

Supporting Information

Asymmetric Total Synthesis of Norzoanthamine and Formal Synthesis of Zoanthenol

Yanyu, Chen,^a Zhengyuan Xin,^a Hui Wang,^a Haibing He,^b Shuanhu Gao^{*a, b}

^aShanghai Key Laboratory of Green Chemistry and Chemical Processes, School of Chemistry and Molecular Engineering, East China Normal University, 3663N Zhongshan Road, Shanghai 200062, China

^bShanghai Engineering Research Center of Molecular Therapeutics and New Drug Development, East China Normal University, 3663 North Zhongshan Road, Shanghai 200062, China

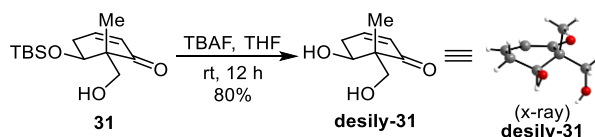
Table of contents

Experimental Procedures and Spectroscopic Data	S2
Reference.....	S35
Copy of NMR spectrum	S36

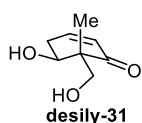
General Experimental Procedures:

Oxygen- and moisture-sensitive reactions were carried out under nitrogen atmosphere. Anhydrous dichloromethane (DCM), 1,2-dichloroethane (DCE) and toluene were distilled from calcium hydride. Tetrahydrofuran (THF) was distilled from sodium-benzophenone ketyl, anhydrous diethyl ether was distilled from sodium. Anhydrous acetone was dried with activated 4Å molecular sieves. All reactions were monitored by thin-layer chromatography with Huang Hai silica gel HSGF254 pre-coated plates (0.2 mm). Column chromatography was carried out on silica gel (200–300 mesh) purchased from Qingdao Haiyang. ^1H and ^{13}C NMR spectra were recorded on a Bruker-500, 400, 300 spectrometers. Chemical shifts for ^1H and ^{13}C NMR spectra are reported in ppm (δ) relative to residue protium in the solvent (CDCl_3 : δ 7.26, 77.0 ppm and the multiplicities are presented as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). High-resolution mass spectra (HRMS) were acquired on Waters Micromass GCT Premier or Bruker Daltonics, Inc. APEXIII 7.0 TESLA FTMS. Mass spectra were acquired on Agilent 5975C.

The compound **23**, **27**, **31**, **32**, **33**, **34**, **35**, **36**, **40a**, **40b**, **41**, **42**, **56-63**, norzoanthamine have been reported by our group.^[1]

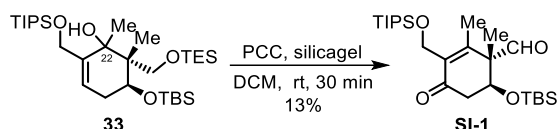


To a solution of **31** (50.0 mg, 0.18 mmol, 1.0 equiv.) in tetrahydrofuran (2 mL) was added tetrabutylammonium fluoride (TBAF, 1.0 M in tetrahydrofuran, 0.6 mL, 0.60 mmol, 3.3 equiv.) at room temperature. It was then stirred at that temperature for 12 h before it was quenched with saturated aqueous ammonium chloride (3 mL) and extracted with ethyl acetate (3×15 mL). The combined organic phases were washed with water and brine, then dried over anhydrous sodium sulfate, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (50% ethyl acetate-petroleum ether) to give **desily-31** (24 mg, 84%).

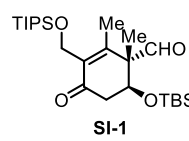


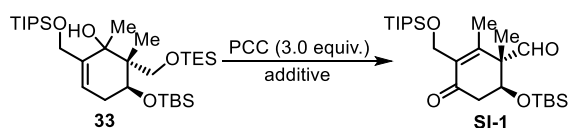
Compound **desily-31**: $R_f = 0.12$ (60% ethyl acetate-petroleum ether), $[\alpha]_D^{20} = -4.46$ ($c = 0.26$ in DCM). ^1H NMR (400 MHz, Acetonitrile- d_3) δ 6.88 (ddd, $J = 10.1, 5.6, 2.7$ Hz, 1H), 5.88 (ddd, $J = 10.1, 2.7, 1.3$ Hz, 1H), 4.23 - 4.18 (m, 1H), 3.77 (dd, $J = 10.8, 5.7$ Hz, 1H), 3.54

(dd, $J = 10.8, 6.2$ Hz, 1H), 3.28 (d, $J = 4.9$ Hz, 1H), 2.83 (t, $J = 5.9$ Hz, 1H), 2.66 – 2.51 (m, 1H), 2.46 – 2.34 (m, 1H), 0.94 (s, 3H) ppm. ^{13}C NMR (100 MHz, Acetonitrile- d_3) δ 204.0, 147.9, 129.3, 69.1, 64.9, 53.7, 32.4, 13.3. IR (neat, cm^{-1}) ν_{max} 3282, 2358, 2368, 1662, 1388, 1197, 1091, 738 cm^{-1} . HRMS–EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_8\text{H}_{12}\text{O}_3$, 156.0786; found, 156.0789. Recrystallization of **desily-31** from ethyl acetate/ petroleum ether gave a crystal suitable for X-ray analysis (CCDC: 2052987).



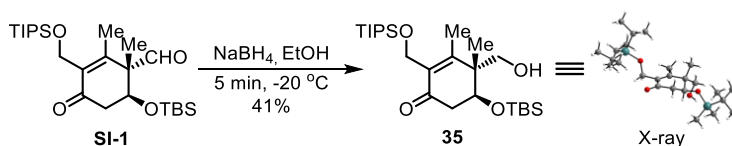
To a stirred mixture of pyridinium chlorochromate (PCC, 32.3 mg, 0.15 mmol, 3.0 equiv.) and silica gel (32.3 mg) in dichloromethane (1 mL) was added a solution of **33** (30.0 mg, 0.05 mmol, 1.0 equiv.) in dichloromethane (1 mL) dropwise at room temperature. The resulting mixture was stirred at room temperature for 1 h. It was then cooled to room temperature and diluted with diethyl ether (2 mL). After stirring for 30 min at room temperature, the resulting mixture was filtrated and the organic phases were concentrated under vacuum. The residue was purified by column chromatography on silica gel (5% ethyl acetate-petroleum ether) to give **SI-1** (3.1 mg, 13%) as a brown oil.


 Compound **SI-1**: $R_f = 0.31$ (1% ethyl acetate-petroleum ether), $[\alpha]_D^{20} = -4.35$ ($c = 0.40$ in DCM). ^1H NMR (500 MHz, CDCl_3) δ 9.54 (s, 1H), 4.56 – 4.39 (m, 3H), 2.72 – 2.52 (m, 2H), 1.99 (s, 3H), 1.35 (s, 3H), 1.11 – 0.99 (m, 21H), 0.83 (s, 9H), 0.07 (s, 3H), 0.01 (s, 3H) ppm. ^{13}C NMR (125 MHz, CDCl_3) δ 201.9, 194.7, 157.9, 137.2, 68.2, 59.3, 55.4, 42.5, 25.6, 18.0, 17.9, 17.6, 12.8, 12.0, -4.1, -5.1. IR (neat, cm^{-1}) ν_{max} 2961, 2858, 1647, 1539, 1112, 1086, 1057, 813 cm^{-1} . $^1\text{HRMS}$ –ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{25}\text{H}_{49}\text{O}_4\text{Si}_2$, 469.3164; found, 469.3159.

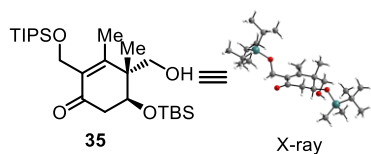


entry	additive	solvent	temp.	yield
1	silicagel	DCM	rt	13%
2	silicagel/CaCO ₃	DCM	rt	0%
3	silicagel	DCE	reflux	23%
4	silicagel/NaOAc	DCE	reflux	28%
5	4ÅMS	DCE	reflux	20%
6	4ÅMS	PhMe/CH ₃ CN	60 °C	35%

Table 1 PCC-mediated oxidation rearrangement

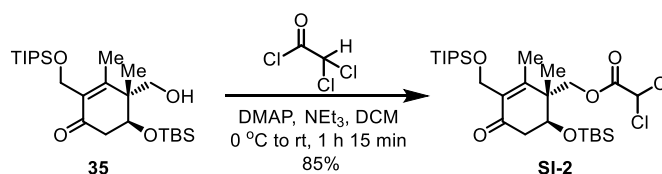


To a solution of **SI-1** (10.0 mg, 0.021 mmol, 1.0 equiv.) in EtOH (1.5 mL) at -20 °C was added NaBH₄ (0.5 mg, 0.013 mmol, 0.6 equiv.). The mixture was stirred for 5 min at -20 °C, and then quenched with saturated ammonium chloride, extracted with ethyl acetate (3×10 mL). The combined organic phase was washed with brine, dried over anhydrous sodium sulfate, concentrated, and purified by silica gel column chromatography (10% ethyl acetate – petroleum ether) to give **35** as a brown solid (4.2 mg, 41%).



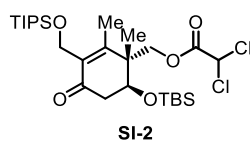
Compound **35**: $R_f = 0.35$ (10% ethyl acetate-petroleum ether); $[\alpha]_D^{20} = -75.5$ ($c = 0.15$ in DCM). ¹H NMR (400 MHz, CDCl₃) δ 4.53 (d, $J = 11.0$ Hz, 1 H), 4.42 (d, $J = 11.0$ Hz, 1 H), 4.27 (dd, $J = 11.1, 5.1$ Hz, 1 H), 3.77

– 3.62 (m, 2 H), 2.66 – 2.50 (m, 2 H), 2.13 (s, 3 H), 1.79 (s, 1 H), 1.12 – 0.96 (m, 24 H), 0.87 (s, 9 H), 0.07 (s, 6 H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ 195.7, 164.0, 136.6, 67.7, 64.3, 55.7, 47.7, 43.0, 25.7, 18.0, 17.9, 15.8, 15.0, 12.0, -4.2, -5.2 ppm. IR (neat, cm⁻¹) ν_{max} 2956, 2349, 1651, 1444, 1201, 777, 680 cm⁻¹. HRMS–EI (m/z): $[M]^+$ calcd for C₂₅H₅₀O₄Si₂, 470.3248; found, 470.3256. M.p. 80–82 °C. Recrystallization of **35** from ethyl acetate gave a crystal suitable for X-ray analysis (CCDC: 2052986).

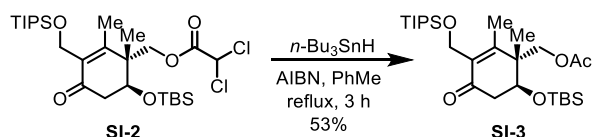


To a solution of **35** (20.0 mg, 0.042 mmol, 1.0 equiv.), 4-dimethylaminopyridine (DMAP) (5.0 mg, 0.042 mmol, 1.0 equiv.) and triethylamine (17.0 μ L, 0.126 mmol, 3.0 equiv.) in dichloromethane (2 mL)

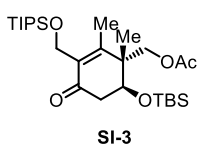
at 0 °C was added dichloroacetyl chloride (6.1 μL, 0.063 mmol, 1.5 equiv.). The resulting mixture was stirred at 0 °C for 15 min and warmed to room temperature while stirring for 1 h before it was quenched with saturated aqueous sodium bicarbonate and extracted with ethyl acetate (3 × 10 mL). The combined organic phases were washed with water, brine and dried over anhydrous sodium sulfate, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (10% ethyl acetate-petroleum ether) to give **SI-2** (21 mg, 85%).



Compound **SI-2**: $R_f = 0.6$ (10% ethyl acetate-petroleum ether); $[\alpha]_D^{20} = +10.5$ ($c = 0.50$ in DCM). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 5.88 (s, 1 H), 4.49 (q, $J = 11.3$ Hz, 2 H), 4.38 – 4.30 (m, 2 H), 4.20 (dd, $J = 11.9, 5.3$ Hz, 1 H), 2.71 – 2.53 (m, 2 H), 2.08 (s, 3 H), 1.12 (s, 3 H), 1.06 – 1.00 (d, $J = 6.4$ Hz, 21 H), 0.88 (s, 9H), 0.08 (s, 3 H), 0.02 (s, 3H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 194.9, 164.0, 161.8, 136.7, 67.8, 67.3, 63.9, 55.6, 46.1, 42.7, 25.7, 18.0, 17.9, 15.7, 14.7, 11.98, 11.95, -4.1, -5.3. IR (neat, cm^{-1}) ν_{max} 2956, 2879, 1771, 1558, 1461, 1086, 777 cm^{-1} . HRMS–ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{27}\text{H}_{51}\text{O}_5\text{Cl}_2\text{Si}_2$, 581.2647; found, 581.2632.



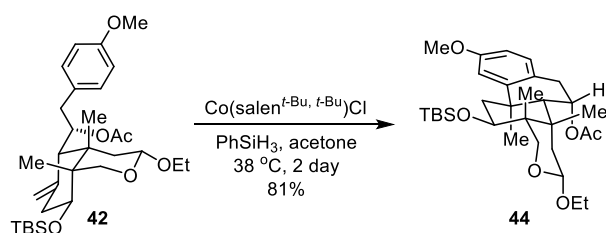
To a stirred solution of **SI-2** (15.0 mg, 0.025 mmol, 1.0 equiv.) in anhydrous degassed toluene (2mL) was heated to reflux and then added dropwise a mixture of tributyltin hydride (35 μL, 0.0125 mmol, 5.0 equiv.) and 2,2'-azoisobutyronitrile (AIBN, 2.1 mg, 0.0125 mmol, 0.5 equiv.) in degassed toluene (0.5 mL) over a period of 20 min. The resultant solution was stirred under reflux for an additional 3 h and cooled to room temperature before it was concentrated under vacuum. The residue was purified by column chromatography on silica gel (5% ethyl acetate-petroleum ether) to give **SI-3** (7.2 mg, 53%) as colorless oil.



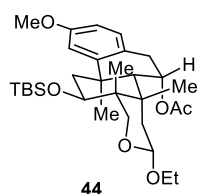
Compound **SI-3**: $R_f = 0.35$ (5% ethyl acetate-petroleum ether); $[\alpha]_D^{20} = +6.84$ ($c = 0.33$ in DCM). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 4.57 (d, $J = 11.4$ Hz, 1 H), 4.43 (d, $J = 11.3$ Hz, 1 H), 4.25 – 4.08 (m, 3 H), 2.65 – 2.55 (m, 2 H), 2.06 (s, 3 H), 2.00 (s, 3 H), 1.14 –

1.00 (m, 24 H), 0.88 (s, 9H), -0.00 (s, 6 H) ppm. ^{13}C NMR (125 MHz, CDCl_3) δ 195.4, 170.7, 163.2, 136.4, 55.7, 45.8, 42.75, 25.7, 20.7, 18.0, 17.9, 15.8, 14.7, 12.0, -4.1, -5.5 ppm. IR (neat, cm^{-1}) ν_{max} 2985, 2880, 1745, 1559, 1260, 1050, 798 cm^{-1} . HRMS–ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{27}\text{H}_{53}\text{O}_5\text{Si}_2$, 513.3426; found, 513.3433.

The preparation of compound 48:

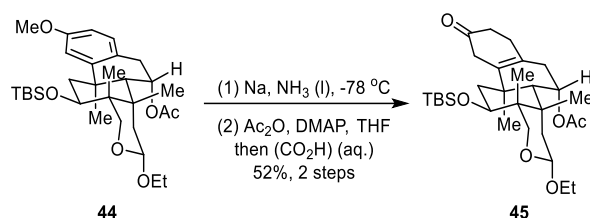


To a solution of compound **42** (370 mg, 0.66 mmol, 1.0 equiv.) in anhydrous acetone (12 mL) was added $\text{Co}(\text{salen}^{t\text{-Bu}}, t\text{-Bu})\text{Cl}$ (42 mg, 0.06 mmol, 0.1 equiv.), then the mixture was degassed through the Freeze-Pump-Thaw cycling before it was added phenylsilane (64 μL , 0.53 mmol, 0.8 equiv.). After stirring for 2 days at 38 $^\circ\text{C}$, the resulting mixture was concentrated under vacuum. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 10/1) to give **44** (300 mg, 81%) as colorless oil.

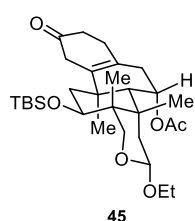


Compound **44**: $R_f = 0.34$ (ethyl acetate/petroleum ether = 1/9); $[\alpha]_{\text{D}}^{20} = +51.9$ ($c = 0.06$ in DCM). ^1H NMR (300 MHz, CDCl_3) δ 6.96 (d, $J = 8.4$ Hz, 1 H), 6.84 (d, $J = 2.5$ Hz, 1 H), 6.72 (dd, $J = 8.4, 2.6$ Hz, 1 H), 5.69 (d, $J = 5.9$ Hz, 1 H), 4.59 – 4.42 (m, 2 H), 3.92 – 3.82 (m, 2 H), 3.81 (s, 3 H), 3.51 (m, 1 H), 3.26 (d, $J = 12.3$ Hz, 1 H), 3.17 (dd,

$J = 18.1, 5.8$ Hz, 1 H), 2.92 (d, $J = 18.1$ Hz, 1 H), 2.24 – 2.13 (m, 2 H), 2.02 (s, 3 H), 1.77 (m, 2 H), 1.68 (s, 3 H), 1.45 – 1.39 (m, 1 H), 1.35 – 1.28 (m, 2 H), 1.26 – 1.21 (m, 4 H), 1.19 (s, 3 H), 0.92 (s, 9 H), 0.59 (s, 3 H), 0.18 (s, 3 H), 0.16 (s, 3 H) ppm. ^{13}C NMR (125 MHz, CDCl_3) δ 170.8, 158.2, 149.6, 130.0, 122.9, 111.1, 110.4, 99.9, 67.9, 67.2, 66.0, 64.1, 55.2, 47.8, 44.8, 41.6, 40.2, 38.6, 38.2, 36.7, 29.1, 25.9, 24.3, 21.9, 18.0, 15.5, 10.1, -4.0, -4.9 ppm. IR (neat, cm^{-1}) ν_{max} 2960, 2885, 2368, 2048, 1556, 1190, 698 cm^{-1} . HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{31}\text{H}_{50}\text{O}_6\text{SiNa}$, 569.3269, found, 569.3266.

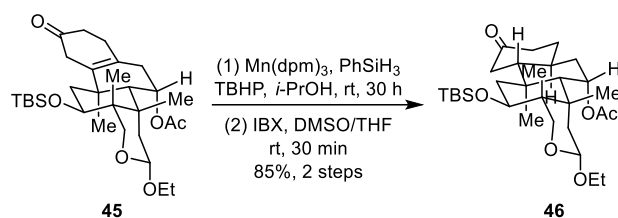


To a stirred anhydrous liquid ammonia (~20 mL) was added sodium (1.3 g, 54.9 mmol, 100.0 equiv.) in small pieces at -78 °C. After stirring for 30 min at -78 °C, a solution of **44** (0.3 g, 0.55 mmol, 1.0 equiv.) in anhydrous tetrahydrofuran (10 mL) was added over 30 min to the solution of sodium in liquid ammonia. After additional stirring for 1 h at -78 °C, the blue reaction solution was treated with ethanol (2.5 mL) dropwise. The resulting suspension was stirring for 5 h at -78 °C and warm to -50 °C for additional 3 h and then quenched with methanol (5 mL), solid ammonium chloride (1.0 g) and diluted with tetrahydrofuran (50 mL) at that temperature. The white mixture was slowly warmed to room temperature to volatilize NH₃ (gas). Then the reaction was quenched with saturated aqueous ammonium chloride (4 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic phases were washed with water, brine and dried over anhydrous sodium sulfate, filtered and concentrated under vacuum for the next step. To a solution of the obtained residue in tetrahydrofuran (10 mL) was added 4-dimethylaminopyridine (DMAP) (0.2 g, 1.65 mmol, 3.0 equiv.) and acetic anhydride (0.16 mL, 1.65 mmol, 3.0 equiv.) at 0 °C. The resulting solution was stirred at 0 °C for 1 h and then warmed to room temperature while stirring for 3 h. the reaction mixture was treated with 1M aqueous oxalic acid (4.4 mL, 4.4 mmol, 8.0 equiv.) and stirred for 3 h. Then the resulting solution was quenched with saturated aqueous ammonium chloride (5 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic phases were washed with water and brine, then dried over anhydrous sodium sulfate, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1/9) to give **45** (0.15 g, 52% over two steps) as colorless oil.

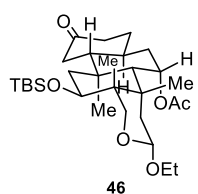


Compound **45**: $R_f = 0.25$ (ethyl acetate/petroleum ether = 1/7); $[\alpha]_D^{20} = +44.9$ (c = 0.15 in DCM). ¹H NMR (500 MHz, CDCl₃) δ 5.53 (d, $J = 5.9$ Hz, 1 H), 4.46 (dd, $J = 13.3, 11.5$ Hz, 1 H), 4.37 (dd, $J = 11.9, 3.9$ Hz, 1 H), 3.88 – 3.77 (m, 2 H), 3.48 (m, 1 H), 3.23 (d, $J = 12.2$ Hz, 1 H), 2.93 – 2.83 (m, 2 H), 2.53 – 2.39 (m, 3 H), 2.32 – 2.24 (m, 2 H), 2.19 – 2.06 (m, 2 H), 2.06 – 2.02 (m, 3 H), 1.66 – 1.61 (m, 1 H), 1.57 (dd, $J = 12.6, 3.9$ Hz, 1 H), 1.48 (s, 3 H), 1.42 (t, $J = 12.2$ Hz, 1 H), 1.30 (dd, $J = 13.6, 1.8$ Hz, 1 H), 1.19 (t, $J = 7.1$ Hz, 3 H), 1.14 (s, 3 H), 0.88 (s, 9 H), 0.60 (s, 3 H), 0.10 (s, 3 H), 0.07 (s, 3 H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ 211.2, 170.8, 135.5,

123.7, 99.8, 67.5, 67.1, 65.7, 64.1, 48.4, 42.4, 41.7, 40.0, 38.7, 38.3, 38.1, 37.9, 37.9, 29.9, 25.9, 24.1, 22.7, 21.9, 18.0, 15.4, 10.1, -4.2, -5.0 ppm. IR (neat, cm^{-1}) ν_{max} 2956, 2873, 2309, 1730, 1653, 1507, 1254, 1070 cm^{-1} . HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{30}\text{H}_{50}\text{O}_6\text{SiNa}$, 557.3269; found, 557.3260. M.p. 150–153 °C.

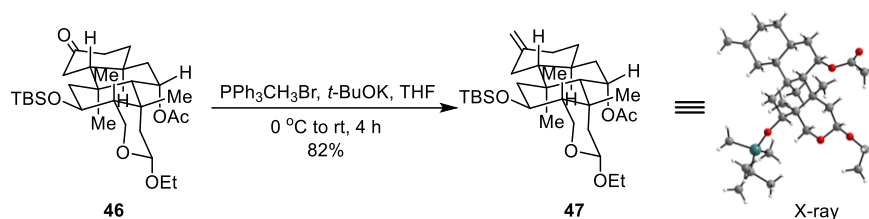


A solution of **45** (140 mg, 0.26 mmol, 1.0 equiv.) in anhydrous isopropanol (3 mL) was added $\text{Mn}(\text{dpm})_3$ (24 mg, 0.04 mmol, 0.15 equiv.) and then subjected to freeze-pump-thaw cycling (four times). To the reaction mixture was added phenylsilane (193 μL , 1.57 mmol, 6.0 equiv.) and tert-butyl hydroperoxide (5.5 M in decane, 307 μL , 1.7 mmol, 6.5 equiv.). After stirring at room temperature for 30 h under nitrogen, the resulting mixture was concentrated under vacuum. The residue was dissolved in the anhydrous dimethyl sulfoxide (4 mL) and tetrahydrofuran (2 mL). The obtained solution was added 2-iodoxybenzoic acid (366 mg, 1.31 mmol, 5.0 equiv.) in three portions and stirred at room temperature for 30 min, then stirred at 50 °C for 5 h. The reaction mixture was cooled to room temperature, diluted with diethyl ether (10 mL) and quenched with saturated aqueous sodium bicarbonate (2 mL) and saturated aqueous sodium thiosulfate (2 mL). The reaction mixture was filtered, washing the filter cake with ethyl acetate (3×30 mL). The filtrate was washed with water and brine, then dried over anhydrous sodium sulfate, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1/5) to give **46** (120 mg, 85%) as colorless oil.

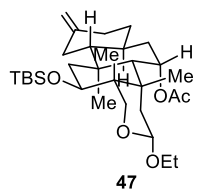


Compound **46**: $R_f = 0.54$ (ethyl acetate/petroleum ether = 1/9); $[\alpha]_{\text{D}}^{20} = +31.2$ ($c = 0.34$ in DCM). ^1H NMR (500 MHz, CDCl_3) δ 5.45 (d, $J = 1.0$ Hz, 1 H), 4.43 (dd, $J = 9.7, 2.1$ Hz, 1 H), 4.31 (dd, $J = 12.1, 4.0$ Hz, 1 H), 3.92 – 3.76 (m, 2 H), 3.48 (m, 1 H), 3.22 (d, $J = 12.2$ Hz, 1 H), 2.36 (m, 3 H), 2.24 – 2.10 (m, 2 H), 2.07 (s, 3 H), 2.02 – 1.83 (m, 3 H), 1.44 (dd, $J = 12.67, 3.83$ Hz, 1 H), 1.37 (s, 3 H), 1.32 – 1.25 (m, 6 H), 1.20 (t, $J = 7.1$ Hz, 3 H), 1.12 (s, 3 H), 0.88 (s, 9 H), 0.58 (s, 3 H), 0.09 (s, 3 H), 0.05 (s, 3 H) ppm. ^{13}C NMR (125 MHz, CDCl_3) δ 212.4, 170.5, 99.8, 69.2, 67.0, 65.2, 64.2, 56.3, 51.5, 44.1, 41.8, 40.9, 40.5, 40.4, 39.2, 38.5, 38.4, 33.4,

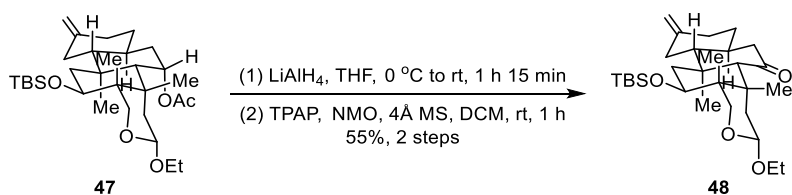
30.6, 25.9, 24.3, 22.0, 18.6, 18.0, 15.5, 10.0, -4.2, -5.1 ppm. IR (neat, cm^{-1}) ν_{max} 2985, 2846, 2379, 1734, 1558, 1246, 1082 cm^{-1} . HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{30}\text{H}_{52}\text{O}_6\text{SiNa}$, 559.3409; found, 559.3409.



To a stirred solution of $\text{PPh}_3\text{CH}_3\text{Br}$ (200 mg, 0.56 mmol, 4.0 equiv.) in tetrahydrofuran (2 mL) was added *t*-BuOK (54 mg, 0.49 mmol, 3.5 equiv.) at room temperature. The resulting mixture was stirred at that temperature for 30 min before a solution of **46** (73 mg, 0.14 mmol, 1.0 equiv.) in tetrahydrofuran (2 mL) was added dropwise at 0 °C. The resulted mixture was stirred at room temperature for 4 h before it was quenched with saturated aqueous ammonium chloride (2 mL) at that temperature and extracted with ethyl acetate (3×10 mL). The combined organic phases were washed with water and brine, then dried over anhydrous sodium sulfate, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1/9) to give **47** (60 mg, 82%) as white solid.

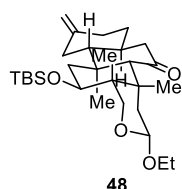


Compound **47**: $R_f = 0.84$ (ethyl acetate/petroleum ether = 1/9); $[\alpha]_{\text{D}}^{20} = +49.2$ ($c = 0.22$ in DCM). ^1H NMR (500 MHz, CDCl_3) δ 5.40 (s, 1 H), 4.64 (s, 2 H), 4.42 (dd, $J = 9.8$, 1.9 Hz, 1 H), 4.35 – 4.28 (m, 1 H), 3.90 – 3.68 (m, 2 H), 3.47 (m, 1 H), 3.21 (d, $J = 12.2$ Hz, 1 H), 2.30 – 2.19 (m, 2 H), 2.14 (dd, $J = 13.5$, 9.9 Hz, 1 H), 2.04 (s, 3 H), 2.00 – 1.93 (m, 1 H), 1.88 – 1.79 (m, 2 H), 1.73 (dd, $J = 12.7$, 2.0 Hz, 1 H), 1.67 – 1.55 (m, 3 H), 1.33 (s, 3 H), 1.31 – 1.28 (m, 1 H), 1.27 – 1.24 (m, 2 H), 1.19 (t, $J = 7.1$ Hz, 3 H), 1.16 – 1.12 (m, 1 H), 1.09 (s, 3 H), 1.03 – 0.92 (m, 1 H), 0.90 (s, 9 H), 0.58 (s, 3 H), 0.10 (s, 3 H), 0.08 (s, 3 H) ppm. ^{13}C NMR (125 MHz, CDCl_3) δ 170.6, 149.6, 107.2, 99.9, 69.7, 67.1, 65.6, 64.1, 57.5, 51.9, 44.4, 41.8, 40.4, 40.0, 38.5, 38.3, 35.4, 34.5, 33.5, 31.2, 25.9, 24.3, 22.0, 18.9, 18.0, 15.5, 10.1, -4.1, -5.0 ppm. IR (neat, cm^{-1}) ν_{max} 2944, 2880, 2331, 1653, 1539, 1086, 794 cm^{-1} . HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{31}\text{H}_{54}\text{O}_5\text{SiNa}$, 557.3633; found, 557.3618. Recrystallization of **47** from ethyl ether/dichloromethane gave a crystal suitable for X-ray analysis (CCDC: 2048713).



