Total Synthesis of (+)-Dactylolide

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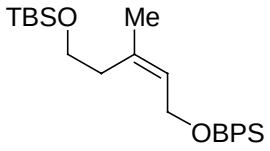
Supplemental Information: Selected Experimentals and ^{1}H and ^{13}C NMR Data

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 using 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 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, m, and ABq stand for the resonance multiplicities singlet, doublet, triplet, quartet, multiplet, and AB quartet, respectively. Optical rotations were obtained (Na D

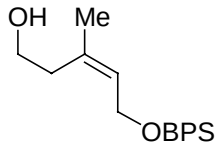
line) using a micro cell with a 1 dm path length. Concentrations are reported in g/100 mL. Melting points were obtained on an Electro thermal melting point apparatus and are uncorrected. Analytical elemental combustion analyses were performed by Atlantic Microlab, Inc., Norcross, Georgia. Glassware for 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 1-[(2Z)-3-methyl-5-(1,1,2,2-tetramethyl-1-silapropoxy)pent-2-enyloxy]-2,2-dimethyl-1,1-diphenyl-1-silapropane. To a cold (- 0 ^{o}C) solution of ester **18** (2.45 g, 9.0 mmol,) in PhMe (90 mL, 0.1 M), was added DIBAL-H (1M in CH_2Cl_2, 22.5 mL, 22.5 mmol, 2.5 equiv). The resulting mixture was stirred at this temperature for 30 min. This mixture was quenched with 10 mL of EtOAc. Saturated aqueous Rochelle's salts (100 mL) were added and the mixture was allowed to stir overnight (8 h). The layers were separated, and the aqueous layer was extracted with EtOAc (2 x 50 mL). The combined organic layers were dried (Na_2SO_4), and concentrated to give a clear, colorless oil. This crude alcohol mixture was taken on without further purification to the next step. Spectral data for crude alcohol: R_f = 0.26 (20% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 5.64 (t, J = 7.3 Hz, 1H), 3.98 (d, J = 6.8 Hz, 2H), 3.66 – 3.63 (m, 2H), 2.66 (s, 1H), 2.31 – 2.29 (m, 2H), 1.70 (s, 3H), 0.86 (s, 9H), 0.03 (s, 6H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 137.4, 126.9, 60.9, 58.1, 35.2, 26.1, 23.4, 18.6, - 5.4.

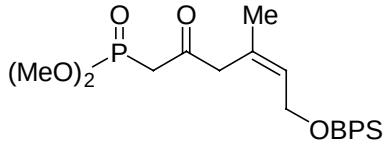
To a stirring solution of the above alcohol in CH_2Cl_2 (90 mL, 0.1 M) was added successively TBDPSCl (3.5 mL, 13.5 mmol, 1.5 equiv), and imidazole (1.23 g, 18.0 mmol, 2 equiv). The resulting mixture was stirred at room temperature for 30 min. The

mixture was then partitioned between 50 mL of 40% EtOAc/hexanes and 15 mL of saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with 40% EtOAc/hexanes (2 x 50 mL). The organic extracts were combined, washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was then purified via flash chromatography, eluting with 2% EtOAc/hexanes, to afford the desired silyl ether (3.38 g, 80%) as a colorless oil: R_f = 0.73 (20% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.73 - 7.71 (m, 4H), 7.46-7.39 (m, 6H), 5.50 (t, *J* = 5.4 Hz, 1H), 4.24 (d, *J* = 6.3 Hz, 2H), 3.55 (t, *J* = 7.1 Hz, 2H), 2.13 (t, *J* = 7.1 Hz, 2H), 1.75 (s, 3H), 1.08 (s, 9H), 0.86 (s, 9H), -0.01 (s, 6H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 135.8, 134.6, 134.2, 129.7, 127.8, 126.8, 62.0, 61.1, 36.1, 27.1, 26.1, 24.3, 19.4, 18.5, -5.2; IR (neat) 3071, 2932, 1469, 1255, 1108, 834, 704 cm $^{-1}$; Anal. Calcd for $C_{28}H_{44}O_2Si_2$: C, 71.73; H, 9.46. Found: C, 71.73; H, 9.57.



Preparation of (3Z)-5-(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)-3-methylpent-3-en-1-ol (19). To a cold (- 0 ^{o}C) solution of disilyl ether 1-[(2Z)-3-methyl-5-(1,1,2,2-tetramethyl-1-silapropoxy)pent-2-enyloxy]-2,2-dimethyl-1,1-diphenyl-1-silapropane (5.02 g, 10.7 mmol,) in MeOH (89 mL, 0.12 M), was added CSA (375 mg, 1.6 mmol, 0.15 equiv). The resulting mixture was stirred at this temperature for 30 min. This mixture was quenched with 1 mL of triethylamine. The solvents were evaporated under reduced pressure and the crude material was purified by flash chromatography, eluting with 5% and 10% ethyl acetate in hexanes to afford **19** (3.52 g, 93%) as a colorless oil: R_f = 0.16 (20% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.72 – 7.70 (m, 4H), 7.45 – 7.38 (m, 6H), 5.60 (dd, *J* = 7.1 Hz, 1H), 4.16 (d, *J* = 6.8 Hz, 2H),

3.62 (q, *J* = 5.9 Hz, 2H), 2.26 (t, *J* = 5.9 Hz, 2H), 2.09 – 2.04 (m, 1H), 1.76 (s, 3H), 1.05 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 136.4, 135.8, 133.8, 129.9, 127.9, 127.0, 60.3, 60.1, 35.5, 27.0, 23.7, 19.3; IR (neat) 3380, 3070, 2990, 1490, 1384, 1153 cm $^{-1}$; Anal. Calcd for $C_{22}H_{30}O_2Si$: C, 74.53; H, 8.53. Found: C, 74.33; H, 8.55.

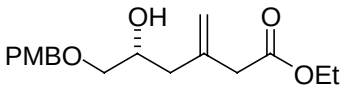


Preparation of [6-(tert-Butyl-diphenyl-silanyloxy)-4-methyl-2-oxo-hex-4-enyl]-phosphonic acid dimethyl ester (5). To a cold (0 ^{o}C) stirring solution of CrO_3 (3.75g, 37.3 mmol, 10 equiv) in CH_2Cl_2 (55 mL) was added pyridine (6.1 mL, 74.6 mmol, 20 equiv) and the ice bath was removed. The mixture was allowed to stir for 15 minutes at ambient temperature before alcohol **19** (1.32 g, 3.73 mmol) in CH_2Cl_2 (3.5 mL + 3.5 mL wash) was added. The mixture was allowed to stir for 30 additional minutes. The mixture was partitioned between 50% EtOAc/hexanes and 1M HCl (50 mL). The layers were separated, and the organic layer was washed with saturated, aqueous $NaHCO_3$, followed by brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. This crude aldehyde was directly taken to the next reaction without any purification. Spectral data for crude aldehyde: R_f = 0.30 (20% EtOAc); 500 MHz ^{1}H NMR ($CDCl_3$) δ 9.45 (t, *J* = 2.2 Hz, 1H), 7.70 – 7.68 (m, 4H), 7.46 – 7.39 (m, 6H), 5.73 – 5.70 (m, 1H), 4.19 (d, *J* = 6.3 Hz, 2H), 2.96 (d, *J* = 2.0 Hz, 2H), 1.77 (d, *J* = 1.5Hz, 3H), 1.06 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 199.2, 135.8, 133.8, 129.9, 129.3, 128.8, 127.9, 60.8, 47.7, 27.0, 24.6, 19.3.

To a cold (- 78 ^{o}C) solution of methyl dimethylphosphonate (1.2 mL, 11.2 mmol, 3 equiv) in PhMe (83 mL) was added *n*-BuLi (4.5 mL, 11.2 mmol, 3 equiv). The mixture was allowed to stir for 30 minutes. The aldehyde in a solution of PhMe (5 mL + 5 mL

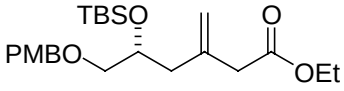
rinse) was transferred via cannula to the cold reaction mixture. This mixture was allowed to stir for 30 minutes. The mixture was poured into a separatory funnel containing 100 mL of pH 7 buffer and further diluted with EtOAc. The layers were separated and the aqueous layer was washed with EtOAc (2 X, 50 mL). The combined organic layers were dried (Na_2SO_4), and concentrated to give a yellow oil. This yellow oil was taken on to the next reaction without further purification.

To a stirring solution of the crude alcohol in CH_2Cl_2 (33 mL, 0.1 M) was added Dess Martin Periodinane (1.7 g, 3.9 mmol, 1.2 equiv). The resulting mixture was stirred at room temperature for 2 h. The mixture was then quenched by addition of 1 : 1 mixture of saturated aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$ solution (10 mL). This mixture was allowed to stir until the solution turned clear (30 minutes). The aqueous layer was extracted with CH_2Cl_2 (2 x 50 mL). The organic extracts were combined, washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was then purified via flash chromatography, eluting with 80% EtOAc/hexanes to 100% EtOAc, to afford **5** (1.23 g, 70%) as a yellow oil: R_f = 0.30 (100% EtOAc); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.70-7.67 (m, 4H), 7.44-7.37 (m, 6H), 5.65 (t, *J* = 6.8 Hz, 1H), 4.18 (d, *J* = 6.8 Hz, 2H), 3.67 (d, *J* = 11.2 Hz, 6H), 3.15 (s, 2H), 3.00 (d, *J* = 23.0 Hz, 2H), 1.72 (s, 3H), 1.07 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 199.2 (*J* = 6.1 Hz), 135.7, 133.8, 130.0, 129.8, 129.1, 127.8, 60.9, 53.1 (*J* = 6.1 Hz), 47.6, 40.5 (*J* = 128 Hz), 26.9 24.1, 19.3; IR (neat) 3070, 2957, 1917, 1262, 1109, 1035 cm $^{-1}$; HRMS (CI+) calcd for. $C_{25}H_{36}PO_5Si$ 475.6171, found 475.2065.

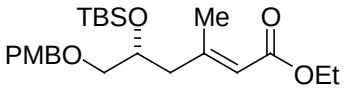


Preparation of ethyl 3-{(2R)-2-hydroxy-3-[(4-methoxyphenyl)methoxy]propyl}but-3-enoate (8). A mixture of (*R*)-BINOL (681 mg,

2.38 mmol, 0.4 equiv), 0.77 M Ti(O*i*Pr)$_4$ (1.54 mL, 1.19 mmol, 0.2 equiv), 0.1M TFA (0.3 mL, 0.03 mmol, 0.005 eq) and dried 4Å MS (805 mg) in 15 mL of CH_2Cl_2 was heated at reflux for 1 h. The brown mixture was cooled to room temperature and aldehyde **9** (1.0732 g, 5.96 mmol) was added *via* cannula. This flask was then rinsed with 2 x 2.5 mL of CH_2Cl_2. After stirring for 10 min at room temperature, the mixture was then cooled to –78 ^oC and stannane **10** (5.0 g, 11.9 mmol, 2.0 equiv) in 1 mL of CH_2Cl_2 was added. The reaction was stirred at –78 ^oC for 10 min and then placed in a –20 ^oC freezer without stirring for 5 d. The reaction mixture was quenched with aqueous saturated $NaHCO_3$ solution. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated to give a brown oil. The residue was purified *via* a silica gel chromatography, eluting with 10% EtOAc/hexanes to give 1.4574 g (79%) of a colorless oil: R_f = 0.16 (30% EtOAc/hex); $[\alpha]^{20}_D$ = - 1.7 (*c* = 1.18, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.27 – 7.25 (m, 2H), 6.89 – 6.87 (m, 2H), 5.04 (d, *J* = 12.7 Hz, 2H) 4.49 (s, 2H), 4.14 (q, *J* = 10.5 Hz, 2H), 3.96 (m, 1H), 3.81 (s, 3H), 3.48 (dd, *J* = 9.5, 3.9 Hz, 1H), 3.37 (dd, *J* = 9.5, 7.1 Hz, 1H), 3.11 (dd, *J* = 15.6, 4.9 Hz, 2H), 2.33 (dd, *J* = 14.4, 4.2 Hz, 1H), 2.26 (dd, *J* = 14.7, 8.8 Hz, 1H), 1.25 (t, *J* = 7.1 Hz, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 171.9, 159.5, 139.1, 130.2, 129.6, 117.3, 114.0, 73.9, 73.2, 68.6, 61.0, 55.4, 42.0, 40.5, 14.3; IR (neat) 3474, 2939, 1733, 1613, 1514, 1175, 1035, 821 cm^{-1}; Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.84. Found: C, 65.98; H, 7.82. Assay of enantiomeric excess: HPLC (Chiralcel OD-H 25 cm column, 5% *i*PrOH/hexanes; 1.0 mL/min); t_r (major) = 13.42 min, t_r (minor) = 14.73 min; 93% ee.

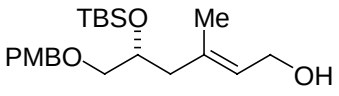


Preparation of ethyl 3 - {(2R) -3- [(4 - methoxyphenyl) methoxy] – 2 - (1,1,2,2-tetramethyl-1-silapropoxy) propyl} but-3-enoate (11). To a stirring solution of alcohol **8** (1.0565 g, 3.43 mmol) in DMF (34 mL, 0.1 M) was added successively TBSCl (775 mg, 5.14 mmol), and imidazole (467 mg, 6.86 mmol). The resulting mixture was stirred at room temperature overnight (8 h). The mixture was then partitioned between 50 mL of 40% EtOAc/hexanes and 15 mL of saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with 40% EtOAc/hexanes (2 x 50 mL). The organic extracts were combined, washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was then purified *via* flash chromatography, eluting with 3% EtOAc/hexanes, to afford **11** (1.400 g, 97%) as a colorless oil: R_f = 0.34 (15% EtOAc/hex); $[\alpha]^{20}_D$ = - 6.7 (*c* = 0.960, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.27 – 7.25 (m, 2H), 6.89 – 6.87 (m, 2H), 4.98 (s, 2H), 4.45 (s, 2H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.97 – 3.94 (m, 1H), 3.81 (s, 3H), 3.37 (d, *J* = 5.4 Hz, 2H), 3.10 (dd, *J* = 15.1, 8.8 Hz, 2H), 2.42 (dd, *J* = 14.2, 5.4 Hz, 1H), 2.28 (dd, *J* = 14.2, 6.8 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 171.7, 159.3, 139.5, 130.7, 129.4, 117.0, 113.9, 74.2, 73.1, 70.6, 60.8, 55.5, 42.5, 41.3, 26.1, 18.4, 14.4, - 4.3, - 4.6; IR (neat) 2931, 2857, 1738, 1614, 1514, 1250, 1097, 836 cm^{-1}; Anal. Calcd for $C_{23}H_{38}O_5Si$: C, 65.36; H, 9.06. Found: C, 65.61; H, 9.07.



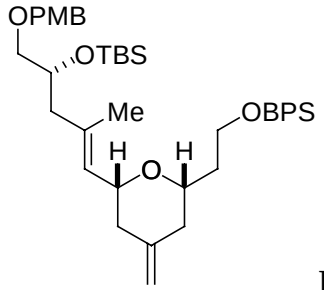
Preparation of ethyl (2E)(5R)-6-[(4-methoxyphenyl)methoxy]-3-methyl-5-(1,1,2,2-tetramethyl-1-silapropoxy)hex-2-

enoate (12). To a stirring solution of olefin **11** (1.4 g, 3.31 mmol) in THF (55 mL, 0.06 M) was added pure NaH (80 mg, 3.31 mmol). The resulting mixture was stirred at room temperature for 2 h. The mixture was then partitioned between 50 mL of 40% EtOAc/hexanes and 15 mL of saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with 40% EtOAc/hexanes (2 x 50 mL). The organic extracts were combined, washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was then purified *via* flash chromatography, eluting with 3% EtOAc/hexanes, to afford **12** (1.4 g, 100%, 32 : 1 *E* : *Z*) as a colorless oil: R_f = 0.34 (15% EtOAc/hex); $[\alpha]^{20}_D$ = + 16.4 (*c* = 1.24, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.27 – 7.25 (m, 2H), 6.89 – 6.87 (m, 2H), 5.70 (m, 1H), 4.45 (s, 2H), 4.20 - 4.10 (m, 2H), 4.0 – 3.96 (m, 1H), 3.81 (s, 3H), 3.39 (dd, *J* = 9.8, 5.4 Hz, 1H), 3.32 (dd, *J* = 9.8, 5.9 Hz, 1H), 2.18 (d, *J* = 1.5 Hz, 3H), 1.27 (t, *J* = 7.08 Hz, 3H), 0.86 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 166.8, 159.4, 156.5, 130.5, 129.5, 118.7, 113.9, 74.3, 73.2, 70.1, 59.6, 55.5, 46.5, 26.0, 19.7, 18.3, 14.6, - 4.3, - 4.7; IR (neat) 2932, 2857, 1716, 1514, 1250, 1151 cm^{-1}; Anal. Calcd for $C_{23}H_{38}O_5Si$: C, 65.36; H, 9.06. Found: C, 65.28; H, 9.07.



Preparation of (2E)(5R)-6-[(4-methoxyphenyl)methoxy]-3-methyl-5-(1,1,2,2-tetramethyl-1-silapropoxy) hex-2-en-1-ol (13). To a stirring solution of ester **12** (921 mg, 2.18 mmol) in Et_2O (22 mL, 0.1 M) at 0 ^oC was added LAH (166 mg, 4.36 mmol). The resulting mixture was warmed to room temperature and stirred for 30 minutes. 3g of $NaSO_4 \cdot 10H_20$/Celite® (1 : 1 mixture) was added to the solution and the solution was allowed to stir for 3 hours. The mixture was then filtered through a pad

of Celite® and concentrated under reduced pressure. The residue was then purified via flash chromatography, eluting with 15% EtOAc/hexanes, to afford **13** (772 mg, 93%) as a colorless oil: R_f = 0.19 (20% EtOAc/hex); $[\alpha]^{20}_D$ = + 5.2 (*c* = 0.975, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.27 – 7.25 (m, 2H), 6.89 – 6.87 (m, 2H), 5.45 – 5.42 (m, 1H), 4.45 (s, 2H), 4.17 – 4.10 (m, 2H), 3.97 – 3.92 (m, 1H), 3.81 (s, 3H), 3.35 (dd, *J* = 5.4, 2.4 Hz, 2H), 2.28 (dd, *J* = 13.7, 5.4 Hz, 1H), 2.14 (dd, *J* = 13.2, 7.3 Hz, 1H), 1.69 (s, 3H), 0.87 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 159.3, 136.4, 130.7, 129.4, 126.8, 113.9, 74.4, 73.1, 70.3, 59.6, 55.5, 45.2, 26.0, 18.4, 17.1, - 4.2, - 4.6; IR (neat) 3385, 2930, 2857, 1613, 1514, 1250, 1107, 836, 776 cm^{-1}; Anal. Calcd for $C_{21}H_{36}O_4Si$: C, 66.27; H, 9.53. Found: C, 66.34; H, 9.61.

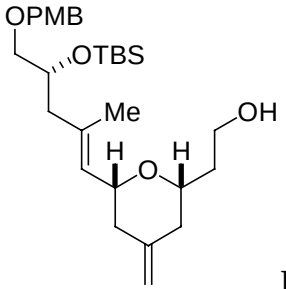


Preparation of (4E)(2R)-5-{(6S,2R)-6-[2-(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)ethyl] – 4 - methylene (2H-3,5,6-trihydropyran-2-yl)} – 1 - [(4- methoxyphenyl)methoxy]-4-methyl-2-(1,1,2,2-tetramethyl-1-silapropoxy)pent-4-ene (16). To a cold (0 °C) solution of alcohol **13** (641 mg, 1.68 mmol) in CH_2Cl_2 (17 mL, 0.1 M) were successively added 4Å MS (640 mg), NMO (590 mg, 5.04 mmol, 3 equiv), and TPAP (59 mg, 0.17 mmol). The resulting mixture was stirred at 0 °C for 5 min and the cold bath was removed. The reaction was stirred at ambient temperature for 30 min before the mixture was filtered through a plug of Florisil®. This plug was washed several times with 80% EtOAc/hexanes. The mixture was concentrated under reduced pressure to give a black oil (589 mg of the crude aldehyde, 91% crude yield). Spectra

data for the crude aldehyde: R_f = 0.55 (30% EtOAc/hex); 500 MHz ^{1}H NMR ($CDCl_3$) δ 9.97 (d, *J* = 7.8 Hz, 1H), 7.23 (d, *J* = 8.3 Hz, 2H), 6.87 (d, *J* = 7.8 Hz, 2H), 5.90 (d, *J* = 7.8 Hz, 1H), 4.44 (s, 2H), 4.04 – 4.00 (m, 1H), 3.80 (s, 3H), 3.40 (dd, *J* = 9.8, 5.4 Hz, 1H), 3.30 (dd, *J* = 9.3, 6.3 Hz, 1H), 2.48 (dd, *J* = 13.2, 4.4 Hz, 1H), 2.32 (dd, *J* = 13.2, 7.8 Hz, 1H), 2.19 (s, 3H), 0.85 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 191.0, 161.0, 159.4, 130.2, 130.0, 129.4, 113.9, 74.0, 73.2, 70.2, 55.4, 46.1, 25.9, 18.6, 18.2, - 4.3, -4.7.

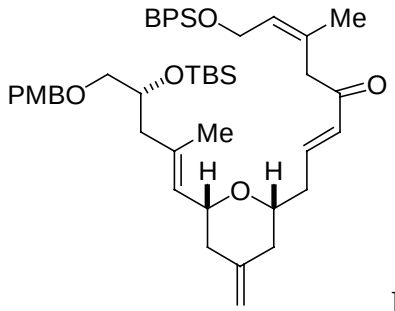
To a cold solution (- 78 ^{o}C) of β-hydroxy allylsilane **6** (0.823 g, 1.87 mmol, 1.2 equiv) and aldehyde **7** (0.589 g, 1.56 mmol) in diethyl ether (11 mL, 0.15 M), was added TMSOTf (340 μL, 1.87 mmol, 1.2 equiv). The resulting mixture was stirred at this temperature for 40 min, then 200 μL of Hünig's base was added. The resulting mixture was then stirred at 0 ^{o}C for 10 min before quenching with saturated aqueous $NaHCO_3$ solution and wet ether (10 mL total, 1:1). The mixture was brought to rt, then transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 25 mL). The organic layers were combined and dried over Na_2SO_4. The solvents were evaporated under reduced pressure and the crude material was purified *via* flash chromatography, eluting with 5% ethyl acetate in hexanes to afford **16** (967 mg, 85%) as a colorless oil: R_f = 0.51 (20% EtOAc/hex); $[\alpha]^{20}_D$ = - 1.7 (*c* = 0.58, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.69 - 7.67 (m, 4H), 7.45 – 7.36 (m, 6H), 7.28 – 7.26 (m, 2H), 6.90 – 6.88 (m, 2H), 5.26 (d, *J* = 7.8 Hz, 1H), 4.75-4.73 (m, 2H), 4.46 (s, 2H), 3.99 (ddd, *J* = 11.2, 8.3, 4.9 Hz, 1H), 3.97 – 3.93 (m, 1H), 3.87 – 3.83 (m, 1H), 3.82 (s, 3H), 3.78 – 3.74 (m, 1H), 3.58 – 3.56 (m, 1H), 3.36 (dd, *J* = 4.9, 1.5 Hz, 2H), 2.32 (dd, *J* = 13.7, 6.8 Hz, 1H), 2.23 (d, *J* = 13.2 Hz, 1H), 2.16 – 2.11 (m, 2H), 2.07

– 1.93 (m, 2H), 1.89 – 1.82 (m, 1H), 1.78 – 1.73 (m, 1H), 1.70 – 1.69 (m, 3H), 1.06 (s, 9H), 0.89 (s, 9H), 0.06 (s, 3H), 0.06 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 159.3, 145.1, 135.8, 135.8, 134.3, 134.1, 130.8, 129.7, 129.7, 129.4, 128.9, 127.8, 127.8, 113.9, 108.6, 75.7, 75.3, 74.3, 73.1, 70.8, 60.6, 55.5, 45.2, 41.1, 40.9, 39.4, 27.1, 26.1, 19.4, 18.4, 17.9, - 4.3, - 4.5; IR (neat) 3071, 2934, 3858, 1513, 1250, 1110, 833 cm^{-1}; Anal. Calcd for $C_{44}H_{34}O_5Si_2$: C, 72.48; H, 8.85. Found: C, 72.43; H, 9.05.



Preparation of 2-(6-{(1E)(4R)-5-[(4-methoxyphenyl)methoxy]-2-methyl-4-(1,1,2,2-tetramethyl-1-silapropoxy)pent-1-enyl}(2S,6R)-4-methylene-2H-3,5,6-trihydropyran-2-yl)ethan-1-ol. To a stirring solution of silyl ether **16** (61.1 mg, 0.08 mmol) in DMF (2 mL, 0.05 M), was successively added TBAF (0.92 mL, 0.09 mmol. 1.1 equiv) and HOAc (5 μL, 0.09 mmol, 1.1 equiv). The resulting mixture was stirred at ambient temperature for 15 h before quenching by the addition of 5 mL each of saturated aqueous $NaHCO_3$ solution and 50% EtOAc/hexanes. The mixture was further diluted with 10 mL of water and the aqueous layer was extracted with EtOAc (2 x 15 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified *via* silica gel chromatography, eluting with 5%, 10%, and 15% EtOAc/hexanes to give the desired alcohol as a colorless oil (31 mg, 89%): R_f = 0.40 (40% EtOAc/hex); $[\alpha]^{20}_D$ = - 2.7 (*c* = 1.16, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.27 – 7.25 (m, 2H), 6.89 – 6.87 (m, 2H), 5.23 (d, J = 8.8 Hz, 1H), 4.75 – 4.74 (m, 2H), 4.45 (s, 2H), 4.02 (ddd, J = 10.7, 4.8, 2.4

Hz, 1H), 3.96 – 3.93 (m, 1H), 3.81 (s, 3H), 3.78 – 3.74 (m, 1H), 3.59 – 3.55 (m, 1H), 3.34 (d, J = 5.4 Hz, 2H), 2.68 – 2.63 (m, 1H), 2.27 (dd, J = 13.4, 5.1, 1H), 2.20 – 2.00 (m, 2H), 2.08 – 1.99 (m, 2H), 1.86 – 1.78 (m, 3H), 1.77 – 1.72 (m, 2H), 1.70 – 1.69 (m, 3H), 0.88 (s, 9H), 0.05 (s, 6H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 159.3, 144.3, 136.4, 130.8, 129.4, 128.4, 113.9, 109.1, 78.8, 76.0, 74.2, 73.1, 70.7, 61.6, 55.5, 45.0, 40.8, 40.7, 38.3, 26.1, 18.4, 18.0, - 4.3, - 4.5; IR (neat) 3450, 2936, 1304, 1094, 835 cm^{-1}; Anal. Calcd for $C_{28}H_{46}O_5Si$: C, 68.53; H, 9.45. Found: C, 68.43; H, 9.51.

