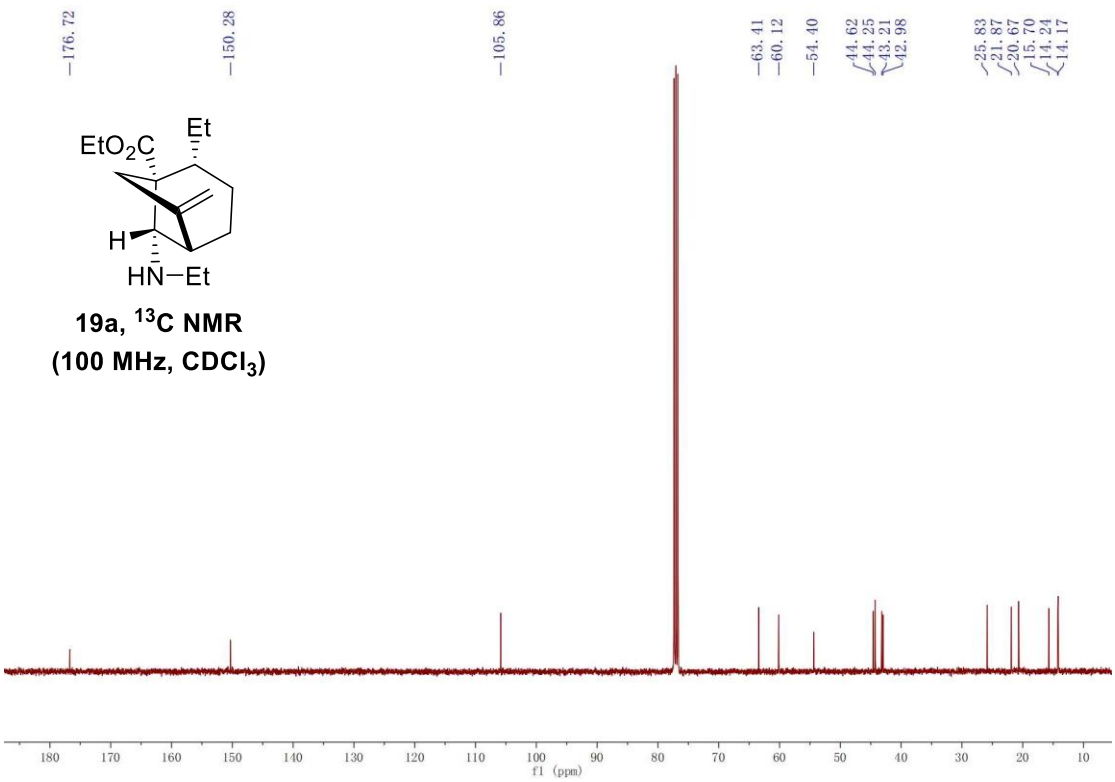
19, ^{1}H NMR
(400 MHz, $CDCl_3$)



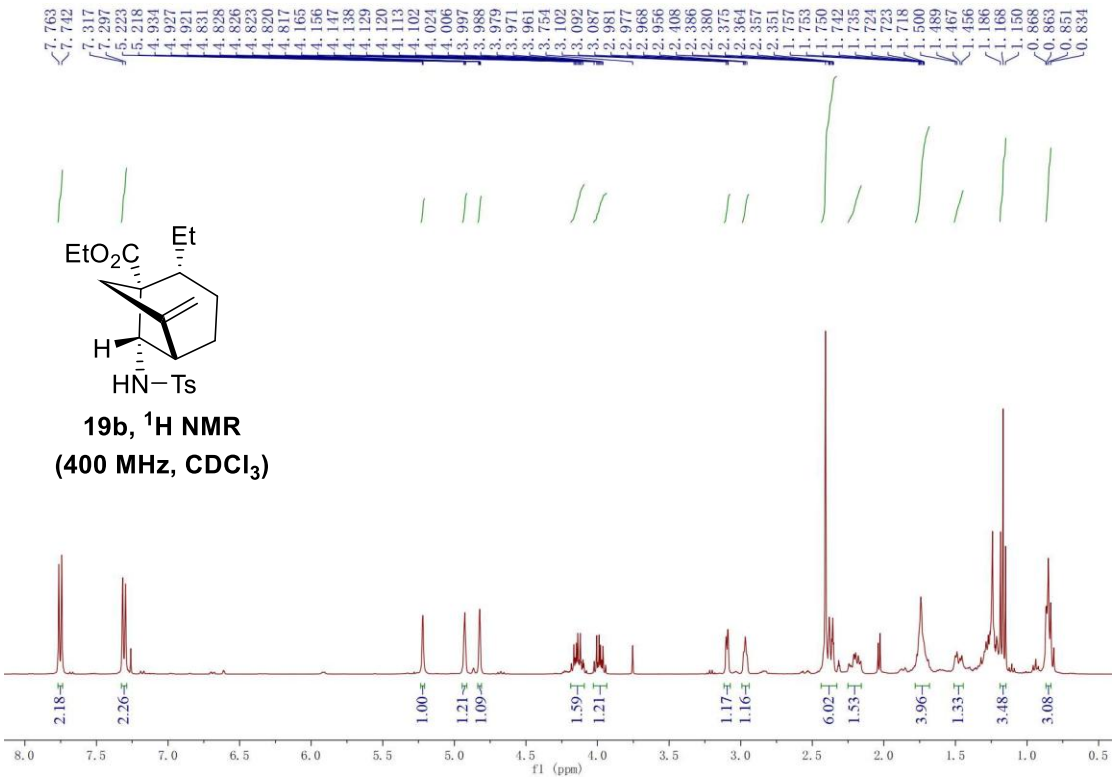
19, ^{13}C NMR
(100 MHz, $CDCl_3$)



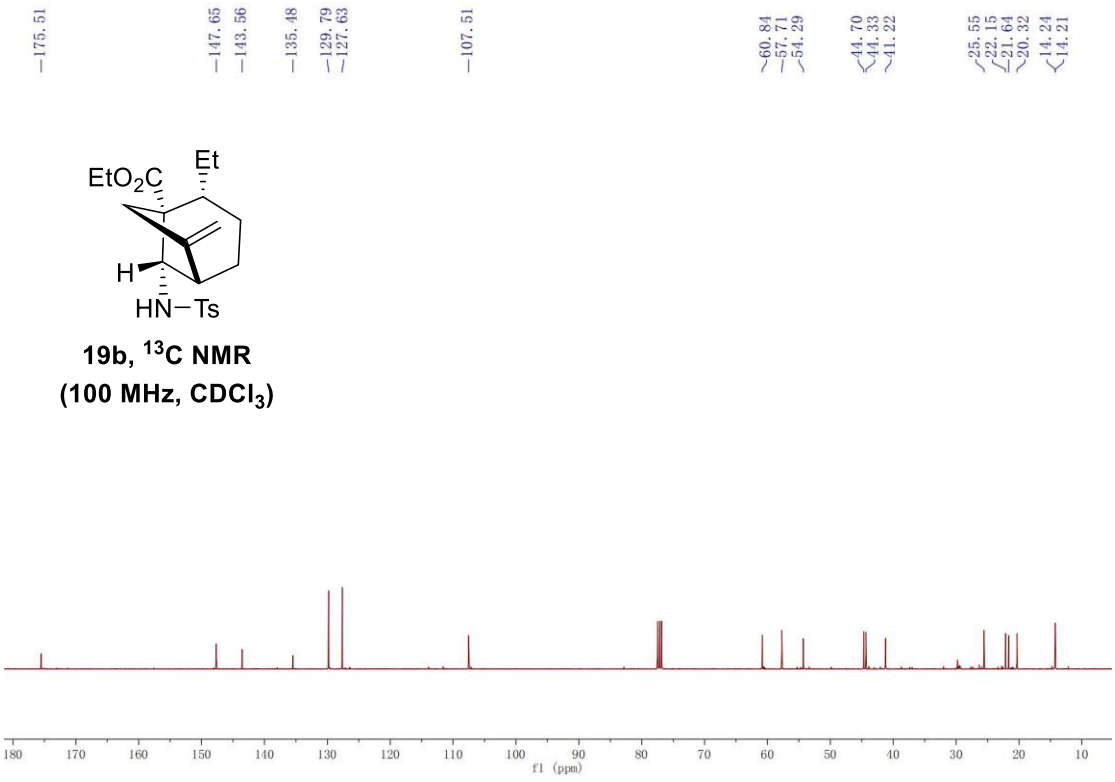
19a, ^{1}H NMR
(400 MHz, $CDCl_3$)



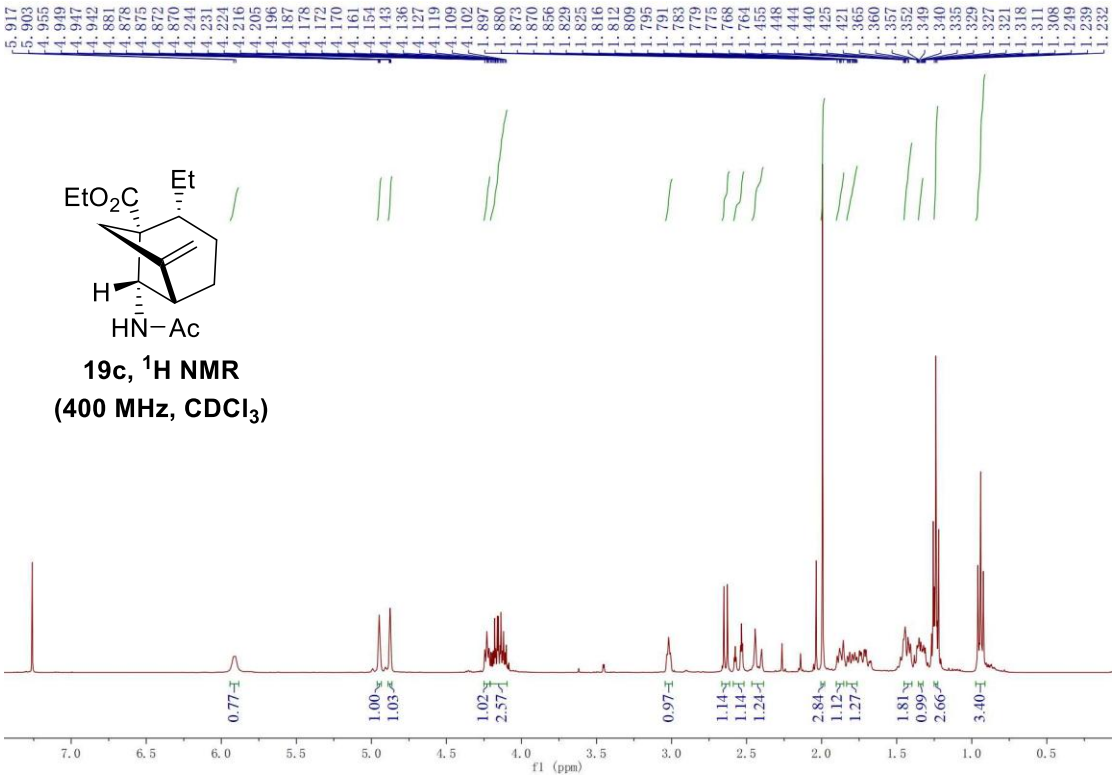
19a, ^{13}C NMR
(100 MHz, $CDCl_3$)



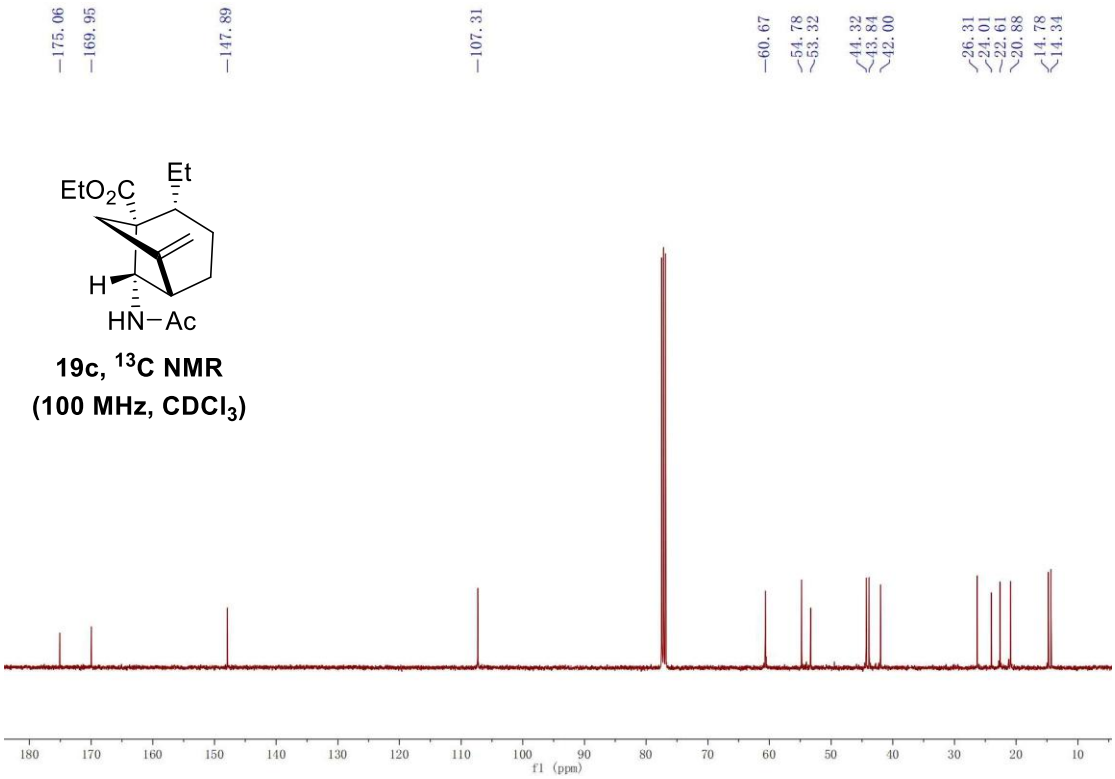
19b, ^{1}H NMR
(400 MHz, $CDCl_3$)



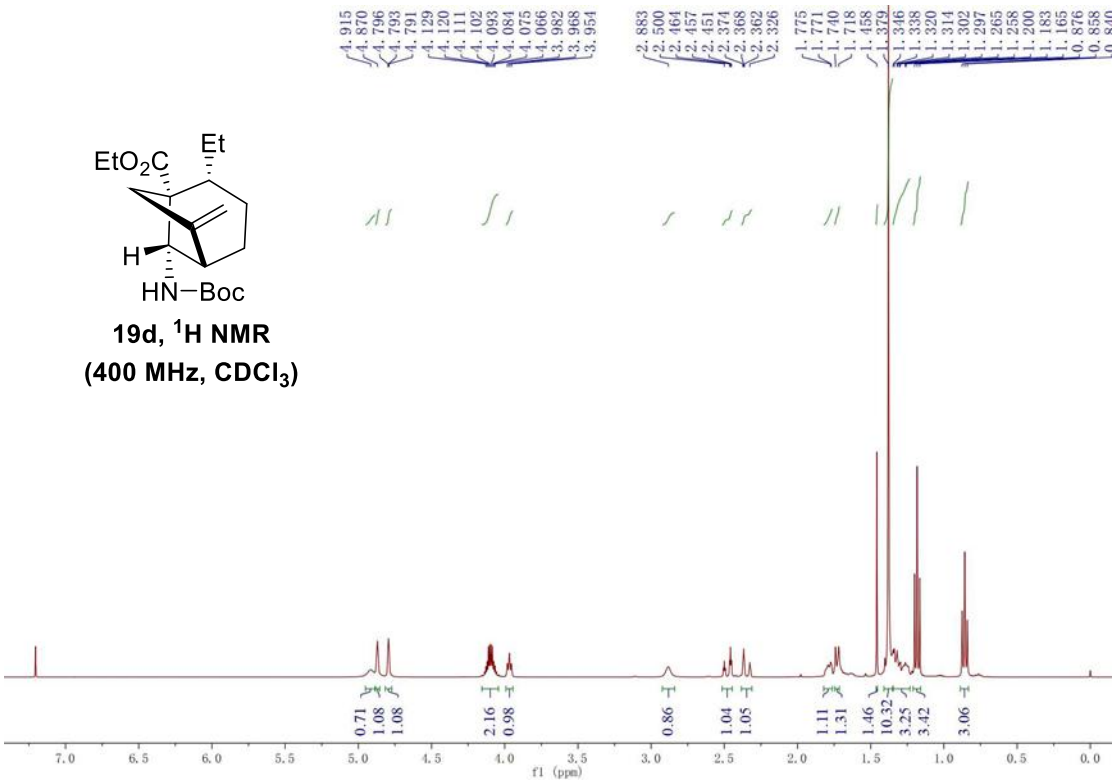
19b, ^{13}C NMR
(100 MHz, $CDCl_3$)



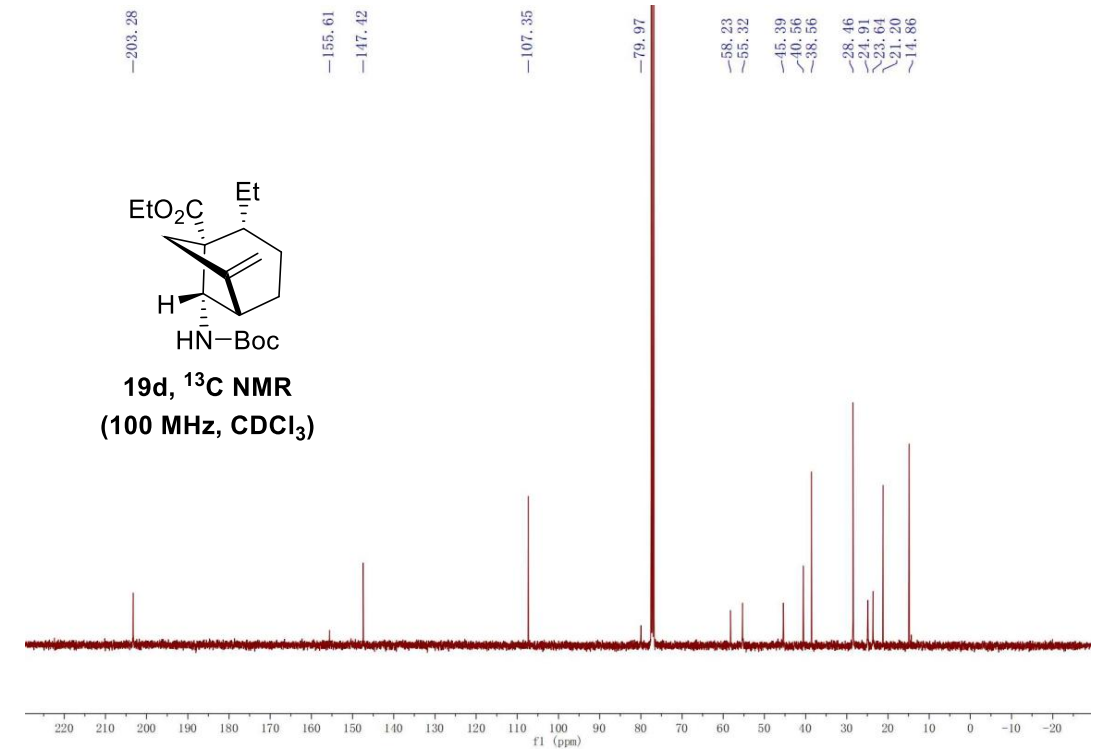
19c, ^{1}H NMR
(400 MHz, $CDCl_3$)



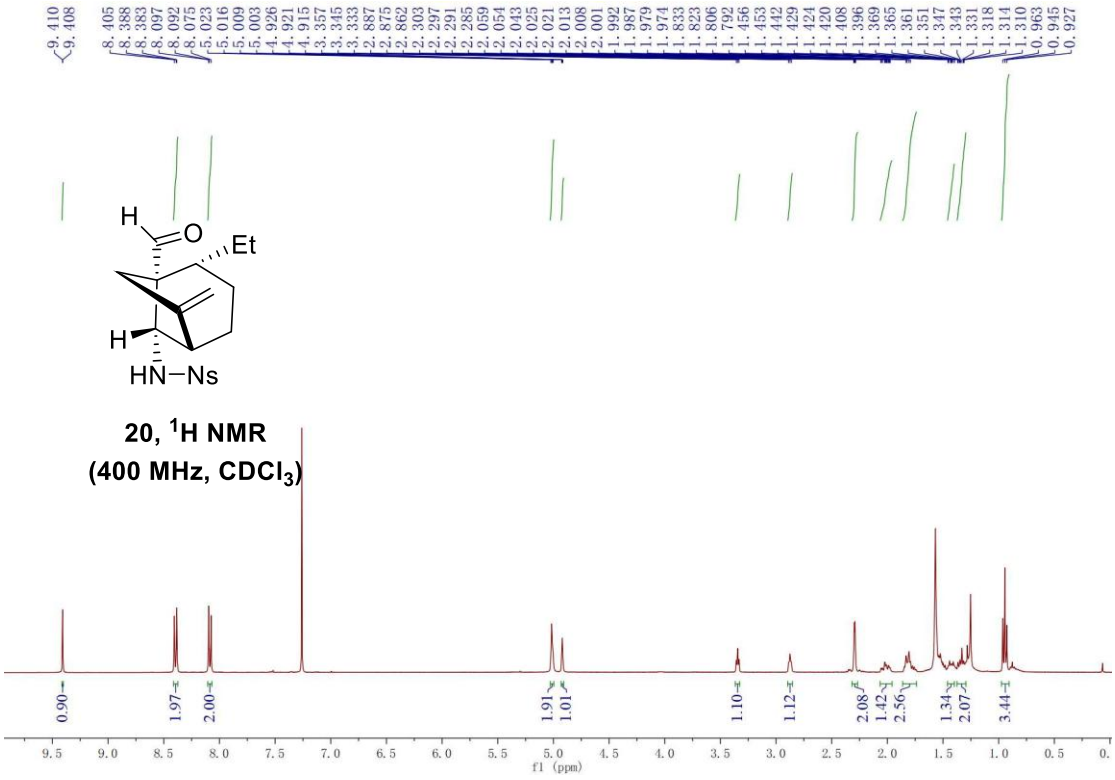
19c, ^{13}C NMR
(100 MHz, $CDCl_3$)



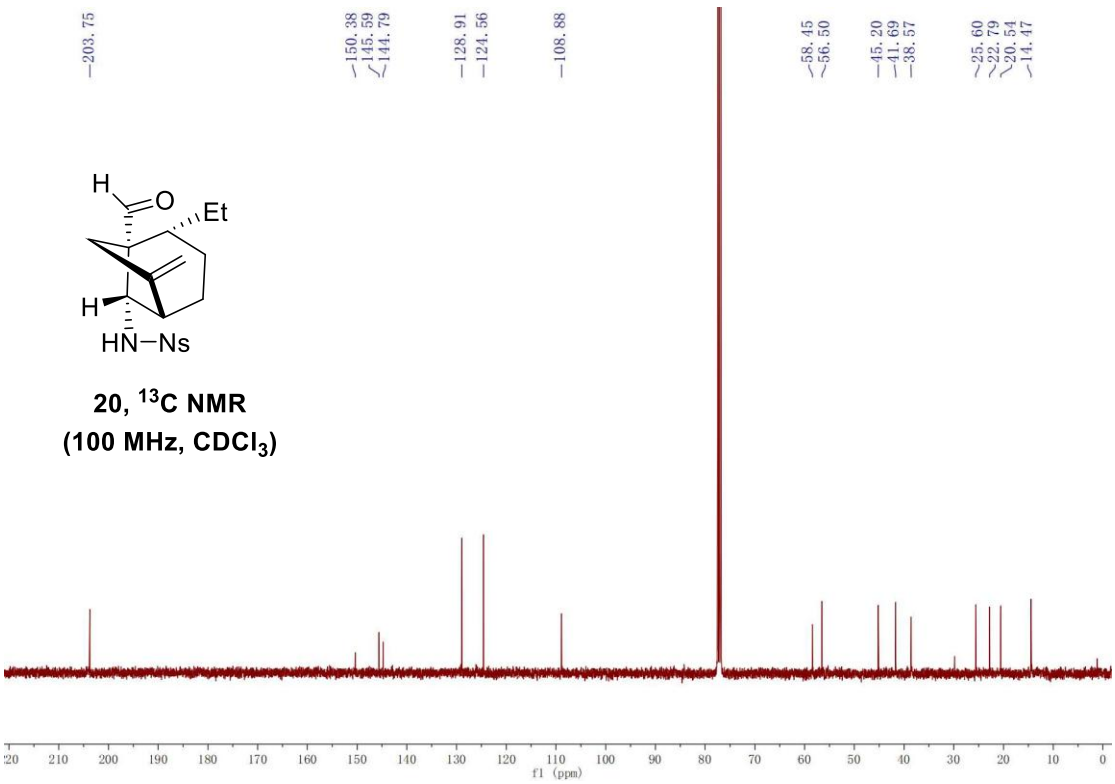
19d, ^{1}H NMR
(400 MHz, $CDCl_3$)



