# Synthetic Studies Toward the Bryostatins: A Substrate-Controlled Approach to the A-Ring

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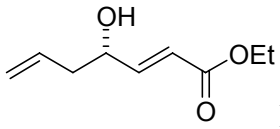
Supplementary Information

## Experimental Section

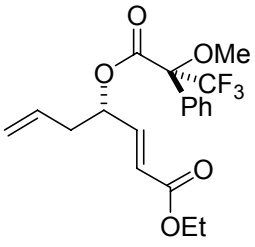
Solvents were purified according to the guidelines in *Purification of Laboratory Chemicals, 3rd Ed.* (Perrin and Armarego, Pergamon: Oxford, U.K., 1988). Reagent-grade dimethoxypropane, methanol, and acetone were purchased and used without further purification. Diisopropylamine, diisopropylethylamine, pyridine, and triethylamine were distilled from $CaH_2$ prior to use. Ozone was generated using a Welsbach model T-816 generator. All other reagents were purchased from Aldrich and used without further purification. The titer of *n*-butyllithium was determined by the method of Eastham and Watson. Yields were calculated for material judged homogeneous by thin-layer chromatography and NMR. Thin-layer chromatography was performed on Merck Kieselgel 60 $F_{254}$ plates eluting with the solvents indicated, visualized by a 254 nm UV lamp, and stained with either an ethanolic solution of 12-molybdophosphoric acid, *p*-anisaldehyde, or a solution of ammonium molybdate/ceric ammonium sulfate. Medium pressure liquid chromatography (MPLC) and flash column chromatography were performed with Davisil 62 silica gel, slurry packed with solvents indicated in glass columns. Radial chromatography (RPLC) was performed using a Chromatotron and glass plates coated with silica gel (P.F. 245 60) of 2 and 4 mm thicknesses. Preparative chromatography was also carried out using preparative HPLC using a Dynamax-60A column with solvents indicated. Nuclear magnetic resonance spectra were acquired at 300 and 500 MHz for $^1H$, and 75 and 125 MHz for $^{13}C$. Chemical shifts for proton nuclear magnetic resonance ($^1H$ NMR) spectra are reported in parts per million downfield relative to the line of the $CDCl_3$ singlet at 7.27 ppm. Chemical shifts for carbon nuclear magnetic resonance ($^{13}C$ NMR) spectra are reported in parts per million downfield

relative to the center line of the $CDCl_3$ triplet at 77.23 ppm. The abbreviations s, d, t, q, quin, m, and ABq stand for the resonance multiplicities singlet, doublet, triplet, quartet, quintet, multiplet, and AB quartet, respectively. Optical rotations were obtained (Na D line) using a micro cell with a 1 dm path length. Concentrations are reported in g/100 mL. Melting points were obtained on an Electro thermal melting point apparatus and are uncorrected. Elemental combustion analyses were performed by Atlantic Microlab, Inc., Norcross, Georgia. Glassware for all reactions was oven-dried at 125 °C and cooled in a desiccator, or flame-dried and cooled under vacuum prior to use.

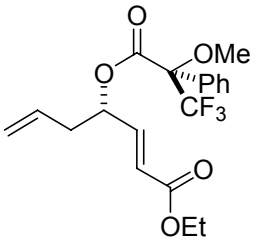



**Preparation of (*E*)-(*S*)-4-hydroxy-hepta-2,6-dienoic acid ethyl ester (9a).** A 100 mL round bottom flask was charged with a magnetic stir bar, oven dried 4 Å molecular sieves (6.25 g), and $CH_2Cl_2$ (62 mL). To the stirring mixture, under an atmosphere of Ar, were added (*S*)-BINOL (893 mg, 3.12 mmol, 0.2 equiv) in one portion, a 1.0 M solution of Ti(O*i*Pr)$_4$ (1.55 mL, 1.56 mmol, 0.1 equiv) in $CH_2Cl_2$ via syringe, and a freshly prepared 0.5 M solution of TFA (0.219 mL, 0.109 mmol, 0.007 equiv) in $CH_2Cl_2$. The reaction mixture was heated at reflux (~38 °C) for a period of 1 h, and then allowed to cool to rt. Commercially available aldehyde **9** (2.00 g, 15.6 mmol, 1.0 equiv) was added to the reaction mixture via syringe. After the mixture was stirred for 0.5 h at rt and cooled to -78 °C, allyltributyltin (7.75 g, 23.42 mmol, 1.5 equiv) was added, dropwise via syringe, to the stirring mixture down the inside of the reaction flask. The reaction mixture was stirred for an additional 10 min at -78 °C then transferred to a -20 °C freezer. After 12 h, TLC analysis indicated complete consumption of aldehyde starting material. The reaction mixture was filtered over a pad of Celite® into a 250 mL

Erlenmeyer flask that contained a stirring saturated aqueous $NaHCO_3$ solution (100 mL). An additional portion of $CH_2Cl_2$ (200 mL) was used to dilute the slurry and the resulting mixture was stirred for 1 h, then the layers were separated. The aqueous layer was extracted with $CH_2Cl_2$ (4 × 25 mL). The combined organic phases were washed with brine (2 × 50 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give the crude product as a red oil. Purification was accomplished by flash column chromatography on a 4.5 × 25 cm column, eluting with 5% acetone/hexanes (1 L) and 10% acetone/hexanes (1 L), collecting 8 mL fractions. The product containing fractions (35–50) were combined and concentrated under reduced pressure to give homoallylic alcohol **9a** (2.57 g, 97% yield) as colorless oil: $R_f$ = 0.30 (15% acetone/hexanes); $[\alpha]^{20}_D$ = - 13.2 (*c* = 0.72, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 6.93 (dd, *J* = 15.8, 4.4 Hz, 1H), 6.04 (dd, *J* = 15.8, 1.8 Hz, 1H), 5.78 (dddd, *J* = 16.8, 9.5, 7.0, 7.0 Hz, 1H), 5.18 – 5.14 (m, 2H), 4.37 – 4.32 (m, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.42 – 2.38 (m, 1H), 2.37 (d, *J* = 1.5 Hz, 1H), 2.30 (ddd, *J* = 14.7, 7.0, 7.0 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 2H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 166.7, 149.4, 133.3, 120.7, 119.3, 70.0, 60.7, 41.2, 14.4; IR (thin film) 3445, 3079, 2984, 2936, 2908, 1716, 1657, 1442, 1395, 1370, 1306, 1277, 1178, 1094, 1042, 987, 921, 869 $cm^{-1}$; Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.29; H, 8.41. Assay of enantiomeric excess: HPLC (Chiralcel OD-H 25 cm column, 10% *i*PrOH/hexanes; 0.5 mL/min); $t_r$ (major) = 12.32 min, $t_r$ (minor) = 13.96 min; 99% ee.

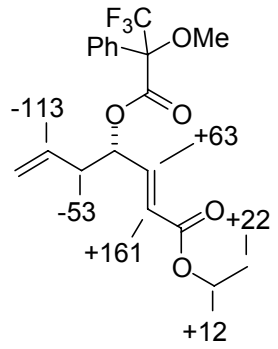


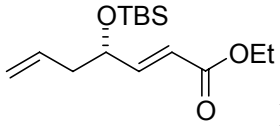

**Preparation of (*E*)-(*S*)-4-((*S*)-3,3,3-trifluoro-2-methoxy-2-phenyl-propionyloxy)-hepta-2,6-dienoic acid ethyl ester (9b).** To a solution of alcohol **9a** (10.0 mg, 0.059 mmol, 1.0 equiv) and pyridine (500 μL) in a 2 mL vial, at rt, was added (*R*)-(–)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (18.6 mg, 0.074 mmol, 1.25 equiv) dropwise via syringe. The mixture was allowed to stand for 12 h, during which time a white precipitate formed. TLC analysis after 12 h indicated complete consumption of alcohol starting material. The mixture was subjected directly to flash column chromatography on a 2.0 × 6.0 cm column, collecting 4 mL fractions. The product containing fractions (3–7) were combined and concentrated under reduced pressure to give acylated product **9b** (22.7 mg, quant. yield) as colorless oil: $R_f$ = 0.35 (20% EtOAc/hexanes); $[\alpha]^{20}_D$ = - 28.0 (*c* = 0.77, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 7.53 – 7.51 (m, 2H), 7.44 – 7.39 (m, 3H), 6.87 (dd, *J* = 15.7, 5.4 Hz, 1H), 6.00 (dd, *J* = 15.7, 1.5 Hz, 1H), 5.69 (dddd, *J* = 7.7, 6.2, 5.9, 1.5 Hz, 1H), 5.62 (dddd, *J* = 17.6, 10.6, 7.0, 7.0 Hz, 1H), 5.09 – 5.05 (m, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.54 (d, *J* = 1.1 Hz, 3 H), 2.50 – 2.47 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 165.9, 165.8, 143.0, 132.1, 131.4, 129.9, 128.7, 127.6, 123.5, 123.4 (q, $J_{C\text{-}F}$ = 288 Hz), 119.8, 84.9 (q, $J_{C\text{-}F}$ = 28 Hz), 74.3, 61.0, 55.7, 38.3, 14.4; IR (thin film) 2985, 2951, 2850, 1751, 1724, 1663, 1251, 1176, 1119, 1024, 988, 927 $cm^{-1}$; HRMS (CI+) calcd for $C_{19}H_{22}F_3O_5$ (M + H) 387.2419, found 387.1422.




**Preparation of (*E*)-(*S*)-4-((*R*)-3,3,3-trifluoro-2-methoxy-2-phenyl-propionyloxy)-hepta-2,6-dienoic acid ethyl ester (9c).** To a solution of alcohol **9a** (10.0 mg, 0.059 mmol, 1.0 equiv) and pyridine (500 μL) in a 2 mL vial, at rt, was added (*S*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (18.6 mg, 0.074 mmol, 1.25 equiv) dropwise via syringe. The mixture was allowed to stand for 12 h, during which time a white precipitate formed. TLC analysis after 12 h indicated complete consumption of alcohol starting material. The mixture was subjected directly to flash column chromatography on a 2.0 × 7.0 cm column, collecting 4 mL fractions. The product containing fractions (3–7) were combined and concentrated under reduced pressure to give the acylated product **9c** (20.7 mg, 91% yield) as a colorless oil: $R_f$ = 0.35 (20% EtOAc/hexanes); $[\alpha]^{20}_D$ = - 28.6 (*c* = 1.03, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 7.55 – 7.52 (m, 2H), 7.45 – 7.39 (m, 3H), 6.80 (dd, *J* = 15.7, 5.5 Hz, 1H), 5.84 (dd, *J* = 15.7, 1.5 Hz, 1H), 5.74 (dddd, *J* = 17.2, 9.9, 7.3, 7.3 Hz, 1H), 5.69 (dddd, *J* = 8.1, 6.6, 5.5, 1.5 Hz, 1H), 5.18 – 5.14 (m, 2H), 4.19 (q, *J* = 7.3 Hz, 2H), 3.57 (d, *J* = 1.5 Hz, 3 H), 2.55 – 2.52 (m, 2H), 1.29 (t, *J* = 7.3 Hz, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 165.9, 165.8, 143.0, 132.2, 131.8, 129.9, 128.7, 127.5, 123.5 (q, $J_{C-F}$ = 289 Hz), 123.1, 119.8, 84.8 (q, $J_{C-F}$ = 28 Hz), 74.3, 60.9, 55.9, 38.3, 14.4; IR (thin film) 2985, 1752, 1724, 1663, 1452, 1370, 1270, 1177, 1122, 1022, 988 $cm^{-1}$; HRMS (CI+) calcd for $C_{19}H_{22}F_3O_5$ (M + H) 387.2419, found 387.1424.

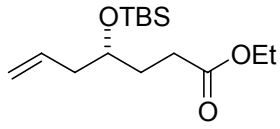
**Stereochemical proof of the homoallylic alcohol.** The observed chemical shift differences (Δδ(**9b**-**9c**), ppb) indicated are all consistent for a hydroxyl stereocenter of the (*S*) configuration. This is the expected result for a CAA reaction using (*S*)-BINOL with substrate **2.211**.



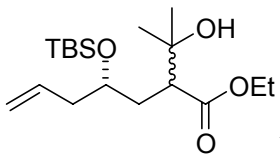

**Preparation of (*E*)-(*S*)-4-(*tert*-butyl-dimethyl-silanyloxy)-hepta-2,6-dienoic acid ethyl ester (10).** To a stirring solution of alcohol **9a** (11.63 g, 68.15 mmol, 1.0 equiv), triethylamine (41.5 g, 410.0 mmol, 6.0 equiv), and DMF (682 mL) in a 1 L round bottom flask under an atmosphere of $N_2$, at 0 °C, was added *tert*-butyl(chloro)dimethylsilane (12.35 g, 82.0 mmol, 1.2 equiv) dropwise via syringe. After 24 h at rt TLC analysis shows complete consumption of alcohol starting material. The reaction was quenched by transfer directly into a 2 L Erlenmeyer flask that contained a stirring mixture of 10% EtOAc/hexanes (400 mL) and $H_2O$ (100 mL). The layers were separated. The organic layer was washed with brine (2 × 100 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a pale yellow oil. Purification was accomplished by flash column chromatography on a 7.3 × 26 cm column, eluting with 5% EtOAc/hexanes, collecting 25 mL fractions. The product containing fractions

(35–67) were combined and concentrated under reduced pressure to give protected alcohol **10** (18.53 g, 96% yield) as a colorless oil: $R_f$ = 0.75 (3% EtOAc/hexanes); $[\alpha]^{20}_D$ = + 4.3 (*c* = 0.10, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 6.93 (dd, *J* = 15.4, 4.6 Hz, 1 H), 5.99 (dd, *J* = 15.4, 1.8 Hz, 1 H), 5.78 (dddd, *J* = 16.5, 9.5, 7.0, 7.0 Hz, 1H), 5.10 – 5.06 (m, 2H), 4.35 (dddd, *J* = 8.1, 6.2, 1.8, 1.8 Hz, 1 H), 4.25 – 4.15 (m, 2H), 2.33 – 2.30 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 0.92 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 166.9, 150.5, 133.9, 120.3, 118.1, 71.6, 60.5, 42.2, 26.0, 18.4, 14.5, -4.4, -4.6; IR (thin film) 3079, 2935, 2859, 1724, 1659, 1468, 1366, 1261, 1167, 1095, 1045, 975, 914, 837 $cm^{-1}$; Anal. Calcd for $C_{15}H_{28}O_3Si$: C, 63.33; H, 9.92. Found: C, 63.31; H, 9.92.




**Preparation of (*R*)-4-(*tert*-butyl-dimethyl-silanyloxy)-hepta-6-enoic acid ethyl ester (10a).** To a stirring suspension of CuBr (804 mg, 5.60 mmol, 8.0 equiv) and THF (9.0 mL) in a 25 mL round bottom flask under an atmosphere of $N_2$, at -5 °C, was added a 3.28 M solution of sodium bis(2-methoxyethoxy) aluminum hydride (1.71 mL, 5.60 mmol, 8.0 equiv), Red-Al®, dropwise via syringe. The reaction mixture was stirred at -5 °C for 30 min then cooled to -78 °C. After 10 min, 2-butanol (935 mg, 12.6 mmol, 18.0 equiv) was added to the reaction mixture drowise via syringe. After 10 min, α,β-unsaturated ester **10** (200 mg, 0.70 mmol, 1 equiv) in THF (1.3 mL) was added dropwise via cannula to the stirring suspension. An additional THF (1.3 mL) rinse was used to transfer remaining ester residue into the reaction flask via cannula. The reaction was stirred for 10 min at -78 °C, and then was warmed to -20 °C. TLC analysis after 2h indicated complete consumption of unsaturated starting material (as evidenced by lack of UV detection). The reaction was quenched by addition of ice to the stirring mixture then

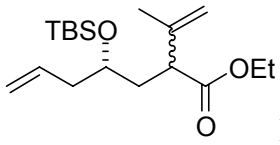
directly transferred into a 125 mL Erlenmeyer flask that contained a vigorously stirring mixture of 10% EtOAc (50 mL) and saturated aqueous $NH_4Cl$ solution (20 mL). The layers were separated and the aqueous phase was extracted with 10% EtOAc/hexanes (2 × 10 mL). The combined organic layers were washed with a saturated aqueous $NaHCO_3$ solution (2 × 10 mL), brine (2 × 10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give the crude product as a pale yellow oil. Purification was accomplished by flash column chromatography on a 2.5 × 10 cm column, eluting with 10% EtOAc/hexanes, collecting 8 mL fractions. The product containing fractions (7–15) were combined and concentrated under reduced pressure to give saturated ester **10a** (187 mg, 93% yield) as a colorless oil: $R_f$ = 0.55 (15% EtOAc/hexanes); $[\alpha]^{20}_D$ = + 25.4 (*c* = 1.04, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 5.79 (dddd, *J* = 17.6, 10.3, 7.0, 7.0 Hz, 1H), 5.07 – 5.06 (m, 1H), 5.03 – 5.02 (m, 1H), 4.12 (q, *J* = 7.3 Hz, 2H), 3.75 (dddd, *J* = 11.7, 7.3, 5.9, 4.4 Hz, 1H), 2.41 – 2.30 (m, 2H), 2.23 – 2.20 (m, 2H), 1.81 (dddd, *J* = 13.9, 8.8, 7.3, 6.4 Hz, 1H), 1.69 (dddd, *J* = 13.9, 8.8, 7.3, 6.4 Hz, 1H), 1.25 (t, *J* = 7.3 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 174.0, 134.9, 117.3, 71.0, 60.4, 42.0, 31.7, 30.2, 26.0, 18.3, 14.4, -4.2, -4.5; IR (thin film) 3078, 2934, 2859, 1738, 1467, 1369, 1255, 1172, 1089, 914, 837 $cm^{-1}$; Anal. Calcd for $C_{15}H_{30}O_3Si$: C, 62.89; H, 10.55. Found: C, 63.19; H, 10.63.




**Preparation of (*R*)-4-(*tert*-butyl-dimethyl-silanyloxy)-2-(1-hydroxy-methyl-ethyl)-hexanoic acid ethyl ester (11).** To a cooled (0 °C) stirring solution of diisopropylamine (2.46 g, 24.4 mmol, 1.4 equiv) and THF (80 mL) in a flame-

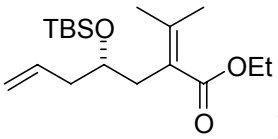
dried 250 mL round bottom flask under an atmosphere of $N_2$, at rt, was added a 2.5 M solution of *n*-BuLi (8.70 mL, 21.8 mmol, 1.25 equiv) in hexanes, dropwise via syringe. The resulting yellow solution was stirred for 30 min at 0 °C and then cooled to -78 °C. A solution of ester **10a** (5.00 g, 17.4 mmol, 1.0 equiv) and THF (3 mL), in a 25 mL pear-shaped flask, was added dropwise via cannula to the reaction mixture. Additional THF (3 × 1 mL) rinses were used to transfer the remaining ester residue from the substrate flask to the reaction flask, via cannula. After 1h, acetone (1.52 g, 26.1 mmol, 1.5 equiv), extra dry (<50 ppm $H_2O$ at time of bottling) from Aldrich, was added slowly down the inside of the flask to the stirring solution. The reaction was allowed to proceed for 2 h, at -78 °C, after which time TLC analysis indicated complete consumption of ester starting material. The reaction was quenched by transfer into a 250 mL Erlenmeyer flask containing a stirring solution of pH 7.0 phosphate buffer (50 mL). After THF was removed under reduced pressure, the resulting slurry was diluted with 10% EtOAc/hexanes (200 mL) and the layers were separated. The aqueous phase was extracted with 10% EtOAc/hexanes (3 × 30 mL). The combined organic layers were washed with brine (3 × 25 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give the crude product as a yellow oil. Purification was accomplished by flash column chromatography on a 4.5 × 25 cm column, eluting with 10% EtOAc/hexanes (1 L) and 15% EtOAc/hexanes (1 L), collecting 8 mL fractions. The product containing fractions (159–269) were combined and concentrated under reduced pressure to give tertiary alcohol **11** (5.24 g, 91% yield) as a colorless oil, and a 2.9 to 1 inseparable mixture of diastereomers: $R_f$ = 0.56 (30% EtOAc/hexanes); $[\alpha]^{20}_D$ = + 25.4 (*c* = 1.04, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) major isomer: δ 5.85 – 5.70 (m, 1

H), 5.05 – 5.02 (m, 2H), 4.23 – 4.11 (m, 2H), 3.70 – 3.61 (m, 1H), 2.89 (s, 1H), 2.43 (dd, $J$ = 10.3, 3.7 Hz, 1H), 1.93 – 1.78 (m, 2H), 1.30 (t, $J$ = 7.0 Hz, 3H), 1.22 (s, 3H), 1.19 (s, 3H), 0.87 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H): minor isomer: δ 5.85 – 5.70 (m, 1 H), 5.05 – 5.02 (m, 2H), 4.23 – 4.11 (m, 2H), 3.70 – 3.61 (m, 1H), 2.75 (s, 1H), 2.60 (dd, $J$ = 11.4, 2.2 Hz, 1H), 1.93 – 1.78 (m, 1H), 1.64 (ddd, $J$ = 13.9, 9.2, 2.2 Hz, 1H), 1.30 (t, $J$ = 7.0 Hz, 3H), 1.22 (s, 3H), 1.19 (s, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) major isomer: δ 175.8, 134.9, 117.4, 71.3, 70.8, 60.7, 51.9, 40.7, 34.8, 28.9, 26.0, 18.2, 14.4, -4.4, -4.5: minor isomer: δ 176.0, 134.3, 117.6, 71.6, 70.4, 60.6, 52.1, 42.7, 35.1, 29.2, 26.1, 18.3, 14.4, -3.9, -4.7; IR (thin film) 3500, 3077, 2934, 2859, 1729, 1642, 1468, 1376, 1254, 1181, 1092, 1004, 914, 836 cm$^{-1}$; Anal. Calcd for $C_{15}H_{30}O_3Si$: C, 62.74; H, 10.53. Found: C, 62.71; H, 10.69.



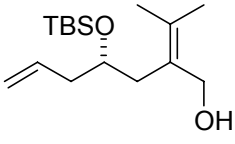

**Preparation of (*S*)-4-(*tert*-butyl-dimethyl-silanyloxy)-2-isoprop-enyl-hept-6-enoic acid ethyl ester (11a).** To a stirring solution of alcohol **11** (1.00 g, 2.90 mmol, 1.0 equiv) and pyridine (9 mL) in a 15 mL round bottom flask under an atmosphere of $N_2$, at -10 °C, was added thionyl chloride (690 mg, 5.80 mmol, 2.0 equiv) dropwise via syringe. The reaction was allowed to proceed for 1 h at -10 °C, after which time TLC analysis indicated complete consumption of starting material. The reaction was quenched by transfer into a 250 mL separatory funnel that contained a mixture of a saturated aqueous $NaHCO_3$ solution (50 mL) and $Et_2O$ (100 mL). The mixture was agitated and the layers were separated. The aqueous layer was extracted with $Et_2O$ (2 × 50 mL). The combined organic phases were washed with brine (2 × 25 mL), dried over

$MgSO_4$, filtered, and concentrated under reduced pressure. Purification was accomplished by flash column chromatography on a 3.5 × 21 cm column, eluting with 5% EtOAc/hexanes, collecting 8 mL fractions. The product containing fractions (23–55) were combined and concentrated under reduced pressure to give alkene **11a** (5.24 g, 91% yield) as a 2.6 to 1 inseparable mixture of diastereomers, along with 6% of the α,β-unsaturated ester isomer, taken on as a colorless oil: $R_f$ = 0.55 (10% EtOAc/hexanes); $[\alpha]^{20}_D$ = + 29.5 (*c* = 0.51, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 5.85 – 5.70 (m, 1 H), 5.07 – 5.02 (m, 2H), 4.91 – 4.84 (m, 2H), 4.13 (t, *J* = 7.0 Hz, 2H), 3.72 – 3.64 (m, 1H), 3.18 (t, *J* = 7.3 Hz, 1H), 2.27 – 2.17 (m, 2H), 1.96 – 1.90 (m, 1H), 1.78 – 1.74 (m, 1.73 (s, 3H), 1.24 (t, *J* = 7.0 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 3H), 0.05 (s, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) major isomer: δ 173.9, 142.5, 135.7, 117.4, 114.1, 69.9, 60.7, 49.3, 42.0, 37.0, 26.1, 20.5, 18.2, 14.3, -4.0, -4.3: minor isomer: δ 173.7, 143.6, 135.6, 117.3, 113.1, 70.0, 60.6, 49.2, 42.5, 37.9, 26.0, 21.0, 18.2, 14.3, -4.0, -4.7; IR (thin film) 3079, 2933, 2859, 1735, 1645, 1466, 1370, 1254, 1163, 1466, 1370, 1254, 1163, 1093, 912, 835 $cm^{-1}$; Anal. Calcd for $C_{18}H_{34}O_3Si$: C, 66.21; H, 10.41. Found: C, 65.92; H, 10.53.



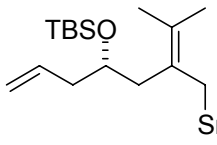

**Preparation of (*S*)-4-(*tert*-butyl-dimethyl-silanyloxy)-2-isopropylidene-hept-6-enoic acid ethyl ester (12).** A flame-dried 15 mL round bottom flask was charged with potassium *tert*-butoxide (73.0 mg, 0.612 mmol, 1.0 equiv), a magnetic stir bar, and then was purged with Ar for 15 min. THF (5 mL), drawn from a 50 mL round bottom flask that was purged with Ar for 30 min, was added to the reaction flask via Gastight® syringe. After cooling the mixture to 0 °C, alkene **11a** (200.0 mg, 0.612 mmol, 1.0 equiv) in Ar purged THF (750 μL) was added to the reaction mixture via

cannula. An Ar purged THF (250 μL) rinse was used to transfer remaining alkene residue into the reaction flask via cannula. The reaction was allowed to proceed for 2 h at 0 °C and then quenched by transfer into a 125 mL Erlenmeyer flask that contained a stirring mixture of a saturated aqueous $NH_4Cl$ solution (10 mL) and $Et_2O$ (50 mL). The layers were separated. The organic phase was washed with brine (2 × 10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give ester **12** (195 mg, 98% yield) as a 99 to 1 ratio of conjugated ester to starting material, which was carried on to the next reaction without further purification as a colorless oil: $R_f$ = 0.47 (15% EtOAc/hexanes); $[\alpha]^{20}_D$ = + 10.6 (*c* = 0.70, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 5.84 (dddd, *J* = 18.3, 9.5, 7.3, 7.3 Hz, 1H), 5.06 – 5.03 (m, 2H), 4.24 – 4.15 (m, 2H), 3.84 – 3.79 (m, 1H), 2.52 (dd, *J* = 13.9, 7.5 Hz, 1H), 2.46 (dd, *J* = 13.9, 5.5 Hz, 1H), 2.27 – 2.22 (m, 1H), 2.21 – 2.15 (m, 1H), 1.99 (s, 3 H), 1.84 (s, 3H), 1.30 (t, *J* = 7.3 Hz, 3H), 0.87 (s, 9H), 0.02 (s, 3H), -0.02 (s, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 169.8, 145.0, 135.3, 125.2, 117.1, 71.7, 60.1, 42.3, 37.5, 26.0, 23.4, 18.2, 14.5, -4.5, -4.6; IR (thin film) 2933, 2859, 2361, 1715, 1641, 1466, 1369, 1254, 1191, 1091, 913, 835 $cm^{-1}$; Anal. Calcd for $C_{18}H_{34}O_3Si$: C, 66.21; H, 10.49. Found: C, 66.33; H, 10.61.