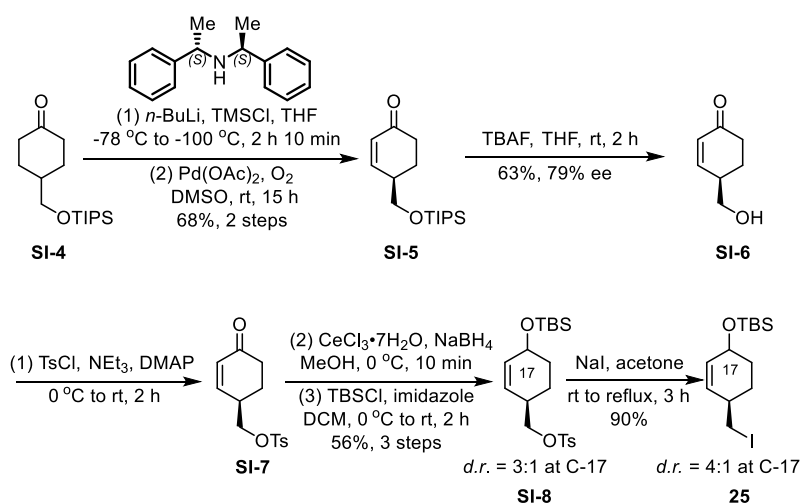
To a stirred solution of **47** (50 mg, 0.09 mmol, 1.0 equiv.) in tetrahydrofuran (3 mL) at 0 °C was added lithium aluminum hydride (9 mg, 0.23 mmol, 2.5 equiv.). After stirring for 15 min at 0 °C, the reaction mixture was warmed to room temperature and stirred for 1 h. The reaction mixture was cooled to 0 °C and quenched with water (50 μ L) carefully and added 10% aqueous sodium hydroxide (50 μ L). Then the resulting suspension was warmed up to room temperature and vigorously stirred for 1 h. The reaction mixture was filtered, washing the filter cake with ethyl acetate (20 mL), and the filtrate was dried over anhydrous sodium sulfate, filtrated and concentrated under vacuum to get crude alcohol compound for the next step.

An oven-dried flask was charged with the obtained alcohol compound, 4-methylmorpholine N-oxide (18 mg, 0.15 mmol, 17.0 equiv.) and 4Å molecule sieve (50 mg) in dichloromethane (2 mL). tetrapropylammonium perruthenate (TPAP) (4.2 mg, 0.011 mmol, 0.12 equiv.) was added at 0 °C and the resulting mixture was warmed to room temperature. After stirring at room temperature for 2 h, the mixture was directly loaded onto column chromatography and purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1/9) to give ketone **48** (25 mg, 55% over two steps) as colorless oil.

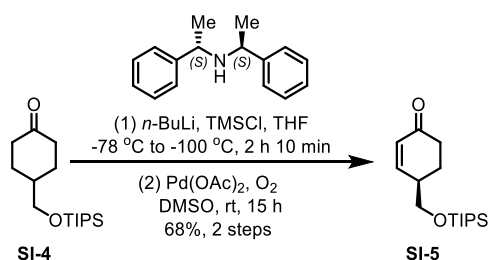


Compound **48**: R_f = 0.6 (ethyl acetate/petroleum ether = 1/9) $[\alpha]_D^{20} = +30.5$ ($c = 0.41$ in DCM). ¹H NMR (500 MHz, CDCl₃) δ 4.72 – 4.68 (m, 2 H), 4.53 (dd, $J = 9.8, 2.2$ Hz, 1 H), 4.36 (dd, $J = 12.0, 4.4$ Hz, 1 H), 3.92 – 3.82 (m, 1 H), 3.75 (d, $J = 12.1$ Hz, 1 H), 3.53 – 3.47 (m, 1 H), 3.26 (d, $J = 12.1$ Hz, 1 H), 2.58 (dd, $J = 13.8, 2.1$ Hz, 1 H), 2.40 (s, 1 H), 2.29 (dd, $J = 13.2, 4.9$ Hz, 3 H), 2.08 – 1.93 (m, 2 H), 1.89 (dd, $J = 13.8, 9.9$ Hz, 1 H), 1.82 – 1.78 (m, 3 H), 1.65 (dd, $J = 12.9, 4.4$ Hz, 1 H), 1.44 (t, $J = 12.4$ Hz, 1 H), 1.38 (td, $J = 11.9, 3.4$ Hz, 1 H), 1.21 (t, $J = 7.1$ Hz, 3 H), 1.14 (dd, $J = 13.2, 3.5$ Hz, 1 H), 1.11 (s, 3 H), 0.97 (s, 3 H), 0.90 (s, 9 H), 0.60 (s, 3 H), 0.11 (s, 3 H), 0.08 (s, 3 H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ 210.6, 148.2, 108.4, 99.8, 66.3, 65.3, 64.1, 62.5, 57.0, 50.9, 42.4, 42.2, 41.0, 39.1, 38.3, 36.0, 35.5, 34.3, 33.7, 25.9, 22.3, 18.0, 17.6, 15.5, 9.8, -4.2, -5.0 ppm. IR (neat, cm⁻¹) ν_{max} 2961, 2855, 1734, 1653, 1520, 1096 cm⁻¹. EI (m/z): $[M-C_4H_9]^+$ calcd for C₂₉H₅₀O₄Si-57,433; found, 433.

The preparation of the perhydrophenanthrene A-B-C ring via Fe-catalyzed hydrogen atom transfer (HAT) reaction:

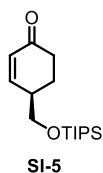


Scheme S1: Synthesis of Compound 25

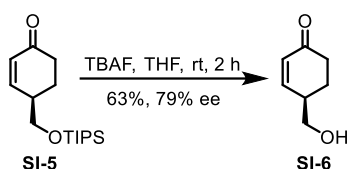


To a stirred solution of (-)-Bis[(*S*)-1-phenylethyl]amine (0.43 g, 1.89 mmol, 1.8 equiv) in dry tetrahydrofuran (10 mL) at -78 °C was added *n*-BuLi (2.5 M in hexane, 0.84 mL, 2.1 mmol, 2.0 equiv.) dropwise. The mixture was stirred at this temperature for 10 min. The resulting solution was cooled to -100 °C and chlorotrimethylsilane (0.53 mL, 4.2 mmol, 4.0 equiv.) was added, followed by a solution of **SI-4** (0.3 g, 1.05 mmol, 1.0 equiv.) in tetrahydrofuran (2.5 mL). The mixture was stirred at this temperature for 2 h, then triethylamine (0.5 mL) was added dropwise. The solution was transferred to cooled (0 °C) aqueous sodium bicarbonate in portions. The organic layer was separated, and the aqueous phase was extracted with ethyl acetate (3 × 50 mL). The combined organic phases were dried over anhydrous sodium sulfate, filtered and evaporated in vacuum. The residue was purified by column chromatography on silica gel (ethyl acetate /petroleum ether, 1/19) to give the silyl enol ether (380 mg) as colorless oil. The obtained oil was dissolved in dimethyl sulfoxide (5 mL) and treated with palladium (II) acetate (47 mg, 0.21 mmol, 0.2 equiv.) under an atmosphere of O₂ at room temperature for 15 h. The

reaction mixture was filtered through silica gel, washing the filter cake with ethyl acetate (2 × 50 mL). The filtrate was evaporated in vacuum and the residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1/15) to give ketone **SI-5** (0.26 g, 68% over two steps).^[2]

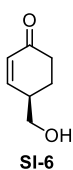


Compound **SI-5**: $R_f = 0.25$ (ethyl acetate/petroleum ether = 1/10); $[\alpha]_D^{20} = +191.8$ ($c = 0.24$ in DCM). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 6.98 (dd, $J = 10.2, 1.1$ Hz, 1 H), 6.03 (dd, $J = 10.2, 2.3$ Hz, 1 H), 3.76 (dd, $J = 9.6, 6.4$ Hz, 1 H), 3.69 (dd, $J = 9.6, 6.9$ Hz, 1 H), 2.67 – 2.57 (m, 1 H), 2.54 – 2.48 (m, 1 H), 2.40 – 2.33 (m, 1 H), 2.14 – 2.00 (m, 1 H), 1.83 – 1.71 (m, 1 H), 1.13 – 1.00 (m, 21 H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 199.9, 152.1, 129.9, 65.9, 39.5, 36.7, 25.4, 18.0, 11.9 ppm. IR (neat, cm^{-1}) ν_{max} 2866, 2361, 2341, 2141, 689, 656 cm^{-1} . HRMS–ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{16}\text{H}_{31}\text{O}_2\text{Si}$, 283.2088, found, 283.2081.

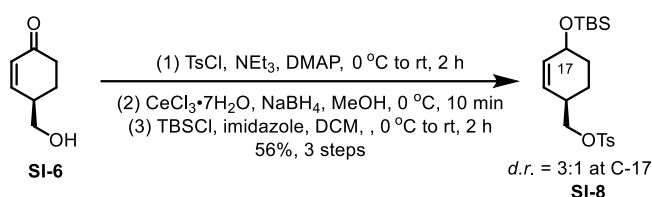


To a stirred solution of compound **SI-5** (260 mg, 0.92 mmol, 1.0 equiv.) in tetrahydrofuran (10 mL) was added tetrabutylammonium fluoride (1.0 M in tetrahydrofuran, 1.84 mmol, 1.84 mL, 2.0 equiv.) at room temperature. The resulting solution was stirred for 2 h, before it was quenched with saturated aqueous ammonium chloride (2 mL) and extracted with ethyl acetate (3 × 40 mL). The combined organic phases were washed with water and brine, then dried over anhydrous sodium sulfate, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 2/1) to give compound **SI-6** (74 mg, 63%, 80 ee) as a yellow oil.

Enantiomeric excess was determined by HPLC analysis, ee = 79% (Chiralpak column AS-H, $\lambda = 240$ nm, n -hexane/ i -PrOH = 70:30, flow rate: 0.8 mL/min, $t_r(\text{major}) = 13.23$ min, $t_r(\text{minor}) = 27.99$). $[\alpha]_D^{20} = +66.0$ ($c = 0.10$ in CDCl_3)(79% ee). Litt^[3] $[[\alpha]_D^{20} = +135$ ($c = 1.21$ in CHCl_3)(98% ee).



Compound **SI-6**: $R_f = 0.33$ (methanol/dichloromethane 1/19) ; $[\alpha]_D^{20} = +66.0$ ($c = 0.10$ in CDCl_3). $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.01 – 6.86 (m, 1 H), 6.07 (dd, $J = 10.2, 2.0$ Hz, 1 H), 3.77 – 3.65 (m, 2 H), 2.70 – 2.57 (m, 1 H), 2.62 – 2.25 (m, 2 H), 2.17 – 2.03 (m, 1 H), 1.87 – 1.77 (m, 1 H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 199.5, 151.1, 130.4, 65.3, 39.0, 36.6, 25.4 ppm. IR (neat, cm^{-1}) ν_{max} 2388, 2338, 1247, 603, 572 cm^{-1} . HRMS–EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_7\text{H}_{10}\text{O}_2$, 126.0681; found, 126.0682. The NMR and specific rotation data were in consistent with the report of Rawal group.^[4]

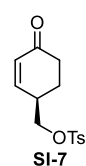


To a stirred solution of **SI-6** (74 mg, 0.59 mmol, 1.0 equiv.), triethylamine (0.2 mL, 1.46 mmol, 2.5 equiv.) and 4-dimethylaminopyridine (DMAP) (36 mg, 0.29 mmol, 0.5 equiv.) in dichloromethane (4 mL) at 0 °C was added 4-tosyl chloride (233 mg, 1.17 mmol, 2.0 equiv.) in one portion. Then the resulting solution was warmed to room temperature and stirred for 2 h, before it was quenched with saturated aqueous sodium bicarbonate (2 mL) and extracted with ethyl acetate (3×50 mL). The combined organic phases were washed with water and brine, then dried over anhydrous sodium sulfate, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1/3) to give unstable ketone **SI-7** (130 mg, 80%) as a yellow oil.

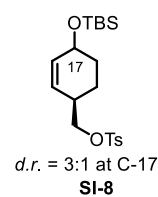
To a stirred solution of the obtained crude ketone (130 mg, 0.46 mmol, 1.0 equiv.) in methanol (5 mL) was added cerium (III) chloride heptahydrate (172 mg, 0.46 mmol, 1.0 equiv.). The resulting mixture was cooled to 0 °C and added NaBH_4 (35 mg, 0.92 mmol, 2.0 equiv.) in portions. After stirring for 10 min at 0 °C, The resulting mixture was quenched with saturated aqueous ammonium chloride (2 mL) and extracted with ethyl acetate (3×40 mL). The combined organic phases were washed with water and brine, then dried over anhydrous sodium sulfate, filtered and concentrated under vacuum to give crude alcohol (100 mg) as a yellow oil for the next step.

To a stirred solution of the obtained crude alcohol (100 mg) in dichloromethane (3 mL) was added imidazole (78 mg, 1.15 mmol, 2.5 equiv.), 4-dimethylaminopyridine (DMAP) (28 mg, 0.23 mmol, 0.5

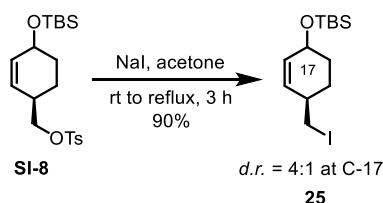
equiv.) at 0 °C. Then the resulting solution was added tertbutyldimethylsilyl chloride (103 mg, 0.69 mmol, 1.5 equiv.) and warmed to room temperature while stirring for 2 h. The resulting mixture was quenched with saturated aqueous ammonium chloride (2 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic phases were washed with water and brine, then dried over anhydrous sodium sulfate, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1/19) to give compound **SI-8** [130 mg, 71% over two steps, *d.r.* = 3:1 at C-17 (by ¹H NMR)] as a yellow oil.



Compound **SI-7**: $R_f = 0.3$ (ethyl acetate/petroleum ether = 1/1). ¹H NMR (300 MHz, CDCl₃) δ 7.79 (d, $J = 8.3$ Hz, 2 H), 7.36 (d, $J = 8.3$ Hz, 2 H), 6.74 (d, $J = 10.2$ Hz, 1 H), 6.03 (dd, $J = 10.2$, 2.4 Hz, 1 H), 4.07 – 3.97 (m, 2 H), 2.87 – 2.74 (m, 1 H), 2.54 – 2.47 (m, 1 H), 2.46 (s, 3 H), 2.42 – 2.28 (m, 1 H), 2.15 – 2.01 (m, 1 H), 1.87 – 1.58 (m, 1 H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ 198.2, 148.0, 145.2, 132.5, 131.1, 123.0, 127.8, 71.1, 36.1, 35.9, 25.2, 21.6 ppm.

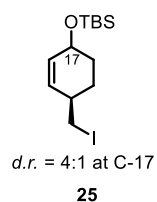


Compound **SI-8**: $R_f = 0.27$ (ethyl acetate/petroleum ether = 1/20); ¹H NMR (500 MHz, CDCl₃) δ 7.79 – 7.77 (m, 2 H), 7.34 (d, $J = 8.1$ Hz, 2 H), 5.76 – 5.72 (m, 0.24 H), 5.70 – 5.66 (m, 0.66 H), 5.52 (dd, $J = 10.1$, 2.1 Hz, 0.24 H), 5.46 (d, $J = 10.1$ Hz, 0.76 H), 4.21 – 4.08 (m, 1 H), 3.90 – 3.80 (m, 2 H), 2.45 (s, 3 H), 1.95 – 1.79 (m, 2 H), 1.64 – 1.43 (m, 2 H), 1.32 – 1.17 (m, 1 H), 0.88 – 0.86 (m, 9 H), 0.06 – 0.04 (m, 6 H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ 144.7, 134.6, 133.7, 133.0, 129.8, 127.9, 127.9, 127.0, 126.9, 73.3, 72.5, 67.1, 65.4, 35.2, 34.8, 31.2, 29.7, 29.5, 25.9, 23.6, 21.6, 20.9, 18.2, 18.2, -4.6, -4.7 ppm. IR (neat, cm⁻¹) ν_{\max} 3061, 2908, 2804, 2368, 1550, 1120, 777, 574 cm⁻¹. HRMS–ESI (*m/z*): [M+Na]⁺ calcd for C₂₀H₃₂O₄SiNa, 419.1688; found, 419.1676.

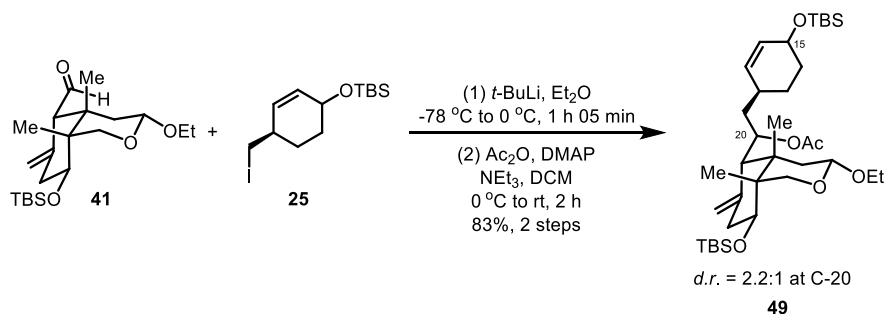


To a solution of **SI-8** (260 mg, 0.66 mmol, 1.0 equiv.) in acetone (5 mL) was added sodium iodide (492 mg, 3.28 mmol, 5.0 equiv.) in one portion at room temperature. The resulting mixture was stirred under reflux for 3 h and cooled to room temperature, then it was quenched with saturated aqueous sodium thiosulfate (2 mL) and extracted with ethyl acetate (3 × 40 mL). The combined organic phases were

washed with water and brine, then dried over anhydrous sodium sulfate, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1/49) to give compound **25** [210 mg, 90%, *d.r.* = 3:1 (by ^1H NMR)] as pink oil.



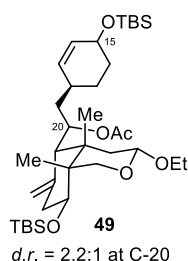
Compound **25**: $R_f = 0.77$ (ethyl acetate/petroleum ether = 1/20). ^1H NMR (500 MHz, CDCl_3) δ 5.77 – 5.66 (m, 1.2 H), 5.56 (dd, $J = 10.1, 1.6$ Hz, 0.8 H), 4.22 – 4.17 (m, 0.8 H), 4.16 – 4.12 (m, 0.2 H), 3.22 – 3.06 (m, 2 H), 2.38 – 2.28 (m, 2 H), 2.01 – 1.92 (m, 1 H), 1.58 – 1.51 (m, 1 H), 1.35 – 1.29 (m, 1 H), 0.90 – 0.84 (m, 9 H), 0.10 – 0.05 (m, 6 H) ppm. ^{13}C NMR (125 MHz, CDCl_3) δ 133.8, 132.2, 131.0, 130.8, 67.5, 65.4, 37.8, 37.3, 31.9, 30.0, 28.1, 25.9, 25.0, 18.2, 18.2, 14.0, 12.0, -4.5, -4.5, -4.6, -4.7 ppm.



To a solution of alkyl iodide fragment **25** (194 mg, 0.55 mmol, 3.0 equiv.) in diethyl ether (5 mL) at -78 °C was added $t\text{-BuLi}$ (1.3M solution in pentane, 0.61 mL, 0.80 mmol, 4.3 equiv.) dropwise. After stirring at -78 °C for 15 min, a solution of aldehyde **41** (71 mg, 0.184 mmol, 1.0 equiv.) in tetrahydrofuran (2 mL) was added. The reaction flask was stirred at -78 °C for additional 20 min and then slowly warmed to 0 °C over the course of 0.5 h. The reaction mixture was quenched with saturated aqueous ammonium chloride and warmed to room temperature. The aqueous layer was extracted with ethyl acetate (3×35 mL) and the combined organic layers were washed with brine, dried over anhydrous sodium sulfate and concentrated in vacuum. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1/5) afforded fragment-coupling product (100 mg) as a colorless oil for the next step.

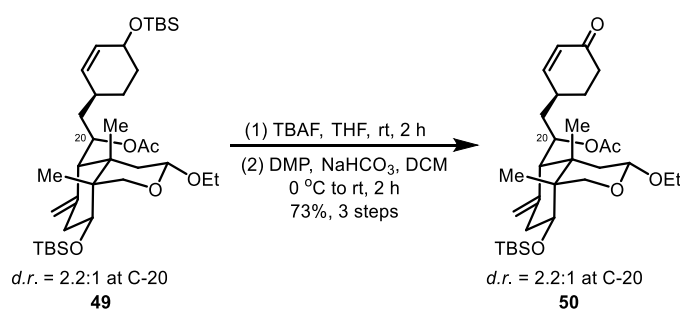
To a stirred solution of the obtained crude oil (100 mg, 0.186 mmol, 1.0 equiv.) in dichloromethane (3 mL) was added acetic anhydride (37 μL , 0.373 mmol, 2.0 equiv.), 4-dimethylaminopyridine (DMAP) (23 mg, 0.186 mmol, 1.0 equiv.) at 0 °C. Then the resulting solution was warmed to room temperature while stirring for 2 h. The obtained mixture was quenched with saturated aqueous ammonium chloride (2 mL)

and extracted with ethyl acetate (3 × 30 mL). The combined organic phases were washed with water and brine, then dried over anhydrous sodium sulfate, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1/9) to give compound **49** [100 mg, 83% over two steps, *d.r.* = 2.2:1 at C-20 (by ¹N NMR analysis)] as a colorless oil.



Compound **49**: R_f = 0.61 (ethyl acetate/petroleum ether = 1/9). ¹H NMR (500 MHz, CDCl₃) δ 5.68 – 5.55 (m, 2 H), 5.51 – 5.45 (m, 1 H), 5.20 (s, 1 H), 5.07 (s, 1 H), 4.48 (dd, J = 10.2, 2.3 Hz, 1 H), 4.31 – 4.10 (m, 2 H), 3.92 – 3.79 (m, 1 H), 3.65 (d, J = 12.1 Hz, 1 H), 3.50 – 3.40 (m, 1 H), 3.28 (d, J = 12.1 Hz, 1 H), 2.29 (dd, J = 12.0, 5.0 Hz, 1 H), 2.21 – 2.13 (m, 2 H), 2.04 – 1.98 (m, 4 H), 1.95 – 1.90 (m, 2 H), 1.87 – 1.75 (m, 2

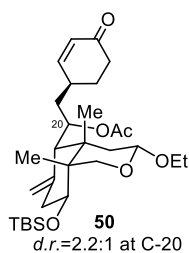
H), 1.70 – 1.60 (m, 2 H), 1.53 – 1.43 (m, 1 H), 1.21 – 1.15 (m, 6 H), 1.07 (dd, J = 13.6, 2.0 Hz, 1 H), 0.89 – 0.86 (m, 18 H), 0.68 (s, 1 H), 0.68 (s, 2 H), 0.07 – 0.05 (m, 12 H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ 170.7, 170.6, 140.6, 140.5, 133.2, 132.3, 132.2, 132.0, 130.5, 113.50, 113.46, 99.70, 99.68, 70.4, 70.0, 69.9, 69.3, 67.8, 67.5, 66.8, 65.3, 64.1, 51.5, 51.1, 50.7, 44.4, 42.23, 41.16, 41.1, 40.5, 40.3, 39.9, 36.3, 32.8, 32.7, 32.6, 32.3, 32.1, 30.6, 27.6, 27.2, 26.0, 25.9, 25.9, 23.9, 21.9, 21.78, 21.75, 18.3, 18.0, 15.4, 9.94, 9.90, 9.86, -4.1, -4.5, -4.6, -4.7, -5.1 ppm. IR (neat, cm⁻¹) ν_{\max} 2968, 2862, 2360, 1737, 1099, 1057, 837, 556 cm⁻¹. HRMS–ESI (m/z): [$M+Na$]⁺ calcd for C₃₆H₆₆O₆Si₂Na, 673.4296; found, 673.4282.



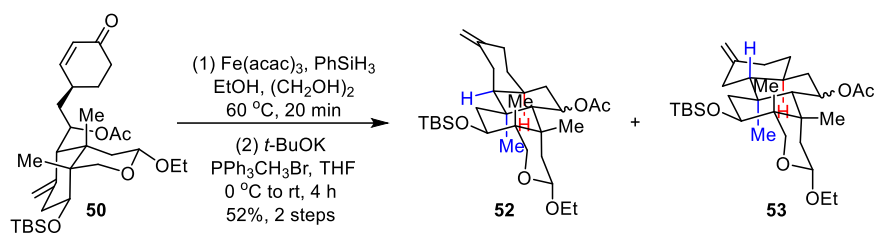
To a stirred solution of diastereomers **49** (472 mg, 0.73 mmol, 1.0 equiv.) in tetrahydrofuran (10 mL) was added tetrabutylammonium fluoride (1.0 M in tetrahydrofuran, 2.17 mL, 2.17 mmol, 3.0 equiv.) at room temperature. The resulting solution was stirred for 2 h, before it was quenched with saturated aqueous ammonium chloride (2 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic phases were washed with water and brine, then dried over anhydrous sodium sulfate, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum

ether, 1/4) to give crude alcohol (390 mg) as a colorless oil for the next step.

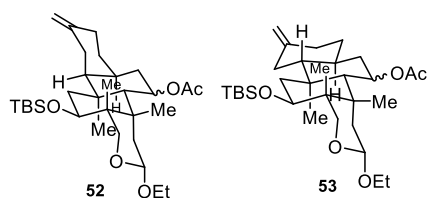
A stirred solution of the obtained crude alcohol (390 mg) in anhydrous dichloromethane (30 mL) at 0 °C was added sodium bicarbonate (123 mg, 1.46 mmol, 2.0 equiv.) and then treated with Dess–Martin periodinane (462 mg, 1.05 mmol, 1.5 equiv.) in four portions. The reaction mixture was stirred at 0 °C for 1 h and slowly warmed to room temperature while stirring for 2 h before it was diluted with diethyl ether (20 mL) and quenched with saturated aqueous sodium bicarbonate (3mL) and sodium thiosulfate (3 mL). After stirring at room temperature for 1 h, the resulting mixture was extracted with ethyl acetate (3 × 20 mL). The combined organic phases were washed with water, brine and dried over anhydrous sodium sulfate, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1/9) to give diastereomers **50** (285 mg, 73% over two steps, *d.r.* = 2.3:1 at C-20 by ¹N NMR analysis) as colorless oil.



Compound **50**: $R_f = 0.35$ (ethyl acetate/petroleum ether = 1/7). ¹H NMR (500 MHz, CDCl₃) δ 7.02 (dd, $J = 10.2, 2.1$ Hz, 0.66 H), 6.85 (dd, $J = 10.2, 1.0$ Hz, 0.28 H), 6.06 – 5.97 (m, 1 H), 5.61 – 5.48 (m, 1 H), 5.24 – 5.07 (m, 1 H), 4.78 – 4.63 (m, 1 H), 4.54 – 4.47 (m, 1 H), 4.24 – 4.08 (m, 1 H), 3.94 – 3.85 (m, 1 H), 3.76 – 3.61 (m, 1 H), 3.57 – 3.43 (m, 1 H), 3.42 – 3.17 (m, 1 H), 2.56 – 2.44 (m, 2 H), 2.42 – 2.28 (m, 3 H), 2.28 – 2.19 (m, 2 H), 2.15 – 2.01 (m, 5 H), 1.87 – 1.80 (m, 1 H) 1.69 (m, 1 H), 1.43 – 1.36 (m, 1 H), 1.29 – 1.18 (m, 6 H), 0.92 – 0.88 (m, 9 H), 0.78 – 0.71 (m, 3 H), 0.15 – 0.07 (m, 6 H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ 199.4, 199.3, 199.2, 170.9, 170.6, 170.5, 154.0, 153.2, 153.0, 144.8, 143.7, 140.5, 129.5, 129.42, 129.35, 113.6, 112.1, 111.2, 99.60, 99.55, 97.1, 70.9, 70.5, 69.8, 69.5, 69.3, 66.8, 66.4, 64.2, 64.1, 62.24, 60.16, 51.8, 51.7, 51.6, 44.4, 43.92, 43.87, 42.8, 42.6, 42.3, 41.6, 41.22, 40.18, 39.6, 36.9, 36.7, 36.6, 36.3, 35.9, 33.7, 33.4, 33.0, 32.7, 32.6, 29.4, 29.3, 28.8, 25.9, 25.8, 25.1, 23.4, 22.0, 21.8, 21.74, 21.72, 18.00, 17.98, 15.5, 15.4, 15.3, 10.6, 10.1, 9.9, -4.07, -4.09, -4.14, -5.03, -5.09 ppm. IR (neat, cm⁻¹) ν_{\max} 2985, 2939, 1736, 1684, 1248, 1147, 1066, 838 cm⁻¹. HRMS–ESI (m/z): [M+Na]⁺ calcd for C₃₀H₅₀O₆SiNa, 557.3269; found, 557.3261.