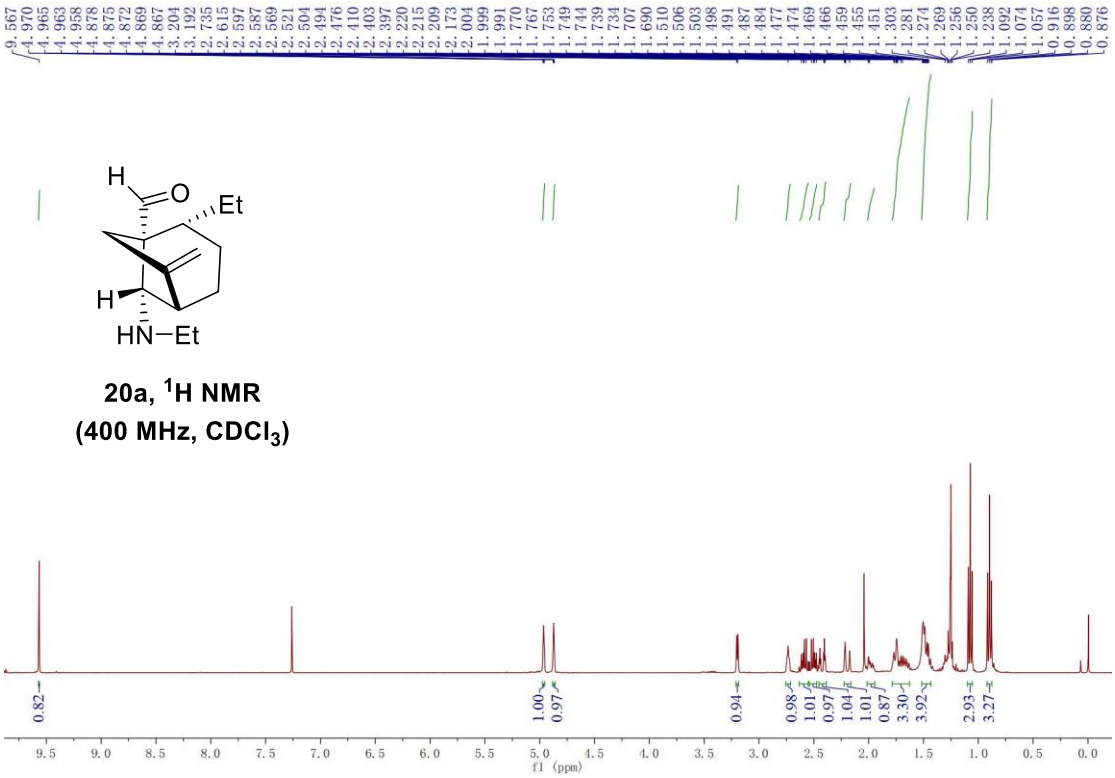
19d, ^{13}C NMR
(100 MHz, $CDCl_3$)



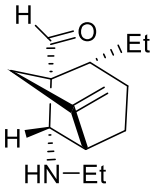
20, ^{1}H NMR
(400 MHz, $CDCl_3$)



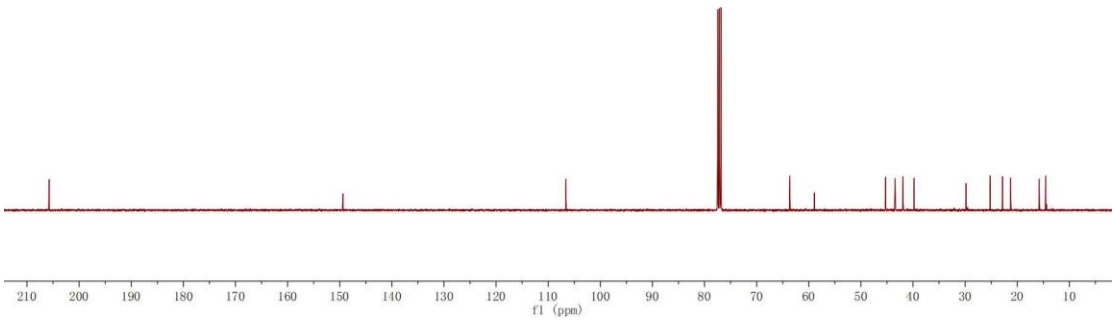
20, ^{13}C NMR
(100 MHz, $CDCl_3$)

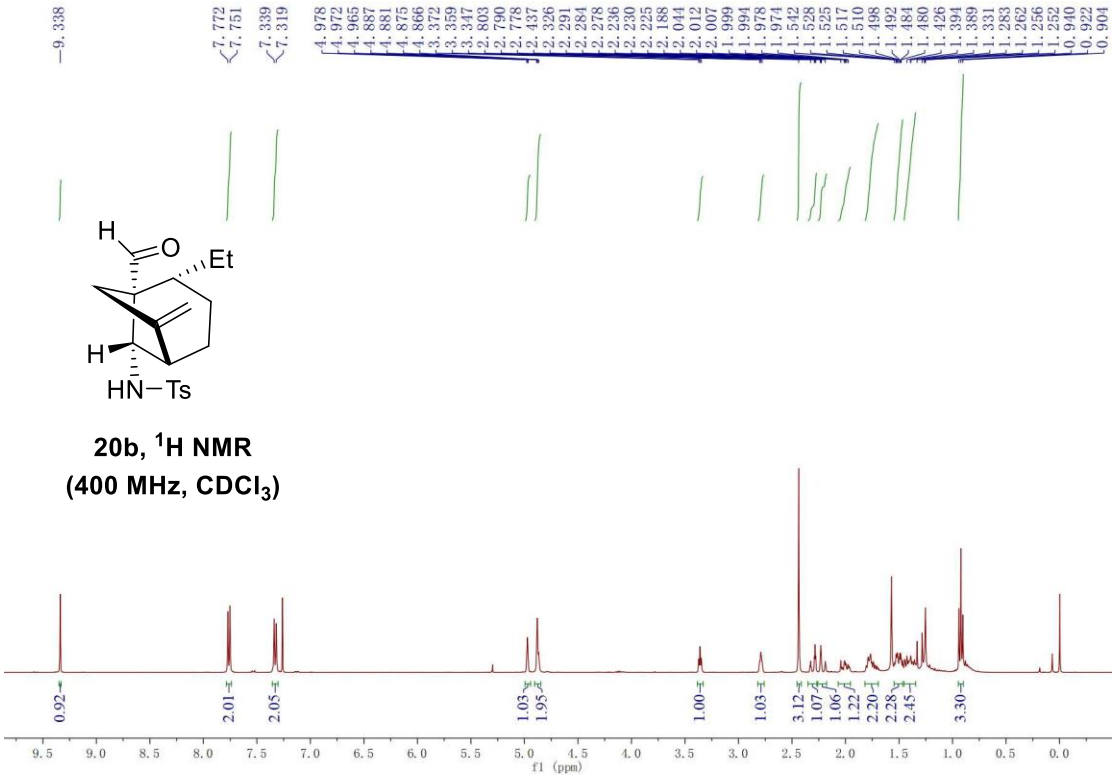


20a, ^{1}H NMR
(400 MHz, $CDCl_3$)

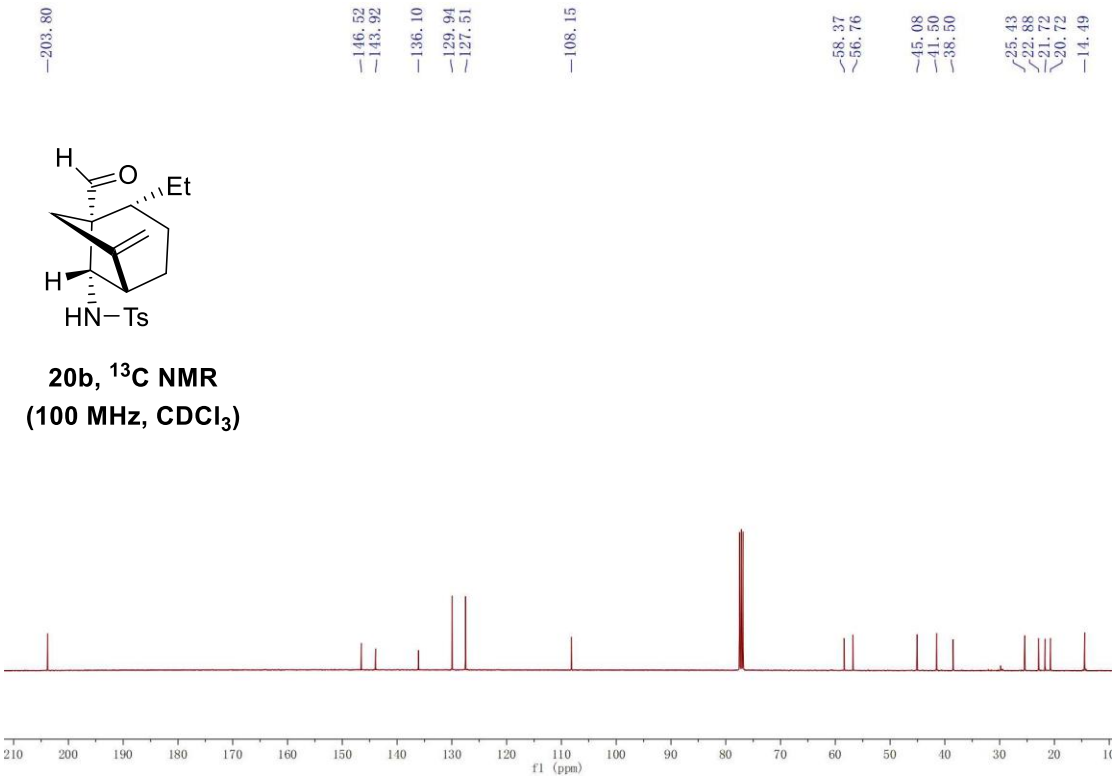


20a, ^{13}C NMR
(100 MHz, $CDCl_3$)

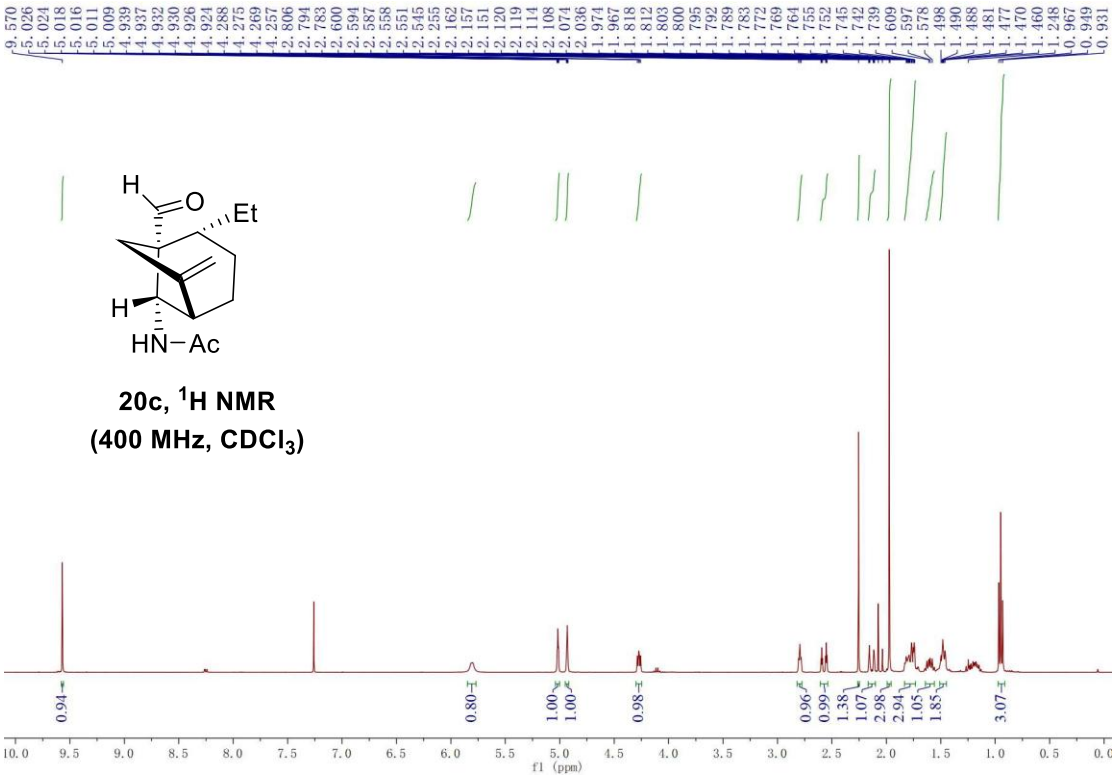




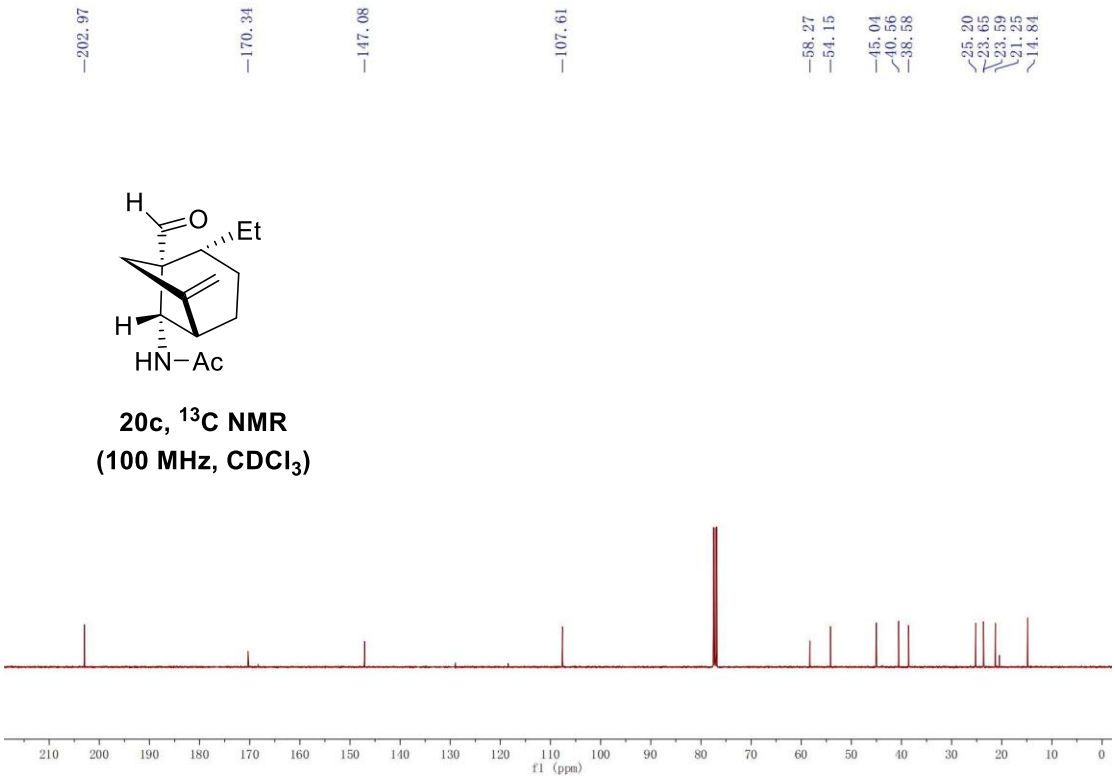
20b, ^{1}H NMR
(400 MHz, $CDCl_3$)



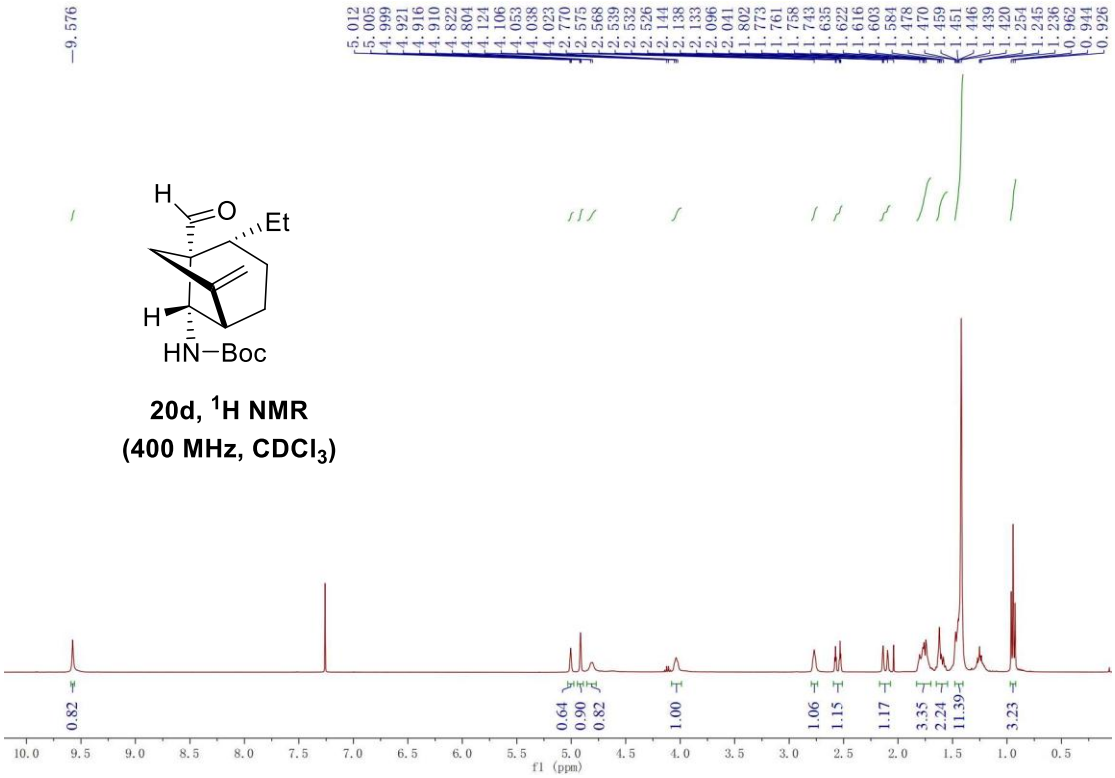
20b, ^{13}C NMR
(100 MHz, $CDCl_3$)



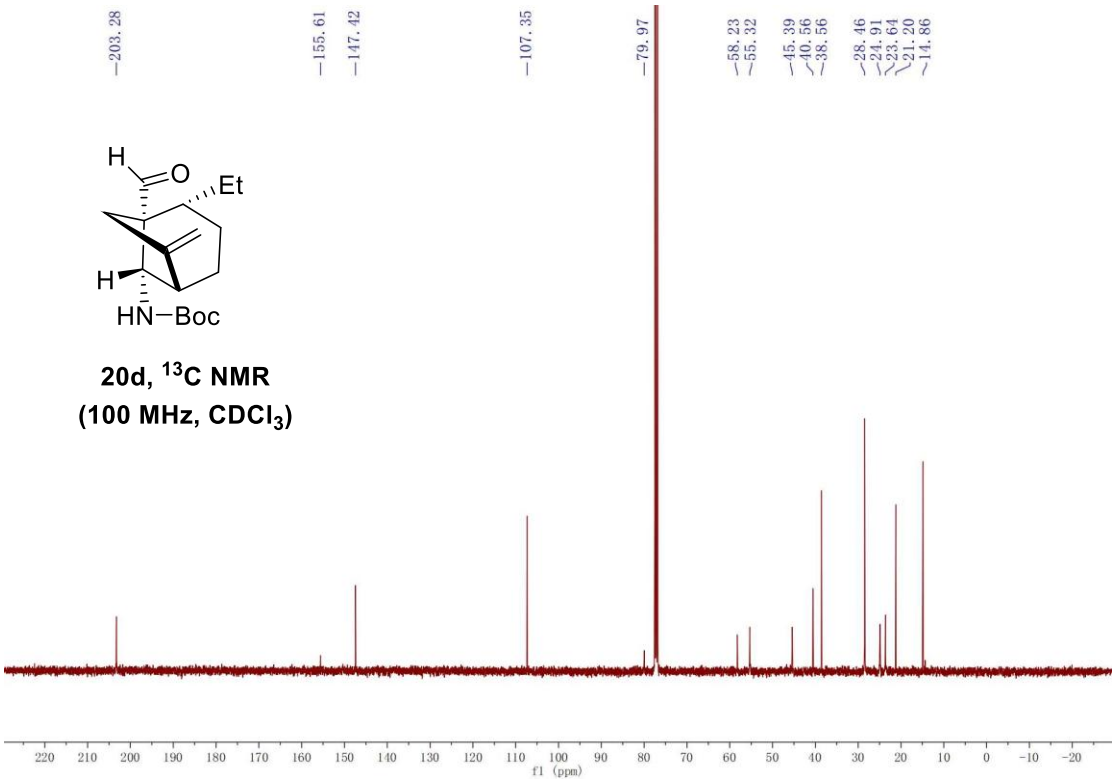
20c, ^{1}H NMR
(400 MHz, $CDCl_3$)



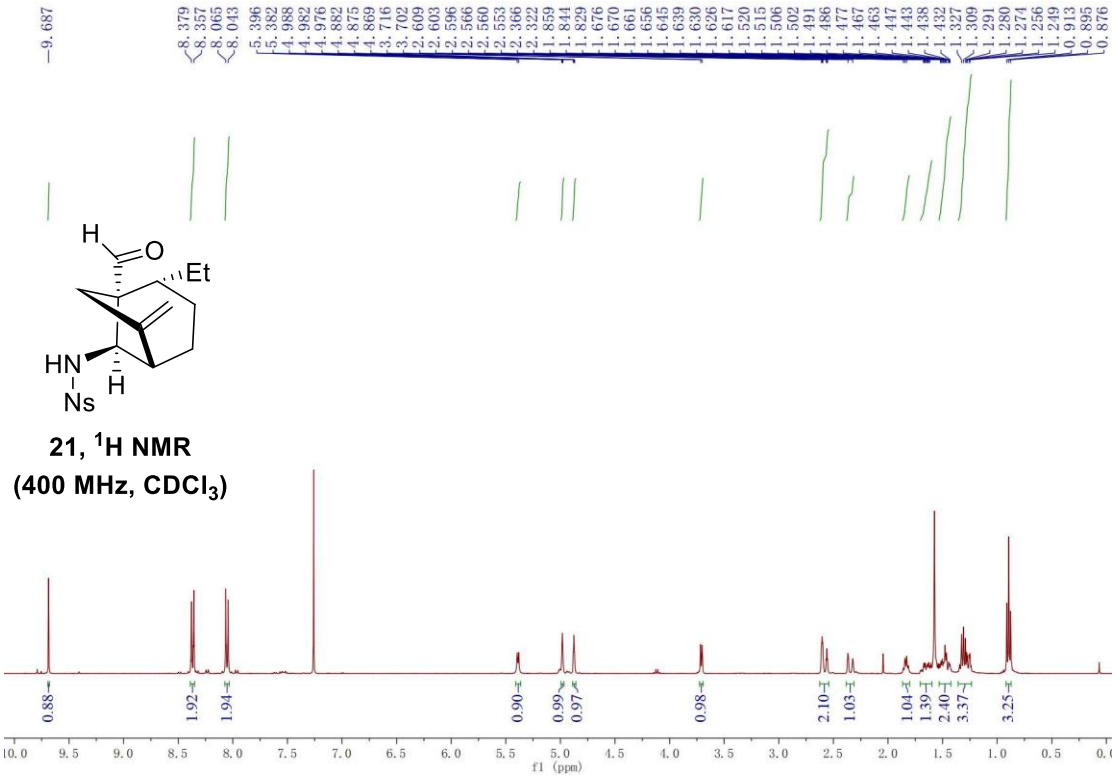
20c, ^{13}C NMR
(100 MHz, $CDCl_3$)



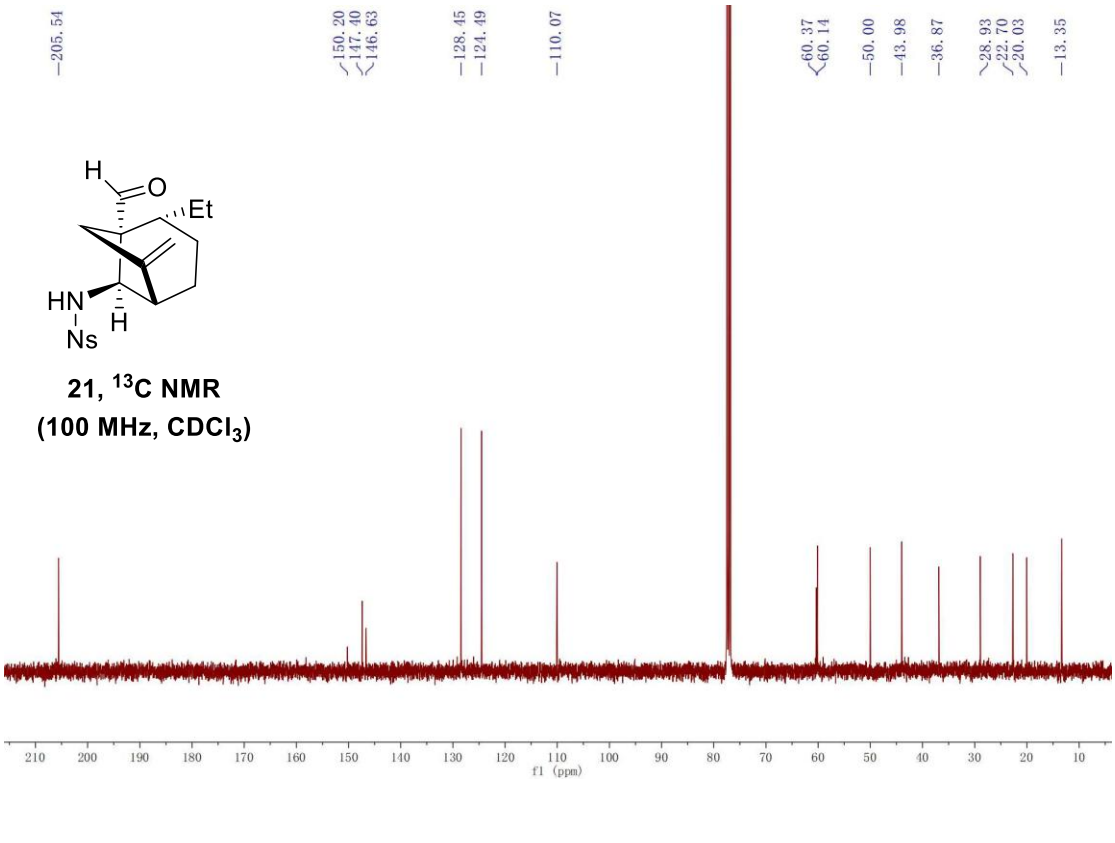
20d, ^{1}H NMR
(400 MHz, $CDCl_3$)