**Preparation of (*S*)-4-(*tert*-butyl-dimethyl-silanyloxy)-2-isopropyl-idene-hept-6-en-1-ol (12a).** To a stirring solution of α,β-unsaturated ester **12** (2.67 g, 8.17 mmol, 1.0 equiv) and $CH_2Cl_2$ (82 mL) in a 250 mL round bottom flask under an atmosphere of Ar, at 0 °C, was added a 1.5 M solution of diisobutylaluminum hydride (16.35 mL, 24.53 mmol, 3.0 equiv) in toluene, dropwise via syringe. The reaction was allowed to proceed for 1 h, after which time TLC analysis indicated complete

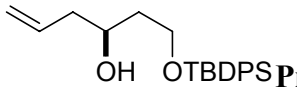
consumption of starting material. The reaction was quenched by transfer into a 1 L Erlenmeyer flask that contained a vigorously stirring mixture of $CH_2Cl_2$ (200 mL) and saturated aqueous potassium sodium tartrate solution (200 mL). The mixture was allowed to stir for 12 h and then the layers were separated. The aqueous phase was extracted with $CH_2Cl_2$ (3 × 50 mL). The combined organic layers were washed with brine (2 × 100 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification was accomplished by column chromatography on a 5.1 × 25 cm column, eluting with 10% EtOAc, collecting 8 mL fractions. The product containing fractions (39–81) were combined and concentrated under reduced pressure to give allylic alcohol **12a** (2.19 g, 94% yield) as a pale yellow oil: $R_f$ = 0.50 (30% EtOAc/hexanes); $[\alpha]^{20}_D$ = + 32.4 (*c* = 1.0, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 5.83 (dddd, *J* = 16.5, 11.0, 7.3, 7.3 Hz, 1H), 5.09 – 5.06 (m, 2H), 4.17 (dd, *J* = 12.1, 4.0 Hz, 1H), 4.06 (dd, *J* = 12.1, 7.3 Hz, 1H), 3.87 (m, 1H), 2.85 (dd, *J* = 7.3, 4.0 Hz, 1H), 2.39 – 2.38 (m, 2H), 2.31 – 2.22 (m, 2H), 1.73 (s, 3 H), 1.69 (m, 3H), 0.90 (s, 9H), 0.08 (s, 3H), 0.03 (s, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 135.0, 130.7, 129.6, 117.5, 72.5, 63.2, 42.3, 37.4, 26.0, 21.2, 20.2, 18.2, -4.5, -4.5; IR (thin film) 3380, 3077, 2932, 2859, 1642, 1467, 1368, 1254, 1059, 1001, 914, 835 cm$^{-1}$; Anal. Calcd for $C_{16}H_{32}O_2Si$: C, 67.54; H, 11.34. Found: C, 67.74; H, 11.50.




**Preparation of ((*S*)-1-allyl-4-methyl-3-tributylstannanylmethyl-pent-3-enyloxy)-*tert*-butyl-dimethyl-silane (6).** To a stirring solution of allylic alcohol **12a** (526 mg, 1.85 mmol, 1.0 equiv) and THF (11 mL) in a flame-dried 50 mL round bottom flask under an atmosphere of Ar, at -78 °C, was added a 2.5 M solution of *n*-BuLi

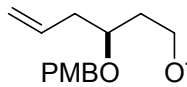
(806 μL, 1.85 mmol, 1.0 equiv) in hexanes dropwise via syringe. The resulting yellow solution was stirred for 15 min at -78 °C. Simultaneously, to a stirring solution of diisopropylamine (206 mg, 2.03 mmol, 1.1 equiv) and THF (4 mL) in a 10 mL round bottom flask under an atmosphere of Ar, at 0 °C, was added a 2.5 M solution of *n*-BuLi (776 μL, 1.94 mmol, 1.05 equiv) in hexanes dropwise via syringe. After 10 min, freshly prepared tributyltin hydride (497 μL, 1.85 mmol, 1.0 equiv) was added via syringe to the freshly prepared LDA solution. After 15 min, methanesulfonyl chloride (212 mg, 1.85 mmol, 1.0 equiv) was added to the lithium alkoxide solution at -78 °C. After 35 min, the $Bu_3SnLi$ solution was added dropwise to the reaction flask via cannula. An additional THF (1 mL) rinse was used to transfer $Bu_3SnLi$ residue from flask into reaction mixture via cannula. The reaction was allowed to proceed for 2 h at -78 °C, then for an additional 10 h during which time the -78 °C bath was allowed to expire to reach rt. The reaction mixture was concentrated, diluted with 10% EtOAc/hexanes (100 mL), washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification was accomplished by flash column chromatography on a 4.5 × 15 cm column, eluting with hexanes, collecting 8 mL fractions. The product containing fractions (28–50) were combined and concentrated under reduced pressure to give allyl stannane **6** (601 mg, 58% yield) as a colorless oil: $R_f$ = 0.55 (hexanes); $[\alpha]^{20}_D$ = + 2.6 (*c* = 0.11, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 5.83 (dddd, *J* = 17.5, 10.6, 7.3, 7.3 Hz, 1H), 5.08 – 5.03 (m, 2H), 3.85 – 3.80 (m, 1H), 2.29 – 2.15 (m, 2H), 2.13 (dd, *J* = 13.2, 7.7 Hz, 1H), 2.03 (dd, *J* = 13.2, 5.5 Hz, 1H), 1.68 (app d, *J* = 11.9 Hz, flanked by Sn satellites, 1H), 1.69 – 1.64 (m, 4H), 1.59 (app s, flanked by Sn satellites, 1H), 1.50 – 1.44 (m, 6H), 1.30 (sextet, *J* = 7.3 Hz, 6 H), 0.90 (t, *J* = 7.3 Hz, 9H), 0.89 (s, 9H), 0.84 – 0.80 (m, 6H),

0.03 (s, 3H), 0.00 (s, 3H); 125 MHz $^{13}C$ NMR ($CDCl_3$) δ 136.0, 129.2 (flanked by Sn satellites, $J_{C\text{-}Sn}$ = 24 Hz), 120.7 (flanked by Sn satellites, $J_{C\text{-}Sn}$ = 22 Hz), 116.8, 72.0 (s, flanked by Sn satellites), 42.7, 42.0, 29.4 (flanked by Sn satellites, $J_{C\text{-}Sn}$ = 10 Hz), 27.7 (flanked by Sn satellites, $J_{C\text{-}Sn}$ = 27 Hz), 26.2, 21.2 (flanked by Sn satellites, $J_{C\text{-}Sn}$ = 6 Hz), 20.9 (flanked by Sn satellites, $J_{C\text{-}Sn}$ = 6 Hz), 18.3, 17.4, 13.9, 10.8 (flanked by Sn satellite doublets, $J_{C\text{-}Sn}$ = 7 Hz), -4.3, -4.4; IR (thin film) 3077, 2956, 2926, 2857, 1463, 1253, 1073, 1002, 957, 912, 834 $cm^{-1}$; Anal. Calcd for $C_{28}H_{58}OSiSn$: C, 60.32; H, 10.49. Found: C, 59.99; H, 10.56.



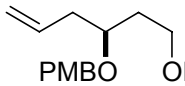

**Preparation of (3*S*)-1-(*tert*-butyl-diphenyl-silanyloxy)-hex-5-en-3-ol (14).**[1] A 250 mL round bottom flask was charged with a magnetic stir bar, oven dried 4 Å molecular sieves (15.0 g), and $CH_2Cl_2$ (80 mL). To the stirring solution, under an atmosphere of $N_2$, was added (*S*)-BINOL (1.44 g, 5.03 mmol, 0.2 equiv) in one portion, a 1.0 M solution of Ti(O*i*Pr)$_4$ (2.52 mL, 2.52 mmol, 0.1 equiv) in $CH_2Cl_2$ via syringe, and a freshly prepared 1.0 M solution of TFA (0.352 mL, 0.176 mmol, 0.007 equiv) in $CH_2Cl_2$. The reaction mixture was heated at reflux (~38 °C) for a period of 1 h, and then allowed to cool to rt. Aldehyde **13**[2] (7.86 g, 25.15 mmol, 1.0 equiv), in $CH_2Cl_2$ (10 mL), was added to the reaction flask via cannula. An additional $CH_2Cl_2$ (6 mL) rinse was used to transfer the remaining aldehyde residue into the reaction flask via cannula. After the mixture was stirred for 0.5 h at rt and cooled to -78 °C, allyltributyltin (12.49 g, 37.73 mmol, 1.3 equiv) was added, dropwise via syringe, to the stirring mixture down the inside of the reaction flask. The reaction mixture was stirred for an additional 10 min at -78 °C then transferred to a -20 °C freezer where it was briefly manually agitated every 24

h. After 4 days, the reaction mixture was filtered over a pad of Celite® into a 500 mL Erlenmeyer flask that contained a stirring saturated aqueous $NaHCO_3$ solution (100 mL). An additional portion of $CH_2Cl_2$ (200 mL) was used to dilute the slurry and the resulting mixture was stirred for 1 h, then the layers were separated. The aqueous layer was extracted with $CH_2Cl_2$ (2 × 50 mL). The combined organic phases were washed with brine (4 × 50 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give the crude product as a red oil. Purification was accomplished by flash column chromatography on a 7.0 × 40 cm column, eluting with 5% acetone/hexanes, collecting 25 mL fractions. The product containing fractions (77–99) were combined and concentrated under reduced pressure to give homoallyic alcohol **14** (7.73 g, 90% yield) as colorless oil: $R_f$ = 0.48 (30% EtOAc/hexanes); $[\alpha]^{20}_D$ = - 5.3 (*c* = 1.03, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 7.72 – 7.69 (m, 4H), 7.48 – 7.40 (m, 6H), 5.87 (dddd, *J* = 17.6, 10.3, 7.3, 7.3 Hz, 1H), 5.16 – 5.10 (m, 2H), 4.02 – 3.96 (m, 1H), 3.93 – 3.84 (m, 2H), 3.23 (d, *J* = 2.6 Hz, 1H), 2.34 – 2.25 (m, 2H), 1.79 – 1.68 (m, 2H), 1.08 (s, 9H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 135.8, 135.8, 135.2, 133.3, 133.2, 130.0, 130.0, 128.0, 117.6, 71.1, 63.5, 42.2, 38.1, 27.0, 19.2; IR (thin film) 3449, 3072, 2934, 2860, 1642, 1470, 1428, 1391, 1109, 1001, 916, 823 cm $^{-1}$; Anal. Calcd for $C_{22}H_{30}O_2Si$: C, 74.53; H, 8.53. Found: C, 74.42; H, 8.60. Assay of enantiomeric excess: HPLC (Chiralcel OD-H 25 cm column, 2.5% *i*PrOH/hexanes; 0.5 mL/min); $t_r$ (major) = 8.13 min, $t_r$ (minor) = 8.92 min; 93% ee.



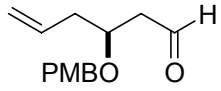

**Preparation of *tert*-butyl-[(3*S*)-(4-methoxy-benzyloxy)-hex-5-enyl-oxy]-diphenylsilane (15).** To a stirring solution of alcohol **14** (671 mg, 1.97 mmol**,** 1.0 equiv), freshly prepared 4-methoxybenzyl trichloroacetimidate (832 mg, 2.96 mmol,

1.5 equiv), and $CH_2Cl_2$ (4 mL) in a 15 mL round bottom flask, under an atmosphere of $N_2$, was added (±)-camphor-10-sulfonic acid (46.0 mg, 0.197 mmol, 0.1 equiv) in one portion. The reaction was allowed to proceed for 12 h at rt, after which time TLC analysis indicated essentially complete consumption of starting material. The reaction mixture was concentrated under reduced pressure, diluted with 20% EtOAc/hexanes (100 mL), filtered over a pad of Celite®, and concentrated under reduced pressure to give a red slurry. Purification was accomplished by flash column chromatography, eluting with 5% EtOAc/hexanes, collecting 8 mL fractions. The product containing fractions were combined and concentrated under reduced pressure to give PMB ether **15** (712 mg, 76% yield) as colorless oil: $R_f$ = 0.49 (20% EtOAc/hexanes); $[\alpha]^{20}_D$ = + 10.6 (*c* = 0.68, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 7.73 – 7.70 (m, 4H), 7.48 – 7.40 (m, 6H), 7.26 – 7.23 (m, 2H), 6.89 – 6.86 (m, 2H), 5.89 (dddd, *J* = 17.2, 10.3, 7.0, 7.0 Hz, 1H), 5.14 – 5.10 (m, 2H), 4.48 (ABq, *J* = 11.0 Hz, Δν = 55.7 Hz, 2H), 3.91 – 3.84 (m, 1H), 3.83 (s, 3H), 3.81 – 3.74 (m, 2H), 2.37 (t, *J* = 7.0 Hz, 2H), 1.87 – 1.77 (m, 2H), 1.10 (s, 9H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 159.3, 135.8, 135.1, 134.1, 134.1, 131.2, 129.8, 129.5, 127.8, 117.1, 113.9, 75.3, 71.0, 60.7, 55.4, 38.7, 37.2, 27.1, 19.4; IR (thin film) 3071, 2934, 2859, 1613, 1513, 1466, 1429, 1390, 1352, 1248, 1176, 1108, 1001, 913, 822 $cm^{-1}$; Anal. Calcd for $C_{30}H_{38}O_3Si$: C, 75.90; H, 8.07. Found: C, 76.13; H, 8.20.



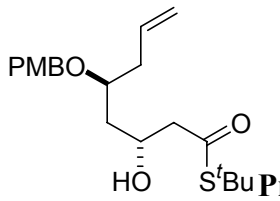

**Preparation of *tert*-butyl-[(3*S*)-(4-methoxy-benzyloxy)-hex-5-enyl-oxy]-diphenylsilane (15a).** To a stirring solution of BPS ether **15** (4.74 g, 10.0 mmol**,** 1.0 equiv) and THF (80 mL) in a 250 mL round bottom flask under an atmosphere of $N_2$, at rt, was added a 1.0 M solution of tetrabutylammonium fluoride (20.0 mL, 20.0 mmol,

2.0 equiv) in THF, dropwise via syringe. The reaction was allowed to proceed for 12 h at rt, after which time TLC analysis indicated complete consumption of starting material. The reaction mixture was then concentrated under reduced pressure. Purification was accomplished by flash column chromatography on a 4.5 × 20.0 cm column, eluting with 10% EtOAc/hexanes (500 mL), 25% EtOAc/hexanes (250 mL), and 50% EtOAc/hexanes, collecting 8 mL fractions. The product containing fractions (126–190) were combined and concentrated under reduced pressure to give primary alcohol **15** (2.23 g, 95% yield) as colorless oil: $R_f$ = 0.25 (40% EtOAc/hexanes); $[\alpha]^{20}_D$ = + 66.2 (*c* = 0.48, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 7.29 – 7.25 (m, 2H), 6.90 – 6.87 (m, 2H), 5.82 (dddd, *J* = 17.2, 10.3, 7.3, 7.3 Hz, 1 H), 5.14 – 5.09 (m, 2H), 4.59 (ABq, *J* = 11.0 Hz, Δν = 80.9 Hz, 2H), 3.80 (s, 3 H), 3.78 – 3.65 (m, 3H), 2.61 (s, 1H), 2.45 – 2.40 (m, 1H), 2.35 (ddd, *J* = 14.2, 7.0, 7.0 Hz, 1H), 1.81 – 1.71 (m, 2H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 159.4, 134.4, 130.5, 129.5, 117.6, 114.0, 77.4, 70.8, 60.6, 55.3, 38.2, 36.1; IR (thin film) 3049, 2936, 1613, 1514, 1441, 1348, 1301, 1248, 1176, 1037, 916, 821 $cm^{-1}$; Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.64. Found: C, 70.95; H, 8.64.



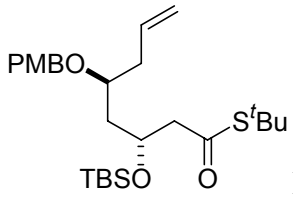

**Preparation of (*S*)-3-(4-methoxy-benzyloxy)-hex-5-enal (16).**[3] To a stirring solution of alcohol **15a** (691 mg, 2.92 mmol**,** 1.0 equiv) and $CH_2Cl_2$ (29 mL) in a 50 mL round bottom flask under an atmosphere of $N_2$, at -5 °C, was added freshly distilled *N,N*-diisopropylethylamine (2.64 g, 20.4 mmol, 7.0 equiv), dropwise via syringe. After 10 min at -5 °C, dimethyl sulfoxide (2.28 g, 29.2 mmol, 10.0 equiv) was added to the reaction mixture via syringe and the solution was allowed to stir for an additional 10 min. Sulfur trioxide pyridine complex (1.86 g, 11.7 mmol, 4.0 equiv) was then added in

one portion. The reaction was allowed to proceed for 30 min at -5 °C, after which time TLC analysis indicated complete consumption of starting material. The reaction was quenched by transfer into an 125 mL Erlenmeyer flask that contained a stirring saturated aqueous $NaHCO_3$ solution. The reaction mixture was then concentrated under reduced pressure, diluted with 20% EtOAc/hexanes (100 mL), and the layers were separated. The aqueous phase was extracted with 20% EtOAc/hexanes (4 × 10 mL). The combined organic layers were washed with brine (2 × 25 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give the crude product as a pale yellow oil. Purification was accomplished by flash column chromatography on a 2.5 × 16.0 cm column, eluting with 10% EtOAc/hexanes, collecting 8 mL fractions. The product containing fractions (26–60) were combined and concentrated under reduced pressure to give aldehyde **16** (664 mg, 97% yield) as colorless oil: $R_f$ = 0.42 (40% EtOAc/hexanes); $[\alpha]^{20}_D$ = + 39.8 (*c* = 0.61, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 9.77 (t, *J* = 1.8 Hz, 1H), 7.27 – 7.24 (m, 2H), 6.90 – 6.87 (m, 2H), 5.81 (dddd, *J* = 16.9, 9.9, 7.3, 7.3 Hz, 1 H), 5.15 – 5.14 (m, 1H), 5.12 (s, 1H), 4.51 (ABq, *J* = 11.3 Hz, Δν = 49.2 Hz, 2H), 4.05 – 4.01 (m, 1H), 3.81 (s, 3 H), 2.67 (ddd, *J* = 16.7, 7.7, 2.6 Hz, 1H), 2.56 (ddd, *J* = 16.7, 4.4, 1.8 Hz, 1H), 2.47 – 2.42 (m, 1H), 2.40 – 2.35 (m, 1H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 201.7, 159.5, 133.8, 130.3, 129.6, 118.5, 114.0, 73.5, 71.1, 55.5, 48.2, 38.5; IR (thin film) 3075, 2839, 2729, 1725, 1613, 1514, 1463, 1348, 1301, 1248, 1176, 1081, 920, 823 $cm^{-1}$; Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.51; H, 7.81.



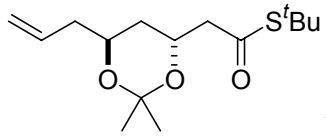

**Preparation of (3*R*, 5*S*)-3-hydroxy-5-(4-methoxy-benzyloxy)-oct-7-enethioic acid *S-tert*-butyl ester (17).** To a stirring solution of aldehyde **16** (1.43 g, 6.10 mmol, 1.0 equiv) and toluene (40 mL) in a 100 mL round bottom flask under an atmosphere of Ar, at -78 °C, was added a freshly prepared 1.0 M solution of $TiCl_2(O\textit{i}Pr)_2$ (15.25 mL, 15.25 mmol, 2.5 equiv) dropwise via syringe. The resulting bright yellow solution was allowed to stir for 15 min, followed by dropwise addition of thioketene acetal **8** (3.24 g, 15.86 mmol, 2.6 equiv), in toluene (4 mL), down the inside of the reaction flask over a 5 min period. An additional toluene (1 mL) rinse was used to transfer the remaining thioketene acetal residue from the syringe into the reaction flask. TLC analysis after 4 h, at -78 °C, indicated complete consumption of the aldehyde starting material. The reaction was quenched by transfer directly into a 500 mL Erlenmeyer flask that contained a vigorously stirring mixture of $CH_2Cl_2$ (240 mL) and pH 7.0 phosphate buffer (50 mL). The layers were separated and the aqueous phase was extracted with $CH_2Cl_2$ (3 × 20 mL). The combined organic layers were washed with a saturated aqueous $NH_4Cl$ solution (2 × 50 mL), brine (2 × 50 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a pale yellow oil. Purification was accomplished by flash column chromatography on a 5.1 × 22.0 cm column, eluting with 10% EtOAc/hexanes (500 mL), 20% EtOAc/hexanes (250 mL), and 30% EtOAc/hexanes (250 mL), collecting 8 mL fractions. The product containing fractions (80–110) were combined and concentrated under reduced pressure to give β-hydroxy thiol ester **17** (2.11 g, 95% yield) as colorless oil: $R_f$ = 0.45 (30% EtOAc/hexanes);

$[\alpha]^{20}_{D}$ = + 23.5 (*c* = 0.30, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 7.29 – 7.26 (m, 2H), 6.90 – 6.87 (m, 2H), 5.81 (dddd, *J* = 17.6, 10.3, 7.3, 7.3 Hz, 1 H), 5.13 – 5.07 (m, 2H), 4.51 (ABq, *J* = 11.0 Hz, Δν = 70.6 Hz, 2H), 4.33 – 4.27 (m, 1H), 3.81 (s, 3 H), 3.79 – 3.76 (m, 1H), 3.19 (d, *J* = 4.0 Hz, 1H), 2.64 – 2.57 (m, 2H), 2.45 – 2.40 (m, 1H), 2.34 (ddd, *J* = 14.0, 7.0, 7.0 Hz, 1H), 1.68 – 1.57 (m, 2H), 1.47 (s, 9H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 200.2, 159.5, 134.5, 130.6, 129.8, 117.8, 114.1, 75.5, 71.3, 66.0, 55.5, 51.5, 48.6, 40.2, 38.4, 30.0; IR (thin film) 3483, 2918, 1679, 1514, 1451, 1248, 1080 cm $^{-1}$; Anal. Calcd for $C_{20}H_{30}O_4S$: C, 65.54; H, 8.25. Found: C, 65.40; H, 8.43. Assay of diastereomeric ratio: HPLC (Microsorb 25 cm column, 2.5% *i*PrOH/hexanes; 0.5 mL/min); $t_r$ (major) = 10.44 min, $t_r$ (minor) = 11.54 min; 41:1.




**Preparation of (3*R*, 5*S*)-3-(*tert*-butyl-dimethyl-silanyloxy)-5-(4-methoxy-benzyloxy)-oct-7-enethioic acid *S*-*tert*-butyl ester (17a).** To a stirring solution of a β-hydroxy thiol ester **17** (857 mg, 2.33 mmol**,** 1.0 equiv) and $CH_2Cl_2$ (23 mL) in a 50 mL round bottom flask under an atmosphere of $N_2$, at -78 °C, was added 2,6-lutidine (902 mg, 8.41 mmol, 3.0 equiv) via syringe. The solution was cooled to -78 °C and *tert*-butyldimethylsilyl trifluoromethanesulfonate (742 mg, 2.81 mmol, 1.2 equiv) was added dropwise via syringe. The reaction was allowed to proceed for 30 min, after which time TLC analysis indicated complete consumption of alcohol starting material. The reaction was quenched by transfer into a 125 mL Erlenmeyer flask containing a stirring solution of $CH_2Cl_2$ (50 mL) and pH 7.0 phosphate buffer (10 mL). The phases were separated and the aqueous layer was extracted with $CH_2Cl_2$ (2 × 10 mL). The

combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give the crude product as an opaque oil. Purification was accomplished by flash column chromatography on a 4.5 × 16.0 cm column, eluting with 5% EtOAc/hexanes, collecting 8 mL fractions. The product containing fractions (28–40) were combined and concentrated under reduced pressure to give silyl ether **17a** (1.05 g, 94% yield) as a colorless oil: $R_f$ = 0.65 (30% EtOAc/hexanes); $[\alpha]^{20}_D$ = - 1.8 (*c* = 0.90, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 7.29 – 7.26 (m, 2 H), 6.90 – 6.87 (m, 2H), 5.83 (dddd, *J* = 17.2, 9.9, 7.0, 7.0 Hz, 1 H), 5.14 – 5.08 (m, 2H), 4.46 (ABq, *J* = 11.0 Hz, Δν = 71.7 Hz, 2H), 4.31 (tt, *J* = 6.6, 5.5 Hz, 1H), 3.62 – 3.57 (m, 1H), 2.65 (dd, *J* = 14.6, 6.2 Hz, 1H), 2.61 (dd, *J* = 14.6, 5.9 Hz, 1H), 2.40 – 2.30 (m, 2H), 1.76 (ddd, *J* = 14.3, 8.4, 5.1 Hz, 1H), 1.67 (ddd, *J* = 14.3, 7.3, 4.0 Hz, 1H), 1.46 (s, 9H), 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 198.2, 159.2, 134.6, 131.0, 129.3, 117.5, 113.9, 75.4, 70.1, 67.4, 55.4, 53.3, 48.2, 42.6, 38.5, 30.0, 26.1, 18.2, -4.2, -4.3; IR (thin film) 2955, 2858, 1683, 1614, 1514, 1464, 1301, 1250, 1173, 1085, 1039, 917, 833 $cm^{-1}$; Anal. Calcd for $C_{26}H_{44}O_4SSi$: C, 64.95; H, 9.22. Found: C, 64.84; H, 9.28.



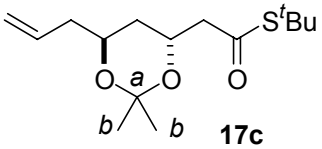

**Preparation of ((4*R*, 6*S*)-6-allyl-2,2-dimethyl-[1,3]dioxan-4-yl-thioacetic acid *S*-*tert*-butyl ester (17c).** To a stirring solution of a diprotected thiol ester **17a** (200 mg, 0.415 mmol**,** 1.0 equiv), $CH_2Cl_2$ (6.6 mL), and $H_2O$ (1.6 mL) in a 15 mL round bottom flask under an atmosphere of $N_2$, at rt, was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (142 mg, 0.623 mmol, 1.5 equiv) in one portion. The reaction was allowed to proceed for 1 h, during which time solution color changed from dark

green to orange. TLC analysis at 1 h indicated complete consumption of PMB ether starting material. The reaction mixture was diluted with 30% EtOAc/hexanes (50 mL) and filtered over a plug (3.3 × 5.0 cm) of Celite®, Florisil®, and $MgSO_4$. The filtrate was concentrated under reduced pressure to give a mixture of anisaldehyde and mono deprotected product (188 mg), which was taken on directly to the next reaction without further purification.