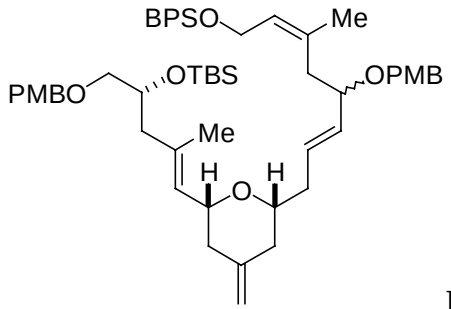


Preparation of 1-(6-{(1E)(4R)-5-[(4-methoxyphenyl)methoxy]-2-methyl-4-(1,1,2,2-tetramethyl-1-silapropoxy)pent-1-enyl}(2R,6R)-4-methylene(2H-3,5,6-trihydropyran-2-yl))(6Z,2E)-8-(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)-6-methylocta-2,6-dien-4-one (20). To a cold (0 ^oC) solution of 2-(6-{(1E)(4R)-5-[(4-methoxyphenyl)methoxy]-2-methyl-4-(1,1,2,2-tetramethyl-1-silapropoxy)pent-1-enyl}(2S,6R)-4-methylene-2H-3,5,6-trihydropyran-2-yl)ethan-1-ol (206 mg, 0.49 mmol) in CH_2Cl_2 (6.2 mL, 0.1 M) were successively added 4Å MS (200 mg), NMO (172 mg, 1.47 mmol, 3 equiv), and TPAP (14 mg, 0.04 mmol, 0.08 equiv). The resulting mixture was stirred at 0 ^oC for 5 min and the cold bath was removed. The reaction was stirred at ambient temperature for 30 min before the mixture was filtered through a plug of Florisil®. This plug was washed several times with EtOAc. The mixture was concentrated under reduced pressure to give a black oil. This crude aldehyde was immediately subjected to the next reaction. Spectra data for the crude

aldehyde: 500 MHz ^{1}H NMR ($CDCl_3$) 9.79 (t, *J* = 2.0 Hz, 1H), 7.26 – 7.24 (m, 2H), 6.88 – 6.86 (m, 2H), 5.22 (d, *J* = 8.3 Hz, 1H), 4.77 – 4.76 (m, 1H), 4.44 (s, 2H), 4.02 (ddd, *J* = 11.5, 9.1, 3.7 Hz, 1H), 3.94 – 3.90 (m, 1H), 3.89 – 3.84 (m, 1H), 3.33 (ddd, *J* = 14.7, 9.8, 5.6 Hz 2H), 2.66 (ddd, *J* = 16.6, 8.3, 2.4 Hz, 1H), 2.49 (ddd, *J* = 16.6, 4.9, 2.0 Hz, 1H), 2.30 – 2.24 (m, 2H), 2.14 – 2.08 (m, 2H), 2.03 – 1.98 (m, 2H), 1.68 (d, *J* = 1 Hz, 3H), 0.87 (s, 9H), 0.03 (s, 3H), 0.03 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 201.2, 159.1, 143.5, 136.3, 130.5, 129.2, 128.1, 113.7, 109.4, 75.8, 74.2, 73.3, 72.9, 70.2, 55.2, 49.6, 45.0, 40.4, 40.2, 25.9, 18.2, 17.6, - 4.5, - 4.8.

A mixture of ketophosphonate **5** (285 mg, 0.6 mmol) and $Ba(OH)_2 \cdot 8H_2O$ (103 mg, 0.6 mmol, heated at 140 ^{o}C under vacuum for 2 h before use) in THF (5 mL) was stirred at ambient temperature for 30 minutes. The mixture was cooled to 0 ^{o}C. A solution of aldehyde **17** in wet THF (1 mL, 40 : 1 THF : H_2O, 1 mL rinse) was then added via cannula. The mixture was stirred at this temperature for 30 minutes and then allowed to warm to ambient temperature and stir 1.5 h. Saturated aqueous sodium bicarbonate solution and EtOAc were added to the reaction mixture. The layers were separated and the aqueous layer was extracted with EtOAc (2 x 25 mL). The combined layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue was then purified via flash chromatography, eluting with 5% EtOAc/hexanes, to afford **20** (326 mg, 79%). R_f = 0.26 (2 x 10% EtOAc/hex); $[\alpha]^{20}_{D}$ = + 20.53 (*c* = 0.775, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.69 – 7.67 (m, 4H), 7.44 – 7.37 (m, 6H), 7.27 – 7.25 (m, 2H), 6.88 – 6.86 (m, 2H), 6.79 (dt, *J* = 15.6, 7.3, 7.3 Hz, 1H), 6.10 (d, *J* = 16.1 Hz, 1H), 5.63 (t, *J* = 6.3 Hz, 1H), 5.24 (d, *J* = 7.3 Hz, 1H), 4.74 – 4.73 (m, 2H), 4.45 (s, 2H), 4.19 (d, *J* = 6.4 Hz, 2H), 3.96 (dt, *J* = 8.8, 5.9, 5.4 Hz, 1H), 3.95 - 3.90 (m, 1H), 3.81

(s, 3H), 3.42 – 3.36 (m, 1H), 3.34 (d, *J* = 4.9 Hz, 2H), 3.06 (s, 2H), 2.47-2.41 (m, 1H), 2.35 – 2.27 (m, 2H), 2.17 – 2.10 (m, 3H), 2.00 – 1.89 (m, 2H), 1.71 (s, 3H), 1.68 (s, 3H), 1.05 (s, 9H), 0.88 (s, 9H), 0.05 (s, 6H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 197.3, 159.3, 144.2, 143.8, 136.2, 135.8, 135.0, 134.0, 131.3, 131.2, 130.8, 129.8, 129.4, 128.5, 128.3, 127.9, 127.9, 113.9, 109.2, 75.9, 74.4, 73.1, 70.7, 61.1, 55.5, 45.2, 44.4, 40.8, 40.4, 39.4, 27.0, 26.8, 26.1, 24.3, 19.4, 18.4, 17.9, - 4.3, - 4.5; IR (neat) 2933, 2857, 1671, 1513, 1250, 1109, 832 cm^{-1}; Anal. Calcd for $C_{52}H_{74}O_6Si_2$: C, 73.16; H, 8.67. Found: C, 72.92; H, 8.70.

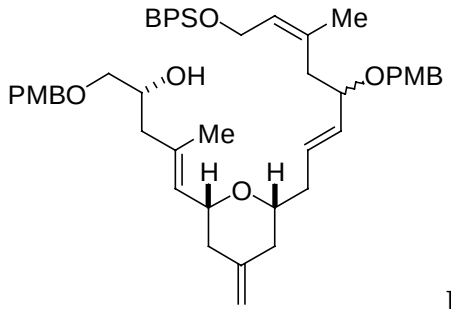


Preparation of 1-[(1E)-3-(6-{(1E)(4R)-5-[(4-methoxyphenyl)methoxy]-2-methyl-4-(1,1,2,2-tetramethyl-1-silapropoxy) pent-1-enyl}(2R,6R)-4-methylene(2H-3,5,6-trihydropyran-2-yl))prop-1-enyl] (3Z)-5-(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)-1-[(4-methoxyphenyl)methoxy]-3-methylpent-3-ene (21). To a cold (-30 ^{o}C) solution of **20** (117mg, 0.14mmol) in 7 mL of MeOH/THF (3:1) was added $CeCl_3 \cdot 7H_2O$ (782 mg, 2.1 mmol, 15 equiv). This was followed by the addition of solid $NaBH_4$ (42 mg, 1.12 mmol, 8 equiv). The resulting mixture was stirred for 40 min. This reaction was then poured into 50% EtOAc/hexanes (10 mL) and saturated aqueous sodium bicarbonate was added. The layers were separated and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford a clear oil.

The residue was directly subjected to the next reaction. Spectral data for the crude alcohol: R_f= 0.25 (20% EtOAc/hex); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.73 – 7.69 (m, 4H), 7.45 – 7.38 (m, 6H), 7.27 - 7.25 (m, 2H), 6.89 – 6.87 (m, 2H), 5.72 – 5.67 (m, 1H), 5.61 – 5.59 (m, 1H), 5.50 (dd, *J* = 15.1, 6.3 Hz, 1H), 5.25 (d, *J* = 7.3 Hz, 1H), 4.72 (s, 2H), 4.45 (s, 2H), 4.20 (dd, *J* = 11.7, 7.3 Hz, 1H), 4.16 – 4.11 (m, 1H), 4.08 (dd, *J* = 11.7, 6.3 Hz, 1H), 3.98 – 3.91 (m, 2H), 3.81 (s, 3H), 3.35 – 3.30 (m, 3H), 2.36 – 2.28 (m, 4H), 2.22 (m, 8H), 1.77 (s, 3H), 1.69 (s, 3H), 1.05 (s, 9H), 0.89 (s, 9H), 0.05 (s, 6H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 159.3, 144.8, 135.9, 135.2, 133.8, 130.8, 129.9, 129.4, 128.8, 127.9, 127.9, 127.4, 127.3, 113.9, 108.8, 77.9, 75.8, 74.4, 73.1, 70.7, 70.2, 60.3, 55.5, 45.2, 41.0, 40.7, 40.2, 39.4, 27.0, 26.1, 24.1, 19.3, 18.4, 17.9, - 4.6, - 4.5.

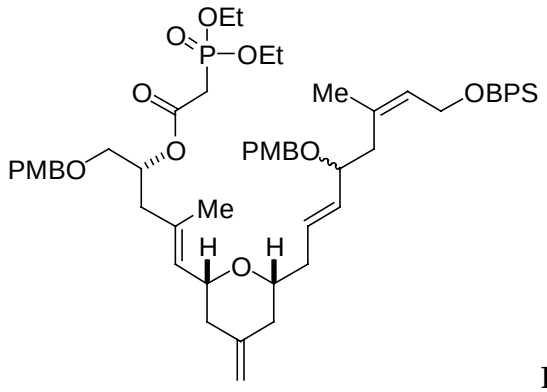
To a cold (- 78 ^{o}C) mixture of the above alcohol, PMBBr (138 mg, 0.68 mmol), NEt_3 (232 μL, 1.65mmol) in THF (1.1 mL) was added KHMDS (0.5 M in PhMe, 660 μL, 0.33mmol). The reaction mixture was allowed to stir for 1 h. The cold bath was removed and the mixture was stirred for 1 h at ambient temperature. The mixture was re-cooled to – 78 ^{o}C and KHMDS (330 μL, 0.17 mmol) was added and allowed to stir for 30 minutes. The cold bath was removed and the mixture was stirred for 1h at ambient temperature. Concentrated NH_4OH (1 mL) was added and the mixture was stirred for 5 h. The mixture was diluted with water and EtOAc and the layers were separated. The aqueous layer was washed with EtOAc (2 x mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was then purified via flash chromatography, eluting with 5% EtOAc/hexanes, to afford **20** (116 mg, 87% from ketone **20**). R_f = 0.56 (30% EtOAc/hex); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.70 – 7.69 (m, 4H), 7.40 – 7.37 (m, 6H), 7.28 – 7.26 (m, 2H), 7.18 – 7.10 (m, 2H), 6.90

– 6.88 (m, 2H), 6.85 – 6.81 (m, 2H), 5.62 – 5.54 (m, 1H), 5.50 – 5.46 (m, 1H), 5.30 – 5.26 (m, 2H), 4.73 (s, 2H), 4.46 (s, 2H), 4.42 (d, *J* = 11.2 Hz, 1H), 4.22 – 4.18 (m, 4H), 3.99 – 3.94 (m, 2H), 3.82 (s, 3H), 3.80 (s, 3H), 3.77 – 3.70 (m, 1H), 3.36 – 3.35 (m, 2H), 3.35 – 3.31 (m, 1H), 2.35 – 2.25 (m, 3H), 2.04 – 1.97 (m, 6H), 1.90- 1.88 (m, 1H), 1.70 (s, 6H), 1.06 (s, 9H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 159.3, 159.1, 144.8, 144.8, 135.9, 135.9, 135.8, 134.2, 134.0, 134.0, 132.9, 132.9, 131.0, 130.8, 130.1, 130.0, 129.9, 129.8, 129.8, 129.7, 129.6, 129.4, 129.3, 129.3, 129.2, 128.8, 128.7, 127.9, 127.8, 127.3, 127.3, 114.0, 114.0, 113.9, 113.8, 108.8, 78.8, 78.7, 78.1, 77.9, 75.8, 74.4, 73.1, 70.7, 69.6, 69.6, 61.2, 55.4, 55.4, 45.2, 40.9, 40.2, 40.2, 39.4, 39.3, 38.8, 38.8, 37.5, 27.1, 26.1, 24.6, 24.6, 19.4, 18.4, 17.9, - 4.3, - 4.5; IR (neat) 2933, 2816, 1612, 1302, 1108, 829 cm^{-1}; Anal. Calcd for $C_{52}H_{74}O_6Si_2$: C, 73.16; H, 8.67. Found: C, 72.92; H, 8.70.



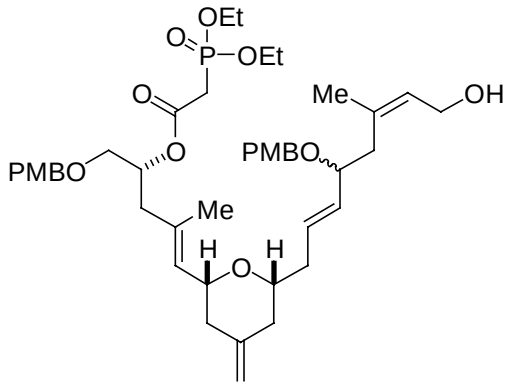
Preparation of (4E)(2R)-5-((2R,6R)-6-{(6Z,2E)-8-(2, 2 - dimethyl-1, 1 - diphenyl - 1 - silapropoxy) - 4 - [(4-methoxyphenyl) methoxy]-6-methylocta-2,6-dienyl}-4-methylene(2H-3,5,6-trihydropyran-2-yl))-1-[(4-methoxyphenyl)methoxy]-4-methylpent-4-en-2-ol. To a mixture of silyl ether **21** (110 mg, 0.12 mmol) and EtOH (1.5 mL) was added PPTs (6 mg, 0.034 mmol, 0.3 equiv) and heated to 55 ^{o}C for 8 h. The reaction mixture was then cooled to ambient temperature and NEt_3 (500 μL) was added. The mixture was concentrated under reduced pressure and

directly subjected to flash chromatography, eluting with 5% EtOAc/hexanes, to afford the desired alcohol (68 mg, 71%). R_f = 0.27 (40% EtOAc/hex); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.67 – 7.66 (m, 4H), 7.42 – 7.35 (m, 6H), 7.26 – 7.24 (m, 2H), 7.16 – 7.14 (m, 2H), 6.89 – 6.87 (m, 2H), 6.80 – 6.79 (m, 2H), 5.56 – 5.50 (m, 1H), 5.46 – 5.42 (m, 1H), 5.29 – 5.25 (m, 2H), 4.77 – 4.75 (m, 2H), 4.48 (s, 2H), 4.40 (d, *J* = 11.7 Hz, 1H), 4.18 – 4.16 (m, 4H), 3.98 – 3.93 (m, 2H), 3.80 (s, 3H), 3.77 (s, 3H), 3.70 – 3.66 (m, 1H), 3.46 – 3.42 (m, 1H), 3.32 – 3.29 (m, 2H), 2.29 – 2.05 (m, 8H), 2.02 – 1.98 (m, 2H), 1.90 – 1.88 (m, 1H), 1.68 (s, 3H), 1.67 (s, 3H), 1.03 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 159.4, 159.1, 145.6, 135.8, 135.6, 135.5, 134.3, 134.0, 134.0, 133.0, 133.0, 131.1, 131.1, 130.3, 129.8, 129.7, 129.6, 129.6, 129.3, 129.3, 128.6, 128.8, 114.1, 113.9, 108.9, 78.7, 78.1, 77.1, 75.7, 73.8, 73.3, 69.7, 69.6, 68.8, 61.2, 55.5, 55.5, 43.7, 43.7, 40.9, 40.2, 40.1, 39.3, 39.2, 38.8, 38.8, 29.9, 27.1, 24.7, 24.7, 19.4, 17.4; IR (neat) 3457, 2935, 1654, 1513, 1248, 1108, 891, 705 cm^{-1}; MS (ESI+) calcd for. $C_{53}H_{68}O_7SiNa$ 867.46, found (M + Na) 867.5.



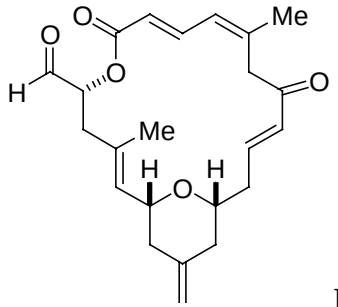
Preparation of (3E)(1R)-4-((2R,6R)-6-{(6Z,2E)-(Diethoxy-phosphoryl)-acetic acid 4-{6-[8-(tert-butyl-diphenyl-silanyloxy)-4-(4-methoxy-benzyloxy)-6-methyl-octa-2,6-dienyl]-4-methylene-tetrahydro-pyran-2-yl}-1-(4-methoxy-benzyloxymethyl)-3-methyl-but-3-enyl ester (22). To a solution

of (4E)(2R)-5-((2R,6R)-6-{(6Z,2E)-8-(2, 2 - dimethyl-1, 1 - diphenyl - 1 - silapropoxy) - 4 - [(4-methoxyphenyl) methoxy]-6-methylocta-2,6-dienyl}-4-methylene(2H-3,5,6-trihydropyran-2-yl))-1-[(4-methoxyphenyl)methoxy]-4-methylpent-4-en-2-ol (12.6 mg, 0.015 mmol) and diethyl phosphonoacetic acid (14.6 mg, 0.075 mmol) in $CHCl_3$ (1.5 mL) were added DMAP (18 mg, 0.15 mmol), DMAP·HCl (24 mg, 0.15 mmol), and PS-carbodiimide (160 mg, 0.15 mmol, 0.94 mmol/g). The mixture was allowed to stir for 30 minutes. The reaction mixture was filtered and concentrated under reduced pressure. The mixture was directly subjected to flash chromatography, eluting with 80% EtOAc/hexanes, to afford **22** (18 mg, 100%). R_f = 0.50 (100% EtOAc); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.68 – 7.67 (m, 4H), 7.43 – 7.36 (m, 6H), 7.24 (d, *J* = 8.5 Hz, 2H), 7.15 (d, *J* = 8.2 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 5.58 – 5.49 (m, 1H), 5.46 (t, *J* = 6.1 Hz, 1H), 5.30 – 5.24 (m, 2H), 5.20 – 5.18 (m, 1H), 4.72 (s, 2H), 4.45 (ABq, *J* = 11.6 Hz, Δν = 7.7 Hz, 2H), 4.40 (d, *J* = 11.3 Hz, 1H), 4.20 – 4.13 (m, 5H), 3.94 (t, *J* = 8.7 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.69 (q, *J* = 7.2 Hz, 1H), 3.49 (s, 2H), 2.98 (d, *J* = 21.4 Hz, 2H), 3.34 – 3.29 (m, 1H), 2.40 – 2.34 (m, 2H), 2.32 – 2.22 (m, 2H), 2.20 –2.12 (m, 2H), 2.10 – 1.99 (m, 2H), 1.96 – 1.86 (m, 2H), 1.70 (s, 3H), 1.68 (s, 3H), 1.32 (t, *J* = 6.9 Hz, 6H), 1.04 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 165.6 (J = 6.2 Hz), 159.5, 144.4, 135.8, 134.2, 134.0, 131.0, 130.2, 129.7, 129.6, 129.5, 129.3, 129.2, 127.8, 114.0, 113.9, 109.0, 78.7, 78.1, 77.9, 75.6, 73.1, 72.7, 70.1, 69.7, 62.8, 61.2, 55.5, 41.0, 40.8, 40.0, 39.4, 39.2, 38.8, 35.2 (J = 134 Hz), 27.1, 24.7, 22.9, 19.4, 17.2, 16.6 (J = 5.8 Hz), 13.8; IR (neat) 2934, 1737, 1513, 1251, 1033, 822, 705 cm^{-1}; MS (CI+) calcd for. $C_{59}H_{79}O_{11}PSi$ 1023.31, found 1023.10.



(3E)(1R)-4-((2R,6R)-6-{(6Z,2E)-8-hydroxy-4-[(4-methoxyphenyl)methoxy]-6-methylocta-2,6-dienyl}-4-methylene(2H-3,5,6-trihydropyran-2-yl))-1-{[(4-methoxyphenyl)methoxy]methyl}-3-methylbut-3-enyl 2-(diethoxycarbonyl)acetate. To a cooled (0 ^{o}C) solution of silyl ether **22** (19 mg, 0.019 mmol) in 1.9 mL of CH_3CN/H_2O (20:1) and 46 μL of pyridine was added 1 mL of HF dropwise over 30 min (48% solution). The reaction was warmed to rt and after 2 h, the solution was poured into a cold mixture of saturated aqueous $NaHCO_3$ solution (20 mL) and EtOAc (10 mL). Additional solid $NaHCO_3$ was added in several portions until pH >> 7 before the layers were separated. The aqueous layer was extracted with EtOAc (2 x 10 mL). The organic extracts were combined and dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The mixture was directly subjected to flash chromatography, eluting with 100% EtOAc, to afford the desired alcohol (10.2 mg, 74%). R_f = 0.10 (100% EtOAc); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.26 (d, *J* = 8.2 Hz, 2H), 7.24 – 7.20 (m, 2H), 6.88 – 6.85 (m, 4H), 5.70 – 5.68 (m, 2H), 5.45 (dd, *J* = 15.6, 8.2 Hz, 1H), 5.28 (d, *J* = 7.6 Hz, 1H), 5.20 – 5.18 (m, 1H), 4.74 (s, 2H), 4.52 (dd, *J* = 11.6, 2.4 Hz, 1H), 4.45 (ABq, *J* = 11.3 Hz, Δν = 8.0 Hz, 2H), 4.24 (d, J = 11.6 Hz, 1H), 4.17 – 4.07 (m, 3H), 3.98 (t, *J* = 9.2 Hz, 1H), 3.80 (s, 3H), 3.80 (s, 3H), 3.50 (s, 2H), 3.40 – 3.32 (m, 1H), 2.98 (dd, J = 2.1, 1.8 Hz, 2H), 2.64 – 2.58 (m, 2H), 2.42 – 2.35 (m, 2H), 2.32 –

2.20 (m, 3H), 2.09 – 2.01 (m, 1H), 1.98 – 1.93 (m, 2H), 1.71 (s, 3H), 1.68 (s, 3H), 1.32 (t, *J* = 7.0 Hz, 6H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 165.6 (*J* = 6.2 Hz), 159.5, 159.4, 144.4, 137.3, 137.3, 134.4, 134.3, 133.0, 133.0, 130.2, 130.1, 130.1, 130.1, 129.8, 129.8, 129.5, 127.2, 114.0, 109.1, 78.0, 77.8, 76.6, 76.6, 75.7, 73.1, 72.7, 70.1, 69.8, 69.8, 39.2, 38.8, 34.6 (*J* = 135 Hz), 24.1, 24.1, 17.2, 16.6 (*J* = 5.8 Hz); IR (neat) 3433, 2962, 1736, 1514, 1257, 1030, 804 cm^{-1}; HRMS (CI+) calcd for. $C_{43}H_{62}O_{11}P$ (M + H) 785.403, found 785.399.



Preparation of (1R,5R,17R)-3,11-dimethyl-19-methylene-7,13-dioxo-6,21-dioxabicyclo[15.3.1]henicosa-2,8,10,14-tetraene-5-carbaldehyde (dactylolide) (1). To a solution of the above alcohol (62.1 mg, 0.079 mmol), in CH_2Cl_2 (8 mL) were successively added 4Å MS (60 mg), NMO (28 mg, 0.24 mmol, 3 equiv), and TPAP (2 mg, 0.006 mmol, 0.08 equiv). The resulting mixture was stirred at 0 ^{o}C for 5 min and the cold bath was removed. The reaction was stirred at ambient temperature for 30 min before the mixture was filtered through a plug of Florisil®. This plug was washed several times with EtOAc. The eluent was concentrated under reduced pressure to give a black oil, which was directly subjected to flash chromatography, eluting with 100% EtOAc, to afford the desired alcohol (53.7 mg, 86%). Spectral data: R_f = 0.25 (100% EtOAc); 500 MHz ^{1}H NMR ($CDCl_3$) δ 9.90 (d, *J* = 7.9 Hz, 1H), 7.24 (d, *J* = 8.6

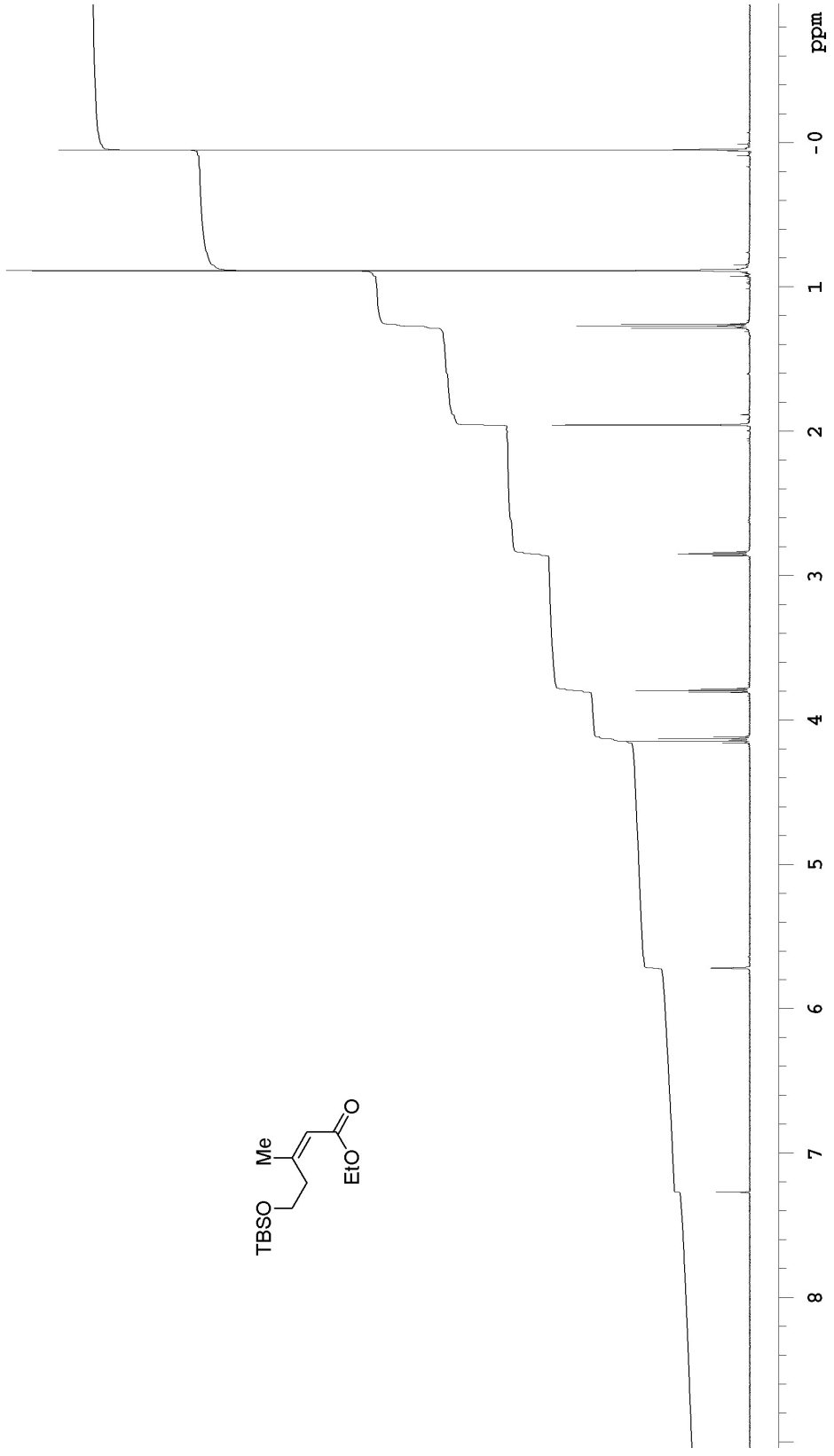
Hz, 2H), 7.18 (d, *J* = 8.6 Hz, 2H), 6.88 – 6.85 (m, 4H), 5.92 (d, *J* = 7.9 Hz, 1H), 5.71 (dddd, *J* = 15.3, 7.3, 7.3, 7.3 Hz, 1H), 5.47 – 5.41 (m, 1H), 5.27 (d, *J* = 7.6 Hz, 1H), 5.18 – 5.15 (m, 1H), 4.74 (s, 2H), 4.48 (ABq, *J* = 11.6 Hz, Δν = 7.9 Hz, 2H), 4.38 (ABq, *J* = 11.6 Hz, Δν = 16.0 Hz, 1H), 4.19 – 4.12 (m, 4H), 3.99 – 3.95 (m, 1H), 3.93 – 3.88 (m, 1H), 3.80 (s, 3H), 3.80 (s, 3H), 3.52 – 3.48 (m, 2H), 3.35 (ddddd, *J* = 8.2, 8.2, 8.2, 4.3, 1.8 Hz, 1H), 3.01 – 2.96 (m, 2H), 2.96 – 2.91 (m, 1H), 2.64 (ddd, *J* = 14.3, 9.5, 5.2 Hz, 1H), 2.42 – 2.34 (m, 2H), 2.32-2.24 (m, 2H), 2.22 – 2.17 (m, 1H), 2.09 – 2.05 (m, 2H), 1.93 (d, *J* = 1.2 Hz, 3H), 1.71 (s, 3H), 1.34 – 1.31 (m, 6H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 191.5, 165.6 (J = 5.8 Hz), 160.2, 159.5, 159.4, 144.3, 144.2, 134.4, 134.3, 132.2, 132.1, 131.1, 130.9, 130.5, 130.4, 130.2, 129.5, 129.5, 129.5, 129.5, 114.0, 109.2, 78.0, 77.9, 77.7, 75.7, 73.1, 72.7, 70.1, 69.9, 68.9, 62.8 (*J* = 6.2 Hz), 55.5, 41.0, 40.9, 40.8, 40.2, 40.2, 39.3, 39.3, 39.2, 35.1 (*J* = 135 Hz), 26.3, 26.2, 17.3, 16.6 (*J* = 6.2 Hz).

