Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Approach to the Synthesis of the C^1-C^{11} and C^{14}-C^{18} portion of Leucascandrolide A[a]

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[a] This manuscript is dedicated to Barry M. Trost on the occasion of this 75th birthday.

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Supporting Information

Section A: General Information

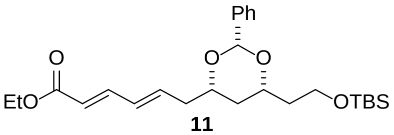
Section B: Experimental Procedures

Section C: ^{1}H and ^{13}C NMR Spectra

Section A: General Information

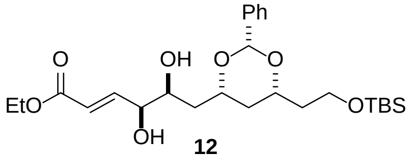
Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded on Varian VXR-300 (300 MHz) or Varian VXR-500 (500 MHz) spectrometers. Chemical shifts are reported relative to internal tetramethylsilane (δ 0.00 ppm) or residual solvent signal. Infrared (IR) spectra were obtained on a Prospect MIDAC FT-IR spectrometer. Optical rotations were measured with a Jasco DIP-370 digital polarimeter in the solvent specified. Flash column chromatography was performed on ICN reagent 60 (60-200 mesh) silica gel. Analytical thin-layer chromatography was performed with precoated glass-backed plates (Whatman K6F 60Å, F_{254}) and visualized by quenching of fluorescence and by charring after treatment with *p*-anisaldehyde or potassium permanganate stain. R_f values are obtained by elution in the stated solvent ratios (v/v). Ether and THF were distilled from benzophenone and sodium metal. Methylene chloride and triethylamine were distilled from calcium hydride. Unless otherwise noted, solvents were reagent grade and were used without purification. Commercial reagents were used without purification unless otherwise noted.

Section B: Experimental Procedures



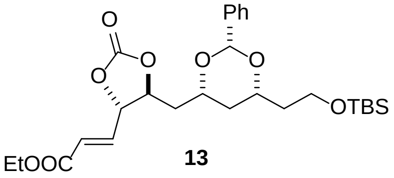
11

Ethyl (2E,4E)-6-((2S,4S,6R)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-phenyl-1,3-dioxan-4-yl)hexa-2,4-dienoate (11): To phosphonate **10** (74 mg, 0.33 mmol) in 2 mL of THF was added 14 mg (0.33 mmol) $LiOH\cdot H_2O$ and 320 mg of 4 Å molecular sieves. This mixture was heated at reflux for 30 min. before 108 mg (0.30 mmol) of aldehyde **9** dissolved in 1 mL of THF was added. This mixture was heated at reflux for 6 h and then filtered through a plug of celite. The solvent was removed under reduced pressure and the crude product was purified by silica gel chromatography to produce dienoate **11** (92 mg) in 68% yield as a clear oil: $[\alpha]_D$ 1.5° (*c* 1.3, CH_2Cl_2) IR (neat) 3035, 2954, 2857, 1644, 1620, 1470, 1462, 1452, 1428, 1402, 1391, 1367, 1345, 1303, 1256, 1221, 1176, 1133, 1097, 1028 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.50 (m, 2H), 7.36 (m, 3H), 7.27 (dd, *J* = 15.5, 10.5 Hz, 1H), 6.27 (dd, *J* = 15,10 Hz, 1H), 6.20 (ddd, *J* = 15, 6.5, 6.5 Hz, 1H), 5.82 (d, *J* = 15.5 Hz, 1H), 5.53 (s, 1H), 4.21 (q, *J* = 7 Hz, 2H), 4.02 (dddd, *J* = 11, 8, 4, 2.5 Hz, 1H), 3.94 (dddd, *J* = 11.5, 6.5, 6.5, 2.5 Hz, 1H), 3.83 (ddd, *J* = 10, 8.5, 5 Hz, 1H), 3.73 (ddd, *J* = 10.5, 5.5, 5.5 Hz, 1H), 2.56 (ddd, *J* = 14.5, 7, 7 Hz, 1H), 2.44 (ddd, *J* = 13, 6.5, 6.5 Hz, 1H), 1.84 (dddd, *J* = 13, 8.5, 5, 5 Hz, 1H), 1.75 (dddd, *J* = 14, 10, 5.5, 5 Hz, 1H), 1.63 (ddd, *J* = 13, 2, 2 Hz, 1H), 1.46 (ddd, *J* = 13, 11, 11 Hz, 1H), 1.30 (t, *J* = 7 Hz, 3H), 0.90 (s, 9H), 0.06 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 196.0, 167.0, 144.3, 138.9, 138.6, 130.6, 128.5, 128.0, 125.9, 120.0, 100.4, 75.8, 73.3, 60.1, 58.7, 39.3, 38.8, 36.6, 25.9, 14.2, -5.4; HRMS (FAB) calcd for $[C_{26}H_{40}O_5Si + H]^+$: 461.2723 Found: 461.2726; Anal. Calcd for C, 67.79; H, 8.75; Found: C, 67.81; H, 9.01.



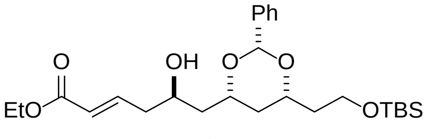
12

Ethyl (4S,5S,E)-6-((2R,4S,6R)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-phenyl-1,3-dioxan-4-yl)-4,5-dihydroxyhex-2-enoate (**12**): Into a 25 mL round bottom flask containing 74 mg (0.16 mmol) of dienoate **11** was added 2 mL of *t*-BuOH, 2 mL of water, $K_3Fe(CN)_6$ (159 mg, 0.482 mmol), K_2CO_3 (67 mg, 0.482 mmol), $MeSO_2NH_2$ (15 mg, 0.16 mmol) and $(DHQ)_2$-PHAL (8 mg, 10 μmol). The mixture was stirred at room temperature for 15 minutes and then cooled to 0°C. To this solution was added OsO_4 (2 mg, 8 μmol) and the reaction was stirred vigorously at 0°C overnight. The reaction was quenched with saturated aqueous sodium sulfite (4 mL) at room temperature. Ethyl acetate (5 mL) was added to the reaction mixture, and after separation of the layers, the aqueous phase was further extracted with the organic solvent (2 x 10 mL). The combined organic layers were washed with 2N KOH (10 mL) to remove the methanesulfonamide, and brine, and then dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel afforded 56 mg (71% yield) of **12** as a clear oil: $R_f = 0.3$ (3:2 hexanes:EtOAc), $[\alpha]_D$ 1.8° (*c* 1.14, CH_2Cl_2); IR (neat) 3435, 3068, 3037, 2955, 2856, 1722, 1714, 1660, 1548, 1512, 1495, 1470, 1454, 1392, 1369, 1344, 1252, 1176, 1100, 1027 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.46 (m, 2H), 7.36 (m, 3H), 6.94 (dd, *J* = 15.5, 5 Hz, 1H), 6.14 (dd, *J* = 15.5, 1.5 Hz, 1H), 5.53 (s, 1H), 4.20 (q, *J* = 7 Hz, 2H), 4.19 (m, 2H), 4.06 (m, 1H), 3.98 (ddd, *J* = 9, 4.5, 3 Hz, 1H), 3.83 (ddd, *J* = 10, 8.5, 5 Hz, 1H), 3.73 (ddd, *J* = 10.5, 5.5, 5.5 Hz, 1H), 1.80-1.93 (m, 3H), 1.72-1.79 (m, 1H), 1.60 (m, 2H), 1.29 (t, *J* = 7.5 Hz, 3H), 0.90 (s, 9H), 0.06 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ166.2, 146.4, 138.4, 128.8, 128.3, 126.0, 122.7, 100.8, 74.2, 74.1, 73.5, 70.5, 60.6, 58.8, 38.9, 38.5, 36.7, 26.0, 18.4, 14.2, -5.3; HRMS (FAB) calcd for [$C_{26}H_{42}O_7$ + H]$^+$: 495.2778 Found: 495.2774.



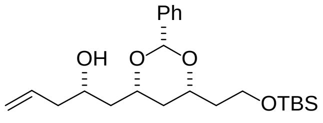
13

Ethyl (E)-3-((4S,5S)-5-(((2R,4R,6R)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-phenyl-1,3-dioxan-4-yl)methyl)-2-oxo-1,3-dioxolan-4-yl)acrylate (13): Into a 10 mL volumetric flask containing 55 mg (0.11 mmol) of diol **12** and 35 μL pyrindine was placed 1 mL of CH_2Cl_2. This mixture was cooled to 0 ºC and 17 mg of triphosgene (0.316 mmol) dissolved in 1 mL of CH_2Cl_2 was added slowly using an addition funnel. The reaction was stirred for 2 h and quenched with saturated aqueous NH_4Cl (5 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with saturated aqueous sodium bicarbonate (10 mL), brine (10 mL), and dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel afforded **13** as a clear, colorless oil (45 mg, 79%): R_f = 0.26 (4:1 hexanes:EtOAc); $[\alpha]_D$ –26.1° (*c* 1.8, CH_2Cl_2); IR (neat) 2930, 2858, 1816, 1725, 1665, 1561, 1546, 1472, 1369, 1344, 1308, 1257, 1170, 1101, 1027 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.46 (m, 2H), 7.36 (m, 3H), 6.78 (dd, *J* = 15.9, 5.4 Hz, 1H), 6.06 (dd, *J* = 15.6, 1.2 Hz, 1H), 5.52 (s, 1H), 4.91 (ddd, *J* = 6.6, 5.4, 1.2 Hz, 1H), 4.67 (ddd, *J* = 12.9, 6.3, 6.3 Hz, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 4.00-4.12 (m, 2H), 3.81 (ddd, *J* = 10.2, 8.4, 4.8 Hz, 1H), 3.72 (ddd, *J* = 10.5, 5.4, 5.4 Hz, 1H), 2.03 (d, *J* = 6 Hz, 1H), 2.01 (d, *J* = 6.9 Hz, 1H), 1.72-1.90 (m, 2H), 1.68 (ddd, *J* = 13.2, 2.4, 2.4 Hz, 1H), 1.48 (ddd, *J* = 12.9, 11.1, 11.1 Hz, 1H), 1.28 (t, *J* = 7.2 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): 164.8, 153.4, 139.0, 138.0, 128.8, 128.2, 126.0, 124.7, 100.8, 80.0, 78.2, 73.2, 72.6, 61.0, 58.5, 39.8, 38.7, 37.1, 25.9, 18.2, 14.1, -5.39, -5.44; HRMS (FAB) calcd for $[C_{27}H_{40}O_8Si + H]^+$: 521.2571 Found: 521.2608.

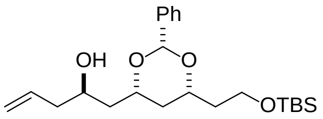


***anti*-14a**

Ethyl (R,E)-6-((2R,4S,6R)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-phenyl-1,3-dioxan-4-yl)-5-hydroxyhex-2-enoate (*anti*-14a): Into a 10 mL, round bottomed flask fitted with a condenser and maintained under nitrogen was placed 37 mg (0.071 mmol) of carbonate **13**, 0.7 mg (0.7 μmol) of $Pd_2(dba)_3 \cdot CHCl_3$, 0.5 mg (0.035 mμmol) of PPh_3, and 1 mL of THF. Triethylamine (50 μL, 0.36 mmol) and formic acid (13 μL, 0.36 mmol) were added and the mixture was allowed to reflux for three hours. The reaction was cooled to room temperature, quenched with saturated aqueous sodium bicarbonate (2 mL), and diluted with ether (4 mL). The aqueous layer was extracted with ether (3 x 10 mL). The organic layer was washed with brine (10 mL) and dried with anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel afforded ***anti*-14a** as a yellow oil (26 mg, 79%): $R_f = 0.16$ (4:1 hexanes:EtOAc); $[\alpha]_D$ 8.1° (*c* 1.25, CH_2Cl_2); IR (neat) 3490, 3036, 2929, 2858, 1786, 1722, 1657, 1630, 1586, 1493, 1462, 1452, 1408, 1390, 1370, 1344, 1255, 1211, 1099, 1028 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.47 (m, 2H), 7.35 (m, 3H), 6.98 (ddd, *J* = 15.6, 7.2, 7.2 Hz, 1H), 5.91 (ddd, *J* = 15.6, 1.2, 1.2 Hz, 1H), 5.53 (s, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 4.18 (m, 2H), 4.05 (m, 1H), 3.82 (ddd, *J* = 10.2, 8.4, 4.8 Hz, 1H), 3.73 (ddd, *J* = 10.5, 5.4, 5.4 Hz, 1H), 2.40 (m, 2H), 1.70-1.90 (m, 4H), 1.57 (m, 2H), 1.28 (t, *J* = 7.2 Hz, 3H), 0.90 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.2, 144.8, 138.4, 128.6, 128.1, 125.8, 123.8, 100.6, 74.0, 73.4, 66.8, 60.2, 58.7, 41.9, 40.3, 38.8, 36.6, 25.9, 18.3, 14.2, -5.4, -5.4; HRMS (FAB) calcd for $[C_{26}H_{42}O_6Si + H]^+$: 479.2829 Found: 479.2817.



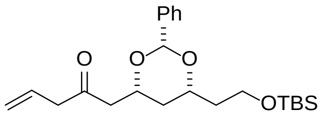
***syn*-16a**



***anti*-16a**

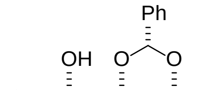
(S)-1-((2R,4S,6R)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-phenyl-1,3-dioxan-4-yl)pent-4-en-2-ol (*syn*-16a) and (R)-1-((2R,4S,6R)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-phenyl-1,3-dioxan-4-yl)pent-4-en-2-ol (*anti*-16a): To a solution of aldehyde **9** in 3 mL of THF at –78 ºC was added 0.62 mL of allylmagnesium chloride (2 M solution in THF). The reaction was allowed to warm to room temperature and stirred for 3 h, after which 1 mL of methanol, 10 mL of a saturated sodium bicarbonate solution, and 10 mL of ether were added. The aqueous layer was extracted with ether (3 x 10 mL). The organic layers were combined and washed with brine and dried over anhydrous sodium sulfate. Removal of the solvents in vacuo followed by silica gel chromatography yielded the alcohol (249 mg, 89%) as a clear oil and a mixture of diastereomers. Spectroscopic data for the *syn* diastereomer ***syn*-16a**: $[\alpha]_D$ 11.7° (*c* 1.25, CH_2Cl_2); IR (neat) 3462, 3072, 3036, 2930, 2859, 2737,1868,1830, 1772, 1734, 1684, 1654, 1541, 1508, 1472, 1404, 1344, 1256, 1018 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.47 (m, 2H), 7.35 (m, 3H), 5.85 (dddd, J = 17.1, 10.2, 6.9, 6.9 Hz, 1H), 5.57 (s, 1H), 5.13 (m, 2H), 4.03-4.19 (m, 2H), 3.99 (dddd, J = 9, 6.5, 6.5, 3 Hz, 1H), 3.83 (ddd, J = 10.2, 8.4, 4.8 Hz, 1H), 3.73 (ddd, J = 10.5, 5.4, 5.4 Hz, 1H), 2.27 (m, 2H), 1.70-1.91 (m, 4H), 1.65 (ddd, J = 13.2, 2.7, 2.7 Hz, 1H), 1.52 (ddd, J = 13.2, 10.8, 10.8 Hz, 1H), 0.91 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.2, 134.6, 128.7, 128.2, 125.8, 117.5, 100.5, 77.4, 73.4, 70.4, 58.6, 41.9, 41.9, 38.7, 37.2, 25.9, 18.3, -5.4, -5.4; HRMS (FAB) calcd for $[C_{23}H_{38}O_4Si + Na]^+$: 429.2437 Found: 429.2425.

Spectroscopic data for the *anti* diastereomer ***anti*-16a**: $[\alpha]_D$ 4.4° (*c* 1.22, CH_2Cl_2); IR (neat) 3446, 3072, 3072, 2951, 2928, 2857, 1472, 1463, 1405, 1387, 1344, 1255, 1215, 1177, 1148, 1102, 1064, 1028 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.48 (m, 2H), 7.34 (m, 3H), 5.84 (dddd, *J* = 17.7, 9.3, 7.2, 7.2 Hz, 1H), 5.54 (s, 1H), 5.12 (m, 2H), 4.19 (m, 1H), 4.04 (m, 2H), 3.83 (ddd, *J* = 10.2, 8.4, 4.8 Hz, 1H), 3.73 (ddd, *J* = 10.5, 5.4, 5.4 Hz, 1H), 2.26 (m, 2H), 1.69-1.90 (m, 4H), 1.57 (m, 2H), 0.90 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.6, 134.6, 128.5, 128.1, 125.9, 117.9, 100.5, 74.1, 73.4, 66.9, 58.7, 42.2, 42.0, 38.8, 36.9, 25.9, 18.3, -5.4, -5.4; HRMS (FAB) calcd for $[C_{23}H_{38}O_4Si + Na]^+$: 429.2437 Found: 429.2425.



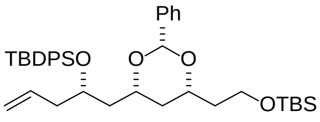
17

1-((2R,4R,6R)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-phenyl-1,3-dioxan-4-yl)pent-4-en-2-one (17): Into a 10 mL round bottomed flask was placed 25 mg (0.062 mmol) of alcohol in 1 mL of CH_2Cl_2. To this solution was added 39 mg (0.092 mmol) of Dess-Martin periodane. The reaction was stirred for 2 h. Ether was added to the reaction and the solution was filtered through a pad of silica gel, followed by removal of the solvents under reduced pressure. The crude product was purified by silica gel chromatography to produce 80 mg (88% yield) of ketone **17** as a clear oil: $[\alpha]_D$ 22.3° (*c* 2.6, CH_2Cl_2); IR (neat) 2952, 2928, 2857, 1720, 1641, 1470, 1453, 1389, 1345, 1253, 1215, 1100, 1025 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.47 (m, 2H), 7.34 (m, 3H), 5.93 (dddd, *J* = 17.4, 10.5, 7.2, 7.2 Hz, 1H), 5.50 (s, 1H), 5.18 (m, 2H), 4.36 (m, 1H), 4.05 (m, 1H), 3.83 (ddd, *J* = 10.5, 8.4, 5.1 Hz, 1H), 3.73 (ddd, *J* = 10.5, 5.4, 5.4 Hz, 1H), 3.25 (m, 2H), 2.91 (dd, J = 16.5, 7.2 Hz, 1H), 2.58 (dd, J = 16.2, 5.4 Hz, 1H), 1.75-1.90 (m, 2H), 1.72 (ddd, J = 12.9, 2.4, 2.4 Hz, 1H), 1.45 (ddd, J = 12.6, 11.1, 11.1 Hz, 1H), 0.90 (s, 9H), 0.06 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 206.3, 138.4, 130.0, 128.4, 128.0, 125.8, 119.0, 100.3, 73.2, 72.9, 58.6, 48.7, 48.0, 38.7, 36.8; 25.8, 18.2, -5.4, -5.5; HRMS (ESI) calcd for $[C_{23}H_{36}O_4Si + Na]^+$: 427.2281 Found: 427.2270.



***syn*-16a**

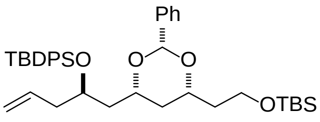
(S)-1-((2R,4S,6R)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-phenyl-1,3-dioxan-4-yl)pent-4-en-2-ol (*syn*-16a): To a solution of ketone (263 mg, 0.65 mmol) in THF (6 mL) at -90 °C was added a 1.0 M solution of L-selectride in THF (1.3 mL, 1.3 mmol). After stirring for 3 h a solution of 30% H_2O_2 and 1 M NaOH was added and the reaction was allowed to warm to room temperature and diluted with Et_2O. The organic layer was separated, washed with a saturated solution of sodium thiosulfate, brine, and then dried (Na_2SO_4), filtered, and concentrated. The crude material was purified by flash chromatography to provide 227 mg (86%) of alcohol ***syn*-16a** as a mixture (4:1) of diastereomers.



***syn*-18a**

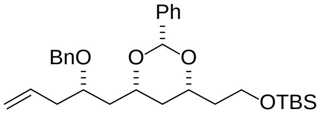
Tert-butyl(((S)-1-((2R,4R,6R)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-phenyl-1,3-dioxan-4-yl)pent-4-en-2-yl)oxy)diphenylsilane l (*syn*-18a): To a solution of alcohol ***syn*-16a** (86 mg, 0.211 mmol) and imidazole (43 mg, 0.56 mmol) in DMF (1 mL) was added TBDPSCl

(116 mg, 0.42 mmol). The reaction stirred for 18 h and then quenched with saturated aqueous sodium bicarbonate (5 mL) and diluted with ether (10 mL). The layers were separated and the aqueous layer was extracted with ether (2 x 10 mL). The combined organic layers were washed with brine (10 mL), and dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel afforded ***syn*-18a** as a clear, colorless oil (113 mg, 83%): $[\alpha]_D$ 12.6° (*c* 1.2, CH_2Cl_2); IR (neat) 3072, 3049, 2930, 2856, 1960, 1898, 1826, 1776, 1736, 1590, 1567, 1546, 1472, 1463, 1428, 1390, 1252, 1109, 1027 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.69 (m, 5H), 7.34 (m, 10H), 5.78 (dddd, *J* = 17, 10, 7, 7 Hz, 1H), 5.51 (s, 1H), 4.98 (m, 2H), 3.94 (m, 2H), 3.79 (m, 2H), 3.69 (ddd, *J* = 10, 5, 5 Hz, 1H), 2.36 (d, *J* = 13.5, 7, 7 Hz, 1H), 2.26 (m, 1H), 1.93 (ddd, *J* = 13.5, 6.5, 6.5 Hz, 1H), 1.72 (dddd, *J* = 13.5, 9, 4.5, 4.5 Hz, 1H), 1.63 (m, 2H), 1.27 (m, 1H), 1.16 (m, 1H), 1.08 (s, 9H), 0.92 (s, 9H), 0.07 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.8, 135.9, 135.8, 135.4, 134.5, 134.1, 134.0, 129.5, 128.2, 127.9, 127.5, 127.4, 125.9, 117.2, 100.2, 73.7, 73.1, 69.4, 58.7, 42.1, 41.4, 38.8, 36.9, 27.0, 26.8, 25.9, 19.3, -5.3, -5.4; HRMS (FAB) calcd for $[C_{39}H_{56}O_4Si_2 + H]^+$: 645.3795 Found: 645.3756.



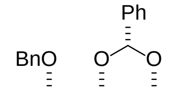
***anti*-18a**

Tert-butyl(((R)-1-((2R,4R,6R)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-phenyl-1,3-dioxan-4-yl)pent-4-en-2-yl)oxy)diphenylsilane (*anti*-18a): Following the procedure above, the TBDPS-protected alcohol ***anti*-18a** was produced (76 mg) in 78% yield from alcohol ***anti*-16a** as a clear, colorless oil: $[\alpha]_D$ –0.4° (*c* 1.2, CH_2Cl_2); IR (neat) 3072, 2953, 2857, 1961, 1898, 1832, 1656, 1590, 1546, 1472, 1428, 1406, 1390, 1344, 1311, 1255, 1106, 1028 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.67 (m, 5H), 7.37 (m, 3H), 7.30 (m, 7H), 5.72 (dddd, *J* = 17, 10, 7, 7 Hz, 1H), 5.12 (s, 1H), 4.96 (m, 1H), 4.91 (m, 1H), 4.19 (m, 1H), 3.95 (m, 1H), 3.84 (m, 1H), 3.79 (ddd, *J* = 10, 8.5, 5 Hz, 1H), 3.70 (ddd, *J* = 11, 6, 6 Hz, 1H), 2.20 (m, 2H), 1.65-1.81 (m, 3H), 1.60 (ddd, *J* = 14, 9, 2.5 Hz, 1H), 1.28 (m, 2H), 1.07 (s, 9H), 0.92 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.8, 135.9, 135.8, 135.4, 134.3, 134.1, 129.5, 129.4, 128.2, 127.9, 127.3, 127.3, 126.0, 117.0, 100.0, 73.2, 73.0, 68.9, 58.8, 42.9, 42.4, 38.8, 37.4, 27.0, 26.8, 25.9, 19.4, -5.3, -5.4; HRMS (FAB) calcd for $[C_{39}H_{56}O_4Si_2 + H]^+$: 645.3795 Found: 645.3756.



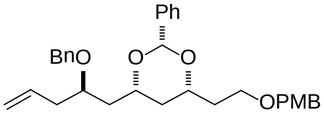
***syn*-18b**

(2-((2R,4R,6S)-6-((S)-2-(benzyloxy)pent-4-en-1-yl)-2-phenyl-1,3-dioxan-4-yl)ethoxy)(tert-butyl)dimethylsilane (*syn*-18b): To a solution of alcohol ***syn*-16a** (382 mg, 0.94 mmol) in methylene chloride (2 mL) was added benzyl trichloroacetimidate (283 mg, 1.13 mmol). The mixture was stirred at room temperature for 24 h and then quenched with saturated aqueous sodium bicarbonate (2 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The organic layers were combined, washed with brine (5 mL), dried (Na_2SO_4), filtered, and concentrated. Purification on a silica gel column gave 224 mg of benzyl ether ***syn*-18b** (48%): R_f = 0.16 (4:1 hexanes:EtOAc); $[\alpha]_D$ 25.9° (*c* 1.05, CH_2Cl_2); IR (neat) 3066, 3033, 2952, 2856, 1640, 1496, 1472, 1454, 1388, 1342, 1253, 1214, 1106, 1028 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.48 (m, 2H), 7.34 (m, 8H), 5.88 (dddd, *J* = 17.1, 10.2, 6.9, 6.9 Hz, 1H), 5.50 (s, 1H), 5.56 (m, 2H), 4.62 (d, *J* = 11.7 Hz, 1H), 4.68 (d, *J* = 11.7 Hz, 1H), 3.99 (m, 2H), 3.83 (ddd, *J* = 10.5, 8.7, 5.4 Hz, 1H), 3.71 (m, 1H), 2.42 (m, 2H), 2.05 (ddd, *J* = 14.1, 6.9, 6.9 Hz, 1H), 1.65-1.85 (m, 4H), 1.44 (m, 2H), 0.91 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.7, 138.4, 134.4, 128.3, 128.2, 127.9, 127.8, 127.5, 125.9, 117.2, 100.3, 74.3, 73.8, 73.2, 70.5, 58.7, 39.8, 38.8, 38.1, 36.9, 25.9, 18.2, -5.4, -5.4; HRMS (ESI) calcd for $[C_{30}H_{44}O_4Si + Na]^+$: 519.2907 Found: 519.2899.



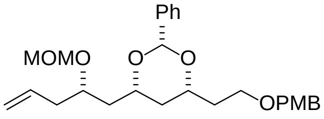
***syn*-18c**

(2R,4S,6R)-4-((S)-2-(benzyloxy)pent-4-en-1-yl)-6-(2-((4-methoxybenzyl)oxy)ethyl)-2-phenyl-1,3-dioxane (*syn*-18c): To a solution of alcohol (111 mg, 0.27 mmol) in THF (2.5 mL) was added benzyl bromide (92 mg, 0.54 mmol), 31 mg (0.8 mmol) of 60% NaH in mineral oil, followed by and tetrabutylammonium iodide (10 mg, 0.027 mmol). The reaction was stirred for 24 h and then quenched with saturated aqueous sodium bicarbonate (5 mL). The layers were separated and the aqueous layer was extracted with ether (3 x 5 mL). The combined organic layers were washed with brine (10 mL) and dried over anhydrous sodium sulfate. After removal of the solvents *in vacuo*, flash chromatography on silica gel afforded ***syn*-18c** as a clear, colorless oil (67 mg, 49%): $R_f = 0.54$ (4:1 hexanes:EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.46 (m, 2H), 7.32 (m, 8H), 7.26 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 5.87 (dddd, *J* = 17.5, 10.5, 7, 7 Hz, 1H), 5.49 (s, 1H), 5.10 (m, 2H), 4.60 (d, *J* = 11.5 Hz, 1H), 4.48 (d, *J* = 12 Hz, 1H), 4.47 (d, *J* = 11.5 Hz, 1H), 4.43 (d, *J* = 12 Hz, 1H), 3.96 (m, 3H), 3.79 (s, 3H), 3.66 (m, 1H), 3.57 (m, 1H), 2.42 (m, 2H), 2.04 (ddd, *J* = 14, 7, 7 Hz, 1H), 1.90 (m, 2H), 1.69 (m, 1H), 1.48 (dddd, *J* = 13.5, 13.5, 2.5, 2.5 Hz, 1H), 1.37 (dddd, *J* = 13, 13, 11, 2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.2, 138.9, 138.7, 134.6, 130.6, 129.3, 128.4, 128.1, 128.1, 127.6, 126.1, 117.4, 113.8, 113.8, 100.4, 76.3, 73.9, 73.8, 72.7, 70.7, 65.8, 55.3, 40.0, 38.3, 36.6, 34.5; HRMS (ESI) calcd for $[C_{32}H_{38}O_5 + Na]^+$: 525.2617 Found: 525.2623.



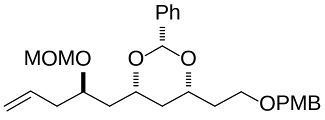
***anti*-18c**

(2R,4S,6R)-4-((R)-2-(benzyloxy)pent-4-en-1-yl)-6-(2-((4-methoxybenzyl)oxy)ethyl)-2-phenyl-1,3-dioxane (*anti*-18c): Following the procedure above, the benzyl-protected alcohol ***anti*-18c** was produced (71 mg) in 52% yield from alcohol ***anti*-16b** as a clear, colorless oil: R_f = 0.54 (4:1 hexanes:EtOAc), $[\alpha]_D$ 23.8° (*c* 1.08, CH_2Cl_2); IR (neat) 3066, 3034, 3006, 2917, 2860, 1698, 1641, 1614, 1586, 1514, 1496, 1455, 1345, 1303, 1247, 1174, 1100, 1030 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.40 (m, 2H), 7.33 (m, 8H), 7.26 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 5.86 (dddd, *J* = 17, 10, 7, 7 Hz, 1H), 5.42 (s, 1H), 5.10 (m, 2H), 4.68 (d, *J* = 11.5 Hz, 1H), 4.48 (d, *J* = 11.5 Hz, 1H), 4.47 (d, *J* = 12 Hz, 1H), 4.43 (d, *J* = 11.5 Hz, 1H), 4.05 (m, 1H), 4.00 (dddd, *J* = 11, 8.5, 4.5, 2.5 Hz, 1H), 3.88 (m, 1H), 3.79 (s, 3H), 3.66 (ddd, *J* = 9.5, 8, 5.5 Hz, 1H), 3.56 (ddd, *J* = 9, 5.5, 5.5 Hz, 1H), 2.37 (m, 2H), 1.91 (dddd, *J* = 14, 8, 5.5, 5.5 Hz, 1H), 1.82 (dddd, *J* = 14, 8, 6, 4.5 Hz, 1H), 1.74 (ddd, *J* = 14.5, 9.5, 3 Hz, 1H), 1.66 (ddd, *J* = 14, 10, 2.5 Hz, 1H), 1.55 (ddd, *J* = 13, 2.5, 2.5 Hz, 1H), 1.41 (ddd, *J* = 13, 11.5, 11.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.2, 139.0, 138.8, 134.5, 130.6, 129.3, 128.4, 128.1, 128.0, 127.7, 126.0, 117.4, 113.8, 112.4, 100.1, 74.1, 73.8, 73.3, 72.7, 71.7, 65.7, 55.3, 41.3, 38.8, 37.5, 36.1; HRMS (ESI) calcd for $[C_{32}H_{38}O_5 + Na]^+$: 525.2617 Found: 525.2623.



***syn*-18d**

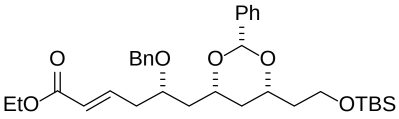
(2R,4R,6S)-4-(2-((4-methoxybenzyl)oxy)ethyl)-6-((S)-2-(methoxymethoxy)pent-4-en-1-yl)-2-phenyl-1,3-dioxane (*syn*-18d): A solution of alcohol (800 mg, 1.94 mmol) and diisopropylethylamine (2 mL) in CH_2Cl_2 (10 mL) was cooled to 0 ºC. To this solution was added DMAP (71 mg, 0.582 mmol), followed by MOMCl (0.59 mL, 7.76 mmol). The reaction was warmed up to room temperature, stirred for 4 h and quenched with saturated aqueous NH_4Cl (10 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with saturated aqueous sodium bicarbonate (10 mL), brine (10 mL), and dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel afforded ***syn*-18d** as a clear, colorless oil (769 mg, 87%): R_f = 0.38 (4:1 hexanes:EtOAc); $[\alpha]_D$ 33.6° (*c* 1.1, CH_2Cl_2); IR (neat) 2924, 1640, 1614, 1586, 1514, 1456, 1344, 1303, 1248, 1213, 1098, 1032 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.46 (m, 2H), 7.35 (m, 3H), 7.27 (d, *J* = 9 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 5.85 (dddd, *J* = 17.1, 10.2, 7.2, 7.2 Hz, 1H), 5.52 (s, 1H), 5.11 (m, 2H), 4.69 (d, *J* = 6.9 Hz, 1H), 4.65 (d, *J* = 6.9 Hz, 1H), 4.49 (d, *J* = 11.7 Hz, 1H), 4.43 (d, *J* = 11.7 Hz, 1H), 4.02 (m, 2H), 3.86 (ddd, *J* = 12, 5.7, 5.7, Hz, 1H), 3.79 (s, 3H), 3.68 (ddd, *J* = 9.3, 8.1, 5.4 Hz, 1H), 3.58 (ddd, *J* = 9.3, 5.4, 5.4 Hz, 1H), 3.38 (s, 3H), 2.39 (m, 2H), 1.99 (ddd, *J* = 14, 6.9, 6.9 Hz, 1H), 1.88 (dddd, *J* = 13.8, 8.1, 5.7, 5.7 Hz, 1H), 1.85 (m, 1H), 1.72 (ddd, *J* = 14.5, 6, 6 Hz, 1H), 1.67 (ddd, *J* = 13.2, 2.1, 2.1 Hz, 1H), 1.43 (ddd, *J* = 12.9, 11.1, 11.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.0, 138.7, 134.4, 130.4, 129.1, 128.3, 128.0, 125.9, 117.4, 113.6, 100.3, 95.3, 73.7, 73.6, 73.4, 72.5, 65.5, 55.5, 55.1, 40.2, 38.8, 36.9, 36.0; HRMS (ESI) calcd for $[C_{27}H_{36}O_6 + Na]^+$: 479.2410 Found: 479.2406.



***anti*-18d**

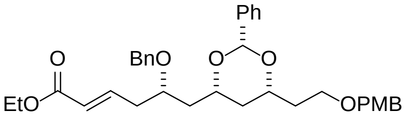
(2R,4R,6S)-4-(2-((4-methoxybenzyl)oxy)ethyl)-6-((R)-2-(methoxymethoxy)pent-4-en-1-yl)-2-phenyl-1,3-dioxane (*anti*-18d): Following the procedure above, the MOM-protected alcohol

***anti*-18d** was produced (195 mg) in 85% yield from alcohol ***anti*-16b** as a clear, colorless oil: R_f = 0.38 (4:1 hexanes:EtOAc), $[\alpha]_D$ –2.7° (*c* 1.0, CH_2Cl_2); IR (neat) 3071, 3035, 2950, 1641, 1614, 1586, 1515, 1455, 1404, 1344, 1303, 1248, 1102, 1040 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.47 (m, 2H), 7.35 (m, 3H), 7.28 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.83 (dddd, *J* = 17.7, 10.8, 7.2, 7.2 Hz, 1H), 5.52 (s, 1H), 5.09 (m, 2H), 4.76 (d, *J* = 6.6 Hz, 1H), 4.69 (d, *J* = 6.6 Hz, 1H), 4.49 (d, *J* = 11.4 Hz, 1H), 4.44 (d, *J* = 11.4 Hz, 1H), 4.05 (m, 3H), 3.79 (s, 3H), 3.69 (ddd, *J* = 9.6, 8.1, 5.4 Hz, 1H), 3.58 (ddd, *J* = 9.3, 5.4, 5.4 Hz, 1H), 3.40 (s, 3H), 2.35 (m, 2H), 1.83-1.97 (m, 2H), 1.65-1.81 (m, 2H), 1.59 (ddd, *J* = 13.2, 2.7, 2.7 Hz, 1H), 1.44 (ddd, *J* = 12.6, 10.8, 10.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.0, 138.8, 134.2, 130.4, 129.2, 128.3, 128.0, 125.8, 118.4, 113.6, 100.0, 95.8, 73.6, 73.9, 73.0, 72.6, 72.6, 65.5, 55.5, 55.0, 41.1, 39.5, 37.4, 36.0; HRMS (ESI) calcd for $[C_{27}H_{36}O_6 + Na]^+$: 479.2410 Found: 479.2423.