To a stirring solution of crude silyl ether (assumed to be 0.415 mmol, 1.0 equiv) and MeOH (4 mL) in a 15 mL round bottom flask under $N_2$, at rt, was added *p*-toluenesulfonic acid monohydrate (8.0 mg, 0.04 mmol, 0.1 equiv) in one portion. TLC analysis after 30 min shows complete consumption of TBS ether starting material. The reaction mixture was diluted with 2,2-dimethoxypropane (DMP, 4 mL) and stirred for an additional 10 min. The magnetic stir bar was extracted and the solvent was removed under reduced pressure. The concentrate was diluted with DMP (2 mL) and the mixture was again concentrated under reduced pressure. DMP (4 mL) was added to the concentrated mixture and the reaction was allowed to proceed for 15 min, after which time TLC analysis indicated complete consumption of diol. The reaction mixture was diluted with $CH_2Cl_2$ (50 mL), washed with a saturated aqueous $NaHCO_3$ solution (10 mL), brine (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give the crude product as a red oil. Purification was accomplished by flash column chromatography on a 2.5 × 10.0 cm column, eluting with 5% EtOAc/hexanes, collecting 8 mL fractions. The product containing fractions (11–15) were combined and concentrated under reduced pressure to give acetonide **17c** (39 mg, 33% yield over two steps) as a colorless oil: $R_f$ = 0.25 (5% EtOAc/hexanes); $[\alpha]^{20}_D$ = + 21.2 (*c* = 0.45,

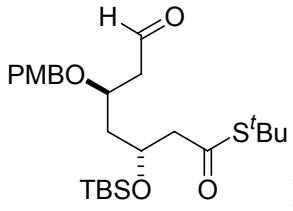
$CHCl_3$); 500 MHz $^1H$ NMR ($CDCl_3$) δ 5.79 (dddd, *J* = 17.2, 10.3, 7.0, 7.0 Hz, 1 H), 5.11 – 5.04 (m, 2H), 4.26 (dddd, *J* = 9.5, 8.1, 5.9, 5.5 Hz, 1H), 3.86 (dddd, *J* = 12.8, 8.8, 6.6, 6.2 Hz, 1H), 2.69 (dd, *J* = 14.6, 8.1 Hz, 1H), 2.54 (dd, *J* = 14.6, 5.5 Hz, 1H), 2.31 (ddd, *J* = 13.9, 7.0, 6.6 Hz, 1H), 2.20 (ddd, *J* = 14.2, 7.0, 6.2 Hz, 1H), 1.71 – 1.58 (m, 2H), 1.46 (s, 9H), 1.35 (s, 3H), 1.34 (s, 3H); 125 MHz $^{13}C$ NMR ($CDCl_3$) δ 197.7, 134.5, 117.2, 100.8, 66.2, 64.0, 50.6, 48.3, 40.2, 37.5, 30.0, 25.0, 24.8; IR (thin film) 2988, 2928, 1685, 1456, 1367, 1224, 1165, 1116, 1024, 991, 944, 914 $cm^{-1}$; HRMS (CI+) calcd for $C_{15}H_{26}O_3S$ (M + H) 287.1681, found 287.1690.

**Stereochemical proof of the Mukaiyama aldol bond construction.** The observed $^{13}C$ NMR chemical shifts of the indicated carbons are consistent for a 1,3-*anti* relative hydroxyl relationship. This is the expected result for addition of thioketene acetal **8** into aldehyde **16**.



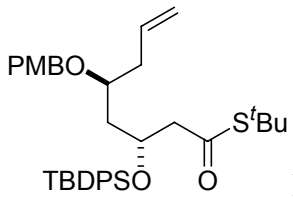

**17c**

*a* = 100.81 ppm
*b* = 24.96, 24.82 ppm



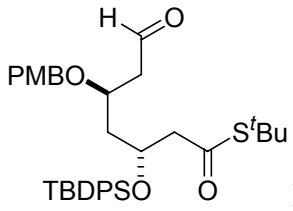

**Preparation of (3*R*, 5*S*)-3-(*tert*-butyl-dimethyl-silanyl-oxy)-5-(4-methoxy-benzyloxy)-oxo-heptanethioic acid *S*-*tert*-butyl ester (18).** To a stirring solution of alkene **17a** (30 mg, 0.063 mmol**,** 1.0 equiv) and $CH_2Cl_2$ (630 μL) in a 4 mL vial, at -78 °C, was bubbled a steady stream of ozone for 0.5 min, during which time solution color changed to grey. The solution was then purged with a steady stream of $N_2$.

Triphenylphosphine (17.3 mg, 0.065 mmol, 1.05 equiv) was added in one portion to the reaction, which was allowed to warm to rt over a period of 1 h. The reaction mixture was concentrated under reduced pressure. Purification was accomplished by flash column chromatography on a 2.5 × 10.0 cm column, eluting with 5% EtOAc/hexanes (250 mL), 10% EtOAc/hexanes (100 mL), 15% EtOAc/hexanes (100 mL), and 20% EtOAc/hexanes, collecting 4 mL fractions. The product containing fractions (41–54) were combined and concentrated under reduced pressure to give aldehyde **18** (26.5 mg, 88% yield) as a colorless oil: $R_f$ = 0.49 (30% EtOAc/hexanes); $[\alpha]^{20}_D$ = - 14.3 (*c* = 0.13, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 9.78 (t, *J* = 1.8 Hz, 1H), 7.26 – 7.23 (m, 2H), 6.89 – 6.86 (m, 2H), 4.46 (s, 2H), 4.32 – 4.27 (m, 1H), 4.09 – 4.04 (m, 1H), 3.81 (s, 3H), 2.71 – 2.64 (m, 3H), 2.60 (dd, *J* = 14.6, 6.2 Hz, 1H), 1.96 (ddd, *J* = 13.9, 7.3, 4.4 Hz, 1H), 1.70 (ddd, *J* = 13.9, 7.3, 4.8 Hz, 1H), 1.46 (s, 9H), 0.88 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 201.3, 198.0, 159.5, 130.3, 129.5, 114.1, 71.5, 70.6, 67.1, 55.5, 53.0, 48.9, 48.4, 43.0, 30.0, 26.1, 18.2, -4.2, -4.4; IR (thin film) 2956, 2931, 2858, 1725, 1681, 1587, 1514, 1461, 1364, 1302, 1251, 1174, 1097, 1037, 938, 834 $cm^{-1}$; HRMS (CI+) calcd for $C_{25}H_{42}O_5SSi$ (M + H) 483.2601, found 453.2588.




**Preparation of (3*R*, 5*S*)-3-(*tert*-butyl-diphenyl-silanyloxy)-5-(4-methoxy-benzyloxy)-oct-7-enethioic acid *S*-*tert*-butyl ester (17d).** To a stirring solution of a β-hydroxy thiol ester **17** (300 mg, 0.818 mmol**,** 1.0 equiv), imidazole (167 mg, 2.46 mmol, 3.0 equiv), and DMF (2.7 mL) in a 10 mL round bottom flask under an atmosphere of Ar, at rt, was added *tert*-butyl(chloro)diphenylsilane (270 mg, 0.982

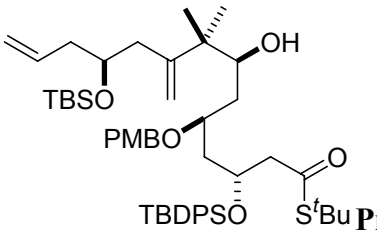
mmol, 1.2 equiv) via syringe. The reaction was allowed to proceed for 24 h, after which time TLC analysis indicated complete consumption of alcohol starting material. The reaction was quenched by transfer into a 125 mL separatory funnel and agitation with a mixture of 10% EtOAc/hexanes (75 mL) and $H_2O$ (10 mL). The phases were separated and the organic layer was washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification was accomplished by flash column chromatography on a 2.5 × 21.0 cm column, eluting with 5% EtOAc/hexanes, collecting 8 mL fractions. The product containing fractions (24–33) were combined and concentrated under reduced pressure to give silyl ether **17d** (454 mg, 92% yield) as a pale yellow oil: $R_f$ = 0.25 (5% EtOAc/hexanes); $[\alpha]^{20}_D$ = - 11.9 (*c* = 0.16, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 7.74 – 7.70 (m, 4H), 7.45 – 7.36 (m, 6H), 7.14 – 7.11 (m, 2H), 6.86 – 6.83 (m, 2H), 5.61 (dddd, *J* = 17.6, 10.6, 7.3, 7.3 Hz, 1 H), 4.99 – 4.95 (m, 2H), 4.41 (tt, *J* = 6.6, 5.9 Hz, 1H), 4.31 (d, *J* = 11.0 Hz, 1H), 4.06 (d, *J* = 11.0 Hz, 1H), 3.81 (s, 3 H), 3.38 – 3.34 (m, 1H), 2.72 (dd, *J* = 14.6, 6.2 Hz, 1H), 2.66 (dd, *J* = 14.6, 5.9 Hz, 1H), 2.14 – 2.05 (m, 2H), 1.76 (ddd, *J* = 14.3, 8.4, 5.9 Hz, 1H), 1.66 (ddd, *J* = 14.3, 6.2, 3.9 Hz, 1H), 1.44 (s, 9H), 1.05 (s, 9H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 198.0, 159.1, 136.2, 136.1, 134.6, 134.0, 131.0, 129.9, 129.8, 129.3, 127.8, 127.8, 117.3, 113.8, 75.7, 70.3, 69.2, 55.4, 53.1, 48.1, 42.4, 38.6, 30.0, 27.2, 19.6; IR (thin film) 3071, 2959, 2859, 1682, 1614, 1514, 1463, 1428, 1364, 1248, 1174, 1108, 918, 822 $cm^{-1}$; Anal. Calcd for $C_{36}H_{48}O_4SSi$: C, 71.48; H, 8.00. Found: C, 71.41; H, 8.14.




**Preparation of (3*R*, 5*S*)-3-(*tert*-butyl-diphenyl-silanyloxy)-5-(4-methoxy-benzyloxy)-oct-7-oxo-heptanethioic acid *S*-*tert*-butyl ester (19).** To a stirring solution of olefin **17d** (1.00 g, 1.65 mmol**,** 1.0 equiv), THF (7.5 mL), *t*-butanol (7.5 mL), and $H_2O$ (1.5 mL) in a 25 mL round bottom flask under $N_2$, at rt, was added 4-methylmorpholine *N*-oxide (242 mg, 2.06 mmol, 1.25 equiv) in one portion. A 0.1 M solution of $OsO_4$ (825 μL, 0.083 mmol, 0.05 equiv) in THF was added dropwise, via syringe. The reaction was allowed to proceed for 14 h, after which time TLC analysis indicated complete consumption of olefin starting material. The reaction was quenched by addition of sodium metabisulfite ($Na_2S_2O_5$) in one portion. The mixture was stirred for 1 h, during which time a color change from yellow to dark brown was observed. The quenched reaction mixture was diluted with $H_2O$ (10 mL), EtOAc (100 mL), and the layers were separated. The aqueous phase was extracted with EtOAc (2 × 25 mL). The combined organic layers were washed with brine (2 × 10 mL), dried over $MgSO_4$, filtered, concentrated under reduced pressure and then high vacuum to give crude diol **17e** (1.06 g) as a thick paste that was taken directly onto the next reaction without further purification.

To a stirring solution of crude diol **17e** (assumed to be 1.65 mmol, 1.0 equiv) and benzene (17 mL) under an atmosphere of Ar, at rt, was added $Pb(OAc)_4$ (735 mg, 1.65 mmol, 1.1 equiv) in three portions over 10 min. After 1 h TLC analysis indicated complete consumption of starting material. The reaction mixture was diluted with hexanes (100 mL) then filtered over a pad of Celite® and $Na_2SO_4$. The filtrate was

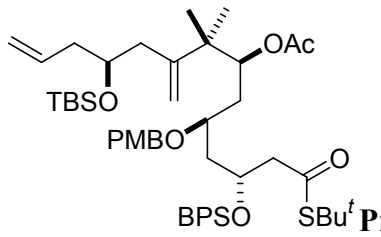
concentrated under reduced pressure then high vacuum to yield aldehyde **19** (991 mg, 99% yield over 2 steps) as a viscous colorless oil: $R_f$ = 0.39 (25% EtOAc/hexanes); $[\alpha]^{20}_D$ = - 25.3 (*c* = 1.72, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 9.54 (t, *J* = 2.3 Hz, 1H), 7.73 – 7.69 (m, 4H), 7.46 – 7.37 (m, 6H), 7.11 – 7.08 (m, 2H), 6.85 – 6.82 (m, 2H), 4.43 (tt, *J* = 6.4, 5.9 Hz, 1H), 4.19 ABq, *J* = 11.0 Hz, Δν = 42.0 Hz, 2H), 3.85 – 3.80 (m, 2H), 3.80 (s, 3H), 2.72 (dd, *J* = 14.6, 5.9 Hz, 1H), 2.63 (dd, *J* = 14.6, 6.4 Hz, 1H), 2.34 (ddd, *J* = 16.5, 6.6, 2.3 Hz, 1H), 2.26 (ddd, *J* = 16.5, 4.9, 2.3 Hz, 1H), 1.96 (ddd, *J* = 14.3, 6.8, 5.9 Hz, 1H), 1.64 (ddd, *J* = 14.3, 5.9, 5.5 Hz, 1H), 1.43 (s, 9H), 1.05 (s, 9H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 201.2, 197.7, 159.4, 136.1, 136.1, 133.9, 133.7, 130.3, 130.0, 130.0, 129.5, 127.9, 127.9, 113.9, 71.4, 70.7, 68.5, 55.5, 52.6, 48.6, 48.3, 42.8, 29.9, 27.1, 19.6; IR (thin film) 3070, 2958, 2860, 2724, 1725, 1680, 1613, 1514, 1464, 1364, 1302, 1249, 1175, 1108, 1037, 823 $cm^{-1}$; HRMS (CI+) calcd for $C_{35}H_{47}O_5SSi$ (M + H) 607.2913, found 607.2883.




**Preparation of (3*R*, 5*S*, 7*S*, 11*S*)-11-(*tert*-butyl-dimethyl-silanyloxy)-3-(*tert*-butyl-diphenyl-silanyloxy)-7-hydroxy-5-(4-methoxy-benzyloxy)-8, 8-dimethyl-9-methylene-tetradec-13-enethioic acid *S-tert*-butyl ester (21).** To a stirring solution of aldehyde **19** (200.0 mg, 0.329 mmol, 1.0 equiv) and toluene (2.8 mL) in a 15 mL round bottom flask under an atmosphere of Ar, at -78 °C, was added a freshly prepared 3.0 M solution of $Me_2AlCl$ (740 μL, 1.85 mmol, 1.0 equiv) in toluene dropwise, via syringe. The solution was stirred for 10 min at -78 °C, then stannane **6** (239.0 mg,

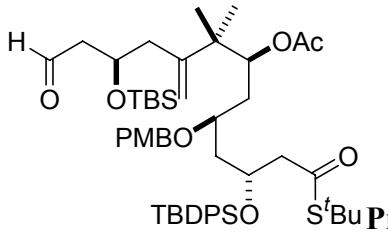
0.428 mmol, 1.3 equiv) in toluene (500 μL) was added dropwise, via syringe, down the inside of the reaction flask. The reaction was allowed to proceed for 2 h at -78 °C, and then quenched by direct transfer into a 250 mL Erlenmeyer flask that contained a vigorously stirring mixture of a saturated aqueous potassium sodium tartrate solution (30 mL) and 20% EtOAc/hexanes (30 mL). The resulting mixture was allowed to stir for 12 h and then the layers were separated. The aqueous layer was extracted with 20% EtOAc/hexanes (2 × 30 mL). The combined organic phases were washed with brine (2 × 20 mL), dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure to give the crude product as a pale yellow oil. Purification was accomplished by flash column chromatography on a 2.0 × 20 cm column, eluting with 7.5% EtOAc/hexanes, collecting 4 mL fractions. The product containing fractions (19–37) were combined and concentrated under reduced pressure to give coupled product **21** (255 mg, 88% yield) as a as a single diastereomer, and a colorless oil: $R_f$ = 0.43 (15% EtOAc/hexanes); $[\alpha]^{20}_D$ = -13.9 (*c* = 0.20, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 7.75 – 7.71 (m, 4H), 7.45 – 7.37 (m, 6H), 7.16 – 7.13 (m, 2H), 6.85 – 6.83 (m, 2H), 5.83 (dddd, *J* = 16.5, 11.0, 7.3, 7.3 Hz, 1H), 5.08 – 5.07 (m, 1H), 5.05 (s, 1H), 5.02 (s, 1H), 4.97 (s, 1H), 4.33 (app quin, *J* = 6.0 Hz, 1H), 4.23 (ABq, *J* = 10.6 Hz, Δν = 53.9 Hz, 2H), 3.89 (app quin, *J* = 6.0 Hz, 1H), 3.81 (s, 3H), 3.68 – 3.66 (m, 1H), 3.63 – 3.58 (m, 1H), 2.71 (dd, *J* = 14.5, 6.0 Hz, 1H), 2.65 (dd, *J* = 14.5, 5.7 Hz, 1H), 2.33 – 2.23 (m, 2H), 2.18 (d, *J* = 2.2 Hz, 1H), 2.16 – 2.10 (m, 2H), 1.95 (td, *J* = 13.9, 7.0 Hz, 1H), 1.59 (td, *J* = 13.9, 5.9 Hz, 1H), 1.45 (s, 9H), 1.25 – 1.14 (m, 2H), 1.06 (s, 9H), 0.96 (s, 3H), 0.91 (s, 9H), 0.87 (s, 3H), 0.10 (s, 3H), 0.06 (s, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 197.9, 159.3, 151.3, 136.2, 136.2, 135.2, 134.2, 134.0, 131.0, 130.0, 129.0, 129.6, 127.8, 117.4, 113.9, 112.2, 74.4, 71.7, 71.5, 71.3, 68.9,

55.5, 52.5, 48.2, 44.0, 42.8, 42.5, 38.3, 35.5, 30.0, 27.2, 26.2, 22.7, 21.6, 19.6, 18.4, -3.9, -4.1; IR (thin film) 3490, 3072, 2957, 2859, 1682, 1614, 1588, 1514, 1467, 1365, 1302, 1251, 1175, 1107, 914, 831 $cm^{-1}$; Anal. Calcd for $C_{52}H_{78}O_6SSi_2$: C, 69.97; H, 8.98. Found: C, 70.26; H, 9.07.




**Preparation of acetic acid (1*S*, 5*S*)-5-(*tert*-butyl-dimethyl-silanyloxy)-1-[(2*S*, 4*R*)-4-(*tert*-butyl-diphenyl-silanyloxy)-5-*tert*-butyl-sulfanyl-carbonyl-2-(4-methoxy-benzyloxy)-pentyl]-2,2-dimethyl-3-methylene-heptyl ester (21a).** To a stirring solution of alcohol **21** (273.0 mg, 0.312 mmol, 1.0 equiv), triethylamine (94.0 mg, 0.936 mmol, 3.0 equiv), DMAP (4.0 mg, 0.031 mmol, 0.1 equiv), and $CH_2Cl_2$ (3.1 mL) in a 10 mL round bottom flask under an atmosphere of Ar, at rt, was added acetic anhydride (64.0 mg, 0.624 mmol, 2.0 equiv) dropwise via syringe. TLC analysis after 12 h indicated complete consumption of alcohol starting material. The stir bar was removed from the reaction flask and the mixture was concentrated under reduced pressure. The concentrate was diluted with 20% EtOAc/hexanes (75 mL), washed with pH 7.0 phosphate buffer (20 mL), brine (25 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to give the crude product as a pale yellow oil. Purification was accomplished by flash column chromatography on a 2.8 × 18 cm column, eluting with 10% EtOAc/hexanes, collecting 8 mL fractions. The product containing fractions (11–19) were combined and concentrated under reduced pressure to give acylated product **21a** (271 mg, 95% yield) as a colorless oil: $R_f$ = 0.60 (10% EtOAc/hexanes); $[\alpha]^{20}_D$ = - 22.3 (*c* = 0.14, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 7.72 –

7.69 (m, 4H), 7.46 – 7.36 (m, 6H), 7.23 – 7.20 (m, 2H), 6.86 – 6.83 (m, 2H), 5.76 (dddd, $J$ = 16.5, 9.2, 7.3, 7.3 Hz, 1H), 5.26 (dd, $J$ = 9.9, 1.1 Hz, 1H), 5.00 (s, 1H), 4.97 – 4.95 (m, 1H), 4.96 (s, 1H), 4.90 (s, 1H), 4.27 – 4.23 (m, 1H), 4.21 (ABq, $J$ = 9.9 Hz, $\Delta\nu$ = 21.0 Hz, 2H), 3.85 (app quin, $J$ = 5.9 Hz, 1H), 3.80 (s, 3H), 3.68 – 3.66 (m, 1H), 3.19 – 3.24 (m, 1H), 2.65 (dd, $J$ = 14.6, 6.2 Hz, 1H), 2.55 (dd, $J$ = 14.6, 5.9 Hz, 1H), 2.23 – 2.05 (m, 4H), 2.00 (s, 3H), 1.97 – 1.90 (m, 1H), 1.52 – 1.46 (m, 1H), 1.45 (s, 9H), 1.32 – 1.18 (m, 2H), 1.05 (s, 9H), 0.96 (s, 3H), 0.94 (s, 9H), 0.88 (s, 3H), 0.04 (s, 3H), 0.00 (s, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 197.7, 170.9, 159.2, 150.2, 136.1, 136.1, 135.6, 133.9, 131.1, 130.0, 129.9, 129.7, 127.8, 127.8, 117.0, 113.8, 112.2, 74.7, 73.4, 71.7, 71.4, 68.7, 55.4, 52.3, 48.2, 43.6, 42.8, 42.2, 38.9, 35.9, 30.0, 27.1, 26.1, 24.1, 21.6, 21.3, 19.6, 18.2, -4.0, -4.2; IR (thin film) 2957, 2858, 1737, 1682, 1614, 1514, 1467, 1367, 1247, 1175, 1085, 831 cm$^{-1}$; Anal. Calcd for $C_{53}H_{80}O_7SSi_2$: C, 69.39; H, 8.79. Found: C, 69.67; H, 8.89.

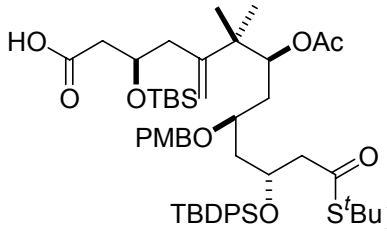



**Preparation of acetic acid (1*S*, 5*S*)-5-(*tert*-butyl-dimethyl-silanyloxy)-1-[(2*S*, 4*R*)-4-(*tert*-butyl-diphenyl-silanyloxy)-5-*tert*-butyl-sulfanyl-carb-onyl-2-(4-methoxy-benzyloxy)-pentyl]-2,2-dimethyl-3-methylene-7-oxo-heptyl ester (22).** To a stirring solution of alkene **21a** (150.0 mg, 0.163 mmol, 1.0 equiv), THF (750 μL), *tert*-butanol (750 μL), and $H_2O$ (150 μL) in a 5 mL round bottom flask under an atmosphere of Ar, at 0 °C, was added 4-methylmorpholine *N*-oxide (21.0 mg, 0.179 mmol, 1.1 equiv) in one portion. A 0.1 M solution of $OsO_4$ (81 μL, 0.008 mmol, 0.05

equiv) in THF was added dropwise, via syringe. The reaction was allowed to proceed for 12 h, allowing the 0 °C bath to expire, after which time TLC analysis indicated complete consumption of olefin starting material. The reaction was quenched by addition of sodium metabisulfite ($Na_2S_2O_5$) in one portion. The mixture was stirred for 1 h, during which time a color change from yellow to dark brown was observed. The quenched reaction mixture was diluted with EtOAc (50 mL), and the layers were separated. The organic layers were washed with brine (2 × 10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give crude diol **21c** (160 mg) as a tan foam that was taken directly onto the next reaction without further purification.

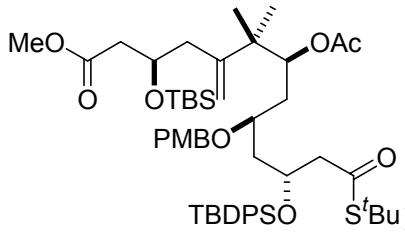
To a stirring mixture of crude diol **21c** (assumed to be 0.163 mmol, 1.0 equiv), THF (3.0 mL), and pH 7.0 phosphate buffer (1.0 mL) in a 25 mL round bottom flask under an atmosphere of $N_2$, at rt, was added sodium meta-periodate (140.0 mg, 0.652 mmol, 4.0 equiv) in one portion. TLC analysis after 3 h indicated complete consumption of diol starting material. The reaction mixture was diluted with 20% EtOAc/hexanes (50 mL) and $H_2O$ (5 mL), and the layers were separated. The aqueous phase was extracted with 20% EtOAc/hexanes (2 × 10 mL). The combined organic layers were washed with brine (2 × 10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give the crude product as a yellow oil. Purification was accomplished by flash column chromatography, eluting with 5% EtOAc/hexanes (500 mL) and 20% EtOAc/hexanes (200 mL), collecting 8 mL fractions. The product containing fractions (56–64) were combined and concentrated under reduced pressure to give aldehyde **22** (134 mg, 89% yield, over 2 steps) as a colorless oil: $R_f$ = 0.46 (20% EtOAc/hexanes); $[\alpha]^{20}_D$ = - 33.7 (*c* = 0.10, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 9.65 (t, *J* = 2.0 Hz, 1H), 7.72 – 7.68 (m,

4H), 7.44 – 7.37 (m, 6H), 7.23 – 7.20 (m, 2H), 6.86 – 6.83 (m, 2H), 5.26 (dd, *J* = 8.4, 2.6 Hz, 1H), 4.98 (s, 1H), 4.89 (s, 1H), 4.38 – 4.33 (m, 1H), 4.26 – 4.21 (m, 1H), 4.19 (s, 2H), 3.80 (s, 3H), 3.21 – 3.16 (s, 1H), 2.65 (dd, *J* = 14.6, 6.2 Hz, 1H), 2.55 (dd, *J* = 14.6, 5.9 Hz, 1H), 2.4 (ddd, *J* = 16.1, 4.4, 2.0 Hz, 1H), 2.35 – 2.28 (m, 2H), 2.14 (dd, *J* = 15.7, 7.0 Hz, 1H), 2.02 (s, 3H), 1.96 – 1.90 (m, 1H), 1.49 – 1.44 (m, 1H), 1.44 (s, 9H), 1.24 – 1.16 (m, 2H), 1.05 (s, 9H), 0.95 (s, 3H), 0.94 (s, 3H), 0.85 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 202.4, 197.7, 170.9, 159.2, 149.7, 136.1, 136.1, 133.8, 131.0, 130.0, 129.9, 129.9, 127.8, 127.8, 113.8, 112.5, 74.3, 73.4, 71.5, 68.6, 67.5, 55.4, 52.2, 50.9, 48.2, 43.5, 42.7, 39.5, 36.0, 29.9, 27.1, 26.0, 24.0, 21.4, 21.3, 19.5, 18.1, -4.0, -4.6; IR (thin film) 3071, 2958, 2858, 2718, 1732, 1681, 1614, 1514, 1467, 1428, 1368, 1247, 1176, 1106, 910, 835 cm$^{-1}$; HRMS (CI+) calcd for $C_{52}H_{79}O_8SSi_2$ (M + H) 919.5034, found 919.4857.