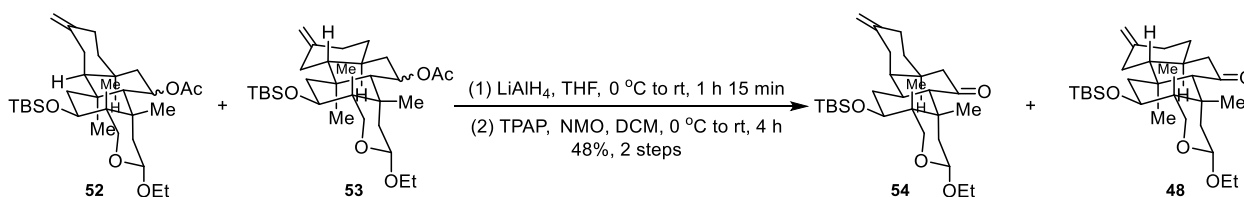
To a solution of diastereomers **50** (60 mg, 0.112 mmol, 1.0 equiv) in ethanol (2.5 mL)/ ethylene glycol (0.5 mL) was added Fe(acac)₃ (19.8 mg, 0.056 mmol, 0.5 equiv.). Then the mixture was degassed through the Freeze-Pump-Thaw cycling before it was added phenylsilane (41 μL, 0.336 mmol, 3.0 mmol). After stirring for 20 min at 60 °C, the resulting mixture was concentrated under vacuum and dissolved subsequently in tetrahydrofuran (2 mL) for Wittig reaction. To a stirred solution of PPh₃CH₃Br (195 mg, 0.55 mmol, 5.0 equiv.) in tetrahydrofuran (2 mL) was added *t*-BuOK (50 mg, 0.45 mmol, .4.0 equiv.) at room temperature. After stirring for 30 min at room temperature, the resulting mixture was cooled to 0 °C and then a solution of the obtained crude oil in tetrahydrofuran (2 mL) was added dropwise. The reaction mixture was warmed to room temperature and stirred for 4 h before it was quenched with saturated aqueous ammonium chloride (2 mL) at that temperature and extracted with ethyl acetate (3 × 20 mL). The combined organic phases were washed with water and brine, then dried over anhydrous sodium sulfate. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1/9) to give a mixture of olefin **52** and **53** (31 mg, 52%) as colorless oil.



Compound **52** and **53**: $R_f = 0.84$ (ethyl acetate/petroleum ether = 1/9).

¹H NMR (500 MHz, CDCl₃) δ 5.42 (d, $J = 14.6$ Hz, 0.34 H), 5.22 – 5.16 (m, 0.71 H), 4.77 – 4.63 (m, 2 H), 4.50 – 4.25 (m, 2 H), 3.90 – 3.73 (m, 2 H), 3.52 – 3.42 (m, 1 H), 3.29 – 3.19 (m, 1 H), 2.32 – 2.20 (m, 2 H), 2.14 – 1.99 (m, 5 H), 1.93 – 1.81 (m, 3 H), 1.76 – 1.69 (m, 2 H), 1.65 – 1.62 (m, 1 H), 1.52 – 1.44 (m, 2 H), 1.33 (s, 1 H), 1.31 – 1.26 (m, 2 H), 1.25 (s, 2 H), 1.22 – 1.17 (m, 5 H), 1.12 – 1.05 (m, 2 H), 0.89 (s, 9 H), 0.64 (s, 1.93 H), 0.59 – 0.57 (m, 0.88 H), 0.1 – 0.06 (m, 6 H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ 170.6, 170.3, 169.9, 149.6, 149.4, 148.0, 108.8, 108.3, 108.2, 107.6, 107.4, 107.2, 103.2, 99.9, 99.8, 72.02, 70.9, 70.5, 70.4, 70.0, 69.9, 69.7, 67.6, 67.1, 67.0, 67.0, 66.9, 66.6, 65.9, 65.62, 65.60, 65.56, 65.5, 65.3, 65.2, 64.4, 64.09, 64.06, 64.0, 63.9, 63.4, 57.5, 55.0, 52.4, 52.3, 52.2, 52.0, 51.9, 49.9, 49.11, 49.07, 45.1, 44.8, 44.7, 44.5, 44.4, 44.3, 44.2, 43.3, 42.7, 42.6, 42.2, 42.0, 41.9, 41.84, 41.79, 41.2, 41.0, 40.8, 40.4, 40.3, 40.21, 40.17, 40.15, 40.1, 40.0, 39.95, 39.90, 39.87, 39.8, 39.6, 39.2, 38.8, 38.70,

38.65, 38.6, 38.54, 38.45, 38.33, 38.31, 38.28, 38.1, 37.6, 37.20, 37.15, 37.1, 36.1, 35.8, 35.4, 35.0, 34.5, 34.0, 33.5, 33.2, 32.7, 32.5, 32.2, 31.9, 31.6, 31.5, 31.2, 31.1, 30.9, 30.6, 30.3, 29.8, 29.5, 29.3, 29.1, 28.9, 28.7, 27.9, 27.3, 27.2, 27.0, 26.3, 25.92, 25.91, 25.88, 25.5, 24.3, 24.2, 24.0, 23.1, 22.0, 22.0, 21.93, 21.90, 21.0, 20.9, 19.9, 18.9, 18.6, 18.04, 18.01, 16.0, 15.5, 15.4, 14.0, 10.3, 10.2, 10.19, 10.17, 10.1, 10.0, 7.8 ppm. IR (neat, cm^{-1}) ν_{max} 2930, 2361, 1735, 1241, 1142, 1067, 885, 668 cm^{-1} . HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{31}\text{H}_{54}\text{O}_5\text{SiNa}$, 557.3633; found, 557.3624.



To a mixture of obtained olefin **52** and **53** (52 mg, 0.097 mmol, 1.0 equiv.) in tetrahydrofuran (4 mL) at 0 °C was added lithium aluminum hydride (7.4 mg, 0.194 mmol, 2.0 equiv.). After stirring for 15 min at 0 °C, the reaction mixture was warmed to room temperature and stirred for 1 h. The reaction mixture was cooled to 0 °C and quenched with water (15 μL) carefully and added 10% aqueous sodium hydroxide (15 μL). Then the resulting suspension was warmed up to room temperature and vigorously stirred for 4 h. The reaction mixture was filtered, washing the filter cake with ethyl acetate (30 mL), and the filtrate was dried over anhydrous sodium sulfate and concentrated under vacuum to get alcoholic mixture (38 mg) for the next step.

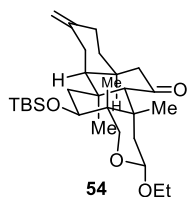
For the preparation of the mixture of Compound **54** and **48**

An oven-dried flask was charged with the obtained mixture (38 mg), 4-methylmorpholine N-oxide (72.3 mg, 0.618 mmol, 8.0 equiv.) and 4Å molecule sieve (38 mg) in dichloromethane (3 mL). tetrapropylammonium perruthenate (TPAP) (2.7 mg, 0.0076 mmol, 0.1 equiv.) was added at 0 °C and the resulting mixture was warmed to room temperature. After stirring for 2 h, the mixture was directly purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1/9) to give a mixture of diastereomers of ketone **54** and **48** (22 mg, 48% over two steps) as colorless oil. [**54**: **48** = 2:1 (calculated by ^1H NMR analysis)]

For the preparation of compound **54**.

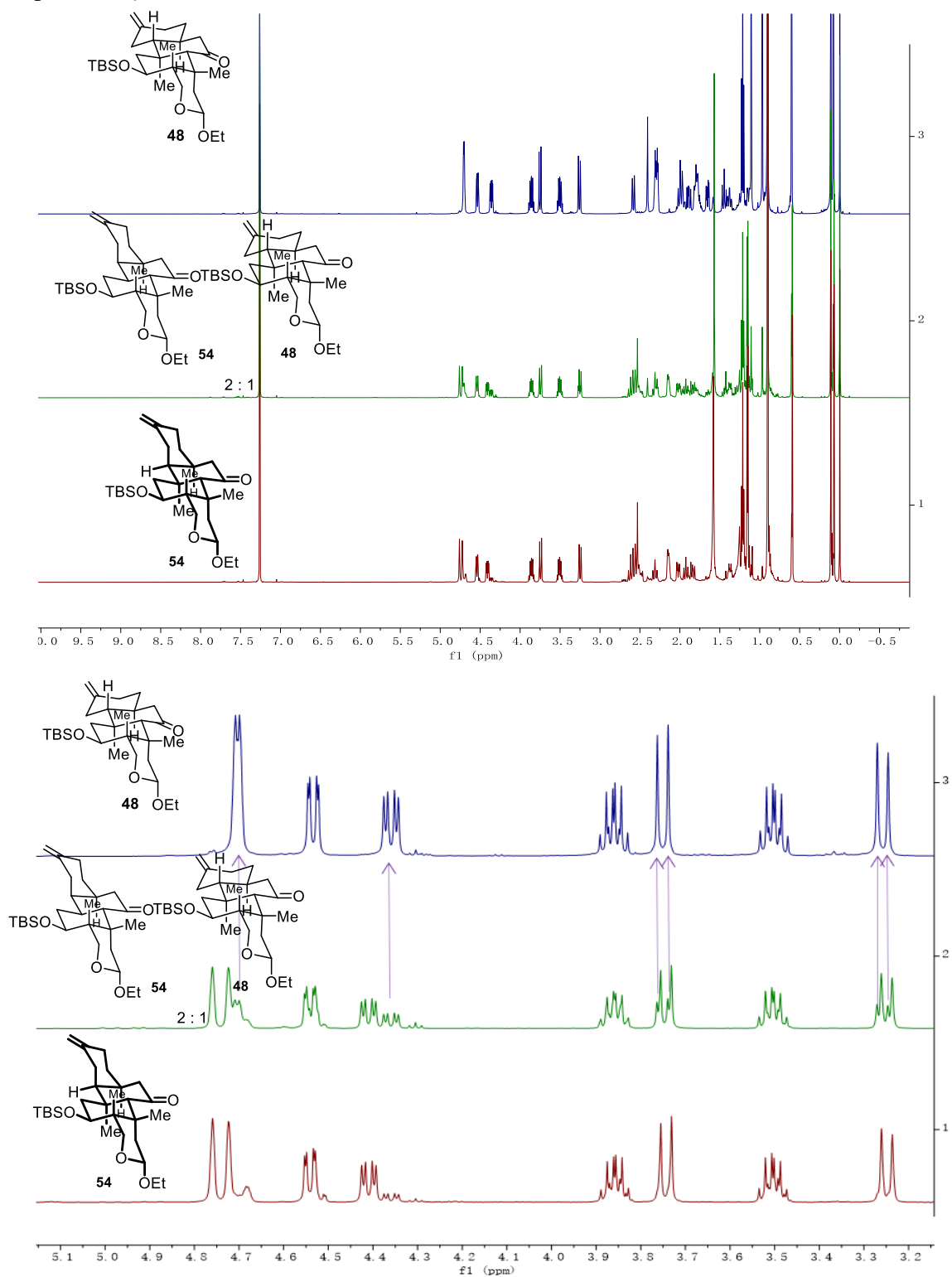
After reduction of the olefin **52** and **53** with lithium aluminum hydride, the obtained alcohol mixture was separated with column chromatography on silica gel to collect the main alcoholic product, which was subjected to the subsequently Ley oxidation to yield the compound **54**. For characterization, compound

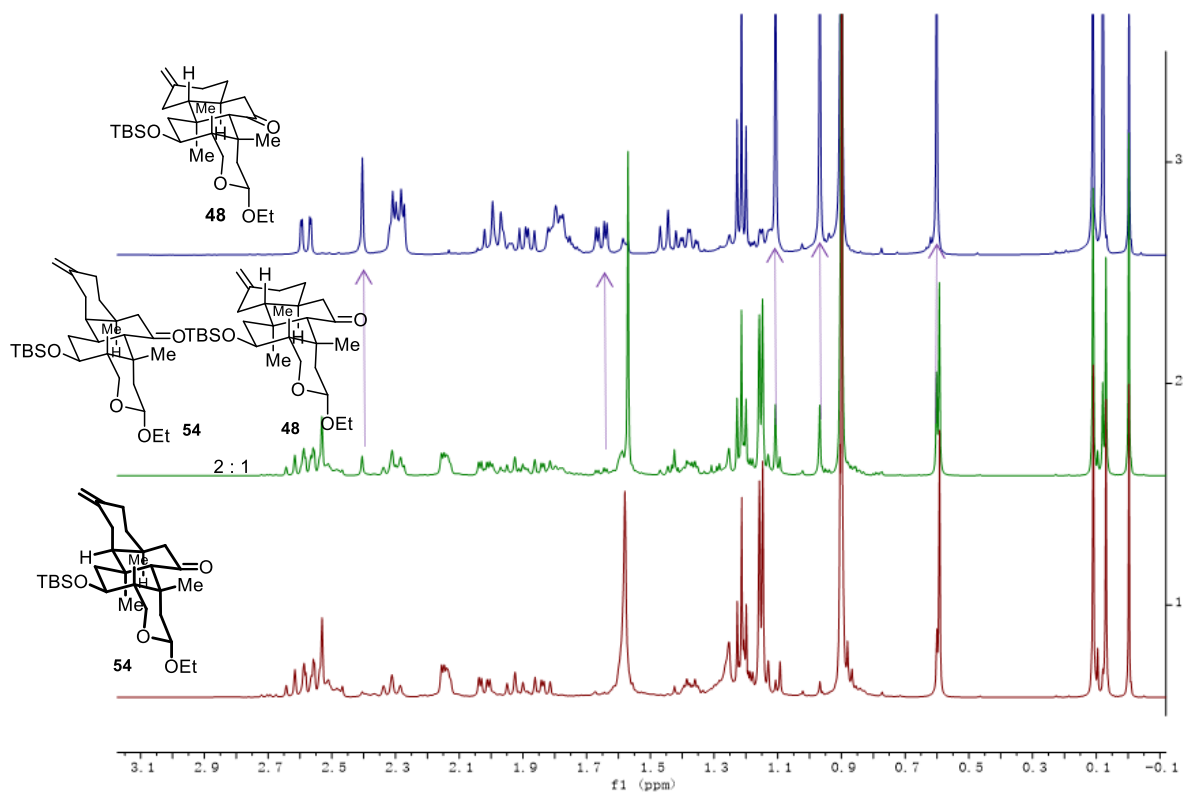
54 was separated by preparative TLC (silica gel, ethyl acetate/petroleum ether, 1/9).



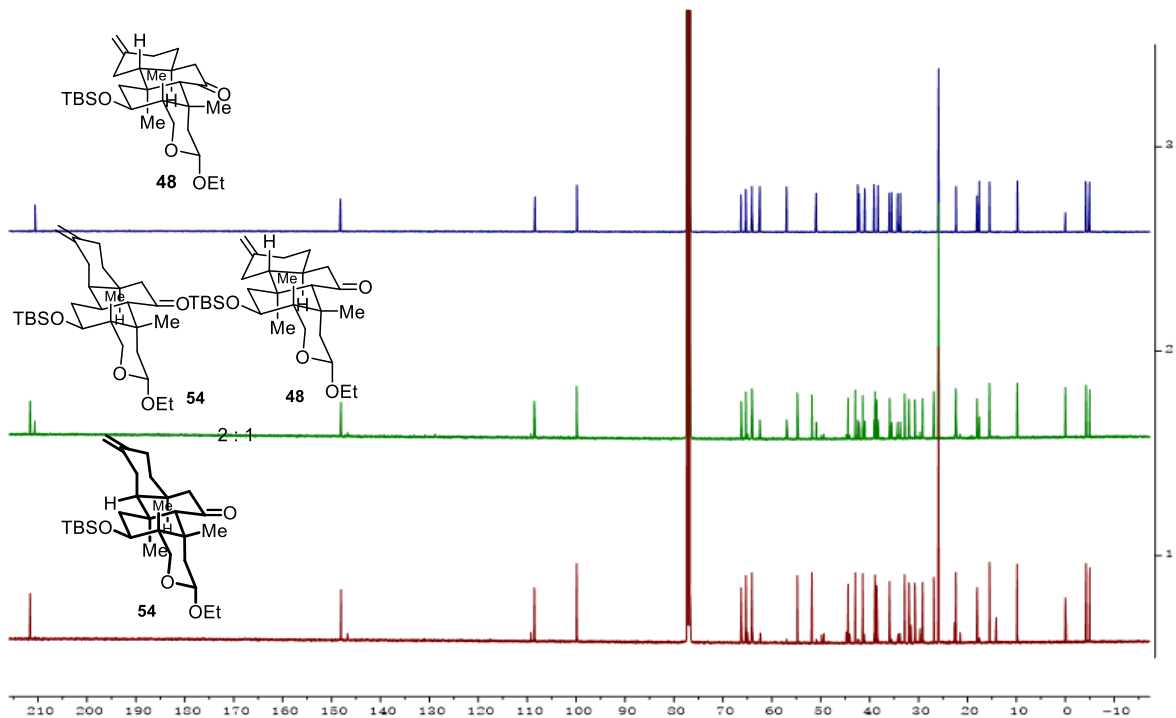
Compound **54**: $R_f = 0.6$ (ethyl acetate/petroleum ether = 1/9); $[\alpha]_D^{20} = +4.7$ ($c = 0.21$ in DCM). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 4.74 (d, $J = 17.9$ Hz, 2 H), 4.54 (dd, $J = 9.8, 2.2$ Hz, 1 H), 4.41 (dd, $J = 11.8, 4.2$ Hz, 1 H), 3.91 – 3.81 (m, 1 H), 3.74 (d, $J = 12.1$ Hz, 1 H), 3.55 – 3.47 (m, 1 H), 3.25 (d, $J = 12.1$ Hz, 1 H), 2.68 – 2.44 (m, 4 H), 2.31 (t, $J = 13.1$ Hz, 1 H), 2.18 – 2.11 (m, 2 H), 2.02 (dd, $J = 13.0, 4.0$ Hz, 1 H), 1.92 (t, $J = 12.4$ Hz, 1 H), 1.84 (dd, $J = 13.8, 9.9$ Hz, 1 H), 1.43 – 1.34 (m, 2 H), 1.26 – 1.22 (m, 2 H), 1.21 (t, $J = 7.1$ Hz, 3 H), 1.16 (s, 3 H), 1.15 (s, 3 H), 1.11 (d, $J = 18.5$ Hz, 1 H), 0.90 (s, 9 H), 0.59 (s, 3 H), 0.11 (s, 3 H), 0.07 (s, 3 H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 211.7, 148.1, 108.6, 99.9, 76.8, 66.3, 65.3, 64.1, 54.8, 51.8, 44.4, 43.0, 41.5, 38.9, 38.6, 36.0, 32.9, 32.0, 30.8, 29.2, 26.9, 25.9, 22.4, 18.1, 15.5, 9.9, -4.2, -5.0 ppm. IR (neat, cm^{-1}) ν_{max} 2885, 1734, 1653, 1539, 1507, 1111, 810 cm^{-1} . EI (m/z): $[\text{M}-\text{C}_4\text{H}_9]^+$ calcd for $\text{C}_{29}\text{H}_{50}\text{O}_4\text{Si}$ -57, 433; found, 433.

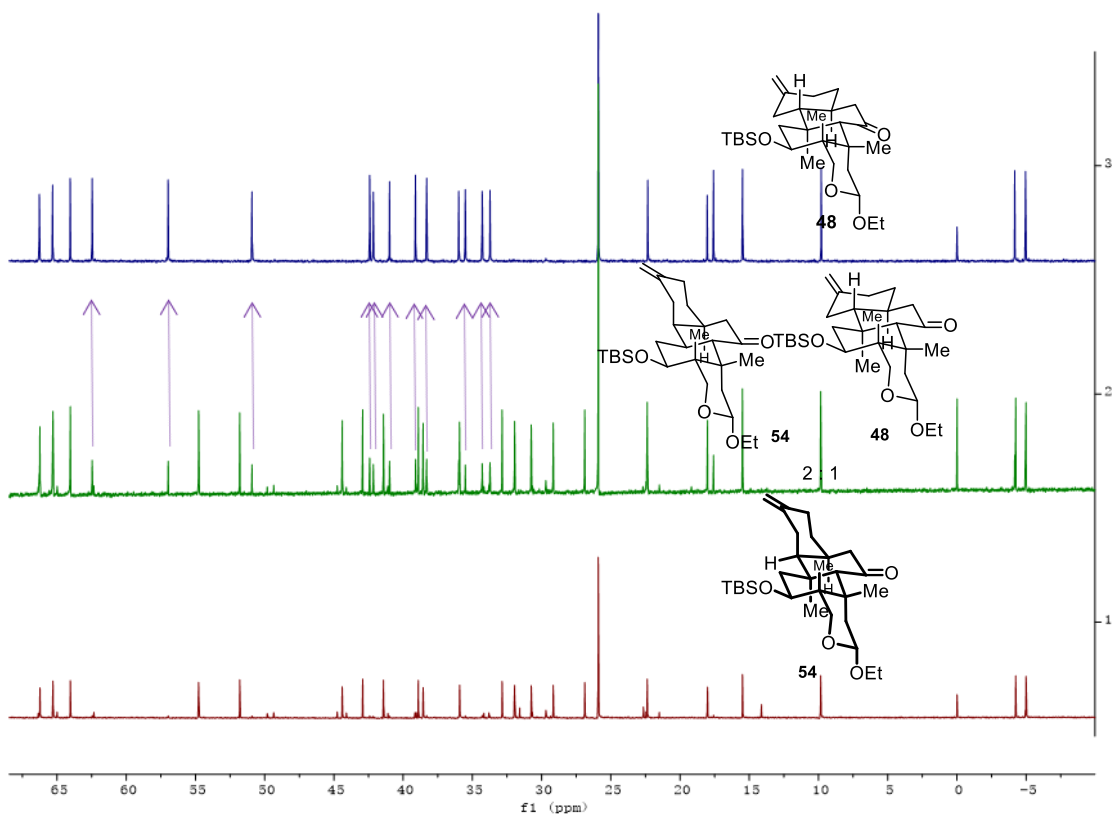
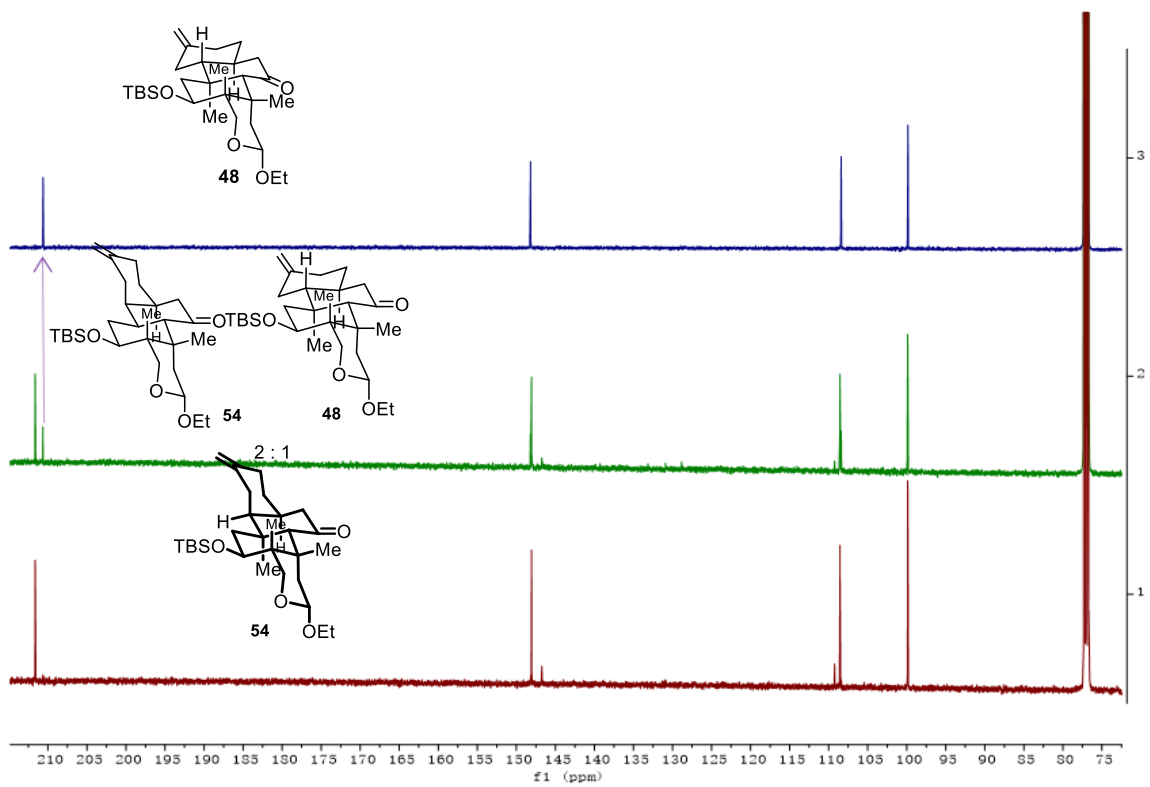
The ^1H NMR spectroscopic data comparison (compound **48**/ the mixture of compound **54** and compound **48**/ compound **54**):



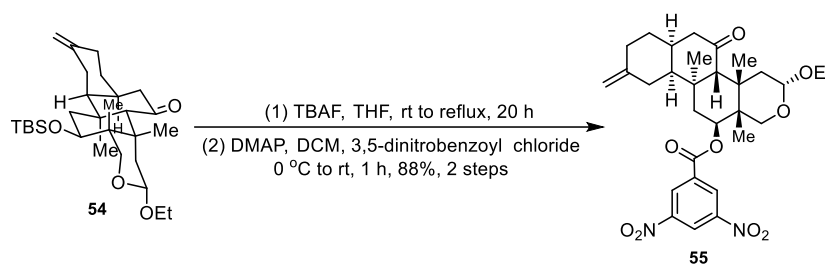


The ^{13}C NMR spectroscopic data comparison (compound **48**/ the mixture of compound **54** and compound **48**/ compound **54**):



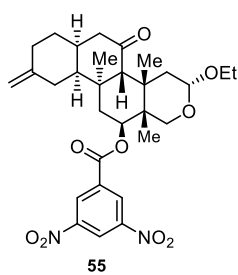


The stereochemistry determination of compound **55**:



To a stirred solution of **54** (8 mg, 0.016 mmol, 1.0 equiv.) in tetrahydrofuran (2 mL) was added tetrabutylammonium fluoride (1.0 M in tetrahydrofuran, 0.32 mL, 0.32 mmol, 20.0 equiv.) at room temperature. After the resulting solution was heated to reflux and stirred for 20 h, it was cooled to room temperature and quenched with saturated aqueous ammonium chloride (2 mL) and then extracted with ethyl acetate (3 × 10 mL). The combined organic phases were washed with water and brine, then dried over anhydrous sodium sulfate, filtered and concentrated under vacuum to get crude alcohol for the next step.