***syn*-15b**

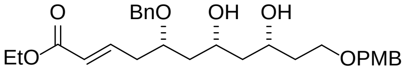
Ethyl (S,E)-5-(benzyloxy)-6-((2R,4S,6R)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-phenyl-1,3-dioxan-4-yl)hex-2-enoate (*syn*-15b): To a solution of alkene ***syn*-18b** (225 mg, 0.453 mmol) in 2 mL of CH_2Cl_2 was added ethyl acrylate (113 mg, 1.13 mmol) and Grubbs's second-generation catalyst (6 mg, 6.8 μmol). This mixture was heated at reflux for 4 h. The reaction was cooled to room temperature and the solvent was removed under reduced pressure. The crude product was purified using column chromatography on silica gel to afford enoate ***syn*-15b** (221 mg, 96%) as a clear oil: R_f = 0.29 (9:1 hexanes:EtOAc); $[\alpha]_D$ 11.5° (*c* 1.05, CH_2Cl_2); IR (neat) 3034, 2953, 2857, 1722, 1657, 1496, 1454, 1368, 1343, 1321, 1258, 1212, 1167, 1100, 1028 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.47 (m, 2H), 7.33 (m, 8H), 7.00 (ddd, *J* = 15.6, 7.5, 7.5 Hz, 1H), 5.90 (d, *J* = 15.6 Hz, 1H), 5.49 (s, 1H), 4.58 (d, *J* = 11.7 Hz, 1H), 4.49 (d, *J* = 11.7 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.97 (m, 2H), 3.77 (m, 3H), 2.54 (m, 2H), 2.06 (ddd, *J* = 14.7, 6.9, 6.9 Hz, 1H), 1.80 (m, 1H), 1.70 (m, 2H), 1.43 (m, 2H), 1.29 (q, *J* = 7.2 Hz, 3H), 0.91 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 166.1, 144.8, 138.6, 138.0, 128.3, 128.2, 128.0, 127.8, 127.6, 125.8, 123.7, 100.3, 73.6, 73.5, 73.2, 70.7, 60.1, 58.7, 39.9, 38.8, 36.9, 36.6, 25.9, 18.2, 14.2, -5.4, -5.4; HRMS (ESI) calcd for [$C_{33}H_{48}O_6Si$ + Na]$^+$: 591.3118 Found: 591.3112.



***syn*-15c**

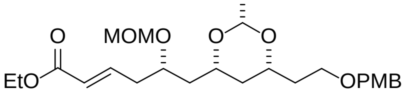
Ethyl (S,E)-5-(benzyloxy)-6-((2R,4S,6R)-6-(2-((4-methoxybenzyl)oxy)ethyl)-2-phenyl-1,3-dioxan-4-yl)hex-2-enoate (*syn*-15c): To a solution of alkene ***syn*-18c** (166 mg, 0.33 mmol) in 2 mL of CH$_2$Cl$_2$ was added ethyl acrylate (83 mg, 0.83 mmol) and Grubbs's second-generation catalyst (4 mg, 5 µmol). This mixture was heated at reflux for 4 h. The reaction was cooled to room temperature and the solvent was removed under reduced pressure. The crude product was purified using column chromatography on silica gel to afford enoate ***syn*-15c** (172 mg, 91%) as a clear oil: [α]$_D$ 12.3° (*c* 1.0, CH$_2$Cl$_2$); IR (neat) 2922, 1715, 1652, 1614, 1514, 1455, 1248, 1172, 1099, 1028 cm^{-1}; ^{1}H NMR (CDCl$_3$, 500 MHz) δ 7.43 (m, 2H), 7.33 (m, 8H), 7.27 (d, *J* = 9 Hz, 2H), 7.00 (ddd, *J* = 15, 7.5, 7.5 Hz, 1H), 6.87 (d, *J* = 8.5 Hz, 1H), 5.89 (d, *J* = 16 Hz, 1H), 5.49 (s, 1H), 4.57 (d, *J* = 11.5 Hz, 1H), 4.49 (d, *J* = 11.5 Hz, 1H), 4.48 (d, *J* = 11.5 Hz, 1H), 4.43 (d, *J* = 11.5 Hz, 1H), 4.19 (q, *J* = 7 Hz, 2H), 3.79 (s, 3H), 3.79 (m, 1H), 3.65 (ddd, *J* = 9.5, 8.5, 5.5 Hz, 1H), 3.56 (ddd, *J* = 9.5, 6, 6 Hz, 1H), 2.54 (m, 2H), 2.05 (ddd, *J* = 14, 7, 7 Hz, 1H), 1.89 (dddd, *J* = 14.5, 9, 6, 6 Hz, 1H), 1.79 (dddd, *J* = 14.5, 8.5, 6, 4.5 Hz, 1H), 1.68 (ddd, *J* = 14.5, 6, 6 Hz, 1H), 1.46 (ddd, J = 13, 3, 3 Hz, 1H), 1.39 (ddd, J = 12.5, 10.5, 10.5 Hz, 1H), 1.29 (q, *J* =

7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 166.4, 159.2, 145.0, 138.7, 138.2, 130.6, 129.3, 128.6, 128.4, 128.2, 128.0, 127.8, 126.0, 123.8, 113.8, 100.4, 73.9, 73.8, 73.7, 72.7, 70.9, 65.7, 60.3, 55.3, 40.0, 37.0, 36.8, 36.1, 14.3; HRMS (ESI) calcd for $[C_{35}H_{42}O_7 + Na]^+$: 597.2828 Found: 597.2844.



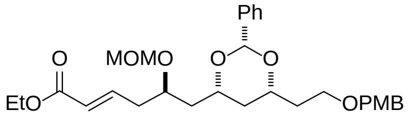
***syn*-15c**

Ethyl (5S,7R,9R,E)-5-(benzyloxy)-7,9-dihydroxy-11-((4-methoxybenzyl)oxy)undec-2-enoate (*syn*-19c): To a flask containing 172 mg (0.30 mmol) of benzylidene ***syn*-15c** was added 1.5 mL of 80% acetic acid. This mixture was heated at 60 ºC for 4 h and then concentrated under reduced pressure to yield 105 mg (72%) of diol ***syn*-19c**: $[\alpha]_D$ 17.1° (*c* 0.9, CH_2Cl_2); IR (neat) 3466, 2937, 1716, 1652, 1614, 1586, 1516, 1456, 1245, 1092 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.33 (m, 5H), 7.25 (d, J = 8.7 Hz, 2H), 6.97 (ddd, J = 15, 7.2, 7.2 Hz, 1H), 6.88 (d, J = 8.4 Hz, 2H), 5.90 (d, J = 15.6 Hz, 1H), 4.64 (d, J = 11.7 Hz, 1H), 4.48 (d, J = 11.7 Hz, 1H), 4.45 (s, 2H), 4.20 (q, J = 7.2 Hz, 2H), 4.01 (m, 2H), 3.82 (m, 1H), 3.81 (s, 3H), 3.64 (m, 2H), 2.53 (m, 2H), 1.66-1.85 (m, 3H), 1.51-1.60 (m, 2H), 1.45 (ddd, J = 14.1, 2.7, 2.7 Hz, 1H), 1.30 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.0, 159.1, 144.1, 137.6, 129.9, 129.2, 128.4, 127.8, 127.8, 123.9, 113.7, 76.8, 72.8, 71.2, 70.8, 70.7, 68.0, 60.1, 55.1, 43.3, 41.5, 36.9, 36.2, 14.1; HRMS (ESI) calcd for $[C_{28}H_{38}O_7 + Na]^+$: 509.2515 Found: 509.2540.



***syn*-19d**

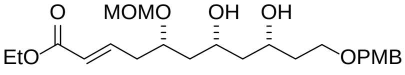
Ethyl (S,E)-6-((2R,4S,6R)-6-(2-((4-methoxybenzyl)oxy)ethyl)-2-phenyl-1,3-dioxan-4-yl)-5-(methoxymethoxy)hex-2-enoate (*syn*-19d): To a solution of alkene ***syn*-15d** (185 mg, 0.405 mmol) in 2.5 mL of CH_2Cl_2 was added ethylacrylate (100 mg, 1.0 mmol) and Grubbs's second-generation catalyst (5.2 mg, 6.1 μmol). This mixture was heated at reflux for 4 h. The reaction was cooled to room temperature and the solvent was removed under reduced pressure. The crude product was purified using column chromatography on silica gel to afford enoate ***syn*-19d** (192 mg, 90%) as a clear oil: $R_f = 0.28$ (4:1 hexanes:EtOAc); $[\alpha]_D$ 16.2° (*c* 1.0, CH_2Cl_2); IR (neat) 2943, 1717, 1684, 1653, 1616, 1586, 1559, 1540, 1507, 1457 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.45 (m, 2H), 7.35 (m, 3H), 7.27 (d, *J* = 9 Hz, 2H), 7.00 (ddd, *J* = 15.6, 7.5, 7.5 Hz, 1H), 6.87 (d, *J* = 9 Hz, 2H), 5.90 (ddd, *J* = 15.6, 1.2, 1.2 Hz, 1H), 5.51 (s, 1H), 4.67 (d, *J* = 6.9 Hz, 1H), 4.64 (d, *J* = 6.9 Hz, 1H), 4.49 (d, *J* = 11.4 Hz, 1H), 4.44 (d, *J* = 11.4 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 4.00 (m, 3H), 3.80 (s, 3H), 3.68 (ddd, *J* = 9.3, 7.8, 5.1 Hz, 1H), 3.58 (ddd, *J* = 9.6, 5.4, 5.4 Hz, 1H), 3.38 (s, 3H), 2.54 (m, 2H), 2.00 (ddd, *J* = 13.8, 7.2, 6 Hz, 1H), 1.80-1.94 (m, 2H), 1.71 (ddd, *J* = 14.4, 5.4, 5.4 Hz, 1H), 1.65 (ddd, *J* = 12.9, 2.7, 2.7 Hz, 1H), 1.45 (ddd, *J* = 12.9, 11.1, 11.1 Hz, 1H), 1.29 (q, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.0, 159.0, 144.8, 138.6, 130.4, 129.1, 128.4, 128.0, 125.9, 123.7, 113.6, 100.3, 95.4, 73.6, 73.4, 72.8, 72.5, 65.4, 60.1, 55.6, 55.1, 40.3, 37.2, 36.9, 36.0, 14.2; HRMS (ESI) calcd for $[C_{30}H_{40}O_8 + Na]^+$: 551.2621 Found: 551.2611.



***anti*-15d**

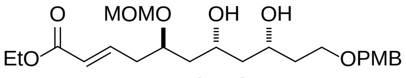
Ethyl (R,E)-6-((2R,4S,6R)-6-(2-((4-methoxybenzyl)oxy)ethyl)-2-phenyl-1,3-dioxan-4-yl)-5-(methoxymethoxy)hex-2-enoate (*anti*-15d): Following the procedure above, the enoate ***anti*-**

15d was produced (208 mg) in 92% yield from alkene ***anti*-18d** as a clear, colorless oil: R_f = 0.28 (4:1 hexanes:EtOAc); $[\alpha]_D$ 2.6° (*c* 1.5, CH_2Cl_2); IR (neat) 2944, 1715, 1694, 1682, 1667, 1651, 1614, 1586, 1556, 1514, 1454, 1367, 1344, 1303, 1247, 1210, 1174, 1153, 1100, 1035 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.45 (m, 2H), 7.35 (m, 3H), 7.28 (d, *J* = 8.4 Hz, 2H), 6.98 (ddd, *J* = 15.3, 7.5, 7.5 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.88 (d, *J* = 15.6 Hz, 1H), 5.50 (s, 1H), 4.72 (d, *J* = 6.9 Hz, 1H), 4.69 (d, *J* = 6.9 Hz, 1H), 4.48 (d, *J* = 11.7 Hz, 1H), 4.43 (d, *J* = 11.7 Hz, 1H), 4.18 (q, *J* = 6.9 Hz, 2H), 4.00-4.18 (m, 3H), 3.78 (s, 3H), 3.68 (ddd, *J* = 9.3, 8.1, 5.4 Hz, 1H), 3.57 (ddd, *J* = 9.3, 5.4, 5.4 Hz, 1H), 3.39 (s, 3H), 2.38-2.60 (m, 2H), 1.80-1.96 (m, 2H), 1.70 (m, 2H), 1.57 (ddd, *J* = 13.2, 2.4, 2.4 Hz, 1H), 1.43 (ddd, *J* = 12.9, 11.4, 11.4 Hz, 1H), 1.29 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.3, 159.2, 144.6, 138.7, 130.5, 129.3, 128.5, 128.2, 125.9, 124.0, 113.8, 100.2, 96.1, 73.7, 73.0, 72.7, 72.3, 65.6, 60.3, 55.8, 55.3, 41.4, 38.0, 37.4, 36.1, 14.3; HRMS (ESI) calcd for $[C_{30}H_{40}O_8 + Na]^+$: 551.2621 Found: 551.2611.



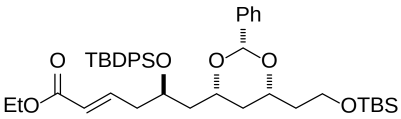
***syn*-19d**

Ethyl (5S,7R,9R,E)-7,9-dihydroxy-11-((4-methoxybenzyl)oxy)-5-(methoxymethoxy)undec-2-enoate (*syn*-19d): To a flask containing 50 mg I_2 in 250 mL MeOH was added 773 mg (1.46 mmol) of enoate ***syn*-15d**. This mixture was heated at reflux for 5 h. The majority of the methanol was then removed under reduced pressure, and the product was dissolved in ethyl acetate (50 mL). The organic layer was washed with aqueous sodium thiosulfate (20 mL), brine (20 mL), and dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel afforded ***syn*-19d** as a clear, colorless oil (512 mg, 80%): R_f = 0.1 (3:2 hexanes:EtOAc); $[\alpha]_D$ 3.3° (*c* 0.9, CH_2Cl_2); IR (neat) 3460, 2942, 1715, 1652, 1614, 1586, 1515, 1446, 1370, 1245 cm^{-1}; ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.27 (d, *J* = 8.7 Hz, 2H), 6.95 (ddd, *J* = 15.6, 7.8, 7.8 Hz, 1H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.90 (ddd, *J* = 15.6, 1.5, 1.5 Hz, 1H), 4.70 (d, *J* = 7.2 Hz, 1H), 4.67 (d, *J* = 7.2 Hz, 1H), 4.46 (s, 2H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.95-4.10 (m, 3H), 3.81 (s, 3H), 3.65 (m, 2H), 3.39 (s, 3H), 2.51 (m, 2H), 1.68-1.88 (m, 3H), 1.50-1.60 (m, 3H), 1.29 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 166.1, 159.1, 144.3, 129.2, 123.8, 113.7, 113.7, 95.3, 74.8, 72.8, 71.7, 70.3, 68.1, 60.1, 55.7, 55.1, 43.2, 41.7, 37.0, 36.8, 14.2; HRMS (ESI) calcd for [$C_{23}H_{36}O_8$ + Na]$^+$: 463.2308 Found: 463.2338.



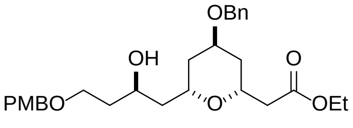
***anti*-19d**

Ethyl (5R,7R,9R,E)-7,9-dihydroxy-11-((4-methoxybenzyl)oxy)-5-(methoxymethoxy)undec-2-enoate (*anti*-19g): Following the procedure above, the diol ***anti*-19d** was produced (225 mg) in 71% yield from enoate ***anti*-15d** as a clear, colorless oil: R$_f$ = 0.1 (3:2 hexanes:EtOAc); $[\alpha]_D$ –33.7° (*c* 1.0, CH$_2$Cl$_2$); IR (neat) 3454, 2938, 1715, 1652, 1586, 1556, 1515, 1445, 1369, 1250, 1174, 1100, 1036 cm^{-1}; ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.25 (d, *J* = 8.7 Hz, 2H), 6.96 (ddd, *J* = 15.6, 7.5, 7.5 Hz, 1H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.88 (ddd, *J* = 15.6, 1.2, 1.2 Hz, 1H), 4.72 (d, *J* = 6.6 Hz, 1H), 4.68 (d, *J* = 6.6 Hz, 1H), 4.46 (s, 2H), 4.19 (q, *J* = 7.2 Hz, 2H), 4.10 (m, 1H), 3.96 (m, 2H), 3.82 (s, 3H), 3.66 (m, 2H), 3.42 (s, 3H), 2.47 (m, 2H), 1.70-1.85 (m, 2H), 1.53-1.63 (m, 3H), 1.49 (ddd, *J* = 14.1, 2.4, 2.4 Hz, 1H), 1.29 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 166.0, 159.1, 144.4, 129.8, 129.2, 123.8, 113.7, 96.4, 73.7, 72.9, 72.0, 68.3, 68.2, 60.1, 55.7, 55.1, 43.2, 42.5, 38.0, 36.8, 14.1; HRMS (ESI) calcd for [$C_{23}H_{36}O_8$ + Na]$^+$: 463.2308 Found: 463.2322.



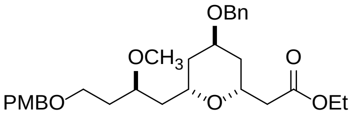
***anti*-15a**

Ethyl (R,E)-6-((2R,4R,6R)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-phenyl-1,3-dioxan-4-yl)-5-((tert-butyldiphenylsilyl)oxy)hex-2-enoate (*anti*-15a): To a solution of alkene ***anti*-18a** (95 mg, 0.15 mmol) in 2 mL of CH_2Cl_2 was added ethyl acrylate (37 mg, 0.37 mmol) and Grubbs's second-generation catalyst (6.4 mg, 7.5 μmol). This mixture was heated at reflux for 4 h. The reaction was cooled to room temperature and the solvent was removed under reduced pressure. The crude product was purified using column chromatography on silica gel to afford enoate ***anti*-15a** (95 mg, 88%) as a clear oil: $[\alpha]_D$ –0.8° (*c* 1.0, CH_2Cl_2); IR (neat) 3072, 3049, 2934, 2857, 1724, 1656, 1590, 1561, 1546, 1472, 1428, 1390, 1368, 1298, 1258, 1104 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.66 (m, 5H), 7.38 (m, 3H), 7.30 (m, 7H), 6.88 (ddd, *J* = 15.5, 7.5, 7.5 Hz, 1H), 5.69 (ddd, *J* = 16, 1.5, 1.5 Hz, 1H), 5.11 (s, 1H), 4.16 (q, *J* = 7 Hz, 2H), 4.16 (m, 1H), 3.93 (m, 1H), 3.83 (m, 1H), 3.79 (ddd, *J* = 10.5, 8.5, 5 Hz, 1H), 3.69 (ddd, *J* = 10.5, 5.5, 5.5 Hz, 1H), 2.31 (m, 2H), 1.76 (ddd, *J* = 13.5, 8.5, 5.5 Hz, 1H), 1.66 (m, 4H), 1.41 (ddd, *J* = 13, 2.5, 2.5 Hz, 1H), 1.28 (t, *J* = 7 Hz, 3H), 1.07 (s, 9H), 0.92 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 166.3, 144.9, 138.8, 136.0, 136.0, 135.6, 134.0, 133.8, 129.7, 128.4, 128.0, 127.6, 127.6, 126.2, 123.8, 100.2, 73.3, 73.0, 68.6, 60.2, 58.8, 43.4, 40.8, 38.9, 37.4, 27.1, 26.9, 26.0, 19.4, 14.3, -5.2, -5.3; HRMS (FAB) calcd for $[C_{42}H_{60}O_6 + H]^+$: 717.4007 Found: 717.3975.



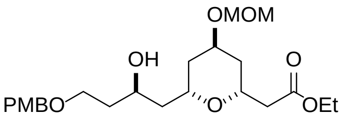
***syn*-20c**

Ethyl 2-((2R,4R,6R)-4-(benzyloxy)-6-((R)-2-hydroxy-4-((4-methoxybenzyl)oxy)butyl)-tetrahydro-2H-pyran-2-yl)acetate (*syn*-20c): To diol ***syn*-19c** (30 mg, 0.062 mmol) in 1 mL THF cooled to –40 ºC was added potassium *tert*-butoxide (0.7 mg, 0.062 mmol). This reaction was allowed to warm up to room temperature and stirred for 4 h, when it was quenched with saturated aqueous ammonium chloride (2 mL) and diluted with ether (5 mL). The aqueous layer was extracted with ether (2 x 5 mL). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by silica gel chromatography to produce ***syn*-20c** (21 mg) in 70% yield as a clear oil: $[\alpha]_D$ 14.5° (*c* 0.95, CH_2Cl_2); IR (neat) 3515, 2944, 1732, 1613, 1514, 1455, 1248, 1173, 1098 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.35 (m, 5H), 7.25 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.55 (d, *J* = 12 Hz, 1H), 4.51 (d, *J* = 11.5 Hz, 1H), 4.45 (d, *J* = 11.5 Hz, 1H), 4.41 (d, *J* = 11.5 Hz, 1H), 4.28 (dddd, *J* = 11.5, 9, 4, 1.5 Hz, 1H), 4.15 (q, *J* = 7 Hz, 2H), 4.12 (m, 1H), 4.01 (dddd, *J* = 12, 7, 4.5, 2.5 Hz, 1H), 3.85 (m, 1H), 3.80 (s, 3H), 3.59 (m, 2H), 2.48 (dd, *J* = 15, 8.5 Hz, 1H), 2.39 (dd, *J* = 15.5, 4.5 Hz, 1H), 1.91 (m, 1H), 1.66-1.83 (m, 3H), 1.59 (ddd, *J* = 14.5, 9.5, 9.5 Hz, 1H), 1.51 (ddd, *J* = 14.5, 2.5, 2.5 Hz, 1H), 1.43 (m, 2H), 1.26 (q, *J* = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.9, 158.9, 138.4, 130.5, 129.1, 128.2, 127.4, 127.2, 113.6, 73.5, 72.5, 70.7, 70.0, 69.5, 68.9, 67.2, 60.5, 55.1, 42.6, 41.0, 37.2, 35.8, 34.8, 14.0; HRMS (ESI) calcd for $[C_{28}H_{38}O_7 + Na]^+$: 509.2515 Found: 509.2514.



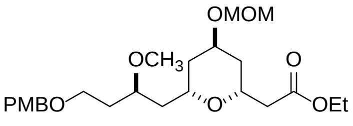
***syn*-21c**

Ethyl 2-((2R,4R,6R)-4-(benzyloxy)-6-((R)-2-methoxy-4-((4-methoxybenzyl)oxy)butyl)-tetrahydro-2H-pyran-2-yl)acetate (*syn*-21c): To a solution of alcohol ***syn*-20c** (19 mg, 0.04 mmol) in CH_2Cl_2 (2 mL) was added Proton Sponge (51 mg, 0.24 mmol), 4 Å molecular sieves (72 mg), and trimethyloxonium tetrafluoroborate (30 mg, 0.2 mmol). After about 1.5 h, the reaction was filtered through a fritted funnel, washing with ethyl acetate (5 x 10 mL). The filtrate was washed with water (1 x 20 mL) and 1M CuSO4 (2 x 20 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by silica gel chromatography to produce methyl ether ***syn*-21c** (15 mg) in 75% yield as a clear oil: R_f = 0.16 (4:1 hexanes:EtOAc); $[\alpha]_D$ 20.4° (*c* 0.7, CH_2Cl_2); IR (neat) 2924, 1732, 1694, 1682, 1652, 1614, 1557, 1538, 1514, 1455, 1372, 1247, 1170, 1092 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.35 (m, 4H), 7.28 (m, 1H), 7.26 (d, *J* = 9 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.54 (d, *J* = 12 Hz, 1H), 4.51 (d, *J* = 12 Hz, 1H), 4.44 (d, *J* = 11.5 Hz, 1H), 4.41 (d, *J* = 11.5 Hz, 1H), 4.22 (dddd, *J* = 13, 7.5, 5, 1.5 Hz, 1H), 4.12 (q, *J* = 7 Hz, 2H), 3.93 (dddd, *J* = 11, 8.5, 5, 2 Hz, 1H), 3.85 (m, 1H), 3.80 (s, 3H), 3.54 (m, 2H), 3.47 (m, 1H), 3.29 (s, 3H), 2.48 (dd, *J* = 15, 8 Hz, 1H), 2.37 (dd, *J* = 14.5, 5 Hz, 1H), 1.93 (m, 1H), 1.74-88 (m, 4H), 1.47 (ddd, *J* = 14, 7, 4.5 Hz, 1H), 1.38 (m, 2H), 1.24 (t, *J* = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.2, 159.1, 138.8, 130.8, 129.3, 128.4, 127.5, 127.4, 113.7, 75.3, 72.6, 71.1, 70.1, 69.3, 69.1, 66.8, 60.4, 56.6, 55.3, 41.7, 40.0, 35.8, 35.2, 33.9, 14.3; HRMS (ESI) calcd for $[C_{29}H_{40}O_7 + Na]^+$: 523.2672 Found: 523.2671.



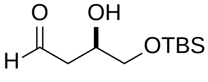
***syn*-20d**

Ethyl 2-((2R,4R,6R)-4-(methoxymethoxy)-6-((R)-2-hydroxy-4-((4-methoxybenzyl)-oxy)butyl)-tetrahydro-2H-pyran-2-yl)acetate (*syn*-20d): To diol ***syn*-19d** (46 mg, 0.104 mmol) in 1 mL THF cooled to –40 ºC was added potassium *tert*-butoxide (12 mg, 0.104 mmol). This reaction was allowed to warm up to room temperature and stirred for 7 h, when it was quenched with saturated aqueous ammonium chloride (2 mL) and diluted with ether (5 mL). The aqueous layer was extracted with ether (2 x 5 mL). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by silica gel chromatography to produce pyran ***syn*-20d** (28 mg) in 61% yield as a clear oil: $[\alpha]_D$ 11.7° (*c* 1.2, CH_2Cl_2); IR (neat) 3522, 2924, 1732, 1615, 1515, 1456, 1248, 1034 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.26 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.68 (s, 2H), 4.45 (d, *J* = 11.5 Hz, 1H), 4.42 (d, *J* = 11.5 Hz, 1H), 4.23 (dddd, *J* = 11.5, 9, 4.5, 2 Hz, 1H), 4.14 (q, *J* = 7 Hz, 2H), 4.14 (m, 1H), 4.03 (m, 2H), 3.81 (s, 3H), 3.59 (m, 2H), 3.38 (s, 3H), 2.48 (dd, *J* = 15.5, 9 Hz, 1H), 2.38 (dd, *J* = 15, 4 Hz, 1H), 1.84-1.68 (m, 4H), 1.60 (ddd, *J* = 14.5, 9.5, 9.5 Hz, 1H), 1.51 (ddd, *J* = 14.5, 2.5, 2.5 Hz, 1H), 1.48-1.41 (m, 2H), 1.26 (t, *J* = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.0, 158.9, 130.4, 129.1, 113.5, 94.8, 73.5, 72.5, 69.5, 69.1, 69.0, 67.2, 60.6, 55.3, 55.1, 42.6, 41.0, 37.1, 36.3, 35.5, 14.0 ; HRMS (ESI) calcd for $[C_{23}H_{36}O_8 + Na]^+$: 463.2308 Found: 463.2329.



***syn*-21d**

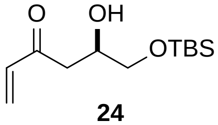
Ethyl 2-((2R,4R,6R)-6-((R)-2-methoxy-4-((4-methoxybenzyl)oxy)butyl)-4-(methoxymethoxy)tetrahydro-2H-pyran-2-yl)acetate (*syn*-21d): To a solution of alcohol ***syn*-20d** (36 mg, 0.082 mmol) in CH_2Cl_2 (4 mL) was added Proton Sponge (105 mg, 0.492 mmol), 4 Å molecular sieves (148 mg), and trimethyloxonium tetrafluoroborate (61 mg, 0.41 mmol). After about 1.5 h, the reaction was filtered through a fritted funnel, washing with ethyl acetate (5 x 10 mL). The filtrate was washed with water (1 x 20 mL) and 1M CuSO4 (2 x 20 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by silica gel chromatography to produce methyl ether ***syn*-21d** (36 mg) in 97% yield as a clear oil: R_f = 0.17 (4:1 hexanes:EtOAc); $[\alpha]_D$ 16.6° (*c* 1.0, CH_2Cl_2); IR (neat) 2934, 1738, 1614, 1586 1514, 1464, 1368, 1302, 1248, 1151, 1099, 1038 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.26 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.68 (d, *J* = 7 Hz, 1H), 4.66 (d, *J* = 7 Hz, 1H), 4.44 (d, *J* = 11.5 Hz, 1H), 4.41 (d, *J* = 11.5 Hz, 1H), 4.17 (dddd, *J* = 14, 8, 5.5, 2 Hz, 1H), 4.11 (q, *J* = 7 Hz, 2H), 4.02 (m, 1H), 3.87 (dddd, *J* = 11.5, 8.5, 4.5, 2 Hz, 1H), 3.81 (s, 3H), 3.53 (m, 2H), 3.46 (m, 1H), 3.37 (s, 3H), 3.29 (s, 3H), 2.48 (dd, *J* = 15, 8.5 Hz, 1H), 2.35 (dd, *J* = 15, 5 Hz, 1H), 1.73-1.88 (m, 5H), 1.35-1.49 (m, 3H), 1.23 (t, *J* = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.1, 159.1, 130.8, 129.2, 113.7, 94.9, 75.3, 72.6, 69.7, 69.3, 69.2, 66.8, 60.4, 56.5, 55.4, 55.3, 41.7, 39.9, 36.5, 35.9, 33.9, 14.3; HRMS (ESI) calcd for $[C_{24}H_{38}O_8 + Na]^+$: 477.2464 Found: 477.2463.



23

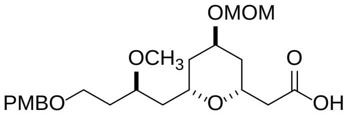
(R)-4-((tert-butyldimethylsilyl)oxy)-3-hydroxybutanal (23): To a solution of alcohol **22** (1.50 g, 5.2 mmol) in CH_2Cl_2 (20 mL) was added NMO (2.44 g of a 50% solution in H_2O, 10.4 mmol).

This solution was cooled down to 0ºC and OsO_4 (13 mg, 0.05 mmol) was added and the reaction was stirred overnight. The reaction was quenched with saturated aqueous sodium sulfite (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 20 mL). The combined organic layers were washed with saturated aqueous ammonium chloride (20 mL), brine (15 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The crude triol was then dissolved in methanol (20 mL) and H_2O (20 mL) and $NaIO_4$ (1.64 g, 7.65 mmol) was added. The reaction was stirred for 4 h when saturated aqueous sodium bicarbonate (30 mL) and EtOAc (150 mL) were added. The layers were separated and the aqueous layer was extracted with EtOAc (2 x 50 mL). The combined organic layers were washed with brine (25 mL), dried over anhydrous sodium sulfate, filtered, and concentrated to give crude aldehyde **23** (772 mg, 68%) as a clear oil: R_f = 0.64 (3:2 hexanes:EtOAc); $[\alpha]_D$ –0.6° (*c* 1.0, CH_2Cl_2); IR (neat) 3439, 2930, 2858, 2739, 1728, 1472, 1464, 1390, 1362, 1255, 1110, 1007 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 9.86 (dd, *J* = 1.5, 1.5 Hz, 1H), 4.21 (m, 1H), 3.67 (dd, *J* = 9.9, 4.2 Hz, 1H), 3.54 (dd, *J* = 9.9, 6.3 Hz, 1H), 2.62 (m, 2H), 0.91 (s, 9H), 0.07 (s, 3H), 0.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 201.4, 67.2, 66.2, 46.9, 25.7, 18.1, -5.6, -5.6; HRMS (ESI) calcd for $[C_{10}H_{22}O_3Si+Na]^+$: 241.1236 Found: 241.1246.



24

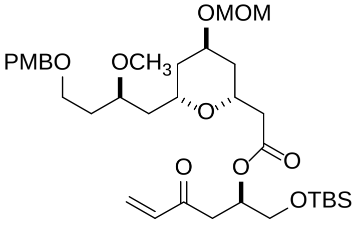
(R)-6-((tert-butyldimethylsilyl)oxy)-5-hydroxyhex-1-en-3-one (24): To a solution of aldehyde **23** (300 mg, 1.37 mmol) in THF (10 mL) cooled to -78 ºC was added vinylMgBr (4.4 mL of a 1M solution in THF). The reaction was stirred for 3 h and then warmed to room temperature. The reaction was quenched with saturated aqueous sodium bicarbonate (10 mL) and diluted with ether. The layers were separated and the aqueous layer was extracted with ether (3 x 10 mL). The organic layers were combined, washed with brine (15 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The crude diol was dissolved in CH_2Cl_2 (10 mL) and MnO_2 (1.08 g, 12.5 mmol) was added. The reaction was stirred overnight and then filtered through a pad of celite. The solvent was removed under reduced pressure and the crude product was purified with silica gel chromatography to give 284 mg (85% yield) of enone **24**: R_f = 0.38 (4:1 hexanes:EtOAc); $[\alpha]_D$ 11.1° (*c* 1.0, CH_2Cl_2); IR (neat) 3472, 2955, 2930, 2858, 1682, 1614, 1472, 1403, 1362, 1256, 1120, 1006 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.38 (dd, *J* = 18, 10.5 Hz, 1H), 6.26 (dd, *J* = 18, 1 Hz, 1H), 5.90 (dd, *J* = 10.5, 1 Hz, 1H), 4.16 (m, 1H), 3.65 (dd, *J* = 10, 5 Hz, 1H), 3.59 (dd, *J* = 10, 5.5 Hz, 1H), 2.93 (d, *J* = 4.5 Hz, 1H), 2.81 (d, *J* = 6 Hz, 1H), 0.90 (s, 9H), 0.08 (s, 3H), 0.08 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 200.1, 136.8, 129.0, 68.3, 66.3, 42.3, 25.9, 18.3, -5.4, -5.4; HRMS (ESI) calcd for $[C_{12}H_{24}O_3Si + Na]^+$: 267.1392 Found: 267.1400.



25

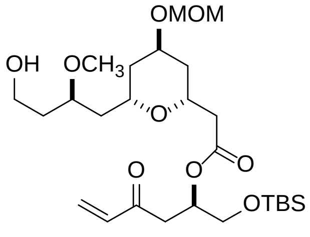
2-((2R,4R,6R)-6-((R)-2-methoxy-4-((4-methoxybenzyl)oxy)butyl)-4-(methoxymethoxy)-tetrahydro-2H-pyran-2-yl)acetic acid (25): To a solution of ester ***syn*-21d** (60 mg, 0.132 mmol) in THF (1 mL) and H_2O (1 mL) was added LiOH (4.5 mg, 0.185 mmol). This solution was allowed to stir for 5 h. The reaction was acidified to pH 4 with 1 M HCl and diluted with ethyl acetate. The layers were separated and the organic layer was washed with brine and dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by silica gel chromatography to produce carboxylic acid **25** (52 mg) in 92% yield as a clear oil:

[α]$_D$ –2.2° (*c* 1.0, CH_2Cl_2); IR (neat) 2936, 1732, 1714, 1614, 1586 1514, 1464, 1442, 1360, 1302, 1248, 1211, 1172, 1150, 1101, 1037 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.27 (d, *J* = 9 Hz, 2H), 6.87 (d, *J* = 9 Hz, 2H), 4.67 (s, 2H), 4.44 (s, 2H), 4.16 (dddd, *J* = 13.5, 7.5, 5.5, 2 Hz, 1H), 4.03 (m, 1H), 3.94 (dddd, *J* = 10.5, 8.5, 3.5, 2 Hz, 1H), 3.80 (s, 3H), 3.47-3.57 (m, 3H), 3.37 (s, 3H), 3.28 (s, 3H), 2.47 (m, 2H), 1.74-1.87 (m, 5H), 1.48 (ddd, J = 14.5, 6, 4 Hz, 1H), 1.40-1.47 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 173.3, 159.2, 130.4, 129.4, 113.8, 95.0, 76.1, 72.7, 70.7, 69.4, 69.0, 66.5, 56.5, 55.5, 55.3, 40.9, 39.8, 36.5, 35.8, 33.5; HRMS (ESI) calcd for $[C_{22}H_{34}O_8 + Na]^+$: 449.2151 Found: 449.2154.



