

Total Synthesis of Etnangien

Pengfei Li,[†] Jun Li,[‡] Fatih Arikan,[‡] Wiebke Ahlbrecht,[†] Michael Dieckmann,[†] Dirk Menche^{*,†,‡}

[†] Ruprecht-Karls-Universität Heidelberg
Institut für Organische Chemie
INF 270, 69120 Heidelberg, Germany
Fax: +49(6221)544205
E-mail: dirk.menche@oci.uni-heidelberg.de

[‡] Helmholtz-Zentrum für Infektionsforschung GmbH
Medizinische Chemie
Inhoffenstr. 7, 38124 Braunschweig, Germany

Contents

I. Experimental Details and Characterization Data.

II. Copies of ¹H and ¹³C NMR spectra.

General Remarks: Optical rotations were determined on a Perkin-Elmer 241 instrument. UV spectra were recorded on a Shimadzu UV-2102 PC scanning spectrometer. IR spectra were measured with a Nicolet 20DXB FT-IR spectrometer. NMR spectra were recorded in CD₃OD and CDCl₃ on a Bruker AM 300, AM 400 and DMX-600 spectrometer. EI and DCI mass spectra (reactant gas ammonia) were obtained on a Finnigan MAT 95 spectrometer, high resolution data were acquired using peak matching (M/DM = 10000). Etnangien was characterized by analytical HPLC on Nucleosil C 18 (column 125 x 2 mm, 5 μm, flow 0.3 ml/min), diode array detection. Analytical TLC (TLC aluminium sheets silica gel Si 60 F₂₅₄ (Merck), solvent: mixtures of ethylacetate/petroleum ether, detection: UV absorption at 254 nm, dark blue spots on staining with cerium(IV)sulfate- phosphomolybdic acid in sulfuric acid followed by charring.

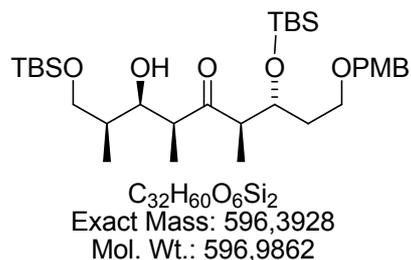
Synthesis of starting materials:

Aldehyde **5**,¹ ketone **6**,¹ epoxide **17**² and ethyl ketone **14**³ and stannane **25**⁴ were prepared according to literature procedures.

¹ Arikan, F.; Li, J.; Menche, D. *Org. Lett.* **2008**, *10*, 3521.

² Myers, A. G.; Lanman, B. A. *J. Am. Chem. Soc.* **2002**, *124*, 12969.

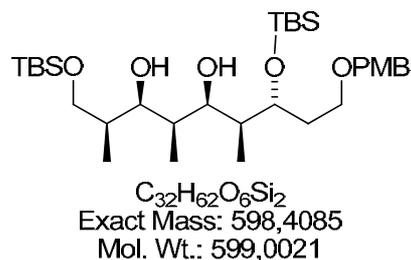
(2*S*,3*R*,4*S*,6*R*,7*R*)-1,7-Bis-(*tert*-butyl-dimethyl-silanyloxy)-3-hydroxy-9-(4-methoxybenzyloxy)-2,4,6-trimethyl-nonan-5-one (7)



To a suspension of 400 mg (0.937 mmol) of stannous triflate in 2 mL of CH_2Cl_2 at ambient temperature was added 156 μ L (1.12 mmol) of Et_3N . The resultant pale yellow slurry was then cooled immediately to -20 °C and stirred for 5 min before a solution of 284 mg (0.720 mmol) of ketone in 700 μ L of CH_2Cl_2 was added via cannula. The resultant nearly clear solution was stirred at -20 °C for 1 h. The reaction was then cooled to -78 °C and treated with 437 mg (2.16 mmol) of aldehyde. After stirring for 1 h at -78 °C, the reaction was quenched with the addition 5 mL pH 7 puffer at 0 °C. The mixture was stirred for 30 min until both layers became clear, whereupon the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2×10 mL). The combined organic extracts were washed with a saturated solution of $NaHCO_3$ (1×4 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo to afford clear colorless oil. The reaction was purified by column chromatography (light petroleum ether /EtOAc 90:10) to afford the aldol (365 mg, 0.612 mmol, 85%) of a clear oil, (dr = 7:1, determined by LCMS). R_f = 0.30 (light petroleum ether /EtOAc 80:20); $[\alpha]_D^{22} = -32$ ($c = 1.1$, $CHCl_3$); 1H -NMR (300 MHz, $CDCl_3$) δ ppm 0.03 (s, 3H) 0.04 (s, 3H), 0.05-0.06 (6H), 0.85 (s, 9H), 0.88 (s, 9H), 0.91 (d, $J = 6.4$ Hz, 3H), 0.91 (d, $J = 6.9$ Hz, 3H), 1.02 (d, $J = 7.0$ Hz, 3H), 1.16 (m, 1H), 1.62 (m, 2H), 1.73 (m, 1H), 2.87 (m, 1H), 2.92 (m, 1H), 3.46 (m, 1H), 3.61 (dd, $J = 10.0, 3.8$ Hz), 3.51 (m, 2H), 3.79 (s, 3H), 3.90 (dd, $J = 5.5, 5.5$ Hz, 1H), 4.13 (ddd, $J = 9.6, 3.8, 1.6$ Hz, 1H), 4.39 (m, 2H), 6.86 (dd, $J = 8.7, 1.9$ Hz, 2H), 7.24 (dd, $J = 8.7, 1.9$ Hz, 2H); ^{13}C -NMR (75 MHz, $CDCl_3$) δ ppm -5.6, -5.5, -4.8, -4.5, 10.8, 11.6, 12.5, 18.0, 18.2, 25.7, 25.9, 32.7, 36.9, 48.9, 51.4, 55.3, 66.0, 68.1, 69.4, 72.7, 74. 4, 113.7, 129.3, 130.6, 159.2, 216.6; HRMS calculated for $C_{32}H_{60}O_6NaSi_2$ $[M+Na]^+$: 619.3826, found: 619.3810.

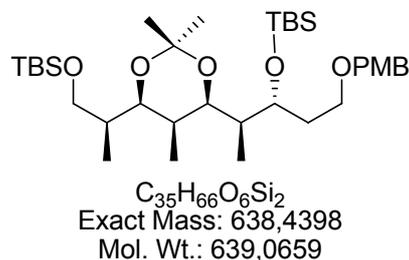
³ Paterson, I.; Wallace, D. J.; Cowden, C. J. *Synthesis* **1998**, 639

⁴ Smith, A. B., III; Wan, Z. *J. Org. Chem.* **2000**, 65, 3738.

(2*S*,3*R*,4*S*,5*R*,6*S*,7*R*)-1,7-Bis-(*tert*-butyl-dimethyl-silanyloxy)-9-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonane-3,5-diol

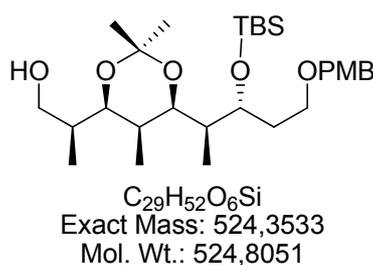
To a solution of chlorodicyclohexylboran (27 μ L, 0.125 mmol) in 300 μ L Et₂O was added Et₃N (18 μ L, 0.125 mmol). The mixture was cooled to -20 °C before a solution of the keton (50 mg, 0.083 mmol) in 50 μ L Et₂O was added. The mixture was stirred at -30 °C for 75 min and then cooled to -78 °C before 200 μ L of a solution of LiBH₄ in THF (2 M, 0.415 mmol) was added. The mixture was stirred again for 60 min at -78 °C and then diluted with Et₂O (1 mL) and quenched with 1 mL satd. aq. NH₄Cl solution. The layers were separated and the aqueous layer was extracted with Et₂O (3 \times 2 mL). The combined organic extracts were washed with brine and concentrated in vacuo to an oil. The crude oil was dissolved in MeOH (330 μ L), 10% NaOH solution (100 μ L), 30% H₂O₂ (150 μ L) and stirred for 60 min at r.t before the reaction was diluted with 2 mL H₂O and 2 mL DCM. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 \times 3 mL). The combined organic Phases were dried with MgSO₄ and concentrated to an oil. The reaction was purified by column chromatography (light petroleum ether /EtOAc 85:15) to afford the diol (42.6 mg, 0.071 mmol, 87 %, dr 19:1) of a clear oil. R_f = 0.28 (light petroleum ether /EtOAc 90:10); $[\alpha]_D^{22} = +2.5$ ($c = 1.1$, CHCl₃); ¹H-NMR (300 MHz, CDCl₃) δ ppm 0.02 (s, 3H), 0.03 (s, 3H), 0.05 (6H), 0.87 (s, 9H), 0.88 (s, 9H), 0.98 (d, $J = 6.8$ Hz, 3H), 1.00 (d, $J = 7.0$ Hz, 3H), 1.01 (d, $J = 6.8$ Hz, 3H), 1.73 (m, 2H), 1.81 (m, 1H), 1.88 (m, 1H), 1.96 (m, 1H), 3.55 – 3.47 (m, 2H), 3.51 - 3.60 (m, 3H), 3.75 (s, 3H), 3.85 (dd, $J = 6.7, 2.9$ Hz, 1H), 3.87 (dd, $J = 7.4, 2.4$ Hz), 4.39 (d, $J = 11.9$ Hz), 4.40 (d, $J = 11.9$ Hz), 6.87 (dd, $J = 8.7, 1.9$ Hz, 2H), 7.24 (dd, $J = 8.7, 1.9$ Hz, 2H); ¹³C-NMR (75 MHz, CDCl₃) δ ppm -5.5, -5.4, -4.6, -4.5, 8.5, 11.4, 13.7, 17.9, 18.3, 23.8, 25.8, 25.9, 29.7, 34.2, 37.3, 37.9, 38.2, 55.5, 66.2, 66.7, 72.7, 73.8, 74.7, 75.9, 113.8, 129.5, 130.2, 159.9; HRMS calculated for C₃₂H₆₂O₆NaSi₂ [M+Na]⁺: 621.3983, found: 621.3990.

(4R,5S,6R)-4-[(1S,2R)-2-(*tert*-Butyl-dimethyl-silyloxy)-4-(4-methoxy-benzyloxy)-1-methyl-butyl]-6-[(S)-2-(*tert*-butyl-dimethyl-silyloxy)-1-methyl-ethyl]-2,2,5-trimethyl-[1,3]dioxane (8)



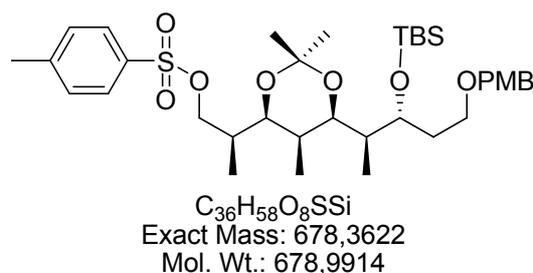
To a solution of diol (620 mg, 1.03 mmol) in 2,2 Dimethoxypropan (15 mL, 0.12 mmol) was added *p*- TsOH x H₂O (60 mg, 0.316 mmol). After the mixture was stirred for 30 min at r.t. the reaction was quenched by addition of 5 ml water. The layers were separated and the aqueous phase was extracted with DCM (2 × 5 mL), the combined organic phases were dried (MgSO₄) and concentrated in vacuo to an oil. The resultant colourless oil was purified by column chromatography (EtOAc/light petroleum ether 96:04) to afford the protected diol (526 mg, 0.824 mmol, 80 %) as a clear oil. $R_f = 0.33$ (light petroleum ether/EtOAc 95:05); $[\alpha]_D^{22} = +9.3$ ($c = 0.8$, CHCl₃); ¹H-NMR (300 MHz, CDCl₃) δ ppm -0.01 (s, 3H), -0.02 (s, 3H), 0.00 (s, 3H), 0.04 (s, 3H), 0.87 (s, 9H), 0.85 (s, 9H), 0.91 (d, $J = 6.3$ Hz, 3H), 0.92 (d, $J = 6.6$ Hz, 3H), 0.93 (d, $J = 6.6$ Hz, 3H), 1.34 (s, 3H), 1.37 (s, 3H), 1.47 (m, 1H), 1.56 (m, 1H), 1.72 (m, 2H), 1.82 (ddq, $J = 10.4, 6.8, 4.1$ Hz, 1H), 3.51 (dd, $J = 8.6, 4.5$ Hz, 1H), 3.47 (dd, $J = 10.6, 4.7$ Hz, 1H), 3.45 (m, 1H), 3.54 (m, 2H), 3.39 (dddd, $J = 7.7, 7.7, 7.7, 7.7$ Hz, 1H), 3.83 (ddd, $J = 10.5, 3.9, 1.9$ Hz, 1H) 4.38 (d, $J = 11.4$ Hz, 1H) 4.40 (d, $J = 11.4$ Hz, 1H), 6.87 (dd, $J = 8.7, 1.9$ Hz, 2H), 7.24 (dd, $J = 8.7, 1.9$ Hz, 2H); ¹³C-NMR (75 MHz, CDCl₃) δ ppm -5.5, -4.8, -4.1, 6.1, 10.0, 14.4, 18.1, 18.2, 19.5, 25.9 30.1, 31.5, 31.6, 36.7, 40.5, 55.3, 64.5, 67.8, 67.9, 72.8, 76.1, 98.9, 113.8, 129.3, 130.7, 159.1; HRMS calculated for C₃₅H₆₆O₆NaSi₂ [$M+Na$]⁺: 661.4296, found: 661.4291.

(S)-2-[(4R,5S,6R)-6-[(1S,2R)-2-(*tert*-Butyl-dimethyl-silyloxy)-4-(4-methoxy-benzyloxy)-1-methyl-butyl]-2,2,5-trimethyl-[1,3]dioxan-4-yl]-propan-1-ol



To a cooled solution (0 °C) of 500 mg protected diol (0.782 mmol) in 10 mL abs. THF was added a 1 M solution of TBAF in THF (2.5 mL, 2.5 mmol). The mixture was stirred for 6 h at 0 °C before the reaction was quenched with addition of satd aq NH₄Cl solution (5 mL). The mixture was extracted with Et₂O (3 × 5 ml). The combined organic extracts were dried (MgSO₄), concentrated in vacuo, and the residue purified by column chromatography. (light petroleum ether/EtOAc 85:15) to give the title amide (333 mg, 81 %) as colourless oil. $R_f = 0,28$ (light petroleum ether/EtOAc 85:15); $[\alpha]_D^{22} = +12.3$ ($c = 0.4$, CHCl₃); ¹H-NMR (300 MHz, CDCl₃) δ ppm -0.04 (s, 3H), 0.04 (s, 3H), 0.87 (s, 9H), 0.89 (d, $J = 7.0$ Hz, 3H), 0.91 (d, $J = 6.6$ Hz, 3H), 0.96 (d, $J = 6.7$ Hz, 3H), 1.35 (s, 3H), 1.38 (s, 3H), 1.55 (m, 2H), 1.57 (m, 1H), 1.65 (m, 1H), 1.18 (ddq, $J = 10.3, 6.7, 4.0$ Hz, 1H), 3.32 (dd, $J = 10.5, 3.5$ Hz, 1H) 3.52 (dd, $J = 10.4, 5.3$ Hz, 1H), 3.42 (ddd, $J = 9.7, 1.6, 0$ Hz, 1H), 3.50 (dd, $J = 9.3, 4.5$ Hz, 1H), 3.52 (m, 1H), 3.54 (m, 1H), 3.80 (s, 3H), 3.95 (ddd, $J = 9.4, 3.7, 1.5$ Hz, 1H), 4.36 (d, $J = 11.0$ Hz, 1H), 4.39 (d, $J = 11.0$ Hz, 1H), 6.87 (dd, $J = 8.7, 1.9$ Hz, 2H), 7.24 (dd, $J = 8.7, 1.9$ Hz, 2H); ¹³C-NMR (75 MHz, CDCl₃) δ ppm -4.7, -4.0, 5.8, 9.9, 14.1, 18.1, 19.6, 25.9, 30.1, 30.7, 32.0, 36.5, 40.1, 55.4, 63.9, 67.3, 67.4, 72.8, 75.8, 76.6, 99.2, 113.8, 129.9, 130.8, 159.3; HRMS calculated for C₂₉H₅₂O₆NaSi [$M+Na$]⁺: 547.3431, found: 547.3411.

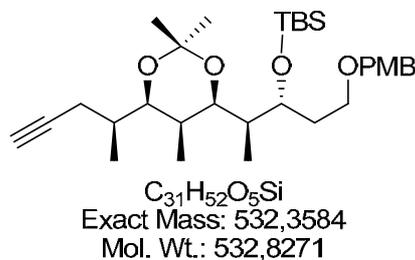
Toluene-4-sulfonic acid (S)-2-{(4R,5S,6R)-6-[(1S,2R)-2-(tert-butyl-dimethyl-silyloxy)-4-(4-methoxy-benzyloxy)-1-methyl-butyl]-2,2,5-trimethyl-[1,3]dioxan-4-yl}-propyl ester



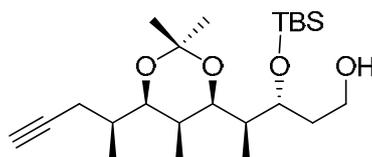
To a cooled (0 °C) solution of alcohol (100 mg, 0.191 mmol) in abs. DCM (3 mL) was added 1,4-Diazabicyclo[2.2.2]octan (85 mg, 0.758 mmol) and p-Toluenesulfonyl chloride (120 mg 0.631 mmol) the reaction mixture was allowed to warm to r.t. After 1 h the mixtures was sequencely washed with 2 N HCl (2 ml), satd aq NaHCO₃ solution (2 mL) and 2 ml water The organic extract was dried (MgSO₄), concentrated in vacuo, and the residue purified by column chromatography. (light petroleum ether/EtOAc 90:10) to give the tosylate (98.3 mg, 76 %) as colourless oil. $R_f = 0,33$ (light petroleum ether/EtOAc 90:10); $[\alpha]_D^{22} = +4.6$ ($c = 0.9$, CHCl₃); ¹H-NMR (300 MHz, CDCl₃) δ ppm 0.00 (s, 3H), 0.03 (s, 3H), 0.86 (s, 9H), 0.84 (d, $J = 7.0$ Hz, 3H), 0.91 (d, $J = 6.6$ Hz, 3H), 0.92 (d, $J = 6.6$ Hz, 3H), 1.31, (s, 3H), 1.34 (s, 3H),

1.50 (m, 2H), 1.65 (m, 1H), 1.78 (m, 1H), 1.88 (m, 1H), 2.41 (s, 3H), 3.41-3.56 (m 4H), 3.78 (s, 3H), 3.81 (ddd, $J = 10.4, 3.7, 1.8$ Hz, 1H), 3.87 (dd, $J = 9.7, 5.9$ Hz, 1H), 3.93 (dd, $J = 9.8, 4.4$ Hz, 1H), 4.39 (d, $J = 11.5$ Hz, 1H), 4.45 (d, $J = 11.5$ Hz, 1H), 6.87 (dd, $J = 8.7, 1.9$ Hz, 2H), 7.24 (dd, $J = 8.7, 1.9$ Hz, 2H), 7.29 (d, $J = 9.7$ Hz, 2H), 7.73 (d, $J = 9.7$ Hz, 2H); ^{13}C -NMR (75 MHz, CDCl_3) δ ppm -4.7, -4.1, 5.7, 9.9, 13.9, 18.1, 19.5, 21.6, 25.8, 29.9, 31.2, 31.8, 34.6, 40.4, 55.3, 67.6, 67.9, 71.2, 72.7, 74.7, 75.8, 99.2, 113.8, 127.9, 129.4, 129.9, 130.8, 133.0, 144.8, 159.1; HRMS calculated for $\text{C}_{36}\text{H}_{58}\text{O}_8\text{NaSSi}$ [$M+\text{Na}$] $^+$: 701.3519, found: 701.2999.

***tert*-Butyl-{(1R,2S)-1-[2-(4-methoxy-benzyloxy)-ethyl]-2-[(4R,5S,6R)-2,2,5-trimethyl-6-((S)-1-methyl-but-3-ynyl)-[1,3]dioxan-4-yl]-propoxy}-dimethyl-silane (9)**

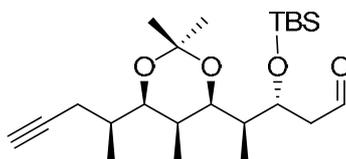


To a cooled (0 °C) solution of tosylate (500 mg, 0.736 mmol) in abs DMSO (3 mL) was added 1.9 mL Sodium acetylide (18 wt. % slurry in xylene). The reaction mixture was allowed to warm to r.t. The resulting red solution was stirred for 30 minutes and then quenched with 1 mL water. The layers were separated and the aqueous phase was extracted with Et_2O (3×5 mL). The combined organic extracts were dried (MgSO_4) and concentrated in vacuo to give colourless oil. Purification of the crude product by column chromatography (light petroleum ether/ EtOAc 95:05) gave the product (282 mg, 72 %) as colourless oil. $R_f = 0,37$ (light petroleum ether/ EtOAc 95:05); $[\alpha]_D^{22} = +3.1$ ($c = 0.40$, CHCl_3); ^1H -NMR (300 MHz, CDCl_3) δ ppm 0.02 (s, 3H), 0.04 (s, 3H), 0.86 (s, 9H), 0.89 (d, $J = 6.7$ Hz, 3H), 0.92 (d, $J = 6.6$ Hz, 3H), 1.05 (d, $J = 6.6$ Hz, 3H), 1.35 (s, 3H), 1.38 (s, 3H), 1.57 (m, 3H), 1.72 (m, 1H), 1.81 (m, 1H), 1.91 (dd, $J = 2.5, 2.5$ Hz, 1H), 3.44-3.52 (m, 4H), 3.80 (s, 3H), 3.88 (ddd, $J = 10.9, 4.0, 2.0$ Hz, 1H) 4.37 (d, $J = 11.1$ Hz, 1H), 4.40 (d, $J = 11.1$ Hz, 1H), 6.86 (dd, $J = 8.7, 1.9$ Hz, 2H), 7.22 (dd, $J = 8.7, 1.9$ Hz, 2H); ^{13}C -NMR (75 MHz, CDCl_3) δ ppm -4.8, -4.1, 5.5, 10.0, 16.4, 18.1, 19.6, 21.0, 25.9, 30.1, 30.4, 31.8, 32.8, 40.3, 55.3, 67.3, 67.5, 69.7, 72.6, 76.3, 77.2, 81.9, 99.1, 113.8, 129.1, 130.8, 159.1; HRMS calculated for $\text{C}_{31}\text{H}_{52}\text{O}_5\text{NaSi}$ [$M+\text{Na}$] $^+$: 555.3482, found: 555.3488.

(3*R*,4*S*)-3-(*tert*-Butyl-dimethyl-silyloxy)-4-[(4*R*,5*S*,6*R*)-2,2,5-trimethyl-6-((*S*)-1-methyl-but-3-ynyl)-[1,3]dioxan-4-yl]-pentan-1-ol

C₂₃H₄₄O₄Si
Exact Mass: 412,3009
Mol. Wt.: 412,6786

To a solution of the product (100 mg, 0.188 mmol) in DCM (6 mL) and pH 7 puffer (0.6 mL) was added 140 mg 2,3-dichloro-5,6-dicyanobenzoquinone (0.617 mmol). The mixture was stirred for 40 min at r.t. before quenched with satd aq NaHCO₃ solution (4 mL). The layers were separated and the aqueous phase was extracted with Et₂O (3 × 5 mL). The combined organic extracts were dried (MgSO₄) and concentrated in vacuo to give brown oil. Purification of the crude product by column chromatography (light petroleum ether/EtOAc 90:10) gave the alcohol (66.7 mg, 86 %) as colourless oil. R_f = 0,36 (light petroleum ether/EtOAc 90:10); [α]²²_D = +7.3 (*c* = 0.4, CHCl₃); ¹H-NMR (300 MHz, CDCl₃) δ ppm 0.09 (6H), 0.89 (s, 9H), 0.91 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 6.6, 3H), 1.06 (d, *J* = 6.6 Hz, 3H), 1.38 (s, 3H), 1.39 (s, 3H), 1.43 (m, 1H), 1.54 (m, 1H), 1.70 (m, 2H), 1.75 (m, 1H), 1.84 (m, 1H), 1.95 (dd, *J* = 2.6, 2.6 Hz, 1H), 2.2 (m, 1H), 3.44 (dd, *J* = 9.6, 1.9 Hz, 1H), 3.50 (dd, *J* = 9.6, 2.2 Hz, 1H), 3.67 (m, 1H), 3.94 (ddd, *J* = 10.0, 4.1, 2.1 Hz, 1H); ¹³C-NMR (75 MHz, CDCl₃) δ ppm -4.7, -4.9, 5.6, 10.0, 16.4, 18.0, 19.6, 21.1, 25.9, 30.0, 30.8, 31.0, 32.5, 33.6, 40.1, 40.4, 60.6, 69.2, 69.8, 76.1, 99.3; HRMS calculated for C₂₃H₄₄O₄NaSi [*M*+Na]⁺: 435.2907, found: 435.2911.

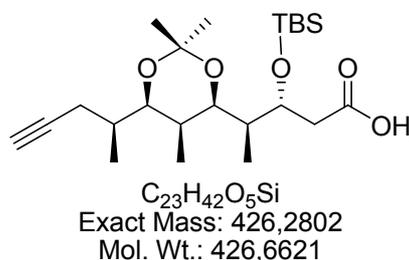
(3*R*,4*S*)-3-(*tert*-Butyl-dimethyl-silyloxy)-4-[(4*R*,5*S*,6*R*)-2,2,5-trimethyl-6-((*S*)-1-methyl-but-3-ynyl)-[1,3]dioxan-4-yl]-pentanal

C₂₃H₄₂O₄Si
Exact Mass: 410,2852
Mol. Wt.: 410,6627

To a mixture of the alcohol (250 mg, 0.605 mmol) and TEA (505 μL, 3.63 mmol) in DMSO (4.8 mL) was added dropwise a solution of SO₃×Pyridine complex (289 mg, 1.82 mmol) in 2 mL DMSO. The mixture was stirred for 30 min at r.t. before diluted with 4.8 mL Et₂O and 4.8

mL EtOAc. The mixture was cooled to 0 °C and quenched with 6 mL of satd aq NH₄Cl solution and water (4 mL). The layers were separated and the aqueous phase was extracted with EtOAc (3 × 8 mL). The combined organic extracts were washed with brine, dried (MgSO₄) and concentrated in vacuo to give colourless oil. Purification of the crude product by column chromatography (light petroleum ether/EtOAc 95:05) gave the aldehyde (223 mg, 90 %) as colourless oil. $R_f = 0.63$ (light petroleum ether/EtOAc 90:10); $[\alpha]_D^{22} = +15.7$ ($c = 0.3$, CHCl₃); ¹H-NMR (300 MHz, CDCl₃) δ ppm 0.05 (s, 3H), 0.09 (s, 3H), 0.86 (s, 9H), 0.91 (d, $J = 6.6$ Hz, 3H), 0.95 (d, $J = 7.0$ Hz, 3H), 1.06 (d, $J = 6.6$ Hz, 3H), 1.36 (s, 3H), 1.38 (s, 3H), 1.50 (m, 1H), 1.75 (m, 1H), 1.89 (m, 1H), 1.93 (dd, $J = 2.9, 2.9$ Hz, 1H), 2.14 (dd, $J = 6.4, 2.8$ Hz, 1H), 2.17 (m, 1H), 2.20 (m, 1H), 2.57 (dd, $J = 9.2, 2.9$ Hz, 1H), 2.59 (dd, $J = 9.2, 3.1$ Hz, 1H), 3.39 (dd, $J = 9.0, 1.7$ Hz, 1H), 3.51 (dd, $J = 9.7, 1.7$ Hz, 1H), 4.29 (ddd, $J = 9.3, 3.9$ Hz, 1H), 9.8 (d, 3.8 Hz, 1H); ¹³C-NMR (75 MHz, CDCl₃) δ ppm -4.8, -4.1, 5.6, 10.1, 16.4, 18.0, 19.6, 21.1, 25.7, 30.0, 31.1, 32.5, 40.5, 46.0, 67.0, 69.9, 75.8, 77.6, 81.6, 94.3, 202.1; HRMS calculated for C₂₃H₄₄O₄Si [$M+H$]⁺: 411.2931, found: 411.2925.

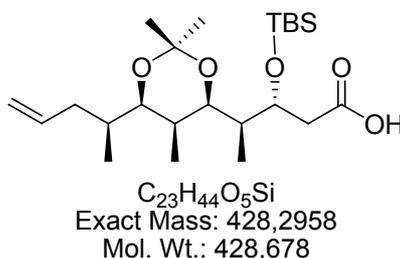
(3*R*,4*S*)-3-(*tert*-Butyl-dimethyl-silyloxy)-4-[(4*R*,5*S*,6*R*)-2,2,5-trimethyl-6-((*S*)-1-methyl-but-3-ynyl)-[1,3]dioxan-4-yl]-pentanoic acid



To a solution of aldehyde (100 mg, 0.243 mmol) in 10 mL *tert*-Butanol was added 2.6 mL water, 3 mL 2-methyl-2-buten, Sodium phosphate (72 mg, 0.60 mmol) and Sodium chlorite (100 mg, 1.11 mmol). The mixture was stirred for 20 min at r.t. and then dissolved with water (4 mL) and EtOAc (6 mL). The layers were separated and the aqueous phase was extracted with EtOAc (2 × 6 mL). The combined organic extracts were dried (MgSO₄) and concentrated in vacuo to give colourless oil. Purification of the crude product by column chromatography (light petroleum ether/EtOAc 85:15) gave the acid (95.4 mg, 92 %) as colourless oil. $R_f = 0.14$ (light petroleum ether/EtOAc 90:10); $[\alpha]_D^{22} = +2.8$ ($c = 0.3$, CHCl₃); ¹H-NMR (300 MHz, CDCl₃) δ ppm 0.05 (s, 3H), 0.09 (s, 3H), 0.86 (s, 9H), 0.91 (d, $J = 6.8$ Hz, 3H), 0.95 (d, $J = 6.8$ Hz, 3H), 1.06 (d, $J = 6.4$ Hz, 3H), 1.37 (s, 3H), 1.38 (s, 3H), 1.55 (ddt, $J = 7.0, 2.0, 2.0$ Hz, 1H), 1.75 (m, 1H), 1.88 (m, 1H), 1.93 (dd, $J = 2.6, 2.6$ Hz, 1H), 2.14 (dd, $J = 6.4, 2.6$ Hz,

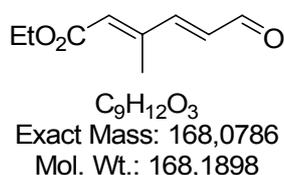
1H), 2.17 (dd, $J = 4.1, 2.7$ Hz, 1H), 2.23 (dd, $J = 15.2, 2.7$ Hz, 1H), 2.45 (dd, $J = 15.2, 8.8$ Hz, 1H), 3.40 (dd, $J = 9.2, 1.7$ Hz, 1H), 3.50 (dd, $J = 9.5, 1.7$, 1H), 4.21 (ddd, $J = 9.1, 3.2, 3.2$ Hz, 1H); ^{13}C -NMR (75 MHz, CDCl_3) δ ppm -4.9, -4.4, 10.0, 16.4, 18.0, 19.6, 21.1, 25.8, 29.8, 30.0, 31.1, 32.6, 37.2, 40.4, 68.6, 69.9, 75.8, 81.7, 99.3, 176.1; HRMS calculated for $\text{C}_{23}\text{H}_{41}\text{O}_5\text{Si}$ $[\text{M}-\text{H}]^-$: 425.2723, found: 425.2720.

(3*R*,4*S*)-3-(*tert*-Butyl-dimethyl-silanyloxy)-4-[(4*R*,5*S*,6*R*)-2,2,5-trimethyl-6-((*S*)-1-methyl-but-3-enyl)-[1,3]dioxan-4-yl]-pentanoic acid (2)



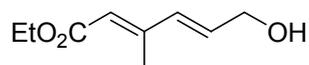
A solution of product (75 mg 0.176 mmol) in MeOH (3 mL) was hydrogenated over Lindlar catalyst (75 mg) at atmospheric pressure for 15 min. After filtration the catalyst was washed with MeOH (2 mL) and the resulting MeOH solution was concentrated by evaporation. The residue was purified by chromatography (light petroleum ether/EtOAc 85:15) gave the product (66.4 mg, 88 %) as colourless oil. $R_f = 0.29$ (light petroleum ether/EtOAc 90:10); $[\alpha]_D^{22} = +10.8$ ($c = 0.4$, CHCl_3); ^1H -NMR (300 MHz, CDCl_3) δ ppm 0.03 (s, 3H), 0.08 (s, 3H), 0.85 (s, 9H), 0.91 (d, $J = 6.5$ Hz, 3H), 0.92 (d, $J = 6.4$ Hz, 3H), 0.98 (d, $J = 6.6$ Hz, 3H), 1.34 (s, 3H), 1.38 (s, 3H), 1.55 (m, 1H), 1.66 (m, 1H), 1.79 (m, 1H), 1.87 (m, 1H), 2.11 (m, 1H), 2.18 (dd, $J = 15.0, 2.2$ Hz, 1H), 2.43 (dd, 14.9, 9.8 Hz, 1H), 3.33 (dd, $J = 7.4, 1.8$ Hz, 1H), 3.36 (dd, $J = 6.9, 1.8$ Hz, 1H), 4.23 (ddd, $J = 9.7, 3.7, 2.5$ Hz, 1H), 5.01 (m, 2H), 5.77 (dddd, $J = 15.9, 10.3, 8.7, 5.7$ Hz, 1H); ^{13}C -NMR (75 MHz, CDCl_3) δ ppm -4.8, -4.4, 5.5, 10.2, 14.2, 18.0, 19.5, 25.8, 30.1, 30.9, 31.3, 32.9, 33.6, 35.9, 40.3, 68.9, 75.8, 98.9, 116.5, 136.2, 177.2; HRMS calculated for $\text{C}_{23}\text{H}_{43}\text{O}_5\text{Si}$ $[\text{M}-\text{H}]^-$: 427.2880, found: 427.2883.

(2*E*,4*E*)-ethyl 3-methyl-6-oxohexa-2,4-dienoate (12)



A flask containing Ph_3PCHCHO (146 mg, 0.481 mmol, 1.0 eq.) was added a solution of (*E*)-Ehyl 3-methyl-4-oxobut-2-enoate (207 μL , 1.52 mmol, 3.0 eq.) in abs. DCM (100 μL). The reaction mixture was stirred for 15 h at room temperature and purified direct by flash chromatography (hexanes / Et_2O = 6:1 to 1:1) to give aldehyde **12** (64.6 mg, 0.384 mmol, 80%) as white needle crystal. R_f = 0.37 (hexanes / EtOAc = 9:1); ^1H NMR (300 MHz, CDCl_3) δ = 1.29 (t, J = 7.2 Hz, 3H), 2.29 (s, 3H), 4.20 (q, J = 7.2 Hz, 2H), 6.11 (s, 1H), 6.43 (dd, J = 15.6, 7.4 Hz, 1H), 7.08 (d, J = 15.6 Hz, 1H), 9.65 (d, J = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ = 13.8, 14.2, 60.5, 127.0, 132.7, 148.6, 154.2, 165.8, 193.3.

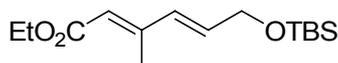
(2*E*,4*E*)-Ethyl 6-hydroxy-3-methylhexa-2,4-dienoate



$\text{C}_9\text{H}_{14}\text{O}_3$
Exact Mass: 170,0943
Mol. Wt.: 170,2057

A solution of sodium borohydride (242 mg, 6.4 mmol, 0.5 eq.) in $\text{EtOH}/\text{H}_2\text{O}$ (1:1, 3 mL) was added to a solution of (2*E*,4*E*)-ethyl 3-methyl-6-oxohexa-2,4-dienoate (2.15 g, 12.8 mmol) in $\text{EtOH}/\text{H}_2\text{O}$ (1:1, 2 mL) at 0 °C. The reaction mixture was stirred at RT for 20 min, saturated with NaCl and extracted with Et_2O (5 x 20 mL). The combined organic extracts were dried over MgSO_4 . Evaporation of the solvent *in vacuo* afforded crude alcohol (3.12 g), which was used for the next steps without further purification. R_f = 0.41 (hexanes / EtOAc = 2:1); ^1H NMR (400 MHz, CDCl_3) δ = 1.27 (t, J = 7.1 Hz, 3H), 2.26 (s, 3H), 4.15 (q, J = 7.1 Hz, 2H), 4.28 (t, J = 4.8, 2H), 5.76 (s, 1H), 6.20 (dt, J = 15.8, 5.1 Hz, 1H), 6.31 (d, J = 15.8 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ = 13.4, 14.3, 59.8, 63.1, 119.7, 133.7, 134.5, 151.4, 167.1.

(2*E*,4*E*)-ethyl 6-(tert-butyldimethylsilyloxy)-3-methylhexa-2,4-dienoate

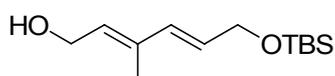


$\text{C}_{15}\text{H}_{28}\text{O}_3\text{Si}$
Exact Mass: 284,1808
Mol. Wt.: 284,4665

To a solution of the crud alcohol (3.12 g) and imidazole (1.13 g, 16.6 mmol, 1.3 eq.) in abs. DMF (2 mL) was added slowly a solution of TBSCl (2.51 g, 16.6 mmol, 1.3 eq.) in abs. DMF (5ml). The reaction mixture was stirred at RT for 30 min. Sat. aq. NaHCO_3 (25 mL) were added, the organic phase separated, and the aq. phase thoroughly extracted with Et_2O (4 x 40 mL). The combined organic extracts were dried over MgSO_4 and concentrated *in vacuo*. After

flash chromatography (hexanes / Et₂O = 9:1) gave TBS-ether (3.25 g, 11.4 mmol, 89%, two steps) as colourless oil. R_f = 0.43 (hexanes / Et₂O = 9:1); ¹H NMR (300 MHz, CDCl₃) δ = 0.07 (s, 6H), 0.91 (s, 9H), 1.27 (t, J = 7.2 Hz, 3H), 2.27 (d, J = 1.5 Hz, 3H), 4.15 (q, J = 7.1 Hz, 2H), 4.30 (dd, J = 4.6, 1.5 Hz, 2H), 5.75 (s, 1H), 6.14 (dt, J = 15.8, 4.6 Hz, 1H), 6.31 (d, J = 15.8 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ = -5.2, 13.9, 14.3, 18.4, 25.9, 59.7, 63.3, 119.0, 132.4, 135.2, 151.8, 167.1; LC-MS (ESI) calculated for C₁₅H₂₈O₃Si: 284.1808, found: 284.1808.

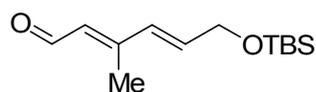
(2E,4E)-6-(tert-butyldimethylsilyloxy)-3-methylhexa-2,4-dien-1-ol



C₁₃H₂₆O₂Si
Exact Mass: 242,1702
Mol. Wt.: 242,4298

To a cooled (0 °C) solution of ester (3.44 g, 12.1 mmol, 1.0 eq.) in THF (50 mL) was added slowly DIBAL-H (1.0 M in hexane, 36.3 mL, 36.3 mmol, 3.0 eq.) in a period of 15 min. The reaction mixture was stirred at 0 °C for 1 h and 200 mL H₂O were added. The organic phase was separated, and the aq. phase extracted with Et₂O (6 × 40 mL). The combined organics were dried over MgSO₄, filtered and evaporated *in vacuo*. Silica gel chromatography (hexanes / Et₂O, gradient elution, 1:1 to 1:2) afforded alcohol (2.85 g, 11.8 mmol, 97%) as a colorless oil. R_f = 0.29 (hexanes / Et₂O = 6:1); ¹H NMR (300 MHz, CDCl₃) δ = 0.06 (s, 6H), 0.90 (s, 9H), 1.78 (s, 3H), 4.24 (d, J = 4.7 Hz, 4H), 5.62 (t, J = 6.6 Hz, 1H), 5.75 (dt, J = 15.6, 5.1 Hz, 1H), 6.24 (d, J = 15.6 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ = -5.2, 12.6, 18.4, 26.0, 59.4, 63.8, 128.6, 129.6, 133.7, 135.8.

(2E,4E)-6-(tert-butyldimethylsilyloxy)-3-methylhexa-2,4-dienal (13)

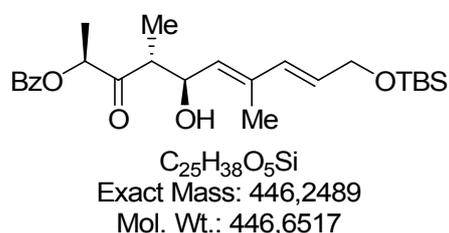


C₁₃H₂₄O₂Si
Exact Mass: 240,1546
Mol. Wt.: 240,414

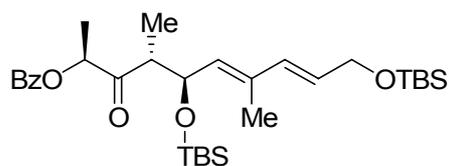
To a stirred solution of alcohol (2.80 g, 11.5 mmol, 1.0 eq.) in Et₂O (10 mL) was added 4 Å MS (7 g) and MnO₂ (15.1 g, 173 mmol, 15 eq.) in portions at 0 °C. The resulting suspension was stirred at room temperature for 30 min. Then the suspension was filtrated through Celite and Silica gel which were washed with Et₂O (10 × 50 mL). The solvent of the filtrate was

removed, to give aldehyde in 95% yield (2.63 g, 10.9 mmol) as yellow oil, which was used for the next step without further purification. $R_f = 0.51$ (hexanes / EtOAc = 6:1); $^1\text{H NMR}$ (300 MHz, CDCl_3) $\delta = 0.07$ (s, 6H), 0.90 (s, 9H), 2.24 (s, 3H), 4.32 (dd, $J = 4.0, 1.4$ Hz, 2H), 5.92 (d, $J = 8.1$ Hz, 1H), 6.30 (dt, $J = 15.6, 4.1$ Hz, 1H), 6.42 (d, $J = 15.6$ Hz, 1H), 10.09 (d, $J = 8.1$ Hz, 1H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) $\delta = -5.3, 13.2, 18.4, 25.9, 63.2, 129.4, 131.9, 137.2, 154.0, 191.4$.

(2*S*,4*R*,5*R*,6*E*,8*E*)-10-(*tert*-butyldimethylsilyloxy)-5-hydroxy-4,7-dimethyl-3-oxodeca-6,8-dien-2-yl benzoate (15)



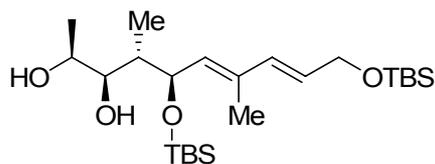
To a stirred solution (-78 °C) of (*S*)-3-oxopentan-2-yl benzoate (1.88 g, 9.12 mmol, 1.0 eq.) in Et_2O (8 mL) was added chlorodicyclohexylborane (3.05 mL, 13.7 mmol, 1.5 eq.) and Me_2NEt (1.9 mL, 18 mmol, 2 eq.). The mixture was warmed to 0 °C, stirred for 2 h and then recooled to -78 °C. A solution of aldehyde (2.63 g, 10.9 mmol, 1.2 eq.) in Et_2O (8 mL) was added dropwise over 2 min. After 3 h, the reaction was kept in the freezer (-22 °C) over night (14 h). The mixture was warmed to 0 °C and quenched by dropwise addition of MeOH (15 mL), pH7 phosphate buffer (15 mL) and 30% H_2O_2 (15 mL) and stirred for 2 h. Water (60 mL) was added, the organic layer was separated and the aqueous layer was extracted with Et_2O (4×50 mL). The combined organics were dried over MgSO_4 , filtered and evaporated *in vacuo*. Silica gel chromatography (hexanes / EtOAc, gradient elution, 9:1 to 6:1) afforded ketone (3.95 g, 8.85 mmol, 97%) as a colorless oil. $R_f = 0.61$ (hexanes / EtOAc = 4:1); $[\alpha]_D^{20} = +30.0$ ($c = 2.16$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3) $\delta = 0.07$ (s, 6H), 0.91 (s, 9H), 1.13 (d, $J = 7.2$ Hz, 3H), 1.55 (d, $J = 7.2$ Hz, 3H), 1.81 (s, 3H), 2.17 (d, $J = 4.3$ Hz, 1H), 2.92 (m, 1H), 4.24 (dd, $J = 5.0, 1.4$ Hz, 2H), 4.70 (m, 1H), 5.36 (d, $J = 9.2$ Hz, 1H), 5.44 (q, $J = 7.0$ Hz, 1H), 5.77 (dt, $J = 15.5, 5.1$ Hz, 1H), 6.23 (d, $J = 15.6$ Hz, 1H), 7.45 (tm, $J = 7.5$ Hz, 2H), 7.57 (tm, $J = 7.4$ Hz, 1H), 8.07 (dm, $J = 7.2$ Hz, 2H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) $\delta = -5.2, 13.3, 14.2, 15.6, 18.4, 26.0, 48.8, 63.7, 70.4, 75.0, 128.5, 129.3, 129.8, 130.9, 133.4, 136.7, 165.9, 211.1$; HRMS calculated for $\text{C}_{25}\text{H}_{38}\text{O}_5\text{SiNa}$ $[\text{M}+\text{Na}]^+$: 469.2386, found: 469.2390.

(2*S*,4*R*,5*R*,6*E*,8*E*)-5,10-bis(tert-butyldimethylsilyloxy)-4,7-dimethyl-3-oxodeca-6,8-dien-2-yl benzoate

$C_{31}H_{52}O_5Si_2$
Exact Mass: 560,3353
Mol. Wt.: 560,9126

To a stirred solution (-78°C) of alcohol (2.70 g, 6.04 mmol, 1.0 eq.) in CH_2Cl_2 (5 mL) was slowly added a solution of Proton-Sponge[®] (1.81 g, 8.46 mmol, 1.4 eq.) in CH_2Cl_2 (15 mL) and TBSOTf (1.52 mL, 6.64 mmol, 1.1 eq.). The mixture was stirred at -78 °C for 20 min. The cooling bath was removed and the reaction quenched with sat. aqueous $NaHCO_3$ (22 mL). The mixture was warmed to room temperature. Et_2O (80 mL) and sat. aqueous $NaHCO_3$ (20 mL) were added. The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 40 mL). The combined organics were washed with sat. aqueous $NaHCO_3$ (50 mL), dried over $MgSO_4$, filtered and evaporated *in vacuo*. Silica gel chromatography (hexanes / Et_2O , gradient elution, 9:1 to 6:1) afforded the desired TBS-ether (2.95 g, 5.26 mmol, 87%) as a white solid. R_f = 0.63 (hexanes / $EtOAc$ = 9:1); $[\alpha]_D^{20}$ = +5.0 (c = 0.52, $CHCl_3$); 1H NMR (300 MHz, $CDCl_3$) δ = -0.06 (s, 3H), -0.04 (s, 3H), 0.07 (s, 6H), 0.80 (s, 9H), 0.91 (s, 9H), 0.99 (d, J = 7.1 Hz, 3H), 1.52 (d, J = 7.1 Hz, 3H), 1.78 (d, J = 1.0 Hz, 3H), 2.89 (m, 1H), 4.24 (dd, J = 5.1, 1.5, 2H), 4.72 (t, J = 9.7 Hz, 1H), 5.26 (d, J = 9.2 Hz, 1H), 5.41 (q, J = 7.0 Hz, 1H), 5.73 (dt, J = 15.3, 5.1 Hz, 1H), 6.21 (d, J = 15.8 Hz, 1H), 7.44 (tm, J = 7.6 Hz, 2H), 7.56 (tm, J = 7.4 Hz, 1H), 8.07 (dm, J = 7.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = -5.1, -4.9, -4.4, 13.5, 14.0, 15.1, 18.0, 18.5, 25.8, 26.0, 49.5, 63.9, 71.7, 75.4, 128.4 (2C), 129.8, 132.8, 133.2, 133.9, 134.6, 165.8, 209.4; HRMS calculated for $C_{31}H_{52}O_5Si_2Na$ $[M+Na]^+$: 583.3251, found: 583.3253.

(2*S*,3*R*,4*S*,5*R*,6*E*,8*E*)-5,10-bis(tert-butyldimethylsilyloxy)-4,7-dimethyldeca-6,8-diene-2,3-diol

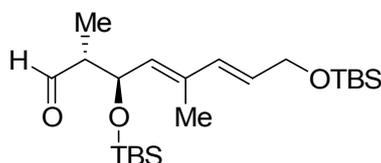


$C_{24}H_{50}O_4Si_2$
Exact Mass: 458,3248
Mol. Wt.: 458,8224

To a cooled ($-78^{\circ}C$) solution of the protected aldol product (1.00 g, 1.78 mmol, 1.0 eq.) in THF (15 mL) was added a solution of $LiBH_4$ (777 mg, 35.6 mmol, 20 eq.) in THF (20 mL). The reaction mixture was warmed slowly to r.t. and stirring was continued for 24 h, before cooling to $0^{\circ}C$ and careful quenching with H_2O (10 mL) and Sat. aq. NH_4Cl (5 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (4×15 mL) and the combined organic extracts washed with brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The colorless residue (1.06 g) was used for the next step without further purification.

$R_f = 0.010$ (hexanes / $EtOAc = 9:1$); $[\alpha]_D^{20} = -9.3$ ($c = 0.67$, $CHCl_3$); 1H NMR (400 MHz, $CDCl_3$) $\delta = 0.005$ (s, 3H), 0.06 (s, 3H), 0.07 (s, 6H), 0.74 (d, $J = 7.1$, 3H), 0.88 (s, 9H), 0.91 (s, 9H), 1.15 (d, $J = 6.6$ Hz, 3H), 1.64 (m, 1H), 1.77 (d, $J = 1.5$ Hz, 3H), 2.52 (d, $J = 7.6$ Hz, 1H), 3.59 (m, 1H), 3.78 (m, 1H), 3.81 (d, $J = 2.0$ Hz, 1H), 4.25 (dd, $J = 5.3, 1.3$, 2H), 4.51 (dd, $J = 9.2, 7.6$ Hz, 1H), 5.36 (d, $J = 9.7$ Hz, 1H), 5.74 (dt, $J = 15.8, 5.1$ Hz, 1H), 6.22 (d, $J = 15.8$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = -5.1, -4.9, -3.9, 12.0, 13.5, 16.3, 18.0, 18.5, 25.8, 26.0, 42.3, 63.9, 68.4, 75.0, 77.6, 128.6, 133.1, 133.8, 133.9$; HRMS calculated for $C_{24}H_{50}O_4Si_2Na$ $[M+Na]^+$: 481.3145, found: 481.3148.

(2*R*,3*R*,4*E*,6*E*)-3,8-bis(tert-butyldimethylsilyloxy)-2,5-dimethylocta-4,6-dienal

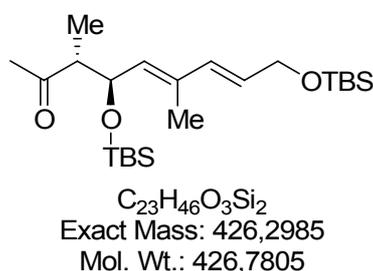


$C_{22}H_{44}O_3Si_2$
Exact Mass: 412,2829
Mol. Wt.: 412,754

To a stirring solution of crude diol (1.06 g) in toluene (10 mL) under an atmosphere of Ar, at r.t., was added $Pb(OAc)_4$ (868 mg, 1.96 mmol, 1.1 equiv) in three portions over 5 min. After 25 min., direct silica gel chromatography (hexanes / Et_2O , 9:1) afforded aldehyde (662 mg,

1.60 mmol, 90%, two steps) as a colorless oil. $R_f = 0.62$ (hexanes / Et₂O = 6:1); $[\alpha]_D^{20} = -15.2$ ($c = 1.29$, CHCl₃); ¹H NMR (300 MHz, CDCl₃) $\delta = -0.03$ (s, 3H), 0.008 (s, 3H), 0.07 (s, 6H), 0.83 (s, 9H), 0.91 (s, 9H), 0.96 (d, $J = 7.2$ Hz, 3H), 1.78 (s, 3H), 2.47 (m, 1H), 4.25 (dd, $J = 5.3, 1.5$ Hz, 2H), 4.63 (dd, $J = 9.1, 7.6$ Hz, 1H), 5.39 (d, $J = 9.2$ Hz, 1H), 5.75 (dt, $J = 15.6, 5.2$ Hz, 1H), 6.22 (d, $J = 15.6$ Hz, 1H), 9.77 (d, $J = 2.8$ Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) $\delta = -5.1, -4.1, 10.5, 13.3, 18.1, 18.5, 25.7, 26.0, 53.3, 63.9, 71.2, 128.8, 132.4, 133.7, 134.2, 204.7$.

(3R,4R,5E,7E)-4,9-bis(tert-butyldimethylsilyloxy)-3,6-dimethylnona-5,7-dien-2-one (16)

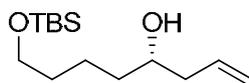


To a stirred solution of the aldehyde prepared above (490 mg, 1.19 mmol, 1.00 eq) in diethyl ether (18 ml) was added MeLi (1.6 M in THF, 2.2 ml, 3.56 mmol, 3.00 eq) at -78 °C. The solution was stirred for 30 min at -78 °C, then for 60 min at -30 °C. Phosphate buffer-solution (15 ml, pH = 7) was added and the mixture was allowed to warm to room temperature. The layers were separated, the aqueous phase was extracted with diethyl ether (4x 15 ml) and the combined organic phases were washed with brine (1x 25 ml) before being dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by column chromatography (60 g SiO₂, hexane/ethyl acetate 9:1) and afforded the corresponding primary alcohol (504 mg, 1.18 mmol, 99%) as a colourless oil: $R_f = 0.33, 0.29$ (hexane/ethyl acetate = 9:1) for the two diastereomers; ¹H NMR (300 MHz, CDCl₃) $\delta = -0.01$ (s, 3H), 0.05 (s, 3H), 0.07 (s, 6H), 0.87 (s, 9H), 0.91 (s, 9H), 0.93 (d, $J = 7.3$ Hz, 3H), 1.11 (d, $J = 6.4$ Hz, 3H), 1.73 (d, $J = 1.1$ Hz, 3H), 1.51 (m, 1H), 3.54 (d, $J = 2.8$ Hz, 1H), 4.17 (m, 1H), 4.24 (dd, $J = 5.4, 1.4$ Hz, 2H), 4.52 (dd, $J = 8.7, 4.7$ Hz, 1H), 5.56 (d, $J = 8.7$ Hz, 1H), 5.72 (dt, $J = 15.6, 5.3$ Hz, 1H), 6.22 (d, $J = 15.6$ Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) $\delta = -5.1, -4.2, 10.9, 13.1, 18.0, 18.5, 25.8, 26.0, 44.2, 64.0, 67.7, 75.1, 128.1, 132.8, 134.0, 134.2$. HRMS (ESI) calculated for C₂₃H₄₈NaO₃Si₂⁺ [M+Na]⁺: 451.3034, found: 451.3041.

To a stirred solution of the above prepared alcohol (415 mg, 0.97 mmol, 1.00 eq) in dichloromethane (3 ml) was added NaHCO₃ (187 mg, 2.23 mmol, 2.30 eq), then a solution of Dess-Martin-Periodinan (492 mg, 1.16 mmol, 1.20 eq) in dichloromethane (7 ml) at room

temperature. After stirring for 90 min sat. aqueous NaHCO₃ (7 ml) and sat. aqueous Na₂SO₃ (7 ml) were added subsequently. The mixture was again stirred for 10 min. The layers were separated and the aqueous phase was extracted with dichloromethane (4x 10 ml). The combined organic phases were washed with brine (1x 20 ml), dried over MgSO₄ and concentrated *in vacuo*. Column chromatography (40 g SiO₂, dichloromethane/0.3% ethyl acetate) afforded the desired (393 mg, 0.92 mmol, 95 %) as a colourless oil. $R_f = 0.50$ (hexanes / Et₂O = 9:1); $[\alpha]_D^{20} = -7.1$ ($c = 0.17$, CHCl₃); ¹H NMR (400 MHz, CDCl₃) $\delta = -0.07$ (s, 3H), -0.04 (s, 3H), 0.07 (s, 6H), 0.80 (s, 9H), 0.85 (d, $J = 6.6$ Hz, 3H), 0.90 (s, 9H), 1.78 (s, 3H), 2.18 (s, 3H), 2.67 (m, 1H), 4.24 (dd, $J = 5.3, 1.3$ Hz, 2H), 4.55 (t, $J = 9.4$ Hz, 1H), 5.26 (d, $J = 9.2$ Hz, 1H), 5.72 (dt, $J = 15.3, 5.7$ Hz, 1H), 6.21 (d, $J = 15.8$ Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) $\delta = -5.1, -4.2, 13.0, 13.5, 18.0, 18.5, 25.8, 26.0, 31.5, 53.3, 63.9, 72.5, 128.5, 132.9, 133.9, 134.3, 212.4$; HRMS calculated for C₂₃H₄₆O₃Si₂Na [M+Na]⁺: 449.2883, found: 449.2881.

(S)-8-(tert-butyldimethylsilyloxy)oct-1-en-4-ol



Chemical Formula: C₁₄H₃₀O₂Si

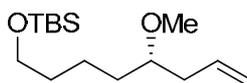
Exact Mass: 258,2015

Molecular Weight: 258,4723

A round-bottomed flask was charged with 4.13 g copper(I) iodide (21.7 mmol, 1 eq.), gently heated under vacuum, and then slowly cooled under a flow of argon. Then THF (100 mL) was added and the resulting suspension was cooled to -20 °C, stirred, and 86.8 mL vinylmagnesium bromide (1M in THF, 86.8 mmol, 4 eq.) added. A solution of 5.00 g epoxide **17** (21.7 mmol, 1eq.) in 75 mL THF was added to the cooled reagent and the mixture was stirred at -20 °C for 1 h. The reaction was quenched with 250 mL saturated aqueous NH₄Cl. The water layer was extracted with EtOAc (3x300 mL) and the combined organic layers were washed with brine (1x300 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo*. The resulting light brown liquid was purified via flash chromatography (hexane/ethyl acetate 10:1) to yield 5.41 g (97%) as a colorless liquid. $R_f = 0.26$ (hexane/ethyl acetate, 10:1); $[\alpha]_D^{20} = -4.8$ ($c = 1.00$, CHCl₃); ¹H NMR (300 MHz, CDCl₃) $\delta = 5.75 - 5.91$ (m, 1 H), 5.09 - 5.18 (m, 2 H), 3.64 - 3.71 (m, 1 H), 3.62 (t, $J = 6.2$ Hz, 2 H), 2.06 - 2.38 (m, 2 H), 1.71 (s, 1 H), 1.32 - 1.61 (m, 6 H), 0.89 (s, 9 H), 0.05 (s, 6 H); ¹³C NMR (75 MHz, CDCl₃) $\delta = 135.3,$

118.5, 71.0, 63.5, 42.3, 36.9, 33.1, 26.4, 22.4, 18.8, -4.88; HRMS calculated for $\text{NaC}_{14}\text{H}_{30}\text{O}_2\text{Si}$ $[\text{M}+\text{Na}]^+$: 281.1913, found: 281.1907.

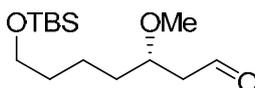
(S)-tert-butyl(5-methoxyoct-7-enyloxy)dimethylsilane (18)



Chemical Formula: $\text{C}_{15}\text{H}_{32}\text{O}_2\text{Si}$
Exact Mass: 272,2172
Molecular Weight: 272,4989

To a cooled (0 °C) suspension of 1.02 g NaH (60% in mineral oil, 25.4 mmol, 1.64 eq.) in 75 ml THF was added a solution of the alcohol (4.00 g, 15.5 mmol, 1 eq.) in 75 ml THF dropwise. Then 4.23 mL iodomethane (68.2 mmol, 4.41 eq.) was added. The reaction mixture was allowed to warm to room temperature slowly in a cold water bath and stirred for 72 h. After that 8 mL water were added at 0 °C to quench the reaction. The solvent was removed under reduced pressure and subsequently 80 mL of water and 60 mL dichloromethane were added and the layers separated. The aqueous layer was extracted with 2x40 mL dichloromethane. The combined organic phases were washed with 120 mL of brine, dried over MgSO_4 , concentrated *in vacuo* providing the crude product as a colorless liquid (4.22 g, 100%). $R_f = 0.78$ (hexane/ethyl acetate, 9:1); $[\alpha]_D^{20} = -9.3$ ($c = 1.00$, CHCl_3); ^1H NMR (300 MHz, CDCl_3) $\delta = 5.73 - 5.90$ (dddd, $J = 7.2, 7.2, 10.4, 17.3$ Hz, 1 H), 5.02 - 5.13 (m, 2 H), 3.61 (t, $J = 6.2$ Hz, 2 H), 3.34 (s, 3 H), 3.21 (quin, $J = 5.7$ Hz, 1 H), 2.26 (t, $J = 6.6$ Hz, 2 H), 1.25 - 1.60 (m, 6 H), 0.89 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (75 MHz, CDCl_3) $\delta = 134.9, 116.8, 80.42, 63.1, 56.6, 37.7, 33.1, 32.9, 26.0, 21.6, 18.3, -5.3$; HRMS calculated for $\text{NaC}_{15}\text{H}_{32}\text{O}_2\text{Si}$ $[\text{M}+\text{Na}]^+$: 295.2069, found: 295.2071.

