Toward More "Ideal" Polyketide Natural Product Synthesis: A Step-Economical Synthesis of Zincophorin Methyl Ester

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Supporting Information

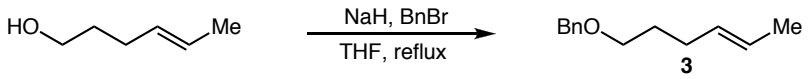
General Information. All reactions were carried out under an atmosphere of nitrogen in flame-dried glassware with magnetic stirring unless otherwise indicated. Degassed solvents were purified by passage through an activated alumina column. Silane **1** was prepared by the previously reported method.[1] Gas chromatographic analyses were performed on a Hewlett-Packard 6890 Series Gas Chromatograph equipped with a capillary split-splitless inlet and flame ionization detector with electronic pneumatics control using a Supelco ß-Dex 120 (30 m x 0.25 mm) capillary GLC column. ^{1}H NMR spectra were recorded on a Bruker DPX-300 (300 MHz) or a Bruker DPX-400 (400 MHz) spectrometer and are reported in ppm from $CDCl_3$ internal standard (7.26 ppm), C_6D_6 (7.16 ppm), or DMSO-d_6 (2.50 ppm). Data are reported as follows: (bs= broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sep = septet, m = multiplet, dd = doublet of doublets, ddd = doublet of doublet of doublets; coupling constant(s) in Hz; integration). Proton decoupled ^{13}C NMR spectra were recorded on a Bruker DPX-300 (75 MHz) or a Bruker DPX-400 (400 MHz) spectrometer and are reported in ppm from $CDCl_3$ internal standard (77.23 ppm), C_6D_6 (128.39 ppm), or DMSO-d_6 (40.45 ppm). Infrared spectra were recorded on a Perkin Elmer Paragon 1000 FT-IR spectrometer. Optical rotations were recorded on a Jasco DIP-1000 digital polarimeter.

Refs 3d and 3e:

(d) Mickel, S. J.; Sedelmeier, G. H.; Niederer, D.; Schuerch, F.; Seger, M.; Schreiner, K.; Daeffler, R.; Osmani, A.; Bixel, D.; Loiseleur, O.; Cercus, J.; Stettler, H.; Schaer, K.; Gamboni, R.; Bach, A.; Chen, G. P.; Chen, W. C.; Geng, P.; Lee, G. T.; Loeser, E.; McKenna, J.; Kinder, F. R.; Konigsberger, K.; Prasad, K.; Ramsey, T. M.; Reel, N.; Repic, O.; Rogers, L.; Shieh, W. C.; Wang, R. M.; Waykole, L.; Xue, S.; Florence, G.; Paterson, I. *Org. Process Res. Dev.* **2004**,

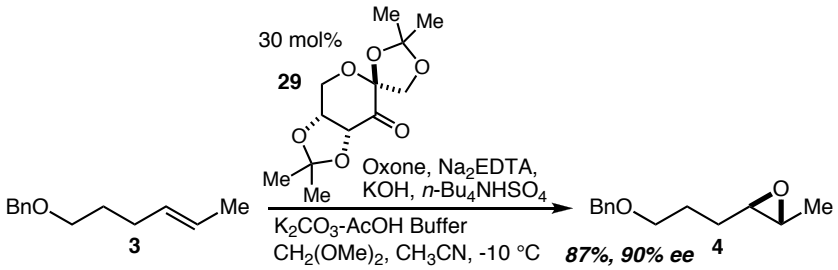
(1) Berger, R.; Duff, K.; Leighton, J. L. *J. Am. Chem. Soc.* **2004**, *126*, 5686-5687.

8, 113. (e) Mickel, S. J.; Niederer, D.; Daeffler, R.; Osmani, A.; Kuesters, E.; Schmid, E.; Schaer, K.; Gamboni, R.; Chen, W. C.; Loeser, E.; Kinder, F. R.; Konigsberger, K.; Prasad, K.; Ramsey, T. M.; Repic, J.; Wang, R. M.; Florence, G.; Lyothier, I.; Paterson, I. *Org. Process Res. Dev.* **2004**, *8*, 122.



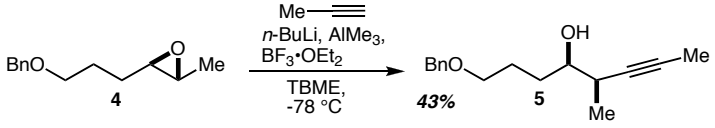
(Procedure adapted from: Nogawa, M.; Sugawara, S.; Iizuka, R.; Shimojo, M.; Ohta, H.; Hatanaka, M.; Matsumoto, K. *Tetrahedron* **2006**, *62*, 12071.)

To a cooled (0 °C) suspension of sodium hydride (7.5 g, 313 mmol, 1.15 equiv) in THF (400 mL, 0.7 M) in a flask fitted with a reflux condenser was added (*E*)-4-hexen-1-ol (32 mL, 272 mmol, 1 equiv) dropwise. After bubbling subsided (~10 min), benzyl bromide (33 mL, 272 mmol, 1 equiv) was added. The reaction mixture was heated to 70 °C (oil bath, external temperature). After 12 h, the reaction mixture was cooled to room temperature and partitioned between saturated aqueous NH_4Cl (100 mL) and Et_2O (100 mL). The aqueous layer was separated and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was filtered over silica gel (180 g), eluting with 10% EtOAc/Hex. The filtrate was purified by distillation (0.3 mm Hg, bp 115 °C) to afford benzyl ether **3** (50 g, 97% yield) as a colorless oil. TLC R_f = 0.67 (20% EtOAc/Hex); IR (neat) 3028, 2936, 2854, 1496, 1453, 1364, 1204, 1103, 966, 735, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.29 (m, 5H, Bn), 5.55 – 5.43 (m, 2H, $C_{12}H$, $C_{13}H$), 4.55 (s, 2H, $C\underline{H}_2Ph$), 3.53 (td, J = 6.5, 1.0 Hz, 2H, $C_{16}H_2$), 2.18 – 1.10 (m, 2H, $C_{14}H_2$), 1.78 – 1.67 (m, 5H, $C_{11}H_3$, $C_{15}H_2$); ^{13}C NMR (100 MHz,$CDCl_3$) δ 138.6, 130.7, 128.2, 127.4, 125.1, 72.8, 69.7, 29.5, 29.1, 23.4, 17.8; Exact mass (FAB+) calcd for $C_{13}H_{17}O$ $[M–H]^+$: 189.13; found 189.36.



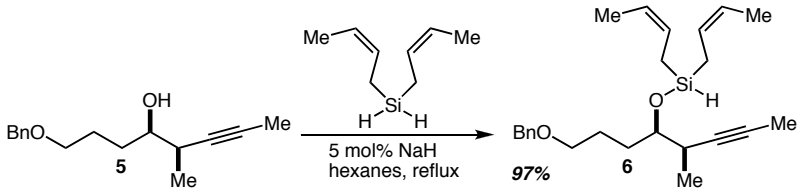
To a cooled (-10 °C) solution of alkene **3** (9.5 g, 50 mmol, 1 equiv) in 2:1 dimethoxymethane:acetonitrile (500 mL) was added a K_2CO_3-AcOH buffer solution (300 mL), Bu_4NHSO_4 (0.375 g), and chiral ketone **29** (4.2 g, 15 mmol, 0.3 equiv). One addition funnel was charged with a solution of Oxone (46.1 g, 75 mmol) in 4 x 10^{-4} M Na_2EDTA (170 mL), and a

second addition funnel was charged with 1.47 M KOH (170 mL). The two solutions were added to the cooled reaction at the same rate over 2 h. The mixture was stirred for 1 h, and was then diluted with pentane (250 mL). The aqueous layer was separated and extracted with pentane (2 x 200 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (10-16% EtOAc/Hex) to afford epoxide **4** (8.9 g, 87% yield, 90% *ee*) as a colorless oil. The enantiomeric excess was determined by HPLC: ADH column, 1% EtOH/Hex, 1 mL/min, T_r (minor) = 8.9 min, T_r (major) = 10.4 min. TLC R_f = 0.27 (17% EtOAc/Hex); $[\alpha]^{23}_D$ +19.5 (*c* 0.99, $CHCl_3$); IR (neat) 2927, 2859, 1496, 1454, 1380, 1363, 1205, 1102, 935, 860, 738, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 5H, Bn), 4.53 (s, 2H, C<u>H</u>$_2$Ph), 3.54 (ddd, *J* = 15.6, 9.3, 6.4 Hz, 2H, $C_{16}H_2$), 2.77 (qd, *J* = 5.2, 2.2 Hz, 1H, $C_{12}H$), 2.68 (td, *J* = 6.7, 2.2 Hz, 1H, $C_{13}H$), 1.89 – 1.55 (m, 4H, $C_{14}H_2$, $C_{15}H_2$), 1.30 (dd, *J* = 5.2 Hz, 3H, $C_{11}H_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 128.3, 127.5, 127.4, 72.8, 69.7, 59.3, 54.4, 28.7, 26.1, 17.5; LRMS (FAB+) calcd for $C_{13}H_{19}O_2$ $[M+H]^+$: 207.14; found 207.39.