To the obtained crude alcohol in dry dichloromethane (2 mL) at 0 °C was added 4-dimethylaminopyridine (DMAP) (23 mg, 0.19 mmol, 12.0 equiv.) and 3,5-dinitrobenzoyl chloride (22 mg, 0.10 mmol, 6.0 equiv.). The reaction mixture was warmed to room temperature and stirred for 1 h before it was quenched with saturated aqueous sodium bicarbonate (2 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic phases were washed with water and brine, then dried over anhydrous sodium sulfate, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether, 1/10) to give compound **55** (8 mg, 88% over two steps) as a yellow oil

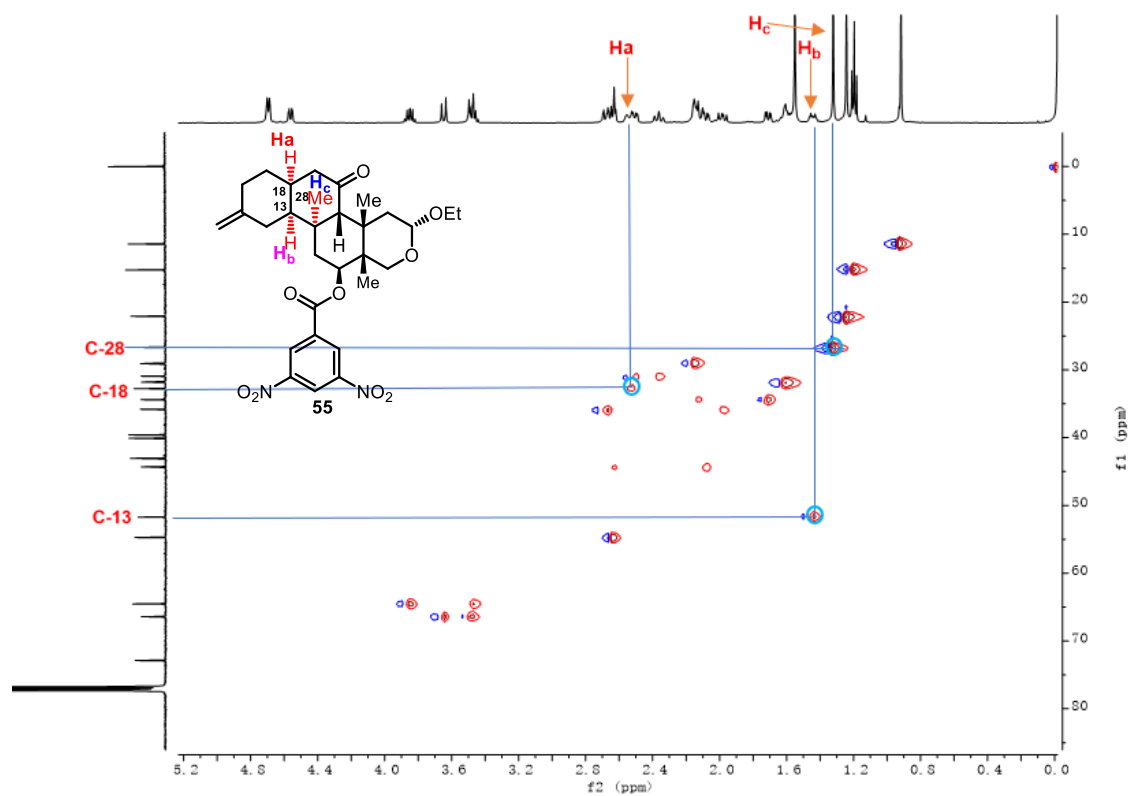


Compound **55**: $R_f = 0.6$ (ethyl acetate/petroleum ether = 1/9); $[\alpha]_D^{20} = +8.8$ ($c = 0.16$ in DCM). $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 9.23 (t, $J = 2.1$ Hz, 1 H), 9.10 (d, $J = 2.1$ Hz, 2 H), 5.97 (dd, $J = 12.0, 4.2$ Hz, 1 H), 4.71 (s, 2 H), 4.58 (dd, $J = 9.7, 2.1$ Hz, 1 H), 3.90 – 3.82 (m, 1 H), 3.67 (d, $J = 12.6$ Hz, 1 H), 3.54 – 3.44 (m, 2 H), 2.75 – 2.62 (m, 3 H), 2.60 – 2.50 (m, 2 H), 2.38 (t, $J = 12.5$ Hz, 1 H), 2.25 – 2.08 (m, 4 H), 2.03

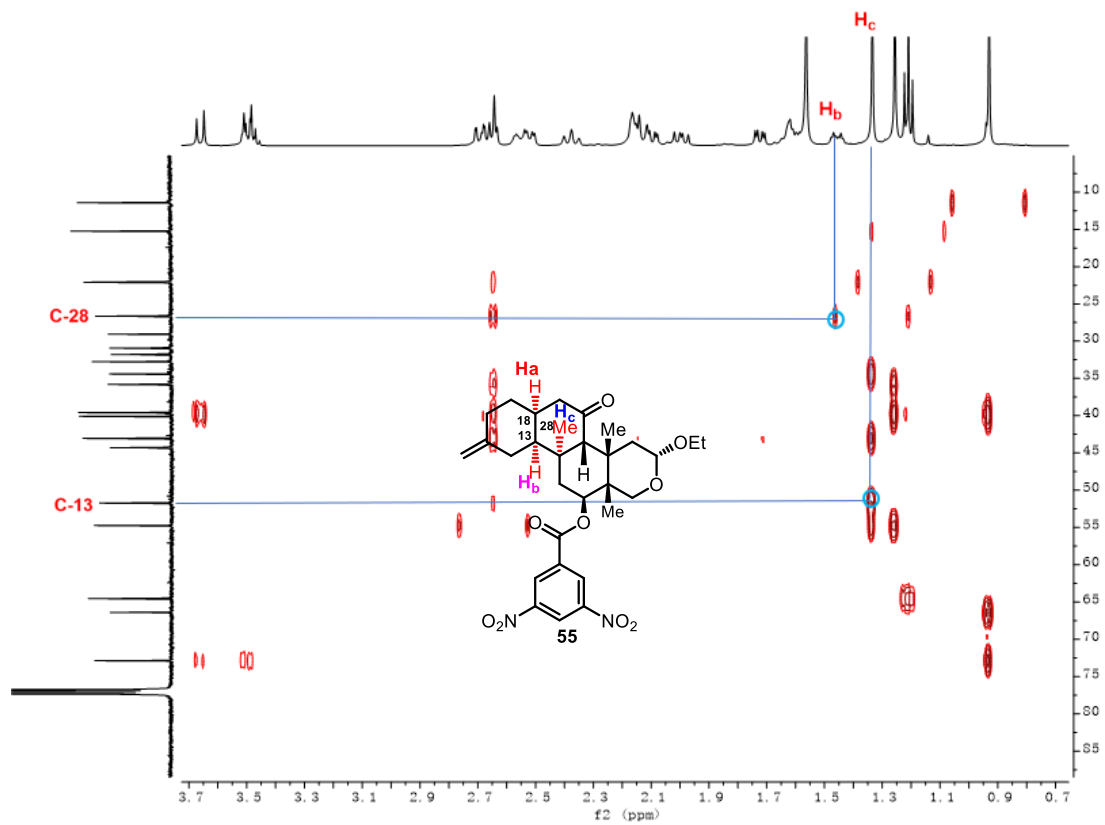
– 1.94 (m, 1 H), 1.73 (dd, $J = 12.6, 4.2$ Hz, 1 H), 1.65 – 1.60 (m, 2 H), 1.50 – 1.42 (m, 1 H), 1.34 (s, 3 H), 1.26 (s, 3 H), 1.21 (t, $J = 7.1$ Hz, 3 H), 0.93 (s, 3 H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 210.55, 161.58, 148.65, 147.36, 134.37, 129.21, 122.31, 108.91, 100.02, 72.84, 66.37, 64.50, 54.70, 51.70, 44.28, 43.02,

40.07, 39.56, 35.79, 34.38, 32.73, 31.78, 30.90, 29.04, 26.64, 22.07, 15.24, 11.40 ppm. IR (neat, cm^{-1}) ν_{max} 2961, 2923, 1734, 1700, 1545, 1270, 1096, 1073, 798, 721 cm^{-1} . HRMS–EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{30}\text{H}_{38}\text{N}_2\text{O}_9$, 570.2577; found, 570.2579.

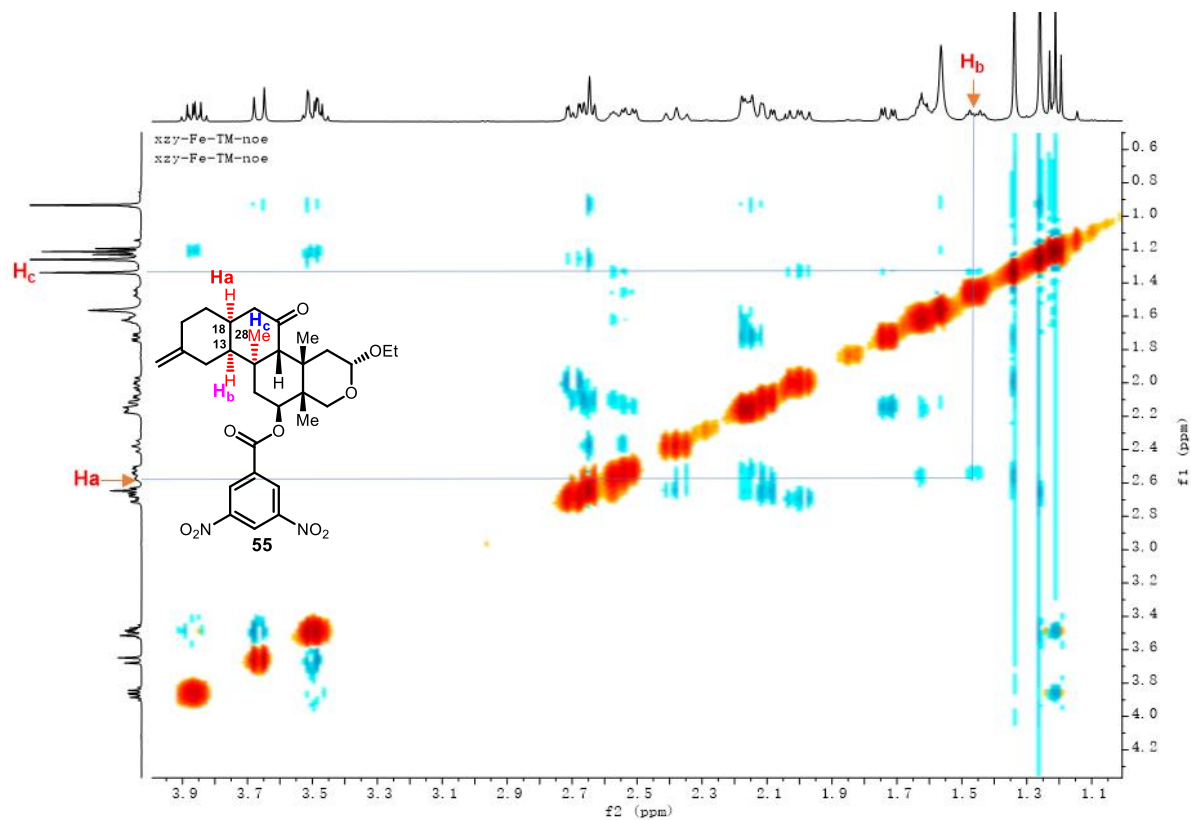
The HSQC spectroscopic data of compound **55**:



The HMBC spectroscopic data of compound **55**:



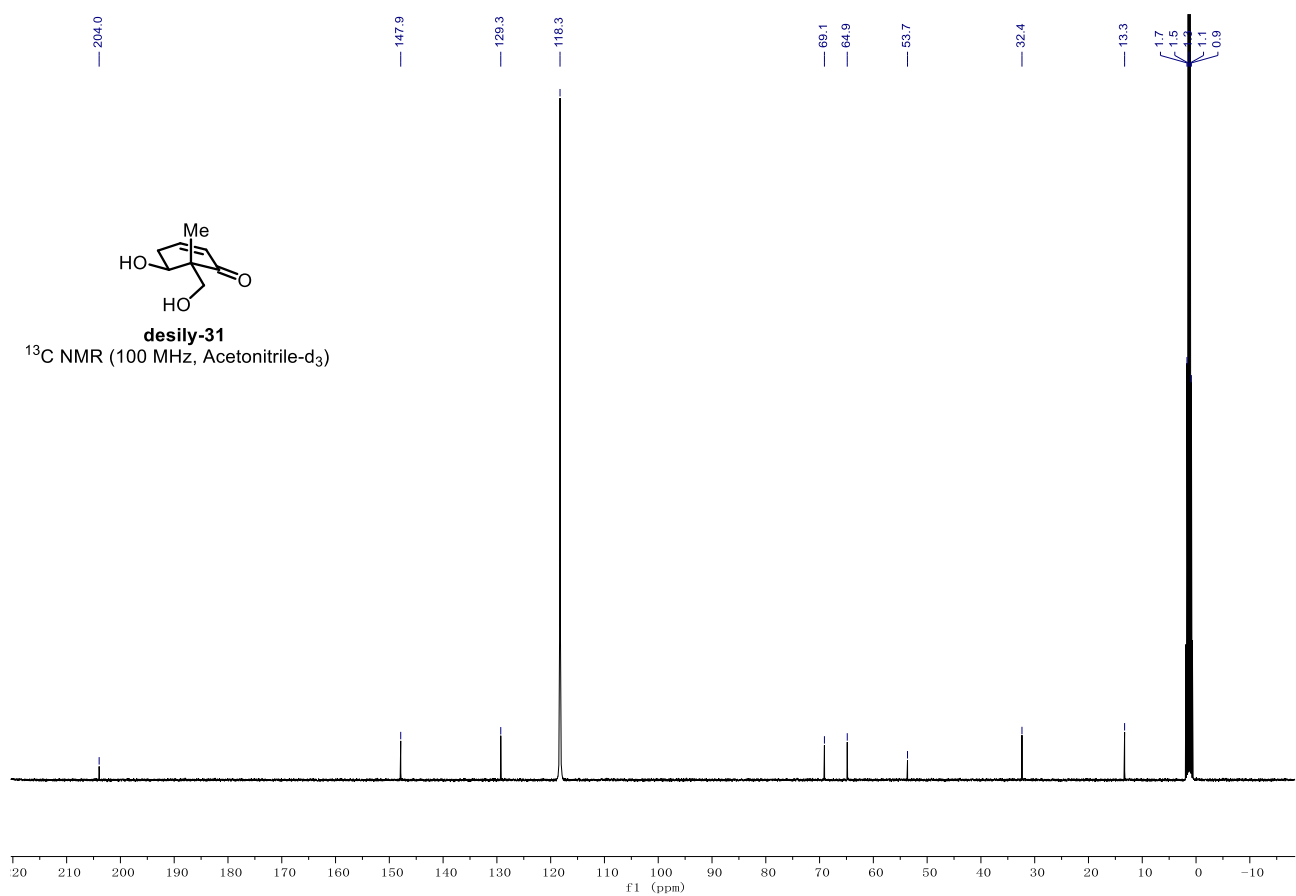
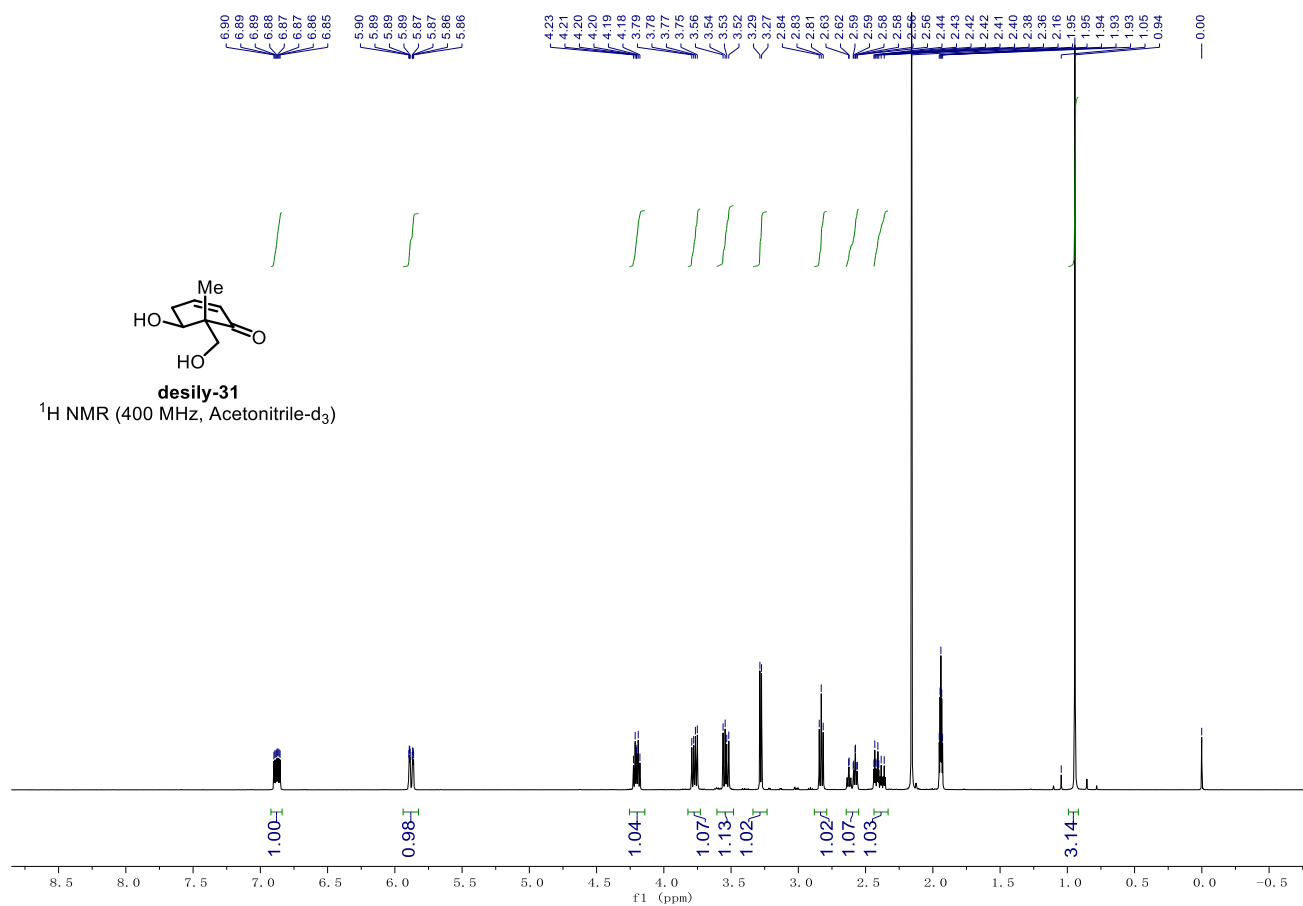
The NOE spectroscopic data of compound **55**:

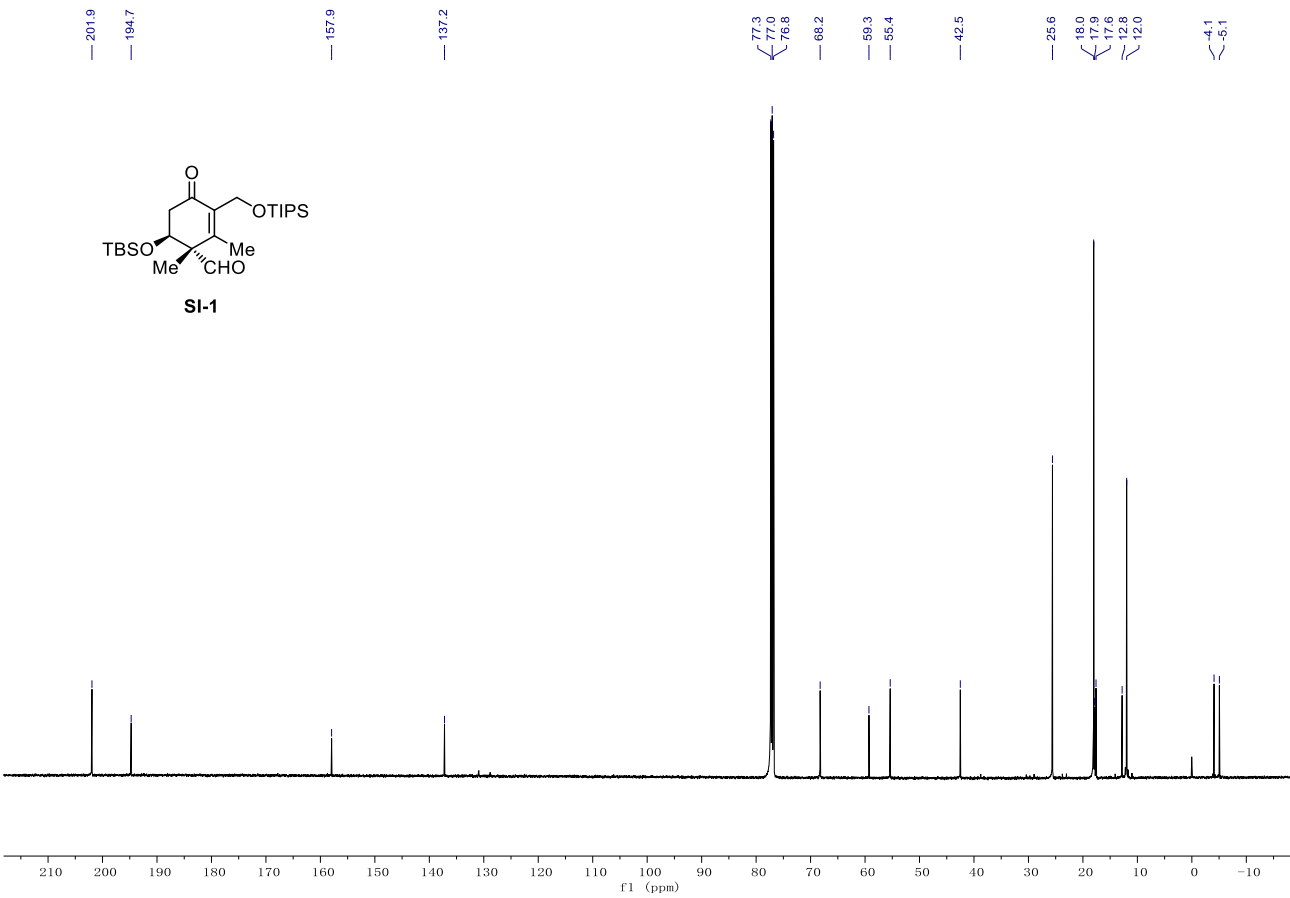
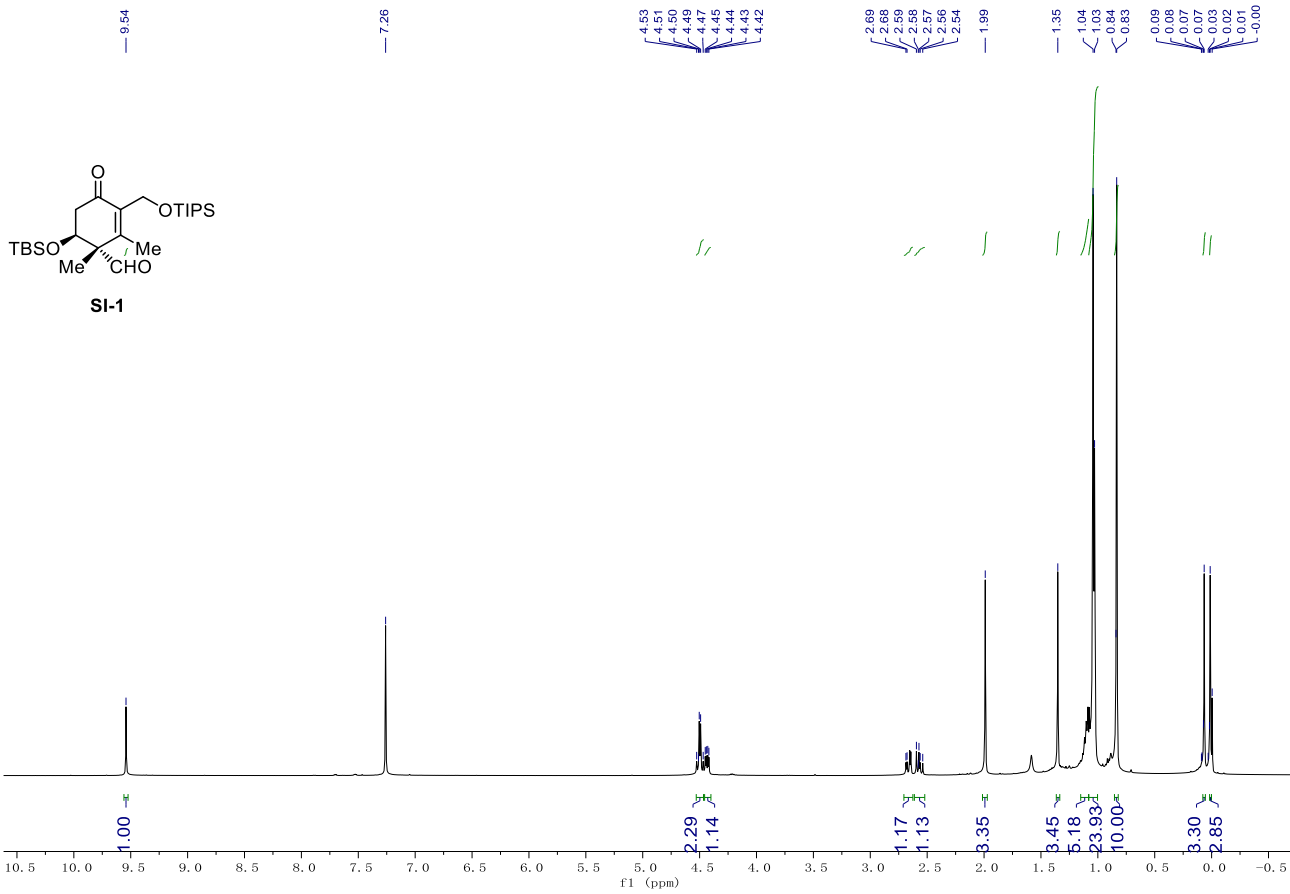


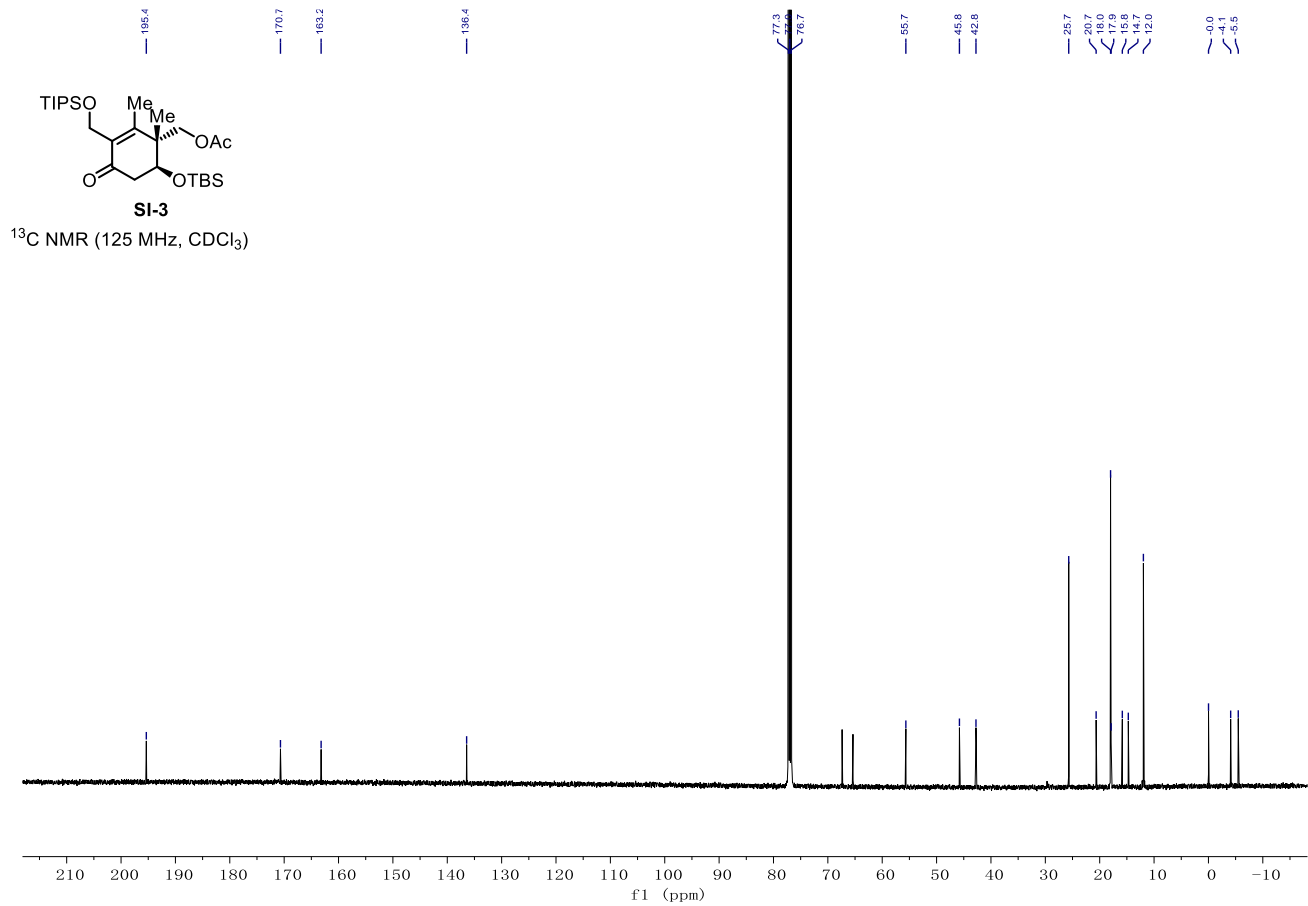
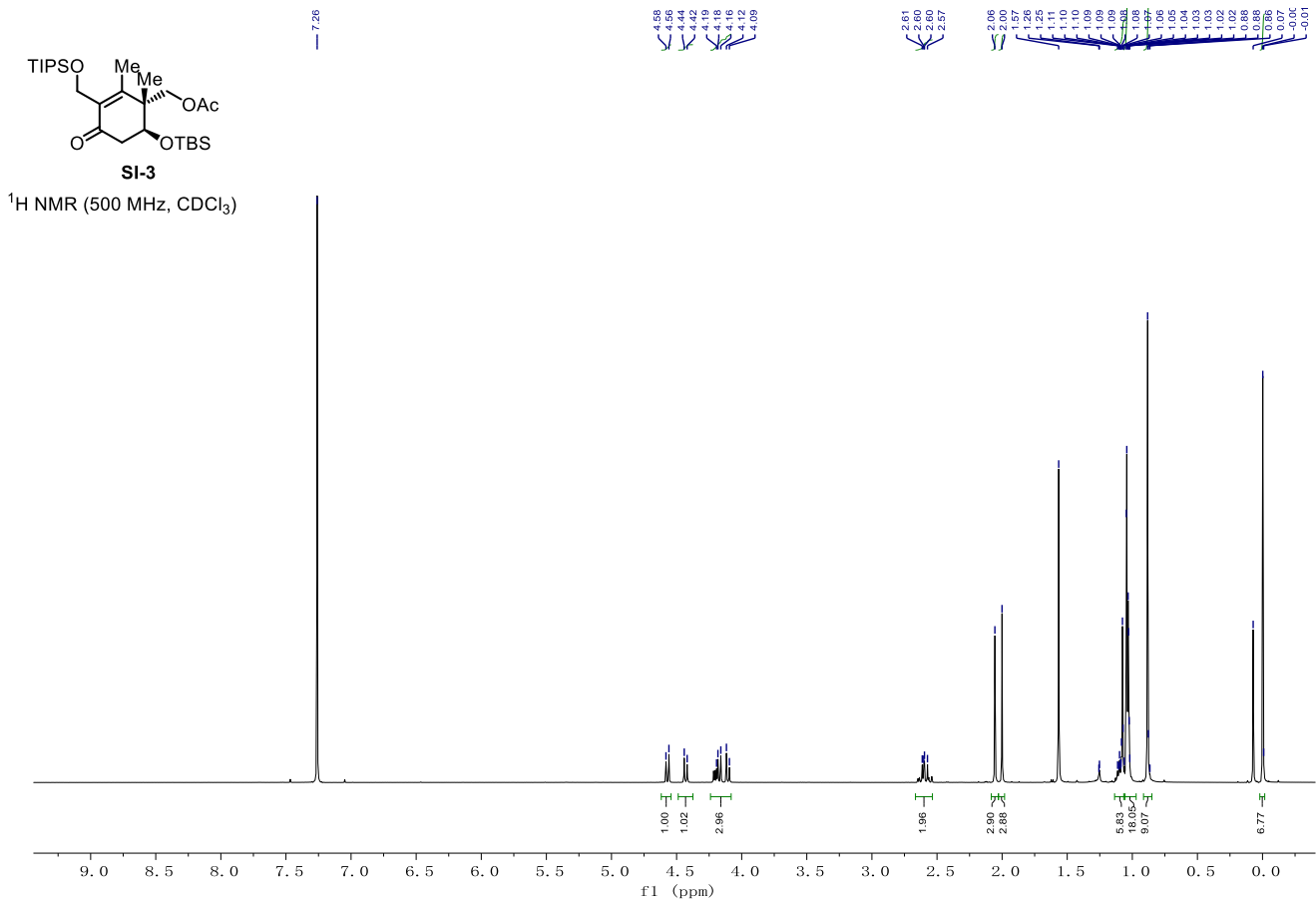
Reference:

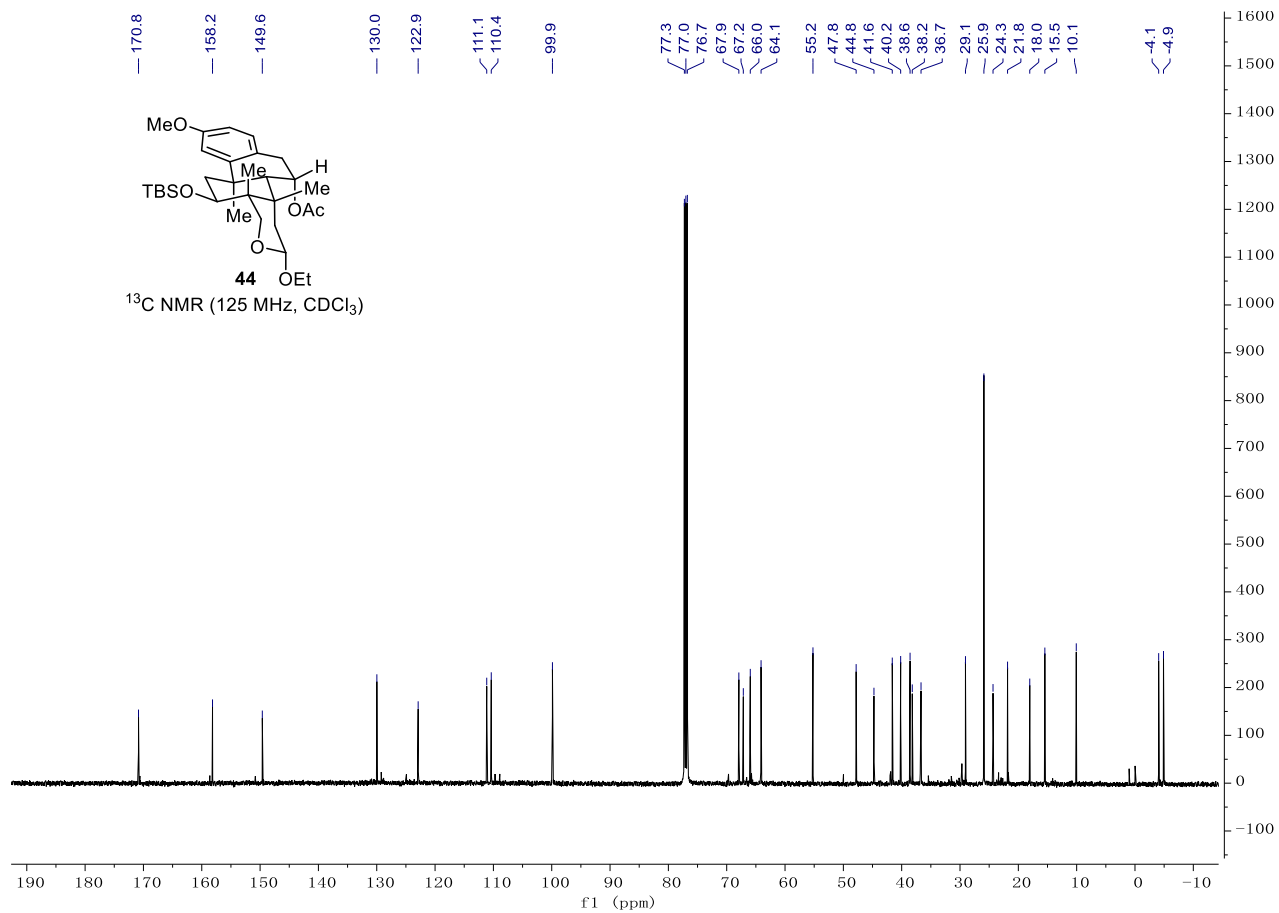
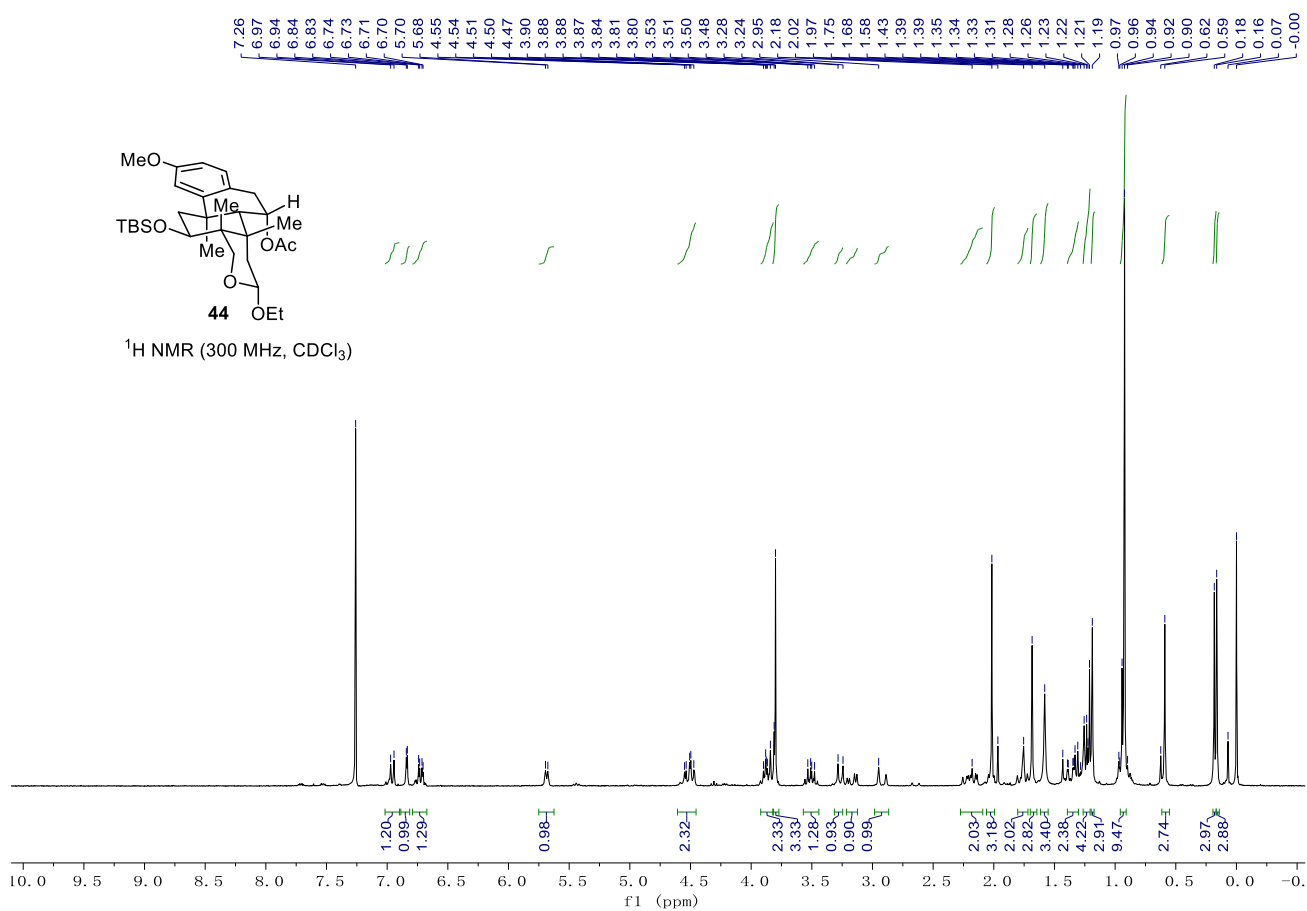
- [1] Z. Xin, H. Wang, H. He, X. Zhao and S. Gao, Asymmetric Total Synthesis of Norzoanthamine, *Angew. Chem. Int. Ed.*, 2021, **60**, 12807-12812.
- [2] A. B. Smith, E. G. Nolen, R. Shi-rai, F. R. Blase, M. Ohta, N. Chida, R. A. Hartz, D. M. Fitch, W. M. Clark and P. A. Sprengeler, Tremorgenic Indole Alkaloids. 9. Asymmetric construction of an Advanced F-G-H-ring Lactone precursor for the Synthesis of Penitrem D, *J. Org. Chem.*, 1995, **60**, 7837-7848.
- [3] S. A. Kozmin and V. H. Rawal, Chiral Amino Siloxy Dienes in the Diels–Alder Reaction: Applications to the Asymmetric Synthesis of 4-Substituted and 4,5-Disubstituted Cyclohexenones and the Total Synthesis of (–)- α -Elemene, *J. Am. Chem. Soc.*, 1999, **121**, 9562-9573.

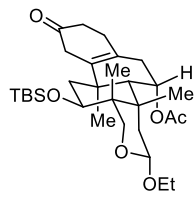
Copy of NMR spectrum:



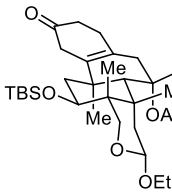
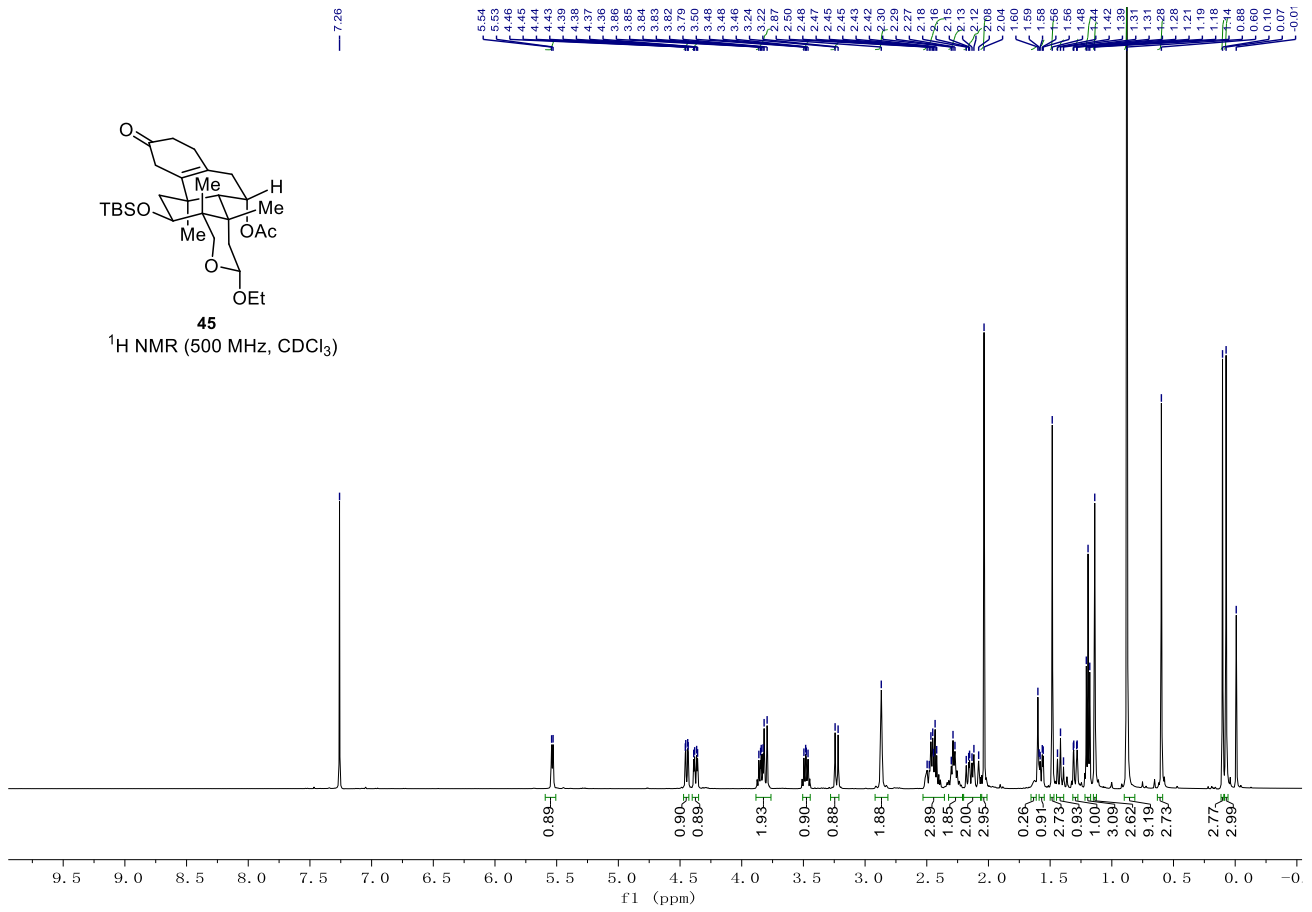




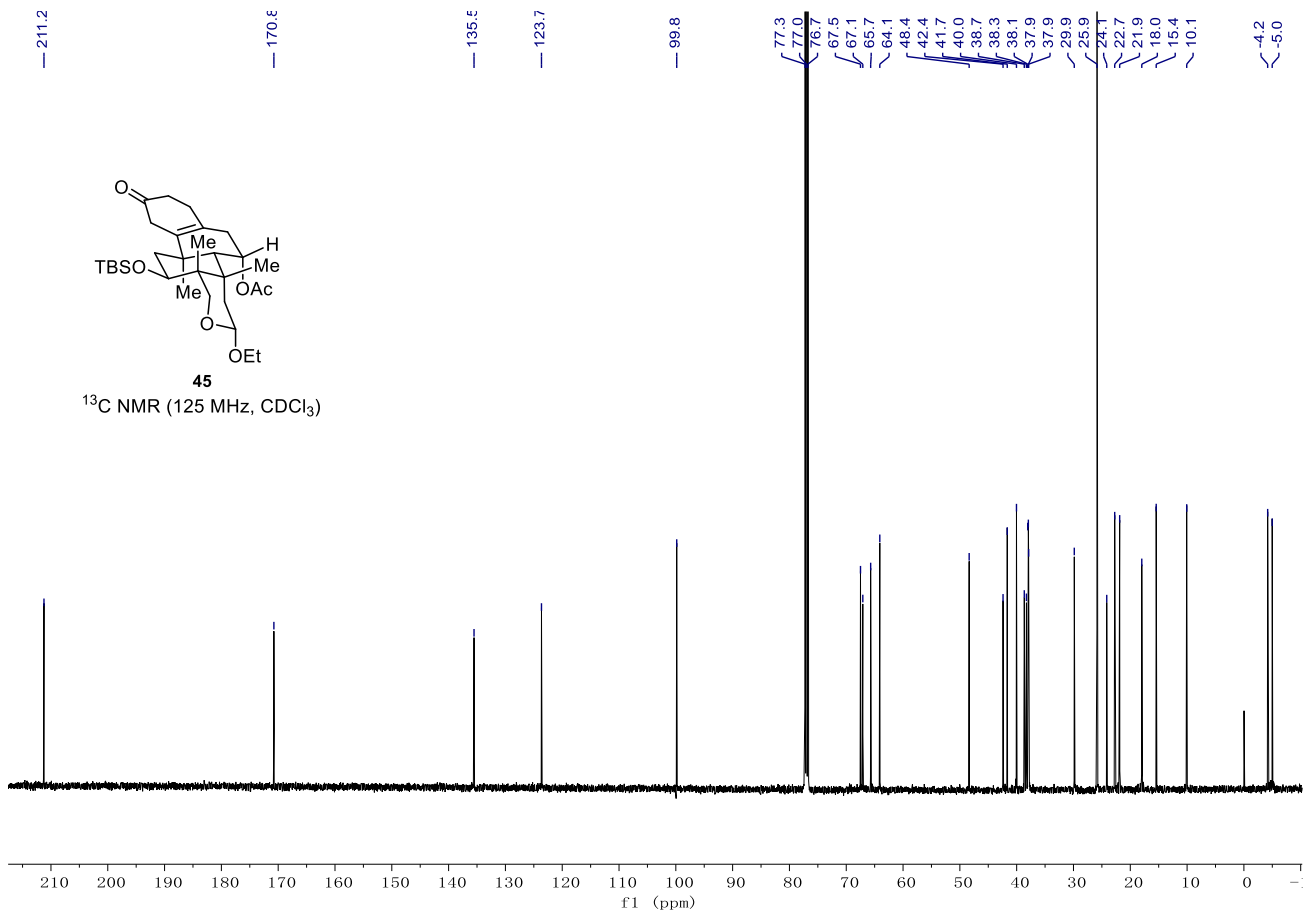


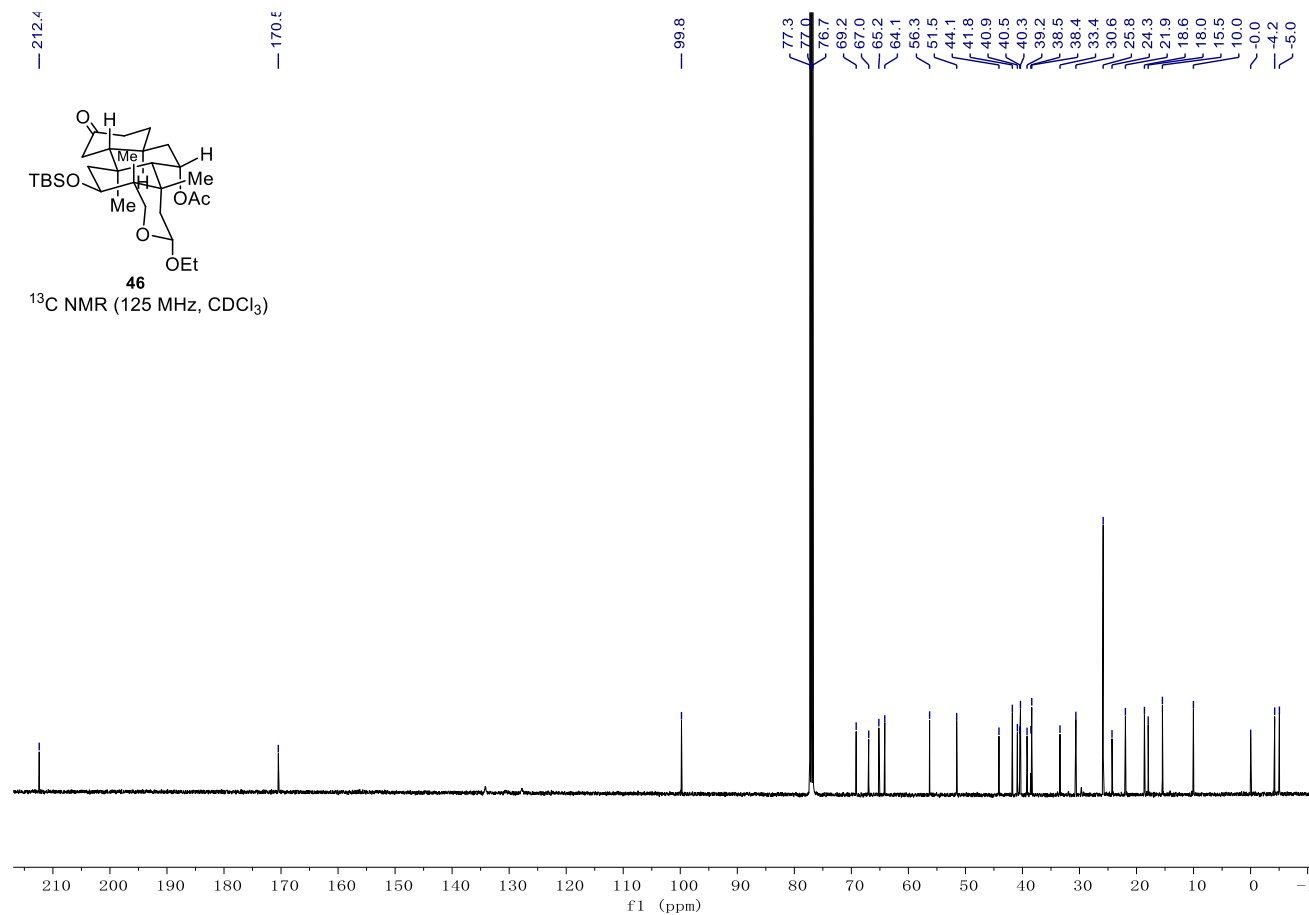
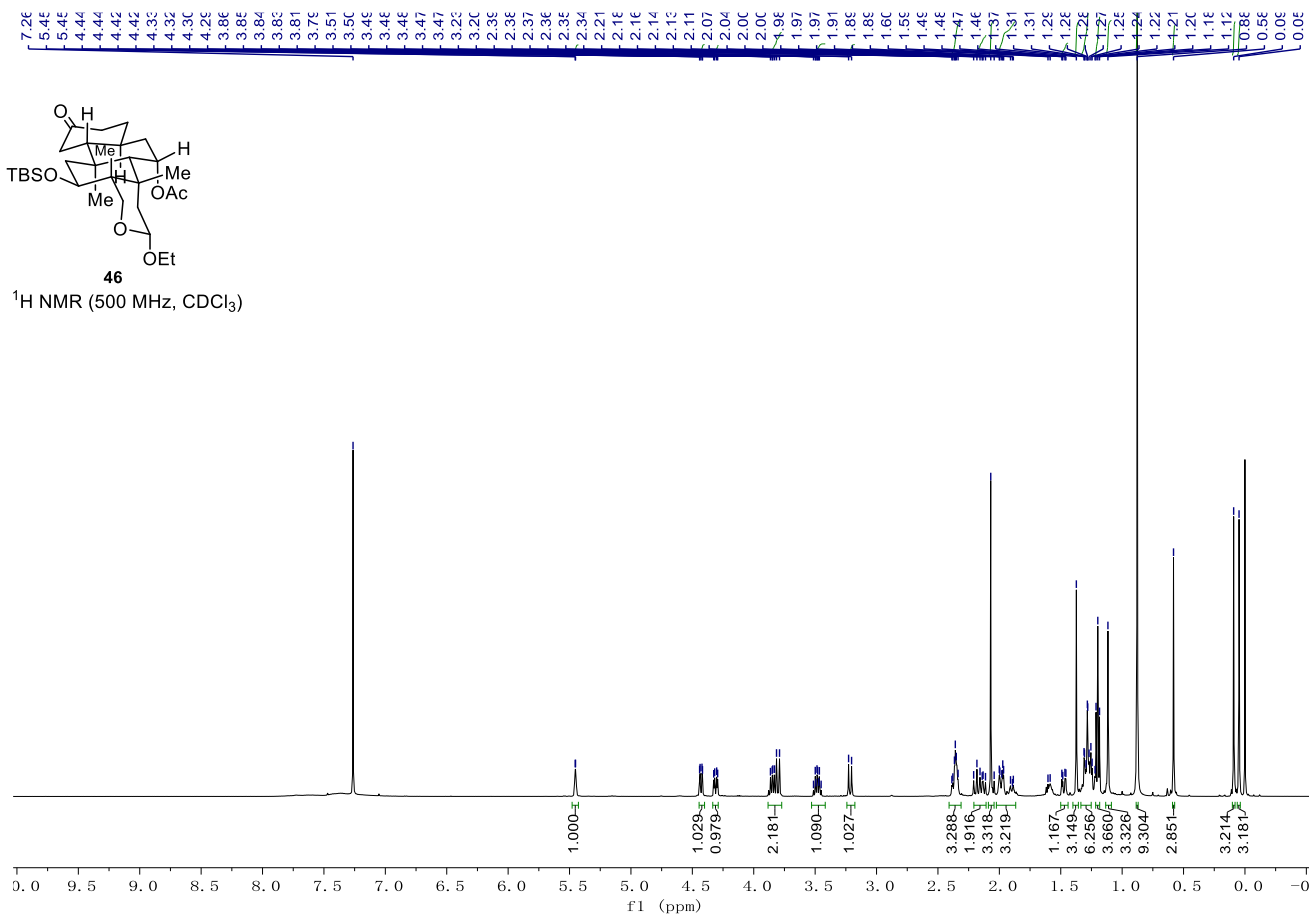


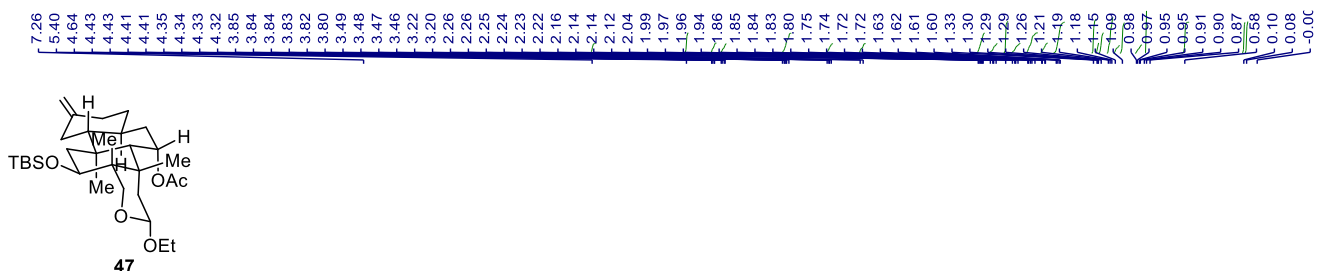
45
¹H NMR (500 MHz, CDCl₃)



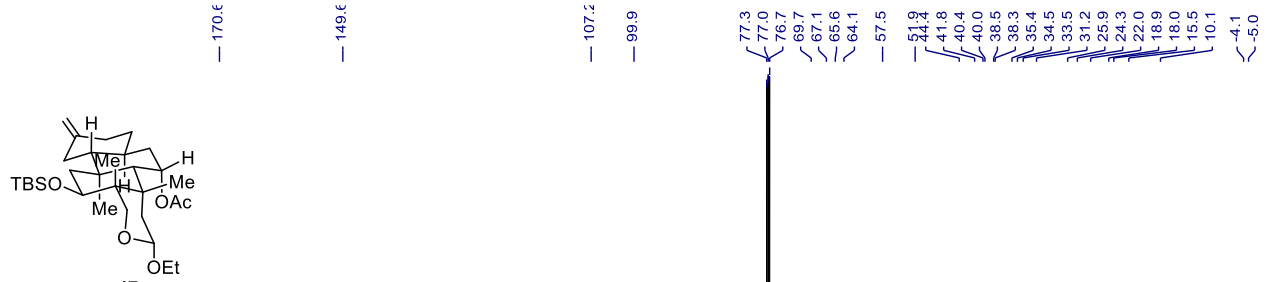
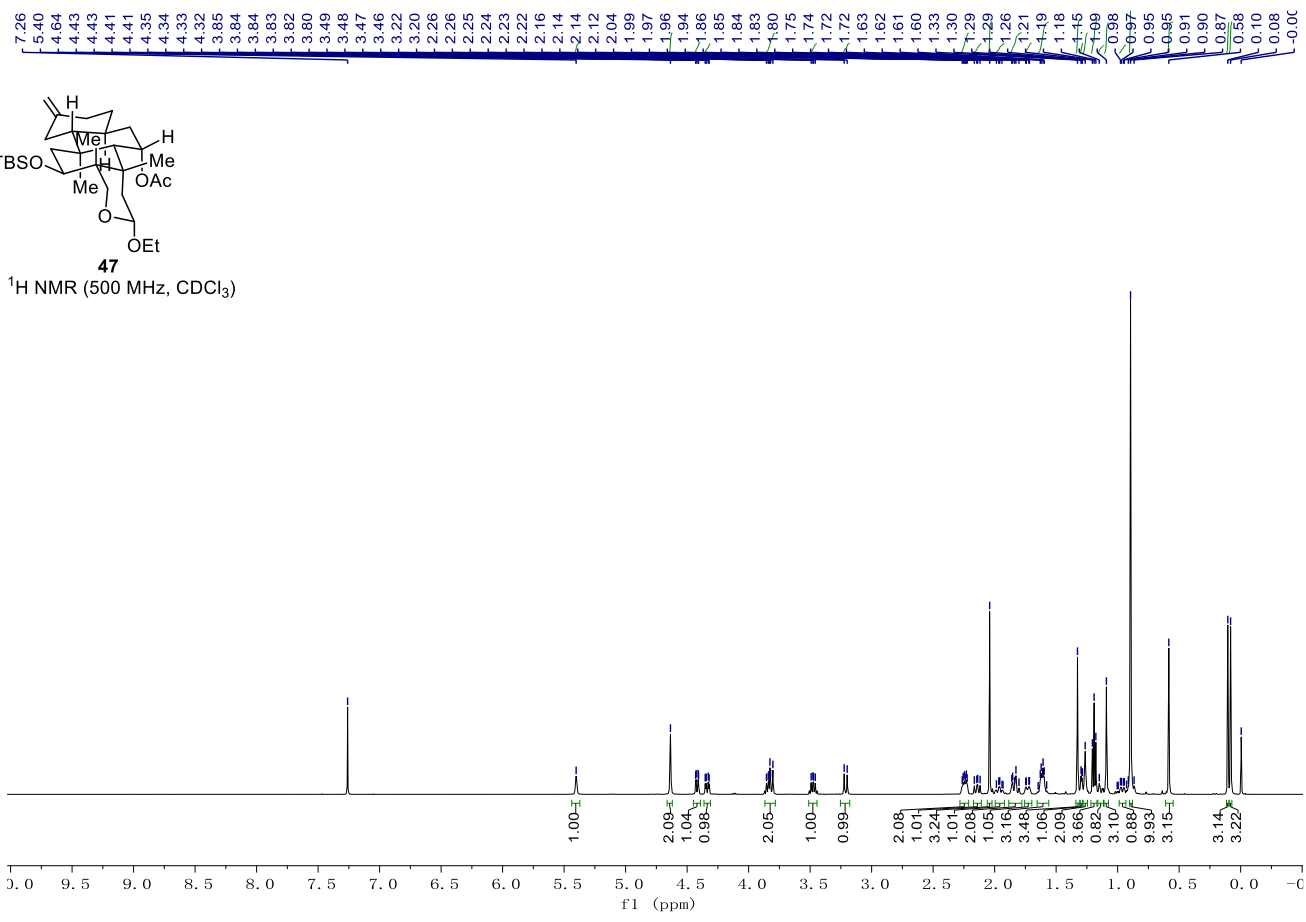
45
¹³C NMR (125 MHz, CDCl₃)



