A Concise Total Synthesis of Saliniketal B

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Contents

1. General Experimental

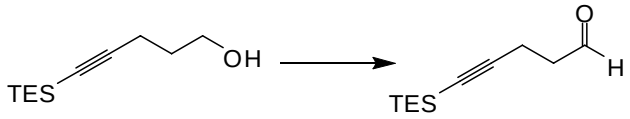
Unless noted otherwise, commercially available materials were used without further purification. All solvents used were of HPLC or ACS grade. Solvents used for moisture sensitive operations were distilled from drying agents under a nitrogen atmosphere: Et_2O and THF from sodium benzophenone ketyl; benzene and toluene from sodium; CH_2Cl_2, CH_3CN, NEt_3 and pyridine from CaH_2. All moisture sensitive reactions were performed under an atmosphere of nitrogen. Flash chromatography (FC) was performed using *E Merck* silicagel 60 (240-400 mesh) according to the protocol of Still, Kahn, and Mitra (*J. Org. Chem.* **1978**, *43*, 2923). Thin Layer chromatography was performed using precoated plates purchased from *E. Merck* (silicagel 60 PF254, 0.25 mm) that were visualized using a $KMnO_4$ or Ce (IV) stain.

Nuclear magnetic resonance (NMR) spectra were recorded in $CDCl_3$ or CD_3OD, unless otherwise specified, on either a *Varian Inova-400* or *Mercury-300* spectrometer at operating frequencies of 400 / 300 MHz (^{1}H NMR) or 100 / 60 MHz (^{13}C NMR). Chemical shifts (δ) are given in ppm relative to residual solvent (usually chloroform; δ 7.26 for ^{1}H NMR or 77.23 for

proton decoupled ^{13}C NMR), and coupling constants (*J*) in Hz. Multiplicity is tabulated as s for singlet, d for doublet, t for triplet, q for quadruplet, and m for multiplet, whereby the prefix *app* is applied in cases where the true multiplicity is unresolved, and *br* when the signal in question is broadened.

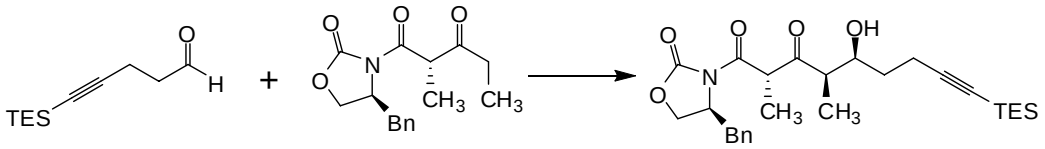
Infrared spectra were recorded on a *Perkin-Elmer 1000* series FTIR with wavenumbers expressed in cm^{-1} using samples prepared as thin films between salt plates. Electrospray ionization mass spectra (ESI-MS) were recorded on a Shimadzu 2010-LCMS. Optical rotations were measured at 20°C on a Rudolph Research Analytical Autopol® IV polarimeter.

2. Experimental Procedures



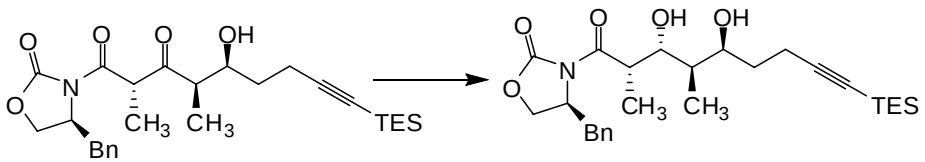
6 **7**

To a solution of oxalyl chloride (5.6 mL, 65 mmol) in dry DCM (150 mL) was added DMSO (9.3 mL, 0.13 mol) dropwise at -78 °C. After stirring for 30 min at -78 °C, **6** (11.65 g, 58.8 mmol) in DCM (8 mL) was added and the reaction was stirred at -78 °C for another 30 min. Then NEt_3 (41 mL, 0.30 mol) was added and the mixture was allowed to warm to RT. The reaction was stirred for 30 min at RT, then poured into 5% HCl (200 mL). The aqueous layer was extracted with DCM (2 × 150 mL) and the combined organic phase was washed with aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated under vacuum. The crude was purified by FC (silica gel, Hexanes/EtOAc 12:1) to give compound **7** (10.6 g, 92%). ^1H NMR (400 MHz, $CDCl_3$) δ: 9.79 (s, 1H), 2.66 (t, J = 7.2, 2H), 2.55 (t, J = 7.2, 2H), 0.95 (q, J = 8.0, 9H), 0.55 (t, J = 8.0, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.8, 106.0, 83.4, 43.0, 13.5, 7.7, 4.7; IR (film, cm^{-1}): 2954, 2874, 2175, 1729, 1413, 1017, 726; MS calcd. for C11H20OSi, 196.13; found: 197.05 $[M + Na]^+$.



7 **8** **9**

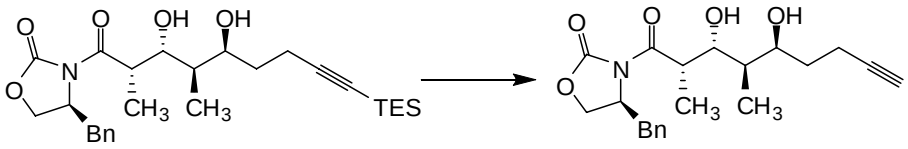
To a stirred suspension of anhydrous, acid-free $Sn(OTf)_2$ (634 mg, 1.52 mmol) in dry DCM (6mL) was added triethylamine (0.212 mL, 1.52 mmol) and then immediately cooled to -20 °C under N_2. After 5 min, a solution of **8** (400 mg in 3 mL dry DCM, 1.38mmol) was added dropwise over 5 min. The mixture was stirred for 1 h at -20 °C and then cooled to -78 °C, followed by the addition of aldehyde **7** (541 mg in 2 mL DCM, 2.76 mmol). The reaction mixture was stirred at -78 °C for 30 min and then quenched rapidly with a cool and vigorously stirred 1:1 mixture of DCM/1 N aqueous $NaHSO_4$ (20mL / 20mL). After stirring at 0°C for 10 min, the mixture was diluted with additional DCM/1 N aqueous $NaHSO_4$ (20mL / 20mL). The aqueous layer was extracted with DCM (2 × 40 mL) and the combined organic phase was washed with aqueous $NaHCO_3$, brine, dried over Na_2SO_4 and concentrated under vacuum. The crude was purified by FC (silica gel, Hexanes/EtOAc 3:1) to give compound **9** (549 mg, 82%). $[\alpha]^{22}_D$ = 28.4 (*c* = 0.50 in DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34-7.20 (m, 5H), 4.85 (q, *J* = 7.2, 1H), 4.79-4.71 (m, 1H), 4.24 (t, *J* = 8.8, 1H), 4.18-4.15 (m, 1H), 4.06 (dt, *J* = 8.4, 3.6, 1H), 3.30 (dd, *J* = 13.2, 3.2, 1H), 2.87 (dq, *J* = 7.2, 2.8, 1H), 2.77 (dd, *J* = 13.6, 9.6, 1H), 2.37 (dt, *J* = 7.2, 3.2, 2H), 1.78-1.67 (m, 1H), 1.60-1.52 (m, 1H), 1.47 (d, *J* = 7.6, 3H), 1.22 (d, *J* = 7.2, 3H), 0.95 (q, *J* = 8.0, 9H), 0.55 (t, *J* = 8.0, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.2, 170.4, 153.8, 135.2, 129.6, 129.2, 127.6, 107.8, 82.7, 70.7, 66.7, 55.5, 52.3, 48.4, 38.1, 32.9, 17.0, 13.1, 10.5, 7.7, 4.6; IR (film, cm^{-1}): 2954, 1779, 1714, 1358, 1214, 1007, 736; MS calcd. for C27H39NO5Si, 485.26; found: 508.50 $[M + Na]^+$.



9 **9a**

To 5 mL of acetic acid at 0°C was added portionwise $NaBH_4$ (293 mg, 7.7 mmol). After completion of gas evolution (about 10 min), the reaction was allowed to warm to RT and stirred

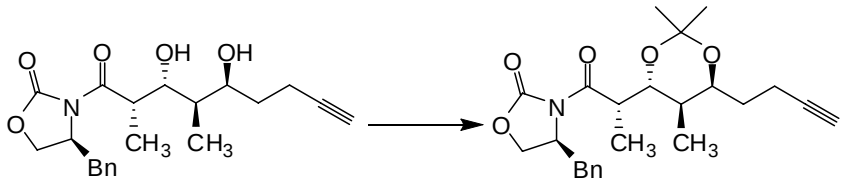
for 1 h. To this solution was added a solution of **9** (373 mg in 2.5 mL acetic acid, 0.77 mmol). After 70 min, the reaction was concentrated under vacuum. The residue was poured into saturated aqueous $NaHCO_3$ (25mL, **caution!**). The aqueous layer was extracted with DCM (3 × 30 mL) and the combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under vacuum. The crude was purified by FC (silica gel, Hexanes/EtOAc 1:1) to give compound **9a** (296 mg, 79%). $[\alpha]^{22}_D$ = 23.4 (*c* = 0.93 in DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35-7.18 (m, 5H), 4.73-4.68 (m, 1H), 4.26-4.18 (m, 2H), 3.98 (d, *J* = 9.6, 1H), 3.85 (dq, *J* = 7.2, 1.6, 1H), 3.80 (d, *J* = 1.6, 1H), 3.24 (dd, *J* = 13.2, 3.2, 1H), 3.16 (d, *J* = 6.4, 1H), 2.78 (dd, *J* = 13.2, 9.6, 1H), 2.52-2.34 (m, 2H), 1.97-1.89 (m, 1H), 1.80-1.63 (m, 3H), 1.26 (d, *J* = 6.8, 3H), 0.98 (q, *J* = 8.0, 9H), 0.84 (d, *J* = 7.2, 3H), 0.57 (t, *J* = 8.0, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.1, 153.0, 135.1, 129.6, 129.2, 127.6, 108.5, 82.3, 74.2 73.7, 66.4, 55.3, 39.6, 39.4, 37.9, 31.9, 17.5, 12.4, 9.8, 7.6, 4.7; IR (film, cm^{-1}): 3436 (br), 2953, 2170, 1781, 1698, 1387, 1210, 736; MS calcd. for C27H39NO5Si, 487.28; found: 510.50 $[M + Na]^+$.



9a **5**

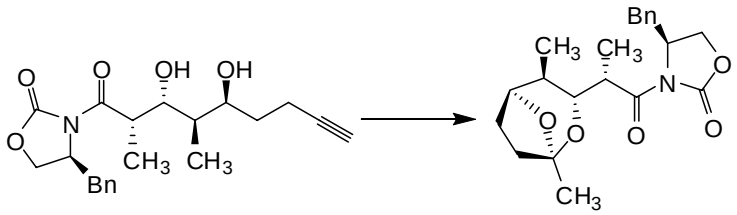
To a solution of **9a** (317 mg, 0.65 mmol) in dry THF (15 mL) was added TBAF (0.72 mL, 1 M in THF) dropwise at 0 °C. After stirring for 3 min at 0 °C, sat. NH_4Cl solution (20 mL) was added. The aqueous layer was extracted with DCM (2 × 25 mL) and the combined organic phase was washed with aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated under vacuum. The crude was purified by FC (silica gel, Hexanes/EtOAc 1:1) to give compound **5** (228 mg, 94%). $[\alpha]^{20}_D$ = 29.5 (*c* = 1.12 in DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34-7.18 (m, 5H), 4.71-4.67 (m, 1H), 4.26-4.17 (m, 2H), 3.98 (dt, *J* = 9.2, 2.4, 1H), 3.91-3.84 (m, 2H), 3.74 (d, *J* = 2.4, 1H), 3.24 (dd, *J* = 13.6, 3.2, 1H), 3.10 (d, *J* = 7.2, 1H), 2.78 (dd, *J* = 13.6, 9.2, 1H), 2.52-2.24 (m, 2H), 1.95 (t, *J* = 2.4, 1H), 1.92-1.84 (m, 1H), 1.78-1.71 (m, 1H), 1.67-1.59 (m, 1H), 1.27 (d, *J* = 6.8, 3H), 0.85 (d, *J* = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.1, 153.0, 135.1, 129.6, 129.2, 127.7, 84.6, 74.0 73.4, 68.8, 66.4, 55.2, 39.7, 39.2, 37.9, 31.8, 15.9, 12.3, 10.2; IR (film, cm^{-1}): 3296, 2937, 1778, 1693, 1386, 1211, 972; MS calcd. for C21H27NO5, 373.19; found: 373.75 $[M + H]^+$.

The relative 1,3-anti diol stereochemistry of **5** was established by 13C NMR analysis of acetonide **5a** using Rychnovsky's method: [1] relevant ^{13}C NMR signals (75 MHz, CDCl3): 100.7, 25.2, 23.9 ppm.



5 **5a**

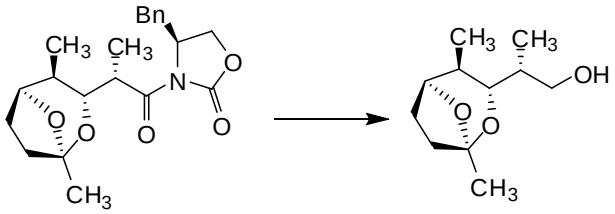
To a stirred solution of **5** (16 mg, 0.043 mmol) in dimethoxypropane / acetone (1.0 mL/1.0 mL) was added 2 mg PPTS. This mixture was stirred at room temperature for 30 min, then concentrated under vacuum. The crude was purified by FC (silica gel, Hexanes/EtOAc 5:1) to give compound **5a** (15 mg, 87%). $[\alpha]^{20}_{D}$ = 46.2 (*c* = 1.43 in DCM); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.34-7.18 (m, 5H), 4.62 (dq, *J* = 6.4, 3.2, 1H), 4.18-4.11 (m, 2H), 4.04-3.98 (m, 1H), 3.92 (dt, *J* = 10.4, 3.2, 1H), 3.60 (dd, *J* = 7.2, 4.8, 1H), 3.33 (dd, *J* = 13.2, 3.2, 1H), 2.76 (dd, *J* = 13.2, 9.6, 1H), 2.34-2.17 (m, 2H), 1.93 (t, *J* = 2.4, 1H), 1.91-1.84 (m, 1H), 1.68-1.61 (m, 1H), 1.53-1.43 (m, 1H), 1.32 (s, 3H), 1.28 (s, 3H), 1.26 (d, *J* = 6.8, 3H), 0.89 (d, *J* = 6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.0, 153.4, 135.5, 129.7, 129.1, 127.5, 100.7, 84.2, 75.4, 68.7, 68.0, 66.3, 56.1, 41.2, 38.0, 37.0, 30.0, 25.2, 23.9, 15.3, 12.3, 11.8; IR (film, cm^{-1}): 3290, 2936, 1781, 1698, 1382, 1210;MS calcd. for C24H31NO5, 413.22; found: 436.70 $[M + Na]^+$.



5 **10**

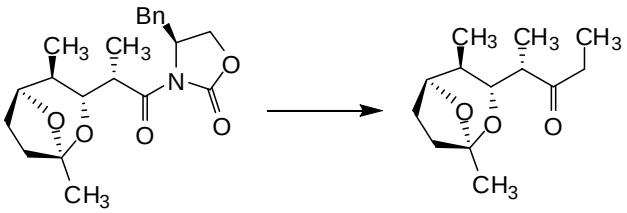
A solution of **5** (69 mg, 0.185 mmol) in fresh distilled THF (1 mL) was added dropwise a solution of Zeise's dimer ($[Cl_2(CH_2CH_2)Pt]_2$, 9.25 μmol, 5% eq) in fresh distilled THF (1.5 ml) at room temperature under N_2. The resultant solution was stirred at room temperature for 5 min, then quenched with 300 μL NEt_3. The mixture was concentrated under vacuum and purified by FC

(silica gel, Hexanes/EtOAc 2:1) to give compound **10** (68 mg, 99%). $[\alpha]^{20}_{D}$ = 38.3 (*c* = 0.60 in DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34-7.20 (m, 5H), 4.66-4.60 (m, 1H), 4.20-4.14 (m, 3H), 3.93 (dq, *J* = 6.8, 2.8, 1H), 3.77 (dd, *J* = 6.8, 2.8, 1H), 3.35 (dd, *J* = 13.2, 3.2, 1H), 2.75 (dd, *J* = 13.6, 9.6, 1H), 2.03-1.95 (m, 1H), 1.92-1.78 (m, 4H), 1.45 (s, 3H), 1.23 (d, *J* = 6.8, 3H), 0.78 (d, *J* = 6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 153.5, 135.6, 129.7, 129.1, 127.5, 105.3, 80.1, 74.8, 66.4, 56.2, 40.0, 37.8, 35.0, 34.5, 24.2, 24.1, 12.9, 9.9; IR (film, cm^{-1}): 2961, 1778, 1705, 1454, 1385, 1194, 973; MS calcd. for C21H27NO5, 373.19; found: 396.10 $[M + Na]^{+}$.



10 **10a**

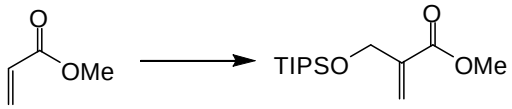
$LiBH_4$ (2M in THF, 0.058mL, 0.117 mmol) was added to the solution of **10** (29 mg, 0.078 mmol) in ether (2 mL, containing 1% H_2O) , and the resulting solution was stirred for 1 h and then poured into a saturated aqueous solution of Rochelle's salt (5 mL). The aqueous layer was extracted with ether (3 × 10 mL) and the combined organic phase was washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by FC (silica gel, Hexanes/EtOAc 1:2) to give compound **10a** (15 mg, 99%). All spectral details match those reported by Paterson.[2] $[\alpha]^{22}_{D}$ = -17.6 (*c* = 0.69 in DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.21 (dd, *J* = 6.8, 3.2, 1H), 3.72 (dd, *J* = 10.4, 2.8, 1H), 3.67-3.59 (m, 2H), 2.35 (dd, *J* = 8.0, 2.8, 1H), 2.07-1.96 (m, 2H), 1.94-1.74 (m, 4H), 1.45 (s, 3H), 0.98 (d, *J* = 7.2, 3H), 0.70 (d, *J* = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 105.2, 80.2, 77.8, 67.8, 35.1, 34.6, 34.2, 24.2, 24.1, 12.8, 9.6; IR (film, cm^{-1}): 3359, 2955, 2924, 1467, 1379, 1200, 1153, 1022; MS calcd. for C11H20O3, 200.14; found: 223.05 $[M + Na]^{+}$.