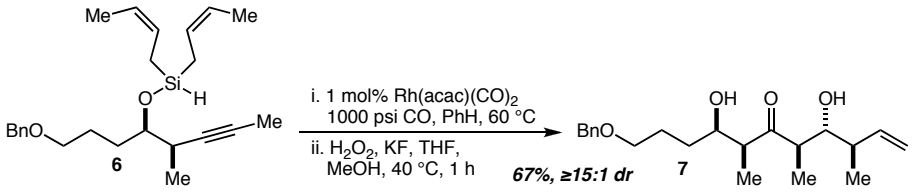


To a cooled (-78 °C) solution of propyne (5 mL, 88 mmol, 2.3 equiv) in *tert*-butyl methyl ether (TBME) (165 mL) was added *n*-BuLi (26 mL, 42.4 mmol, 1.63 M in Hex, 1.08 equiv) dropwise. After 10 min, the reaction was warmed to 0 °C and Me_3Al (20 mL, 40 mmol, 2 M in Tol, 1.03 equiv) was added. The reaction was then warmed to room temperature. After 40 min, epoxide **4** (8.1 g, 39 mmol, 1 equiv) was added and the reaction mixture was recooled to -78 °C. Freshly distilled BF_3•OEt_2 (9.8 mL, 78 mmol, 2 equiv) was added via syringe pump over 2 h. After 2 h, the reaction was quenched with MeOH (7 mL), and the mixture was poured onto a mixture of saturated aqueous $NaHCO_3$ (300 mL) and ice (100 mL), and the resulting mixture was allowed to warm to room temperature. The aqueous layer was separated and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (10-25% EtOAc/Hex) to afford alcohol **5** (4.1 g, 43% yield) as a colorless oil. TLC R_f = 0.26 (25% EtOAc/Hex); $[\alpha]^{23}_D$ +17.4 (*c* 0.95, $CHCl_3$); IR (neat) 3418, 2919, 2859, 1496, 1454, 1364, 1204, 1098, 998, 739, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 5H, Bn), 4.52 (s, 2H, C<u>H</u>$_2$Ph), 3.54 – 3.45 (m, 1H, $C_{13}H$),

3.53 (t, J = 5.9 Hz, 2H, $C_{16}H_2$), 2.57 – 2.48 (m, 1H, $C_{12}H$), 2.45 (d, J = 4.8 Hz, 1H, OH), 1.86 – 1.70 (m, 3H, $C_{14}H_a$, $C_{15}H_2$), 1.80 (d, J = 2.4 Hz, 3H, $C_{10}CH_3$), 1.58 – 1.48 (m, 1H, $C_{14}H_b$), 1.14 (d, J = 5.8 Hz, 3H, $C_{12}CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 128.3, 127.6, 127.6, 80.9, 77.7, 74.3, 72.9, 70.4, 33.0, 30.9, 26.3, 16.5, 3.5; LRMS (FAB+) calcd for $C_{16}H_{23}O_2$ $[M+H]^+$: 247.17; found 247.41.

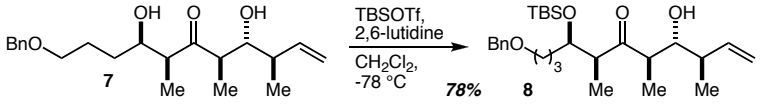


To a solution of alcohol **5** (6.0 g, 24.4 mmol, 1 equiv) in HPLC-grade hexanes (81 mL, 0.3 M) was added di-*cis*-crotylsilane (6.4 mL, 36.6 mmol, 1.5 equiv), and sodium hydride (29 mg, 1.2 mmol, 0.05 equiv). The mixture was heated to reflux (oil bath). After 2 h, the reaction mixture was cooled to room temperature and filtered through a pad of oven-dried silica gel with hexane washes. The filtrate was concentrated to afford silane **6** (9.1 g, 97% yield). The silane was used immediately in the next step without further purification. TLC R_f = 0.55 (14% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 5H, Bn), 5.48 – 5.39 (m, 4H, C<u>H</u>=C<u>H</u>CH_3), 4.51 (s, 2H, C<u>H</u>$_2$Ph), 4.50 – 4.47 (m, 1H, SiH), 3.61 (td, J = 7.0, 3.5 Hz, 1H, $C_{13}H$), 3.53 – 3.45 (m, 2H, $C_{16}H_2$), 2.47 (qdq, J = 7.0, 3.5, 2.4 Hz, 1H, $C_{12}H$), 1.78 (d, J = 2.4 Hz, 3H, $C_{10}CH_3$), 1.74 – 1.61 (m, 8H, $SiCH_2$, $C_{14}H_2$, $C_{15}H_2$), 1.60 – 1.57 (m, 6H, CH=CHC<u>H</u>$_3$), 1.12 (d, J = 7.0 Hz, 3H, $C_{12}CH_3$).



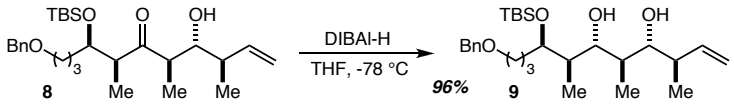
To a glass liner equipped with a stir bar was added silane **6** (3.5 g, 9.1 mmol, 1 equiv) and benzene (46 mL, 0.2 mmol). The glass liner was immersed in a -78 °C bath, and $Rh(acac)(CO)_2$ (24 mg, 0.01 equiv) was added on top of the frozen benzene solution. The glass liner was placed into a Parr bomb, and the pressure gauge/gas inlet apparatus was assembled. The bomb was charged to 600 psi with CO and vented. This procedure was repeated twice, and the bomb was then pressurized to 1000 psi with CO and heated to 60 °C (oil bath, external temperature). After 4.5 h, the bomb was allowed to cool to room temperature and then vented.

The mixture was concentrated and the residue was dissolved in 1:1 MeOH/THF (80 mL). KF (1.1 g, 18 mmol, 2 equiv) was added, followed by 30% aqueous H_2O_2 (12 mL), and the mixture was heated to 40 °C (oil bath, external temperature). After 1 h, the reaction mixture was cooled to room temperature and quenched by the addition of saturated aqueous NaCl (40 mL). The aqueous layer was separated and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (10-33% EtOAc/Hex) to afford ketodiol **7** (2.1 g, 67% yield) as a colorless oil. Analysis by ^{1}H NMR spectroscopy revealed that the product was formed with ≥15:1 overall diastereoselectivity. TLC R_f = 0.20 (33% EtOAc/Hex); $[\alpha]^{23}_D$ -3.7 (*c* 0.99, $CHCl_3$); IR (neat) 3425, 3068, 2965, 2935, 2874, 1702, 1455, 1373, 1102, 994, 915, 738 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 5H, Bn), 5.84 (ddd, *J* = 17.3, 10.3, 8.6 Hz, 1H, C_7H), 5.14 – 5.04 (m, 2H, C_6H_2), 4.51 (s, 2H, C$\underline{H_2}$Ph), 4.02 (app. dq, *J* = 9.9, 3.4 Hz, 1H, $C_{13}H$), 3.69 (ddd, *J* = 8.3, 5.2, 3.1 Hz, C_9H), 3.52 (td, *J* = 6.3, 1.6 Hz, 2H, $C_{16}H_2$), 3.18 (d, *J* = 3.4 Hz, 1H, $C_{13}OH$), 2.93 (dq, *J* = 9.0, 7.0 Hz, 1H, $C_{12}H$), 2.76 (qd, *J* = 7.0, 3.1 Hz, 1H, $C_{10}H$), 2.40 – 2.31 (m, 1H, C_8H), 2.31 (d, *J* = 5.2 Hz, 1H, C_9OH), 1.83 – 1.73 (m, 1H, $C_{14}H_a$), 1.73 – 1.63 (m, 1H, $C_{14}H_b$), 1.59 – 1.53 (m, 2H, $C_{15}H_2$), 1.08 (app. t, *J* = 6.9 Hz, 6H), 1.01 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 219.0 (C_{11}), 138.3, 138.2, 128.3, 127.6, 127.6, 116.0, 77.3, 72.9, 70.8, 70.3, 51.4, 48.4, 40.1, 30.8, 26.6, 17.6, 13.7, 9.1; LRMS (FAB+) calcd for $C_{21}H_{33}O_4$ $[M+H]^+$: 349.24; found 349.33 (FAB+).