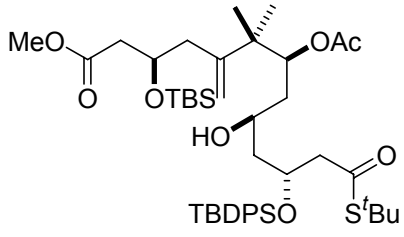

**Preparation of (3*R*, 7*S*, 9*S*, 11*R*)-7-acetoxy-3-(*tert*-butyl-dimethyl-silanyloxy)-11-(*tert*-butyl-diphenyl-silanyloxy)-12-*tert*-butyl-sulfanyl-carb-onyl-9-(4-methoxy-benzyloxy)-6,6-dimethyl-5-methylene-dodecanoic acid (22a).** To a stirring mixture of aldehyde **22** (124.0 mg, 0.134 mmol, 1.0 equiv), 2-methyl-2-butene (406 μL), 1.25 M aqueous solution of $KH_2PO_4$ (650 μL, 0.809 mmol, 6.0 equiv), and *tert*-butanol (670 μL) in a 5 mL round bottom flask under an atmosphere of Ar, at -10 °C, was added sodium chlorite (61.0 mg, 0.674 mmol, 5.0 equiv) in one portion. The mixture was allowed to stir vigorously for 1 h, at -10 °C, after which time TLC analysis indicated

complete consumption of aldehyde starting material. The mixture was diluted with pH 4.0 buffer (10 mL) and $Et_2O$ (40 mL), and the layers were separated. The aqueous phase was extracted with $Et_2O$ (2 × 10 mL). The combined organic layers were washed with brine (2 × 10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give the crude product as a yellow oil. Purification was accomplished by flash column chromatography on a 2.5 × 9 cm column, eluting with 20% EtOAc/hexanes (200 mL) and 20% acetone/hexanes (250 mL), collecting 8 mL fractions. The product containing fractions (15–45) were combined and concentrated under reduced pressure to give acid **22a** (122.6 mg, 97% yield) as a white foam: $R_f$ = 0.24 (20% EtOAc/hexanes); $[\alpha]^{20}_D$ = -26.8 (*c* = 0.40, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 7.71 – 7.67 (m, 4H), 7.45 – 7.36 (m, 6H), 7.21 – 7.18 (m, 2H), 6.85 – 6.82 (m, 2H), 5.24 (dd, *J* = 9.2, 1.8 Hz, 1H), 4.98 (s, 1H), 4.91 (s, 1H), 4.34 – 4.27 (m, 1H), 4.26 – 4.21 (m, 1H), 4.20 (s, 1H), 4.19 (s, 1H), 3.80 (s, 3H), 3.22 – 3.17 (s, 1H), 2.64 (dd, *J* = 14.3, 5.9 Hz, 1H), 2.54 (dd, *J* = 14.3, 5.9 Hz, 1H), 2.45 (dd, *J* = 15.4, 4.0 Hz, 1H), 2.30 (dd, *J* = 15.8, 5.5 Hz, 1H), 2.29 (dd, *J* = 15.4, 7.7 Hz, 1H), 2.14 (dd, *J* = 15.8, 7.7 Hz, 1H), 2.01 (s, 3H), 1.95 – 1.89 (m, 1H), 1.49 – 1.44 (m, 1H), 1.44 (s, 9H), 1.23 – 1.19 (m, 2H), 1.04 (s, 9H), 0.95 (s, 3H), 0.93 (s, 3H), 0.86 (s, 9H), 0.04 (s, 3H), 0.04 (s, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 197.8, 177.0, 159.2, 149.6, 136.1, 136.1, 133.9, 133.8, 131.0, 130.0, 129.9, 129.8, 127.9, 127.8, 113.8, 112.9, 74.5, 73.4, 71.5, 68.9, 68.7, 55.4, 52.3, 48.3, 43.5, 42.7, 42.0, 39.4, 35.8, 30.0, 27.1, 26.0, 24.0, 21.7, 21.3, 19.6, 18.1, -4.1, -4.8; IR (thin film) 2958 (br), 1712, 1614, 1514, 1467, 1368, 1248, 1174, 1105, 971, 911, 831 $cm^{-1}$; HRMS (CI+) and (FAB), unable to obtain meaningful molecular ion data despite multiple sample submissions.



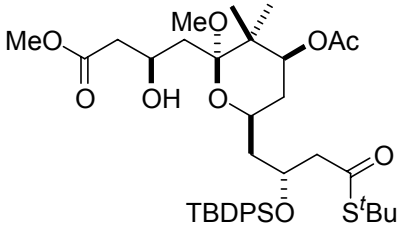

**Preparation of (3*R*, 7*S*, 9*S*, 11*R*)-7-acetoxy-3-(*tert*-butyl-dimethyl-silanyloxy)-11-(*tert*-butyl-diphenyl-silanyloxy)-12-*tert*-butyl-sulfanyl-carbonyl-9-(4-methoxy-benzyloxy)-6,6-dimethyl-5-methylene-dodecanoic acid methyl ester (5).** To a stirring mixture of acid **22a** (113.0 mg, 0.120 mmol, 1.0 equiv), $CH_2Cl_2$ (1.0 mL), and MeOH (250 μL) in a 5 mL round bottom flask under an atmosphere of Ar, at rt, was added a 2.0 M solution of (trimethylsilyl)diazomethane (120 μL, 0.241 mmol, 2.0 equiv) in $Et_2O$ dropwise, via syringe. A solution color change from colorless to yellow and vigorous bubbling gas evolution was observed. The reaction was allowed to proceed for 20 min, after which time TLC analysis indicated complete consumption of acid starting material. The reaction mixture was transferred to a 50 mL round bottom flask and concentrated under reduced pressure. Purification was accomplished by flash column chromatography on a 2.5 × 15 cm column, eluting with 5% EtOAc/hexanes (500 mL) and 10% EtOAc/hexanes (200 mL), collecting 8 mL fractions. The product containing fractions (57–88) were combined and concentrated under reduced pressure to give methyl ester **5** (108.3 mg, 94% yield) as a colorless oil: $R_f$ = 0.52 (20% EtOAc/hexanes); $[\alpha]^{20}_D$ = - 32.7 (*c* = 0.08, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 7.72 – 7.68 (m, 4H), 7.44 – 7.36 (m, 6H), 7.22 – 7.19 (m, 2H), 6.86 – 6.82 (m, 2H), 5.25 (dd, *J* = 9.5, 1.6 Hz, 1H), 4.97 (s, 1H), 4.94 (s, 1H), 4.35 – 4.30 (m, 1H), 4.26 – 4.21 (m, 1H), 4.20 (ABq, *J* = 10.3 Hz, Δν = 17.2 Hz, 2H), 3.80 (s, 3H), 3.63 (s, 3H), 3.22 – 3.18 (s, 1H), 2.64 (dd, *J* = 14.6, 6.2 Hz, 1H), 2.55 (dd, *J* = 14.6, 5.9 Hz, 1H), 2.41 (dd, *J*

= 15.0, 4.0 Hz, 1H), 2.32 – 2.26 (m, 2H), 2.13 (dd, *J* = 16.1, 7.7 Hz, 1H), 2.01 (s, 3H), 1.94 – 1.89 (m, 1H), 1.50 – 1.44 (m, 1H), 1.44 (s, 9H), 1.28 – 1.17 (m, 2H), 1.04 (s, 9H), 0.96 (s, 3H), 0.94 (s, 3H), 0.85 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 197.7, 172.6, 170.9, 159.2, 149.8, 136.1, 136.1, 133.9, 133.8, 131.0, 130.0, 129.9, 129.7, 127.8, 127.8, 113.8, 112.6, 74.6, 73.4, 71.4, 69.0, 68.7, 55.4, 52.3, 51.5, 48.2, 43.5, 42.8, 42.4, 39.6, 35.9, 30.0, 27.1, 26.0, 24.0, 21.6, 21.3, 19.5, 18.1, -4.1, -4.8; IR (thin film) 2957, 2859, 1738, 1681, 1614, 1514, 1466, 1368, 1247, 1168, 1105, 971, 911, 832 cm$^{-1}$; HRMS (CI+) calcd for $C_{53}H_{80}O_9SSi_2$ (M + H) 949.5139, found 949.5102.




**Preparation of (3*R*, 7*S*, 9*S*, 11*R*)-7-acetoxy-3-(*tert*-butyl-dimethyl-silanyloxy)-11-(*tert*-butyl-diphenyl-silanyloxy)-12-*tert*-butyl-sulfanyl-carbonyl-9-hydroxy-6,6-dimethyl-5-methylene-dodecanoic acid methyl ester (5a).** To a stirring solution of PMB ether **5** (107.0 mg, 0.112 mmol, 1.0 equiv), $CH_2Cl_2$ (1.1 mL), and pH 7.0 phosphate buffer (0.4 mL) in a 5 mL round bottom flask under an atmosphere of Ar, at rt, was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (52.0 mg, 0.225 mmol, 2.0 equiv) in one portion. TLC analysis after 1.5 h indicated complete consumption of alcohol starting material. The reaction mixture was transferred to a 50 mL Erlenmeyer flask, containing 20% EtOAc/hexanes (40 mL), and filtered over a plug of Celite®, Florsil®, and $Na_2SO_4$ (5 × 2 cm). The plug was flushed with additional 20% EtOAc/hexanes (3 × 20 mL) portions. The filtrate was concentrated under reduced pressure to give the crude product as a pale yellow oil. Purification was accomplished by flash column chromatography on a 2.5 × 8 cm column, eluting with 10% EtOAc/hexanes,

collecting 4 mL fractions. The product containing fractions (18–25) were combined and concentrated under reduced pressure to give alcohol **5a** (81.3 mg, 88% yield) as a colorless oil: $R_f$ = 0.50 (25% EtOAc/hexanes); $[\alpha]^{20}_D$ = - 19.9 (*c* = 0.15, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 7.70 – 7.66 (m, 4H), 7.47 – 7.38 (m, 6H), 5.05 (dd, *J* = 11.0, 1.5 Hz, 1H), 5.01 (s, 1H), 4.97 (s, 1H), 4.41 – 4.34 (m, 1H), 4.26 – 4.21 (m, 1H), 3.66 (s, 3H), 3.51 – 3.44 (s, 1H), 2.66 – 2.59 (m, 3H), 2.54 (dd, *J* = 15.0, 4.7 Hz, 1H), 2.39 (dd, *J* = 15.0, 7.7 Hz, 1H), 2.27 (dd, *J* = 15.7, 5.5 Hz, 1H), 2.20 (dd, *J* = 15.7, 7.7 Hz, 1H), 1.93 (s, 3H), 1.60 – 1.50 (m, 2H), 1.40 (s, 9H), 1.36 – 1.21 (m, 2H), 1.03 (s, 9H), 1.01 (s, 6H), 0.86 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 197.7, 172.5, 172.1, 149.7, 136.1, 136.0, 133.8, 133.7, 130.0, 127.9, 113.0, 75.3, 69.1, 68.5, 63.7, 52.4, 51.6, 48.1, 44.4, 43.0, 42.4, 38.8, 38.2, 29.9, 27.1, 25.9, 24.1, 22.1, 21.0, 19.6, 18.1, -4.1, -4.7; IR (thin film) 3526, 2957, 2932, 2858, 1738, 1684, 1468, 1430, 1368, 1253, 1163, 1087, 970, 831 $cm^{-1}$; HRMS (FAB) calcd for $C_{45}H_{72}O_8SSi_2$ (M) 829.4565, found 829.4584.



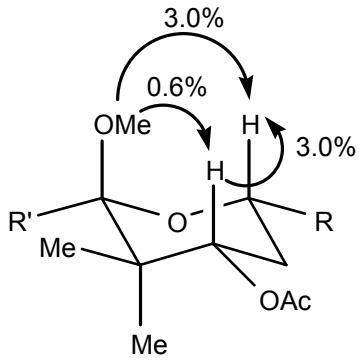

**Preparation of (*R*)-4-{(*S*)-4-((*S*)-(*S*)-acetoxy)-6-[(*R*)-2-(*tert*-butyl-diphenyl-silanyloxy)-3-*tert*-butylsulfanylcarbonyl-propyl]-2-methoxy-3,3-dimethyl-tetrahydropyran-2-yl}-3-hydroxy-butyric acid methyl ester (4).** To a stirring solution of alkene **5a** (47.0 mg, 0.056 mmol, 1.0 equiv) and $CH_2Cl_2$ (3.0 mL) in a 10 mL round bottom flask, at -78°C, was bubbled a steady stream of ozone. After 5 min, during which time the solution color changed from colorless to light blue, ozone bubbling

was ceased and replaced with a steady stream of $N_2$ for 10 min to purge the solution. The reaction mixture was transferred to a 25 mL round bottom flask and concentrated under reduced pressure. Methyl sulfide (10 mL) was added to the concentrated reaction mixture and the resulting solution was stirred for 12 h. The solution was concentrated under reduced pressure, and then diluted with 20% EtOAc/hexanes (50 mL). The organic solution was washed with $H_2O$ (2 × 5 mL), brine (2 × 5 mL), dried over $MgSO_4$, and concentrated under reduced pressure to give a pale yellow oil that was taken onto the next reaction without further purification.

To a stirring solution of a crude equilibrating mixture of cyclic hemiketal and keto-alcohol (assumed to be 0.056 mmol, 1.0 equiv) and MeOH (2 mL) in a 5 mL round bottom flask under an atmosphere of Ar, at rt, was added (±)-camphor-10-sulfonic acid (13.0 mg, 0.056 mmol, 1.0 equiv) in one portion. The reaction was allowed to proceed for 5 h, after which time TLC analysis indicated no noticeable reaction progress. The reaction mixture was transferred into a 50 Erlenmeyer flask containing a stirring mixture of a saturated aqueous $NaHCO_3$ solution (5 mL) and 20% EtOAc/hexanes (50 mL). The resulting layers were separated and the aqueous phase was extracted with 20% EtOAc/hexanes (2 × 5 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification was accomplished by flash column chromatography on a 2.5 × 8 cm column, eluting with 10% EtOAc/hexanes, collecting 4 mL fractions. The product containing fractions (11–19) were combined and concentrated under reduced pressure to give cyclic ketal **4** (24.5 mg, 60% yield over 2 steps) as a colorless oil: $R_f$ = 0.51 (40% EtOAc/hexanes); $[\alpha]^{20}_D$ = + 38.6 (*c* = 0.06, $CHCl_3$); 500 MHz $^1$H NMR ($CDCl_3$) δ 7.70 – 7.64 (m, 4H), 7.46 – 7.37

(m, 6H), 5.07 (dd, $J$ = 11.7, 5.1 Hz, 1H), 4.33 – 4.24 (m, 2H), 3.70 (s, 3H), 3.58 – 3.52 (s, 1H), 3.30 (s, 1H), 3.05 (s, 3H), 2.71 (dd, $J$ = 14.6, 5.9 Hz, 1H), 2.60 (dd, $J$ = 14.6, 6.6 Hz, 1H), 2.54 (dd, $J$ = 15.7, 6.6 Hz, 1H), 2.37 (dd, $J$ = 15.7, 7.0 Hz, 1H), 2.03 (s, 3H), 1.89 (dd, $J$ = 15.6, 9.9 Hz, 1H), 1.83 – 1.76 (m, 2H), 1.51 – 1.43 (m, 2H), 1.43 (s, 9H), 1.08 – 1.00 (m, 1H), 1.04 (s, 9H), 0.91 (s, 3H), 0.83 (s, 3H); 125 MHz $^{13}$C NMR ($CDCl_3$) δ 197.8, 172.2, 170.7, 136.1, 136.0, 134.0, 133.9, 130.0, 127.9, 127.9, 104.6, 73.2, 68.4, 66.2, 65.6, 52.3, 51.8, 49.1, 48.4, 43.8, 41.9, 39.6, 32.8, 29.9, 27.1, 21.4, 20.4, 19.5, 17.5; IR (thin film) 3554, 2957, 1739, 1680, 1431, 1367, 1244, 1164, 1108, 1076, 1030, 824 cm$^{-1}$; HRMS (CI+) calcd for $C_{38}H_{56}O_8SSi$ (M - OMe) 699.3387, found 699.3349.

**Stereochemical proof of the indicated A-ring stereochemistry.** Relevant NOE interactions presented below. The suspected stereochemistry of the fragment coupling event between stannane **6** and aldehyde **19** is also confirmed by this data.




**4**

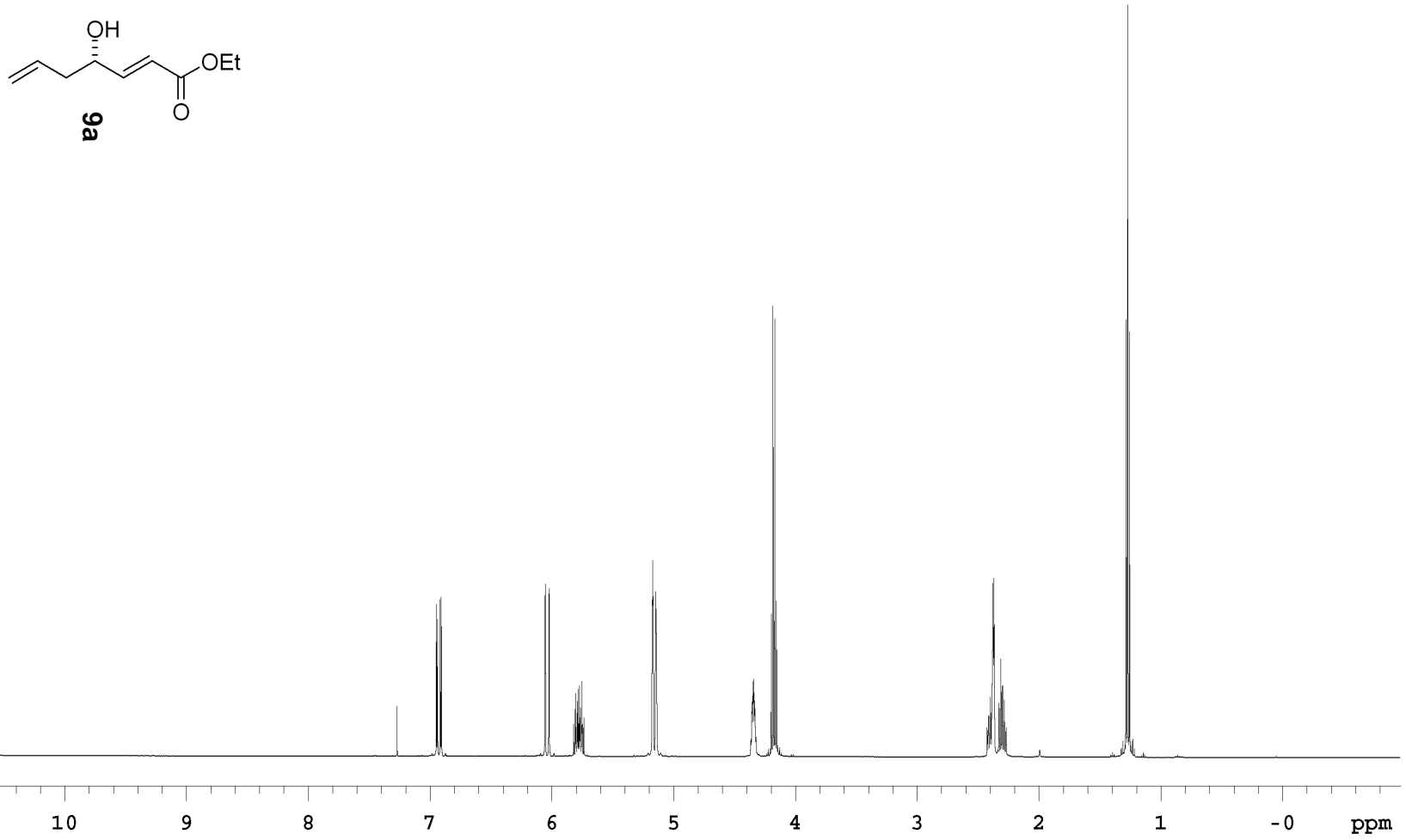
References


1) Roush, W. R; Hoong, L. K.; Palmer, M. A. J.; Straub, J. A.; Palkowitz, A. D. *J. Org. Chem.* **1990**, *55*, 4117.

2) Holmes, A. B.; Hughes, A. B.; Smith, A. L. *J. Chem. Perkin Trans. 1* **1993**, *5*, 633.

3) Yokokawa, F.; Asano, T.; Shioiri, T. *Org. Lett.* **2000**, *2*, 4169.

# $^{1}H$ and $^{13}C$ NMR SPECTRAL DATA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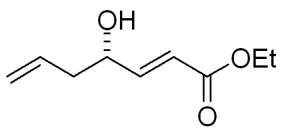


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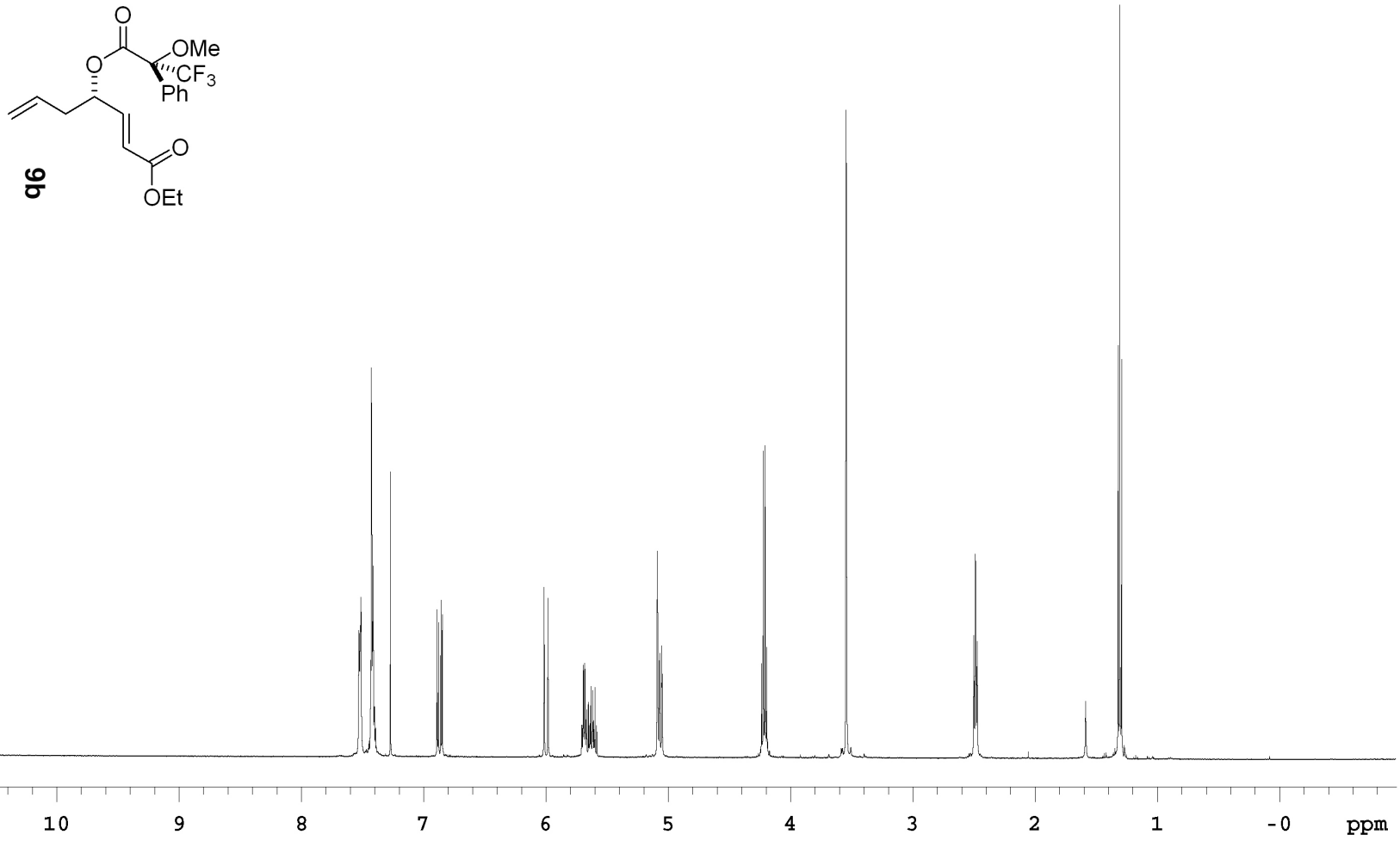
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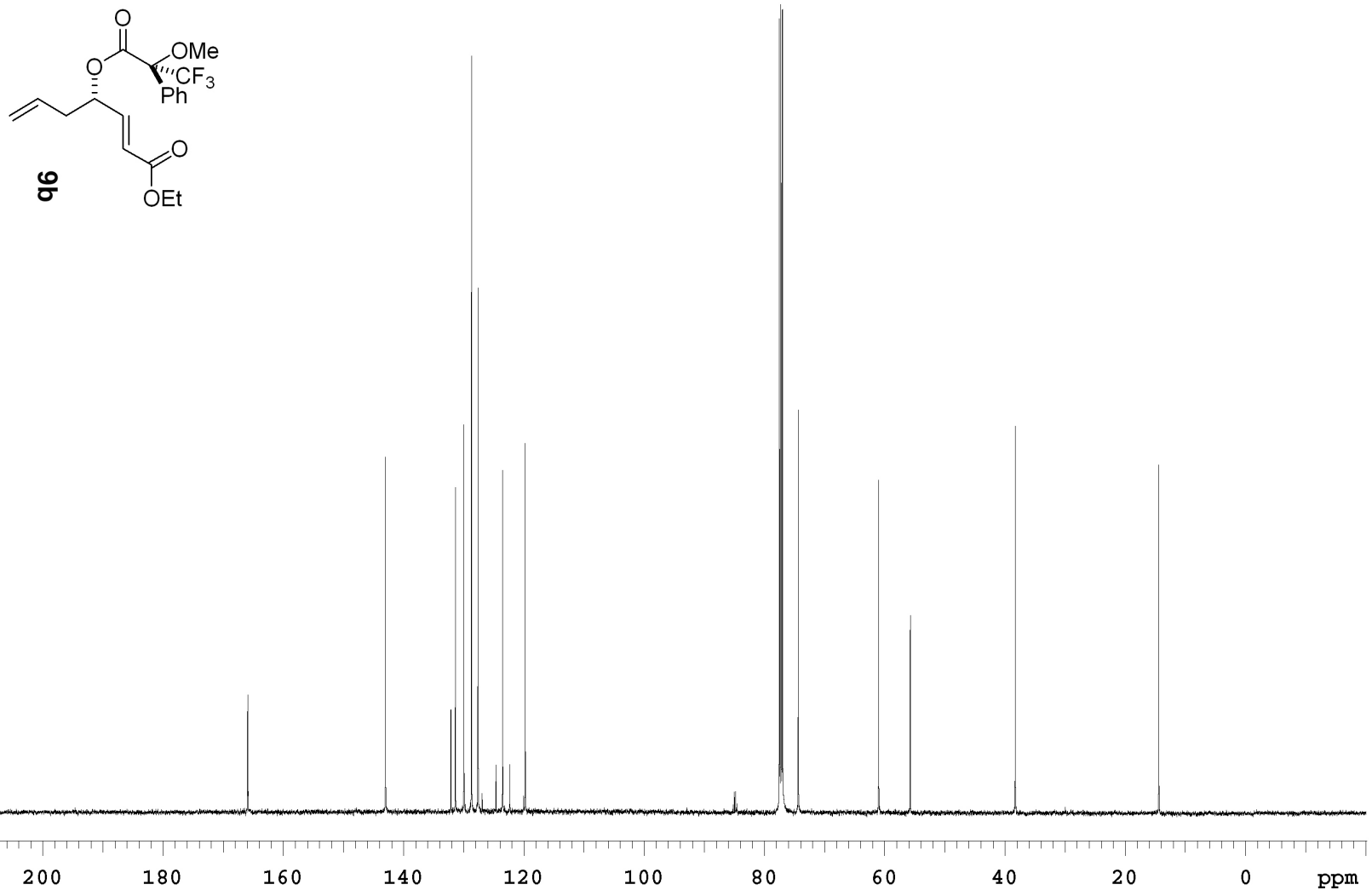
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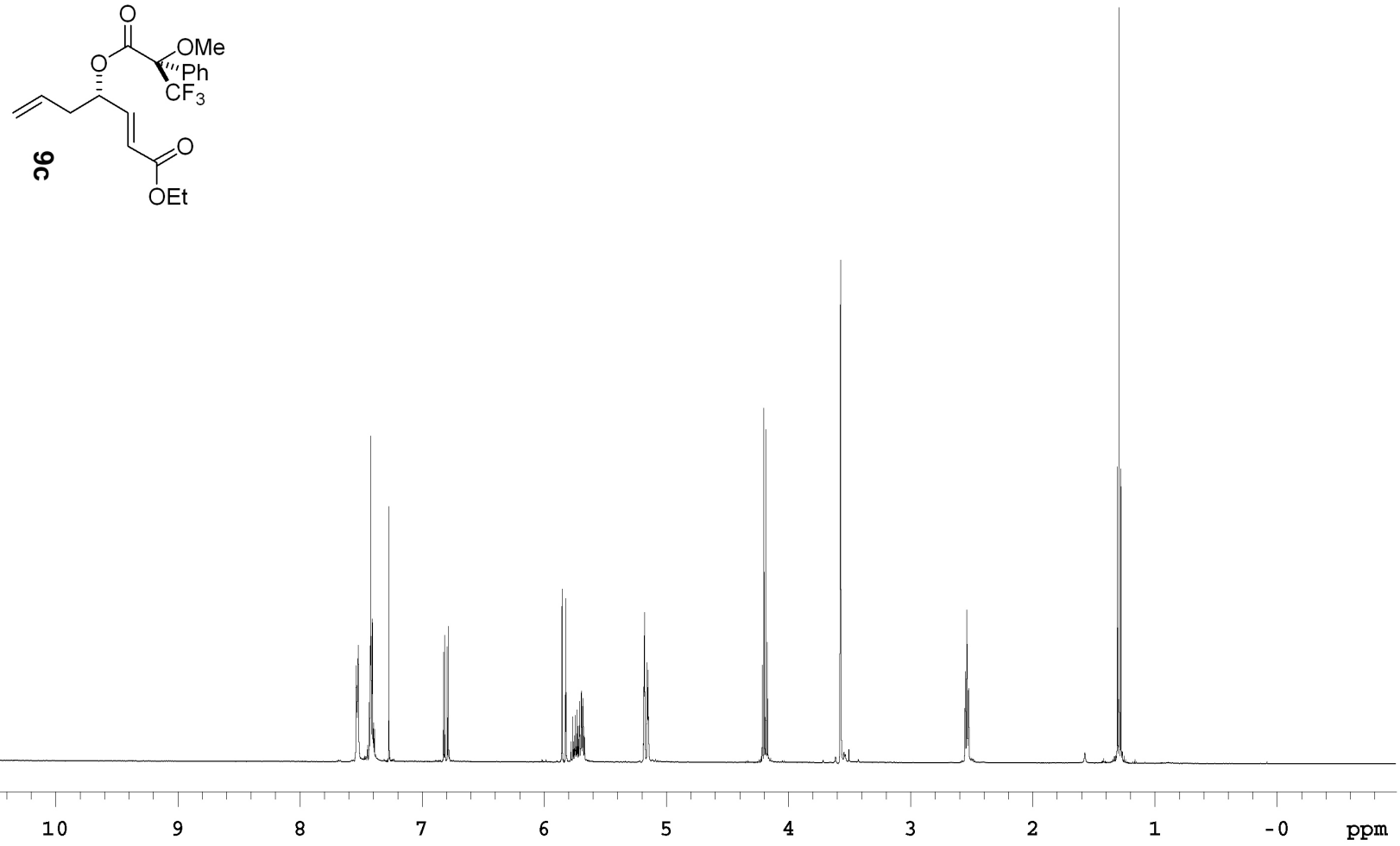
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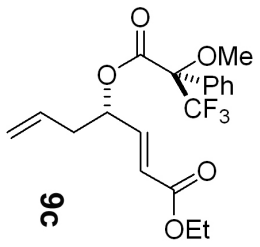