26

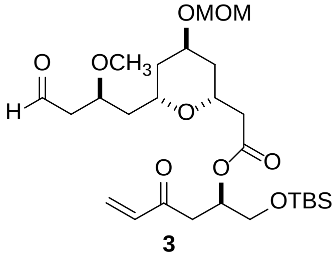
(R)-1-((tert-butyldimethylsilyl)oxy)-4-oxohex-5-en-2-yl 2-((2R,4R,6R)-6-((R)-2-methoxy-4-((4-methoxybenzyl)oxy)butyl)-4-(methoxymethoxy)tetrahydro-2H-pyran-2-yl)acetate (26): To a solution of alcohol **24** (15.5 mg, 0.063 mmol) and acid **25** in CH_2Cl_2 (1 mL) was added DCC (26mg, 0.126 mmol) and 5 mg (0.042 mmol) of DMAP. The reaction was stirred at room temperature and after 4 h, diluted with ether (3 mL), filtered through a glass wool plug, and washed successively with aqueous $NaHSO_4$, saturated aqueous $NaHCO_3$, and brine. The organic layer was dried ($NaSO_4$) and evaporated to yield crude ester. The product was purified with flash chromatography to yield ester **26** as a clear oil (18 mg, 64%): [α]$_D$ 17.6° (*c* 1.3, CH_2Cl_2); IR (neat) 2927, 1739, 1685, 1614, 1514, 1464, 1362, 1248, 1100, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.25 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.35 (dd, *J* = 17.7, 10.2 Hz, 1H), 6.23 (dd, *J* = 17.7, 1.5 Hz, 1H), 5.86 (dd, *J* = 9.9, 1.5 Hz, 1H), 5.29 (m, 1H), 4.67 (d, *J* = 2.1 Hz, 1H), 4.65 (d, *J* = 2.1 Hz, 1H), 4.42 (s, 2H), 4.13 (m, 2H), 4.01 (m, 1H), 3.87 (m, 1H), 3.80 (s, 3H), 3.75 (dd, *J* = 10.8, 4.5 Hz, 1H), 3.66 (dd, *J* = 10.8, 4.8 Hz, 1H), 3.53 (m, 2H), 3.45 (m, 1H), 3.36 (s, 3H), 3.28 (s, 3H), 2.98 (dd, *J* = 16.5, 6.3, Hz, 1H), 2.88 (dd, *J* = 16.5, 6.9 Hz, 1H), 2.48 (dd, *J* = 15.3, 7.5 Hz, 1H), 2.33 (dd, *J* = 15, 5.7 Hz, 1H), 1.79 (m, 5H), 1.31-1.50 (m, 3H), 0.87 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 197.3, 170.0, 158.9, 136.4, 130.5, 129.0, 128.6, 113.6, 94.7, 75.0, 72.4, 70.6, 69.4, 69.2, 68.7, 66.5, 63.4, 56.3, 55.2, 55.1, 41.3, 39.9, 39.9, 36.2, 35.6, 33.8, 25.7, 18.1, -5.5; HRMS (ESI) calcd for $[C_{34}H_{56}O_{10}Si + Na]^+$: 675.3540 Found: 675.3534.



27

(R)-1-((tert-butyldimethylsilyl)oxy)-4-oxohex-5-en-2-yl 2-((2R,4R,6R)-6-((R)-4-hydroxy-2-methoxybutyl)-4-(methoxymethoxy)tetrahydro-2H-pyran-2-yl)acetate (27): To a solution of PMB ether **26** (30 mg, 0.046 mmol) in 1 mL of CH_2Cl_2 was added 5 µL of H_2O and 16 mg (0.69 mmol) of DDQ. This reaction was stirred for 2 h when saturated aqueous sodium bicarbonate (1 mL) was added to the reaction along with more CH_2Cl_2 (5 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The organic layers were combined and washed with brine (5 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified with silica gel chromatography to yield 19 mg (78%) of alcohol **27**:

R_f = 0.12 (3:2 hexanes:EtOAc); $[\alpha]_D$ 26.2° (*c* 1.0, CH_2Cl_2); IR (neat) 3493, 2932, 1738, 1688, 1613, 1546, 1464, 1404, 1360, 1253, 1150, 1101, 1040 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.36 (dd, *J* = 17.5, 10.5 Hz, 1H), 6.24 (dd, *J* = 18, 1 Hz, 1H), 5.88 (dd, *J* = 10.5, 1 Hz, 1H), 5.29 (m, 1H), 4.68 (d, *J* = 7 Hz, 1H), 4.66 (d, *J* = 7 Hz, 1H), 4.13 (m, 1H), 4.02 (m, 1H), 3.88 (dddd, *J* = 11.5, 9.5, 4, 2 Hz, 1H), 3.77 (dd, *J* = 11, 4.5 Hz, 1H), 3.75 (m, 2H), 3.68 (dd, *J* = 10.5, 4.5 Hz, 1H), 3.59 (m, 1H), 3.36 (s, 3H), 3.33 (s, 3H), 2.98 (dd, *J* = 16.5, 5.5 Hz, 1H), 2.91 (dd, *J* = 16.5, 7.5 Hz, 1H), 2.45 (dd, *J* = 15.5, 8 Hz, 1H), 2.34 (dd, *J* = 15.5, 5 Hz, 1H), 1.77-1.91 (m, 3H), 1.64-1.76 (m, 3H), 1.36-1.50 (m, 2H), 0.88 (s, 9H), 0.05 (s, 3H), 0.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 197.6, 170.3, 136.6, 128.8, 94.9, 77.9, 70.8, 69.6, 69.2, 68.9, 65.9, 63.5, 56.4, 55.4, 41.3, 40.1, 39.2, 36.7, 35.7, 35.6, 25.8, 18.3, -5.4; HRMS (ESI) calcd for $[C_{26}H_{48}O_9Si + Na]^+$: 555.2965 Found: 555.2969.

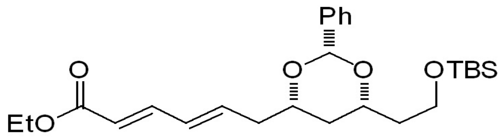


3

(R)-1-((tert-butyldimethylsilyl)oxy)-4-oxohex-5-en-2-yl 2-((2R,4R,6R)-6-((S)-2-methoxy-4-oxobutyl)-4-(methoxymethoxy)tetrahydro-2H-pyran-2-yl)acetate (3): To a solution of alcohol **27** (10 mg, 0.19 mmol) in 0.5 mL of CH_2Cl_2 was added 12 mg (0.029 mmol) of Dess-Martin periodane. The reaction was stirred for 2 h. Ether was added to the reaction and the solution was filtered through a pad of silica gel, followed by removal of the solvents under reduced pressure. The crude product was purified by silica gel chromatography to produce 7 mg (70% yield) of aldehyde **3** as a clear oil: R_f = 0.26 (3:2 hexanes:EtOAc); $[\alpha]_D$ 16.1° (*c* 0.7,

CH_2Cl_2); IR (neat) 2930, 2858, 1732, 1682, 1615, 1464, 1403, 1360, 1253, 1189, 1150, 1104, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.77 (dd, *J* = 2.5, 1.5 Hz, 1H), 6.35 (dd, *J* = 17.5, 10.5 Hz, 1H), 6.24 (dd, *J* = 18, 1 Hz, 1H), 5.87 (dd, *J* = 10.5, 1 Hz, 1H), 5.29 (m, 1H), 4.68 (d, *J* = 7 Hz, 1H), 4.66 (d, *J* = 7 Hz, 1H), 4.13 (m, 1H), 4.02 (m, 1H), 3.82-3.96 (m, 2H), 3.76 (dd, *J* = 11, 4.5 Hz, 1H), 3.68 (dd, *J* = 11, 5 Hz, 1H), 3.37 (s, 3H), 3.32 (s, 3H), 2.98 (dd, *J* = 17, 6 Hz, 1H), 2.90 (dd, *J* = 16.5, 7 Hz, 1H), 2.69 (ddd, *J* = 16.5, 4.5, 1.5 Hz, 1H), 2.58 (ddd, *J* = 16.5, 7.5, 3 Hz, 1H), 2.45 (dd, *J* = 15, 7.5 Hz, 1H), 2.33 (dd, *J* = 15.5, 5 Hz, 1H), 1.86 (ddd, *J* = 14, 9, 4.5 Hz, 1H), 1.81 (m, 1H), 1.73 (m, 3H), 1.54 (ddd, *J* = 14.5, 7.5, 4 Hz, 1H), 1.26 (m, 1H), 0.88 (s, 9H), 0.05 (s, 3H), 0.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 201.9, 197.5, 170.2, 136.6, 128.8, 94.9, 73.4, 70.8, 69.5, 68.8, 63.5, 56.6, 55.4, 47.7, 41.3, 40.1, 39.2, 36.5, 35.6, 31.6, 25.8, 18.3, -5.4; HRMS (ESI) calcd for $[C_{26}H_{46}O_9Si + CH_3OH + Na]^+$: 585.3071 Found: 585.3057.

Section C: ^{1}H and ^{13}C NMR Spectra



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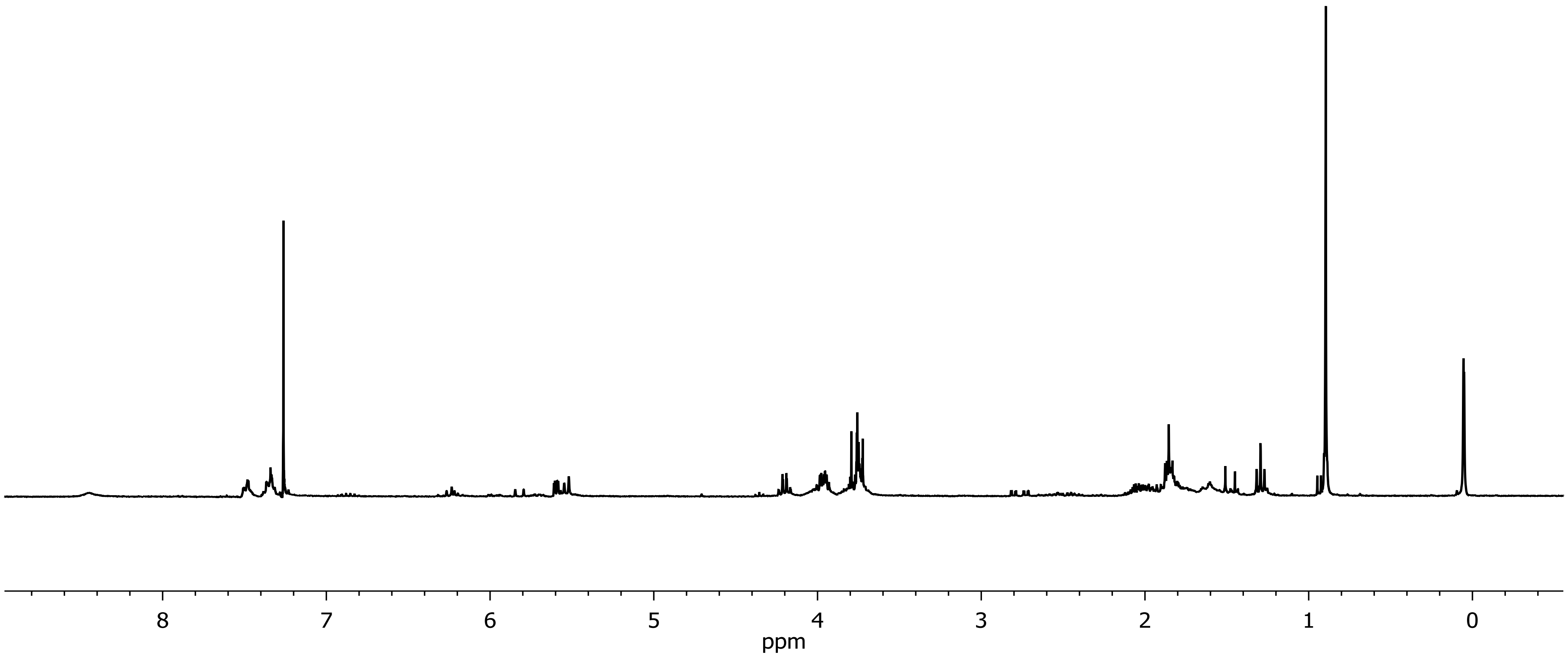
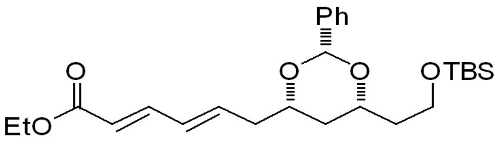
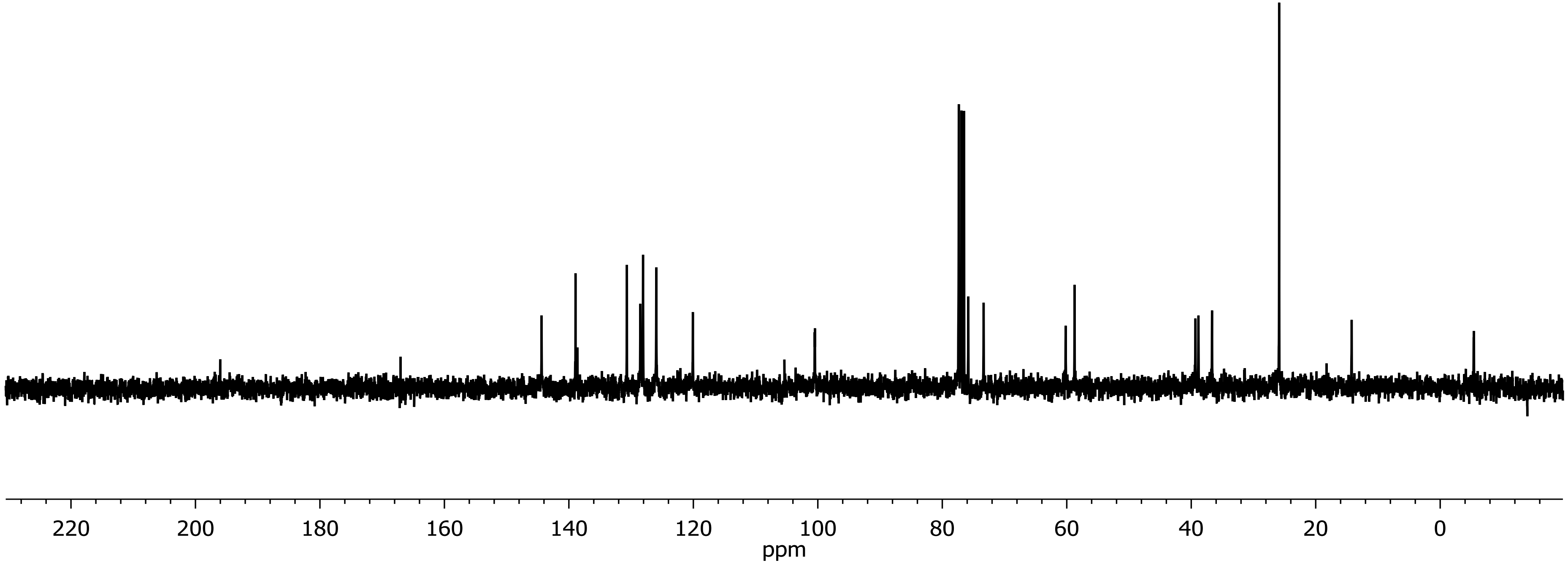
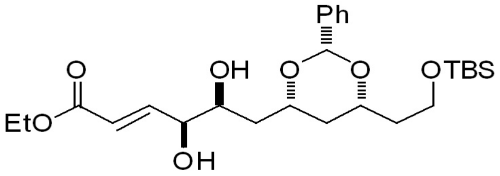


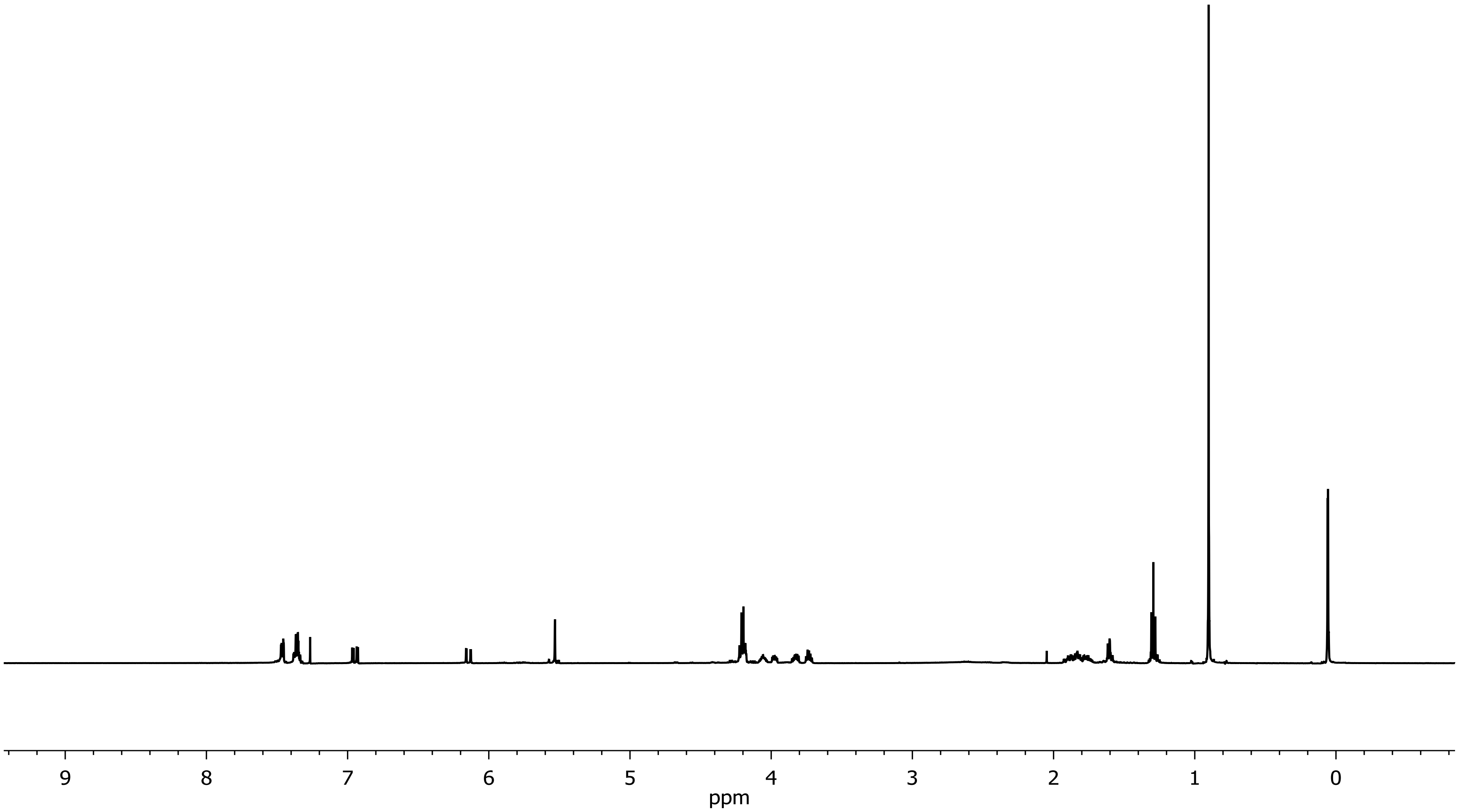


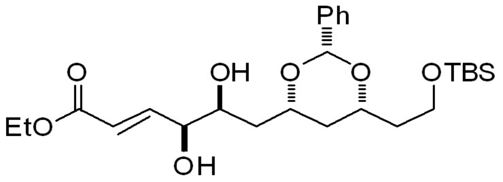
^{13}C NMR(75MHz, CDCl$_3$)



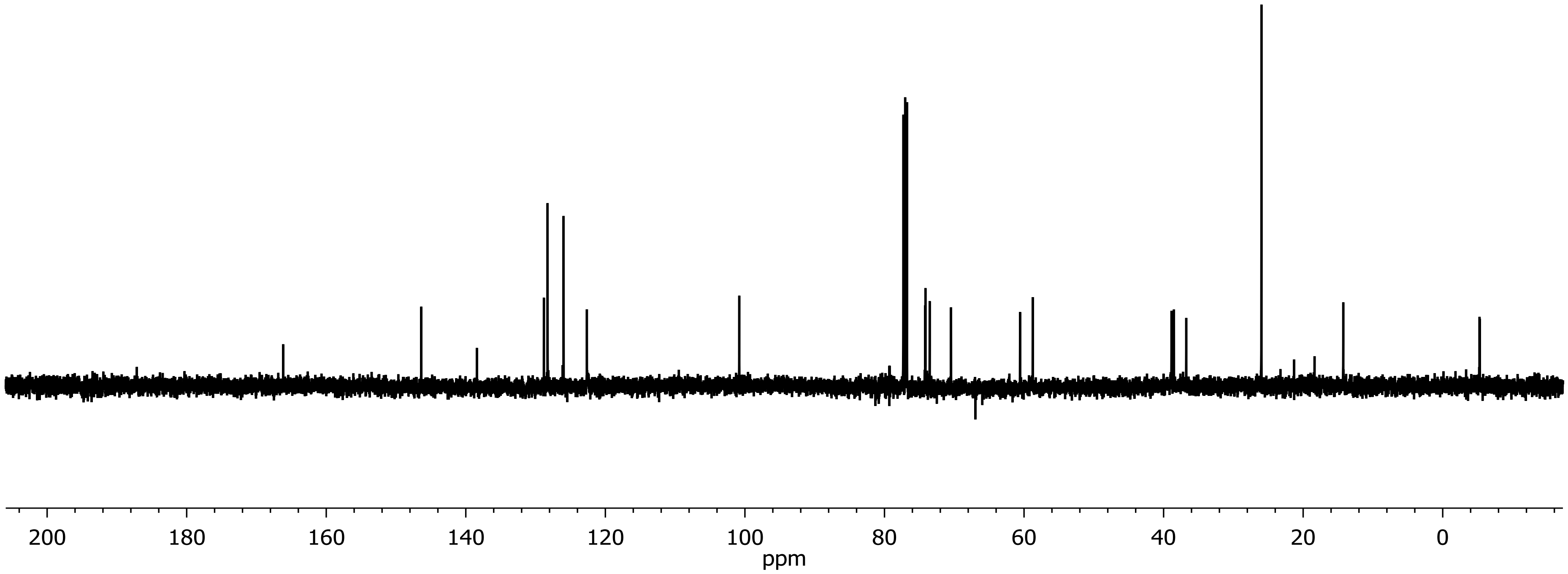


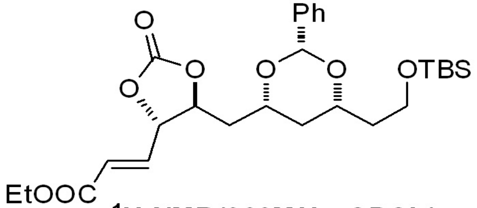
^{1}H NMR(300MHz, CDCl$_3$)



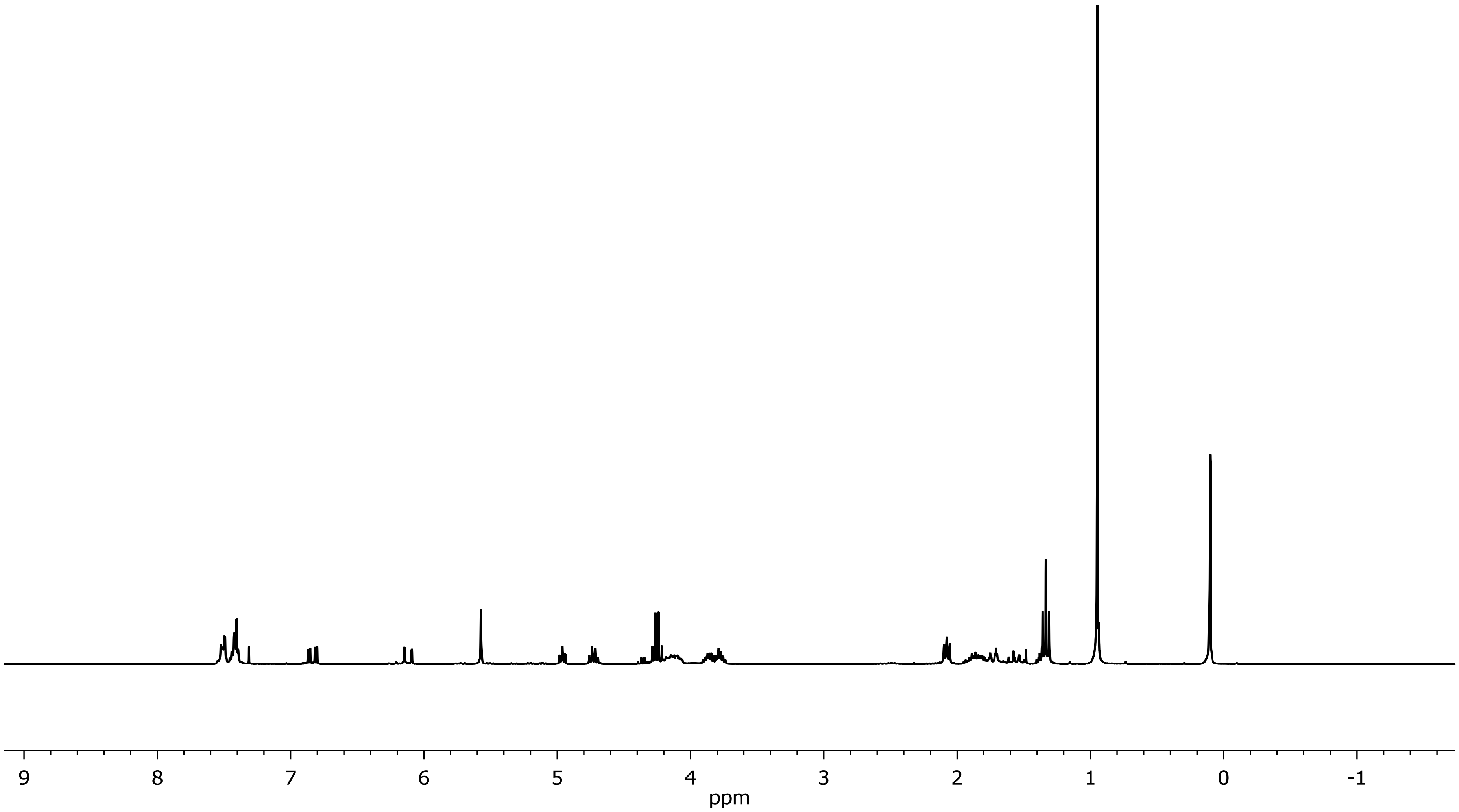


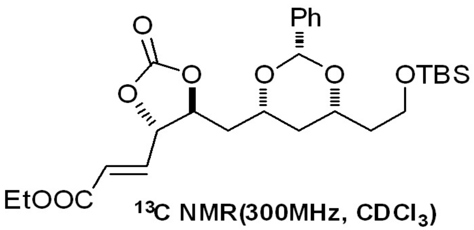
^{13}C NMR(125MHz, CDCl$_3$)



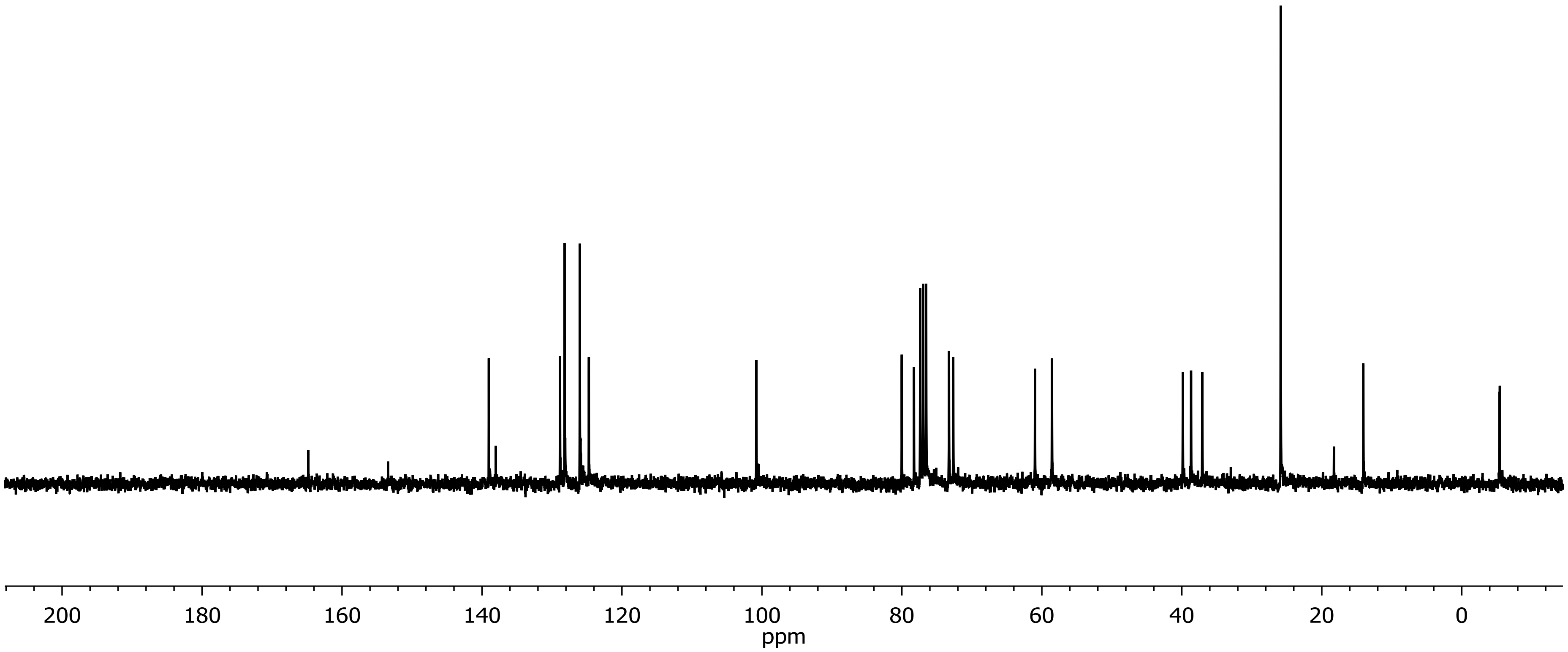


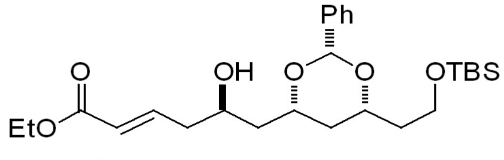
^{1}H NMR(300MHz, $CDCl_3$)





^{13}C NMR(300MHz, CDCl$_3$)





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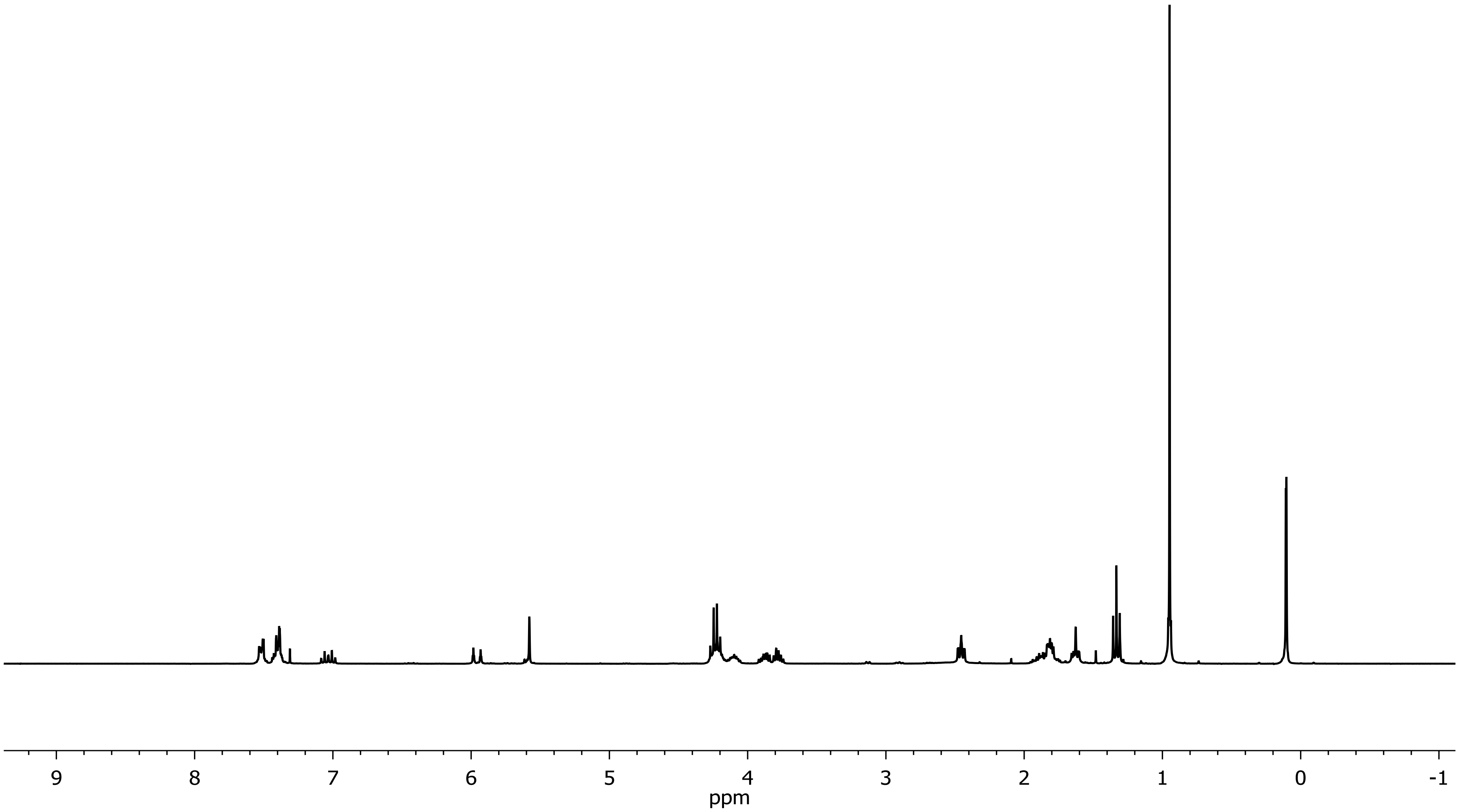
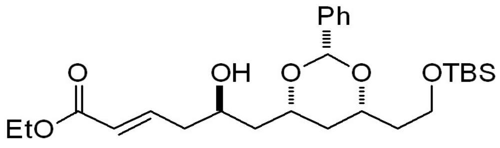
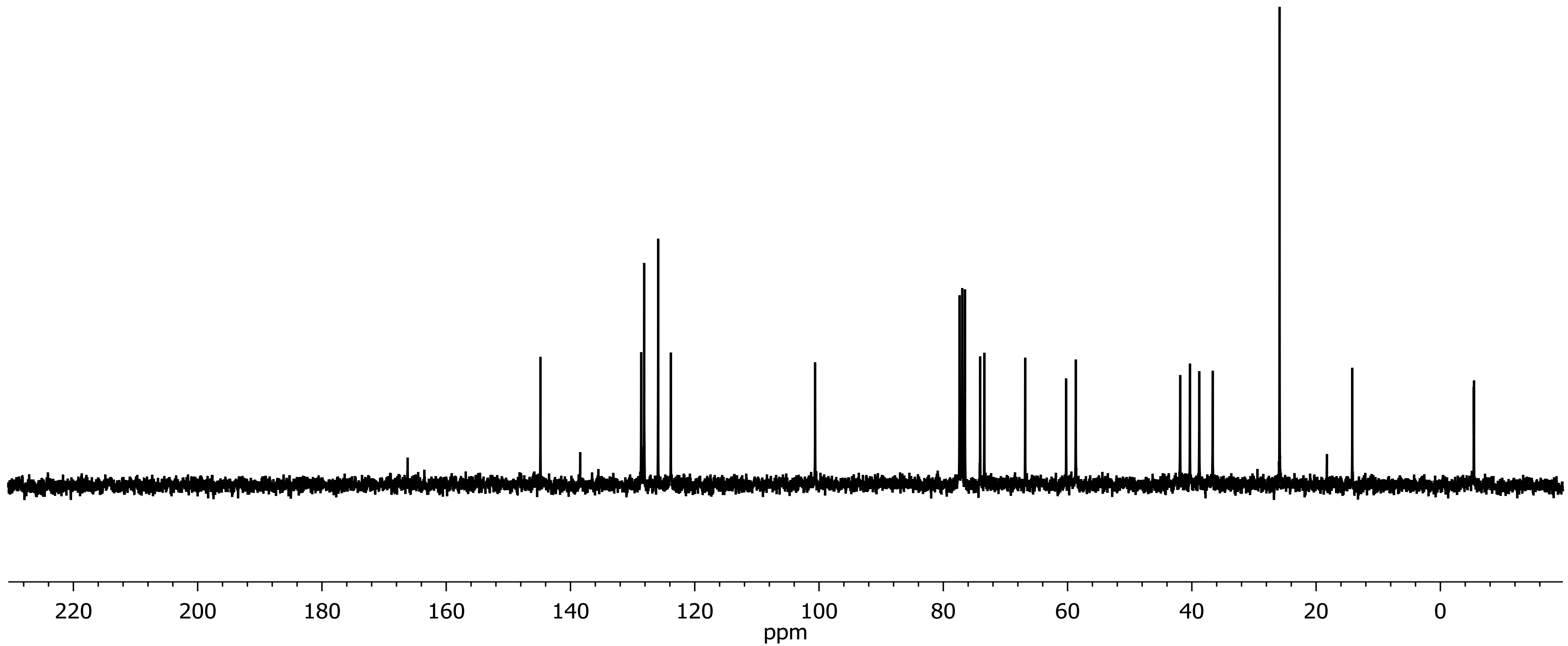
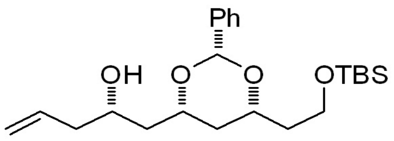