To a cold (- 78 ^{o}C) solution of the phosphono-aldehyde (53.7 mg, 0.069) in THF (12 mL) was added a solution of NaHMDS (82 μL, 0.082 mmol 1.0 M in THF) dropwise. The solution was allowed to stir at this temperature for 10 minutes before warming to 0 ^{o}C and stirring for 1.5 h. The mixture was poured into saturated aqueous NH_4Cl solution and further diluted with EtOAc (10 mL). The layers were separated and the aqueous layer was further extracted with EtOAc (2 x 15 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. This residue was subjected to flash chromatography eluting with 10% EtOAc/hexanes to 20% EtOAc hexanes to afford macrolactone **23** (26 mg, 60%). R_f = 0.44 (20% EtOAc/hex); HRMS (CI+) calcd for. $C_{39}H_{48}O_7$ 628.3400, found 628.3406.

To a stirring solution of PMB ether **23** (3 mg, 0.048 mmol) in CH_2Cl_2/H_2O (500 μL, 20:1) was added DDQ (3 mg, 0.0143 mmol, 3 equiv). The resulting mixture was stirred for 45 min at rt. The mixture was poured into saturated aqueous $NaHCO_3$ and further diluted with CH_2Cl_2. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was then filtered through a plug of Florisil®. The plug was washed with 50% EtOAc/hexanes (20 mL). The solvents were removed under reduced pressure to give the crude product mixture as a yellow oil. This crude product was taken directly to the next reaction without further purification.

To a solution of the above diol in CH_2Cl_2 (250 μL) and pyridine (5 μL, 0.058 mmol) at ambient temperature was added Dess Martin periodinane (10 mg, 0.024 mmol) The resulting mixture was stirred at room temperature for 2 h. The mixture was then quenched by addition of 1 : 1 mixture of saturated aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$ solution (1 mL). This mixture was allowed to stir until the solution turned clear (30 minutes). The aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL). The organic extracts were combined, washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. This residue was subjected to flash chromatography eluting with 10% EtOAc/hexanes to 20% EtOAc hexanes to afford dactylolide **1** (1.3 mg, 76% from **23**): R_f = 0.25 (40% EtOAc/hexanes); $[\alpha]^{20}_D$ = + 134 (*c* = 0.065, MeOH); 500 MHz ^{1}H NMR ($CDCl_3$) δ 9.68 (s, 1H), 7.64 (dd, *J* = 15.3, 11.6 Hz, 1H), 6.86 (ddd, *J* = 14.6, 8.9, 5.8 Hz, 1H), 6.17 (d, *J* = 11.6 Hz, 1H), 6.01 (d, *J* = 17.7 Hz, 1H), 5.98 (d, *J* = 15.6 Hz, 1H), 5.33 (dd, *J* = 11.3, 2.4 Hz, 1H), 5.24 (d, *J* = 7.9 Hz, 1H), 4.76 (br s, 2H), 4.00 – 3.96 (m, 1H), 3.33 (dddd, *J* = 11.3, 9.5, 2.4, 2.4 Hz, 1H), 3.24 (d, *J*