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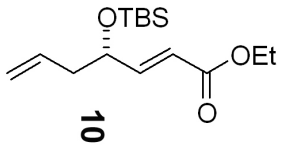


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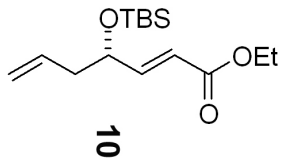


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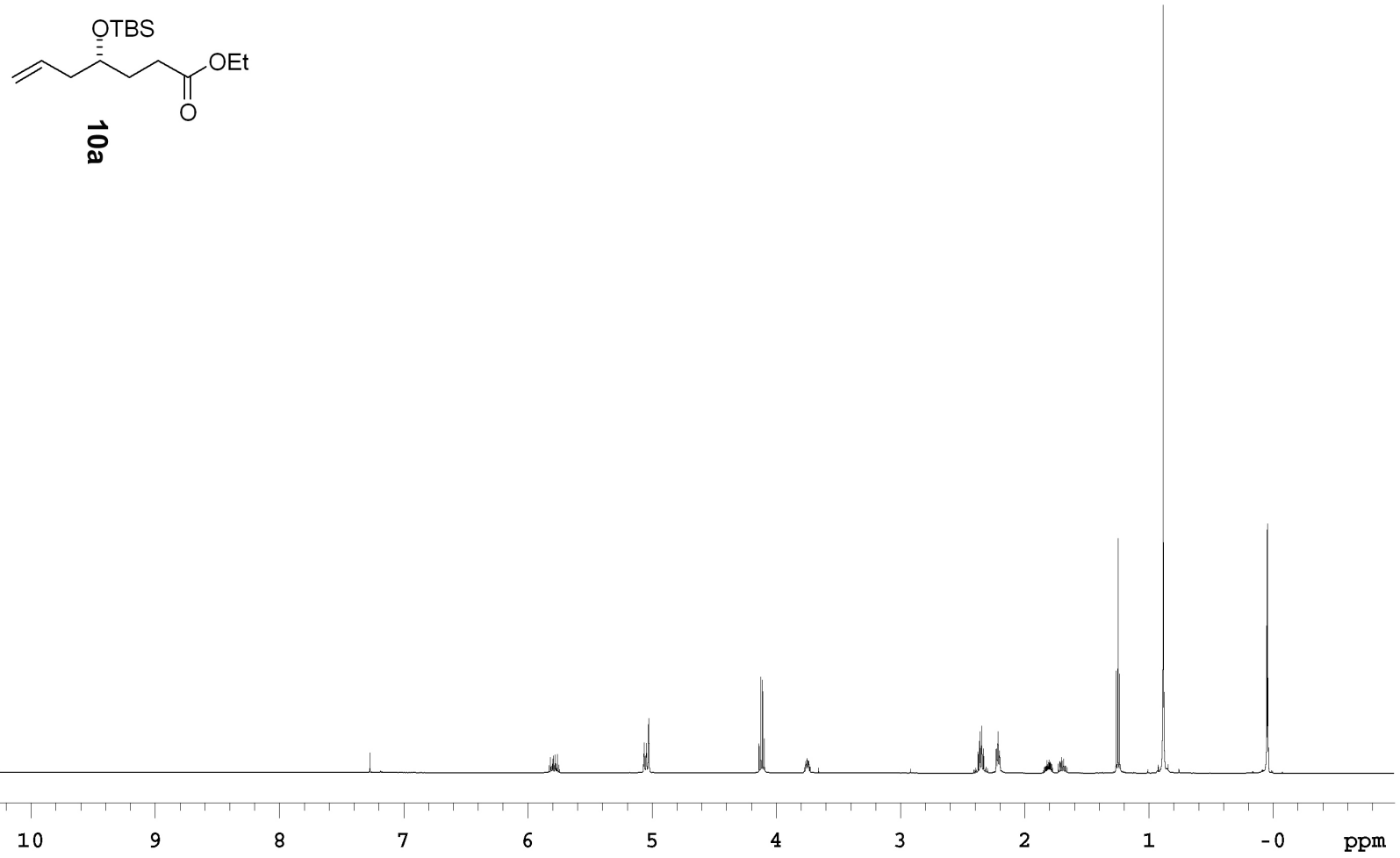
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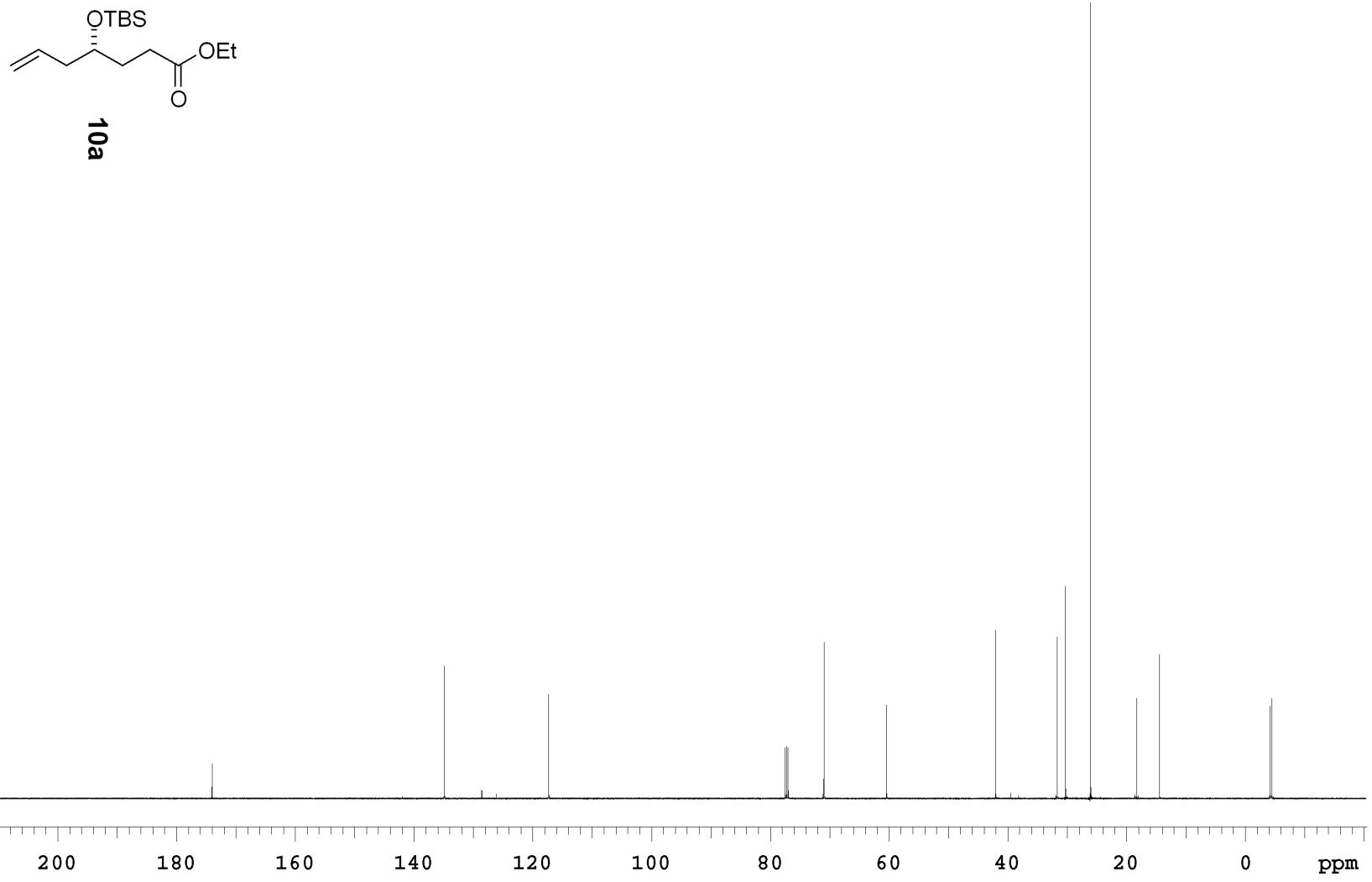
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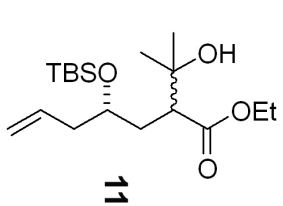


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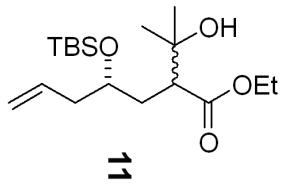


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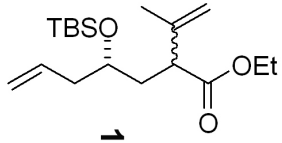


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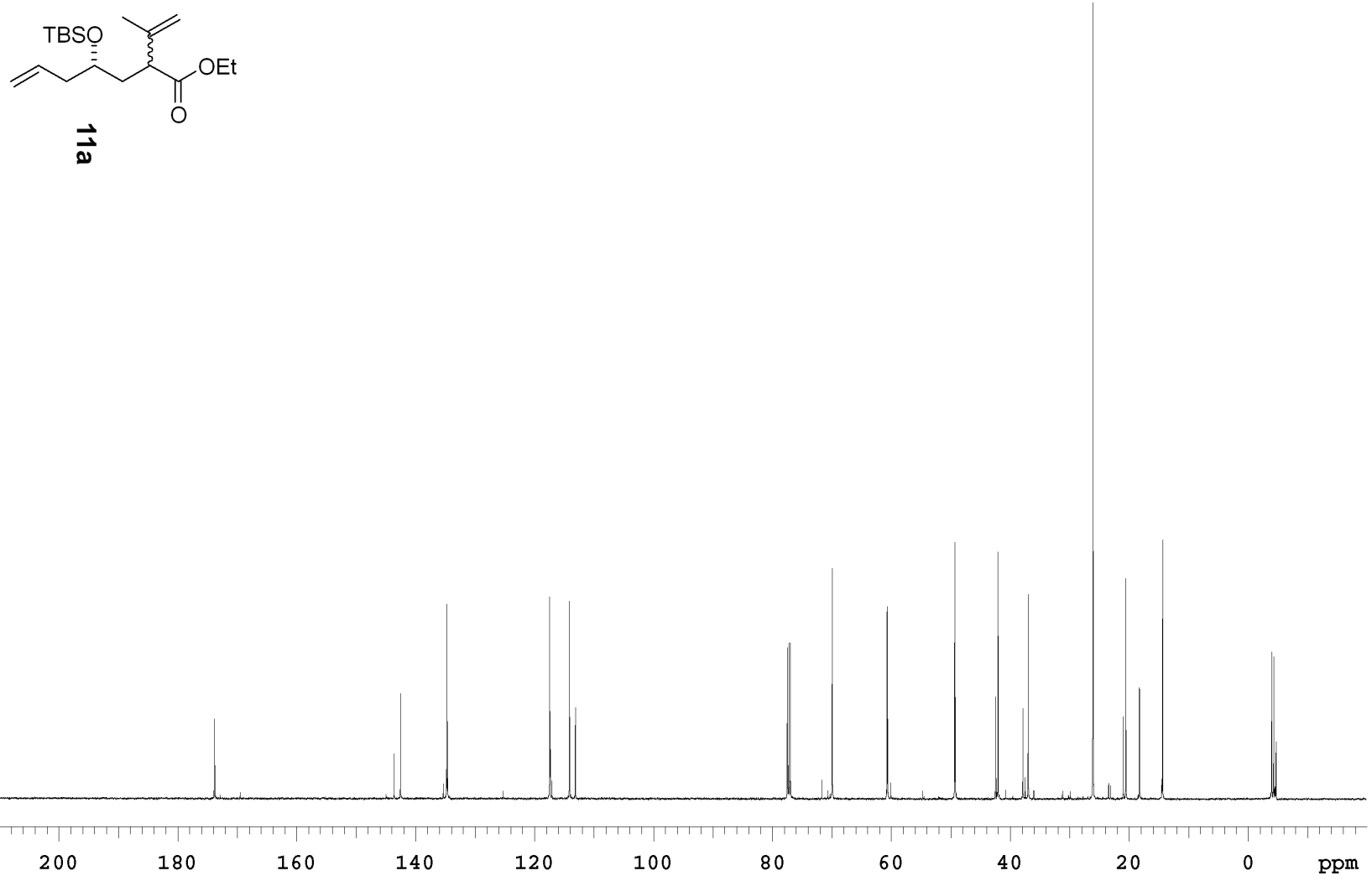
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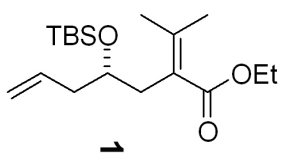


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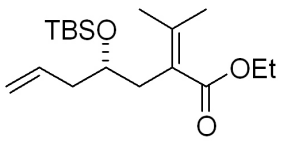


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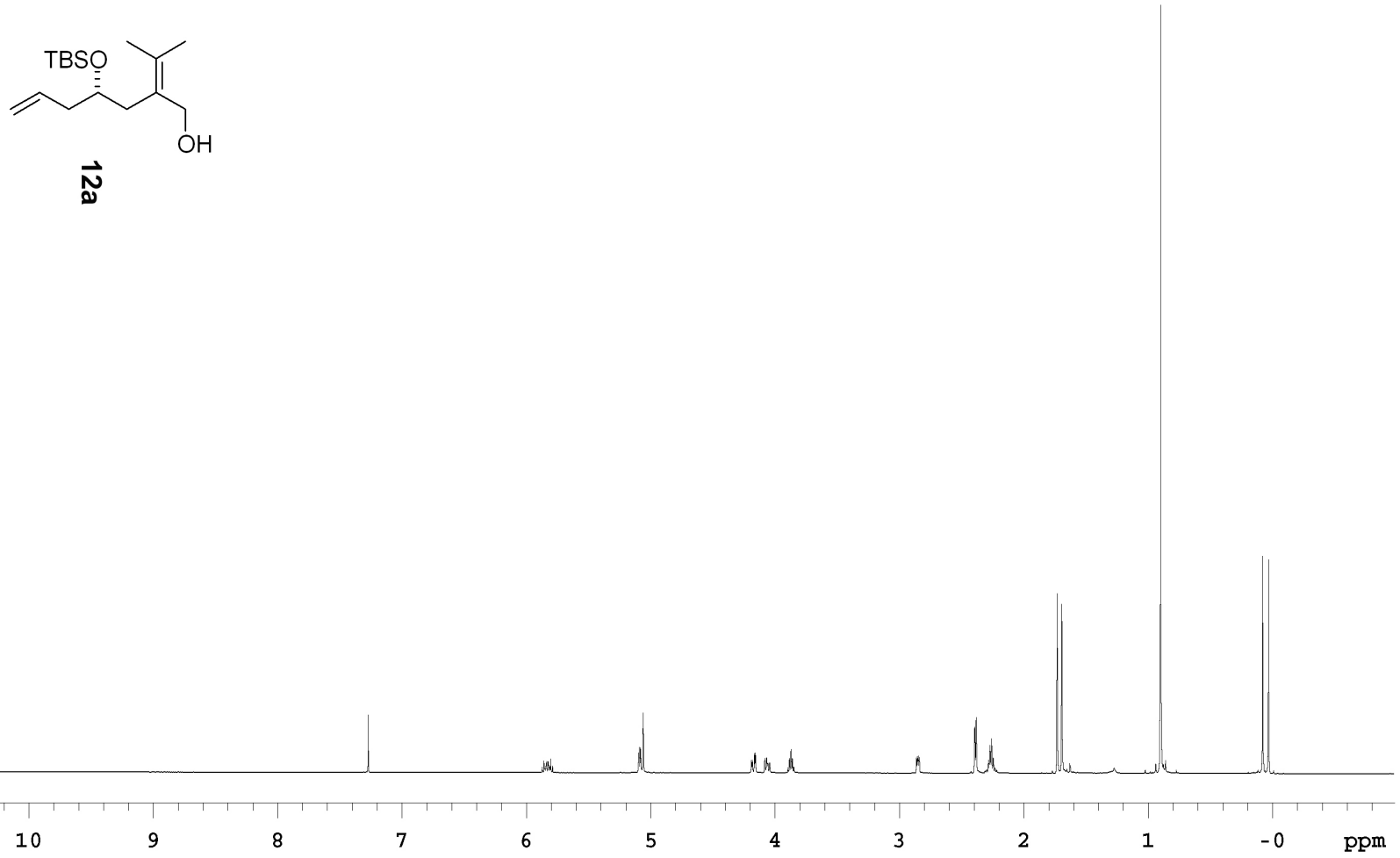
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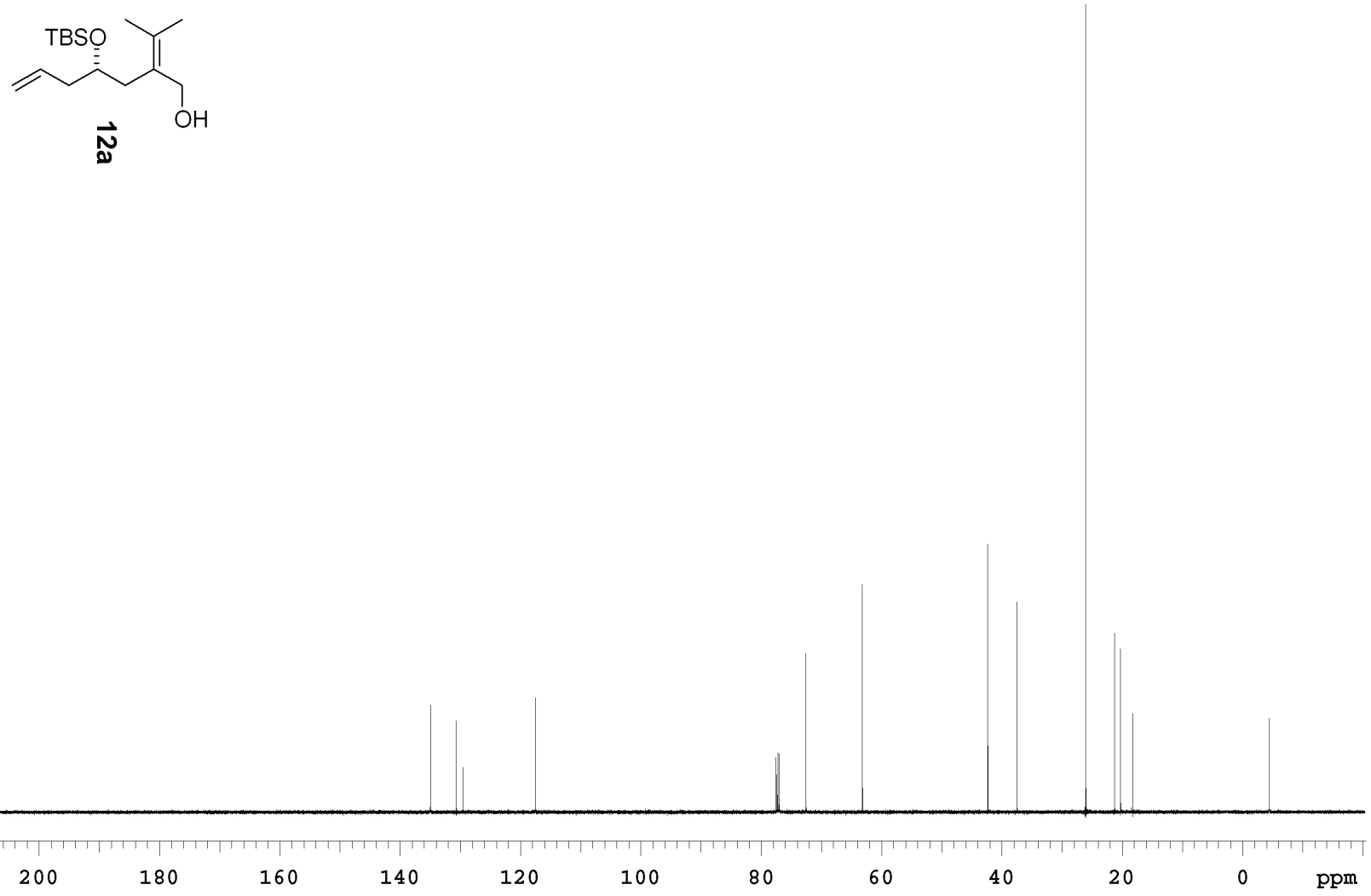
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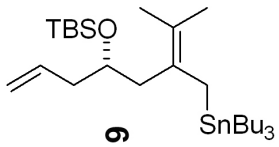


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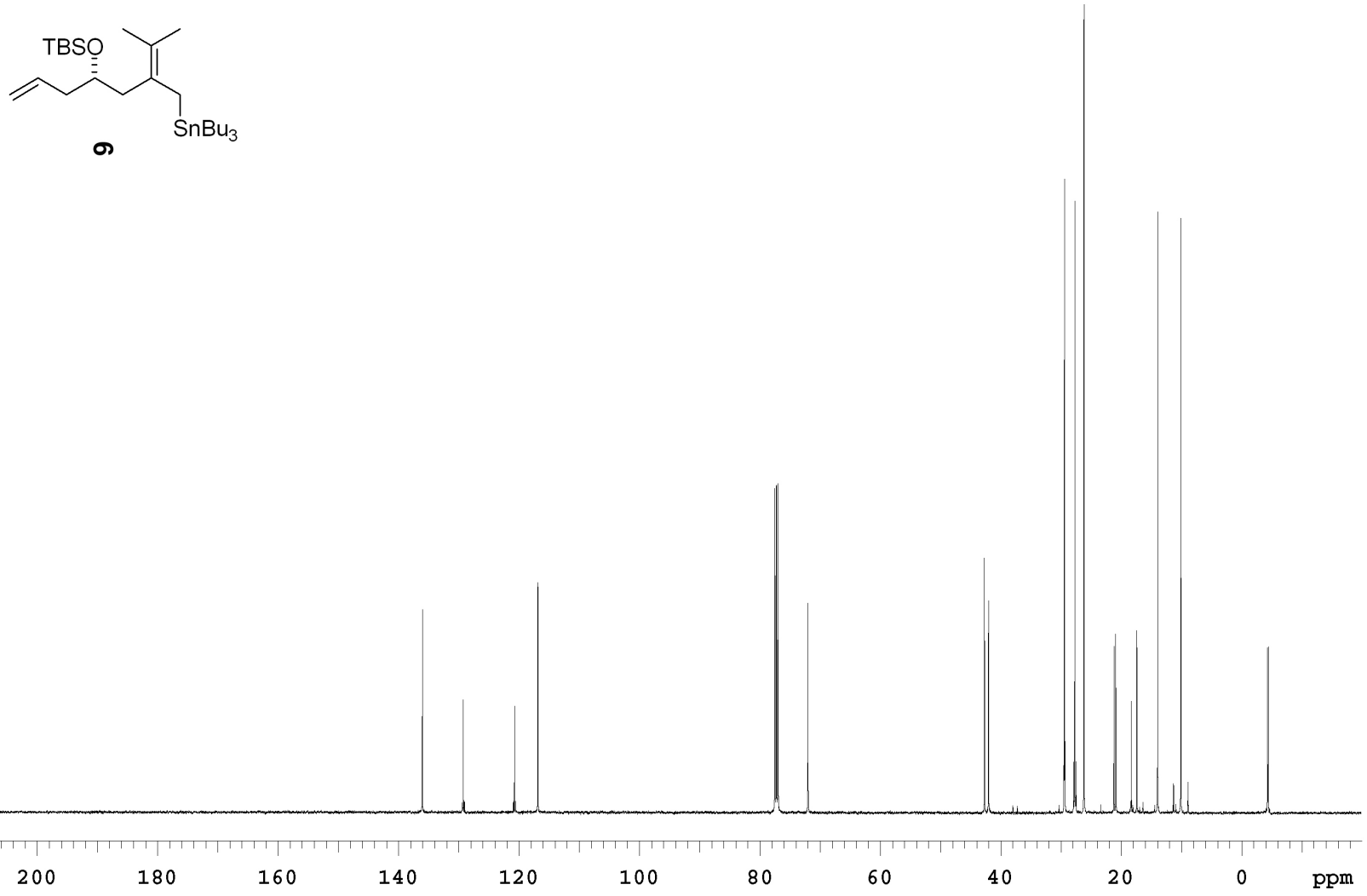
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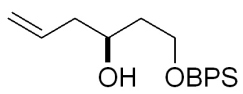