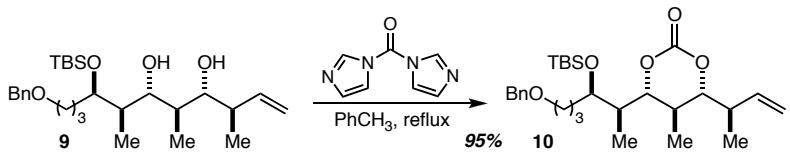


To a cooled (-78 °C) solution of ketodiol **7** (4.35 g, 12.5 mmol, 1 equiv) in CH_2Cl_2 (83 mL, 0.15 M) was added 2,6-lutidine (4.3 mL, 37.5 mmol, 3 equiv) followed by dropwise addition of TBSOTf (3.6 mL, 15.6 mmol, 1.25 equiv). After 1 h, the reaction was quenched with triethylamine (5 mL), and the mixture was poured onto saturated aqueous $NaHCO_3$ (100 mL) and ice (100 mL), and the mixture was allowed to warm to room temperature. The aqueous layer was separated and extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (5-33% EtOAc/Hex) to afford **8** (4.49 g, 78% yield, 86% brsm) as a colorless oil. TLC R_f = 0.67 (33% EtOAc/Hex); $[\alpha]^{23}_D$ -0.4 (*c* 1.06, $CHCl_3$); IR (neat) 3480, 2931, 2858, 1702, 1456, 1363, 1255, 1101, 996, 836, 775 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.24 (m, 5H, Bn), 5.85

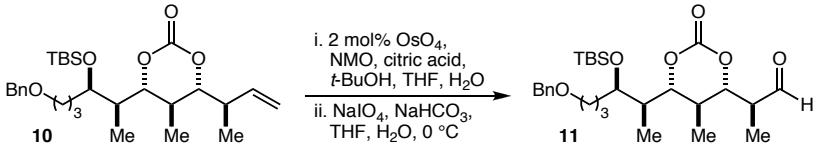
(ddd, J = 16.8, 10.6, 8.7 Hz, 1H, C_7H), 5.08 – 4.99 (m, 2H, C_6H_2), 4.47 (s, 2H, $C\underline{H}_2Ph$), 3.90 (app. dd, J = 10.7, 4.9 Hz, 1H, $C_{13}H$), 3.57 (ddd, J = 8.7, 5.8, 3.1 Hz, 1H, C_9H), 3.47 (app. dt, J = 9.1, 5.8 Hz, 1H, $C_{16}H_a$), 3.39 (ddd, J = 9.0, 7.2, 5.7 Hz, 1H, $C_{16}H_b$), 3.00 – 2.83 (m, 2H, $C_{10}H$, $C_{12}H$), 2.75 (d, J = 5.8 Hz, 1H, OH), 2.36 – 2.26 (m, 1H, C_8H), 1.75 – 1.64 (m, 1H, $C_{14}H_a$), 1.63 – 1.49 (m, 3H, $C_{14}H_b$, $C_{15}H_2$), 1.07 (d, J = 7.1 Hz, 3H), 1.01 (app. d, J = 7.0 Hz, 6H), 0.89 (s, J = 6.5 Hz, 9H, TBS), 0.07 (s, 3H, TBS), 0.06 (s, 3H, TBS); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.5 (C_{11}), 138.9, 138.4, 128.3, 127.6, 127.5, 115.4, 76.6, 73.4, 73.0, 70.4, 50.9, 49.9, 40.1, 30.9, 25.9, 25.1, 18.1, 17.8, 13.6, 13.5, -4.4, -4.5; LRMS (FAB+) calcd for $C_{27}H_{47}O_4Si$ $[M+H]^+$: 463.3; found 463.6.



To a cooled (-78 °C) solution of **8** (563 mg, 1.22 mmol, 1 equiv) in THF (12 mL, 0.1 M) was added DIBAl-H (3.0 mL, 3.0 mmol, 1.0 M in hexanes, 2.5 equiv) dropwise. After 2 h, the reaction was quenched by the addition of saturated aqueous NH_4Cl (750 μL) and the mixture was allowed to warm to room temperature. After 1 h, $MgSO_4$ (3 g) was added and stirring was continued for an additional 1 h. The suspension was then filtered through a pad of Celite with Et_2O washes and the filtrate was concentrated. The residue was purified by silica gel flash column chromatography (5-15% EtOAc/Hex) to afford diol **9** (540 mg, 96% yield) as a colorless oil. TLC R_f = 0.3 (14% EtOAc/Hex); $[\alpha]^{23}_D$ -18.4 (*c* 1.04, $CHCl_3$); IR (neat) 3412, 2932, 2859, 1639, 1456, 1363, 1256, 1098, 1002, 911, 839, 778, 736, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H, Bn), 5.96 (ddd, J = 16.9, 11.0, 8.8 Hz, 1H, C_7H), 5.09 – 4.99 (m, 2H, C_6H_2), 4.92 (s, 1H, OH), 4.50 (s, 2H, $C\underline{H}_2Ph$), 4.48 (s, 1H, OH), 4.05 (app. t, J = 6.2 Hz, 1H, $C_{13}H$), 3.59 (dd, J = 12.9, 6.3 Hz, 1H), 3.52 (app. d, J = 8.8 Hz, 1H), 3.45 (t, J = 6.2 Hz, 2H, $C_{16}H_2$), 2.48 – 2.36 (m, 1H, C_8H), 2.04 – 1.94 (m, 1H), 1.82 – 1.69 (m, 1H), 1.69 – 1.58 (m, 2H, $C_{14}H_2$), 1.58 – 1.47 (m, 2H, $C_{15}H_2$), 1.14 (d, J = 6.9 Hz, 3H), 1.00 (d, J = 7.0 Hz, 3H), 0.89 (s, 9H, TBS), 0.76 (d, J = 6.8 Hz, 3H), 0.14 (s, 3H, TBS), 0.11 (s, 3H, TBS); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.0, 138.4, 128.4, 127.6, 127.6, 114.7, 82.3, 79.6, 74.7, 73.0, 70.0, 41.0, 38.8, 36.6, 30.4, 26.2, 25.9, 18.3, 17.9, 13.8, 11.4, -3.7, -4.2; LRMS (FAB+) calcd for $C_{27}H_{49}O_4Si$ $[M+H]^+$: 465.3; found 465.6.

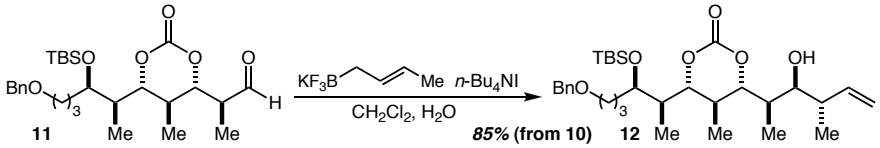


To a solution of diol **9** (2.03 g, 4.38 mmol, 1 equiv) in toluene (22 mL, 0.2 M) was added carbonyl diimidazole (780 mg, 4.81 mmol, 1.1 equiv) and the mixture was then heated to reflux. After 18 h, the mixture was concentrated. The residue was purified by silica gel flash column chromatography (10% EtOAc/Hex) to afford carbonate **10** (2.04 g, 95% yield) as a white solid. $[\alpha]^{23}_{D}$ -17.3 (*c* 1.03, $CHCl_3$); IR (neat) 2932, 2857, 1760, 1460, 1387, 1362, 1253, 1208, 1119, 1076, 1004, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 5H, Bn), 5.77 (ddd, *J* = 17.2, 10.3, 9.1 Hz, 1H, C_7H), 5.14 (dd, *J* = 10.3, 1.6 Hz, 1H, C_6H_a), 5.10 (dd, *J* = 17.2, 1.6 Hz, 1H, C_6H_b), 4.50 (s, 2H, $C\underline{H}_2Ph$), 4.09 – 4.01 (m, 1H, $C_{13}H$), 3.98 (dd, *J* = 8.4, 7.6 Hz, 1H, $C_{11}H$), 3.86 (dd, *J* = 10.4, 2.1 Hz, 1H, C_9H), 3.48 – 3.39 (m, 2H, $C_{16}H_2$), 2.50 (dqd, *J* = 9.1, 7.0, 2.1 Hz, 1H, C_8H), 2.14 – 1.98 (m, 1H, $C_{10}H$), 1.77 (app. pd, *J* = 7.0, 2.2 Hz, 1H, $C_{12}H$), 1.63 – 1.45 (m, 4H, $C_{14}H_2$, $C_{15}H_2$), 1.21 (d, *J* = 7.0 Hz, 3H, $C_{10}CH_3$), 0.98 (d, *J* = 6.5 Hz, 3H, C_8CH_3), 0.95 (d, *J* = 7.0 Hz, 3H, $C_{12}CH_3$), 0.88 (s, 9H, TBS), 0.07 (s, *J* = 3.1 Hz, 6H, TBS); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 138.5, 136.7, 128.3, 127.5, 127.4, 117.4, 85.7, 85.3, 72.8, 70.6, 70.1, 42.0, 39.1, 33.1, 31.4, 26.0, 25.9, 18.0, 17.6, 14.6, 10.0, -4.2, -4.6; LRMS (FAB+) calcd for $C_{28}H_{47}O_5Si$ $[M+H]^+$: 491.3; found 491.4.