10 **3**

To a stirred suspension of Weinreb salt (45 mg, 0.46 mmol) in dry DCM(8 mL) was added $AlMe_3$ (2.0 M in toluene, 0.23 mL, 0.46 mmol) dropwise at -10 °C under N_2. After gas evolution was evident, the solution was stirred at ambient temperature for 45 min before it was cooled to -10 °C and a solution of **10** (57 mg, 0.153 mmol) in 2 mL of DCM was added. The resultant solution was warmed to RT and allowed to sit for 5 h before it was quenched by the addition of 10 mL of a saturated aqueous solution of Rochelle's salt. The mixture was stirred vigorously until the phases became clear. The aqueous layer was then extracted with DCM (3 × 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The crude amide was used for next step without further purification.

To a solution of crude Weinreb amide in 5 mL of dry THF at 0 °C was added ethyl Grignard (2.0 M in THF, 0.23 mL, 0.46 mmol). After 30 min the solution was warmed to ambient temperature and allowed to stir for 2 additional hours. The reaction was recooled to 0 °C and quenched with 10 mL of a saturated aqueous solution of NH_4Cl and 10 mL of Et_2O. The aqueous layer was extracted with ether (3 × 10 mL) and the combined organic phase was washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The crude was purified by FC (silica gel, Hexanes/EtOAc 5:1) to give compound **3** (30 mg, 87% for 2 steps). $[\alpha]^{20}_D$ = -7.8 (*c* = 1.0 in DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.20 (dd, *J* = 6.0, 3.6, 1H), 3.84 (dd, *J* = 10.4, 3.2, 1H), 2.54-2.46 (m, 3H), 1.98-1.76 (m, 5H), 1.41 (s, 3H), 1.12 (d, *J* = 7.2, 3H), 1.02 (t, *J* = 7.2, 3H), 0.72 (d, *J* = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.6, 105.2, 80.1, 75.6, 48.1, 34.8, 34.4, 33.9, 24.2, 24.0, 13.0, 9.5, 7.9.; IR (film, cm^{-1}): 2960, 1713, 1459, 1389, 1155, 1021, 970; MS calcd. for C13H22O3, 226.16; found: 227.00 $[M + H]^+$.

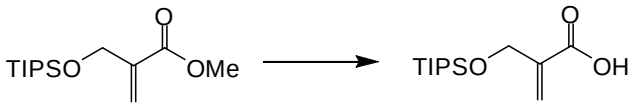


14a

para-Formaldehyde (3.50 g, 117 mmol) was dissolved in a mixture of 1,4-dioxane and H_2O (1:1, 16 mL) and the solution was stirred for 30 min at RT. To this mixture were added methyl acrylate (21.0 mL, 233 mmol) and DABCO (13.1 g, 117 mmol). The mixture was stirred for 72 h and then poured into saturated aqueous NaCl. The aqueous layer was extracted with ether (3 × 50 mL) and

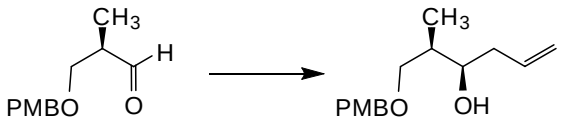
the combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under vacuum to give 15.6 g known alcohol.[3] The crude alcohol was used for next step without further purification.

To a solution of crude alcohol (7.0 g, ca. 60 mmol) and imidazole (6.12 g, 90 mmol) in dry DCM (60 mL) was added TIPSCl (15.3 mL, 72 mmol) by two portions at 0 ^{o}C under N_2 protection. After 30 min, the solution was warmed to room temperature and stirred for another 30 min. The reaction was quenched by the addition of aq. NH_4Cl (50 mL). The aqueous layer was extracted with DCM (3 × 50 mL). The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under vacuum. The crude was purified by FC (silica gel, Hexanes/EtOAc 7:1) to give compound **14a** (11.3 g, 79% for two steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.26 (dd, J = 4.4, 2.0, 1H), 5.98 (dd, J = 4.4, 2.0, 1H), 4.44 (t, J = 2.2, 2H), 3.73 (s, 3H), 1.16-1.02 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 139.8, 124.0, 61.8, 51.8, 18.2, 12.2; IR (film, cm^{-1}): 3537, 2942, 2865, 1721, 1463, 1308, 1104, 882; MS calcd. for C14H28O3Si, 272.18; found: 295.10 [M + Na] $^{+}$.



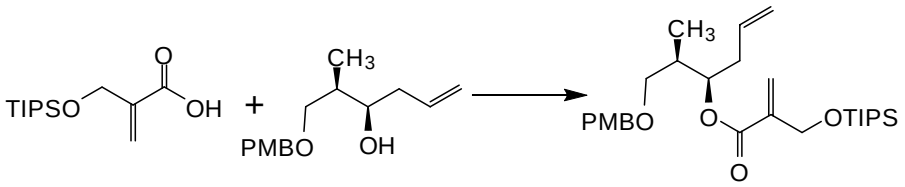
14a **14**

LiOH (115 mg, 2.74 mmol) was added to a solution of **14a** (373 mg, 1.37 mmol) in THF (2.5 mL) and H_2O (2.5 mL). The reaction was stirred vigorously for 24 h and quenched with HCl (5%, 10 mL). The aqueous layer was extracted with ether (3 × 10 mL). The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under vacuum. The crude was purified by FC (silica gel, Hexanes/EtOAc 2:1) to give compound **14** (325 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.2 (br s, 1 H), 6.41 (dd, J = 3.6, 2.4, 1H), 6.10 (dd, J = 4.0, 2.0, 1H), 4.45 (t, J = 2.4, 2H), 1.18-0.95 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 139.3, 126.5, 61.6, 18.2, 12.2; IR (film, cm^{-1}): 2943, 2866, 1698, 1634, 1463, 1280, 1107, 882; MS calcd. for C13H26O3Si, 258.17; found: 281.15 [M + Na] $^{+}$.



12 **13**

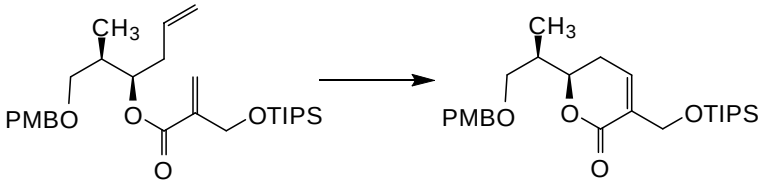
To a solution of (+)diisopinocampheylallylborane in ether (36.8 mmol in 80 mL ether) was added **12** (7.2 g, 35 mmol in 10 mL ether) at - 98°C. The solution was stirred at – 98 °C for 2 h and then warmed to 0 °C. The mixture was treated with 1N NaOH (50 mL) and 30% H_2O_2 (20 mL) and heated under reflux for 1 h. After allowed to reach ambient temperature, the aqueous layer was extracted with ether (3 × 50 mL). The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under vacuum. The crude was purified by FC (silica gel, Hexanes/EtOAc 5:1) to give compound **13** (7.79 g, 90%).[4] $[\alpha]^{22}_D$ = 5.71 (*c* = 0.88 in DCM); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.25-7.21 (m, 2H), 6.89-6.85 (m, 2H), 5.88-5.78 (m, 1H), 5.13-5.05 (m, 2H), 4.43 (s, 2H), 3.83-3.77 (m, 1H), 3.80 (s, 3H), 3.49 (d, *J* = 5.3, 2H), 2.55 (d, *J* = 4.0, 1H, OH), 2.23-2.17 (m, 2H), 1.94-1.84 (m, 1H), 0.94 (d, *J* = 6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 159.4, 135.9, 130.4, 129.5, 117.4, 114.0, 74.4, 73.2, 55.5, 39.1, 37.7, 11.0; IR (film, cm^{-1}): 3462(br), 1640, 1513, 1456, 1247, 1173, 1090, 984, 818; MS calcd. for C15H22O3: 250.16; found: 251.05 $[M + H]^+$.



14 **13** **15a**

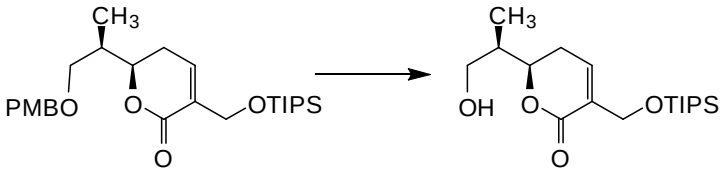
To a solution of acid **14** (206 mg, 0.8 mmol) and alcohol **13** (100 mg, 0.4 mmol) in dry DCM (10 mL) was added DCC (412 mg, 2.0 mmol) and DMAP (25 mg, 0.2 mmol) at 0 °C under N_2. After stirring at 0 °C for 30 min, the solution was warmed to room temperature and stirred for 12 h, then poured into saturated aqueous $NaHCO_3$. The aqueous layer was extracted with DCM (3 × 10 mL) and the combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under vacuum. The crude was purified by FC (silica gel, Hexanes/EtOAc 9:1) to give compound **15a** (160 mg, 82%). $[\alpha]^{22}_D$ = -5.3 (*c* = 0.75 in DCM); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.25-7.21 (m, 2H), 6.88-6.84 (m, 2H), 6.24 (dd, *J* = 4.0, 2.0, 1H), 5.95 (dd, *J* = 4.4, 2.4, 1H), 5.77-5.67 (m, 1H),

5.20-5.15 (m, 1H), 5.07-5.00 (m, 2H), 4.43-4.41 (m, 2H), 4.38 (s, 2H), 3.79 (s, 3H), 3.33-3.25 (m, 2H), 2.42-2.29 (m, 2H), 2.07-2.01 (m, 1H), 1.18-1.04 (m, 21H), 0.96 (d, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 159.3, 140.3, 134.1, 130.7, 129.5, 123.5, 117.9, 114.0, 73.7, 73.1, 72.4, 61.9, 55.5, 36.8, 36.7, 18.2, 18.2, 12.2, 11.7; IR (film, cm^{-1}): 2934, 2865, 1709, 1660, 1634, 1514, 1463, 1248, 1099, 882, 819; MS calcd. for C28H46O5Si, 490.31; found: 513.10 [M + Na] $^+$.



15a **15**

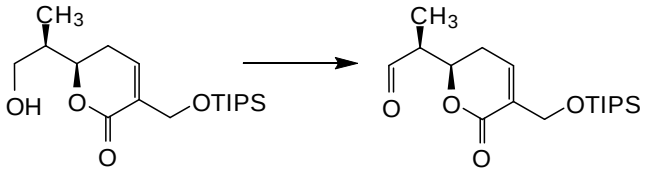
Grubbs' second generation catalyst (1,3-Bis-(2,4,6-trimethylphenyl)-2-(imidazolidinylidene)-(dichlorophenylmethylene)(tricyclohexylphosphine)ruthenium, 28 mg, 0.033 mmol) was added to a solution of **15a** (160 mg, 0.327 mmol) in dry DCM (120 mL). The reaction was refluxed for 14 h under N_2. The solution was concentrated and purified by FC (silica gel, Hexanes/EtOAc 6:1) to give compound **15** (101 mg, 67%) and recover **15a** (24 mg, 15%). $[\alpha]^{22}_D$ = 0.7 (c = 0.60 in DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.25-7.21 (m, 2H), 6.95-6.95 (m, 1H), 6.88-6.85 (m, 2H), 4.57-4.49 (m, 2H), 4.46-4.38 (m, 3H), 3.79 (s, 3H), 3.52 (dd, J = 9.2, 7.6, 1H), 3.41 (dd, J = 9.2, 5.2, 1H), 2.53-2.44 (m, 1H), 2.30-2.24 (m, 1H), 2.03-1.97 (m, 1H), 1.18-1.02 (m, 24H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.2, 159.5, 138.1, 131.8, 130.6, 129.5, 114.1, 78.5, 73.2, 71.5, 61.0, 55.5, 37.8, 27.3, 18.3, 12.2, 12.1; IR (film, cm^{-1}): 2940, 2864, 1717, 1611, 1512, 1462, 1248, 1080, 882, 817; MS calcd. for C26H42O5Si, 462.28; found: 485.60 [M + Na] $^+$.



15 **4a**

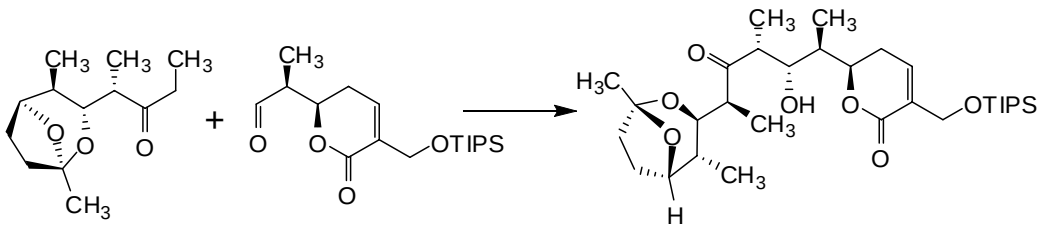
To a solution of **15** (65 mg, 0.14 mmol) in DCM/H_2O (8 mL/ 0.4 mL) was added DDQ (38 mg, 0.17 mmol). After stirring at RT for 1 h, the solution poured into saturated aqueous $NaHCO_3$ (10 mL) and extracted with DCM (3 × 10 mL) and the combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under vacuum. The crude was purified by FC (silica gel,

Hexanes/EtOAc 2:1) to give compound **4a** (44 mg, 91%). $[\alpha]^{22}_{D}$ = 27.8 (*c* = 1.45 in DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.98-6.96 (m, 1H), 4.59-4.51 (m, 2H), 4.41-4.36 (m, 1H), 3.74 (dd, *J* = 10.4, 3.6, 1H), 3.64 (dd, *J* = 10.8, 5.2, 1H), 2.58-2.48 (m, 1H), 2.35-2.27 (m, 1H), 1.97-1.89 (m, 1H), 1.84 (br s, 1H, OH), 1.18-1.01 (m, 24H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 138.2, 131.8, 78.6, 64.4, 60.9, 39.3, 27.1, 18.2, 12.2, 11.6; IR (film, cm^{-1}): 3426 (br), 2941, 2865, 1712, 1462, 1403, 1154, 1081, 1066, 882; MS calcd. for C18H34O4Si, 342.22; found: 365.05 $[M + Na]^{+}$.



4a **4**

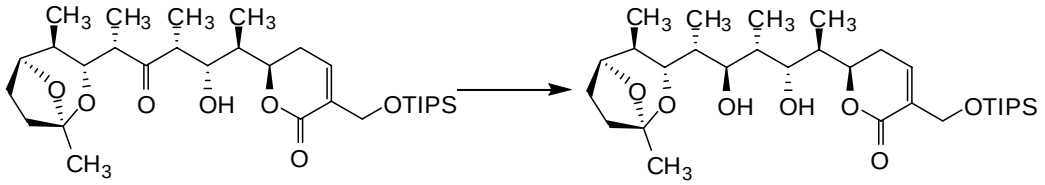
To a solution of **4a** (80 mg, 0.234 mmol) in dry DCM (10 mL) was added Dess-Martin reagent (198 mg, 0.47 mmol) and solid $NaHCO_3$ (79 mg, 0.94 mmol). The reaction was stirred for 30 min at RT, then poured into aqueous $NaHCO_3$ (15 mL). The aqueous layer was extracted with DCM (3 × 10 mL) and the combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under vacuum. The crude was purified by FC (silica gel, Hexanes/EtOAc 3:1) to give compound **4** (79 mg, 99%). $[\alpha]^{22}_{D}$ = 36.7 (*c* = 0.60 in DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.78 (s, 1H), 6.98-6.95 (m, 1H), 4.79-4.74 (m, 1H), 4.57-4.52 (m, 1H), 4.43-4.38 (m, 1H), 2.73-2.70 (m, 1H), 2.49-2.44 (m, 2H), 1.29 (d, *J* = 7.6, 3H), 1.21-1.05 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.0, 164.0, 137.3, 132.0, 76.9, 60.8, 49.8, 27.1, 18.2, 12.1, 9.3; IR (film, cm^{-1}): 2943, 2866, 1725, 1463, 1402, 1224, 1143, 1069, 882; MS calcd. for C18H32O4Si, 340.21; found: 341.15 $[M + H]^{+}$.