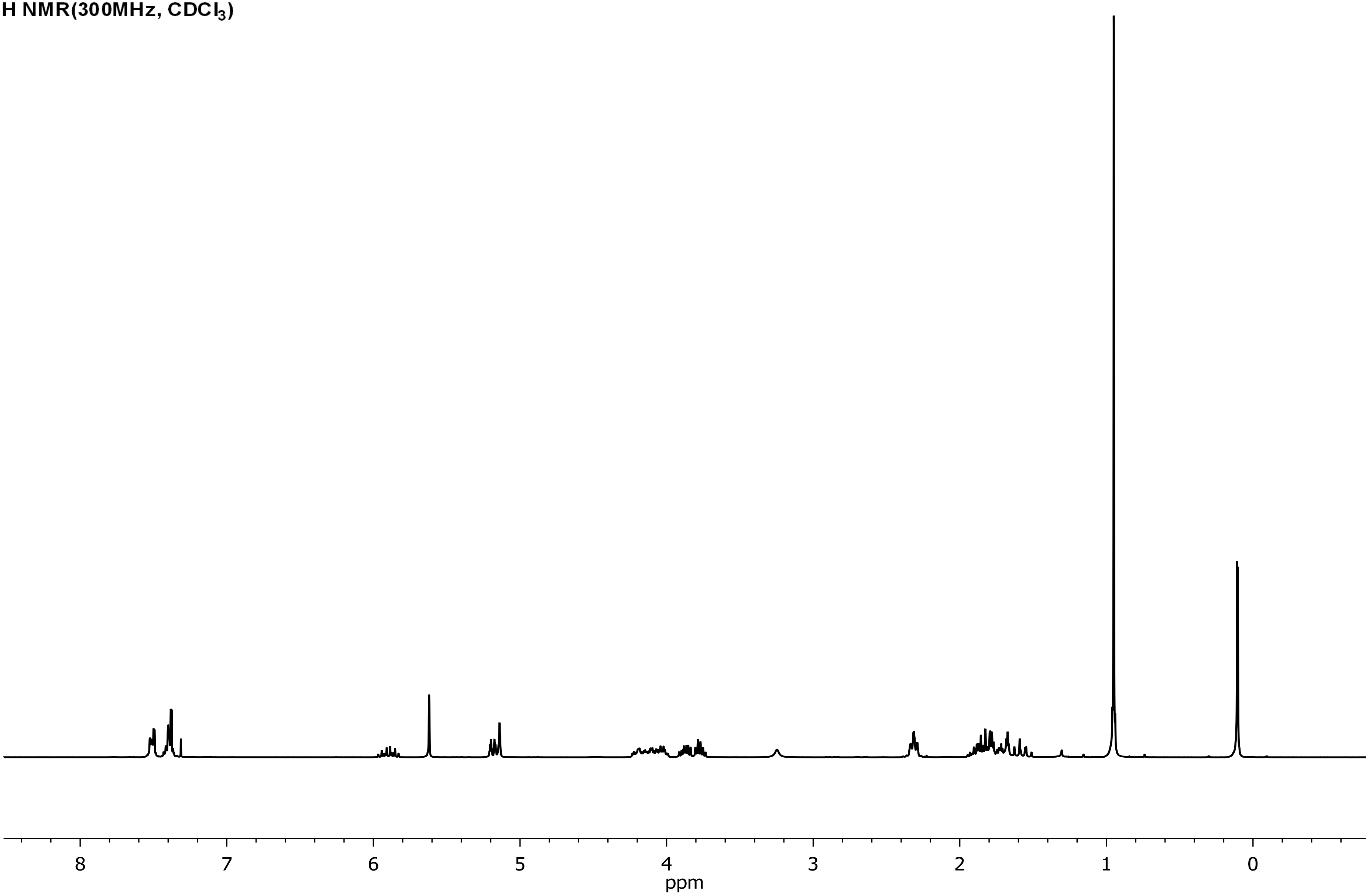


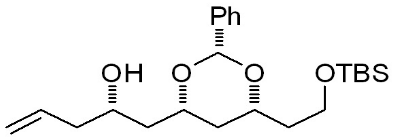
^{13}C NMR(75MHz, CDCl$_3$)



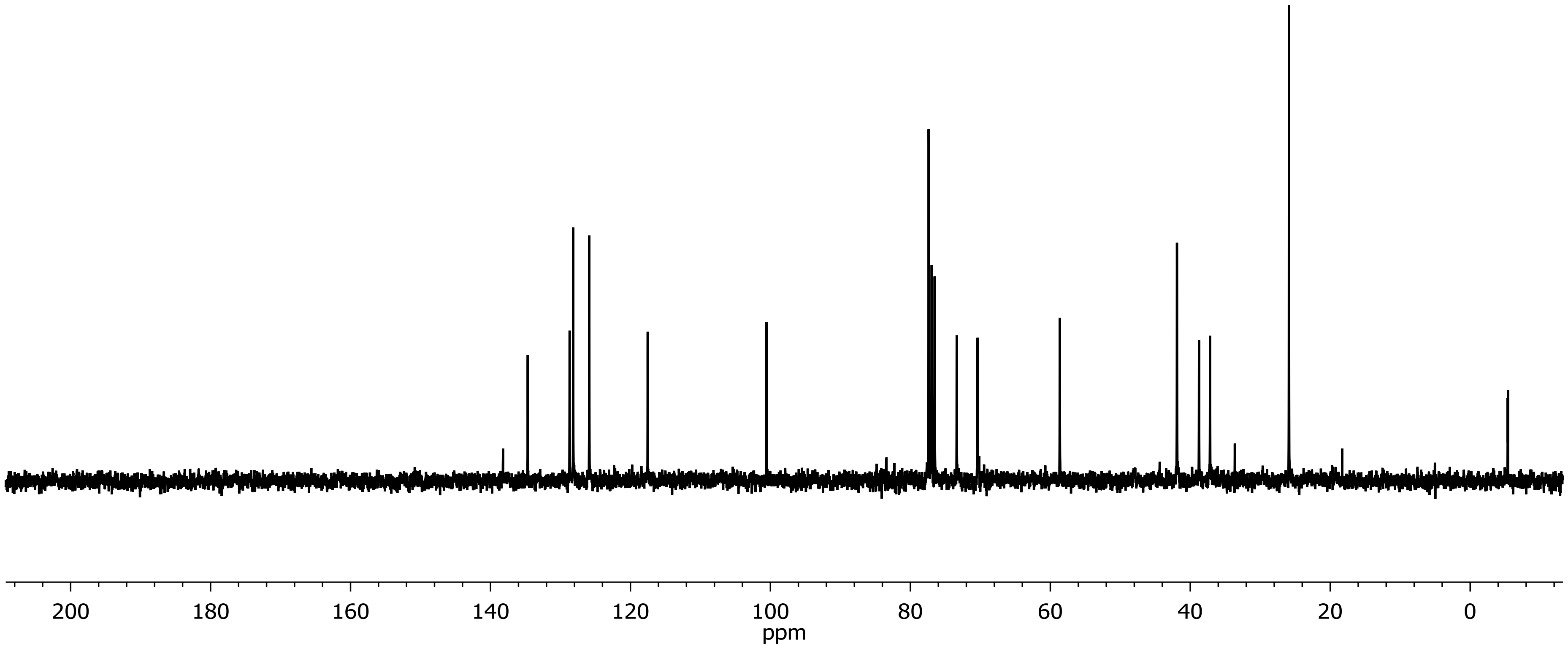


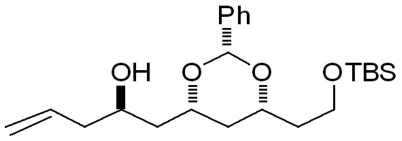
^{1}H NMR(300MHz, CDCl$_3$)



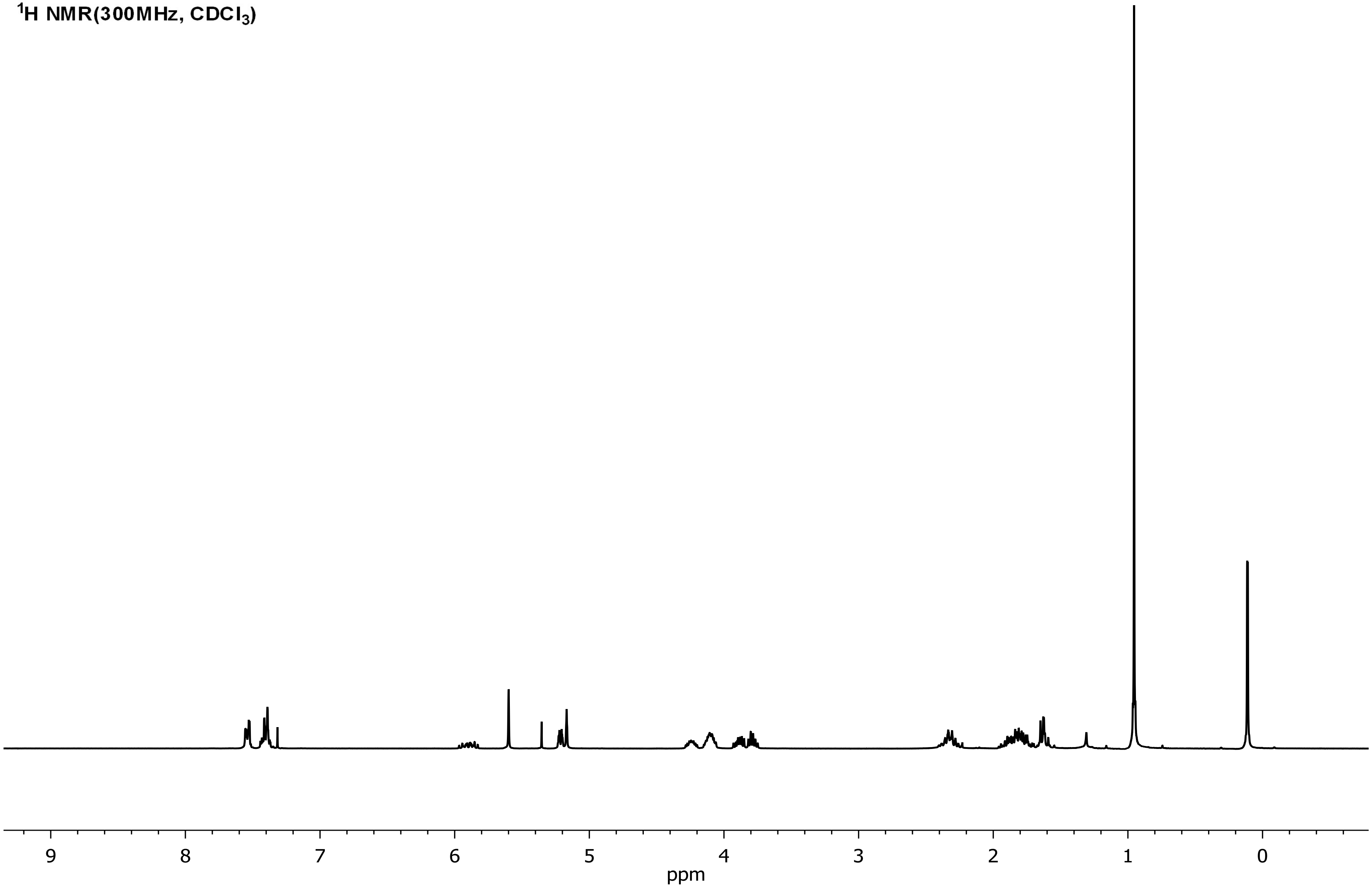


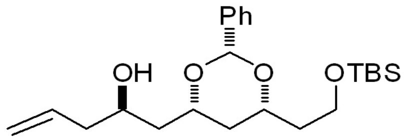
^{13}C NMR(75MHz, $CDCl_3$)



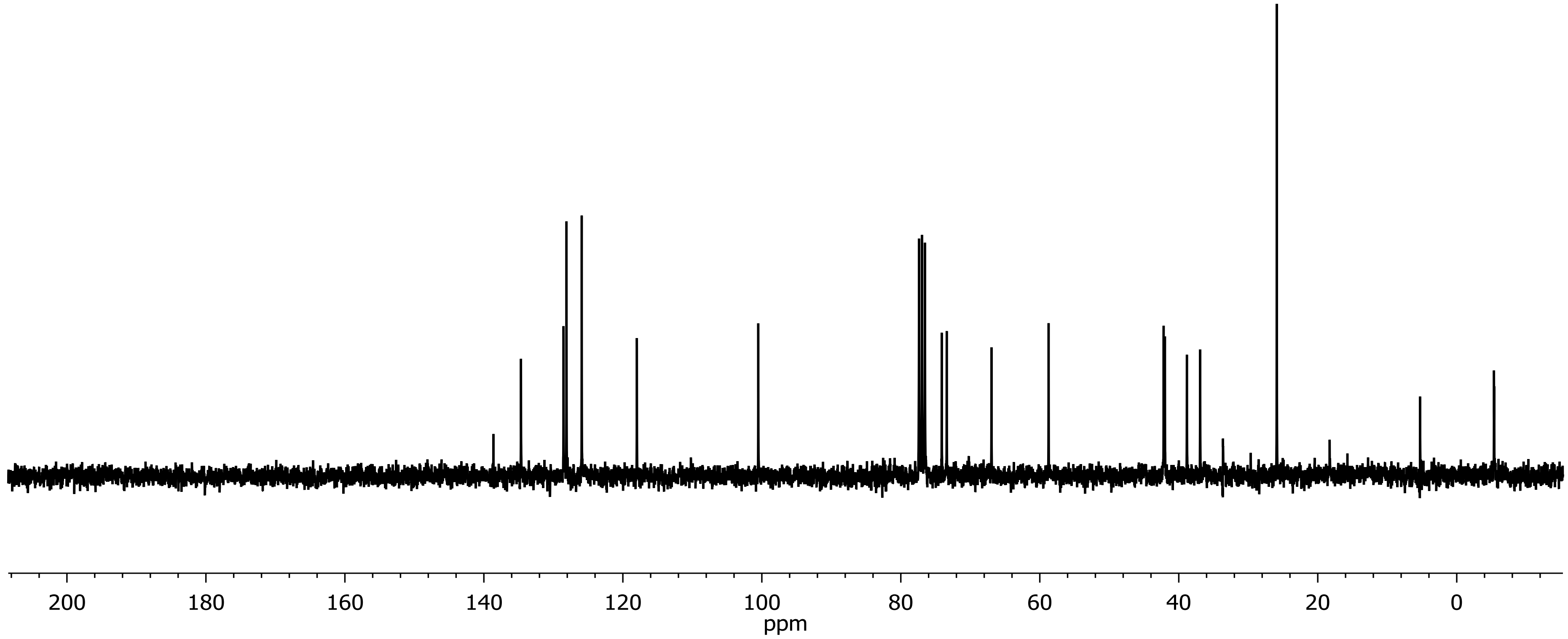


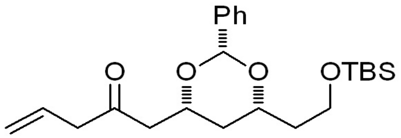
^{1}H NMR(300MHz, CDCl$_3$)



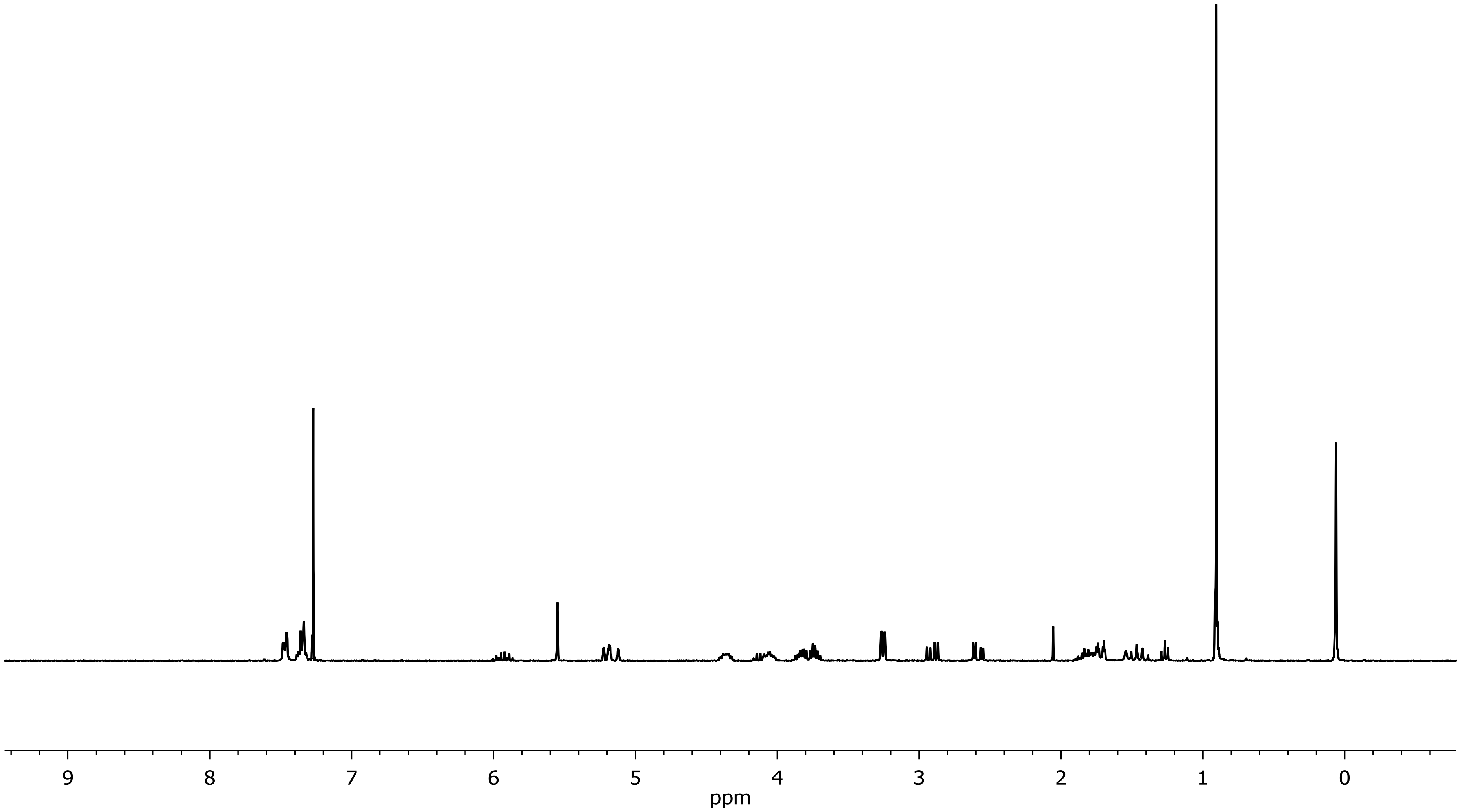


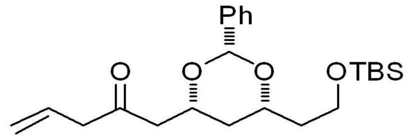
^{13}C NMR(75MHz, CDCl$_3$)



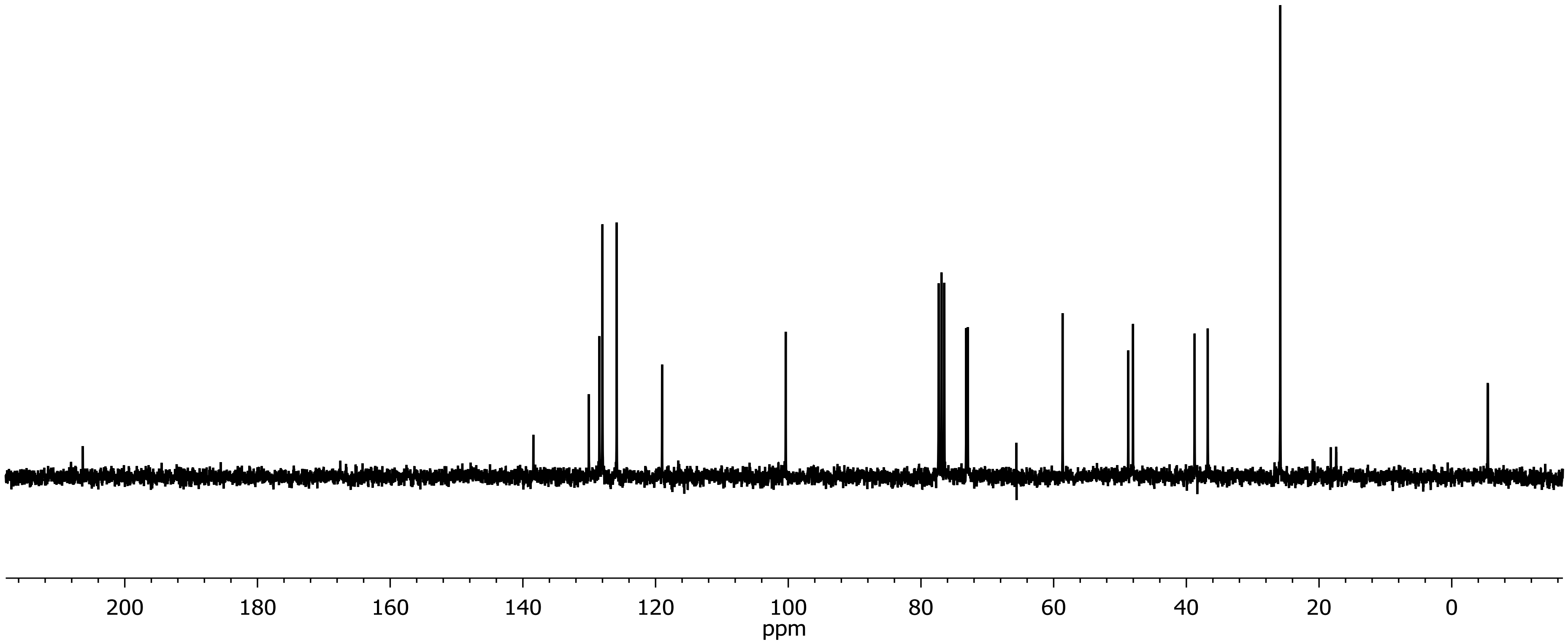


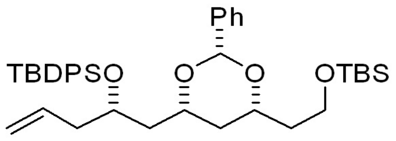
^{1}H NMR(300MHz, CDCl$_3$)



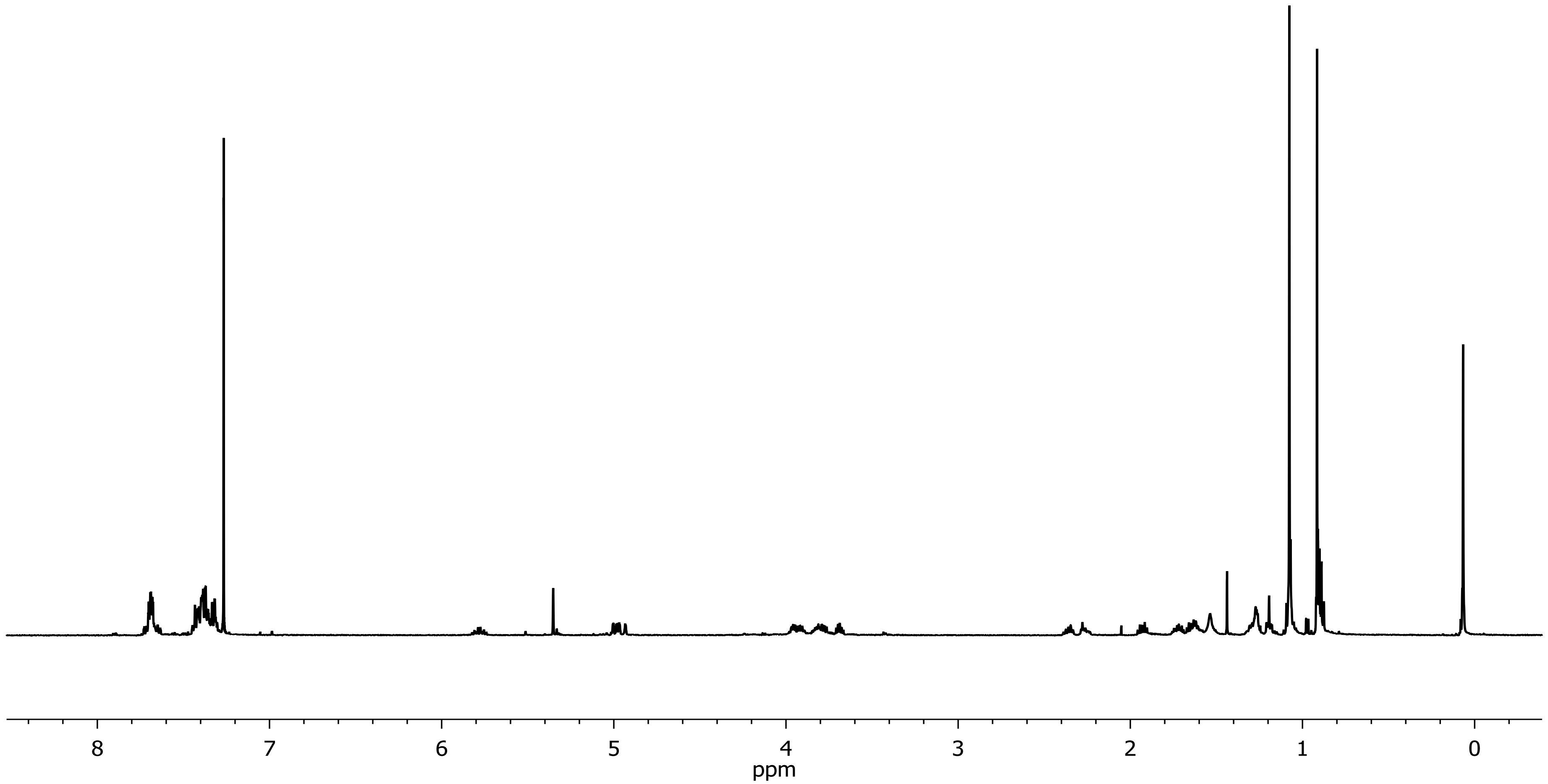


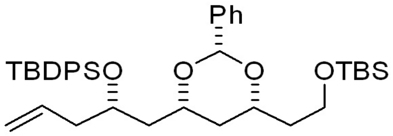
^{13}C NMR(100MHz, CDCl$_3$)



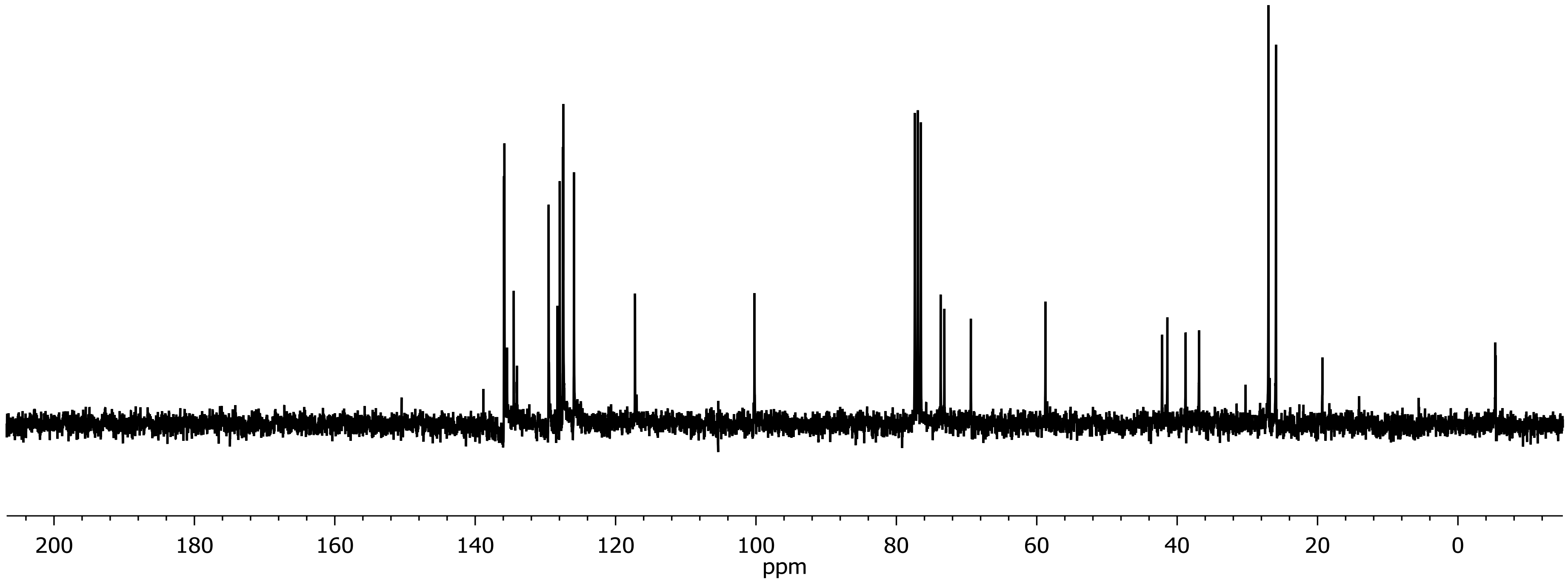


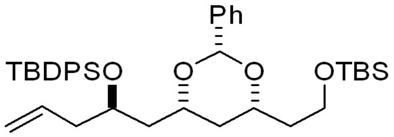
^{1}H NMR(500MHz, CDCl$_3$)



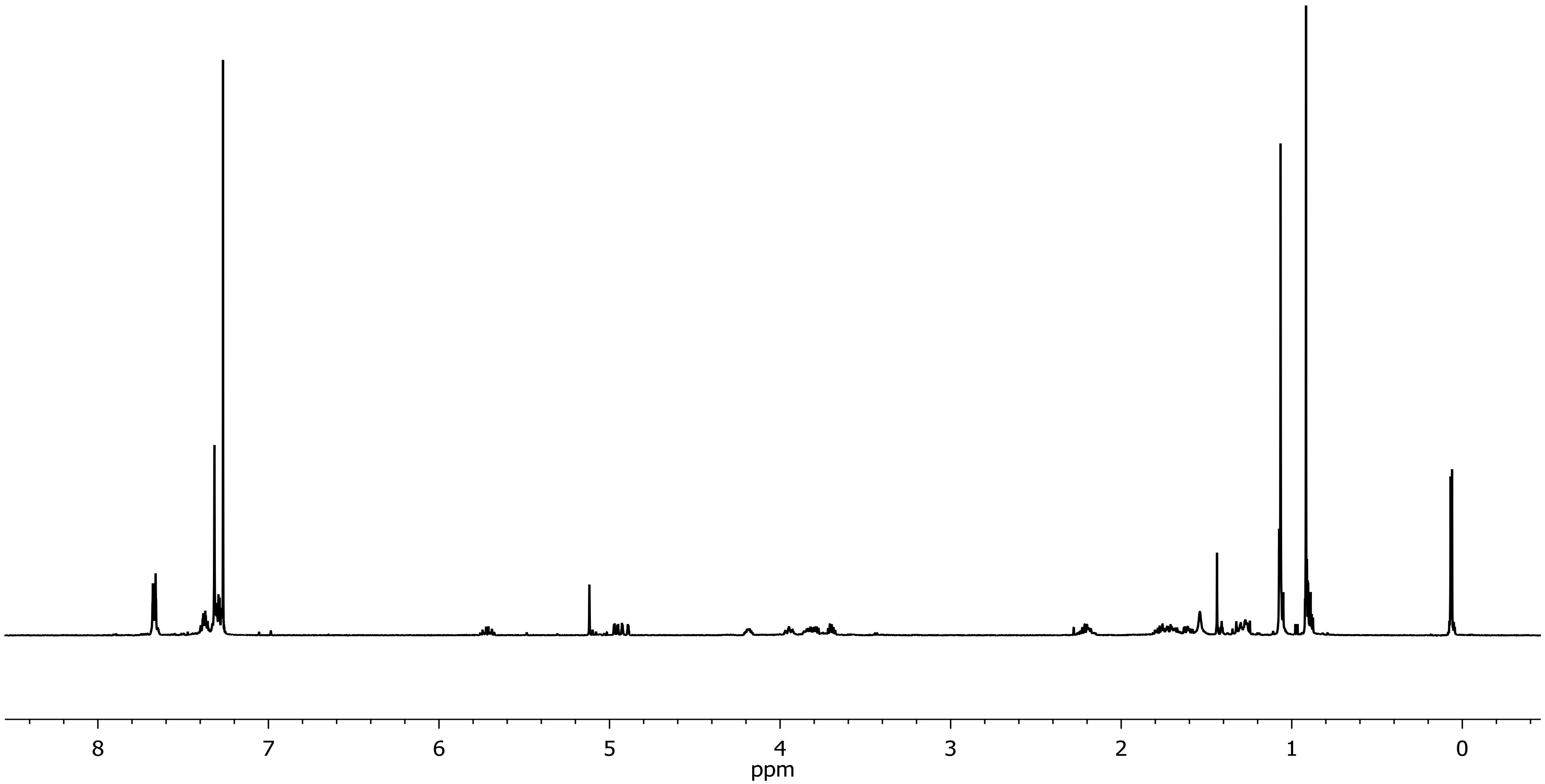


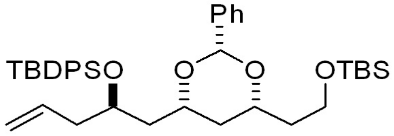
^{13}C NMR(75MHz, CDCl$_3$)