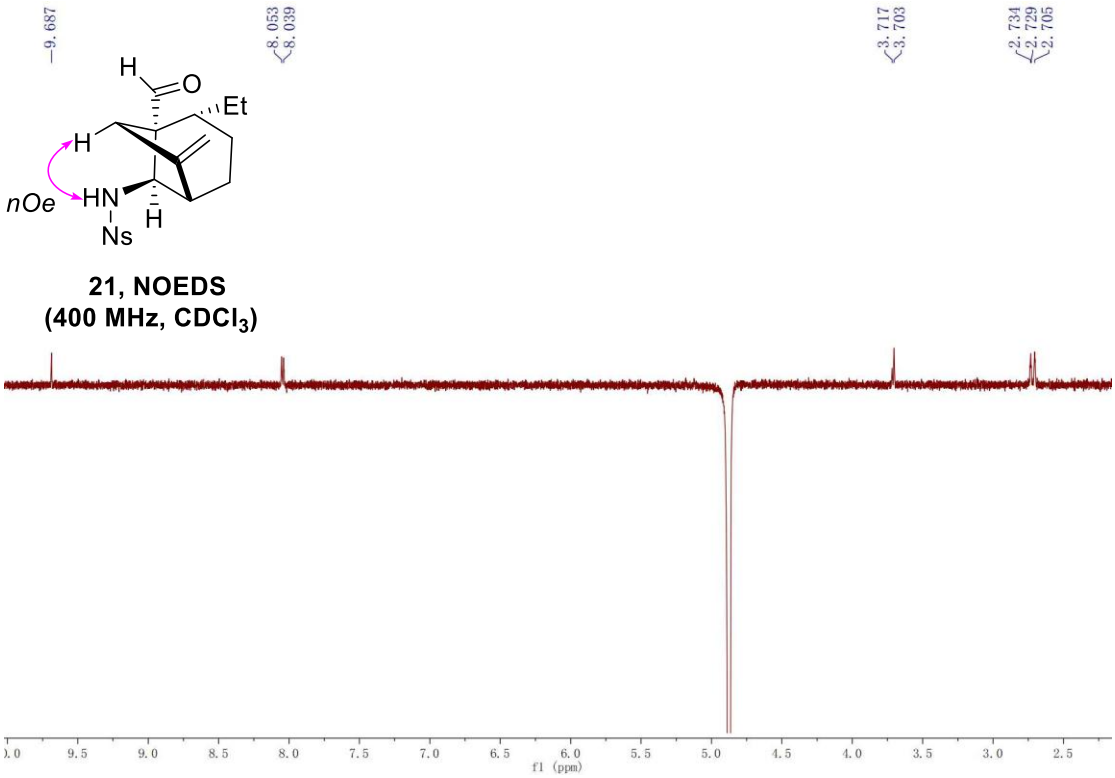
20d, ^{13}C NMR
(100 MHz, $CDCl_3$)



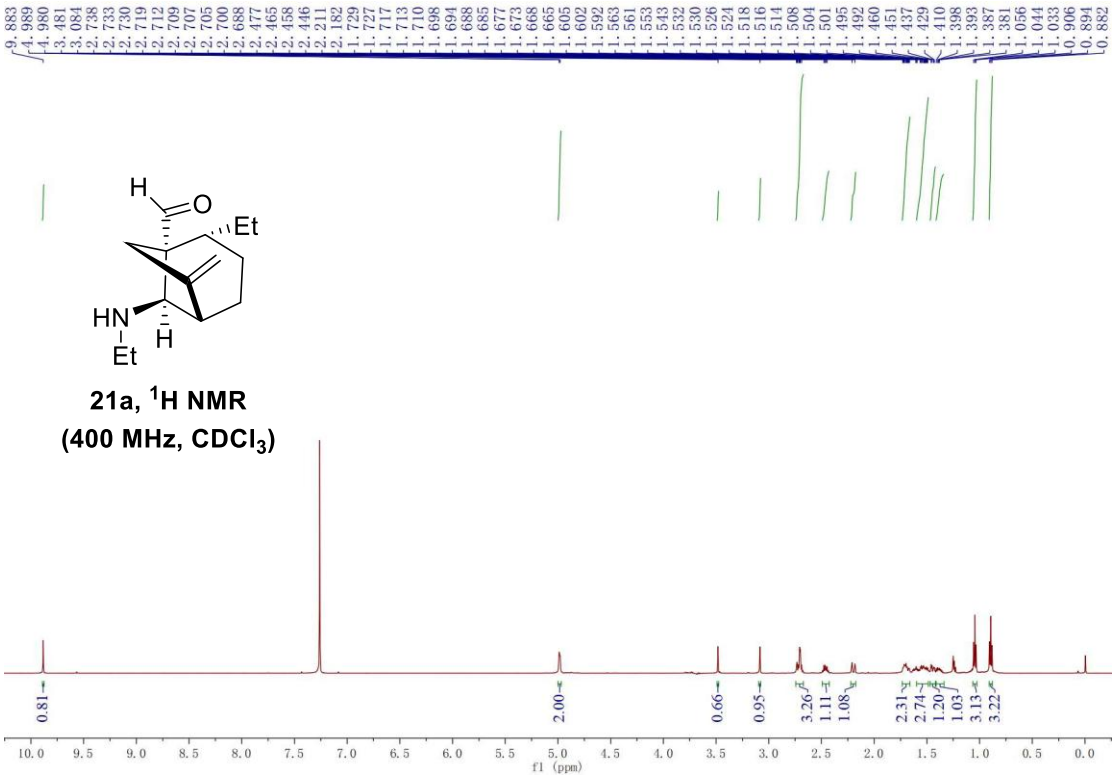
21, ^{1}H NMR
(400 MHz, $CDCl_3$)



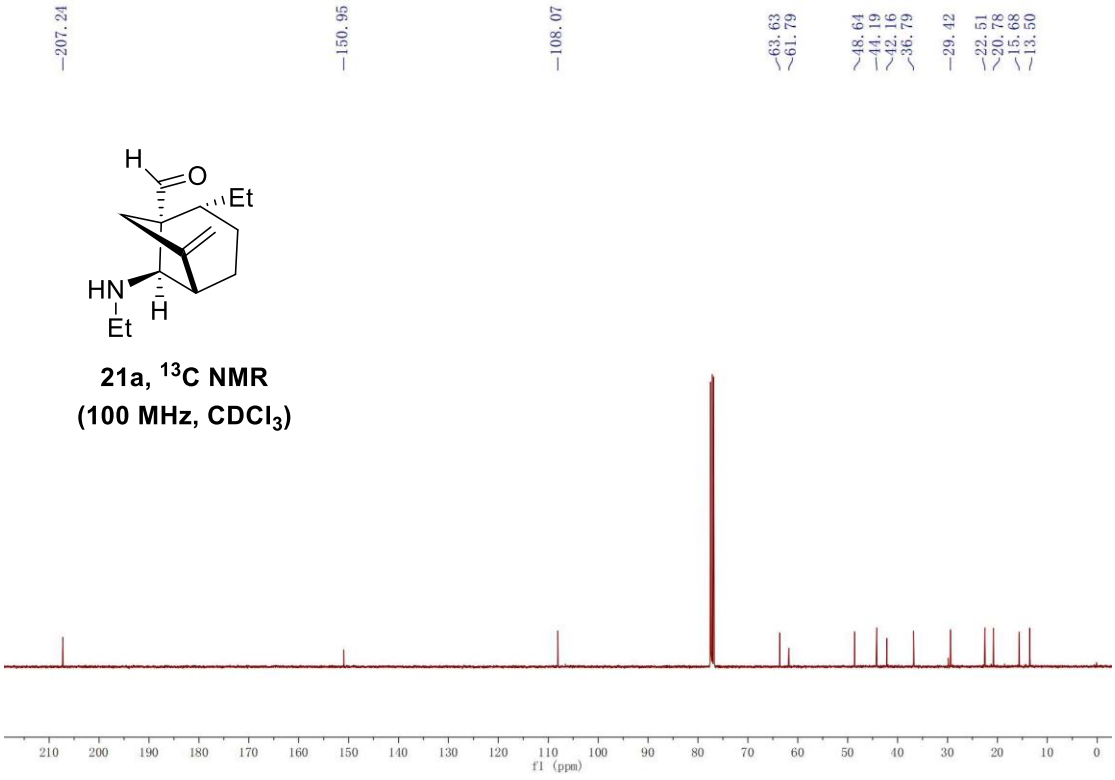
21, ^{13}C NMR
(100 MHz, $CDCl_3$)



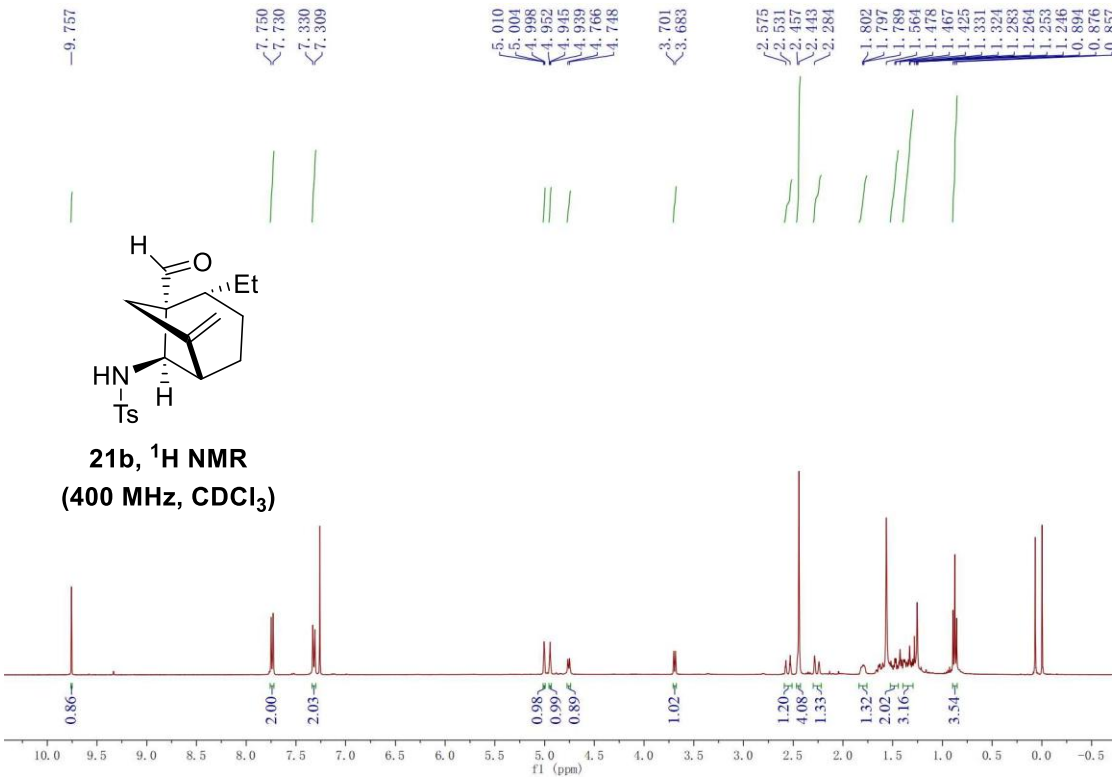
21, NOEDS
(400 MHz, $CDCl_3$)



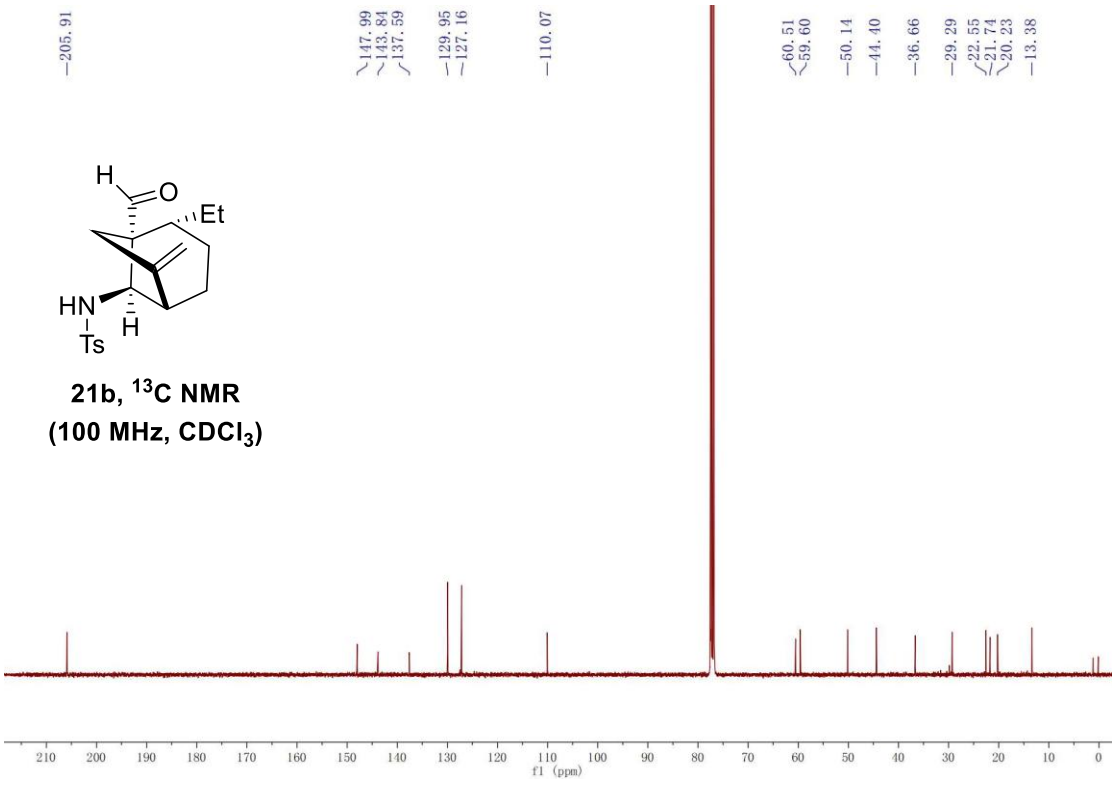
21a, ^{1}H NMR
(400 MHz, $CDCl_3$)



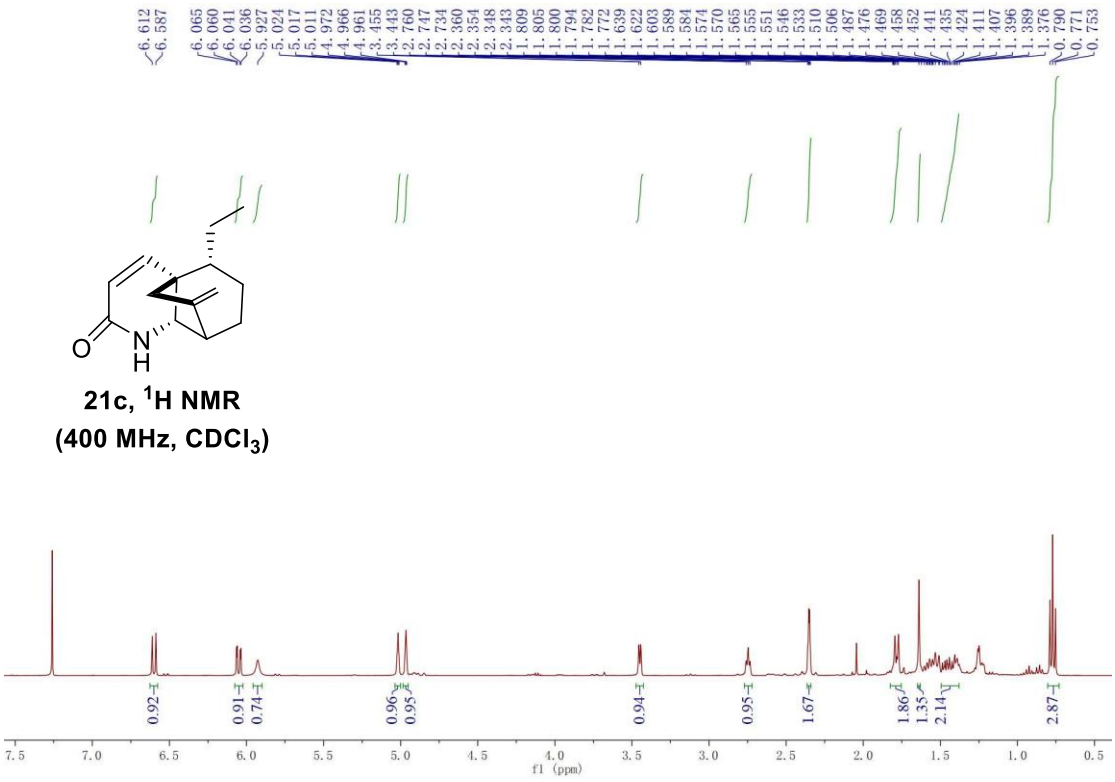
21a, ^{13}C NMR
(100 MHz, $CDCl_3$)



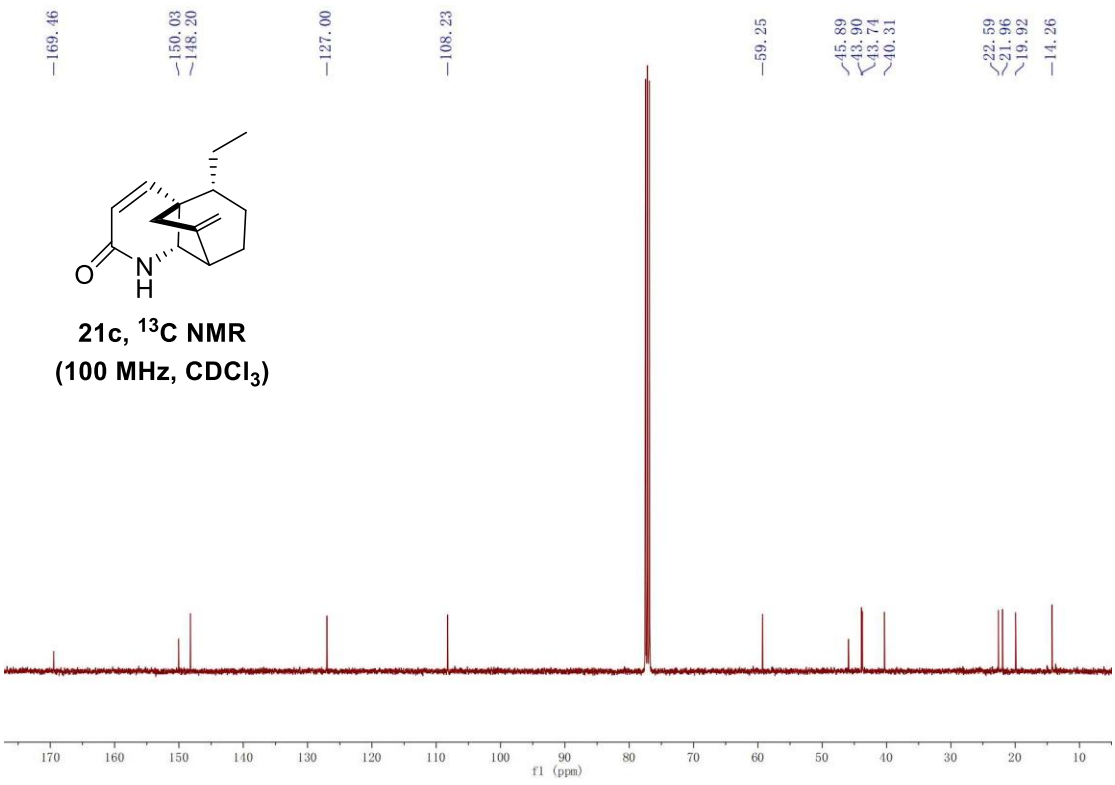
21b, ^{1}H NMR
(400 MHz, $CDCl_3$)



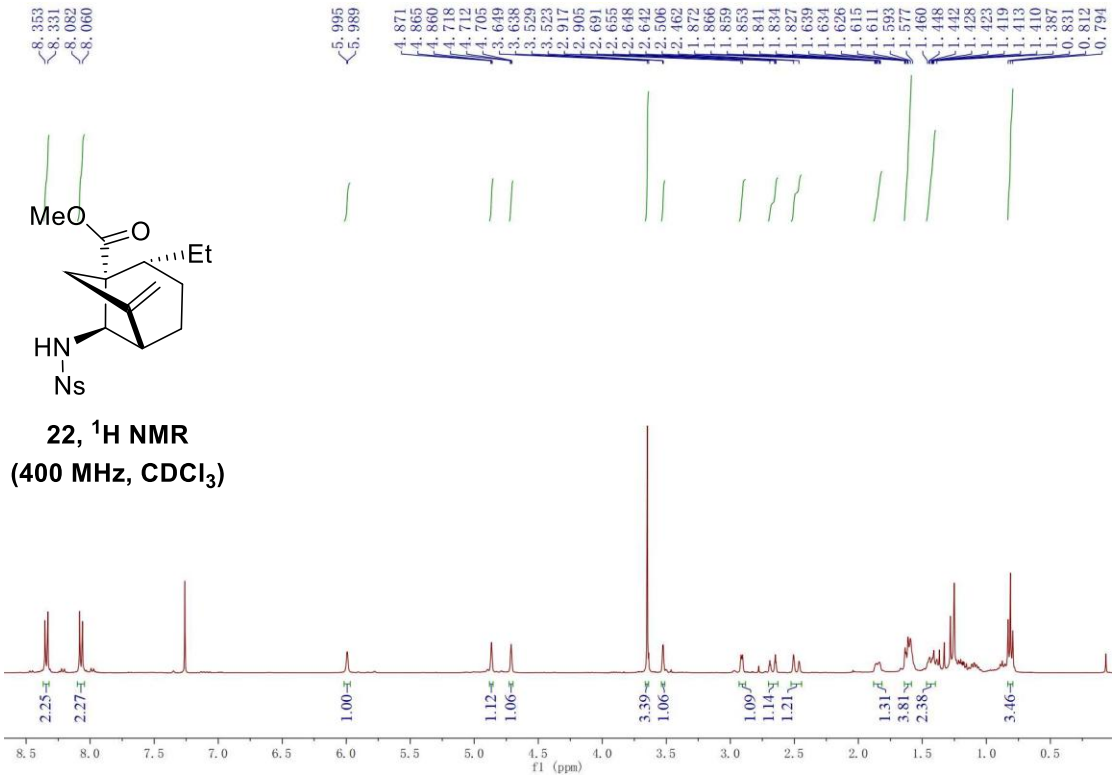
21b, ^{13}C NMR
(100 MHz, $CDCl_3$)



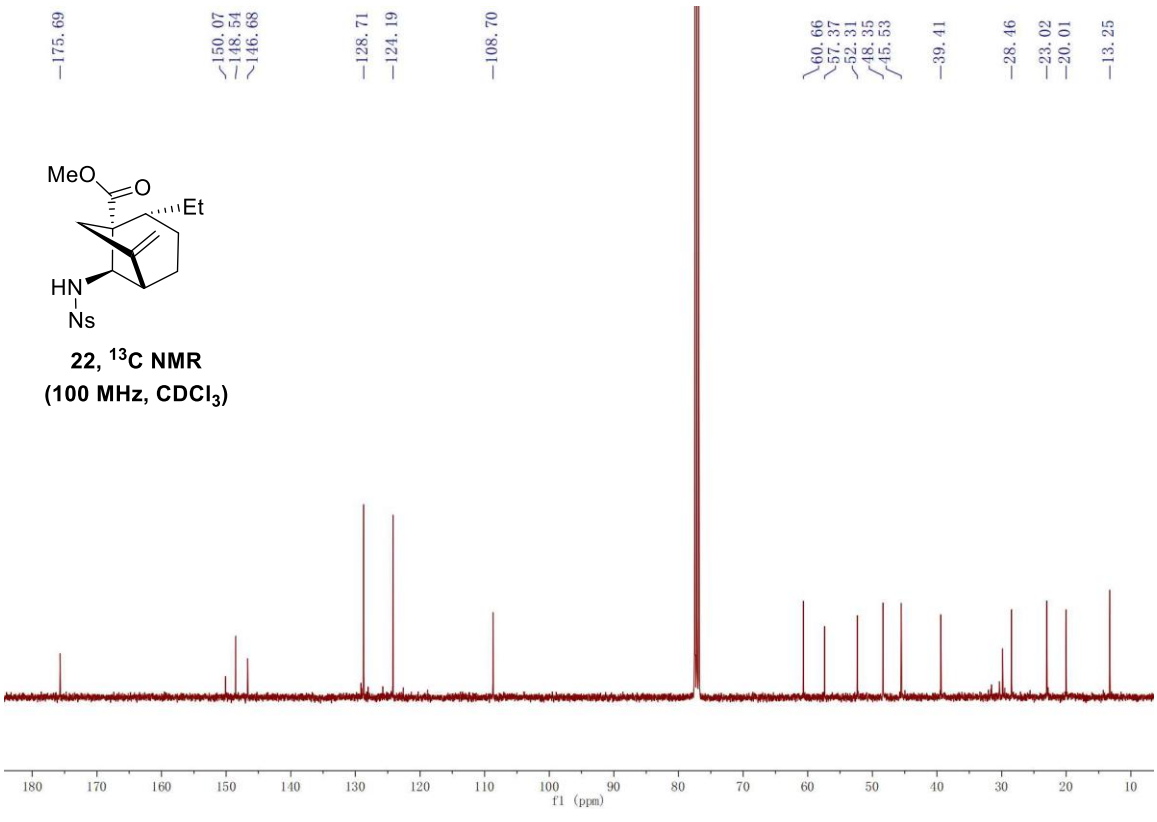
21c, ^{1}H NMR
(400 MHz, $CDCl_3$)