3 **4** **2**

To a solution of ketone **3** (56.5 mg, 0.25 mmol) in dry THF (5 mL) at -78 °C was added a solution of lithium bis(trimethylsilyl)amide (1 M in THF, 0.3 mL, 0.3 mmol) dropwise. The resulting

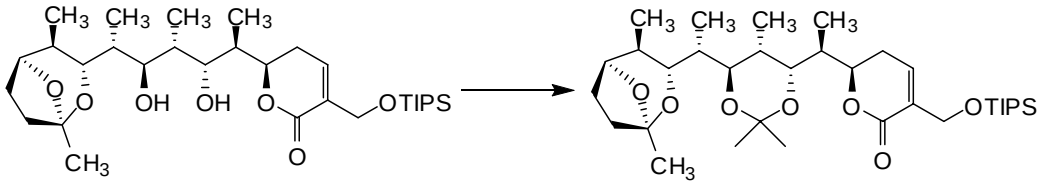
yellow solution was stirred at -78 °C for 2 h and then a solution of aldehyde **4** (119 mg, 0.35 mmol) in 1 mL THF was added. The resulting solution was stirred at -78 °C for another 2 h. The reaction was quenched by the addition of pH 7 phosphate buffer solution (6 mL). The aqueous layer was extracted with ether (3 × 10 mL) and the combined organic phase was washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The crude was purified by FC (silica gel, Hexanes/EtOAc 3:1) to give compound **2** (112 mg, 81%). $[\alpha]^{22}_D$ = 14.2 (*c* = 0.27 in DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.96-6.94 (m, 1H), 4.97 (ddd, *J* = 13.2, 7.2, 1.2, 1H), 4.59-4.52 (m, 1H), 4.40-4.33 (m, 1H), 4.20 (dd, *J* = 6.0, 3.6, 1H), 4.01 (d, *J* = 10.0, 1H), 3.81 (dd, *J* = 10.4, 2.8, 1H), 3.54 (d, *J* = 2.0, 1H, OH), 3.04 (dq, *J* = 7.2, 1.6, 1H), 2.78 (dq, *J* = 7.2, 2.8, 1H), 2.60-2.50 (m, 1H), 2.24-2.15 (m, 1H), 2.00-1.80 (m, 6H), 1.42 (s, 3H), 1.16-1.04 (m, 24H), 1.11 (d, *J* = 7.2, 3H), 0.94 (d, *J* = 7.2, 3H), 0.76 (d, *J* = 6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.6, 165.1, 138.0, 131.8, 105.5, 80.2, 76.5, 75.8, 69.8, 61.0, 47.4, 43.4, 39.3, 34.8, 34.5, 27.7, 24.2, 24.0, 18.3, 13.2, 12.2, 10.0, 9.8, 8.9; IR (film, cm^{-1}): 2941, 2866, 2365, 1710, 1460, 1388, 1066, 969, 882, 814; MS calcd. for C31H54O7Si, 566.36; found: 589.35 $[M + Na]^+$.



Tetramethylammonium triacetoxyborohydride (345 mg, 1.31 mmol) was added to CH_3CN/acetic acid (3 mL / 3 mL), and the resulting solution was stirred for 30 min at RT and cooled to -20 °C before ketone **2** (93 mg, 0.164 mmol) was added. After 48 h at -20 °C, the reaction was quenched by the addition of 20 mL of a saturated aqueous solution of Rochelle's salt. The aqueous layer was then extracted with DCM (3 × 20 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by FC (silica gel, Hexanes/EtOAc 2:1) to give compound **16** (83 mg, 89%). $[\alpha]^{22}_D$ = -24.0 (*c* = 0.58 in DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.98-6.96 (m, 1H), 5.01-4.97 (m, 1H), 4.58-4.54 (m, 1H), 4.40-4.37 (m, 1H), 4.23 (dd, *J* = 5.2, 3.6, 1H), 4.13 (d, *J* = 10.4, 1H), 3.80 (dd, *J* = 10.4, 2.4, 1H), 3.61 (dd, *J* = 12.0, 5.6, 1H), 3.37 (d, *J* = 2.4, 1H, OH), 3.32 (d, *J* = 1.6, 1H), 2.60-2.54 (m, 1H), 2.24-2.18 (m, 1H), 2.12-2.07 (m, 1H), 1.96-1.69 (m, 7H), 1.46 (s, 3H),

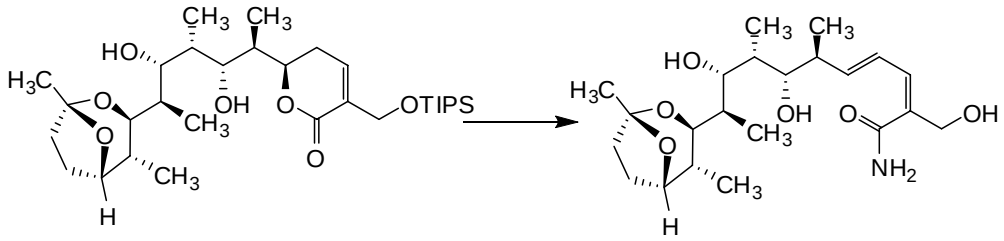
1.16-1.04 (m, 21H), 0.97 (d, J = 7.2, 3H), 0.95 (d, J = 6.8, 3H), 0.92 (d, J = 7.2, 3H), 0.75 (d, J = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 138.3, 131.8, 105.4, 80.5, 79.1, 75.7, 70.2, 61.0, 40.0, 35.7, 35.6, 34.7, 34.0, 27.8, 24.2, 18.3, 13.1, 12.2, 12.0, 10.7, 10.1; IR (film, cm^{-1}): 3424 (br), 2943, 2867, 1719, 1461, 1406, 1329, 1152, 1067, 969, 882, 814; MS calcd. for C31H56O7Si, 568.38; found: 591.55 [M + Na]$^+$.

The relative 1,3-anti diol stereochemistry of **16** was established by ^{13}C NMR analysis of acetonide **17** using Rychnovsky's method[1]: relevant ^{13}C NMR signals (75 MHz, CD_3OD): 102.1, 25.2, 24.0.



16 **17**

To a stirred solution of **16** (13 mg, 0.023 mmol) in dimethoxypropane / acetone (1.5 mL/1.5 mL) was added cat. PPTS (2 mg). This mixture was stirred at room temperature for 10 h, then concentrated under vacuum. The crude was purified by FC (silica gel, Hexanes/EtOAc 5:1) to give compound **17** (12 mg, 87%). $[\alpha]^{22}_D$ = 12.0 (c = 0.23 in DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.97-6.95 (m, 1H), 4.82-4.79 (m, 1H), 4.56-4.40 (m, 2H), 4.19-4.18 (m, 1H), 3.96 (dd, J = 10.8, 3.6, 1H), 3.72 (d, J = 10.8, 1H), 3.27 (dd, J = 9.2, 2.4, 1H), 2.59-2.51 (m, 1H), 2.19-2.13 (m, 1H), 1.97-1.91 (m, 1H), 1.85-1.62 (m, 7H), 1.41 (s, 3H), 1.29 (s, 3H), 1.26 (s, 3H),1.16-1.05 (m, 21H), 0.91 (d, J = 6.8, 3H), 0.88 (d, J = 6.4, 3H), 0.87(d, J = 6.8, 3H), 0.67 (d, J = 6.8, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 167.0, 141.9, 132.4, 106.5, 102.1, 81.8, 78.1, 76.3, 74.4, 70.2, 62.2, 40.2, 37.6, 37.5, 35.3, 28.2, 26.2, 25.2, 24.5, 24.0, 18.7, 14.7, 13.4, 13.2, 12.9, 9.3, 8.5; IR (film, cm^{-1}): 2942, 2866, 1721, 1464, 1381, 1228, 1153, 1081, 1065, 1022, 969, 883, 814; MS calcd. for C34H60O7Si, 608.41; found: 631.50 [M + Na]$^+$.



16 **(-)-Saliniketal B**

To a solution of **16** (13.6 mg, 0.024 mmol) in dry THF (2 mL) was added TBAF (1 M in THF, 0.3 mL, 0.3 mmol). The resulting yellow solution was stirred at RT for 48 h and then anhydrous ammonia gas was bubbling into the solution for 15 min. To the resulting solution was added HOBt (7.3 mg, 0.054 mmol) and EDC (10.4 mg, 0.054 mmol) for 10 h. The mixture was filtered with Celite and washed twice with THF. The combined organic phase was concentrated under vacuum and purified by FC (silica gel, DCM/MeOH 9:1) to give **Saliniketal B** as a white amorphous solid (7.1 mg, 72%). All spectral details match those reported by Fenical.[5] $[\alpha]^{22}_{D}$ = -14.6 (*c* = 0.23 in MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ: 6.71 (dd, *J* = 15.2, 11.2, 1H, H4), 6.38 (dd, *J* = 10.8, 0.8, 1H, H3), 5.94 (dd, *J* = 15.2, 8.4, 1H, H5), 4.22 (m, 3H, H13, H18a, H18b), 3.95 (dd, *J* = 10.4, 1.2, 1H, H11), 3.74 (dd, *J* = 9.6, 1.6, 1H, H7), 3.51 (dd, *J* = 8.4, 4.4, 1H, H9), 2.39 (m, 1H, H6), 2.04-1.79 (m, 7H, H8, H10, H12, H14a, H14b, H15a, H15b), 1.39 (s, 3H, H17), 1.01 (d, *J* = 7.2, 3H, H20), 0.96 (d, *J* = 6.8, 3H, H19), 0.88 (d, *J* = 7.2, 3H, H21), 0.73 (d, *J* = 7.2, 3H, H22); ^{13}C NMR (126 MHz, CD_3OD) δ 173.3, 145.1, 135.4, 134.7, 127.9, 106.4, 81.6, 78.1, 75.7, 75.0, 65.1, 42.4, 37.1, 35.9, 35.2, 24.9, 24.3, 17.0, 12.8, 11.1, 10.3; IR (film, cm^{-1}): 3330 (br), 2931, 2362, 1654, 1458, 1388, 1334, 1090, 1020, 972; MS calcd. for C22H37NO6, 411.26; found 434.20 $[M + Na]^{+}$.

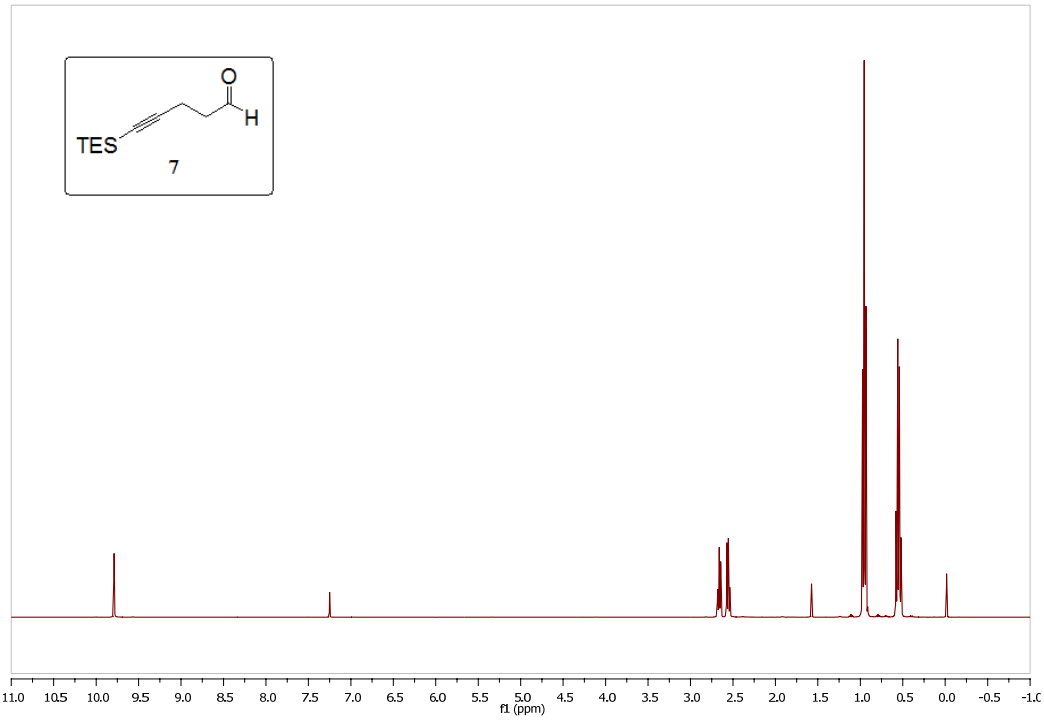
Table 1. Comparison of ^{1}H NMR data of natural and synthetic (-)-Saliniketal B

Position	^{1}H natural	^{1}H synthetic	+/-
1	-	-	
2	-	-	
3	6.38 (br d 11.1, 1.1)	6.38 (br d 10.8, 0.8)	
4	6.71, dd (15.2, 11.2)	6.71, dd (15.2, 11.2)	
5	5.94, dd (15.2, 8.3)	5.94, dd (15.2, 8.4)	
6	2.39, m (9.4, 8.3, 6.7)	2.39, m	
7	3.74, dd (9.4, 1.7)	3.74, dd (9.6, 1.6)	
8	1.86, m (7.4, 4.9, 1.3)	2.04 - 1.79 m	
9	3.51, dd (8.4, 4.9)	3.51, dd (8.4, 4.4)	
10	1.84, br dq (8.4, 7.2)	2.04 - 1.79 m	
11	3.95, br d (10.6)	3.95, dd (10.4, 1.2)	
12	2.00, dqd (10.6, 7.3, 6.3)	2.04 - 1.79 m	
13	4.22, m	4.22, m	
14	1.94, m	2.04 - 1.79 m	
15	2.05, m	2.04 - 1.79 m	
16	-	-	
17	1.39 S	1.39 S	
18	4.22, m	4.22, m	
19	0.96, d (6.8)	0.96, d (6.8)	
20	1.01, d (7.3)	1.01, d (7.2)	
21	0.88, d (7.2)	0.88, d (7.2)	
22	0.73, d (7.3)	0.73, d (7.2)	

Table 2. Comparison of ^{13}C NMR data of natural and synthetic (-)-Saliniketal B

Position	^{13}C Natural	^{13}C Synthetic	+/-
1	173.3, qC	173.3, qC	
2	134.6, qC	134.7, qC	- 0.1
3	135.4, CH	135.4, CH	
4	127.9, CH	127.9, CH	
5	145.1, CH	145.1, CH	
6	42.4, CH	42.4, CH	
7	75.7, CH	75.7, CH	
8	35.9, CH	35.9, CH	
9	78.1, CH	78.1, CH	
10	37.0, CH	37.1, CH	- 0.1
11	75.0, CH	75.0, CH	
12	35.2, CH	35.2, CH	
13	81.6, CH	81.6, CH	
14	24.9, CH_2	24.9, CH_2	
15	35.1, CH_2	35.2, CH_2	- 0.1
16	106.4, qC	106.4, qC	
17	24.3, CH_3	24.3, CH_3	
18	65.1, CH_2	65.1, CH_2	
19	17.0, CH_3	17.0, CH_3	
20	11.1, CH_3	11.1, CH_3	
21	10.3, CH_3	10.3, CH_3	
22	12.8, CH_3	12.8, CH_3	

Figure 1: ^{1}H and ^{13}C NMR spectra of **7**.



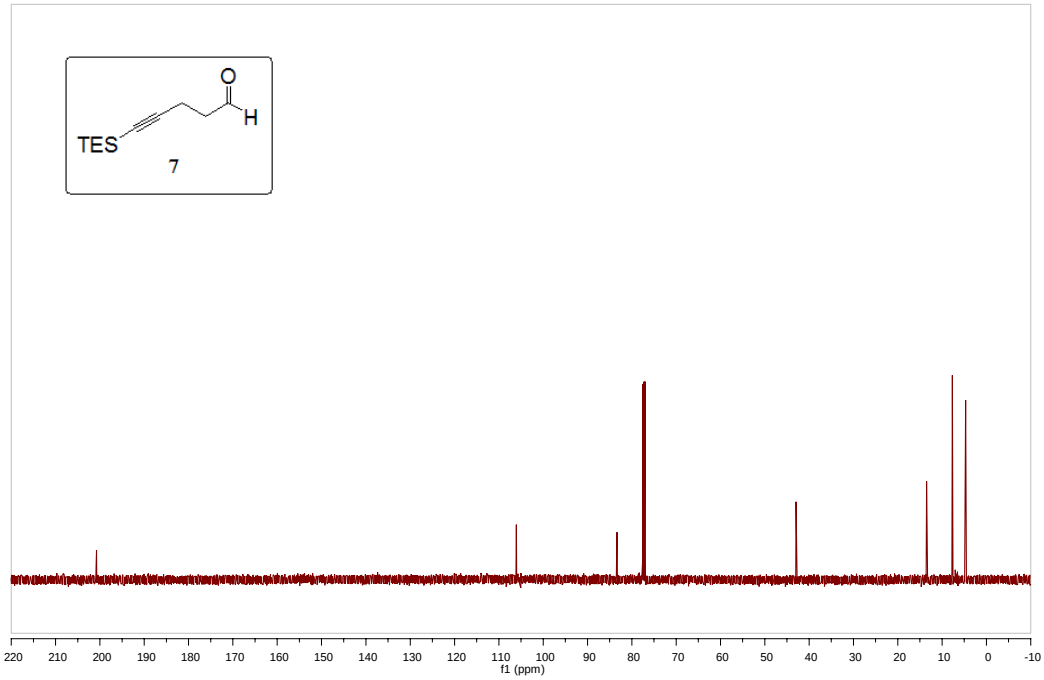
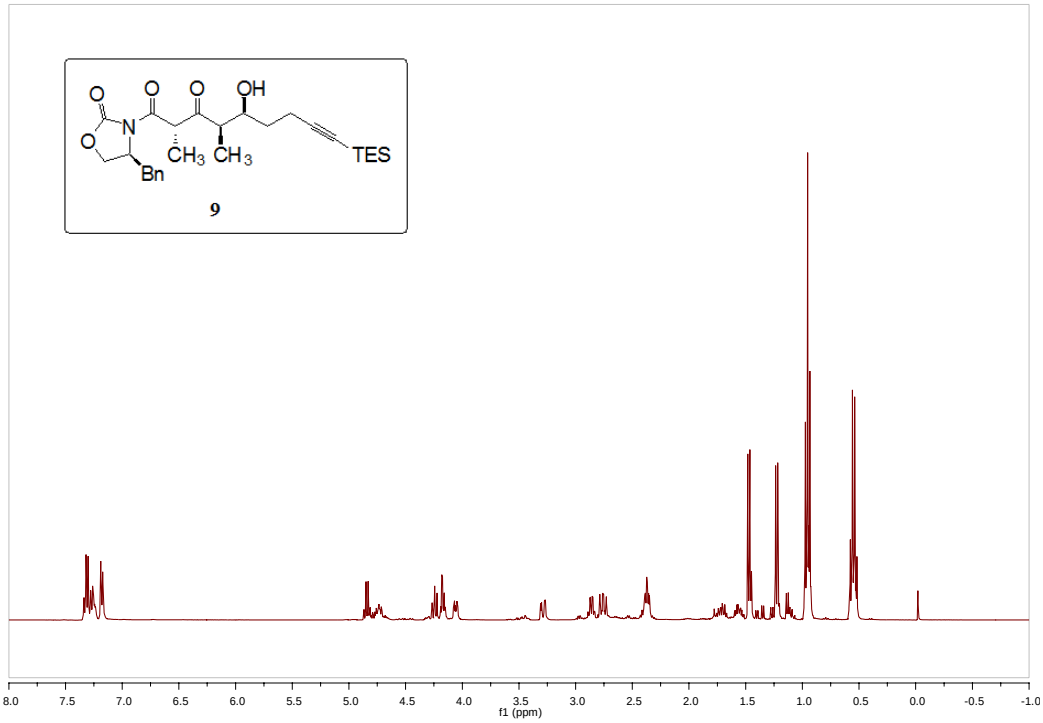


Figure 2: ^{1}H and ^{13}C NMR spectra of **9**.