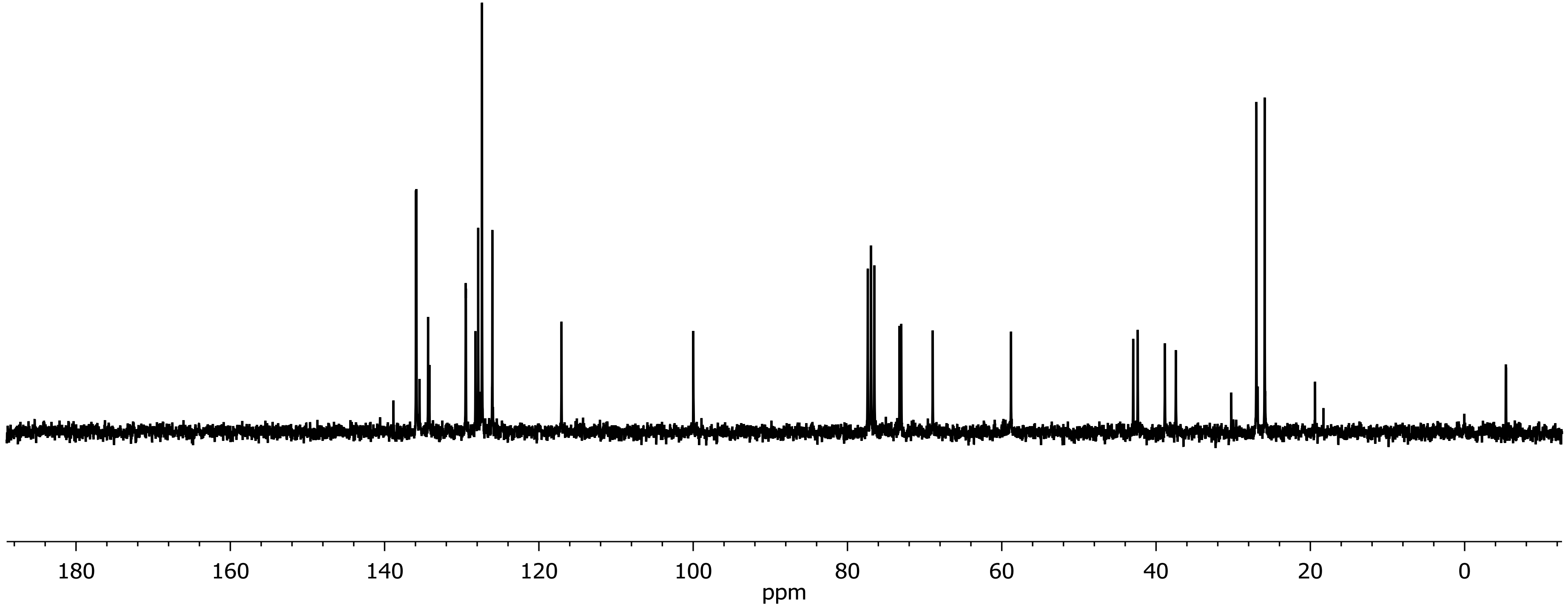


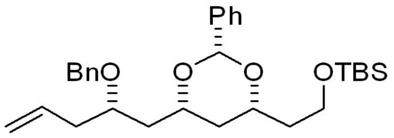
^{1}H NMR(500MHz, $CDCl_3$)



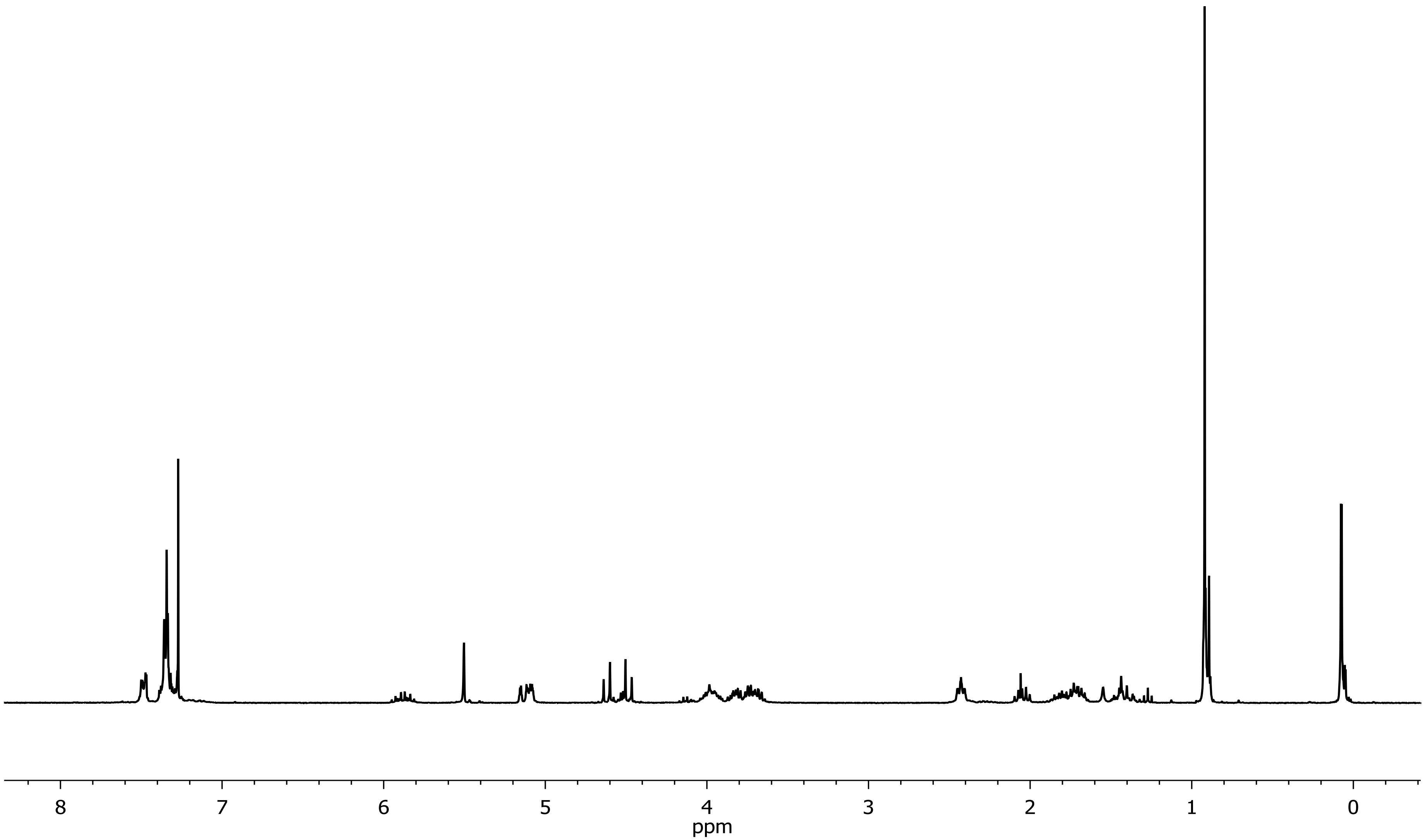


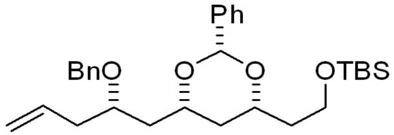
^{13}C NMR(75MHz, $CDCl_3$)



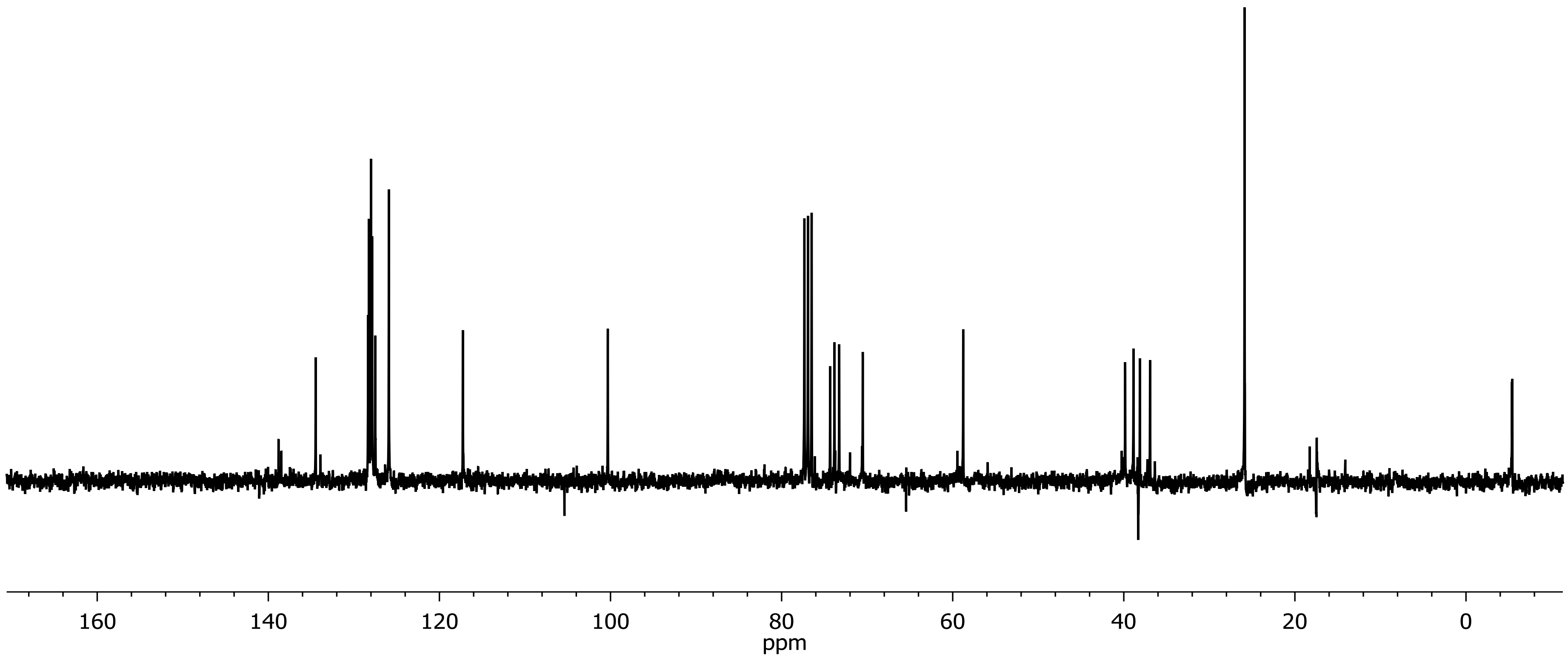


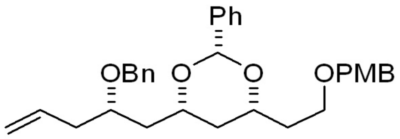
^{1}H NMR(300MHz, CDCl$_3$)



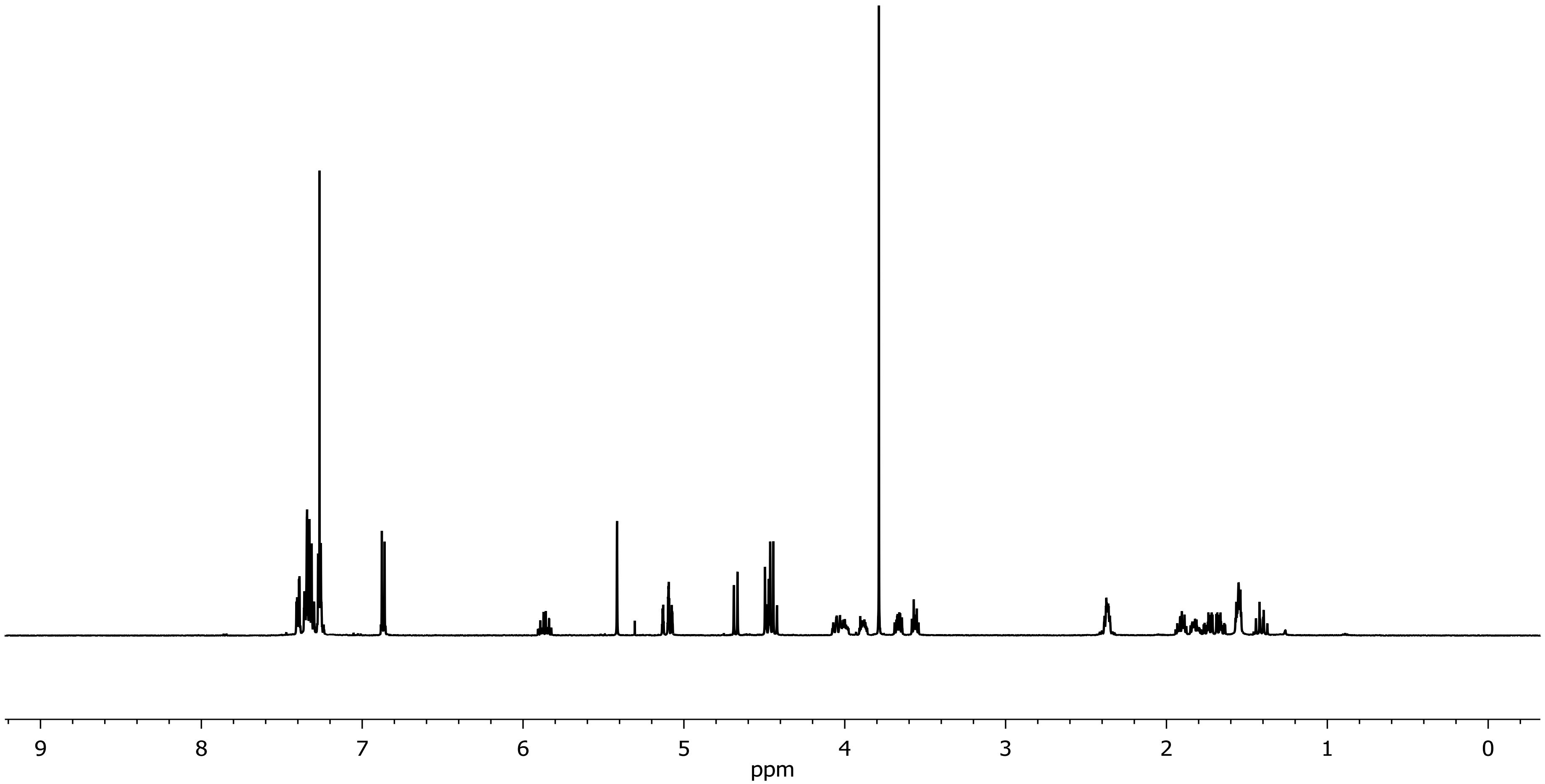


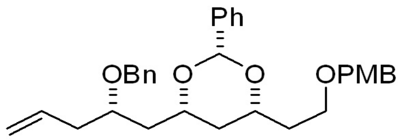
^{13}C NMR(75MHz, $CDCl_3$)



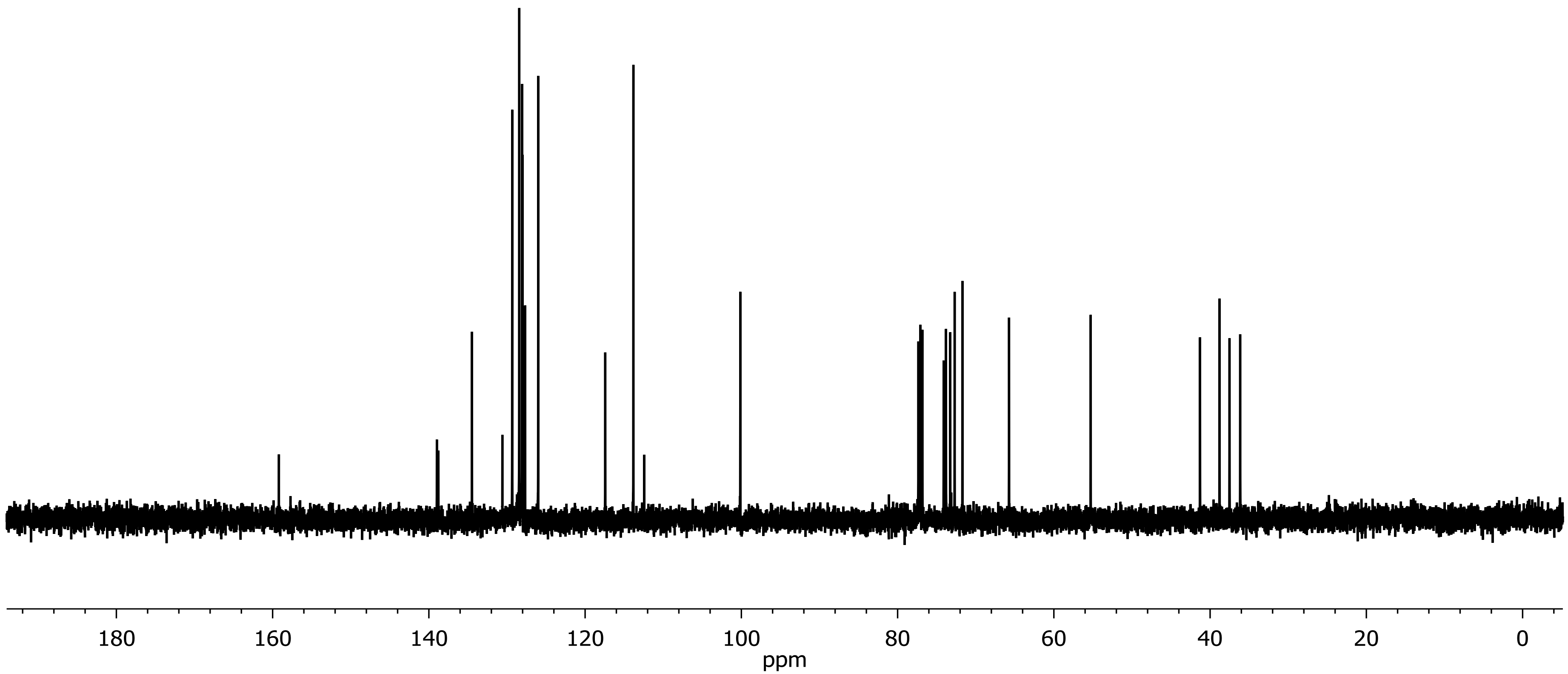


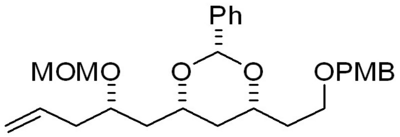
^{1}H NMR(500MHz, CDCl$_3$)



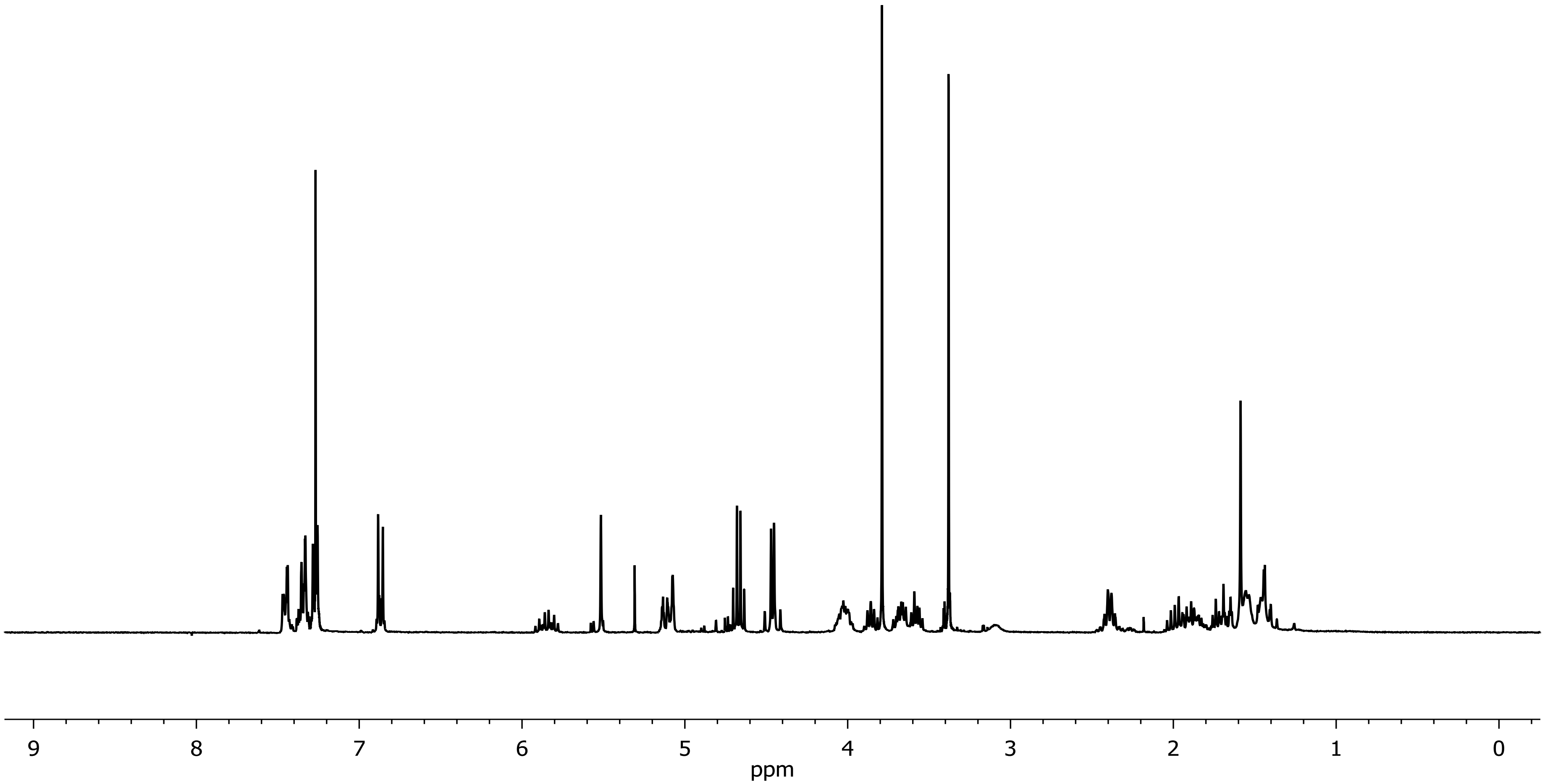


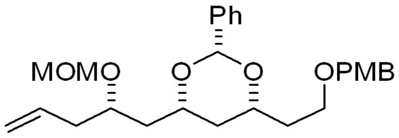
^{13}C NMR(125MHz, CDCl$_3$)



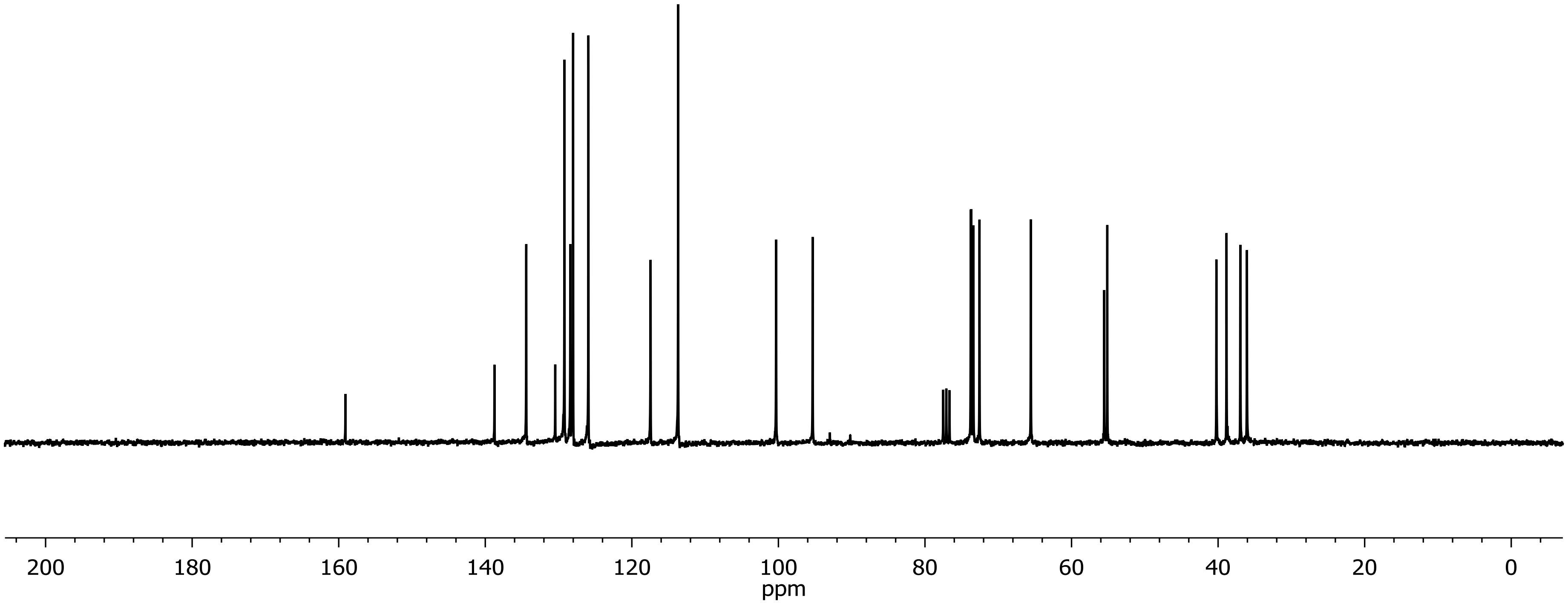


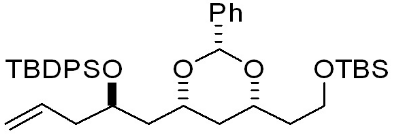
^{1}H NMR(500MHz, $CDCl_3$)



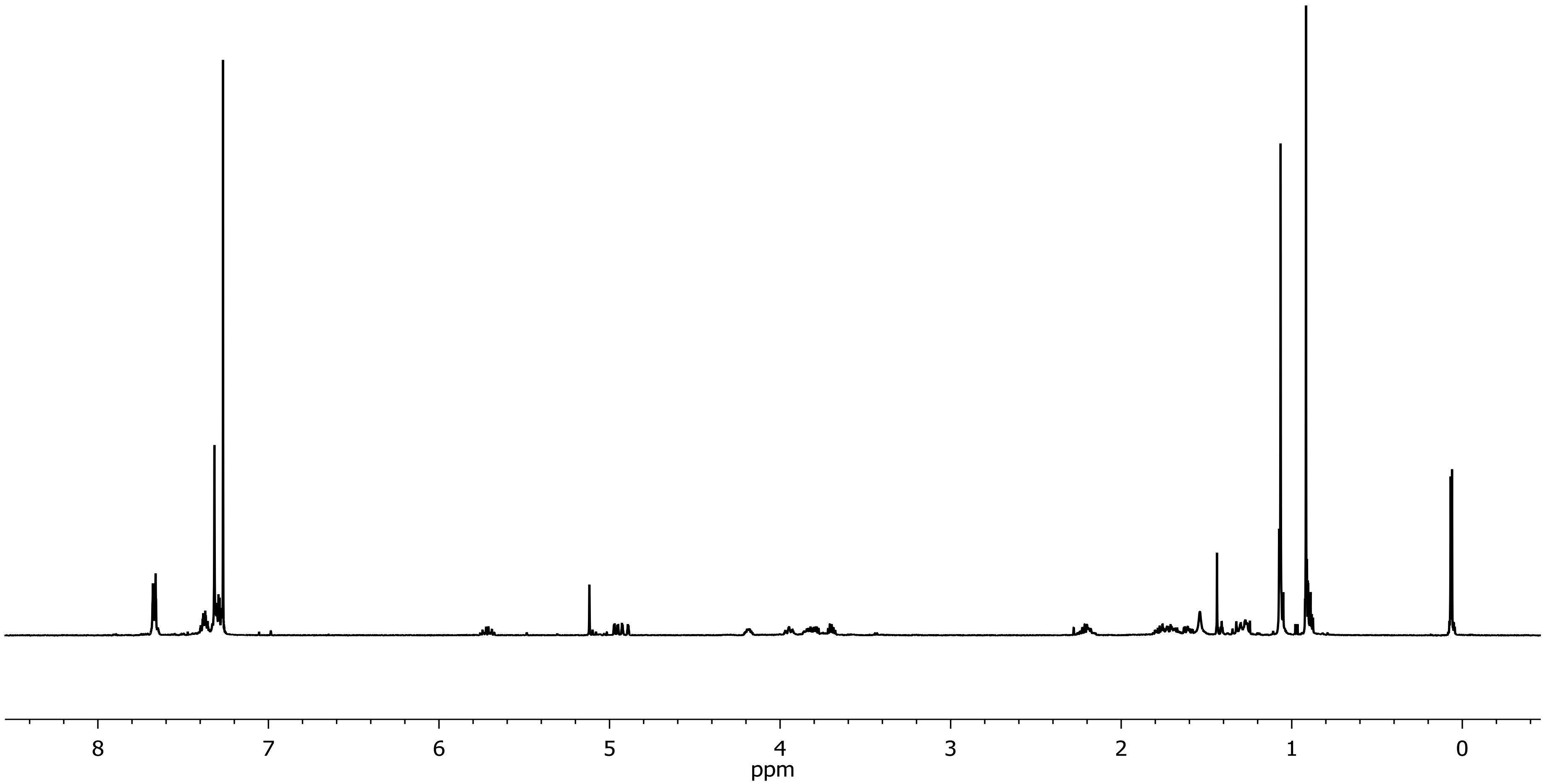


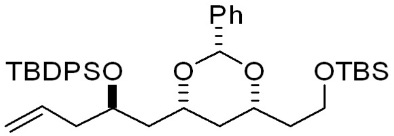
^{13}C NMR(125MHz, CDCl$_3$)



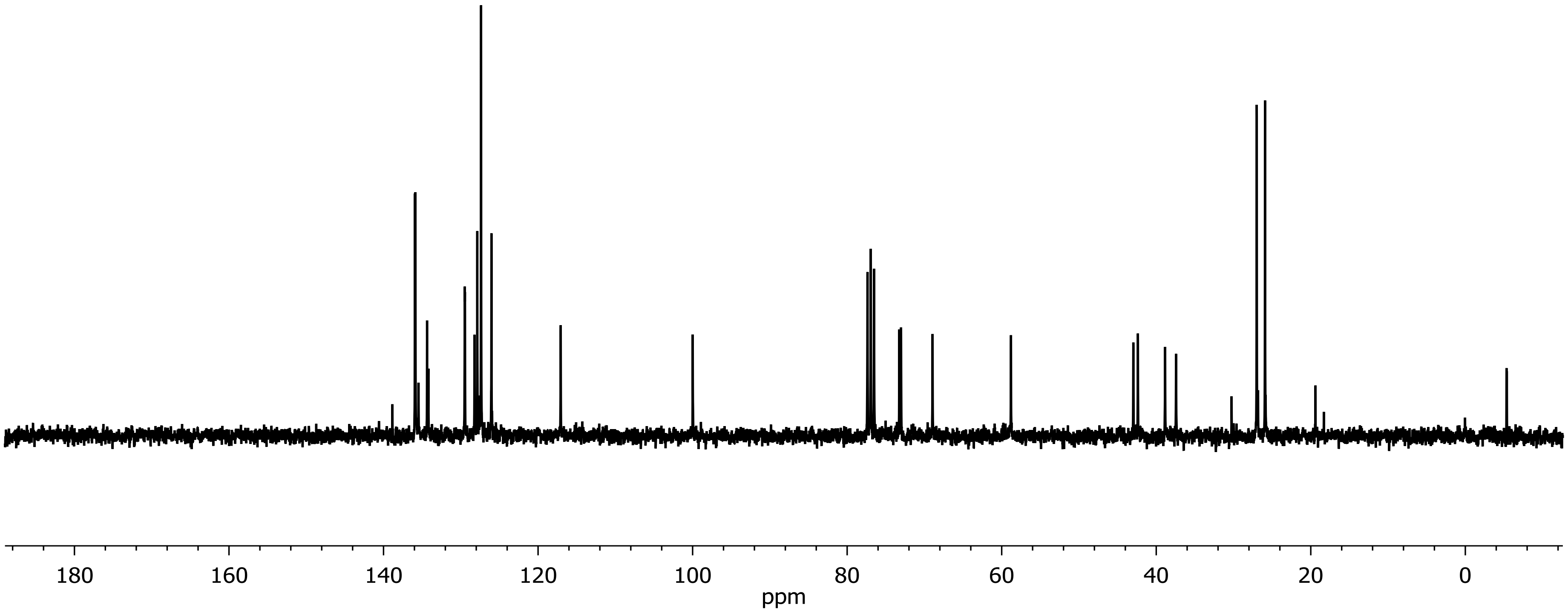


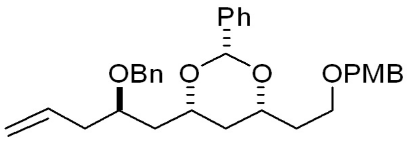
^{1}H NMR(500MHz, CDCl$_3$)





^{13}C NMR(75MHz, CDCl$_3$)





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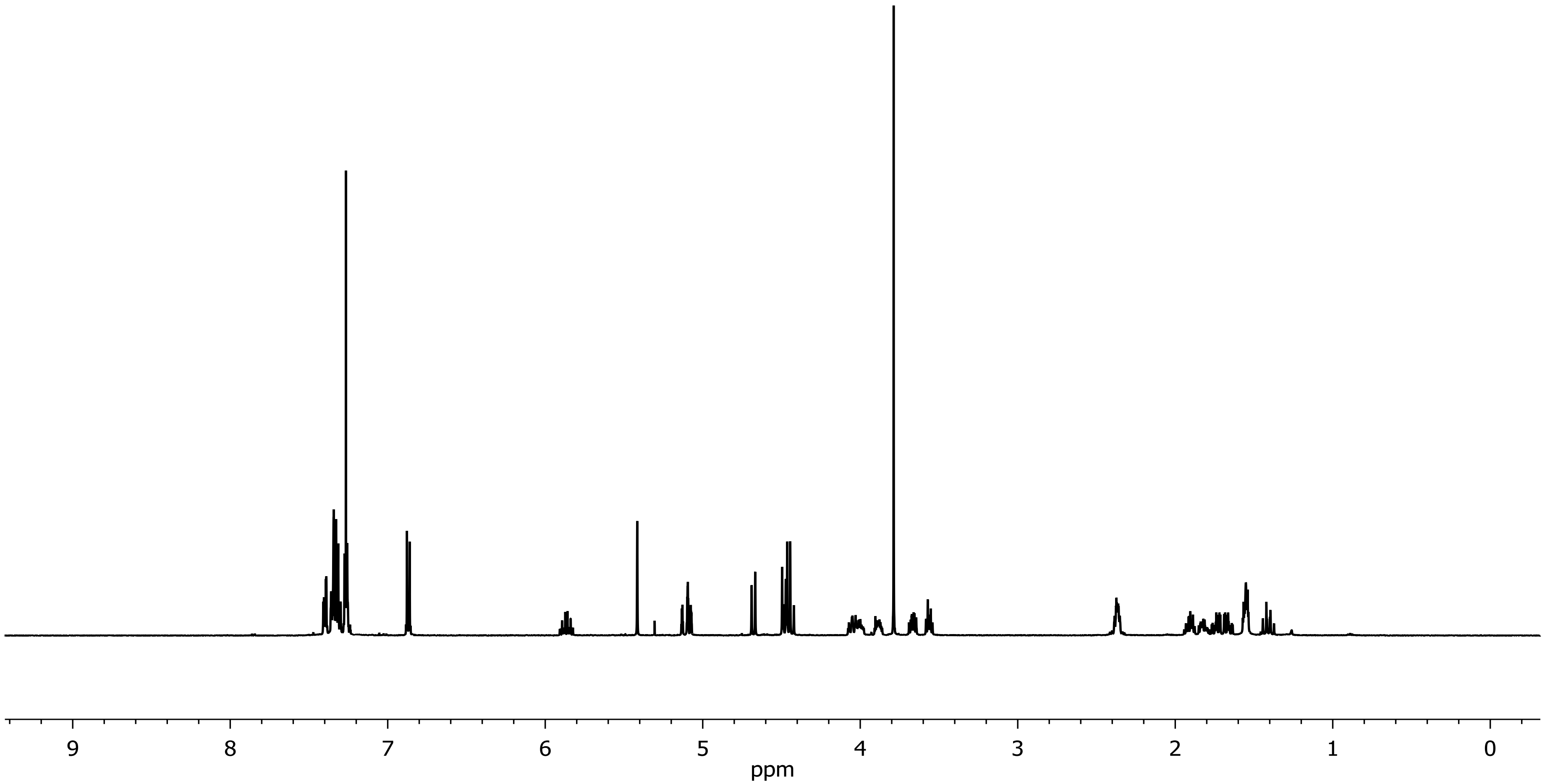
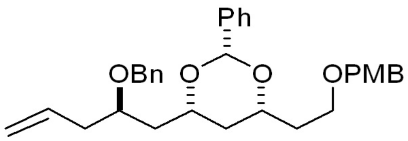
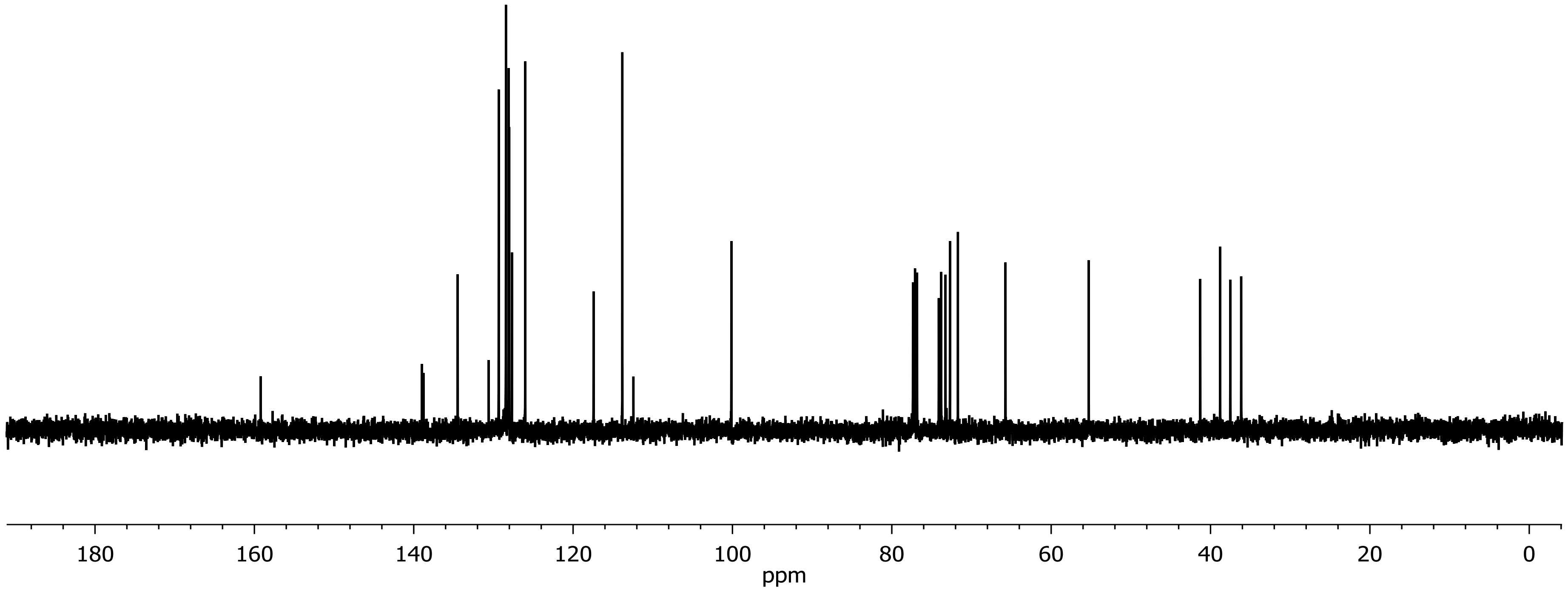
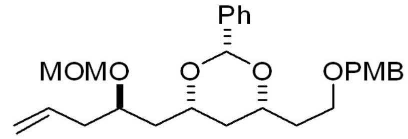