(S)-7-(tert-butyl dimethylsilyloxy)-3-methoxyheptanal

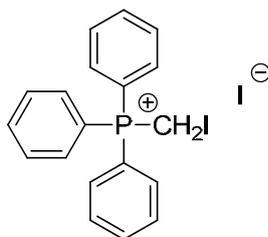


Chemical Formula: $\text{C}_{14}\text{H}_{30}\text{O}_3\text{Si}$
Exact Mass: 274,1964
Molecular Weight: 274,4717

To a precooled (-78 °C) solution of the respective alkene (143 mg, 0.52 mmol, 1.0 eq.) in DCM (6 mL) was bubbled ozone until a light blue color persisted in the solution (c.a. 15 min).

The excess of ozone was removed by exchanging with argon repeatedly and triphenylphosphine (682 mg, 2.60 mmol, 5.0 eq.) was added. The mixture was slowly warmed to room temperature and stirred for 1.5 h. The solvent was removed *in vacuo* and the residue was chromatographed on silica gel (50.0 g, Hexanes / AcOEt = 20 : 1 to 3: 1) to afford the aldehyde as colorless liquid (143 mg, 99%) which was used for next step immediately. $R_f = 0.29$ (Hexanes / EtOAc = 9:1); $[\alpha]_D^{23} = +9.1$ ($c = 1.0$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3) $\delta = 0.05$ (s, 6H), 0.89 (s, 9H), 1.30-1.73 (m, 6H), 2.52 (ddd, $J = 16.2, 4.9, 1.9$ Hz, 1H), 2.61 (ddd, $J = 16.2, 7.0, 2.4$ Hz, 1H), 3.35 (s, 3H), 3.61 (t, $J = 6.2$ Hz, 2H), 3.67-3.76 (m, 1H), 9.81 (t, $J = 2.1$ Hz, 1H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) $\delta = -5.3, 18.3, 21.4, 25.9, 32.7, 33.6, 48.0, 56.8, 62.9, 76.3, 201.6$.

Preparation of (iodomethyl)triphenylphosphonium iodide



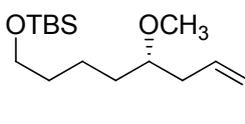
Chemical Formula: $\text{C}_{19}\text{H}_{17}\text{I}_2\text{P}^+$

Exact Mass: 529.9152

Molecular Weight: 530.1204

A solution of PPh_3 (50.0 g, 0.19 mol, 1.00 eq) and diiodomethane (20.0 ml, 0.25 mmol, 1.30 eq) in 250 ml toluene was heated to 50 °C and stirred for 96 h in the absence of light. The mixture was cooled down to room temperature and filtered. The precipitate was washed with dry toluene and dry diethylether subsequently, then dried under vacuum to yield a colourless solid (56.8 g, 0.11 mol, 56 %). $^1\text{H-NMR}$ (300 MHz, DMSO-d_6) $\delta = 5.08$ (d, $J = 8.9$ Hz, 2 H), 7.73-7.96 (m, 15 H). $^{13}\text{C-NMR}$ (75 MHz, DMSO-d_6) $\delta = 117.9, 119.1, 130.4, 134.1, 135.5$. MS calculated for $\text{C}_{19}\text{H}_{17}\text{IP}^+ [\text{M}]^+ = 529.9$; found 529.5.

(*S,Z*)-tert-butyl(8-iodo-5-methoxyoct-7-enyloxy)-dimethylsilane



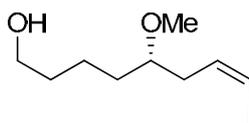
Chemical Formula: $\text{C}_{15}\text{H}_{31}\text{IO}_2\text{Si}$

Exact Mass: 398,1138

Molecular Weight: 398,3954

In the absence of light, to a solution of NaHMDS (1.0 M in THF, 2.96 mL, 2.96 mmol, 1.5 eq.) in absolute THF (58 mL) was added a suspension of the phosphonium iodide (1.57 g, 2.96 mmol, 1.5 eq.) in anhydrous HMPA (dried over 4 Å molecular sieves, 4.0 mL and 2 x 2.5 mL washes) at 10-15 °C (ice-water bath). After 1 min, the mixture was cooled to -78 °C and a solution of the aldehyde (541 mg, 1.97 mmol, 1.0 eq.) in THF (1.0 mL and 2 x 0.5 mL washes) was added dropwise. After stirred at -78 °C for 20 min, the reaction was quenched by addition of aqueous saturated NH₄Cl (25 mL) and water (10 mL). When warmed to room temperature, the insoluble solids were filtered off and the layers of the filtrate were separated. The aqueous layer was extracted with diethyl ether (3 x 25 mL). The combined organic phases were washed with brine (40 mL), dried over MgSO₄, filtered and concentrated. Flash chromatography on silica gel (80 g, hexanes / Et₂O = 35 : 1 to 12:1) afforded the vinyl iodide (607 mg, 1.52 mmol, 77%, Z : E = 27 : 1). R_f = 0.68 (hexanes / EtOAc = 9 : 1); $[\alpha]_D^{23}$ = -9.9 (c = 2.0, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ = 0.06 (s, 6H), 0.90 (s, 9H), 1.36-1.60 (m, 6H), 2.30-2.43 (m, 2H), 3.30 (m, 1H), 3.36 (s, 3H), 3.61 (d, J = 6.6 Hz, 1H), 3.63 (d, J = 6.1 Hz, 1H), 6.24-6.32 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ = -5.2, 18.4, 21.8, 26.0, 32.9, 33.5, 38.6, 56.7, 63.1, 79.6, 84.1, 137.7; HRMS calculated for C₁₅H₃₁IO₂SiNa [M+Na]⁺: 421.1036, found: 421.1039.

(S,Z)-8-iodo-5-methoxyoct-7-en-1-ol



Chemical Formula: C₉H₁₇IO₂

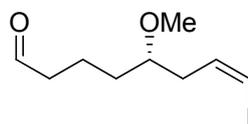
Exact Mass: 284,0273

Molecular Weight: 284,1345

A solution of the TBS ether (870 mg, 2.18 mmol, 1.0 eq.) and (±)-camphor-10-sulfonic acid (152 mg, 0.65 mmol, 0.3 eq.) in MeOH (20 mL) was stirred at room temperature for 15 min then diluted with EtOAc (140 mL). The mixture was washed with aqueous saturated NaHCO₃ (2 x 30 mL) and brine (30 mL). The combined aqueous phases were extracted with EtOAc (2 x 25 mL). The combined organic phases were dried over MgSO₄, filtered and concentrated to produce the alcohol (611 mg, 2.15 mmol, 99%) as essentially pure form which was used directly for next step. R_f = 0.39 (hexanes / EtOAc = 1 : 1); $[\alpha]_D^{23}$ = -20.1 (c = 1.0, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ = 1.40-1.64 (m, 6H), 2.30-2.45 (m, 2H), 3.32 (m, 1H), 3.36 (s, 3H), 3.66 (t, J = 6.4 Hz, 2H), 6.22-6.33 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ = 21.7, 32.8,

33.5, 38.5, 56.8, 62.8, 79.5, 84.2, 137.5; HRMS calculated for $C_9H_{17}IO_2Na$ $[M+Na]^+$: 307.0171, found: 307.0176.

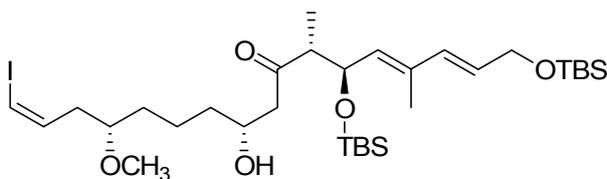
(S,Z)-8-iodo-5-methoxyoct-7-enal (19)



Chemical Formula: $C_9H_{15}IO_2$
Exact Mass: 282,0117
Molecular Weight: 282,1187

At room temperature, to a solution of the alcohol (32.0 mg, 110 μ mol, 1.0 eq.) in anhydrous DMSO (700 μ L) was added triethylamine (93.5 μ L, 670 μ mol, 6.0 eq.) then a solution of sulphur trioxide pyridine complex (53.5 mg, 340 μ mol, 3.0 eq.) in anhydrous DMSO (300 μ L) dropwise over 10 min. After addition, the light yellow clear mixture was stirred at room temperature for additional 60 min, followed by dilution with diethyl ether (1.0 mL) and EtOAc (1.0 mL). The mixture was cooled to 0 $^{\circ}$ C and aqueous saturated NH_4Cl (2.0 mL) was added. The whole mixture was extracted with EtOAc (3 x 3.0 mL) and the combined organics were washed brine (3.0 mL), dried over $MgSO_4$, filtered and concentrated. Column chromatography of the residue produced the pure aldehyde as colorless liquid (30.0 mg, 106 μ mol, 94%) which is used immediately for next step. R_f = 0.66 (hexanes / EtOAc = 1 : 1); $[\alpha]_D^{23}$ = -6.6 (c = 1.0, $CHCl_3$); 1H NMR (300 MHz, $CDCl_3$) δ = 1.47-1.56 (m, 2H), 1.61-1.84 (m, 2H), 2.35-2.40 (m, 2H), 2.46 (td, J = 7.2, 1.6 Hz, 2H), 3.32 (m, 1H), 3.36 (s, 3H), 6.21-6.34 (m, 2H), 9.77 (t, J = 1.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 18.2, 33.1, 38.3, 43.8, 56.8, 79.2, 84.5, 137.2, 202.4.

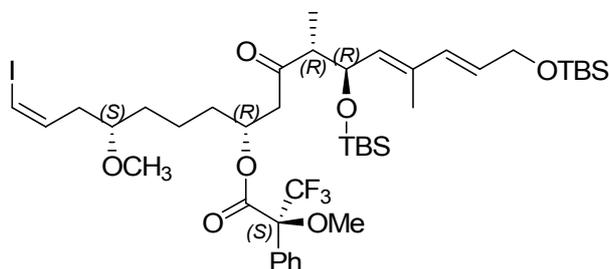
(2E,4Z,6R,7R,10R,14S,16Z)-1,6-bis(*tert*-butyldimethylsilyloxy)-10-hydroxy-17-iodo-14-methoxy-4,7-dimethylheptadeca-2,4,16-trien-8-one (20)



$C_{32}H_{61}IO_5Si_2$
Exact Mass: 708,3102
Mol. Wt.: 708,8992

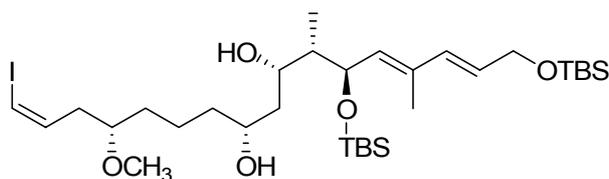
A Schlenk-flask was charged with (+)-DIPCl under inert gas (glove box) to avoid any traces of moisture. (+)-DIPCl was further dried under high vacuum for 4 h to remove traces of HCl. A stirred solution of ketone **16** (243 mg, 0.57 mmol, 1.00 eq) in diethyl ether (0.7 ml) was cooled down to 0 °C. Dry NEt₃ (240 µl, 1.71 mmol, 3.00 eq) and a solution of (+)-DIPCl (475 mg, 1.48 mmol, 2.60 eq) in diethyl ether (2.0 ml) were added subsequently and stirred for 60 min at 0 °C. The white suspension was cooled down to -78 °C and a solution of aldehyde **19** (177 mg, 0.63 mmol, 1.10 eq) in diethyl ether (1.4 ml) was added slowly. The mixture was stirred for 1 h at -78 °C and 3 h at -20 °C. Then it was put into the fridge for 17 h at -20 °C (without stirring) until TLC indicated no more **16** ($R_f = 0.50$ (hexane/ethyl acetate = 9:1) left. The solution was stirred at -20 °C and phosphate buffer solution (5 ml, pH = 7) was added before warming to room temperature (30 min). The layers were separated, the aqueous phase was extracted with diethyl ether (4x 2 ml) and the combined organic phases were concentrated *in vacuo*. The residue was diluted in methanol (6 ml), phosphate buffer solution (3 ml), stirred and cooled down to 0 °C. H₂O₂ (1.0 ml, 30% aqueous solution) was added and the mixture was stirred for 2.5 h at 0 °C. Dichloromethane (6 ml) and water (6 ml) were added. The layers were separated and the aqueous phase was extracted with dichloromethane (4x 5 ml). The combined organic phases were dried over MgSO₄, filtered and concentrated *in vacuo*. The colourless residue could be purified either by flash chromatographed (hexanes / EtOAc, gradient elution, 9:1 to 4:1) to yield an aldol adduct (289 mg, 0.408 mmol, 76%) as a colorless oil. $R_f = 0.11$ (hexanes / EtOAc = 9:1); $[\alpha]_D^{20} = -34.1$ ($c = 0.73$, CHCl₃); ¹H NMR (600 MHz, CDCl₃) $\delta = -0.06$ (s, 3H), -0.04 (s, 3H), 0.07 (s, 6H), 0.80 (s, 9H), 0.85 (d, $J = 7.0$ Hz, 3H), 0.91 (s, 9H), 1.44 (m, 6H), 1.79 (s, 3H), 2.35 (m, 2H), 2.56 (dd, $J = 18.3, 9.5$ Hz, 1H), 2.65 (m, 3H), 2.75 (dd, $J = 18.3, 2.2$ Hz, 1H), 3.18 (s, 1H), 3.30 (m, 1H), 3.34 (s, 3H), 4.05 (m, 1H), 4.25 (d, $J = 5.3$ Hz, 2H), 4.57 (t, $J = 9.3$ Hz, 1H), 5.24 (d, $J = 9.2$ Hz, 1H), 5.74 (dt, $J = 15.8, 5.1$ Hz, 1H), 6.21 (d, $J = 15.8$ Hz, 1H), 6.24 (q, $J = 6.6$ Hz, 1H), 6.29 (d, $J = 7.3$ Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) $\delta = -5.1, -4.2, 13.0, 13.5, 18.0, 18.5, 21.4, 25.8, 26.0, 33.6, 36.2, 38.5, 51.4, 53.0, 56.7, 63.9, 67.0, 72.6, 79.5, 84.2, 128.7, 132.6, 133.7, 134.6, 137.6, 215.9$; HRMS calculated for C₃₂H₆₁IO₅Si₂Na [M+Na]⁺: 731.3000, found: 731.3000.

(S)-((1Z,4S,8R,11R,12R,13E,15E)-12,17-bis(*tert*-butyldimethylsilyloxy)-1-iodo-4-methoxy-11,14-dimethyl-10-oxoheptadeca-1,13,15-trien-8-yl) 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate



C₄₂H₆₈F₃IO₇Si₂
 Exact Mass: 924,35
 Mol. Wt.: 925,0558

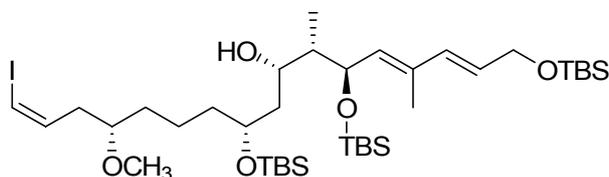
To a stirred solution of (2*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoic acid (3.5 mg, 14.8 μ mol, 5.1 eq.), Et₃N (2.0 μ L, 16.2 μ mol, 5.6 eq.) and DMAP (2.0 mg, 16.4 μ mol, 5.6 eq.) in toluene (50 μ L) were added 2,4,6-Trichlorobenzoyl chloride (2.3 μ L, 14.8 μ mol, 5.1 eq.) and a solution of alcohol (2.0 mg, 2.9 μ mol, 1.0 eq.) in toluene (100 μ L) at room temperature. The resulted white slurry was stirred at room temperature for 20 minutes before being quenched with pH7 phosphate buffer (0.5 mL) and H₂O (1 mL) at 0 °C. DCM (2 mL) was added and the layers were separated. The aqueous layer was extracted with DCM (3 \times 2 mL). The combined organic extracts were dried (MgSO₄) and concentrated *in vacuo*. Flash column chromatography (hexanes / EtOAc = 6:1) afforded the ester (2.4 mg, 2.6 μ mol, 90%) as a colorless oil. R_f = 0.50 (hexanes / EtOAc = 9:1); ¹H NMR (300 MHz, CDCl₃) δ = -0.07 (s, 3H), -0.06 (s, 3H), 0.07 (s, 6H), 0.68 (d, J = 7.0 Hz, 3H), 0.79 (s, 9H), 0.91 (s, 9H), 1.49 (m, 4H), 1.68 (m, 2H), 1.76 (s, 3H), 2.33 (t, J = 5.6 Hz, 2H), 2.55 (m, 1H), 2.68 (dd, J = 18.3, 4.1 Hz, 1H), 2.90 (dd, J = 18.3, 8.1 Hz, 1H), 3.25 (m, 1H), 3.32 (s, 3H), 3.52 (s, 3H), 4.25 (d, J = 5.1 Hz, 2H), 4.52 (t, J = 9.4 Hz, 1H), 5.21 (d, J = 9.2 Hz, 1H), 5.55 (m, 1H), 5.73 (dt, J = 15.6, 5.1 Hz, 1H), 6.22 (m, 2H), 6.30 (m, 1H), 7.37 (m, 3H), 7.52 (m, 2H).

(1Z,4S,8R,10S,11S,12R,13Z,15E)-12,17-bis(*tert*-butyldimethylsilyloxy)-1-iodo-4-methoxy-11,14-dimethylheptadeca-1,13,15-triene-8,10-diol

$C_{32}H_{63}IO_5Si_2$
Exact Mass: 710,3259
Mol. Wt.: 710,9151

To a solution of acetic acid (1.6 mL) in acetonitrile (1.6 mL) was added tetramethylammonium triacetoxyborohydride (274 mg, 1.04 mmol, 4.7 eq.). After stirring for 15 min at room temperature, the mixture was added to a cold (-40 °C) stirred, solution of β -hydroxy ketone (157 mg, 0.221 mmol, 1.0 eq.) in 5:2 acetonitrile/THF (3.2 mL) via cannula. The mixture was then placed in a -20 °C freezer for 40 h (without stirring). The reaction was quenched at -20 °C with a saturated aqueous solution of potassium sodium tartrate tetrahydrate (20 mL) and was stirred for 30 min while warming to room temperature. The mixture was diluted with CH_2Cl_2 (25 mL) and the layers were separated. The aqueous phases were extracted with CH_2Cl_2 (4 \times 15 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ (1 \times 20 mL), and dried ($MgSO_4$), filtered, and concentrated to give a yellow oil. Purification by flash chromatography (hexanes / EtOAc, gradient elution, 6:1 to 4:1) afforded diol (144 mg, 0.203 mmol, 92%) as a clear, colorless oil. $R_f = 0.33$ (hexanes / EtOAc = 4:1); $[\alpha]_D^{20} = -19.0$ ($c = 0.76$, $CHCl_3$); 1H NMR (600 MHz, $CDCl_3$) $\delta = 0.003$ (s, 3H), 0.06 (s, 3H), 0.07 (s, 6H), 0.67 (d, $J = 7.0$ Hz, 3H), 0.87 (s, 9H), 0.91 (s, 9H), 1.41 (m, 2H), 1.54 (m, 4H), 1.65 (m, 2H), 1.74 (m, 1H), 1.76 (s, 3H), 2.35 (m, 2H), 3.30 (m, 1H), 3.34 (s, 3H), 3.50 (s, 1H), 3.93 (m, 2H), 4.25 (dd, $J = 5.3, 1.2$ Hz, 2H), 4.42 (t, $J = 8.9$ Hz, 1H), 4.76 (s, 1H), 5.34 (d, $J = 9.1$ Hz, 1H), 5.74 (dt, $J = 15.5, 5.3$ Hz, 1H), 6.22 (d, $J = 15.3$ Hz, 1H), 6.26 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) $\delta = -5.1, -3.7, 12.8, 13.6, 18.0, 18.5, 21.7, 25.8, 26.0, 33.8, 37.6, 38.5, 39.4, 44.1, 56.7, 63.9, 68.7, 74.2, 76.5, 79.5, 84.1, 128.8, 133.5, 133.8, 133.9, 137.7$; HRMS calculated for $C_{32}H_{63}IO_5Si_2Na$ $[M+Na]^+$: 733.3157, found: 733.3156.

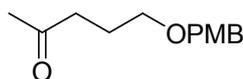
(5R,7S,8S,9R,10Z,12E)-9-(tert-butylidimethylsilyloxy)-5-((S,Z)-7-iodo-4-methoxyhept-6-enyl)-2,2,3,3,8,11,16,16,17,17-decamethyl-4,15-dioxo-3,16-disilaoctadeca-10,12-dien-7-ol
(4)



$C_{38}H_{77}IO_5Si_3$
Exact Mass: 824,4123
Mol. Wt.: 825,1759

A flask containing diol (235 mg, 0.330 mmol, 1.0 eq.), imidazole (112 mg, 1.65 mmol, 5.0 eq.) and TBSCl (124 mg, 0.826 mmol, 2.5 eq.) was charged with argon and abs. DCM (1.1 ml) was added. The reaction mixture was stirred at RT for 30 min. Sat. aq. NaHCO₃ (5 mL) were added, the organic phase separated, and the aq. phase thoroughly extracted with DCM (3 × 10 mL). The combined organic extracts were dried over MgSO₄ and concentrated *in vacuo*. After flash chromatography (hexanes / Et₂O = 9:1) gave TBS-ether (172 mg, 0.208 mmol, 63%, 77%) as colourless oil. $R_f = 0.60$ (hexanes / EtOAc = 9:1); $[\alpha]_D^{20} = -14.4$ ($c = 1.18$, CHCl₃); ¹H NMR (600 MHz, CDCl₃) $\delta = -0.025$ (s, 3H), 0.029 (s, 3H), 0.066 (s, 3H), 0.072 (s, 6H), 0.083 (s, 3H), 0.75 (d, $J = 7.0$ Hz, 3H), 0.86 (s, 9H), 0.88 (s, 9H), 0.91 (s, 9H), 1.32 (m, 1H), 1.41 (m, 2H), 1.49 (m, 4H), 1.63 (m, 2H), 1.77 (d, $J = 1.1$ Hz, 3H), 2.34 (m, 2H), 3.27 (m, 1H), 3.33 (s, 3H), 3.76 (m, 1H), 3.85 (d, $J = 2.2$ Hz, 1H), 4.00 (m, 1H), 4.24 (dd, $J = 5.5, 1.1$ Hz, 2H), 4.52 (dd, $J = 9.2, 6.6$ Hz, 1H), 5.36 (d, $J = 9.2$ Hz, 1H), 5.70 (dt, $J = 15.4, 5.5$ Hz, 1H), 6.21 (d, $J = 15.4$ Hz, 1H), 6.24 (q, $J = 6.8$ Hz, 1H), 6.29 (d, $J = 7.7$ Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) $\delta = -5.1, -4.8, -4.5, -4.2, -3.9, 11.8, 13.4, 18.1, 18.5, 21.3, 25.9, 26.0, 34.0, 37.5, 38.5, 40.0, 46.0, 56.7, 64.1, 70.2, 70.5, 73.5, 79.5, 84.2, 127.9, 133.3, 133.9, 134.4, 137.6$; HRMS calculated for C₃₈H₇₇IO₅Si₃Na [M+Na]⁺: 847.4021, found: 847.4019.

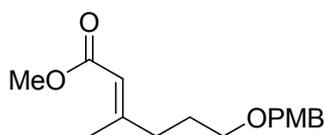
4-(4-methoxybenzyloxy)pentan-2-one



$C_{13}H_{18}O_3$
Exact Mass:
222,1256
Molecular Weight:
222,2802

A solution of CSA (3.36 g, 10.41 mmol, 0.04 eq) in 100 ml CH₂Cl₂ was treated with 3-acetyl-1-propanol (25.00 g, 243.59 mmol, 1.01 eq) in 30 ml CH₂Cl₂. At room temperature, a solution of 4-methoxybenzyl-2,2,2-trichloroacetimidate (68.36 g, 241.95 mmol) in 30 ml CH₂Cl₂ was added and the resulting yellow solution was stirred over night. The white precipitate was removed by filtration. The solution was washed with sat. aqueous NaHCO₃ (200 mL) and the aqueous phase was extracted twice with MTBE (200 ml). The combined organic phases were washed with sat. aqueous NaHCO₃ (300 mL) and brine (100 mL). The organic phase was dried (MgSO₄) and the solvent evaporated *in vacuo*. Silica gel chromatography (hexanes / EtOAc = 3:1) afforded the PMB-protected ketone (41.69 g, 187.56 mmol, 77%) as a yellow oil. R_f = 0.32 (hexanes / EtOAc = 3:1); ¹H NMR (300 MHz, CDCl₃) δ = 1.84 (ddd, J = 13.4, Hz J = 7.2 Hz, J = 6.2 Hz, 2H), 2.10 (s, 3H), 2.51 (t, J = 7.3 Hz, 2H), 3.43 (t, J = 6.1 Hz, 2H), 3.77 (s, 3H), 4.38 (s, 2H), 6.83-6.87 (m, 2H), 7.19-7.25 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ = 23.8, 29.9, 40.3, 55.2, 68.9, 72.5, 113.8, 129.2, 130.4, 159.1, 208.8. The spectroscopic data were in agreement to those previously reported.⁵

(E)-methyl 6-(4-methoxybenzyloxy)-3-methylhex-2-enoate



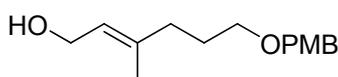
C₁₆H₂₂O₄
Exact Mass: 278,1518
Molecular Weight:
278,3435

To a cooled (0 °C), stirred solution of the Trimethyl phosphonoacetate (22.16 g, 121.80 mmol, 1.25 eq) in THF (180 mL) was added Potassium bis(trimethylsilyl)amide solution (243.60 mL, ~ 0.5 M in toluene, 121.80 mmol, 1.25 eq) over a period of 45 min. The mixture was stirred for 15 min at 0 °C, 30 min at ambient temperature, then a solution of 4-(4-methoxybenzyloxy)pentan-2-one (21.58 g, 97.44 mmol) in THF (10 mL) was added. After stirring for 17 h at ambient temperature, the reaction mixture was quenched with brine (600 mL). The organic layer was separated and the aqueous layer was extracted three times with CH₂Cl₂ (150 mL). The combined organic layers were dried over MgSO₄ and concentrated in vacuum. The residue was purified by column chromatography on silica gel

⁵ K. A. H. Chehade, K. Kiegiel, R. J. Isaacs, J. S. Pickett, K. E. Bowers, C. A. Fierke, D.A. Andres, H. P. Spielmann *J. Am. Chem. Soc.* **2002**, *124*, 8206-8219

(hexanes / EtOAc = 6:1) to give the ester as an *E/Z* mixture (3:1) (16.82 g, 60.41 mmol, 62 %) as a colourless oil. $R_f = 0.49$ (hexanes / Et₂O = 6:1); ¹H NMR (300 MHz, CDCl₃, data for major diastereomer) $\delta = 1.71$ -1.82 (m, 2H), 2.14 (d, $J = 1.2$ Hz, 3H), 2.21 (t, $J = 7.8$ Hz, 2H), 3.42 (t, $J = 6.3$ Hz, 2H), 3.66 (s, 3H), 3.78 (s, 3H), 4.40 (s, 2H), 5.66 (dd, $J = 1.3$ Hz, $J = 1.1$ Hz, 1H), 6.84-6.87 (m, 2H), 7.22-7.26 (m, 2H); ¹³C NMR (75 MHz, CDCl₃, data for major diastereomer) $\delta = 18.7, 27.5, 37.4, 50.7, 55.2, 69.3, 72.6, 113.8, 115.3, 129.2, 130.5, 159.2, 159.7, 167.1$; HRMS calculated for C₁₅H₂₀O₄: 278,1518, found: 278,1518.

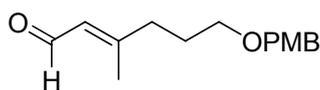
(*E*)-6-(4-methoxybenzyloxy)-3-methylhex-2-en-1-ol



C₁₅H₂₂O₃
Exact Mass: 250,1569
Molecular Weight: 250,3334

To a stirred solution (-78 °C) of ester (13.35 g, 47.97 mmol) in CH₂Cl₂ (150 mL) was added DiBAL-H (143.91 mL, 1M in CH₂Cl₂, 143.91 mmol, 3 eq). After 1 h, Et₂O (11 mL) was added and the mixture was allowed to warm to room temperature. Dropwise addition of water (30 mL) led to the formation of a colourless gel. Upon addition of aqueous 2N NaOH (3.2 mL) and additional water (2.0 mL), a white solid precipitates. The resulting suspension was dried with MgSO₄. The mixture was filtered and the solvent was evaporated *in vacuo* to afford the alcohol as an *E/Z* mixture (3:1) (11.23 g, 44.88 mmol, 94 %). The mixture was purified by column chromatography on silica gel (CH₂Cl₂ / Et₂O = 4:1) to give the *E/Z*-alcohol as a colourless oil. $R_f = 0.42$ (CH₂Cl₂ / Et₂O = 4:1); ¹H NMR (400 MHz, CDCl₃) (data for major diastereomer) $\delta = 1.64$ -1.75 (m, 5H), 2.08 (t, $J = 7.1$ Hz, 2H), 3.42 (t, $J = 6.6$ Hz, 2H), 3.79 (s, 3H), 4.12 (t, $J = 5.6$ Hz, 2H), 4.42 (s, 2H), 5.39 (ddd, $J = 8.1$ Hz, $J = 5.6$ Hz, $J = 1.5$ Hz, 1H), 6.87 (d, $J = 8.7$ Hz, 2H), 7.25 (d, $J = 8.7$ Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) (data for major diastereomer) $\delta = 16.1, 27.6, 35.9, 55.1, 59.1, 69.4, 72.4, 113.7, 123.7, 129.2, 130.5, 138.7, 159.0$; The spectroscopic data were in agreement to those previously reported.⁵

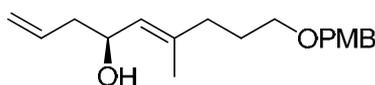
(*E*)-6-(4-methoxybenzyloxy)-3-methylhex-2-enal (21)



C₁₅H₂₀O₃
Exact Mass: 248,1412
Molecular Weight:
248,3175

Activated MnO₂ (62.08 g, 713.05 mmol, 17 eq) was suspended in CH₂Cl₂ (350 mL). 6-(4-methoxybenzyloxy)-3-methylhex-2-enal (10.50 g, 41.94 mmol) was added in CH₂Cl₂ (35 mL) at room temperature and the mixture was stirred for 2 h. The mixture was filtered through a short pad of celite with CH₂Cl₂ (300 mL) and EtOAc (500 mL). The solvent was evaporated *in vacuo* to afford the aldehyde as a *E/Z* mixture (3:1). The mixture was purified by column chromatography on silica gel (hexanes / EtOAc = 3:1) to give the *E/Z*-aldehyde (9.98 g, 40.26 mmol, 96 %) as a colourless oil. R_f = 0.33 (hexanes / EtOAc = 3:1); ¹H NMR (400 MHz, CDCl₃) (data for major diastereomer) δ = 1.78–1.86 (m, 2H), 2.17 (d, *J* = 1.02 Hz, 3H), 2.32 (t, *J* = 7.6 Hz, 2H), 3.48 (t, *J* = 6.1 Hz, 2H), 3.81 (s, 3H), 4.43 (s, 2H), 5.89 (d, *J* = 7.1 Hz, 1H), 6.89 (d, *J* = 8.7 Hz, 2H), 7.26 (d, *J* = 8.7 Hz, 2H), 9.99 (d, *J* = 8.1 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) (data for major diastereomer) δ = 17.7, 27.2, 37.2, 55.2, 68.9, 72.6, 113.7, 127.3, 129.2, 130.3, 159.2, 163.5, 191.1.

(*S,E*)-9-(4-methoxybenzyloxy)-6-methylnona-1,5-dien-4-ol

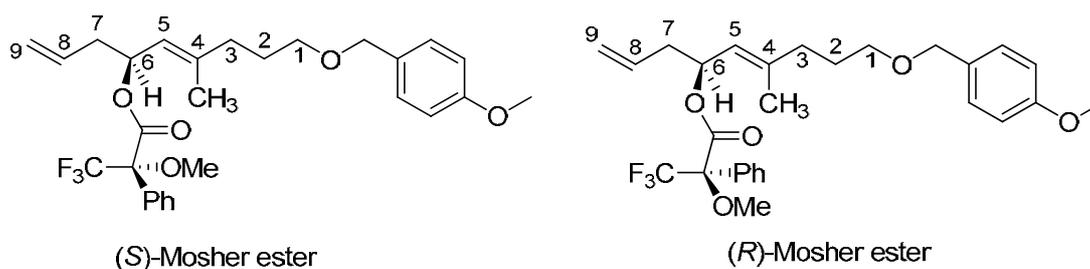


C₁₈H₂₆O₃
Exact Mass: 290,1882
Molecular Weight: 290,3972

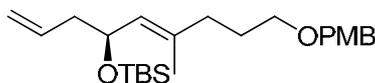
To a stirred solution (0 °C) of (-)-B-Methoxydiisopinocampheylborane (40.28 g, 128.47 mmol, 4 eq) in Et₂O (140 mL) was added Allylmagnesiumbromide (128.47 mL, 1M in Et₂O, 128.47 mmol, 4 eq). After 10 min, it was stirred for 1 h at room temperature. Afterwards the suspension was centrifuged under argon and the solution was separated from the settled magnesium salt. The residue was washed with pentane. The combined organic phases were concentrated, dissolved in 20 ml Ether and cooled down to -100°C. To this solution, (*E*)-6-(4-methoxybenzyloxy)-3-methylhex-2-enal (7.93 g, 31.95 mmol) solved in Et₂O (60 mL) was added and the mixture was stirred for 5 h at -100°C. Then the mixture was allowed to warm to room temperature. After dropwise addition of aqueous 3 N NaOH (26 mL) and H₂O₂ (13 mL, 30% in water) and the mixture was refluxed for 1 h. The organic phase was extracted with water (150 mL) and brine (150 mL) and was dried with MgSO₄. The

mixture was filtered and the solvent was evaporated *in vacuo* to afford the alcohol as an *E/Z* mixture (3:1) (7.42 g, 25.56 mmol, 80 %). The mixture was purified by column chromatography on silica gel (hexanes / EtOAc = 5:1) to give the *E/Z*-alcohol as a colourless oil. $R_f = 0.22$ (hexanes / EtOAc = 5:1); $[\alpha]_D^{23} = +8.0$ ($c = 1.0$, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) (data for major diastereomer) $\delta = 1.66$ -1.73 (m, 5H), 2.03-2.30 (m, 4H), 3.41 (t, $J = 6.6$ Hz, 2H), 3.78 (s, 3H), 4.36-4.42 (m, 3H), 5.06-5.25 (m, 3H), 5.72-5.83 (m, 1H), 6.86 (d, $J = 8.7$ Hz, 2H), 7.25 (d, $J = 6.1$ Hz, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) (data for major diastereomer) $\delta = 17.0$, 28.2, 36.4, 42.6, 55.7, 68.1, 69.9, 73.0, 114.2, 118.2, 127.7, 129.7, 131.1, 134.9, 138.7, 159.6. HRMS calculated for $\text{C}_{18}\text{H}_{26}\text{O}_3\text{Na}$: 313.1780, found: 313.1784. Mosher-Ester analysis gave 90 % ee.

Table. $^1\text{H-NMR}$ data for the Mosher esters of degradation product (300 MHz, CDCl_3)

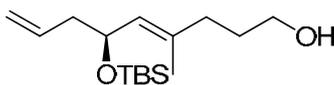


H	δ [ppm], S-Mosher ester	δ [ppm], R-Mosher ester	$\Delta\delta = \delta_S - \delta_R$
1	3.41	3.38	0.03
3	2.105	2.065	0.04
Me-4	1.77	1.76	0.01
5	5.205	5.1155	0.0895
7	2.28-2.45 (2.365)	2.31-2.52 (2.415)	-0.05
8	4.99-5.05 (5.02)	5.07-5.14 (5.105)	-0.085
9	5.55-5.68 (5.615)	5.70-5.78 (5.74)	-0.125

((*S,E*)-9-(4-methoxybenzyloxy)-6-methylnona-1,5-dien-4-yloxy)(*tert*-butyl)dimethylsilane (22)

$C_{24}H_{40}O_3Si$
Exact Mass: 404,2747
Molecular Weight: 404,6581

To a stirred solution of (*S,E*)-9-(4-methoxybenzyloxy)-6-methylnona-1,5-dien-4-ol (2.68 g, 9.04 mmol) in CH_2Cl_2 (30 mL) at $-78^\circ C$ was slowly added 2,6-lutidine (2.29 mL, 19.21 mmol, 2.1 eq.) and TBSOTf (3.29 mL, 14.39 mmol, 1.6 eq.). The mixture was stirred for 1 h. The reaction was quenched with sat. aqueous, ice-cold $NaHCO_3$ (60 mL) and warmed up to room temperature. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic phases were dried over $MgSO_4$, filtered and evaporated *in vacuo*. Silica gel chromatography (hexanes / EtOAc = 30/1) afforded the desired TBS-protected diastereomerically pure *E*-TBS ether (2.27 g, 5.60 mmol, 83 %, based on diastereomeric purity of starting material) as a colorless liquid. $R_f = 0.24$ (hexanes / EtOAc = 30:1); 1H NMR (400 MHz, $CDCl_3$) $\delta = -0.01$ (s, 3H), 0.01 (s, 3H), 0.86 (s, 9H), 1.62 (d, $J = 7.2$ Hz, 3H), 1.60 (d, $J = 1.5$ Hz, 3H), 1.69 (dt, $J = 15.3$ Hz, $J = 6.6$ Hz, 2H), 2.02 (t, $J = 7.2$ Hz, 2H), 2.14 (ddd, $J = 13.6$ Hz, $J = 6.7$ Hz, $J = 6.5$ Hz, 1H), 2.25 (ddd, $J = 13.9$ Hz, $J = 7.1$ Hz, $J = 7.0$ Hz, 1H), 3.41 (t, $J = 6.6$ Hz, 2H), 3.79 (s, 3H), 4.35 (dt, $J = 8.5$ Hz, $J = 6.4$ Hz, 1H), 4.41 (s, 2H), 4.96 – 5.05 (m, 2H), 5.13 (dd, $J = 8.7$ Hz, $J = 1.3$ Hz, 1H), 5.75 (dddd, $J = 17.2$ Hz, $J = 10.1$ Hz, $J = 7.1$ Hz, 1H), 6.87 (d, $J = 8.7$ Hz, 2H), 7.25 (d, $J = 8.7$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = -4.7, -4.24, 16.6, 18.3, 25.9, 27.9, 35.9, 43.3, 55.3, 69.6, 69.7, 72.3, 113.8, 116.4, 129.1, 129.3, 130.7, 134.4, 135.4, 159.2$; HRMS calculated for $C_{24}H_{40}O_3SiNa$: 427.2644, found: 427.2654.

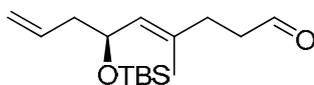
(*S, E*)-6-(*tert*-Butyl-dimethyl-silyloxy)-4-methyl-nona-4,8-dien-1-ol

$C_{16}H_{32}O_2Si$
Exact Mass: 284,2172
Molecular Weight: 284,5096

The PMB-ether (0.49 g, 1.22 mmol) was dissolved in CH_2Cl_2 / H_2O (10:1, 22 mL) under argon atmosphere. Then DDQ (0.42 g, 1.83 mmol, 1.5 eq.) was added fast at $0^\circ C$ and the resulting suspension was stirred for 60 min at room temperature. The reaction mixture was

quenched by addition of 60 mL saturated, aqueous NaHCO₃ solution. The organic layer was separated and the aqueous phase was extracted with CH₂Cl₂ (3 x 20 mL), dried over MgSO₄, filtrated and the solvent was removed under reduced pressure, before the crude product was purified by flash chromatography on silica gel (EtOAc / hexanes = 1:10) to give the desired free alcohol (0.25 g, 0.87 mmol, 71 %) as a colorless liquid. $R_f = 0.17$ (EtOAc / hexanes = 1:10); ¹H NMR (300 MHz, CDCl₃) $\delta = 0.00$ (s, 3H), 0.02 (s, 3H), 0.86 (s, 9H), 1.62 (d, $J = 1.13$ Hz, 3H), 1.67 (dt, $J = 6.5$ Hz, $J = 1.9$ Hz, 2H), 2.05 (t, $J = 7.5$ Hz, 2H), 2.14 (ddd, $J = 13.6$ Hz, $J = 7.0$ Hz, $J = 6.2$ Hz, 1H), 2.26 (ddd, $J = 13.8$ Hz, $J = 7.0$ Hz, $J = 6.8$ Hz, 1H), 3.63 (t, $J = 6.5$ Hz, 2H), 4.36 (dt, $J = 8.6$ Hz, $J = 6.3$ Hz, 1H), 4.97-5.06 (m, 2H), 5.17 (ddd, $J = 8.6$ Hz, $J = 2.4$ Hz, $J = 1.1$ Hz, 1H), 5.76 (dddd, $J = 17.2$ Hz, $J = 10.1$ Hz, $J = 7.1$ Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) $\delta = -4.7, -4.2, 16.6, 18.3, 25.9, 30.7, 35.8, 43.2, 62.7, 69.6, 116.5, 129.3, 134.4, 135.3$; HRMS calculated for C₁₇H₃₆O₃Si: 325.2437, found: 325.1823.

(*S, E*)-6-(*tert*-Butyl-dimethyl-silyloxy)-4-methyl-nona-4,8-dienal

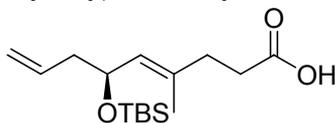


C₁₆H₃₀O₂Si
Exact Mass: 282,2015
Molecular Weight:
282,4937

A solution of the alcohol (1.97 g, 7.00 mmol) in CH₂Cl₂ (40 mL) under argon atmosphere was cooled down to 0 °C, before Dess-Martin Periodinane (7.26 g, 8.40 mmol, 2.4 eq.) was added. The resulting solution was stirred for 100 min at room temperature and quenched by addition of saturated aqueous Na₂SO₃ solution (50 mL) and saturated aqueous NaHCO₃ solution (50 ml) afterwards. The organic layer was separated and the aqueous phase reextracted with CH₂Cl₂ (3 x 100 mL). The combined organic layer was dried (MgSO₄), filtrated and the solvent was evaporated. The residue was purified by column chromatography on silica gel (hexanes / EtOAc = 30:1) to give the aldehyde (1.74 g, 6.16 mmol, 88 %) as colourless liquid. $R_f = 0.33$ (hexanes / EtOAc = 30:1); ¹H NMR (400 MHz, CDCl₃) $\delta = -0.02$ (s, 3H), 0.01 (s, 3H), 0.85 (s, 9H), 1.62 (d, $J = 1.02$ Hz, 3H), 2.13 (ddd, $J = 13.7$ Hz, $J = 7.0$ Hz, $J = 6.2$ Hz, 1H), 2.24 (ddd, $J = 13.7$ Hz, $J = 7.1$ Hz, $J = 6.6$ Hz, 1H), 2.28 – 2.30 (m, 2H), 2.49 – 2.54 (m, 2H), 4.34 (ddd, $J = 8.7$ Hz, $J = 6.6$ Hz, 1H), 5.74 (dddd, $J = 17.3$ Hz, $J = 10.2$ Hz, $J = 7.1$ Hz, 1H), 9.75 (t, $J = 1.8$ Hz, $J = 1.8$ Hz, 1H), ¹³C NMR (100 MHz, CDCl₃) $\delta = -4.7, -4.2, 16.8, 18.2, 25.9, 31.6, 42.0, 43.1, 69.5,$

116.7, 129.8, 132.8, 135.1, 202.1; HRMS calculated for $C_{16}H_{30}O_2SiNa$: 305.1913, found: 305.1914.

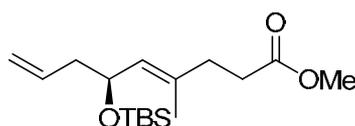
(S, E)-6-(tert-Butyl-dimethyl-silyloxy)-4-methyl-nona-4,8-dienoic acid



$C_{16}H_{30}O_3Si$
Exact Mass: 298,1964
Molecular Weight: 298,4931

The aldehyde (0.80 g, 2.83 mmol) was dissolved in *tert*-butyl alcohol (80 mL) and water (20 mL). To this solution was added sequentially 2-methyl-2-buten (237.91 mmol, 25.15 mL, 16.65 mg, 81 eq), sodium dihydrogen phosphate monohydrate (1.01 g, 2.5 eq), and sodium chlorite (14.58 mmol, 1.32 g, 5 eq). After being stirred at 20 °C for 3 h, the solvents were evaporated and the residue was partitioned between ethyl acetate (50 mL) and brine (50 mL). The separated aqueous layer was extracted three times with ethyl acetate (20 mL). The combined organic extracts were dried and concentrated to give the acid (0.63 g, 2.12 mmol, 75 %) as colourless liquid. $R_f = 0.25$ (hexanes / EtOAc = 5:1); 1H NMR (400 MHz, $CDCl_3$) $\delta = -0.02$ (s, 3H), 0.01 (s, 3H), 0.85 (s, 9H), 1.62 (d, $J = 1.02$ Hz, 3H), 2.13 (ddd, $J = 13.6$ Hz, $J = 6.7$ Hz, $J = 6.6$ Hz, 1H), 2.21 – 2.26 (m, 1H), 2.28 – 2.32 (m, 2H), 2.43 – 2.47 (m, 2H), 4.34 (ddd, $J = 8.5$ Hz, $J = 6.5$ Hz, $J = 6.4$ Hz, 1H), 4.97 – 5.03 (m, 2H), 5.17 (dd, $J = 8.39$, $J = 1.27$, 1H), 5.74 (dddd, $J = 17.2$ Hz, $J = 10.1$ Hz, $J = 7.4$ Hz, $J = 7.1$ Hz, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = -4.8, -4.3, 16.7, 18.2, 25.9, 32.5, 34.0, 43.1, 69.6, 116.6, 129.7, 132.8, 135.2, 178.8$; HRMS calculated for $C_{16}H_{30}O_3Si$: 298.1964, found: 298.1981.

(S, E)-6-(tert-Butyl-dimethyl-silyloxy)-4-methyl-nona-4,8-dienoic acid methyl ester (23)

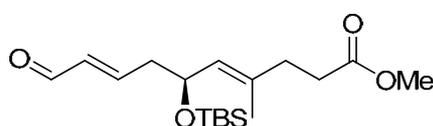


$C_{17}H_{32}O_3Si$
Exact Mass: 312,2121
Molecular Weight: 312,5197

The acid (2.18 mmol, 650.5 mg) was dissolved in 2 mL EtOAc. To this solution was added freshly prepared Diazomethane in Ether. After stirring for 1 h the solvent was evaporated. The

residue was purified by column chromatography on silica gel (hexanes / EtOAc = 30:1) to give the ester (516 mg, 1.65 mmol, 75 %) as colourless liquid. $R_f = 0.35$ (hexanes/EtOAc = 30:1); $^1\text{H NMR}$ (300 MHz, CDCl_3) $\delta = -0.02$ (s, 3H), 0.01 (s, 3H), 0.85 (s, 9H), 1.62 (d, $J = 1.1$ Hz, 3H), 2.08 – 2.13 (m, 4H), 2.38 – 2.44 (m, 2H), 3.65 (s, 3H), 4.34 (dt, $J = 8.6$ Hz, $J = 6.5$ Hz, $J = 6.5$ Hz, 1H), 4.96 – 5.05 (m, 2H), 5.15 (dd, $J = 8.6$, $J = 1.2$, 1H), 5.74 (dddd, $J = 17.2$ Hz, $J = 10.2$ Hz, $J = 7.2$ Hz, 1H), $^{13}\text{C NMR}$ (75 MHz, CDCl_3) $\delta = -4.8$, -4.2, 16.7, 18.2, 25.9, 32.7, 34.3, 43.1, 51.6, 69.6, 116.6, 129.5, 133.1, 135.3, 173.7; HRMS calculated for $\text{C}_{17}\text{H}_{32}\text{O}_3\text{Si}$: 312.2121, found: 312.2063.

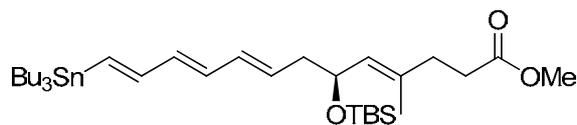
(S,4E,8E)-methyl 6-(tert-butyldimethylsilyloxy)-4-methyl-10-oxodeca-4,8-dienoate (24)



Chemical Formula: $\text{C}_{18}\text{H}_{32}\text{O}_4\text{Si}$
Exact Mass: 340,2070
Molecular Weight: 340,5298

To a solution of the alkene substrate (124.0 mg, 0.397 mmol) and crotonaldehyde (278.1 mg, 3.97 mmol) in anhydrous toluene (3.0 mL) was added a solution of the Grubbs second generation catalyst (16.8 mg, 19.8 μmol) in toluene (1.0 mL). The brown mixture was heated to 60°C in an oil bath and stirred at that temperature for 3 h. After cooled to room temperature, the solvent was removed under reduced pressure and the residue was chromatographed (silica gel, n-Hexane / EtOAc = 9:1 to 4:1). The aldehyde product was obtained as yellow oil (122.0 mg, 90%) and used for next step immediately. $R_f = 0.26$ (n-Hexane / EtOAc = 9:1); $^1\text{H NMR}$ (300 MHz, CDCl_3) $\delta = 0.01$ (s, 3H), 0.03 (s, 3H), 0.87 (s, 9H), 1.66 (d, $J = 1.3$ Hz, 3H), 2.30-2.54 (m, 6H), 3.67 (s, 3H), 4.50 (ddd, $J = 8.5$, 6.9, 5.3 Hz, 1H), 5.19 (dq, $J = 8.6$, 1.2 Hz, 1H), 6.13 (ddt, $J = 15.6$, 8.0, 1.3 Hz, 1H), 6.84 (dt, $J = 15.6$, 7.4 Hz, 1H), 9.51 (d, $J = 8.1$ Hz, 1H); $^{13}\text{C NMR}$ (75.5 MHz, CDCl_3) $\delta = -4.9$, -4.2, 16.7, 18.1, 25.8, 32.5, 34.2, 41.8, 51.6, 68.5, 128.6, 134.3, 134.7, 155.0, 173.4, 193.9.

(S,4E,8E,10E,12E)-methyl 6-(tert-butyldimethylsilyloxy)-4-methyl-13-(tributylstannyl)trideca-4,8,10,12-tetraenoate (25)



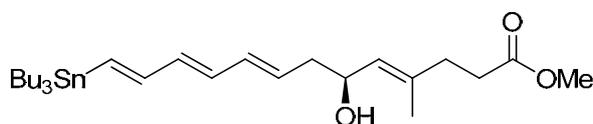
Chemical Formula: C₃₃H₆₂O₃SiSn

Exact Mass: 654,3490

Molecular Weight: 653,6391

To a cooled (-78°C) solution of the phosphonate (**25**) (74.9 mg, 160.3 μmol, 1.2 eq.) and 18-crown-6 (70.6 mg, 267.2 μmol, 1.2 eq.) in dry THF (0.8 mL) was added dropwise a solution of KHMDS (0.5 M in toluene, 320.6 μL, 1.2 eq.). After stirring for 5 min, a solution of the aldehyde (**24**) (45.5 mg, 133.6 μmol, 1.0 eq.) in dry THF (0.2 mL and 0.2 mL washing) was added dropwise. The resulted mixture was stirred at -78°C for 1h followed by dilution with n-hexane (5.0 mL) and quenching with pH7 phosphate buffer (4.0 mL). Warmed to room temperature, the layers were separated and the aqueous layer was extracted with n-hexane (2 x 2.0 mL). The combined organic phased were washed with brine (4.0 mL), dried over anhydrous sodium sulphate, filtered and concentrated under vacuum. The residue was chromatographed by preparative HPLC (Column: LiChrospher® Si 60 (10 μm) 250x10 mm, n-hexane/EtOAc = 97:3, 6.0 mL/min, 254 nm) to produce the pure trienyl stannane (retention time = 8.08 min, 33.1 mg, 50.6 μmol, 38% yield). $R_f = 0.45$ (n-Hexane / EtOAc = 20:1); ¹H NMR (300 MHz, C₆D₆) δ = 0.07 (s, 3H), 0.08 (s, 3H), 0.90-1.02 (m, 24H), 1.31-1.43 (m, 9H), 1.52-1.71 (m, 6H), 2.19-2.46 (m, 6H), 3.36 (s, 3H), 4.39 (m 1H), 5.26 (dd, $J = 8.6, 0.9$ Hz, 1H), 5.77 (dt, $J = 14.6, 7.4$ Hz, 1H), 6.11-6.29 (m, 3H), 6.39 (d, $J = 18.7$ Hz, 1H), 6.79 (ddd, $J = 18.7, 6.8, 2.8$ Hz, 1H); ¹³C NMR (75 MHz, C₆D₆) δ = -4.2, -3.6, 10.2, 14.3, 16.9, 18.8, 26.5, 28.1, 29.9, 33.0, 34.9, 43.0, 51.4, 70.5, 130.2, 132.3, 133.0, 133.5, 134.0, 134.1, 135.0, 148.2, 173.0; ESI-HRMS calculated for C₂₉H₅₃O₃SiSn [M-C₄H₉]⁺: 597.2786, found: 597.2283.

(S,4E,8E,10E,12E)-methyl 6-hydroxy-4-methyl-13-(tributylstannyl)trideca-4,8,10,12-tetraenoate (3)



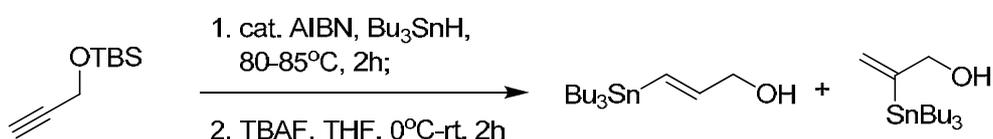
Chemical Formula: C₂₇H₄₈O₃Sn

Exact Mass: 540,2625

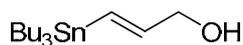
Molecular Weight: 539,3782

To a cooled (0°C) solution of the TBS ether (21.0 mg, 32.1 μmol, 1.0 eq.) in dry THF (500 μL) was added dropwise a solution of TBAF (1.0 M in THF, 321 μL, 10.0 eq.). The resultant mixture was warmed to room temperature and stirred for 1.5 h and then poured into a cooled (0°C) mixture of dichloromethane (3.0 mL) and pH7 phosphate buffer (5.0 mL). The layers were separated and the aqueous layer was extracted with dichloromethane (2 x 3.0 mL). The combined organic phases were washed with brine (2.0 mL), dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure. The residue was chromatographed (Silica gel, n-hexane : EtOAc : triethylamine = 90:10:2 to 80:20:2) to produce the alcohol (11.9 mg, 22.1 μmol, 69% yield). $R_f = 0.30$ (n-Hexane / EtOAc = 2:1); $^1\text{H NMR}$ (600 MHz, C_6D_6) $\delta = 0.94$ (t, $J = 7.3$ Hz, 9H), 1.00 (m, 6H), 1.35-1.42 (m, 9H), 1.58-1.64 (m, 6H), 2.16-2.31 (m, 6H), 3.36 (s, 3H), 4.19-4.23 (m 1H), 5.15 (d, $J = 8.2$ Hz, 1H), 5.66 (dt, $J = 14.8, 7.4$ Hz, 1H), 6.09-6.28 (m, 3H), 6.41 (d, $J = 18.7$ Hz, 1H), 6.80 (dd, $J = 18.8, 9.2$ Hz, 1H); $^{13}\text{C NMR}$ (151 MHz, C_6D_6) $\delta = 10.2, 14.3, 16.8, 28.1, 29.9, 33.1, 35.0, 42.1, 51.4, 68.5, 129.3, 131.8, 132.9, 133.8, 134.2, 135.1, 136.6, 148.2, 173.2$; ESI-HRMS calculated for $\text{C}_{27}\text{H}_{48}\text{O}_3\text{SnNa}$ $[\text{M}+\text{Ma}]^+$: 563.2523, found: 563.2518.

(E)-3-(tributylstannyl)prop-2-en-1-ol



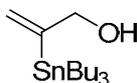
Under argon, a mixture of tert-butyldimethyl(prop-2-ynyl)oxy)silane (2.56 g, 15.0 mmol, 1.0 eq.), AIBN (N,N-Azobisisobutyronitril, 73.9 mg, 0.45 mmol, 0.03 eq.) and tributyltin hydride (4.84 mL, 18.0 mmol, 1.2 eq.) was heated in an oil bath to 80°C and stirred at 80-85°C for 2h, cooled down to room temperature and dissolved in THF (30.0 mL). The resulted solution was cooled to 0°C and a solution of TBAF in THF (1.0 M, 30.0 mL, 30.0 mmol, 2.0 eq.) was added. After stirred at room temperature for additional 2h, aqueous saturated NH_4Cl (50.0 mL) was added and the layers separated. The aqueous phase was extracted with diethyl ether (2x30.0 mL). The combined organic phases were washed with brine (30.0 mL), dried over MgSO_4 , filtered and concentrated under vacuum. Column chromatography of the residue (silica gel, n-Hexane/EtOAc = 20:1 to 9:1) produced two alcohol isomers.

(E)-3-(tributylstannyl)prop-2-en-1-olChemical Formula: C₁₅H₃₂OSn

Exact Mass: 348,1475

Molecular Weight: 347,1240

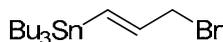
3.68 g, 10.6 mmol, yield 71%. $R_f = 0.40$ (n-Hexane / EtOAc = 9:1); ¹H NMR (300 MHz, CDCl₃) $\delta = 0.88-0.97$ (m, 15H), 1.25-1.37 (m, 6H), 1.45-1.59 (m, 6H), 4.18 (dd, $J = 5.8, 3.2$ Hz, 2H), 6.09-6.32 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) $\delta = 9.4, 13.7, 27.3, 29.1, 66.4, 128.4, 147.0$.

2-(tributylstannyl)prop-2-en-1-olChemical Formula: C₁₅H₃₂OSn

Exact Mass: 348,1475

Molecular Weight: 347,1240

1.08 g (contaminated by about 20% of (Z)-3-(tributylstannyl)prop-2-en-1-ol), 3.1 mmol, yield 21%. $R_f = 0.51$ (n-Hexane / EtOAc = 9:1); ¹H NMR (300 MHz, CDCl₃) $\delta = 0.88-0.97$ (m, 15H), 1.26-1.38 (m, 6H), 1.46-1.56 (m, 6H), 4.29 (dt, $J = 6.0, 1.7$ Hz, 2H), 5.25 (q, $J = 1.7$ Hz, 1H), 5.89 (q, $J = 2.1$ Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) $\delta = 9.5, 13.7, 27.3, 29.1, 69.6, 122.9, 154.8$.

(E)-(3-bromoprop-1-enyl)tributylstannane⁴Chemical Formula: C₁₅H₃₁BrSn

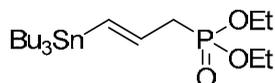
Exact Mass: 410,0631

Molecular Weight: 410,0206

To a solution of the alcohol (724.0 mg, 2.09 mmol, 1.0 eq.) and triphenylphosphine (1.095 g, 4.17 mmol, 2.0 eq.) in dry acetonitrile (20.0 mL) was added 2,6-lutidine (48.4 μ L, 417 μ mol, 0.2 eq.) then CBr₄ solid (1.383 g, 4.17 mmol, 2.0 eq.) at 0°C. The resulted dark red solution was stirred at room temperature for 10 min and then poured into aqueous 5% NaHCO₃ (120 mL). The mixture was extracted with n-hexane (2x150 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and concentrated to about 15 mL. This was chromatographed (silica gel, 50.0 g, n-Hexane / EtOAc = 20:1) quickly to yield the bromide as colorless liquid and used for next step immediately. $R_f = 0.87$ (n-Hexane / EtOAc = 20:1); ¹H NMR (300 MHz, CDCl₃) $\delta = 0.80-0.87$ (m, 15H), 1.18-1.30 (m, 6H), 1.38-1.46 (m, 6H),

3.89 (dd $J = 6.7, 0.9$ Hz, 2H), 6.05 (dt, $J = 18.5, 6.6$ Hz, 1H), 6.22 (d, $J = 18.7$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) $\delta = 9.6, 13.7, 27.2, 29.0, 35.8, 135.1, 143.0$.