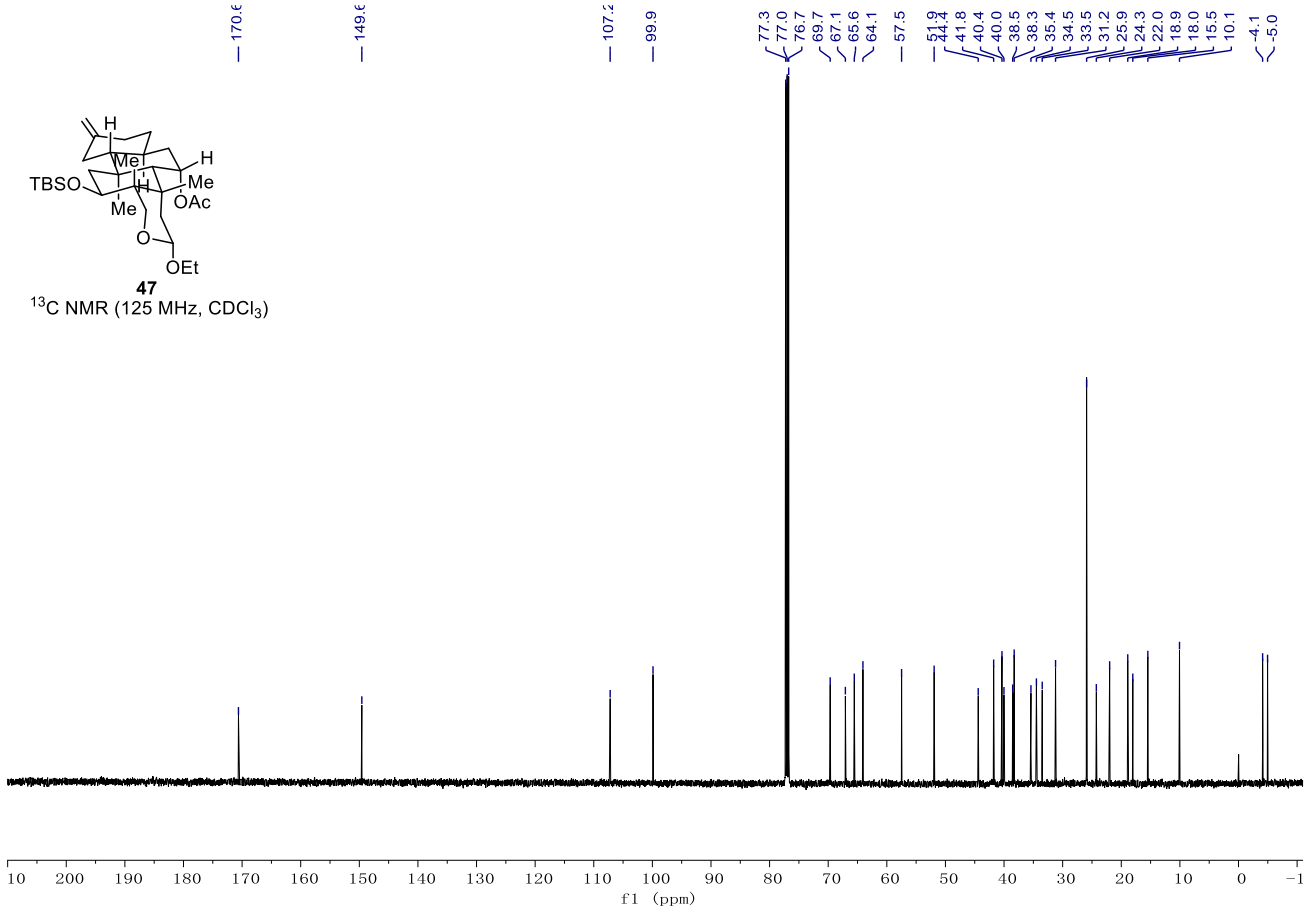


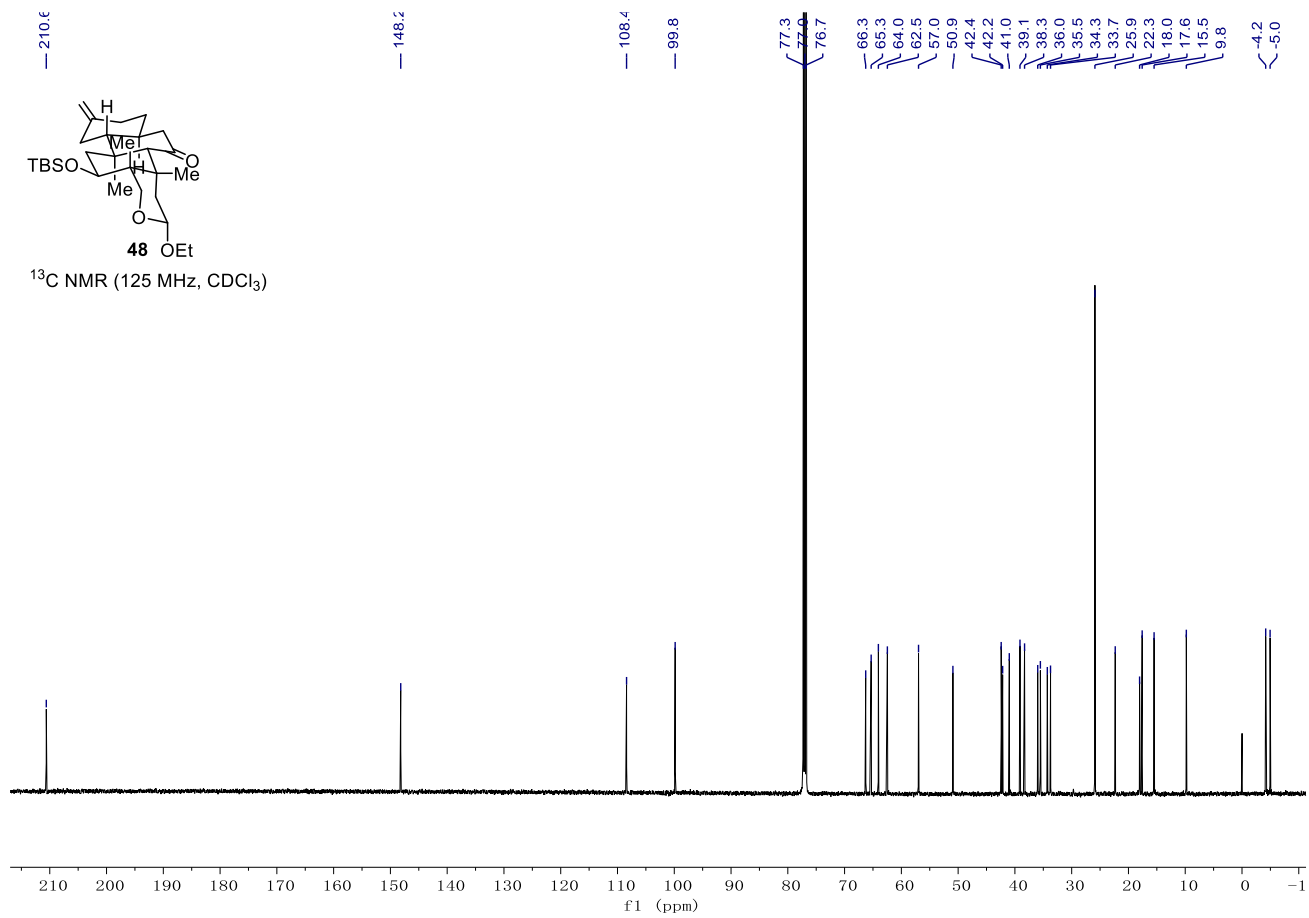
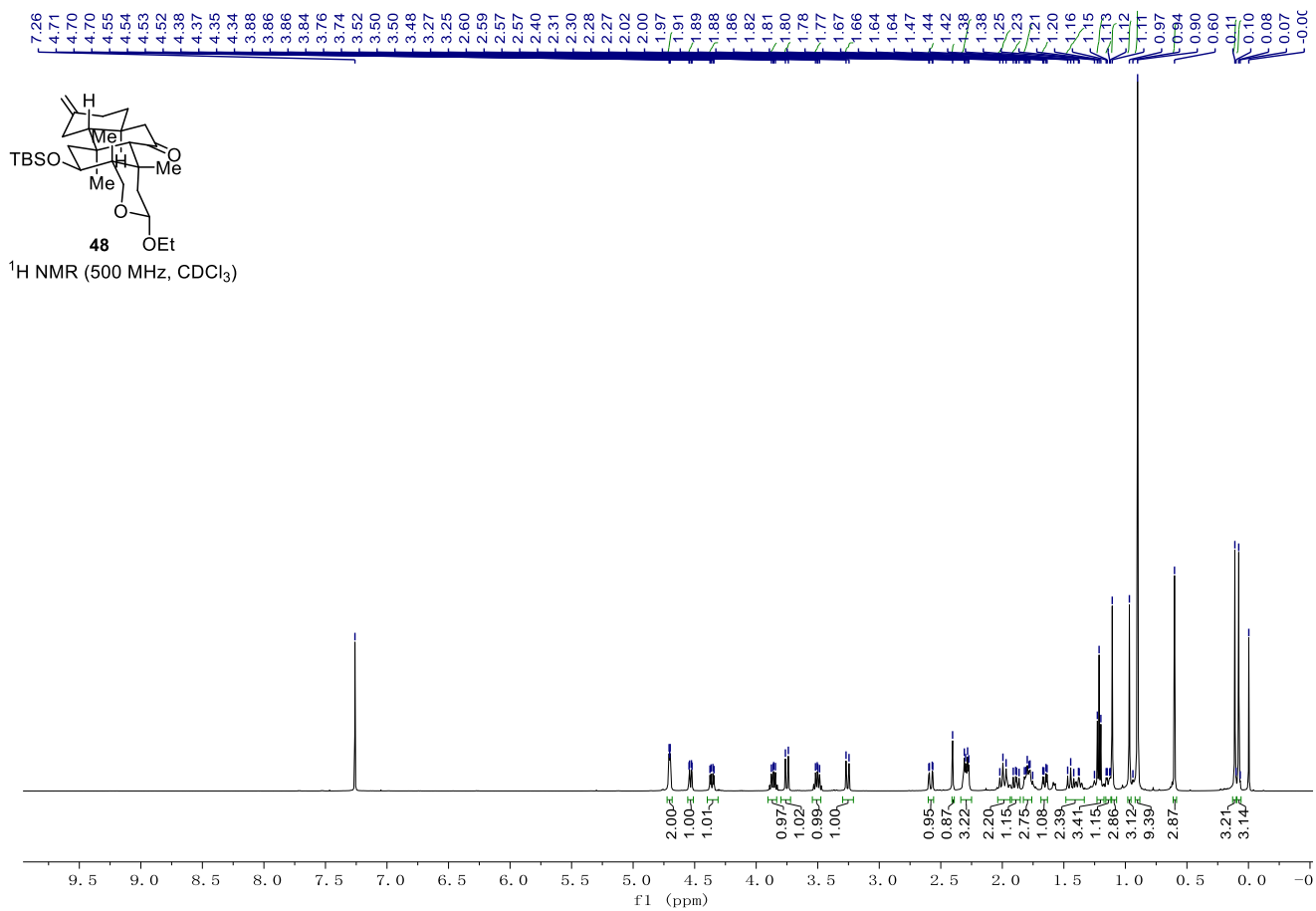


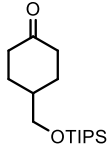
¹H NMR (500 MHz, CDCl₃)



¹³C NMR (125 MHz, CDCl₃)

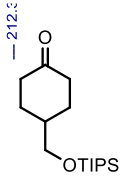
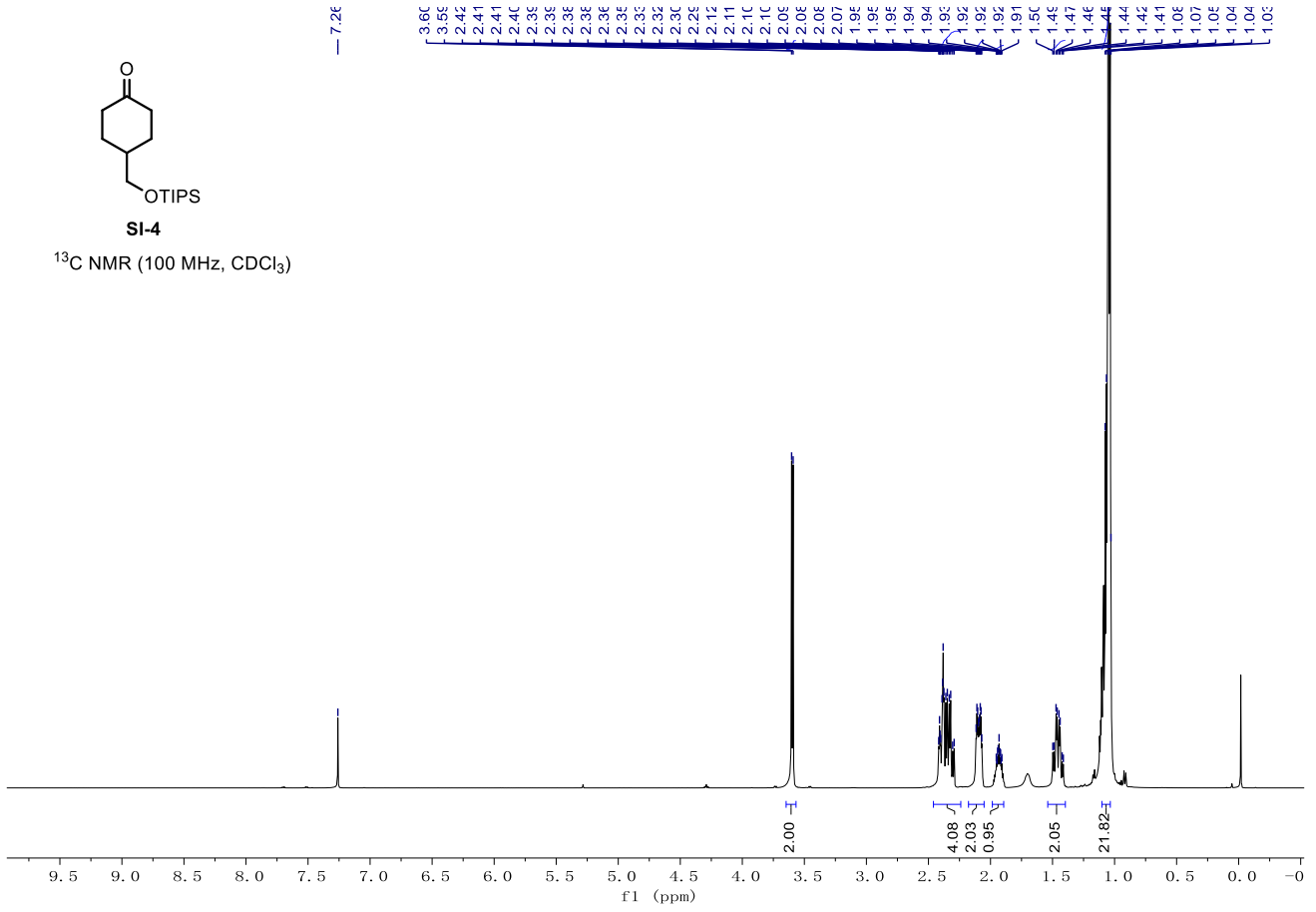






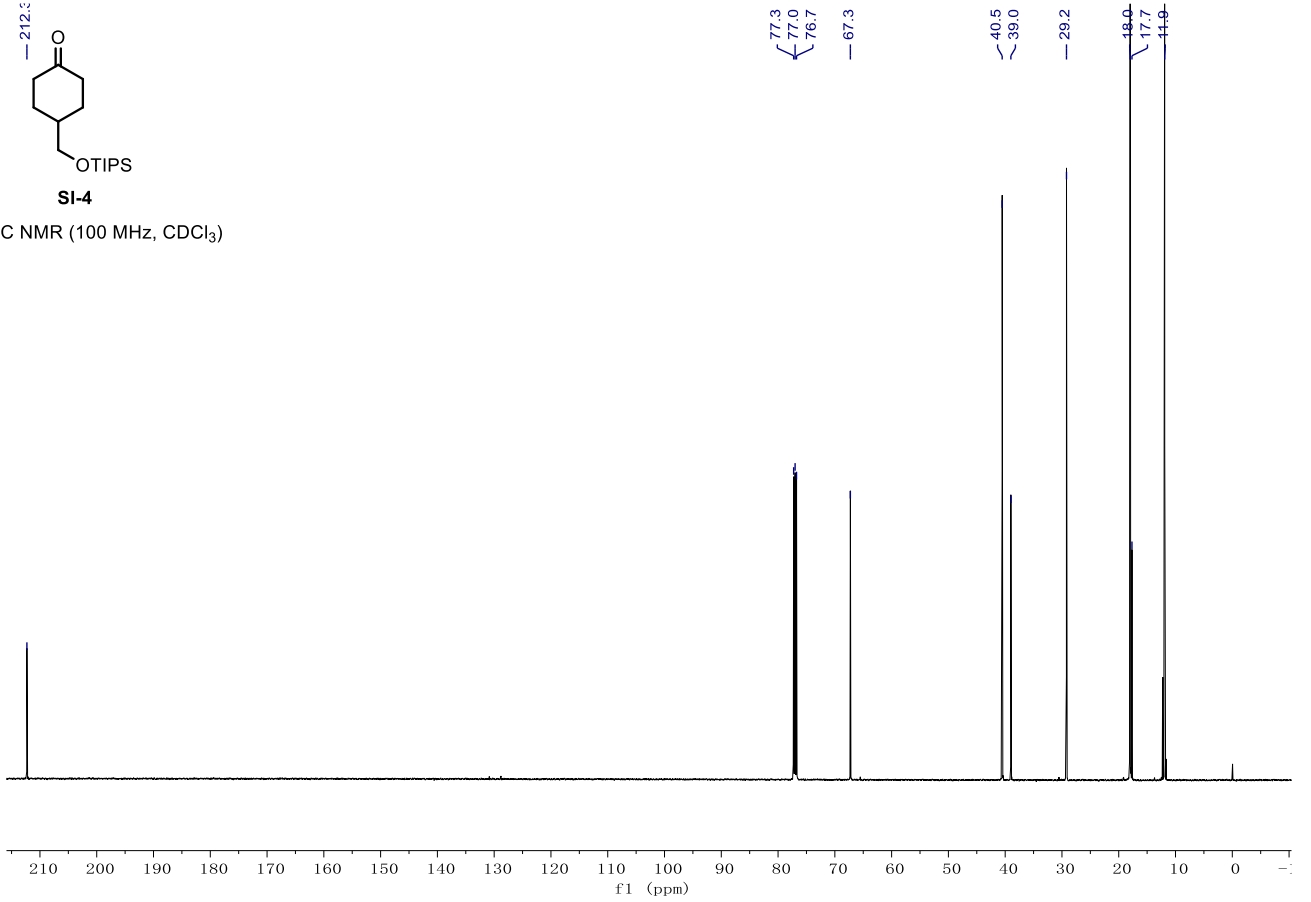
SI-4

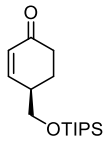
¹³C NMR (100 MHz, CDCl₃)



SI-4

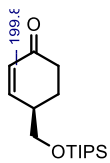
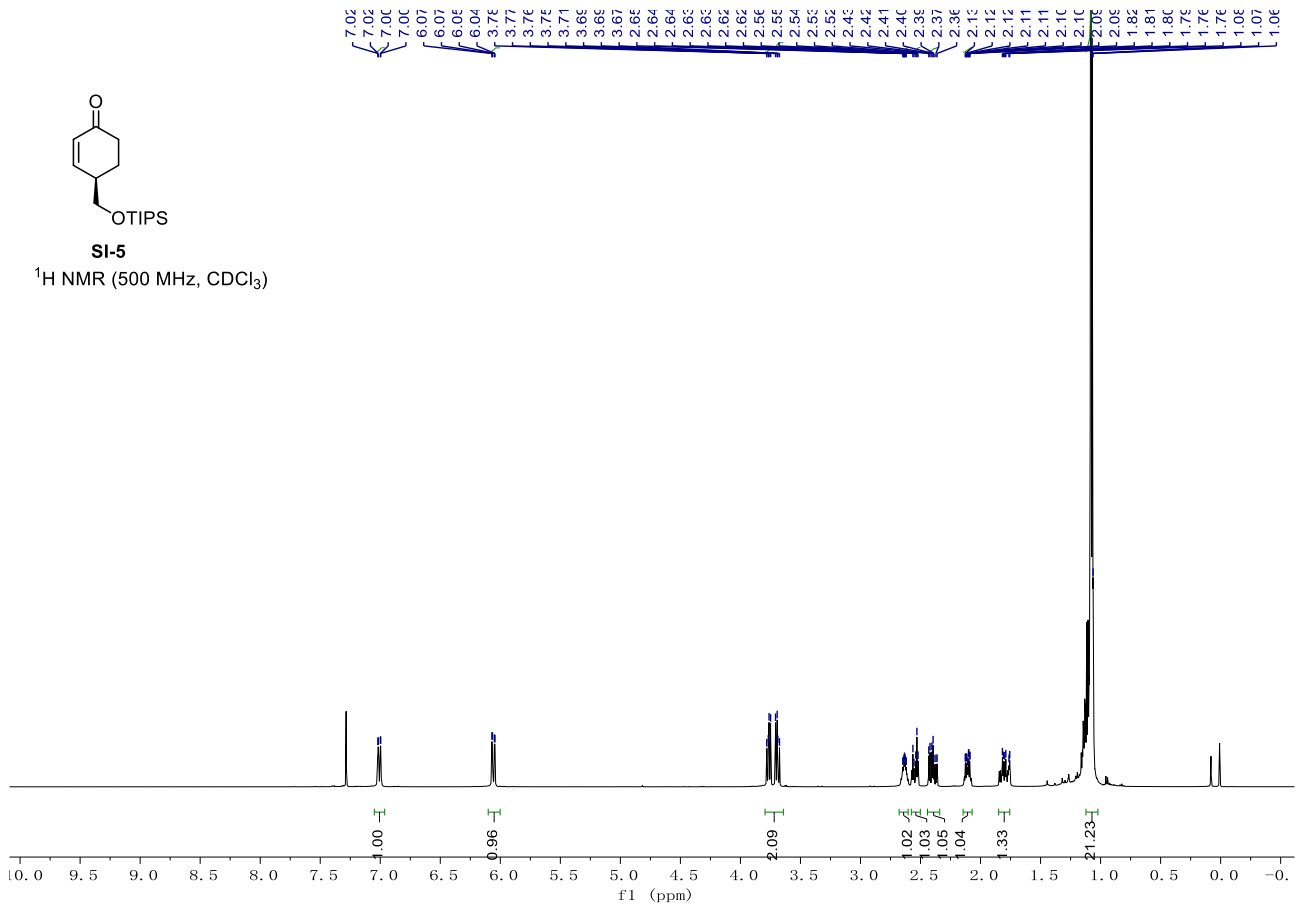
¹³C NMR (100 MHz, CDCl₃)





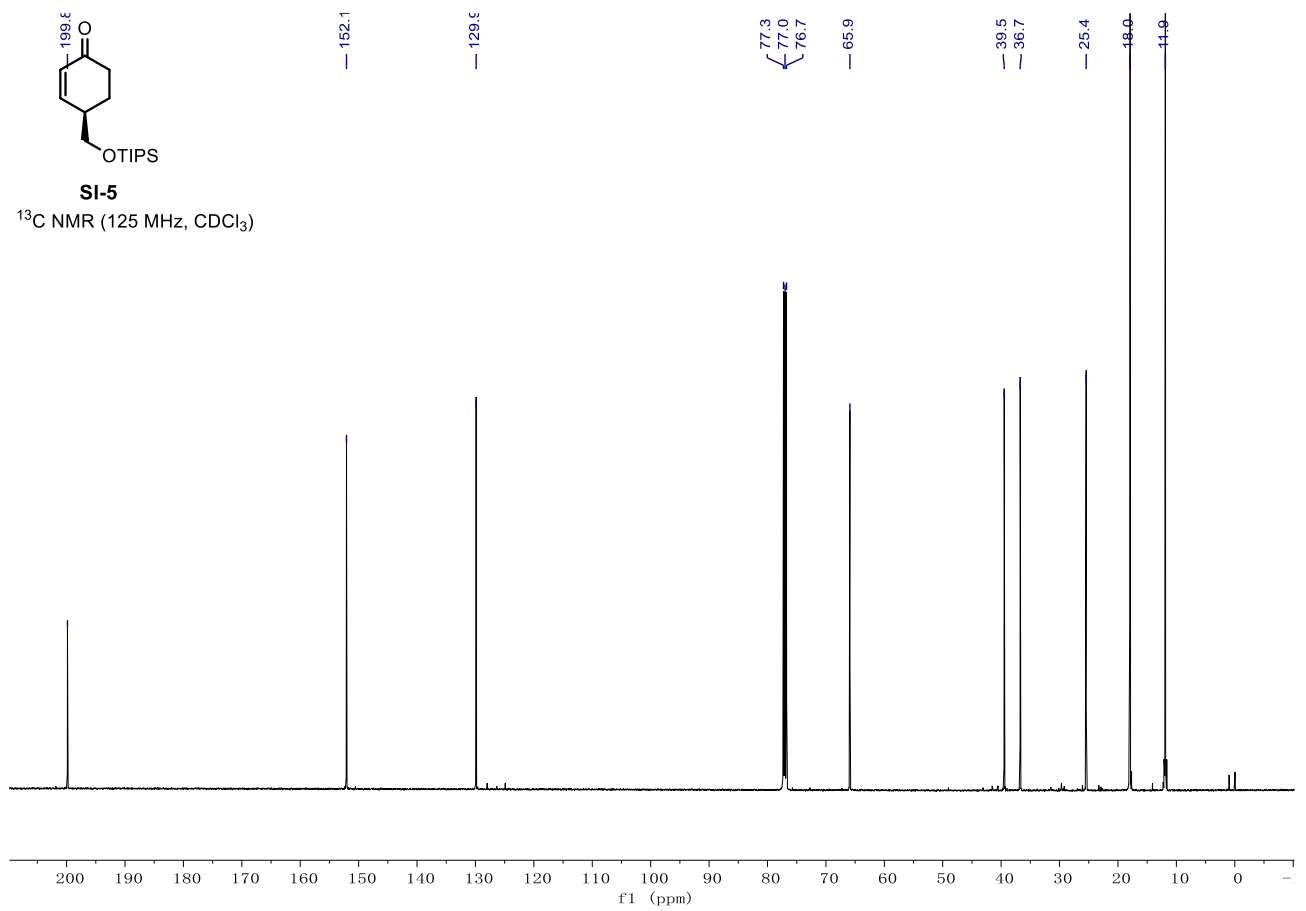
SI-5

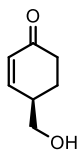
$^1\text{H NMR}$ (500 MHz, CDCl_3)