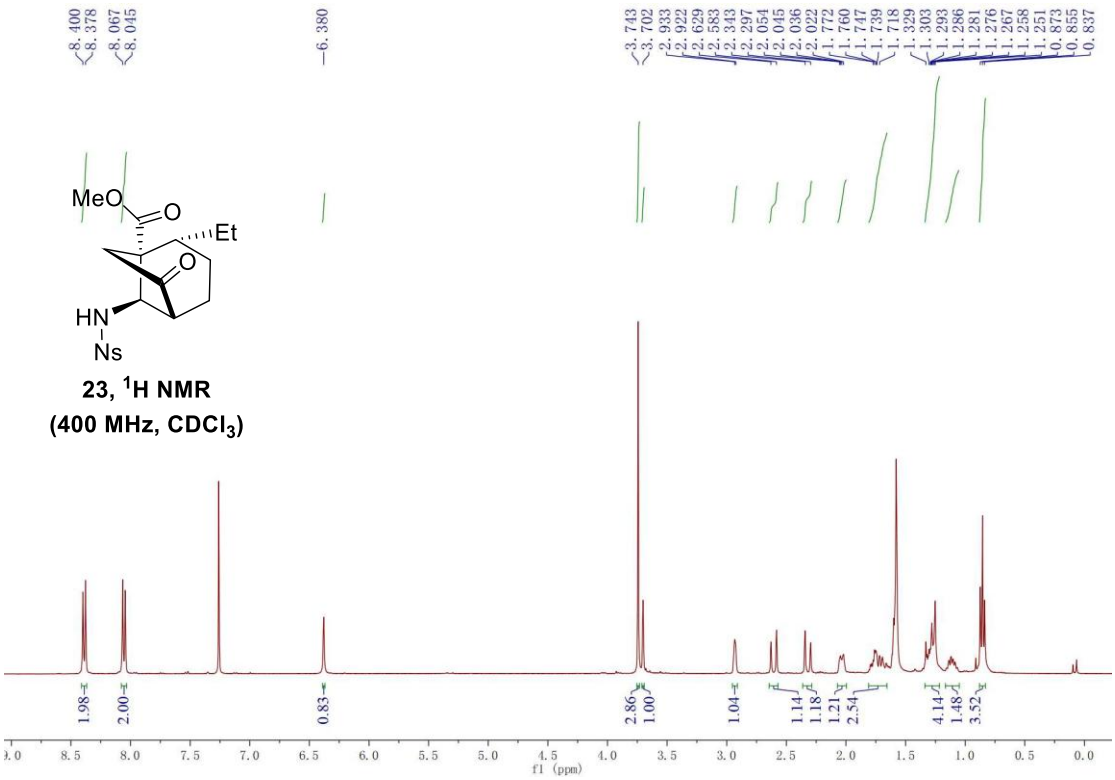
21c, ^{13}C NMR
(100 MHz, $CDCl_3$)



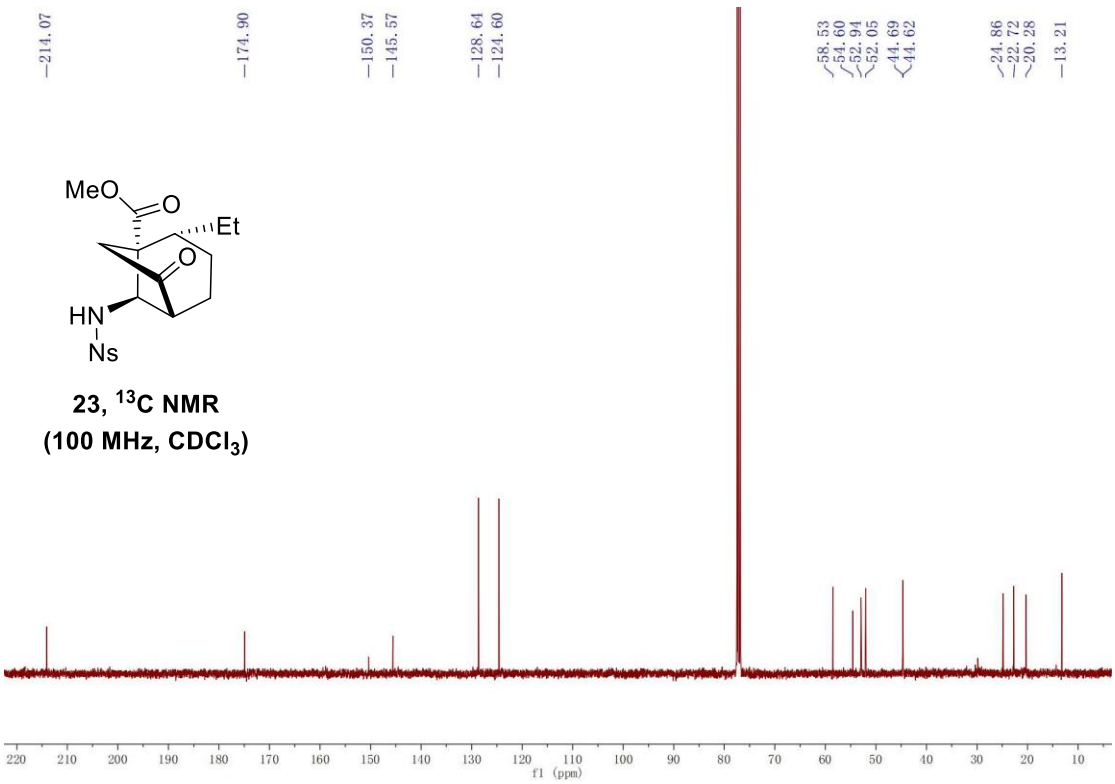
22, ^{1}H NMR
(400 MHz, $CDCl_3$)



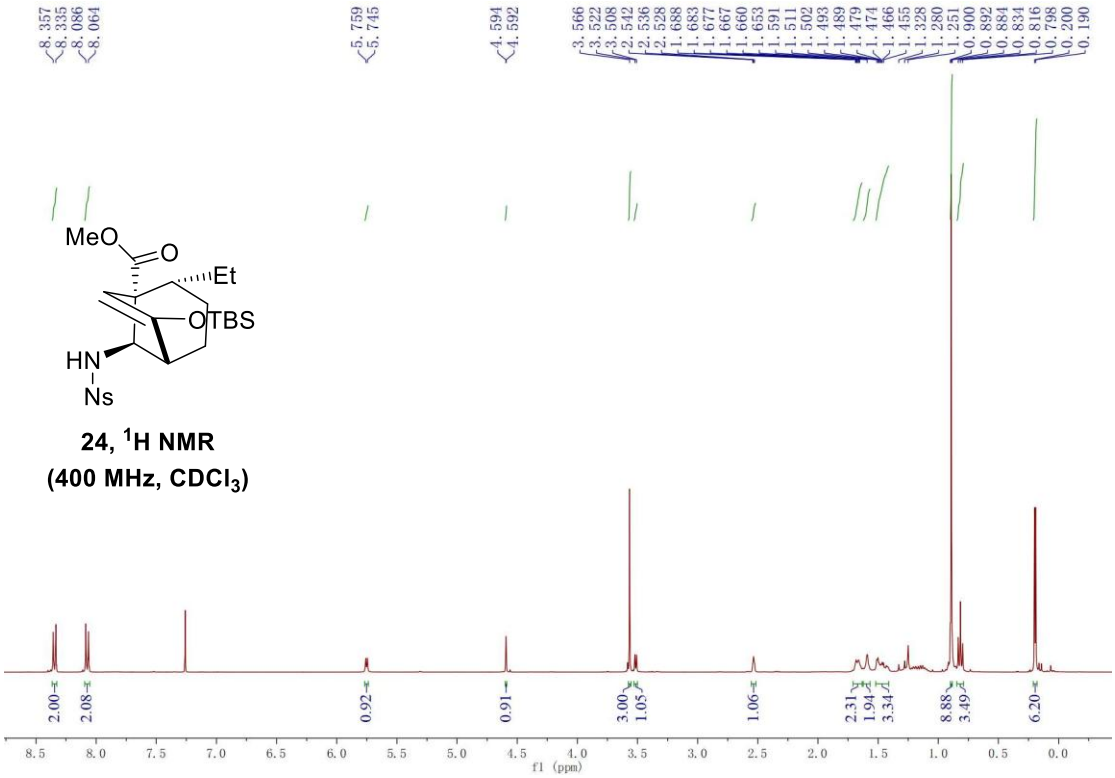
22, ^{13}C NMR
(100 MHz, $CDCl_3$)



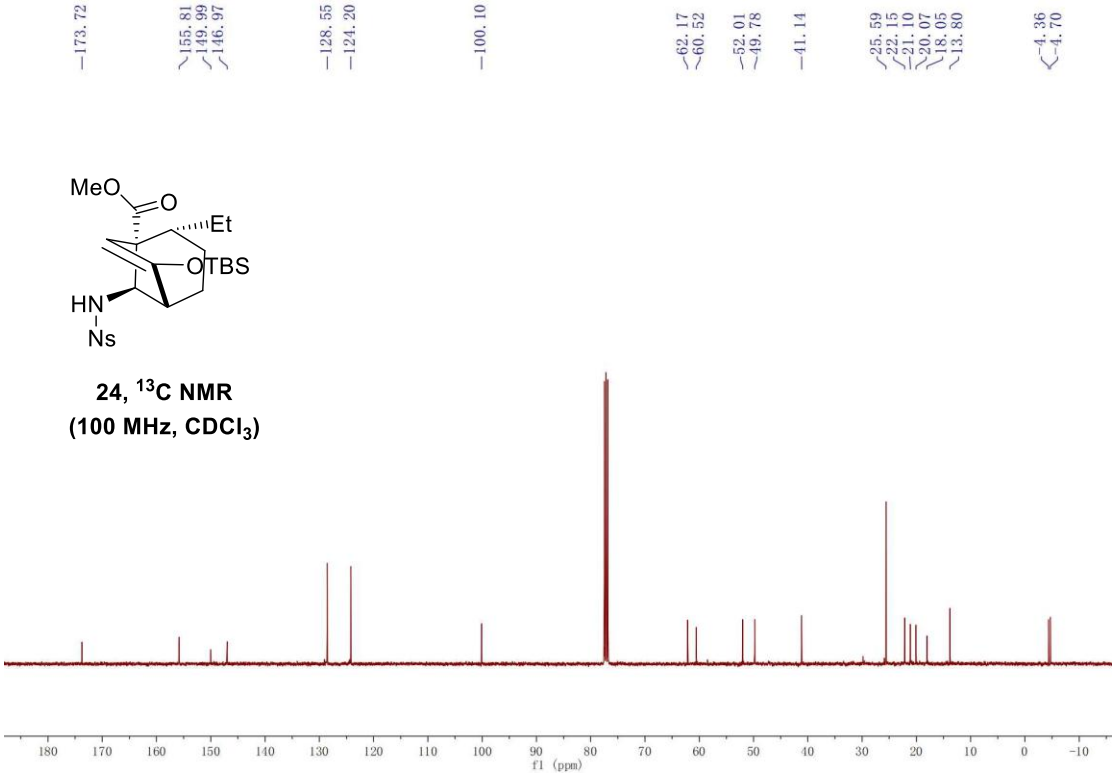
23, ^{1}H NMR
(400 MHz, $CDCl_3$)



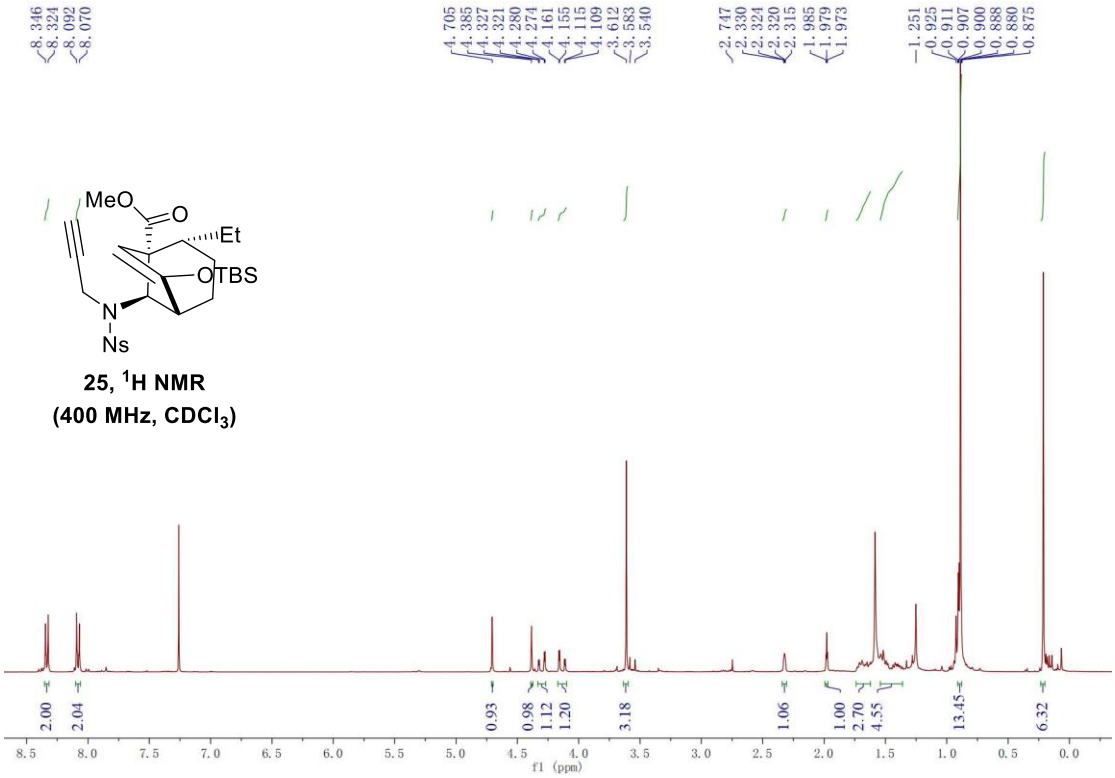
23, ^{13}C NMR
(100 MHz, $CDCl_3$)



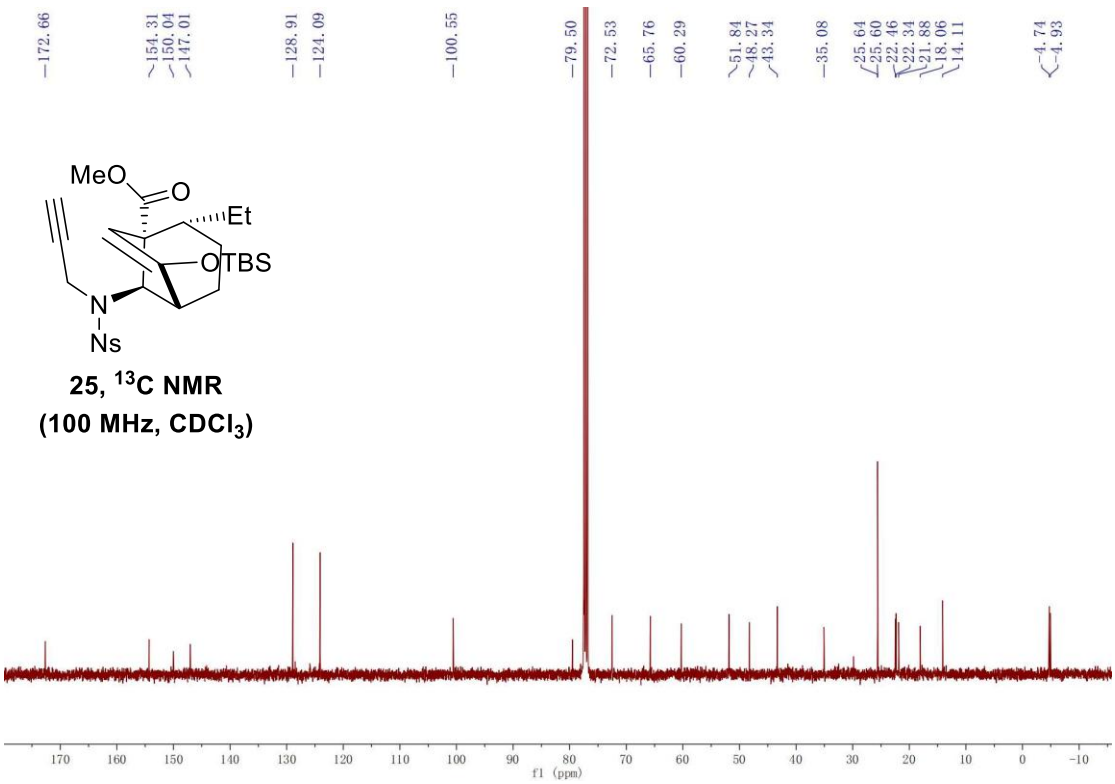
24, ^{1}H NMR
(400 MHz, $CDCl_3$)



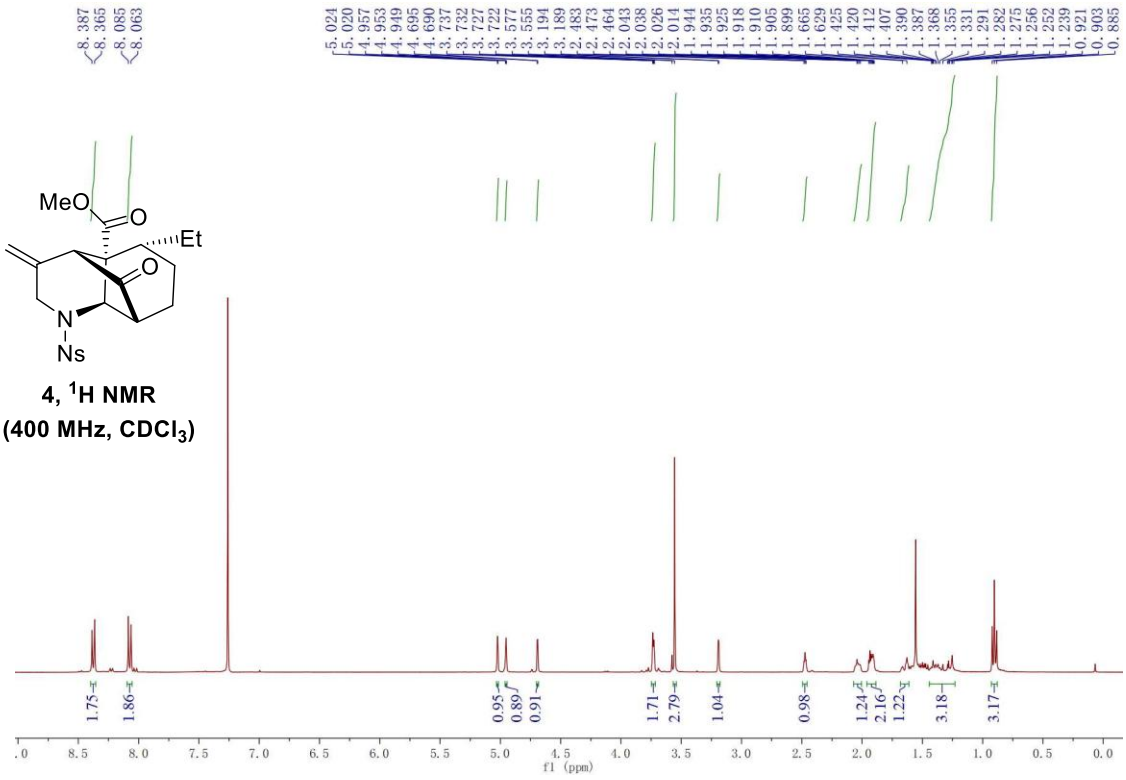
24, ^{13}C NMR
(100 MHz, $CDCl_3$)



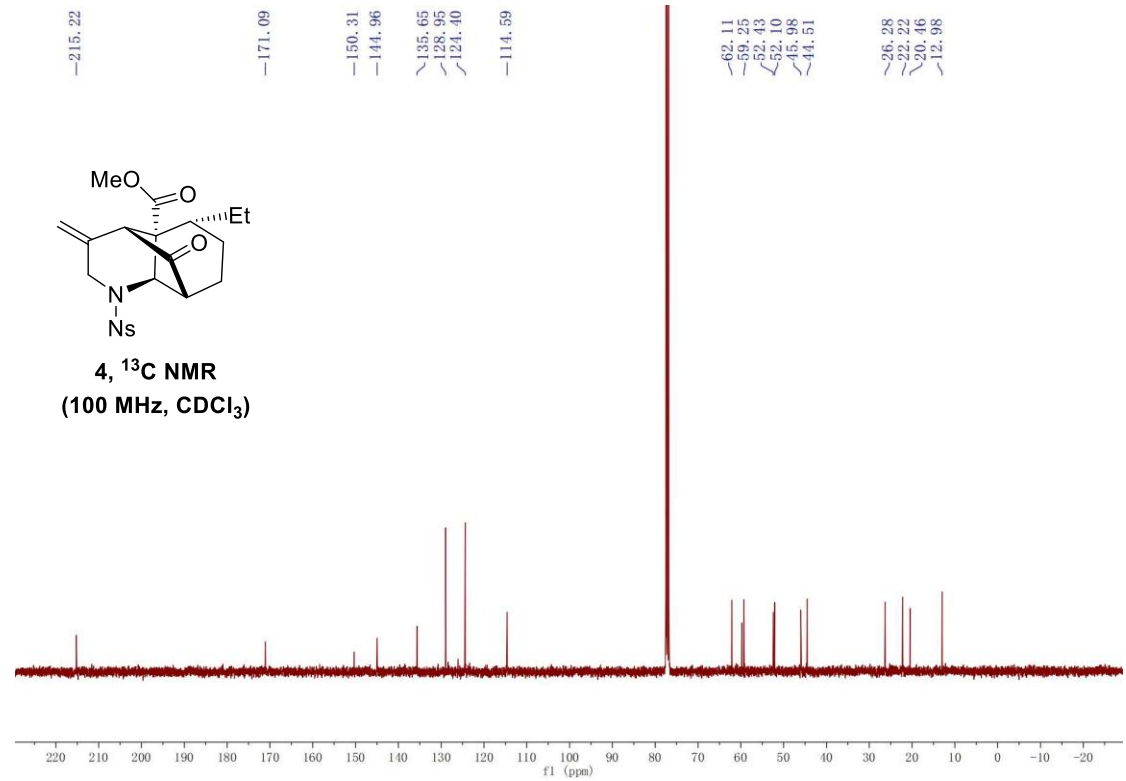
25, ^{1}H NMR
(400 MHz, $CDCl_3$)



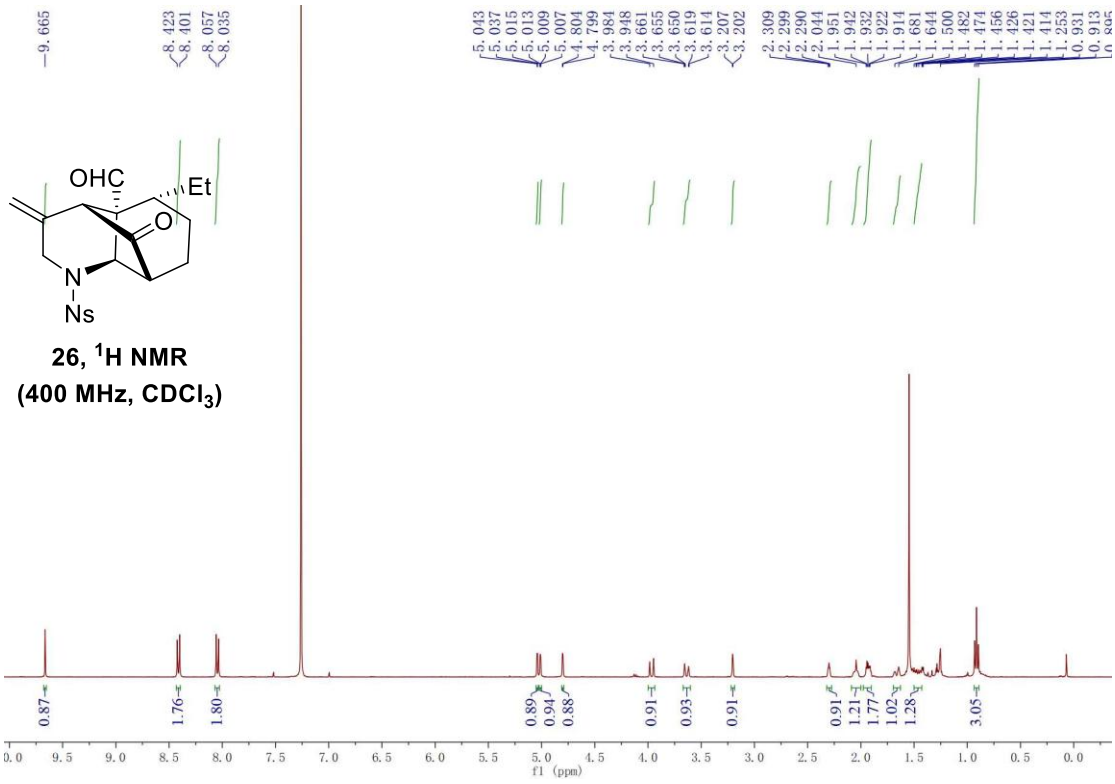
25, ^{13}C NMR
(100 MHz, $CDCl_3$)