(E)-diethyl 3-(tributylstannyl)allylphosphonate⁴ (25)



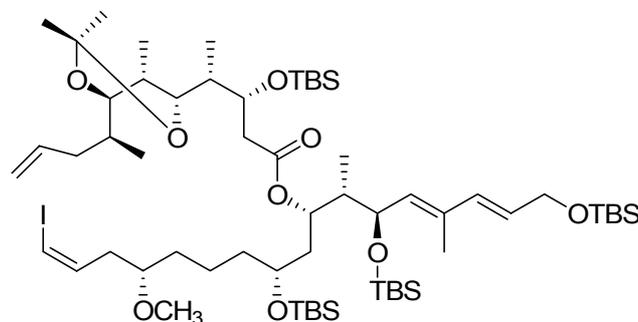
Chemical Formula: $\text{C}_{19}\text{H}_{41}\text{O}_3\text{PSn}$

Exact Mass: 468,1815

Molecular Weight: 467,2108

To a suspension of sodium hydride (60% in paraffin, 240.0 mg, 6.0 mmol, 3.0 eq.) in dry THF (22.0 mL) was added diethyl phosphate (828.0 mg, 6.0 mmol, 3.0 eq.). The mixture was warmed with a heating gun until a clear solution was obtained. Then a solution of the above bromide in dry THF (3.0 mL and 2.0 mL washing) was added. The reaction mixture was stirred at room temperature for 3 h, diluted with diethyl ether (50 mL) and water (30 mL) at 0°C. The layers were separated and the aqueous layer was extracted with diethyl ether (2x30 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated under vacuum. Flash chromatography (silica gel, 50.0 g, n-Hexane / EtOAc = 1:1) provided the pure phosphonate as colorless liquid (634.1 mg, 1.36 mmol, 65% over 2 steps). $R_f = 0.49$ (n-Hexane / EtOAc = 1:1); ^1H NMR (300 MHz, CDCl_3) $\delta = 0.86\text{-}0.91$ (m, 15H), 1.24-1.36 (m, 12H), 1.44-1.54 (m, 6H), 2.67-2.79 (m, 2H), 4.05-4.15 (m, 4H), 5.84-5.97 (m, 1H), 6.12-6.20 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) $\delta = 9.9, 14.1, 16.8$ (d, $J = 6.1$ Hz), 27.7, 29.4, 36.1 (d, $J = 135.5$ Hz), 62.2 (d, $J = 6.4$ Hz), 135.7 (d, $J = 13.2$ Hz), 136.8 (d, $J = 11.0$ Hz); ESI-HRMS calculated for $\text{C}_{19}\text{H}_{41}\text{O}_3\text{PSnNa}$ $[\text{M}+\text{Na}]^+$: 491.1713, found: 491.1711.

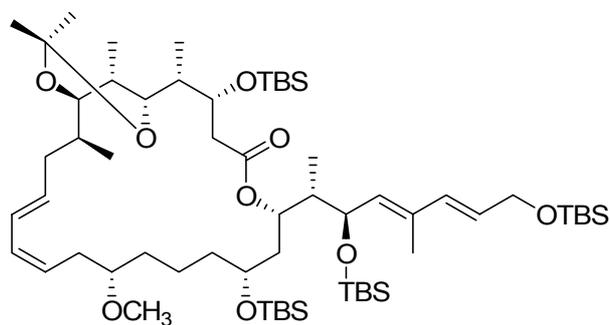
(3*R*,4*S*)-((5*R*,7*S*,8*S*,9*R*,10*E*,12*E*)-9-(*tert*-butyldimethylsilyloxy)-5-((*S*,*Z*)-7-iodo-4-methoxyhept-6-enyl)-2,2,3,3,8,11,16,16,17,17-decamethyl-4,15-dioxo-3,16-disilaoctadeca-10,12-dien-7-yl) 3-(*tert*-butyldimethylsilyloxy)-4-((4*R*,5*S*,6*R*)-2,2,5-trimethyl-6-((*S*)-pent-4-en-2-yl)-1,3-dioxan-4-yl)pentanoate



$C_{61}H_{119}IO_9Si_4$
Exact Mass: 1234,6976
Mol. Wt.: 1235,8386

Et₃N (67.0 μL, 0.482 mmol, 2.5 eq.) and 2,4,6-Trichlorobenzoyl chloride (76.0 μL, 0.482 mmol, 2.5 eq.) were added to a stirred solution of alcohol (4) (159 mg, 0.193 mmol, 1.0 eq.), acid (2) (140 mg, 0.326 mmol, 1.7 eq.), DMAP (118 mg, 0.965 mmol, 5.0 eq.) in toluene (7.0 mL) at 0 °C. The resulted white slurry was stirred at room temperature for 30 minutes before being quenched with pH7 phosphate buffer (7.0 mL) and H₂O (7.0 mL) at 0 °C. Et₂O (20 mL) was added and the layers were separated. The aqueous layer was extracted with Et₂O (4 × 15 mL). The combined organic extracts were dried (MgSO₄) and concentrated *in vacuo*. Flash column chromatography (hexanes / Et₂O = 9:1) afforded the ester (232 mg, 0.188 mmol, 97%) as a colorless oil. $R_f = 0.71$ (hexanes / Et₂O = 9:1); $[\alpha]_D^{20} = -1.9$ ($c = 0.56$, CHCl₃); ¹H NMR (600 MHz, CDCl₃) $\delta = -0.05$ (s, 3H), -0.02 (s, 3H), -0.006 (s, 3H), -0.001 (s, 3H), 0.01 (s, 3H), 0.07 (s, 9H), 0.82 (d, $J = 6.0$ Hz, 3H), 0.83 (s, 9H), 0.87 (s, 9H), 0.89 (s, 9H), 0.91 (s, 9H), 0.89 (d, $J = 5.9$ Hz, 3H), 0.90 (d, $J = 6.6$ Hz, 3H), 0.92 (d, $J = 6.6$ Hz, 3H), 1.34 (s, 3H), 1.37 (s, 3H), 1.37 - 1.50 (m, 6H), 1.73 (s, 3H), 1.80 - 1.86 (m, 2H), 2.05 (dd, $J = 16.1, 1.5$ Hz, 1H), 2.10 (m, 1H), 2.15 (dd, $J = 10.6, 5.9$ Hz, 3H), 2.30 - 2.40 (m, 3H), 3.27 (m, 1H), 3.30 (dd, $J = 9.2, 1.5$ Hz, 1H), 3.34 (s, 3H), 3.32 - 3.37 (m, 1H), 3.72 (m, 1H), 4.24 (d, $J = 5.2$ Hz, 2H), 4.23 - 4.27 (m, 1H), 4.34 (dd, $J = 8.8, 5.9$ Hz, 1H), 4.99 (m, 2H), 5.21 (m, 1H), 5.40 (d, $J = 9.2$ Hz, 1H), 5.68 (dt, $J = 15.4, 5.5$ Hz, 1H), 5.72 (m, 1H), 6.19 (d, $J = 15.8$ Hz, 1H), 6.25 (q, $J = 6.9$ Hz, 1H), 6.30 (d, $J = 7.3$ Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) $\delta = -5.0, -4.8, -4.7, -4.5, -4.4, -4.2, -4.0, 5.5, 10.4, 10.7, 13.2, 14.1, 16.2, 17.9, 18.1, 18.5, 19.5, 20.3, 22.7, 25.8, 26.0, 26.1, 30.1, 31.2, 31.6, 33.8, 34.2, 35.9, 36.2, 37.6, 38.2, 38.5, 40.3, 42.7, 56.8, 64.2, 68.1, 68.8, 71.7, 72.6, 76.1, 77.9, 79.6, 84.2, 99.0, 116.4, 127.6, 132.8, 134.0, 134.5, 136.3, 137.5, 171.1$; HRMS calculated for C₆₁H₁₁₉IO₉Si₄Na [M+Na]⁺: 1257.6874, found: 1257.6882.

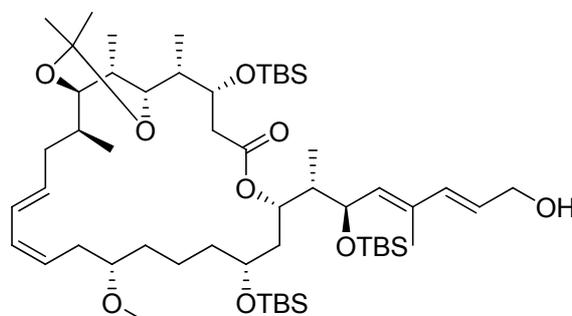
(1*R*,2*S*,3*R*,7*S*,9*R*,13*S*,15*Z*,17*E*,20*S*,21*R*,25*S*)-7-((2*S*,3*R*,4*E*,6*E*)-3,8-bis(*tert*-butyldimethylsilyloxy)-5-methylocta-4,6-dien-2-yl)-3,9-bis(*tert*-butyldimethylsilyloxy)-13-methoxy-2,20,23,23,25-pentamethyl-6,22,24-trioxabicyclo[19.3.1]pentacos-15,17-dien-5-one (27)



C₆₁H₁₁₈O₉Si₄
 Exact Mass: 1106,7853
 Mol. Wt.: 1107,9262

To the above prepared ester iodide (88.0 mg, 71.2 μ mol, 1.0 eq.), Pd(OAc)₂ (16.0 mg, 71.2 μ mol, 1.0 eq.), Bu₄NCl (49.5 mg, 178 μ mol, 2.5 eq.) and K₂CO₃ (78.5 mg, 569 μ mol, 8.0 eq.) was added DMF (18.0 mL) at room temperature. The resulted yellow suspension was stirred at 70 °C for 50 min. The mixture was cooled to room temperature, diluted with Et₂O (40 mL) and filtered through a celite plug (3 \times 10 mL Et₂O). After removing of the solvent, the residue was purified by column chromatography (hexanes / Et₂O = 20:1) to give dien (55.1 mg, 49.7 μ mol, 70%) as a colorless oil. R_f = 0.55 (hexanes / Et₂O = 9:1); $[\alpha]_D^{20}$ = +6.3 (c = 0.57, CHCl₃); ¹H NMR (600 MHz, CDCl₃) δ = -0.04 (s, 3H), 0.005 (s, 3H), 0.02 (s, 3H), 0.04 (s, 3H), 0.07 (s, 9H), 0.08 (s, 3H), 0.83 (d, J = 7.1 Hz, 3H), 0.84 (s, 9H), 0.87 (s, 9H), 0.89 (s, 9H), 0.90 (d, J = 6.6 Hz, 3H), 0.91 (s, 9H), 0.91 (d, J = 7.0 Hz, 3H), 0.93 (d, J = 6.6 Hz, 3H), 1.34 (s, 3H), 1.37 (s, 3H), 1.39-1.53 (m, 6H), 1.61 (m, 1H), 1.68-1.75 (m, 2H), 1.73 (s, 3H), 1.80-1.85 (m, 2H), 1.89-1.93 (m, 2H), 2.11 (m, 1H), 2.20 (m, 2H), 2.34 (dd, J = 16.1, 8.8 Hz, 1H), 2.46 (m, 1H), 3.20 (m, 1H), 3.31 (s, 3H), 3.31-3.36 (m, 2H), 3.78 (m, 1H), 4.24-4.26 (m, 3H), 4.40 (dd, J = 9.2, 6.6 Hz, 1H), 5.17 (m, 1H), 5.36 (d, J = 9.5 Hz, 1H), 5.38 (m, 1H), 5.64 (m, 1H), 5.69 (dt, J = 15.8, 5.3 Hz, 1H), 6.04 (t, J = 10.8 Hz, 1H), 6.20 (d, J = 15.8 Hz, 1H), 6.23 (dd, J = 14.7, 11.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ = -5.1, -4.7, -4.5, -4.4, -4.3, -4.1, -3.8, 5.8, 11.3, 13.3, 16.3, 18.0, 18.1, 18.5, 19.6, 25.9, 26.0, 26.1, 30.1, 31.1, 31.8, 35.0, 37.2, 38.3, 40.1, 44.1, 56.5, 64.1, 70.7, 71.0, 72.9, 80.3, 99.1, 126.0, 127.1, 127.9, 130.2, 132.2, 133.1, 133.6, 134.4, 171.0; HRMS calculated for C₆₁H₁₁₈O₉Si₄Na [M+Na]⁺: 1129.7751, found: 1129.7743.

(1S,2S,3R,7S,9R,13S,15Z,17E,20S,25R)-3,9-bis(tert-butyldimethylsilyloxy)-7-((2S,3R,4E,6E)-3-(tert-butyldimethylsilyloxy)-8-hydroxy-5-methylocta-4,6-dien-2-yl)-13-methoxy-2,20,23,23,25-pentamethyl-6,22,24-trioxabicyclo[19.3.1]pentacos-15,17-dien-5-one

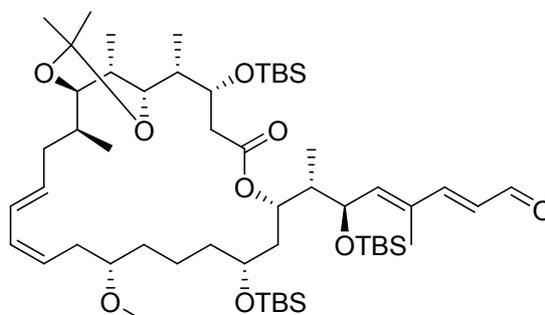


Chemical Formula: C₅₅H₁₀₄O₉Si₃
Exact Mass: 992,6988
Molecular Weight: 993,6654

To a solution of the fully protected macrocycle (**27**) (2.9 mg, 2.62 μ mol) in THF (100 μ L) was added a mixture of acetic acid (65 μ L) and water (35 μ L). The resulted mixture was stirred at room temperature for 18 h and then concentrated under high vacuum. Flash chromatography (silica gel, n-Hexane / EtOAc = 20:1 to 4:1) afforded the monodeprotected product as white solid (2.2 mg, 85%). R_f = 0.23 (n-Hexane / EtOAc = 9:1); $[\alpha]_{20}^D = +9.2$ ($c = 0.10$, CHCl₃); ¹H NMR (600 MHz, Acetone-d₆) $\delta = -0.02$ (s, 3H), 0.04 (s, 6H), 0.07 (s, 3H), 0.09 (s, 3H), 0.11 (s, 3H), 0.85 (s, 9H), 0.89 (s, 9H), 0.91 (s, 9H), 0.87-0.93 (m, 12H), 1.28 (s, 3H), 1.35 (s, 3H), 1.36-1.51 (m, 6H), 1.62 (m, 1H), 1.65-1.69 (m, 2H), 1.77 (s, 3H), 1.80 (m, 1H), 1.84 (m, 1H), 1.93 (m, 1H), 2.01-2.04 (m, 1H), 2.17 (m, 1H), 2.23 (m, 1H), 2.46 (m, 1H), 2.33 (brd, $J = 4.0$ Hz, 2H), 3.20 (m, 1H), 1.84 (m, 1H), 3.24 (s, 3H), 3.44 (dd, $J = 9.4$, 1.4 Hz, 1H), 3.55 (m, 1H), 3.70 (t, $J = 5.6$ Hz, 1H), 3.85 (m, 1H), 4.11 (pseudo-t, $J = 5.6$ Hz, 2H), 4.28 (m, 1H), 4.53 (dd, $J = 9.2$, 6.0 Hz, 1H), 5.27 (ddd, $J = 8.1$, 3.0, 3.0 Hz, 1H), 5.35 (m, 1H), 5.44 (d, $J = 9.1$ Hz, 1H), 5.68 (ddd, $J = 14.8$, 6.9, 6.9 Hz, 1H), 5.79 (dt, $J = 15.6$, 5.6 Hz, 1H), 6.03 (pseudo-t, $J = 10.9$ Hz, 1H), 6.26 (d, $J = 15.7$ Hz, 1H), 6.29 (dd, $J = 14.8$, 11.1 Hz, 1H); ¹³C NMR (151 MHz, Acetone-d₆) $\delta = -4.4$, -4.2, -4.0, -4.0, -3.7, -3.5, 6.2, 11.8, 13.6, 13.7, 16.8, 18.7, 18.8, 18.8, 19.6, 20.0, 26.3, 26.4, 26.4, 26.5, 26.5, 26.6, 30.4, 30.5, 30.7, 31.8, 32.1, 32.1, 34.7, 35.7, 38.4, 39.1, 41.3, 45.0, 55.5, 56.5, 63.2, 63.3, 72.1, 73.4, 78.2, 99.6, 99.7, 127.1, 128.2, 130.3, 131.1, 133.3, 134.0, 134.2, 134.5, 171.9; ESI-HRMS calculated for C₅₅H₁₀₄O₉Si₃Na [M+Na]⁺: 1015.6886, found: 1015.6887.

^1H NMR (600 MHz, CDCl_3) δ = -0.04 (s, 3H), 0.01 (s, 3H), 0.02 (s, 3H), 0.04 (s, 3H), 0.06 (s, 3H), 0.07 (s, 3H), 0.84 (s, 9H), 0.87 (s, 9H), 0.89 (d, J = 6.6 Hz, 3H), 0.90 (s, 9H), 0.91 (d, J = 6.6 Hz, 3H), 0.93 (d, J = 6.6 Hz, 3H), 1.34 (s, 3H), 1.37 (s, 3H), 1.34-1.43 (m, 7H), 1.48-1.52 (m, 3H), 1.59 (m, 1H), 1.69 (m, 1H), 1.73-1.84 (m, 3H), 1.75 (s, 3H), 1.89-1.94 (m, 2H), 2.13 (m, 1H), 2.19 (m, 2H), 2.34 (dd, J = 15.8, 8.8 Hz, 1H), 2.47 (m, 1H), 3.21 (m, 1H), 3.31 (s, 3H), 3.31-3.36 (m, 2H), 3.77 (m, 1H), 4.21 (m, 3H), 4.42 (dd, J = 9.2, 6.2 Hz, 1H), 5.16 (m, 1H), 5.37 (m, 1H), 5.43 (d, J = 9.2 Hz, 1H), 5.64 (m, 1H), 5.78 (dt, J = 15.8, 6.0 Hz, 1H), 6.04 (t, J = 10.8 Hz, 1H), 6.23 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ = -4.7, -4.5, -4.4, -4.3, -4.1, -3.9, 5.7, 11.2, 13.3, 16.3, 18.0, 18.1, 19.6, 25.9, 26.1, 30.1, 31.1, 31.4, 35.0, 37.4, 38.2, 40.2, 44.1, 56.4, 64.0, 70.4, 70.9, 72.9, 80.3, 99.1, 126.0, 127.1, 127.4, 130.3, 132.4, 132.8, 134.3, 135.9, 171.1; ESI-HRMS calculated for $\text{C}_{55}\text{H}_{104}\text{O}_9\text{Si}_3\text{Na}$ $[\text{M}+\text{Na}]^+$: 1015.6886, found: 1015.6887.

(2E,4E,6R,7S)-7-((1S,2S,3R,7S,9R,13S,15Z,17E,20S,25R)-3,9-bis(tert-butyl dimethylsilyloxy)-13-methoxy-2,20,23,23,25-pentamethyl-5-oxo-6,22,24-trioxabicyclo[19.3.1]pentacos-15,17-dien-7-yl)-6-(tert-butyl dimethylsilyloxy)-4-methylocta-2,4-dienal

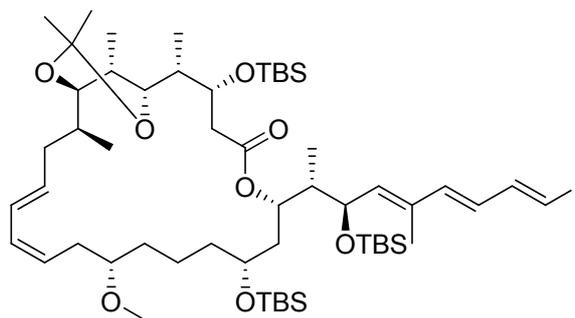


Chemical Formula: $\text{C}_{55}\text{H}_{102}\text{O}_9\text{Si}_3$
Exact Mass: 990,6832
Molecular Weight: 991,6495

To a solution of the alcohol (13.0 mg, 13.1 μmol , 1.0 eq.) in dry dichloromethane (300 μL) was added active manganese dioxide (11.4 mg, 131 μmol , 10.0 eq.). After stirring at room temperature for 4h, the mixture was filtered through a pad of celite. The filter cake was washed with dichloromethane. The filtrate was concentrated under reduced pressure to give the aldehyde as white solid (13.0 mg, 13.1 μmol , 100% yield) which was used for next step immediately. R_f = 0.42 (n-Hexane / EtOAc = 9:1); ^1H NMR (600 MHz, CDCl_3) δ = -0.02 (s, 3H), 0.01 (s, 3H), 0.06 (s, 3H), 0.06 (s, 3H), 0.07 (s, 3H), 0.09 (s, 3H), 0.86 (s, 9H), 0.91 (s, 9H), 0.92 (s, 9H), 0.89-0.94 (m, 12H), 1.36 (s, 3H), 1.39 (s, 3H), 1.34-1.42 (m, 3H), 1.46 (m,

1H), 1.51 (m, 2H), 1.58 (m, 1H), 1.64 (m, 1H), 1.71 (m, 1H), 1.76-1.85 (m, 2H), 1.84 (s, 3H), 1.94-2.02 (m, 2H), 2.13 (m, 1H), 2.22 (m, 2H), 2.34 (m, 1H), 2.49 (m, 1H), 3.23 (m, 1H), 3.33 (s, 3H), 3.34-3.47 (m, 2H), 3.79 (m, 1H), 4.23 (m, 1H), 4.51 (dd, $J = 8.7, 5.4$ Hz, 1H), 5.14 (m, 1H), 5.41 (m, 1H), 5.67 (m, 1H), 5.98 (d, $J = 8.7$ Hz, 1H), 6.07 (pseudo-t, $J = 10.9$ Hz, 1H), 6.17 (dd, $J = 15.6, 7.8$ Hz, 1H), 6.24 (dd, $J = 14.3, 11.0$ Hz, 1H), 7.12 (d, $J = 15.6$ Hz, 1H), 9.60 (d, $J = 7.8$ Hz, 1H); ^{13}C NMR (151 MHz, CDCl_3) $\delta = -4.9, -4.6, -4.5, -4.3, -4.2, -4.1, 5.7, 11.6, 13.1, 16.2, 18.0, 18.1, 18.1, 19.1, 19.5, 25.8, 25.8, 26.0, 26.1, 29.7, 30.0, 31.1, 31.5, 34.9, 37.6, 38.5, 40.0, 43.6, 56.4, 70.2, 71.1, 72.7, 77.5, 80.2, 99.1, 126.1, 127.1, 128.3, 130.2, 132.2, 132.4, 144.5, 156.7, 171.0, 194.0$.

(1S,2S,3R,7S,9R,13S,15Z,17E,20S,25R)-3,9-bis(tert-butyldimethylsilyloxy)-7-((2S,3R,4E,6E,8E)-3-(tert-butyldimethylsilyloxy)-9-iodo-5-methylnona-4,6,8-trien-2-yl)-13-methoxy-2,20,23,23,25-pentamethyl-6,22,24-trioxabicyclo[19.3.1]pentacos-15,17-dien-5-one (28)

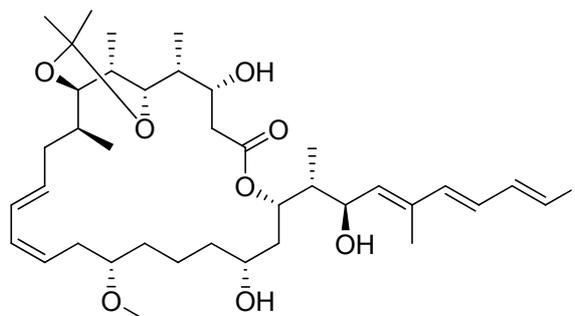


Chemical Formula: $\text{C}_{56}\text{H}_{103}\text{IO}_8\text{Si}_3$
Exact Mass: 1114,6005
Molecular Weight: 1115,5732

To a cooled (0°C) suspension of CrCl_2 (48.3 mg, 393 μmol , 30.0 eq.) in THF/dioxane (1:6 v/v, 0.6 mL) was added a solution of the aldehyde (13.0 mg, 13.1 μmol , 1.0 eq.) and iodoform (41.3 mg, 105 μmol , 8.0 eq.) in THF/dioxane (1:6 v/v, 0.2 mL and 2x0.1 mL washes) in dark. The mixture was stirred at 0°C for 15 min then room temperature 1.5 h, quenched with aqueous saturated ammonium chloride (4.0 mL) and aqueous saturated $\text{Na}_2\text{S}_2\text{O}_3$ (1.0 mL). The whole mixture was extracted with EtOAc (3 x 3.0 mL) and the combined organic phases were dried over anhydrous MgSO_4 , filtered and concentrated under reduced pressure. The residue was flash chromatographed (silica gel, n-hexane / EtOAc = 60 : 1 to 20 : 1) to produce the trienyl iodide as light yellow solid (13.5 mg, 12.1 μmol , 92% yield, as a mixture of C14-C15 *E/Z* isomers with the ratio $E : Z = 4 : 1$) which is extremely sensitive (undergoing *E* to *Z* isomerization) to light. $R_f = 0.34$ (n-Hexane / EtOAc = 20:1); $[\alpha]_{20}^D = +9.2$ ($c = 1.0, \text{CHCl}_3$);

E isomer ^1H NMR (600 MHz, CDCl_3) δ = -0.03 (s, 3H), 0.02 (s, 3H), 0.03 (s, 3H), 0.06 (s, 3H), 0.08 (s, 3H), 0.09 (s, 3H), 0.86 (s, 9H), 0.89 (s, 9H), 0.91 (s, 9H), 0.88-0.96 (m, 12H), 1.36 (s, 3H), 1.39 (s, 3H), 1.33-1.46 (m, 4H), 1.51 (m, 2H), 1.62 (m, 1H), 1.71 (m, 1H), 1.76 (d, J = 1.1 Hz, 3H), 1.82 (m, 3H), 1.94 (m, 2H), 2.13 (br, 1H), 2.22 (m, 2H), 2.36 (dd, J = 16.0, 9.0 Hz, 1H), 2.49 (m, 1H), 3.23 (m, 1H), 3.33 (s, 3H), 3.34-3.40 (m, 2H), 3.79 (m, 1H), 4.25 (m, 1H), 4.43 (dd, J = 9.1, 6.1 Hz, 1H), 5.16 (m, 1H), 5.41 (m, 1H), 5.54 (d, J = 9.2 Hz, 1H), 5.67 (m, 1H), 6.06 (pseudo-t, J = 10.9 Hz, 1H), 6.12 (dd, J = 15.4, 10.7 Hz, 1H), 6.25 (m, 1H), 6.25 (d, J = 15.4 Hz, 1H), 6.32 (d, J = 14.2 Hz, 1H), 7.08 (dd, J = 14.2, 10.6 Hz, 1H); ^{13}C NMR (151 MHz, CDCl_3) δ = -5.0, -4.8, -4.7, -4.6, -4.4, -4.2, 5.5, 11.2, 12.8, 13.8, 16.0, 17.8, 17.8, 17.9, 17.9, 19.3, 22.8, 25.6, 25.8, 28.7, 29.8, 30.8, 31.4, 34.7, 38.5, 39.8, 43.7, 56.2, 67.9, 70.3, 70.8, 72.6, 77.2, 77.9, 80.0, 98.8, 125.8, 126.8, 127.4, 130.0, 132.0, 132.7, 136.3, 137.6, 145.3, 170.8; ESI-HRMS for $\text{C}_{56}\text{H}_{103}\text{IO}_8\text{Si}_3\text{K}$ $[\text{M}+\text{K}]^+$: calculated 1153.5642, found: 1153.5633, for $\text{C}_{56}\text{H}_{103}\text{IO}_8\text{Si}_3\text{Na}$ $[\text{M}+\text{Na}]^+$: calculated 1137.5903, found: 1137.5899 and for $\text{C}_{56}\text{H}_{107}\text{INO}_8\text{Si}_3\text{Na}$ $[\text{M}+\text{NH}_4]^+$: calculated 1132.6349, found: 1132.6329.

(1R,2R,3R,7S,9R,13S,15Z,17E,20S,25R)-3,9-dihydroxy-7-((2R,3R,4E,6E,8E)-3-hydroxy-9-iodo-5-methylnona-4,6,8-trien-2-yl)-13-methoxy-2,20,23,23,25-pentamethyl-6,22,24-trioxabicyclo[19.3.1]pentacos-15,17-dien-5-one

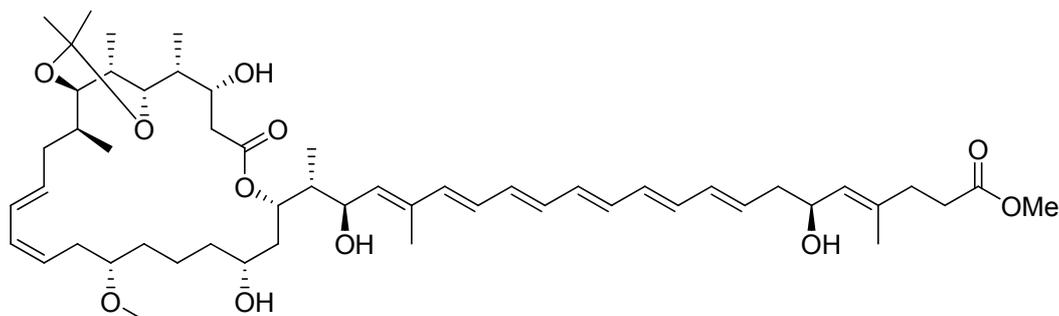


Chemical Formula: $\text{C}_{38}\text{H}_{61}\text{IO}_8$
Exact Mass: 772,3411
Molecular Weight: 772,7906

A cooled (0°C) solution of the substrate (11.0 mg, 9.86 μmol) in a freshly prepared solution of TBAF (2.0 M) and AcOH (0.2 M) in anhydrous DMF (300 μL) was stirred at 0°C for 1 h and then gradually (in around 1 h) warmed to room temperature, further 1 h. To this mixture then was added calcium carbonate (124.5 mg), DOWEX[®] 50WX8-200 (373.5 mg) and methanol (2.2 mL) sequentially. The resultant mixture was vigorously stirred at room temperature for 1.5 h and filtered through a pad of Celite. The filtering cake was thoroughly washed with methanol. The combined filtrate was concentrated and chromatographed through a short silica

gel column (eluent: dichloromethane / methanol = 20 : 1). All visible spots were collected and concentrated together. The product (0.8 mg, 1.04 μmol , 11%) was isolated with normal phase preparative HPLC (Column: LiChrospher® Si 60 (10 μm) 250 x 10 mm, dichloromethane / *i*-PrOH = 96 : 4, 6.0 mL/min, 254 nm, retention time: 26.3 min). R_f = 0.34 (dichloromethane / methanol = 20 : 1); $[\alpha]_{20}^D$ = + 10.0 (c = 0.03, MeOH); ^1H NMR (600 MHz, Acetone- d_6) δ = 0.85 (d, J = 7.0 Hz, 3H), 0.89 (d, J = 6.7 Hz, 3H), 0.94 (d, J = 6.8 Hz, 6H), 1.31 (s, 3H), 1.39 (s, 3H), 1.29-1.52 (m, 6H), 1.58-1.70 (m, 4H), 1.80, (s, 3H), 1.83 (m, 1H), 1.90 (m, 1H), 2.02 (m, 1H), 2.23 (ddd, J = 14.0, 6.8, 3.6 Hz, 1H), 2.30 (ddd, J = 14.4, 8.8, 4.9 Hz, 1H), 2.36 (dd, J = 15.7, 10.1 Hz, 1H), 2.42 (dd, J = 15.7, 2.0 Hz, 1H), 2.47 (ddd, J = 13.6, 6.5, 6.5 Hz, 1H), 3.23 (m, 1H), 3.28 (s, 3H), 3.49 (dd, J = 9.9, 1.9 Hz, 1H), 3.58 (m, 1H), 3.62 (d, J = 5.1 Hz, 1H), 3.64 (dd, J = 9.3, 1.8 Hz, 1H), 3.93 (d, J = 4.5 Hz, 1H), 3.98 (d, J = 3.8 Hz, 1H), 4.15 (m, 1H), 4.40 (ddd, J = 9.2, 7.9, 4.6 Hz, 1H), 5.40 (m, 1H), 5.43 (m, 1H), 5.61 (d, J = 9.2 Hz, 1H), 5.78 (ddd, J = 14.5, 7.4, 7.4 Hz, 1H), 6.08 (dd, J = 10.9, 10.9 Hz, 1H), 6.28 (dd, J = 15.4, 10.5 Hz, 1H), 6.39 (d, J = 15.1 Hz, 1H), 6.40 (dd, J = 14.4, 10.6 Hz, 1H), 6.53 (d, J = 14.3 Hz, 1H), 7.16 (dd, J = 14.3, 10.5 Hz, 1H); ^{13}C NMR (151 MHz, Acetone- d_6) δ = 5.7, 10.9, 11.1, 13.2, 16.4, 20.1, 23.4, 30.5, 30.6, 31.8, 32.7, 35.2, 35.5, 37.8, 38.4, 39.4, 40.8, 43.6, 56.5, 67.9, 68.1, 69.6, 73.5, 76.6, 78.3, 79.1, 81.8, 99.7, 126.9, 128.5, 128.8, 131.0, 132.5, 135.4, 137.3, 139.1, 146.8, 174.1 (Characterization of ^{13}C NMR data was aided by HMBC- and HSQC-measurements); ESI-HRMS calculated for $\text{C}_{38}\text{H}_{61}\text{IKO}_8$ $[\text{M}+\text{K}]^+$: 811.3048, found: 811.3046, calculated for $\text{C}_{38}\text{H}_{61}\text{INaO}_8$ $[\text{M}+\text{Na}]^+$: 795.3309, found: 795.3308.

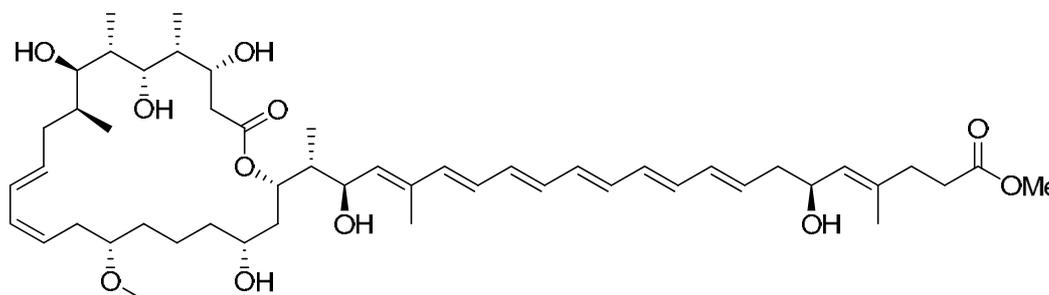
**(4E,6S,8E,10E,12E,14E,16E,18E,20R,21R)-methyl 21-
((1R,2R,3R,7S,9R,13S,15Z,17E,20S,25R)-3,9-dihydroxy-13-methoxy-2,20,23,23,25-
pentamethyl-5-oxo-6,22,24-trioxabicyclo[19.3.1]pentacos-15,17-dien-7-yl)-6,20-
dihydroxy-4,18-dimethyldocosa-4,8,10,12,14,16,18-heptaenoate (29)**



Chemical Formula: $\text{C}_{53}\text{H}_{82}\text{O}_{11}$
Exact Mass: 894,5857
Molecular Weight: 895,2116

In the absence of light, to a cooled (0°C) solution of the trienyl iodide (0.70 mg, 0.91 μmol, 1.0 eq.) and the trienyl stannane (1.3 mg, 2.40 μmol, 2.6 eq.) in degassed DMF (100 μL) was added a solution of PdCl₂(CH₃CN)₂ (0.073 mg, 0.28 μmol, 0.3 eq.) in degassed DMF (30 μL). The mixture was stirred at 0°C for 3 h until TLC showed the disappearance of the trienyl iodide. Phosphate buffer (pH7, 3.0 mL) and ethyl acetate (2.0 mL) were added and the layers separated. The aqueous phase was further extracted with ethyl acetate (9 x 2.0 mL) and the combined organic phases were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The residue was flash chromatographed (silica gel, dichloromethane / methanol = 30 : 1 to 20 : 1) to afford the acetonide protected etnangien methyl ester (0.6 mg, 0.67 μmol, 74% yield). R_f = 0.29 (dichloromethane / methanol = 20 : 1); ¹H NMR (600 MHz, Aceton-d₆) δ = 0.85 (d, *J* = 7.1 Hz, 3H), 0.89 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 6.3 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 1.31 (s, 3H), 1.39 (s, 3H), 1.29-1.52 (m, 6H), 1.62 (m, 1H), 1.65 (s, 3H), 1.67 (m, 1H), 1.68 (m, 2H), 1.82 (s, 3H), 1.83 (m, 1H), 1.90 (m, 1H), 2.02 (m, 1H), 2.19-2.32 (m, 6H), 2.34-2.44 (m, 4H), 2.48 (m, 1H), 3.23 (m, 1H), 3.28 (s, 3H), 3.49 (dd, *J* = 9.8, 1.7 Hz, 1H), 3.58 (m, 1H), 3.61 (s, 3H), 3.62 (d, *J* = 5.0 Hz, 1H), 3.64 (d, *J* = 10.0 Hz, 1H), 3.88 (d, *J* = 4.4 Hz, 1H), 3.99 (d, *J* = 3.9 Hz, 1H), 4.15 (m, 1H), 4.35 (dddd, *J* = 6.7, 8.7, 6.7, 4.5 Hz, 1H), 4.40 (ddd, *J* = 8.8, 8.3, 4.4 Hz, 1H), 5.21 (dd, *J* = 8.6, 1.3 Hz, 1H), 5.40 (m, 1H), 5.44 (ddd, *J* = 9.1, 4.8, 2.8 Hz, 1H), 5.52 (d, *J* = 8.8 Hz, 1H), 5.75 (m, 1H), 5.77 (ddd, *J* = 14.7, 7.3, 7.3 Hz, 1H), 6.09 (dd, *J* = 10.8, 10.8 Hz, 1H), 6.16 (dd, *J* = 15.3, 10.3 Hz, 1H), 6.25 (m, 2H), 6.31-6.36 (m, 6H), 6.40 (dd, *J* = 15.7, 11.3 Hz, 1H); ESI-HRMS calculated for C₂₇H₄₈O₃SnNa [M+Ma]⁺: 563.2523, found: 563.2518.

Etnangien methyl ester

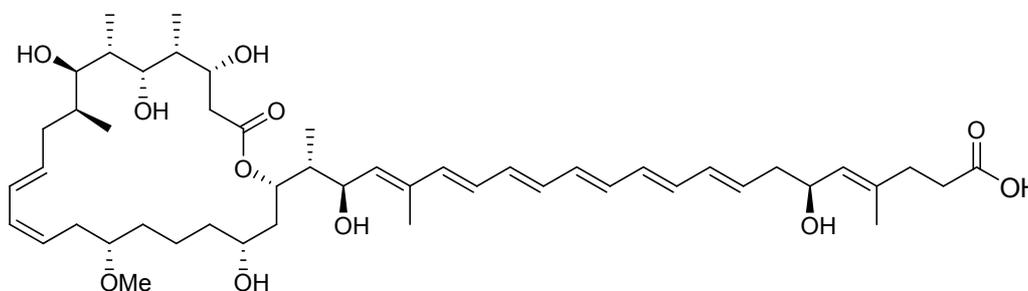


Chemical Formula: C₅₀H₇₈O₁₁
Exact Mass: 854,5544
Molecular Weight: 855,1477

A cooled (0°C) solution of the acetonide (0.3 mg, 0.34 μmol) in AcOH / water (65 / 35 v / v, 100 μL) was stirred at this temperature for 80 min. Aqueous saturated NaHCO₃ (1.5 mL) and

EtOAc (1.5 mL) were added and the layers were separated. The aqueous layer was extracted with EtOAc (9 x 2.0 mL). The combined organic phases were dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure. The residue was flash chromatographed (silica gel, dichloromethane / methanol = 15 : 1 to 10 : 1) to afford the product (0.1 mg, 0.12 μ mol, 35% yield). R_f = 0.31 (dichloromethane / methanol = 10 : 1); $[\alpha]_D^{22} = +17.0^\circ$ (c = 0.20, MeOH); $^1\text{H NMR}$ (600 MHz, Acetone- d_6) δ ppm 0.84 (d, J = 7.2 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H), 0.97 (d, J = 7.0 Hz, 3H), 0.98 (d, J = 6.8 Hz, 3H), 1.31 (m, 2H), 1.41 (m, 1H), 1.42 (m, 1H), 1.46 (m, 1H), 1.65 (m, 1H), 1.66 (d, J = 0.7 Hz, 1H), 1.75 (m, 1H), 1.82 (d, J = 0.7 Hz, 1H), 1.84 (m, 1H), 1.87 (m, 1H), 1.95 (m, 1H), 1.98 (m, 1H), 2.22 (m, 1H), 2.23 (m, 1H), 2.27 (m, 1H), 2.33 (ddd, J = 14.9, 7.5, 6.8, 1H), 2.37 (m, 1H), 2.38 (m, 1H), 2.40 (d, J = 5.5 Hz, 1H), 2.44 (m, 1H), 3.25 (m, 1H), 3.29 (s, 3H), 3.44 (dd, J = 6.8, 3.8 Hz, 1H), 3.51 (m, 1H), 3.56 (m, 1H), 3.61 (s, 3H), 3.61 (dd, J = 7.9, 2.6 Hz, 1H), 3.72 (m, 1H), 3.81 (d, J = 2.6 Hz, 1H), 3.89 (m, 1H), 3.98 (d, J = 4.4 Hz, 1H), 4.17 (dt, J = 5.5, 5.5 Hz, 1H), 4.37 (ddd, J = 8.4, 6.8, 6.8 Hz, 1H), 4.39 (dd, J = 8.7, 8.3 Hz, 1H), 5.25 (d, J = 8.3 Hz, 1H), 5.35 (m, 1H), 5.44 (ddd, J = 8.5, 4.4, 4.4 Hz, 1H), 5.53 (d, J = 9.0 Hz, 1H), 5.71 (ddd, J = 14.9, 8.5, 6.2 Hz, 1H), 5.76 (ddd, J = 14.9, 6.8, 7.5 Hz, 1H), 6.06 (dd, J = 10.9, 10.9 Hz, 1H), 6.16 (dd, J = 14.9, 10.4 Hz, 1H), 6.24 (m, 1H), 6.25 (m, 1H), 6.31 (m, 2H), 6.33 (d, J = 17.9 Hz, 1H), 6.35 (m, 3H); $^{13}\text{C NMR}$ (100 MHz, Acetone- d_6) δ ppm 7.2, 10.9, 11.1, 13.2, 15.1, 16.7, 22.2, 30.7, 33.0, 33.2, 35.2, 36.5, 37.3, 37.7, 38.6, 38.7, 39.2, 42.4, 42.8, 43.8, 51.7, 56.4, 67.9, 68.4, 69.0, 69.1, 73.5, 76.9, 79.4, 81.1, 126.0, 128.3, 129.5, 130.0, 130.9, 132.1, 132.6, 133.3, 133.6, 133.7, 133.9, 134.0, 134.1, 134.3, 135.5, 135.9, 136.2, 138.3, 173.6, 174.2; HRMS: calculated for $\text{C}_{50}\text{H}_{78}\text{O}_{11}\text{Na}$ $[\text{M}+\text{Na}]^+$: 877.5444, found 877.5442.

Etnangien



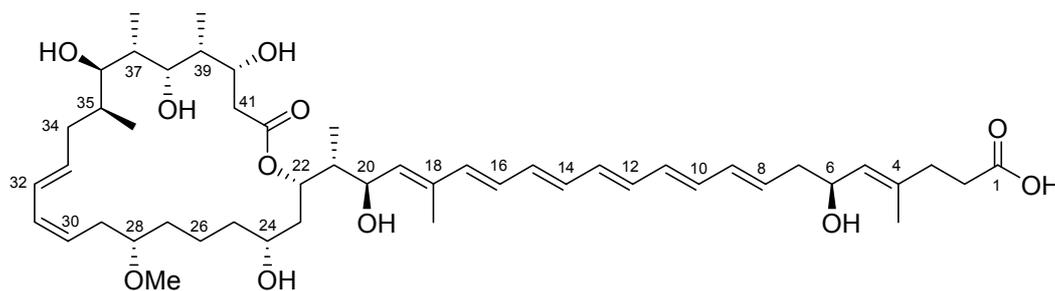
$\text{C}_{49}\text{H}_{76}\text{O}_{11}$
Exact Mass: 840,5388
Mol. Wt.: 841,1211

A solution of etnangien methyl ester (1.00 mg, 1.17 μ mol) in 500 μ L DMSO/water = 1:3 was treated under argon at room temperature with 2 mg porcine liver esterase (obtained from

Sigma) and stirred for 24 h. The crude product was purified by HPLC (Nucleosil 100-7 C18, 250/21; MeOH / H₂O, 0.01 M phosphate buffer = 75:25, flow: 18 mL/min; UV detection 355 nm) to give etnangien (0.65 mg, 0.71 μ mol, 61%) as a colorless oil. $[\alpha]_D^{20} = +16.2$ ($c = 0.65$ mg/mL, MeOH) [Lit: $[\alpha]_D^{21} = +18.7$ ($c = 0.9$, MeOH)]⁷; ¹H NMR (600 MHz, Acetone-*d*₆) δ ppm 0.84 (d, $J = 7.2$ Hz, 3H), 0.92 (d, $J = 6.4$ Hz, 3H), 0.97 (d, $J = 7.0$ Hz, 3H), 0.98 (d, $J = 6.8$ Hz, 3H), 1.31 (m, 2H), 1.41 (m, 1H), 1.42 (m, 1H), 1.46 (m, 1H), 1.65 (m, 2H), 1.66 (d, $J = 1.1$ Hz, 1H), 1.75 (m, 1H), 1.82 (d, $J = 0.7$ Hz, 1H), 1.84 (m, 1H), 1.87 (m, 1H), 1.95 (m, 1H), 1.98 (m, 1H), 2.22 (m, 1H), 2.23 (m, 1H), 2.27 (m, 1H), 2.33 (ddd, $J = 14.9, 7.5, 6.8$, 1H), 2.37 (m, 1H), 2.38 (m, 1H), 2.40 (m, 2H), 2.44 (m, 1H), 3.25 (dddd, $J = 6.0, 6.0, 5.6, 4.5$ Hz, 1H), 3.29 (s, 3H), 3.44 (dd, $J = 6.8, 3.8$ Hz, 1H), 3.51 (tt, $J = 8.3, 4.1$ Hz, 1H), 3.56 (m, 1H), 3.61 (dd, $J = 7.9, 2.6$ Hz, 1H), 3.73 (m, 1H), 3.84 (d, $J = 2.6$ Hz, 1H), 3.89 (m, 1H), 3.98 (m, 1H), 4.17 (dt, $J = 5.4, 6.2$ Hz, 1H), 4.37 (ddd, $J = 8.4, 6.4, 6.8$ Hz, 1H), 4.39 (dd, 9.2, 7.8 Hz, 1H), 5.25 (d, $J = 8.3$ Hz, 1H), 5.35 (ddd, $J = 10.7, 7.4, 7.4$ Hz, 1H), 5.44 (m, 1H), 5.53 (d, $J = 9.0$, 1H), 5.71 (ddd, $J = 14.9, 8.5, 6.2$ Hz, 1H), 5.76 (ddd, $J = 14.9, 6.8, 7.5$ Hz, 1H), 6.06 (dd, $J = 11.2, 11.2$ Hz, 1H), 6.16 (dd, $J = 14.9, 10.4$ Hz, 1H), 6.24 (m, 1H), 6.25 (m, 1H), 6.31 (m, 2H), 6.33 (d, $J = 17.9$ Hz, 1H), 6.35 (m, 4H); ¹³C NMR (100 MHz, Acetone-*d*₆) δ ppm 7.2, 10.9, 11.1, 13.2, 15.1, 16.7, 22.0, 30.7, 33.1, 33.2, 35.1, 36.5, 37.3, 37.8, 38.71, 38.72, 39.2, 42.3, 42.8, 43.9, 56.4, 68.1, 68.4, 69.0, 69.6, 73.5, 76.8, 79.4, 81.1, 126.0, 128.3, 129.5, 129.9, 130.9, 132.1, 132.6, 133.4, 133.5, 133.7, 133.8, 134.0, 134.2, 134.3, 135.5, 135.9, 136.4, 138.6, 173.5, 174.3. HRMS: calculated for C₄₉H₇₅O₁₁ [M-H]: 839.5309, found: 839.5312. All data were identical to those previously reported for etnangien from *Sorangium cellulosum*.⁶

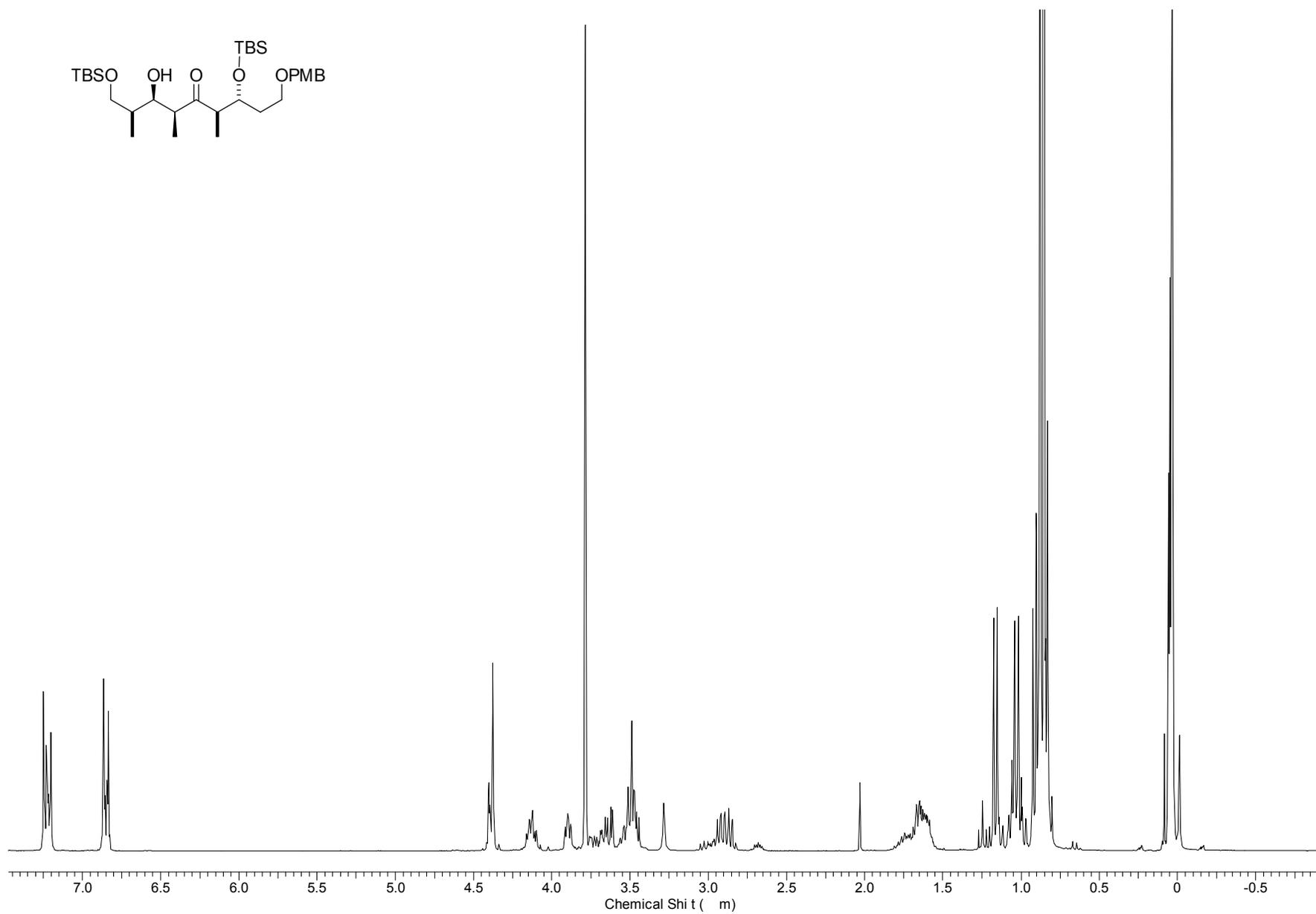
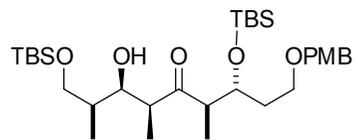
⁶ Irschik, H.; Schummer, D.; Höfle, G.; Reichenbach, H.; Steinmetz, H.; Jansen, R. *J. Nat. Prod.* **2007**, *70*, 1060.

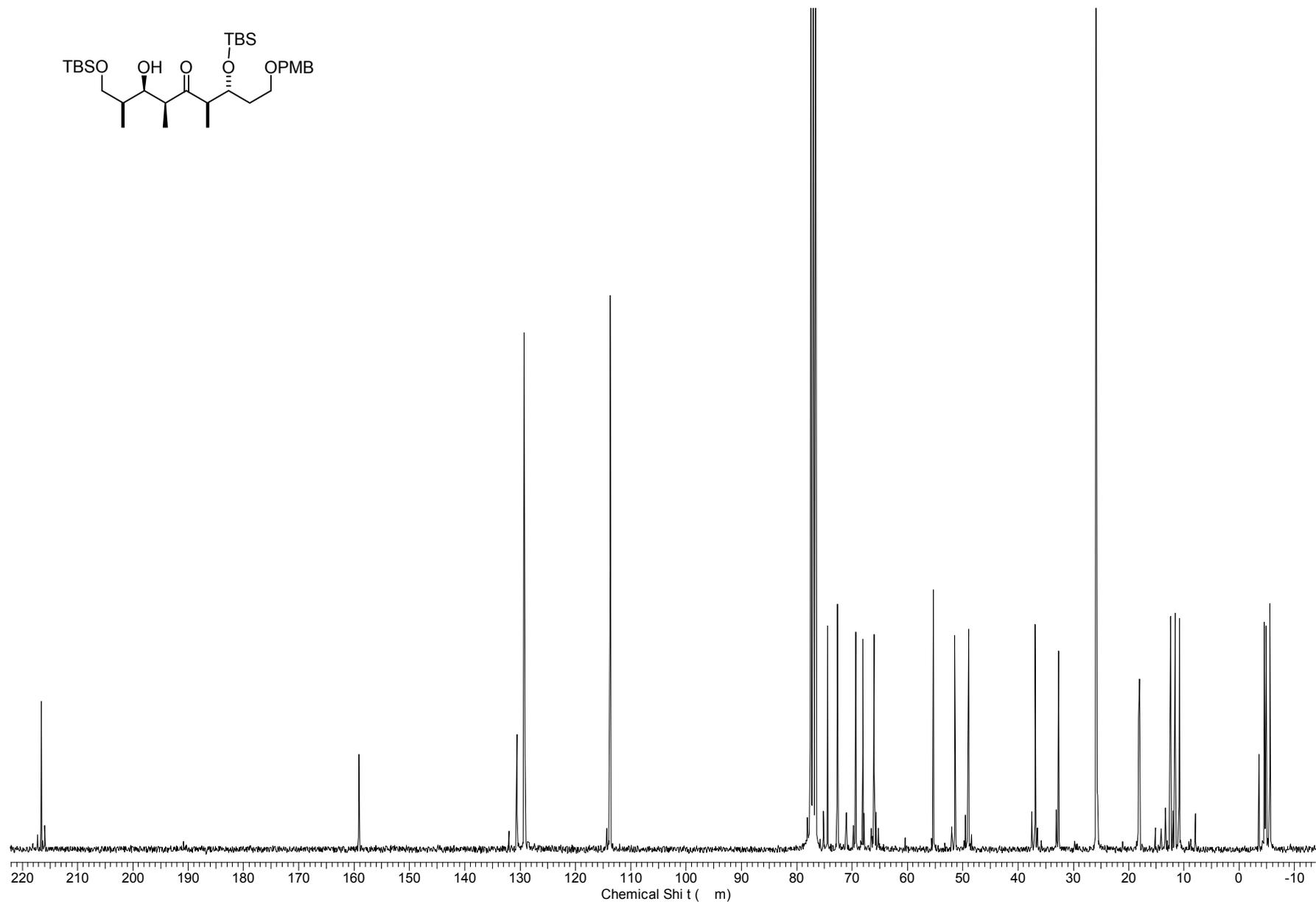
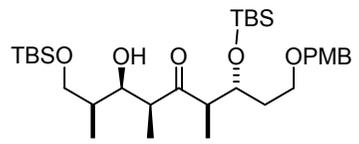
Table: Comparison of ^1H - and ^{13}C -NMR data for synthetic and natural etnangien (recorded in acetone- d_6 at 600 (^1H NMR) and 100 MHz (^{13}C)).