= 14.0 Hz, 1H), 2.56 (d, *J* = 14.0 Hz, 1H), 2.37 – 2.30 (m, 3H), 2.19 (d, *J* = 13.1 Hz, 1H), 2.12 (d, *J* = 13.1 Hz, 1H), 1.99 – 1.94 (m, 1H), 1.97 (t, *J* = 12.2 Hz, 1H), 1.87 (s, 3H), 1.73 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 199.3, 197.7, 166.5, 146.2, 144.3, 143.7, 140.6, 131.7, 131.2, 130.7, 125.8, 120.0, 109.6, 76.7, 76.0, 75.5, 45.1, 41.0, 40.7, 40.0, 39.9, 24.3, 16.3; IR (neat) 2928, 1710, 1668, 1634, 1424, 1356, 1255, 1145, 1085, 978, 890 cm^{-1};HRMS (CI+) calcd for $C_{23}H_{28}O_5$ (M) 384.1937, found 384.1931.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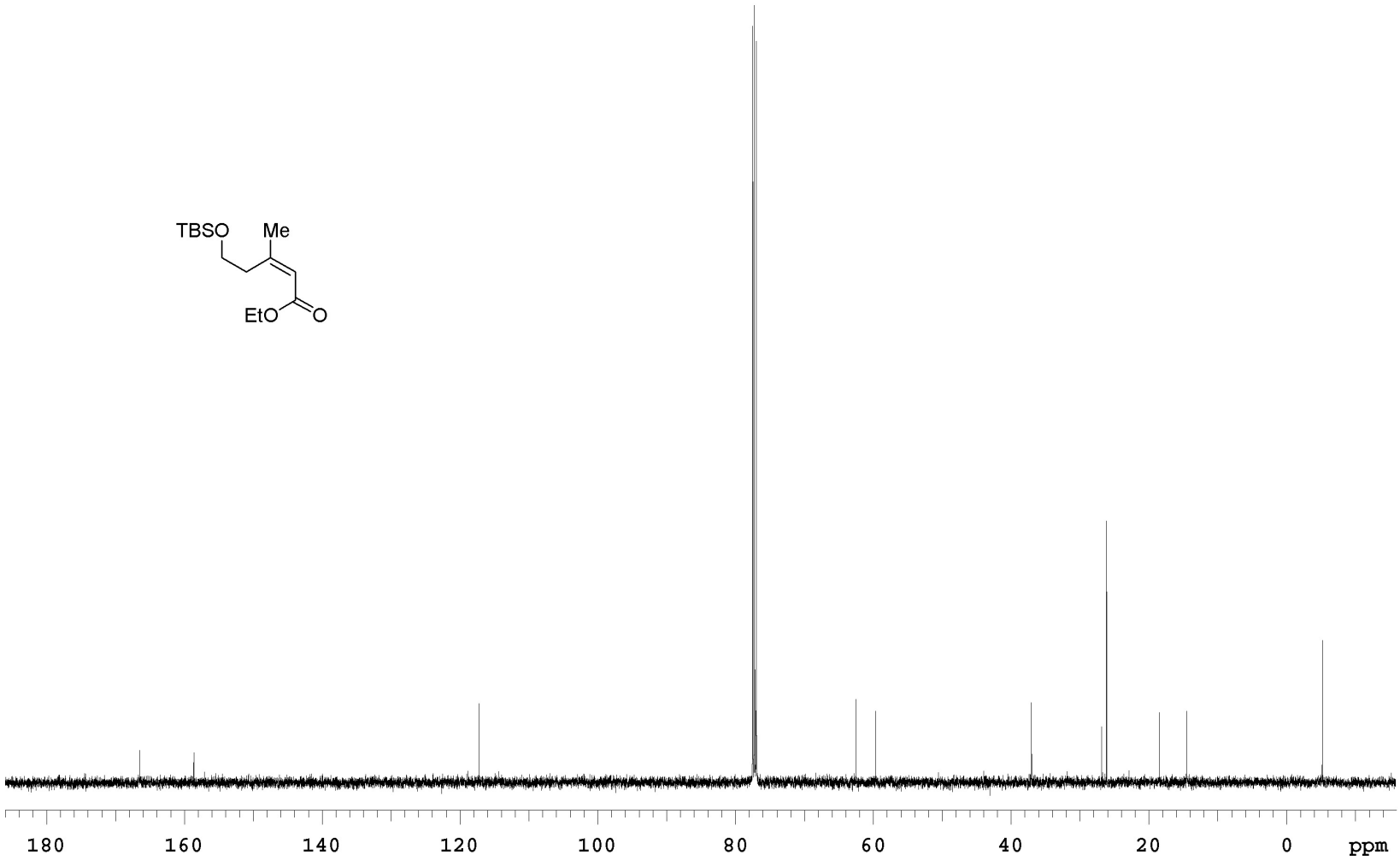
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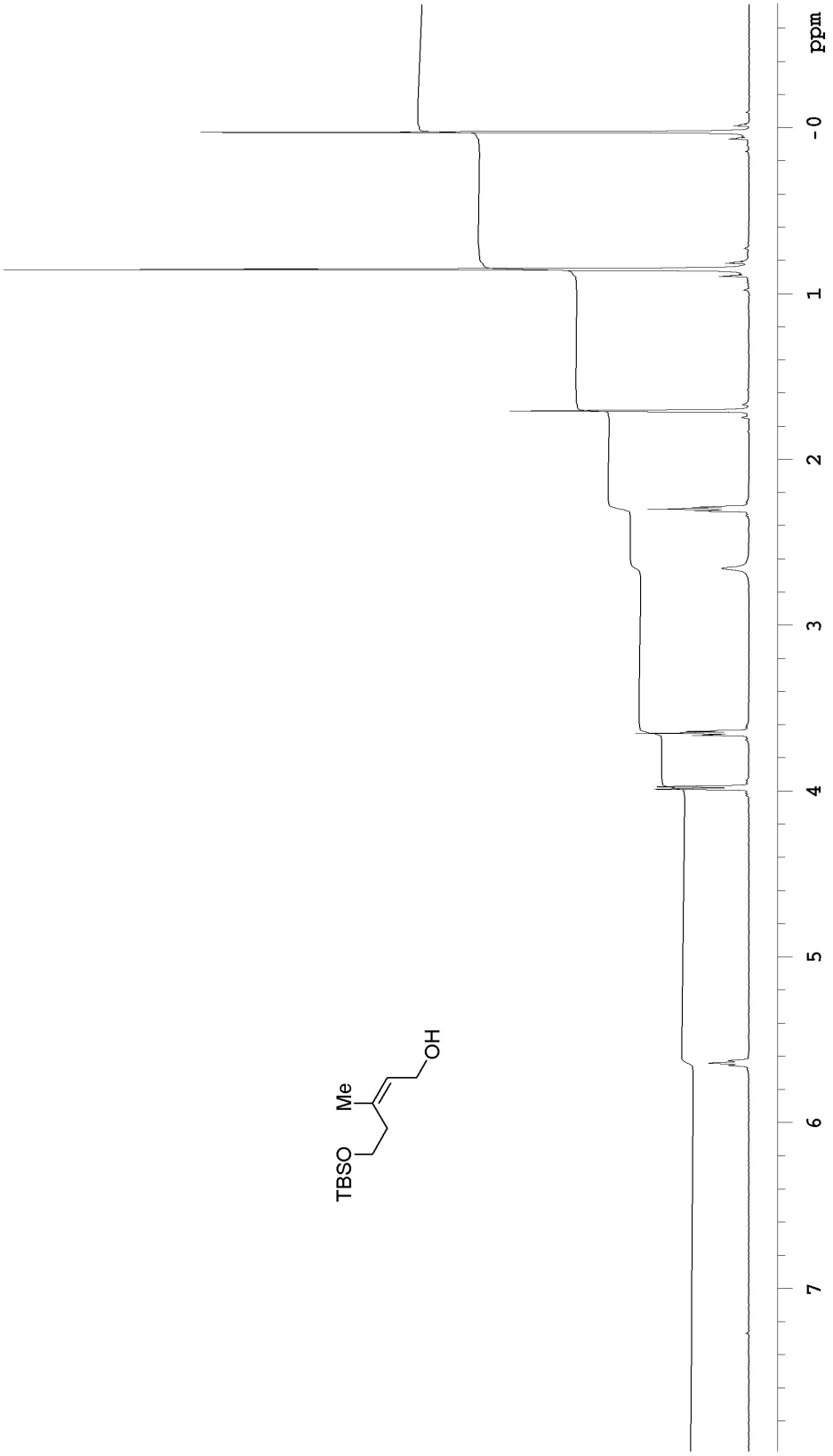
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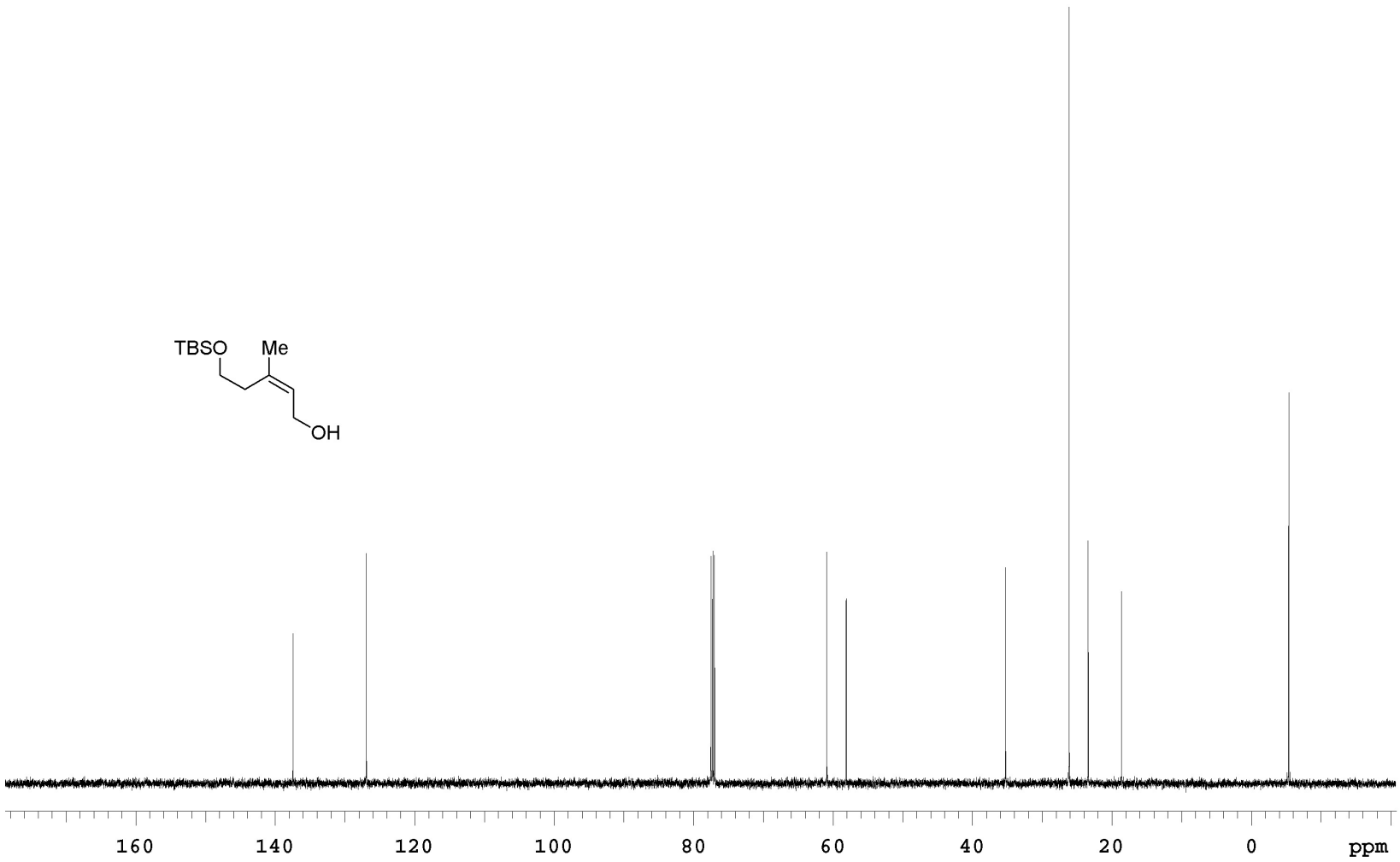
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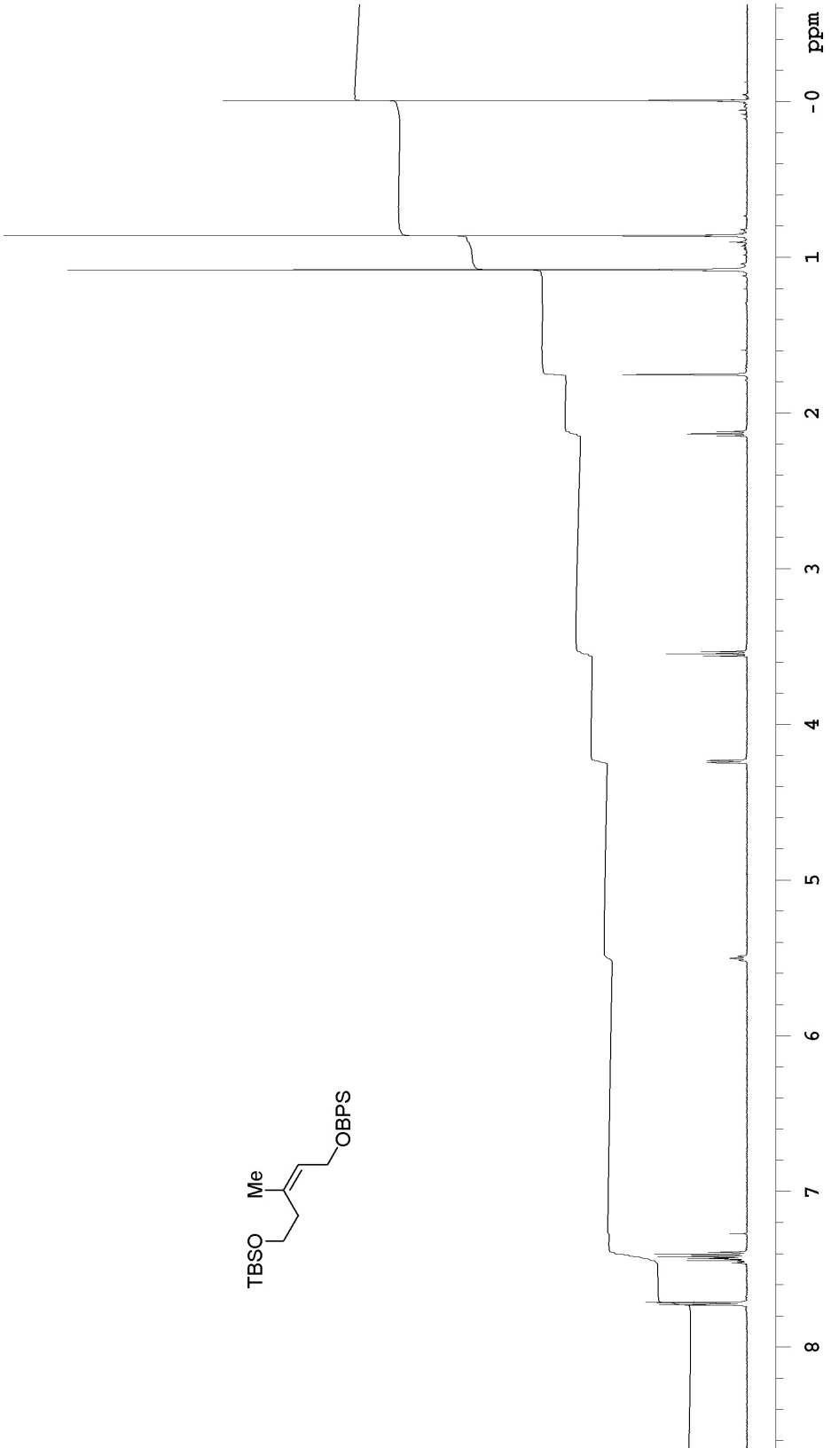
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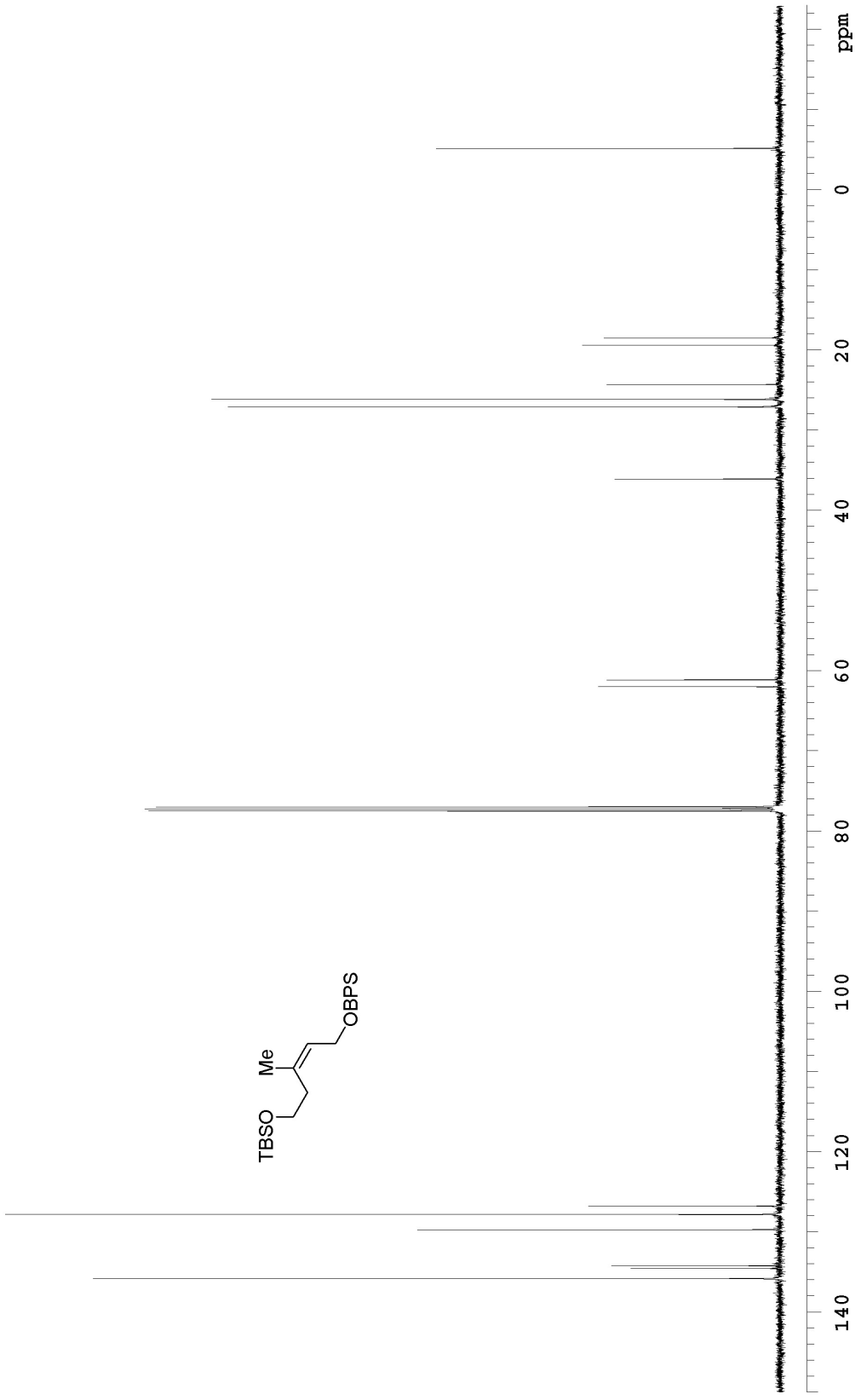
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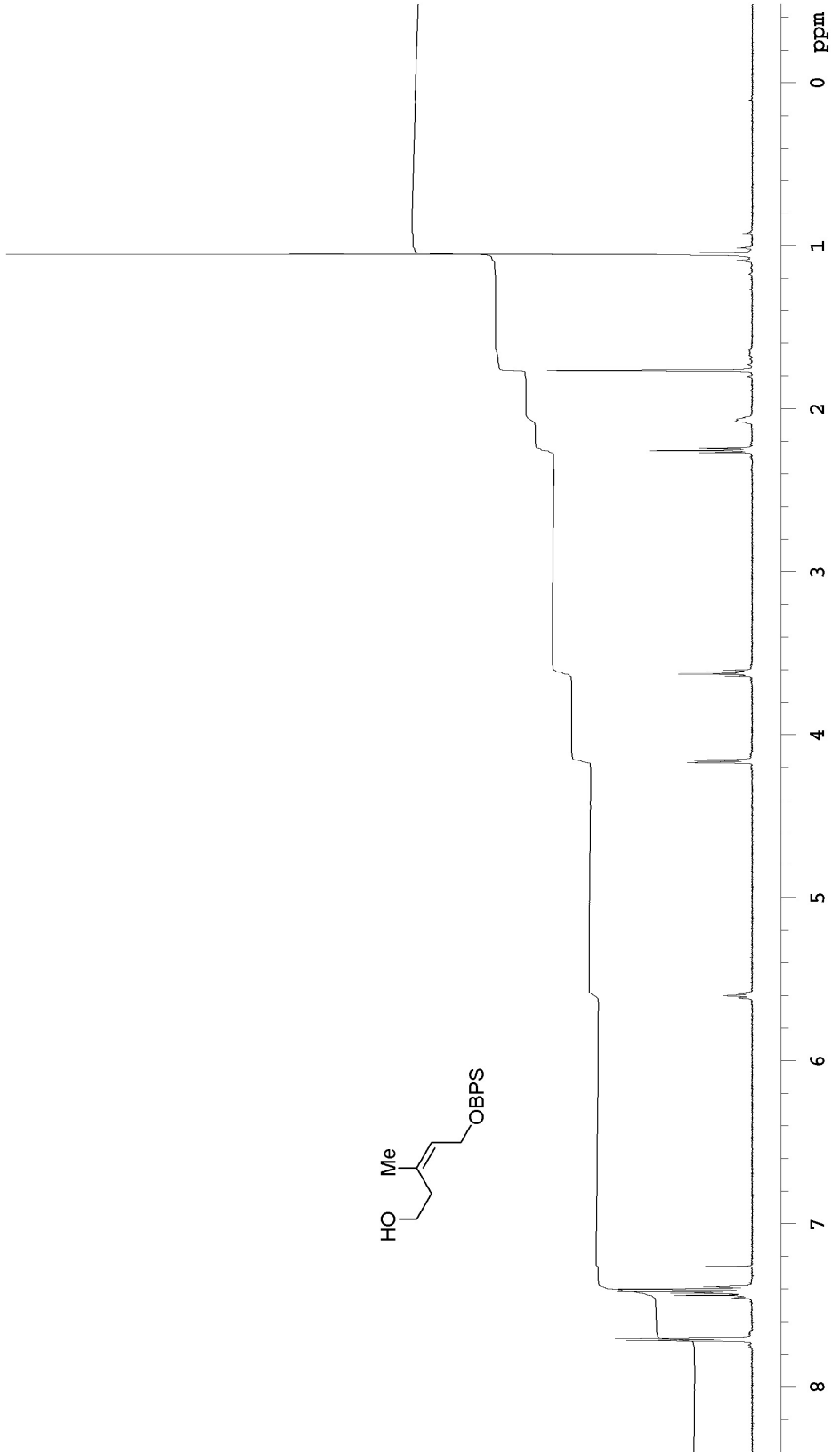
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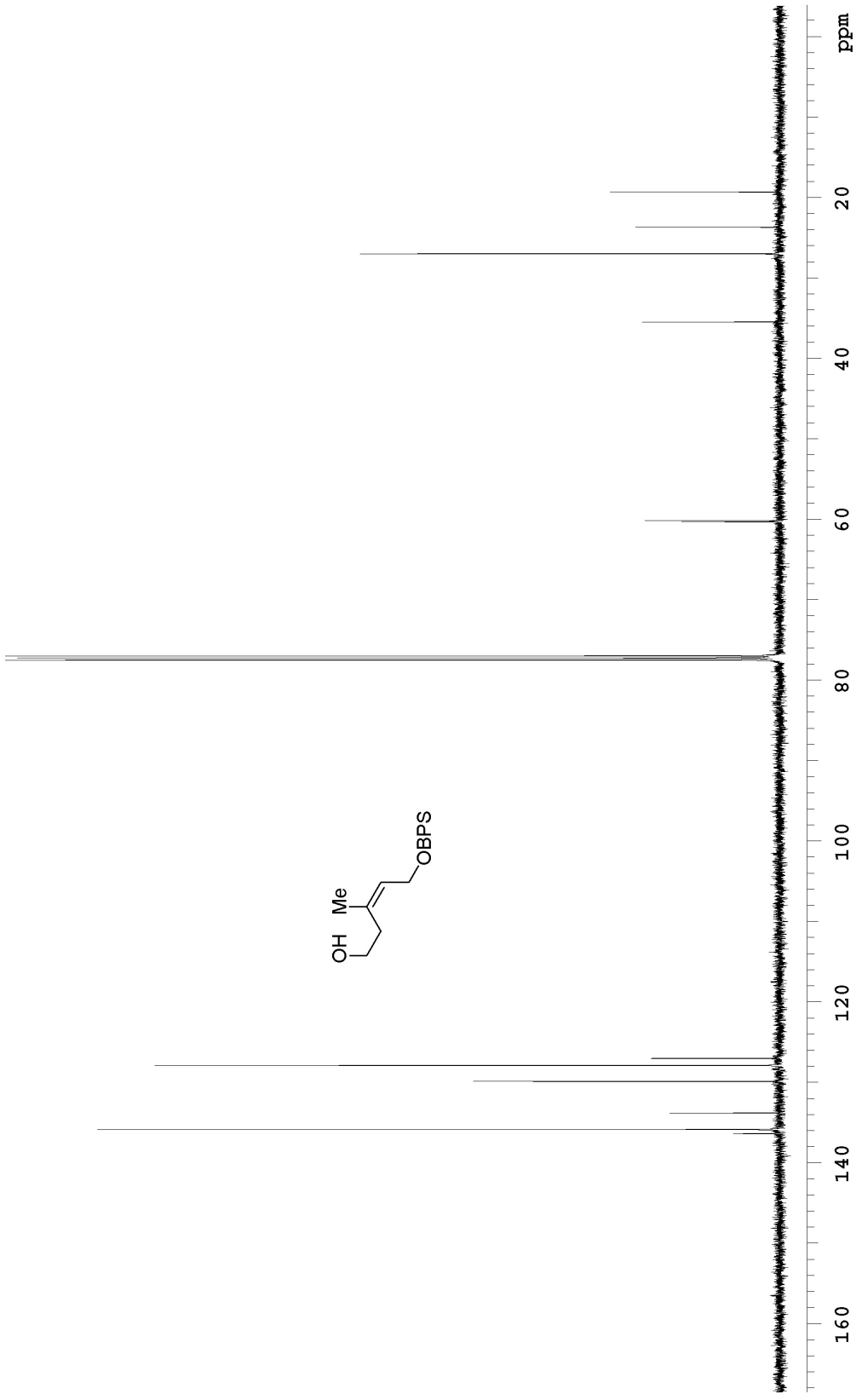
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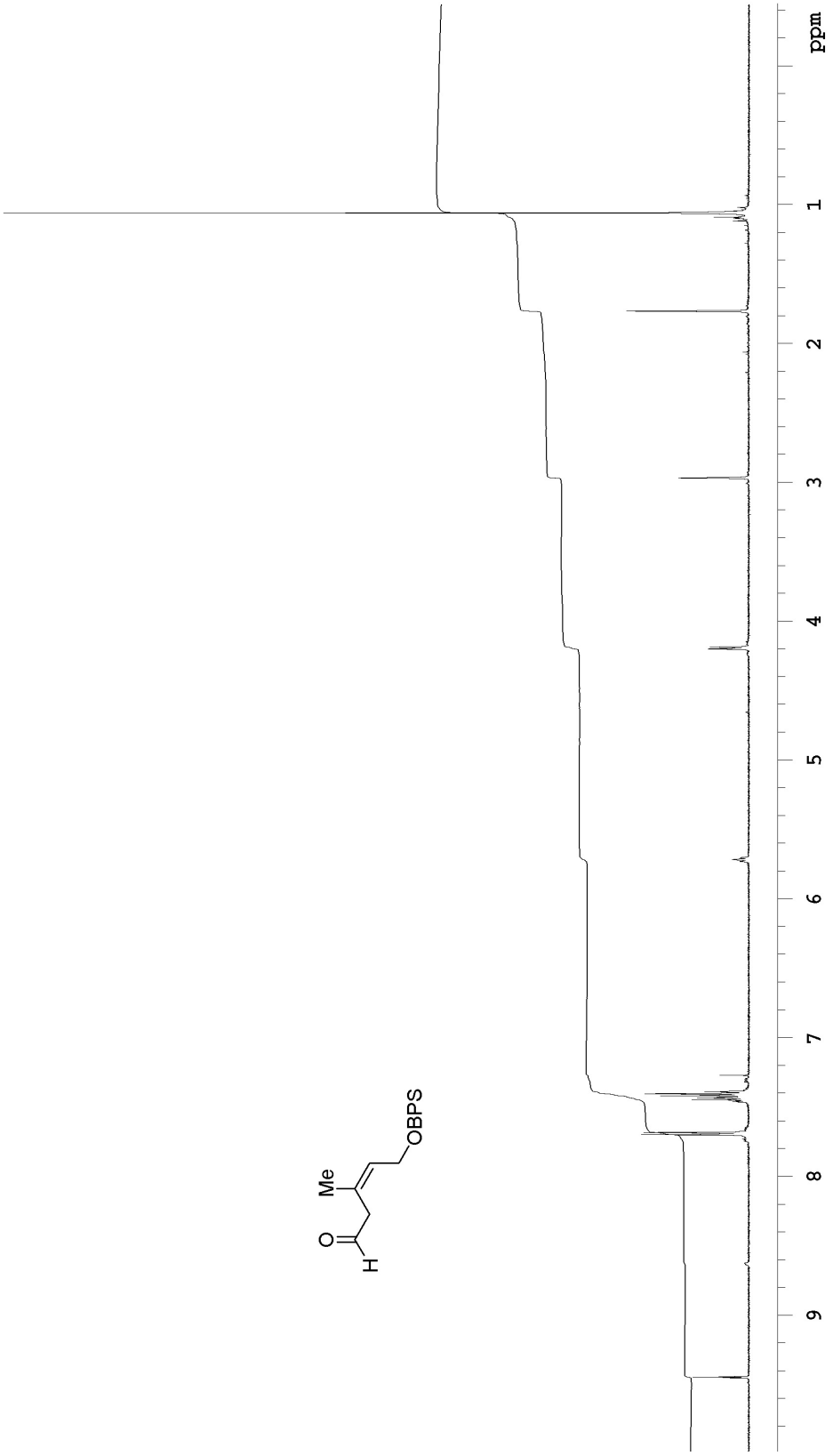
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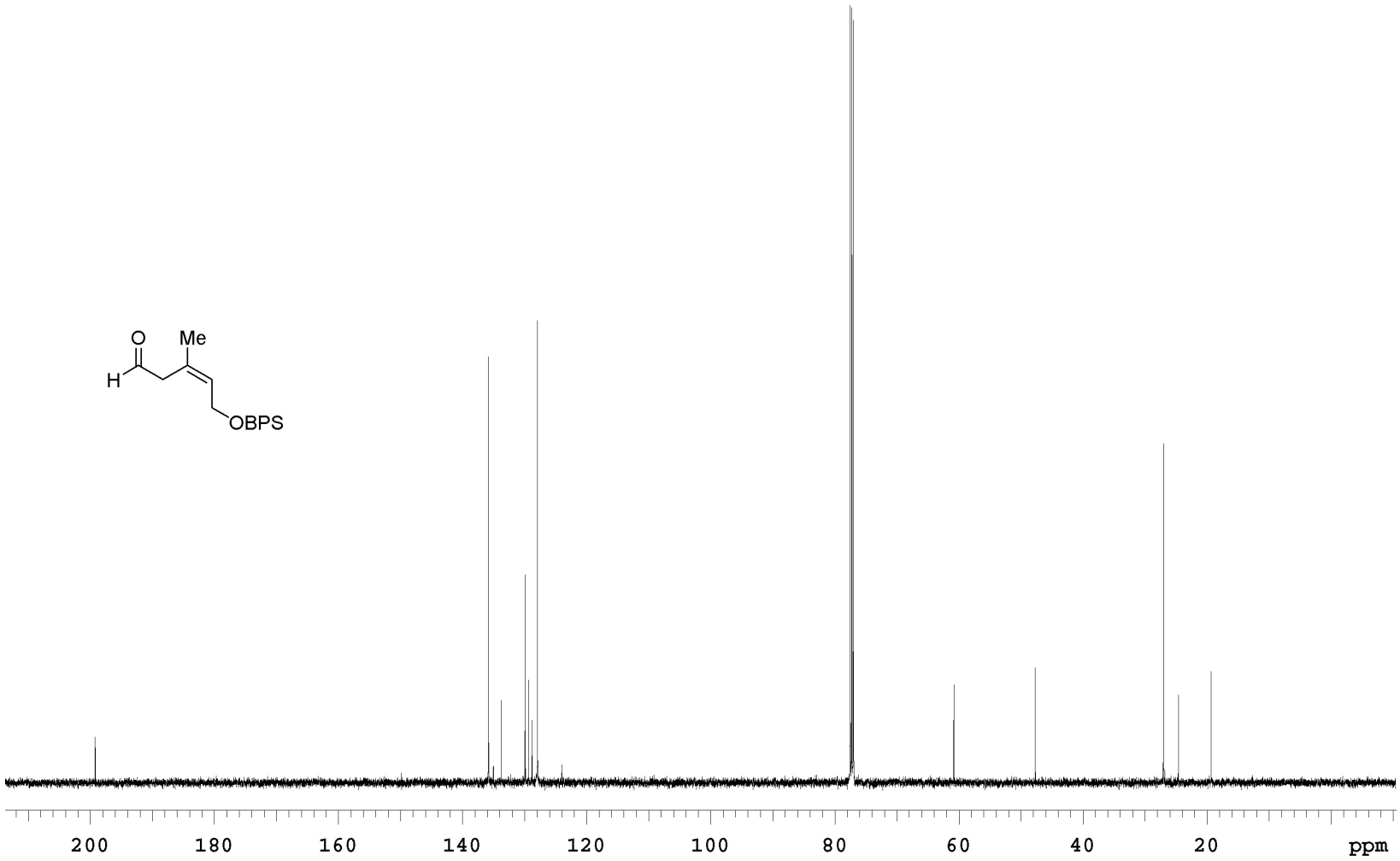
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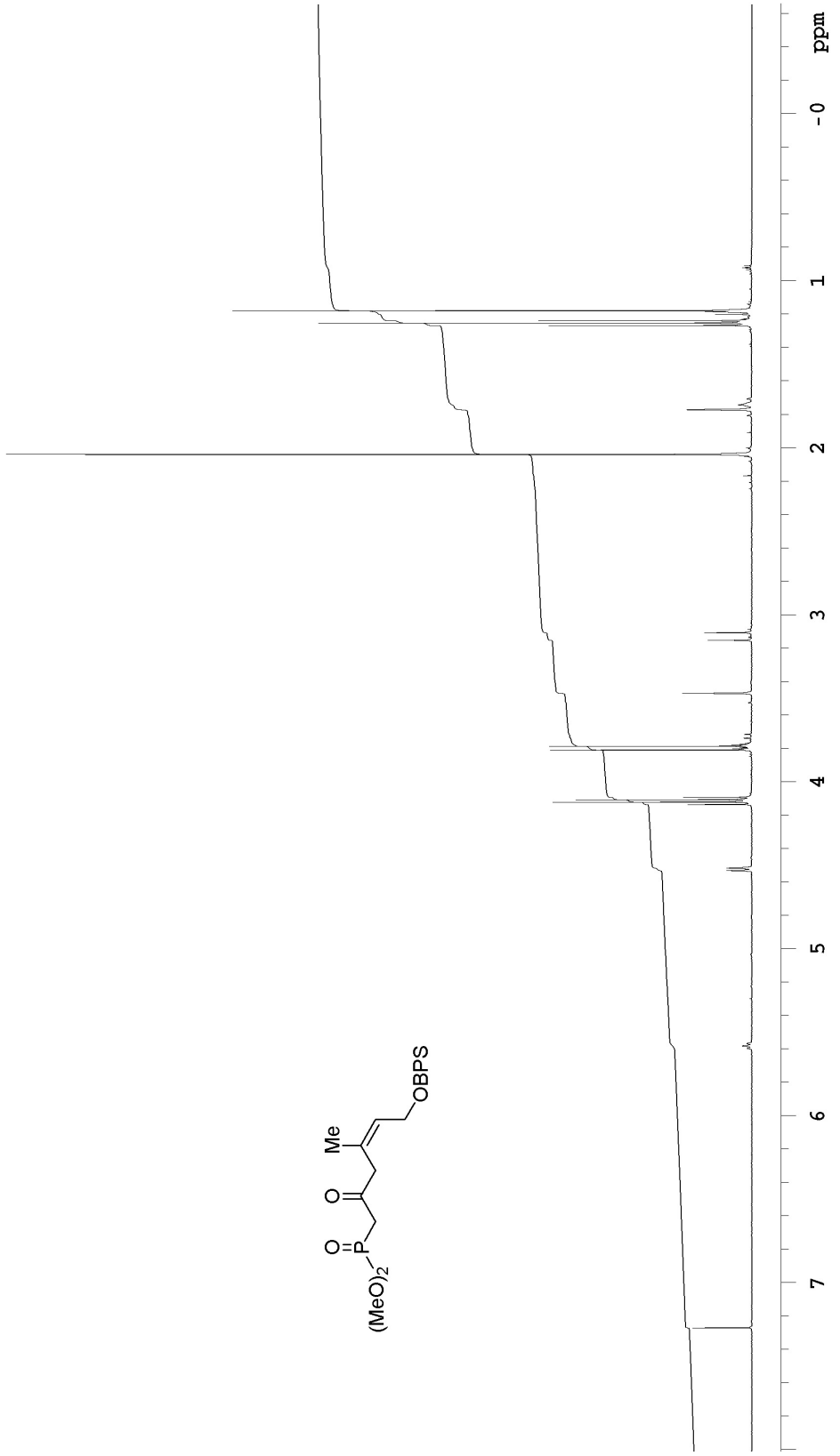
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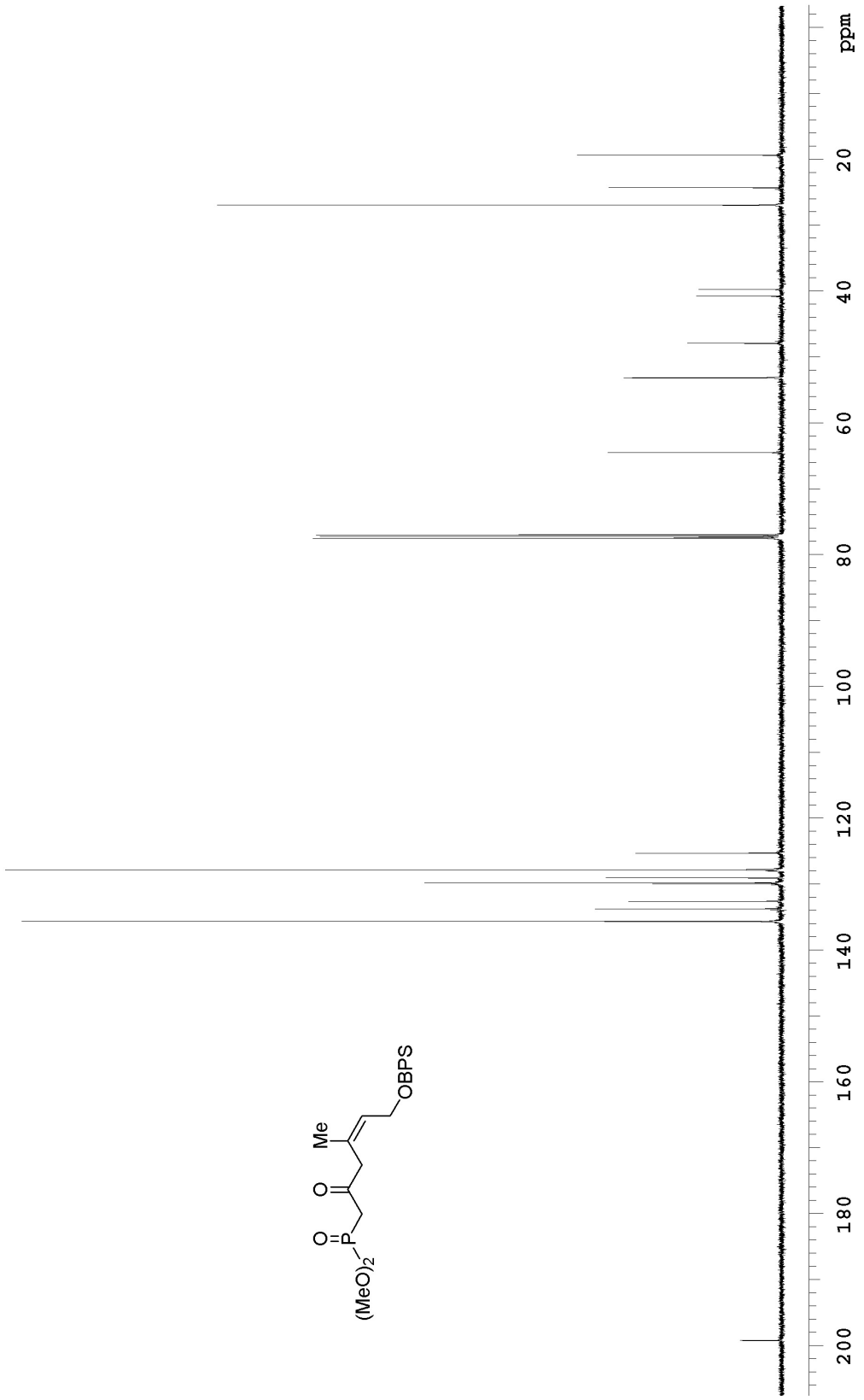
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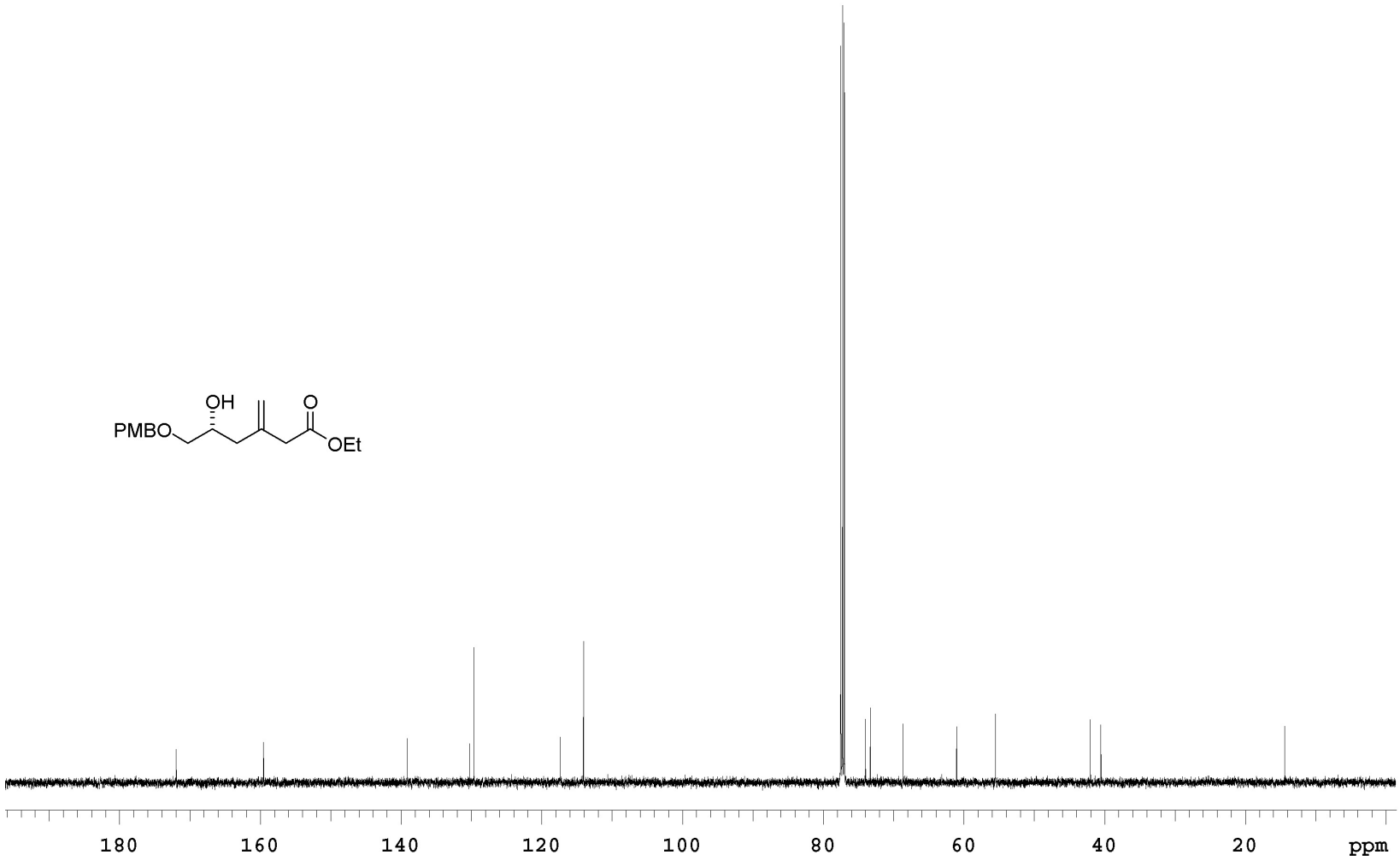
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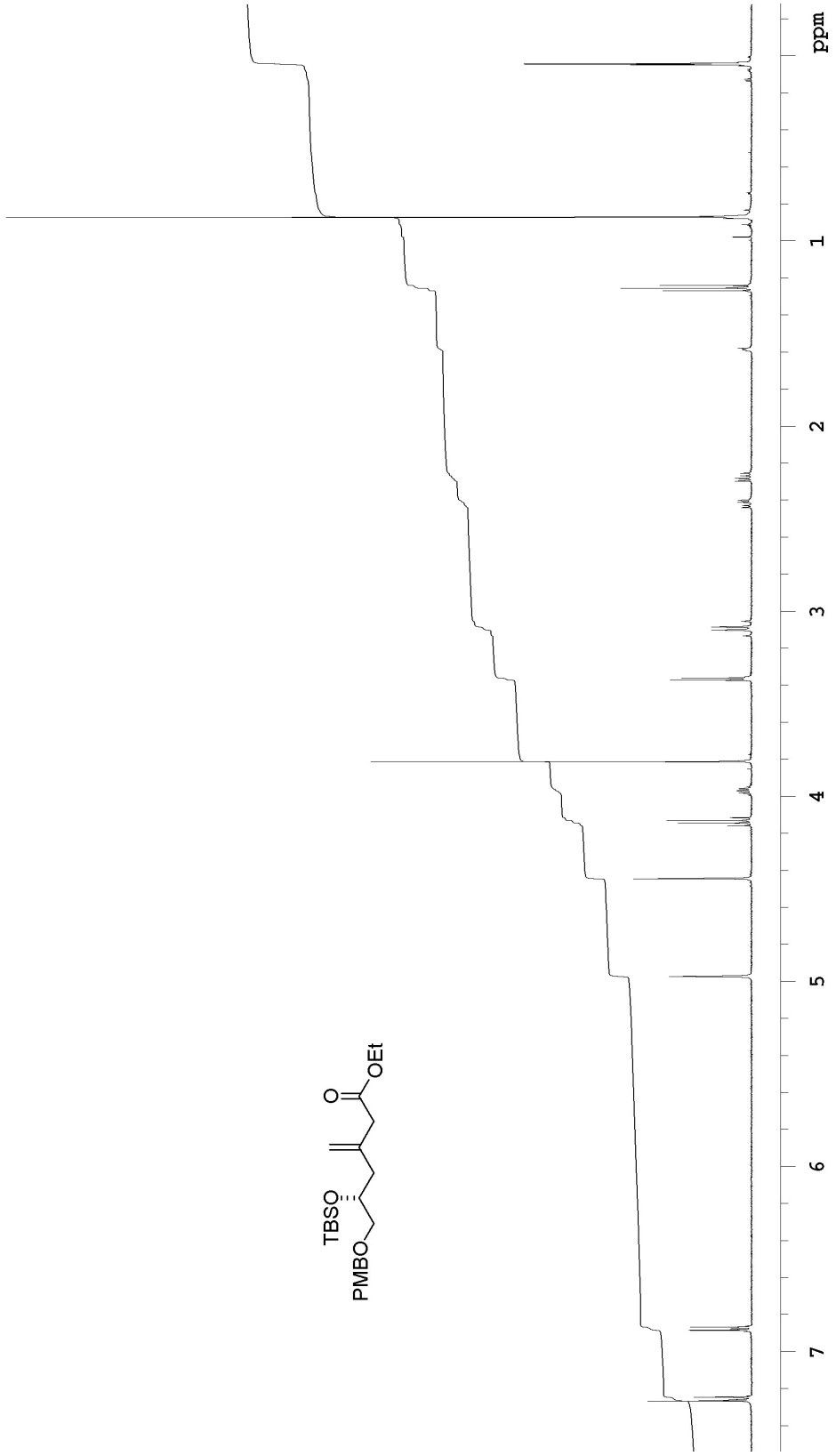
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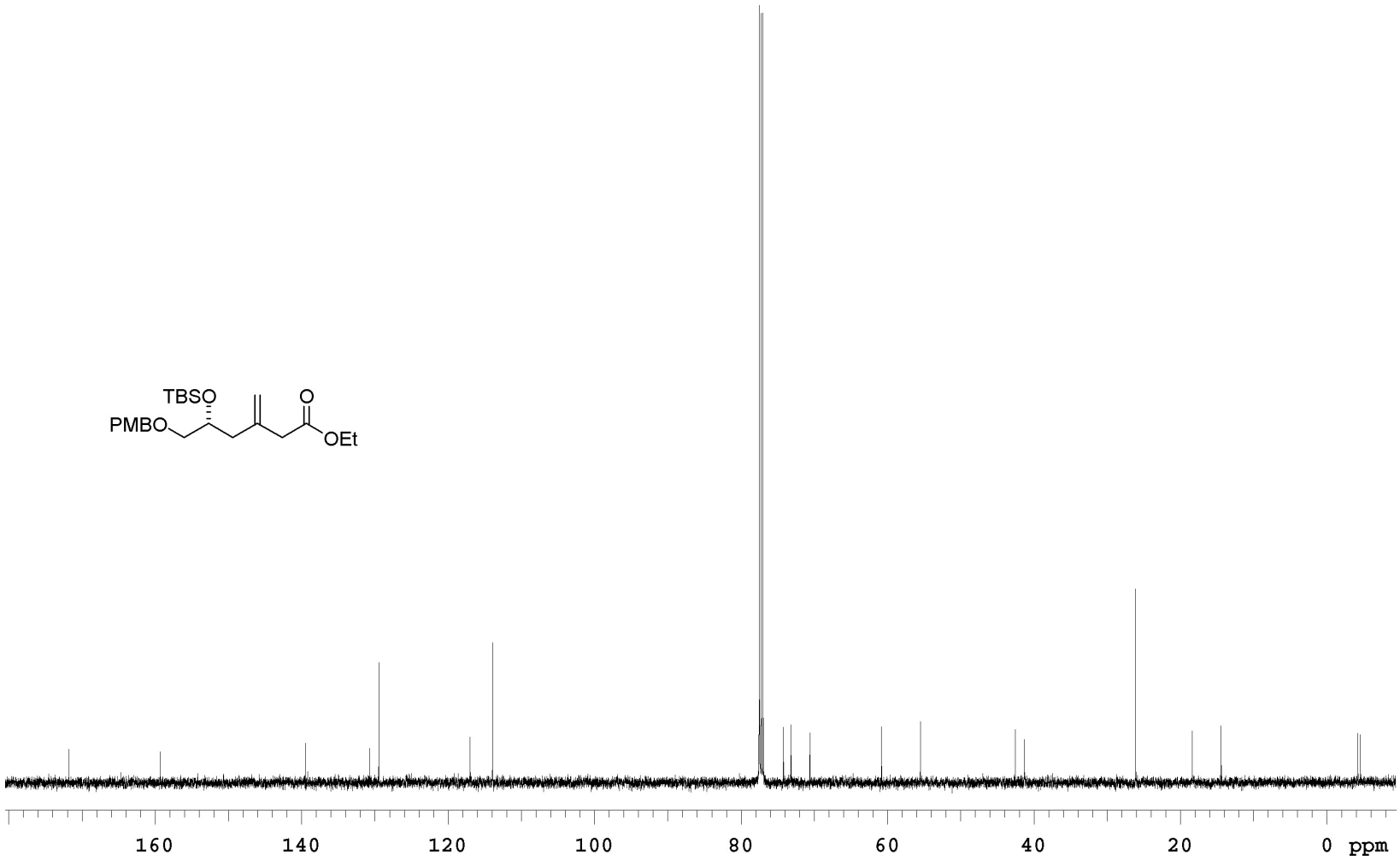
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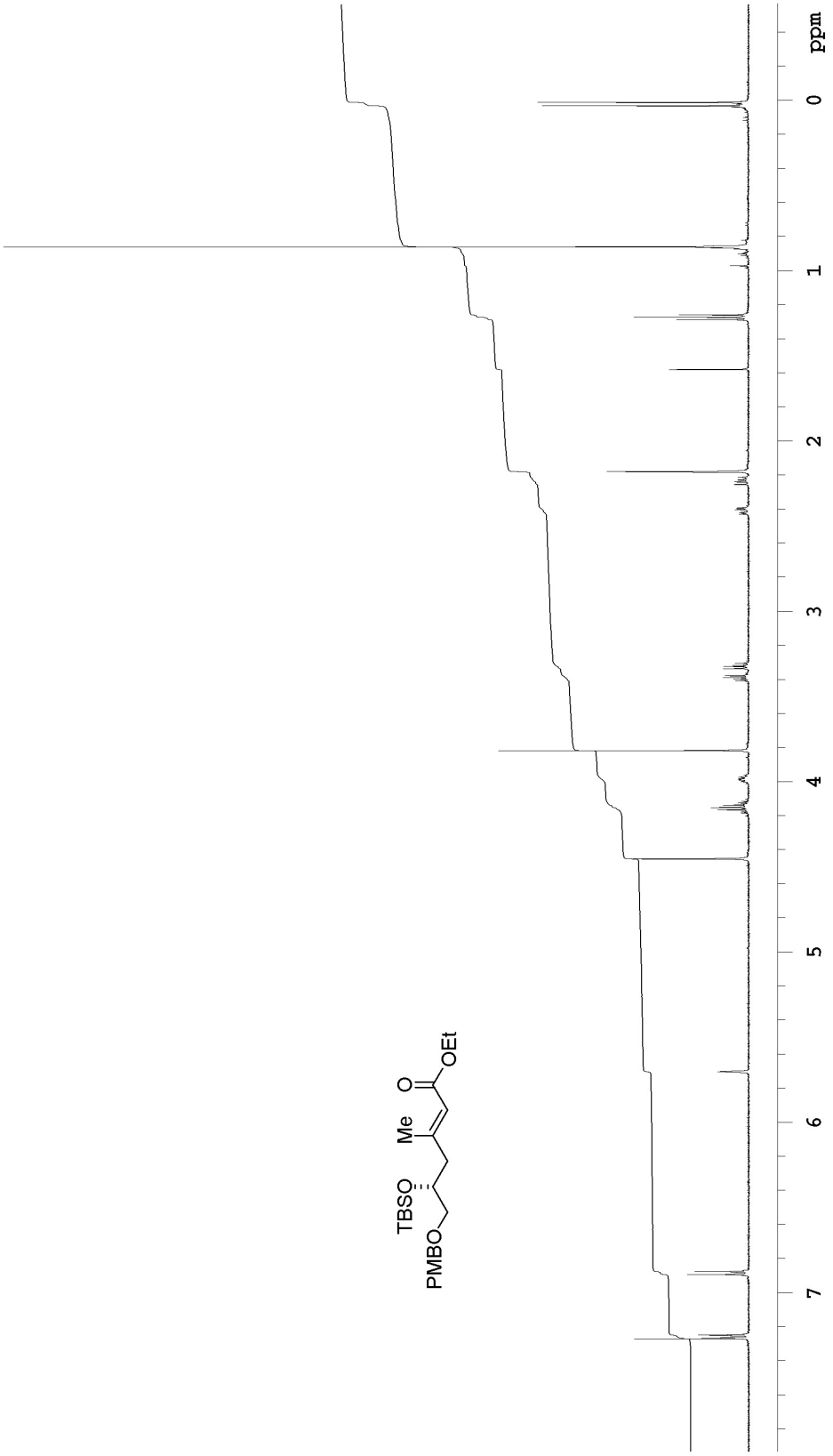
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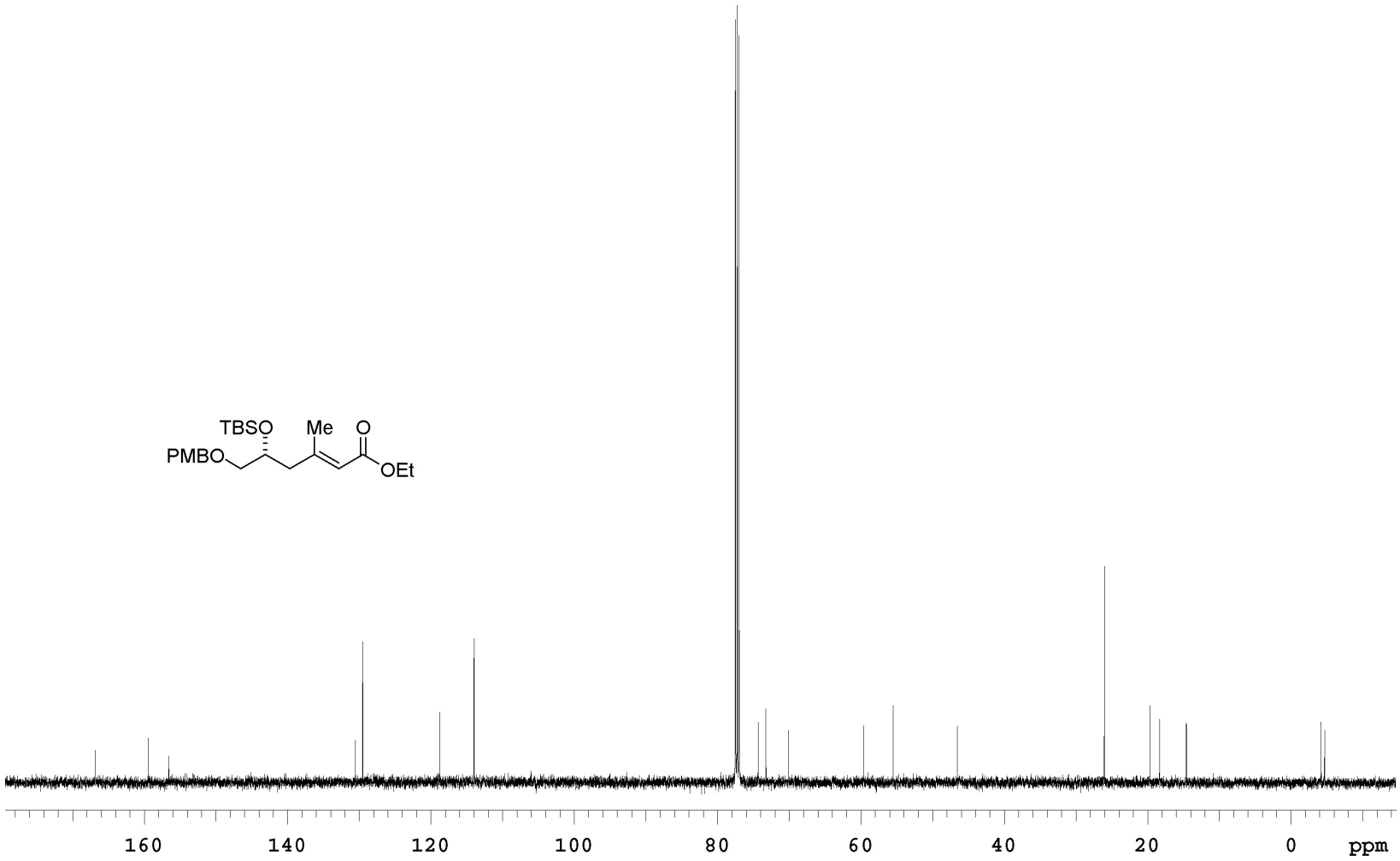
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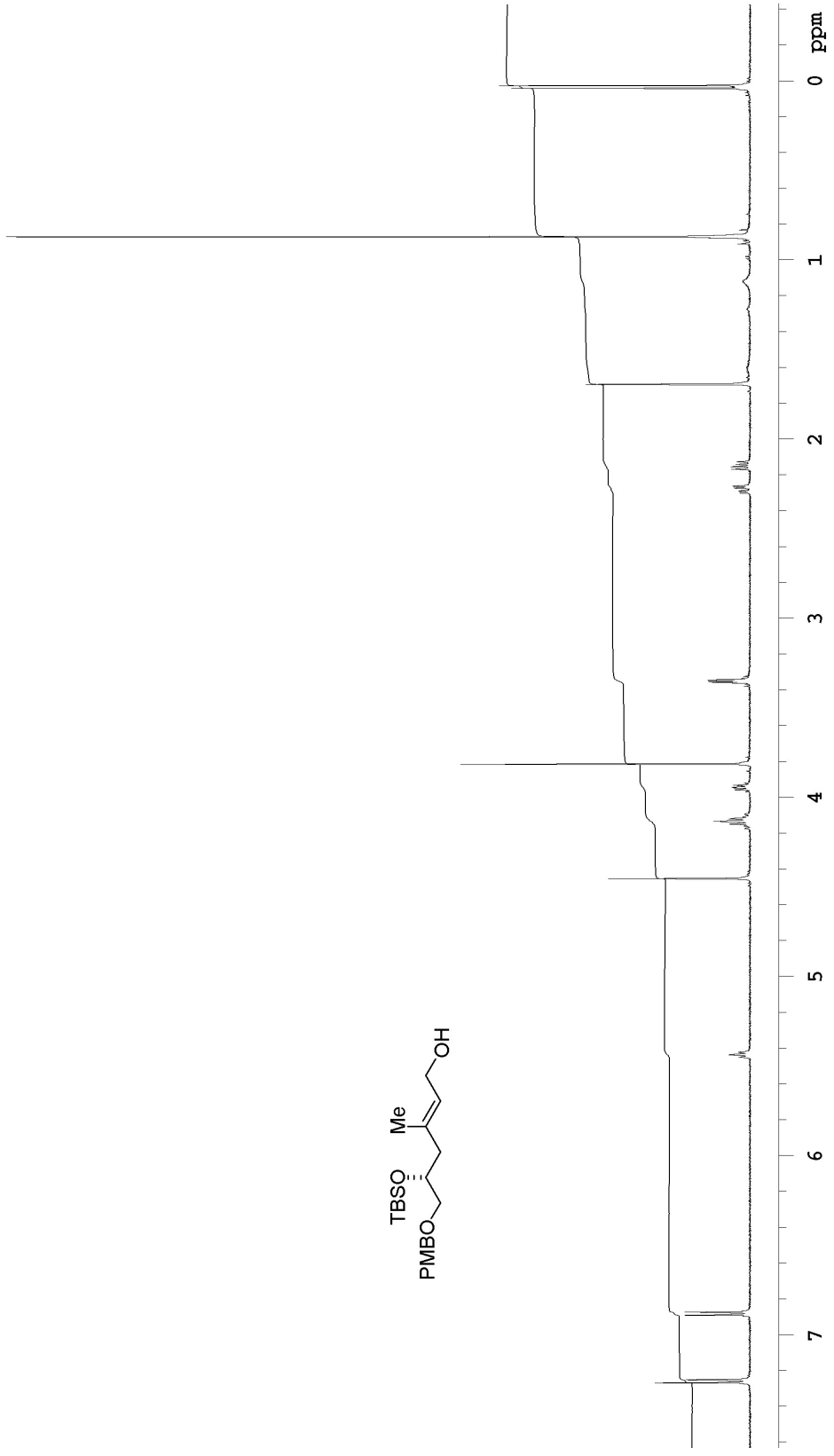
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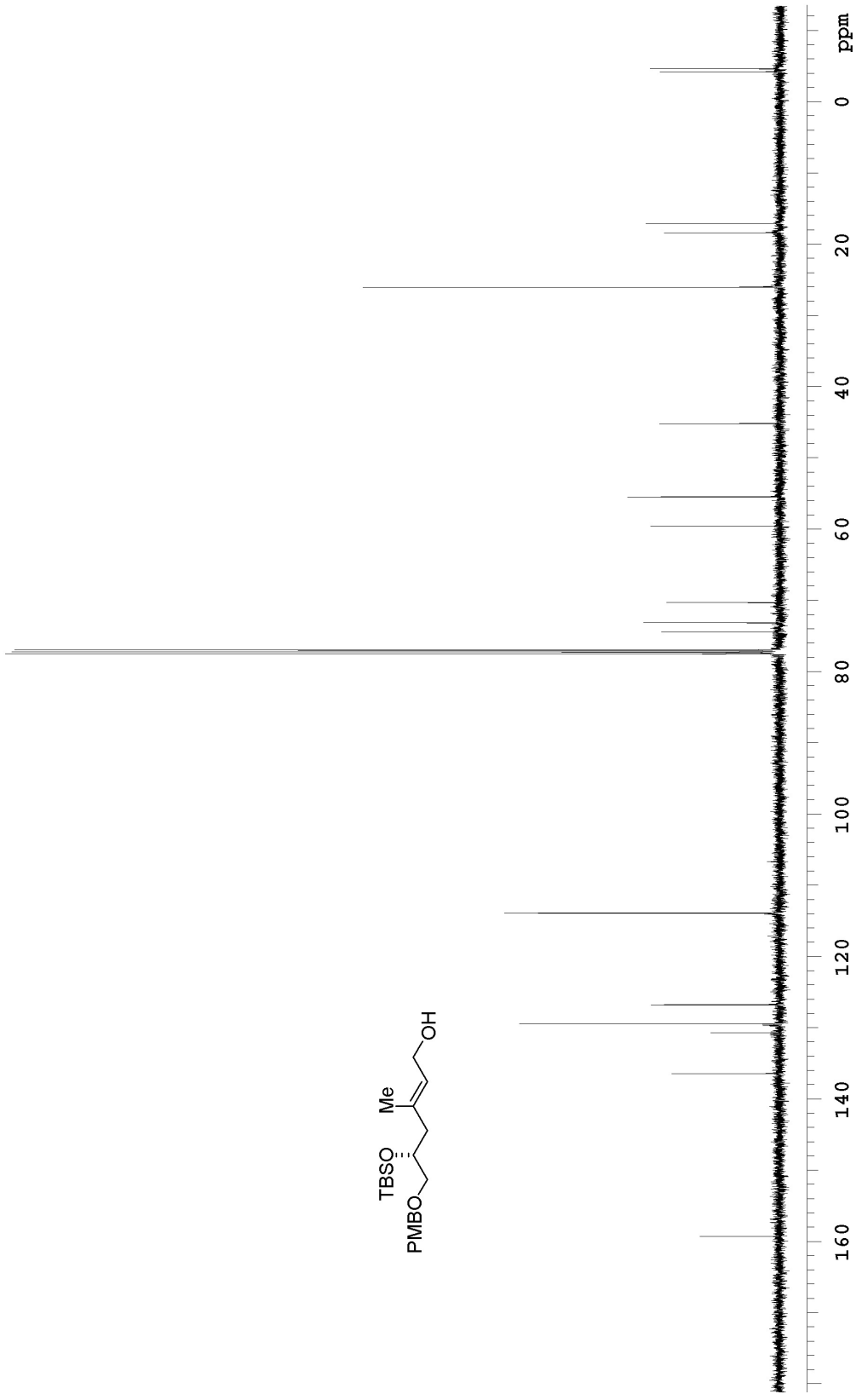