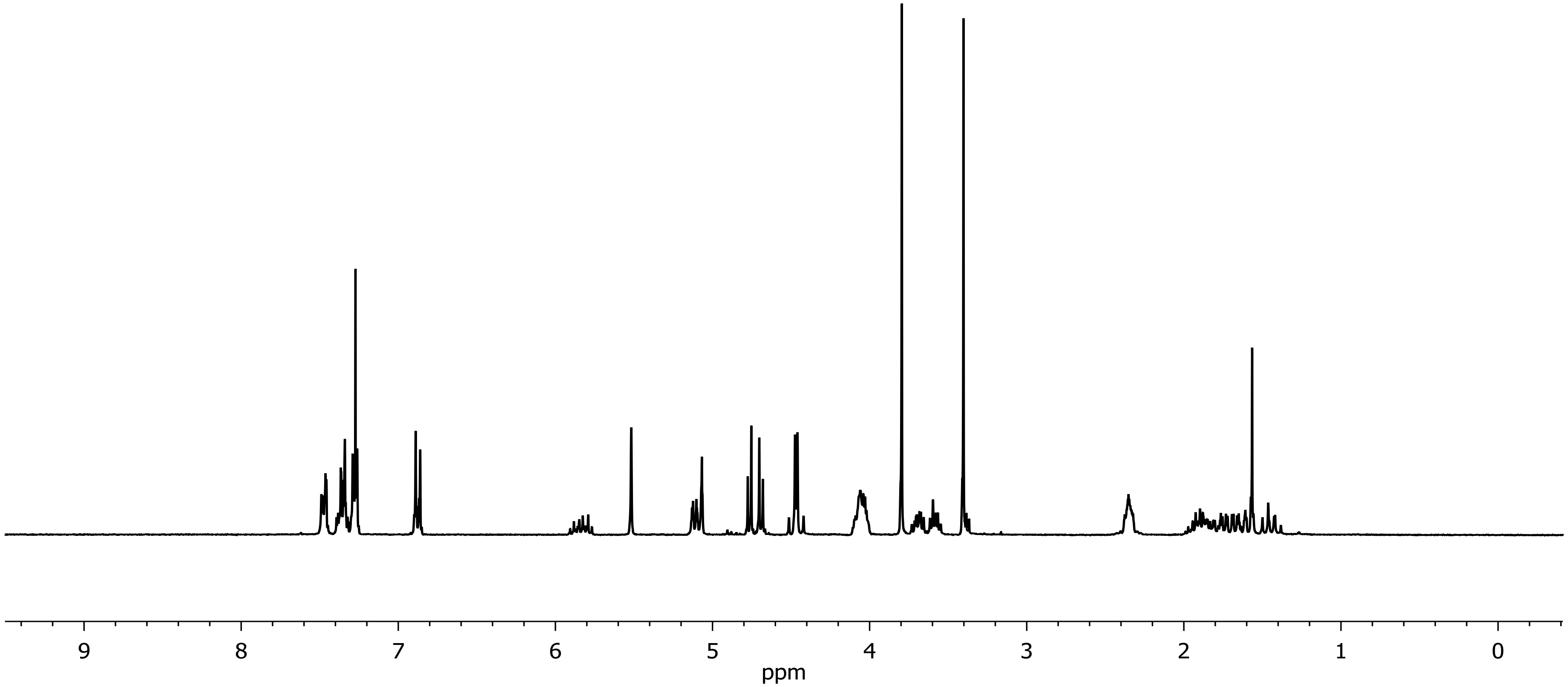


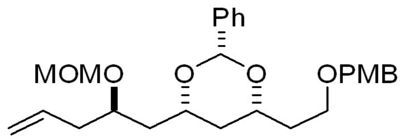
^{13}C NMR(125MHz, $CDCl_3$)



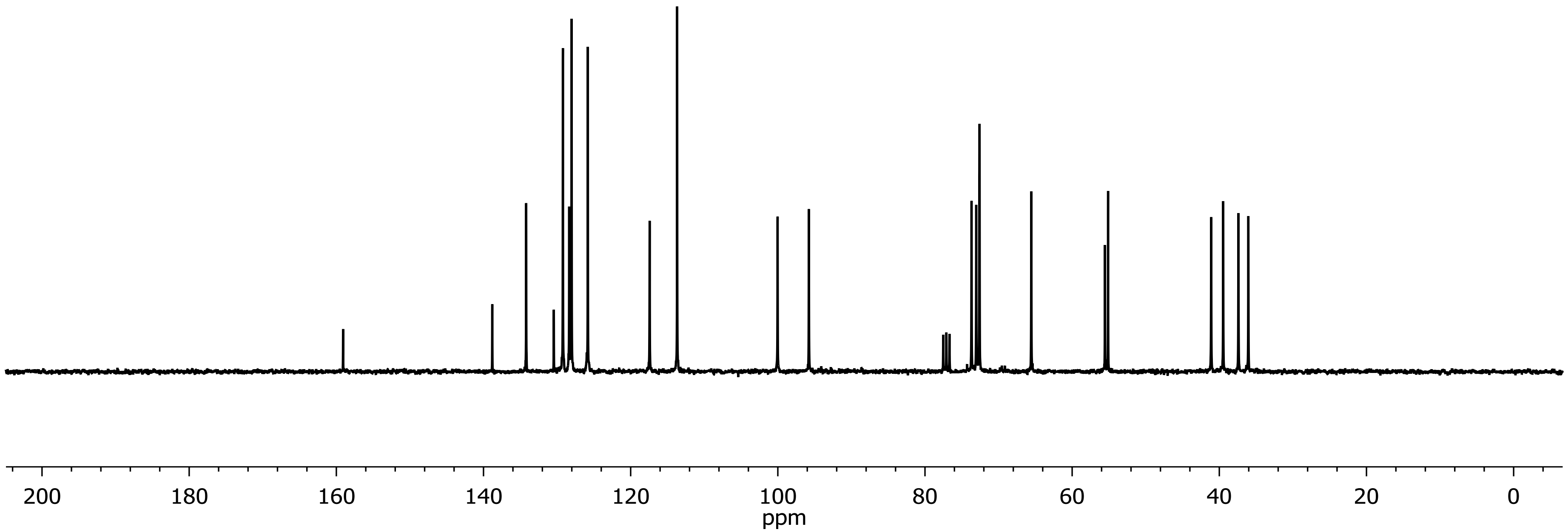


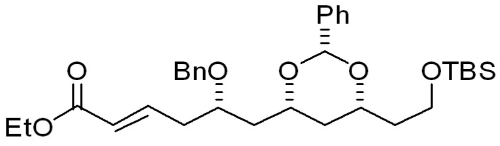
^{1}H NMR(500MHz, $CDCl_3$)



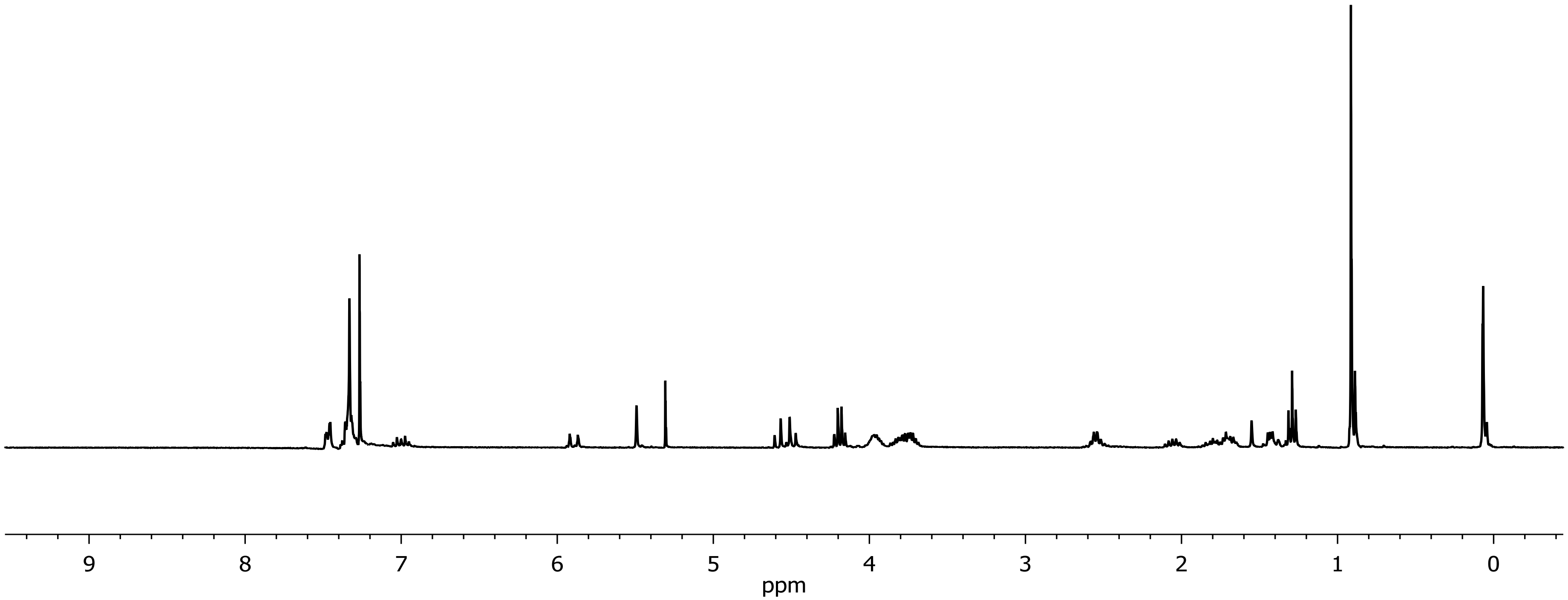


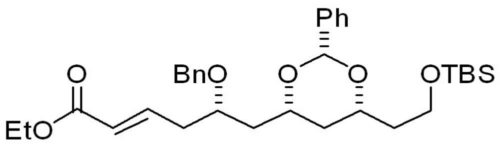
^{13}C NMR(125MHz, CDCl$_3$)



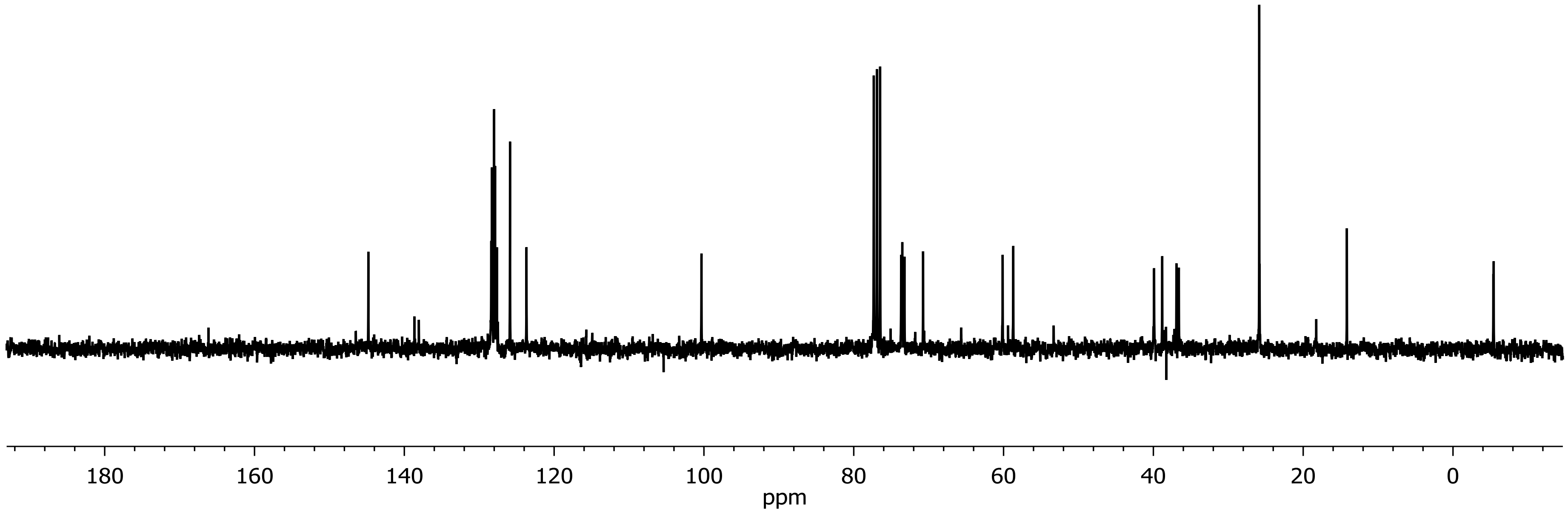


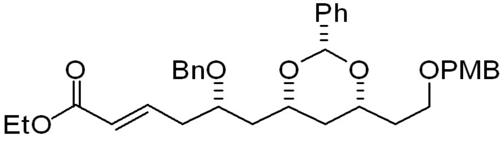
^{1}H NMR(300MHz, CDCl$_3$)



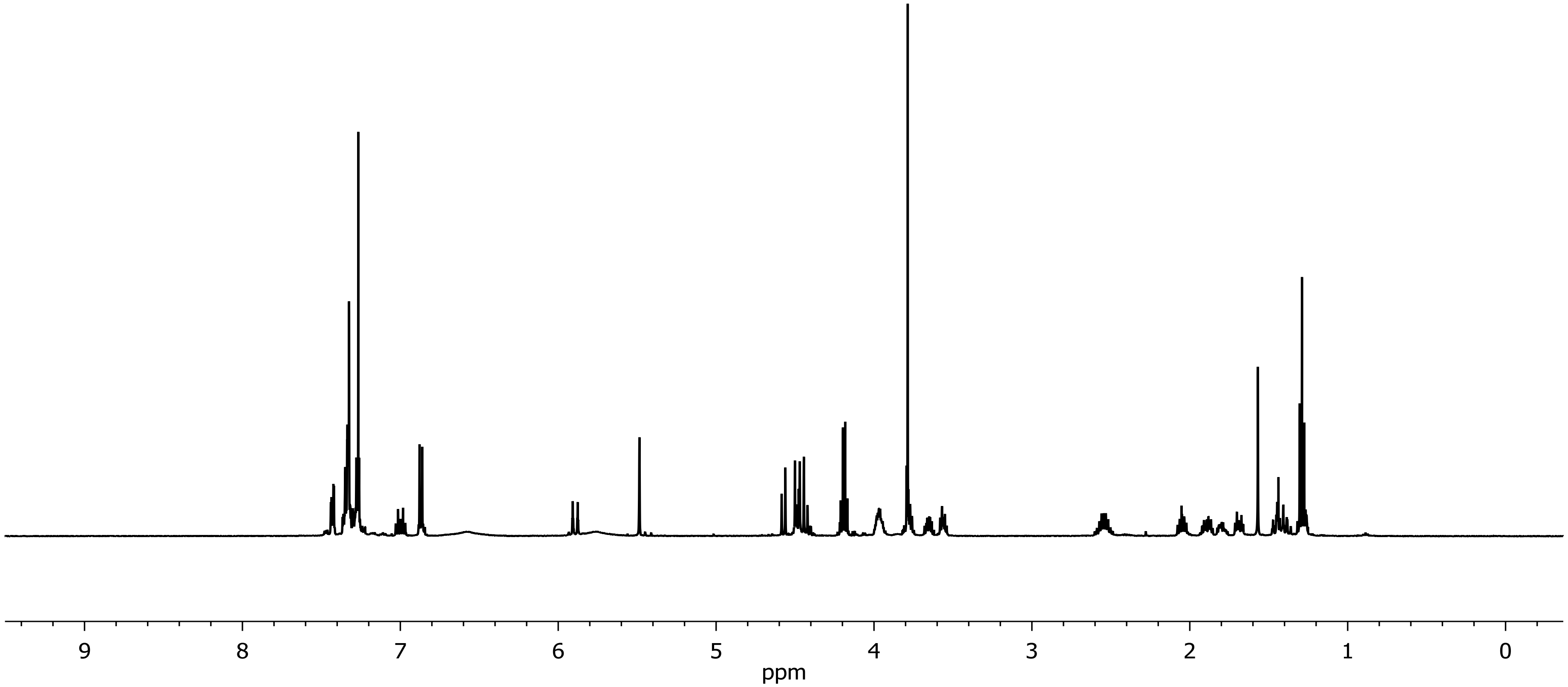


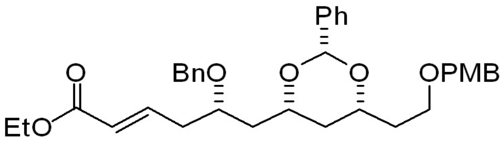
^{13}C NMR(75MHz, CDCl$_3$)



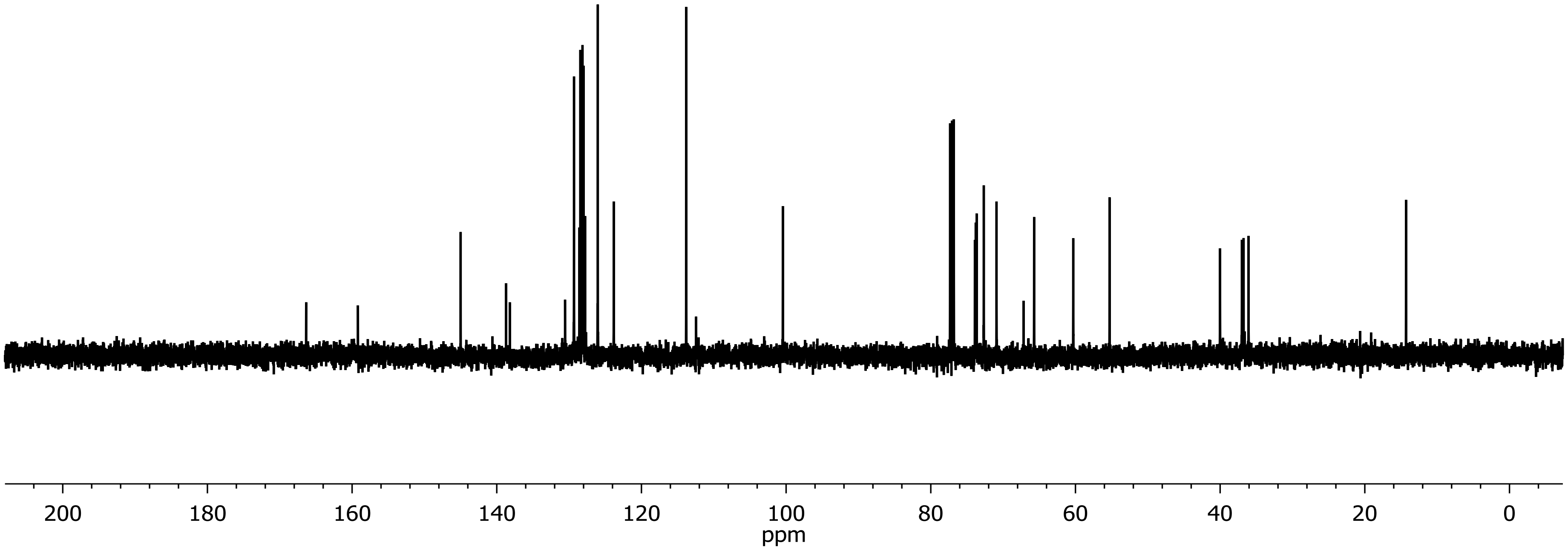


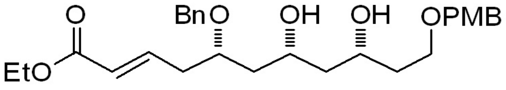
^{1}H NMR(500MHz, CDCl$_3$)





^{13}C NMR(125MHz, CDCl$_3$)





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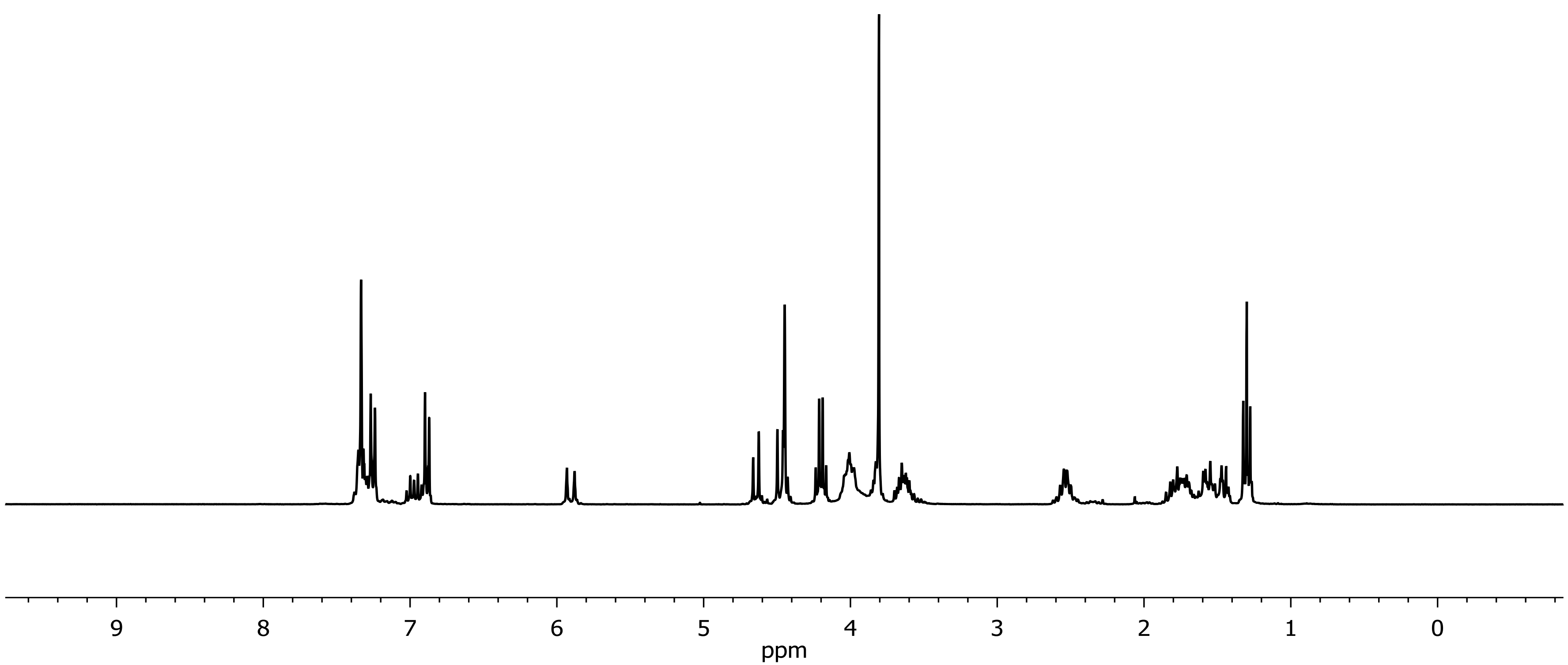

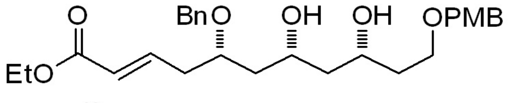

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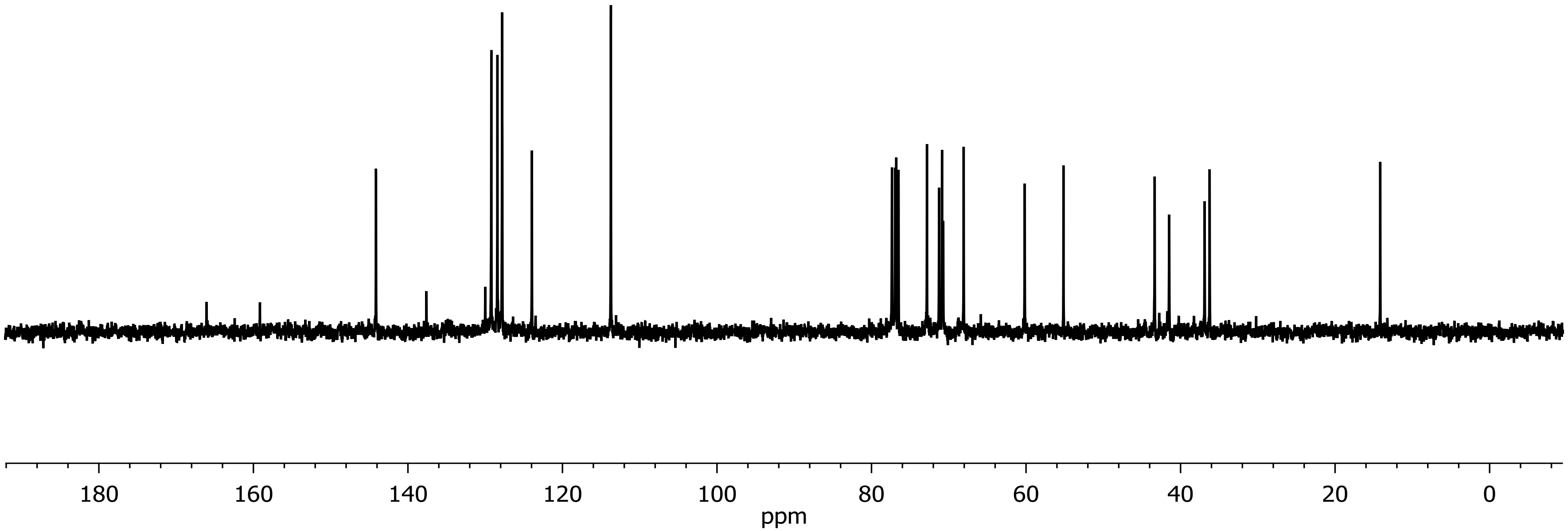

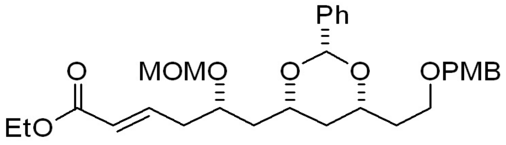

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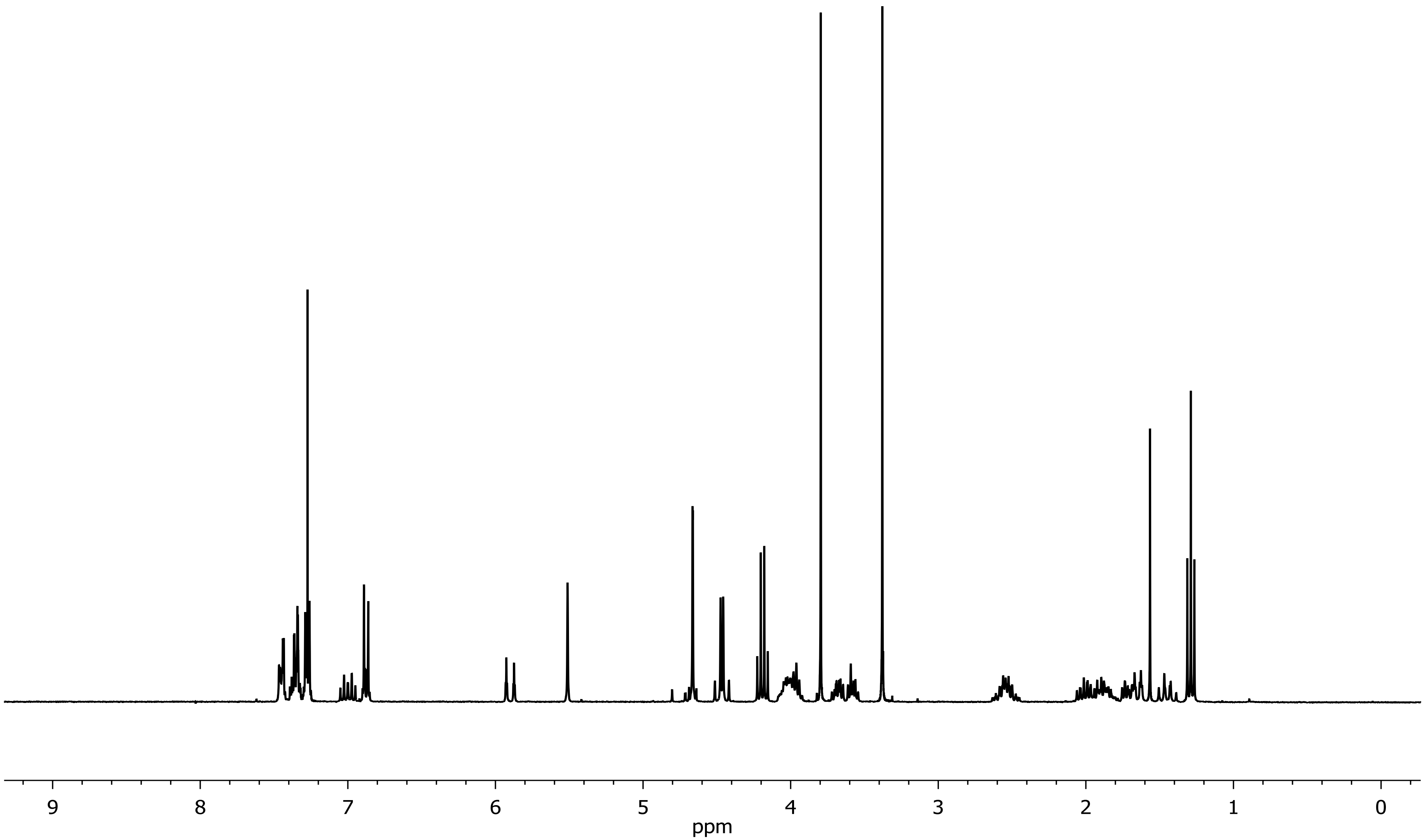
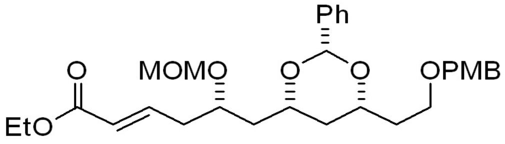
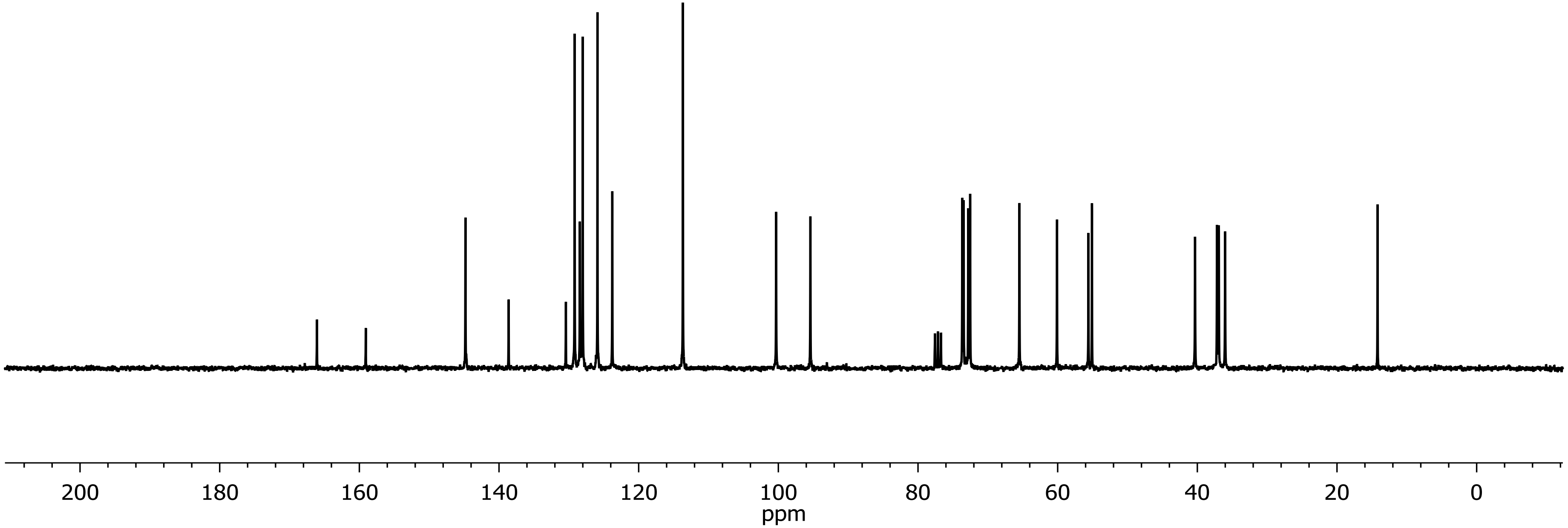
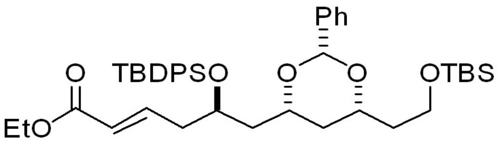




^{13}C NMR(125MHz, CDCl$_3$)