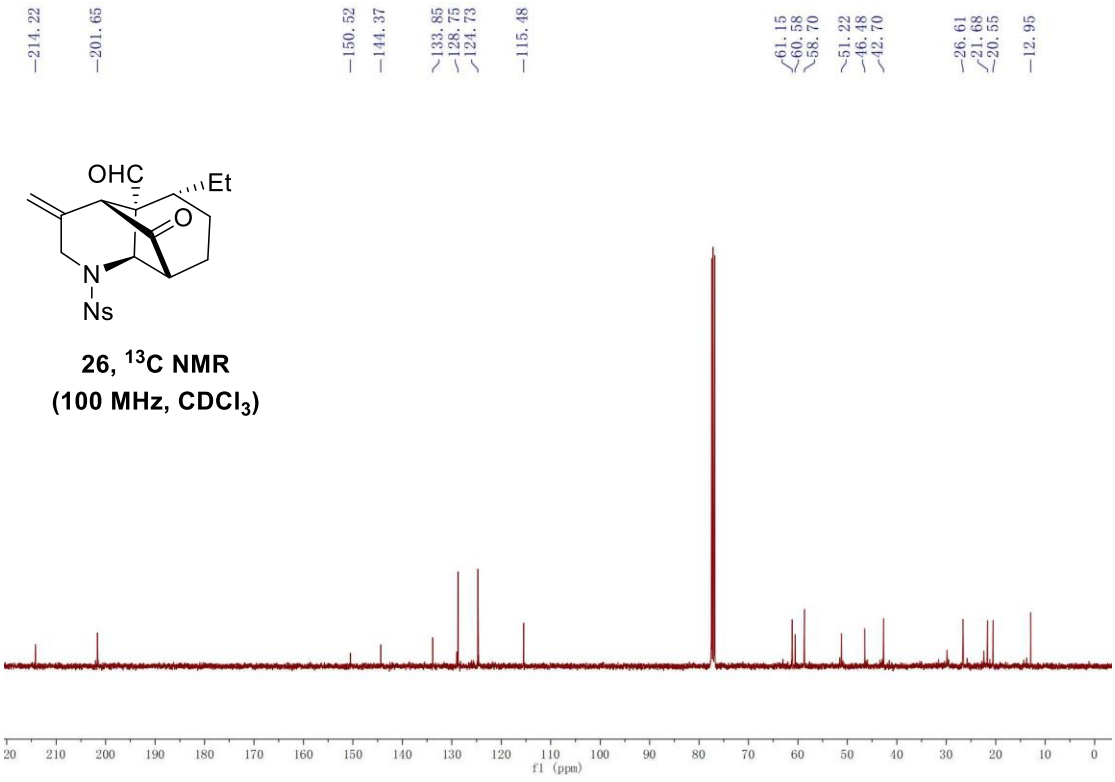
4, ^{1}H NMR
(400 MHz, $CDCl_3$)



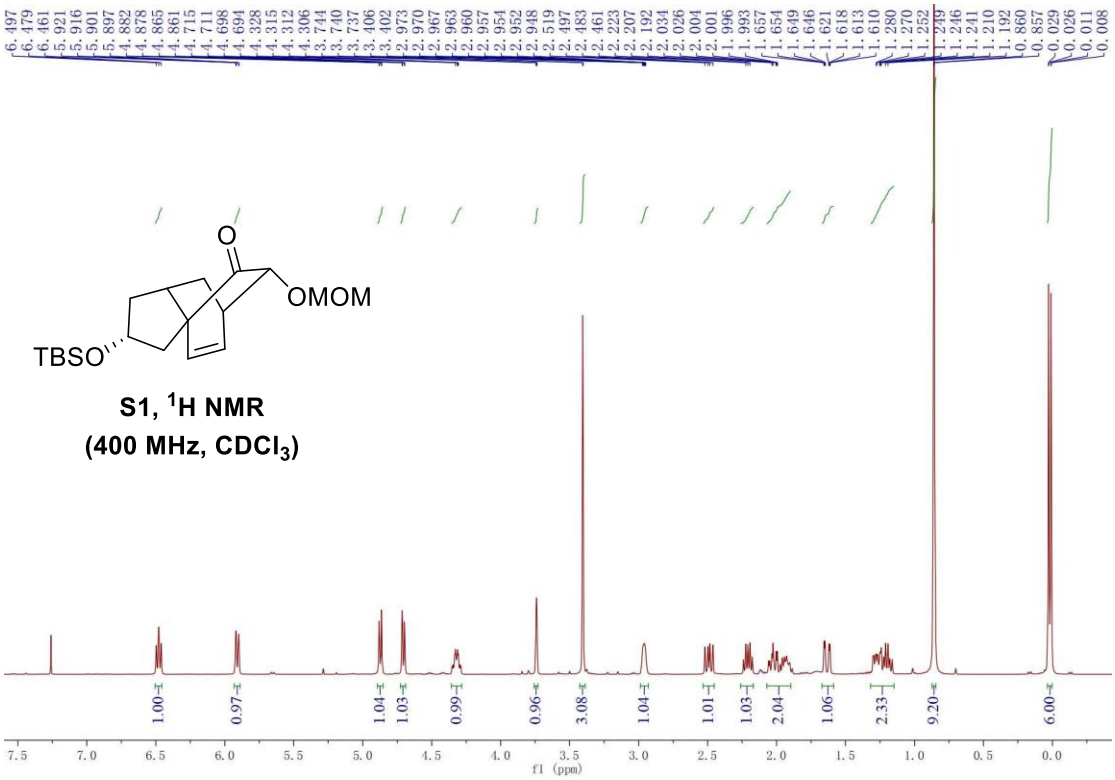
4, ^{13}C NMR
(100 MHz, $CDCl_3$)



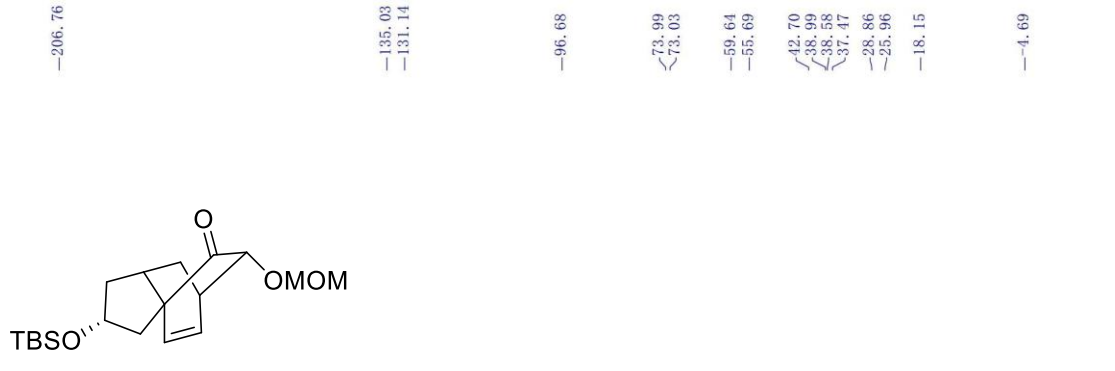
26, ^{1}H NMR
(400 MHz, $CDCl_3$)



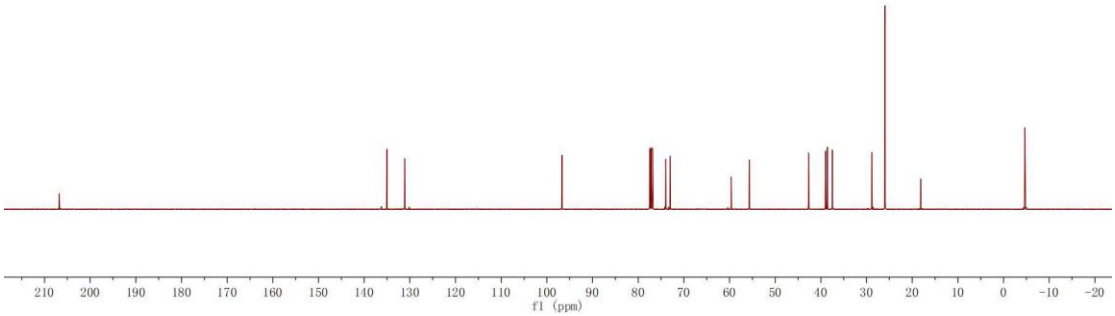
26, ^{13}C NMR
(100 MHz, $CDCl_3$)

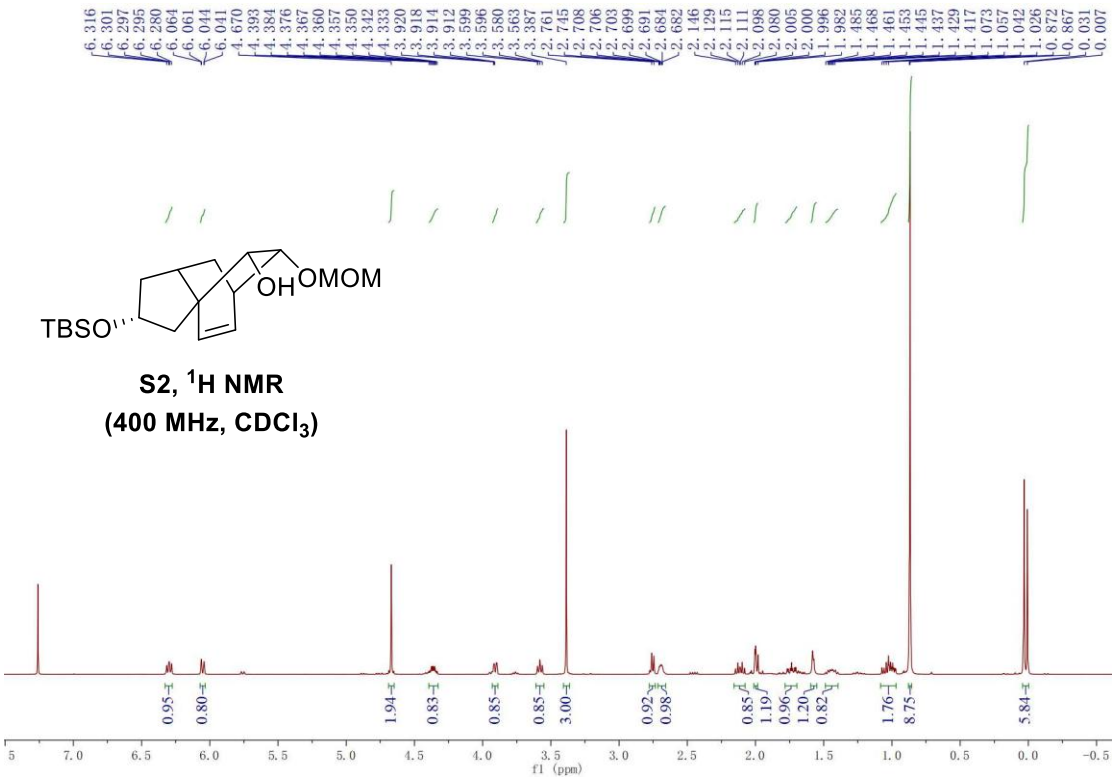


S1, ^{1}H NMR
(400 MHz, $CDCl_3$)

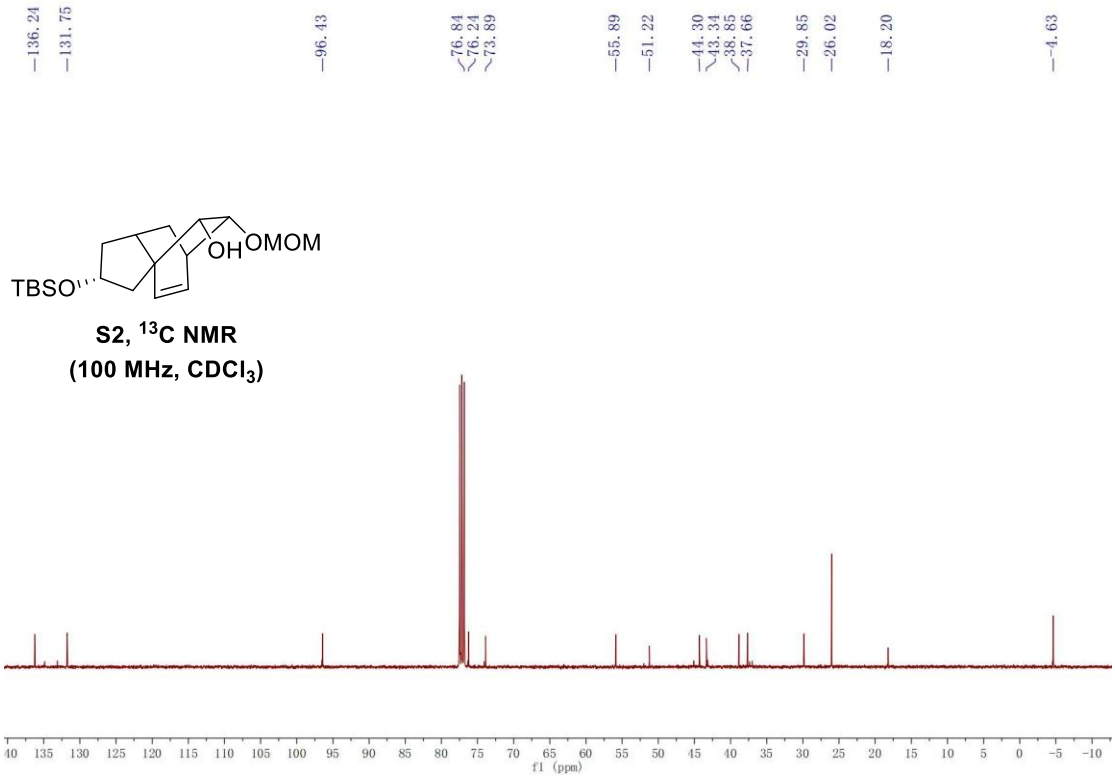


S1, ^{13}C NMR
(100 MHz, $CDCl_3$)

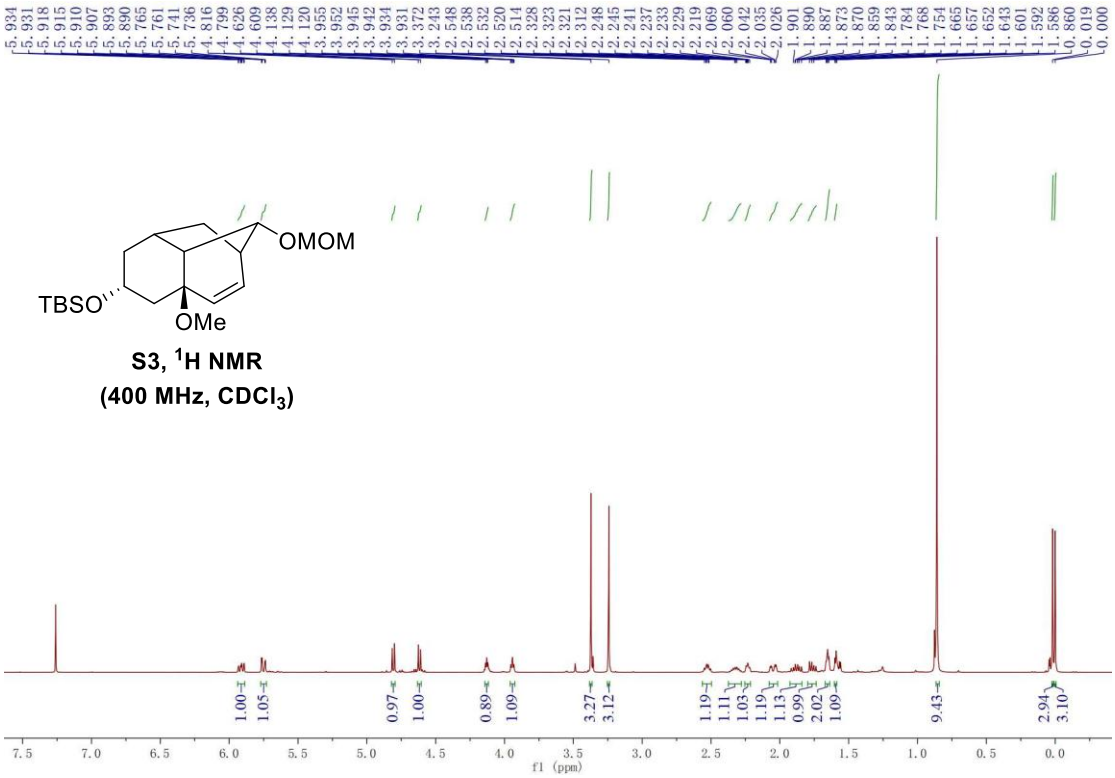




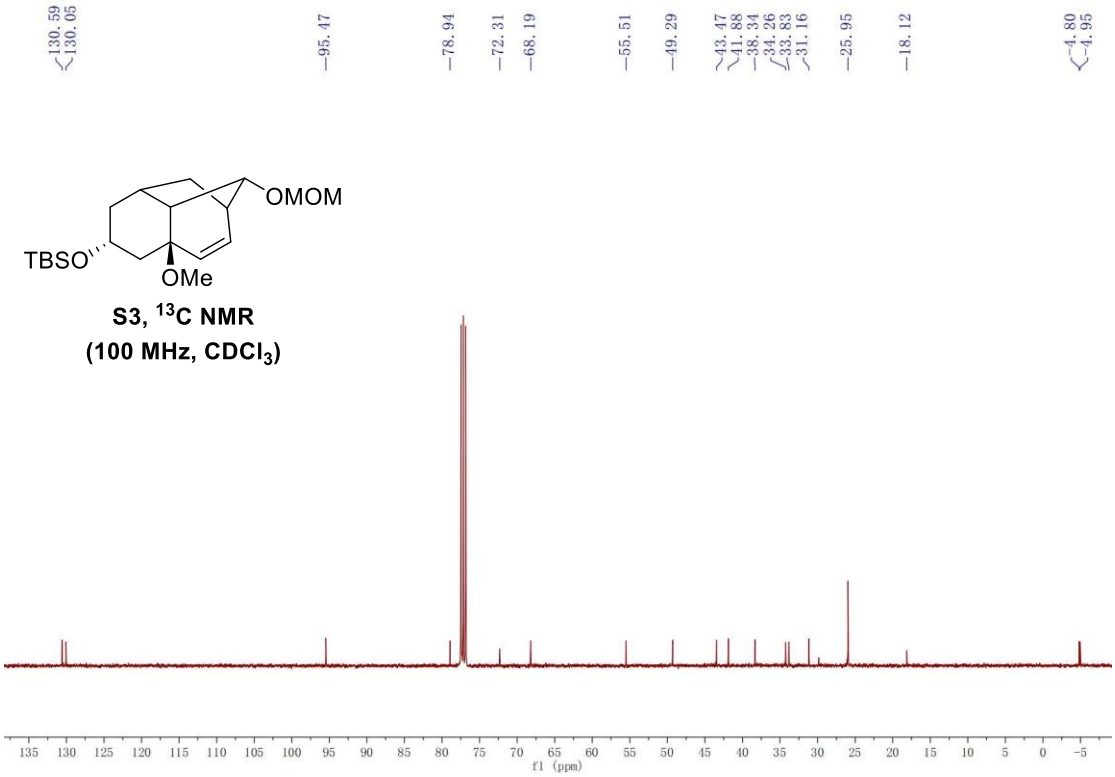
S2, ^{1}H NMR
(400 MHz, $CDCl_3$)



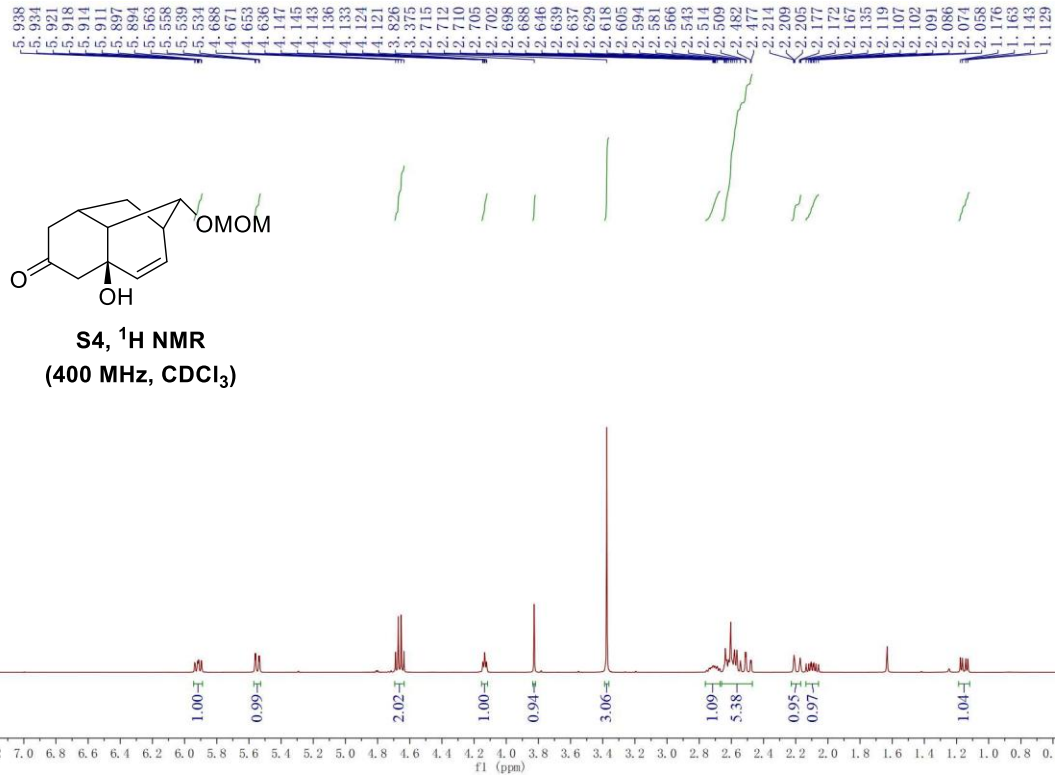
S2, ^{13}C NMR
(100 MHz, $CDCl_3$)



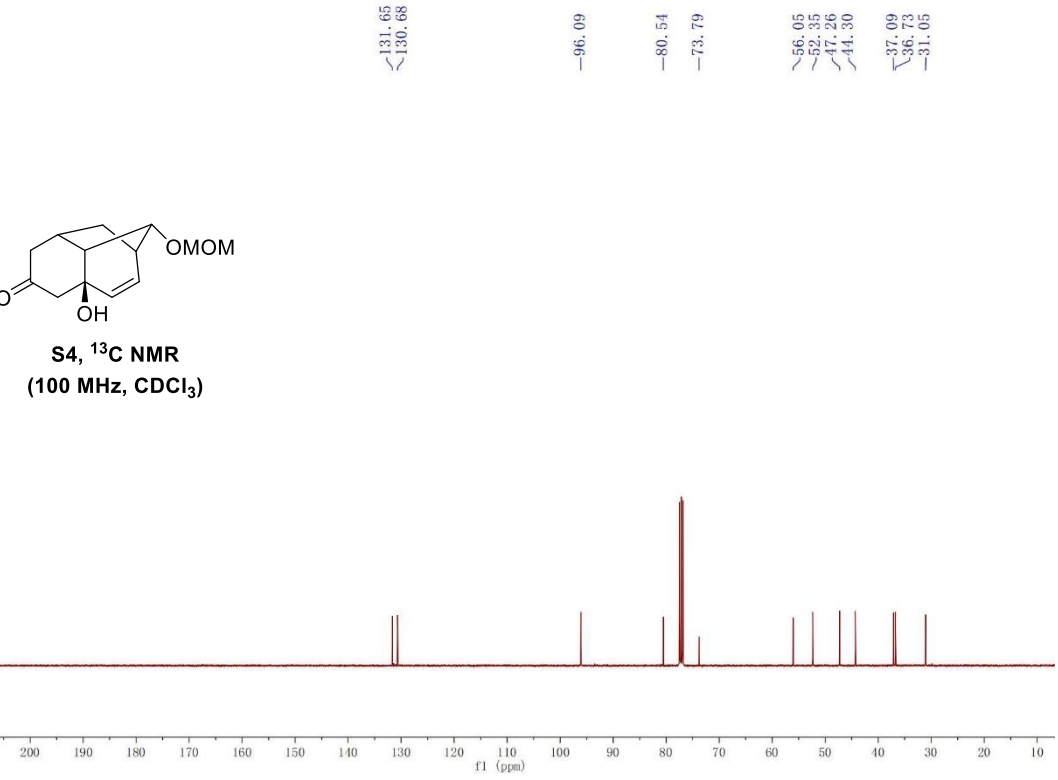
S3, ^{1}H NMR
(400 MHz, $CDCl_3$)