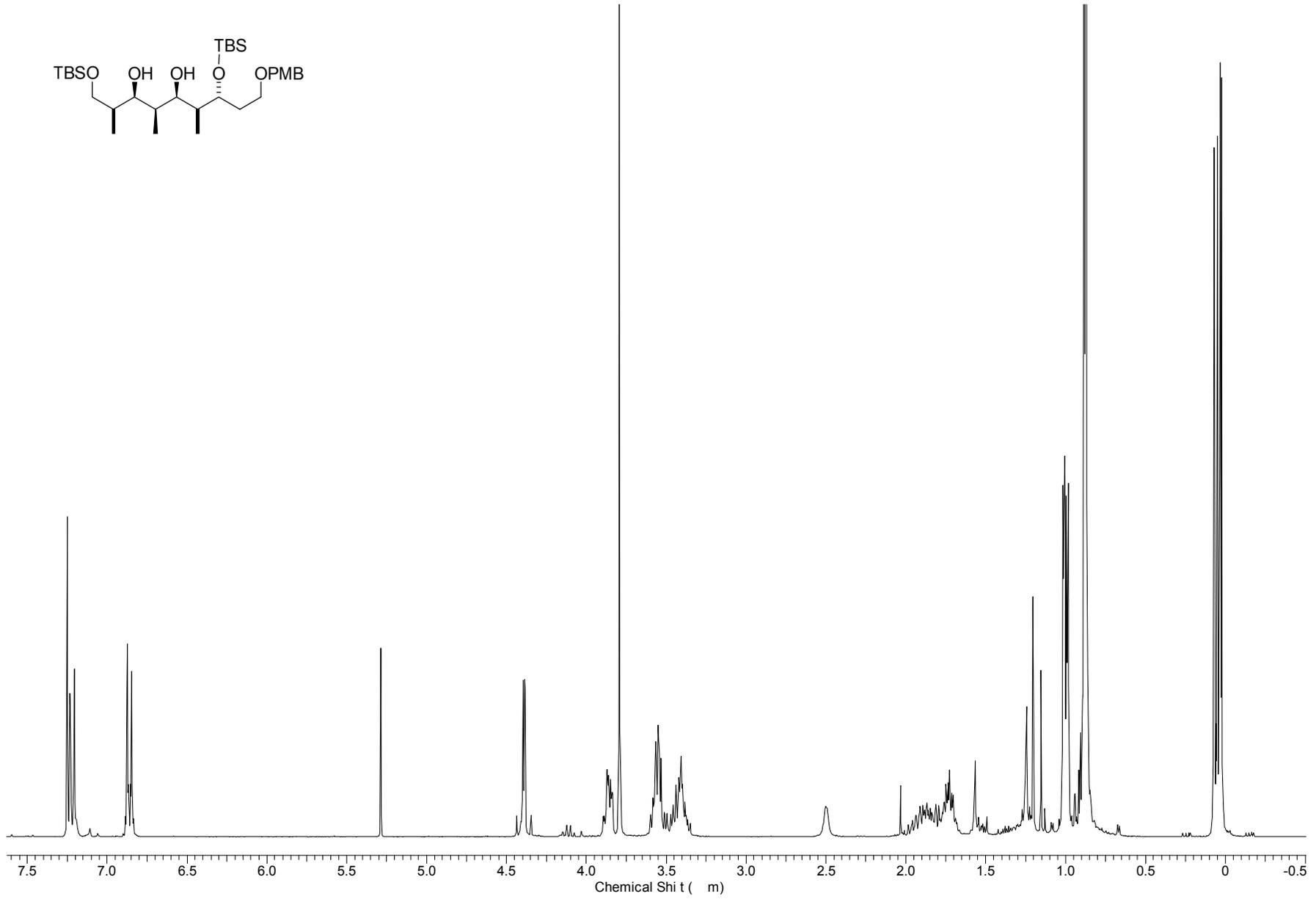
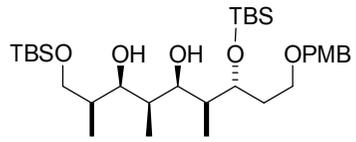


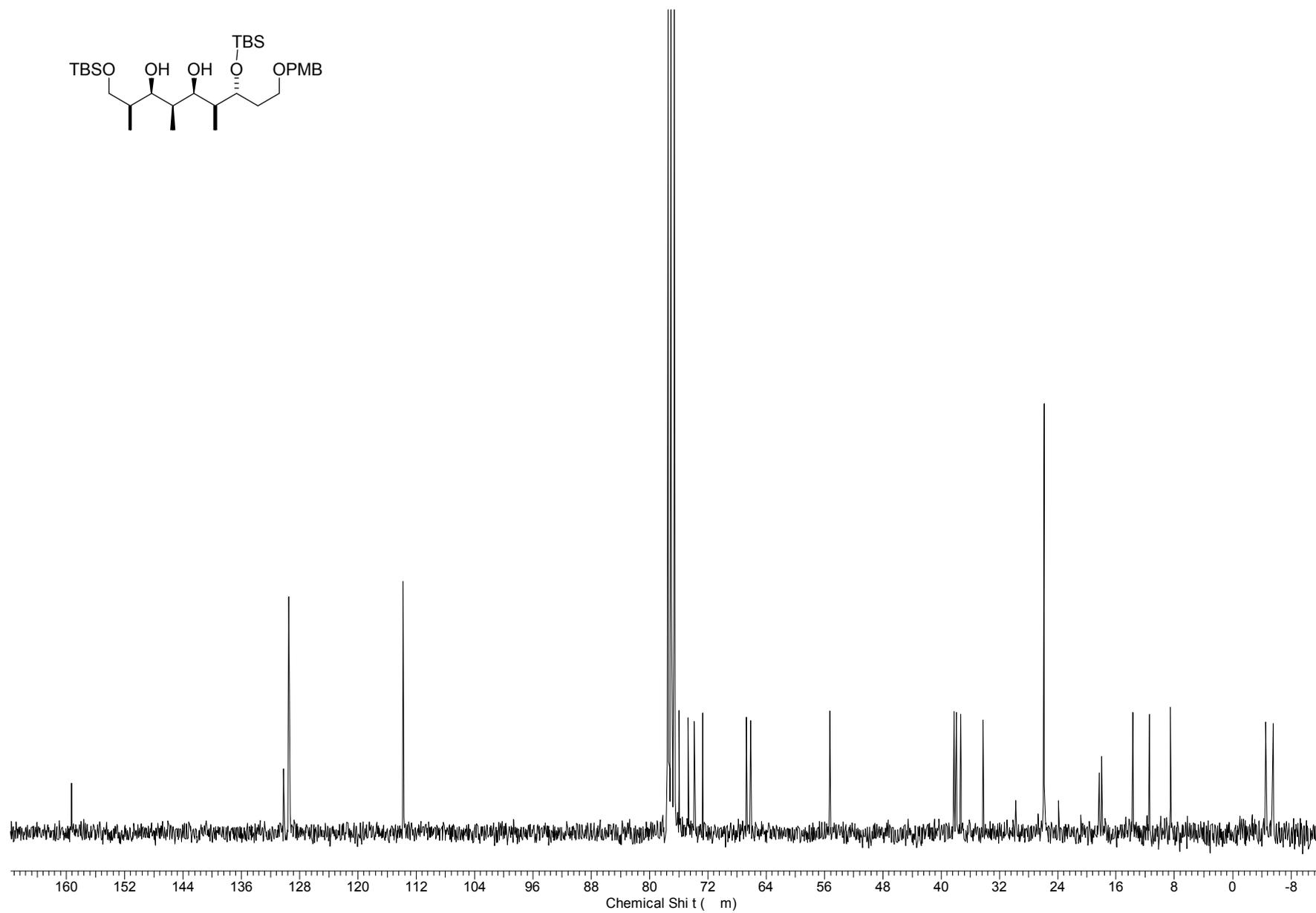
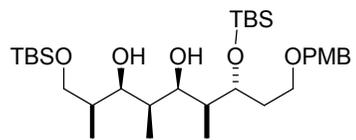
No	synthetic Etnangien		natural Etnangien ⁶	
	^{13}C	^1H mult., J (Hz)	^{13}C	^1H mult., J (Hz)
1	174.3	-	174.2	-
2	33.1	2.38 m	33.0	2.38 m
3	35.1	2.27 m	35.2	2.27 m
4	135.9	-	135.9	-
5	129.9	5.25 d, 8.3	129.9	5.24 dq, 8.5, 1.3
6	68.4	4.37 ddd, 8.4, 6.4, 6.8	68.5	4.37 dt, 8.3, 6.4
7	42.3	2.22 m / 2.33 (ddd, 14.9, 7.5, 6.8	42.4	2.22 m / 2.33 m
8	132.6	5.76 ddd, 14.9, 6.8, 7.5	132.6	5.76 dt, 15.0, 7.6
9	133.5	6.16 dd, 14.9, 10.4	133.5	6.16 dd, 15.0, 10.2
10	132.1	6.25 m	132.1	6.25 m
11	134.3	6.24 m	134.3	6.24 m
12	134.2	6.31 m	134.1	6.31 m
13	134.0	6.35 m	134.0	6.35 m
14	133.8	6.35 m	133.9	6.35 m
15	133.7	6.35 m	133.6	6.35 m
16	129.5	6.31 m	129.5	6.31 m
17	138.6	6.33 d, 17.9	138.3	6.33 m
18	136.4	-	136.1	-
19	135.5	5.53 d, 9.0	135.5	5.53 dd, 9.0, 1.0 br
20	69.6	4.39 dd, 9.2, 7.8	69.6	4.39 dd, 9.0, 8.1
21	43.9	1.98 m	43.8	1.98 m
22	73.5	5.44 m	73.5	5.44 dt, 8.5, 4.4
23	38.7	1.65 m (2H)	38.7	1.65 m (2H)
24	68.1	3.51 tt, 8.3, 4.1	67.9	3.51 tt, 8.3, 4.1
25	39.2	1.31 m / 1.42 m	39.2	1.31 m / 1.42 m
26	22.0	1.31 m / 1.46 m	22.1	1.31 m / 1.46 m
27	33.2	1.41 m	33.2	1.41 m
28	81.1	3.25 dddd, 6.0, 6.0,	81.1	3.25 ddt, 4.5, 5.6, 5.9

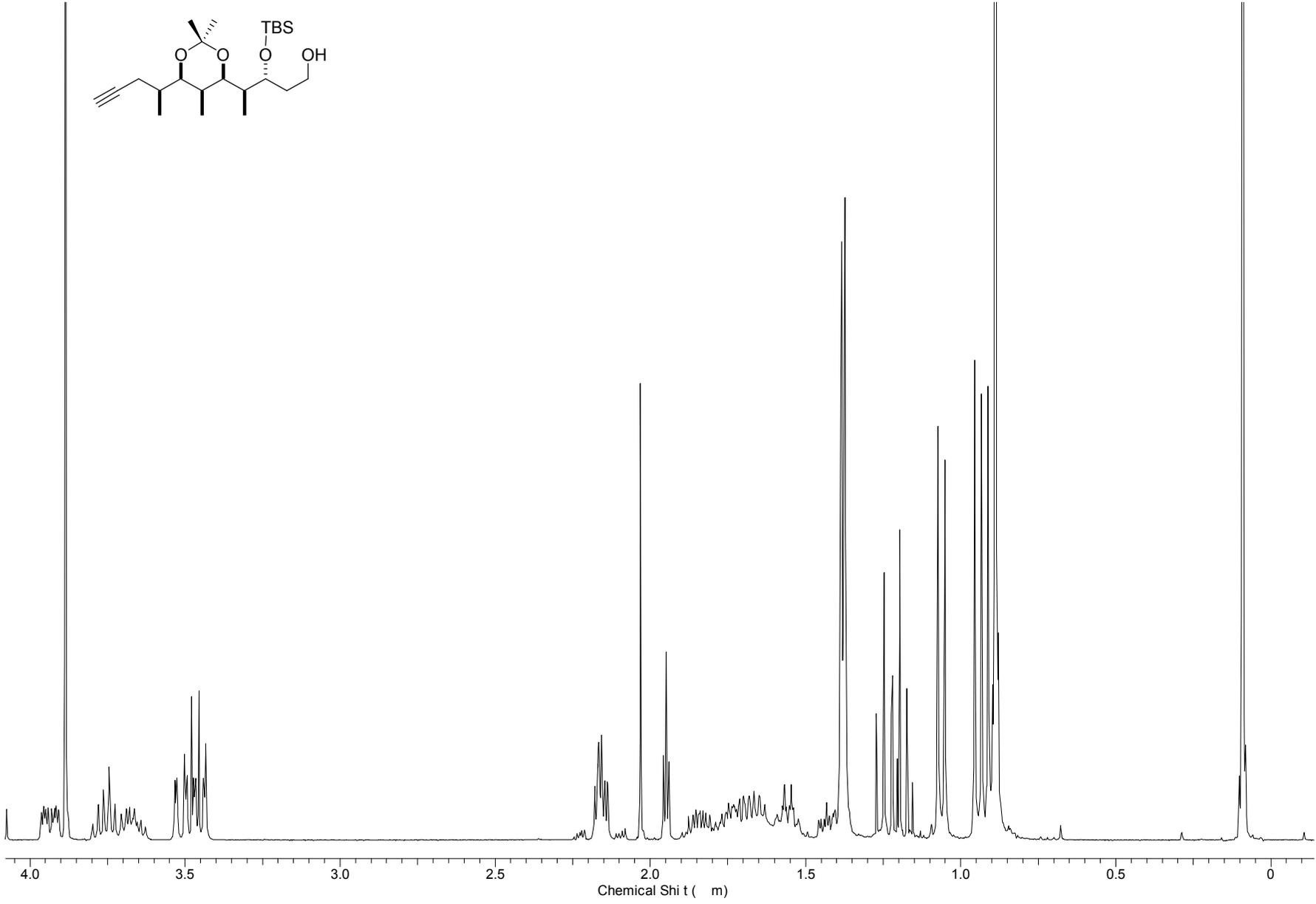
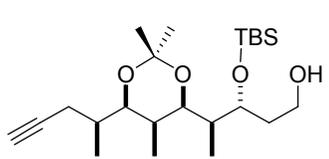
5.6, 4.5				
29	30.7	2.37 m / 2.44 m	30.7	2.37 m / 2.44 m
30	126.0	5.35 ddd, 10.7, 7.4, 7.4	126.0	5.35 dt, 10.7, 7.7 br
31	130.9	6.06 dd, 11.2, 11.2	130.9	6.06 t, 11.0
32	128.3	6.35 m	128.3	6.36 m
33	133.4	5.71 ddd, 14.9, 8.5, 6.2	133.3	5.71 ddd, 14.8, 8.3, 6.0
34	37.8	1.95 m / 2.23 m	37.6	1.95 m / 2.23 m
35	36.5	1.75 m	36.5	1.75 m
36	79.4	3.44 dd, 6.8, 3.8	79.3	3.44 dd, 7.2, 3.8
37	37.3	1.84 m	37.3	1.84 m
38	76.8	3.61 dd, 7.9, 2.6	76.9	3.61 dd, 7.2, 3.2
39	42.8	1.87 m	42.8	1.87 m
40	69.0	4.17 dt, 5.4, 6.2	69.0	4.17 dt, 5.4, 6.2
41	38.7	2.40 (2H) m	38.7	2.40 (2H) m
42	173.5	-	173.6	-
Me-4	16.7	1.66 d, 1.1	16.7	1.66 d, 1.1
Me-18	13.2	1.82 d, 0.7	13.2	1.82 d, 0.7
Me-21	11.1	0.84 d, 7.2	11.1	0.84 d, 7.2
Me-35	15.1	0.92 d, 6.4	15.1	0.92 d, 6.8
Me-37	7.2	0.98 d, 6.8	7.2	0.98 d, 6.8
Me-39	10.9	0.97 d, 7.0	10.9	0.97 d, 6.8
OMe-28	56.4	3.29 s	56.5	3.29 s

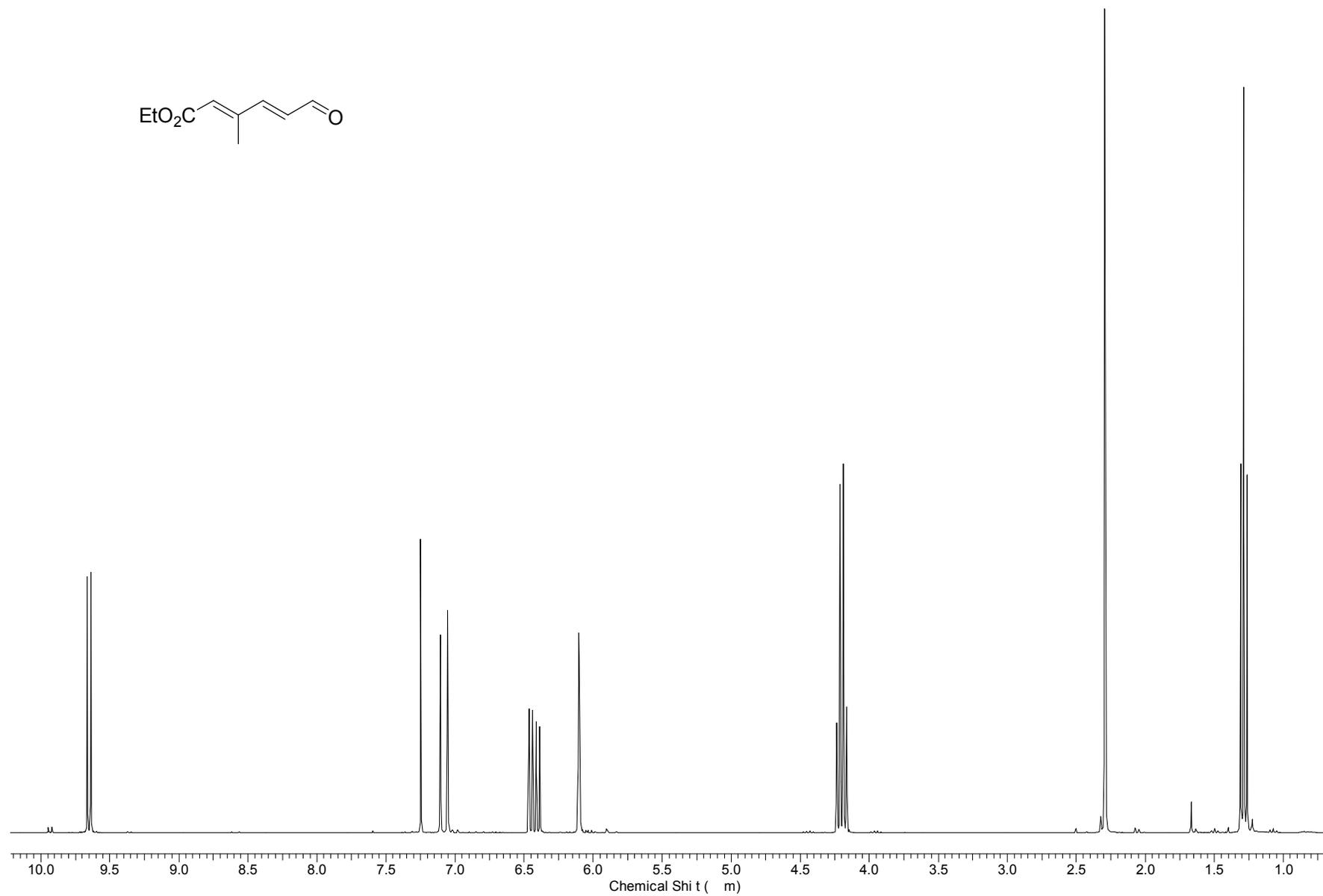
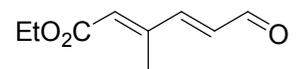


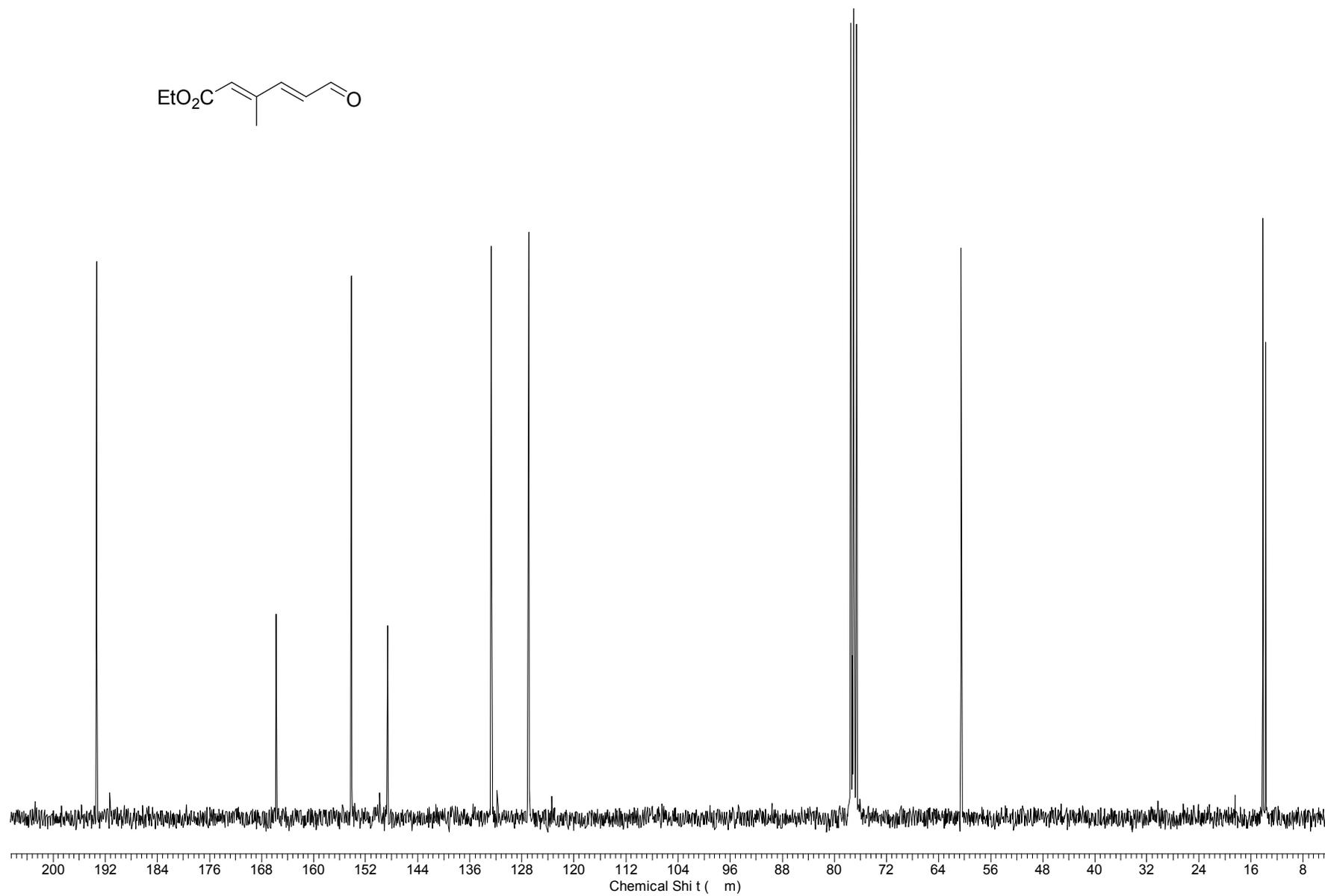
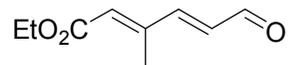


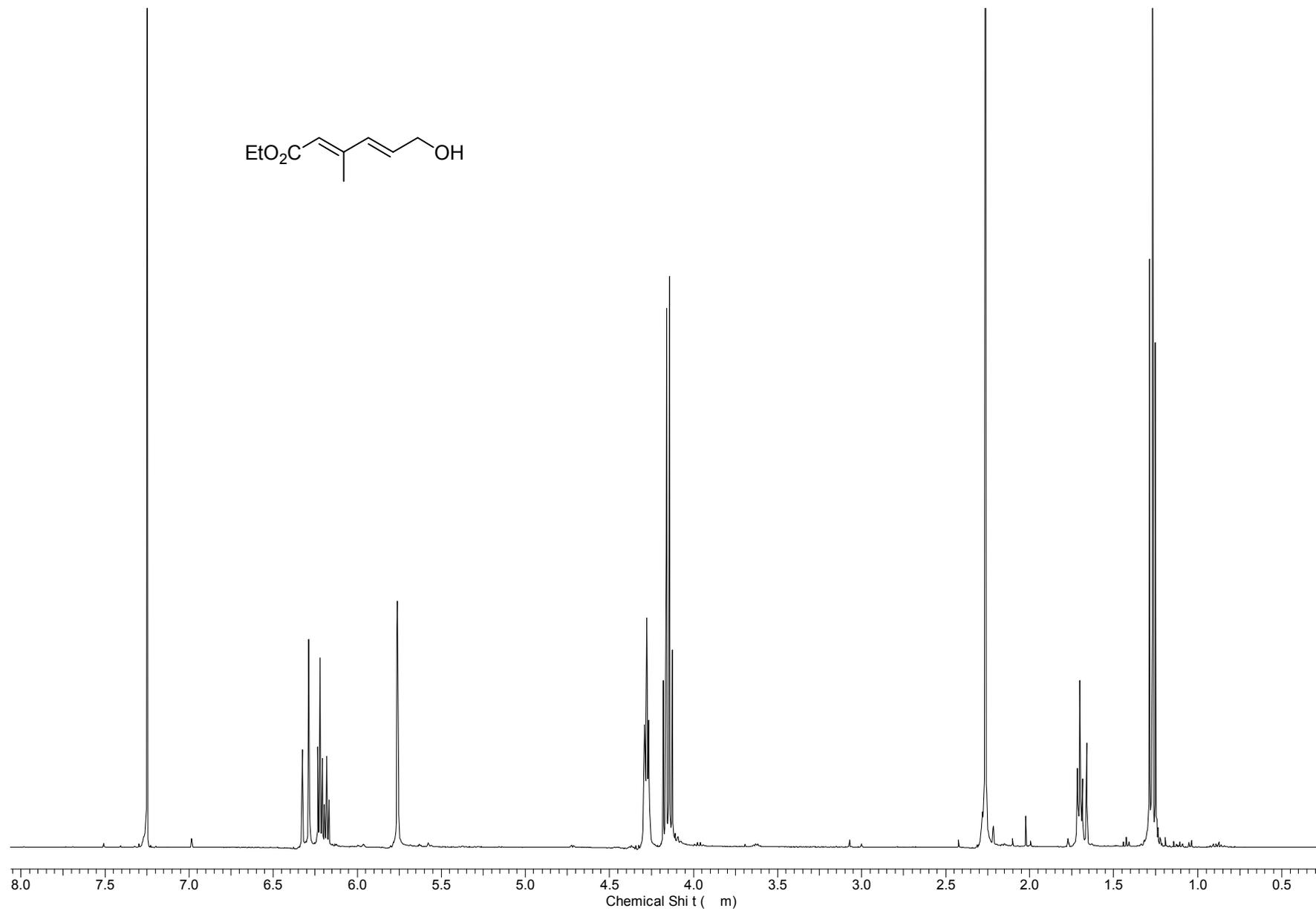
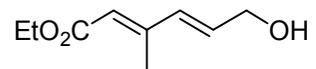


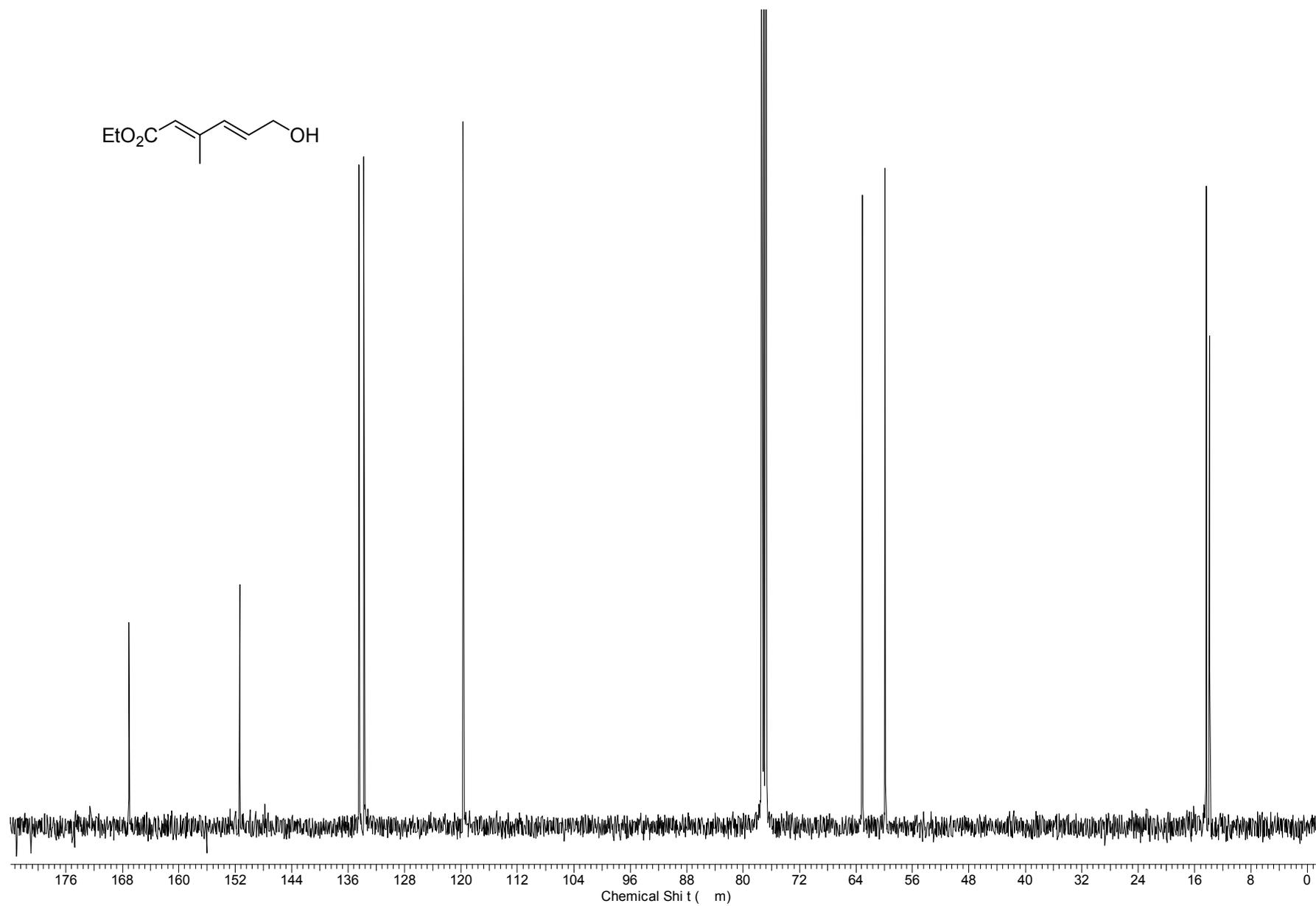
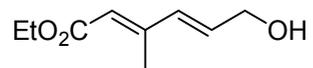


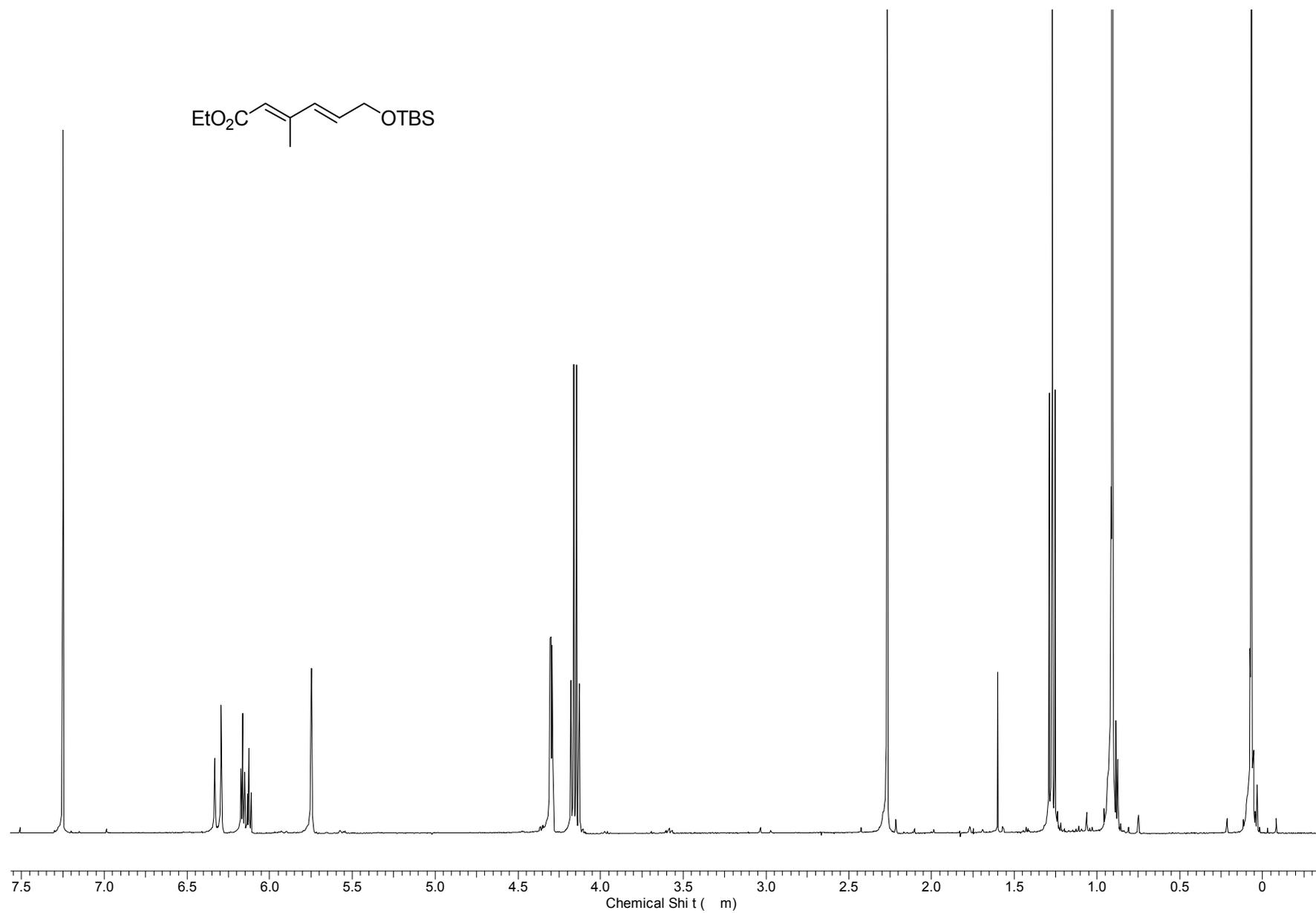
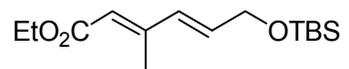


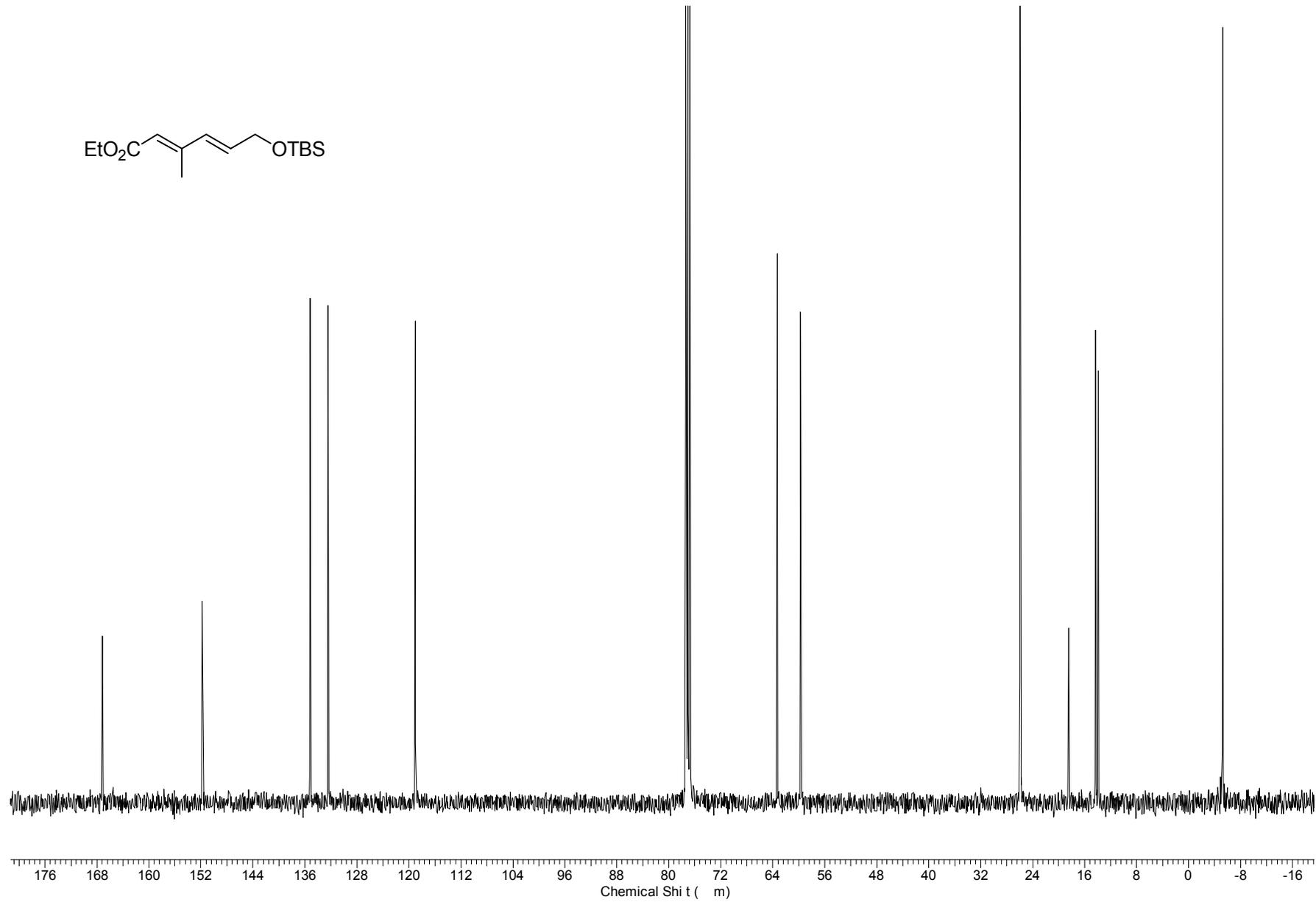
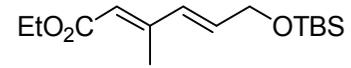


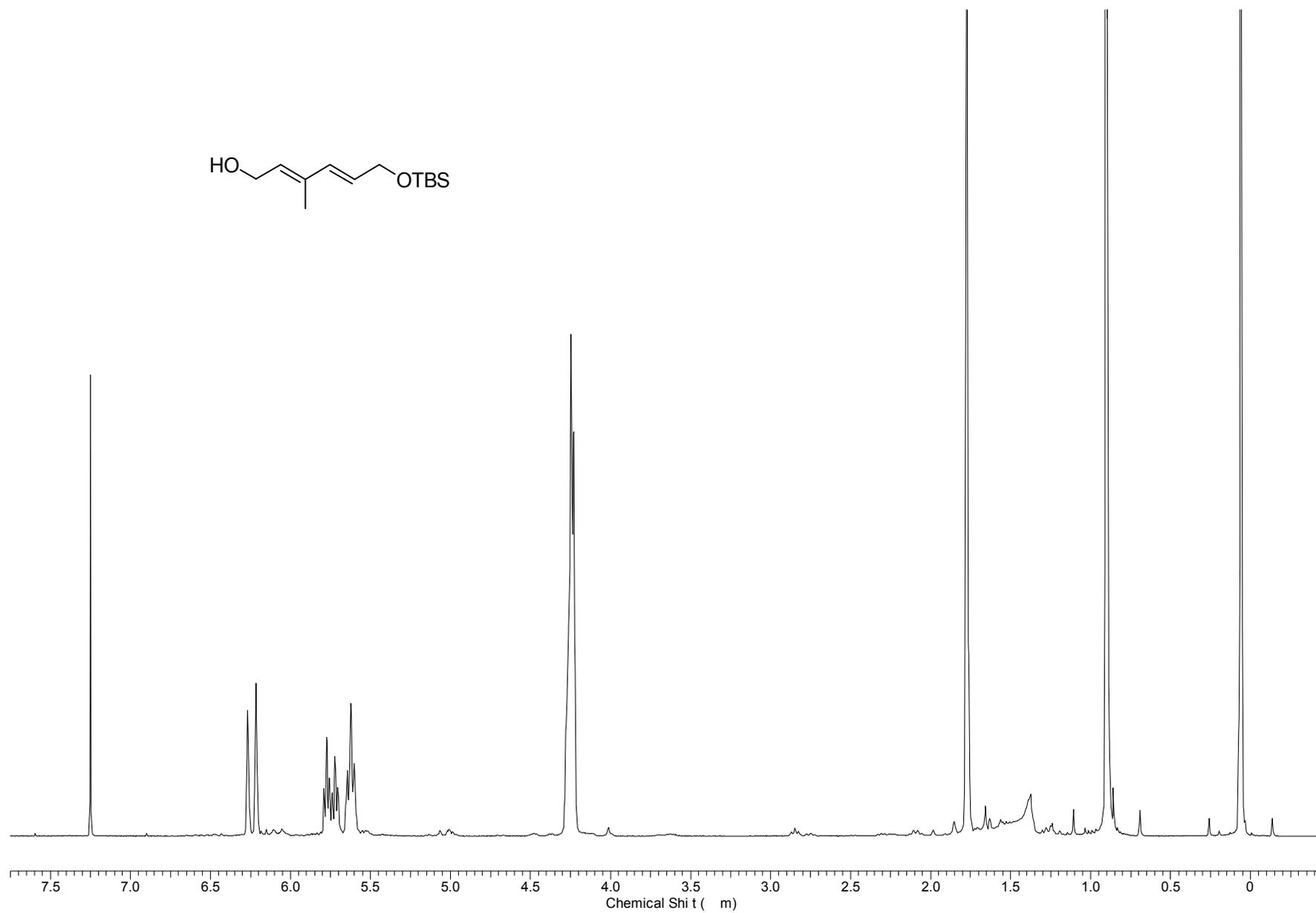
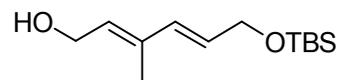


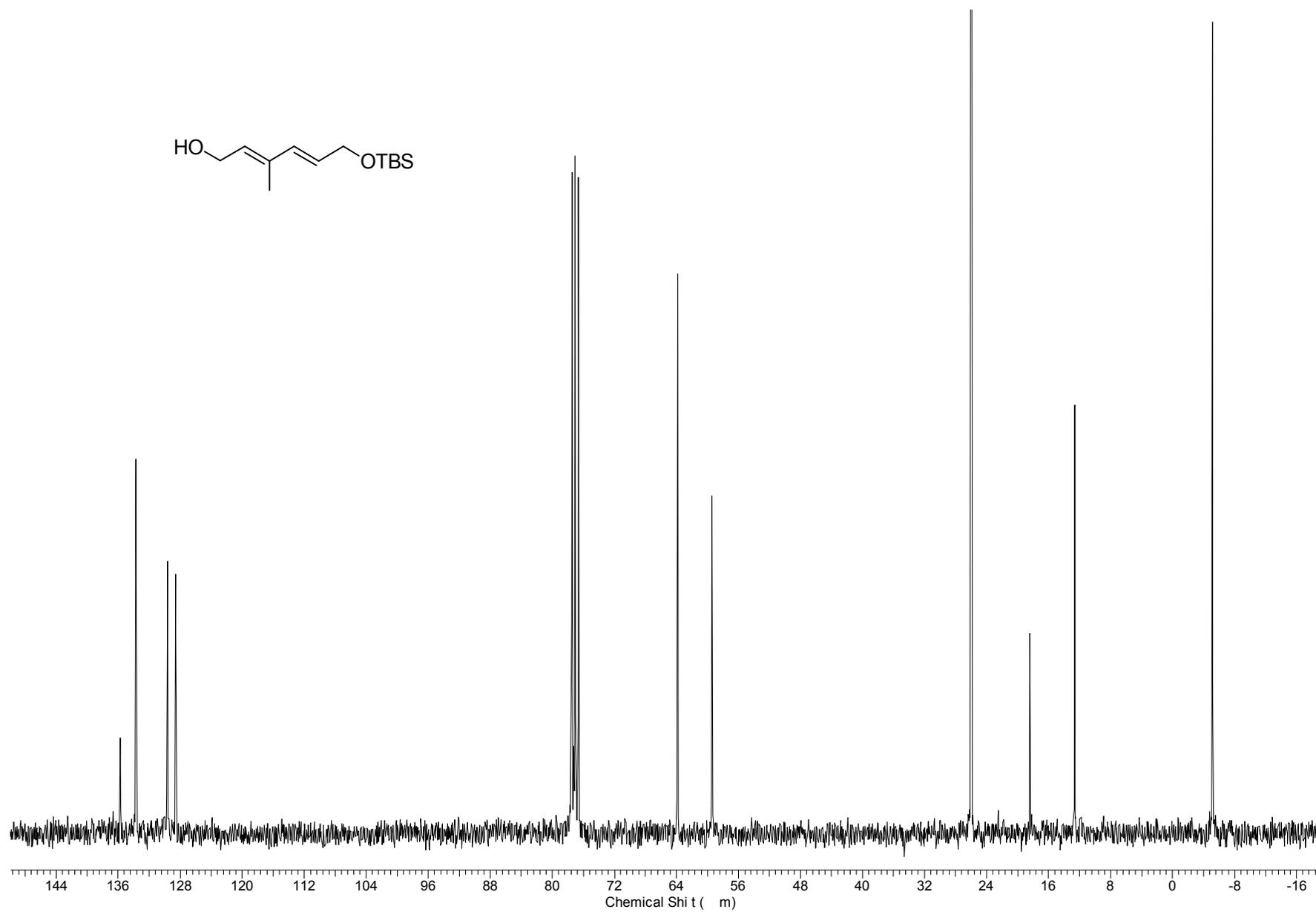
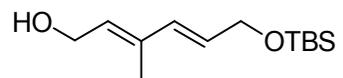


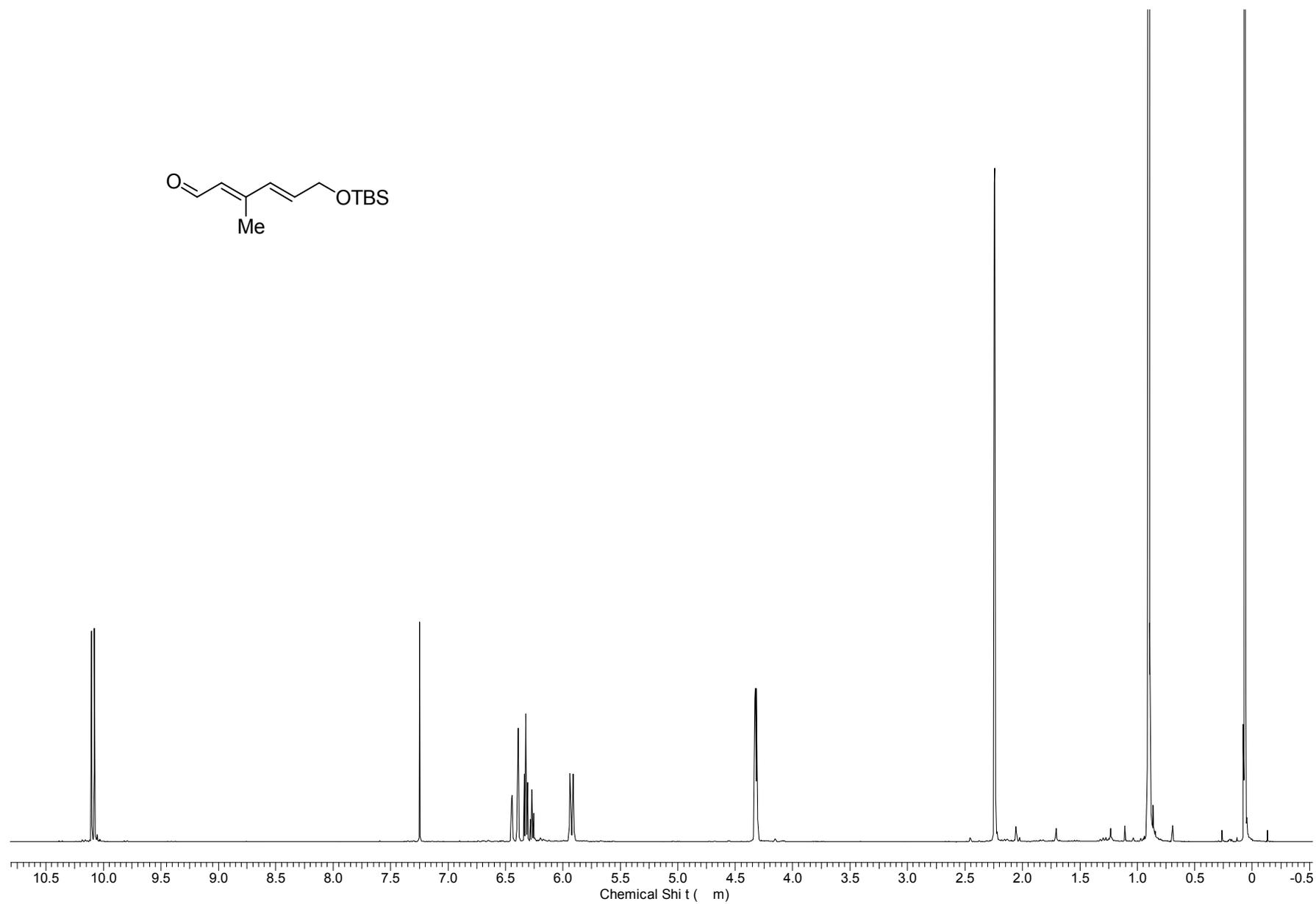
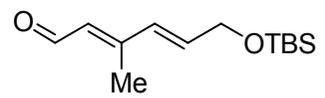


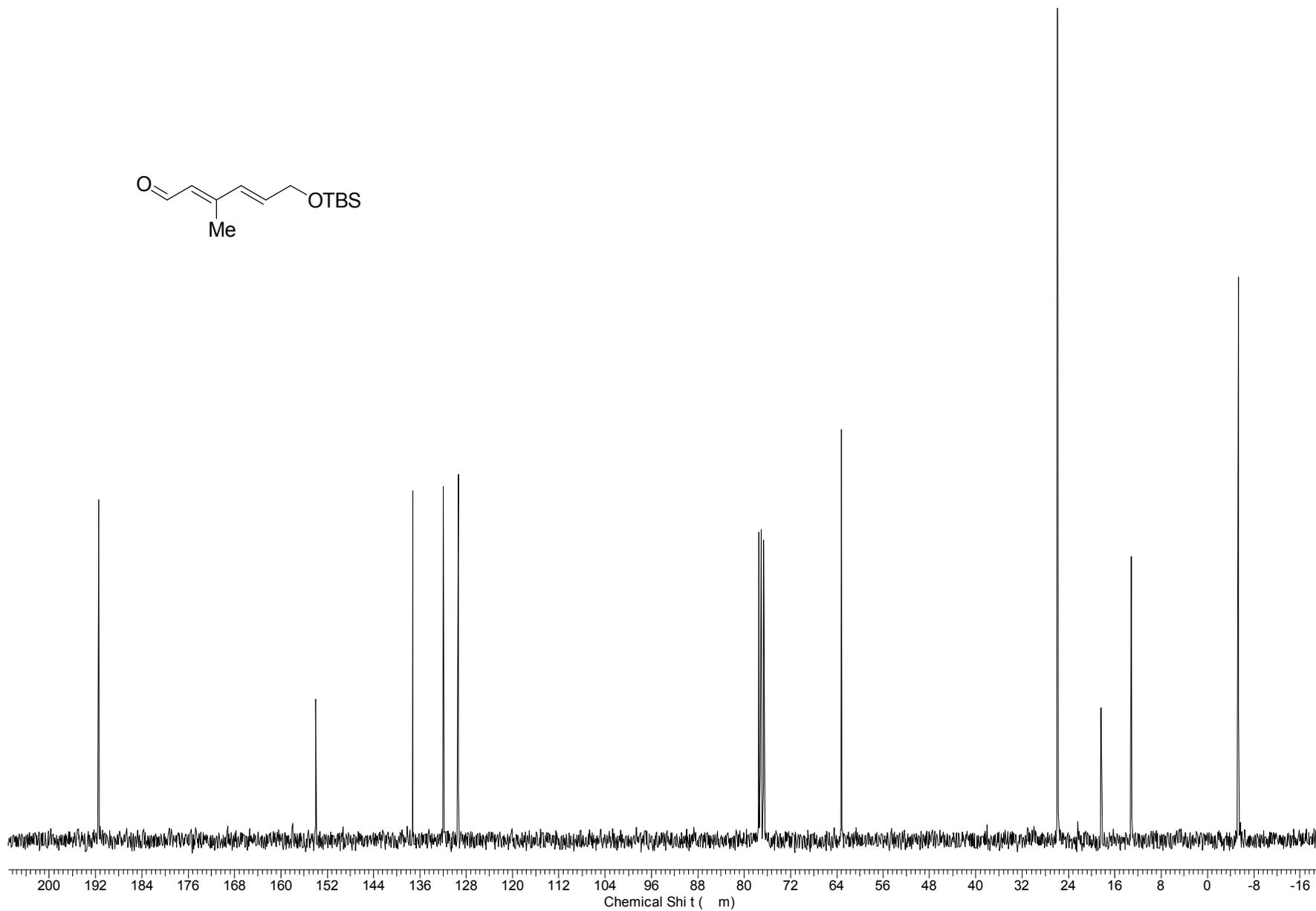
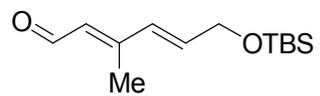


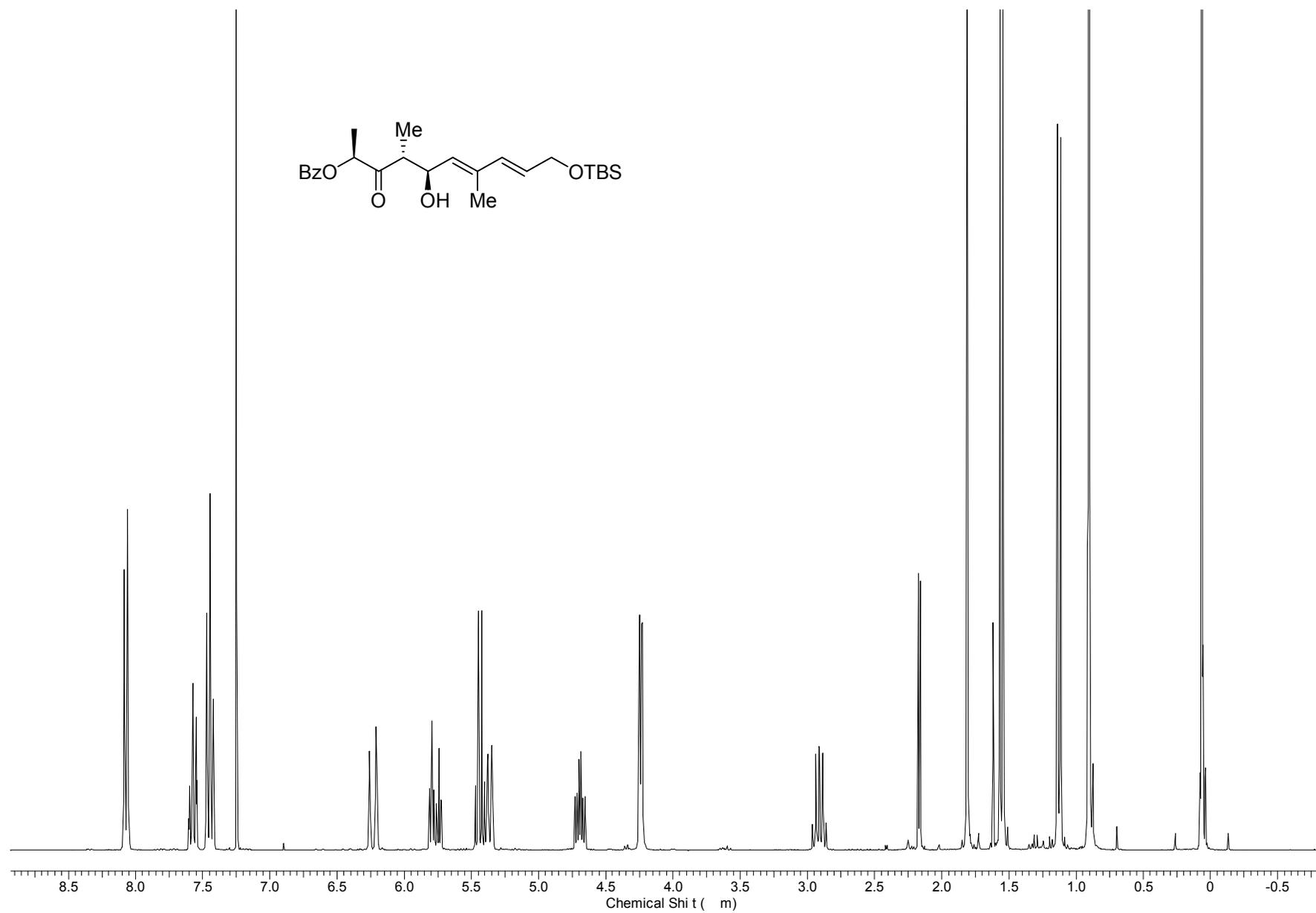
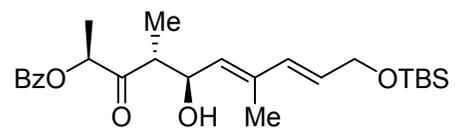


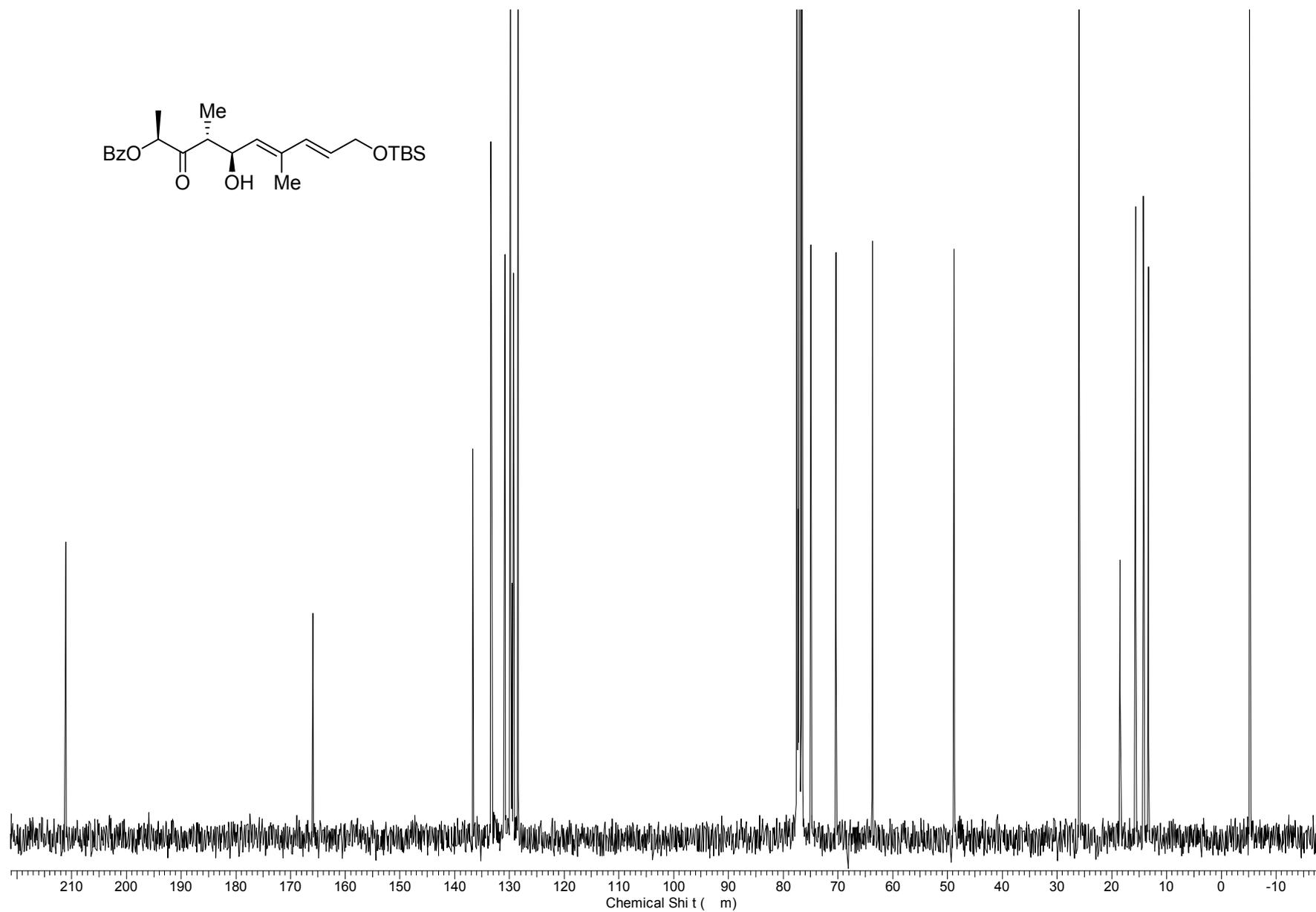
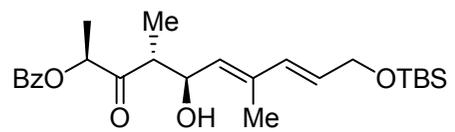