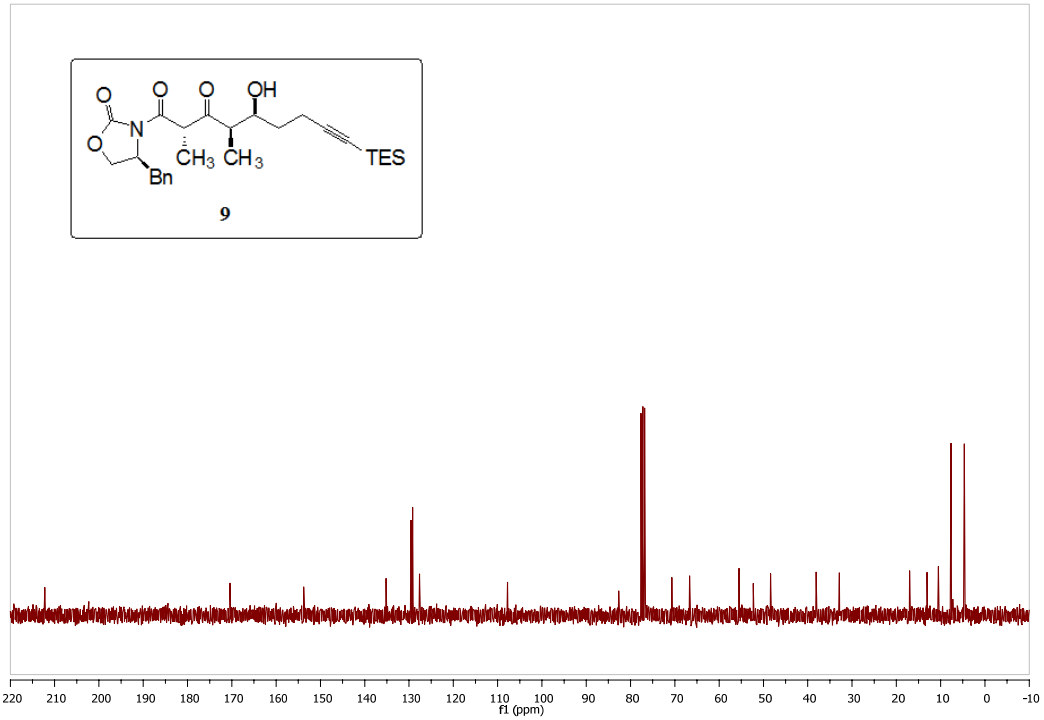
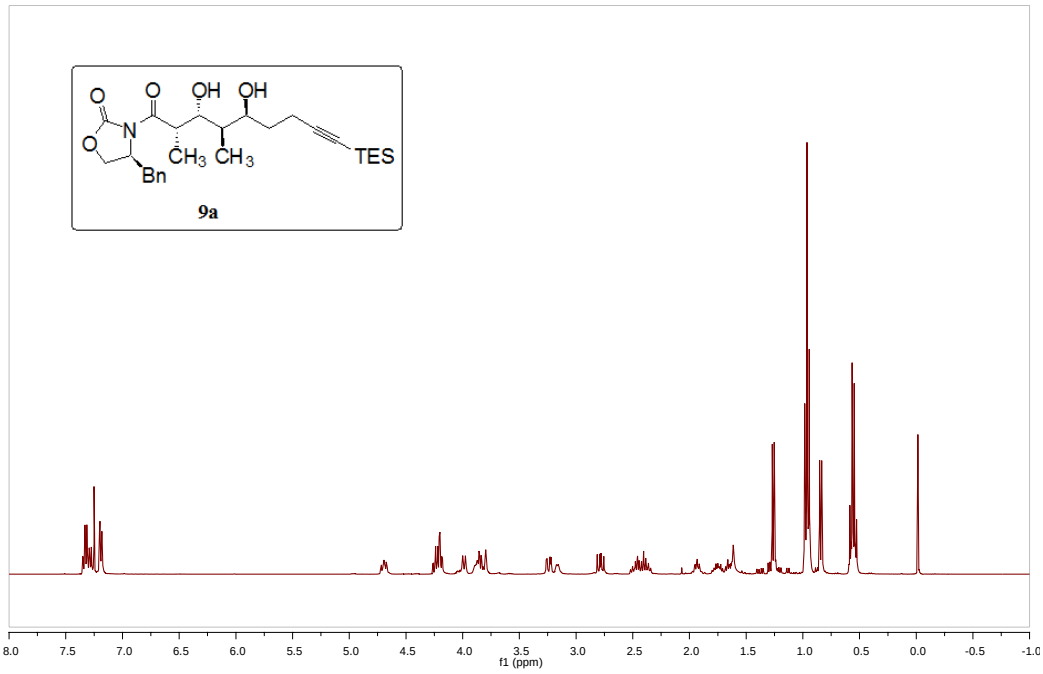


Figure 3: ^{1}H and ^{13}C NMR spectra of **9a**.



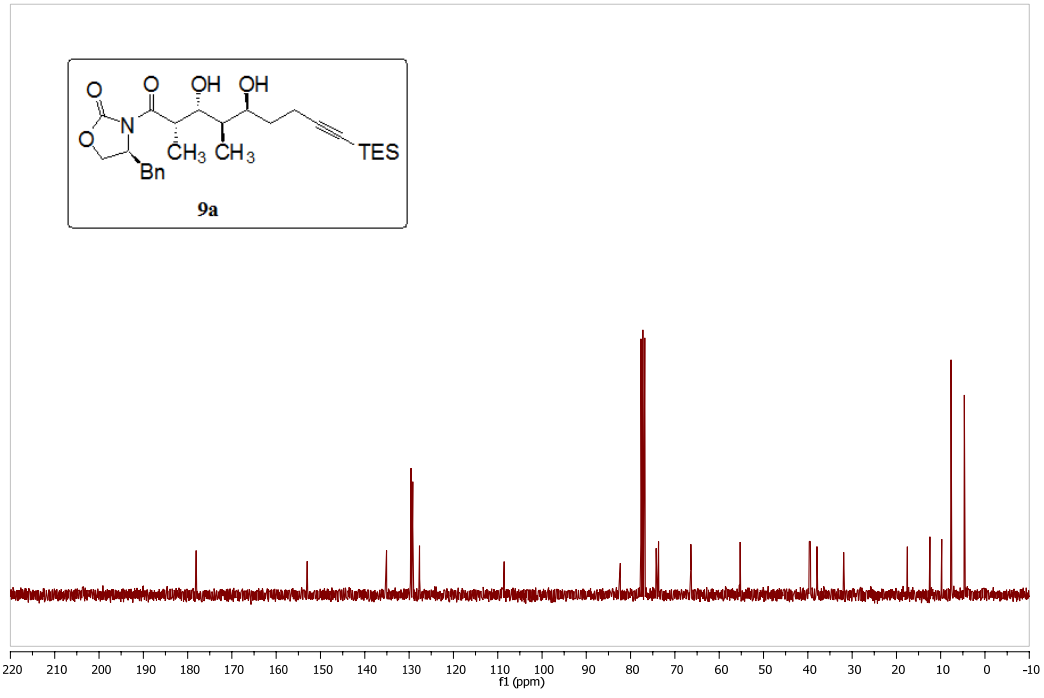
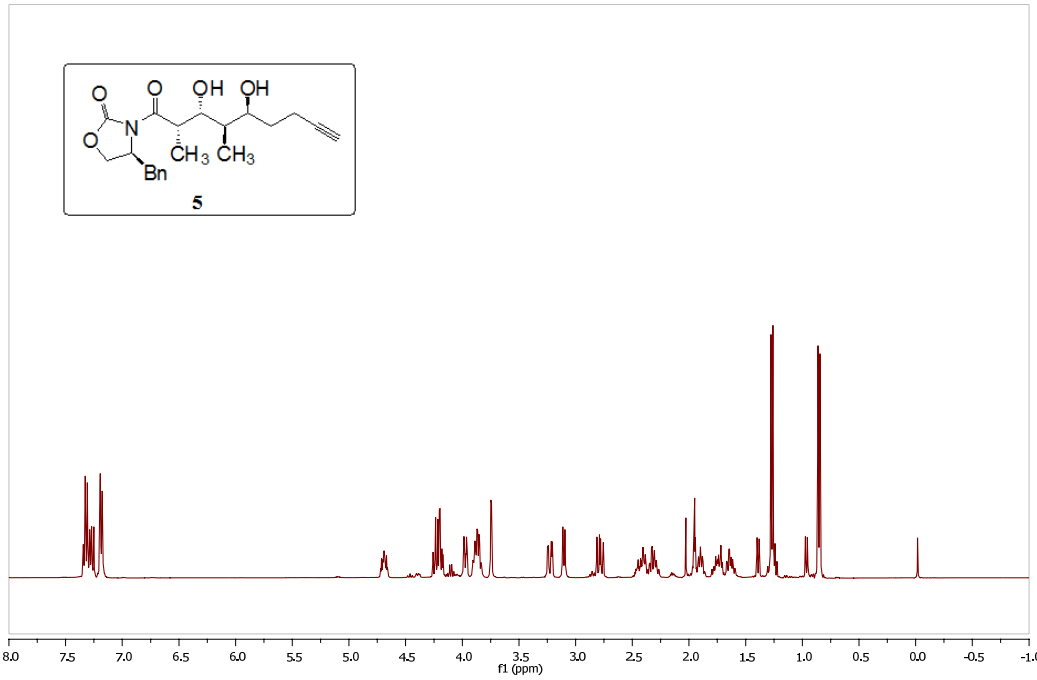


Figure 4: ^{1}H and ^{13}C NMR spectra of **5**.



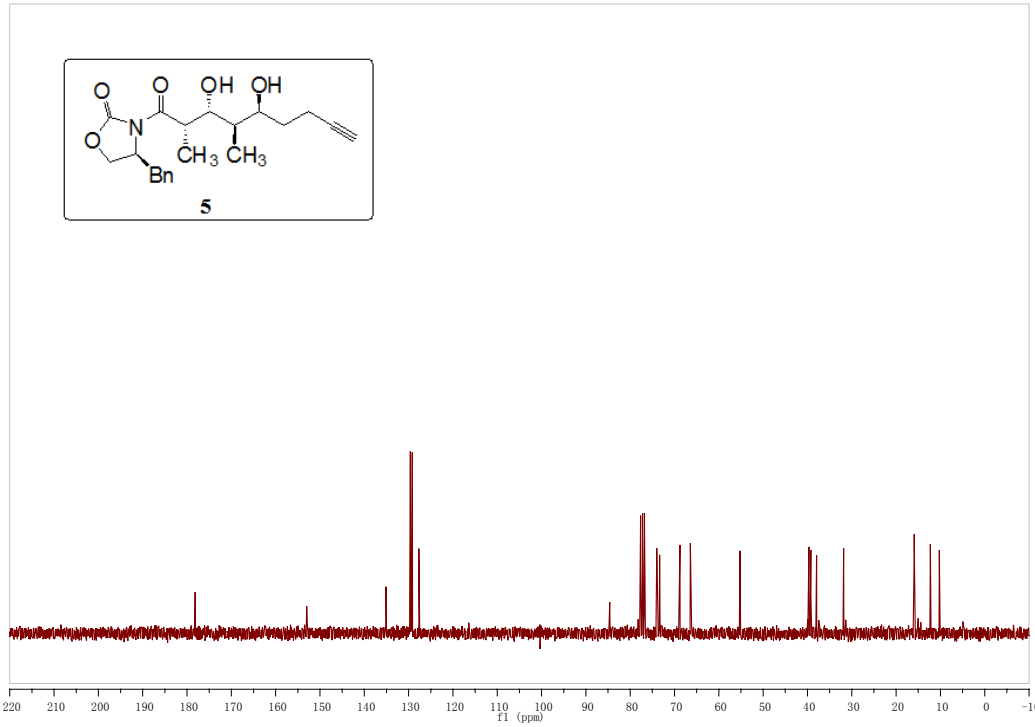
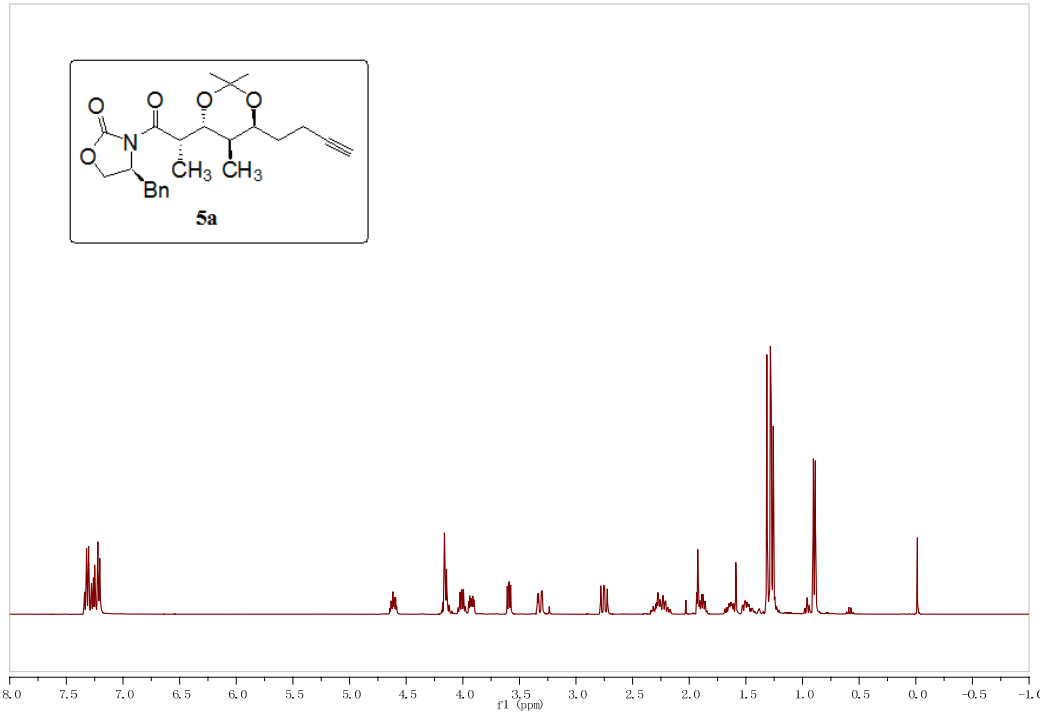


Figure 5: ^{1}H and ^{13}C NMR spectra of **5a**.



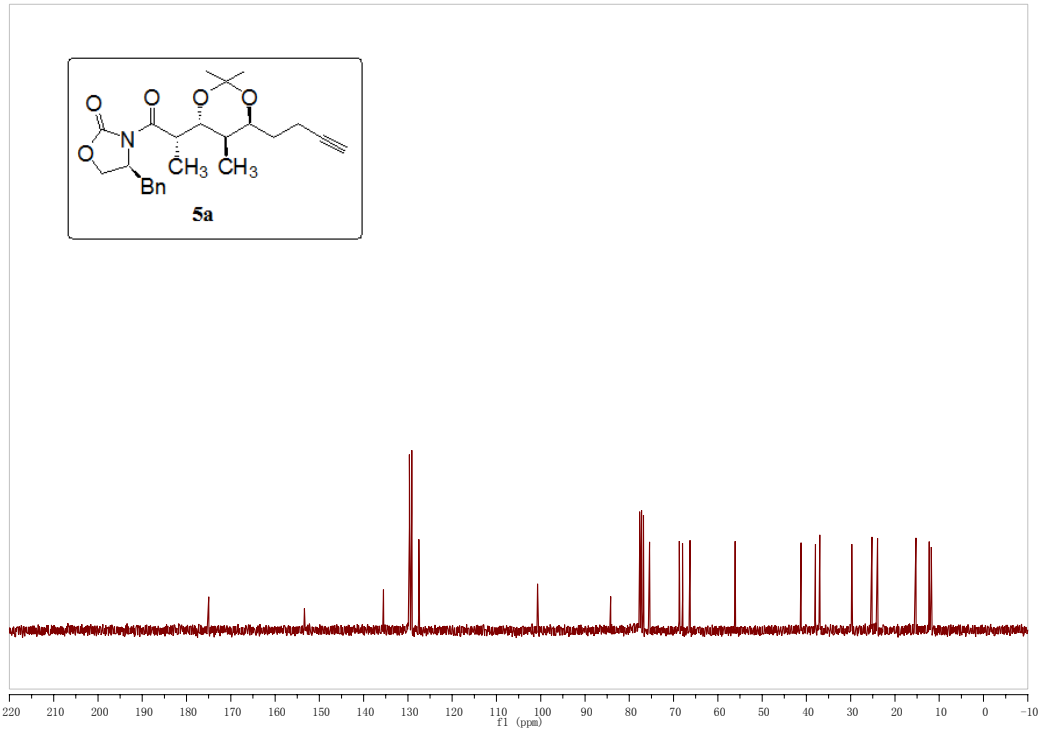
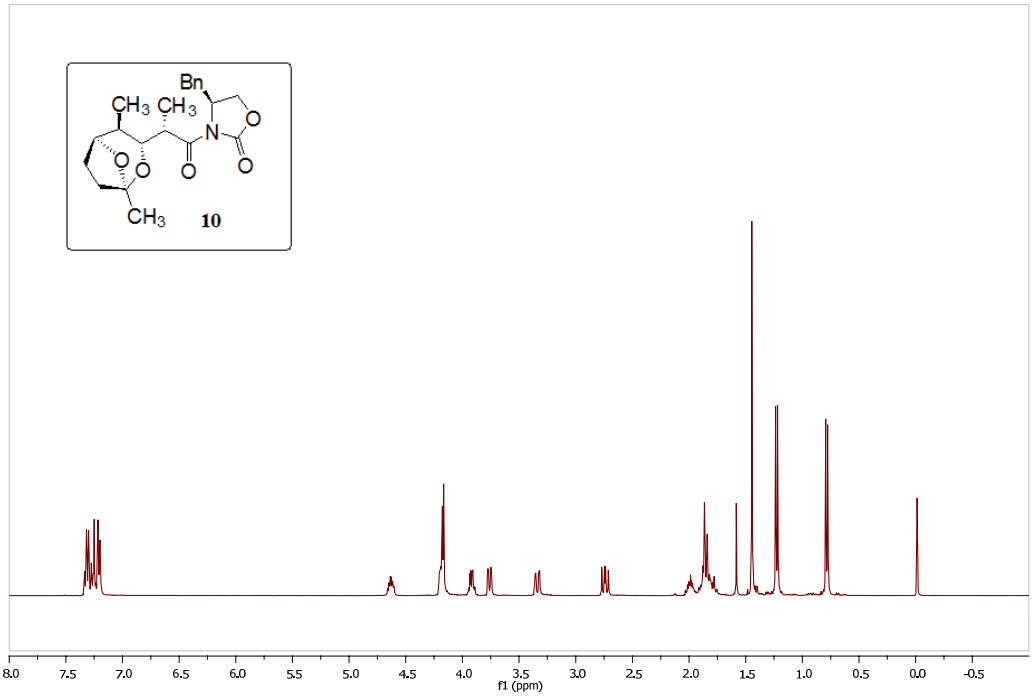


Figure 6: ^{1}H and ^{13}C NMR spectra of **10**.