SI-5

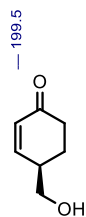
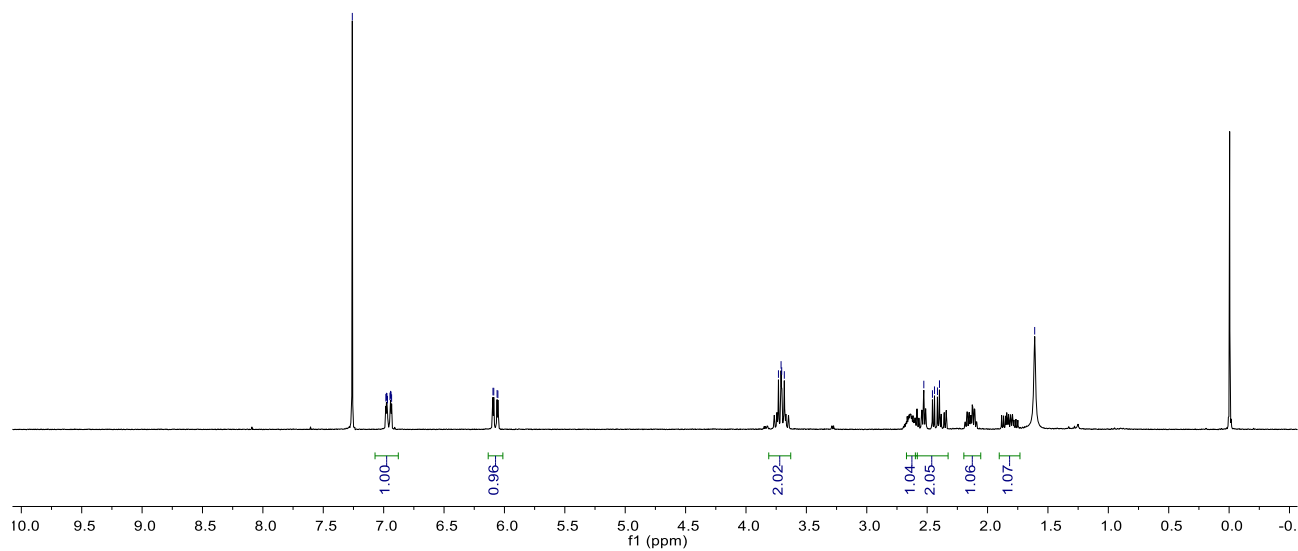
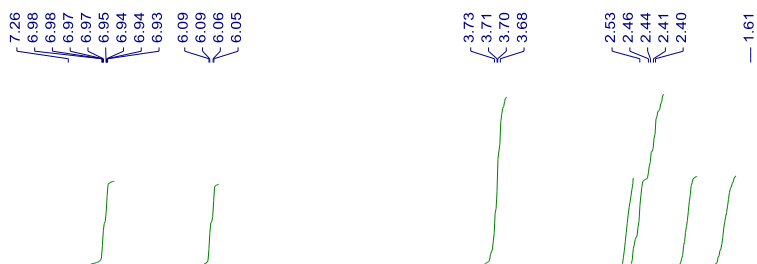
$^{13}\text{C NMR}$ (125 MHz, CDCl_3)





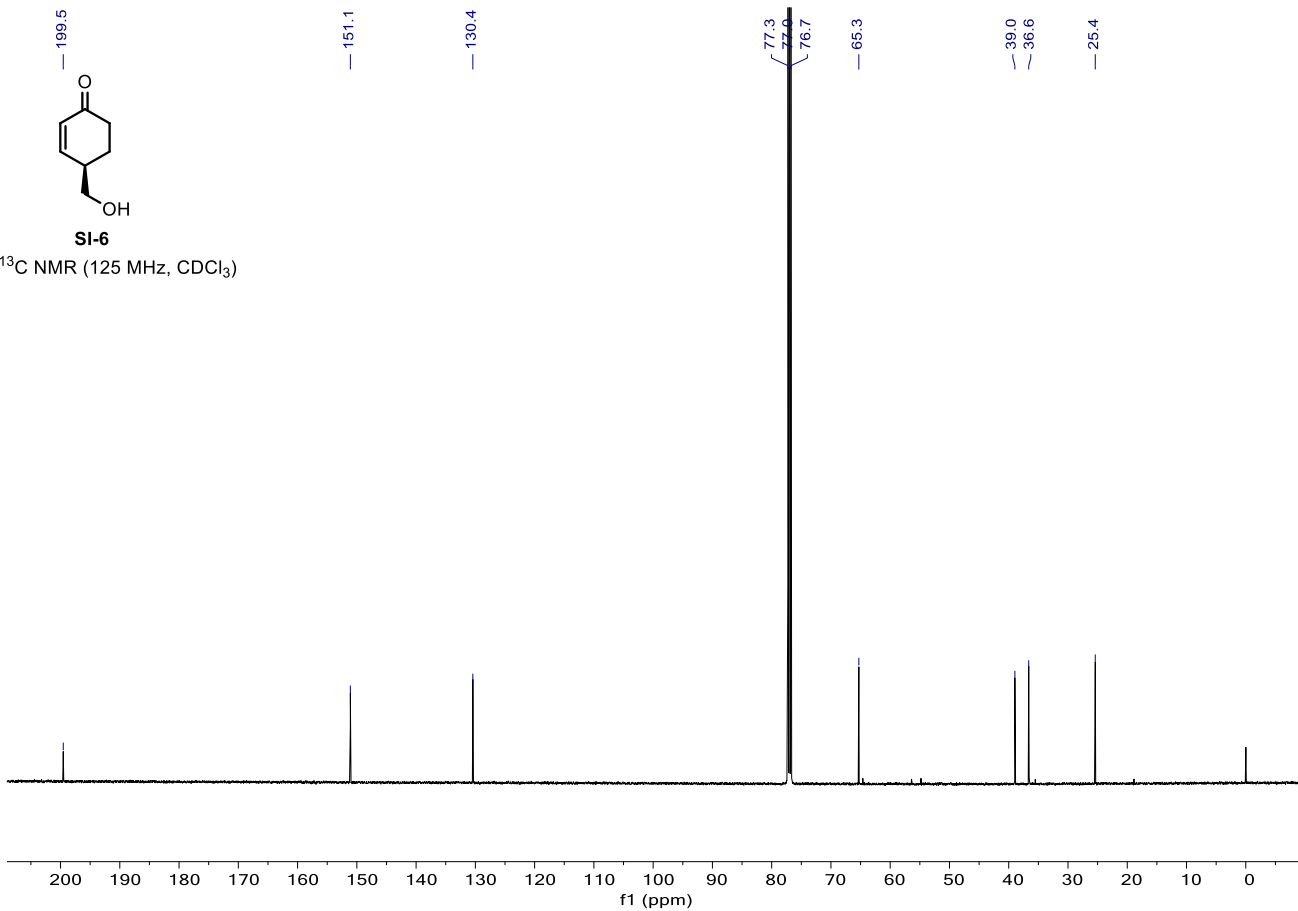
SI-6

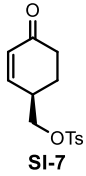
¹H NMR (300 MHz, CDCl₃)



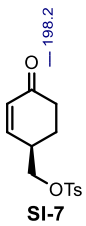
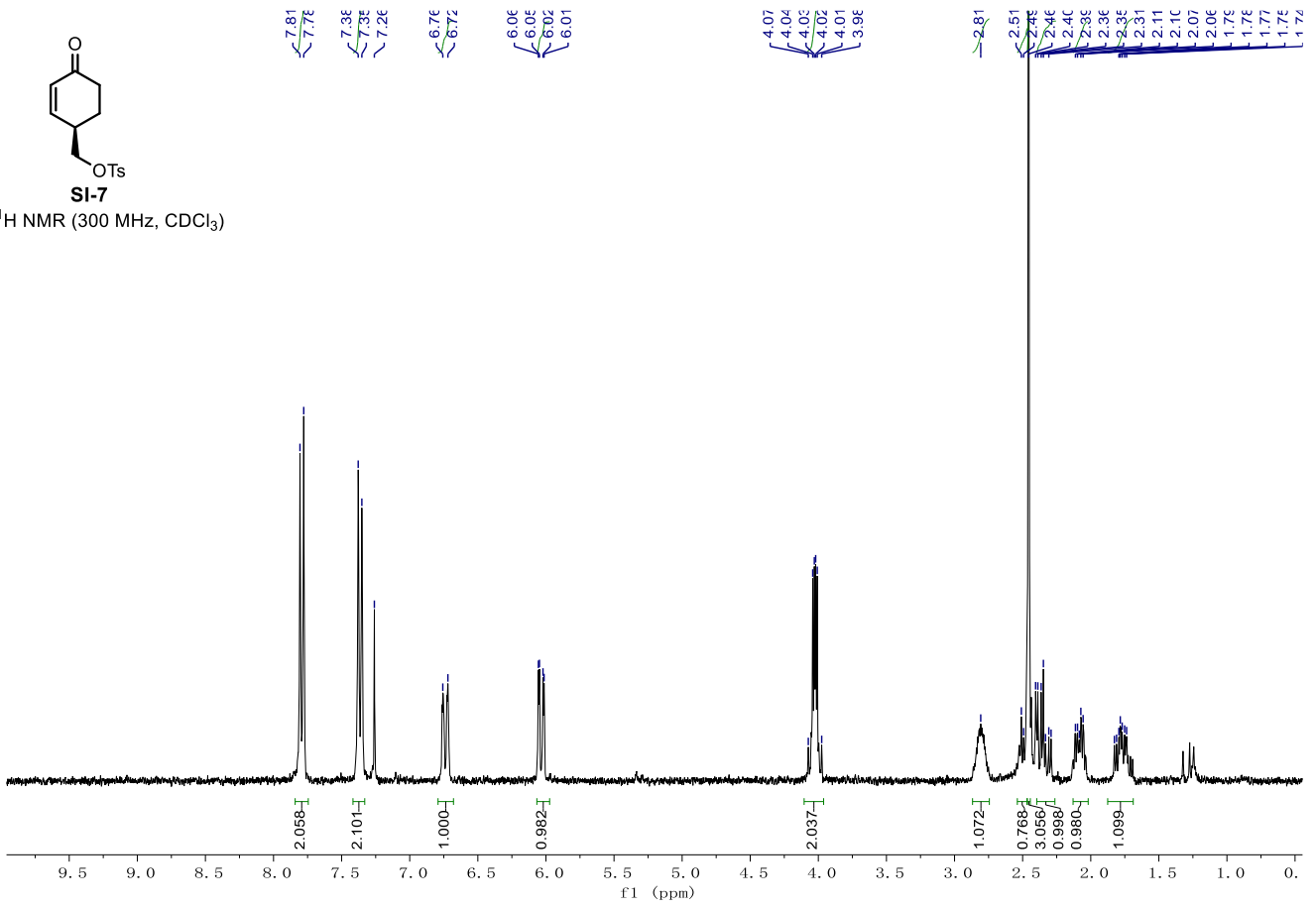
SI-6

¹³C NMR (125 MHz, CDCl₃)

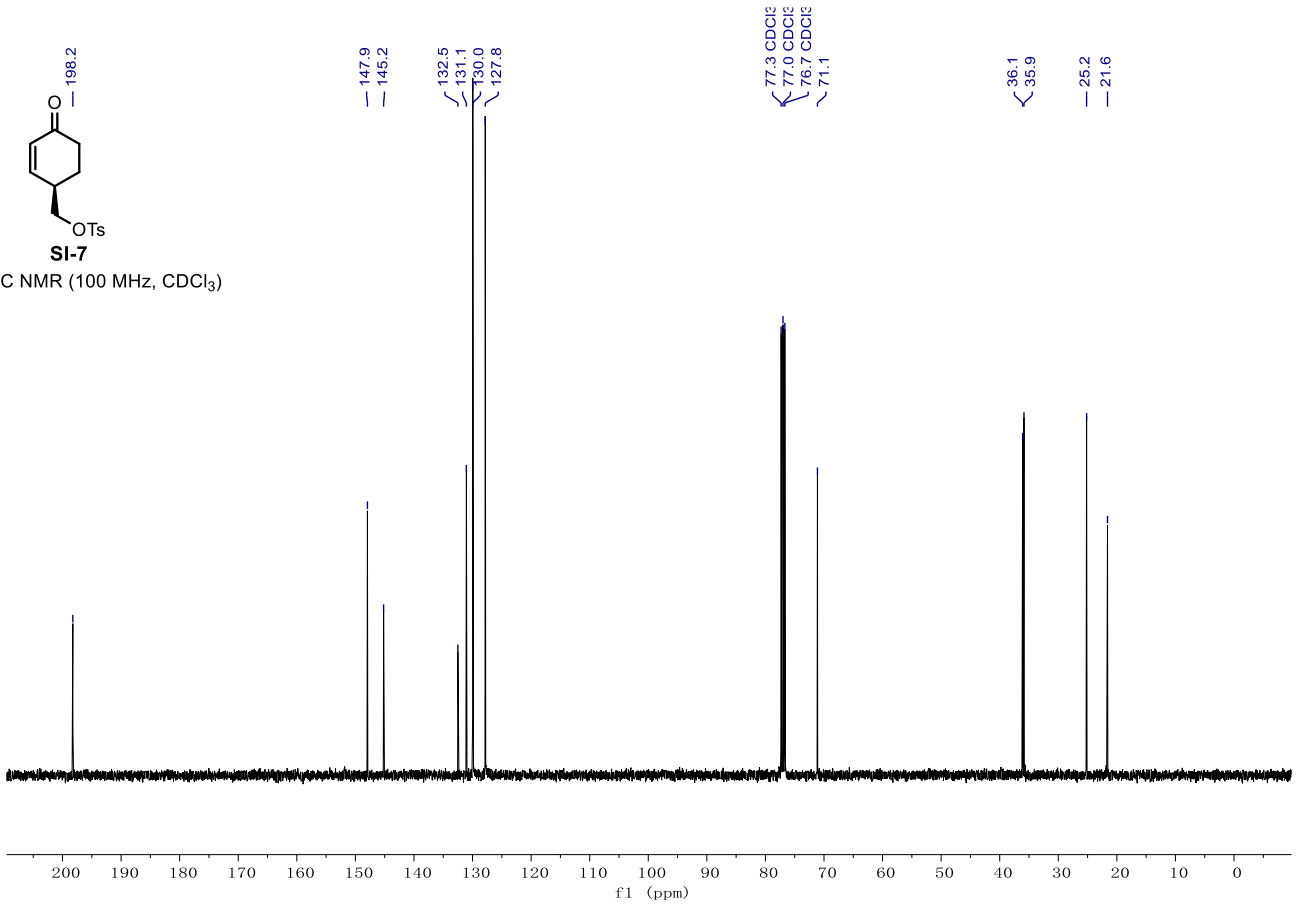


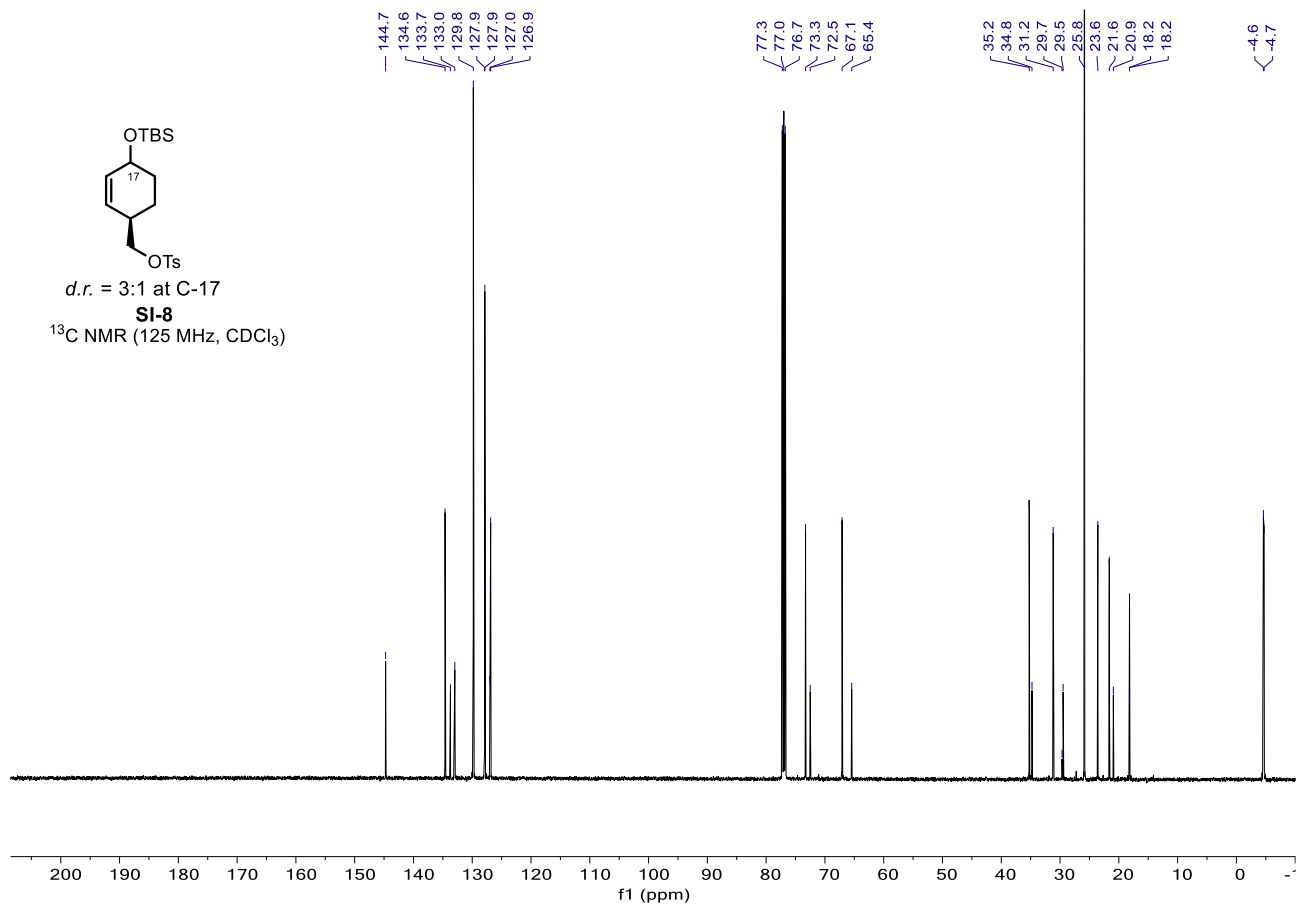
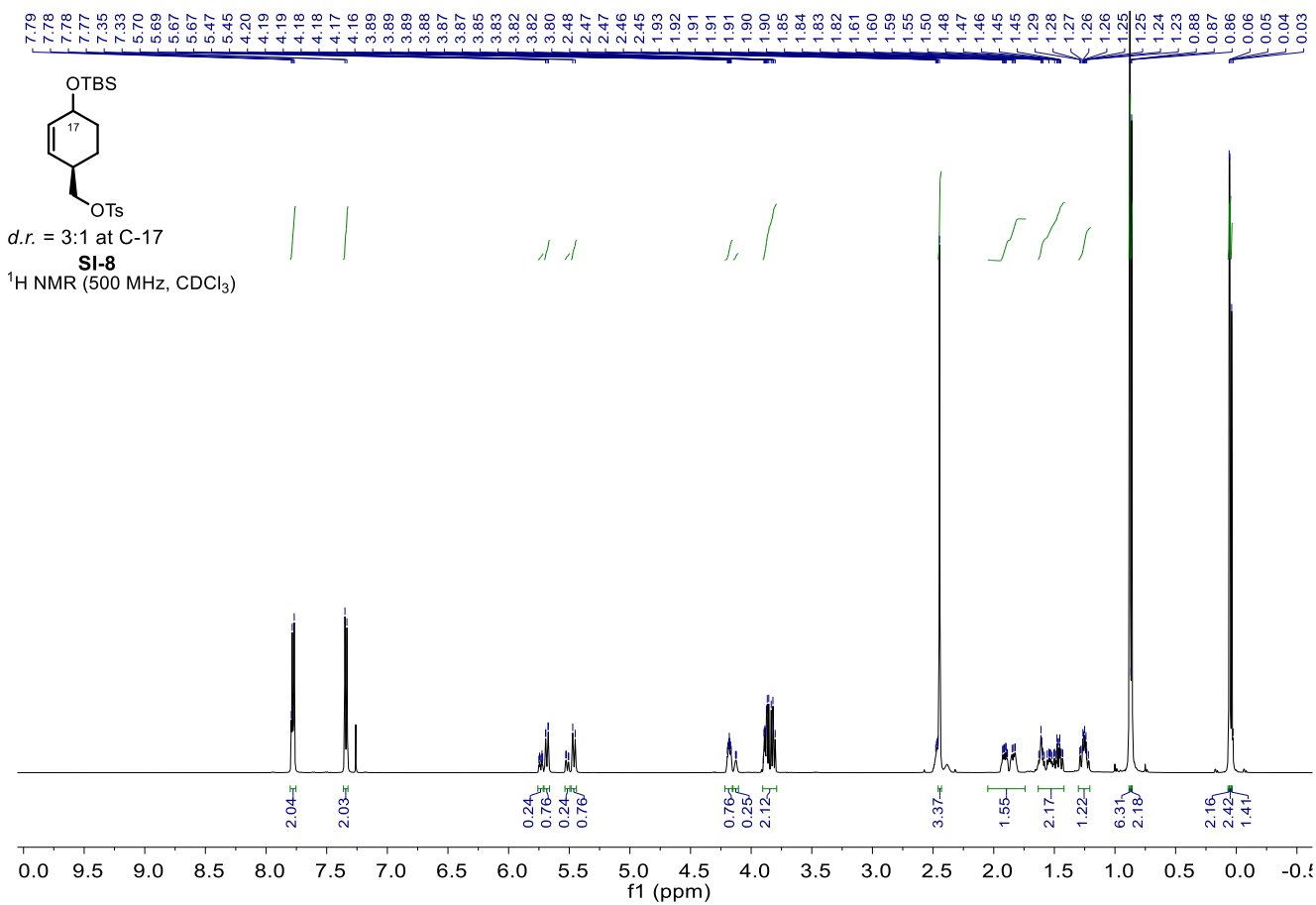


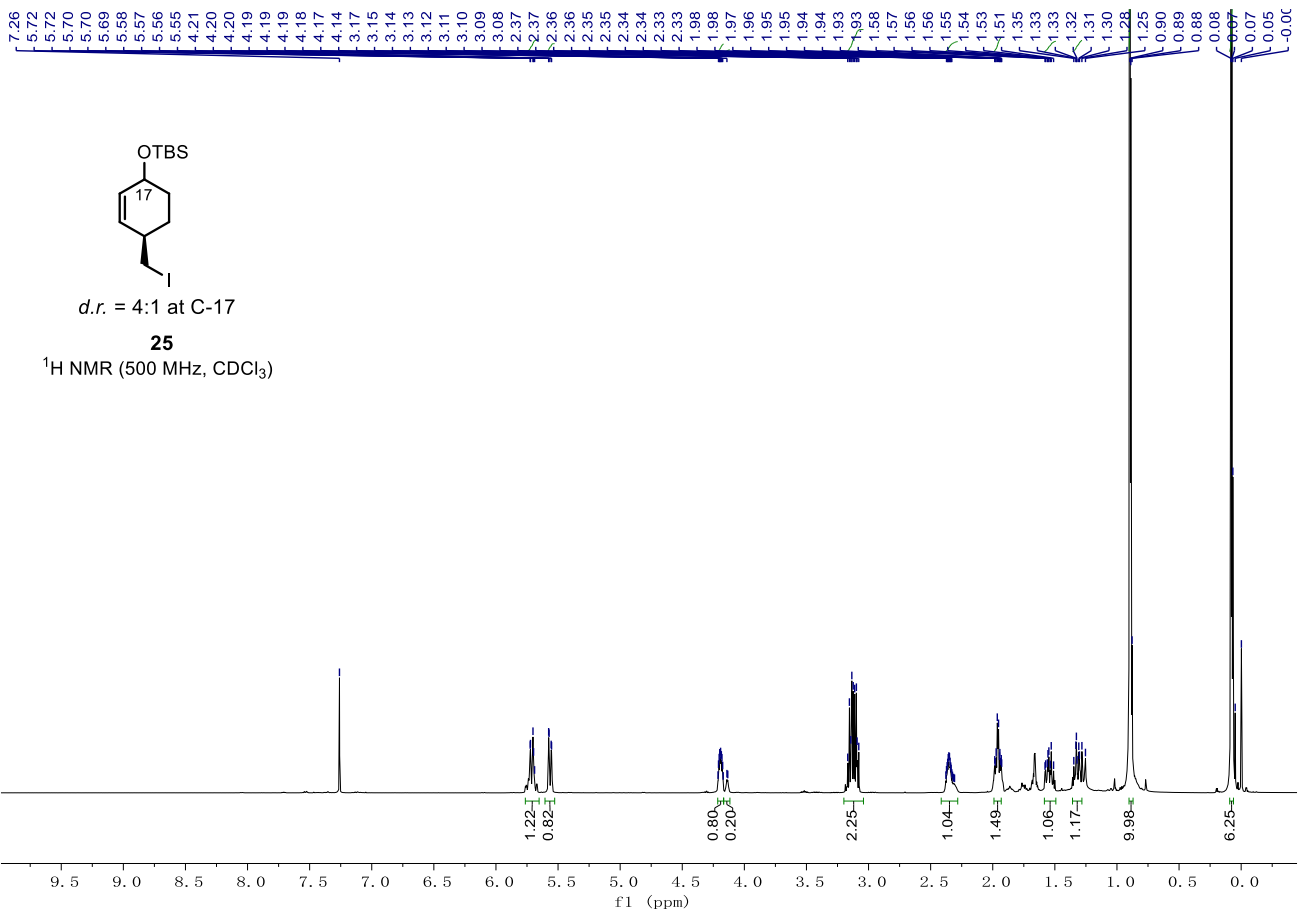
¹H NMR (300 MHz, CDCl₃)



¹³C NMR (100 MHz, CDCl₃)