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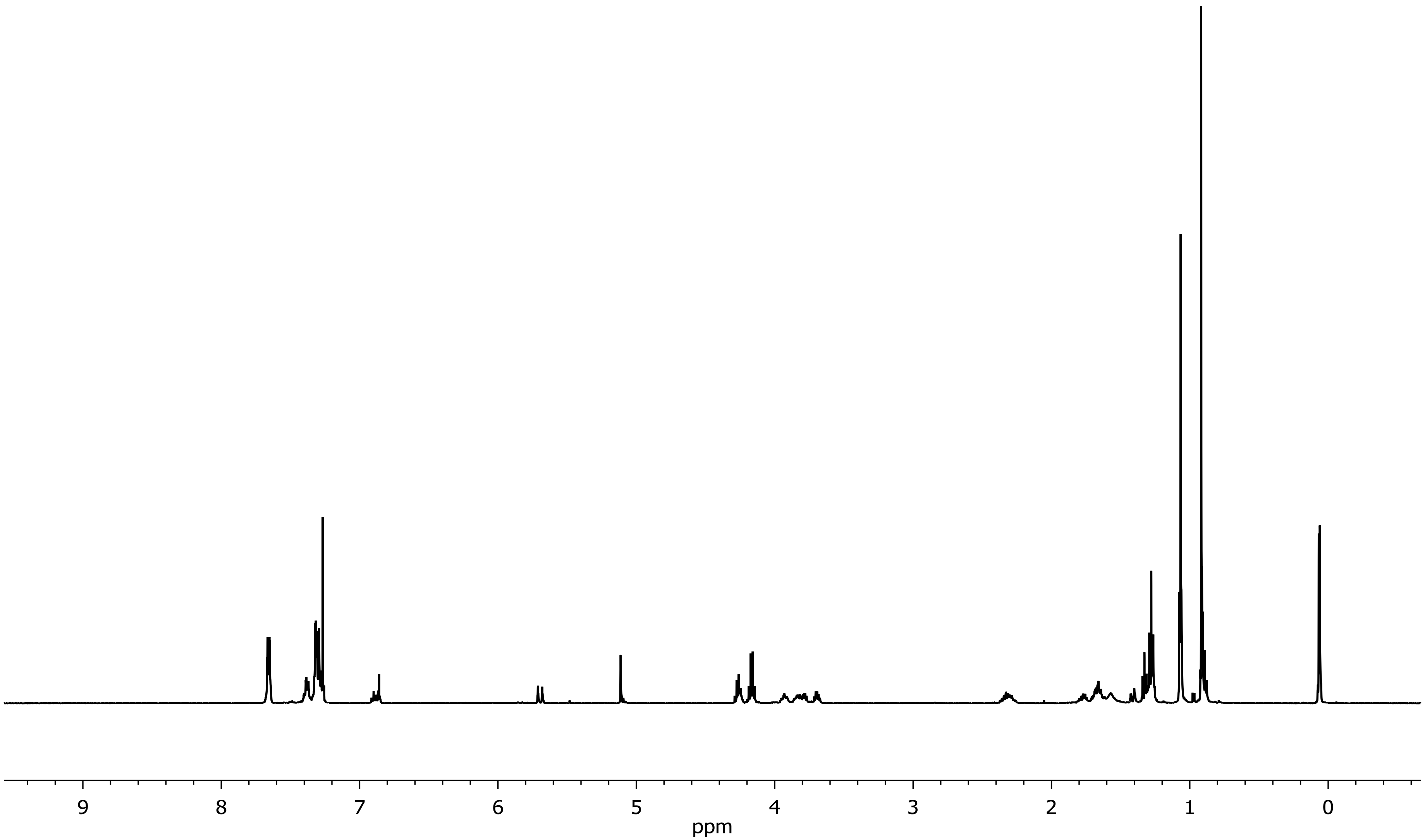
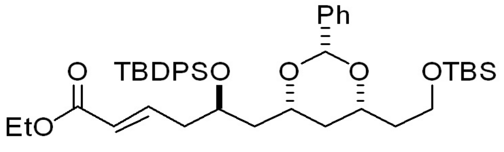
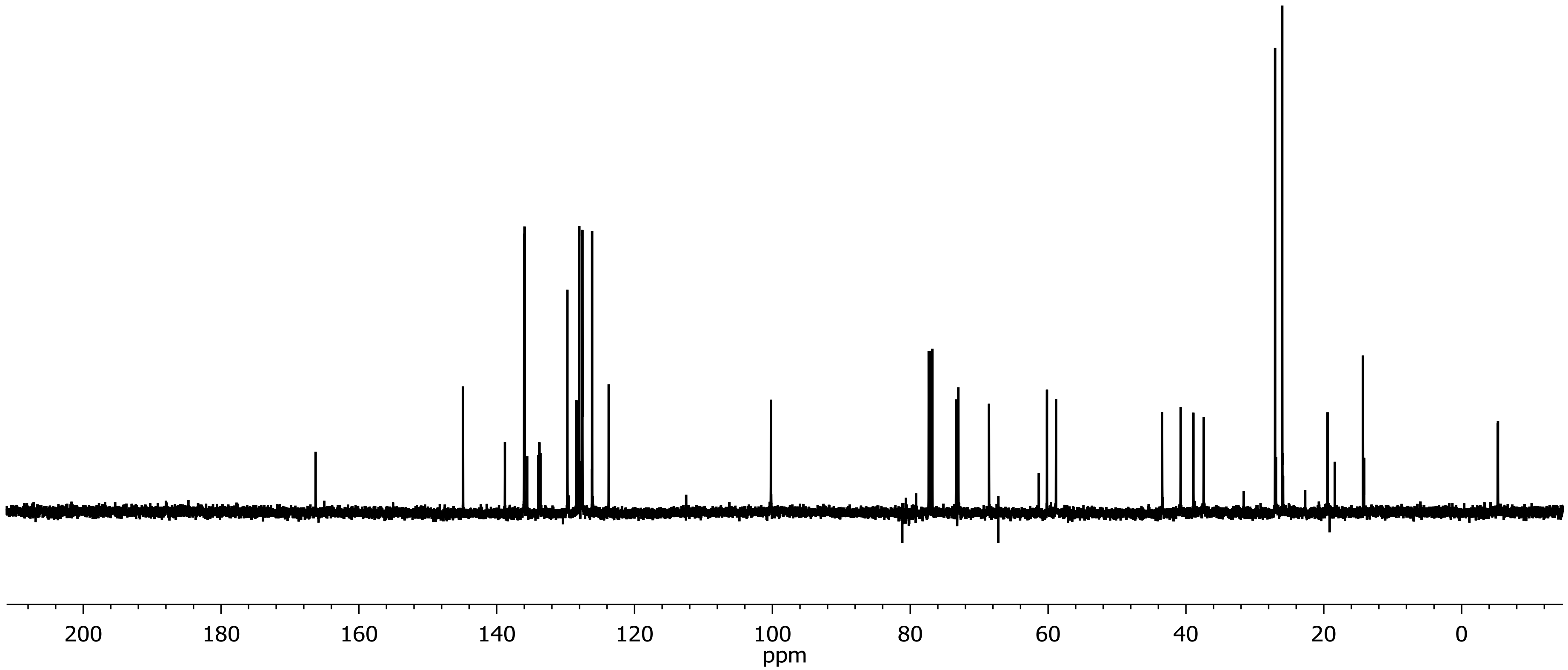
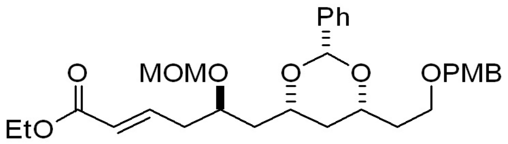




^{13}C NMR(125MHz, CDCl$_3$)





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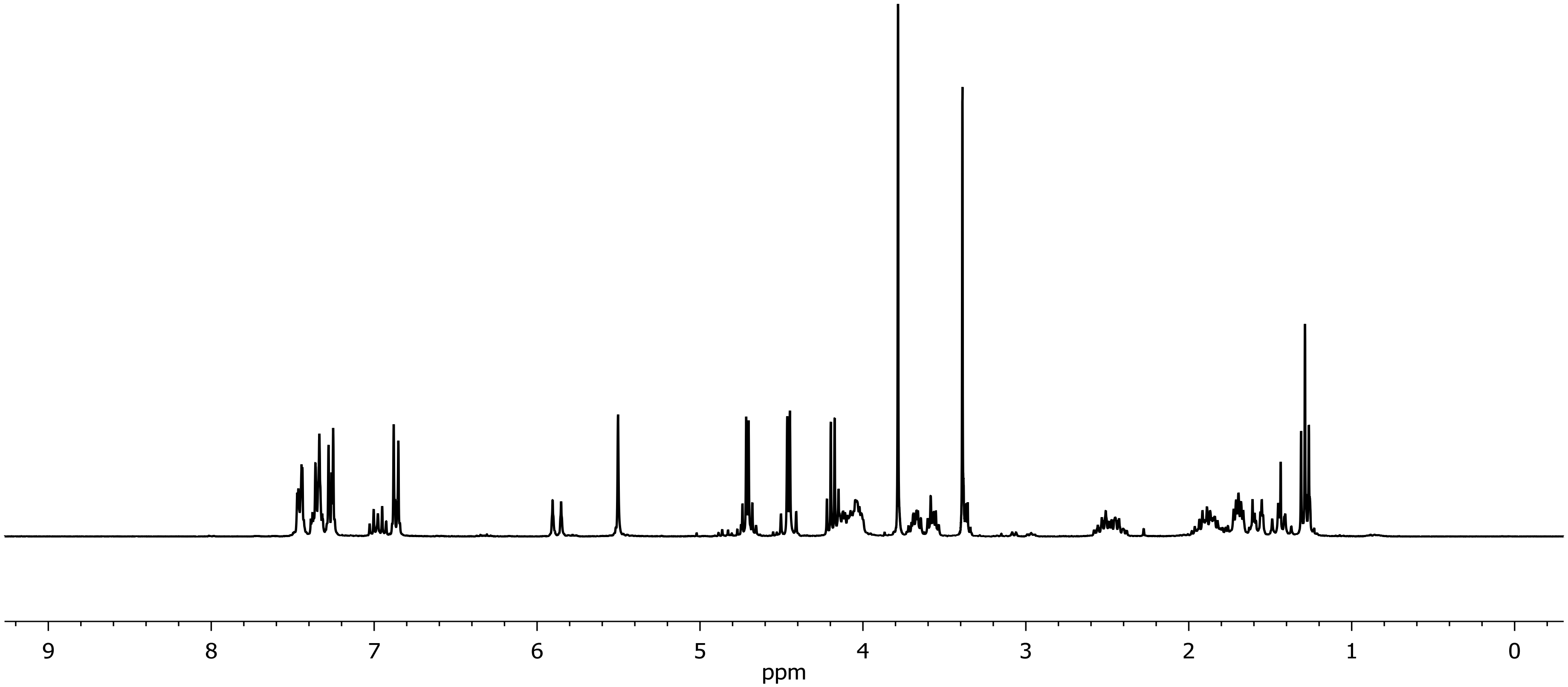
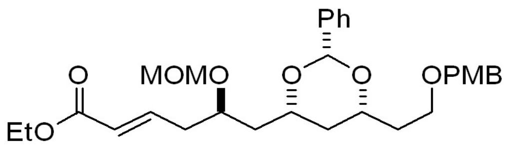
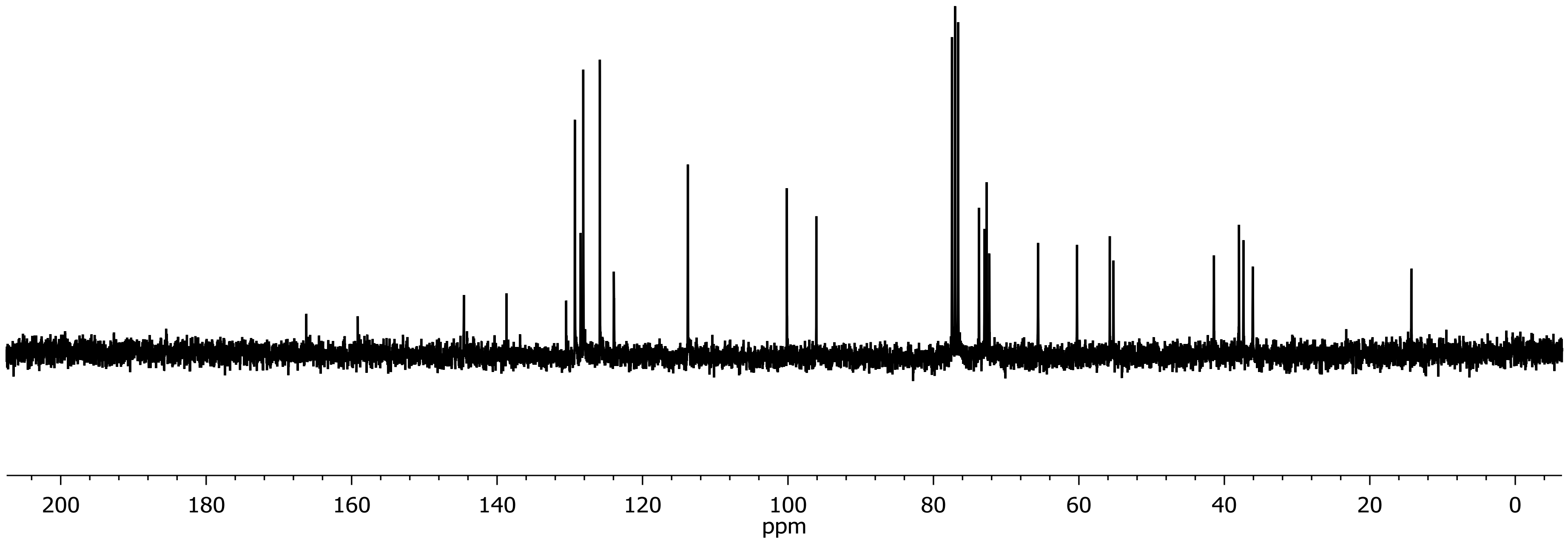
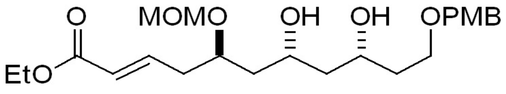




^{13}C NMR(125MHz, $CDCl_3$)





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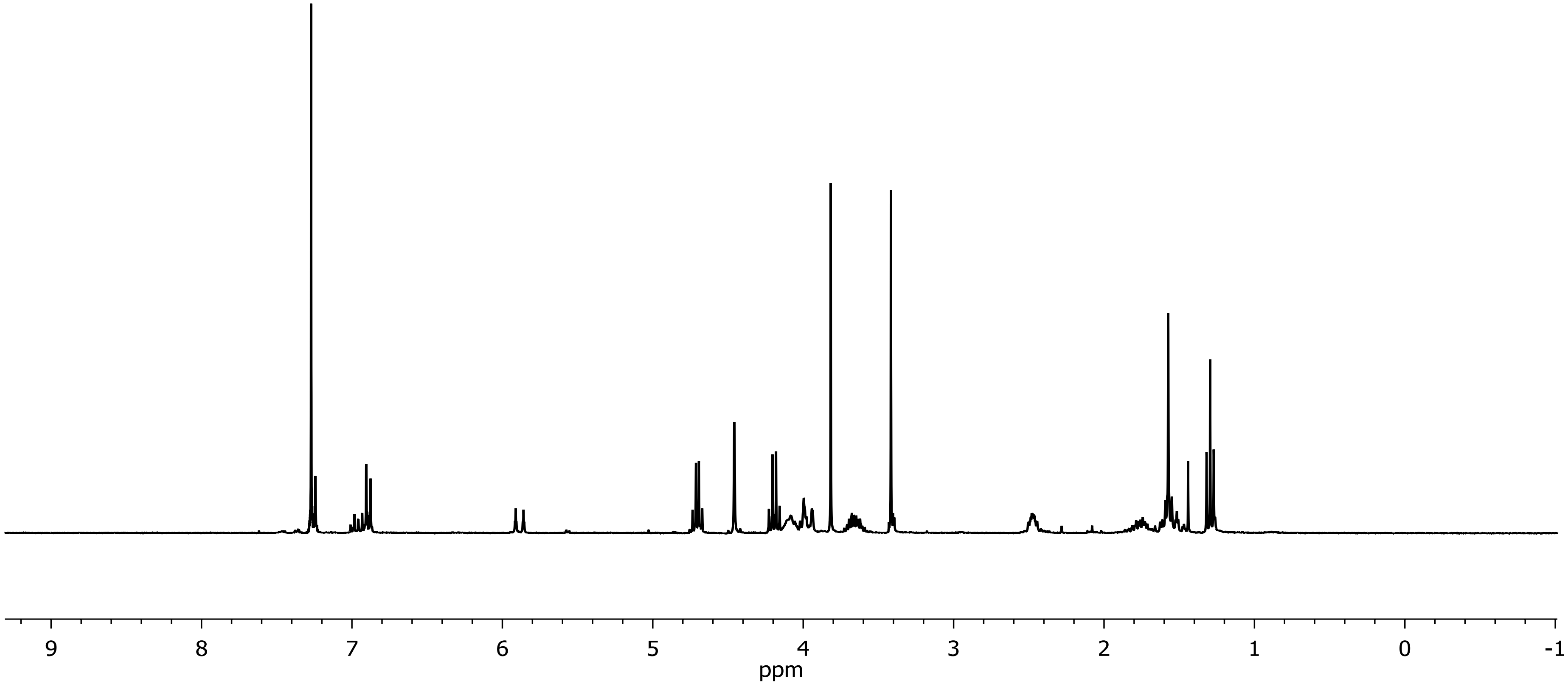

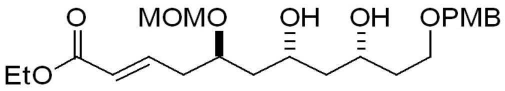

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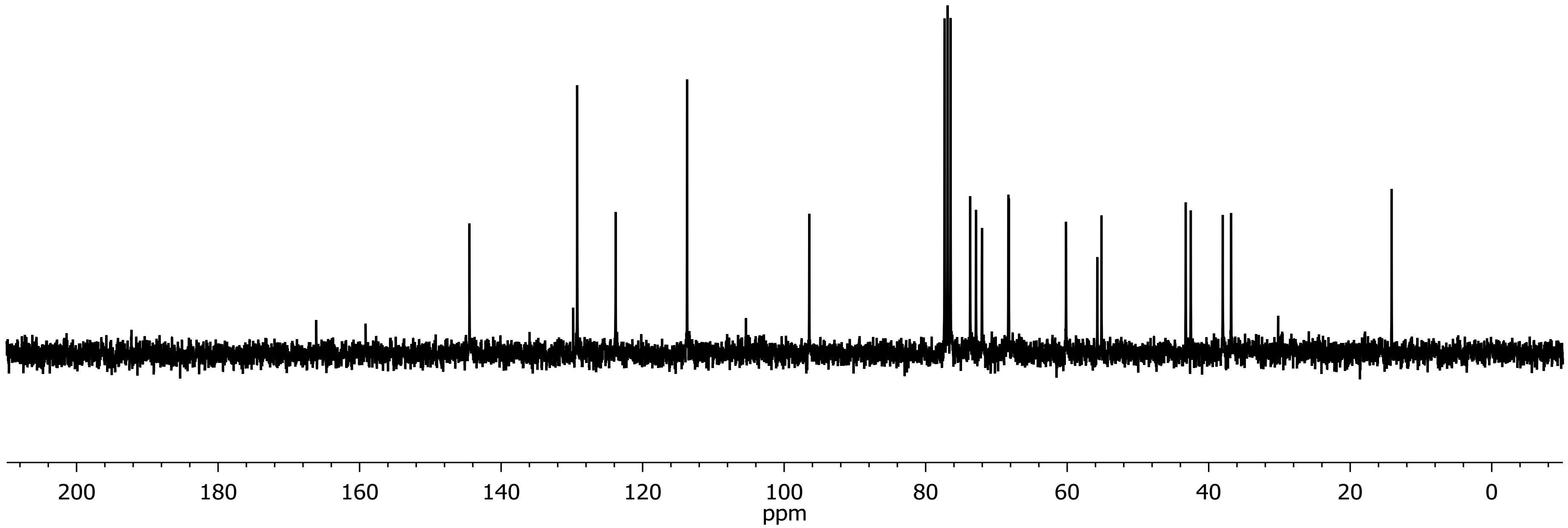

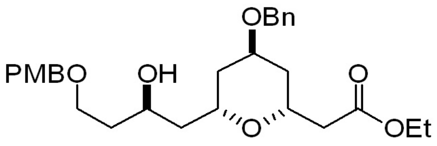

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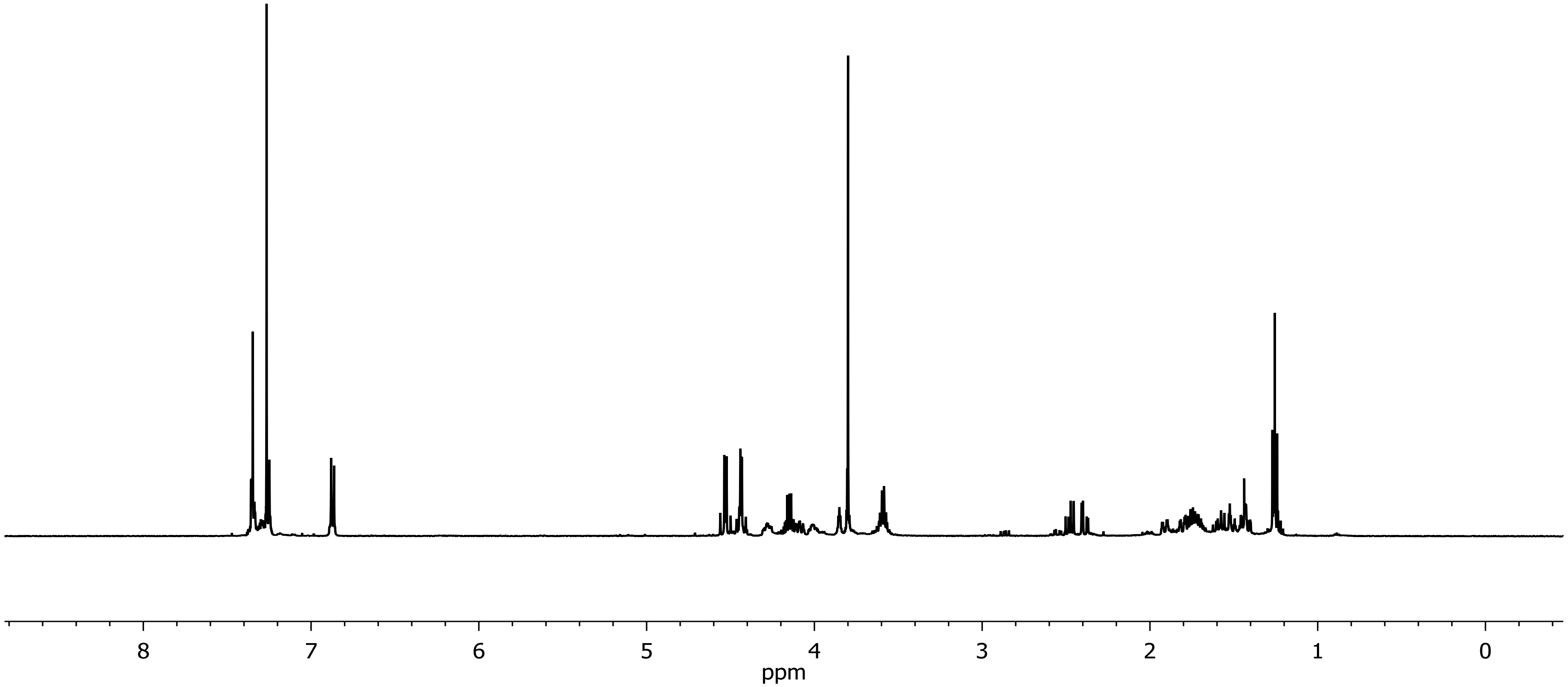

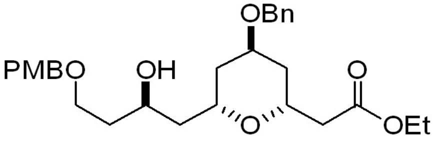

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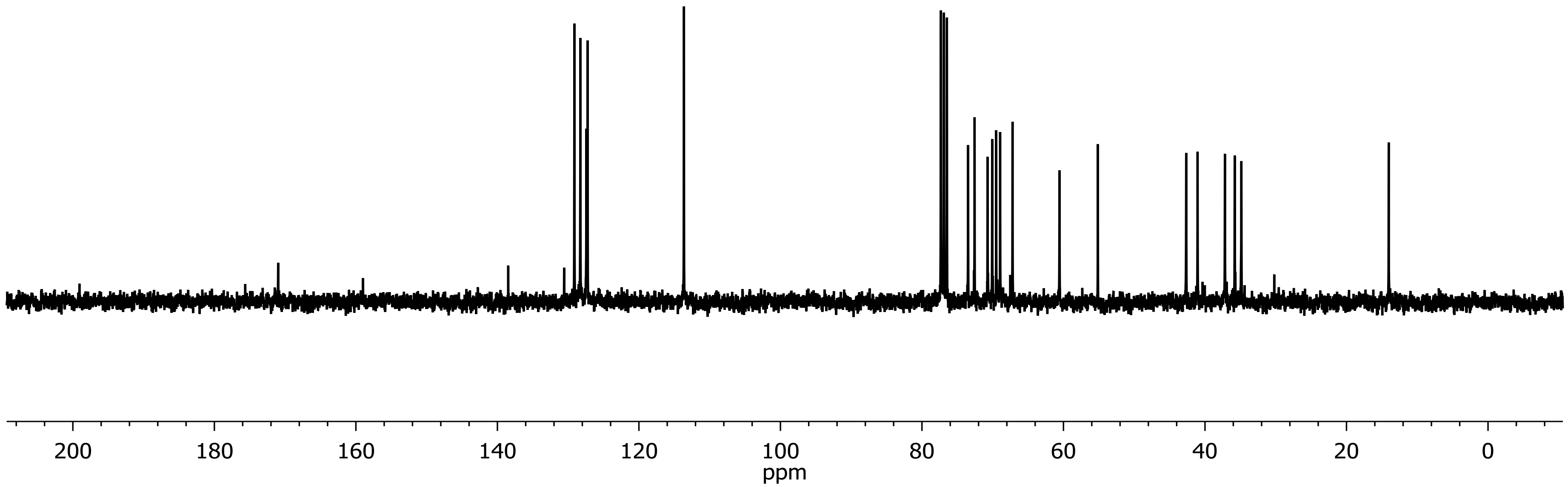
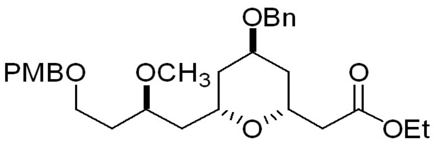
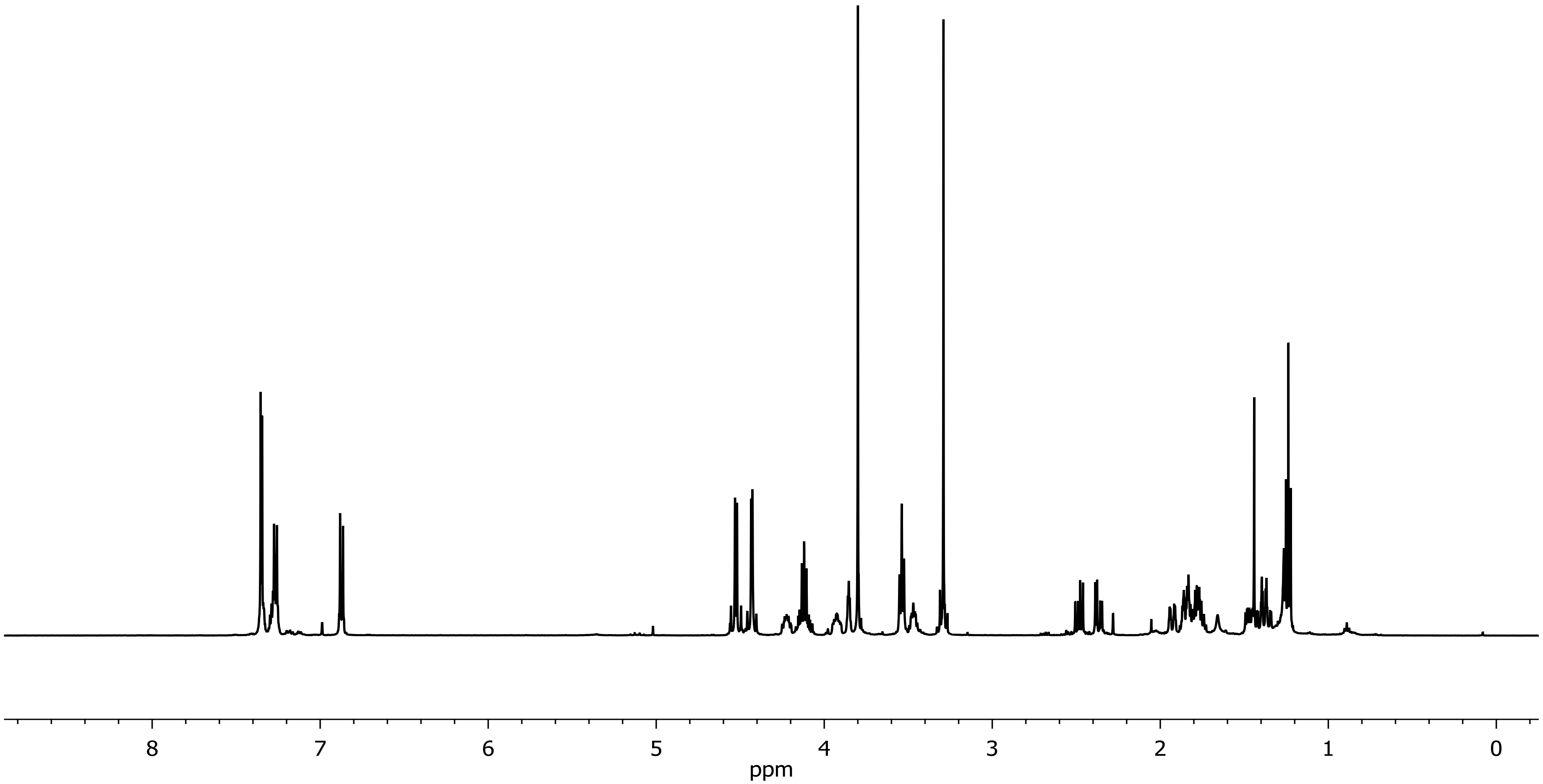
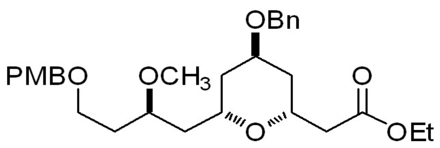


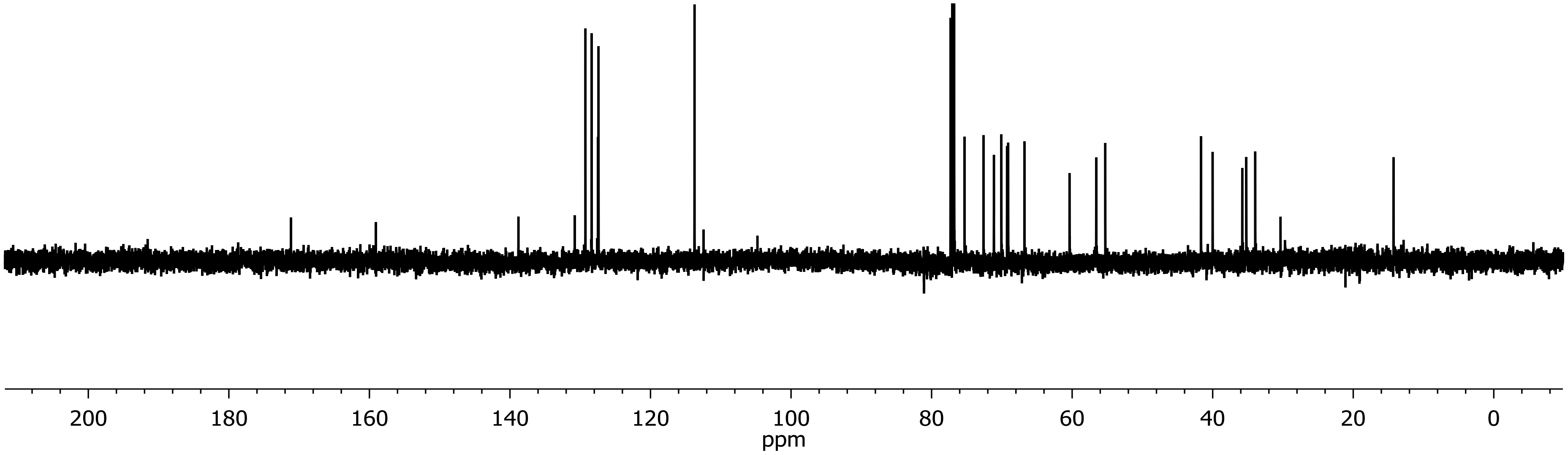


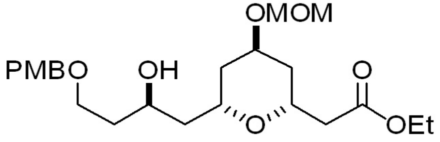
^{1}H NMR(500MHz, CDCl$_3$)



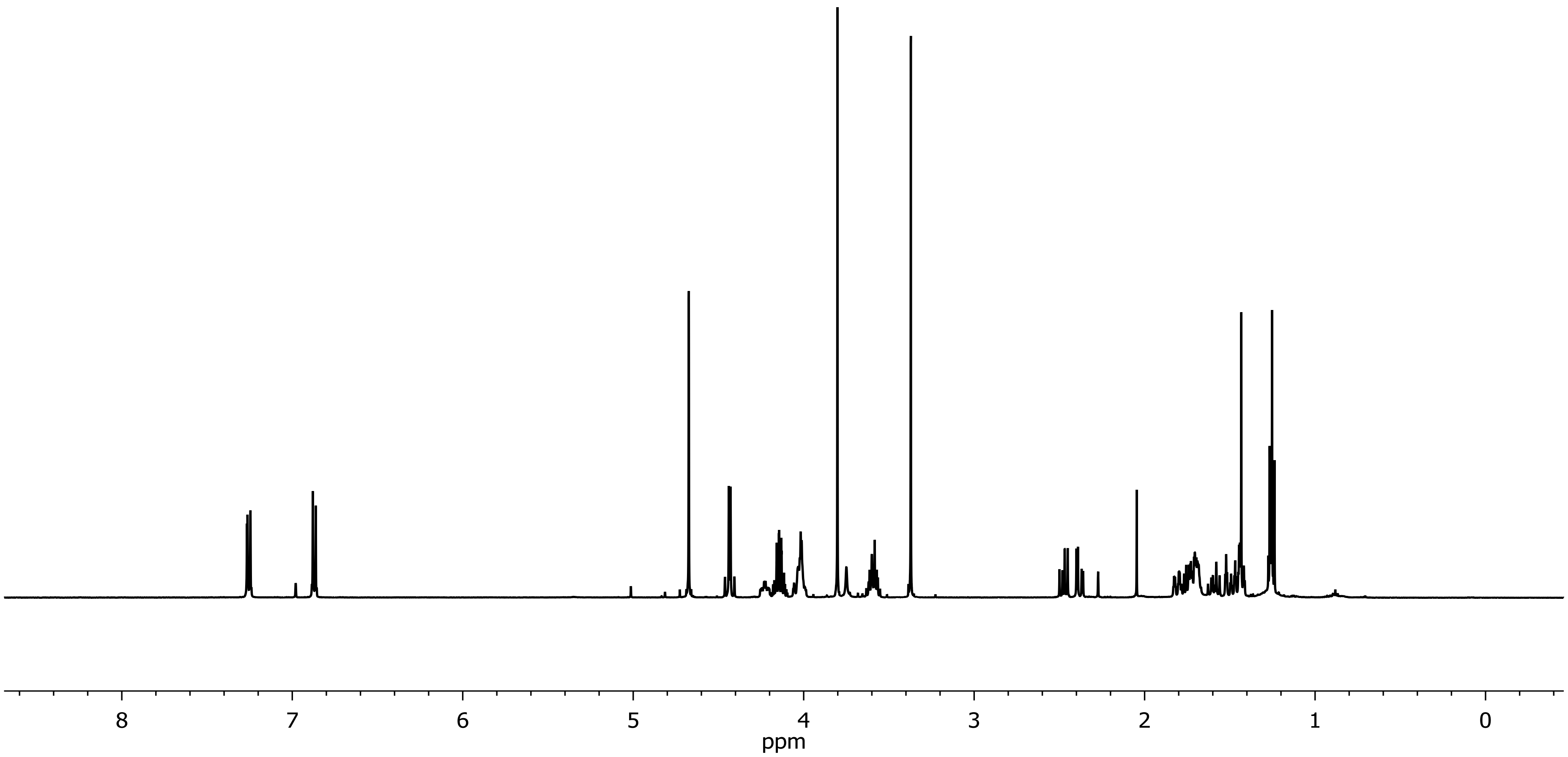


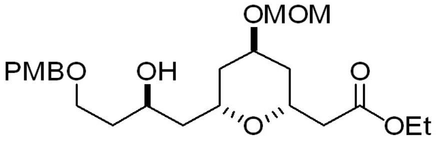
^{13}C NMR(125MHz, CDCl$_3$)