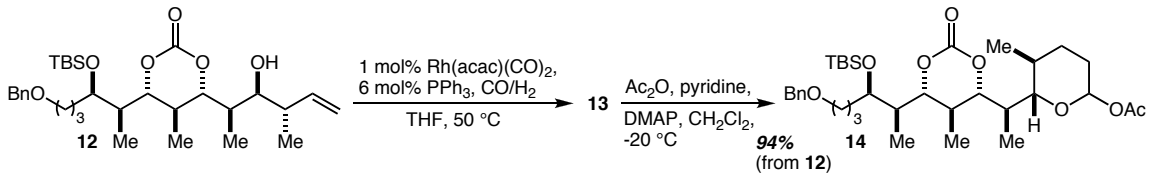


To a solution of **10** (136 mg, 0.28 mmol, 1 equiv) in 3:1:1 *t*-BuOH/THF/H_2O (4 mL) was added N-methylmorpholine N-oxide (130 μL, 0.56 mmol, 50% wt in H_2O, 2 equiv), citric acid (56 mg, 0.29 mmol, 1.05 equiv), and OsO_4 (111 ΀L, 0.0056 mmol, 0.05 M in *t*-BuOH, 0.02 equiv). After 24 h, the reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$ (8 mL) and stirred for 30 min. The aqueous layer was separated and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. To a cooled (0 °C) solution of the residue in 10:1 THF/0.1 M $NaHCO_3$ (2.2 mL) was added a solution of $NaIO_4$ (237 mg, 1.11 mmol, 4 equiv) in H_2O (2.2 mL) dropwise. After 1 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ (8 mL). The aqueous layer was separated and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated to afford aldehyde

11 as a colorless oil. The aldehyde was used immediately in the next step without further purification. TLC R_f = 0.29 (33% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.70 (d, *J* = 2.1 Hz, 1H, C_7H), 7.36 – 7.26 (m, 5H, Bn), 4.49 (s, 1H, C<u>H</u>$_2$Ph), 4.20 (dd, *J* = 10.4, 2.5 Hz, 1H), 4.06 (td, *J* = 5, 2.2 Hz, 1H), 4.02 (app. t, *J* = 8.0 Hz, 1H), 3.45 (t, *J* = 5.4 Hz, 2H, $C_{16}H_2$), 2.72 (app. qt, *J* = 7.2, 2.3 Hz, 1H, C_8H), 2.26 (ddq, *J* = 13.2, 10.4, 6.6 Hz, 1H), 1.81 (app. pd, *J* = 7.0, 2.2 Hz, 1H), 1.62 – 1.48 (m, 2H, $C_{14}H_2$, $C_{15}H_2$), 1.36 (d, *J* = 7.2 Hz, 3H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.88 (s, 9H, TBS), 0.08 (s, 3H, TBS), 0.07 (s, 3H, TBS); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.5 (C_7), 149.9, 138.6, 128.3, 127.6, 127.4, 86.0, 82.8, 72.8, 70.6, 70.1, 46.9, 42.2, 33.2, 31.4, 26.0, 25.9, 18.1, 15.1, 10.8, 9.9, -4.1, -4.6.

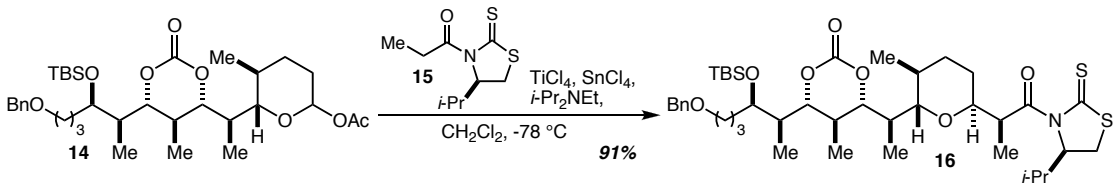


To a solution of aldehyde **11** in 1:1 CH_2Cl_2:H_2O (4 mL) was added Bu_4NI (10 mg, 0.028 mmol, 0.1 equiv) and potassium *trans*-crotyltrifluoroborate (67 mg, 0.40 mmol, 1.44 equiv). After 3h, the reaction was quenched with H_2O (5 mL). The aqueous layer was separated and extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (16-25% EtOAc/Hex) to afford alcohol **12** (129 mg, 85% yield from **10**) as a colorless oil. TLC R_f = 0.45 (33% EtOAc/Hex); $[\alpha]^{23}_D$ -7.7 (*c* 0.94, $CHCl_3$); IR (neat) 3485, 2955, 2931, 2857, 1765, 1462, 1388, 1253, 1210, 1102, 1005, 837, 776 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 5H, Bn), 5.76 (ddd, *J* = 17.0, 10.4, 8.4 Hz, 1H, C_5H), 5.17 – 5.10 (m, 2H, C_4H_2), 4.50 (s, 2H, C<u>H</u>$_2$Ph), 4.09 – 4.04 (td, *J* = 5.8, 2.1 Hz, 2H), 4.04 (app. t, *J* = 6.8 Hz, 1H), 3.96 (dd, *J* = 8.6, 6.3 Hz, 1H), 3.66 (dt, *J* = 9.0, 1.9 Hz, 1H), 3.48 – 3.41 (m, 2H, $C_{16}H_2$), 2.33 – 2.20 (m, 2H, C_6H, $C_{10}H$), 2.01 (app. pd, *J* = 7.0, 1.4 Hz, 1H), 1.90 (d, *J* = 2.5 Hz, 1H, OH), (dqd, *J* = 8.6, 6.8, 1.9 Hz, 1H), 1.62 – 1.49 (m, 4H, $C_{14}H_2$, $C_{15}H_2$), 1.12 (d, *J* = 6.8 Hz, 3H), 1.03 (d, *J* = 7.0 Hz, 3H), 0.95 (app. d, *J* = 7.0 Hz, 6H), 0.89 (s, 9H, TBS), 0.09 (s, 3H, TBS), 0.08 (s, 3H, TBS); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.6, 141.2, 138.5, 128.3, 127.5, 127.4, 116.2, 86.2, 85.4, 72.8, 71.8, 70.3, 70.1, 42.2, 41.4, 36.8, 32.1, 31.5, 26.0, 25.9, 18.1, 17.9, 16.2, 9.5, 9.4, -4.2, -4.7; LRMS (FAB+) calcd for $C_{31}H_{53}O_6Si$ $[M+H]^+$: 549.4; found 549.7.

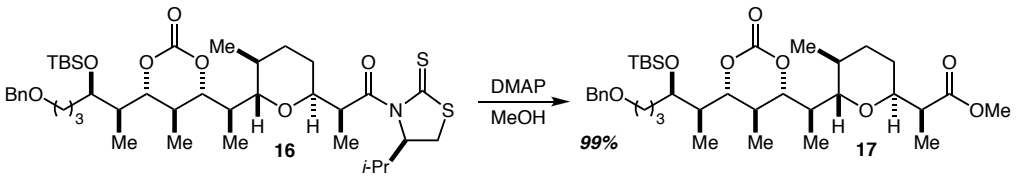


To a glass liner equipped with a stir bar was added $Rh(acac)(CO)_2$ (0.6 mg, 0.01 equiv), PPh_3 (3 mg, 0.06 equiv), and THF (1 mL). The glass liner was placed into a Parr bomb, and the pressure gauge/gas inlet apparatus was assembled. The bomb was charged to 500 psi with 1/1 H_2/CO and vented. This procedure was repeated twice, and the bomb was then pressurized to 500 psi with 1/1 H_2/CO and heated to 75 °C (oil bath, external temperature). After 3 h, the bomb was allowed to cool to room temperature and then vented. To the residue was added a solution of alcohol **12** (92 mg, 0.17 mmol) in THF (1 mL), $Rh(acac)(CO)_2$ (0.6 mg, 0.01 equiv), and PPh_3 (3 mg, 0.06 equiv). The bomb was charged to 500 psi with 1/1 H_2/CO and vented. This procedure was repeated twice, and the bomb was then pressurized to 500 psi with 1/1 H_2/CO and heated to 50 °C (oil bath, external temperature). After 4 h the oil bath was removed and the bomb was allowed to stand at room temperature for 20 h. The bomb was vented and the residue was concentrated. Purification by silica gel flash column chromatography (10-33% EtOAc/Hex) afforded hemiacetal **13** as a colorless oil.

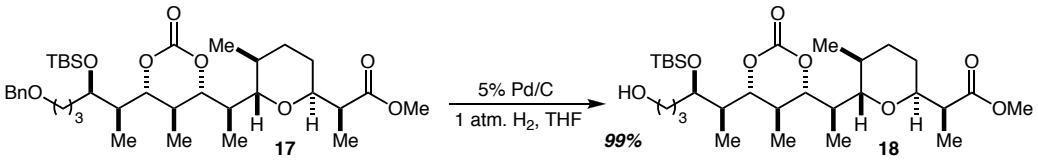
To a cooled (-20 °C) solution of hemiacetal **13** in CH_2Cl_2 (2 mL) was added pyridine (40 μL), acetic anhydride (60 μL), and DMAP (2 mg). After 16 h, the reaction mixture was diluted with Et_2O. The combined organic layers were washed with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated to afford acetate **14** (98 mg, 94% yield over 2 steps) as a colorless oil. The acetal was used immediately in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 5H, Bn), 5.60 (dd, J = 9.9, 2.0 Hz, 1H, C_3H), 4.50 (s, 2H, $C\underline{H}_2Ph$), 4.12 – 4.05 (m, 1H, $C_{13}H$), 4.03 (app. t, J = 7.0 Hz, 1H, C_9H), 3.89 (dd, J = 8.5, 6.0 Hz, 1H, $C_{11}H$), 3.51 – 3.40 (m, 3H, C_7H, $C_{16}H_2$), 2.30 – 2.20 (m, 1H, $C_{10}H$), 2.07 (s, 3H, AcO), 2.04 – 1.97 (m, 1H, C_8H), 1.89 – 1.76 (m, 3H, $C_{12}H$, $C_{16}H_2$), 1.62 – 1.49 (m, 7H, C_4H_a, C_5H_a, C_6H, $C_{14}H_2$, $C_{15}H_2$), 1.38 – 1.23 (m, 2H, C_4H_b, C_5H_b), 1.11 (d, J = 6.8 Hz, 3H, $C_{10}CH_3$), 1.01 (d, J = 7.1 Hz, 3H, C_8CH_3), 0.95 (d, J = 6.8 Hz, 3H, $C_{12}CH_3$), 0.88 (s, 9H, TBS), 0.79 (d, J = 6.6 Hz, 3H, C_6CH_3), 0.08 (s, 3H, TBS), 0.08 (s, 3H, TBS); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 150.9, 138.6, 128.3, 127.6, 127.5, 94.9, 84.9, 84.8, 80.0, 72.8, 70.2, 70.0, 41.0, 37.5, 31.7, 31.7, 31.1, 30.6, 30.3, 26.0, 25.9, 21.2, 18.6, 18.1, 16.5, 9.4, 9.1, -4.1, -4.7.