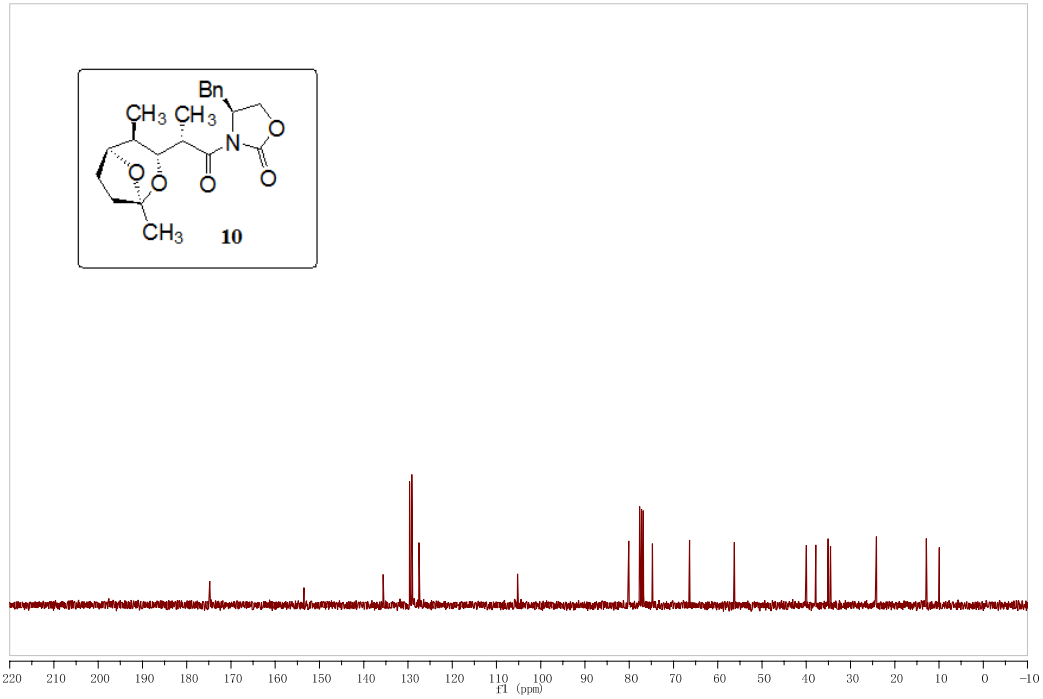
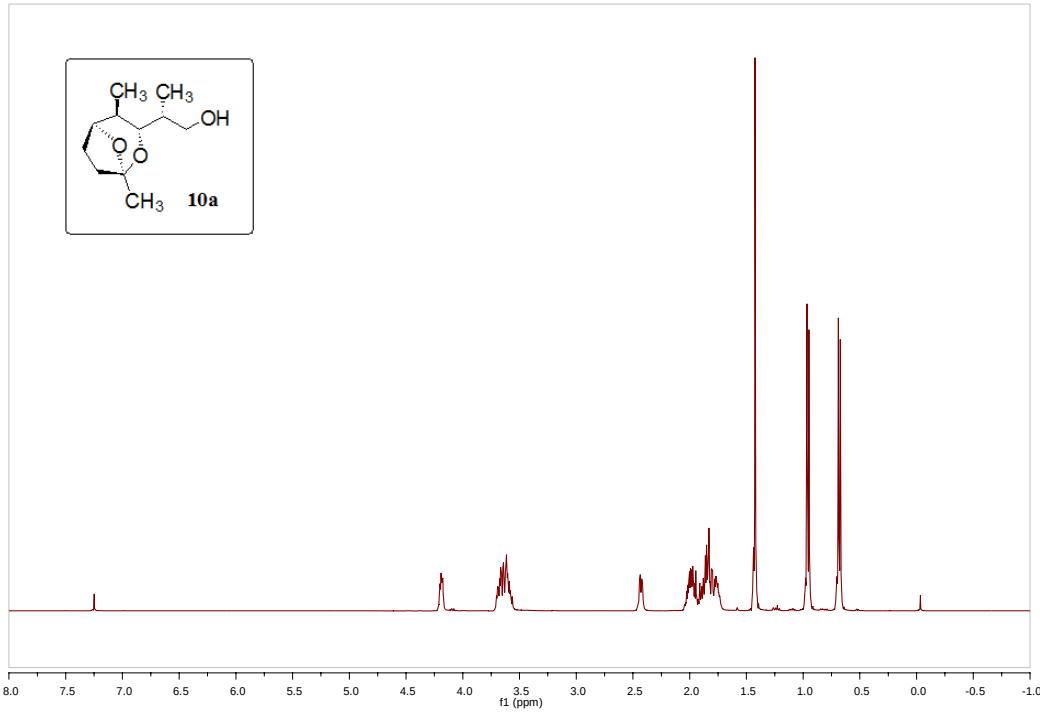


Figure 7: ^{1}H and ^{13}C NMR spectra of **10a**.



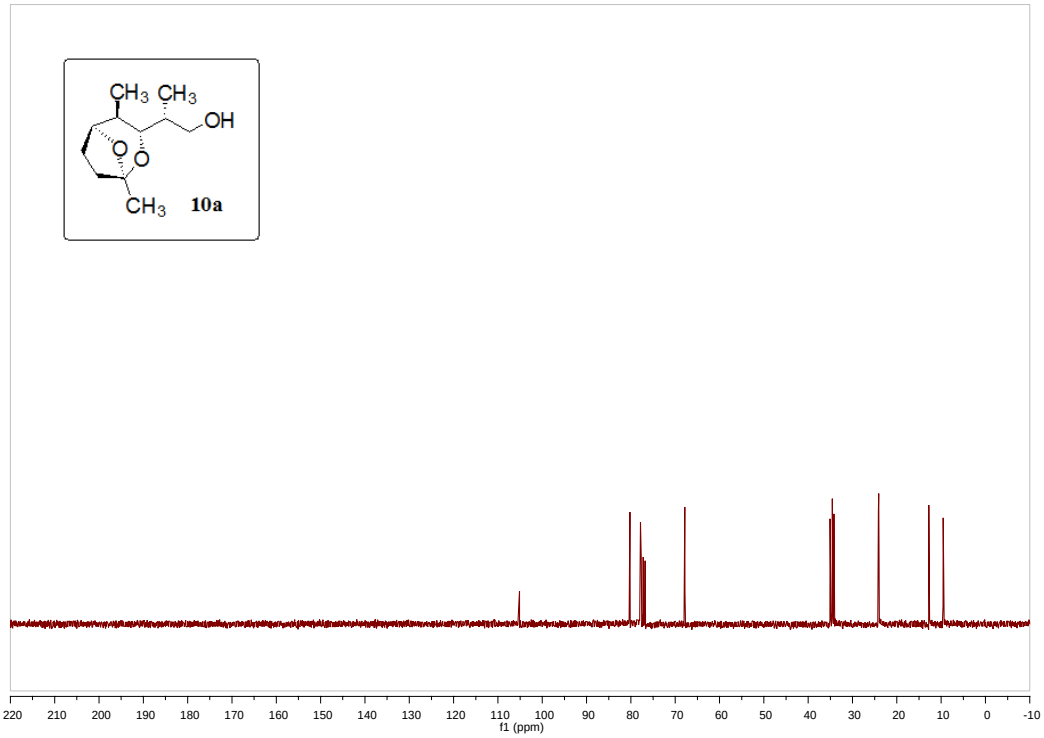
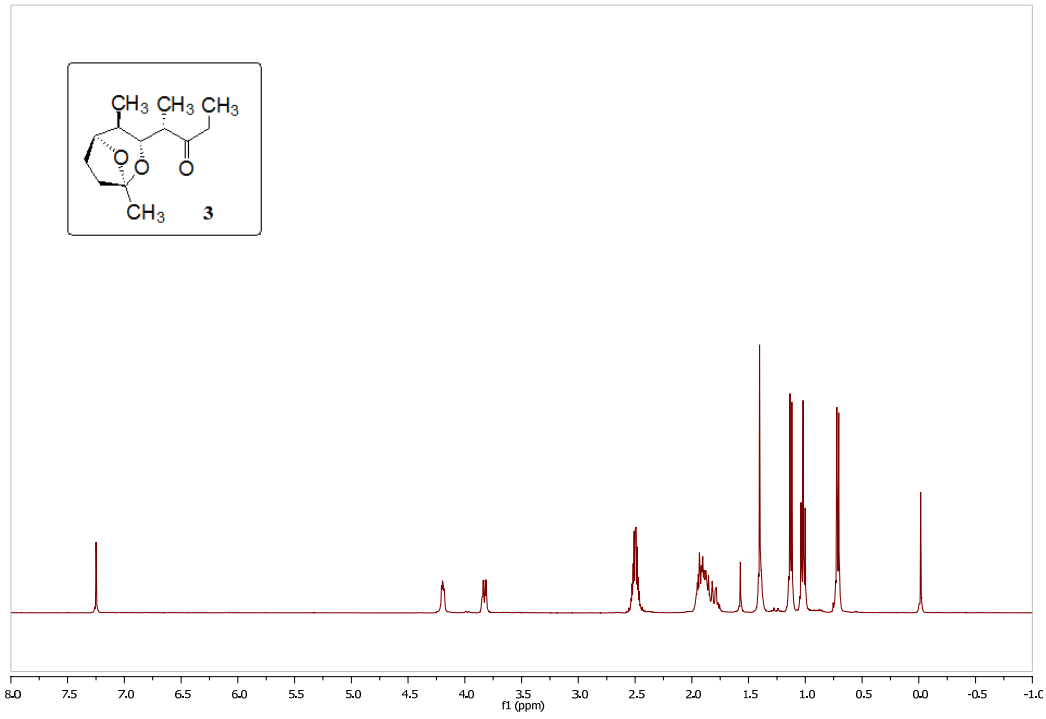


Figure 8: ^{1}H and ^{13}C NMR spectra of **3**.



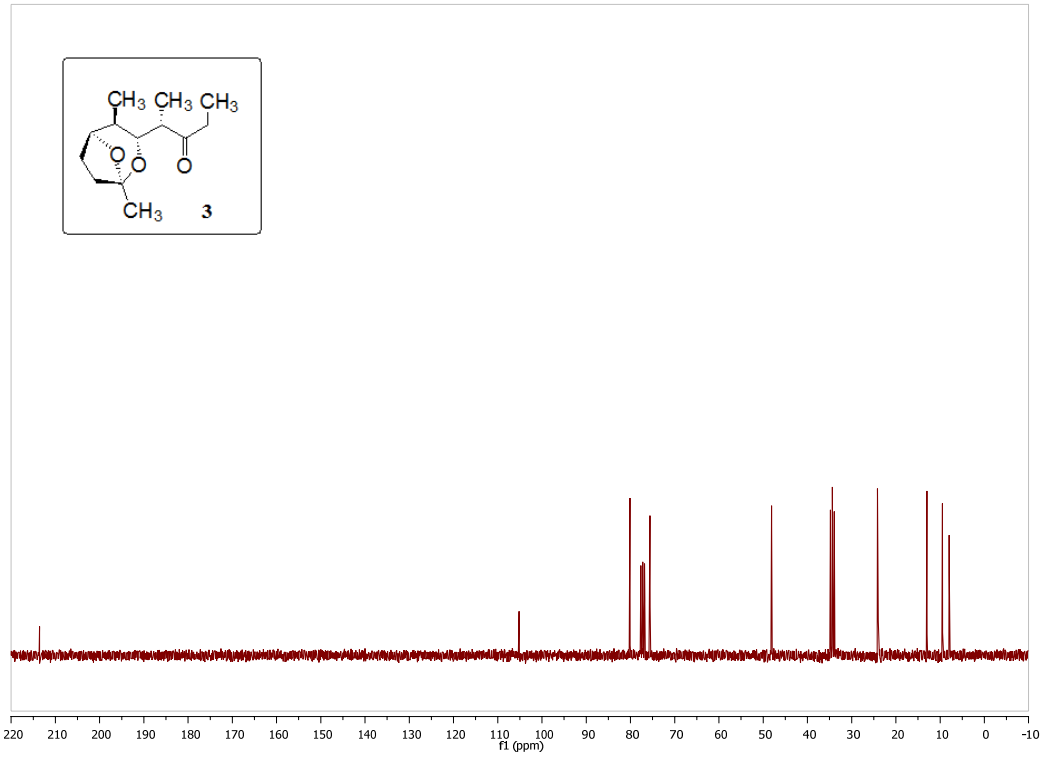
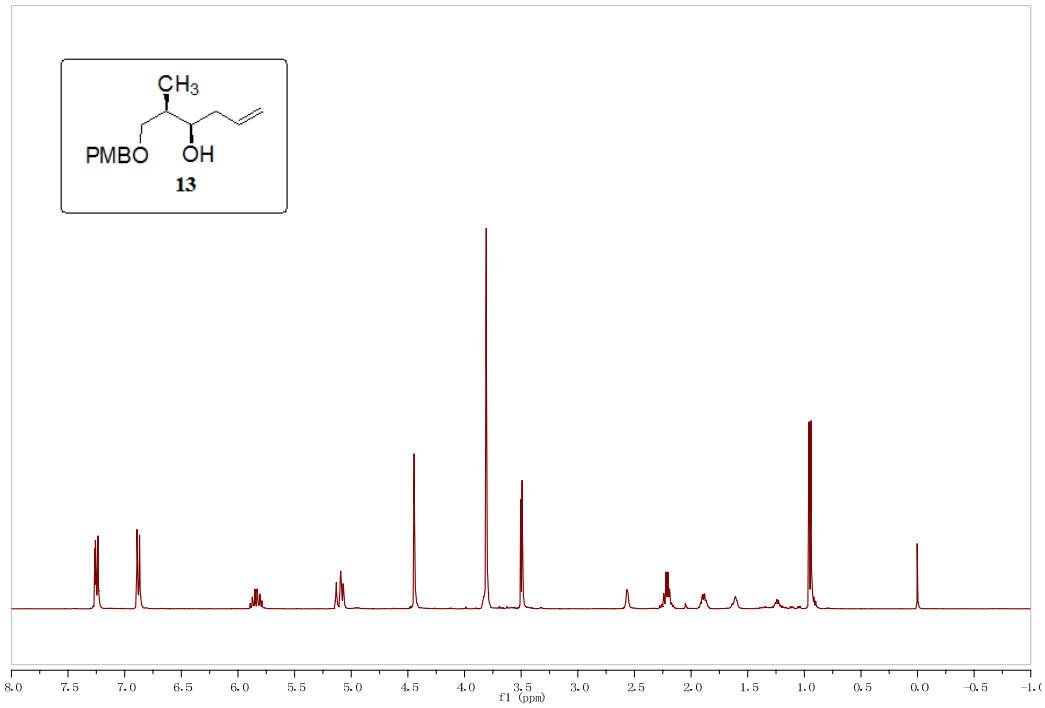


Figure 9: ^{1}H and ^{13}C NMR spectra of **13**.