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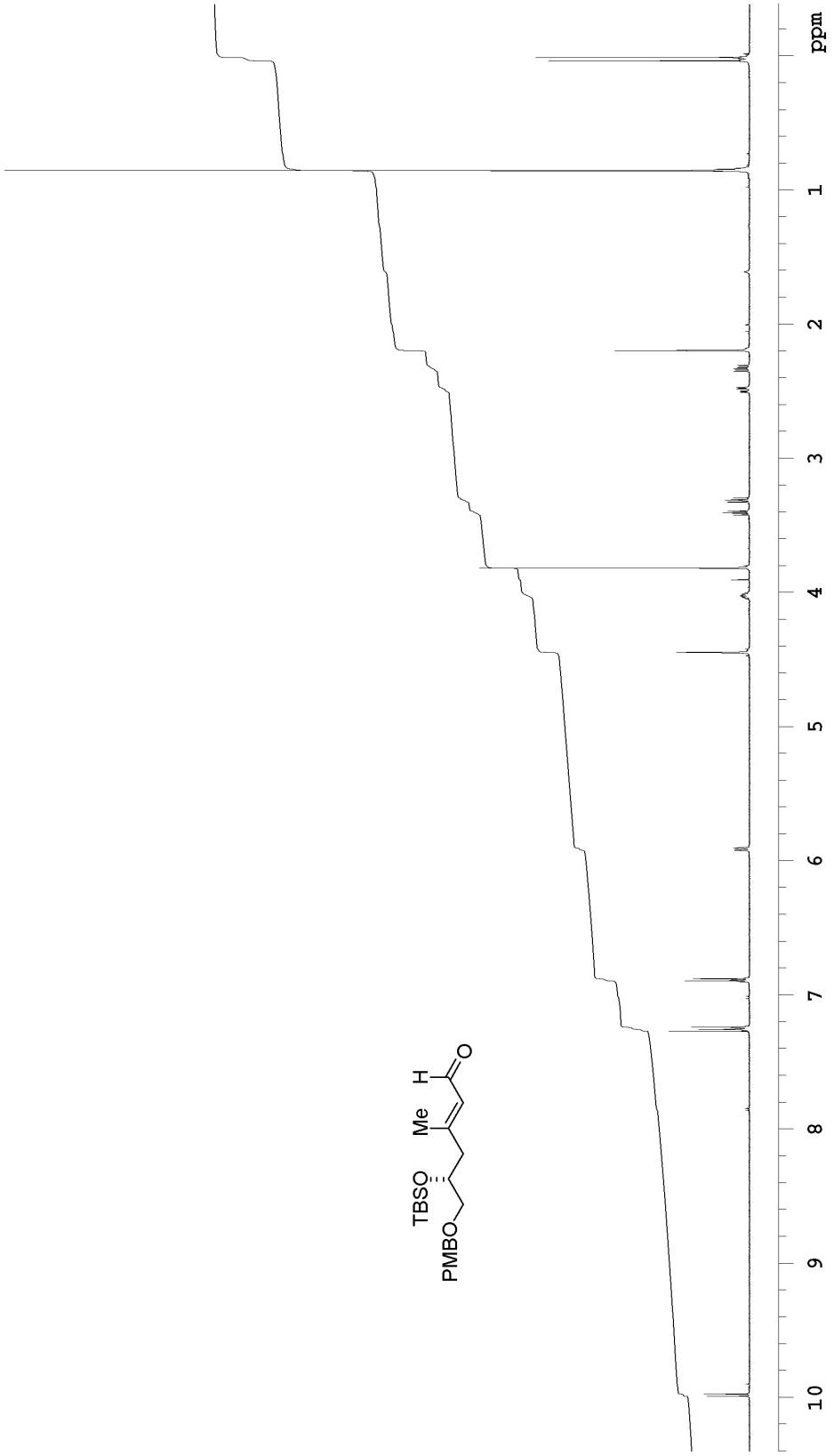
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PMBO
ppm
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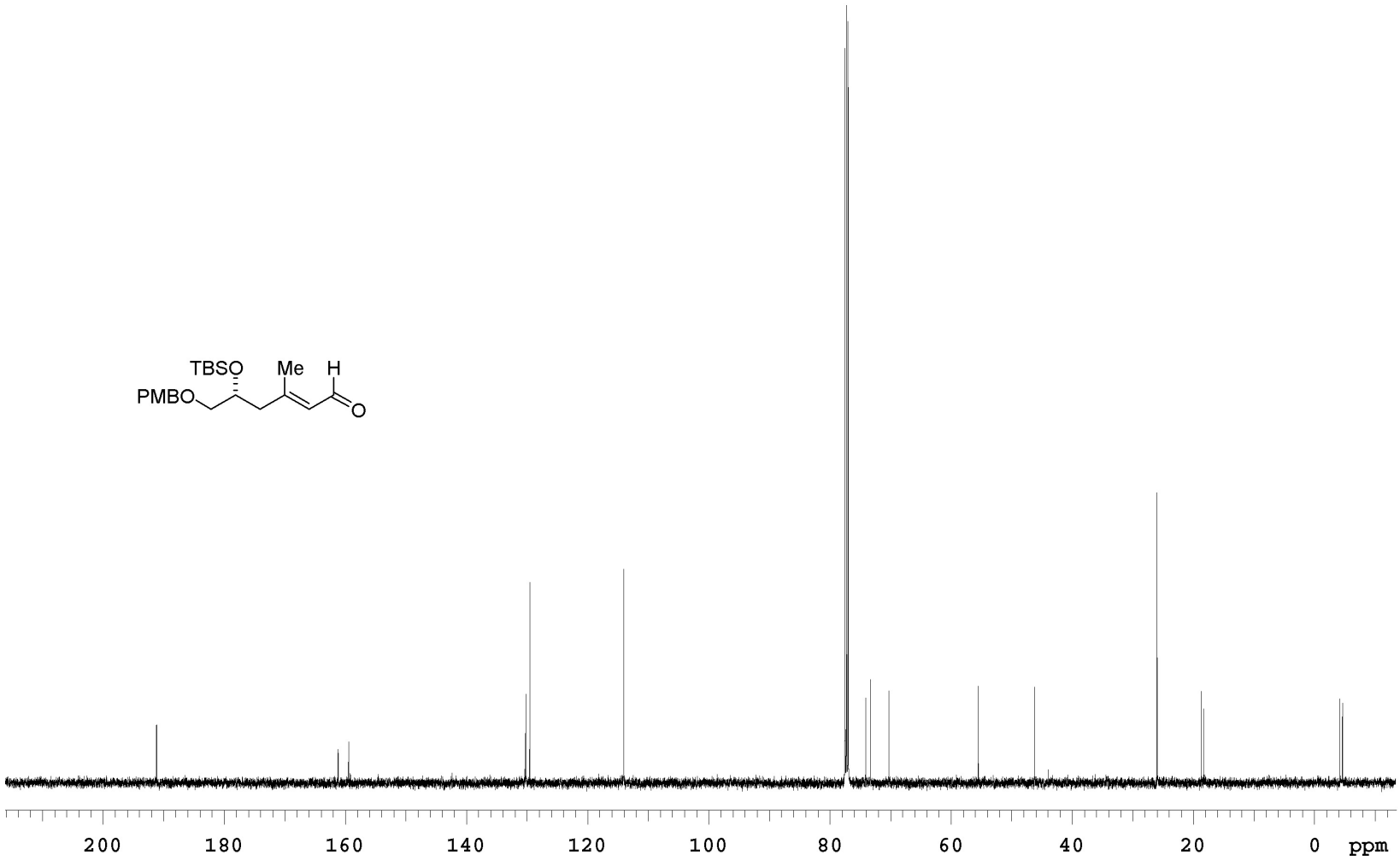
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PMBO
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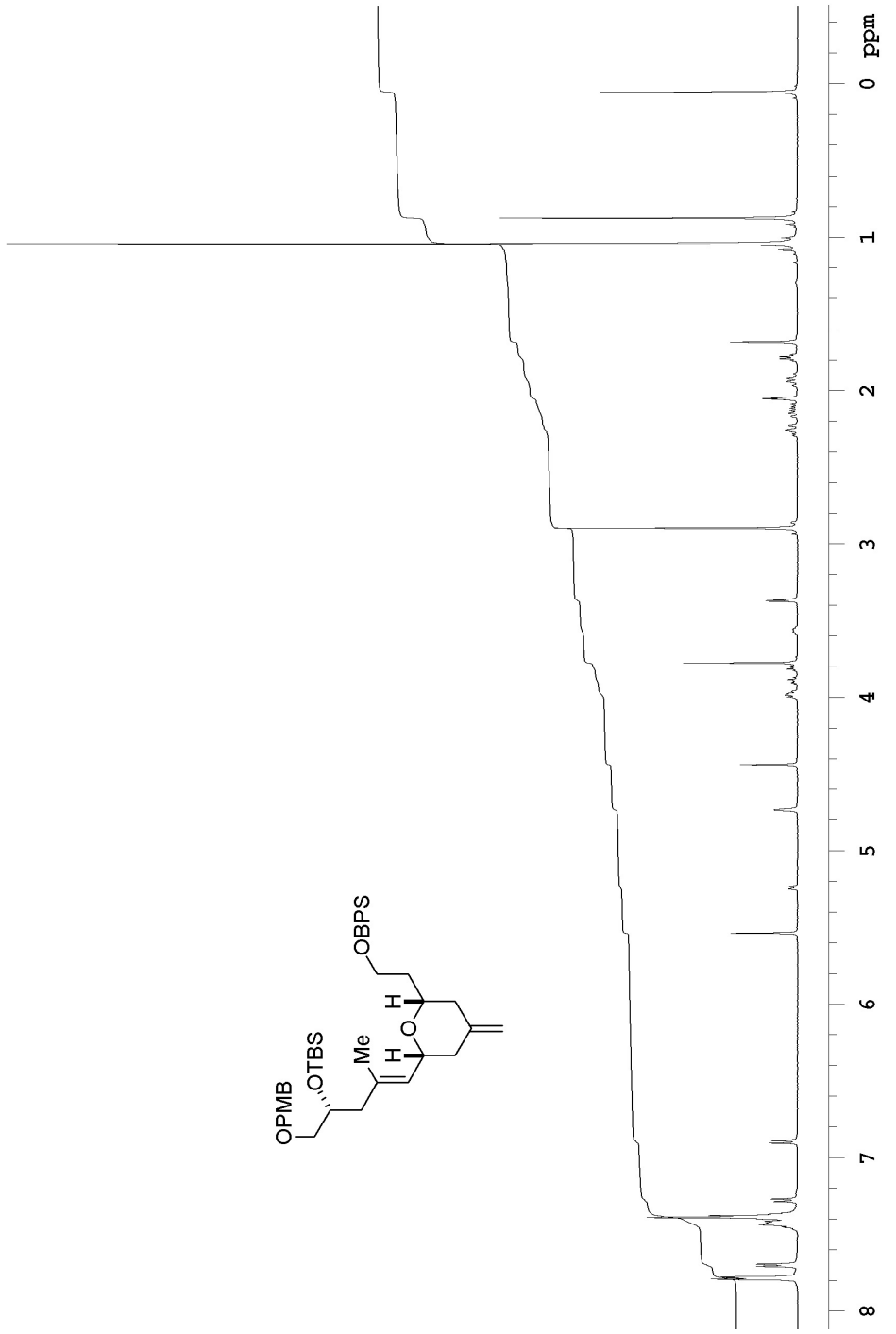
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OTBS
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OBPS
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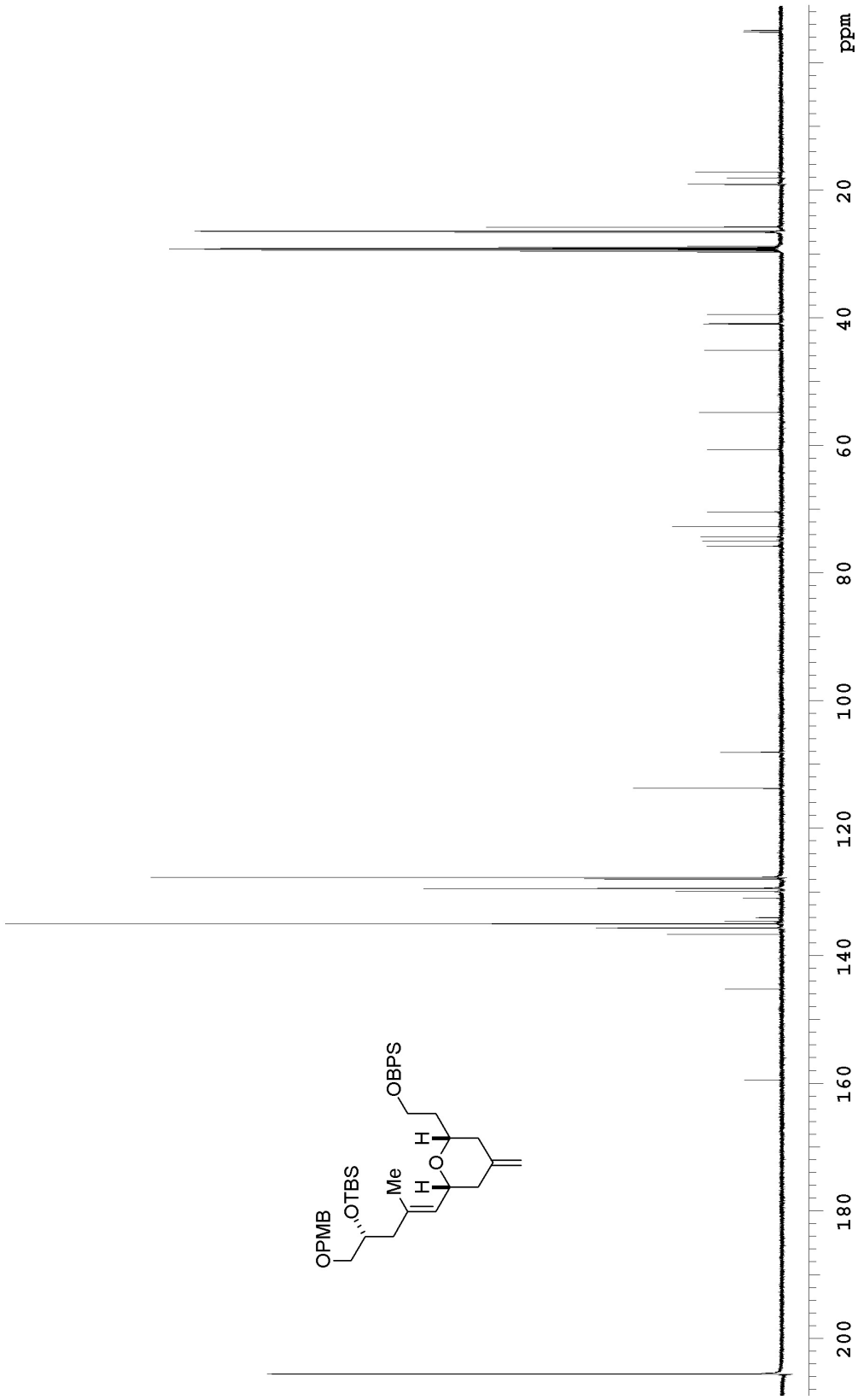
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OTBS
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O
H
OBPS
ppm
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60
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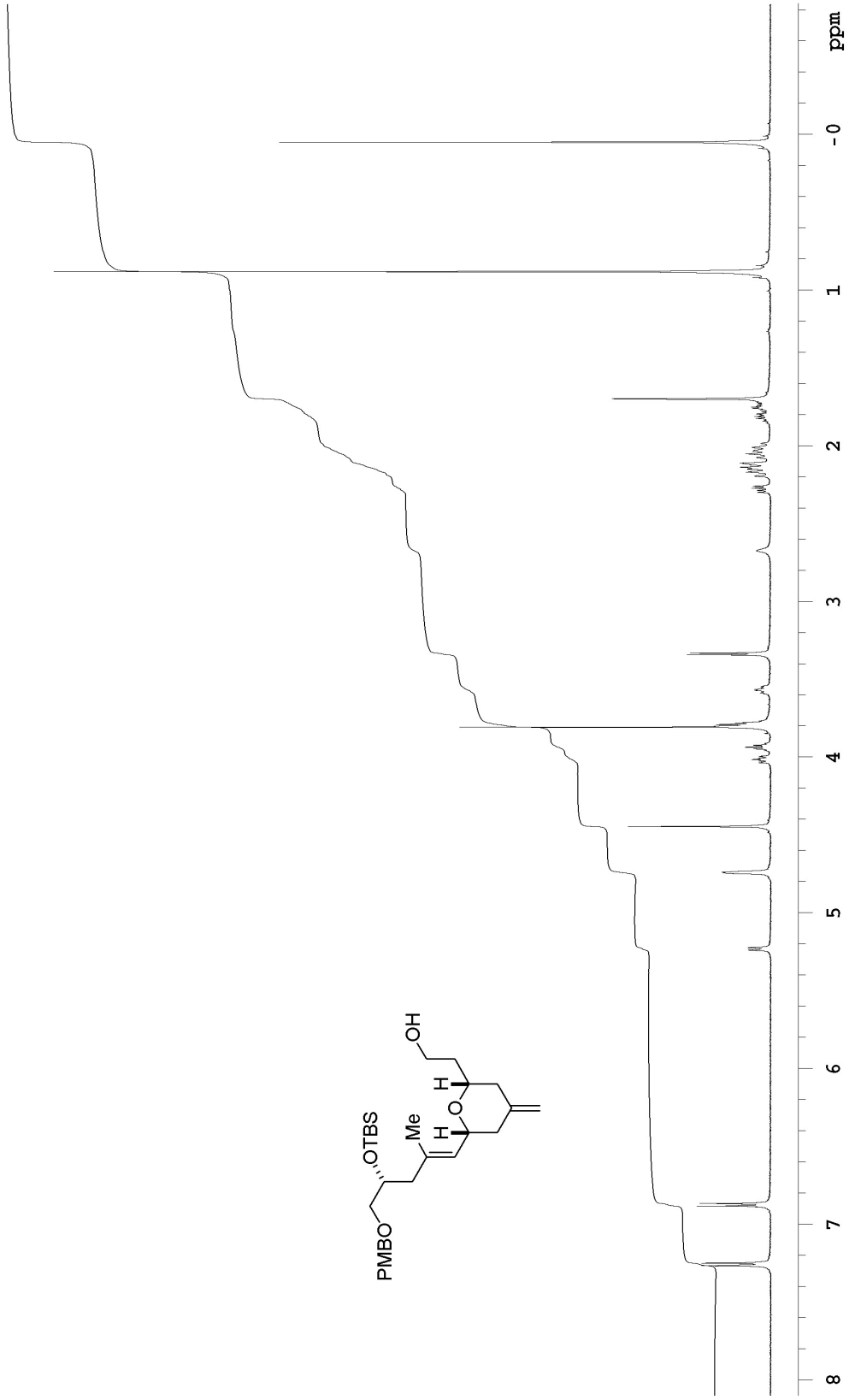
20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OTBS
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H
OH
ppm
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1
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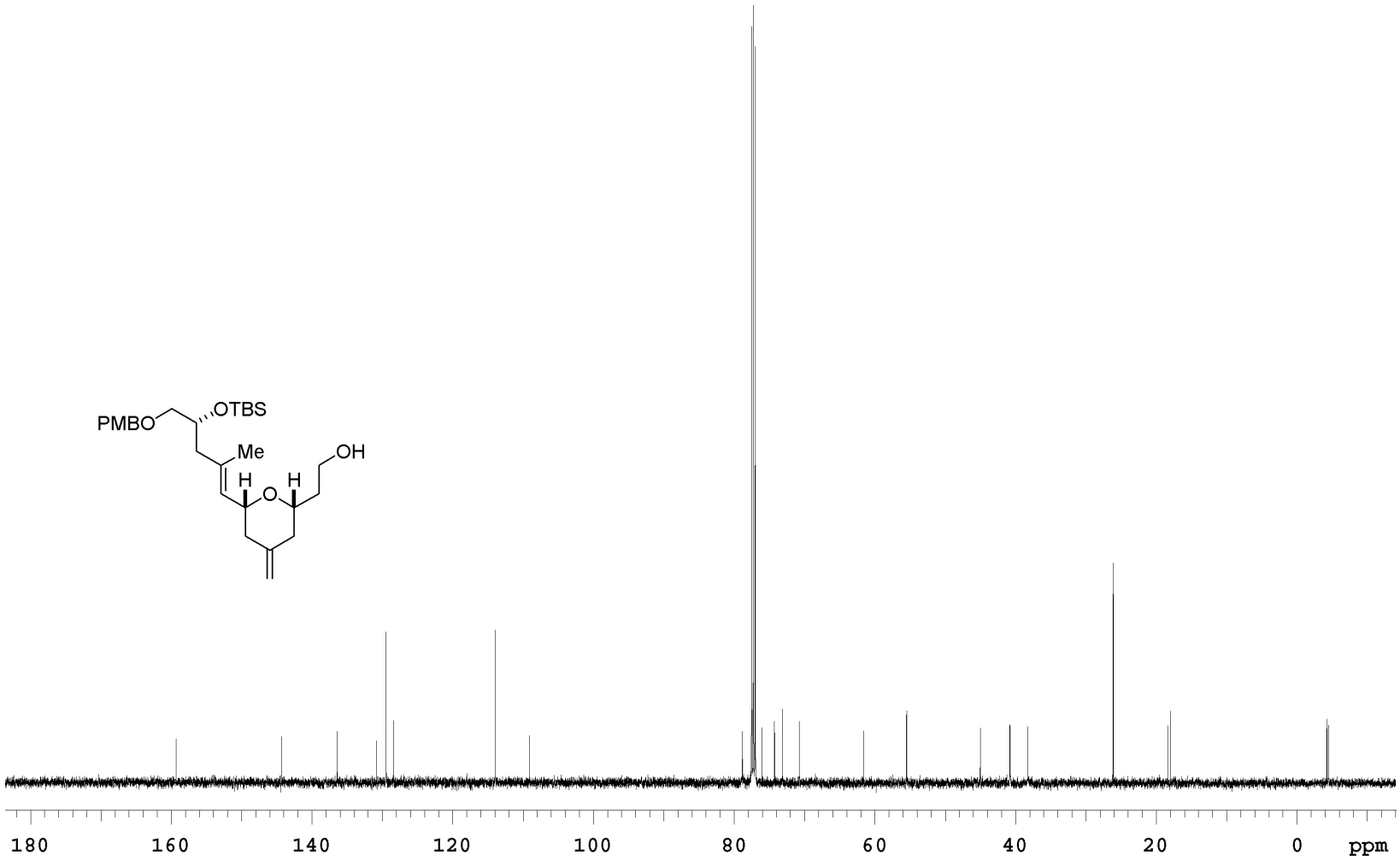
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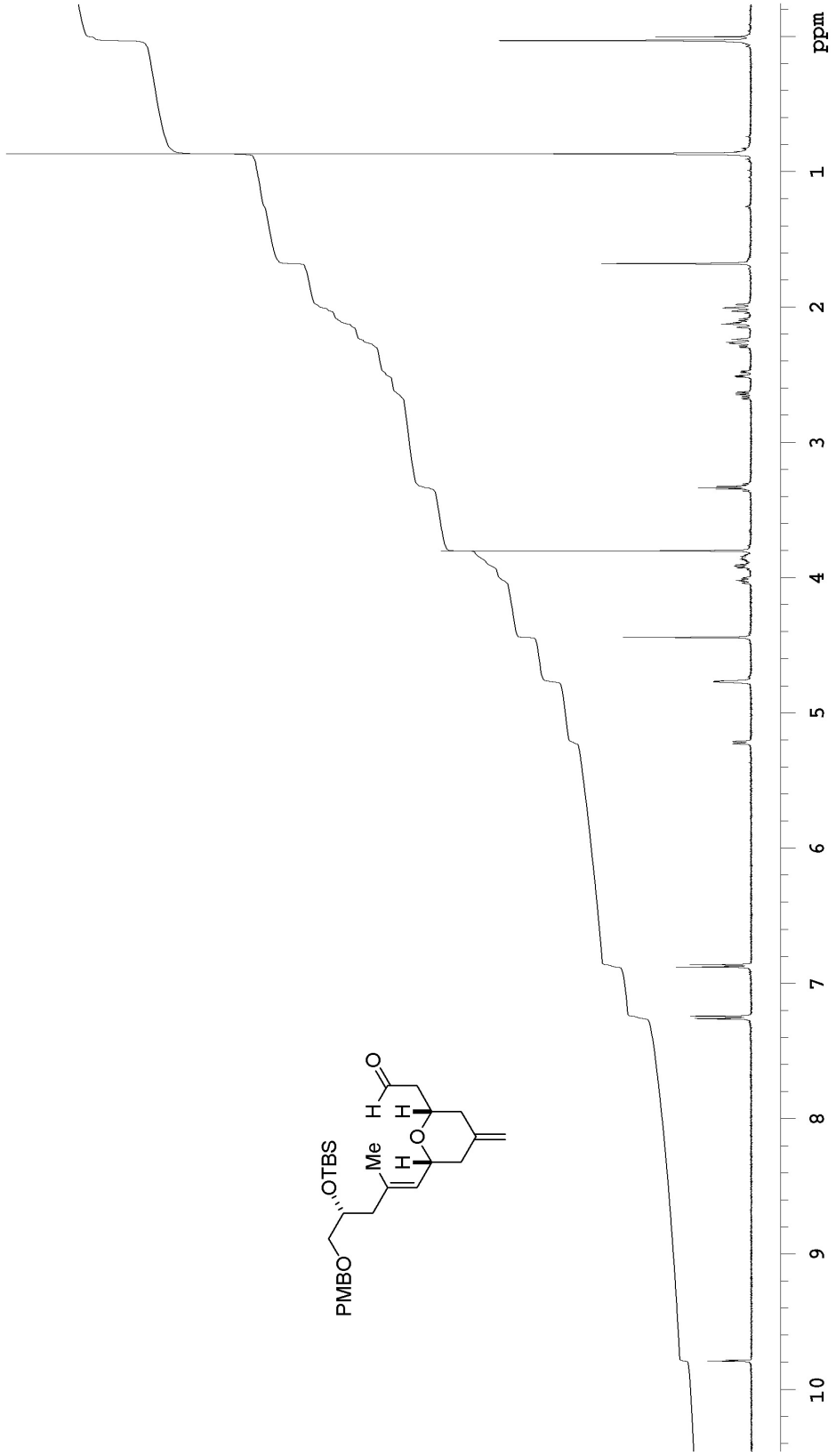
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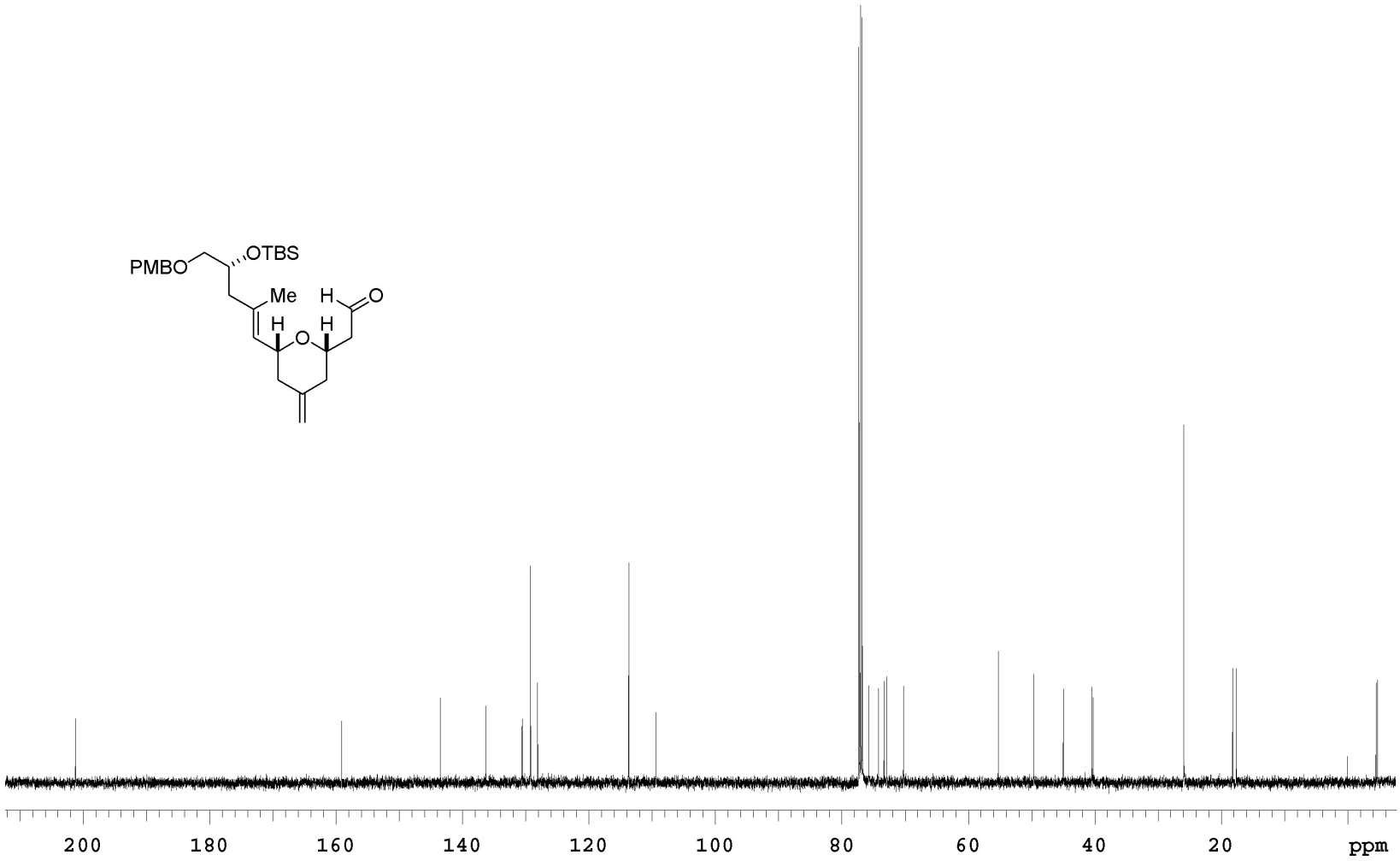
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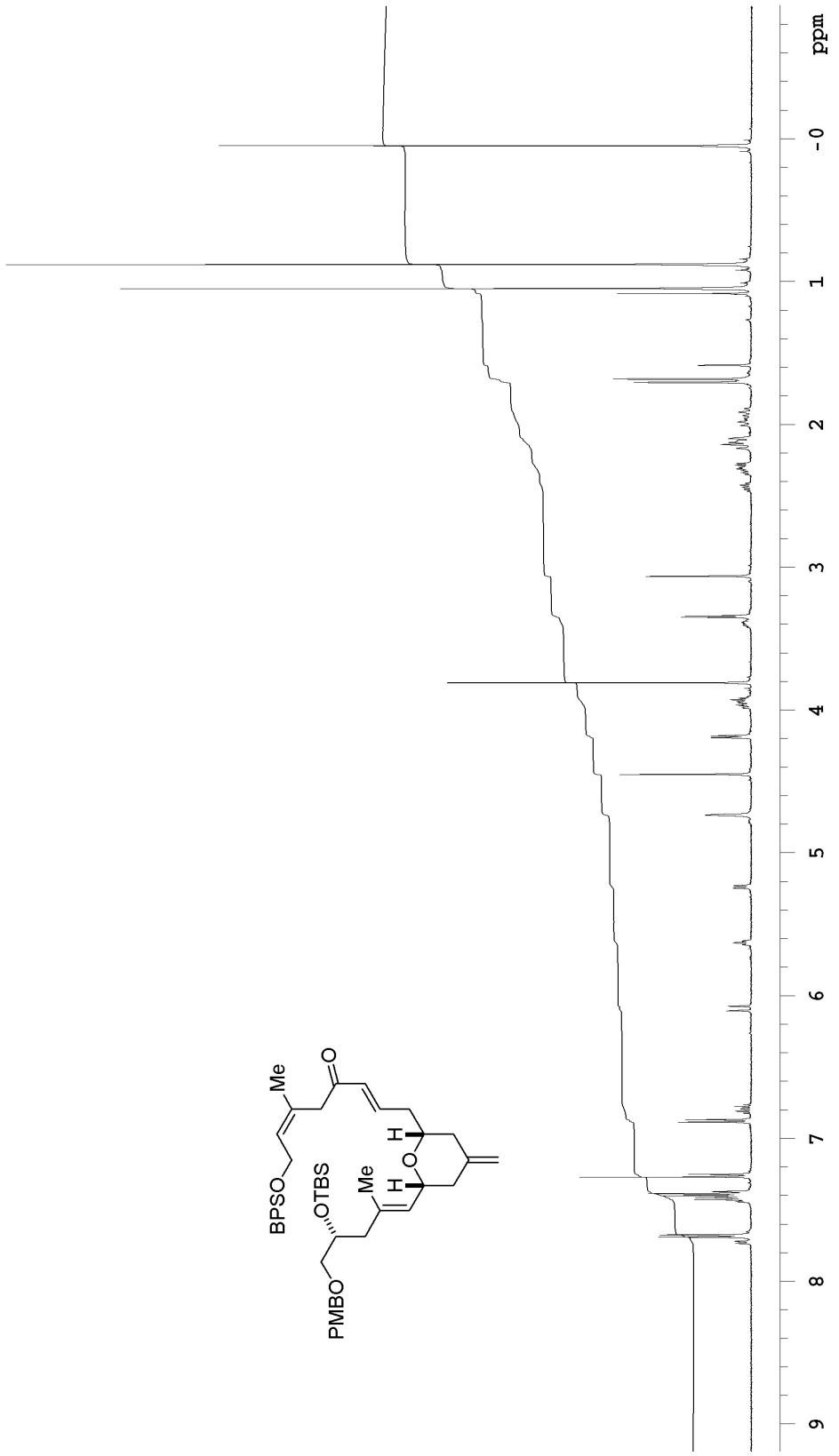
BPSO
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H
PMBO
ppm
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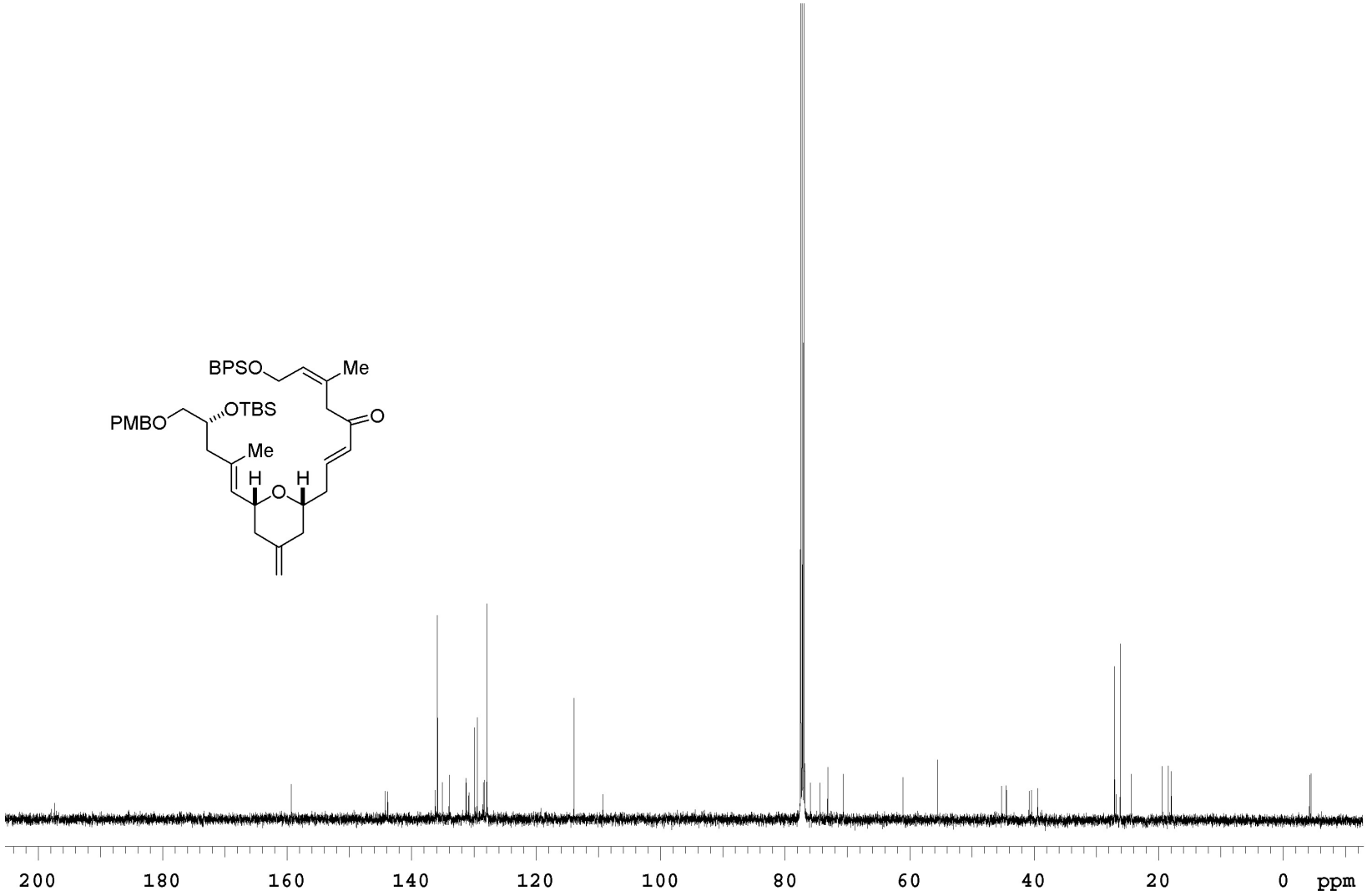
2
1
-0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PMBO
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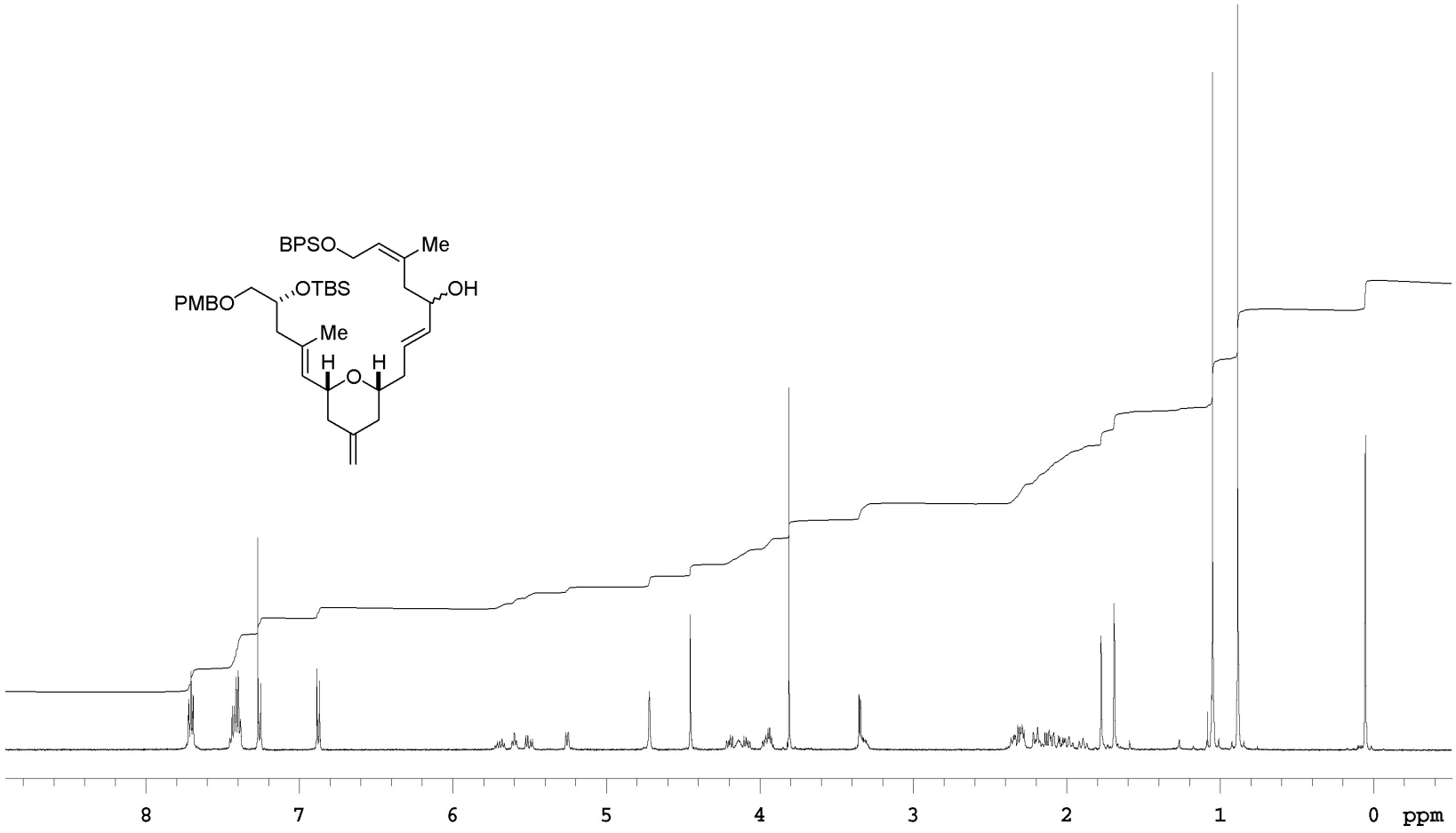
ppm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PMBO
OTBS
OH
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H
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H
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4
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2
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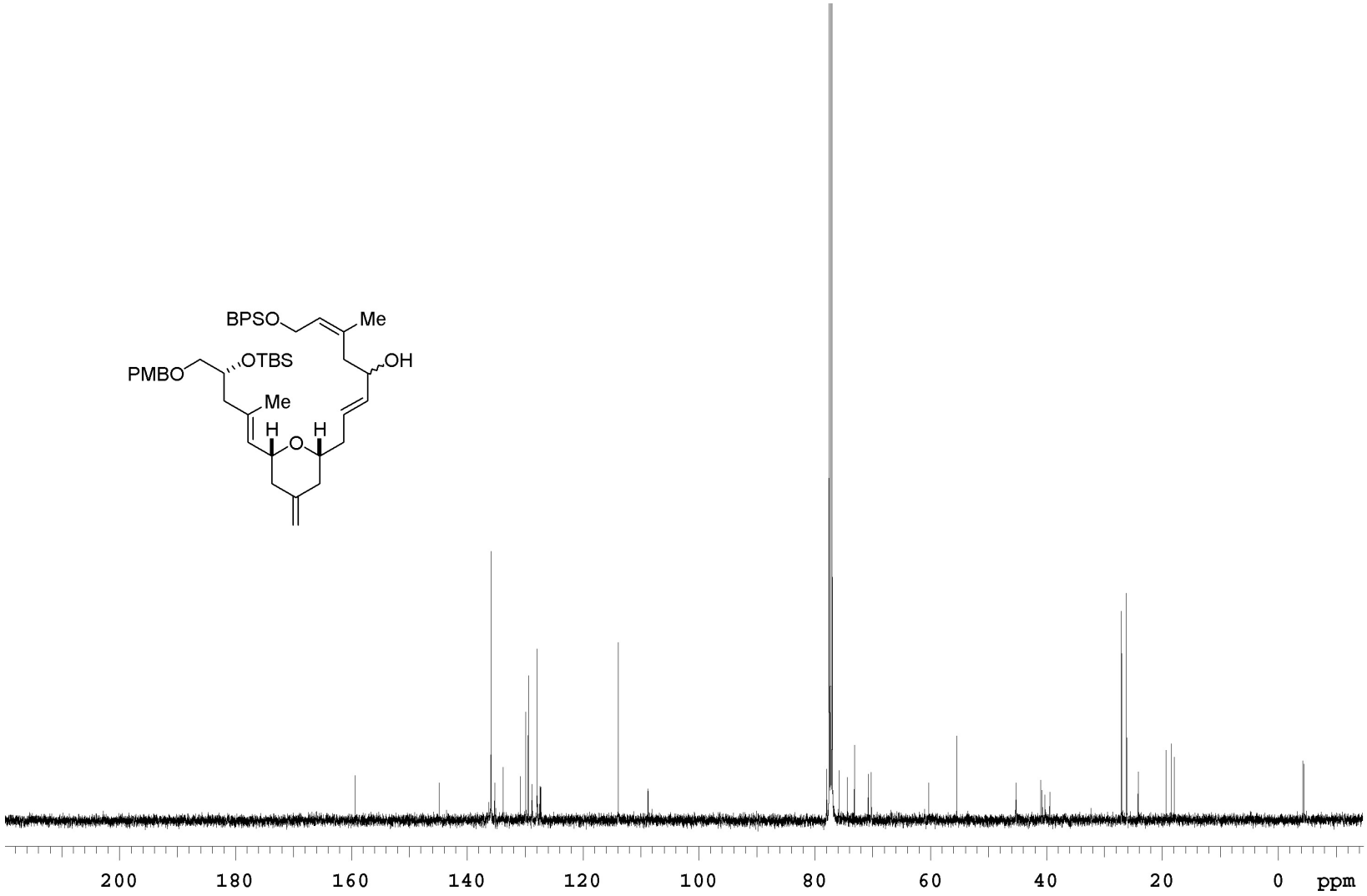
0
ppm