To a cooled (0 °C) solution of **15** (103 mg, 0.48 mmol, 3 equiv) in CH_2Cl_2 (3 mL) was added titanium tetrachloride (480 µL, 0.48 mmol, 1 M in CH_2Cl_2, 3 equiv) dropwise. After 5 min, the reaction mixture was cooled to -40 °C and diisopropylethylamine (480 µL, 0.48 mmol, 1 M in CH_2Cl_2, 3 equiv) was added resulting in a deep red color. After 3 h, a solution of acetate **14** (98 mg, 0.16 mmol, 1 equiv) in CH_2Cl_2 (2 mL) was added, followed by tin tetrachloride (160 µL, 0.16 mmol, 1 M in CH_2Cl_2, 1 equiv). The reaction mixture was then allowed to warm to -15 °C. After 2 h, the reaction mixture was cooled to -78 °C, and then quenched with saturated aqueous NH_4Cl (8 mL), and the mixture was allowed to warm to room temperature. The aqueous layer was separated and extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (10-20% EtOAc/Hex) to afford **16** (112 mg, 91% yield) as a yellow oil. TLC R_f = 0.33 (20% EtOAc/Hex); $[\alpha]^{23}_D$ -123.5 (*c* 1.06, $CHCl_3$); IR (neat) 2949, 2854, 1766, 1694, 1463, 1373, 1308, 1242, 1201, 1153, 1022, 832 cm^{-1}; ^1H NMR (500 MHz, CDCl3) δ 7.36 – 7.26 (m, 5H, Bn), 5.20 – 5.12 (m, 2H, C<u>H</u>N, C_2H), 4.49 (s, 2H, C<u>H</u>$_2$Ph), 4.15 (dt, *J* = 9.4, 4.8 Hz, 1H, C_3H), 4.05 (m, 1H, $C_{13}H$), 3.95 (dd, *J* = 6.9, 6.1 Hz, 1H, C_9H), 3.84 (dd, *J* = 8.6, 6.0 Hz, 1H, $C_{11}H$), 3.56 (dd, *J* = 7.1, 4.7 Hz, 1H, C_7H), 3.48 – 3.40 (m, 3H, SC<u>H</u>$_{2a}$, $C_{16}H_2$), 2.97 (dd, *J* = 11.4, 0.7 Hz, 1H, SC<u>H</u>$_{2b}$), 2.34 (m, 1H, C<u>H</u>$(CH_3)_2$), 2.26 – 2.18 (m, 1H, $C_{10}H$), 2.18 – 2.08 (m, 1H, C_8H), 1.83 – 1.74 (m, 1H, $C_{12}H$), 1.71 – 1.61 (m, 3H, C_4H_a, C_5H_a, C_6H), 1.60 – 1.48 (m, 4H, $C_{14}H_2$, $C_{15}H_2$), 1.36 – 1.22 (m, 2H, C_4H_b, C_5H_b), 1.06 (app. dd, *J* = 6.8, 1.7 Hz, 9H, CH(C<u>H</u>$_{3a}$)$_2$, C_2CH_3, $C_{10}CH_3$) 0.98 (d, *J* = 7.0 Hz, 3H, CH(C<u>H</u>$_{3b}$)$_2$), 0.96 (d, *J* = 7.0 Hz, 3H, C_8CH_3), 0.92 (d, *J* = 6.9 Hz, 3H, $C_{12}CH_3$), 0.90 (d, *J* = 6.4 Hz, 3H, C_6CH_3), 0.87 (s, 9H, TBS), 0.07 (s, 3H, TBS), 0.07 (s, 3H, TBS); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.2, 176.1, 150.5, 138.6, 128.3, 127.6, 127.5, 85.0, 84.6, 76.0, 72.8, 72.7, 72.1, 70.2, 70.0, 41.1, 39.9, 37.9, 31.7, 31.5, 31.1, 30.0, 29.2, 26.4, 26.0, 25.9, 24.4, 19.3, 18.6, 18.1, 17.9, 17.4, 14.8, 10.4, 9.3, -4.2, -4.6; LRMS (FAB+) calcd for $C_{41}H_{66}NO_7S_2Si$ $[M–H]^+$: 776.41; found 776.89.

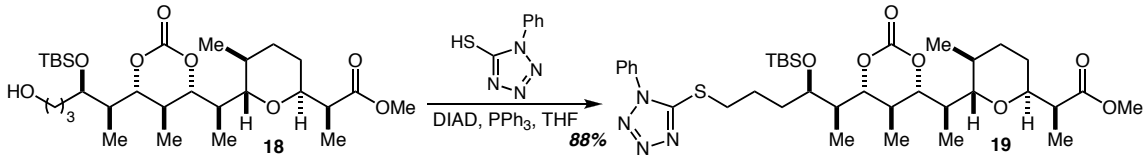


To a solution of **16** (230 mg, 0.30 mmol, 1 equiv) in MeOH (1.2 mL, 0.25 M) was added DMAP (36 mg, 0.30 mmol, 1 equiv). After 24 h, the mixture was concentrated. The residue was dissolved in pentane and washed with 1 M NaOH. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (16% EtOAc/Hex) to afford methyl ester **17** (190 mg, 99% yield) as a colorless oil. TLC R_f = 0.56 (33% EtOAc/Hex); $[\alpha]^{23}_D$ +18.5 (*c* 0.94, $CHCl_3$); IR (thin film) 2942, 2851, 1751, 1455, 1384, 1256, 1204, 1095, 909, 831, 735 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.23 (m, 5H, Bn), 4.48 (s, 2H, $C\underline{H}_2Ph$), 4.10 (app. t, *J* = 5.4 Hz, 1H, $C_{13}H$), 4.00 – 3.93 (m, 1H, C_3H), 3.89 (app. t, *J* = 6.7 Hz, 1H, C_9H), 3.87 (app. t, *J* = 6.0 Hz, 1H, $C_{11}H$), 3.66 (s, 3H, MeO), 3.60 (dd, *J* = 9.2, 1.8 Hz, 1H, C_7H), 3.47 – 3.39 (m, 2H, $C_{16}H_2$), 3.08 (dq, *J* = 10.9, 6.9 Hz, 1H, C_2H), 2.27 – 2.19 (m, 1H, $C_{10}H$), 2.02 – 1.93 (m, 1H, C_8H), 1.84 (app. p, *J* = 7.1 Hz, 1H, $C_{12}H$), 1.73 – 1.63 (m, 2H, C_4H_2), 1.62 – 1.48 (m, 6H, C_5H_a, C_6H, $C_{14}H_2$, $C_{15}H_2$), 1.31 – 1.21 (m, 1H, C_5H_b), 1.09 (d, *J* = 6.8 Hz, 3H, $C_{10}CH_3$), 1.04 (d, *J* = 6.9 Hz, 3H, C_2CH_3), 0.92 (app. d, *J* = 6.9 Hz, 6H, C_8CH_3, $C_{12}CH_3$), 0.87 (s, 9H, TBS), 0.81 (d, *J* = 6.4 Hz, 3H, C_6CH_3), 0.08 (s, 3H, TBS), 0.07 (s, 3H, TBS); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.0, 150.9, 138.6, 128.3, 127.5, 127.4, 85.1, 84.2, 74.4, 73.9, 72.8, 70.1, 69.7, 51.5, 41.2, 39.7, 37.8, 31.6, 31.5, 31.0, 26.9, 25.9, 25.9, 24.8, 19.1, 18.1, 17.7, 14.5, 9.3, 8.9, -4.2, -4.8; LRMS (FAB+) calcd for $C_{36}H_{61}O_8Si$ $[M+H]^+$: 649.4; found 649.5.