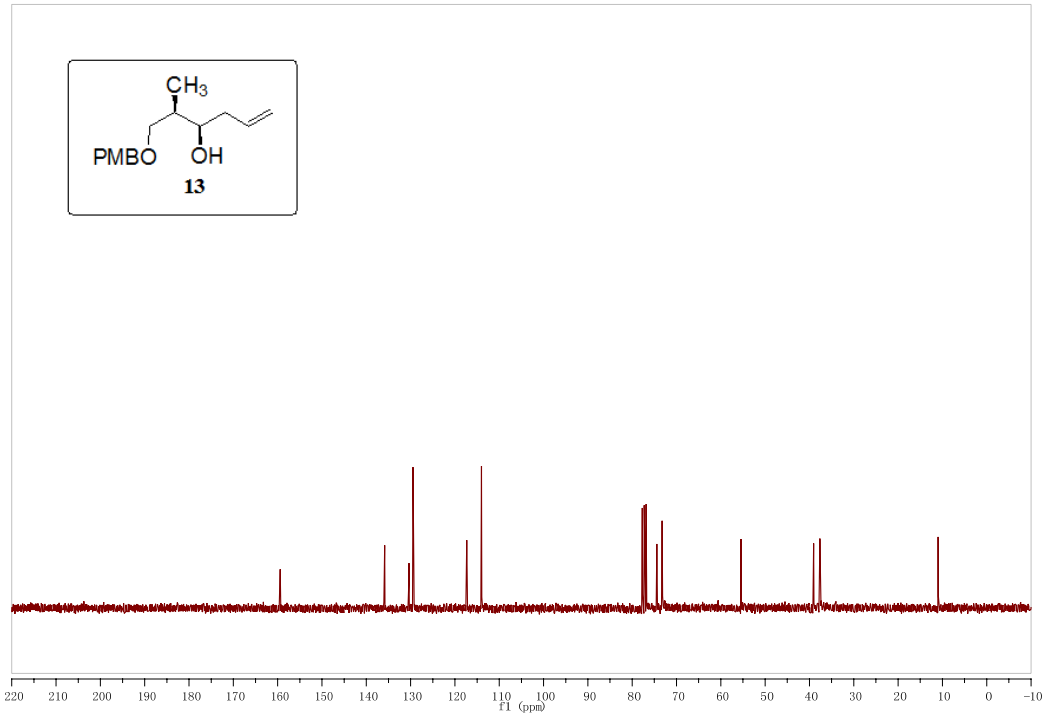
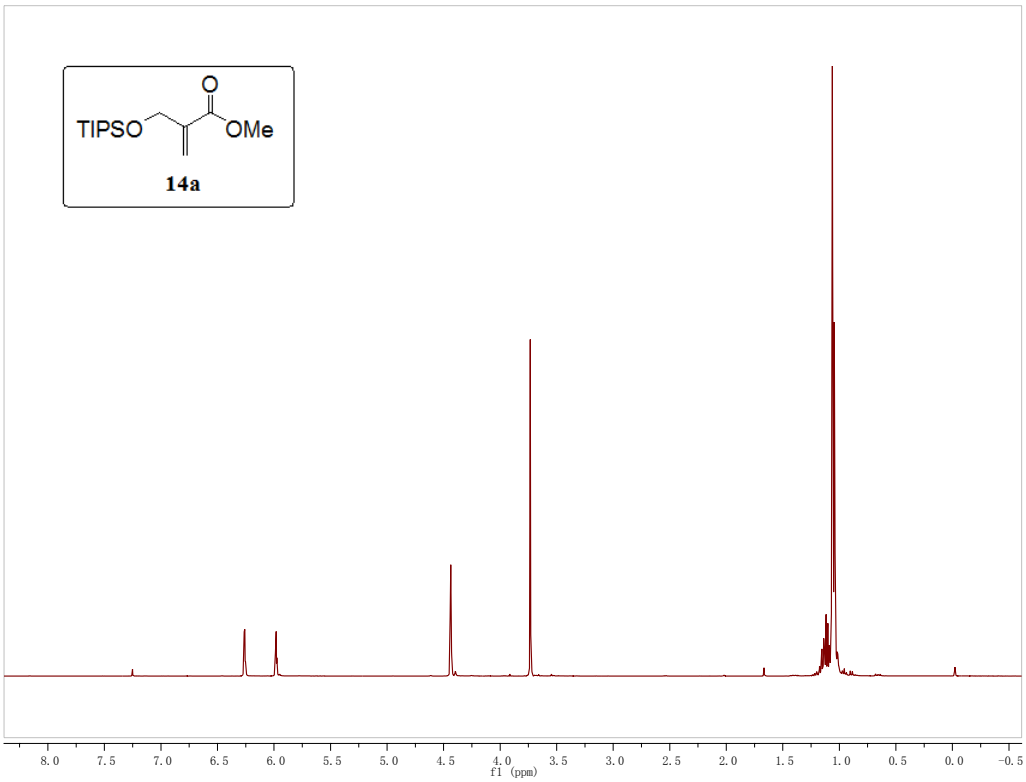


Figure 10: ^{1}H and ^{13}C NMR spectra of **14a**.



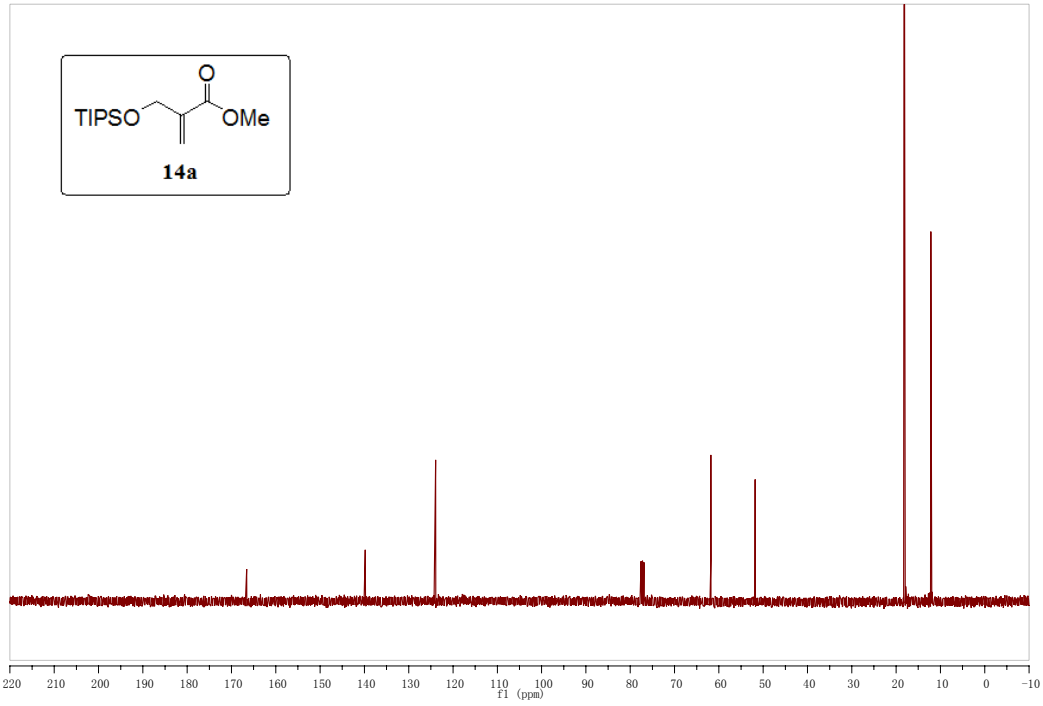
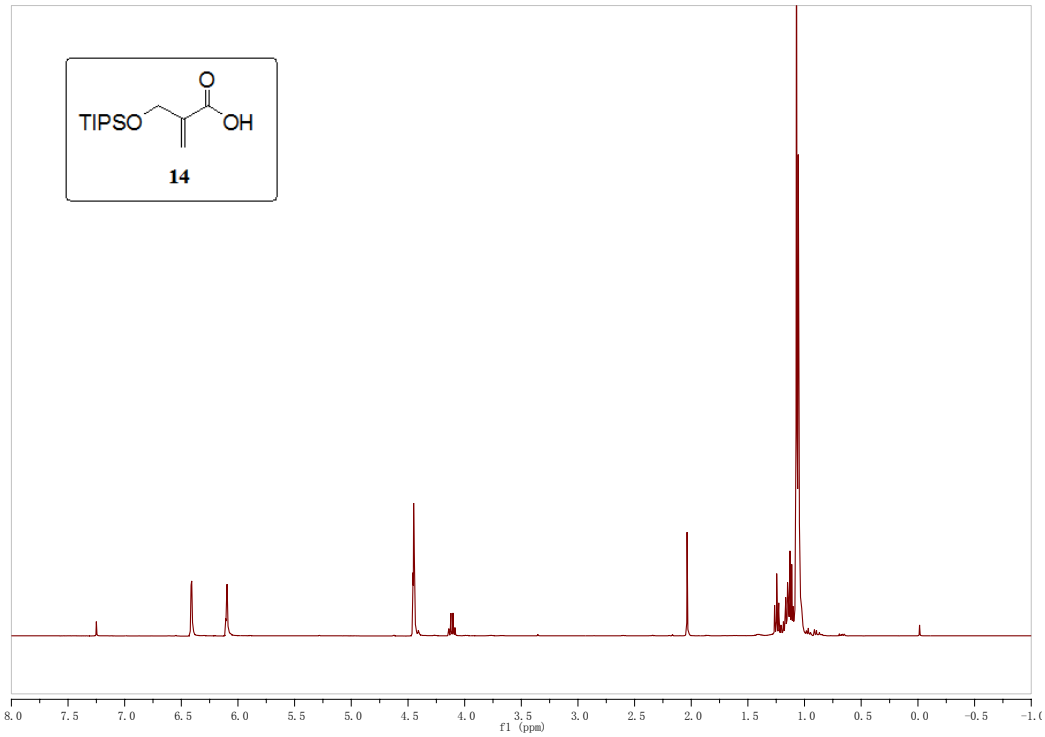


Figure 11: ^{1}H and ^{13}C NMR spectra of **14**.



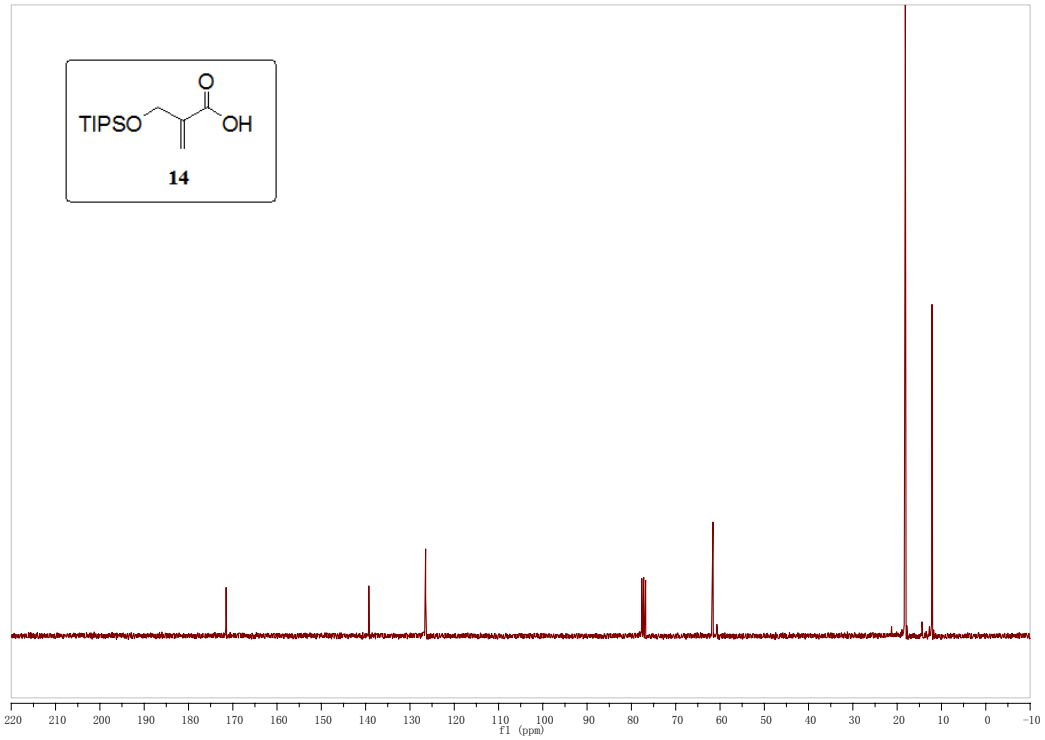
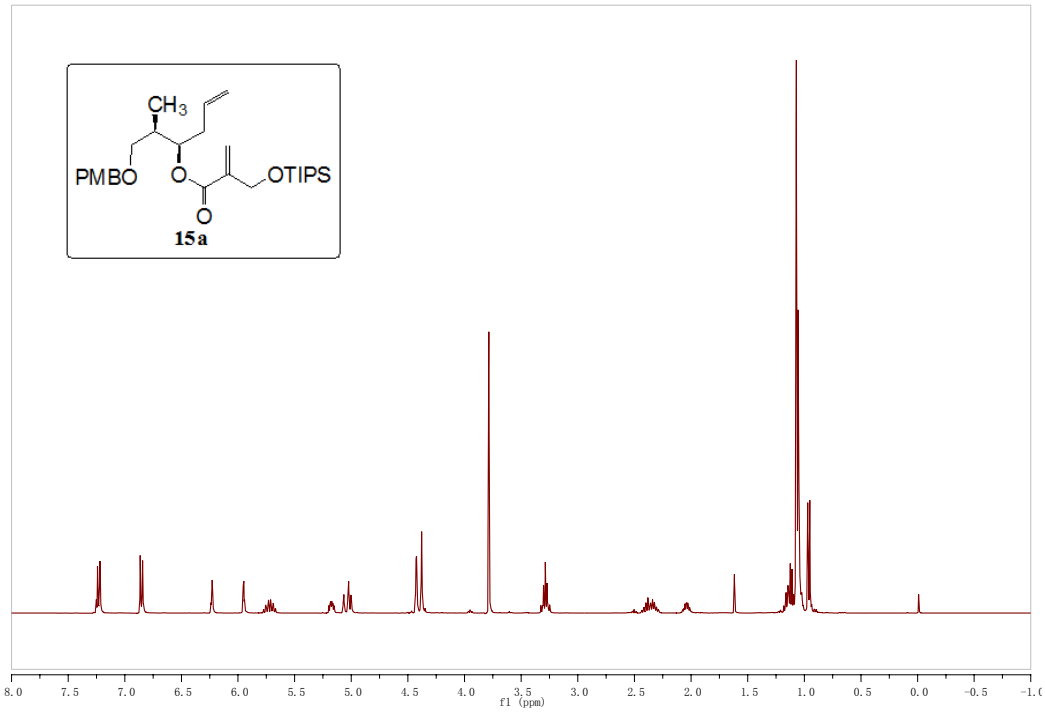


Figure 12: ^{1}H and ^{13}C NMR spectra of **15a**.



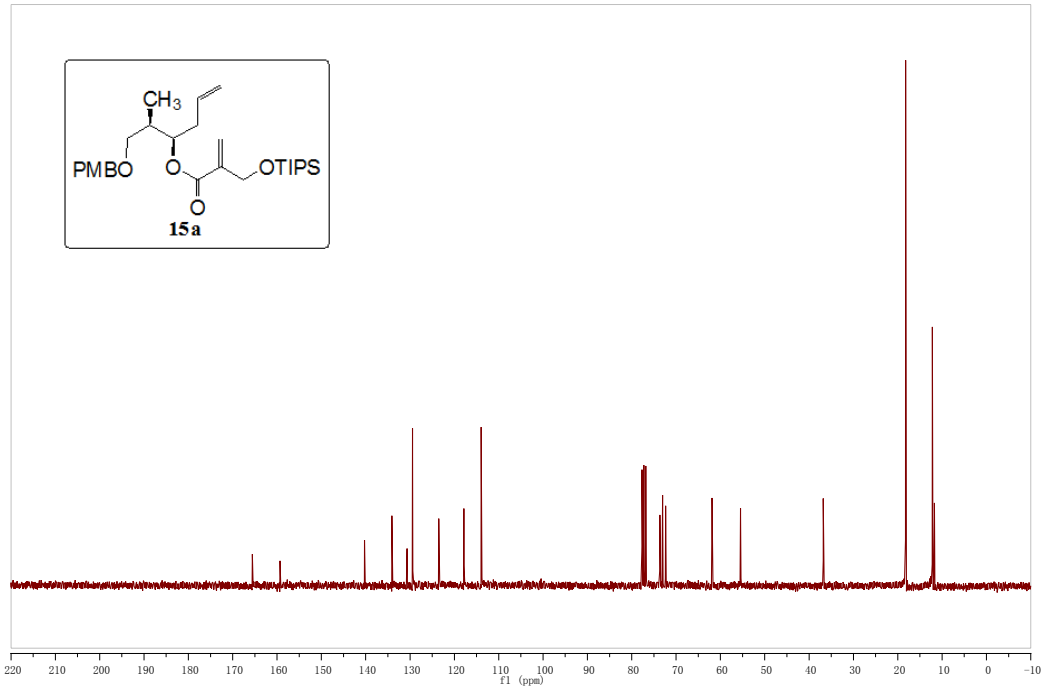
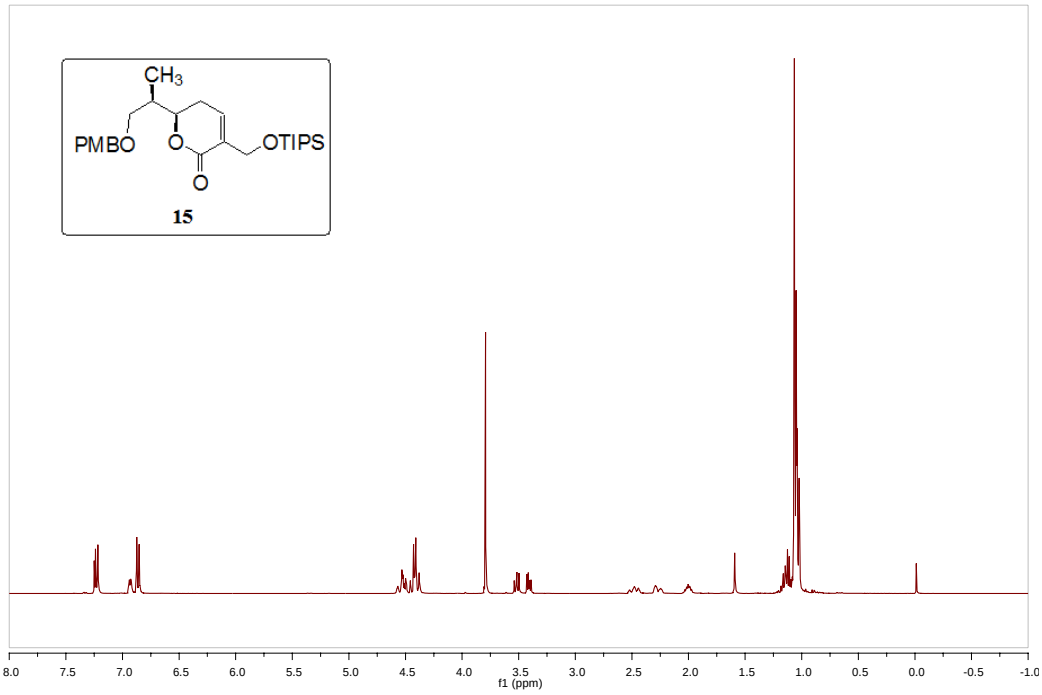


Figure 13: ^{1}H and ^{13}C NMR spectra of **15**.