BPSO
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OTBS
OH
PMBO
Me
H
H
O
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140
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100
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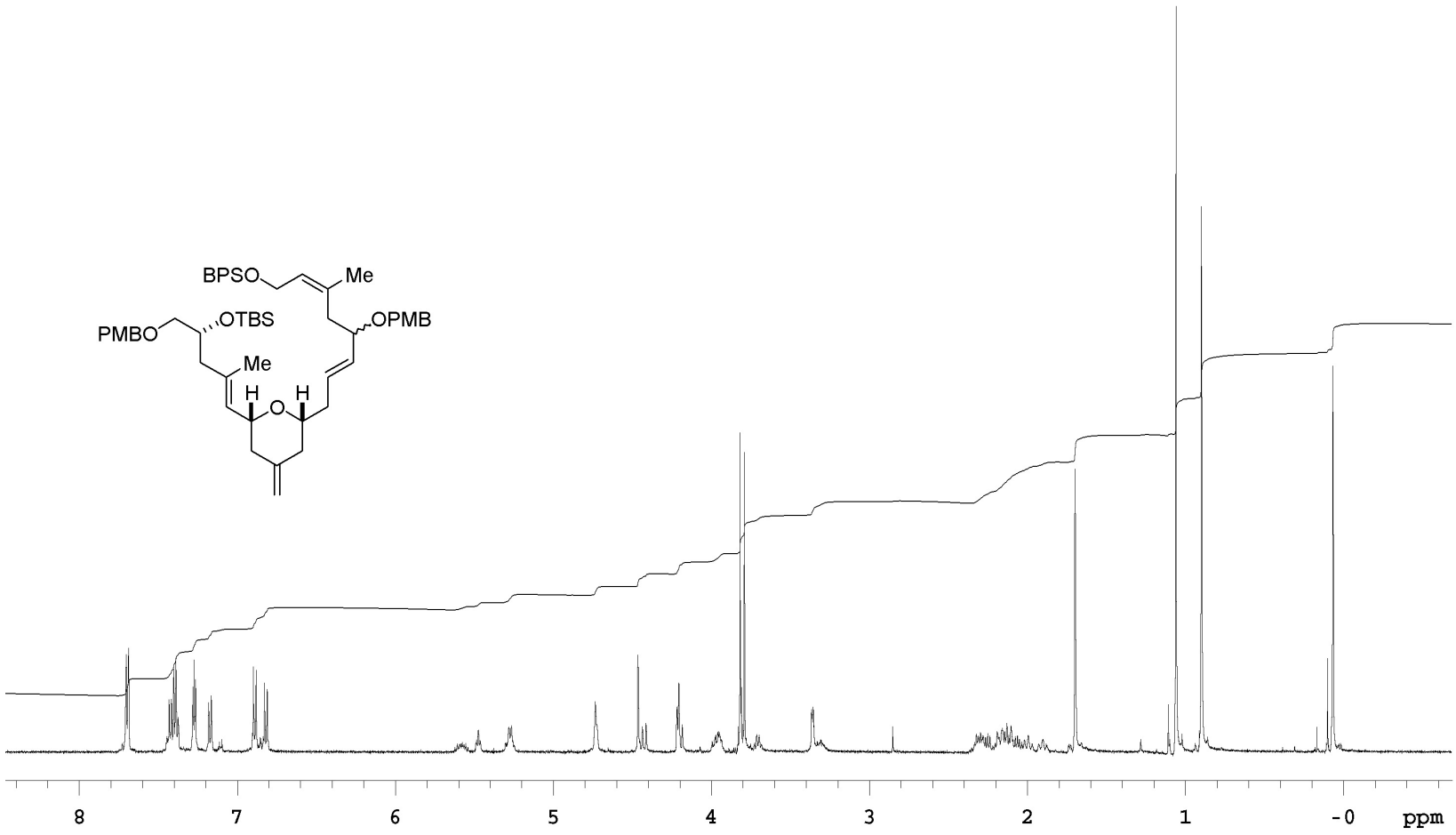
20
0
ppm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PMBO
OTBS
OPMB
Me
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H
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6
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4
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2
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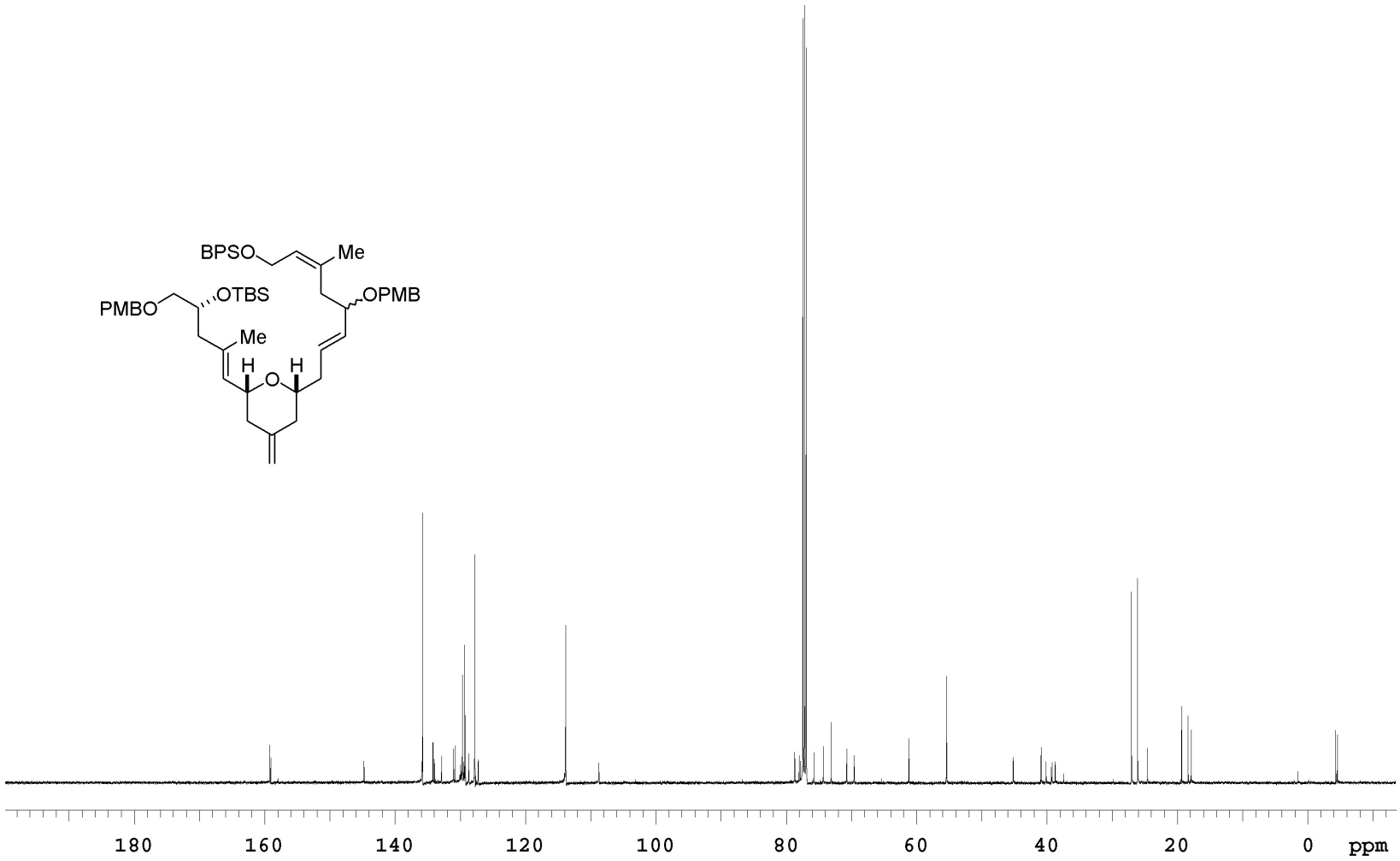
-0
ppm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PMBO
OTBS
OPMB
Me
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O
H
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140
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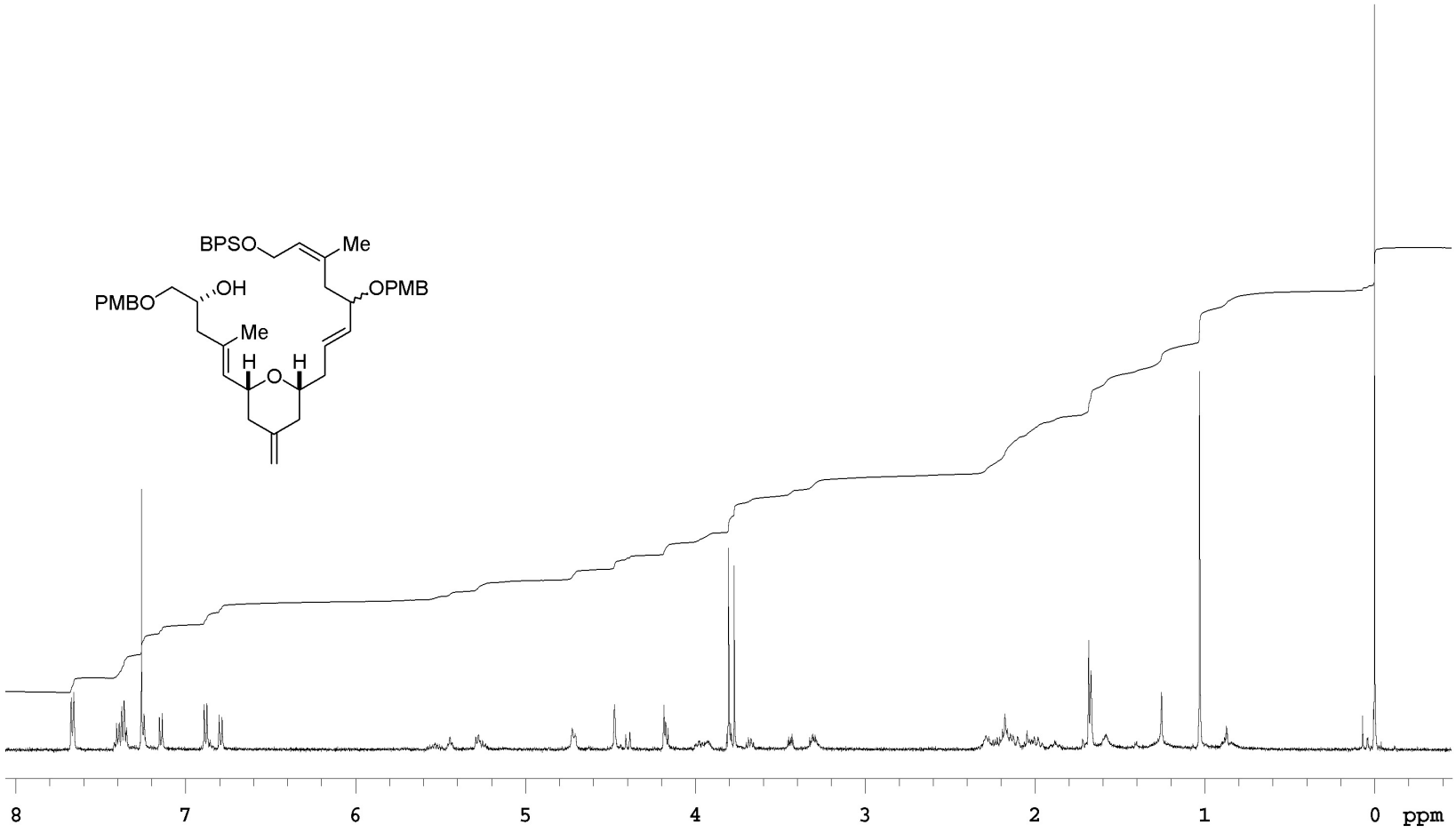
100
80
60
40
20
0
ppm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PMBO
OH
OPMB
Me
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O
H
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4
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2
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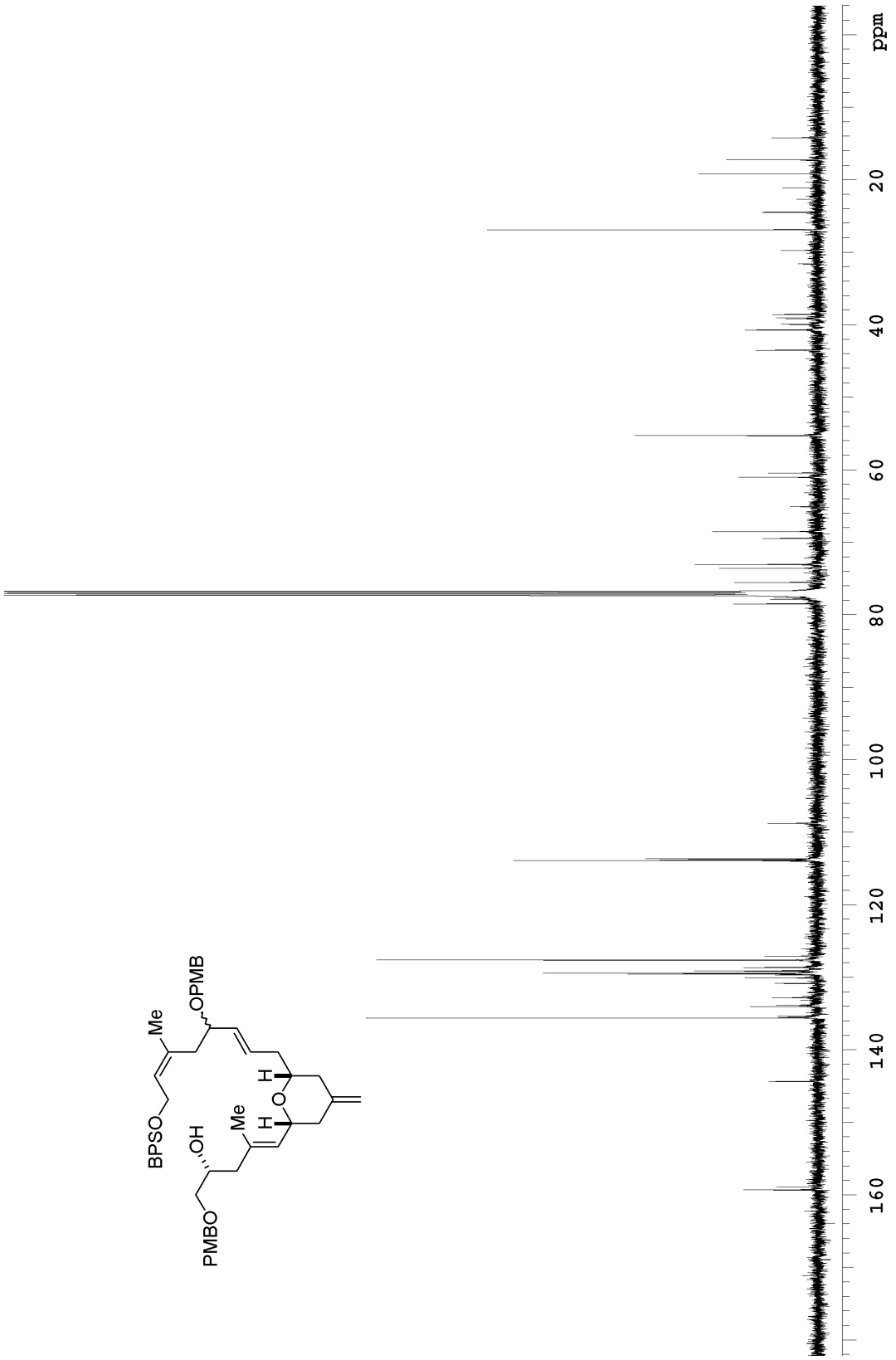
0
ppm