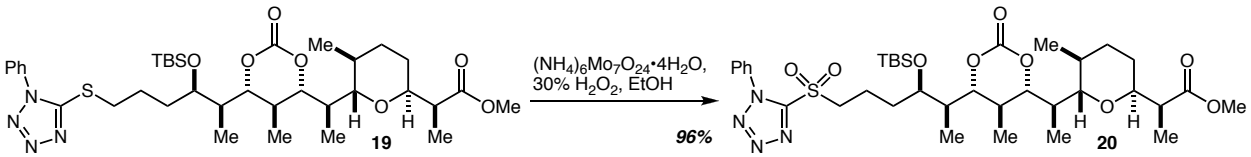


To a solution of benzyl ether **17** (204 mg, 0.31 mmol, 1 equiv) in THF (1.5 mL, 0.2 M) was added 5% Pd/C (100 mg, 50% wt.). A balloon of H_2 was attached to the flask by way of a needle through the septum. After 2 h, the reaction mixture was filtered over oven-dried Celite with Et_2O washes and the filtrate was concentrated. The residue was purified by silica gel flash column chromatography (6-50% EtOAc/Hex) to afford alcohol **18** (173 mg, 99% yield) as a colorless oil. TLC R_f = 0.1 (33% EtOAc/Hex); $[\alpha]^{23}_D$ +30.4 (*c* 0.97, $CHCl_3$); IR (neat) 3476,

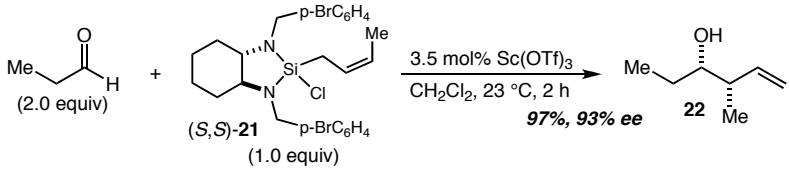
2942, 2858, 1739, 1459, 1381, 1251, 1206, 1069, 835 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.11 (td, *J* = 6.6, 1.9 Hz, 1H, $C_{13}H$), 3.98 (ddd, *J* = 10.8, 4.9, 2.9 Hz, 1H, C_3H), 3.92 – 3.85 (m, 2H, C_9H, $C_{11}H$), 3.67 (s, 3H, MeO), 3.66 – 3.58 (m, 3H, C_7H, $C_{16}H_2$), 3.08 (dq, *J* = 10.8, 6.9 Hz, 1H, C_2H), 2.29 – 2.21 (m, 1H, $C_{10}H$), 1.99 (app. pd, *J* = 7.1, 2.2 Hz, 1H, C_8H), 1.90 – 1.82 (m, 1H, $C_{12}H$), 1.74 – 1.46 (m, 8H, C_4H_2, C_5H_a, C_6H, $C_{14}H_2$, $C_{15}H_2$), 1.32 – 1.22 (m, 1H, C_5H_b), 1.10 (d, *J* = 6.8 Hz, 3H, $C_{10}CH_3$), 1.05 (d, *J* = 6.9 Hz, 3H, C_2CH_3), 0.95 (d, *J* = 7.1 Hz, 3H, C_8CH_3), 0.94 (d, *J* = 6.9 Hz, 3H, $C_{12}CH_3$), 0.88 (s, 9H, TBS), 0.83 (d, *J* = 6.4 Hz, 3H, C_6CH_3), 0.09 (s, 6H, TBS); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.0, 151.0, 85.2, 84.3, 74.4, 74.0, 69.9, 62.7, 51.6, 41.3, 39.8, 37.7, 31.5, 31.3, 31.0, 28.9, 26.9, 25.9, 24.8, 18.9, 18.1, 17.7, 14.5, 9.3, 9.1, -4.2, -4.8; Exact mass (FAB+) calcd for $C_{29}H_{55}O_8Si$ $[M+H]^+$: 559.3666; found 559.3662.



To a solution of alcohol **18** (125 mg, 0.22 mmol, 1 equiv) in THF (2.2 mL, 0.1 M) was added triphenylphosphine (65 mg, 0.25 mmol, 1.1 equiv), 1-phenyl-1*H*-tetrazole-5-thiol (44 mg, 0.25 mmol, 1.1 equiv), and diisopropyl azodicarboxylate (50 μL, 0.25 mmol, 1.1 equiv) dropwise. After 24 h, the reaction mixture was concentrated. The residue was purified by silica gel flash column chromatography (10-33% EtOAc/Hex) to afford sulfide **19** (142 mg, 88% yield) as a colorless oil. TLC R_f = 0.37 (33% EtOAc/Hex); $[\alpha]^{23}_D$ +24.9 (*c* 1.05, $CHCl_3$); IR (neat) 2949, 2854, 1748, 1492, 1457, 1385, 1248, 1213, 1165, 1082, 1017, 909, 832 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.60 – 7.49 (m, 5H, Ph), 4.10 (app. t, *J* = 6.7 Hz, 1H, $C_{13}H$), 4.00 – 3.93 (m, 1H, C_3H), 3.87 (dd, *J* = 6.6, 5.1 Hz, 1H, C_9H), 3.85 (dd, *J* = 8.1, 4.4 Hz, 1H, $C_{11}H$), 3.64 (s, 3H, MeO), 3.59 (dd, *J* = 9.2, 1.6 Hz, 1H, C_7H), 3.37 (t, *J* = 7.2 Hz, 2H, $C_{16}H_2$), 3.07 (dq, *J* = 11.0, 6.9 Hz, 1H, C_2H), 2.28 – 2.18 (m, 1H, $C_{10}H$), 2.02 – 1.92 (app. pd, *J* = 7.1, 1.7 Hz, 1H, C_8H), 1.85 – 1.73 (m, 3H, $C_{12}H$, $C_{15}H_2$), 1.68 – 1.54 (m, 6H, C_4H_2, C_5H_a, C_6H, $C_{14}H_2$), 1.33 – 1.22 (m, 1H, C_5H_b), 1.08 (d, *J* = 6.7 Hz, 3H, $C_{10}CH_3$), 1.04 (d, *J* = 6.9 Hz, 3H, C_2CH_3), 0.93 (d, *J* = 7.0 Hz, 3H, C_8CH_3), 0.92 (d, *J* = 6.8 Hz, 3H, $C_{12}CH_3$), 0.86 (s, 9H, TBS), 0.79 (d, *J* = 6.4 Hz, 3H, C_6CH_3), 0.07 (s, 3H, TBS), 0.05 (s, 3H, TBS); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.9, 154.1, 150.9, 133.6, 130.0, 129.7, 123.8, 85.0, 84.3, 74.4, 73.9, 69.5, 51.5, 41.5, 39.7, 37.7, 34.0, 33.2, 31.7, 31.0, 26.9, 25.8, 25.5, 24.7, 18.9, 18.0, 17.7, 14.5, 9.3, 9.1, -4.2, -4.7; LRMS (FAB+) calcd for $C_{36}H_{59}N_4O_7SSi$ $[M+H]^+$: 719.4; found 719.4.

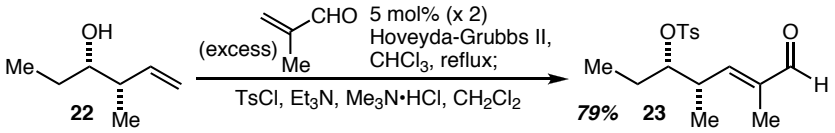


To a solution of sulfide **19** (27 mg, 0.038 mmol, 1 equiv) in EtOH (380 μL, 0.1 M) was added a solution of $(NH_4)_6Mo_7O_{24}•4H_2O$ (9 mg, 0.0071 mmol, 0.19 equiv) in 30% aqueous H_2O_2 (81 μL, 0.71 mmol, 19 equiv). After 12 h, the reaction mixture was diluted with H_2O (5 mL). The aqueous layer was separated and extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (10-33% EtOAc/Hex) to afford sulfone **20** (27 mg, 96% yield) as a white solid. TLC R_f = 0.37 (33% EtOAc/Hex); $[\alpha]^{23}_D$ +21.6 (*c* 0.63, $CHCl_3$); IR (neat) 2955, 2855, 1742, 1462, 1345, 1258, 1211, 1147, 1077, 1019, 832 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 – 7.66 (m, 2H, Ph), 7.65 – 7.54 (m, 3H, Ph), 4.10 (td, *J* = 6.6, 1.4 Hz, 1H, $C_{13}H$), 4.00 – 3.94 (m, 1H, C_3H), 3.88 (app. t, *J* = 7.1 Hz, 1H, C_9H), 3.85 (dd, *J* = 8.9, 6.1 Hz, 1H, $C_{11}H$), 3.79 – 3.68 (m, 2H, $C_{16}H_2$), 3.64 (s, 3H, MeO), 3.59 (dd, *J* = 9.3, 1.7 Hz, 1H, C_7H), 3.07 (dq, *J* = 10.8, 6.9 Hz, 1H, C_2H), 2.30 – 2.21 (m, 1H, $C_{10}H$), 2.02 – 1.93 (m, 2H, C_8H, $C_{15}H_a$), 1.93 – 1.80 (m, 2H, $C_{12}H$, $C_{15}H_b$), 1.73 – 1.64 (m, 4H, C_4H_2, $C_{14}H_2$), 1.64 – 1.52 (m, 2H, C_5H_a, C_6H), 1.30 – 1.21 (m, 1H, C_5H_b), 1.07 (d, *J* = 6.7 Hz, 3H, $C_{10}CH_3$), 1.04 (d, *J* = 6.9 Hz, 3H, C_2CH_3), 0.95 (d, *J* = 6.8 Hz, 3H, $C_{12}CH_3$), 0.94 (d, *J* = 7.0 Hz, 3H, C_8CH_3), 0.87 (s, 9H, TBS), 0.80 (d, *J* = 6.4 Hz, 3H, C_6CH_3), 0.08 (s, 3H, TBS), 0.07 (s, 3H, TBS); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.9, 153.4, 150.9, 133.0, 131.4, 129.7, 125.1, 85.0, 84.4, 74.4, 73.9, 69.6, 55.9, 51.6, 41.7, 39.8, 37.6, 33.6, 31.9, 31.1, 26.9, 25.8, 24.8, 18.8, 18.6, 18.1, 17.7, 14.5, 9.5, 9.4, -4.2, -4.6; LRMS (FAB+) calcd for $C_{36}H_{59}N_4O_9SSi$ $[M+H]^+$: 751.4; found 751.4.