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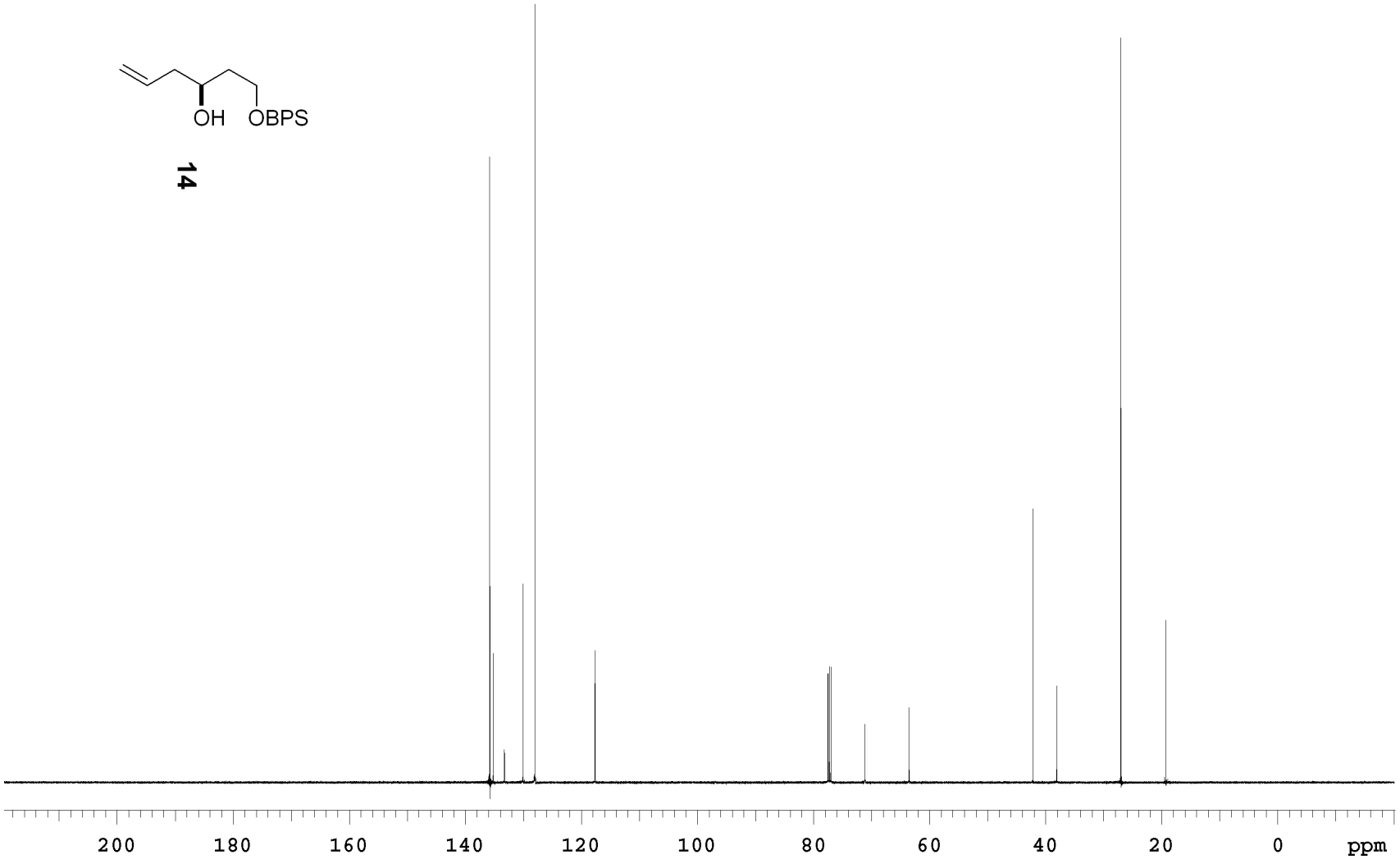
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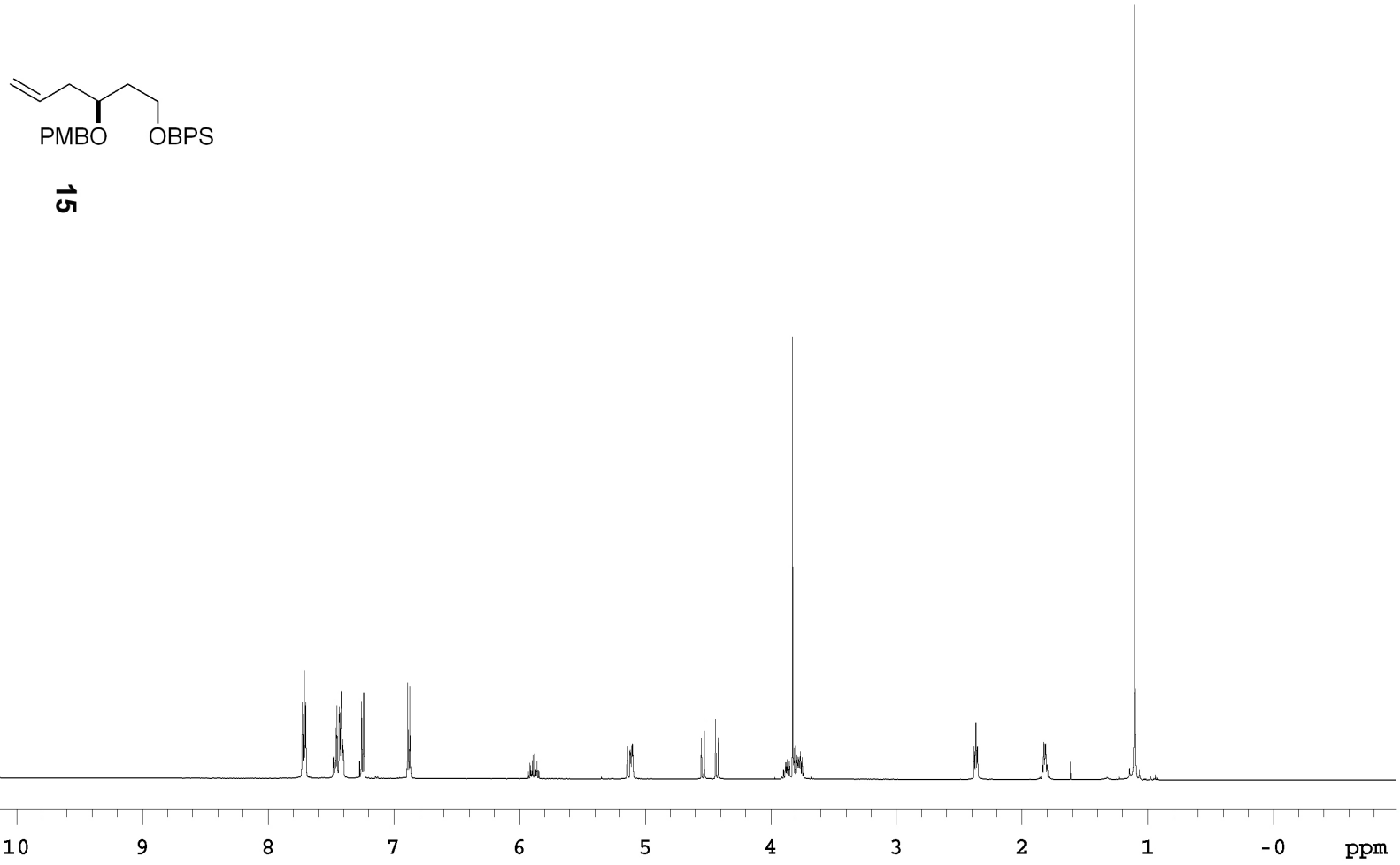
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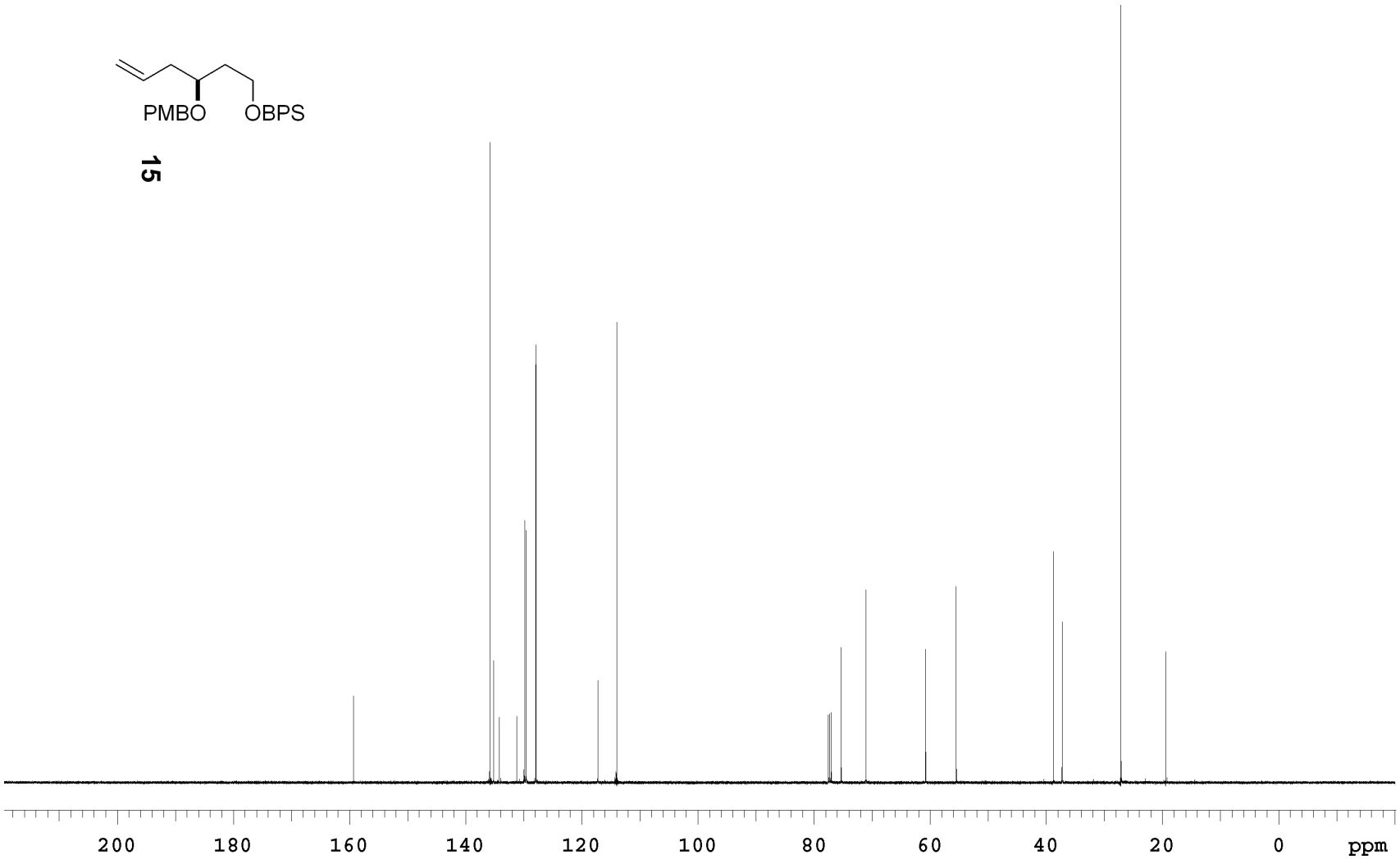
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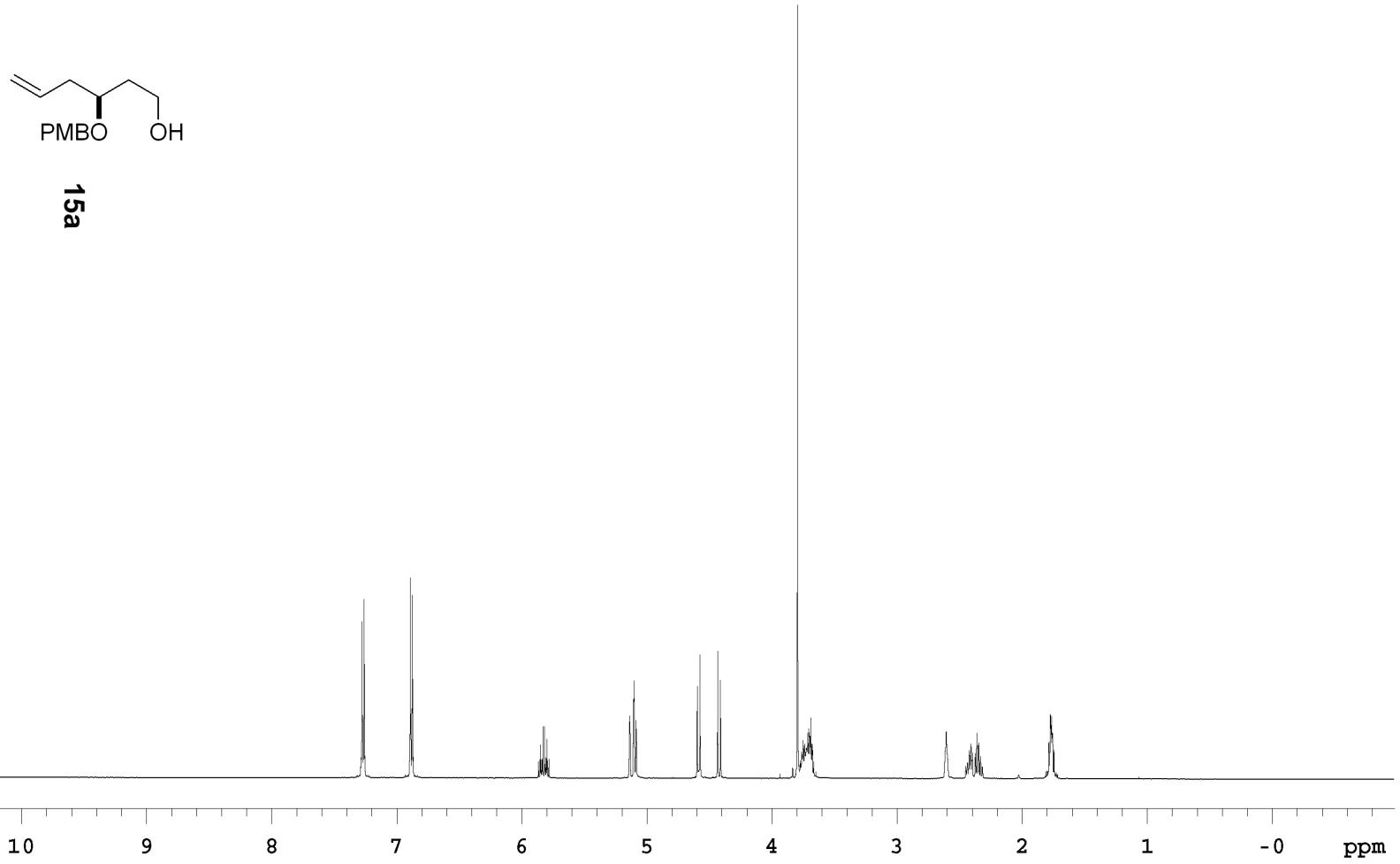
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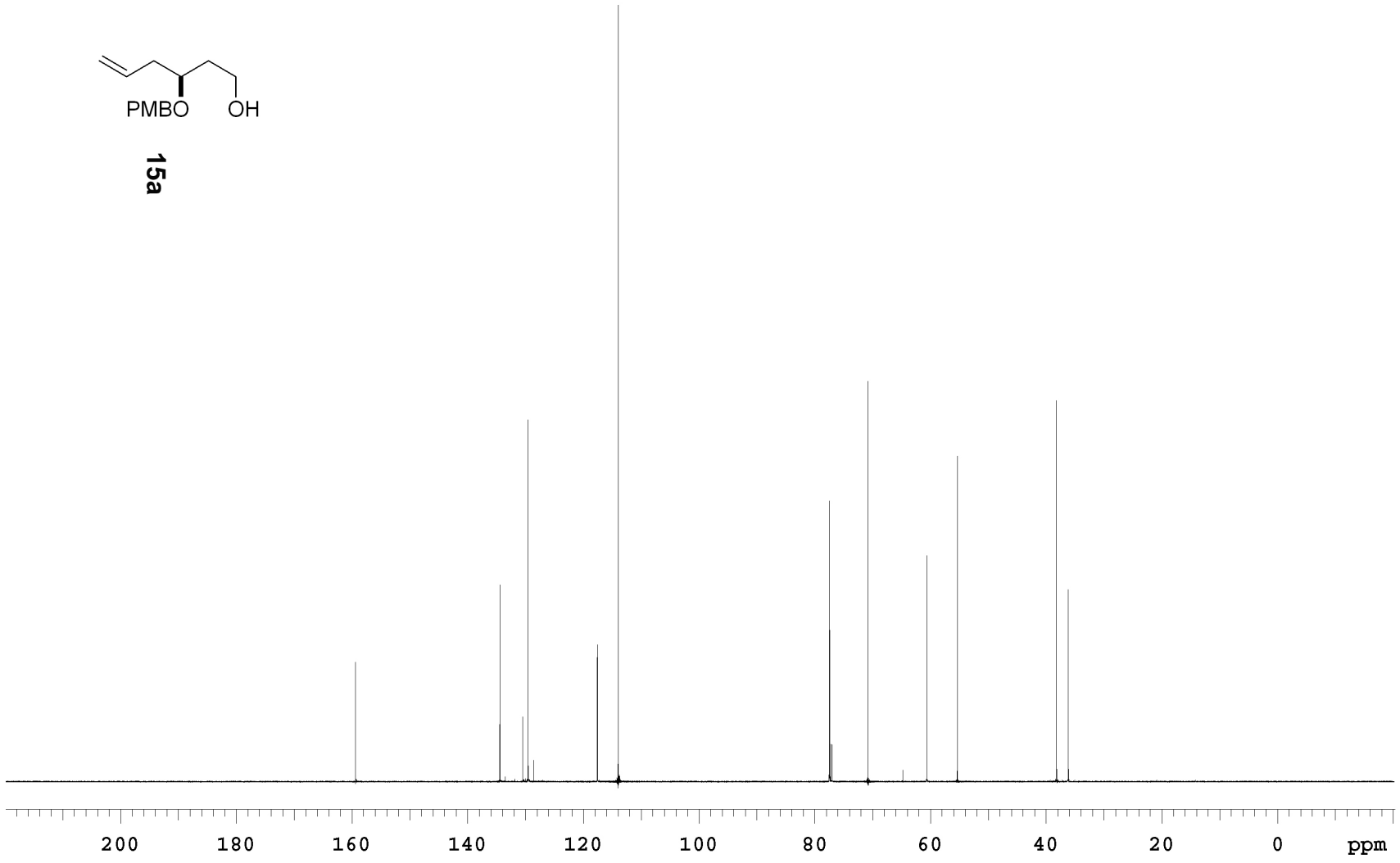
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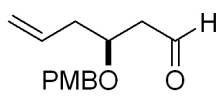


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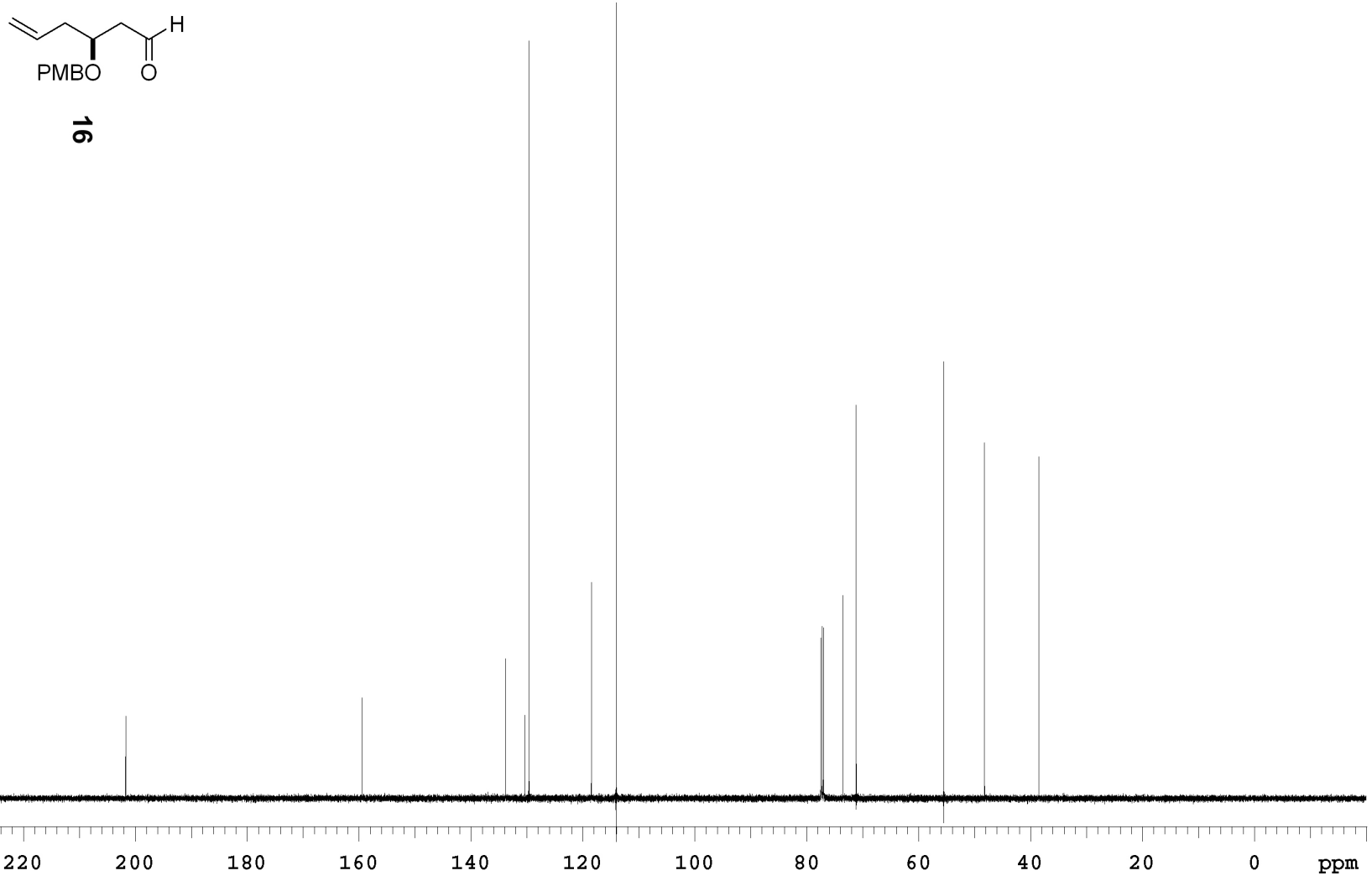
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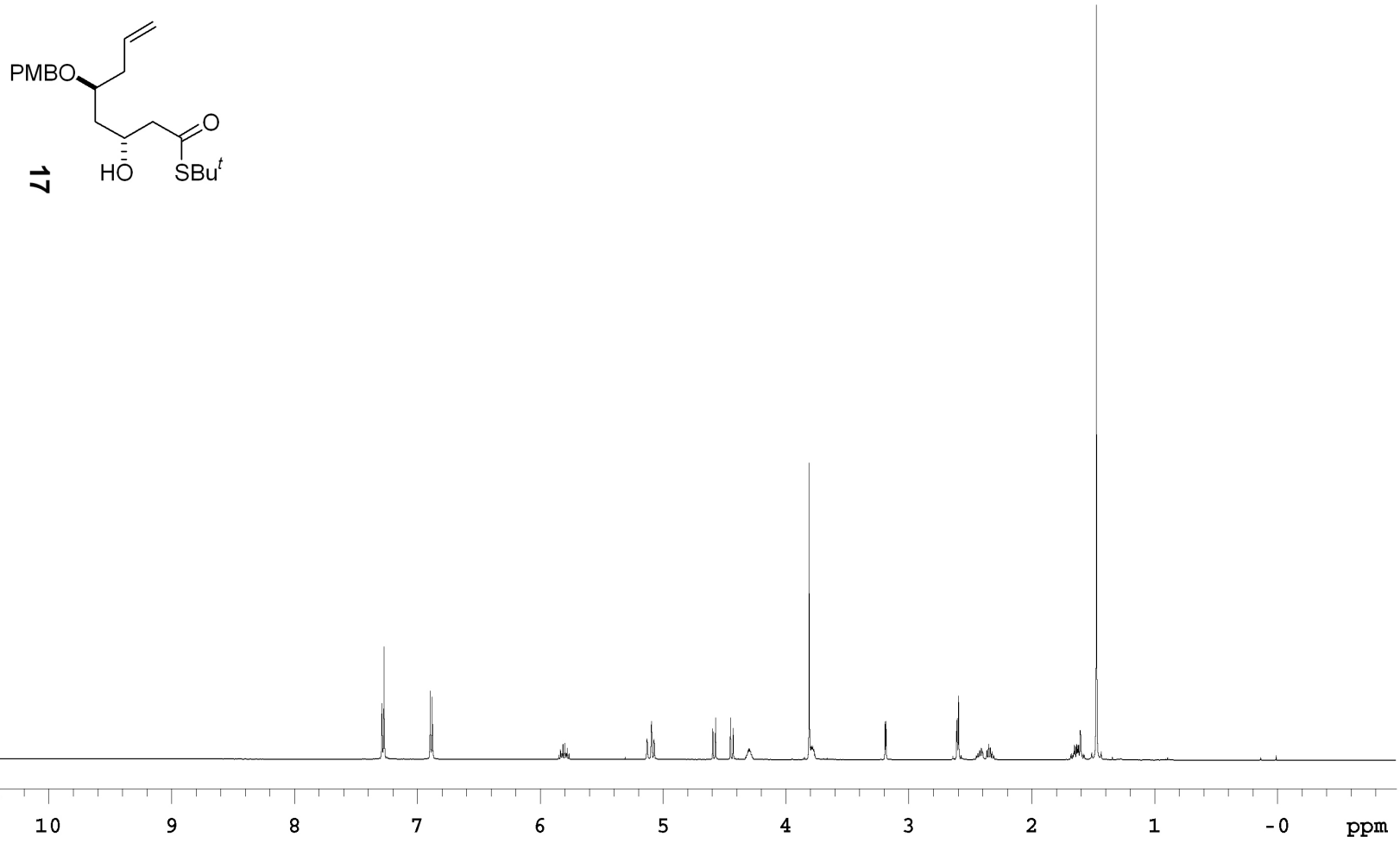
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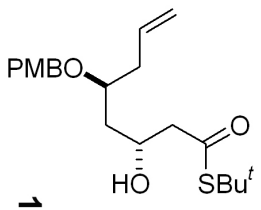


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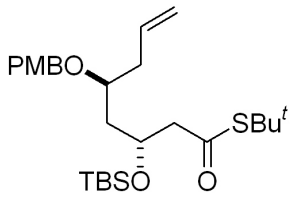