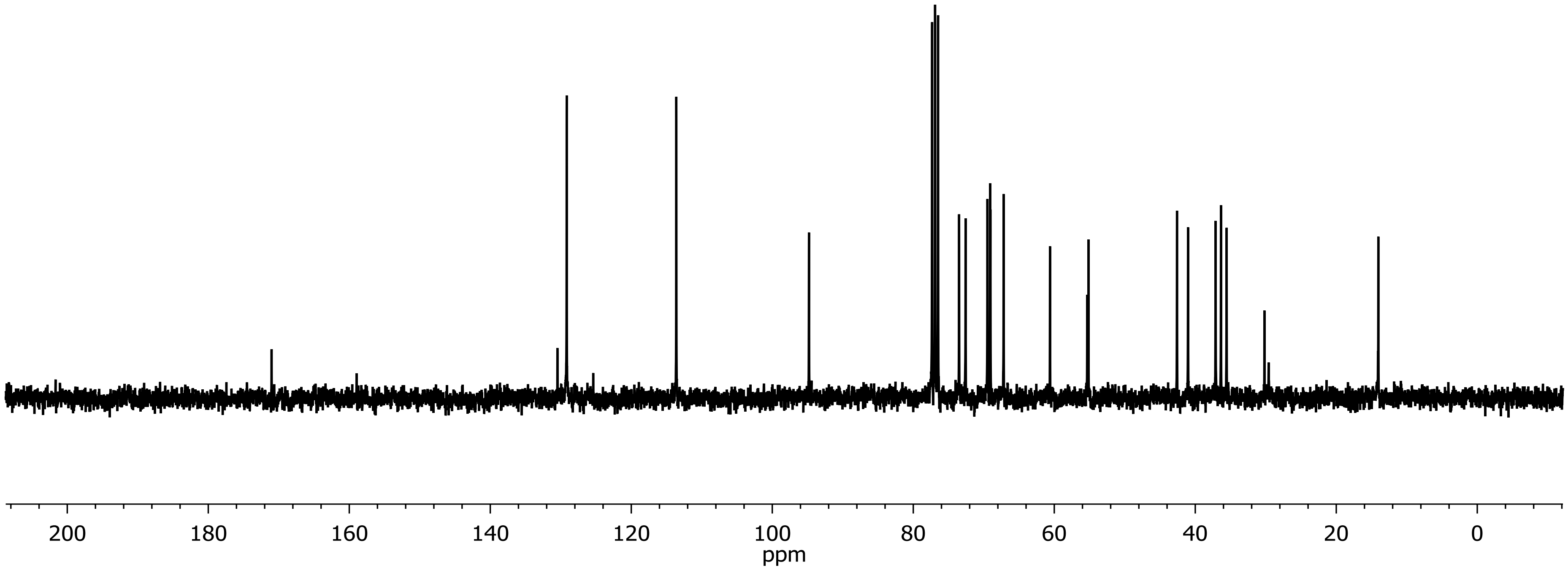


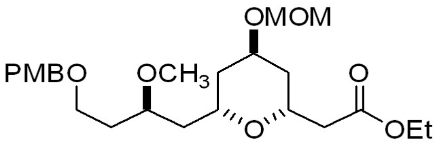
^{1}H NMR(500MHz, $CDCl_3$)



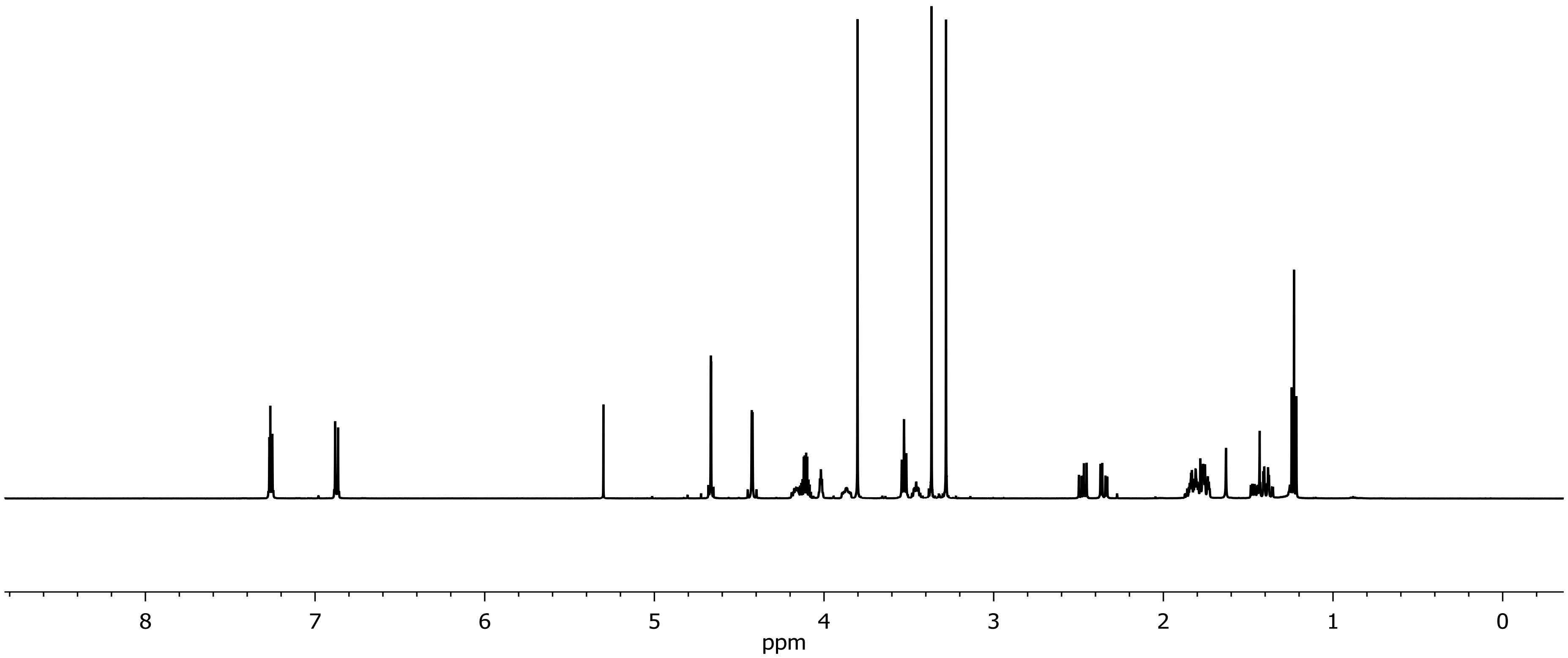


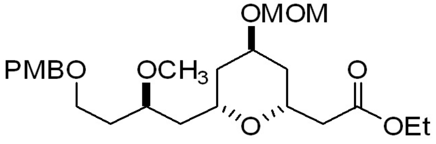
^{13}C NMR(75MHz, $CDCl_3$)



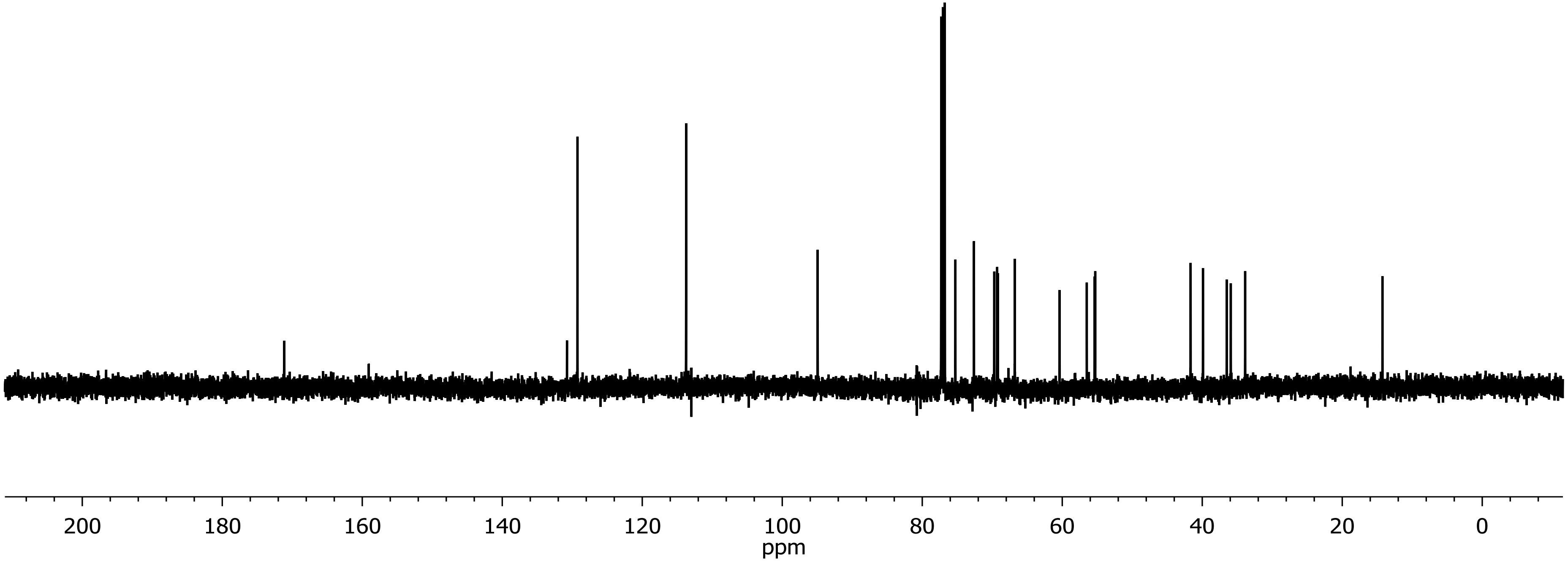


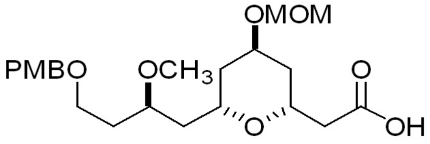
^{1}H NMR(500MHz, CDCl$_3$)



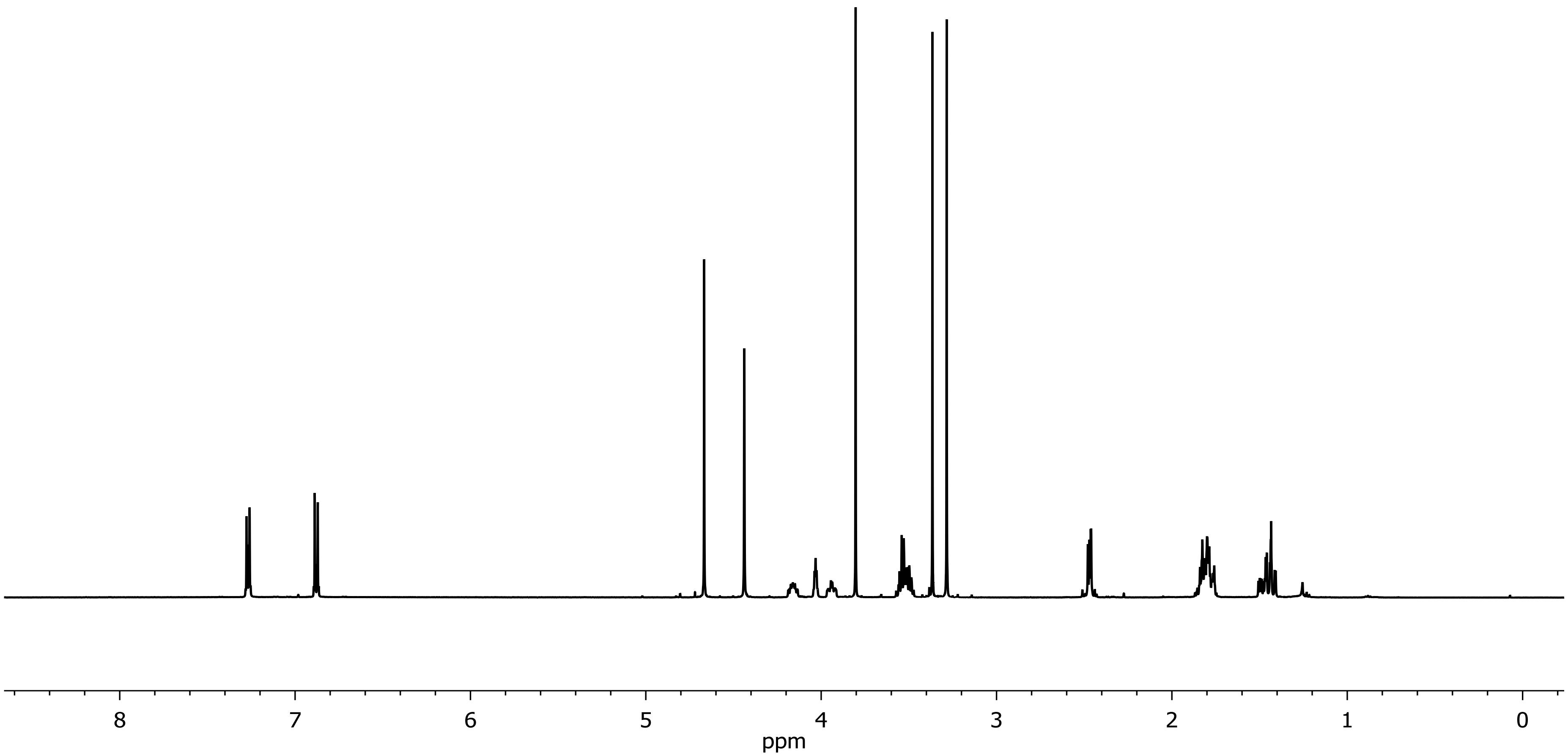


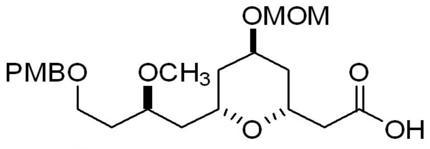
^{13}C NMR(125MHz, $CDCl_3$)



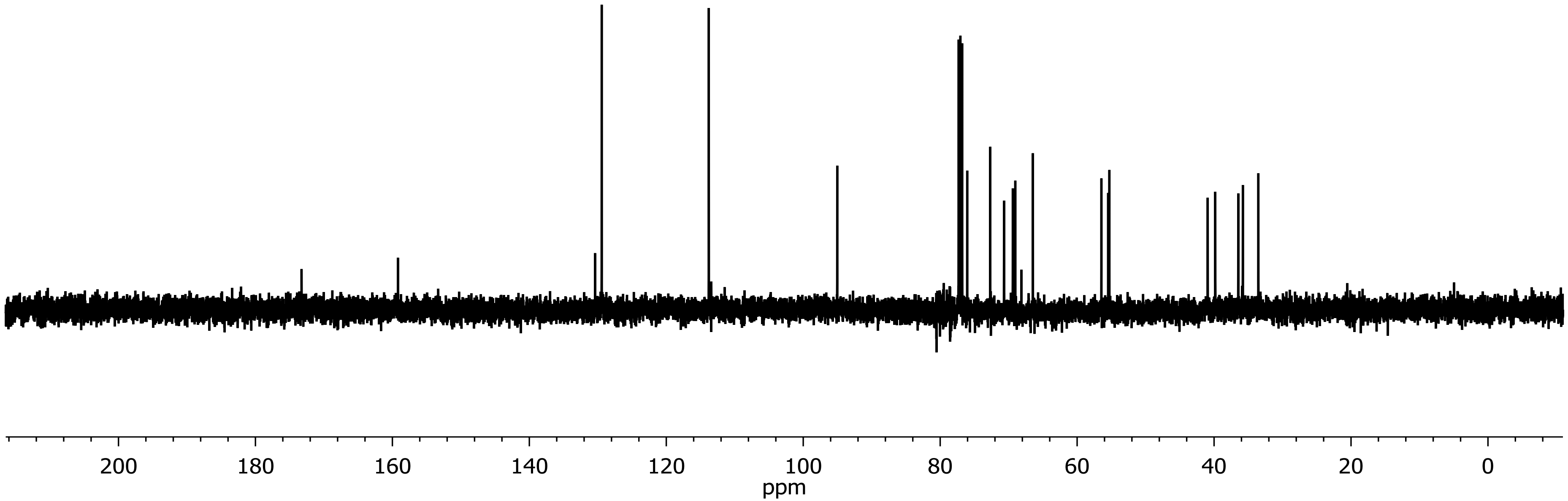


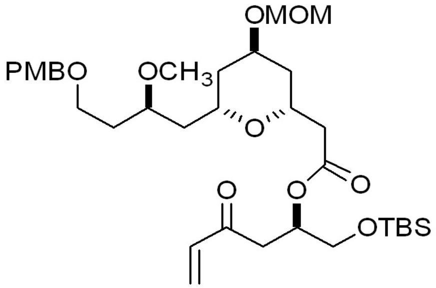
^{1}H NMR(500MHz, CDCl$_3$)



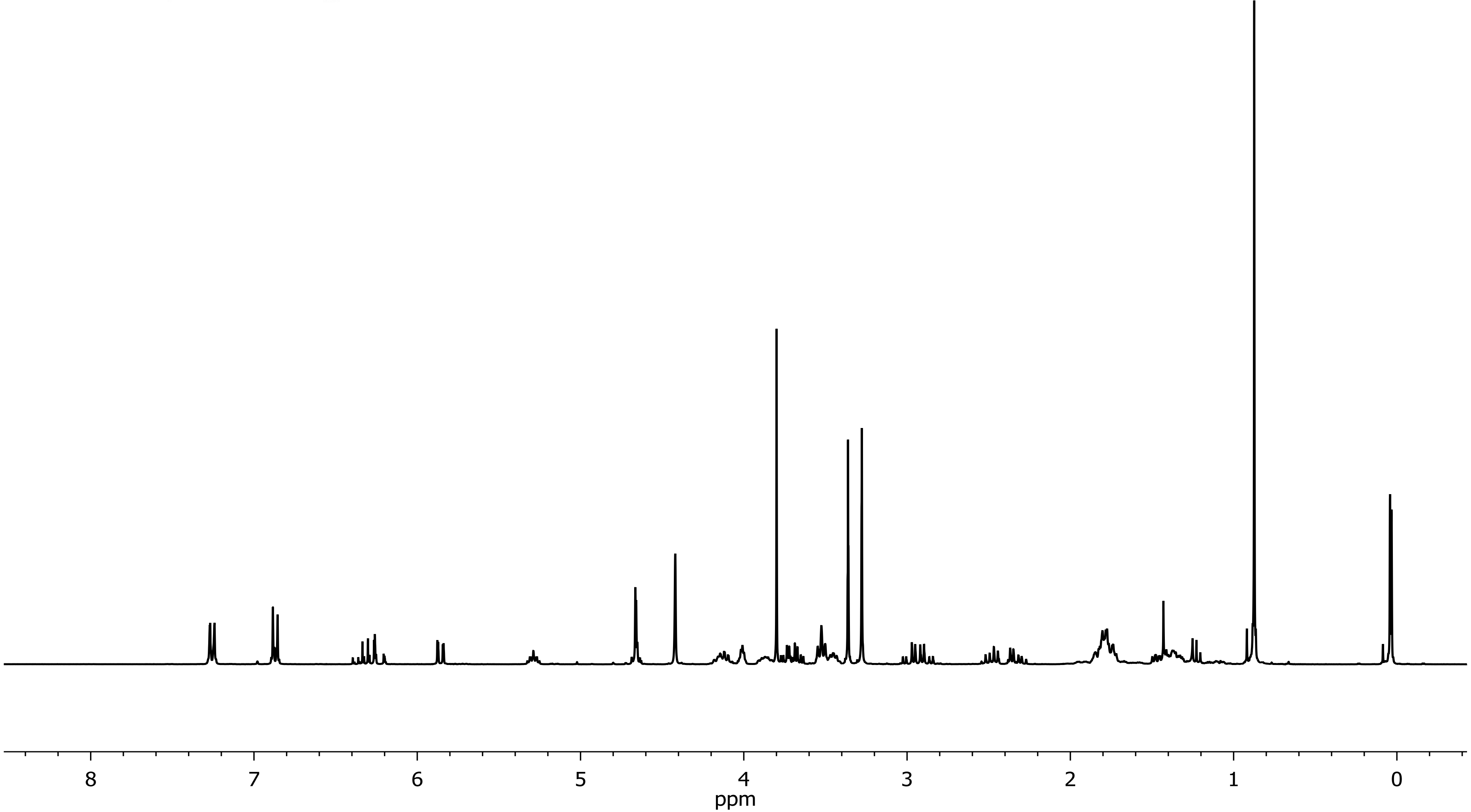


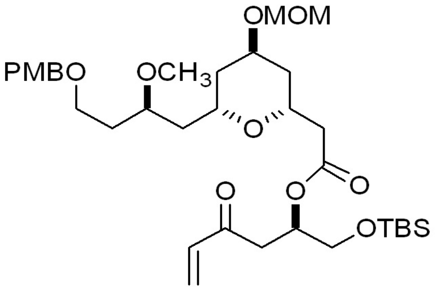
^{13}C NMR(125MHz, CDCl$_3$)



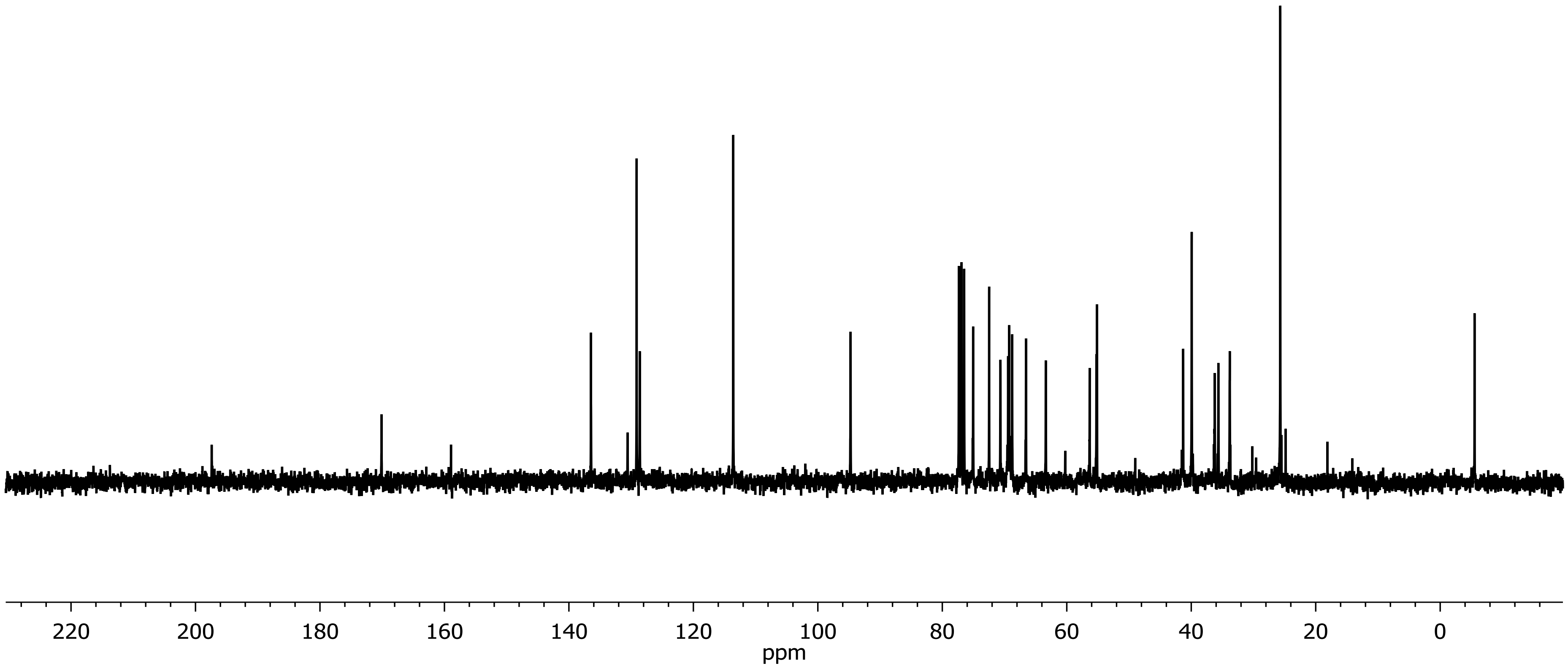


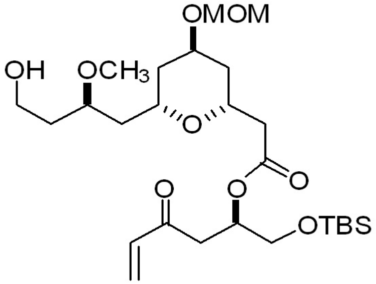
^{1}H NMR(300MHz, CDCl$_3$)



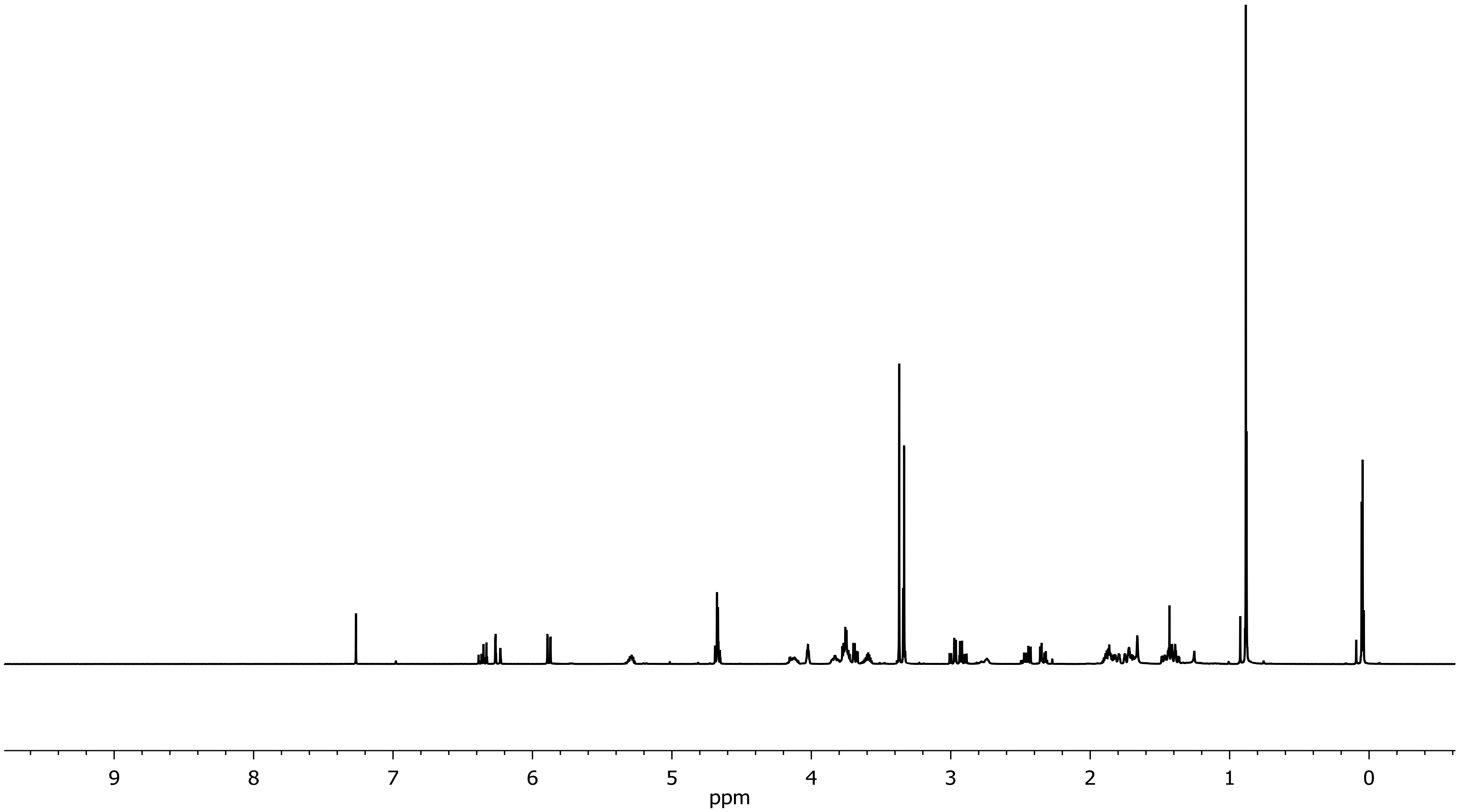


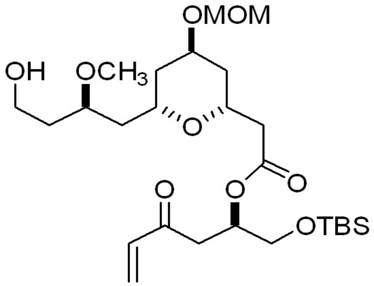
^{13}C NMR(75MHz, CDCl$_3$)



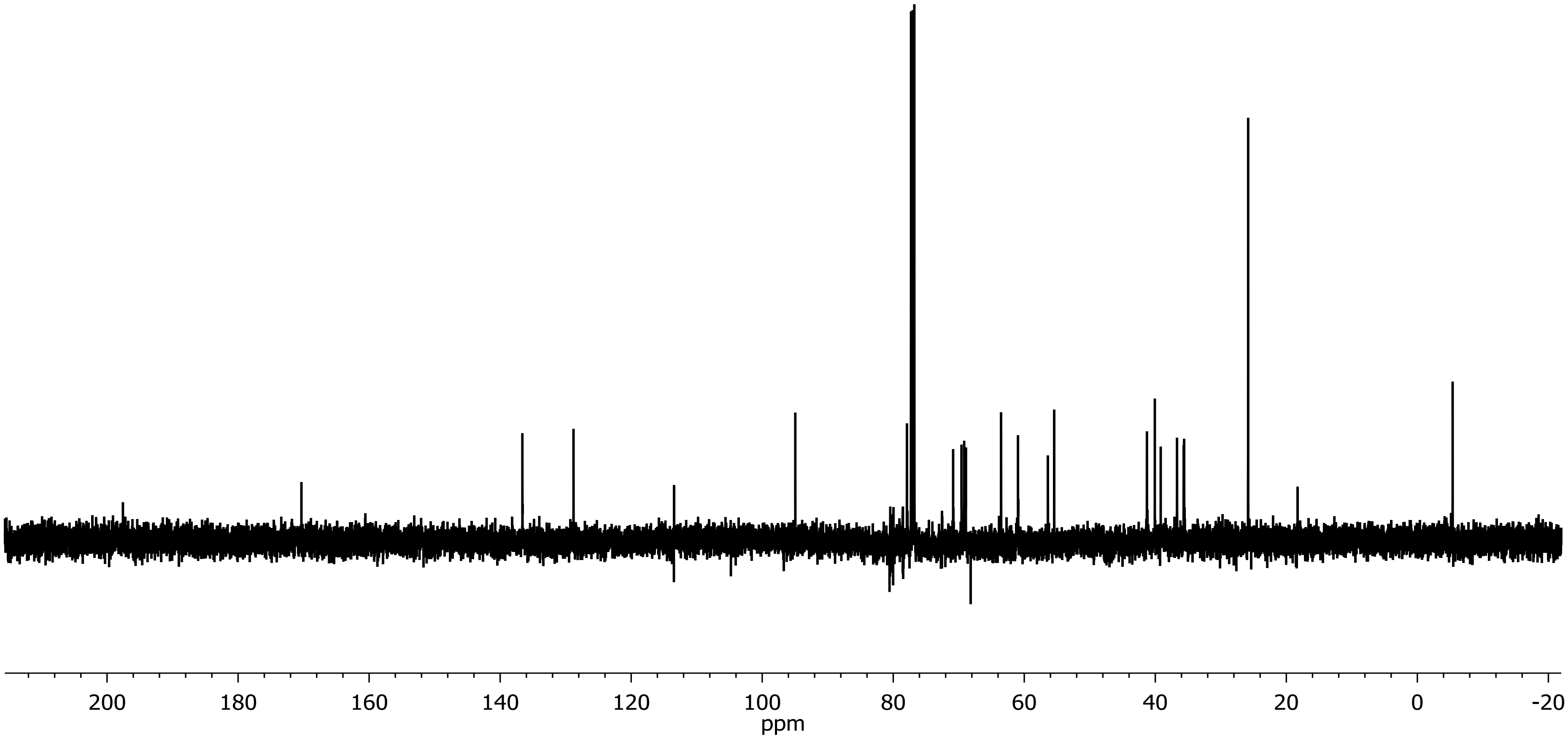


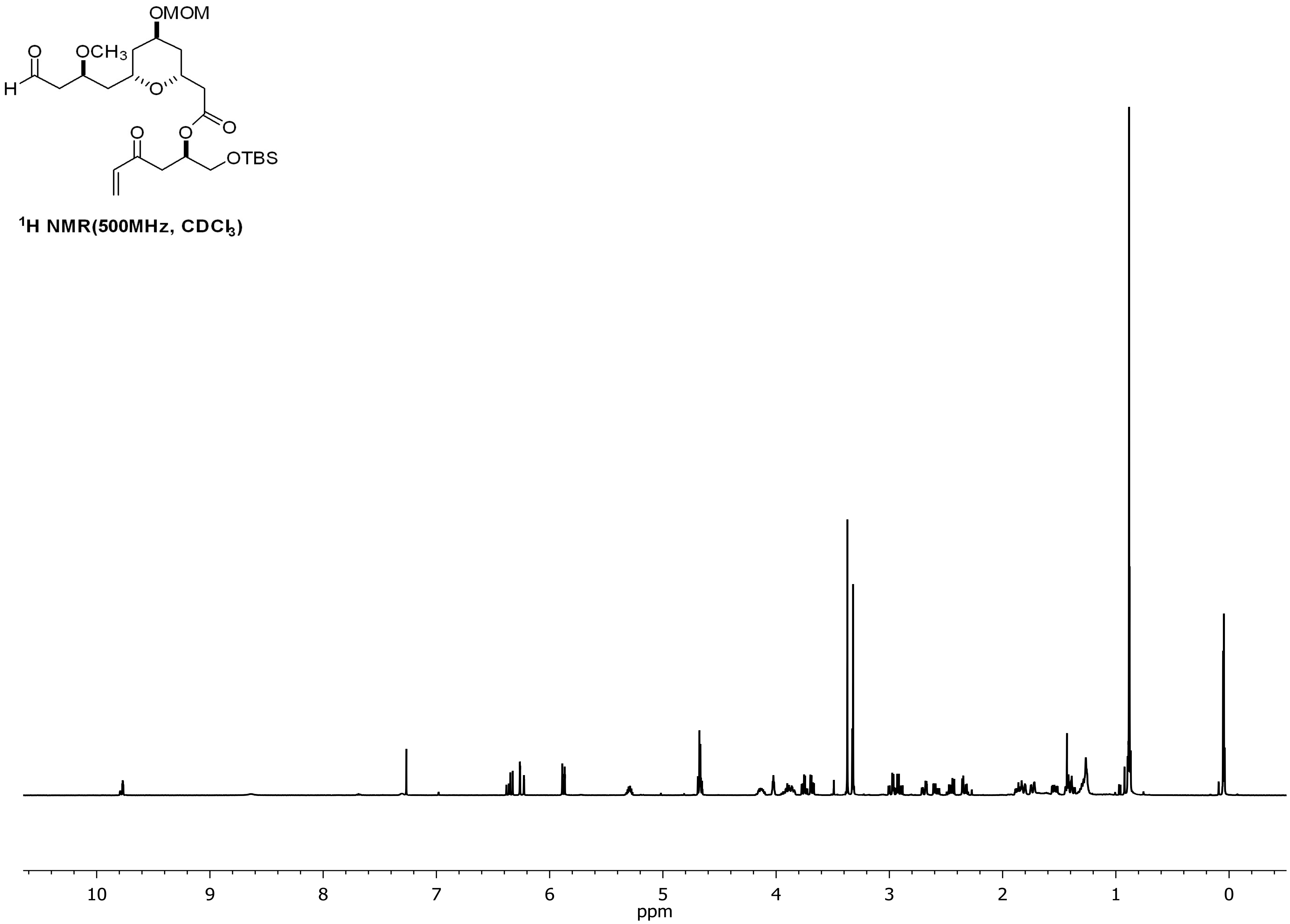
^{1}H NMR(500MHz, $CDCl_3$)



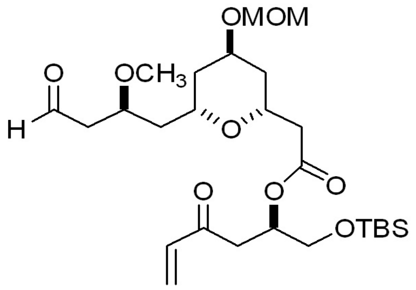


^{13}C NMR(125MHz, CDCl$_3$)





^{1}H NMR(500MHz, CDCl$_3$)



^{13}C NMR(125MHz, CDCl$_3$)