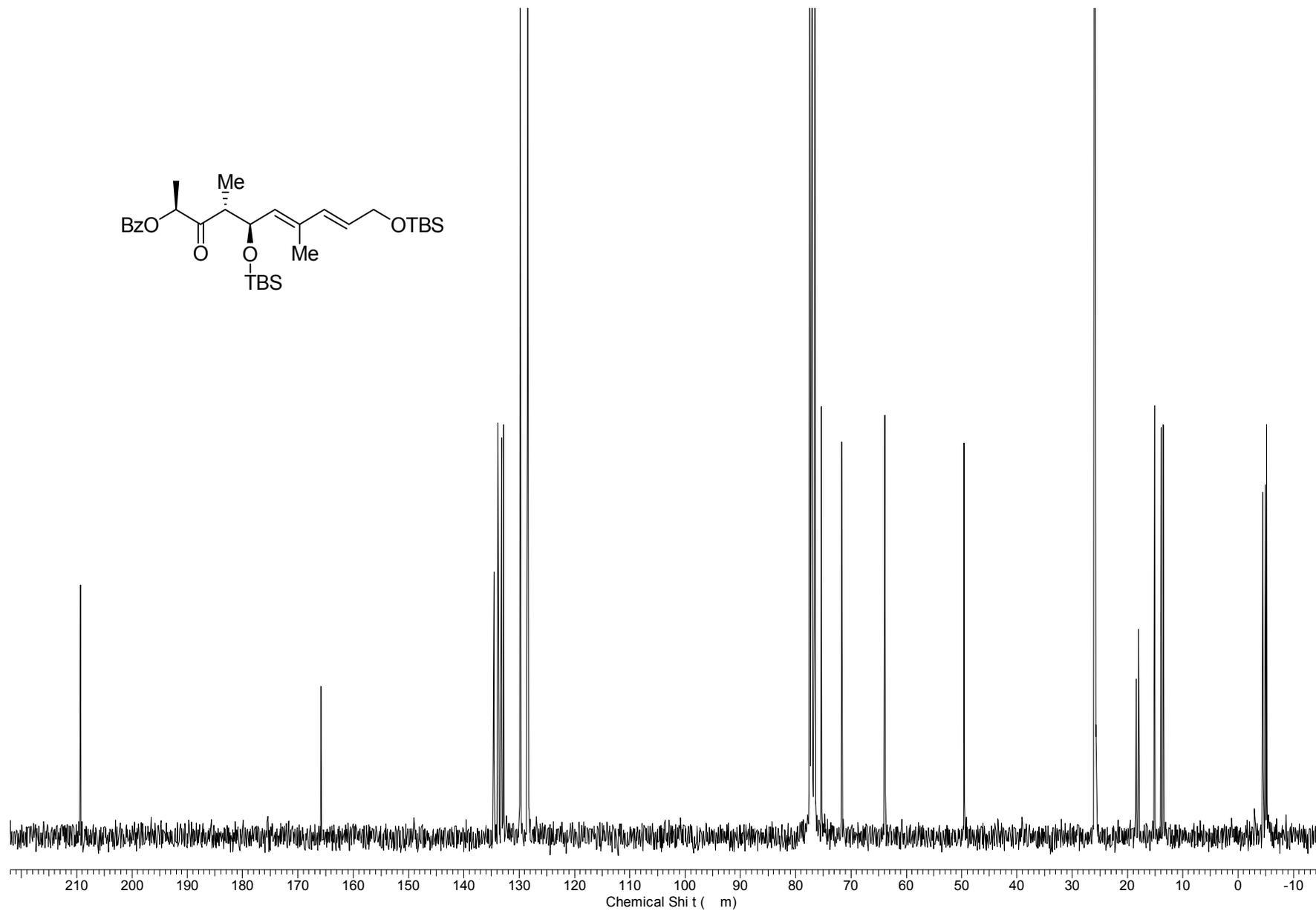
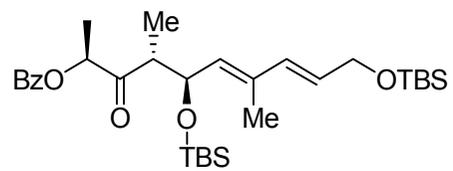


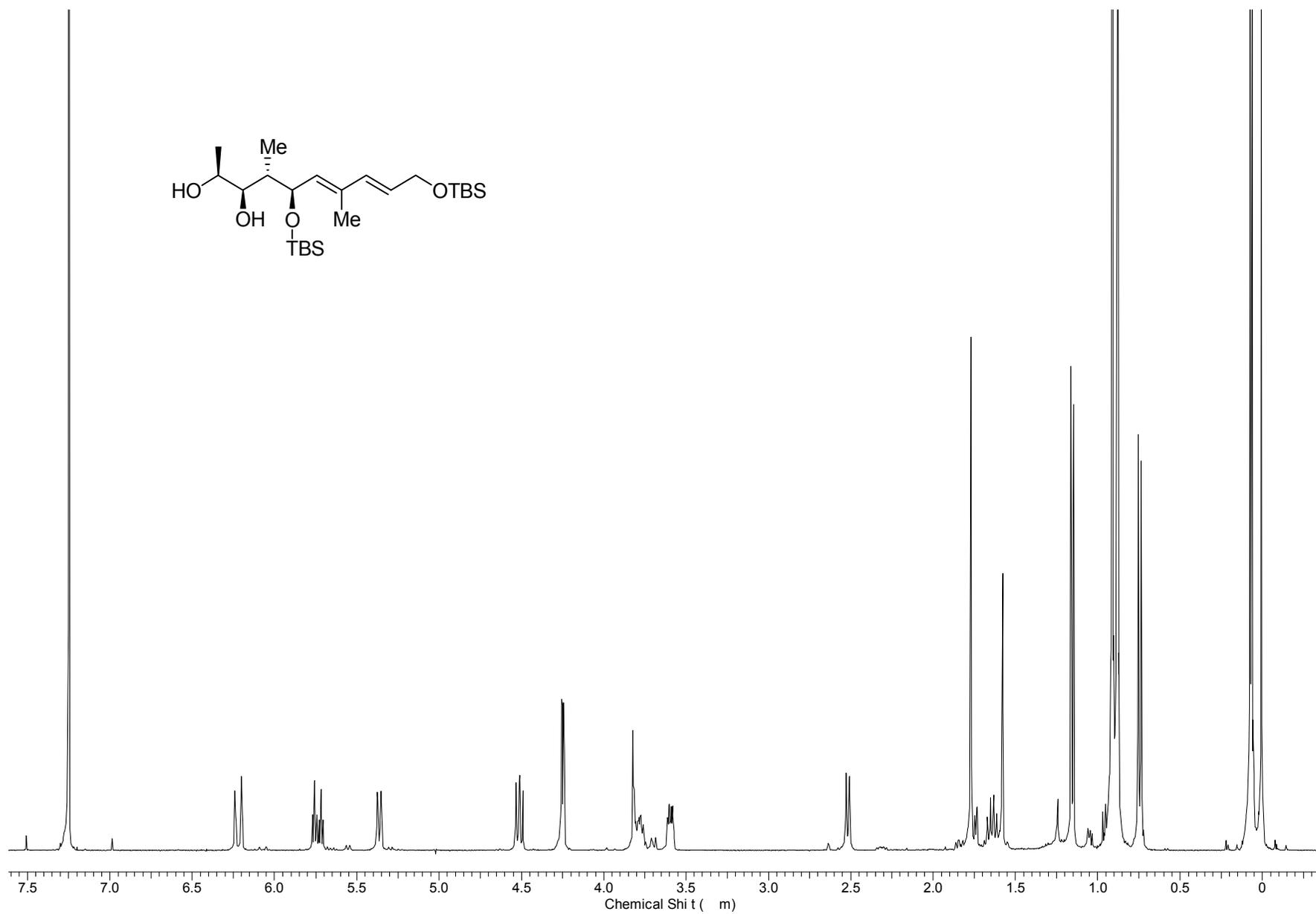
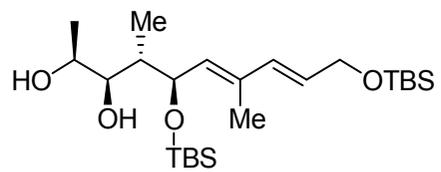


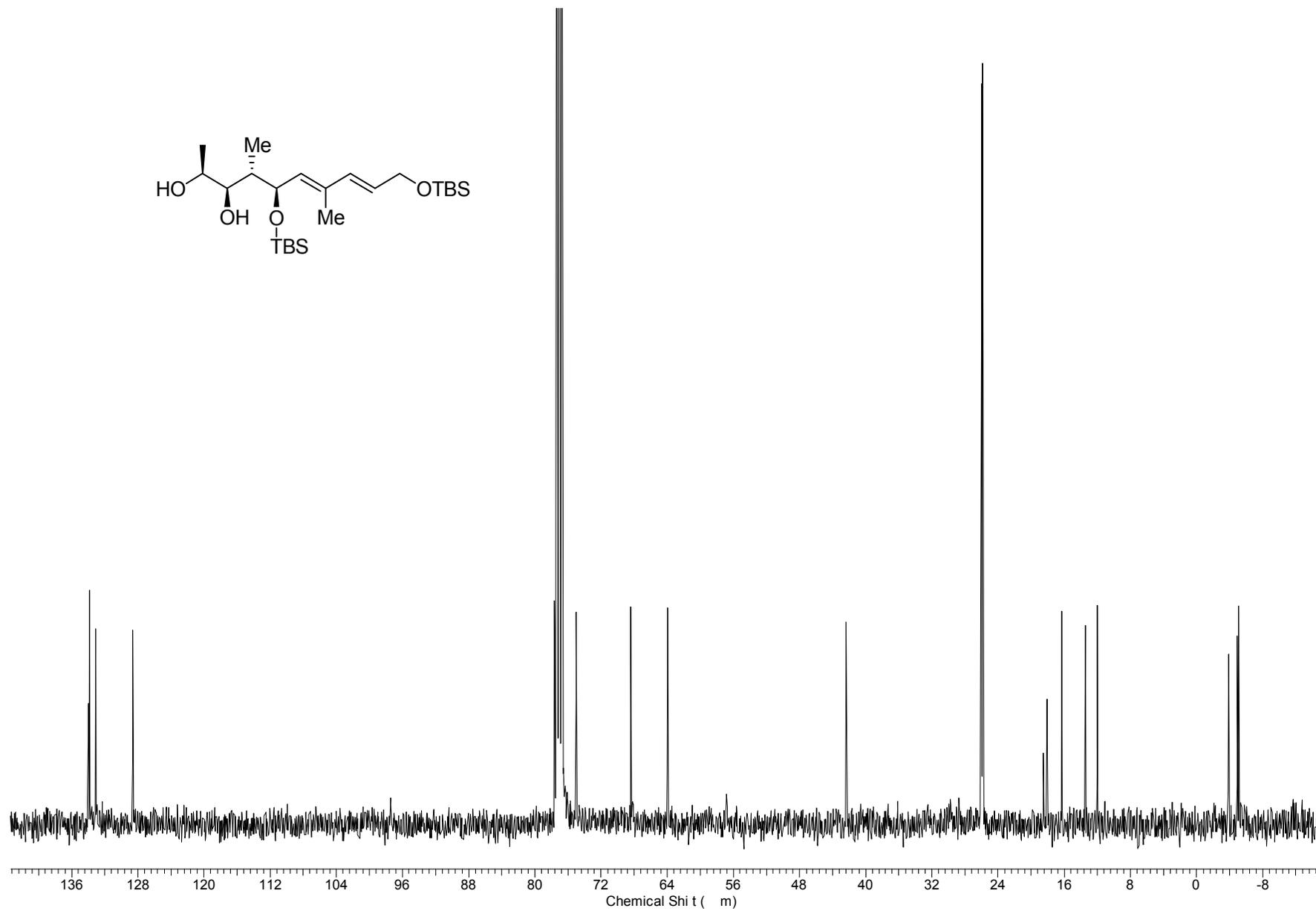
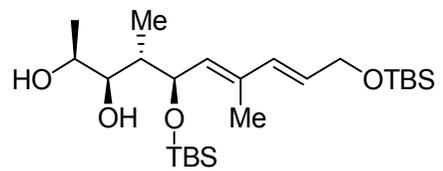


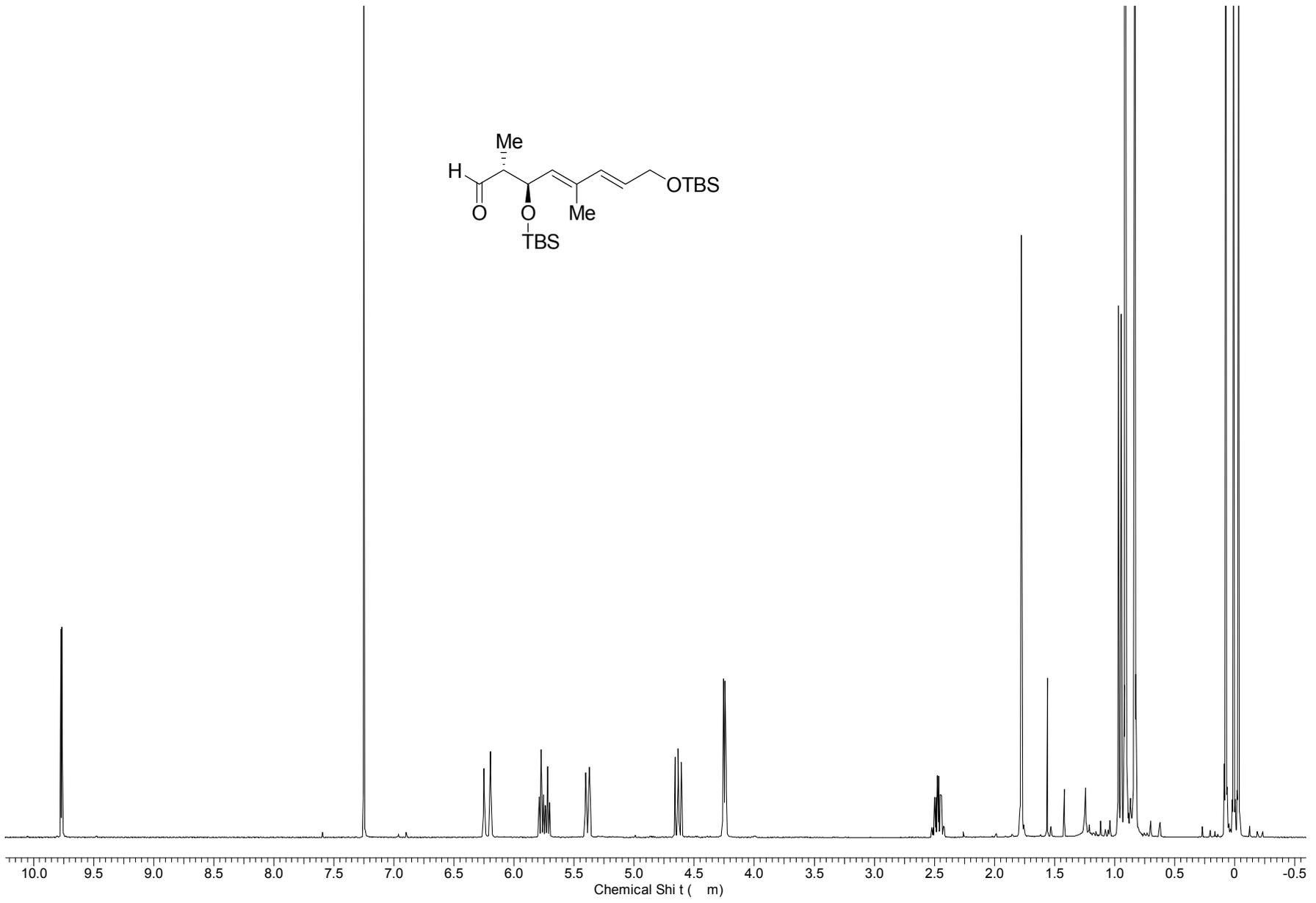
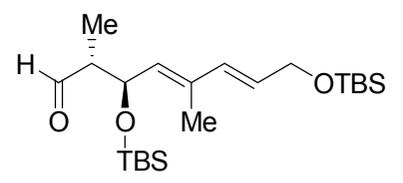


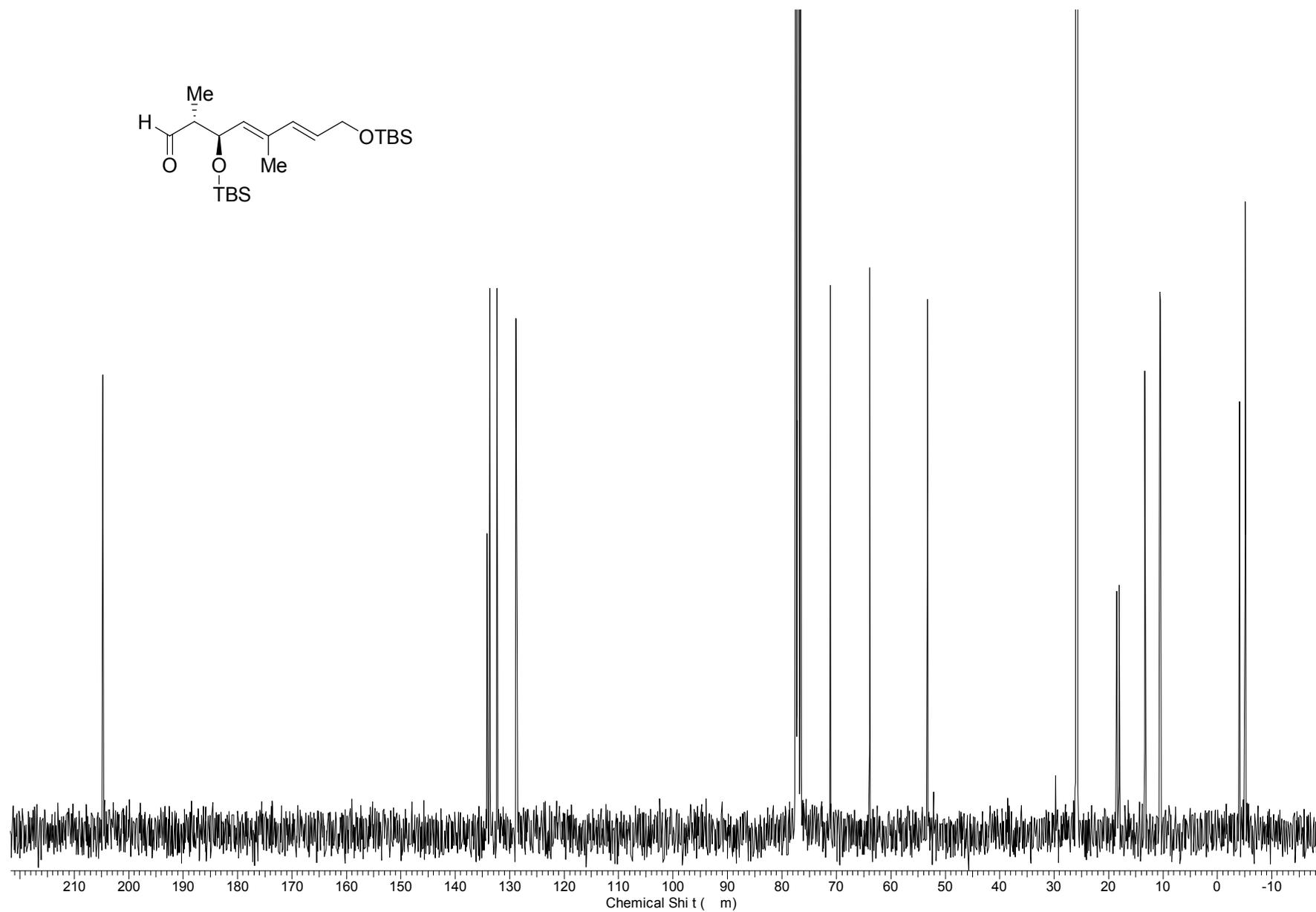
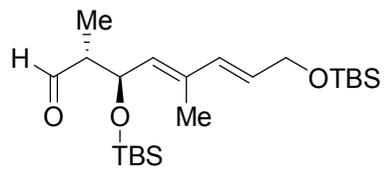


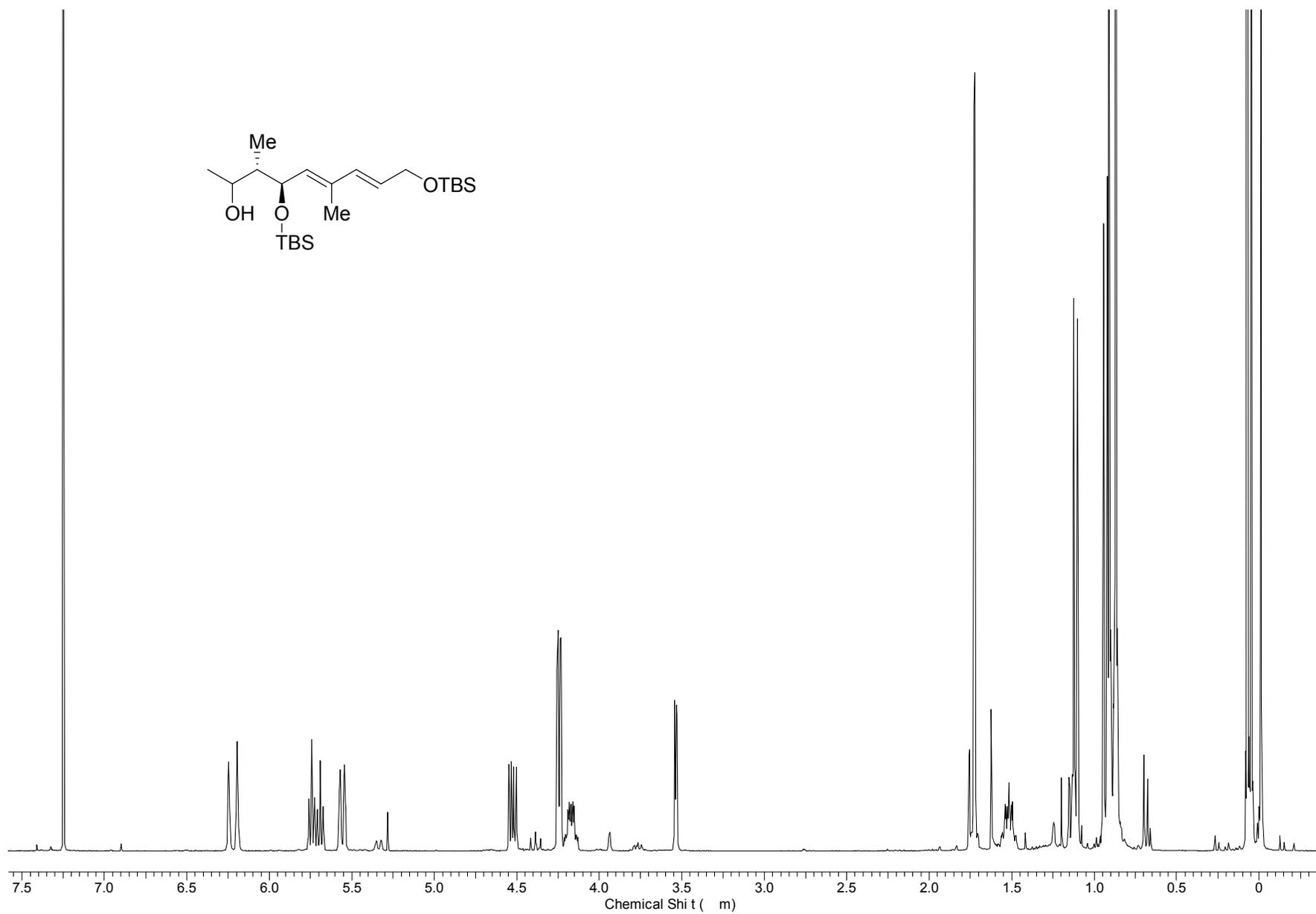
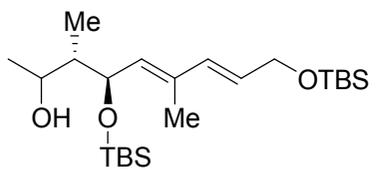


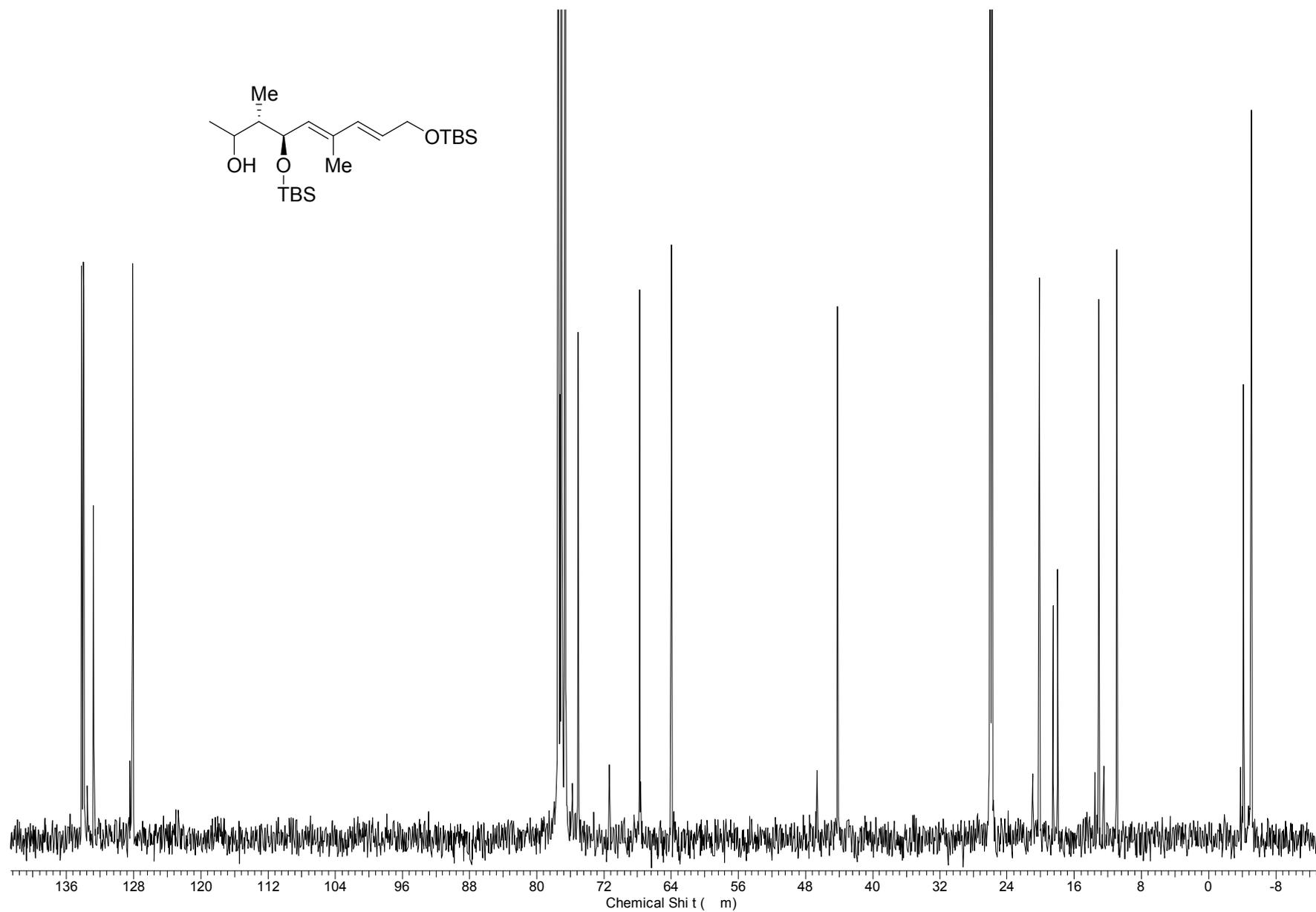
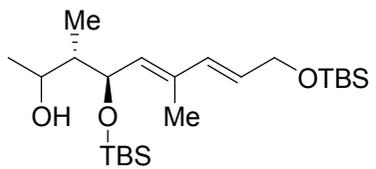


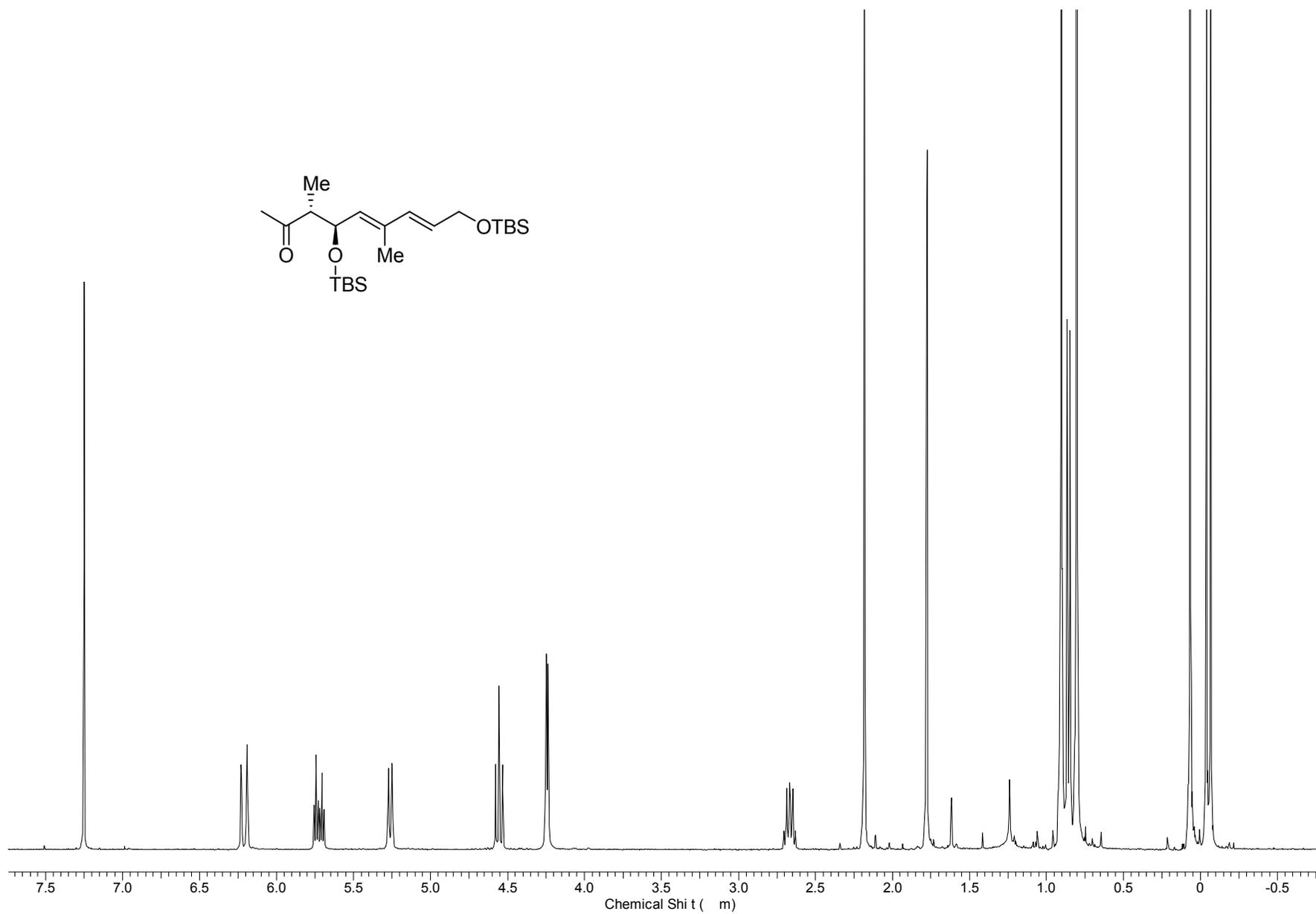
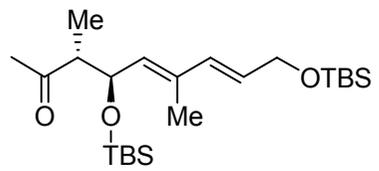


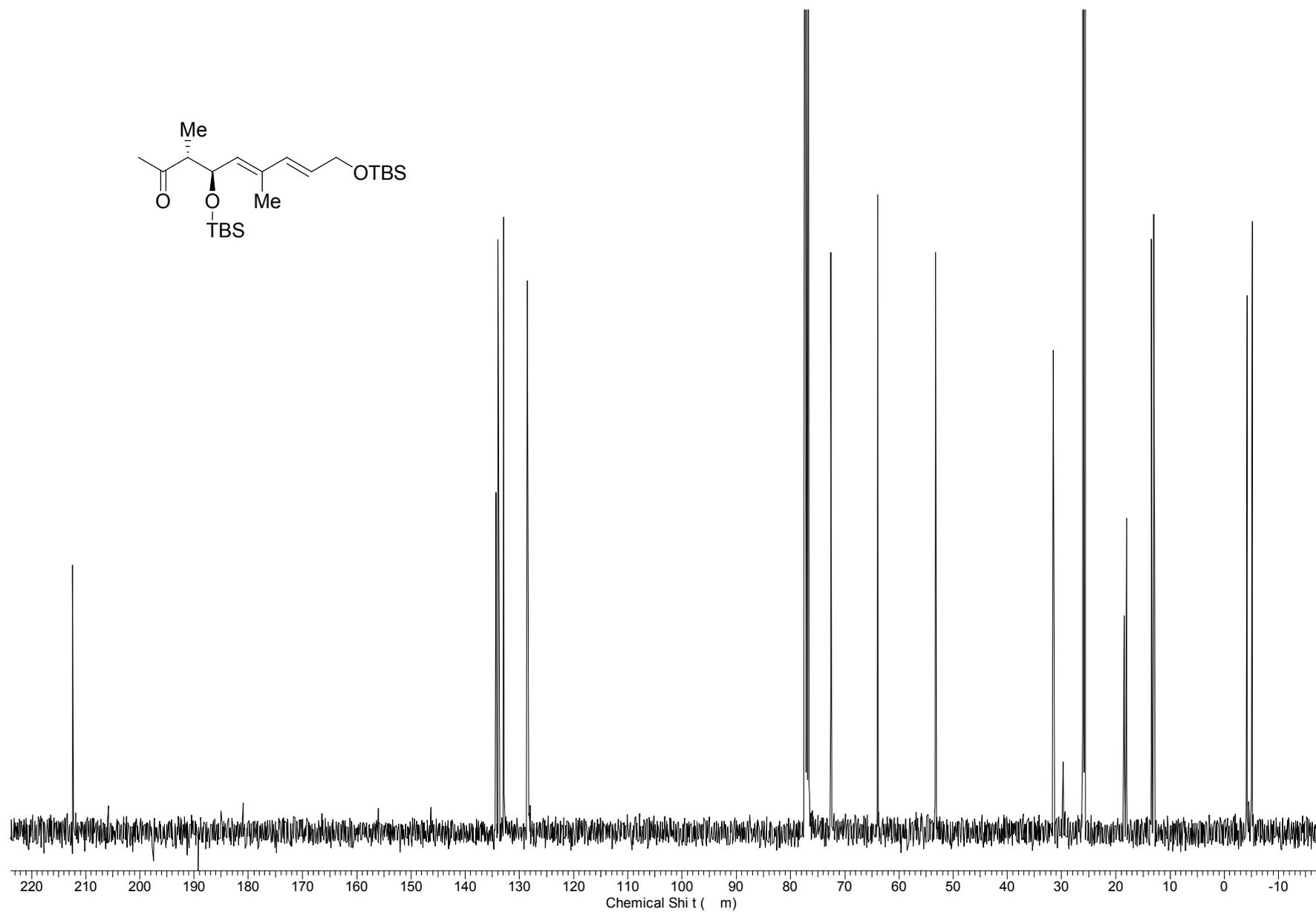
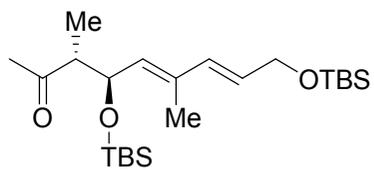


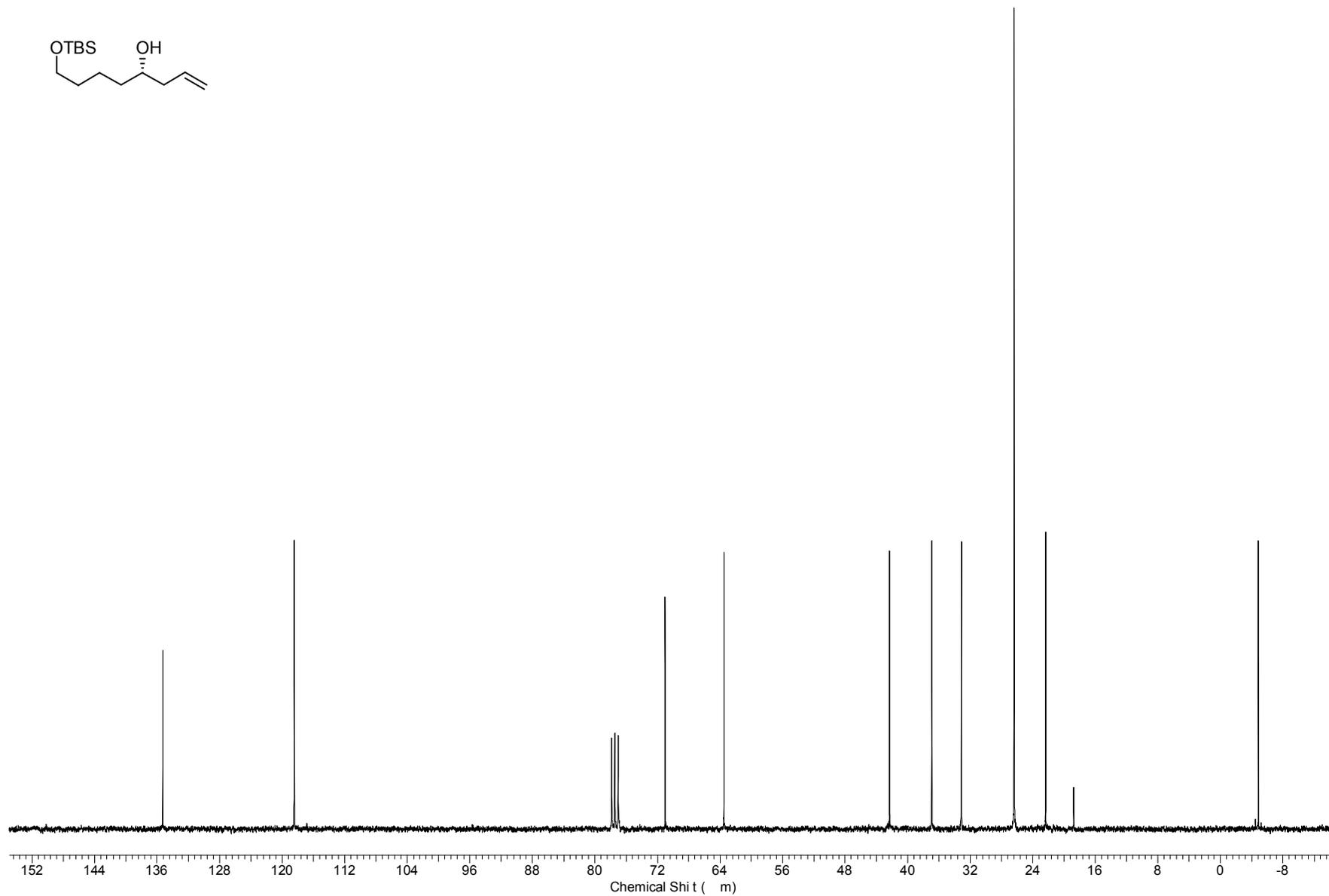
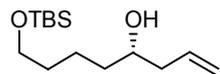


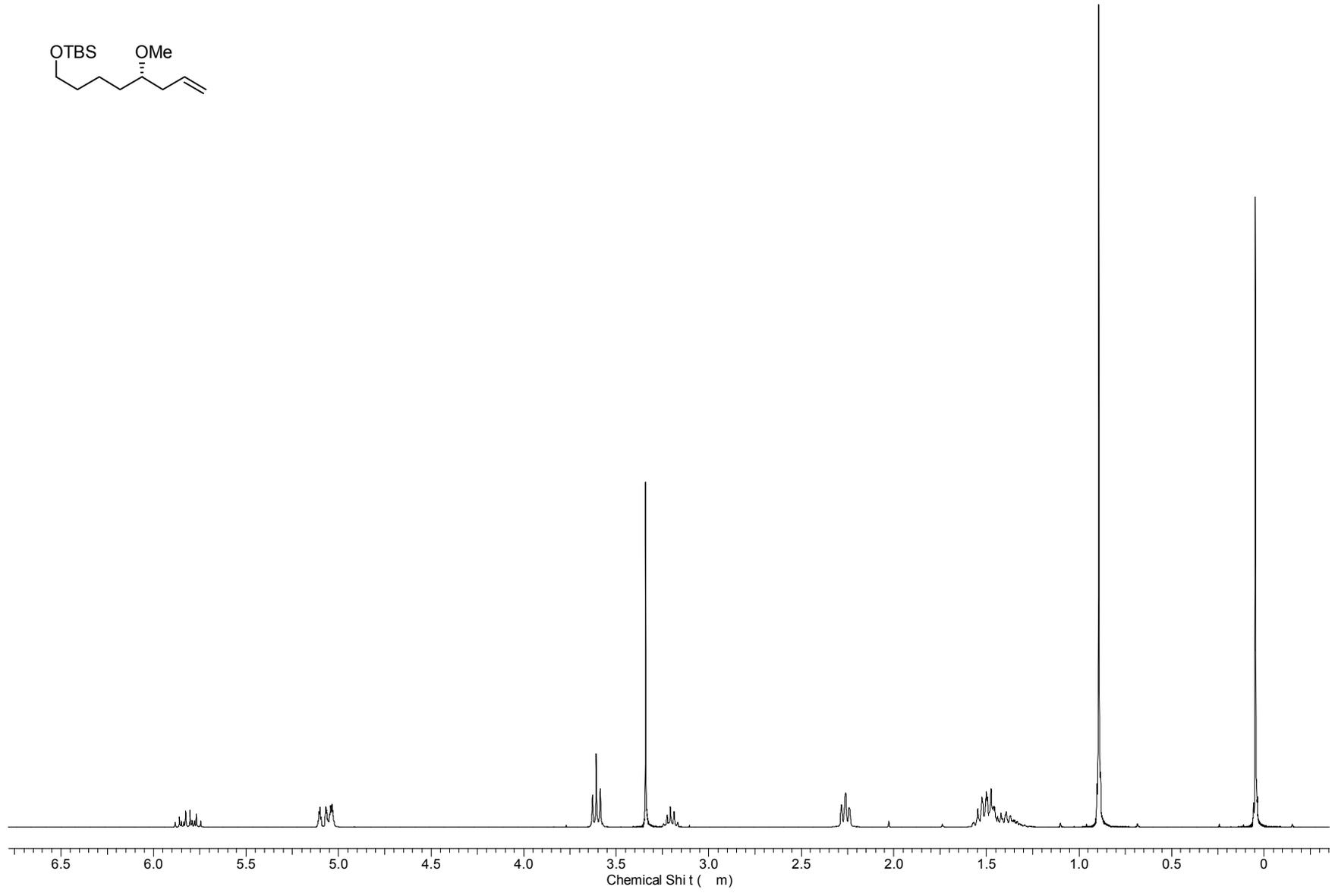
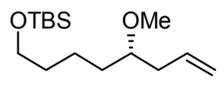


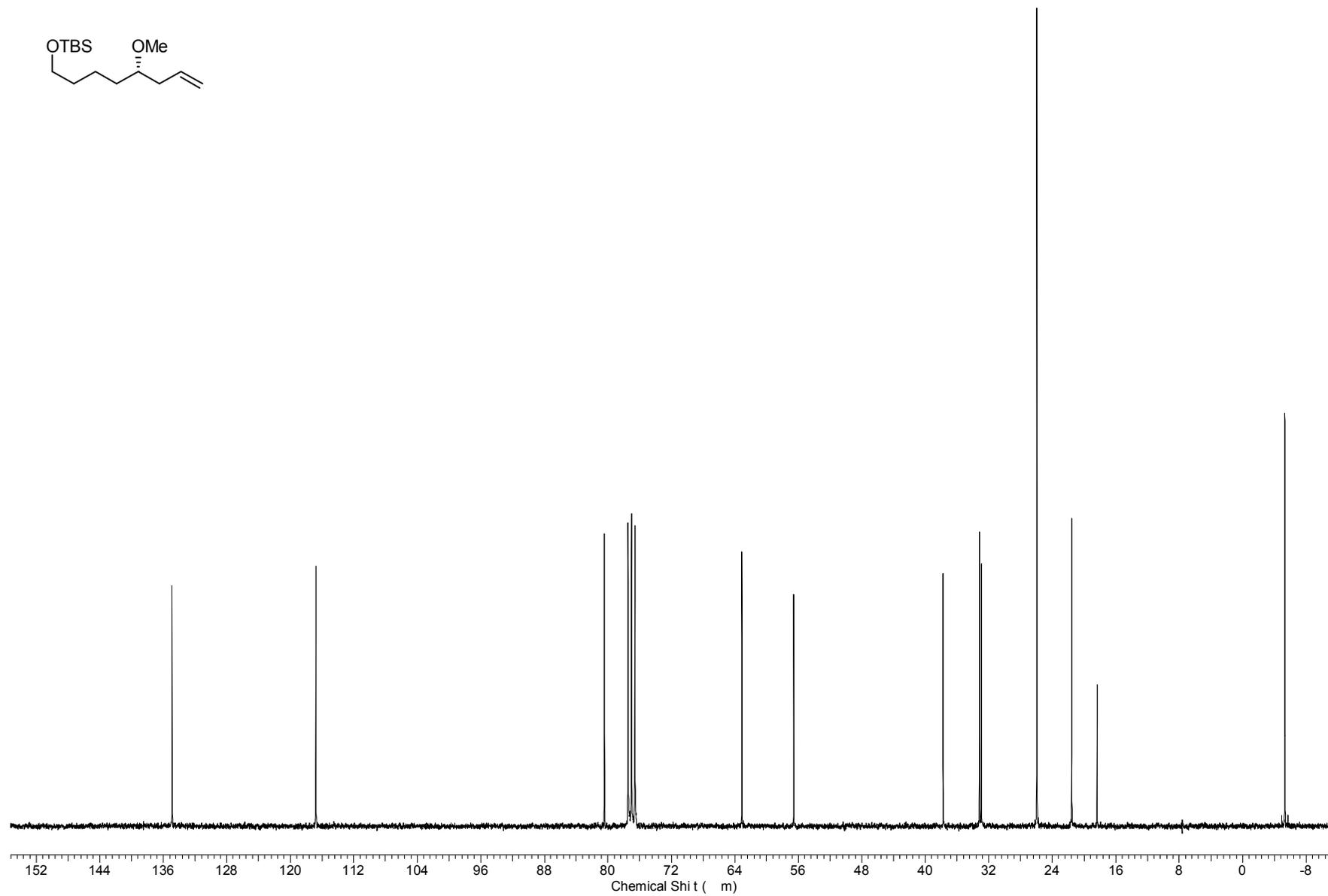
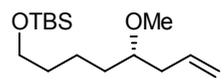


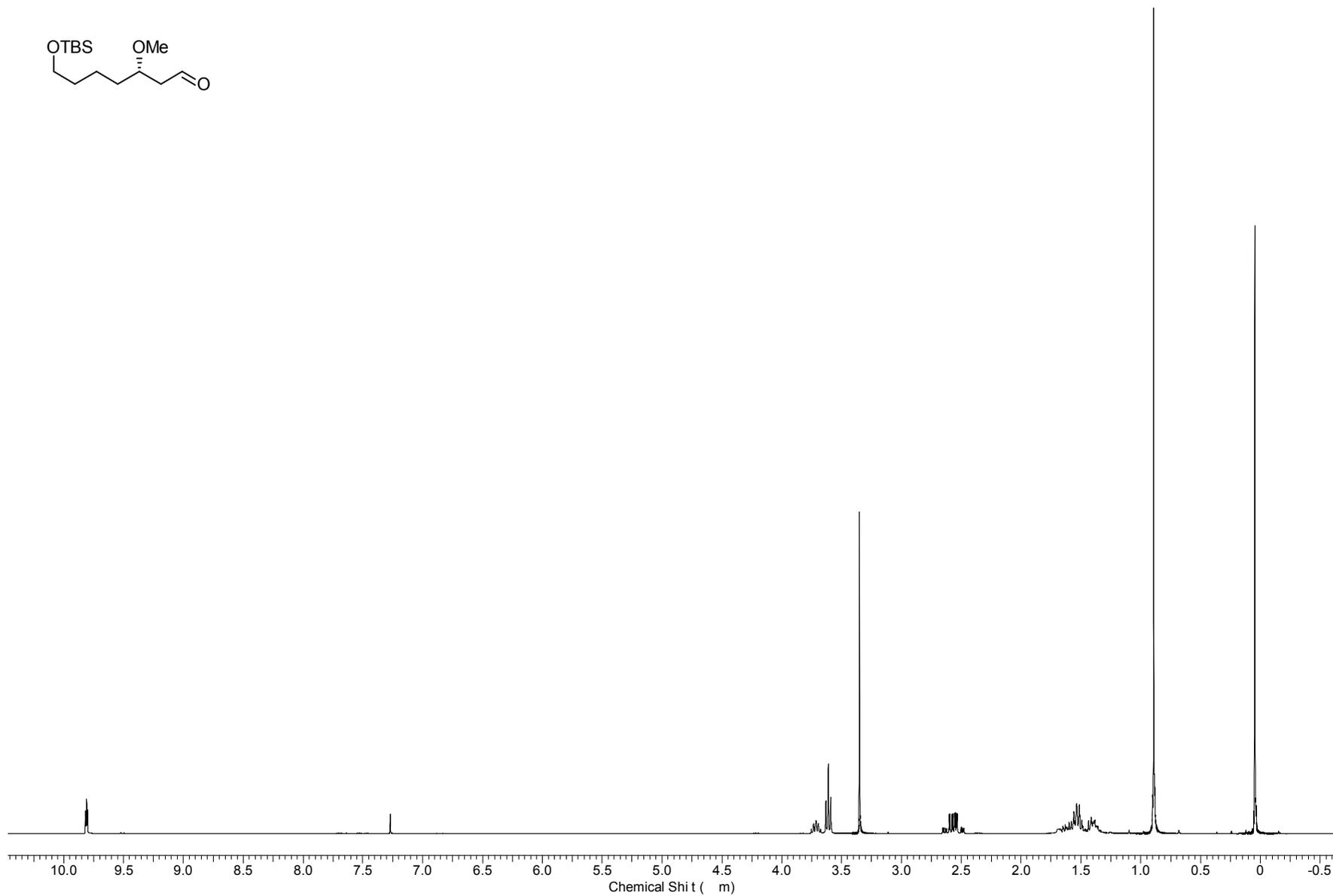
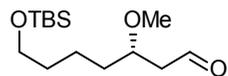


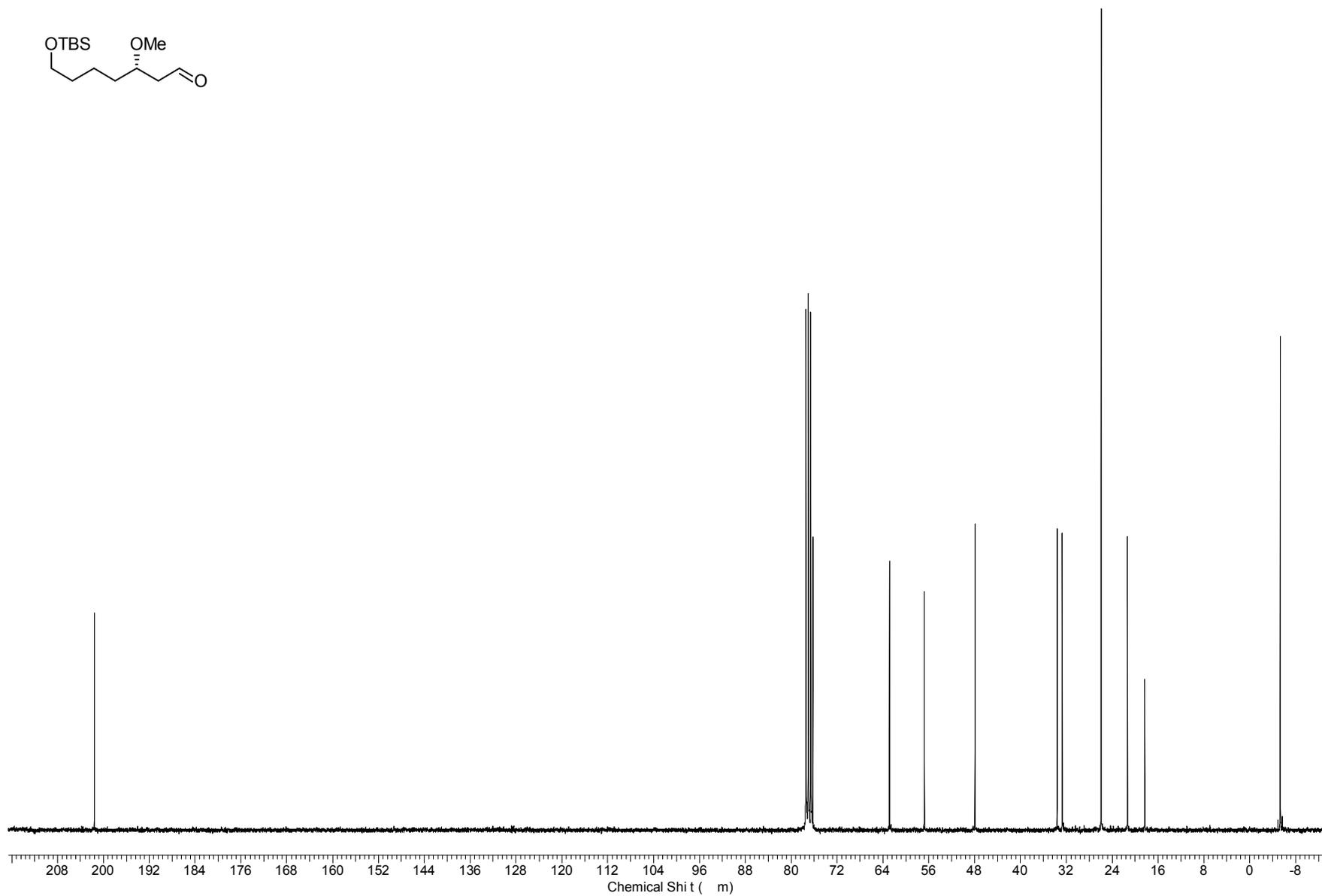
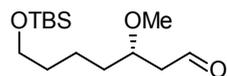


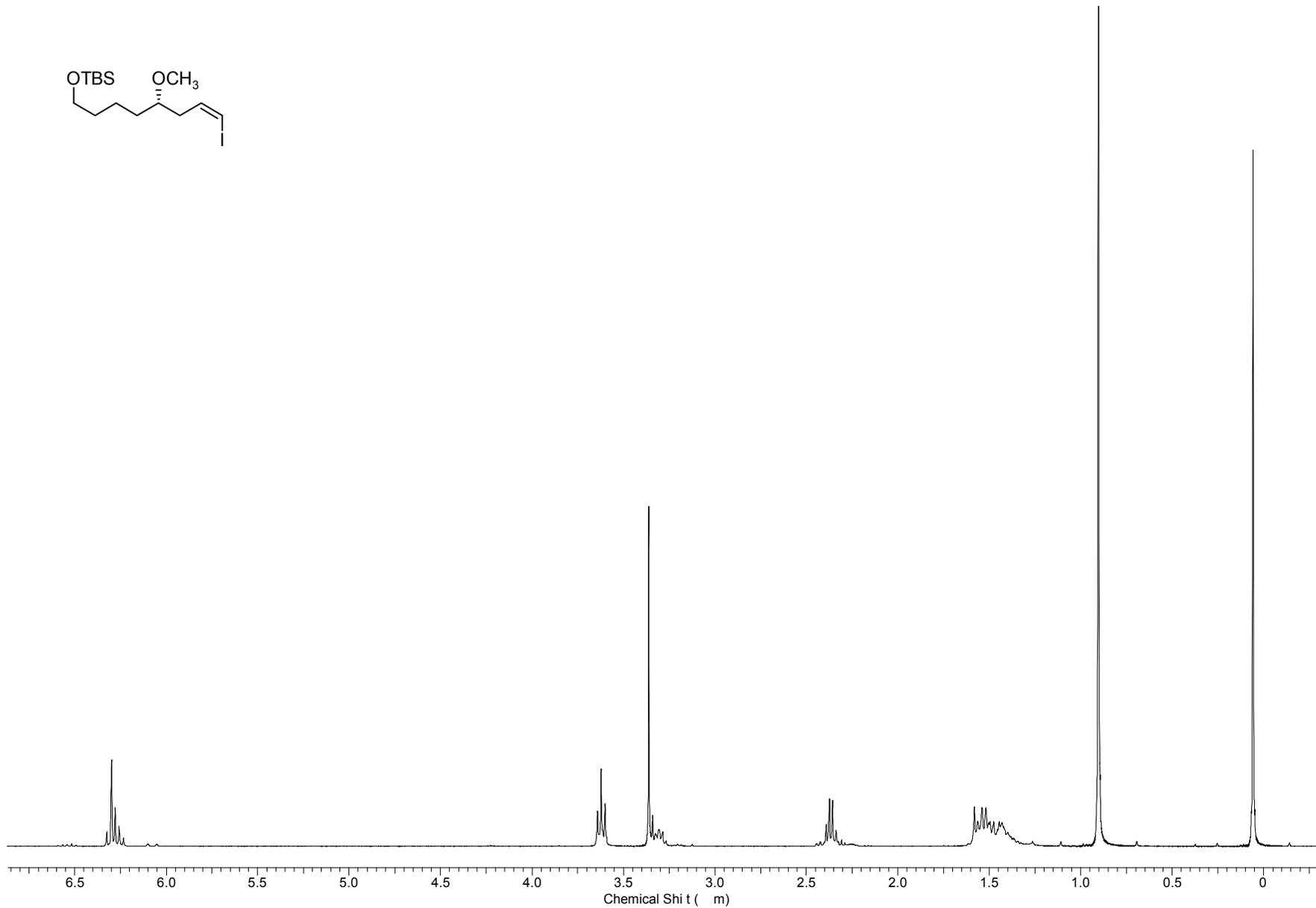
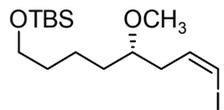


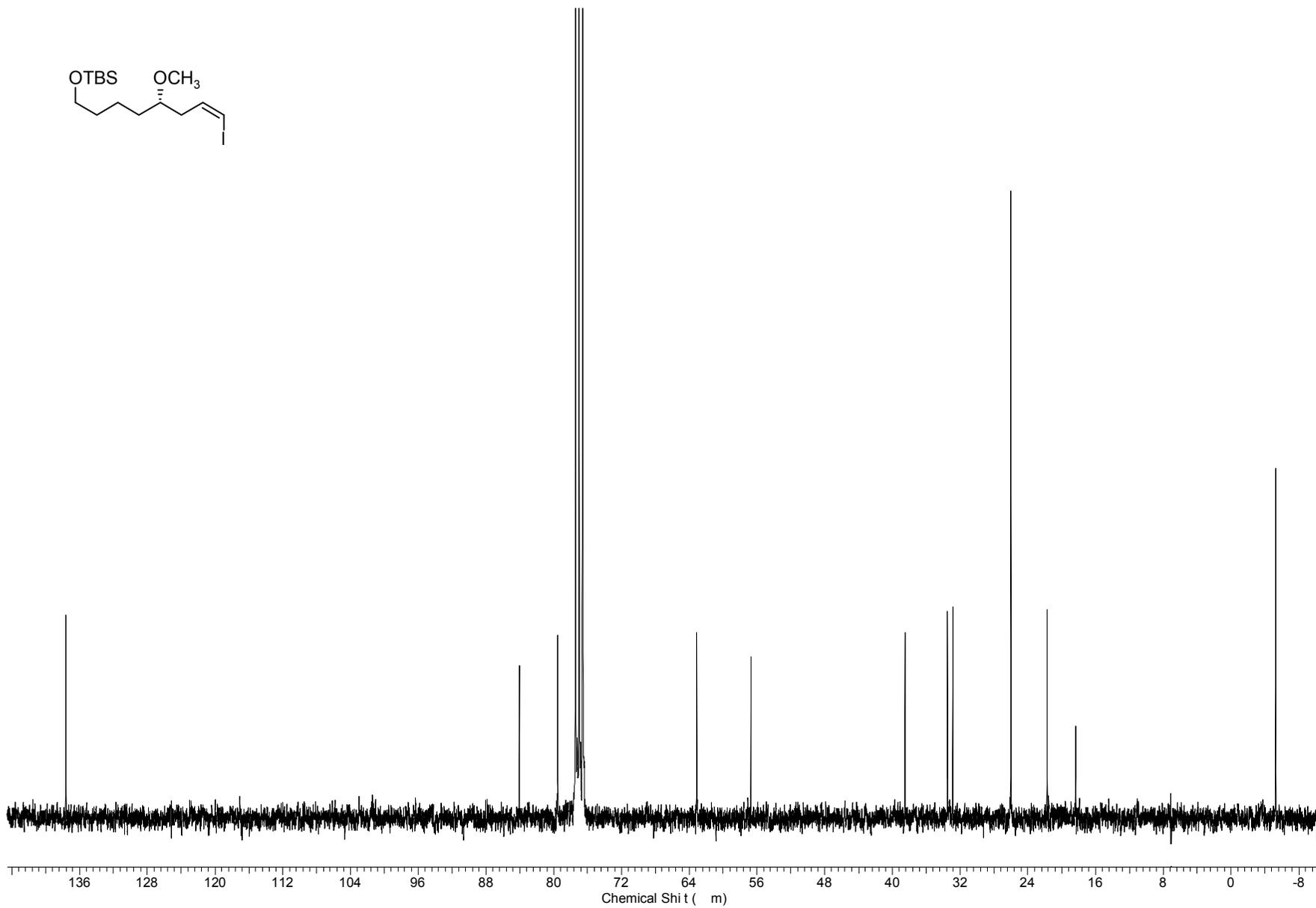
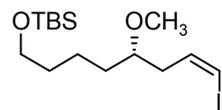