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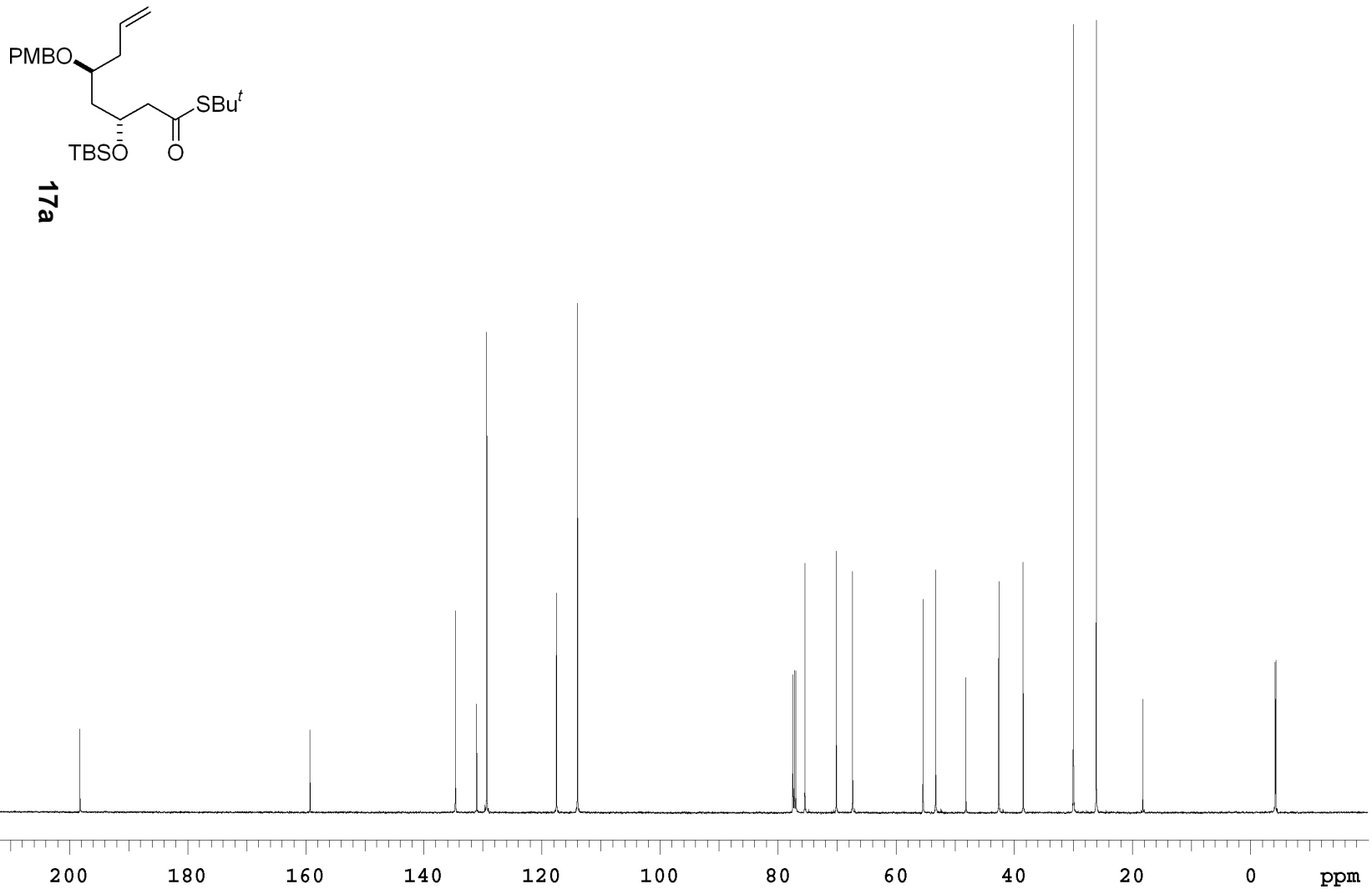
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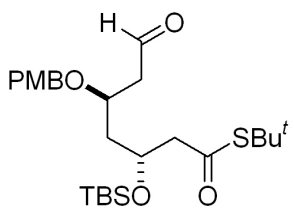


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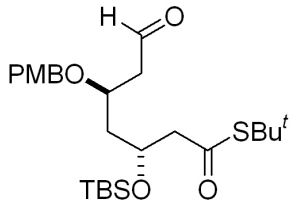


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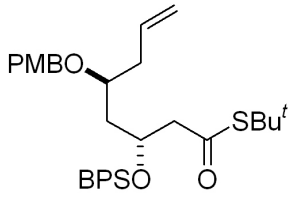


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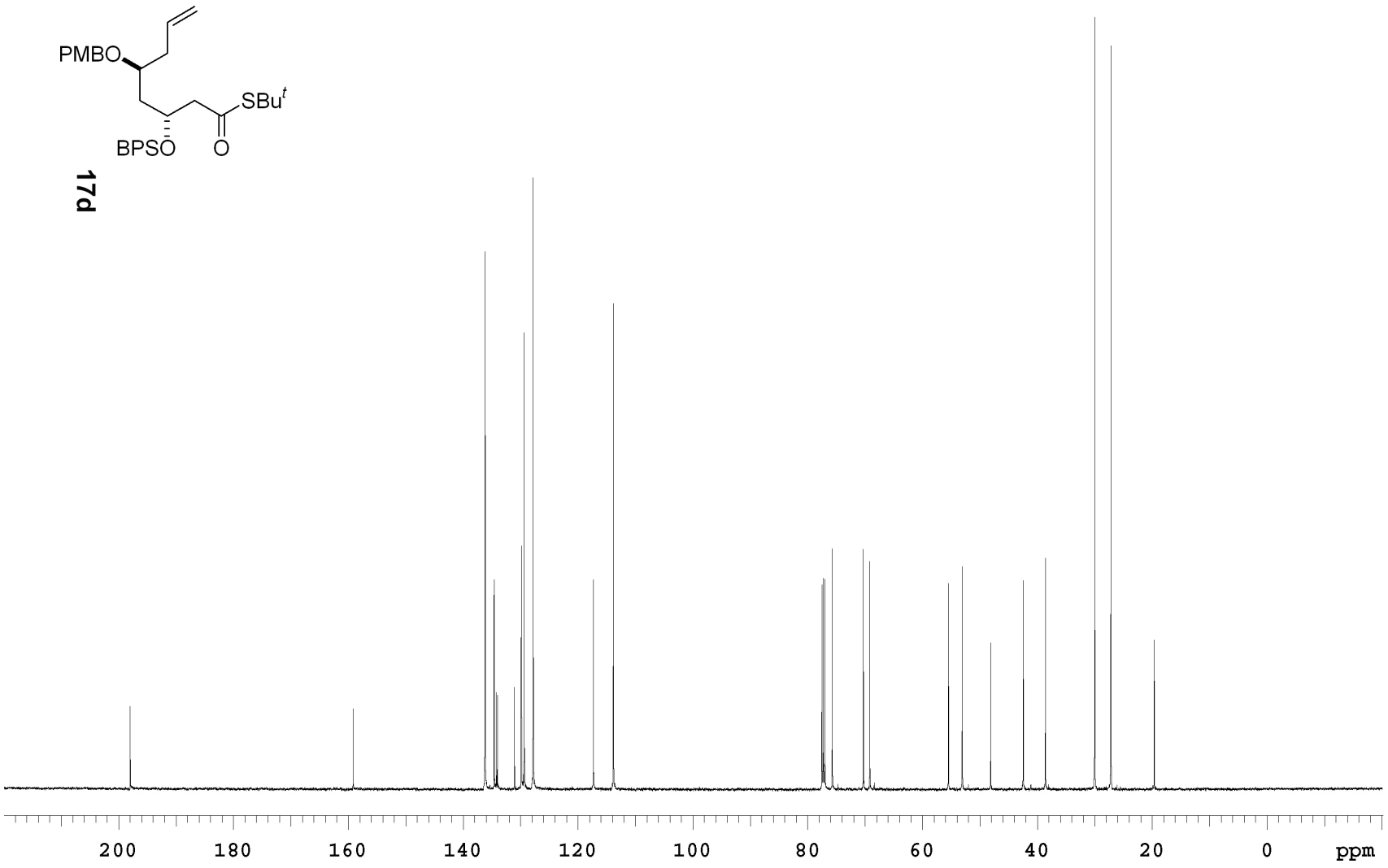
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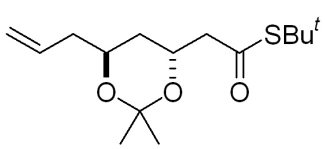


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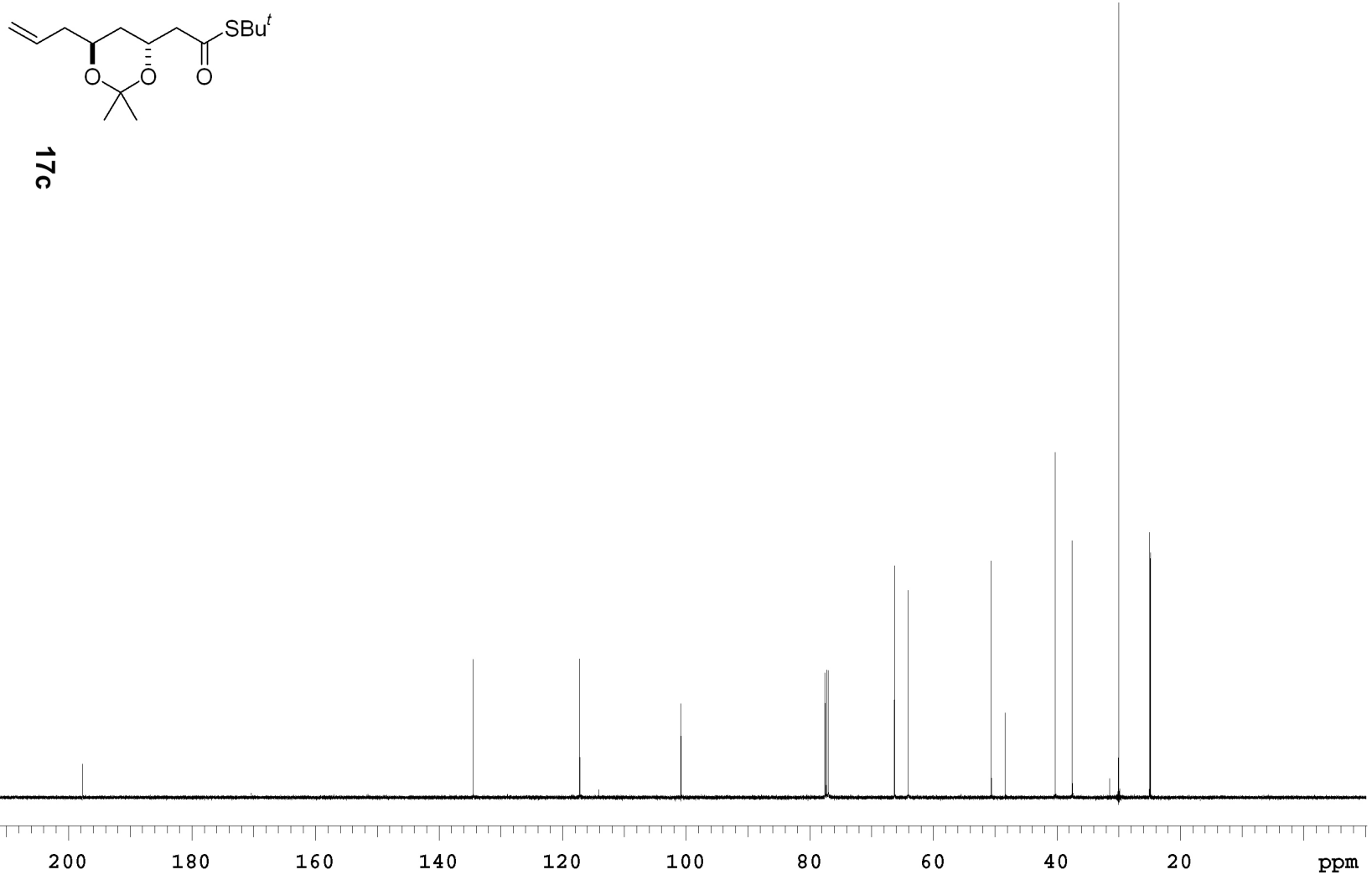
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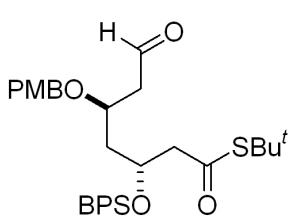


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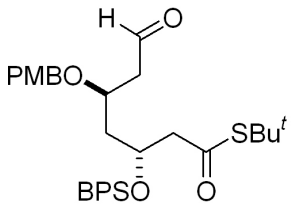
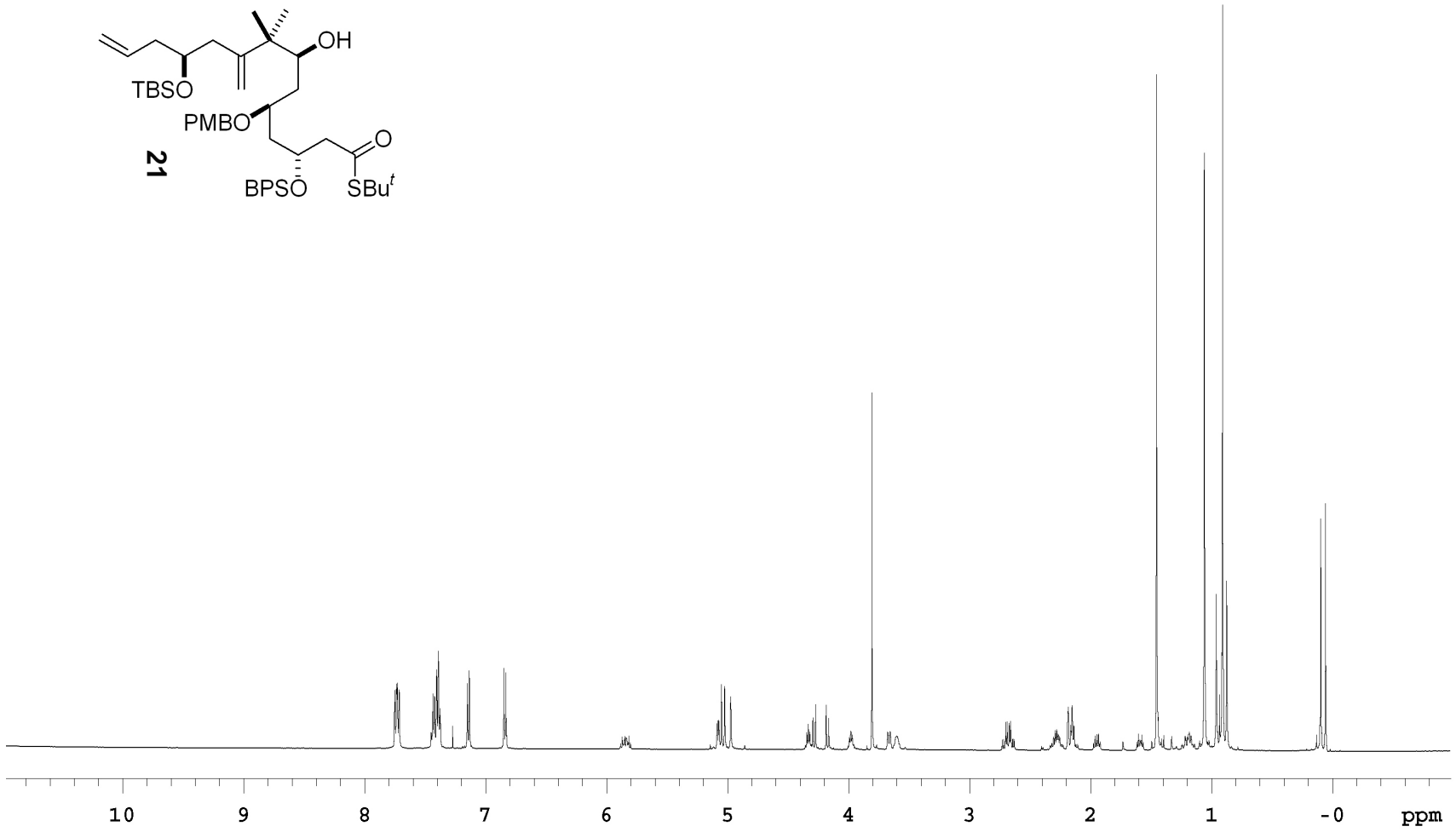
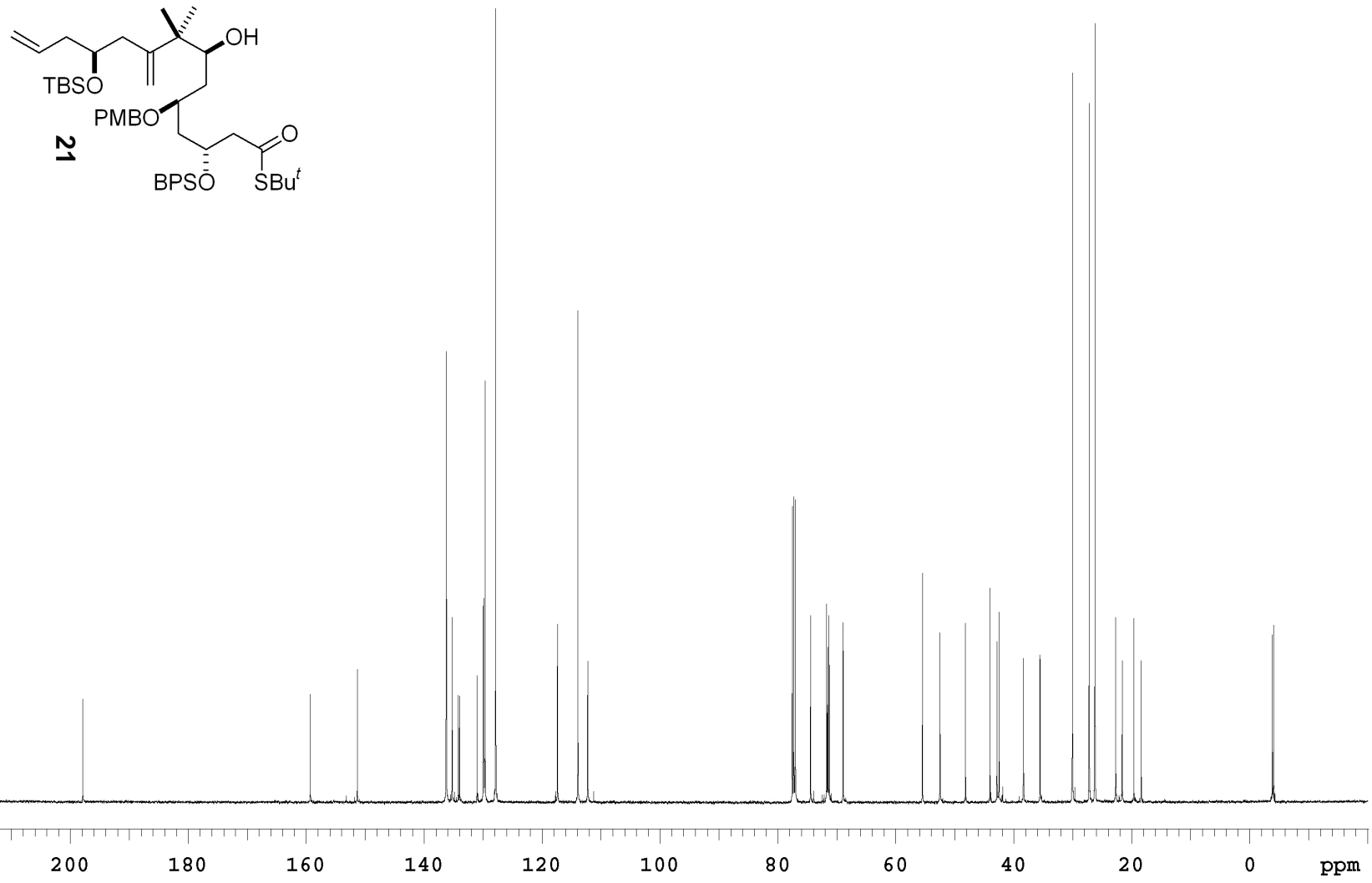
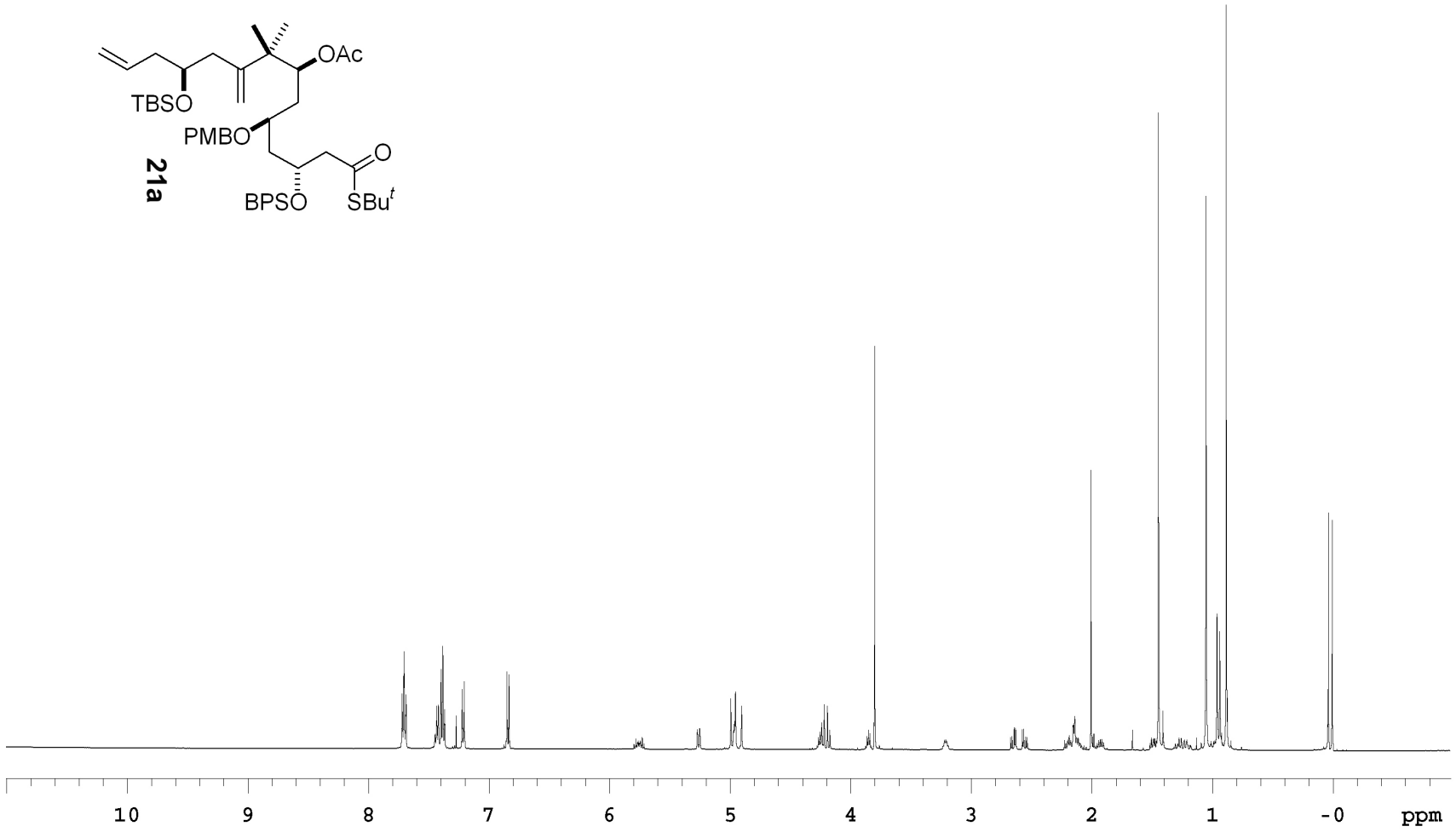
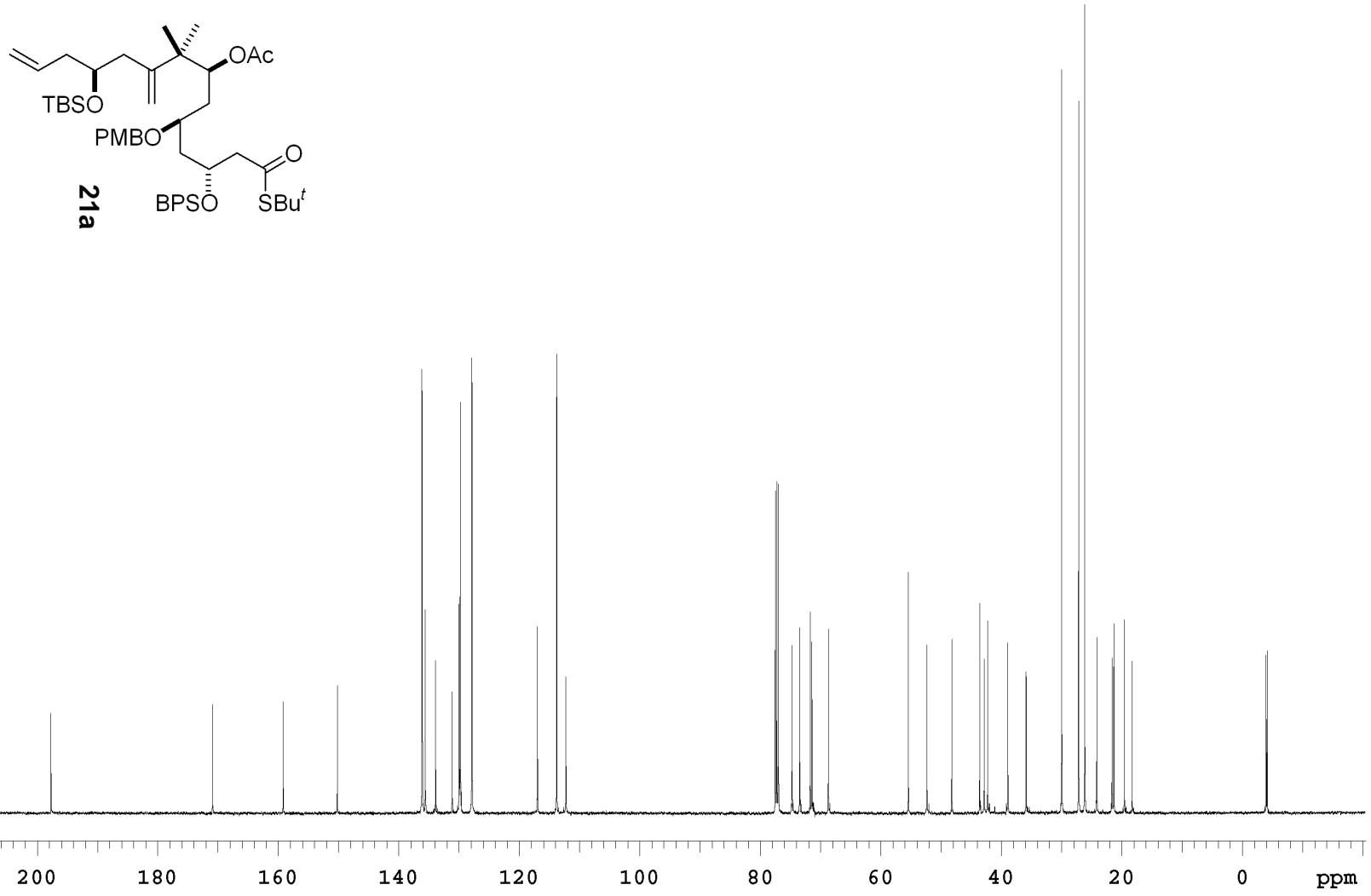