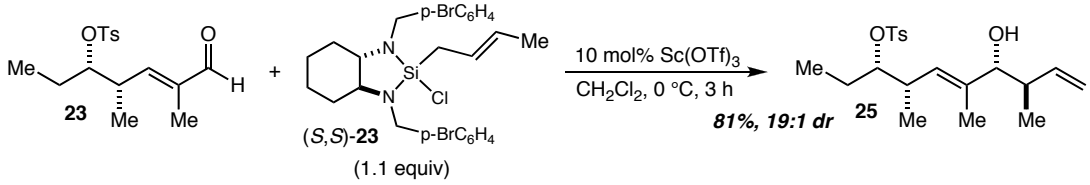
To a cooled (0 °C) solution of (*S*,*S*)-**21** (2.8 g, 5.0 mmol, 1 equiv) and scandium triflate (86 mg, 0.175 mmol, 0.035 equiv) in CH_2Cl_2 (50 mL, 0.1 M) was added propanal (720 μL, 10 mmol, 2 equiv). The mixture was stirred vigorously for 2 h, and then was concentrated. To the cooled (0 °C) residue was added Et_2O (25 mL) and 1N HCl (25 mL). The mixture was warmed to room temperature and stirred for 1 h during which time a precipitate forms. The mixture was

filtered to collect the diamine as its bis HCl salt as a white powder (2.5 g, 96% yield). The filtrate was then carefully neutralized with $NaHCO_3$ and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (20-40% EtOAc/Hex) to afford known alcohol **22** (550 mg, 97% yield, 93% ee) as a colorless oil. The enantiomeric excess was determined by HPLC analysis of the derived 3,5-dinitrobenzoate ester: ADH column, 1.5% EtOH/Hex, 1 mL/min, T_r (major) = 28.5 min, T_r (minor) = 38.5 min. TLC R_f = 0.5 (20% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 (ddd, *J* = 16.8, 11.0, 7.4 Hz, 1H, $C_{21}H$), 5.09 (ddd, *J* = 16.8, 1.8, 1.3 Hz, 1H, $C_{20}H_a$), 5.08 (ddd, *J* = 11.0, 1.8, 1.1 Hz, 1H, $C_{20}H_b$), 3.42 (td, *J* = 9.0, 5.0 Hz, 1H, $C_{23}H$), 2.34 – 2.24 (m, 1H, $C_{22}H$), 1.61 – 1.50 (m, 1H, $C_{24}H_a$), 1.46 – 1.32 (m, 2H, $C_{24}H_b$, OH), 1.02 (d, *J* = 6.9 Hz, 3H, $C_{22}CH_3$), 0.97 (t, *J* = 7.4 Hz, 3H, $C_{25}H_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 115.2, 76.2, 43.0, 26.8, 13.9, 10.4.

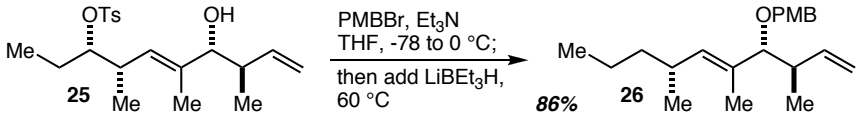


To a solution of alkene **22** (21 mg, 0.18 mmol, 1 equiv) and methacrolein (1.8 mL) in $CHCl_3$ (3.7 mL) was added the Hoveyda-Grubbs 2nd gen. catalyst (6 mg, 0.009 mmol, 0.05 equiv). The mixture was heated to reflux and after 10h, a second batch of the Hoveyda-Grubbs 2nd gen. catalyst (6 mg) was added. After 14h, the mixture was concentrated and the residue dissolved in CH_2Cl_2 (3.7 mL). To this solution was added Et_3N (64 μL, 0.46 mmol, 2.5 equiv), Me_3N-HCl (35 mg, 0.37 mmol, 2 equiv), and then TsCl (88 mg, 0.46 mmol, 2.5 equiv). This was repeated at t = 12h and t = 24h. After an additional 12h, H_2O was added to the reaction mixture. The aqueous layer was separated and extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (5-20% EtOAc/Hex) affording aldehyde **23** (45 mg, 79% yield). TLC R_f = 0.20 (20% EtOAc/Hex); $[\alpha]^{23}_D$ -3.8 (*c* 0.3, $CHCl_3$); IR (thin film) 2975, 2937, 2881, 1686, 1642, 1598, 1459, 1359, 1175, 1099, 913, 854, 816, 741, 666 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (s, 1H, $C_{19}H$), 7.76 (d, *J* = 8.3 Hz, 2H, Ts), 7.31 (d, *J* = 8.1 Hz, 2H, Ts), 6.12 (dd, *J* = 9.9, 1.3 Hz, 1H, $C_{21}H$), 4.49 (dt, *J* = 6.7, 5.3 Hz, 1H, $C_{23}H$), 3.08 – 2.96 (ddq, *J* = 9.9, 6.9, 6.7 Hz, 1H, $C_{22}H$), 2.42 (s, 3H, Ts), 1.75 – 1.60 (m, 2H, $C_{24}H_2$), 1.67 (d, *J* = 1.3 Hz, 3H, $C_{20}CH_3$), 1.04 (d, *J* = 6.9 Hz, 3H, $C_{22}CH_3$), 0.83 (t, *J* = 7.4 Hz, 3H, $C_{25}H_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9 (C_{19}),

153.0, 144.9, 139.6, 134.2, 129.8, 127.7, 86.8, 36.3, 24.8, 21.6, 14.9, 9.4, 9.4; Exact mass (EI+) calcd for $C_{16}H_{23}O_4S$ [M]: 310.1239; found 310.1242.

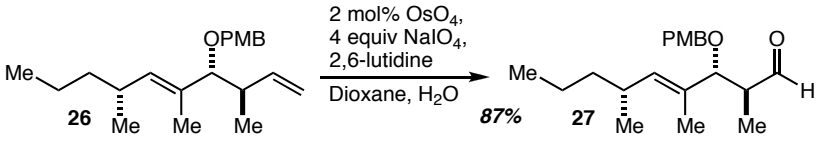


To a cooled (0 °C) solution of aldehyde **23** (900 mg, 2.90 mmol, 1 equiv) in CH_2Cl_2 (29 mL, 0.1 M) was added (*S*,*S*)-**24** (4.76 mL, 3.19 mmol, 0.67 M in CH_2Cl_2, 1.1 equiv) and scandium triflate (143 mg, 0.29 mmol, 0.10 equiv). The mixture was stirred vigorously for 3 h, and the reaction was then quenched by the addition of *n*-Bu_4NF (12 mL, 1 M in THF, 4 equiv). The mixture was allowed to warm to room temperature, and, after 15 min, was concentrated. The residue was purified by silica gel flash column chromatography (2-50% EtOAc/Hex) to afford alcohol **25** (857 mg, 81% yield, 19:1 dr) as a colorless oil and recovered diamine (1.39 g, 96% yield). TLC R_f = 0.17 (20% EtOAc/Hex); $[\alpha]^{23}_D$ +5.5 (*c* 0.13, $CHCl_3$); IR (thin film) 3445, 2967, 2929, 1738, 1455, 1361, 1247, 1176, 1188, 1099, 1020, 913, 671, 665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H, Ts), 7.32 (d, *J* = 8.0 Hz, 2H, Ts), 5.70 (ddd, *J* = 17.2, 10.3, 8.4 Hz, 1H, $C_{17}H$), 5.19 – 5.11 (m, 3H, $C_{16}H_2$, $C_{21}H$), 4.42 (td, *J* = 6.6, 4.2 Hz, 1H, $C_{23}H$), 3.58 (dd, *J* = 8.6, 2.1 Hz, 1H, $C_{19}H$), 2.82 (app. dp, *J* = 9.9, 6.8 Hz, 1H, $C_{22}H$), 2.44 (s, 3H, Ts), 2.34 – 2.23 (m, 1H, $C_{18}H$), 1.75 (d, *J* = 2.4 Hz, 1H, OH), 1.71 – 1.62 (m, 1H, $C_{24}H_a$), 1.60 (d, *J* = 1.3 Hz, 3H, $C_{20}CH_3$), 1.58 – 1.47 (m, 1H, $C_{24}H_b$), 0.93 (d, *J* = 6.8 Hz, 3H, $C_{22}CH_3$), 0.86 (d, *J* = 6.8 Hz, 3H, $C_{18}CH_3$), 0.79 (t, *J* = 7.4 Hz, 3H, $C_{25}H_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 141.0, 136.6, 134.8, 129.6, 128.9, 127.7, 116.6, 88.7, 81.2, 42.3, 35.4, 24.4, 21.6, 16.9, 16.7, 11.4, 9.1; LRMS (FAB+) calcd for $C_{20}H_{30}NaO_4S$ $[M+Na]^+$: 389.18; found 389.06.