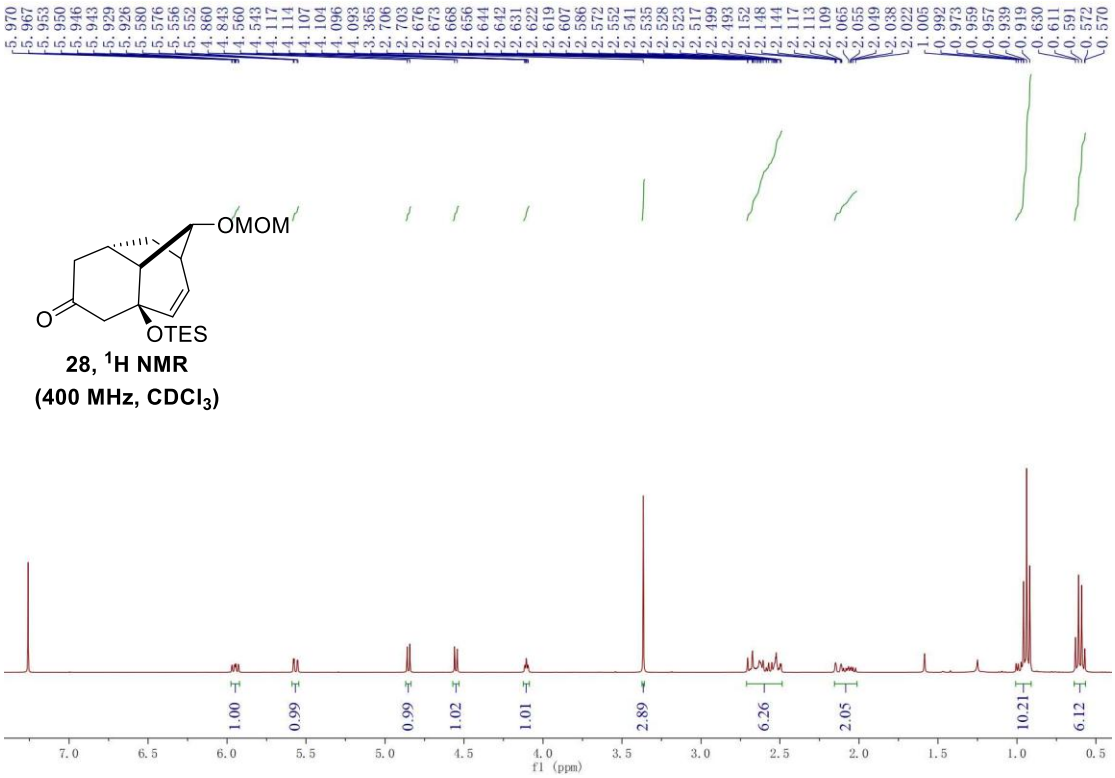
S3, ^{13}C NMR
(100 MHz, $CDCl_3$)



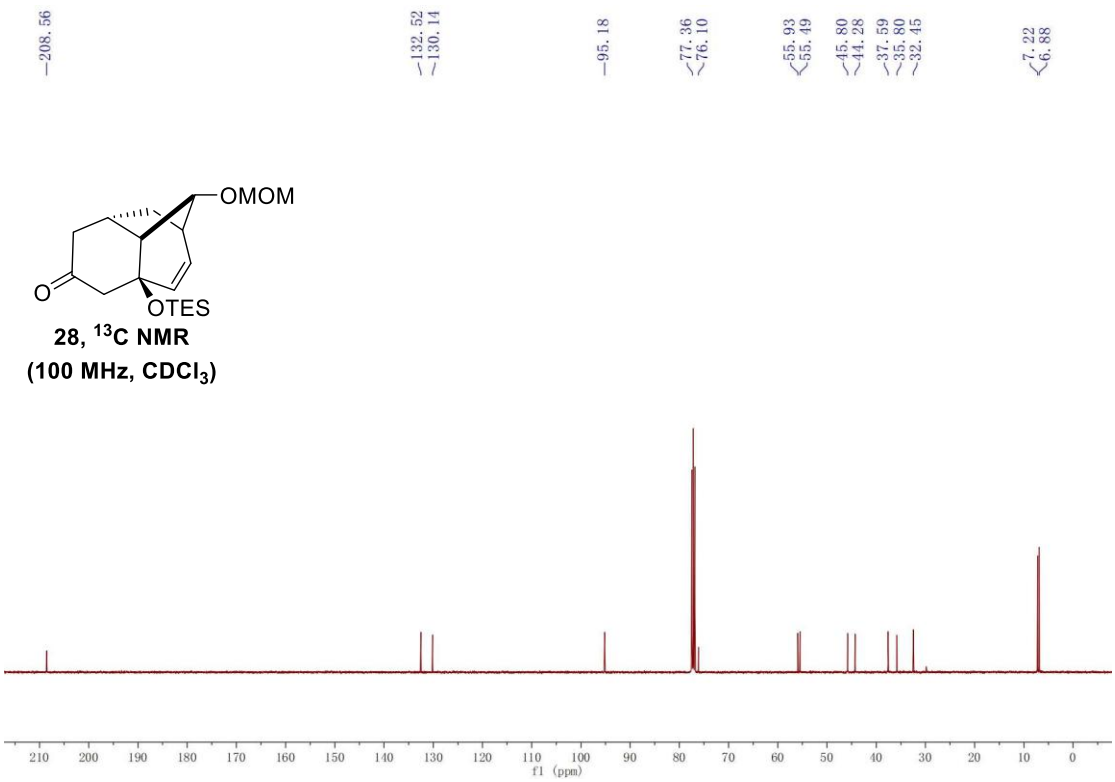
S4, ^{1}H NMR
(400 MHz, $CDCl_3$)



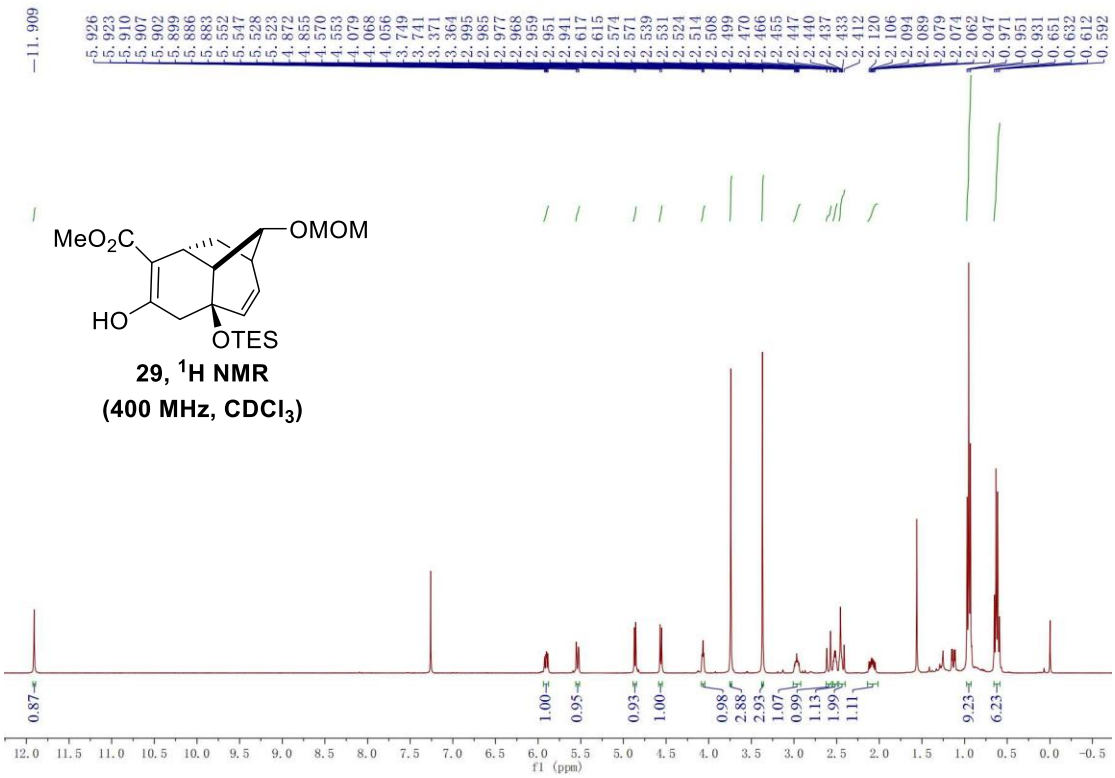
S4, ^{13}C NMR
(100 MHz, $CDCl_3$)



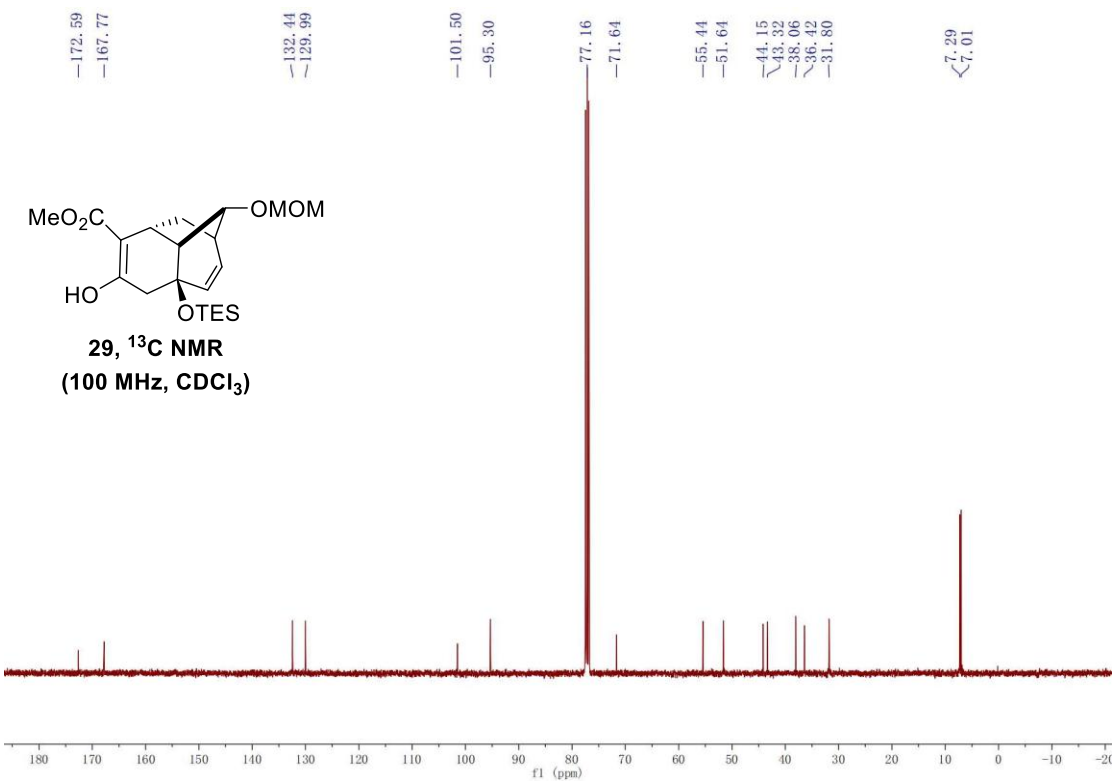
28, ^{1}H NMR
(400 MHz, $CDCl_3$)



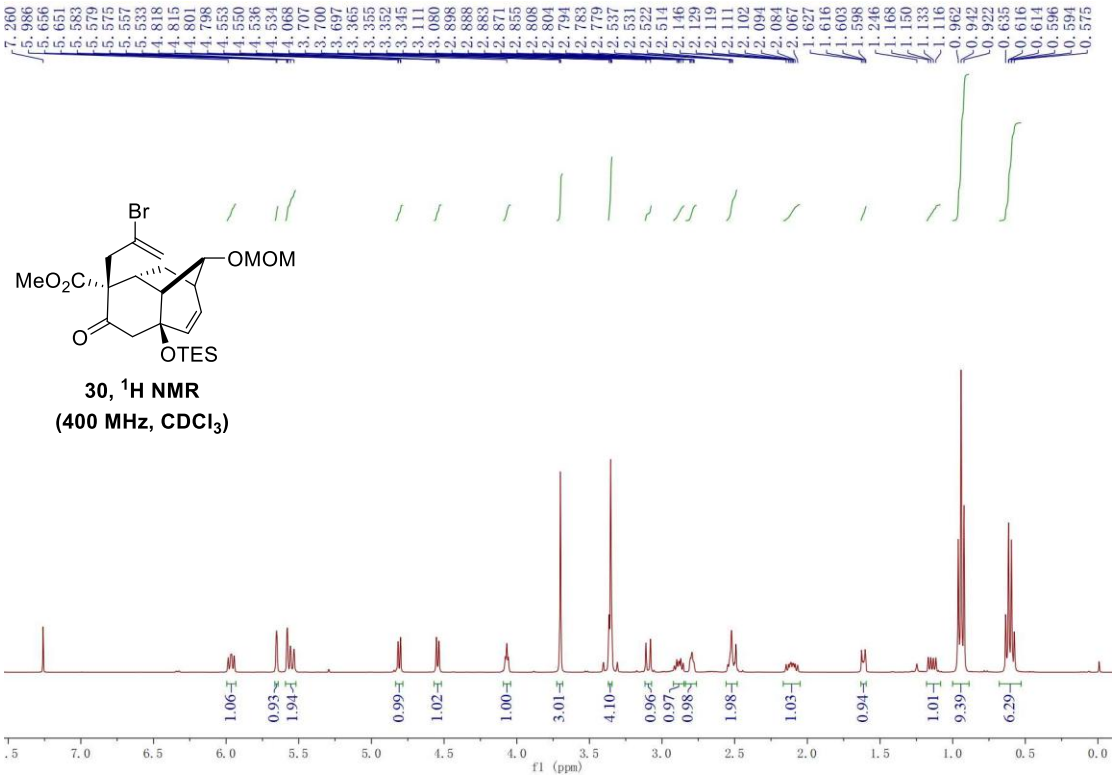
28, ^{13}C NMR
(100 MHz, $CDCl_3$)



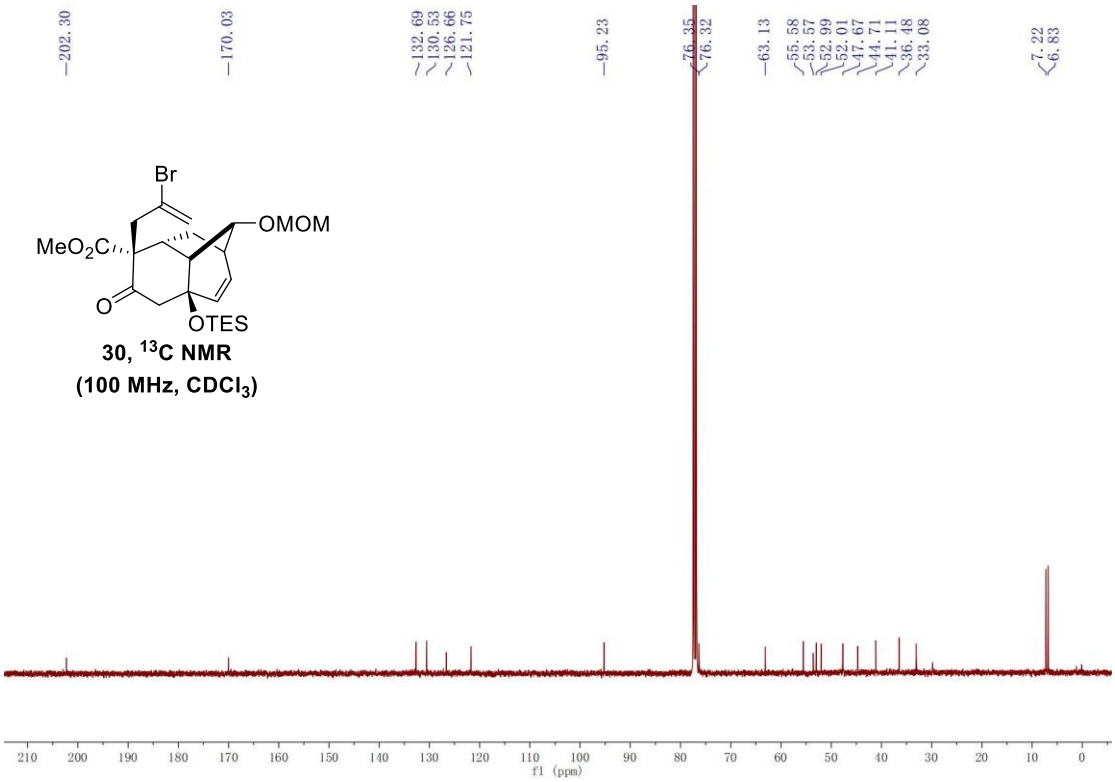
29, ^{1}H NMR
(400 MHz, $CDCl_3$)



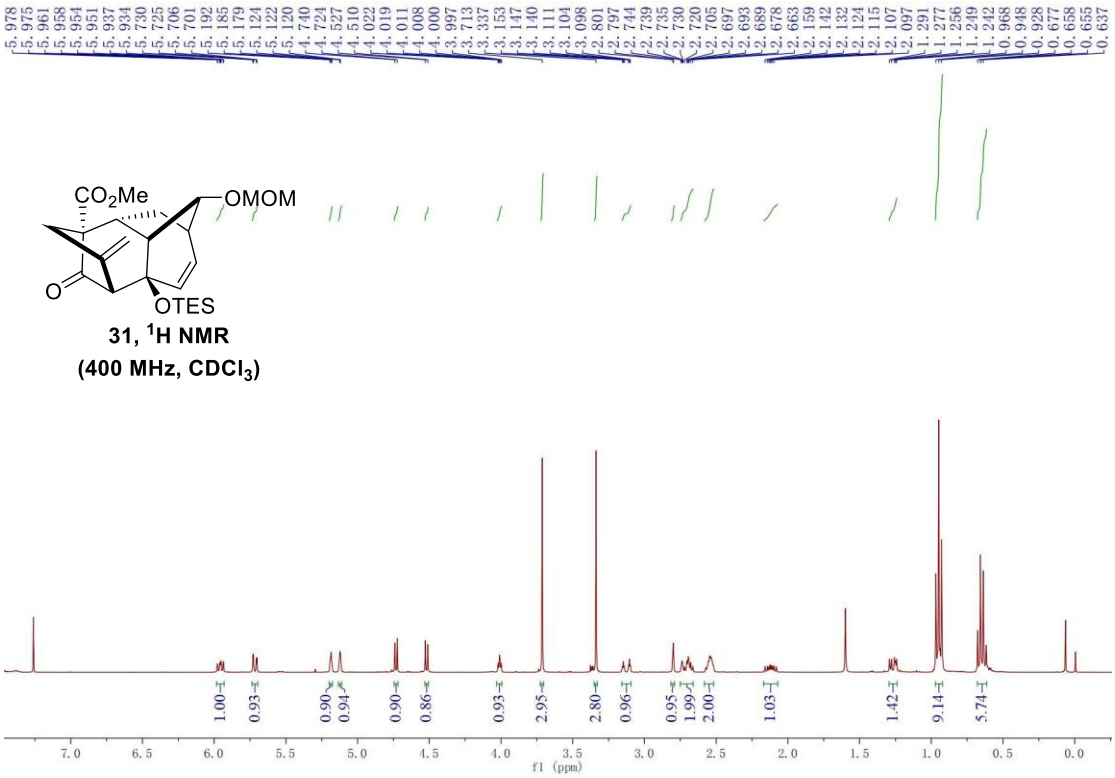
29, ^{13}C NMR
(100 MHz, $CDCl_3$)



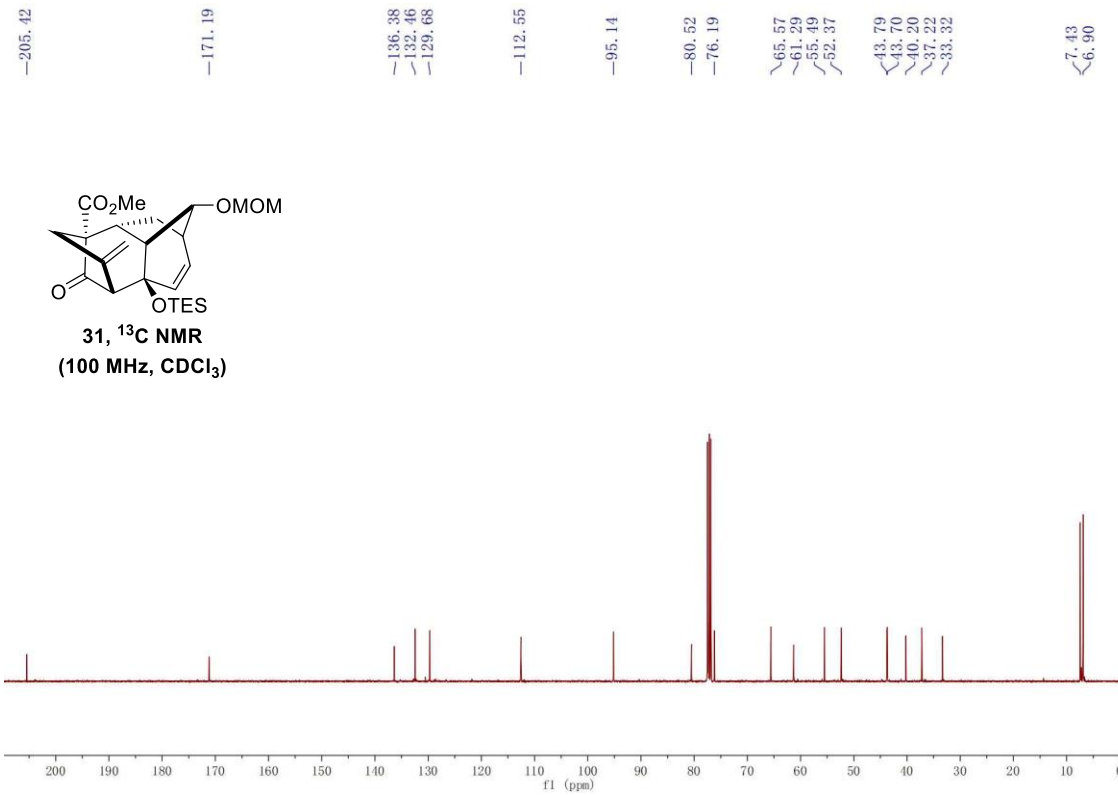
30, ^{1}H NMR
(400 MHz, $CDCl_3$)



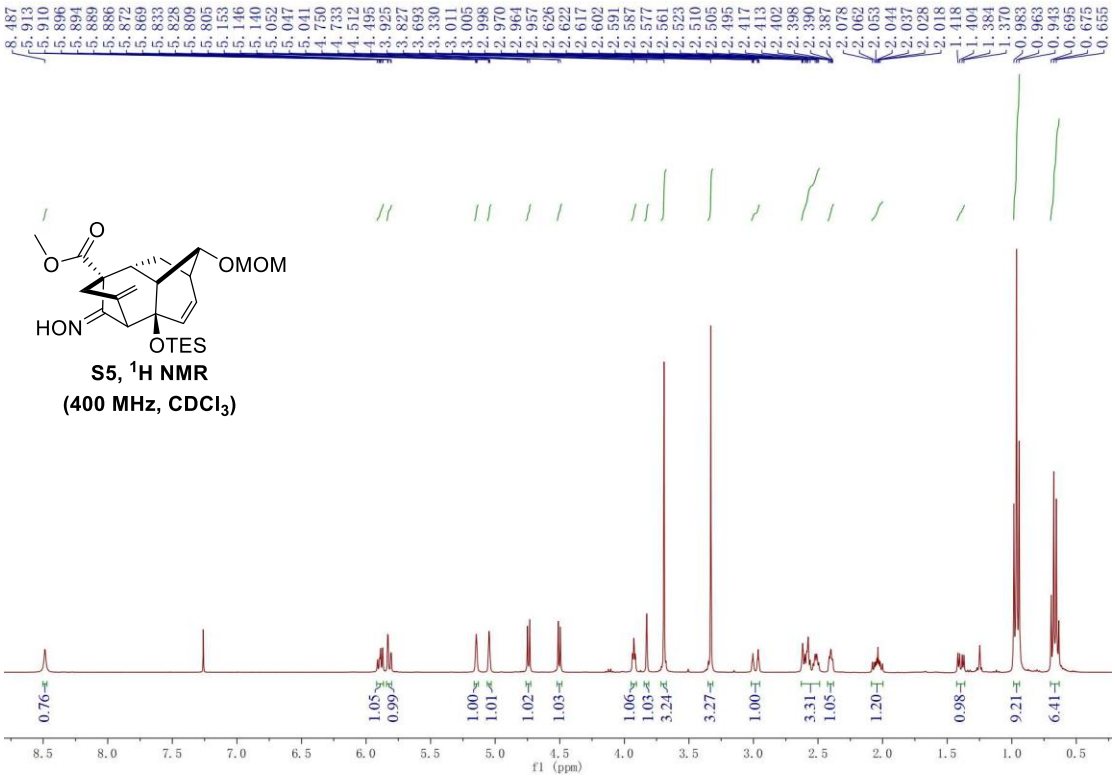
30, ^{13}C NMR
(100 MHz, $CDCl_3$)



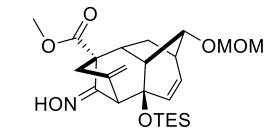
31, ^{1}H NMR
(400 MHz, $CDCl_3$)



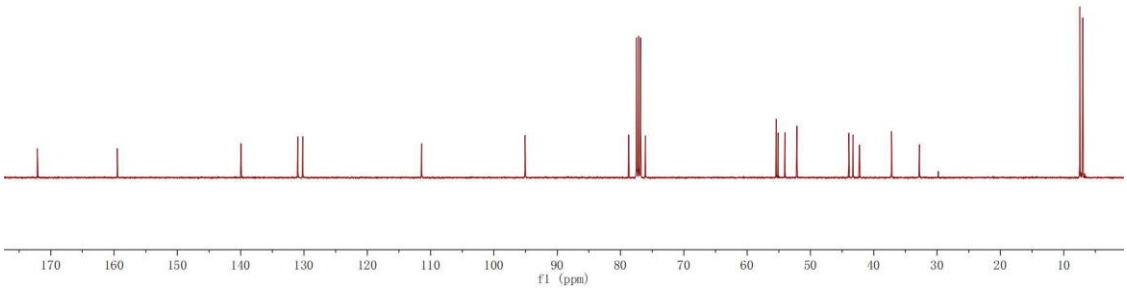
31, ^{13}C NMR
(100 MHz, $CDCl_3$)