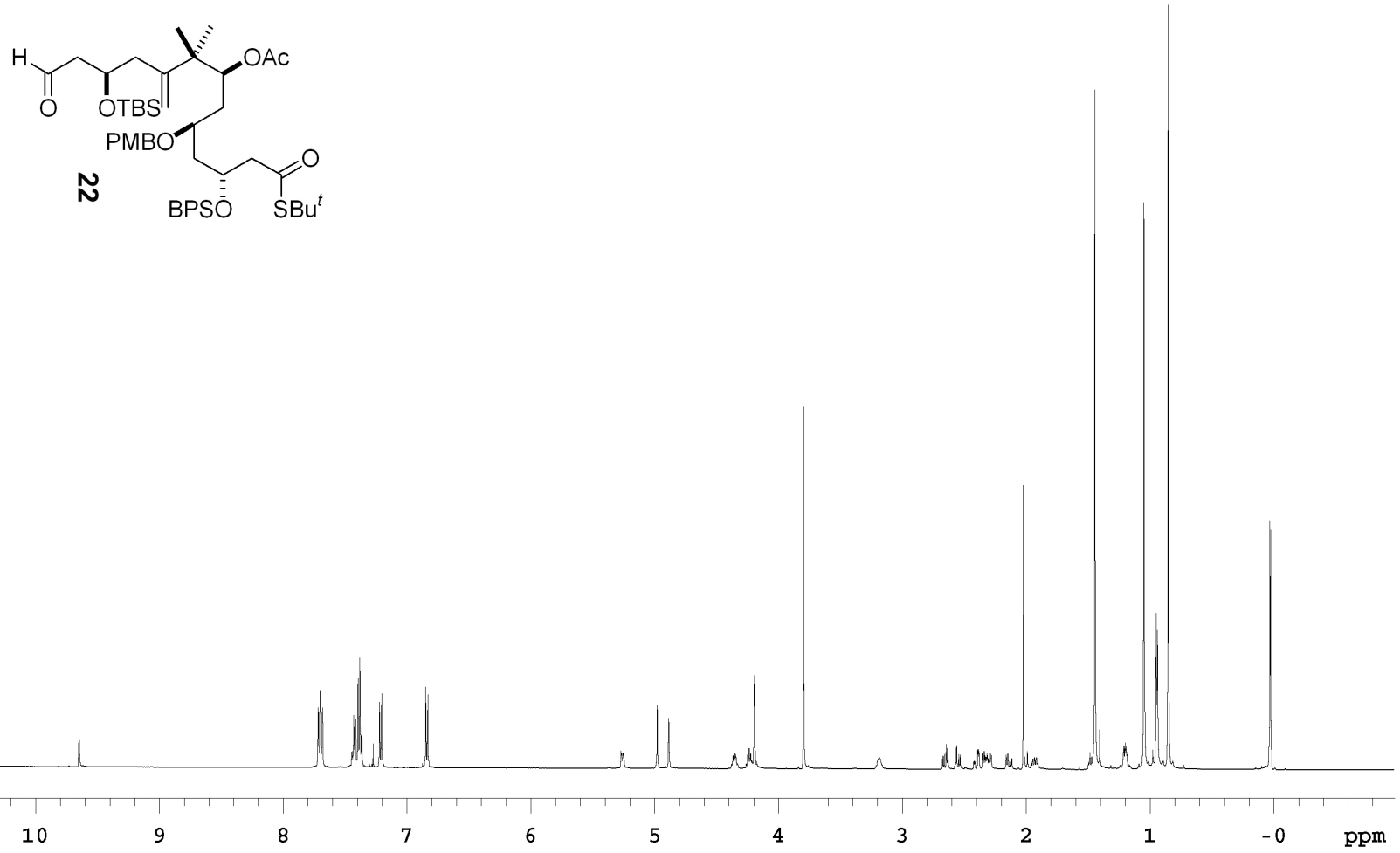

**19**

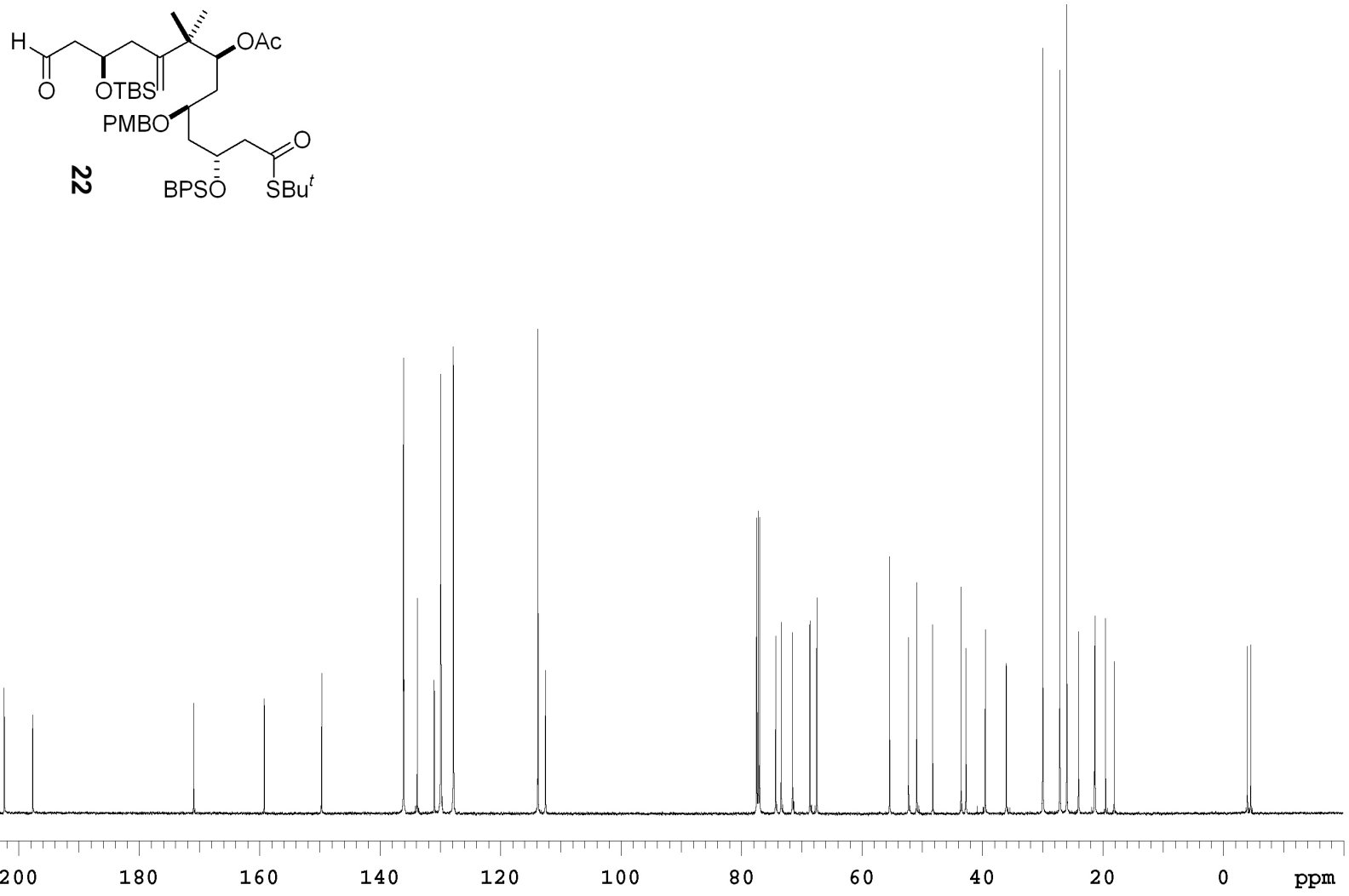

OH
TBSO
PMBO
O
21
BPSO
SBu$^t$
10
9
8
7
6
5
4
3
2
1
-0
ppm

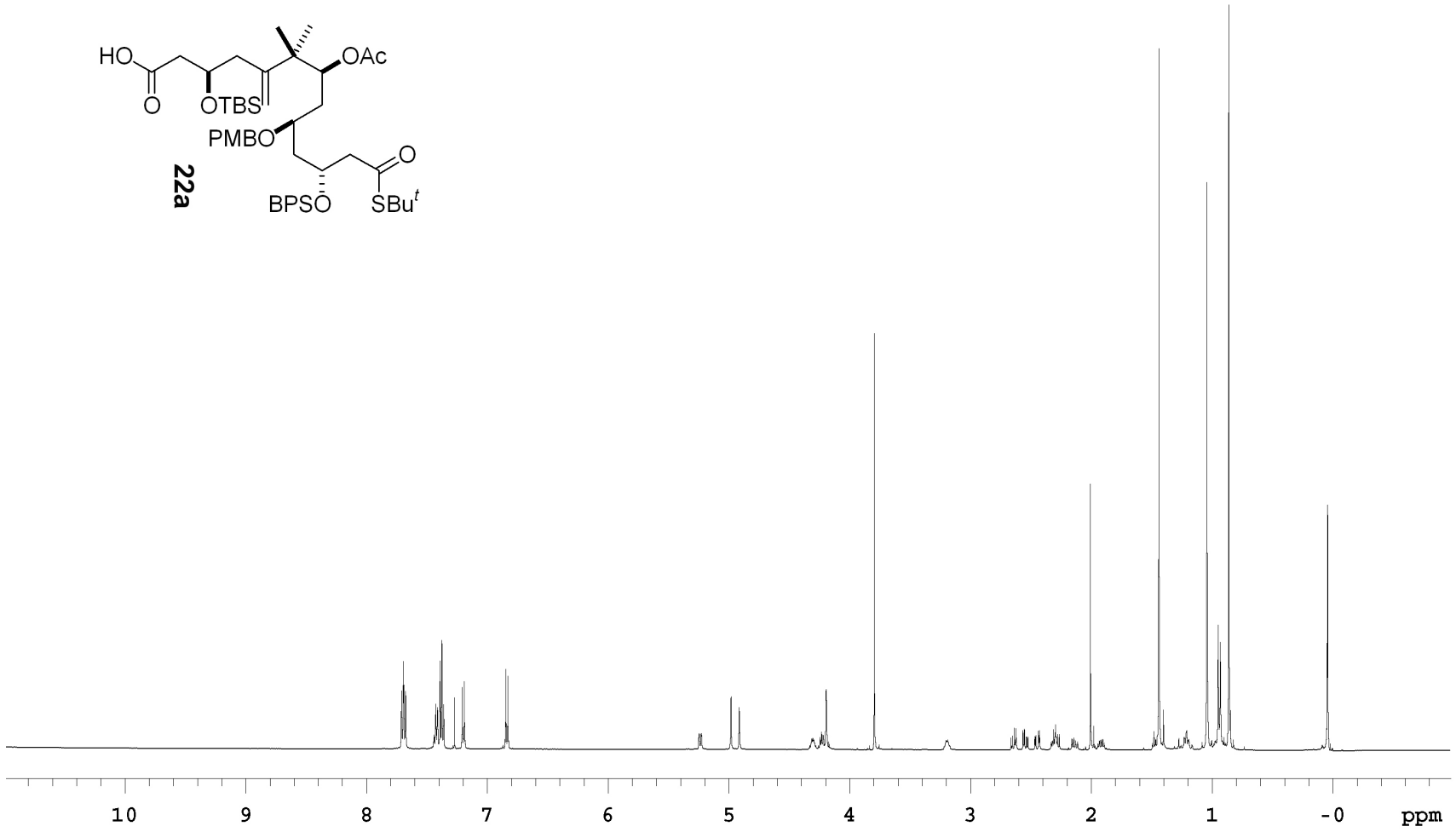

OH
TBSO
PMBO
O
21
BPSO
SBu$^t$
200
180
160
140
120
100
80
60
40
20
0
ppm

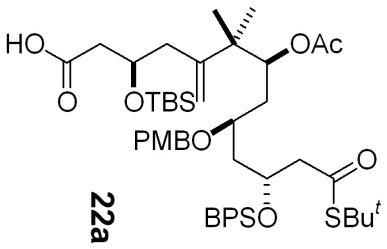

OAc
TBSO
PMBO
O
BPSO
SBu$^t$
21a
10
9
8
7
6
5
4
3
2
1
-0
ppm


OAc
TBSO
PMBO
O
BPSO
SBu$^t$
21a
200
180
160
140
120
100
80
60
40
20
0
ppm


H
O
OTBS
OAc
PMBO
O
BPSO
SBu$^t$
22
10
9
8
7
6
5
4
3
2
1
-0
ppm

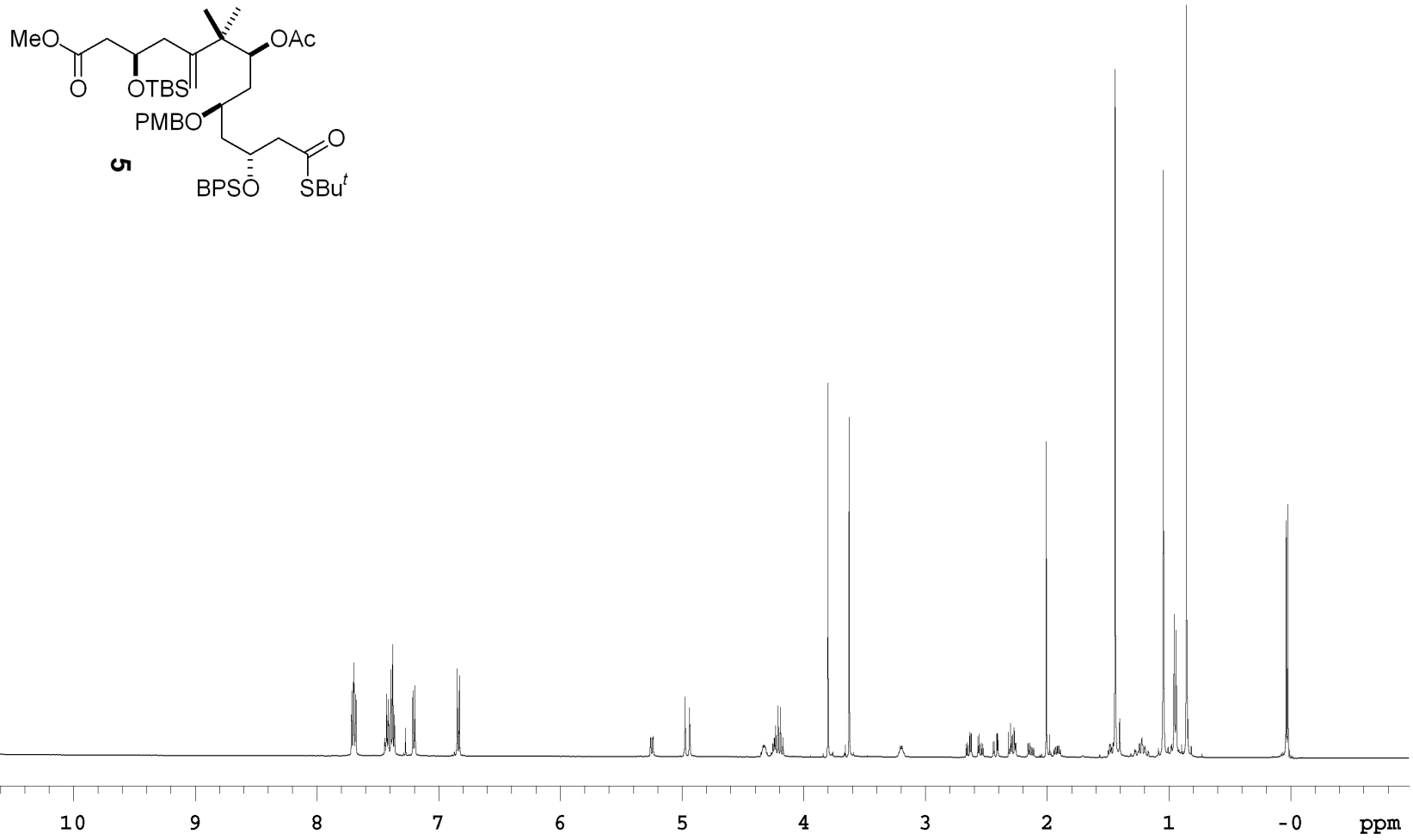

H
O
OTBS
OAc
PMBO
O
BPSO
SBu$^t$
22
200
180
160
140
120
100
80
60
40
20
0
ppm

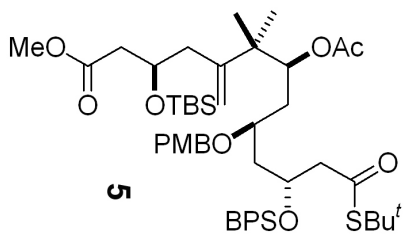

HO
O
OTBS
OAc
PMBO
O
BPSO
SBu$^t$
22a
10
9
8
7
6
5
4
3
2
1
-0
ppm


HO
O
OTBS
OAc
PMBO
O
BPSO
SBu$^t$

**22a**

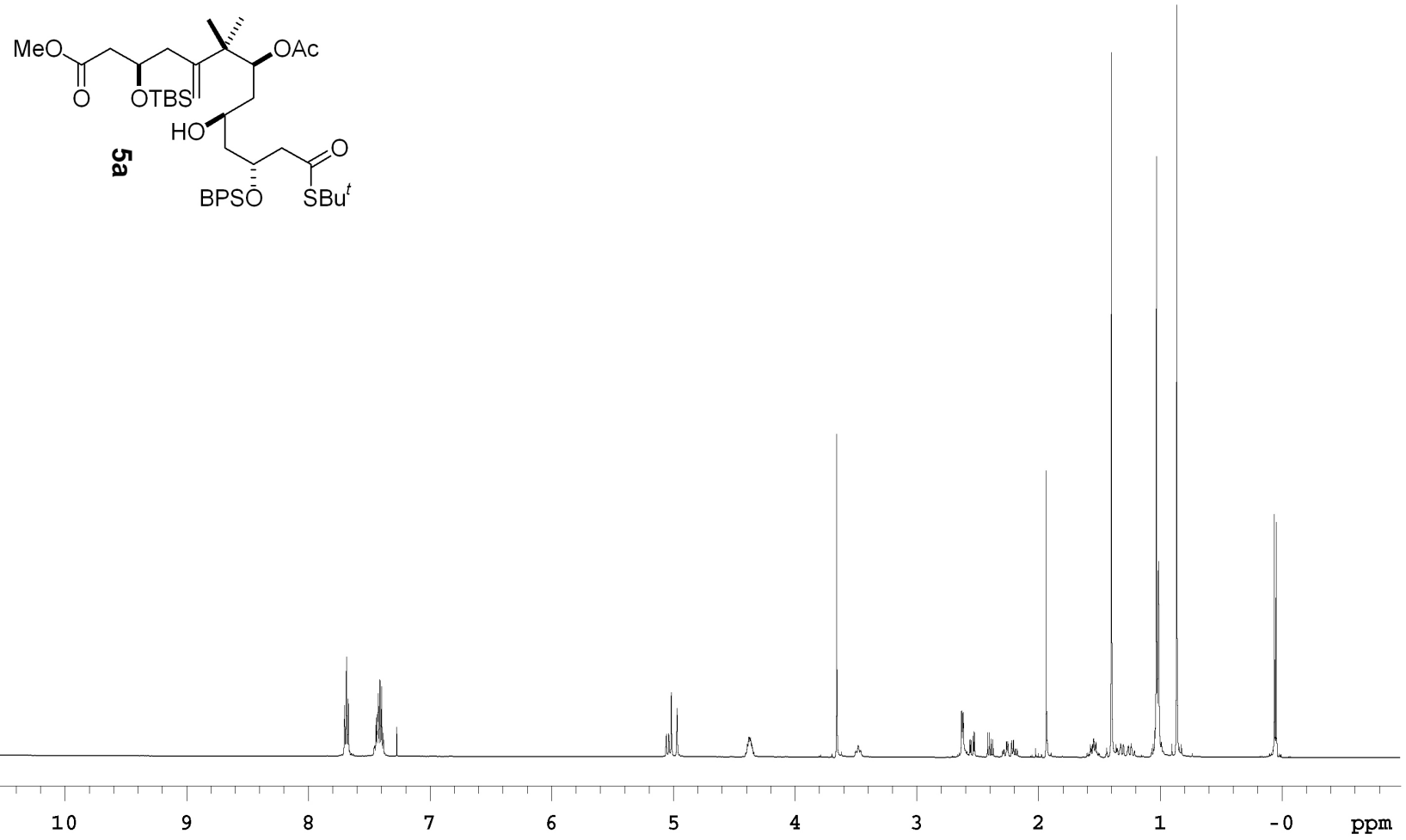

200
180
160
140
120
100
80
60
40
20
0
ppm

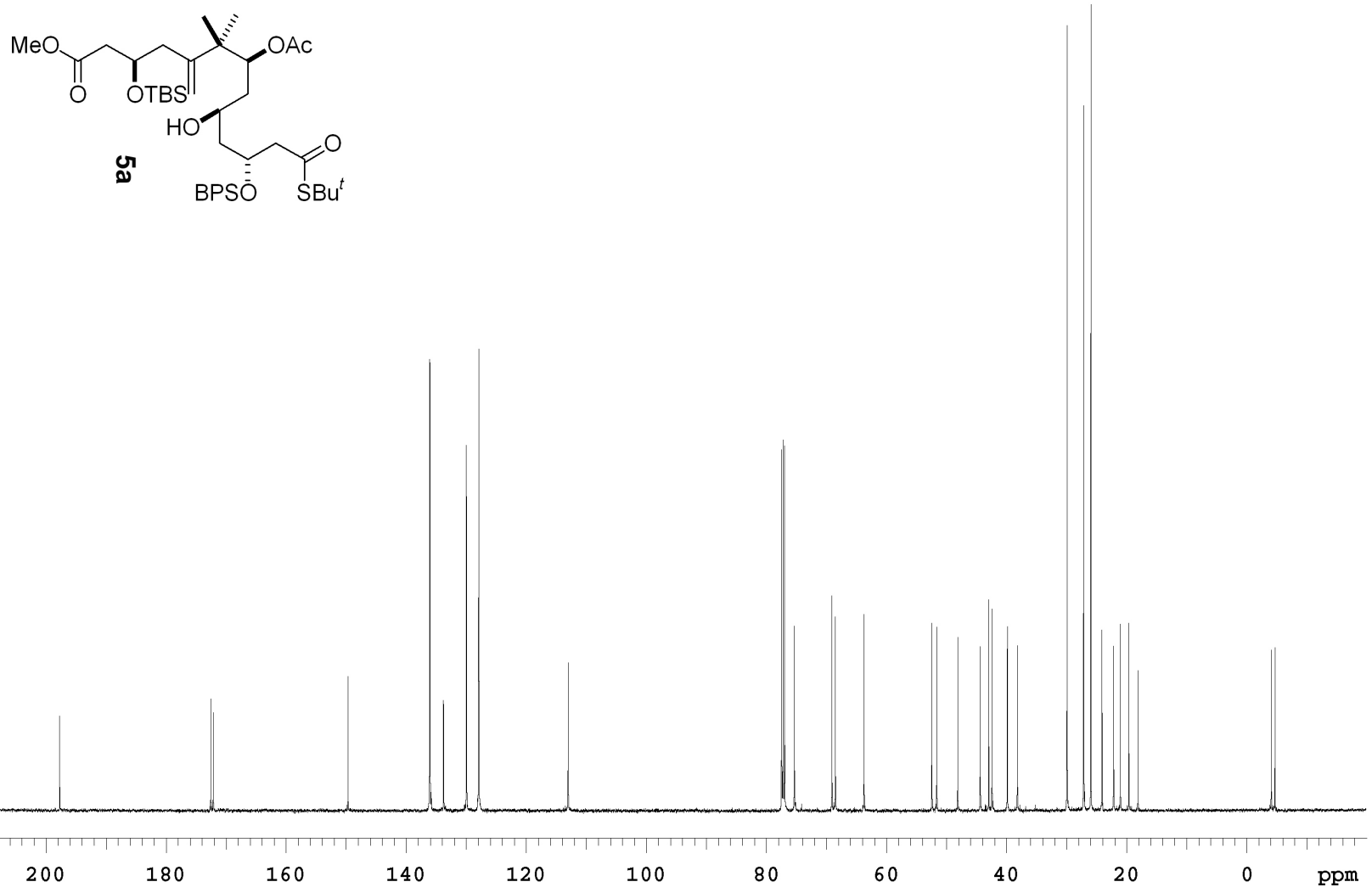

MeO
O
OTBS
OAc
PMBO
O
BPSO
SBu$^t$
5
10
9
8
7
6
5
4
3
2
1
-0
ppm

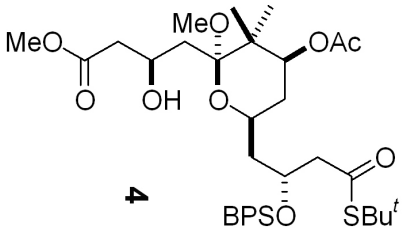

MeO
O
OTBS
OAc
PMBO
O
BPSO
SBu$^t$

**5**

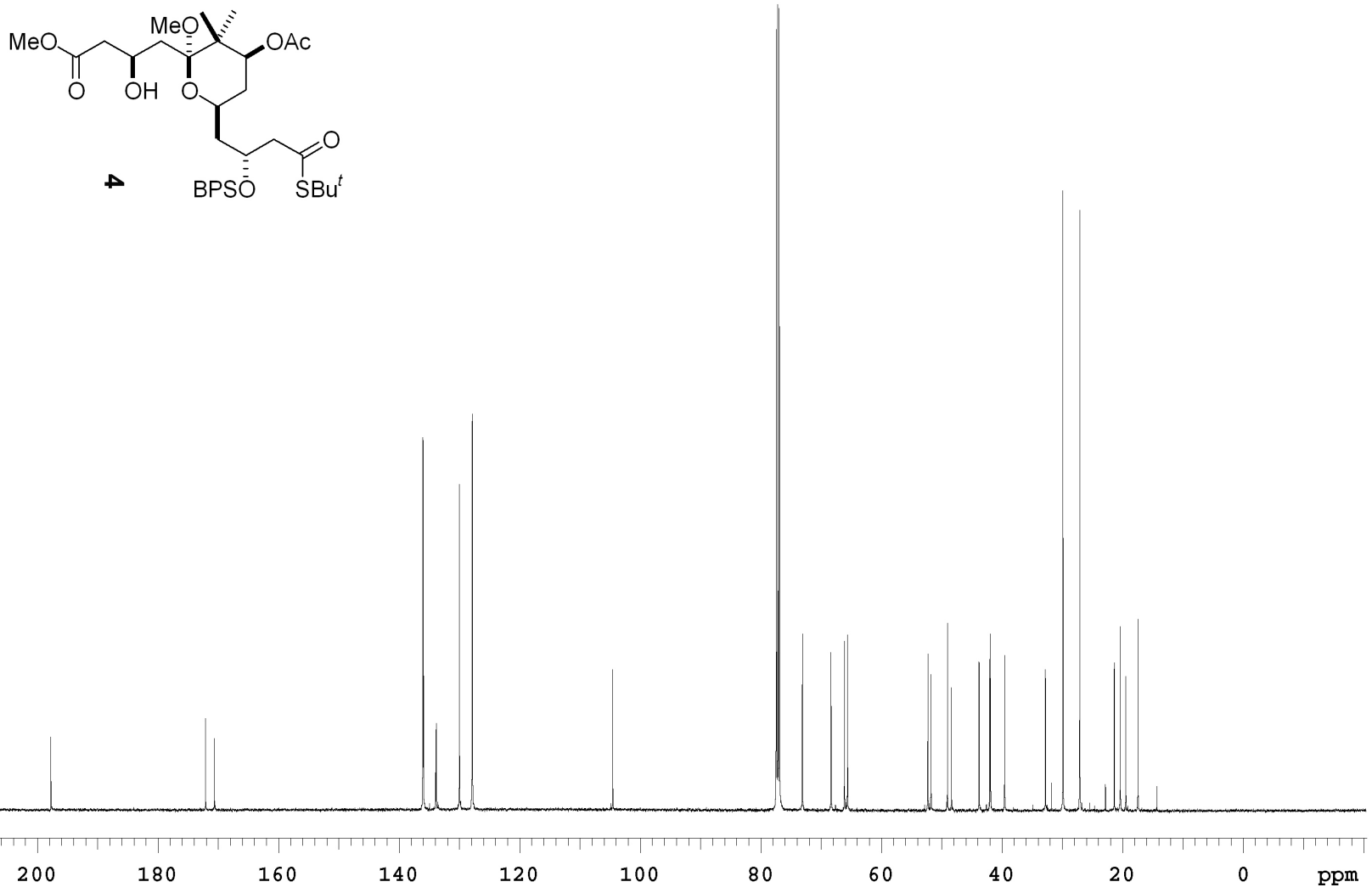

200
180
160
140
120
100
80
60
40
20
0
ppm


MeO
O
OTBS
HO
OAc
BPSO
O
SBu$^t$
5a
10
9
8
7
6
5
4
3
2
1
-0
ppm


MeO
O
OTBS
OAc
HO
O
BPSO
SBu$^t$
5a
200
180
160
140
120
100
80
60
40
20
0
ppm




**4**


MeO
MeO
OAc
O
OH
O
O
BPSO
SBu$^t$
4
200
180
160
140
120
100
80
60
40
20
0
ppm