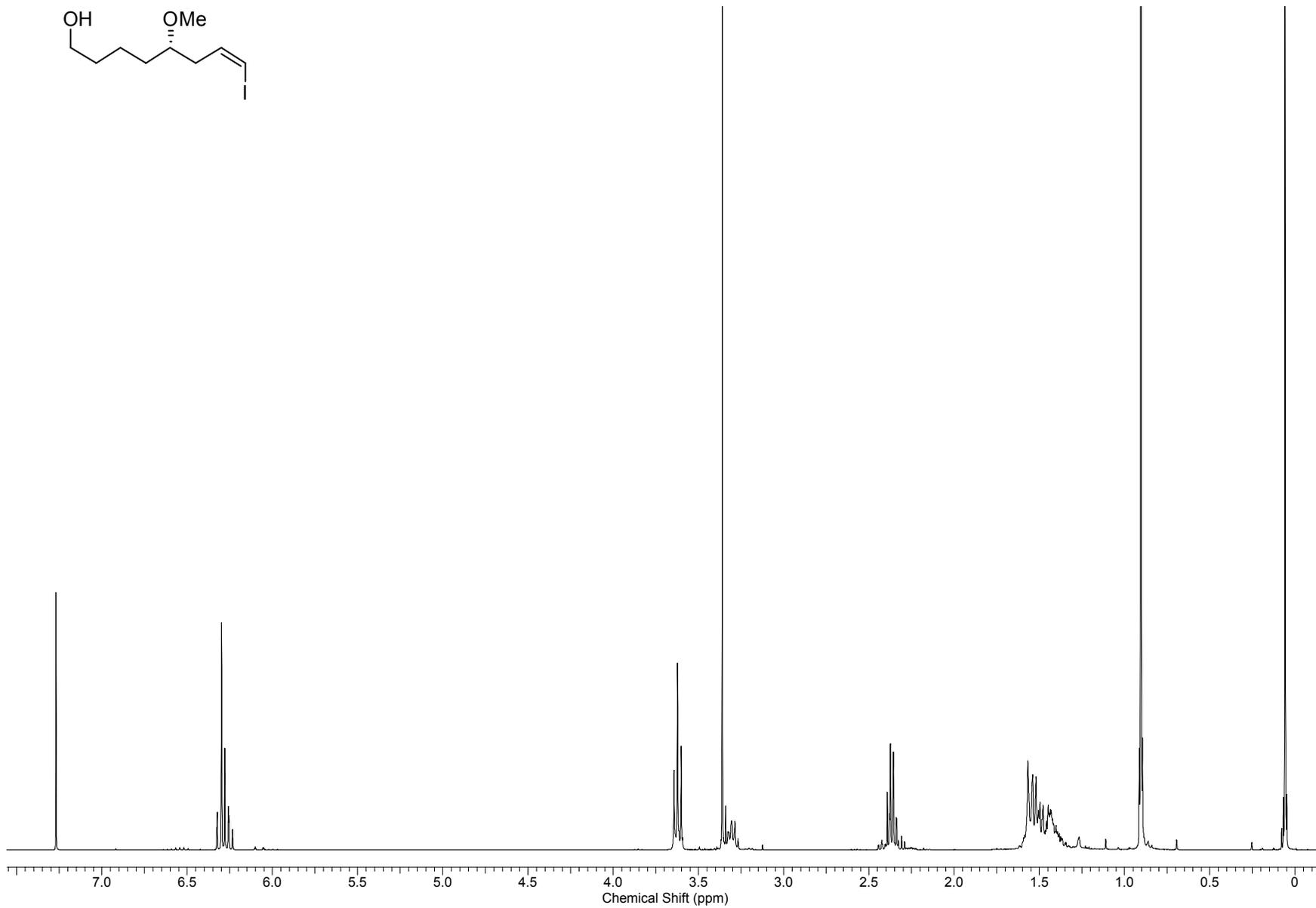
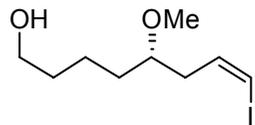


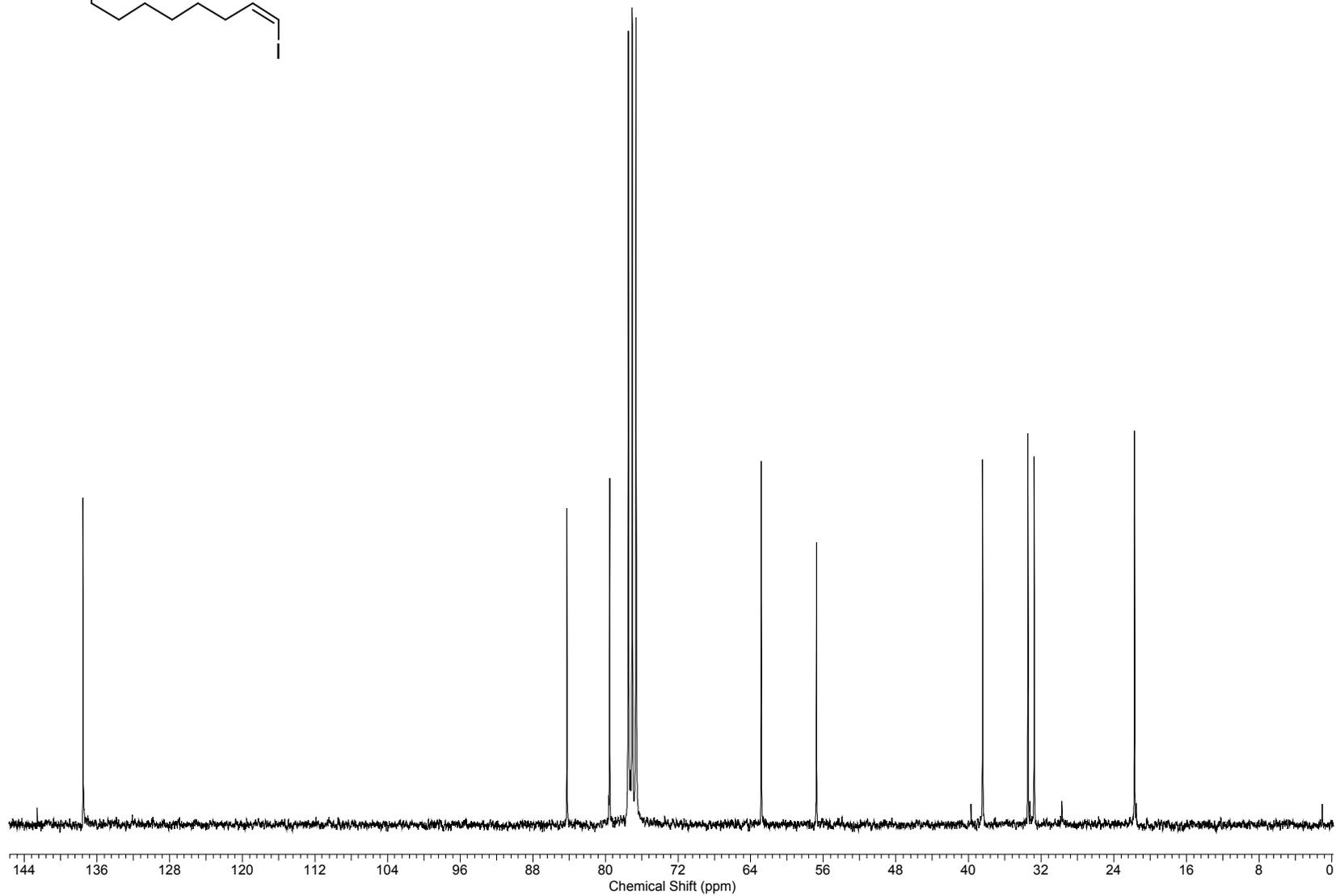
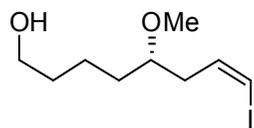


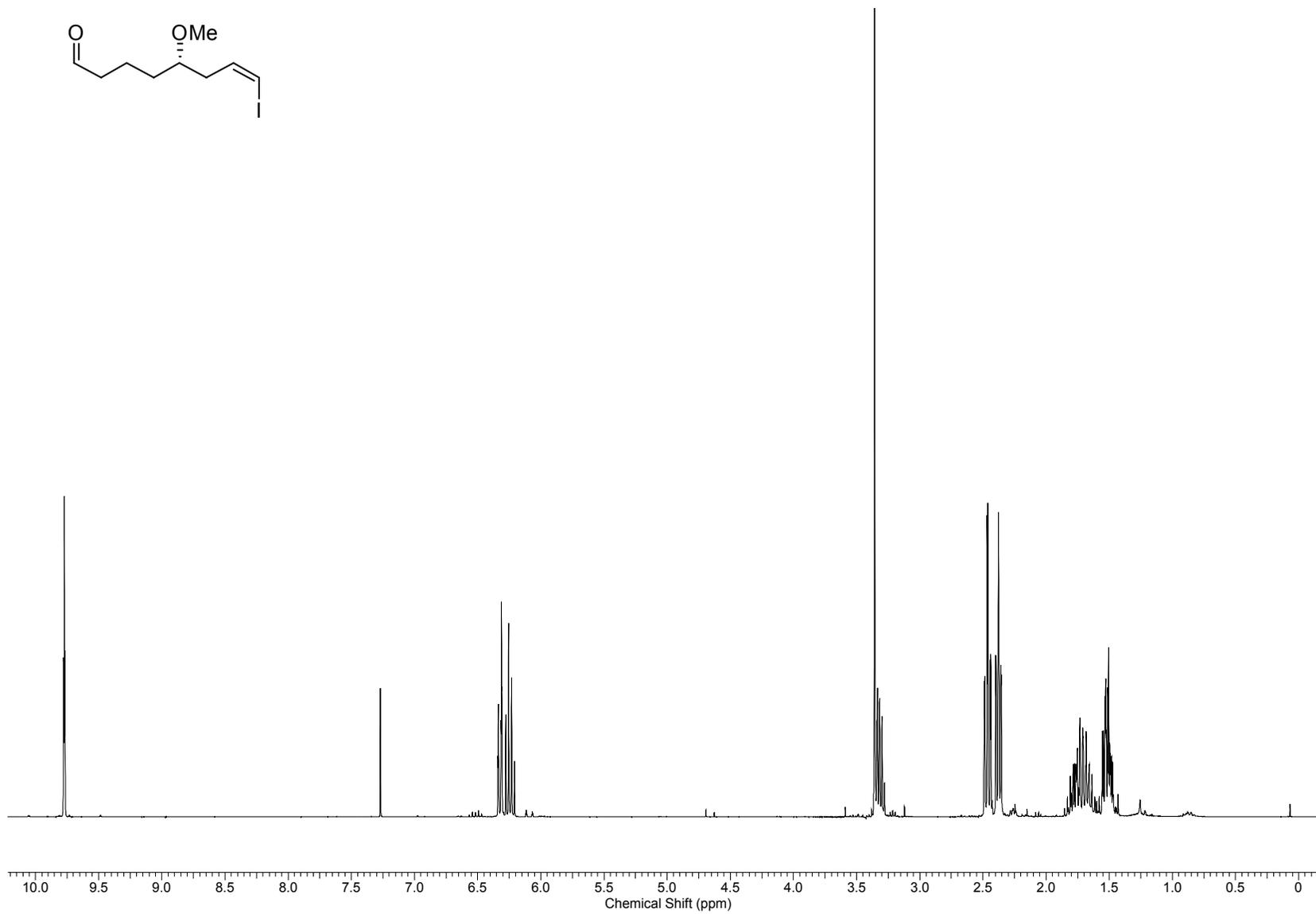
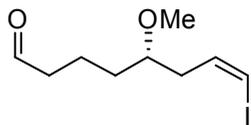


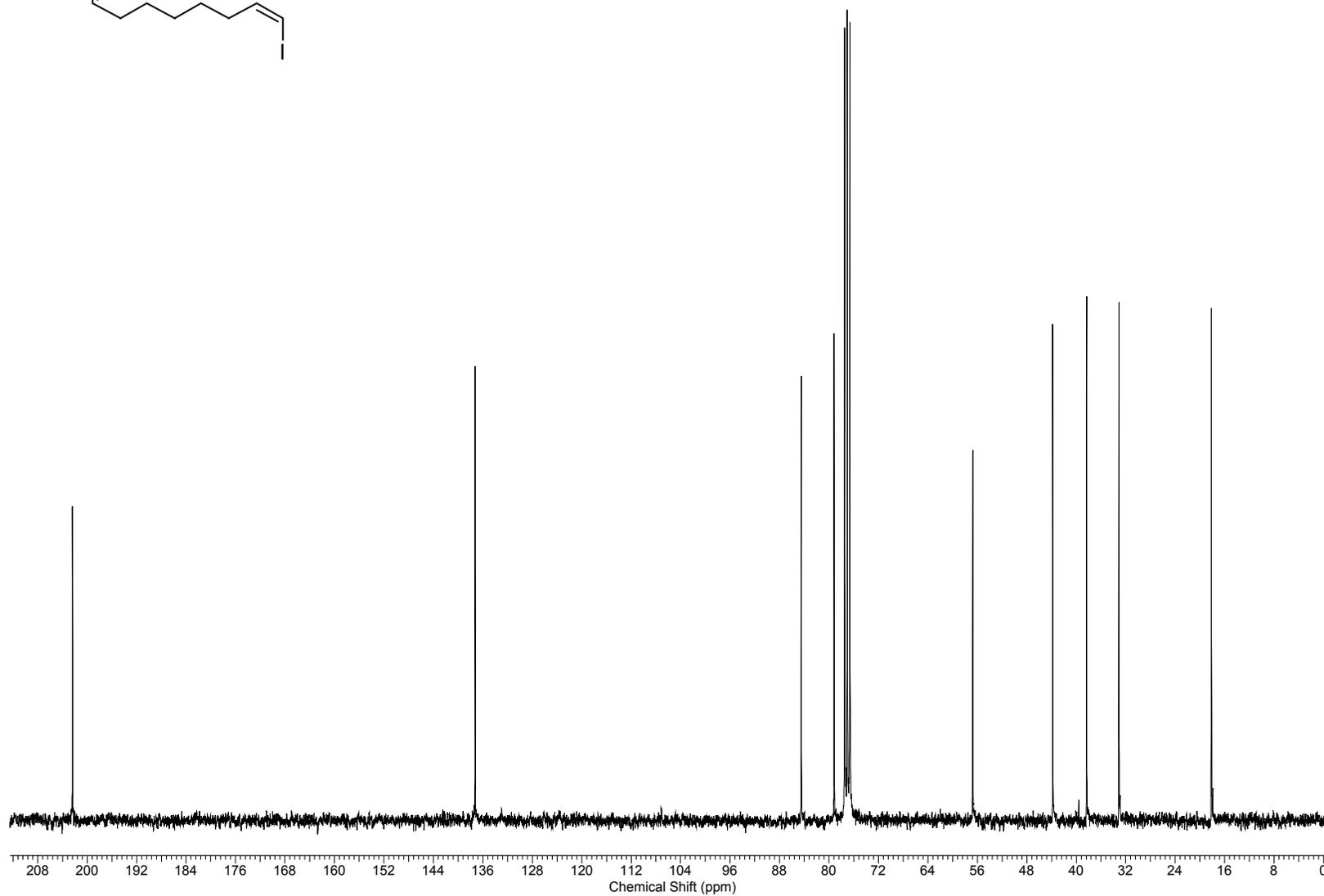
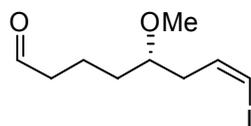


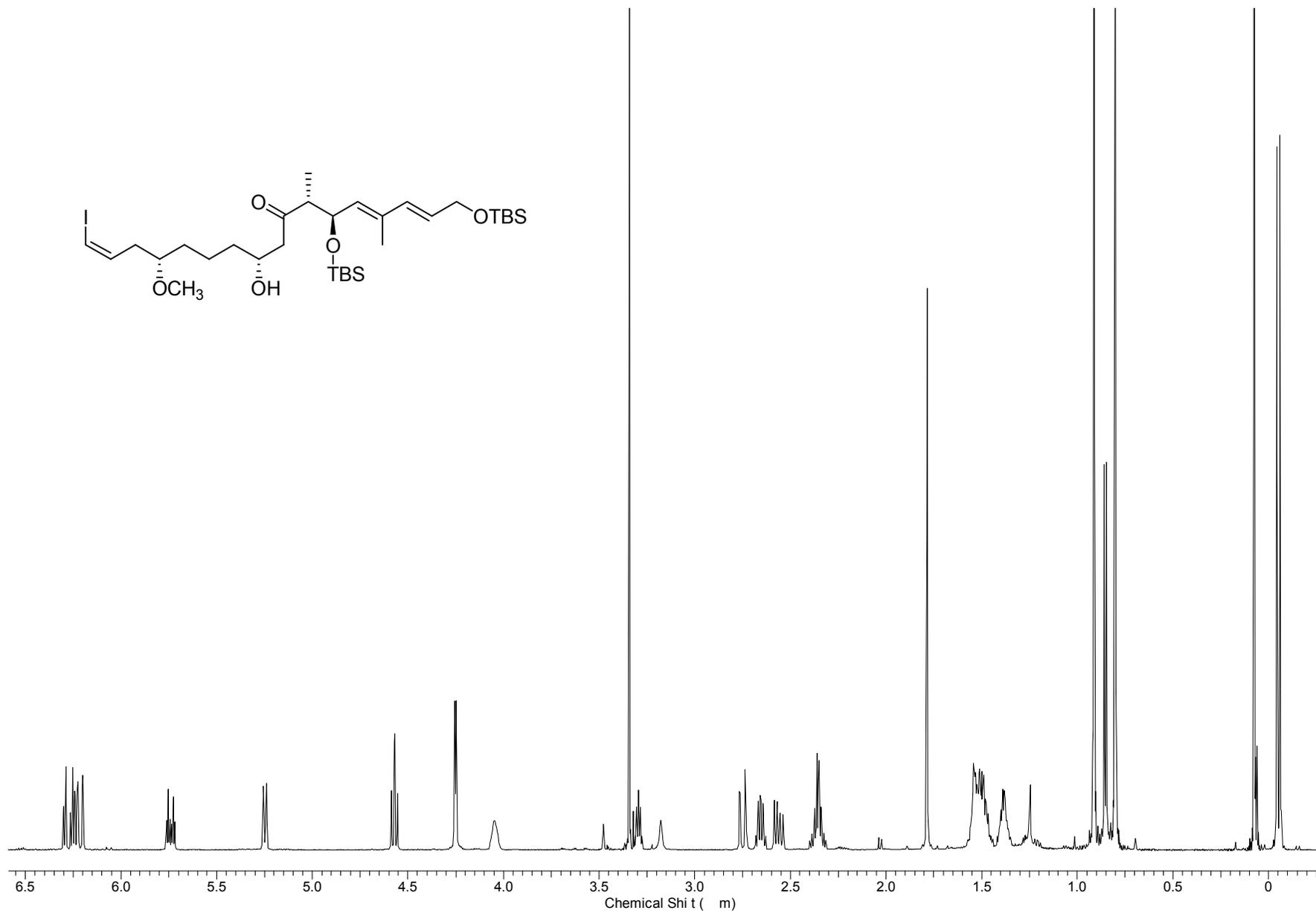
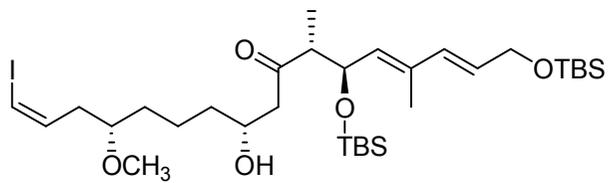


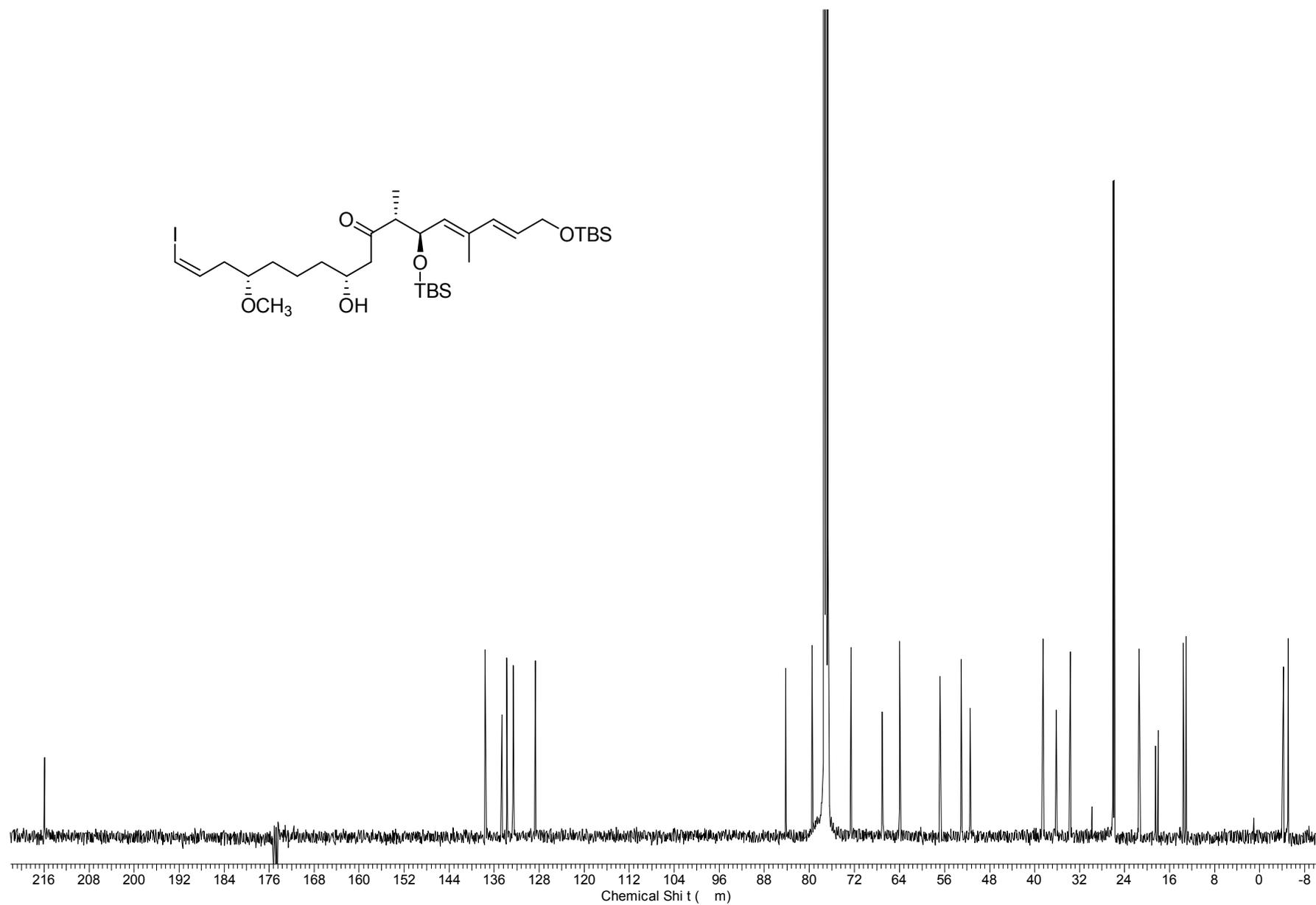
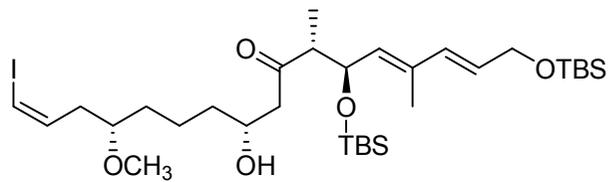


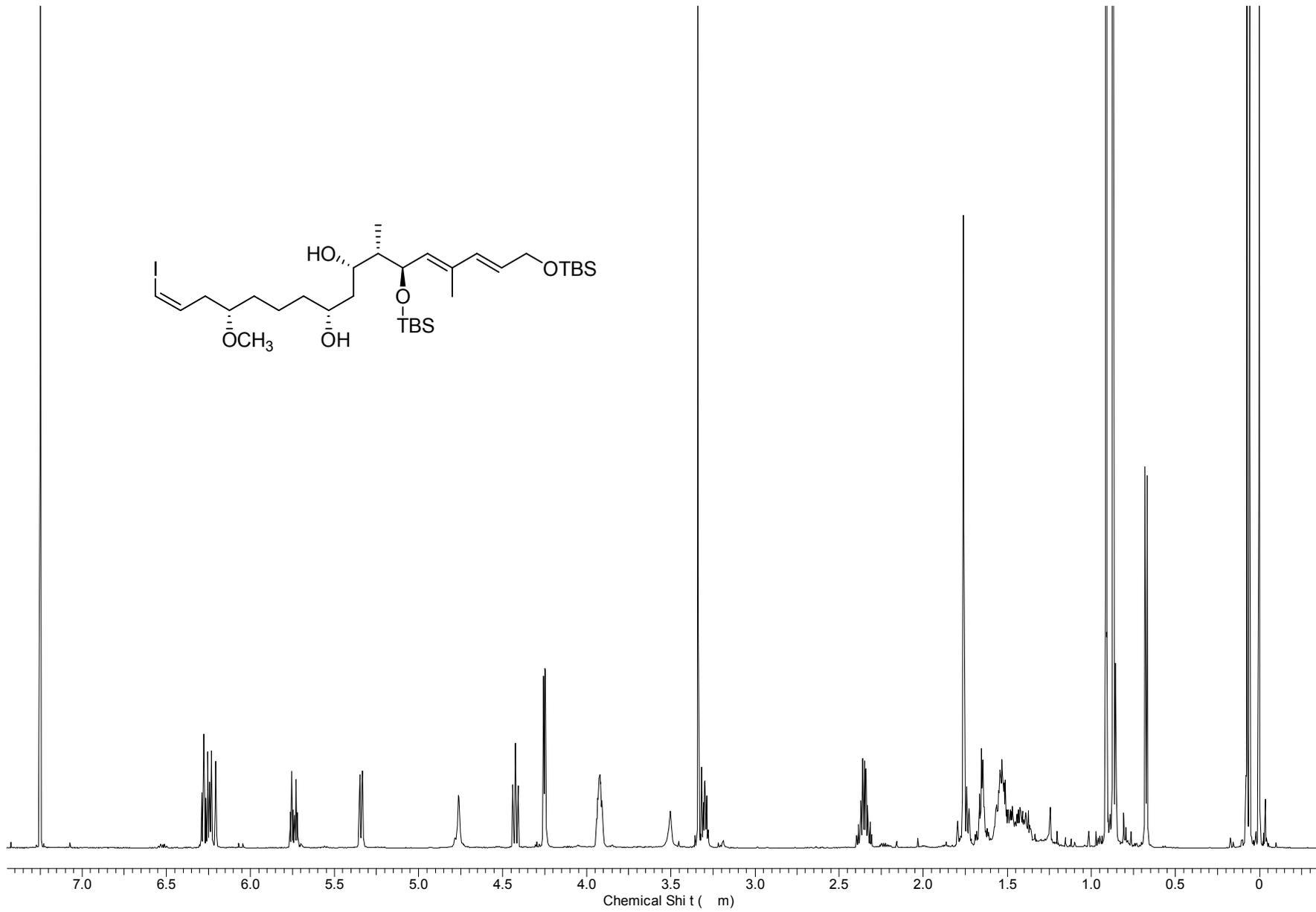
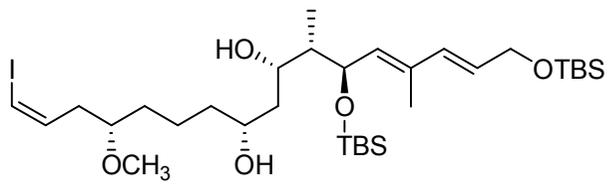


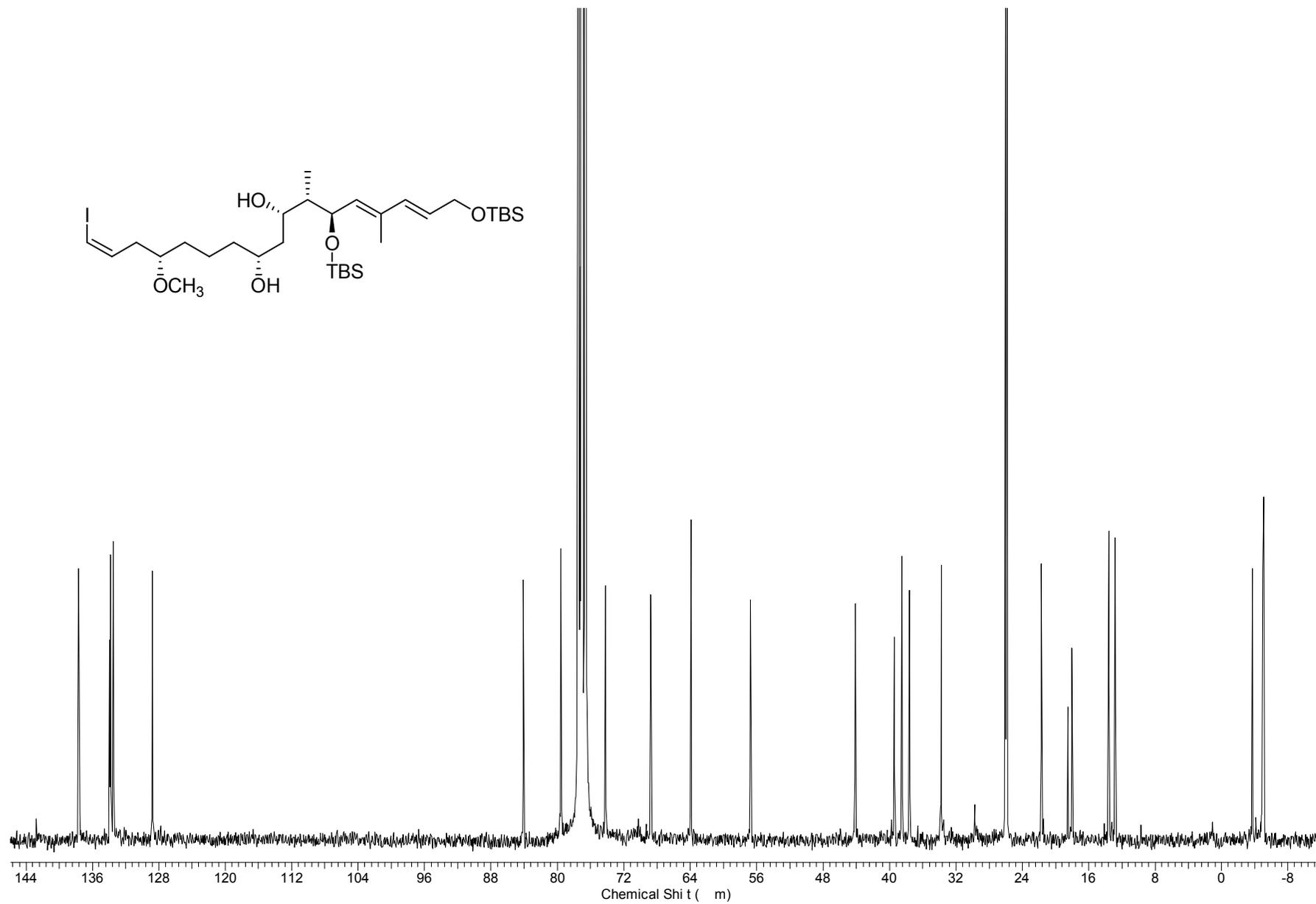
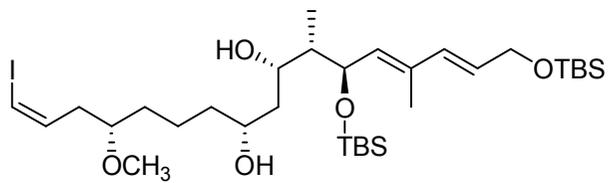


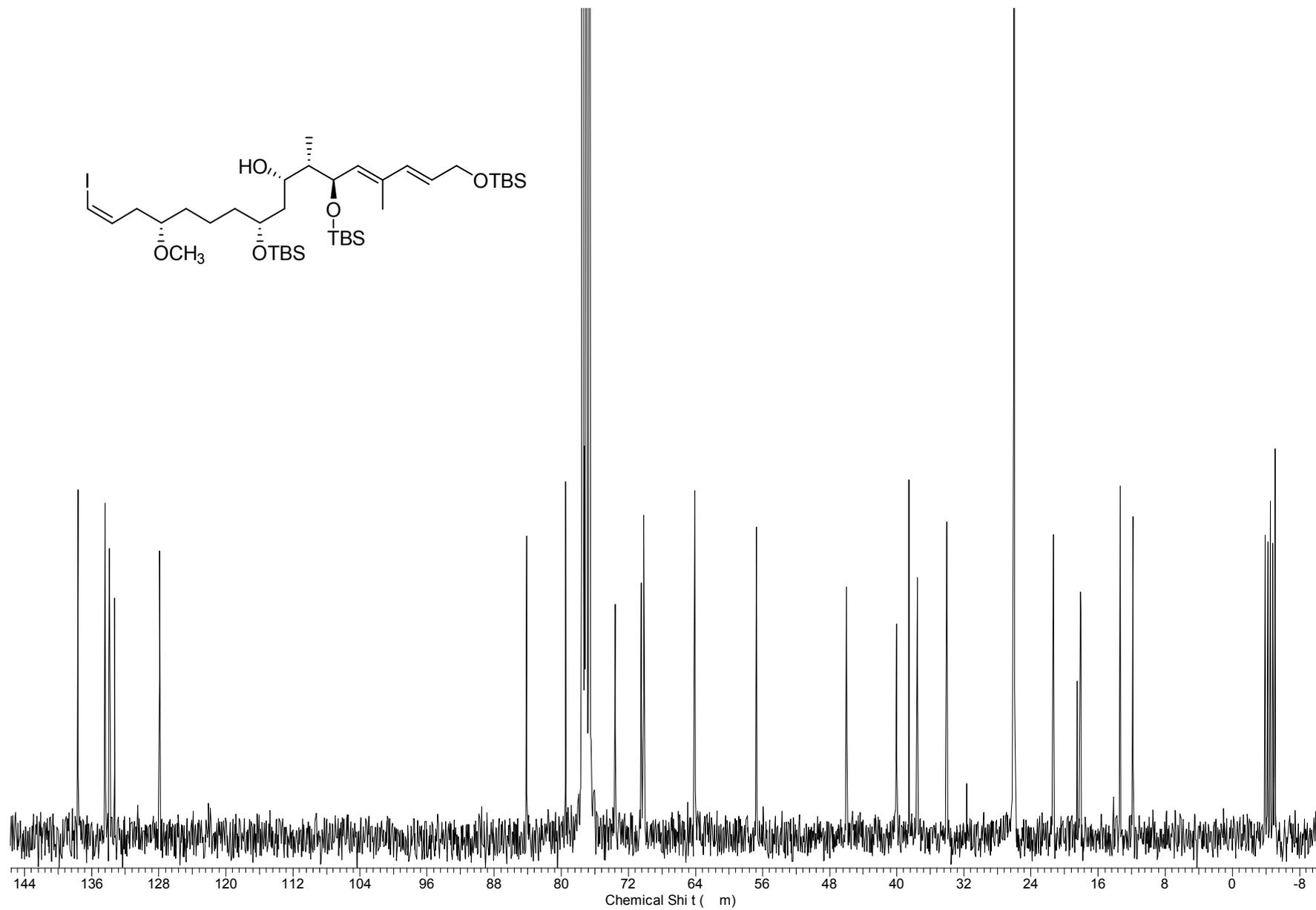
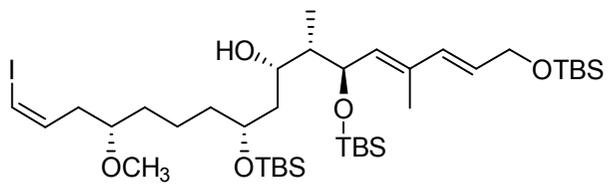


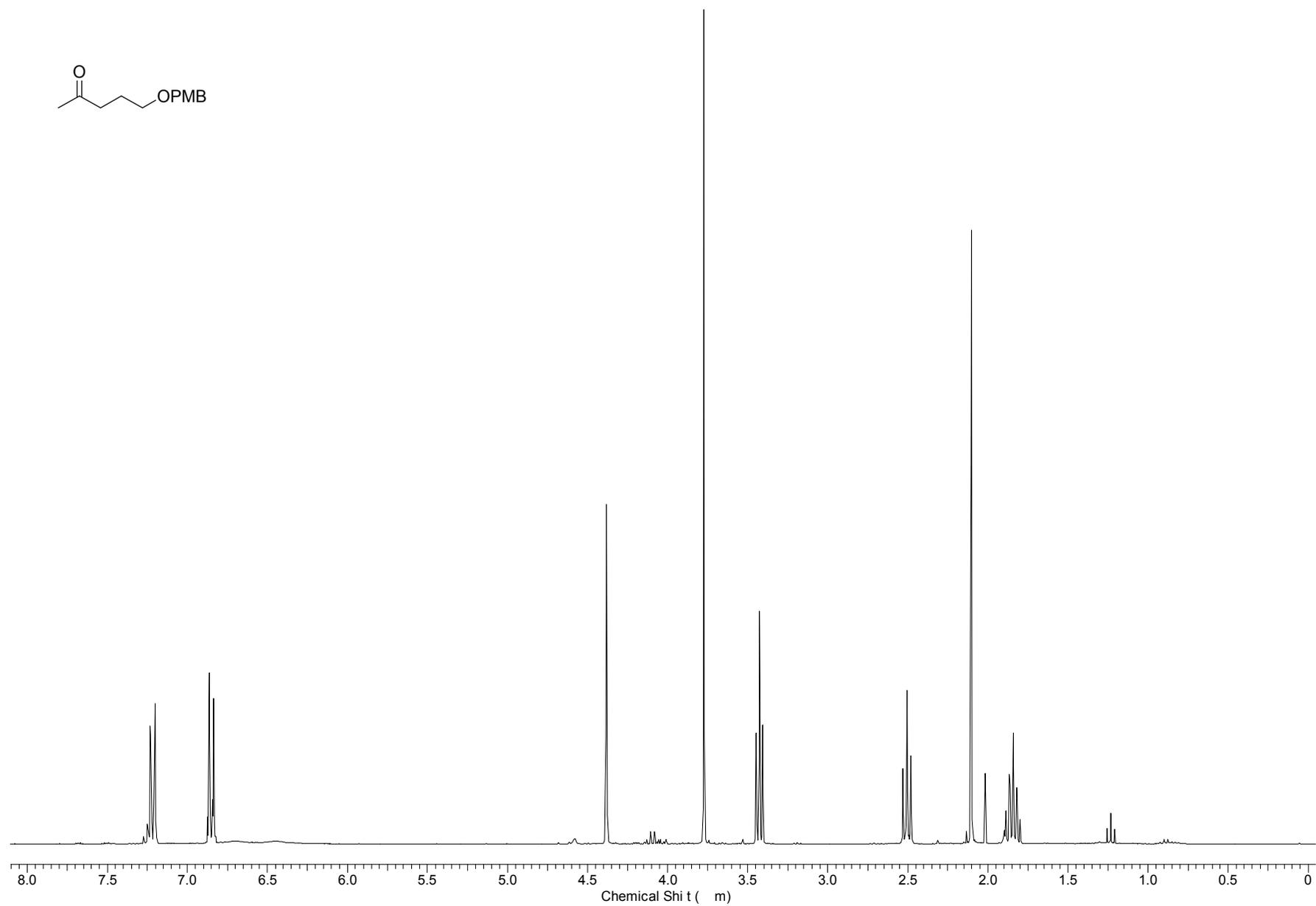
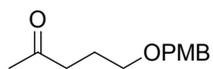


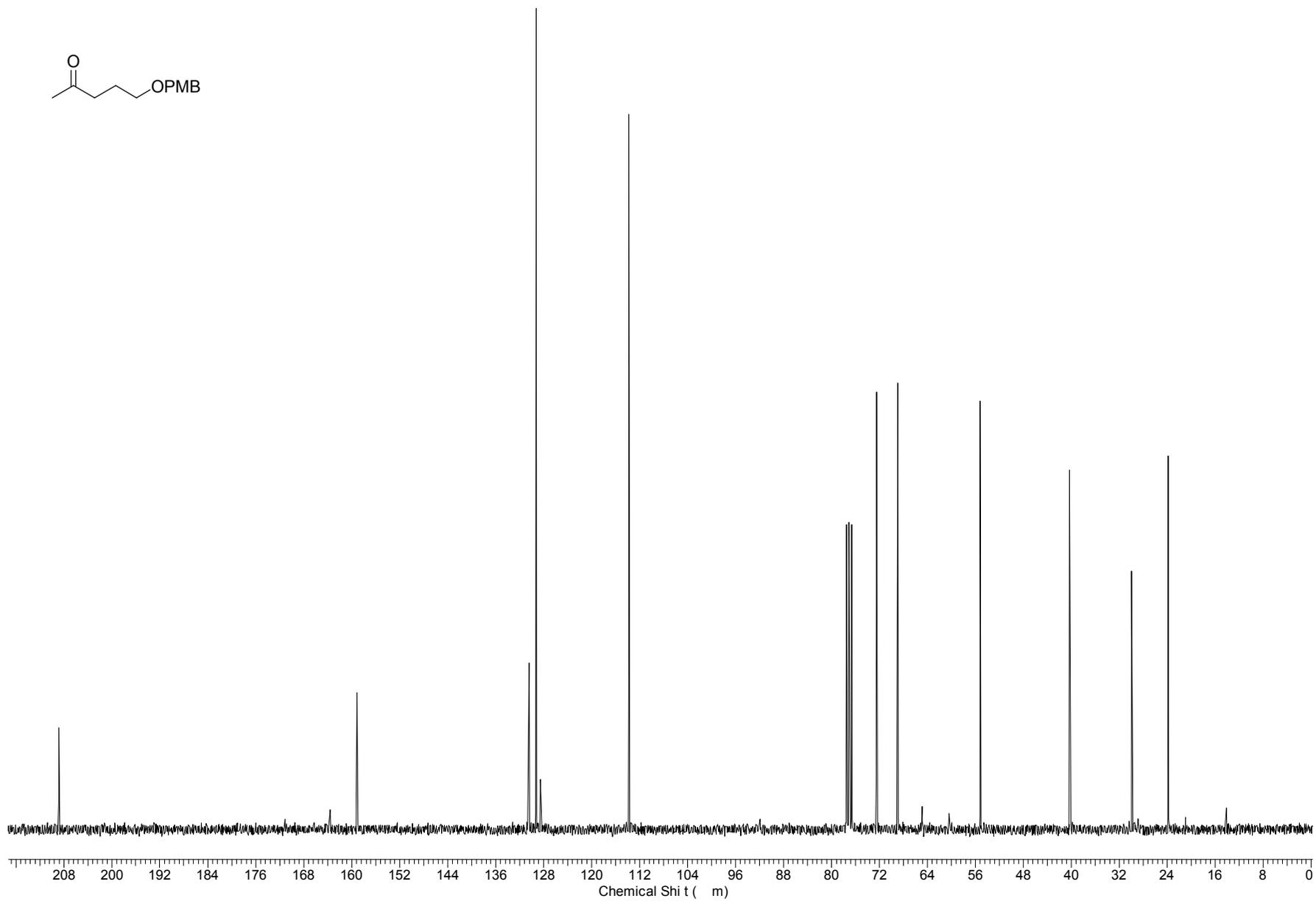
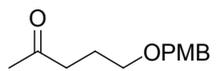


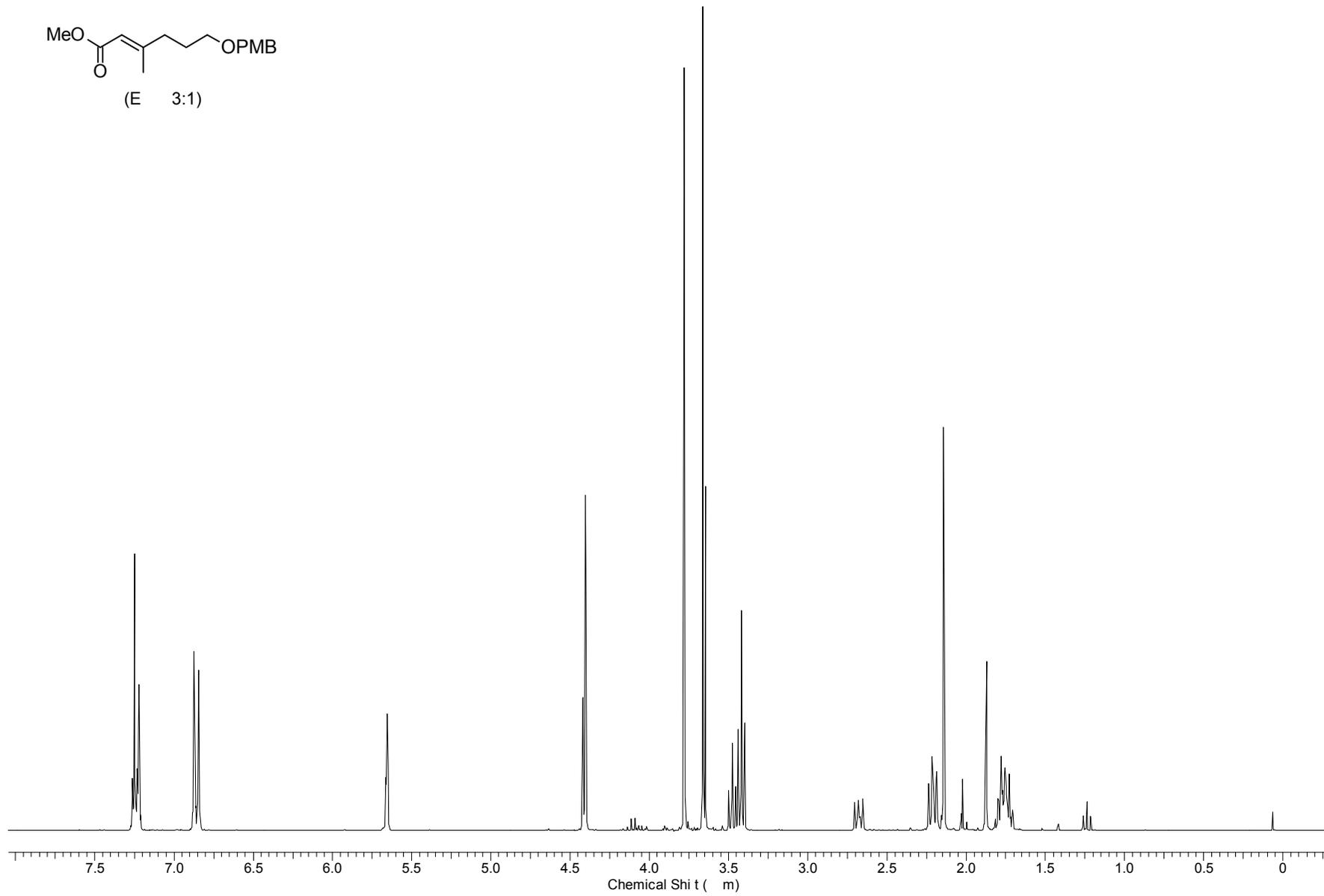
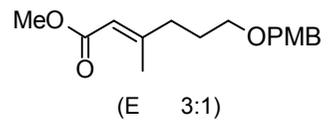


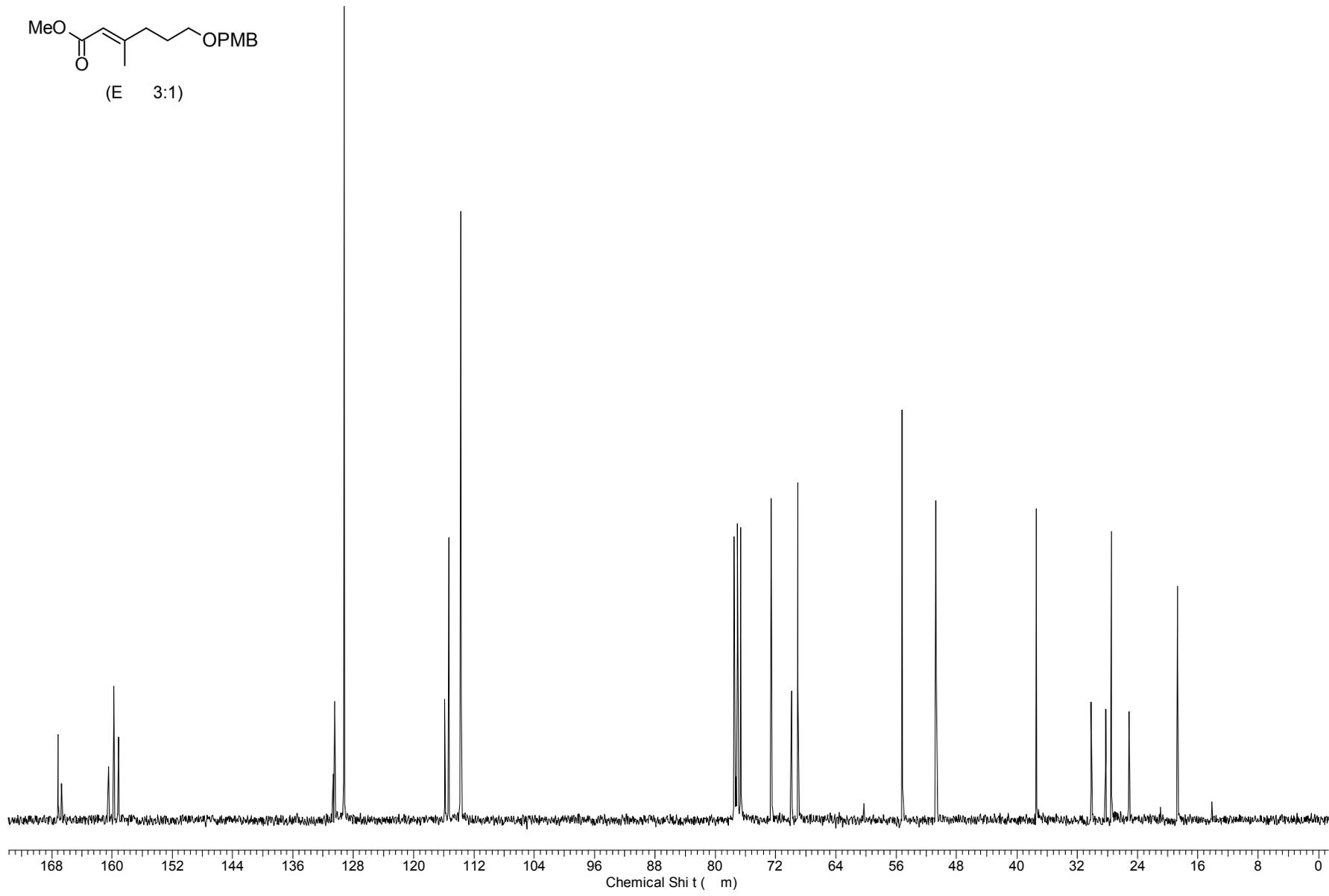
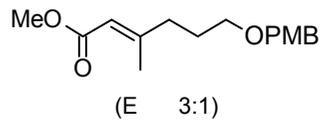


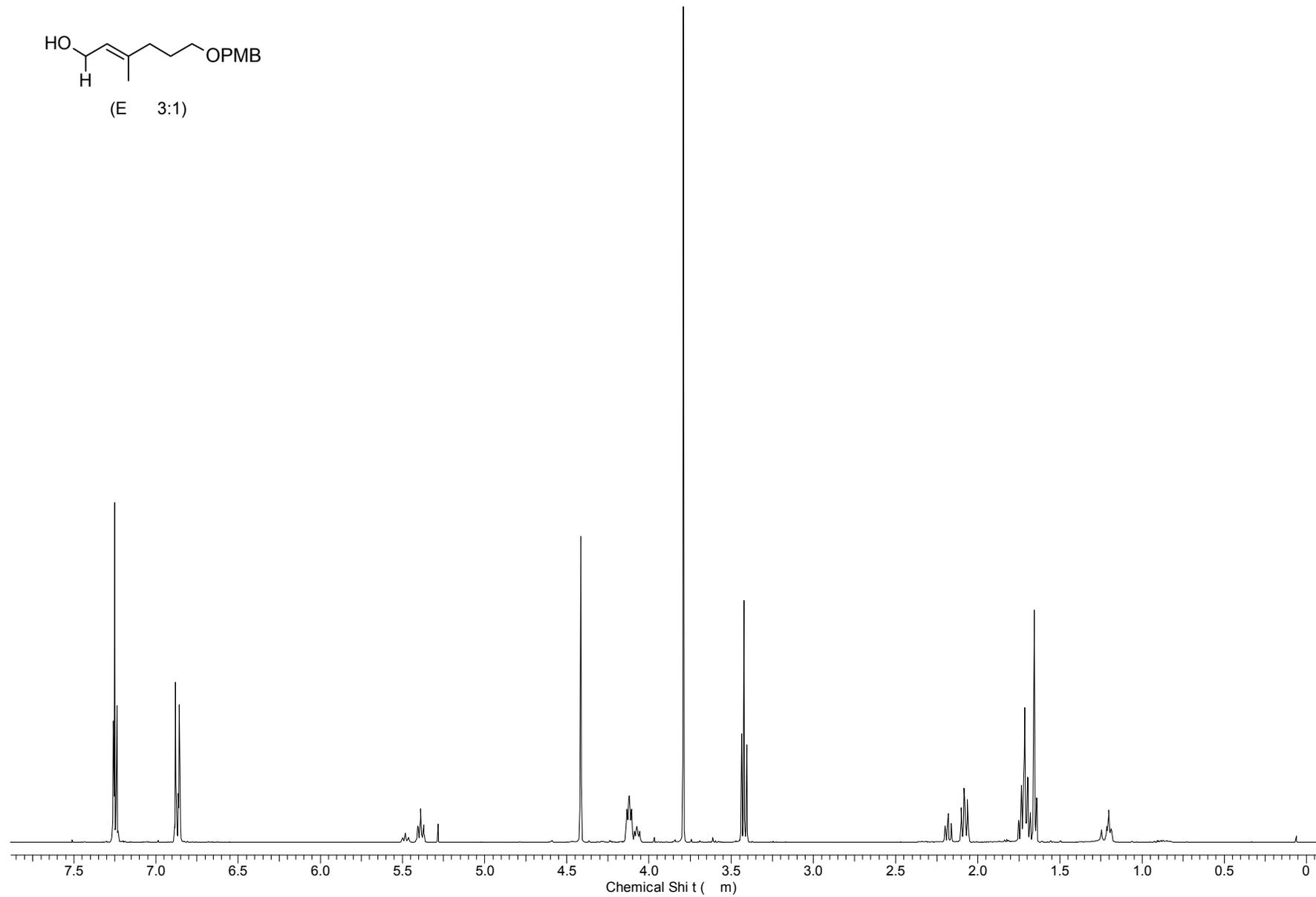
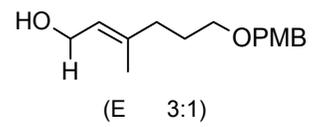


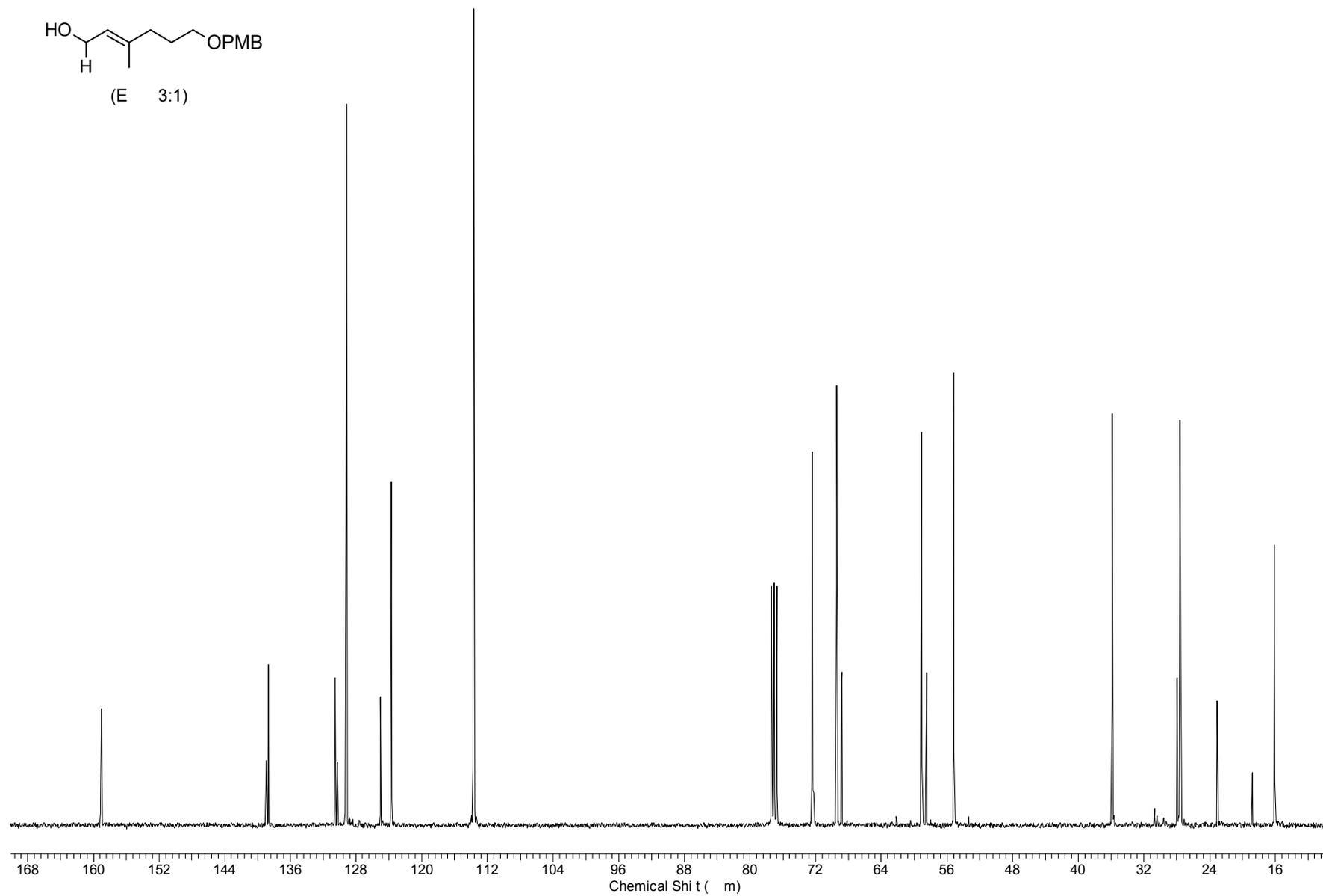
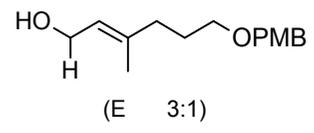