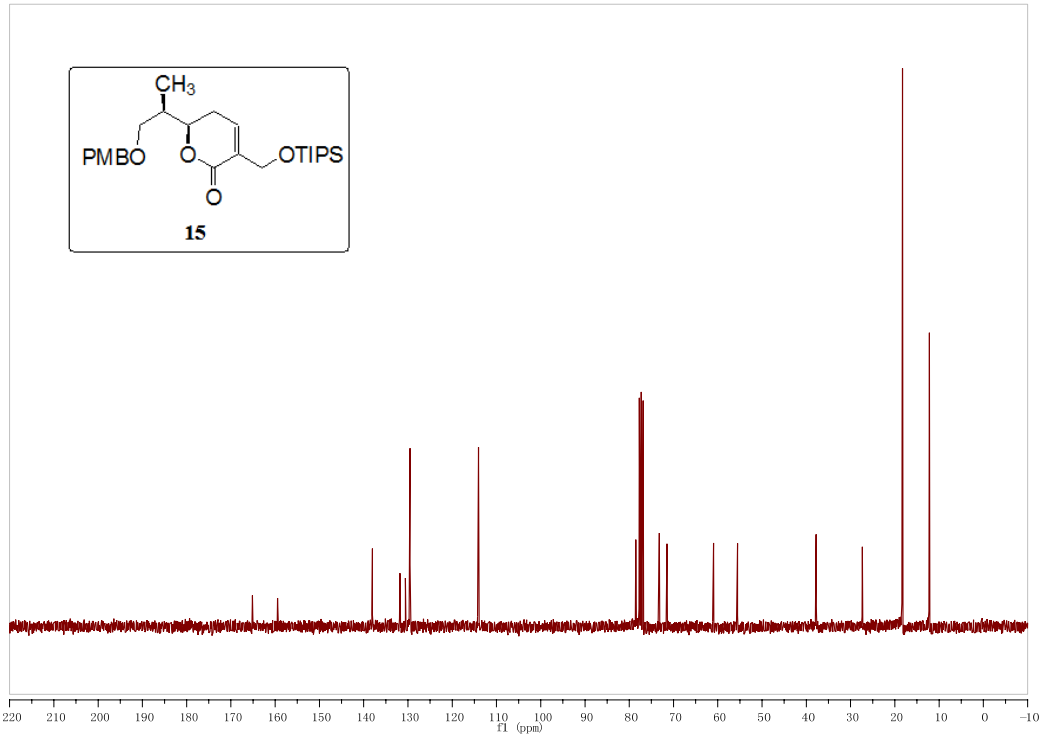
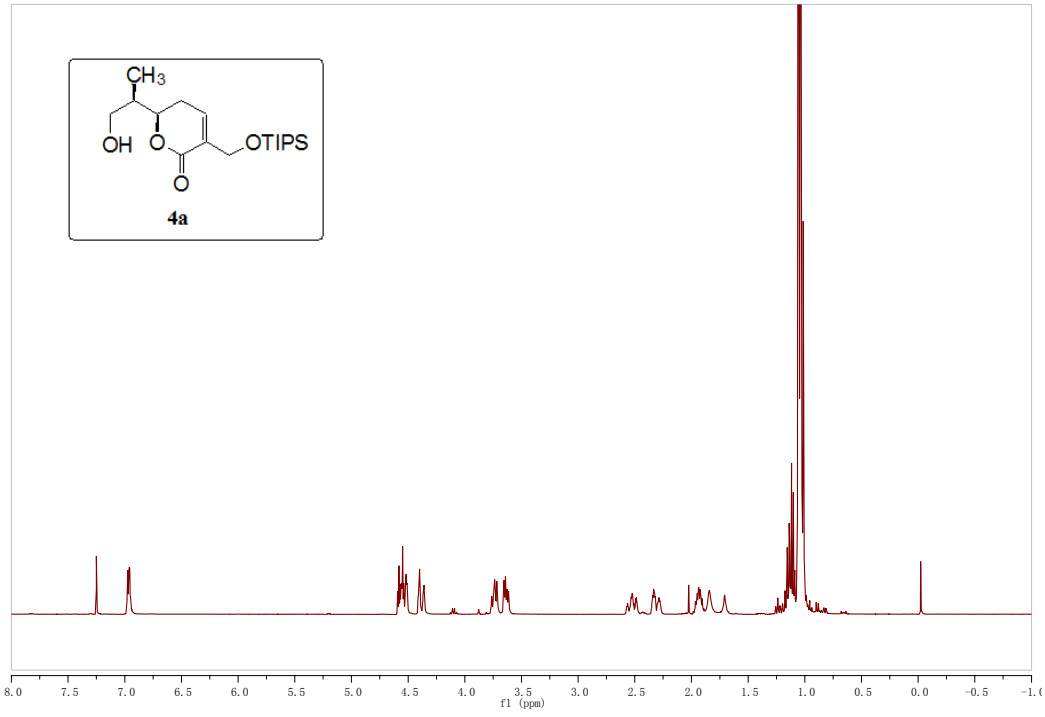


Figure 14: ^{1}H and ^{13}C NMR spectra of **4a**.



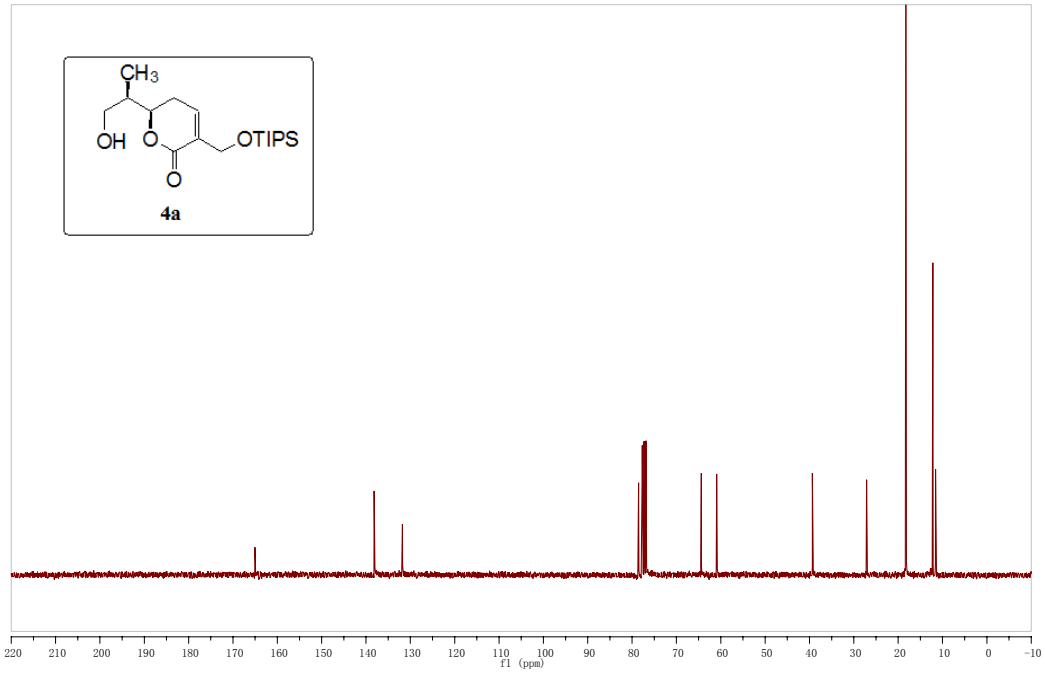
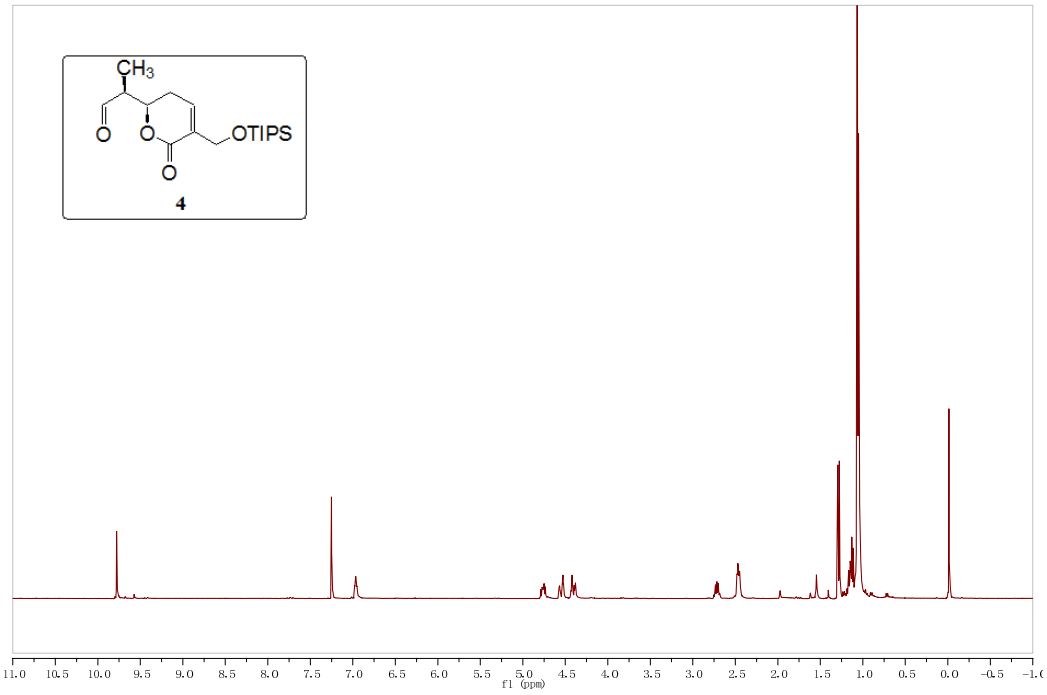


Figure 15: ^{1}H and ^{13}C NMR spectra of **4**.



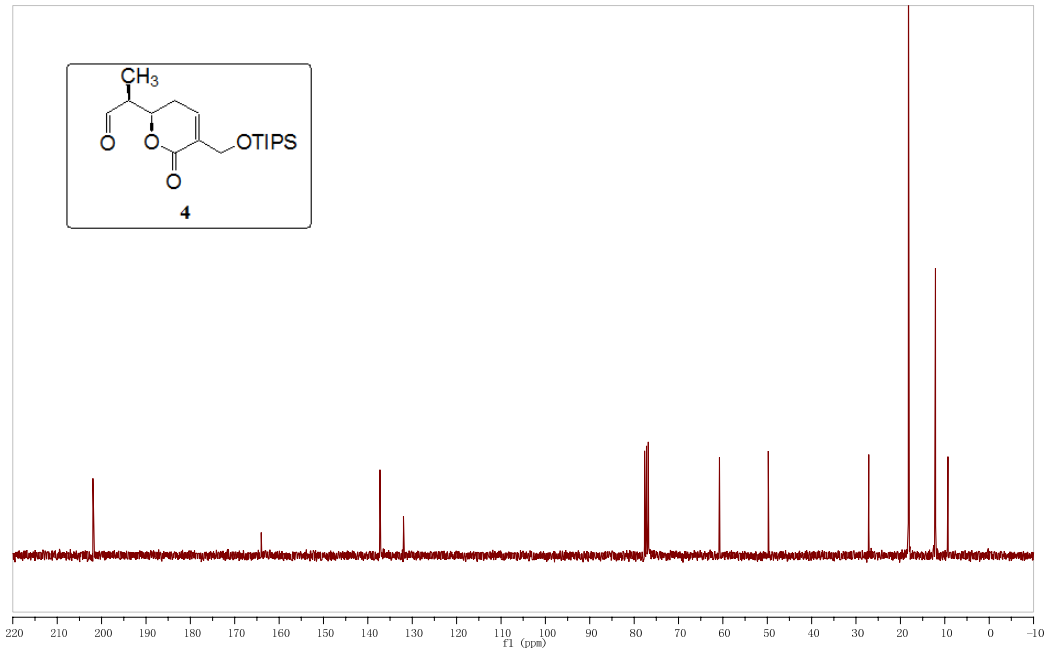
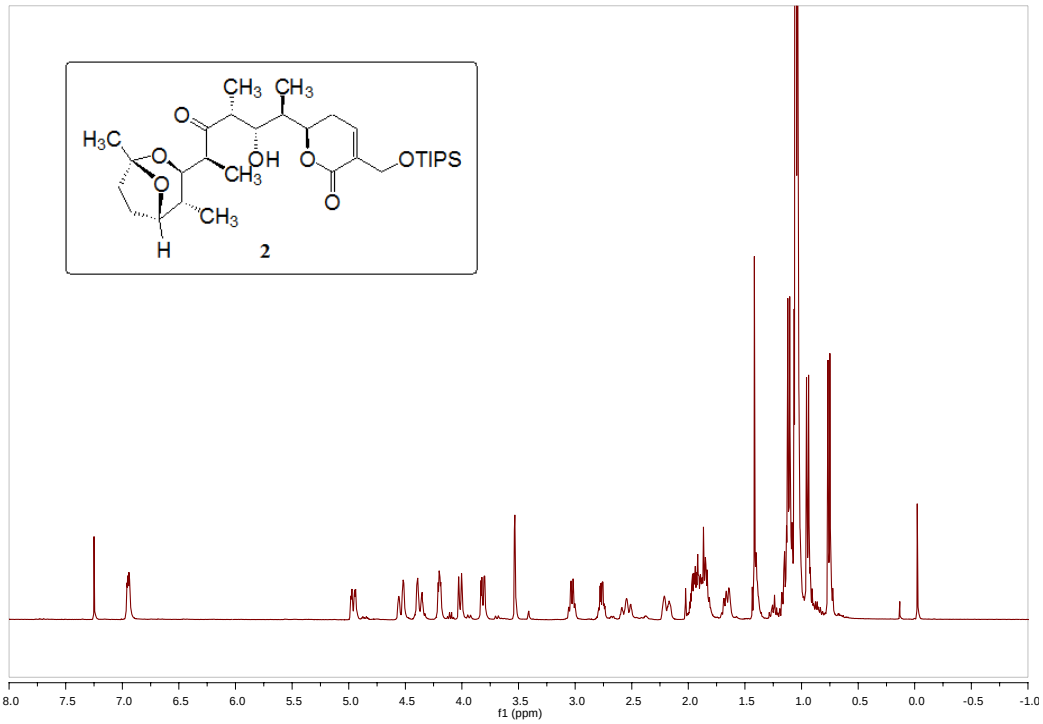


Figure 16: ^{1}H and ^{13}C NMR spectra of **2**.