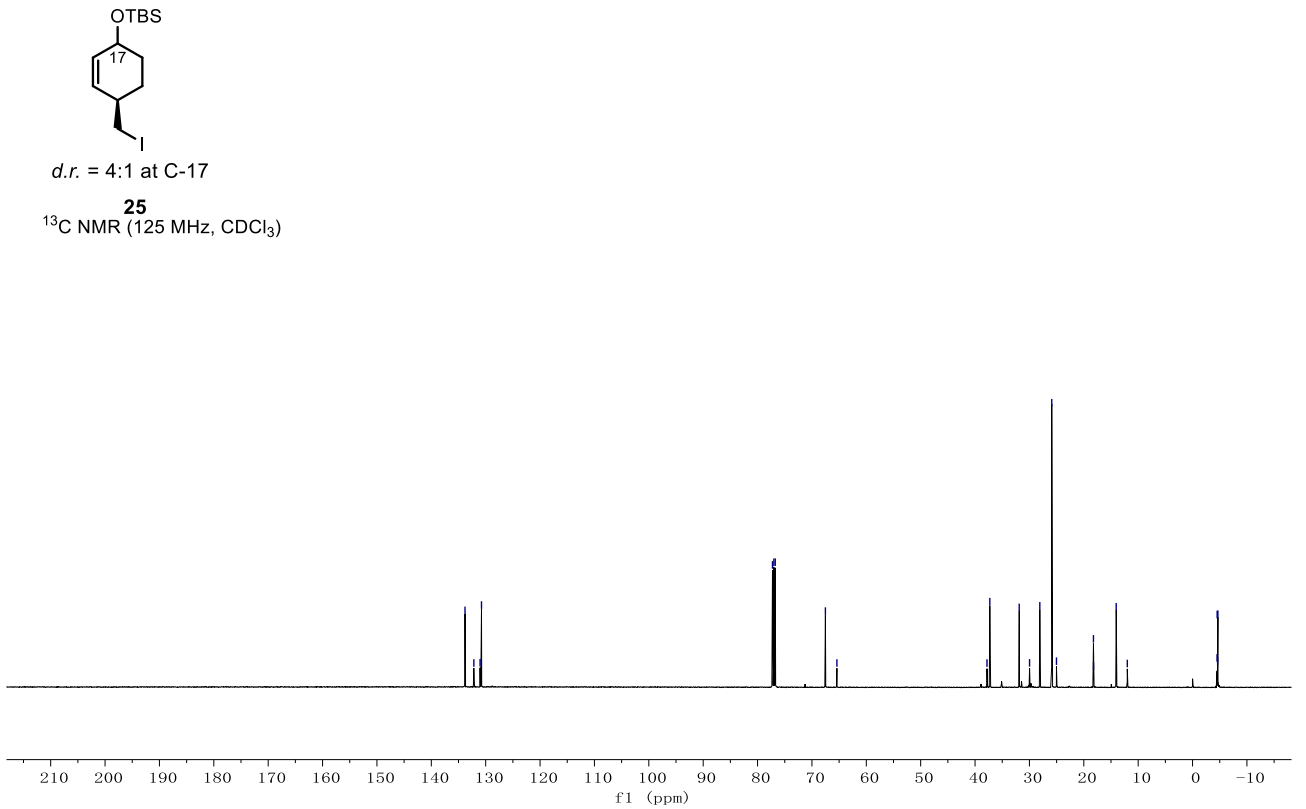


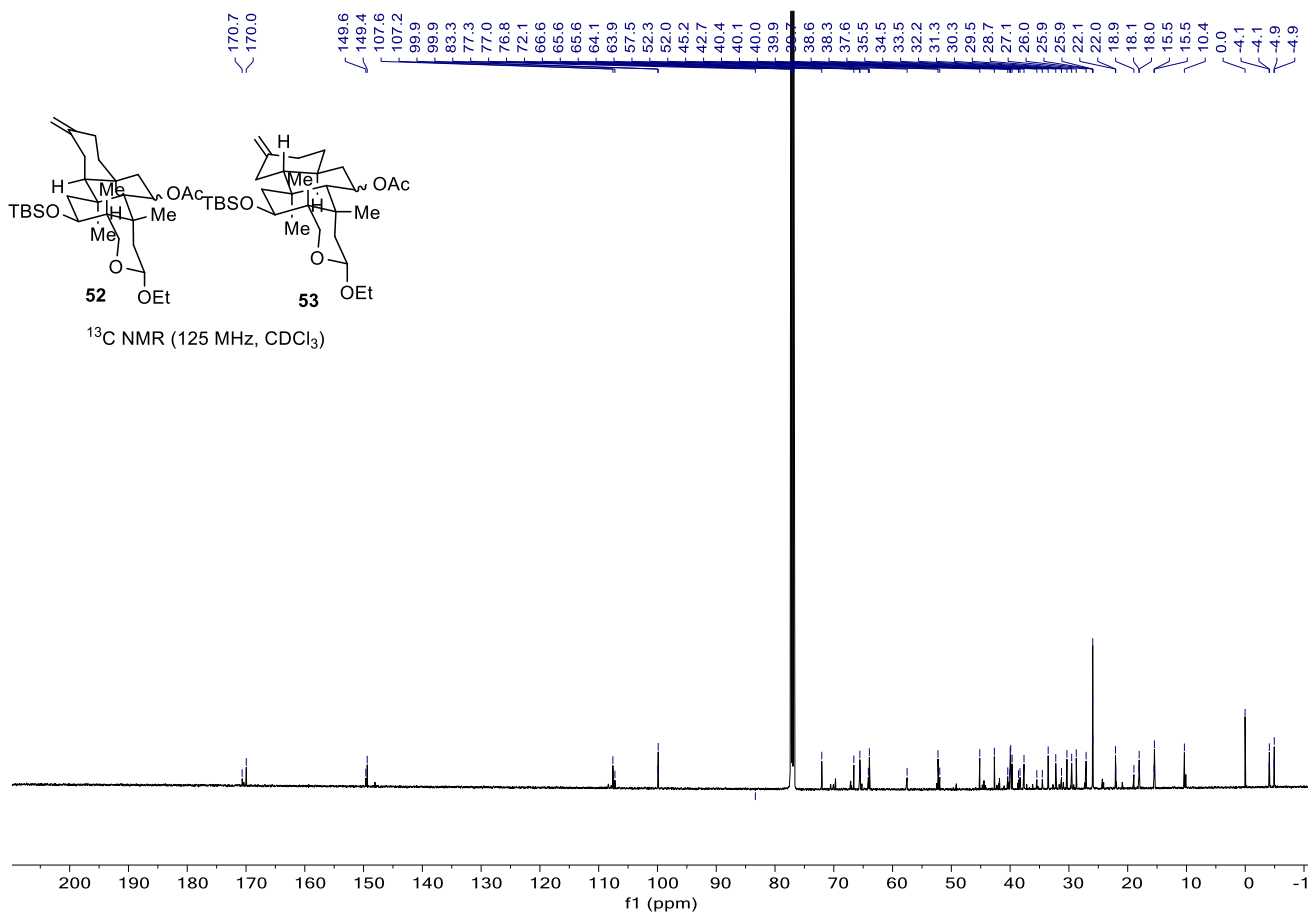
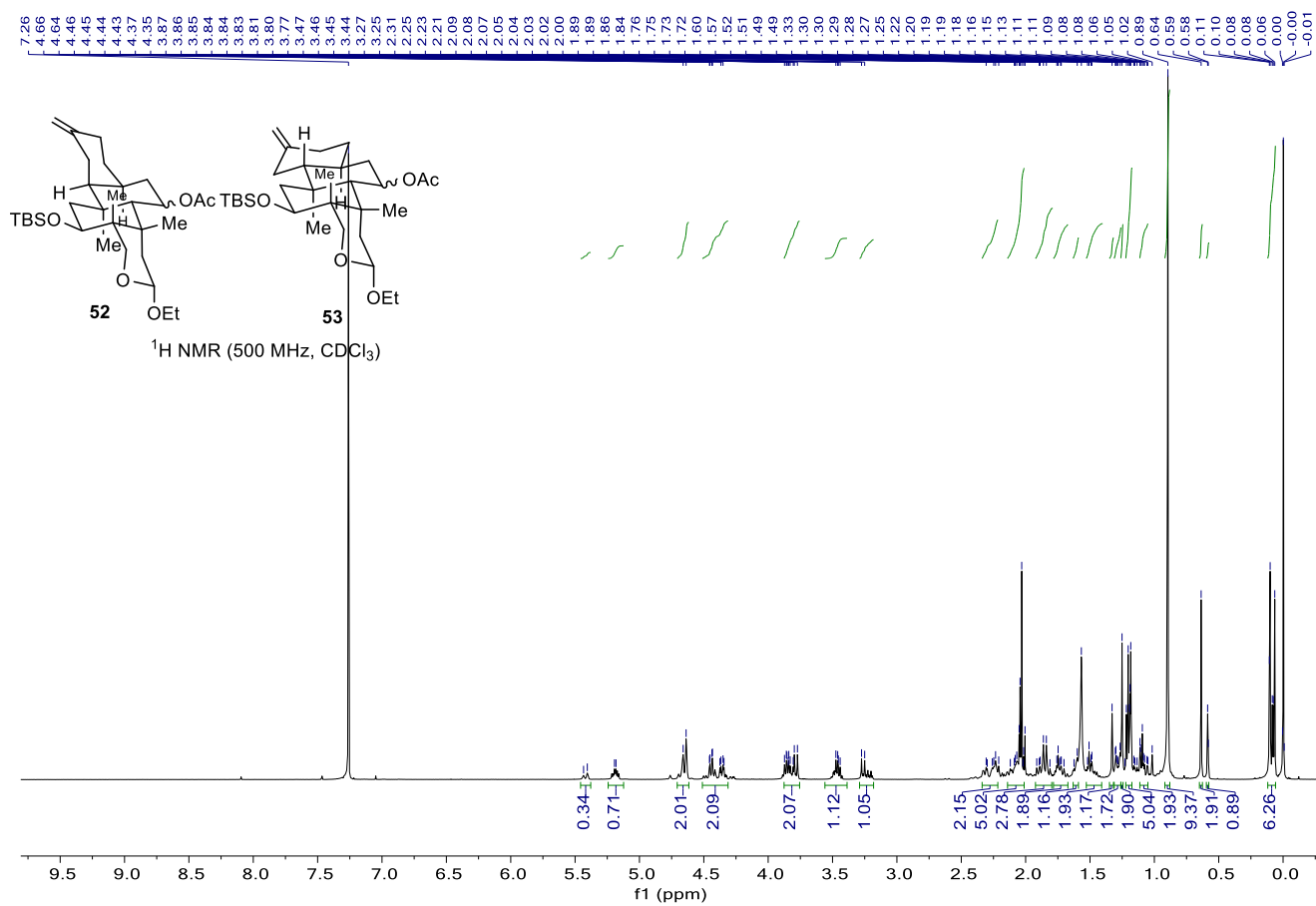
133.8
132.2
131.0
130.8

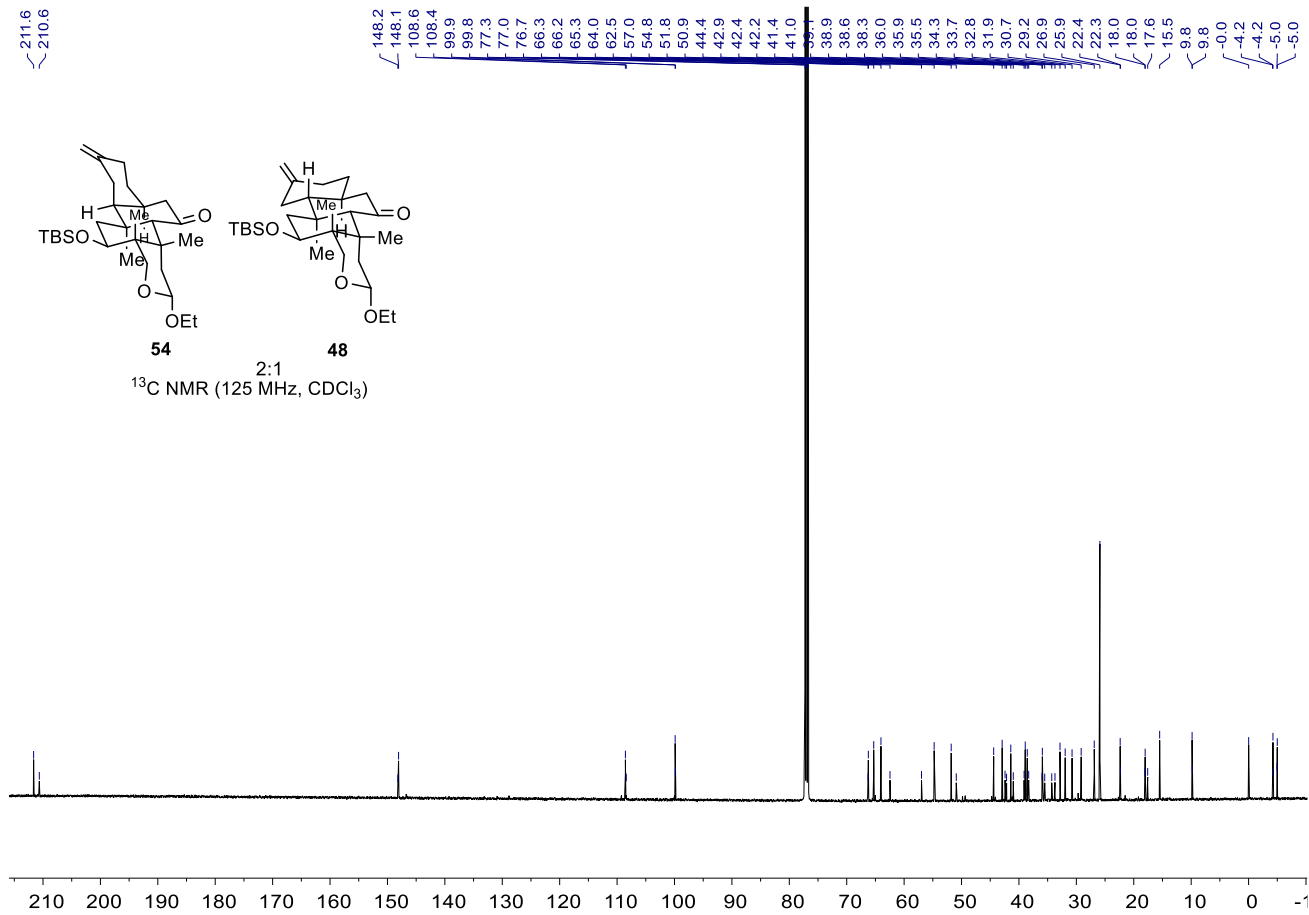
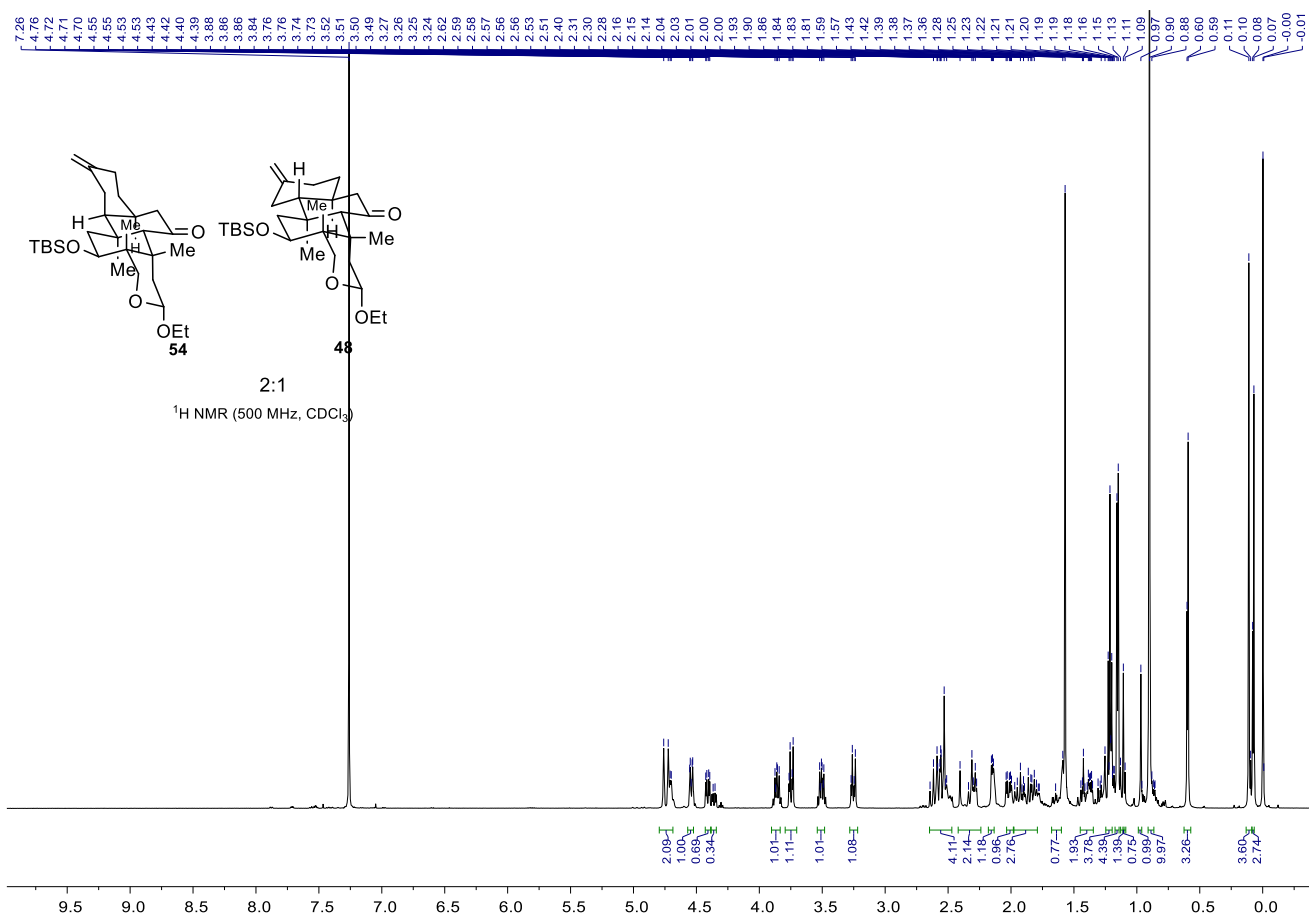
77.3
77.0
76.7
67.5
65.4

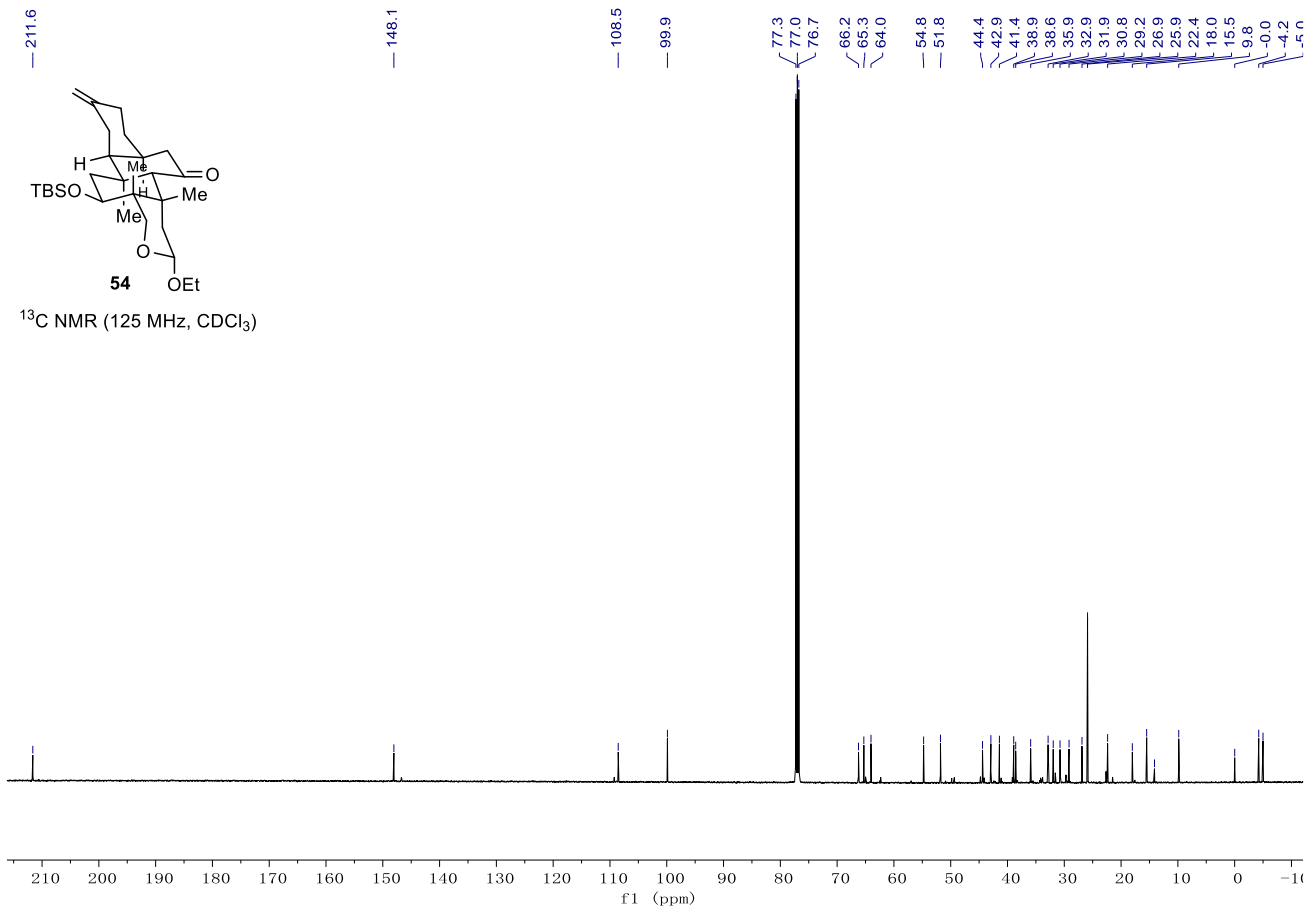
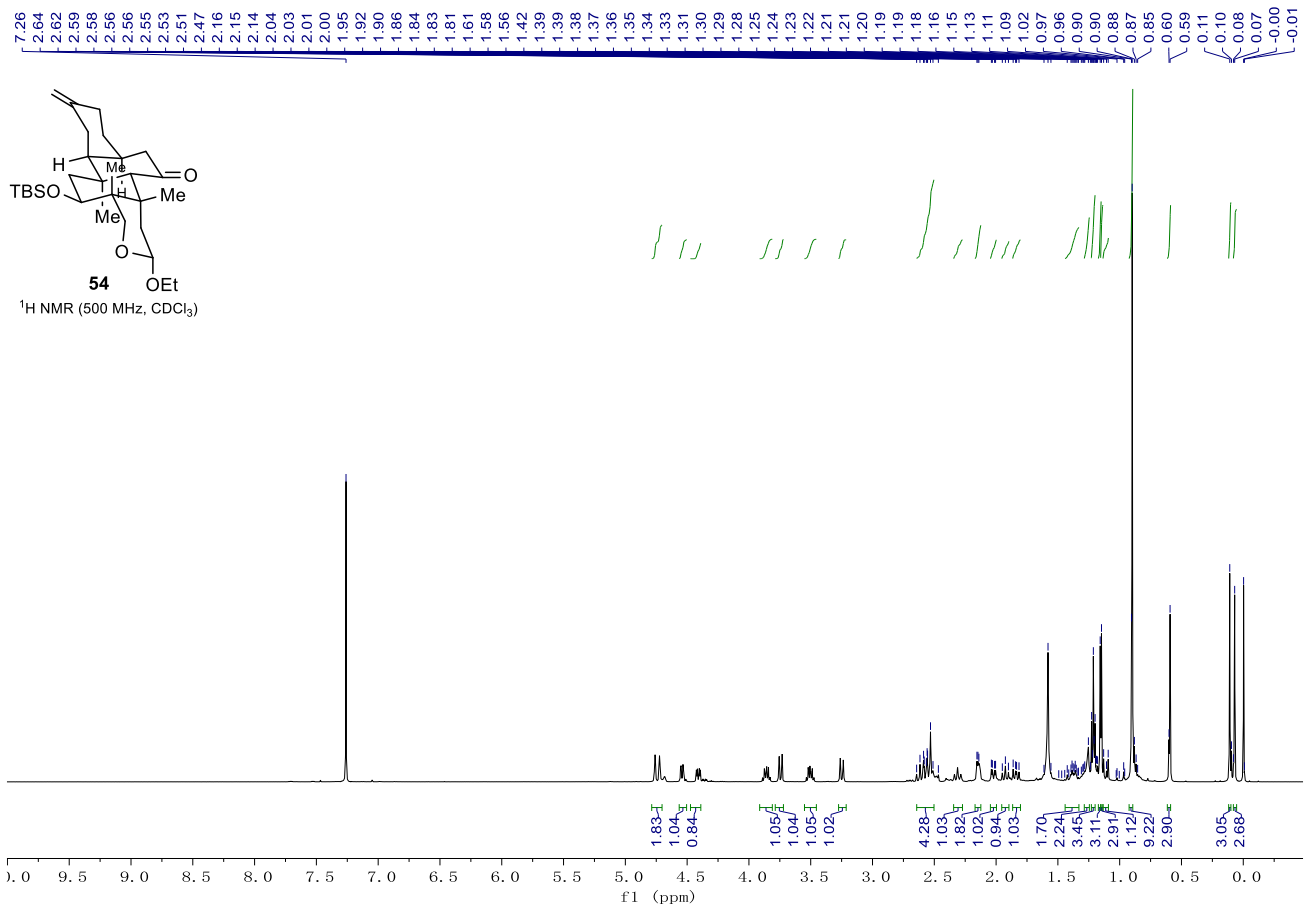
37.8
37.3
31.9
30.0
28.1
25.9
25.0
18.2
18.2
14.0
12.0

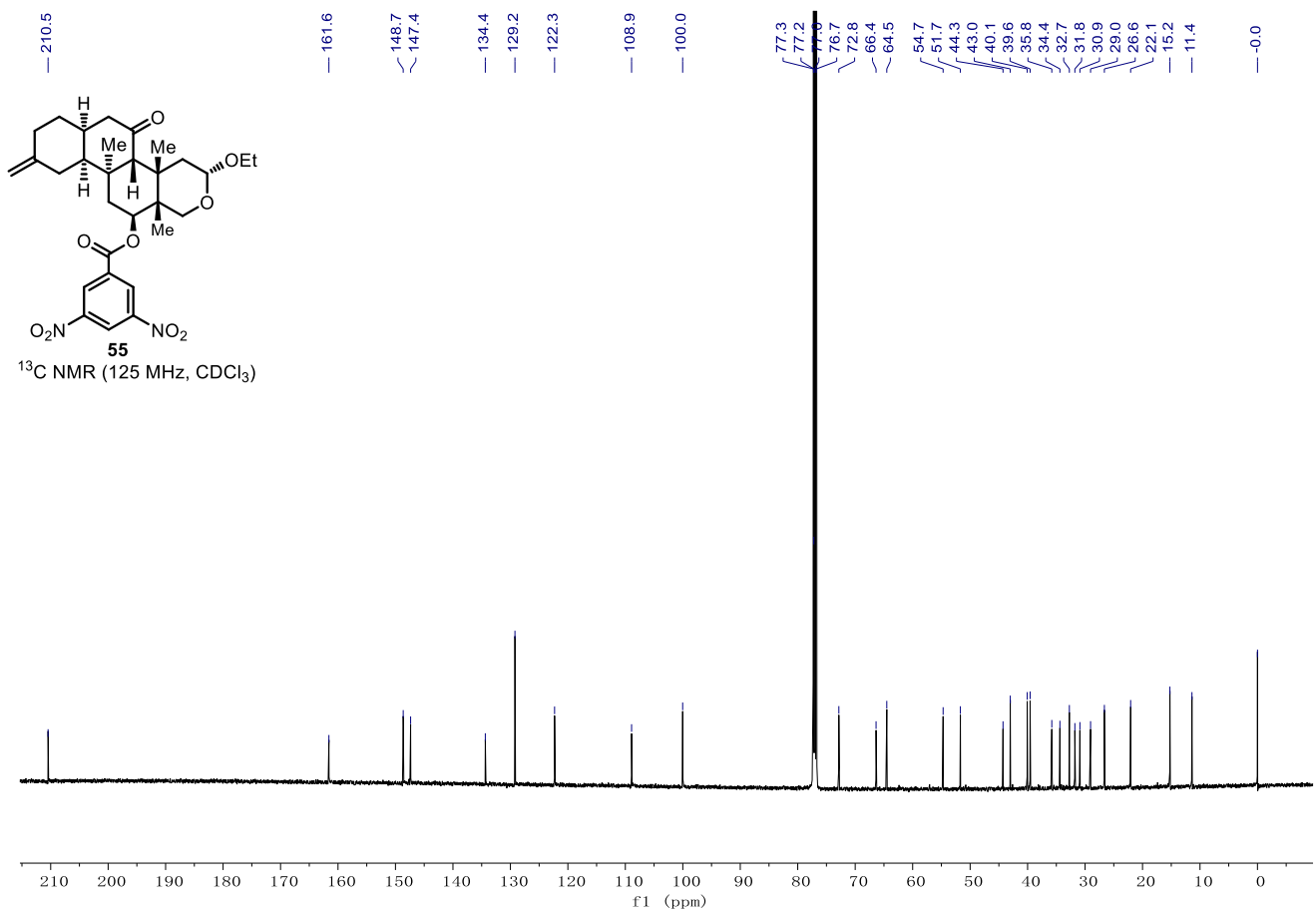
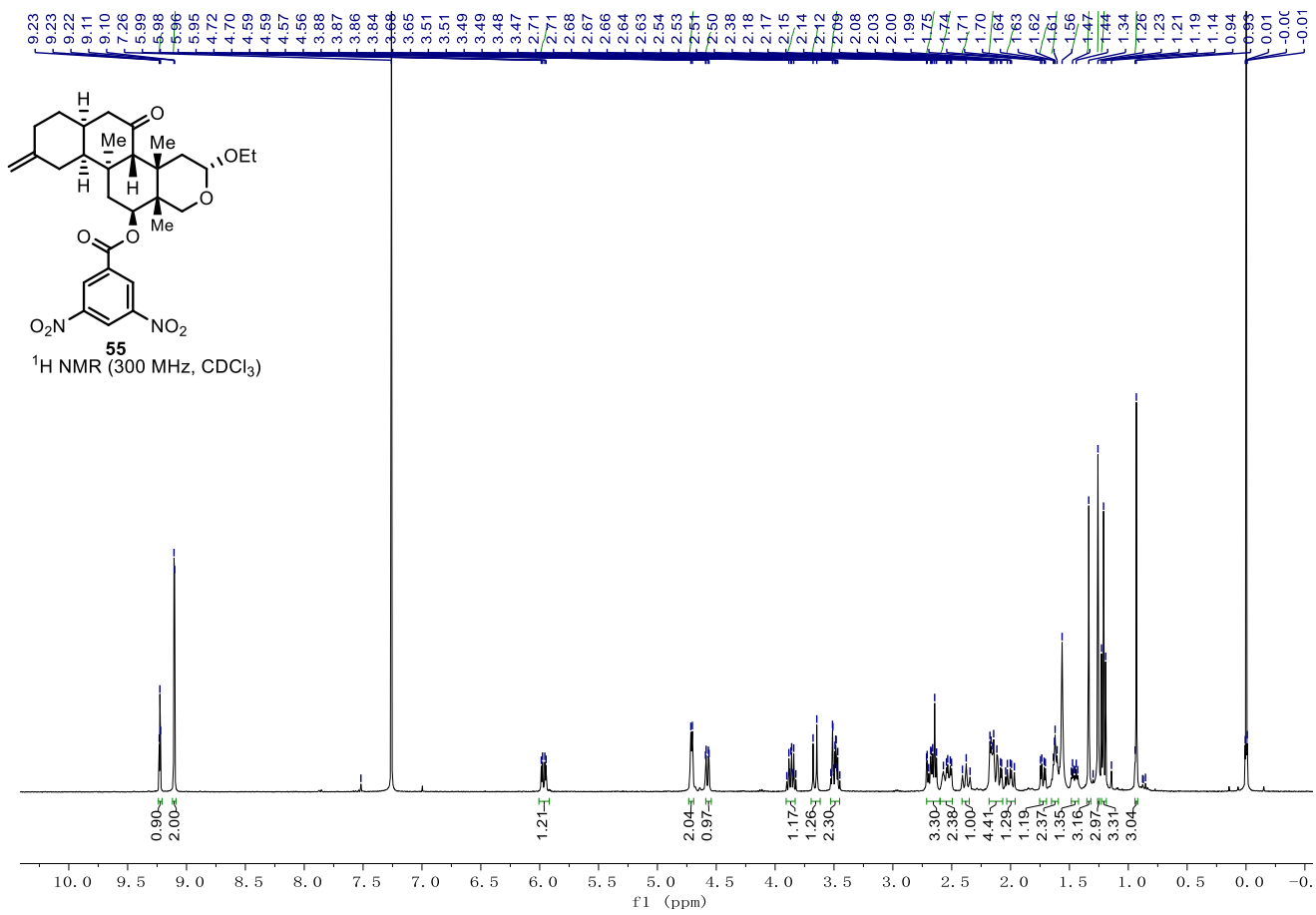
4.5
4.5
4.6
4.7

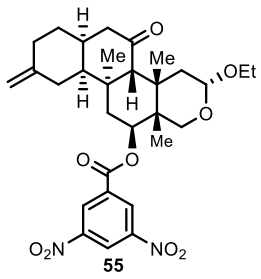












¹³C NMR (125 MHz, CDCl₃)