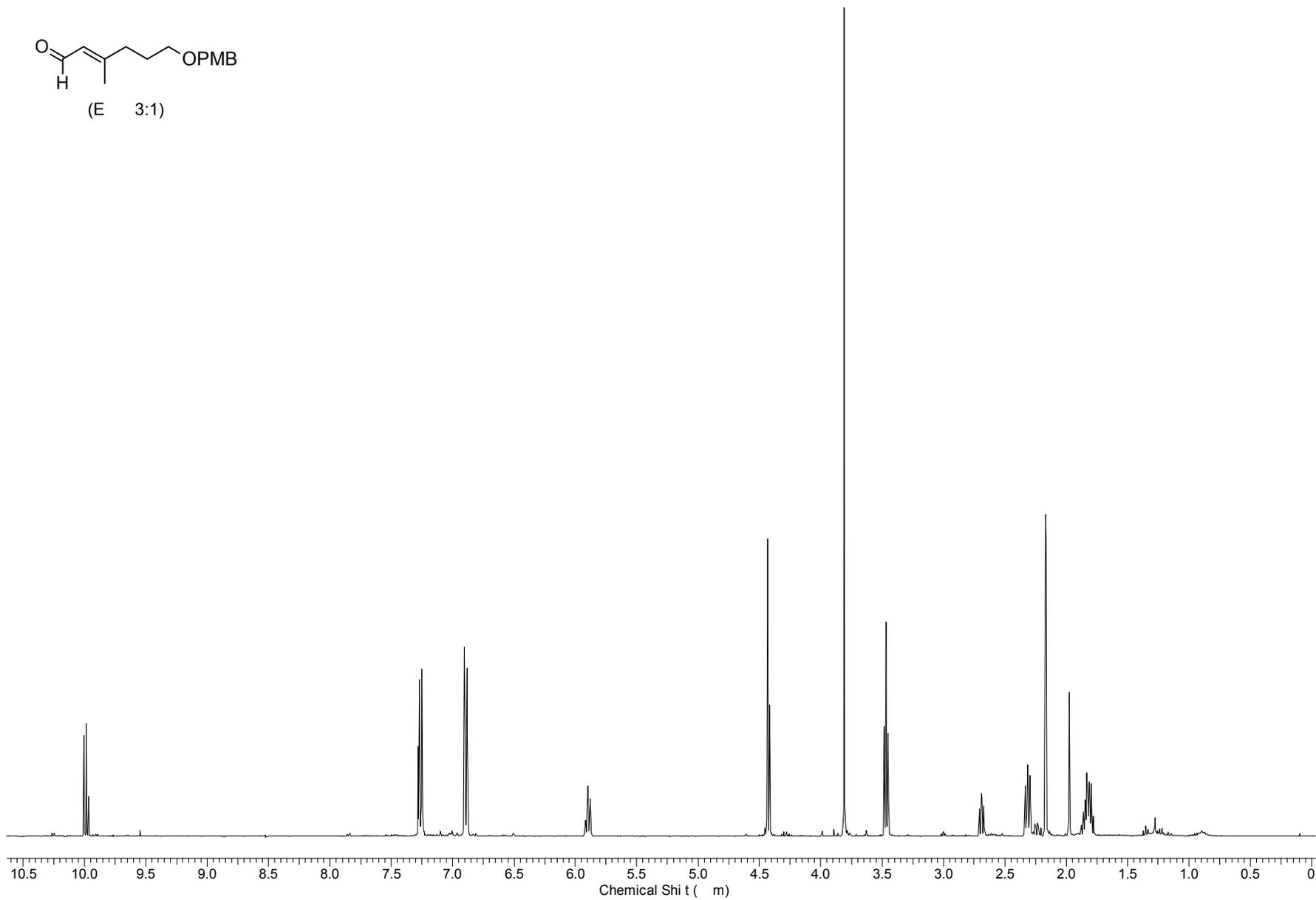
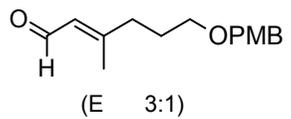


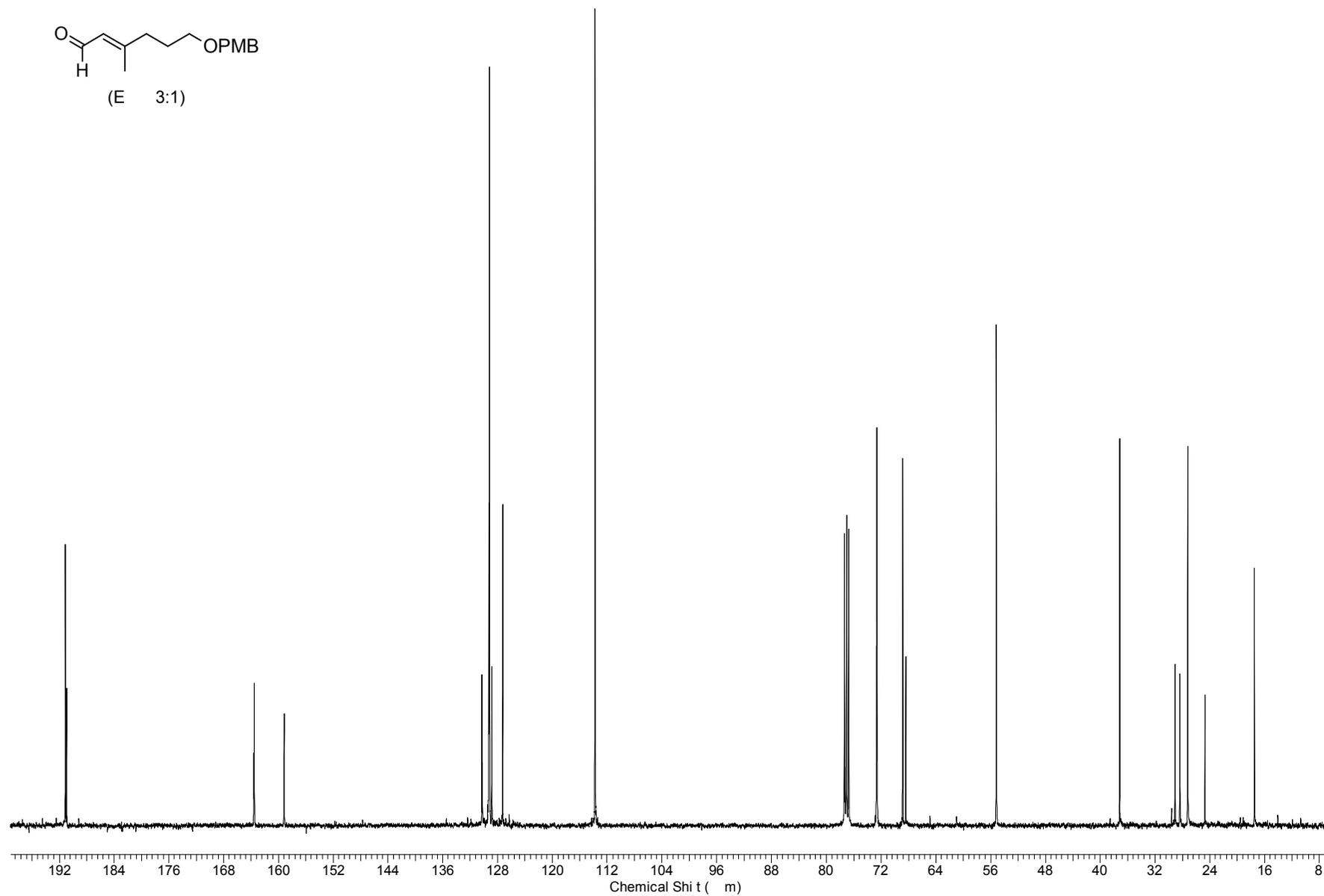
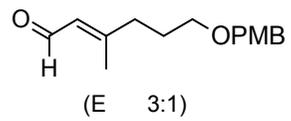


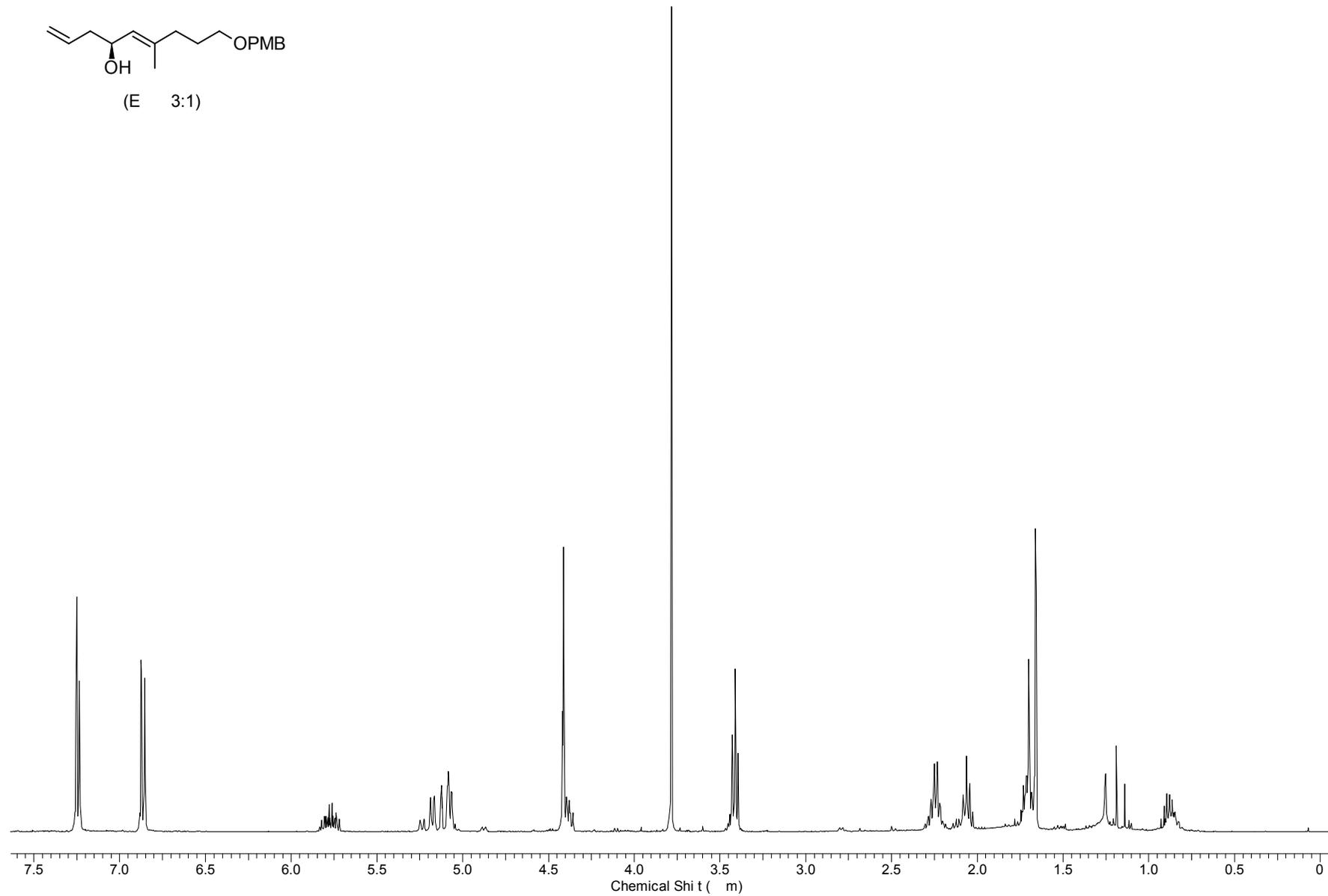
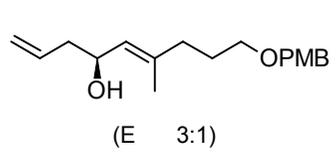


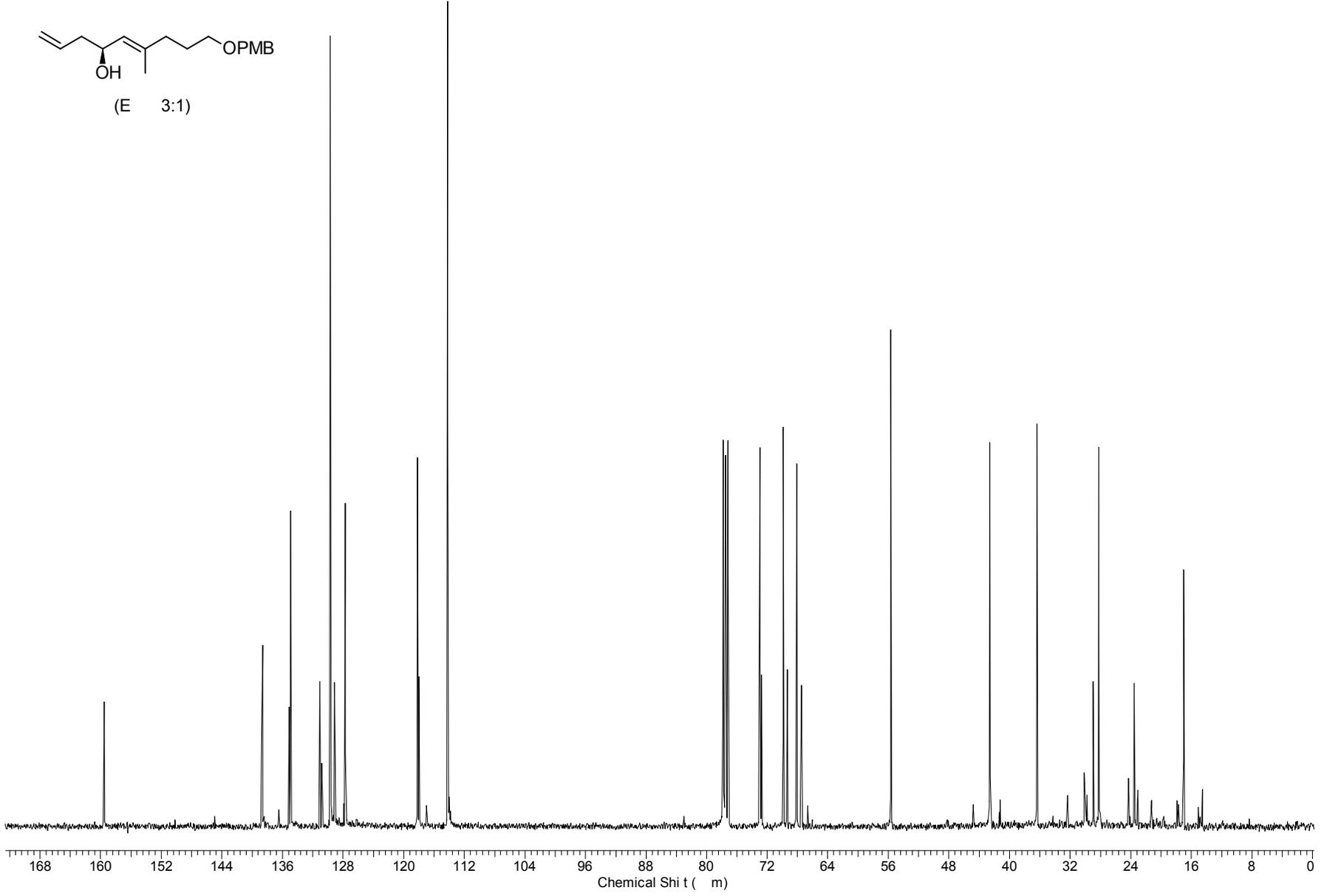
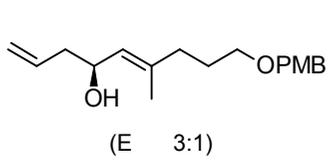


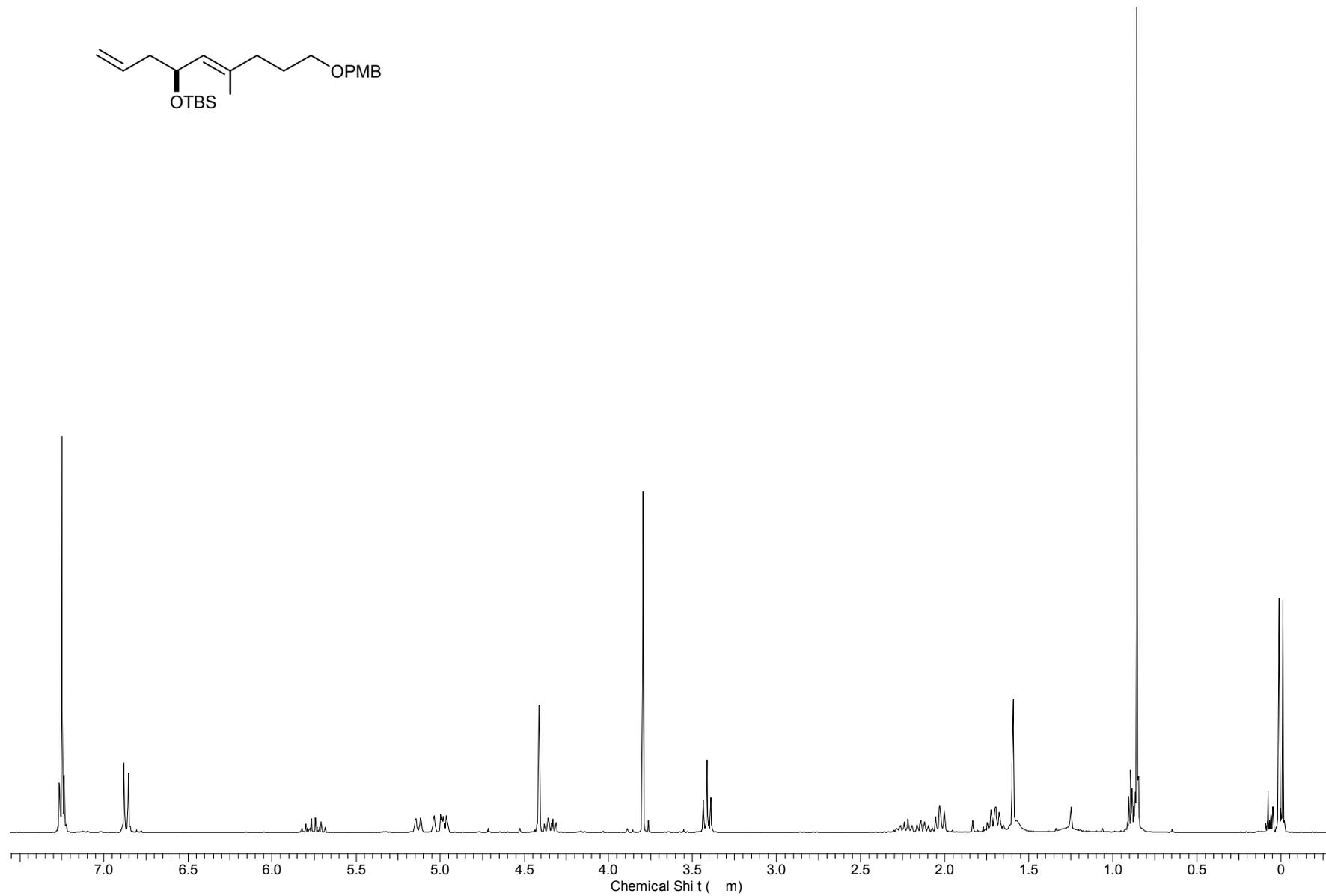
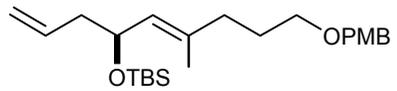


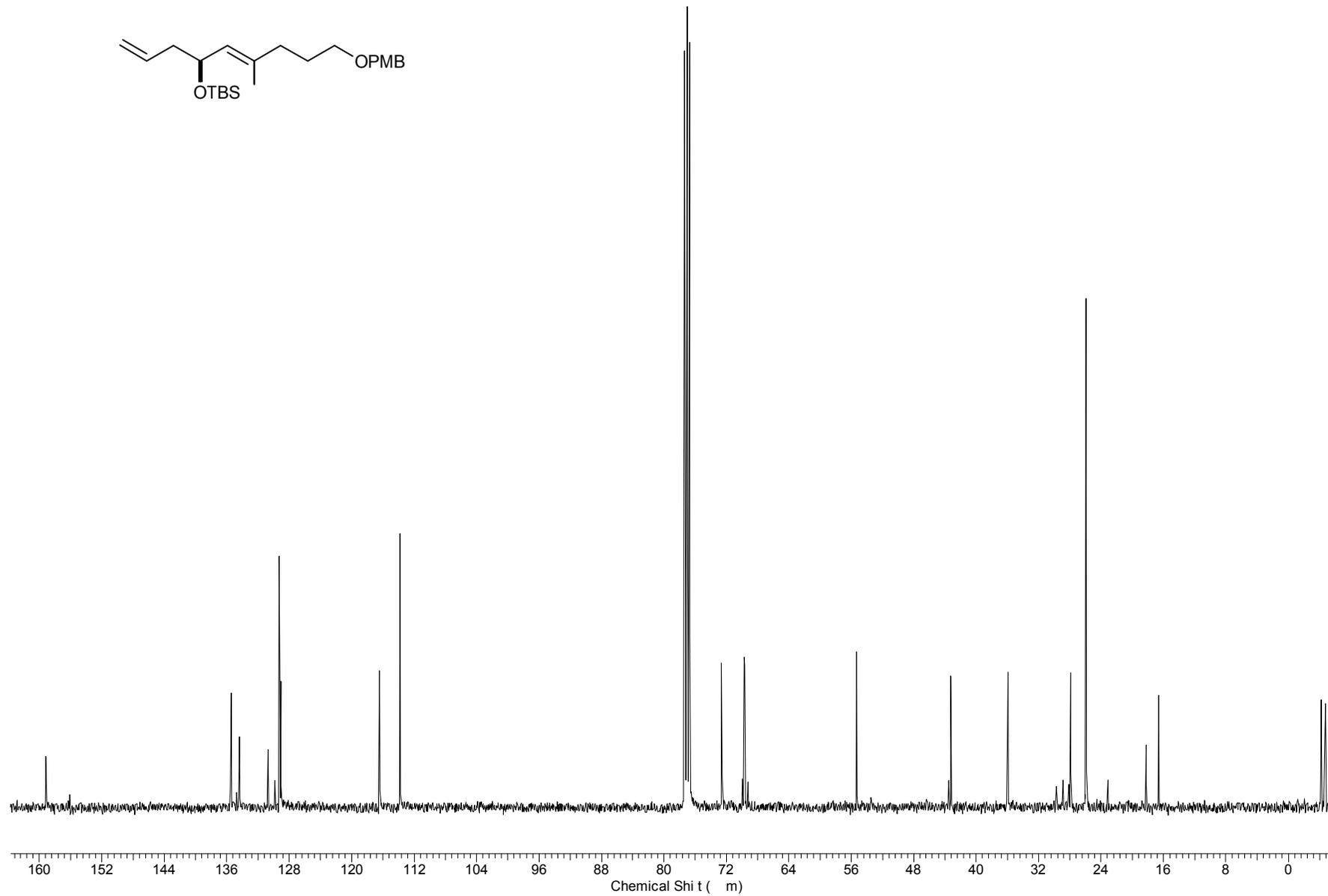
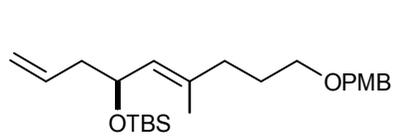


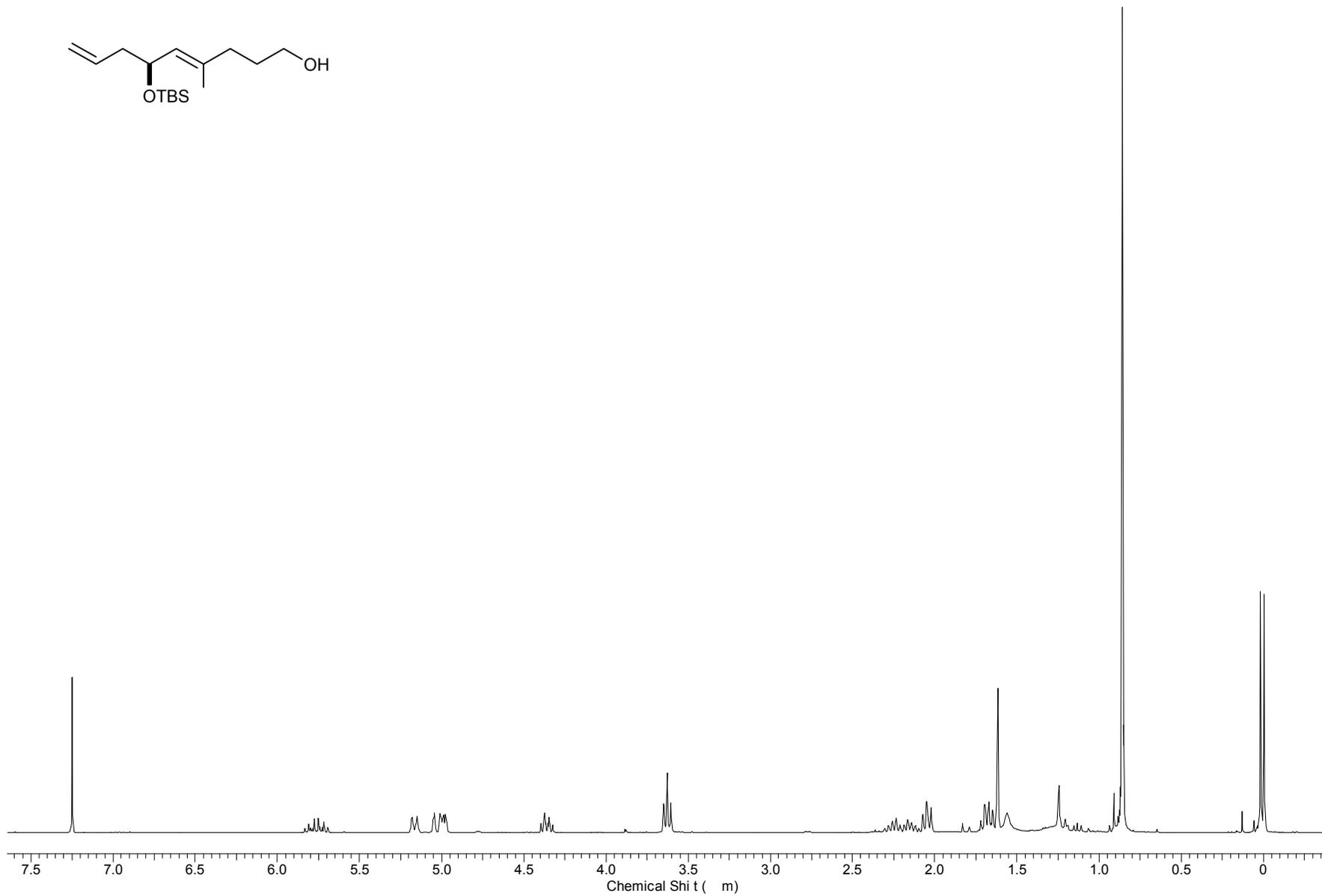
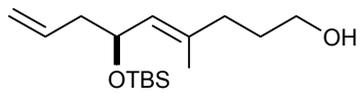


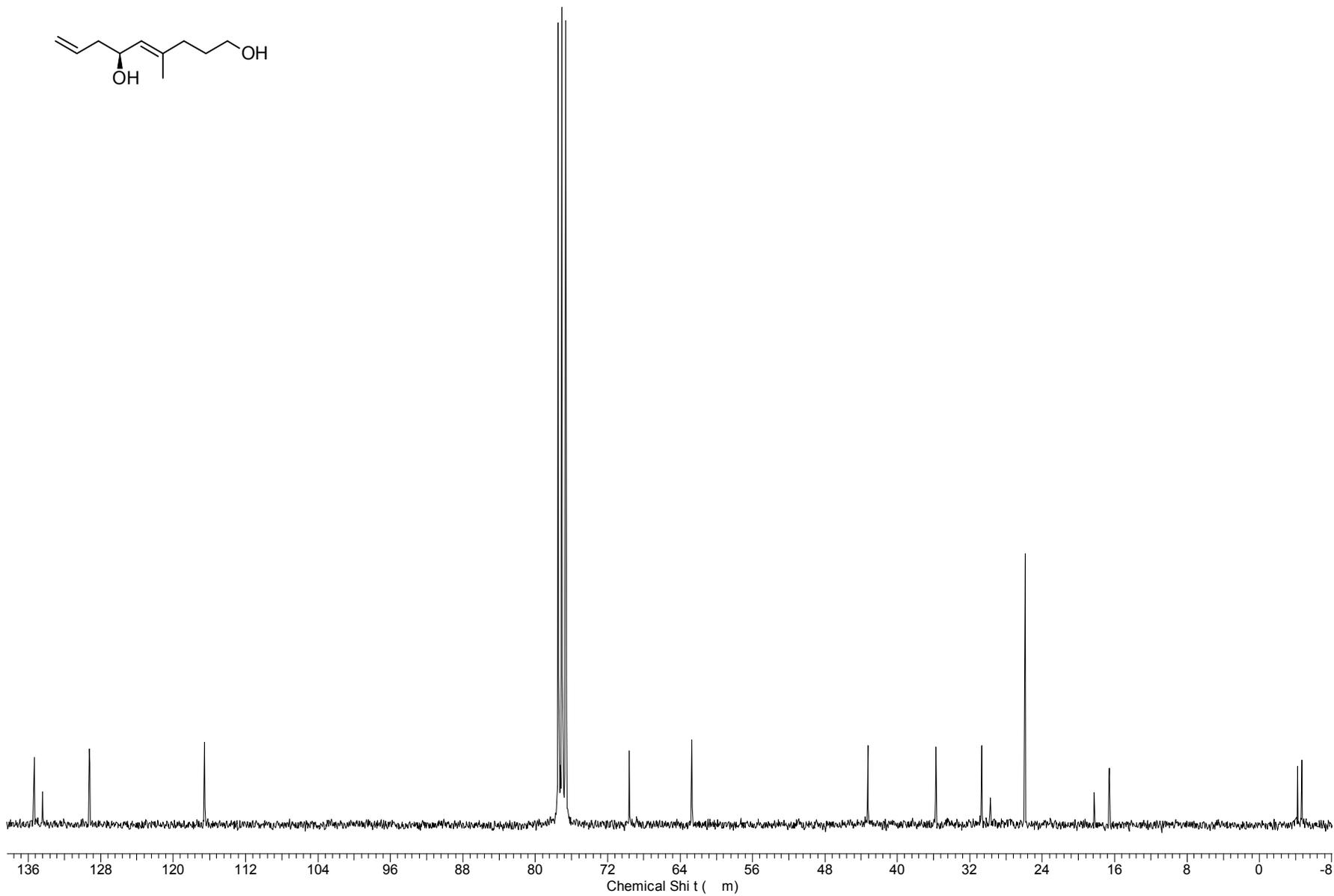
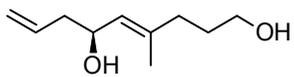


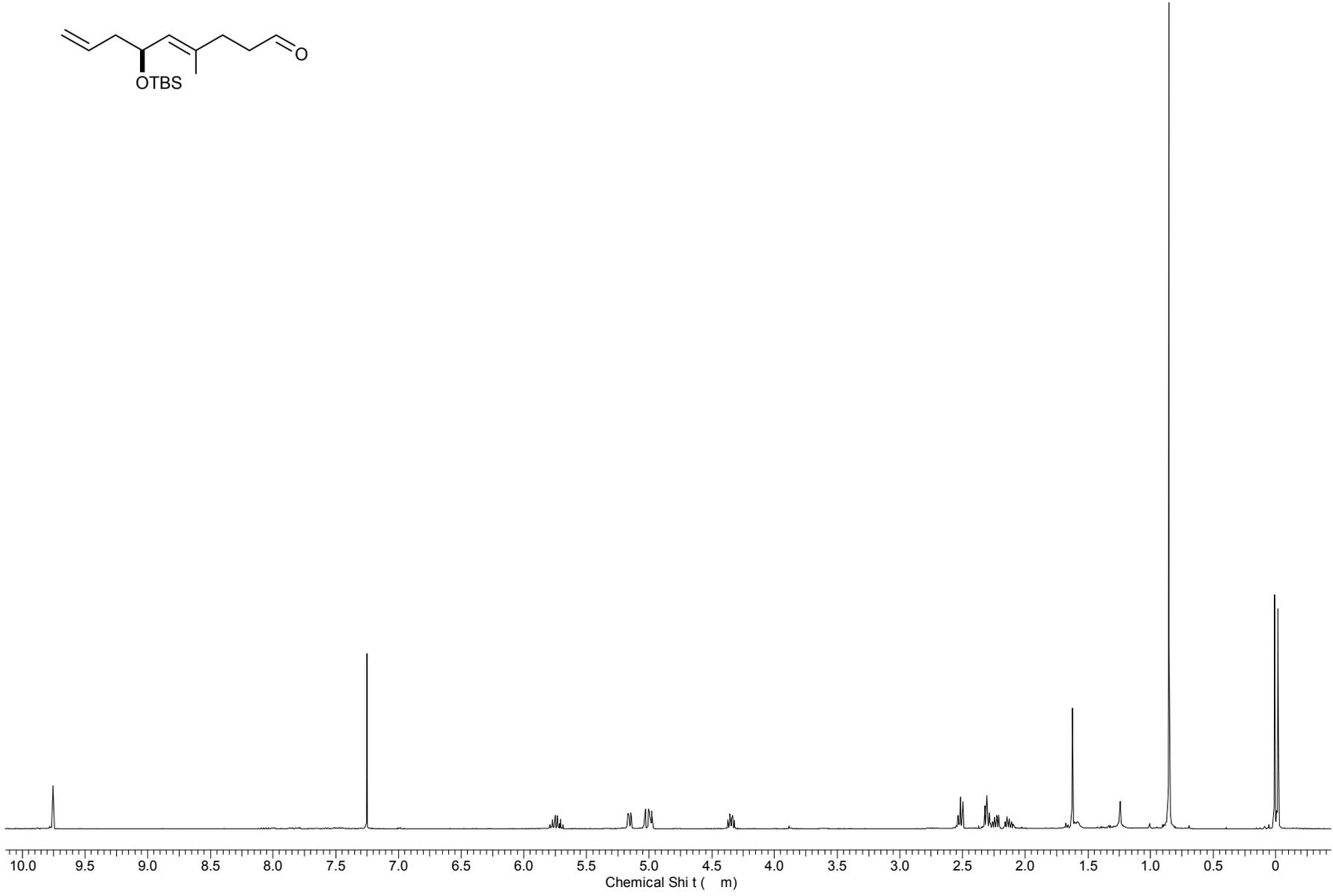
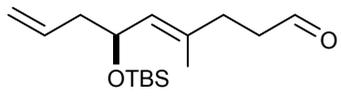


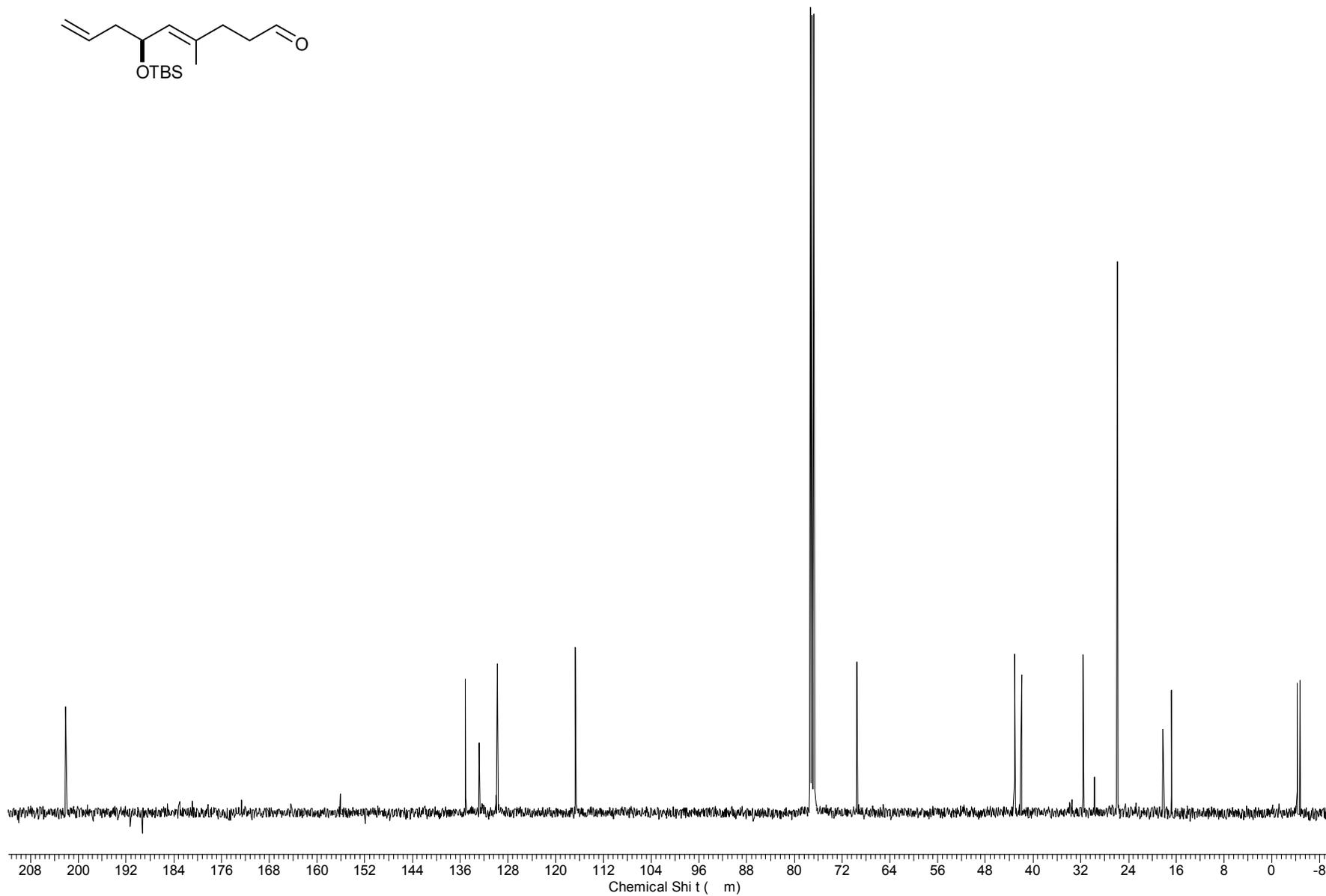
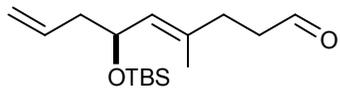


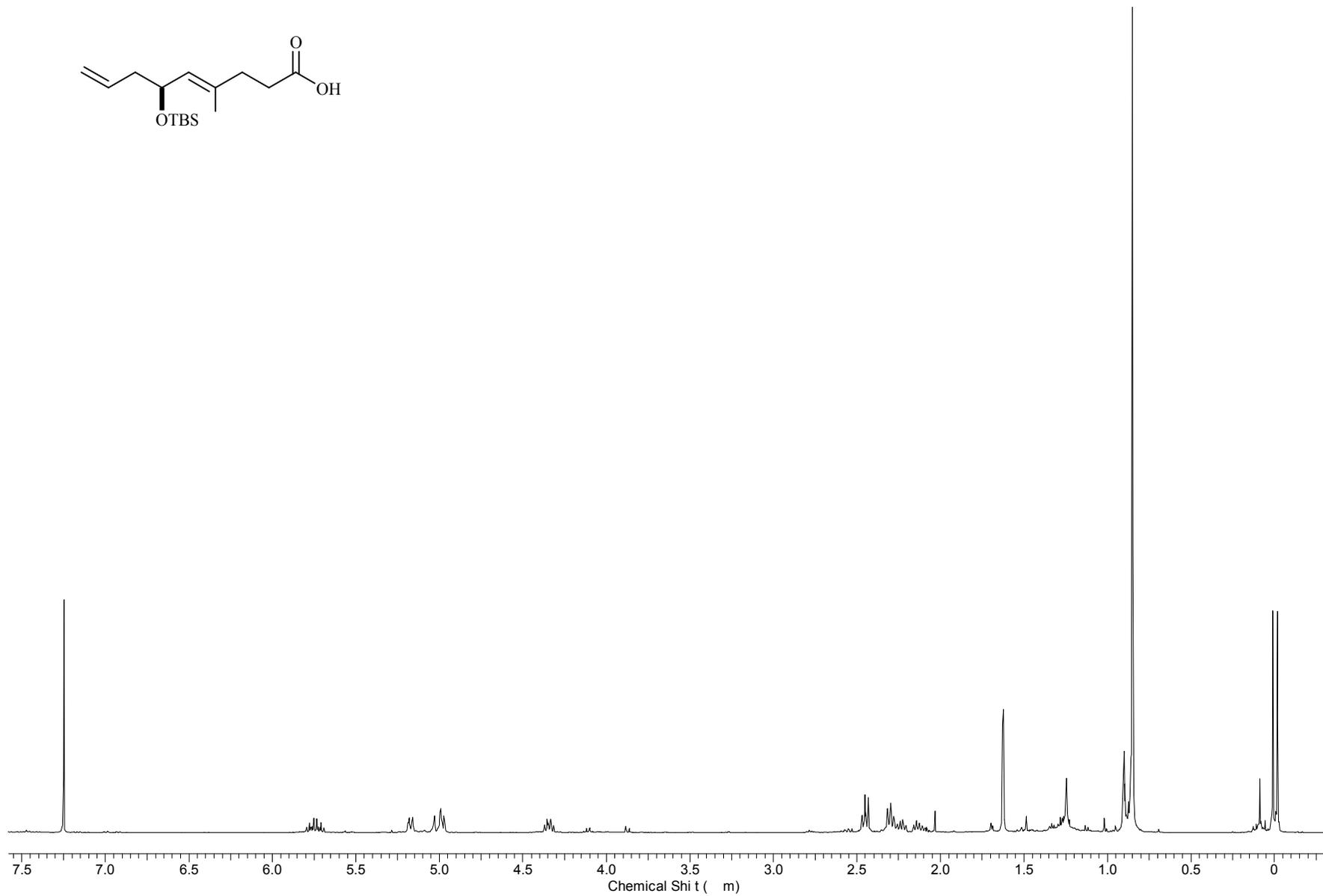
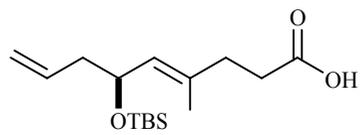


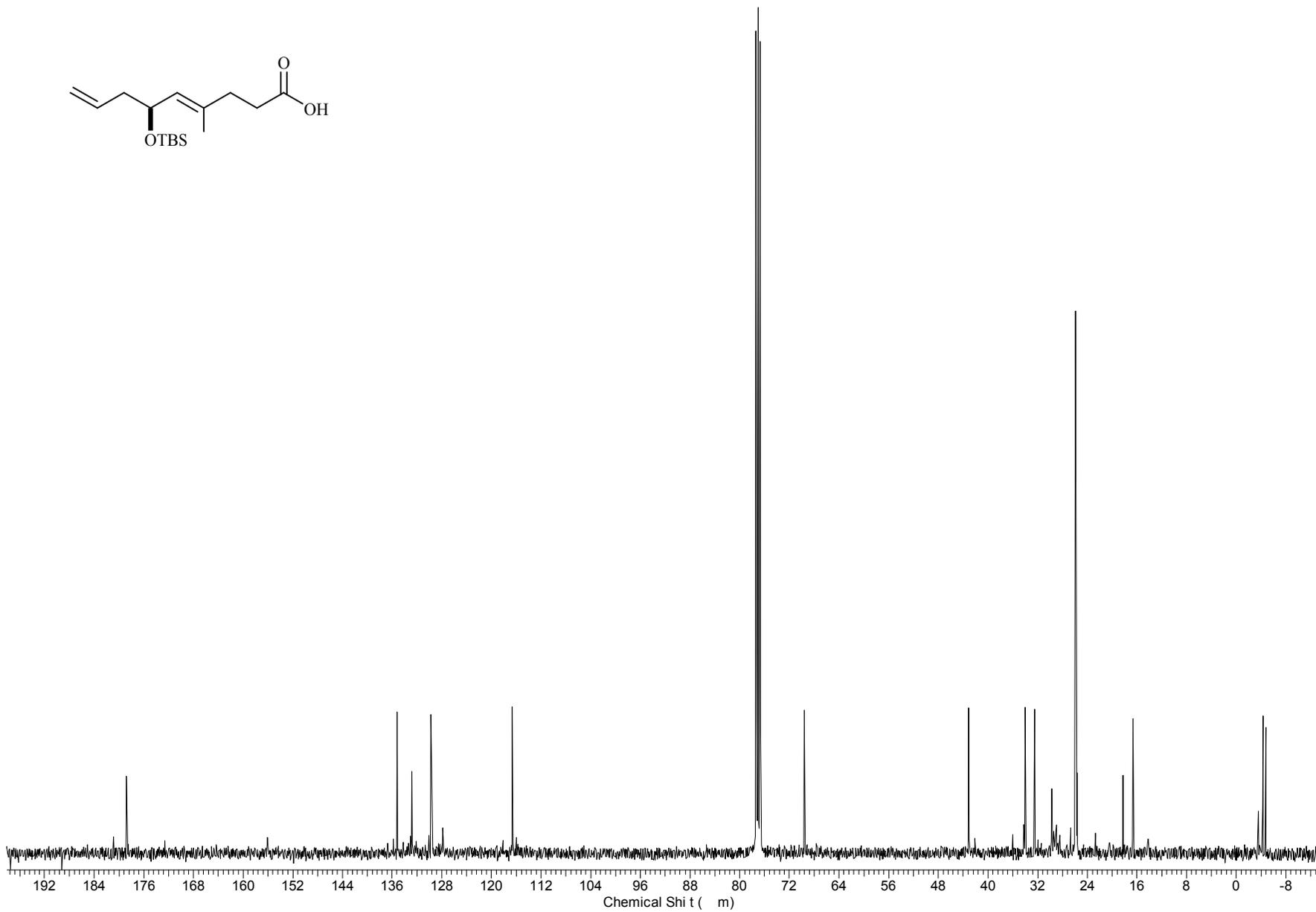
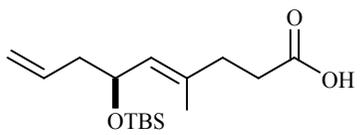


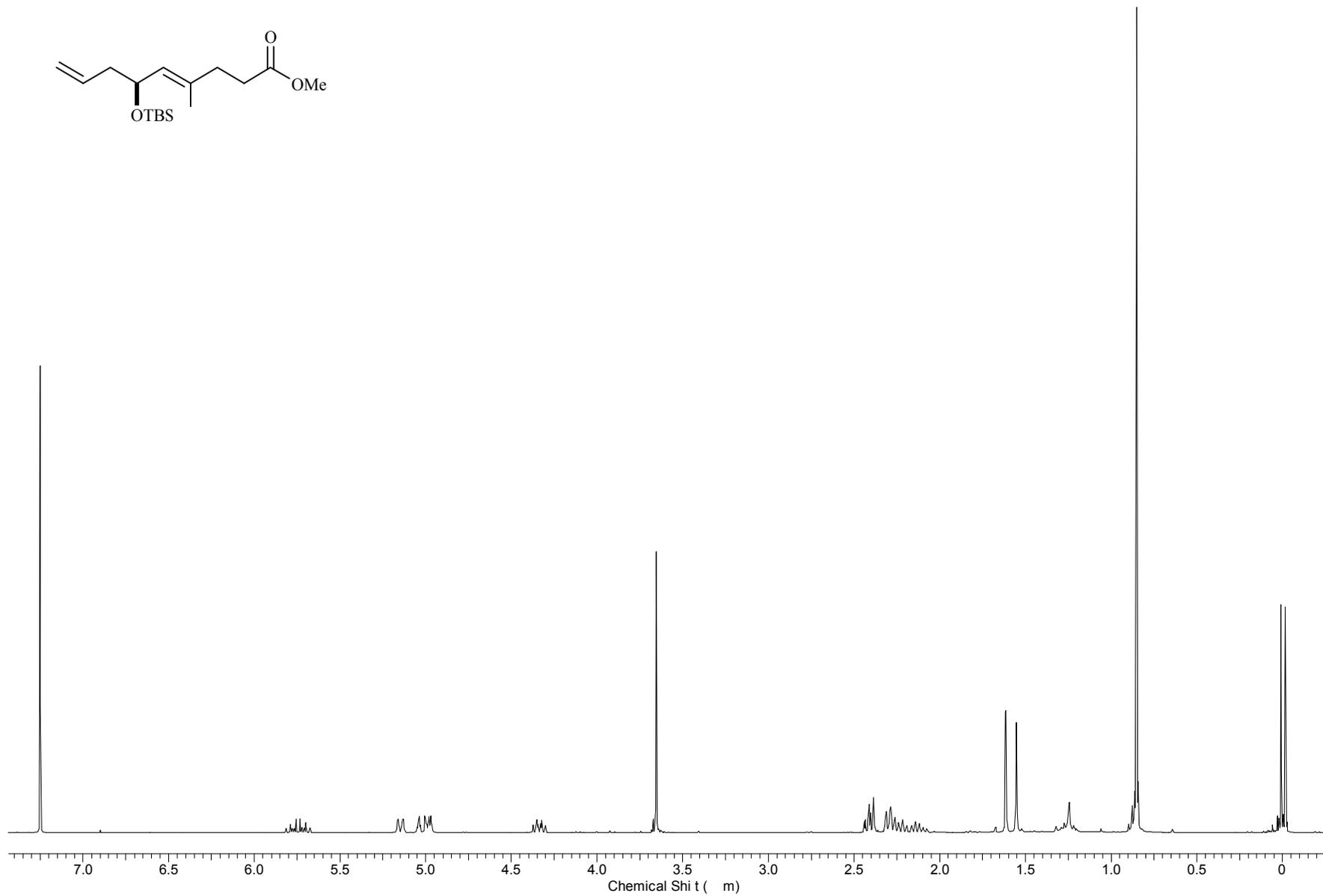
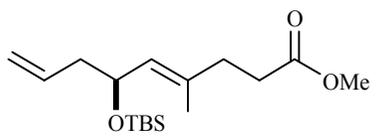


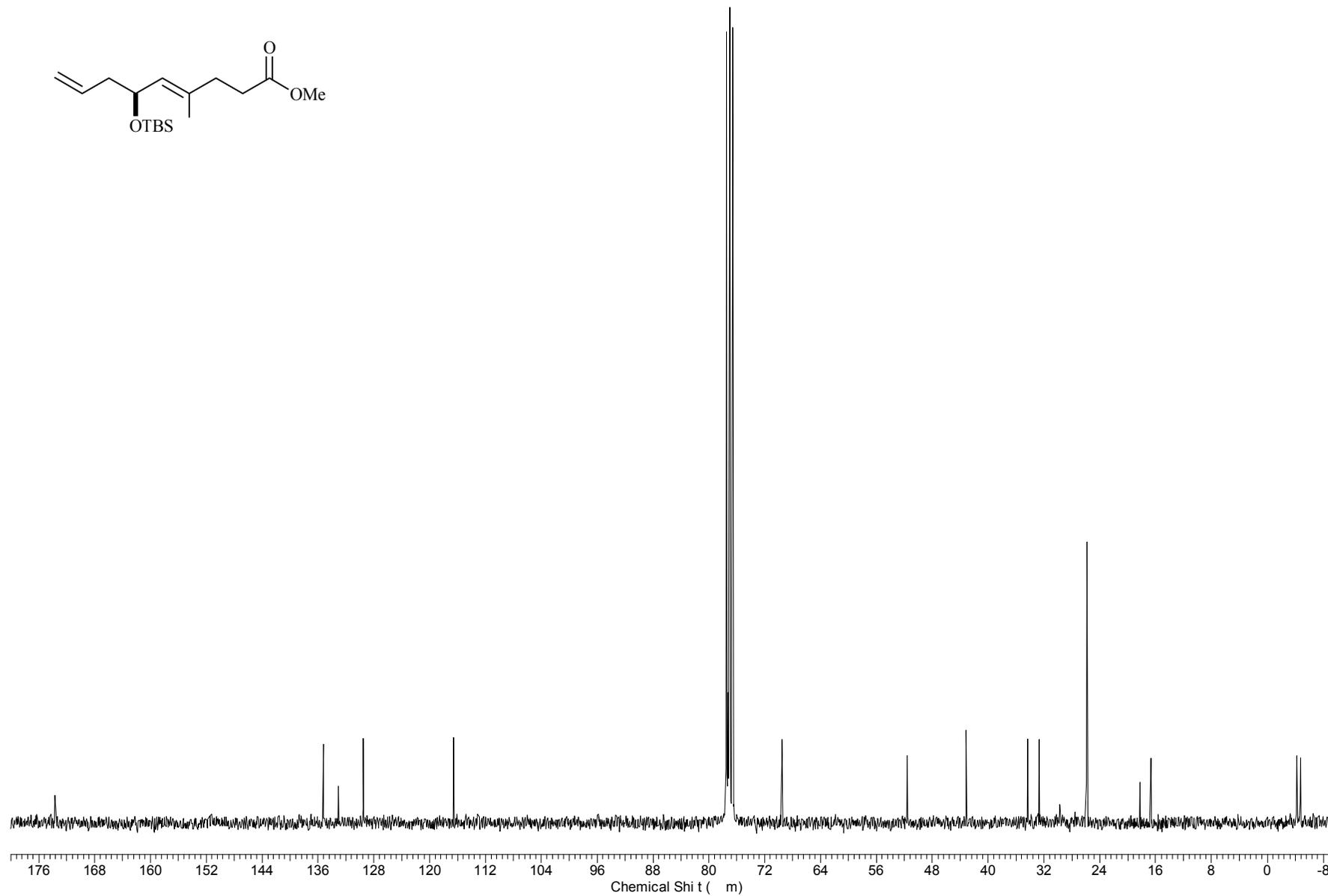
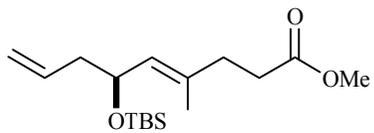


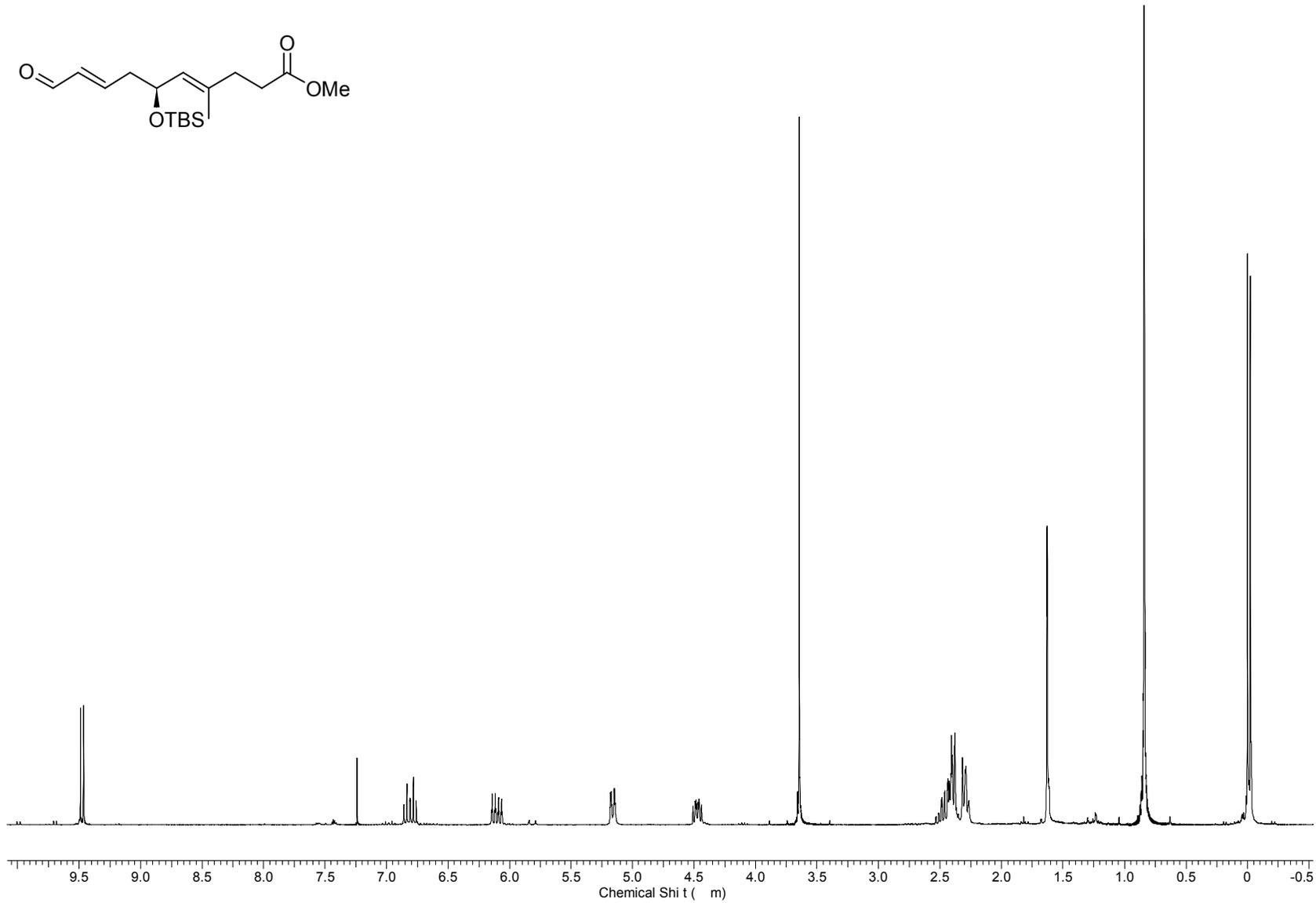
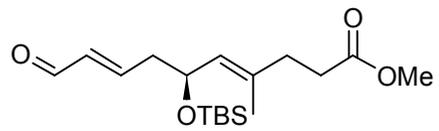


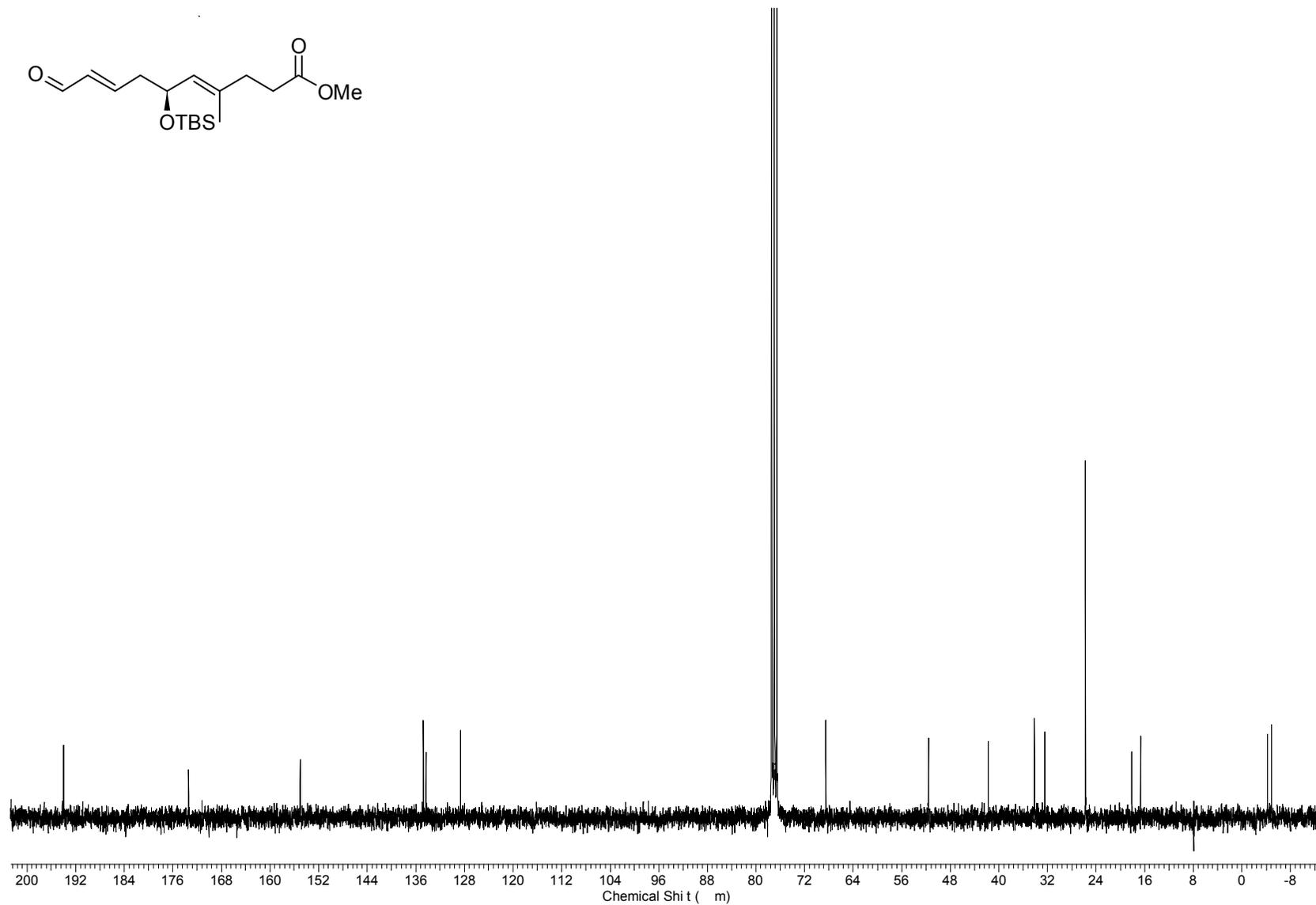
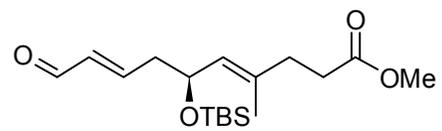