BPSO
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OPMB
OH
Me
H
O
H
PMBO
ppm
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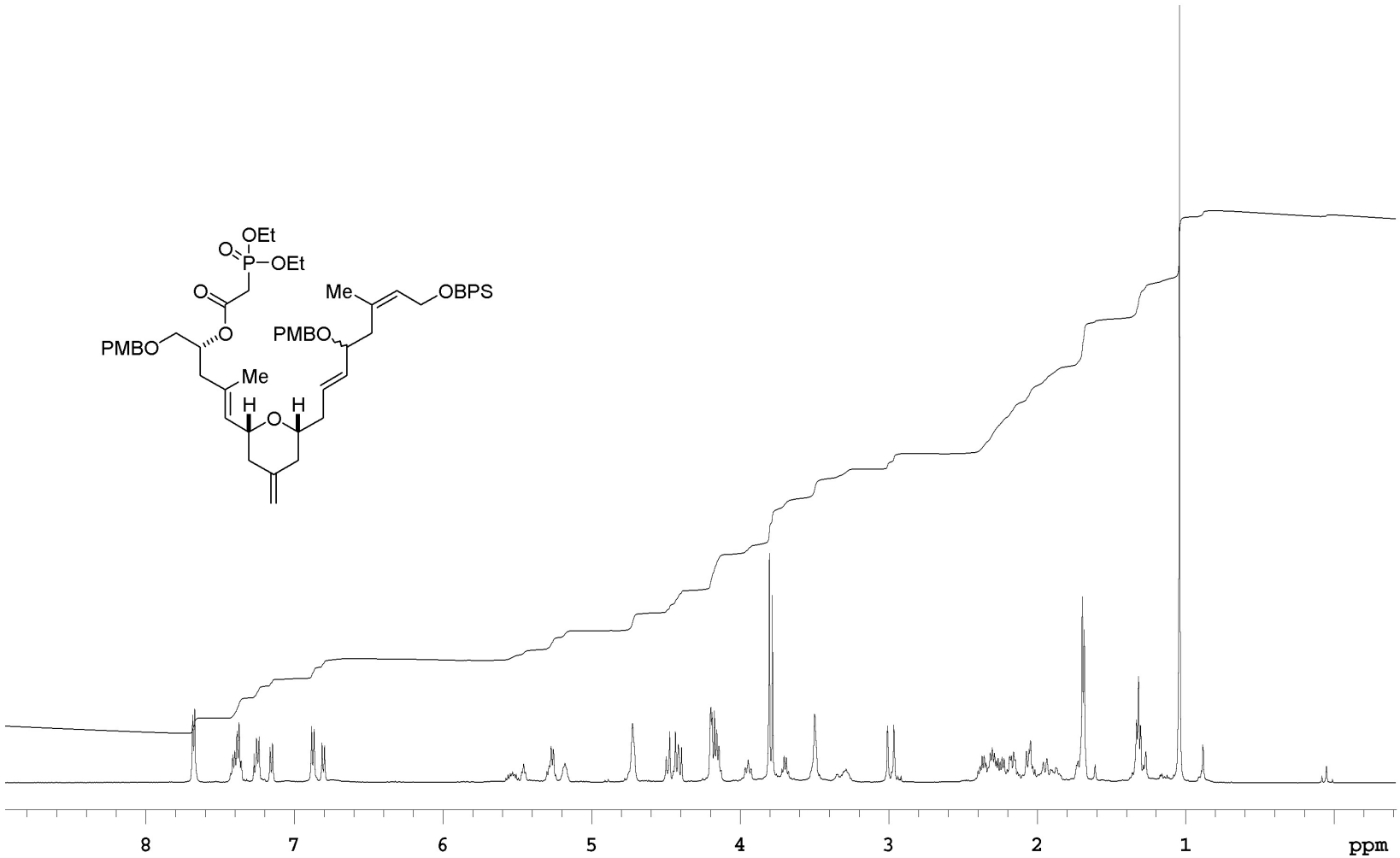
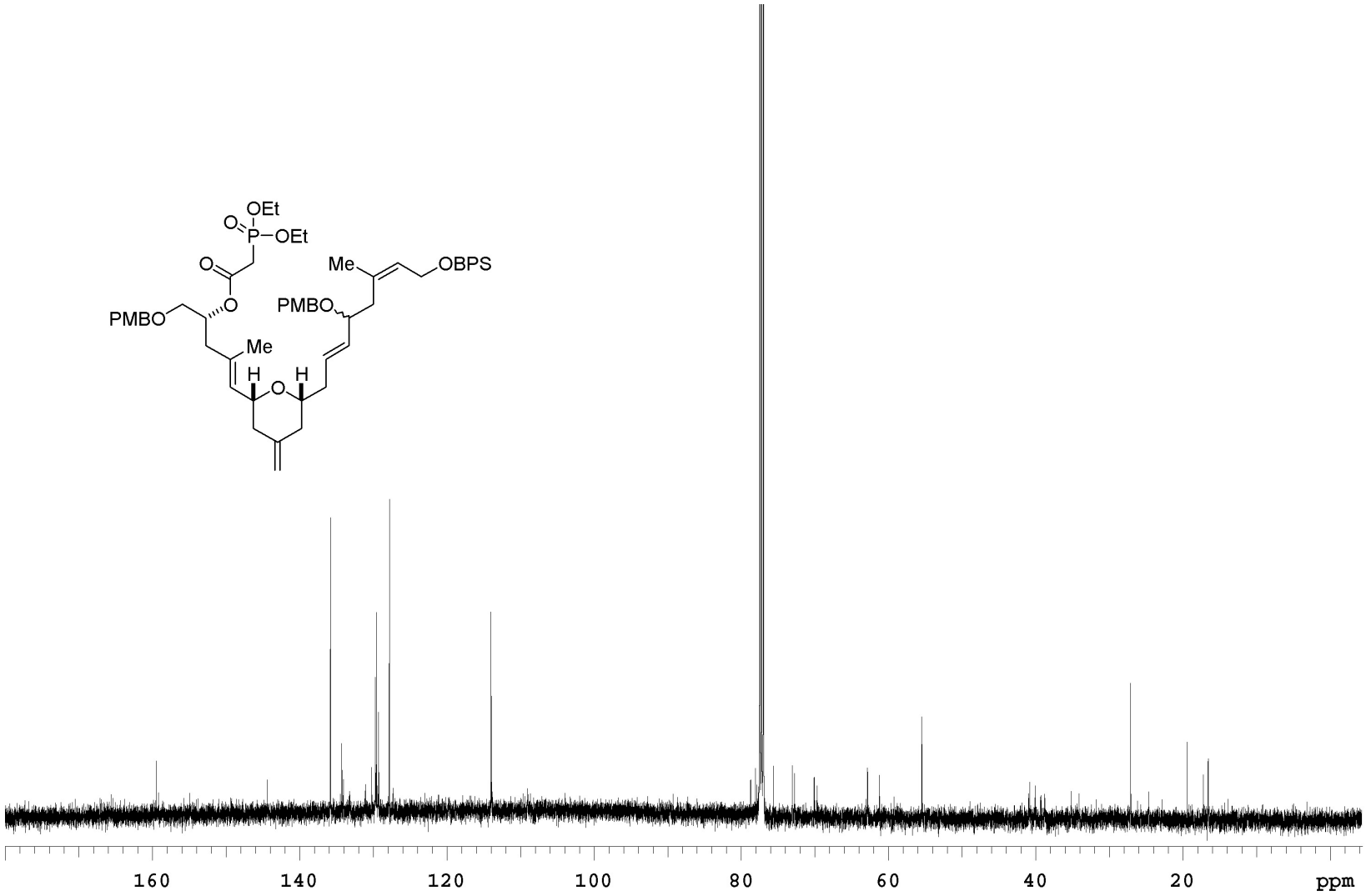
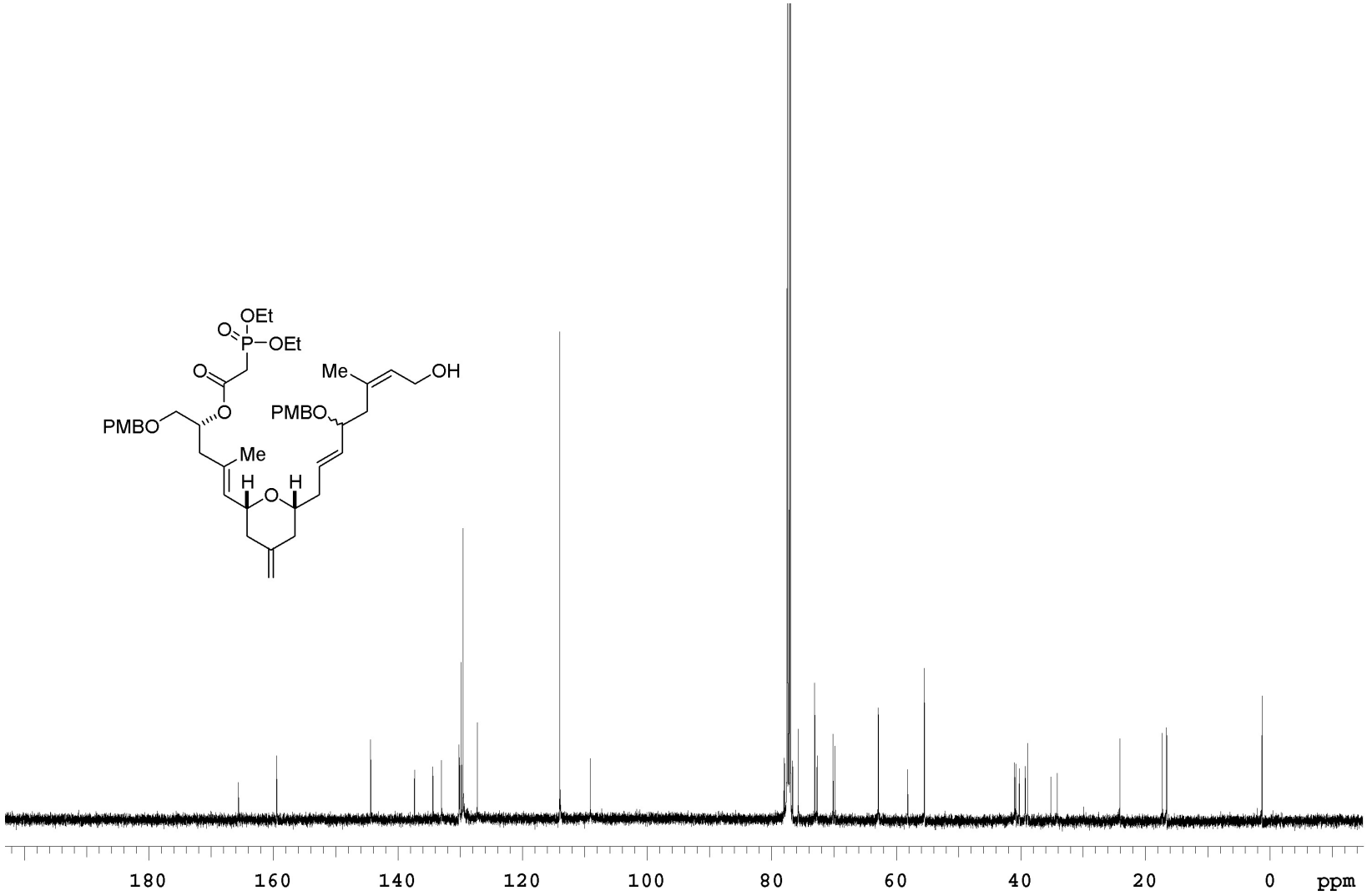
40
60
80
100
120
140
160