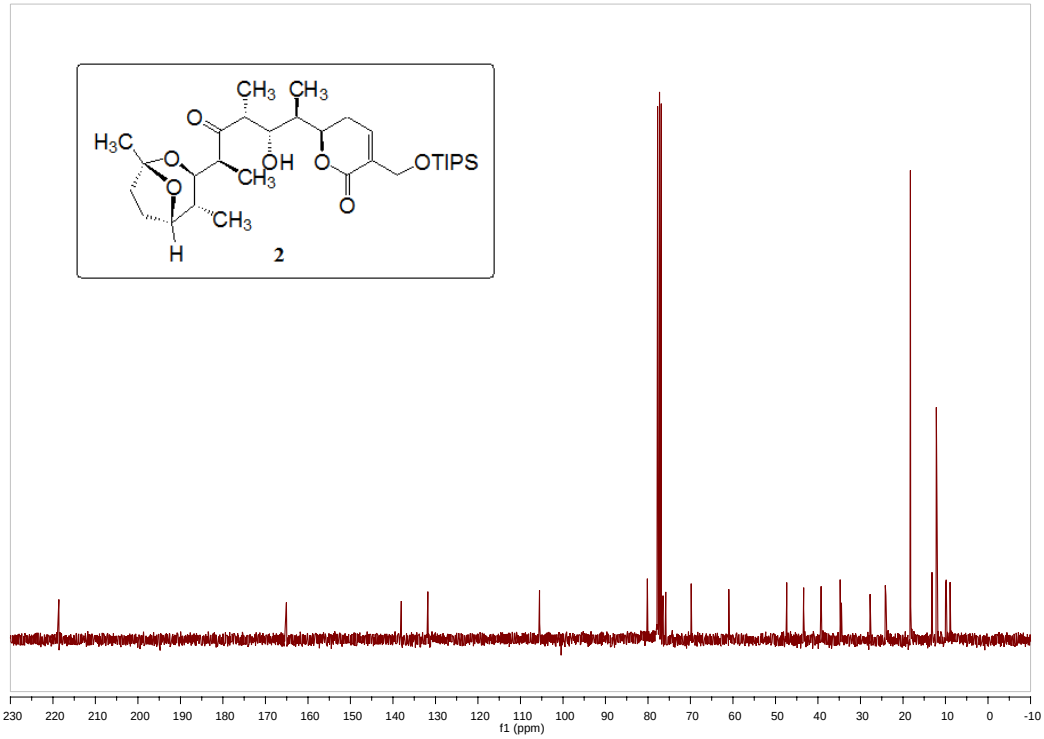
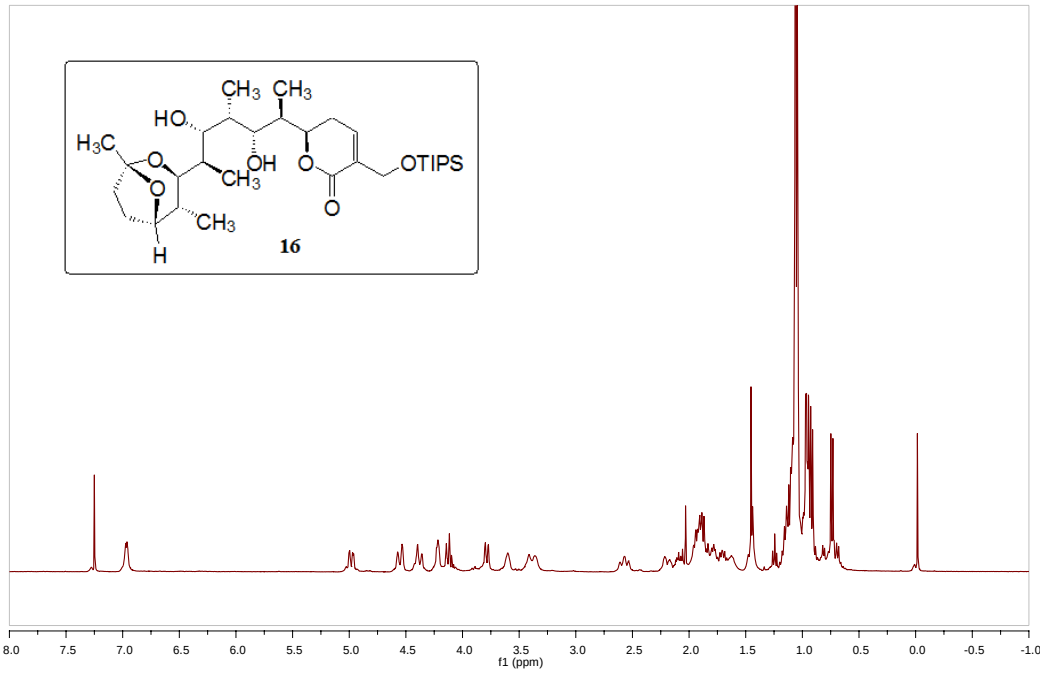


Figure 17: ^{1}H and ^{13}C NMR spectra of **16**.



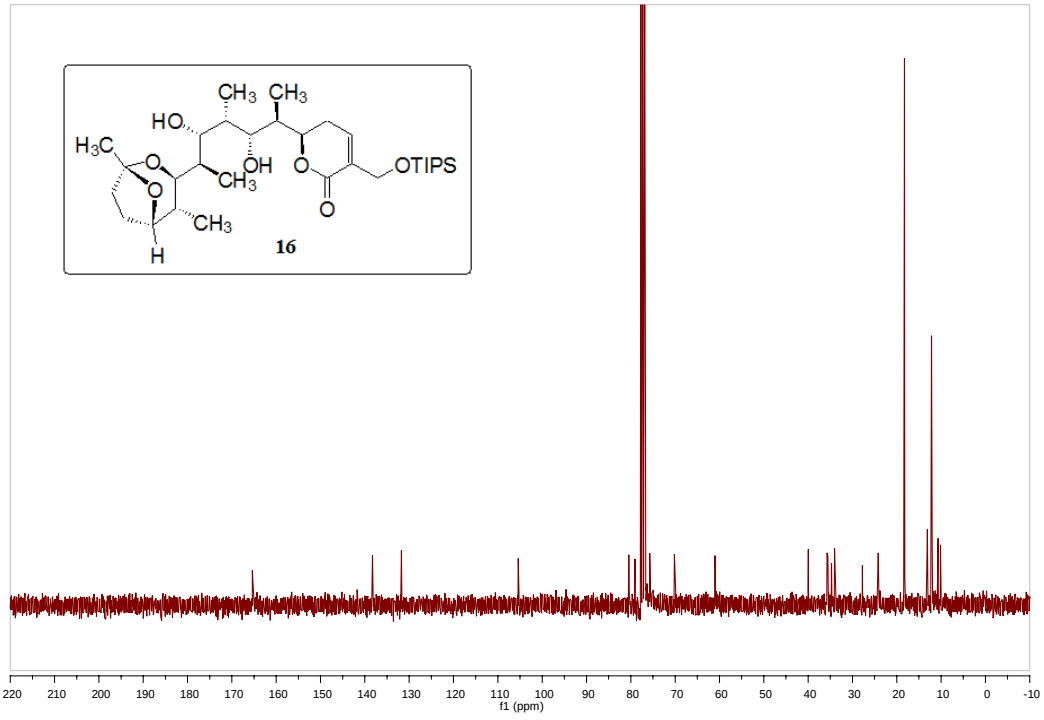
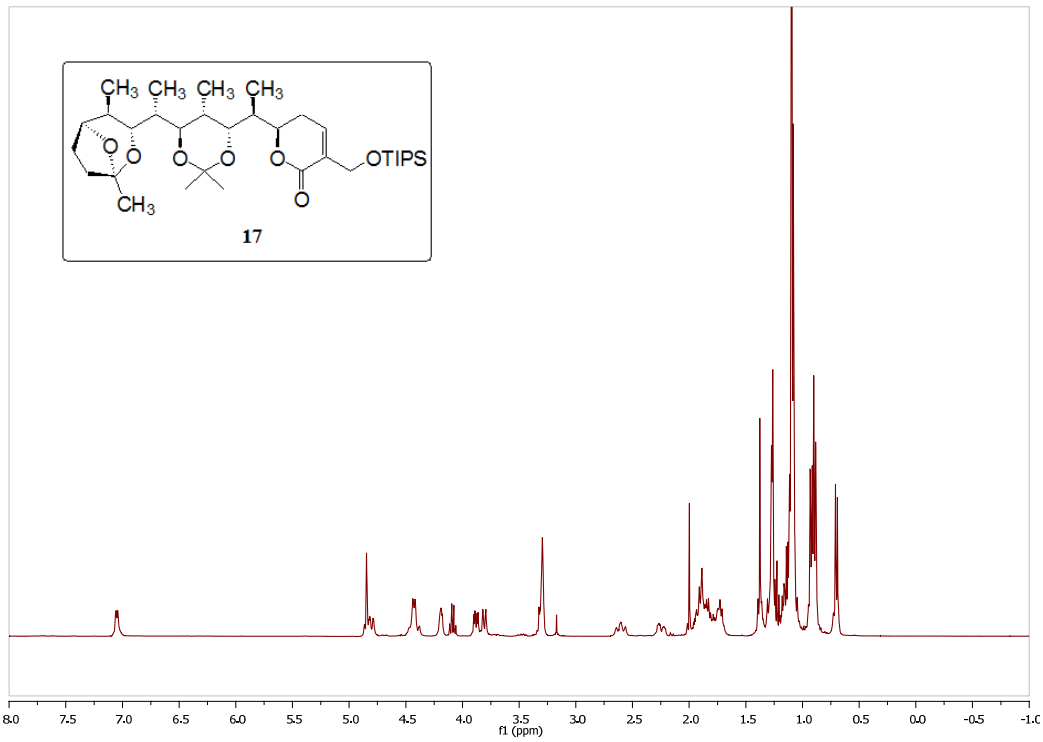


Figure 18: ^{1}H and ^{13}C NMR spectra of 17.



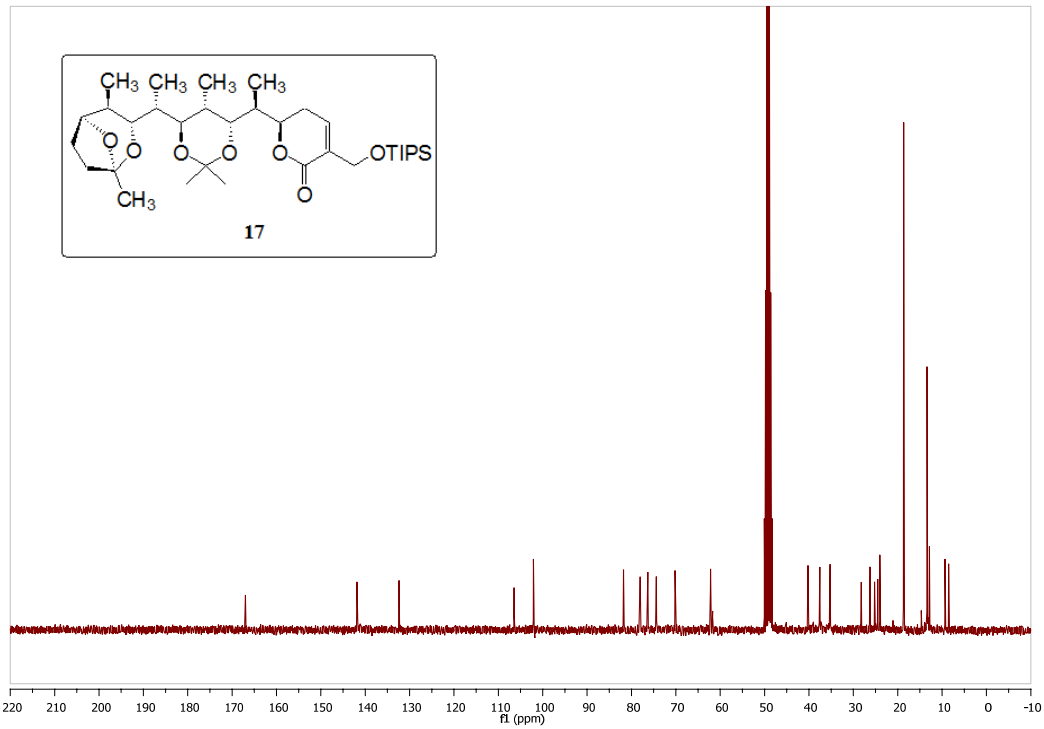


Figure 19: Comparison of ^{1}H NMR resonances between natural (–)-**Saliniketal B** (top) and synthetic (–)-**Saliniketal B** (bottom).

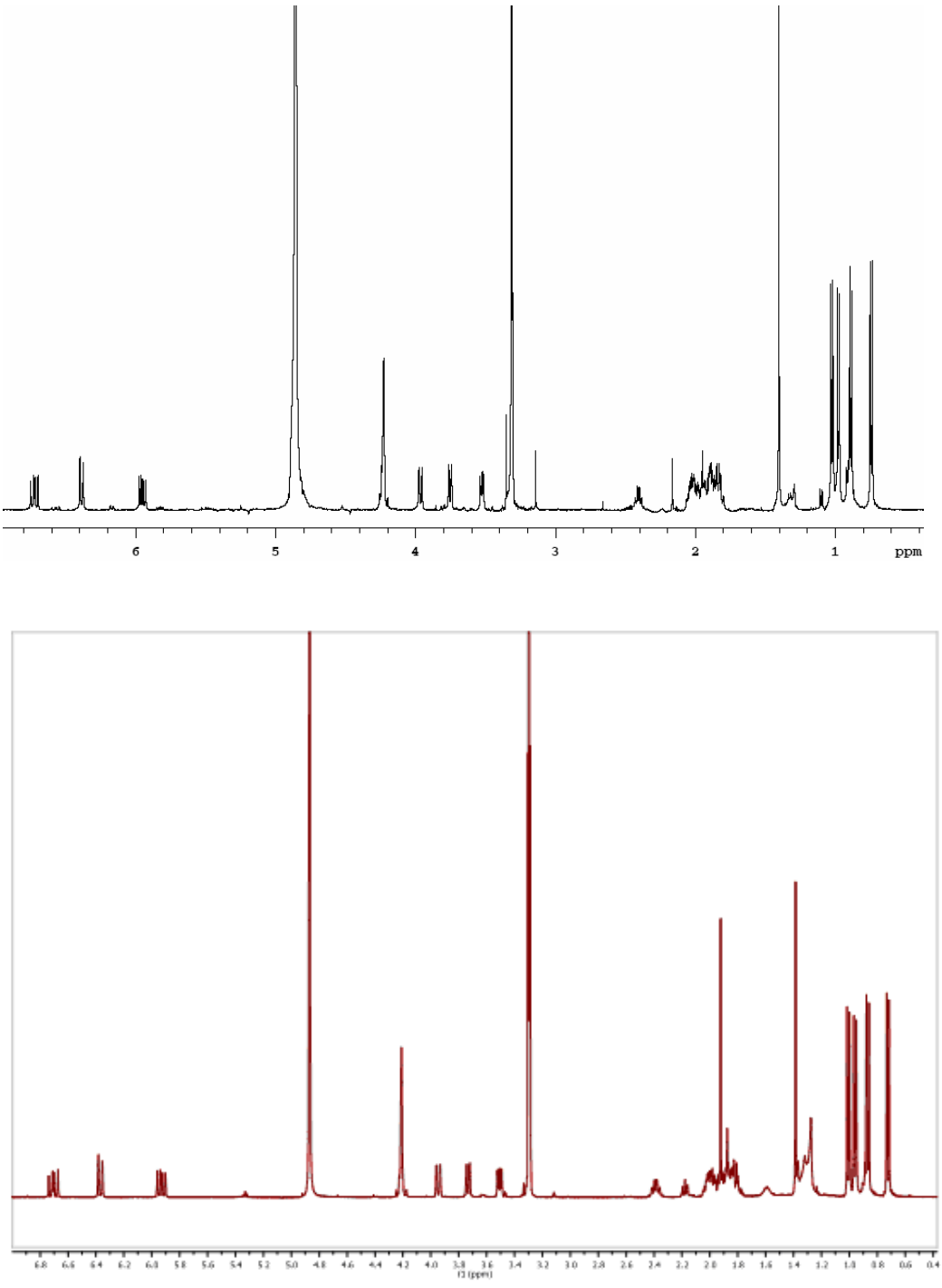
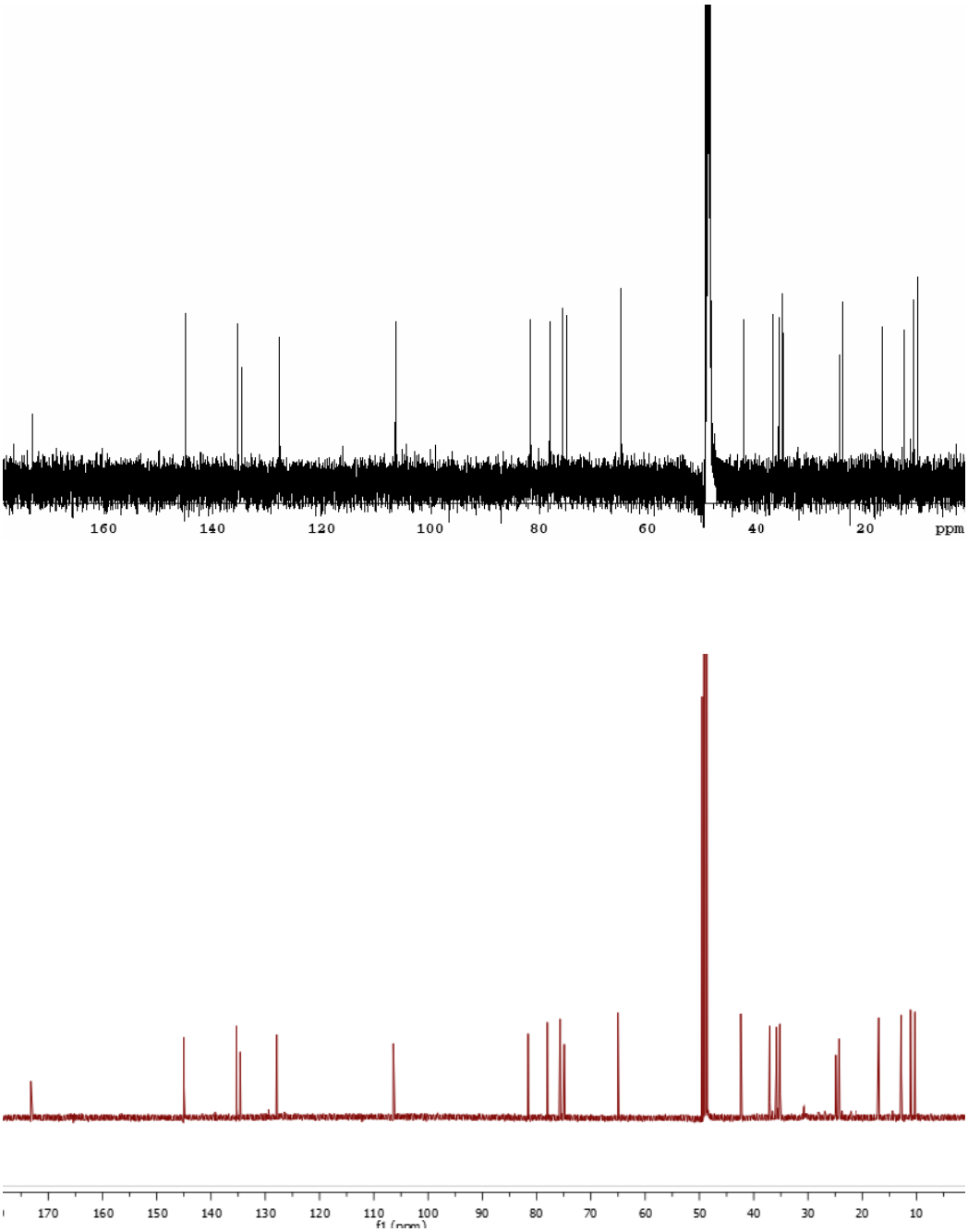


Figure 20: Comparison of ^{13}C NMR resonances between natural (–)-**Saliniketal B** (top) and synthetic (–)-**Saliniketal B** (bottom).



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