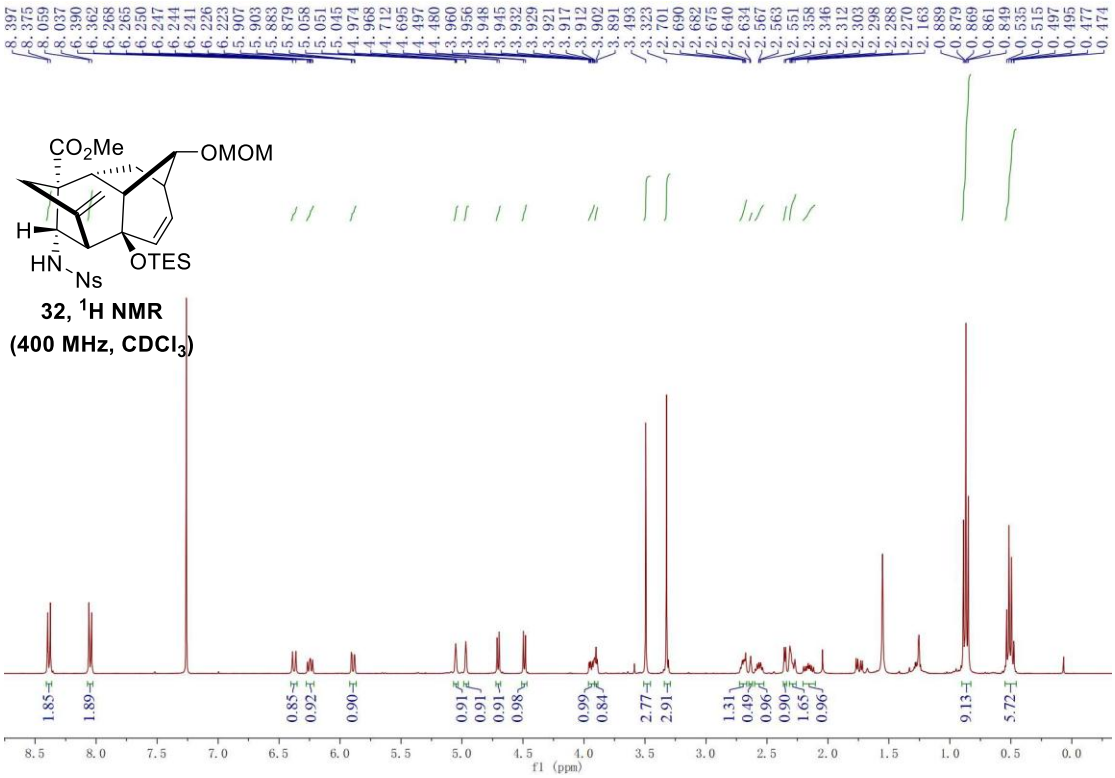


S5, ^{1}H NMR
(400 MHz, $CDCl_3$)

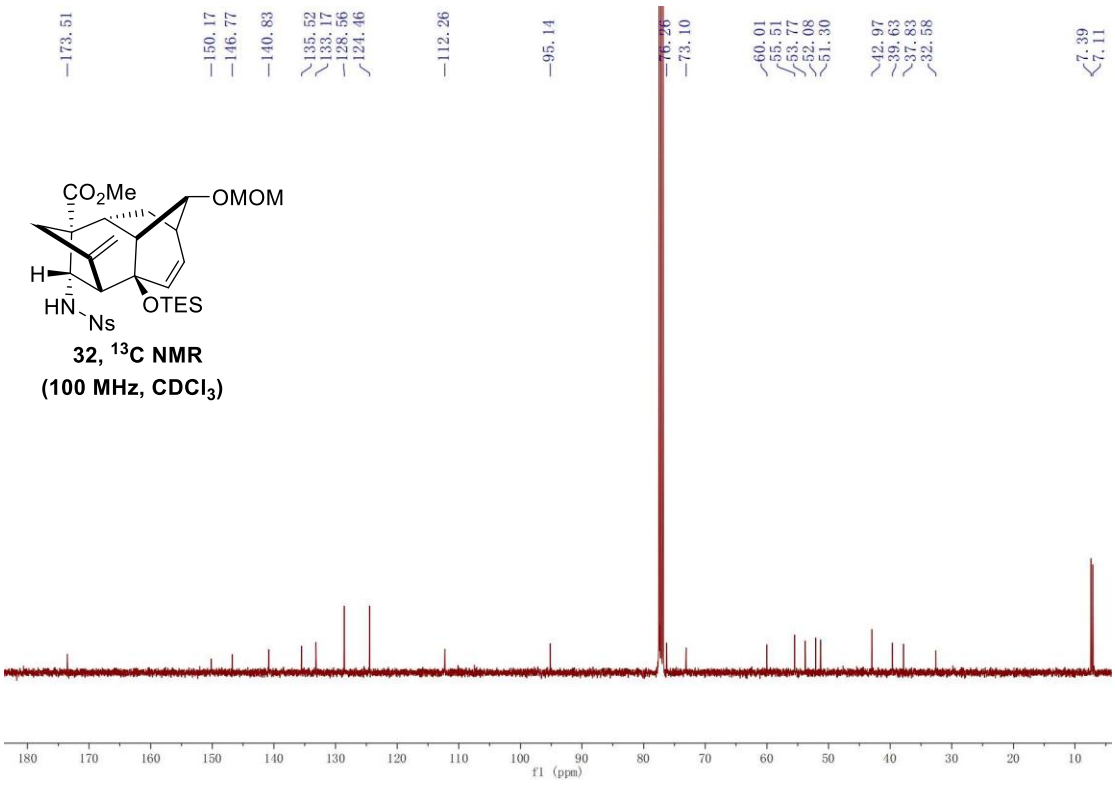


S5, ^{13}C NMR
(100 MHz, $CDCl_3$)

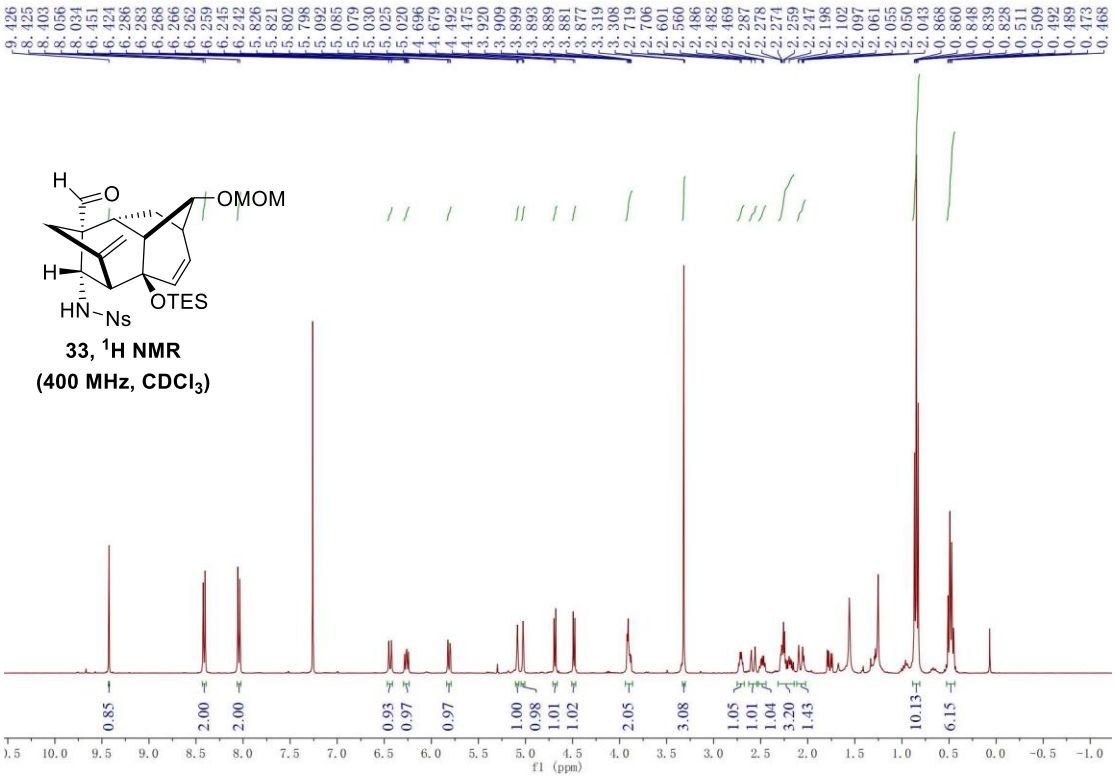




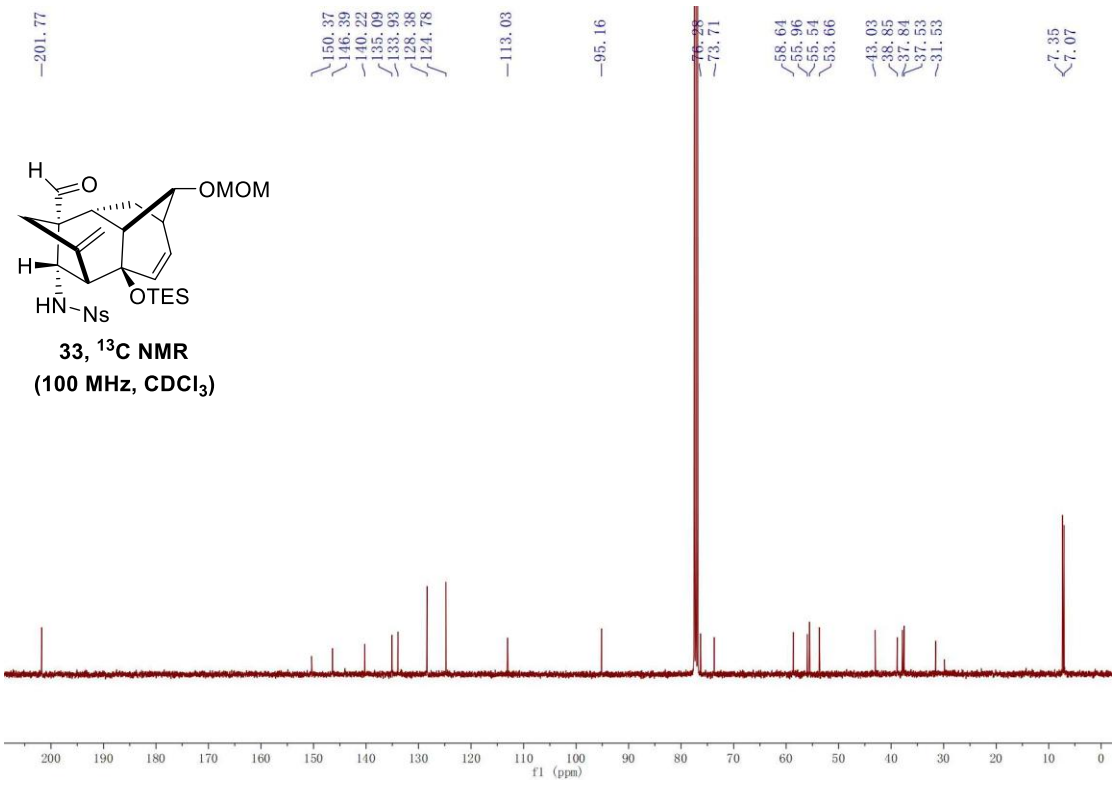
32, ^{1}H NMR
(400 MHz, $CDCl_3$)



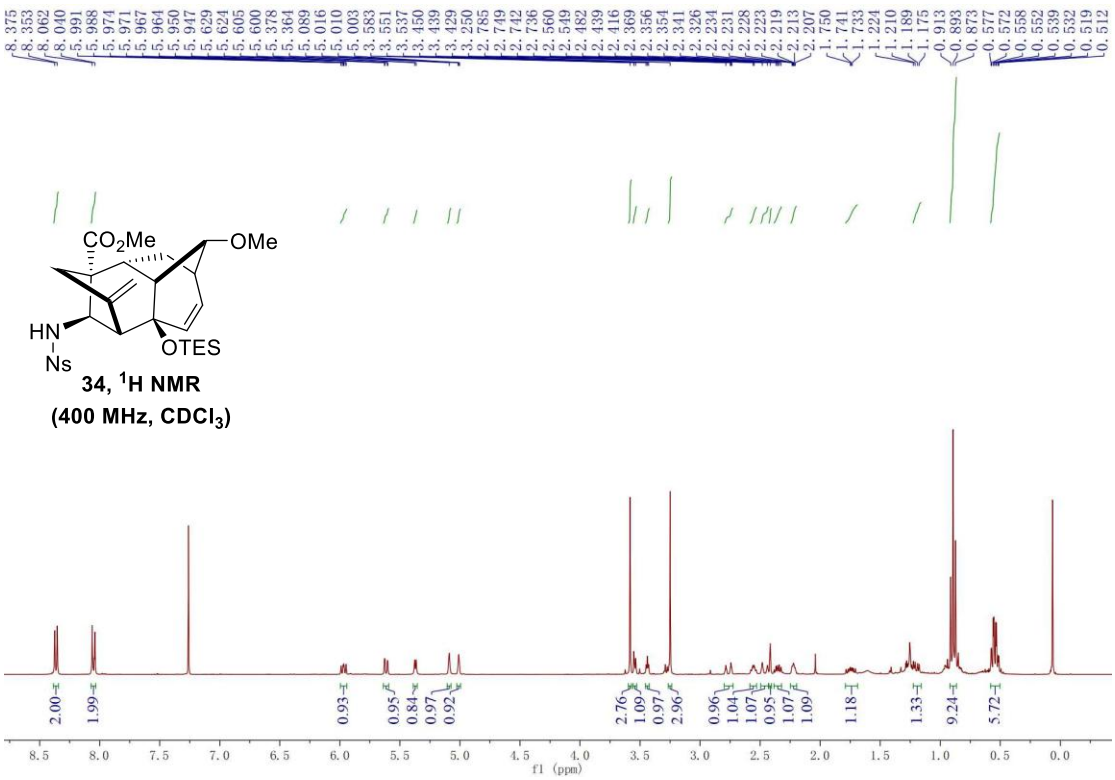
32, ^{13}C NMR
(100 MHz, $CDCl_3$)



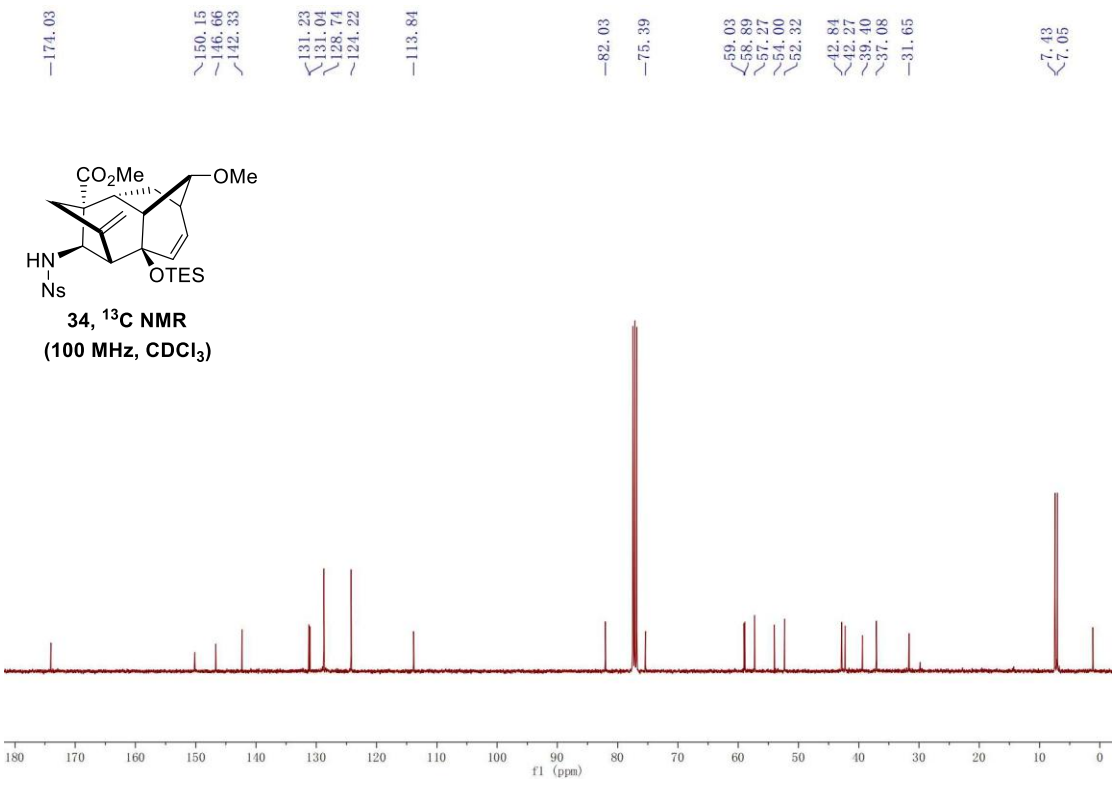
33, ^{1}H NMR
(400 MHz, $CDCl_3$)



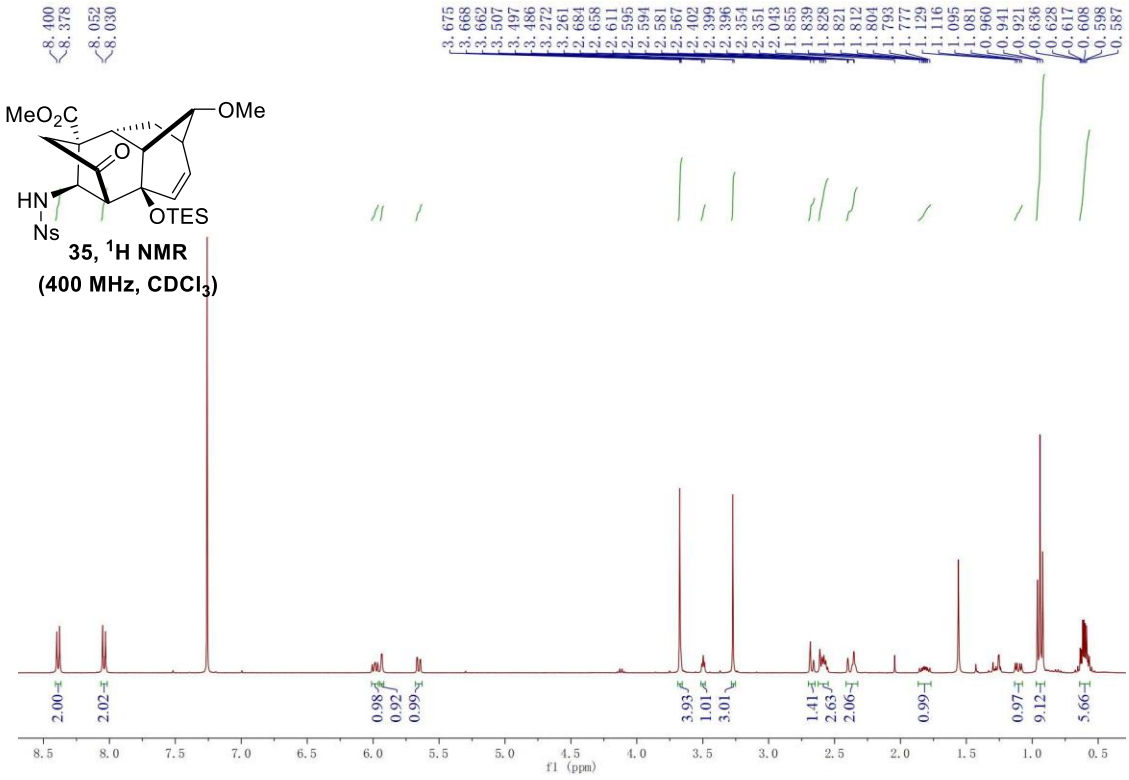
33, ^{13}C NMR
(100 MHz, $CDCl_3$)



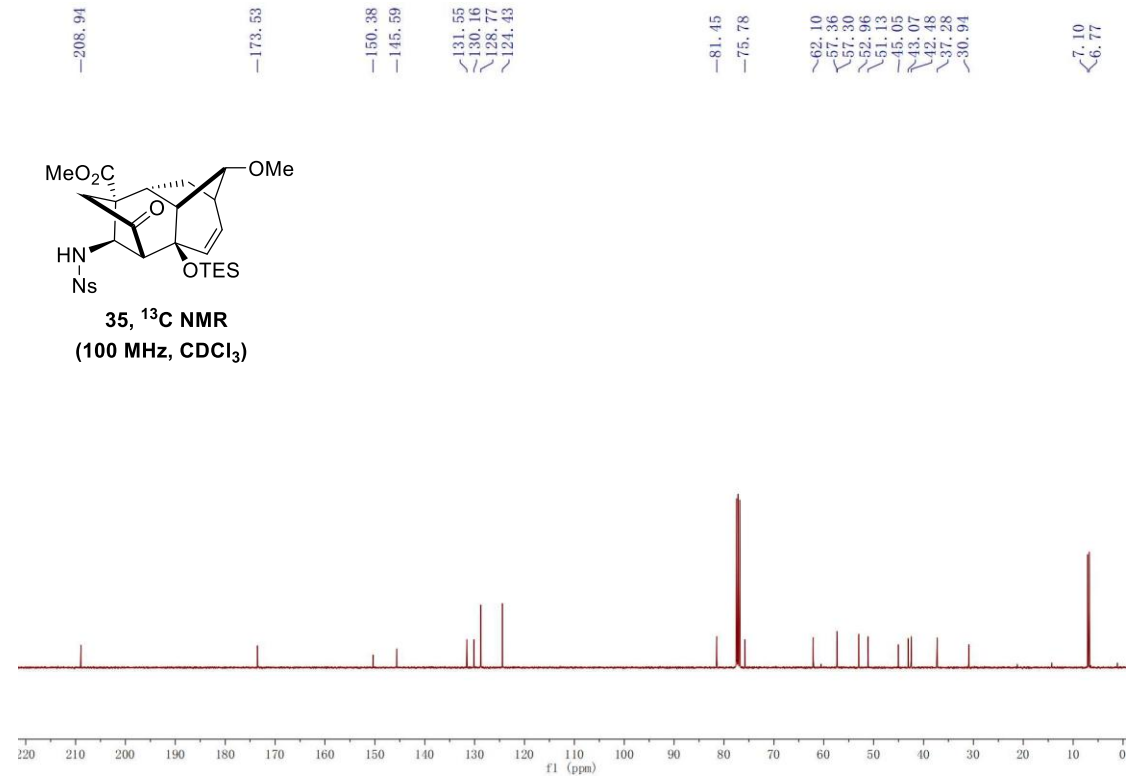
34, ^{1}H NMR
(400 MHz, $CDCl_3$)



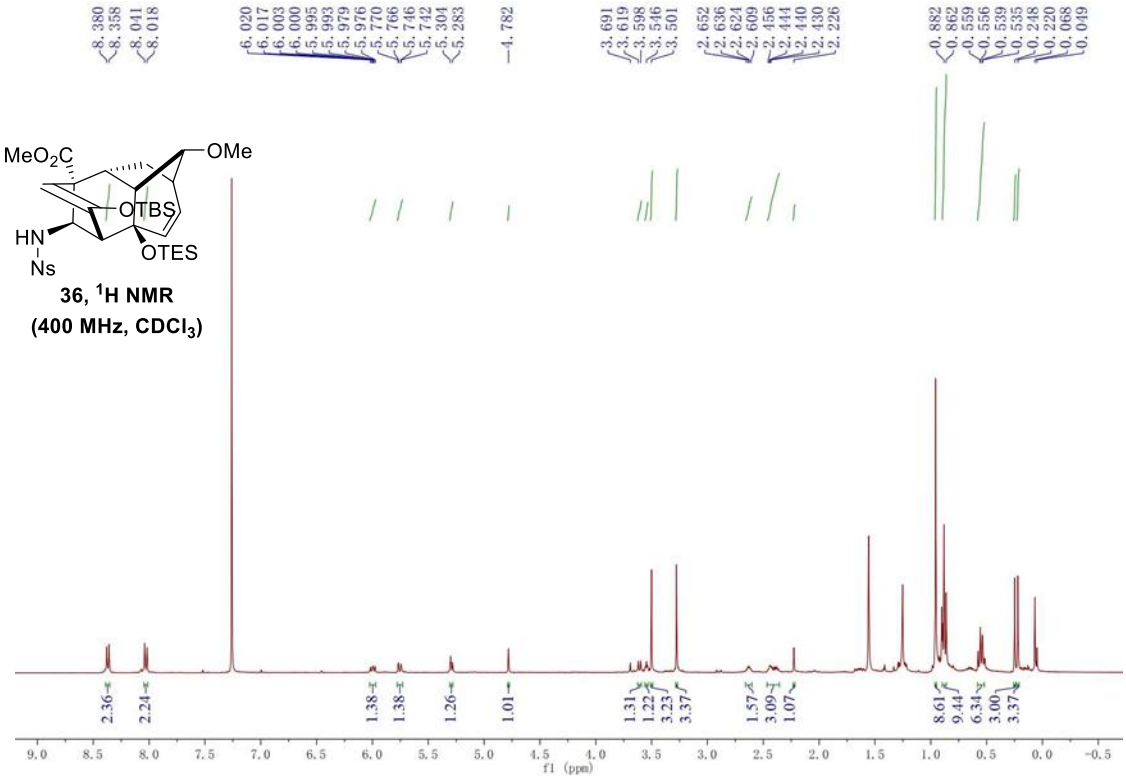
34, ^{13}C NMR
(100 MHz, $CDCl_3$)