OEt
O
P
OEt
O
O
PMBO
Me
OBPS
PMBO
Me
H
H
O
8
7
6
5
4
3
2
1
ppm


OEt
O
P
OEt
O
Me
OBPS
PMBO
O
PMBO
Me
H
O
H
160
140
120
100
80
60
40
20
ppm

OH
Me
PMBO
OEt
O=P–OEt
O
O
Me
H
O
H
PMBO
ppm
1
2
3
4
5
6
7
8


OEt
O
P
OEt
O
O
PMBO
Me
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O
H
Me
OH
PMBO
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100
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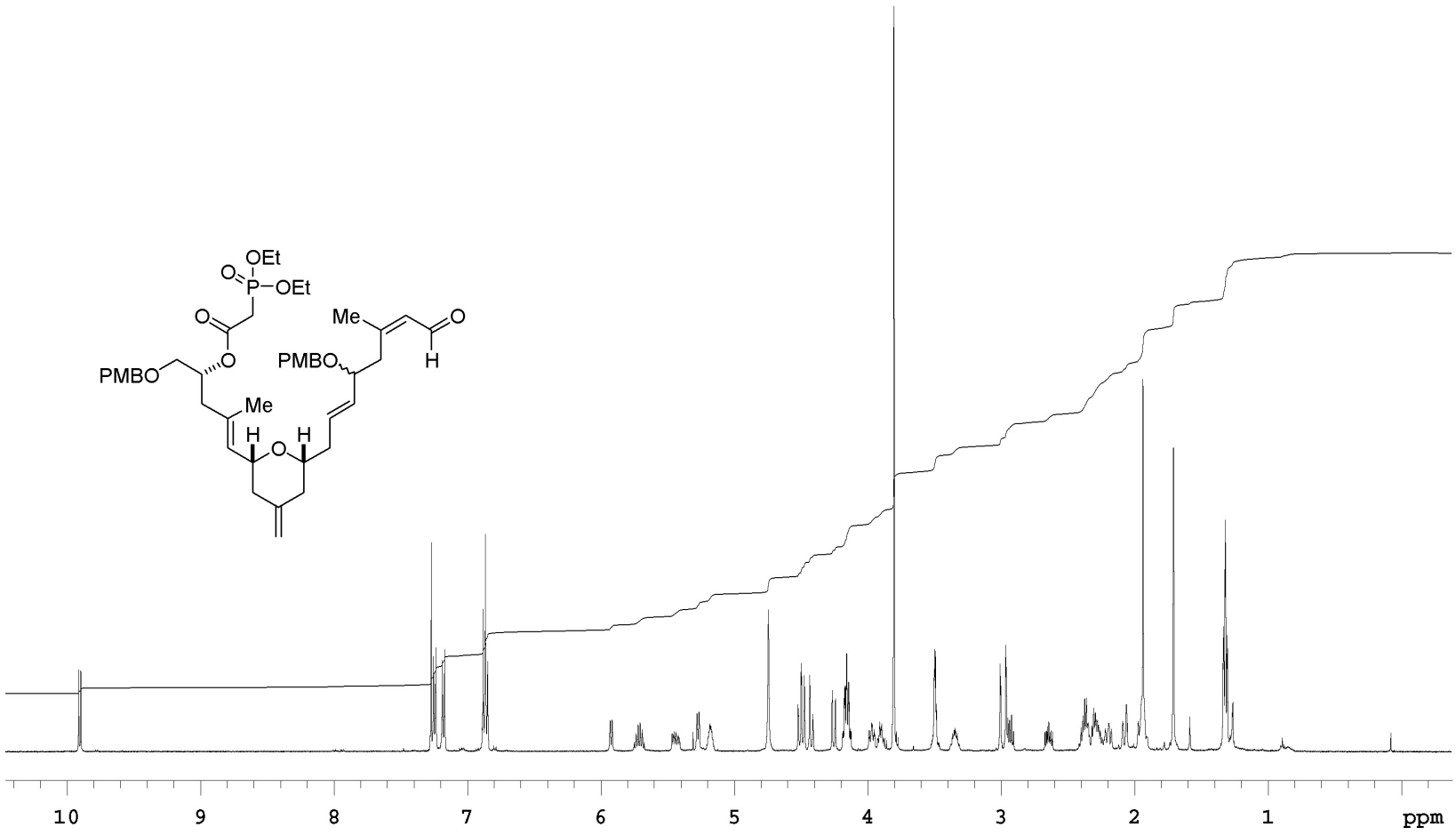
40
20
0
ppm


OEt
O
P
OEt
O
O
Me
O
PMBO
O
PMBO
H
Me
H
H
O
10
9
8
7
6
5
4
3
2
1
ppm

ppm
20
40
60
80
100
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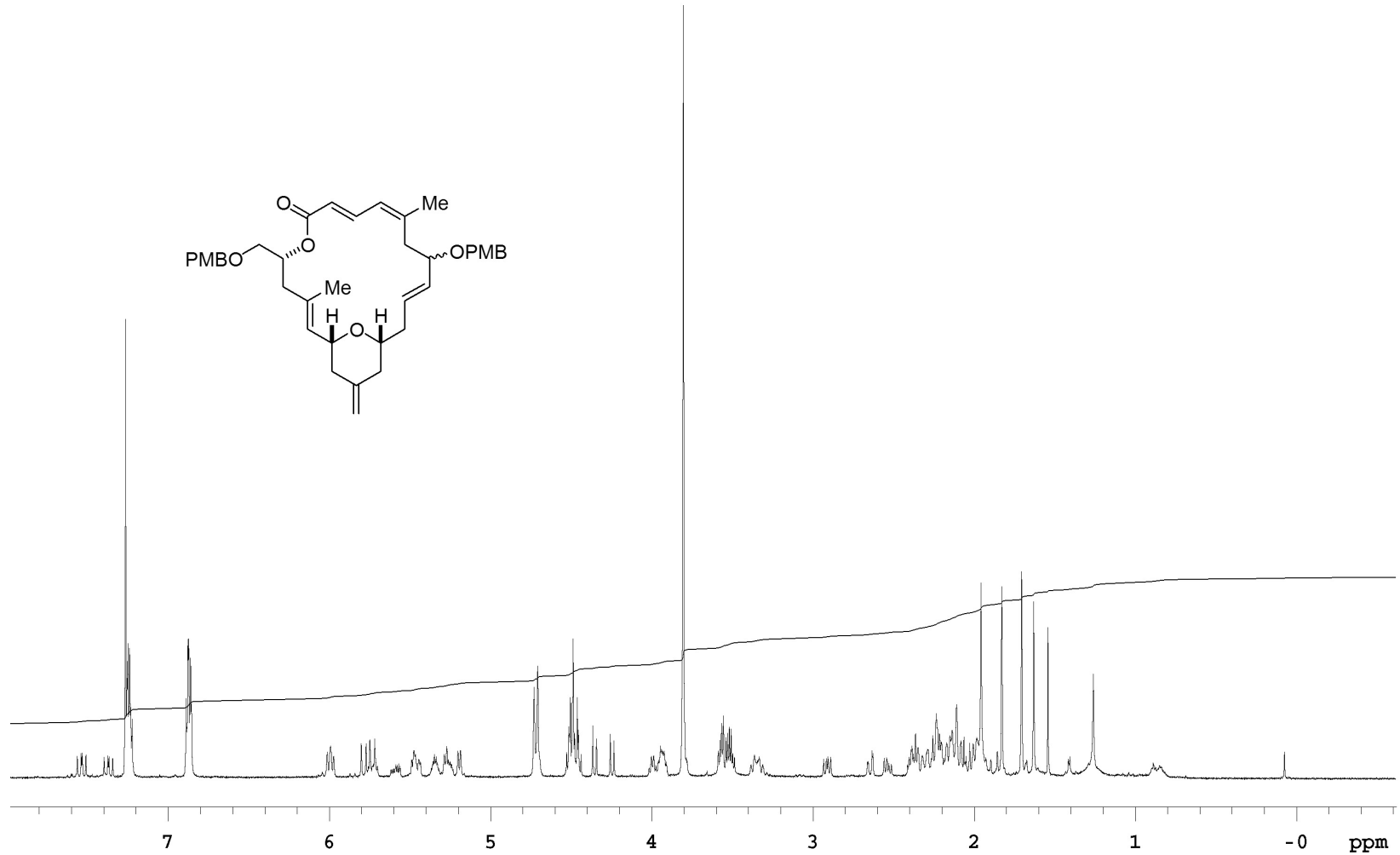
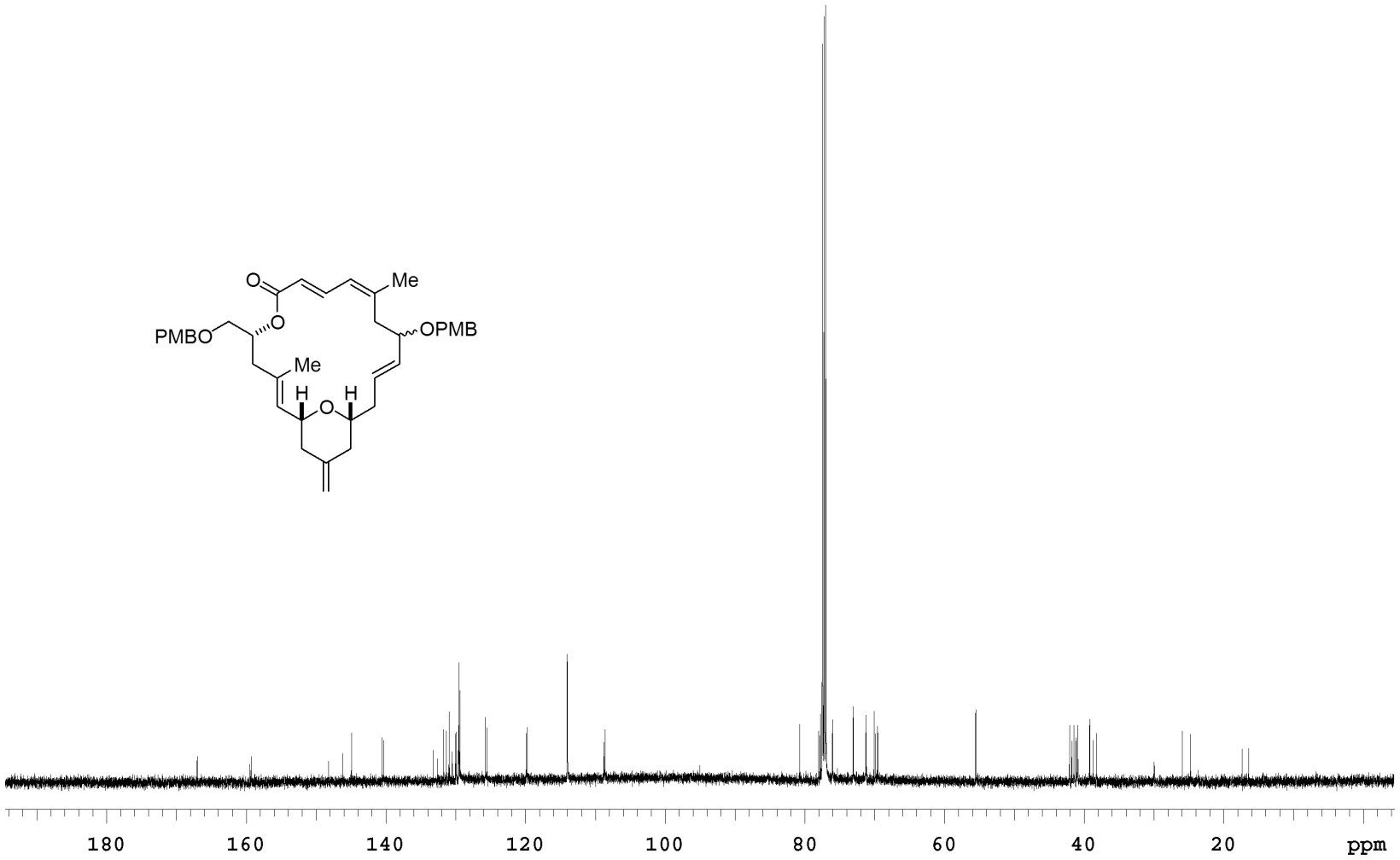
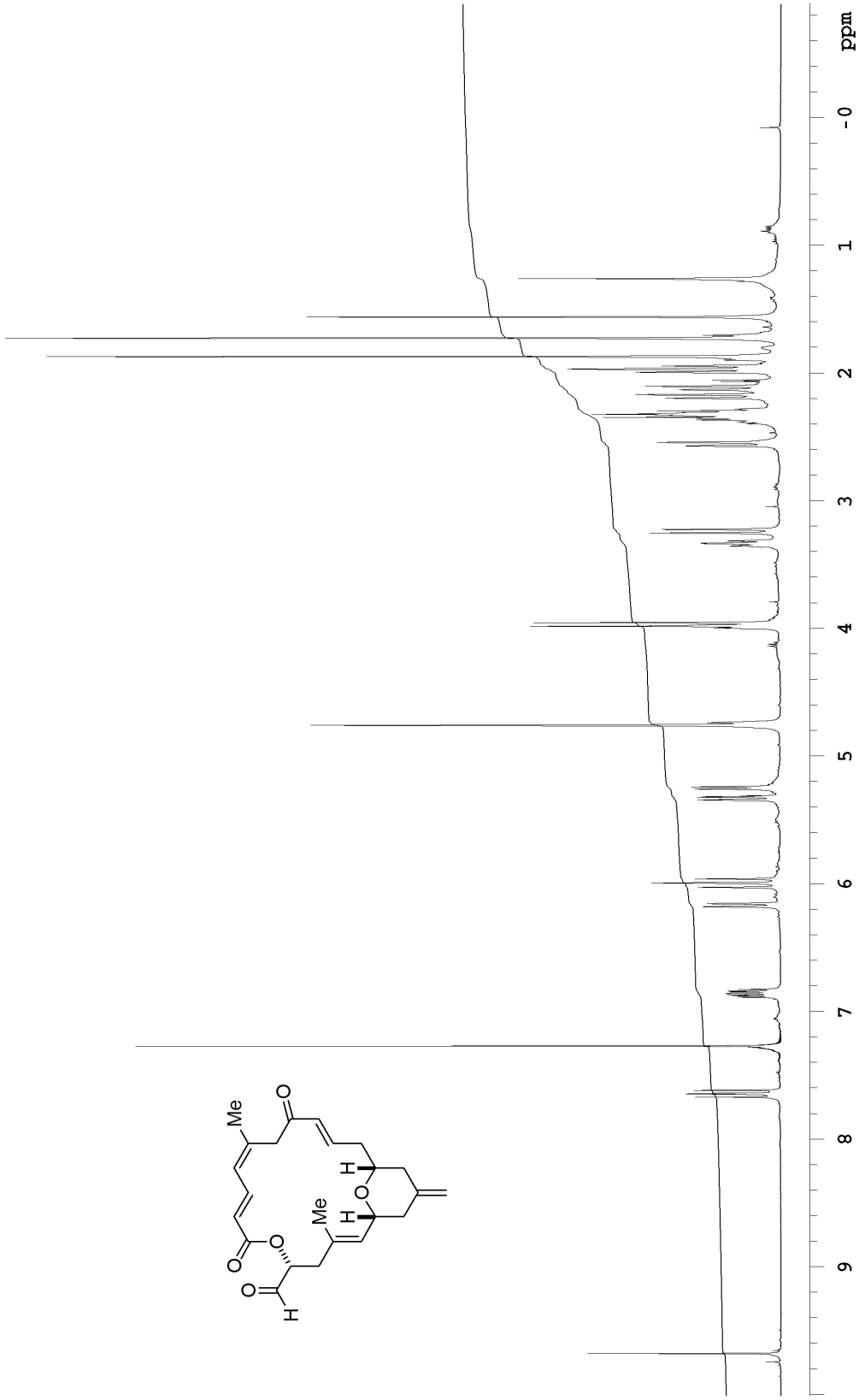
OEt
P
OEt
O
O
O
PMBO
Me
H
O
H
PMBO
Me
O
H


O
Me
PMBO
O
OPMB
Me
H
O
H
7
6
5
4
3
2
1
-0
ppm


O
Me
PMBO
O
OPMB
Me
H
O
H
180
160
140
120
100
80
60
40
20
ppm


ppm
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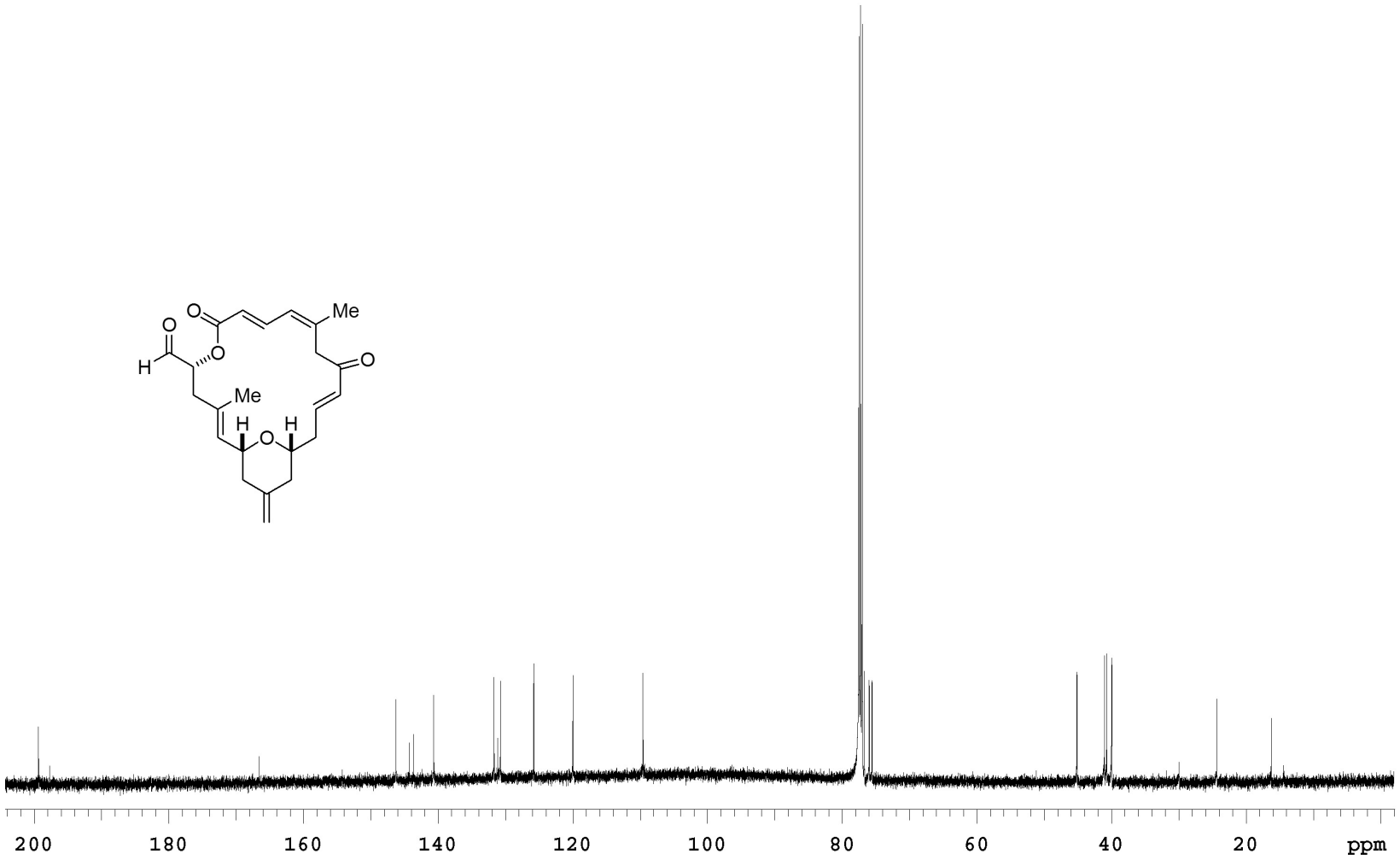
5
4
3
2
1
0
Me
Me
O
O
O
O
H
H
H
O


O
O
H
O
Me
O
Me
H
O
H
200
180
160
140
120
100
80
60
40
20
ppm