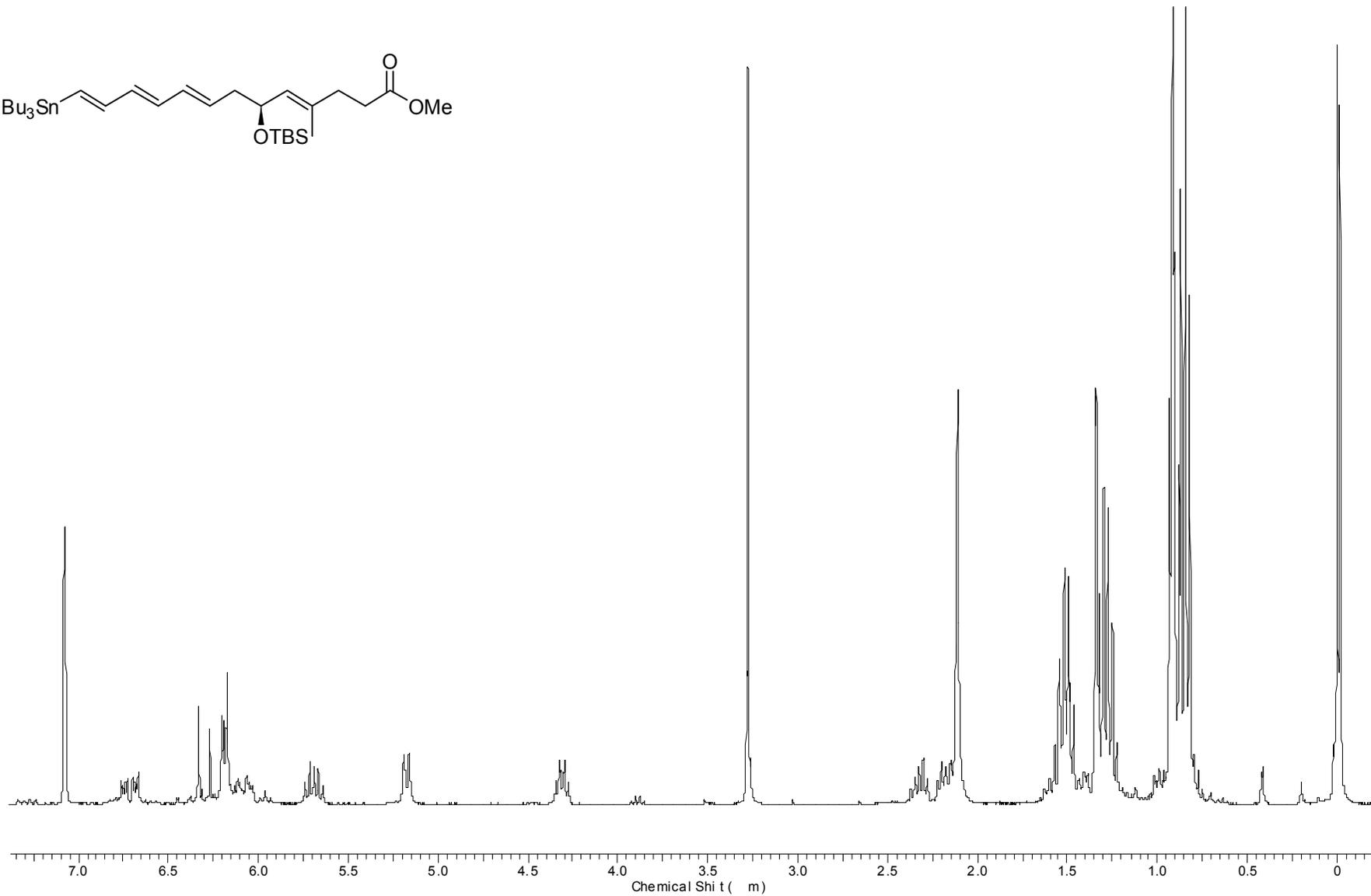
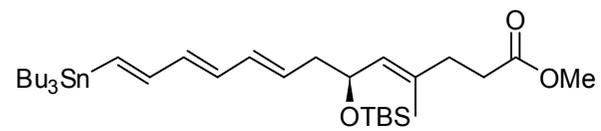


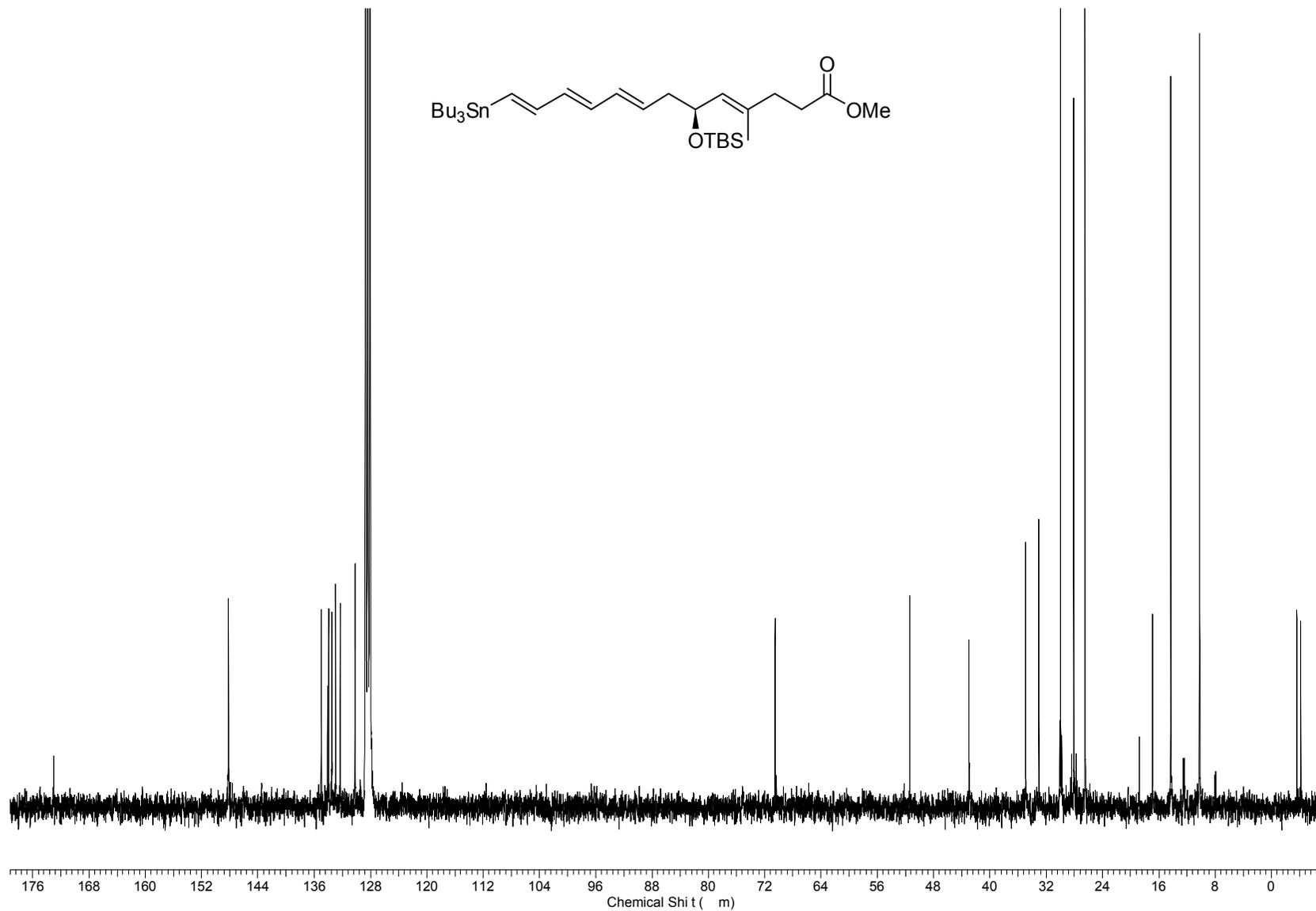
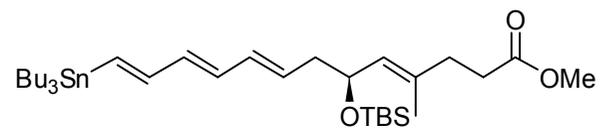


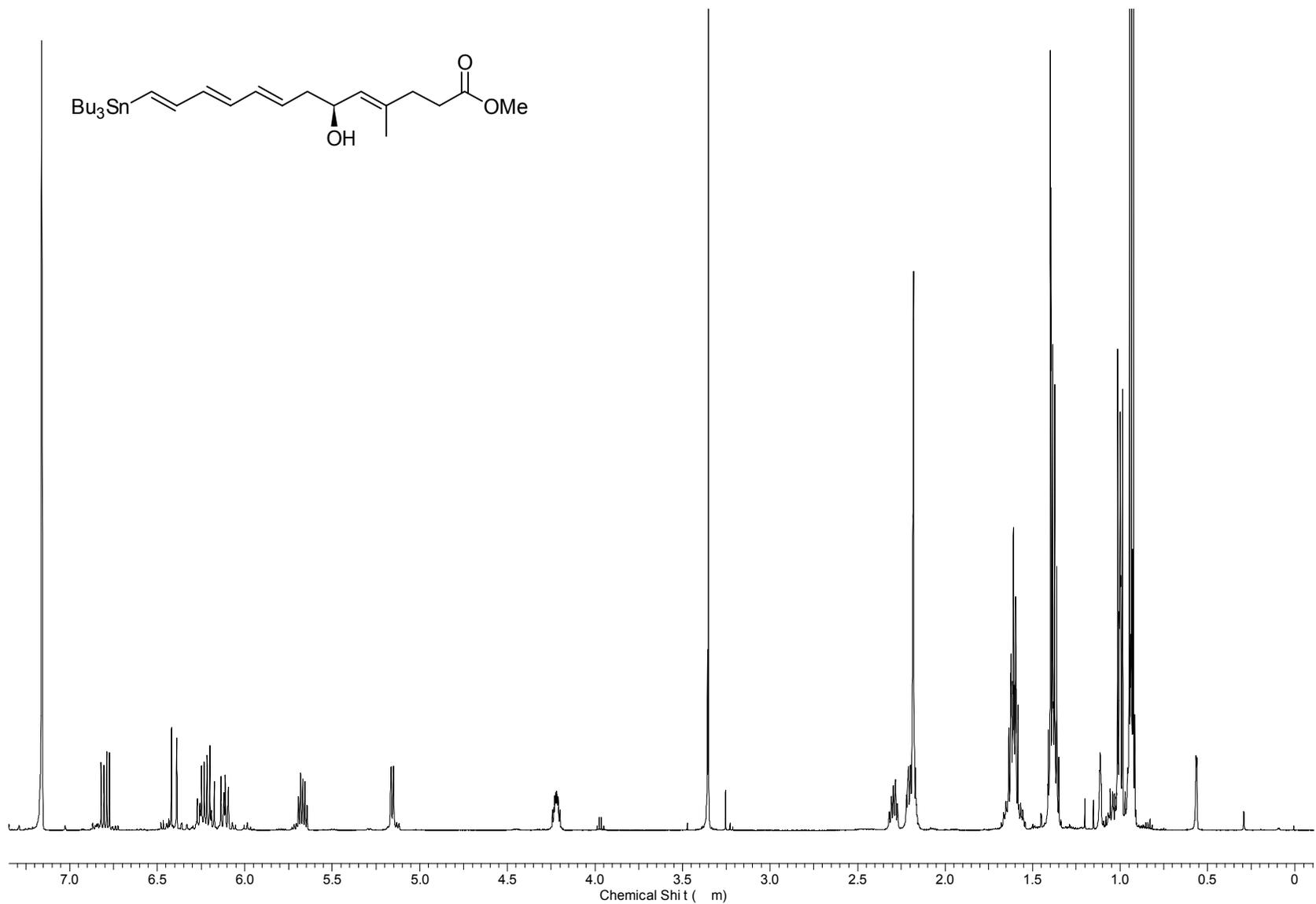
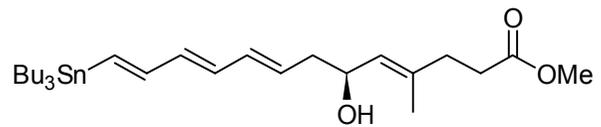


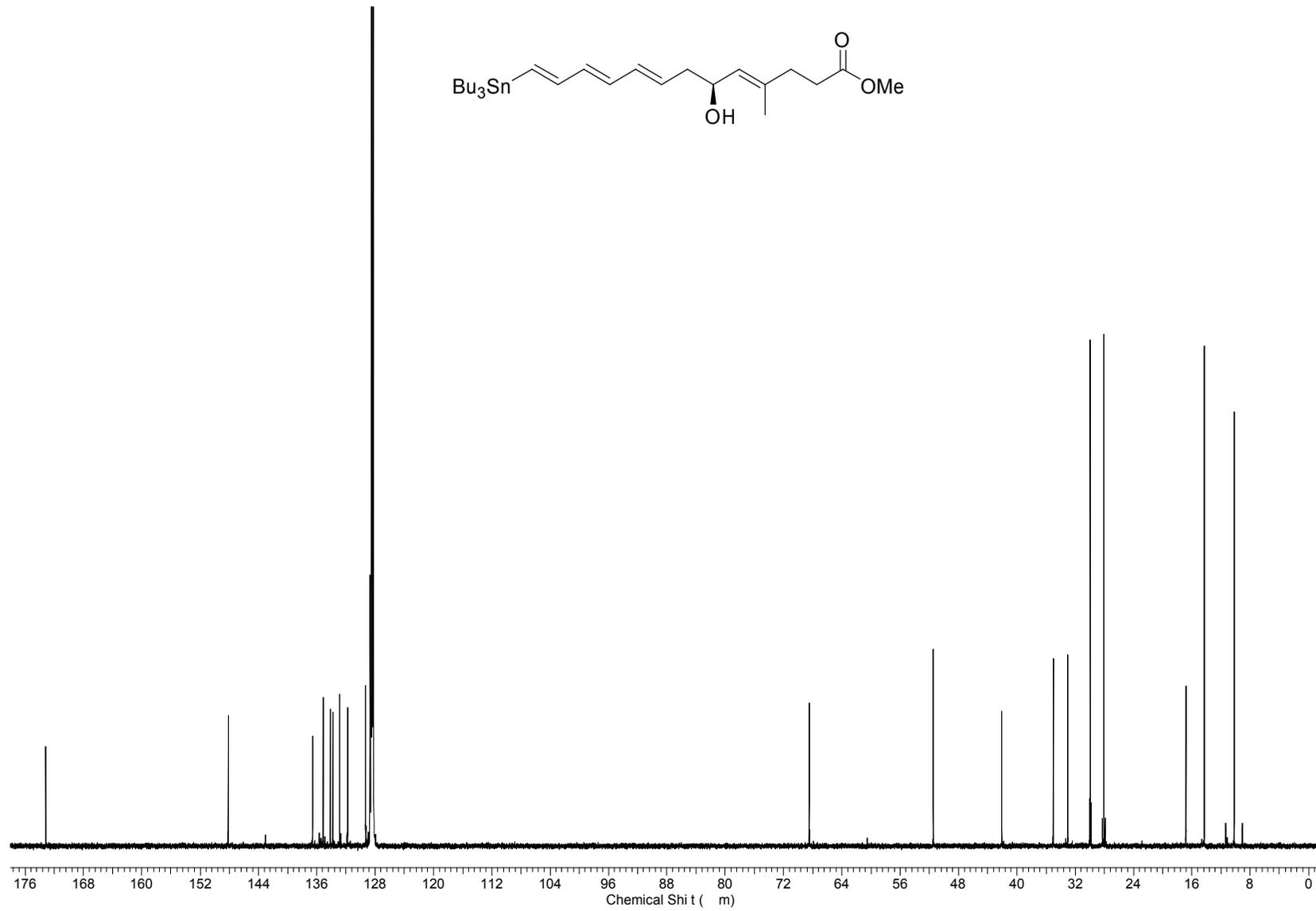
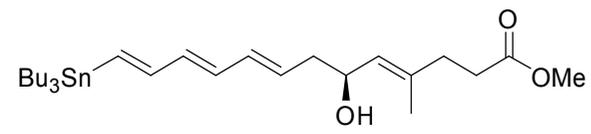


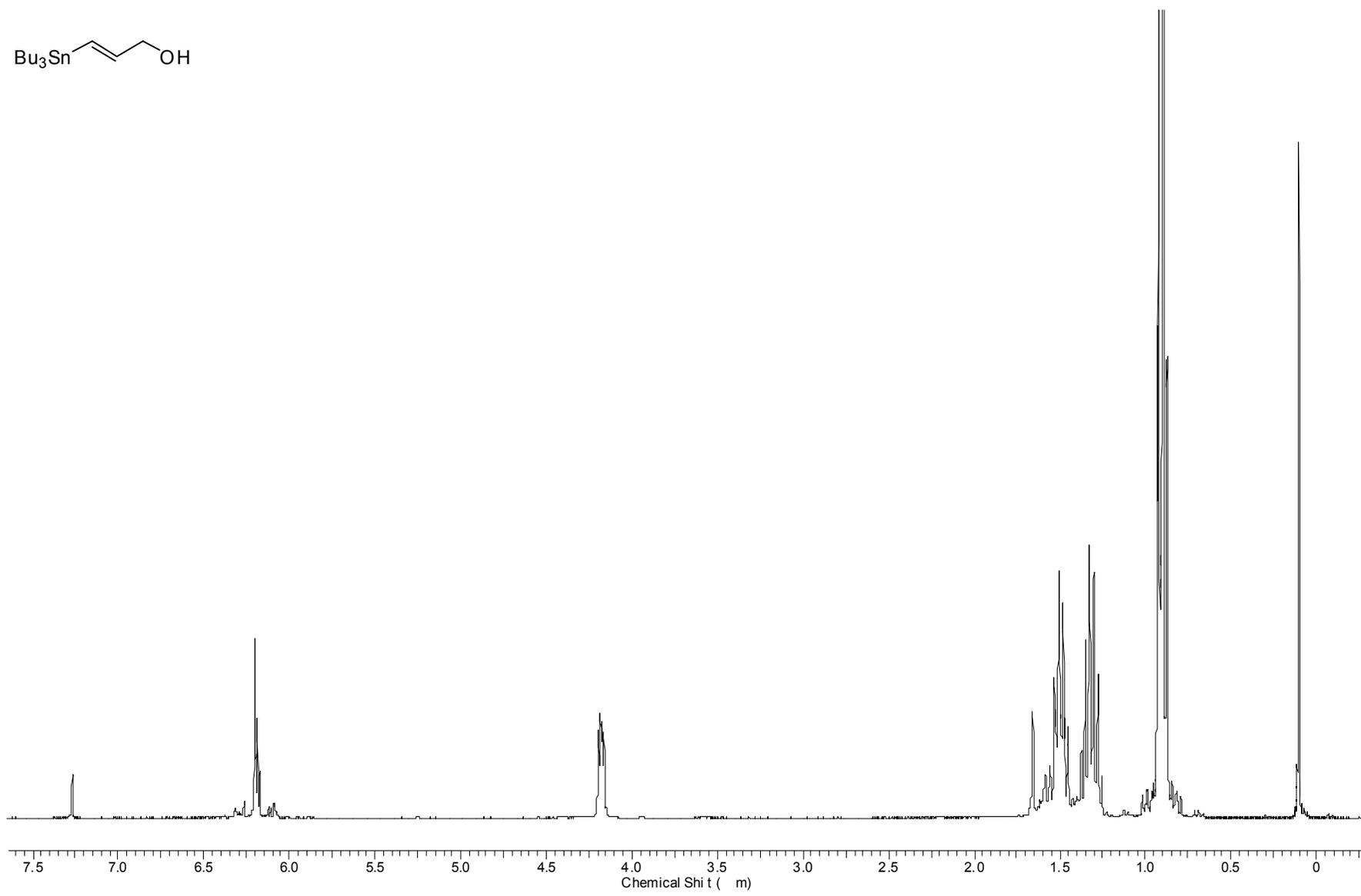
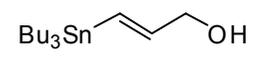


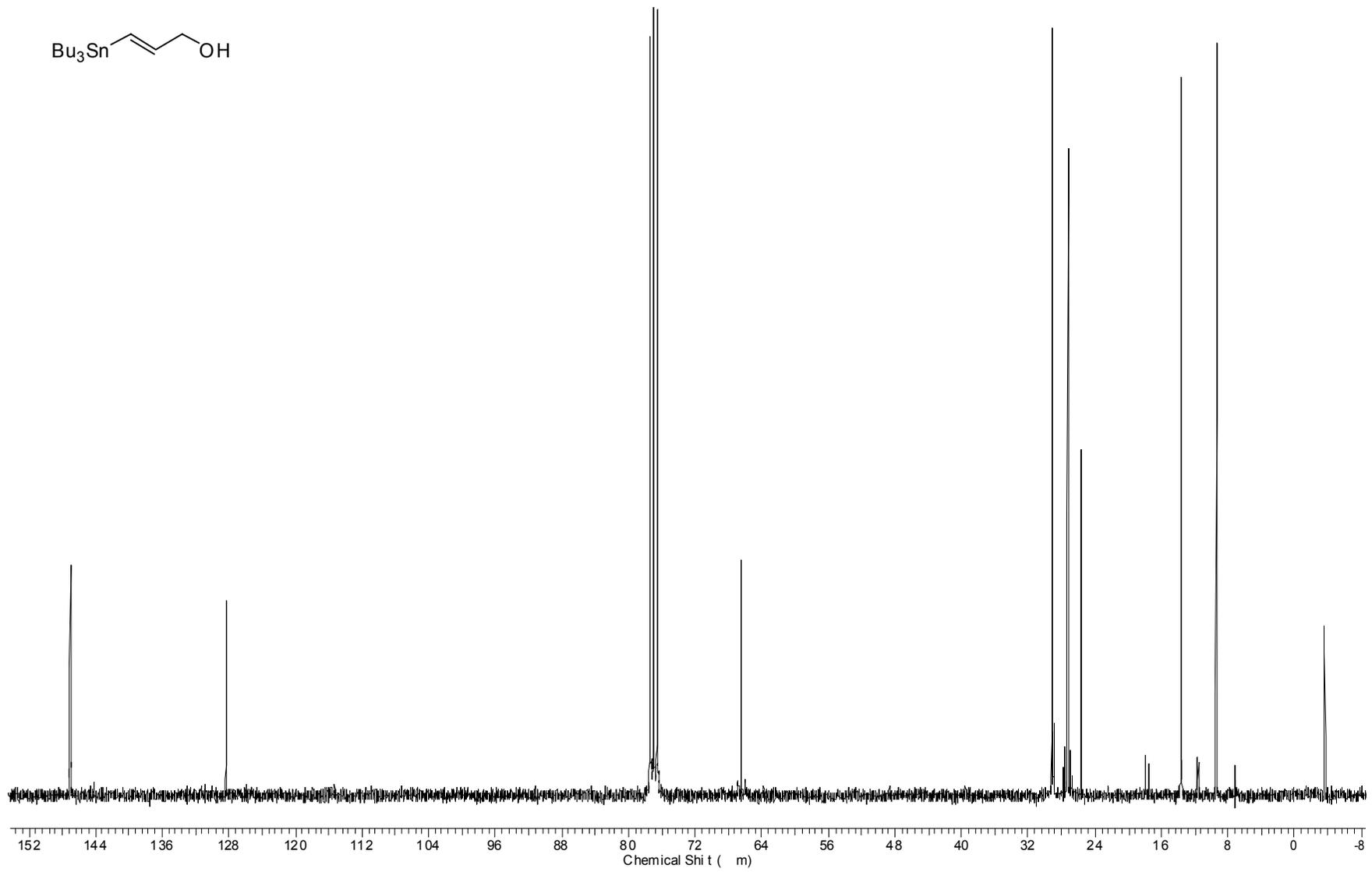
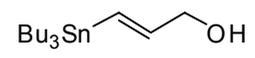


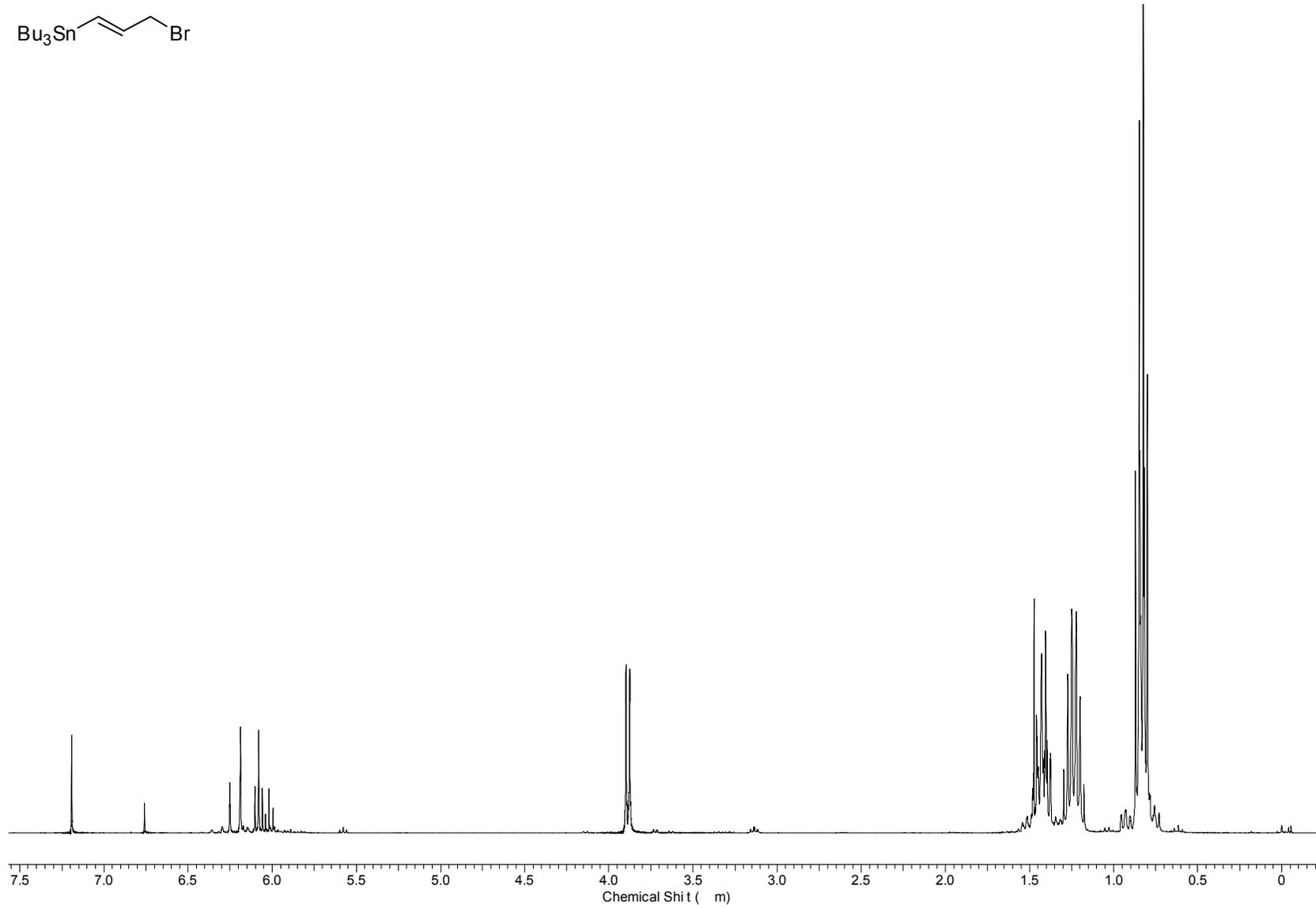
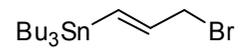


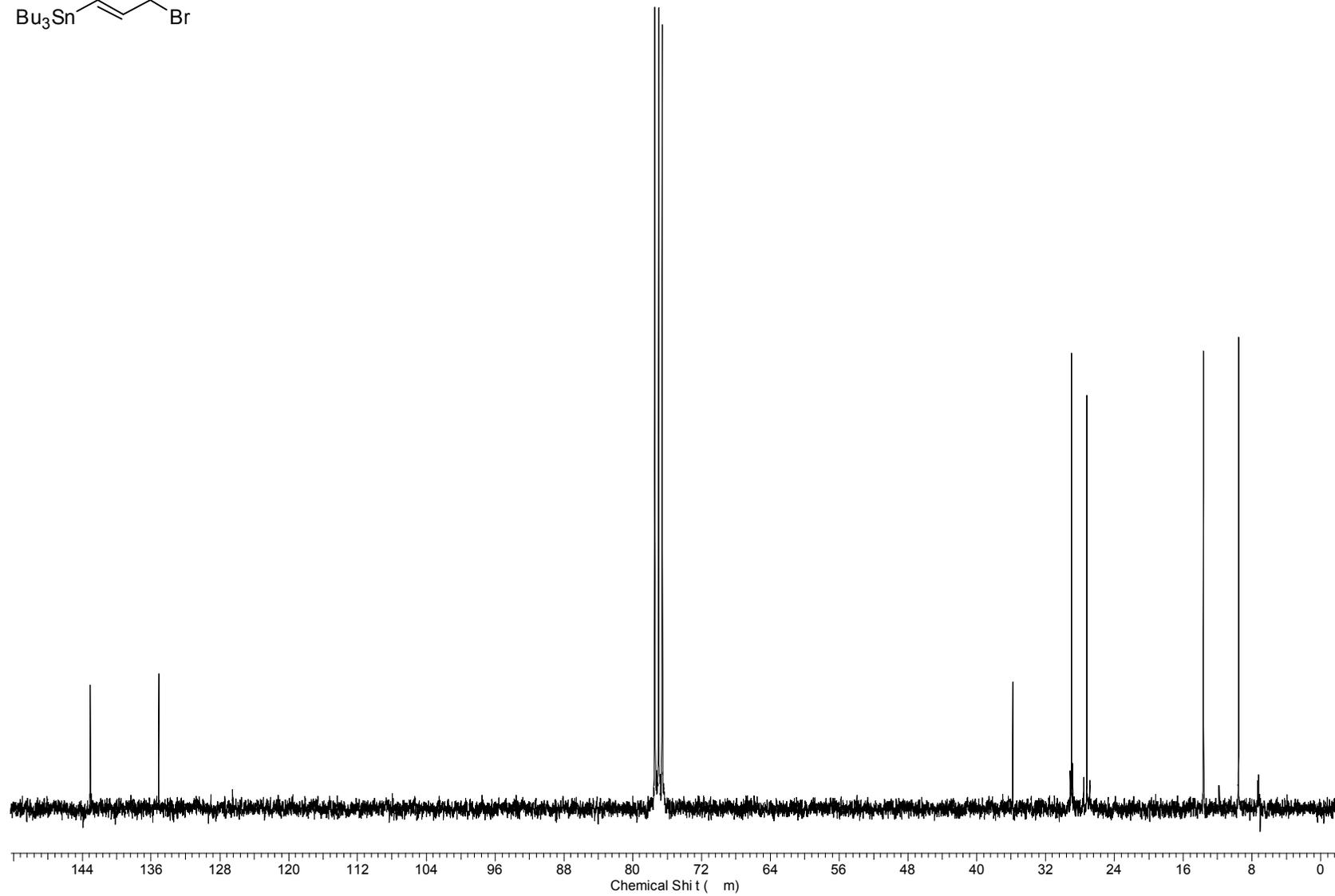
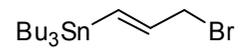


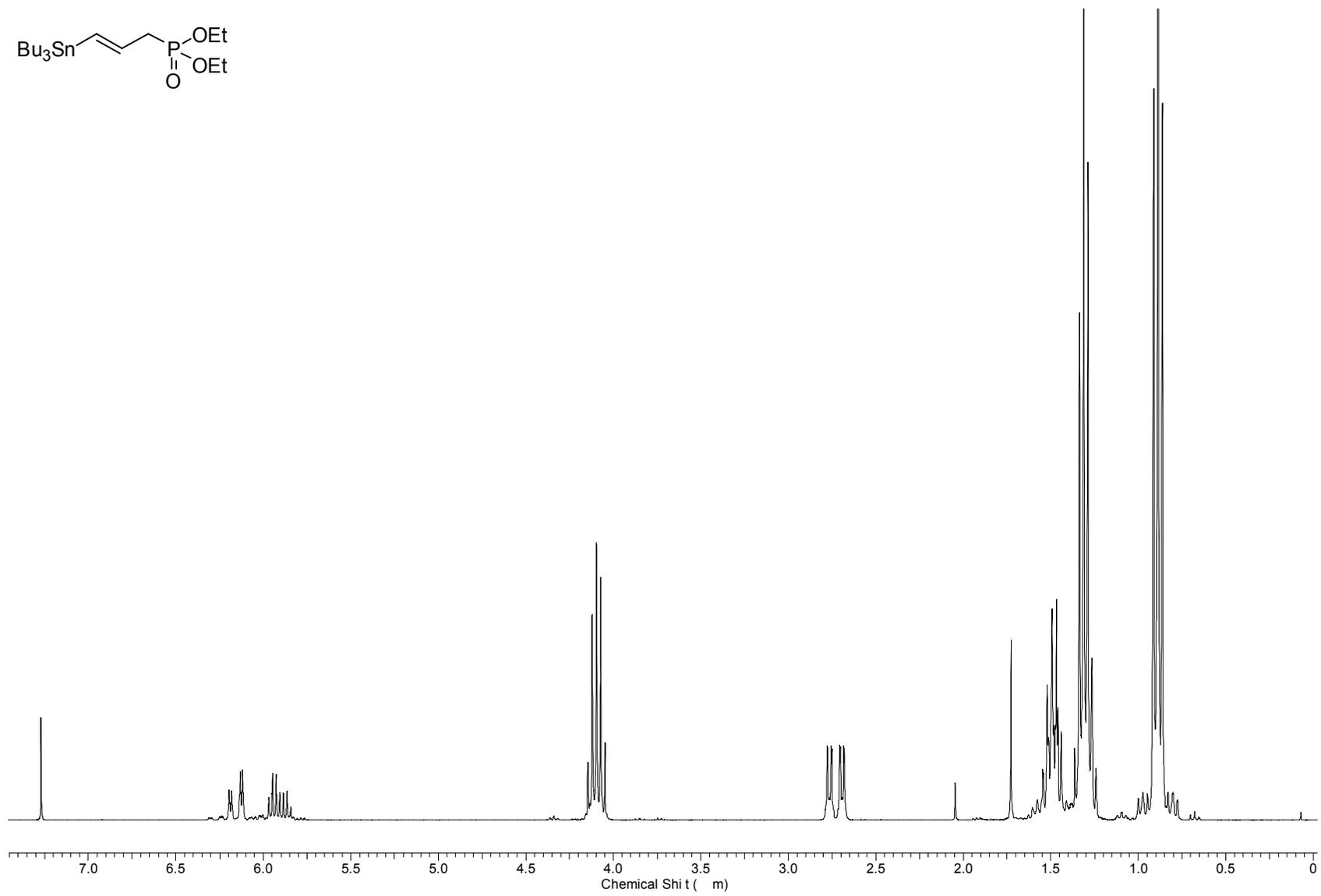
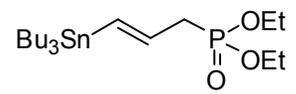


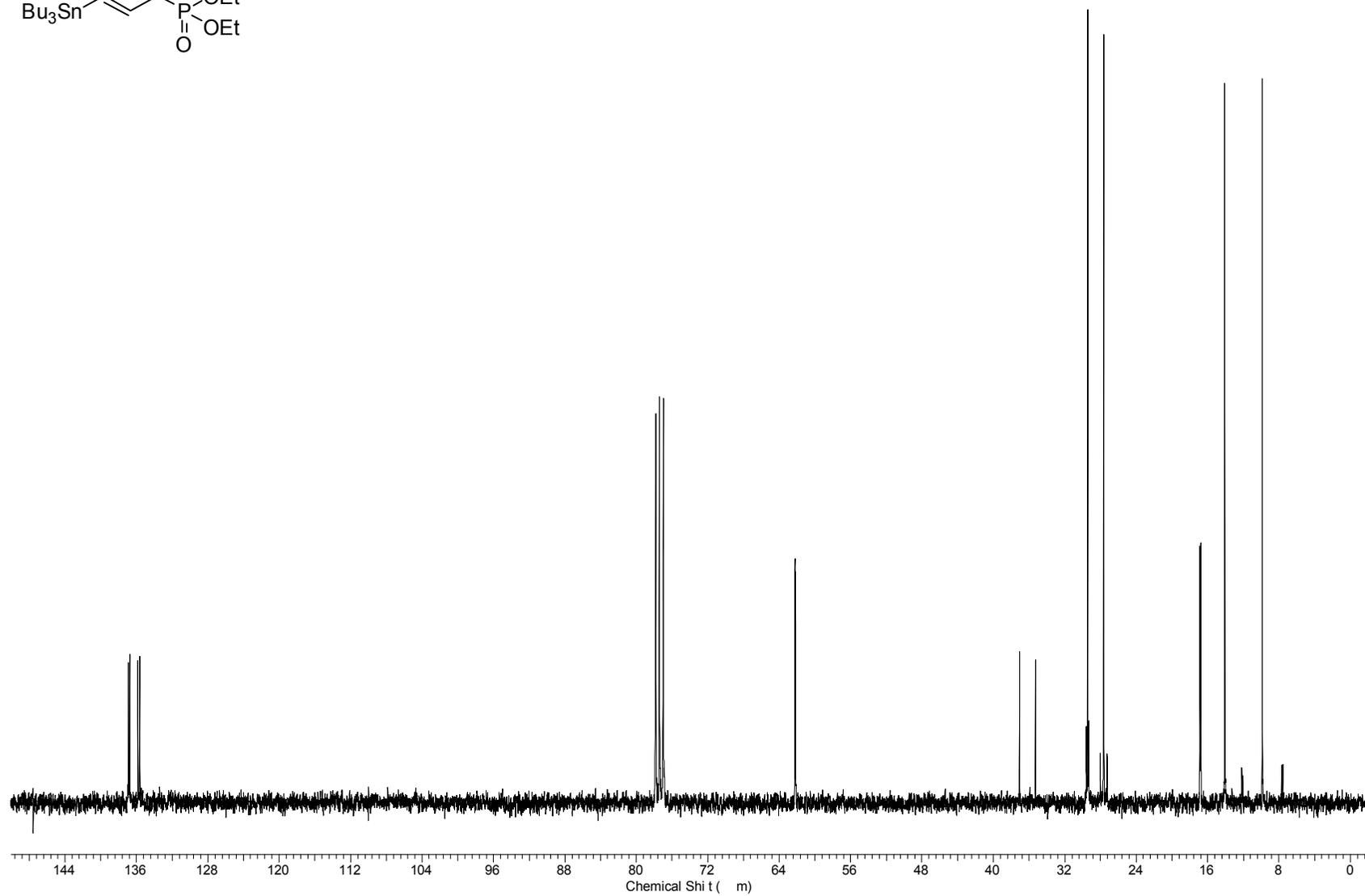
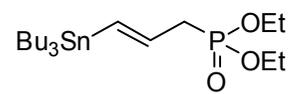


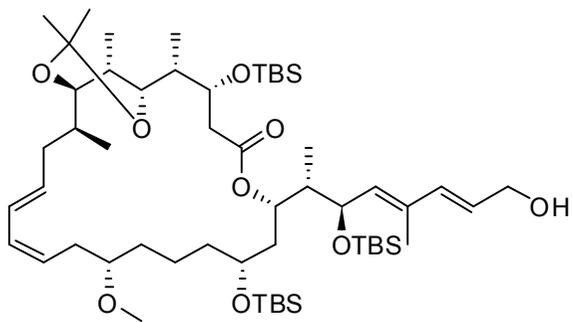




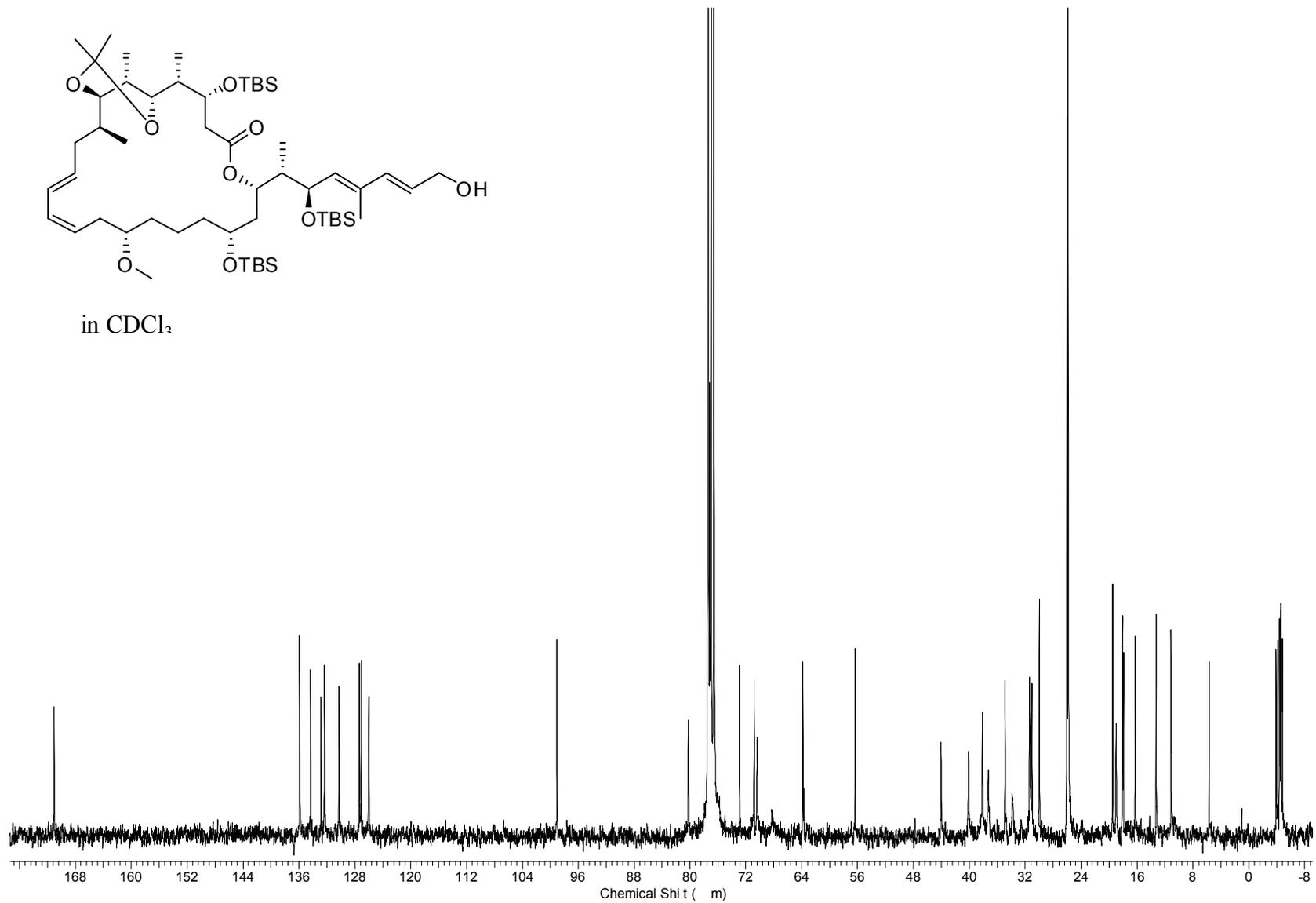


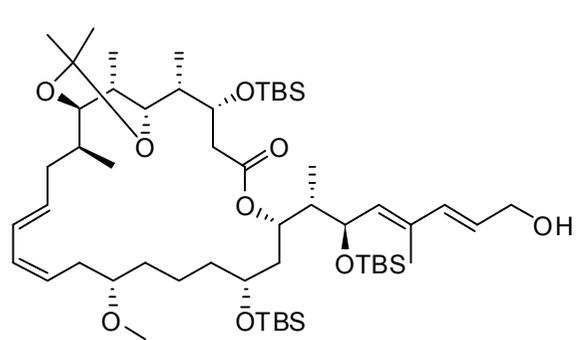




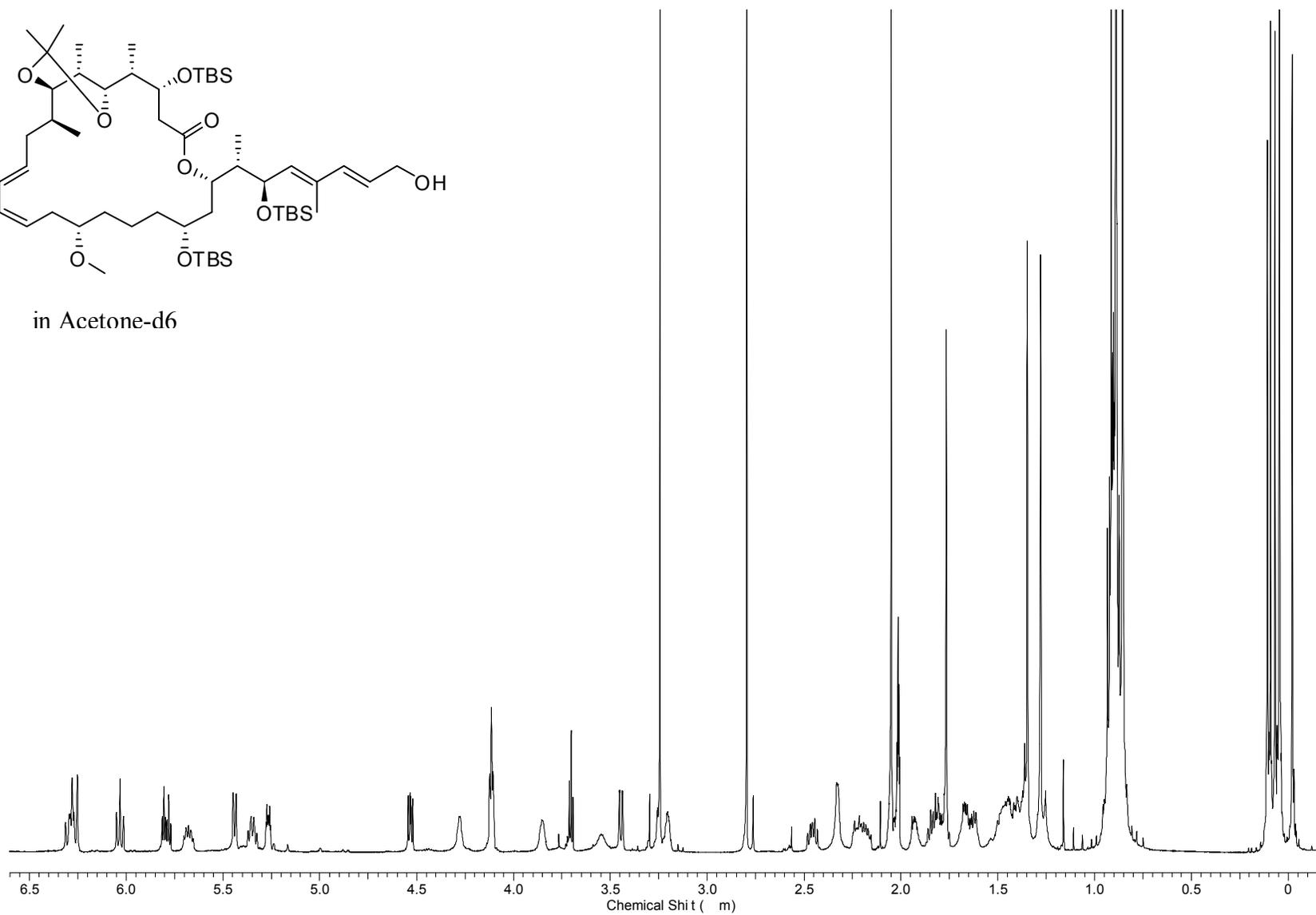


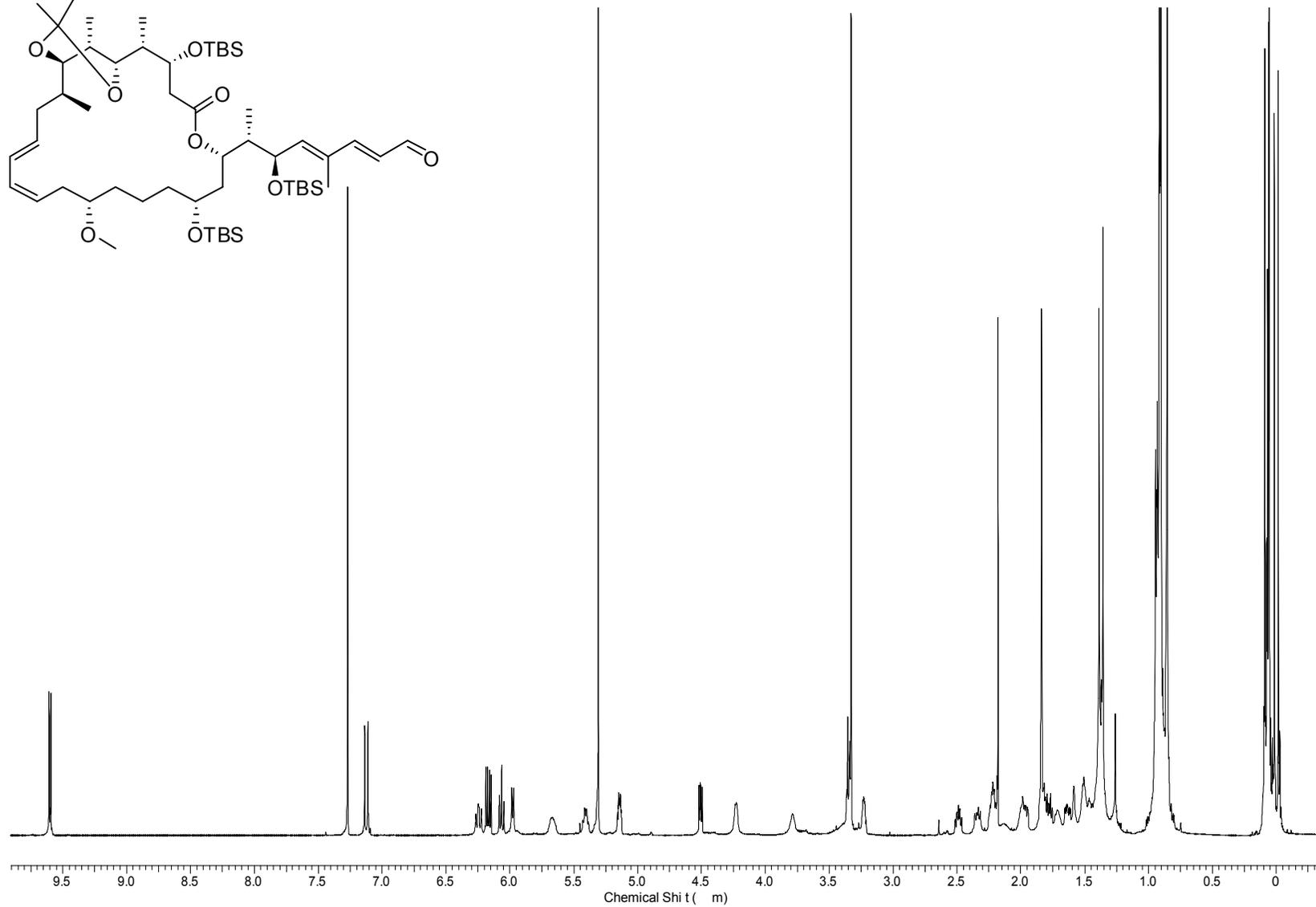
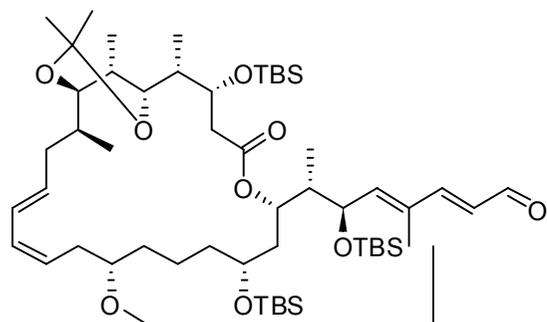
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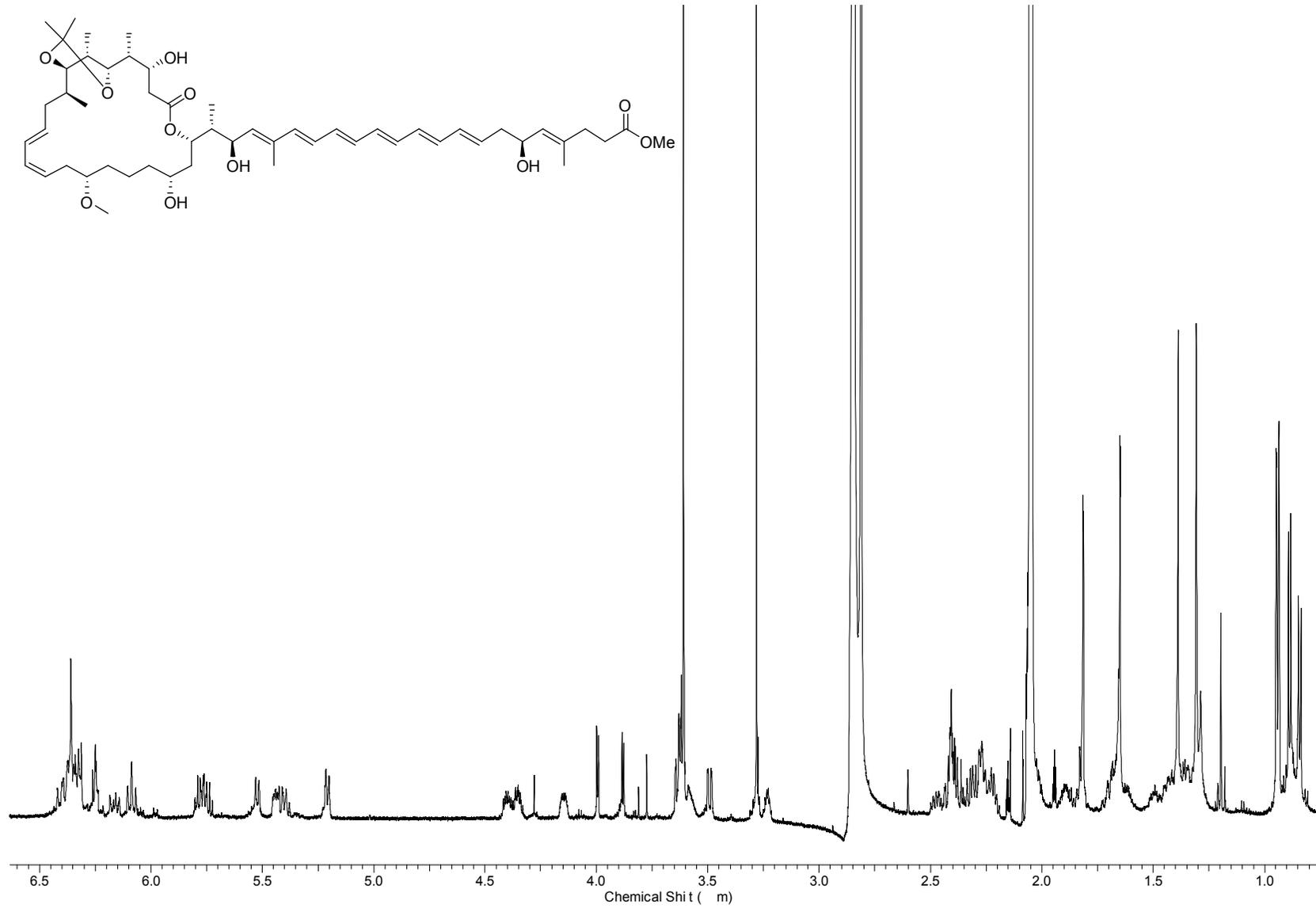
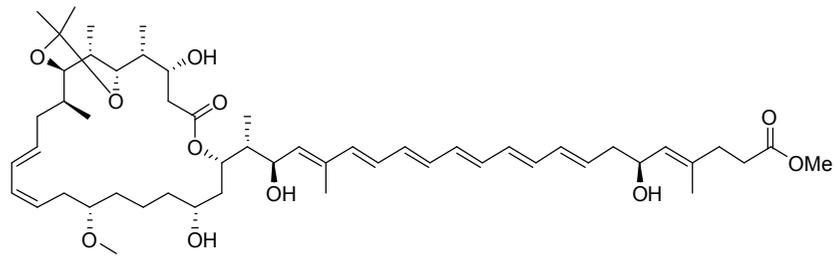




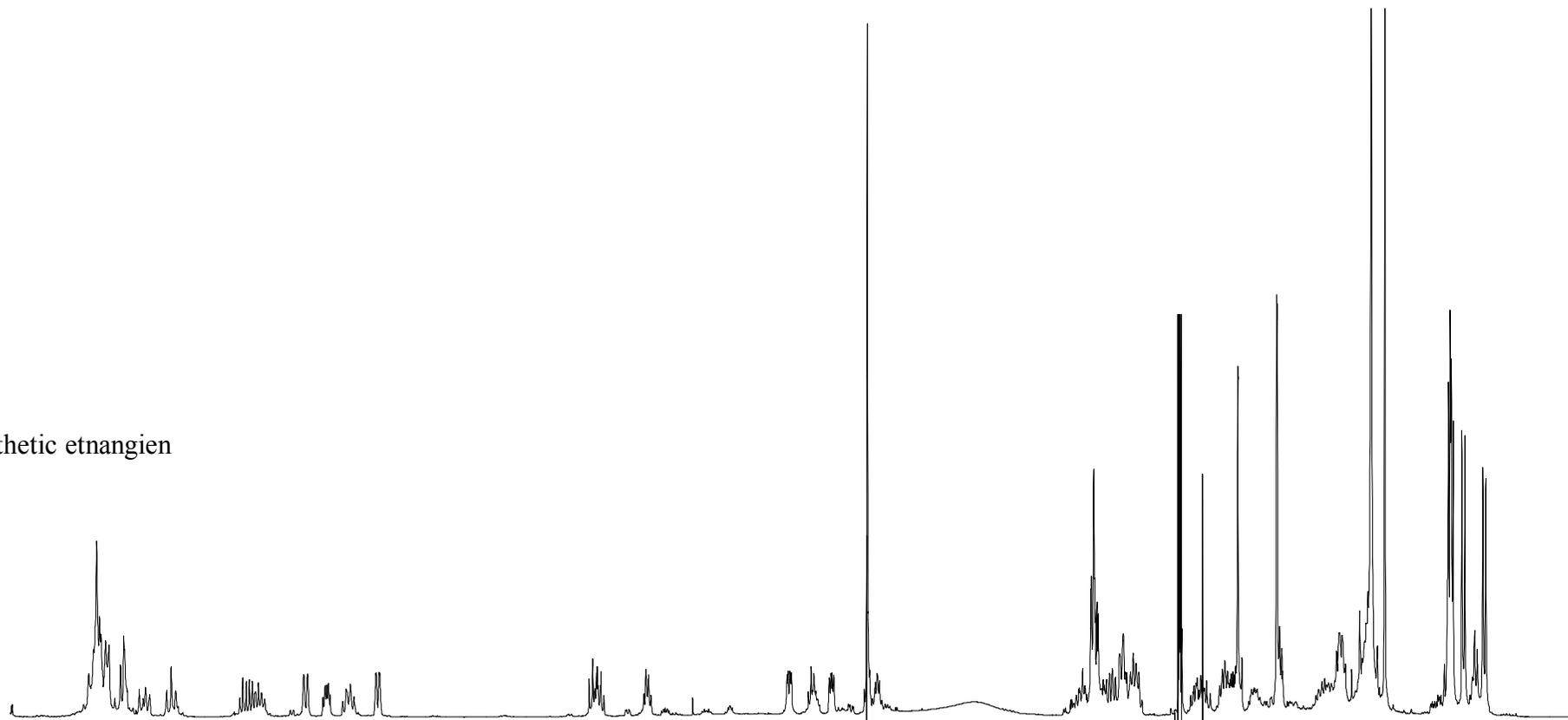
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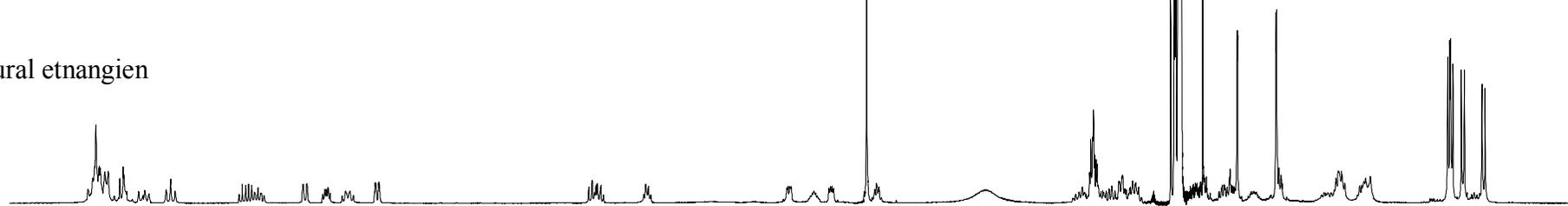




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Chemical Shift (ppm)