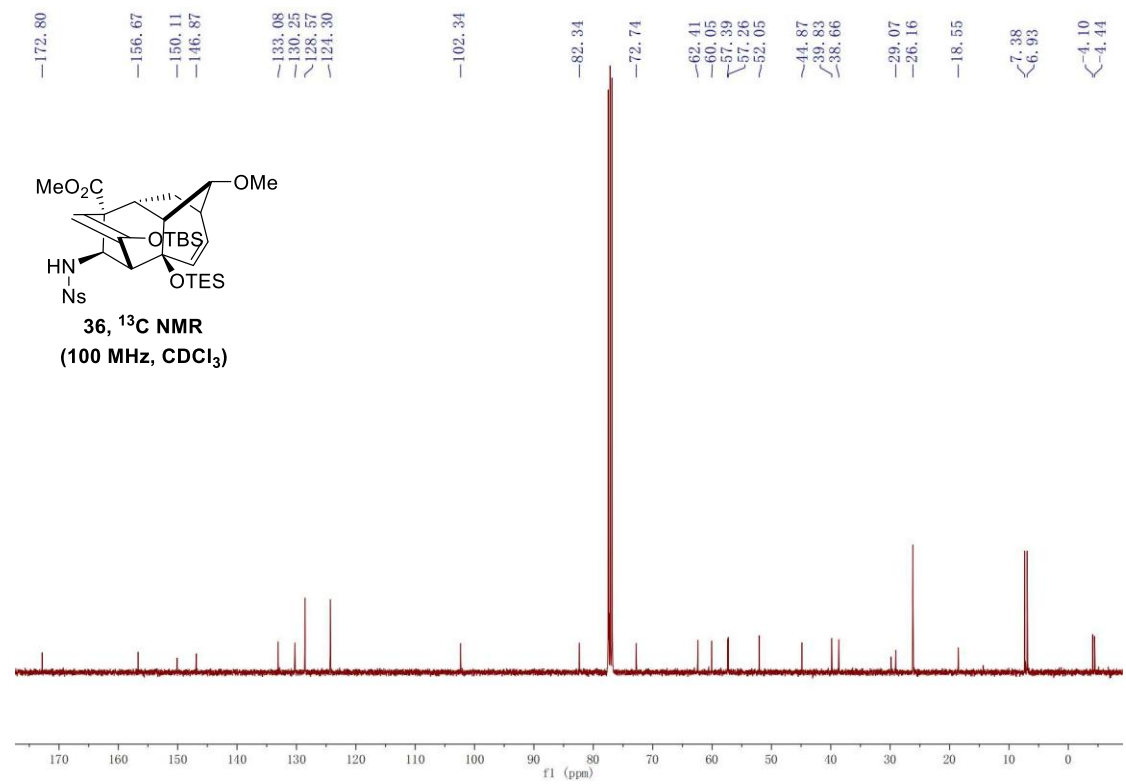
35, ^{1}H NMR
(400 MHz, $CDCl_3$)



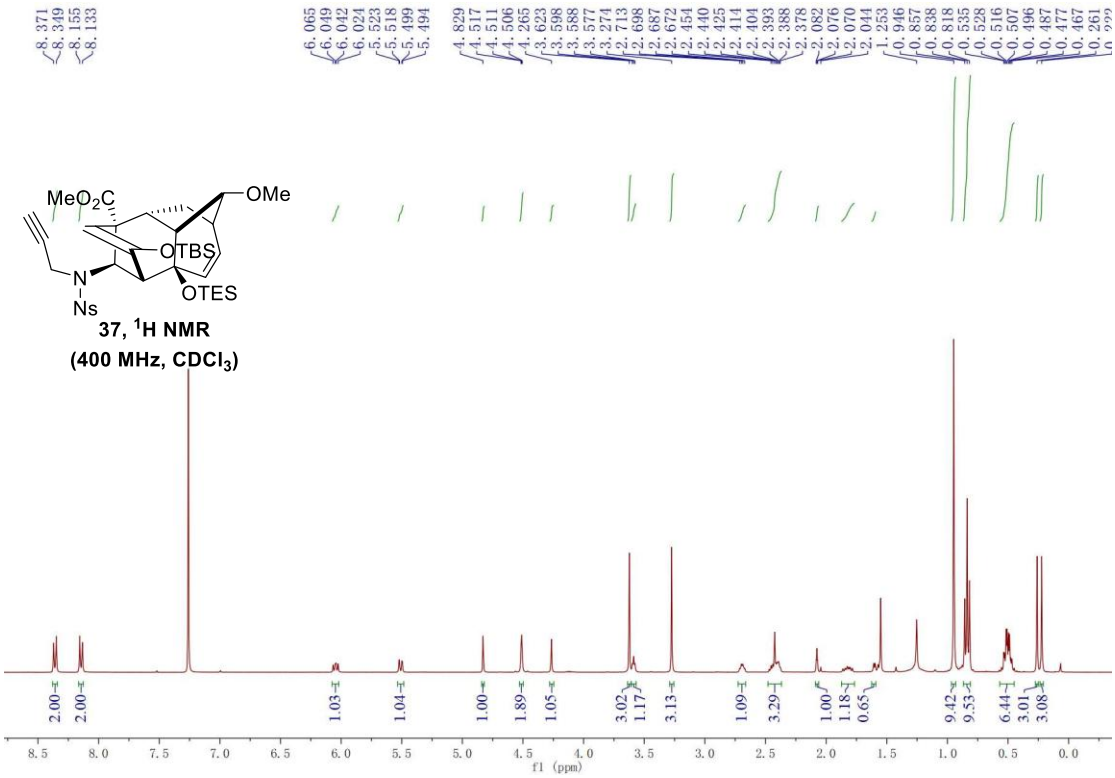
35, ^{13}C NMR
(100 MHz, $CDCl_3$)



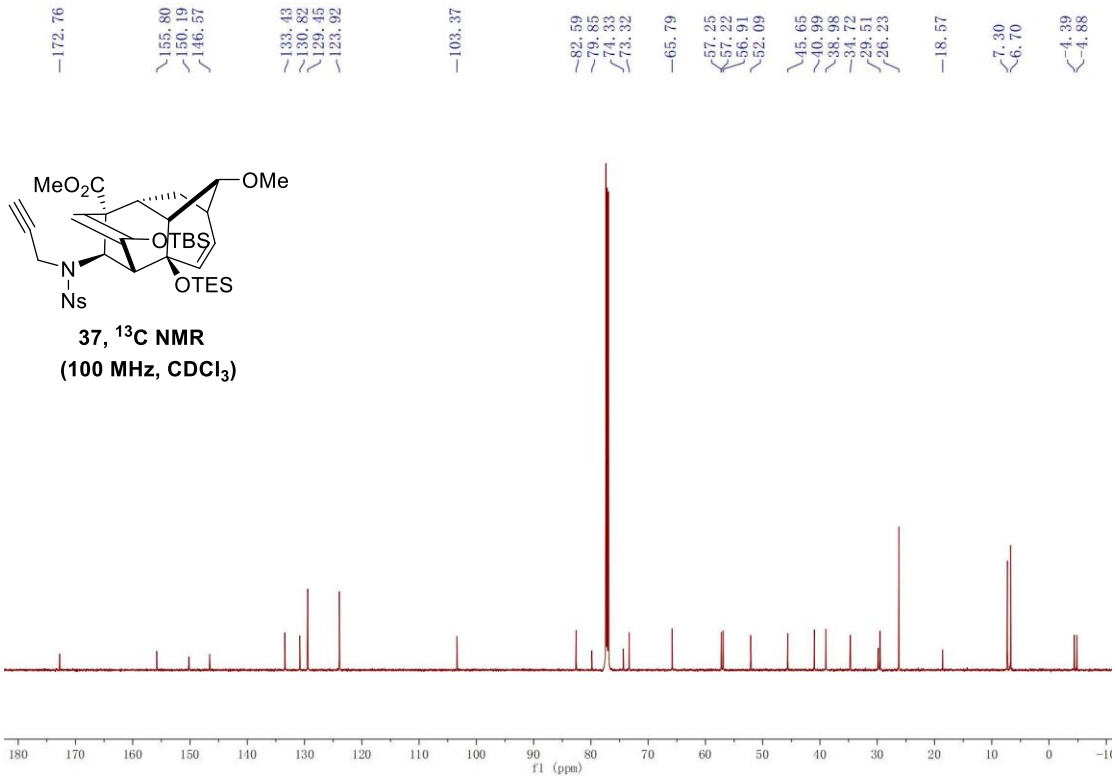
36, ^{1}H NMR
(400 MHz, $CDCl_3$)



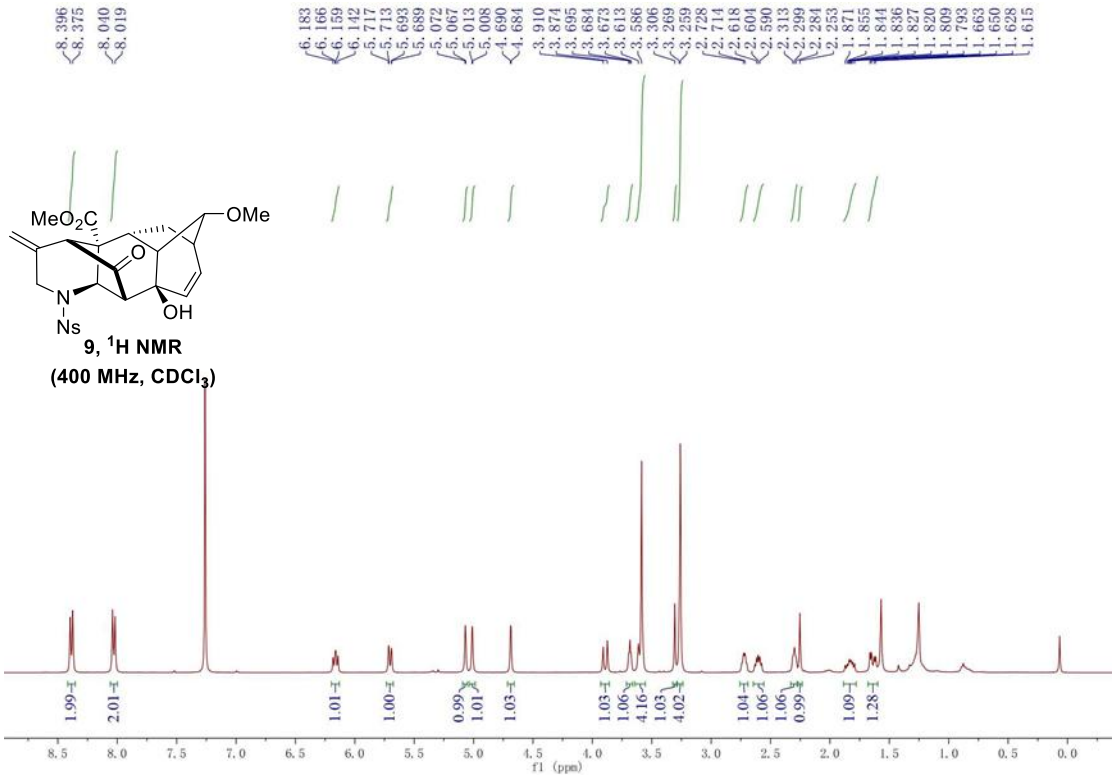
36, ^{13}C NMR
(100 MHz, $CDCl_3$)



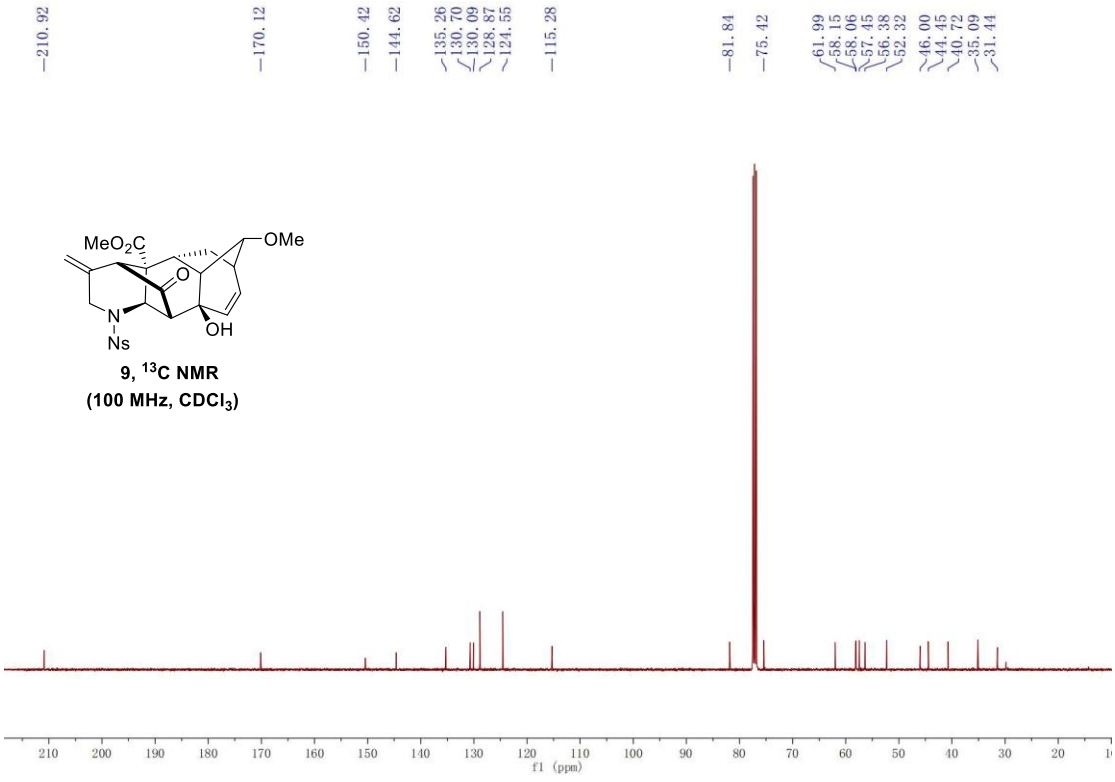
37, ^{1}H NMR
(400 MHz, $CDCl_3$)



37, ^{13}C NMR
(100 MHz, $CDCl_3$)

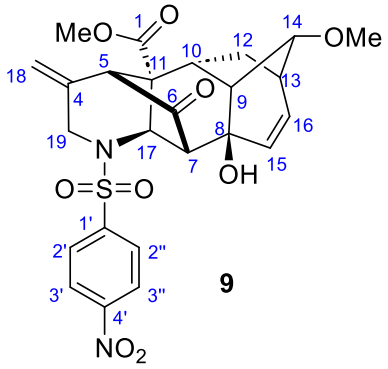


9, ^{1}H NMR
(400 MHz, $CDCl_3$)



9, ^{13}C NMR
(100 MHz, $CDCl_3$)

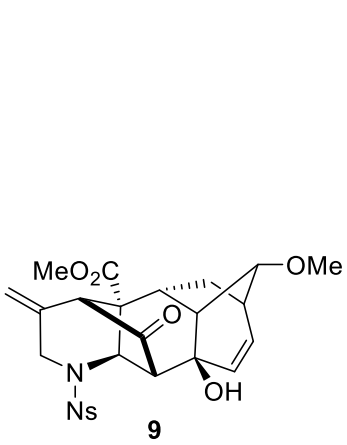
7. 2D-NMR spectra and their interpretations for compound 9



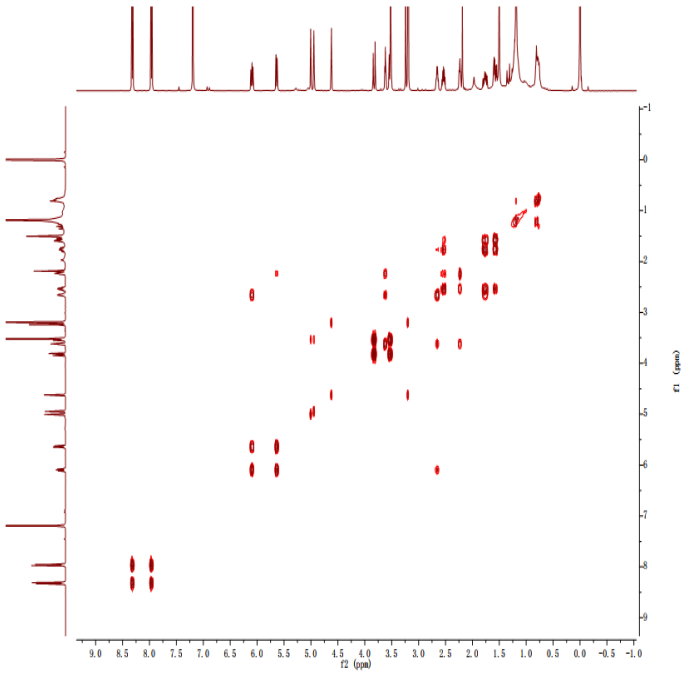
9

Position	δ_C	δ_H	H-H COSY	HMBC (from H to C)	Key-NOESY
1	170.1 (C)	-	-	-	
4	135.3 (C)	-	-	-	
5	62.0 (CH)	3.26 (d, J = 2.4 Hz, 1H)	H_{17}	C_4, C_{18}	H_9, H_{10}, H_{18b}
6	210.9 (C)	-	-	-	-
7	58.1 (CH)	2.25 (s, 1H)	-	C_6, C_8, C_9, C_{15}, C_{17}	H_{15}, $H_{19\beta}$
8	75.4 (C)	-	-	-	-
9	44.4 (CH)	2.30 (t, J = 5.6 Hz, 1H)	H_{10}, H_{14}, H_{15}	C_7, C_8	H_5
10	40.7 (CH)	2.65 – 2.56 (m, 1H)	H_9, H_{12}	C_{11}	H_5, H_{14}
11	56.4 (C)	-	-	-	
12	31.4 (CH_2)	1.87 – 1.79 (m, 1H) β	H_{10}, $H_{12\alpha}$, H_{13}	C_{16}	H_{14}
		1.64 (dd, J = 14.0, 5.2 Hz, 1H) α	H_{10}, $H_{12\beta}$	C_{10}, C_{11}, C_{14}, C_{16}	H_{17}
13	35.1 (CH)	2.74 – 2.70 (m, 1H)	H_{12}, H_{14}		
14	81.8 (CH)	3.68 (t, J = 4.4 Hz, 1H)	H_9, H_{13}	C_8, 14-OMe	H_{10}, $H_{12\beta}$
15	130.1 (CH)	5.70 (dd, J = 9.6, 2.0 Hz, 1H),	H_9, H_{16}		H_7, H_{17}
16	130.7 (CH)	6.16 (dd, J = 9.6, 6.8 Hz, 1H)	H_{13}, H_{15}		
17	58.1 (CH)	4.69 (d, J = 2.4 Hz, 1H)	H_5	C_6, C_7	$H_{12\alpha}$, H_{15}
18	115.3 (CH_2)	5.07 (d, J = 2.0 Hz, 1H) b	H_{18a}	C_5	H_5
		5.01 (d, J = 2.0 Hz, 1H) a	H_{18b}		
19	46.0 (CH_2)	3.89 (d, J = 14.4 Hz, 1H) α	$H_{19\beta}$	C_4, C_{17}, C_{18}	1-OMe
		3.67 (d, J = 14.4 Hz, 1H) β	$H_{19\alpha}$		H_7
1-OMe	52.3 (CH_3)	3.59 (s, 3H)	-	C_1	$H_{19\alpha}$
14-OMe	57.4 (CH_3)	3.26 (s, 3H)	-	C_{14}	
1’	144.6 (C)	-	-	-	-
2’	128.9 (CH)	8.03 (d, J = 8.4 Hz, 2H)	$H_{3'}$	$C_{3'}$	
3’	124.6 (CH)	8.39 (d, J = 8.4 Hz, 2H)	$H_{2'}$	$C_{2'}$	
4’	150.4 (C)	-	-	-	-

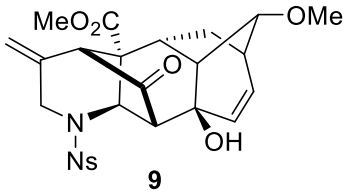
H-H COSY of Compound 9 ($CDCl_3$, 400 MHz)



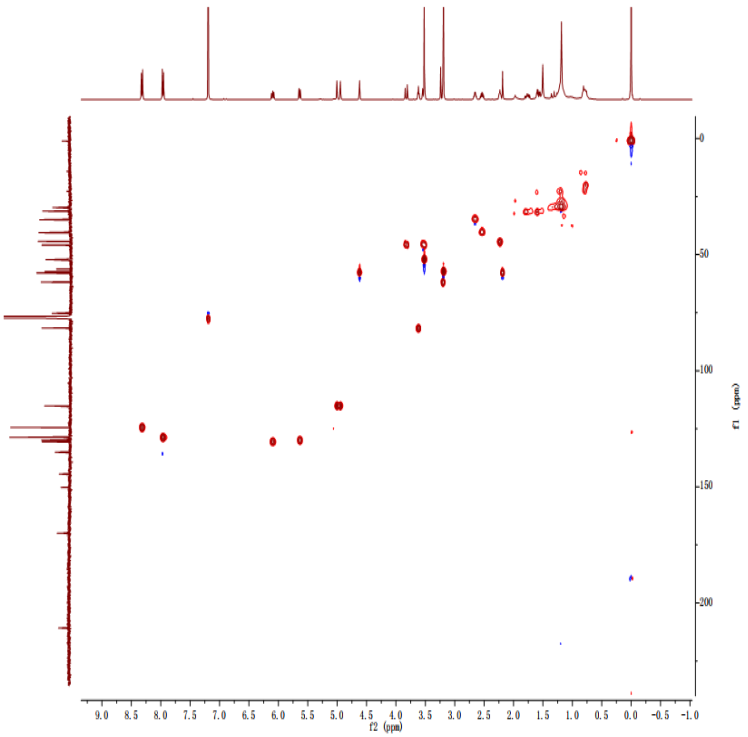
9



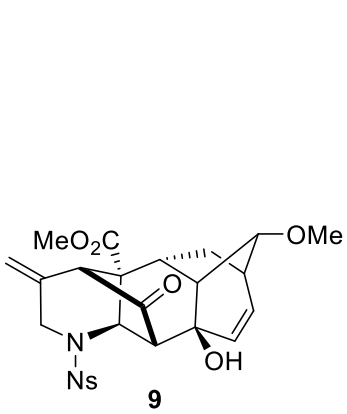
HMQC of Compound 9 ($CDCl_3$, 400 MHz)



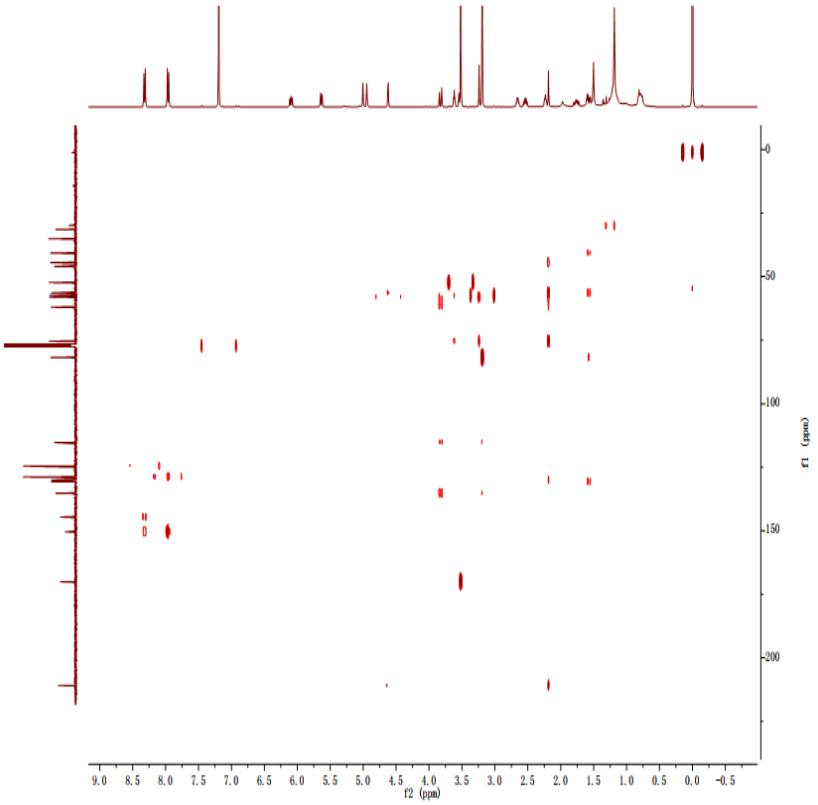
9



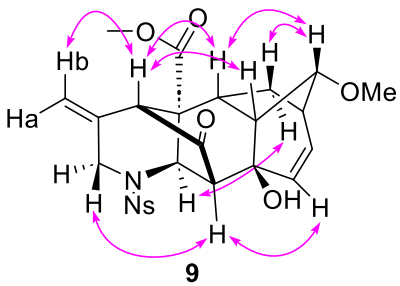
HMBC of Compound 9 ($CDCl_3$, 400 MHz)



9



NOSEY of Compound 9 ($CDCl_3$, 400 MHz)



9