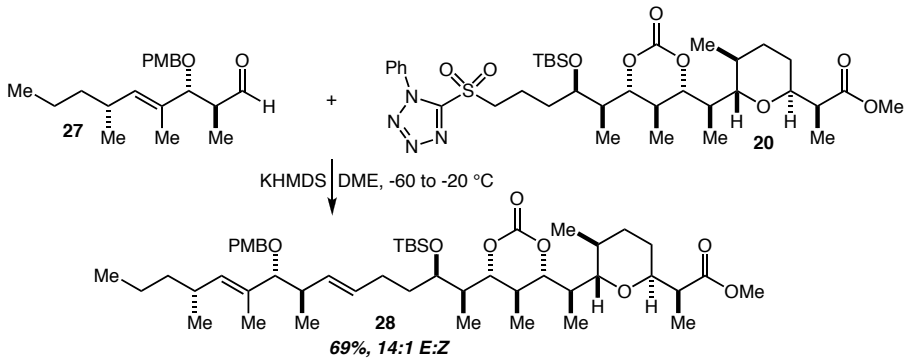
To a solution of **25** (338 mg, 0.92 mmol, 1 equiv) in THF (9.2 mL, 0.1 M) was added triethylamine (390 µL, 2.8 mmol, 3 equiv) and *para*-methoxybenzyl bromide (270 µL, 1.8 mmol, 2 equiv). The reaction mixture was cooled to -78 °C and KHMDS (1.2 mL, 1.2 mmol, 1 M in THF, 1.25 equiv) was added dropwise. After 15 min, the mixture was warmed to 0 °C, and held at that temperature for 75 min. $LiEt_3BH$ (5.5 mL, 5.5 mmol, 1M in THF, 6 equiv) was added and the mixture was heated to 60 °C. After 2 h, the mixture was cooled to 0 °C and quenched with

saturated aqueous NH_4Cl. The aqueous layer was separated and extracted with 20% EtOAc/Hex. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (1-5% EtOAc/Hex) to afford **26** (252 mg, 86% yield) as a colorless oil. TLC R_f = 0.5 (5% EtOAc/Hex); $[\alpha]_{23}^{D}$ +19.0 (c 0.60, $CHCl_3$); IR (thin film) 2958, 2927, 2869, 1613, 1513, 1455, 1301, 1248, 1172, 1070, 1038, 1010, 820 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.6 Hz, 2H, PMB), 6.86 (d, *J* = 8.7 Hz, 2H, PMB), 5.89 (ddd, *J* = 17.4, 10.4, 7.1 Hz, 1H, $C_{17}H$), 5.10 – 4.96 (m, 3H, $C_{16}H_2$, $C_{21}H$), 4.42 (d, *J* = 11.8 Hz, 1H, PMB), 4.14 (d, *J* = 11.8 Hz, PMB), 3.80 (s, 3H, PMB), 3.27 (d, *J* = 9.3 Hz, 1H, $C_{19}H$), 2.53 – 2.43 (m, 1H, $C_{22}H$), 2.43 – 2.32 (m, 1H, $C_{18}H$), 1.58 (d, *J* = 1.3 Hz, 3H, $C_{20}CH_3$), 1.33 – 1.17 (m, 4H, $C_{23}H_2$, $C_{24}H_2$), 1.00 (d, *J* = 6.7 Hz, 3H, $C_{22}CH_3$), 0.87 (t, *J* = 6.8 Hz, 3H, $C_{25}H_3$), 0.82 (d, *J* = 6.9 Hz, 3H, $C_{18}CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 142.6, 137.8, 131.1, 129.4, 113.6, 113.5, 88.9, 69.0, 55.3, 39.8, 39.7, 32.0, 21.5, 20.7, 16.7, 14.2, 10.9; Exact mass (EI+) calcd for $C_{21}H_{32}O_2$ [M]: 316.2402; found 316.2406.



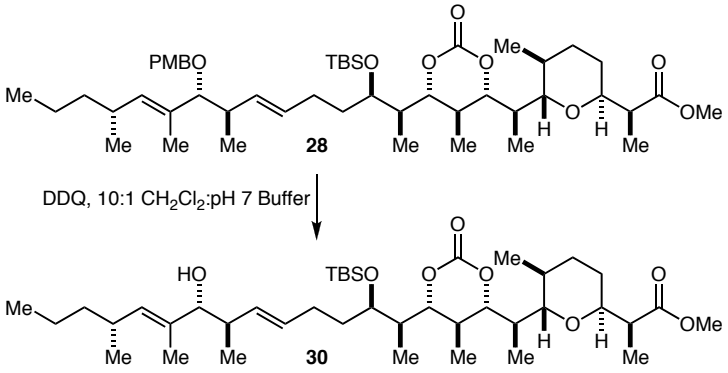
To a solution of **26** (140 mg, 0.44 mmol, 1 equiv) in 3:1 dioxane-H_2O (4.4 mL, 0.1 M) was added 2,6-lutidine (100 µL, 0.88 mmol, 2 equiv), OsO_4 (120 µL, 0.0088 mmol, 2.5% in *t*-BuOH, 0.02 equiv), and $NaIO_4$ (380 mg, 1.8 mmol, 4 equiv). After 4 h, the mixture was partitioned between H_2O and CH_2Cl_2. The aqueous layer was separated and extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (2-6% EtOAc/Hex) to afford **27** (120 mg, 87%) as a colorless oil. TLC R_f = 0.43 (10% EtOAc/Hex); $[\alpha]^{23}_{D}$ +27.3 (*c* 1.00, $CHCl_3$); IR (thin film) 2957, 2926, 2869, 1731, 1611, 1516, 1510, 1459, 1377, 1301, 1251, 1175, 1061, 1036, 814 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (d, *J* = 3.0 Hz, 1H, $C_{17}H$), 7.18 (d, *J* = 8.6 Hz, 2H, PMB), 6.86 (d, *J* = 8.6 Hz, 2H, PMB), 5.18 (d, *J* = 9.6 Hz, 1H, $C_{21}H$), 4.42 (d, *J* = 11.6 Hz, 1H, PMB), 4.15 (d, *J* = 11.6 Hz, 1H, PMB), 3.80 (s, 3H, PMB), 3.71 (d, *J* = 10.1 Hz, 1H, $C_{19}H$), 2.61 (dqd, *J* = 10.1, 7.1, 3.0 Hz, 1H, $C_{18}H$), 2.54 – 2.43 (m, 1H, $C_{22}H$), 1.60 (d, *J* = 1.2 Hz, 3H, $C_{20}CH_3$), 1.33 – 1.17 (m, 4H, $C_{23}H_2$, $C_{24}H_2$), 1.02 (d, *J* = 6.7 Hz, 3H, $C_{22}CH_3$), 0.87 (t, *J* = 6.5 Hz, 3H, $C_{25}H_3$), 0.84 (d, *J* = 7.1 Hz, 3H, $C_{18}CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ

205.1 (C_{17}), 159.2, 139.4, 130.2, 129.5, 129.3, 113.8, 85.5, 69.0, 55.3, 48.2, 39.6, 32.1, 21.3, 20.7, 14.2, 10.9, 10.5; Exact mass (EI+) calcd for $C_{20}H_{30}O_3$ [M]: 318.2195; found 310.2180.

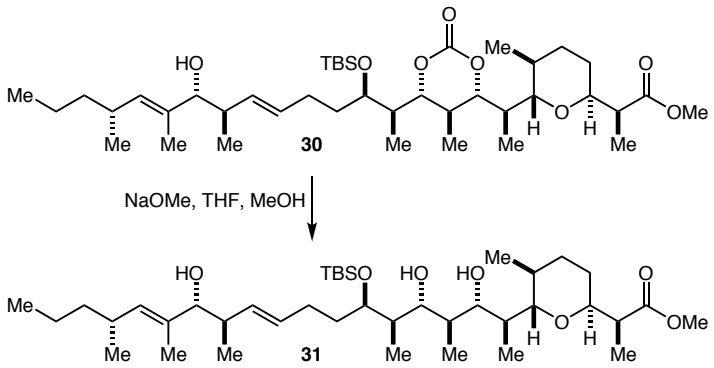


To a cooled (-60 °C) solution of sulfone **20** (140 mg, 0.19 mmol, 1 equiv) in DME (1.9 mL) was added KHMDS (205 μL, 1 M in THF, 1.1 equiv), followed immediately by a solution of aldehyde **27** (59 mg, 0.19 mmol, 1 equiv) in DME (1.9 mL). After 90 min, at which point the temperature had naturally increased to -20 °C, the reaction was quenched with saturated aqueous NH_4Cl. The aqueous layer was separated and extracted with 20% EtOAc/Hex. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (5-50% EtOAc/Hex) to afford **28** (100 mg, 14:1 *E*:*Z*, 69% yield, 82% brsm) as a colorless oil. TLC R_f = 0.5 (20% EtOAc/Hex); $[\alpha]^{23}_D$ +14.8 (*c* 1.20, $CHCl_3$); IR (thin film) 2954, 2929, 2858, 1766, 1739, 1513, 1461, 1249, 1211, 1171, 1074, 1038, 836, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.6 Hz, 2H, PMB), 6.85 (d, *J* = 8.7 Hz, 2H, PMB), 5.46 – 5.33 (m, 2H, $C_{16}H$, $C_{17}H$), 5.04 (dd, *J* = 9.6, 1.2 Hz, 1H, $C_{21}H$), 4.41 (d, *J* = 11.9 Hz, 1H, PMB), 4.13 (d, *J* = 11.9 Hz, 1H, PMB), 4.08 (td, *J* = 6.9, 1.4 Hz, 1H, $C_{13}H$), 4.01 – 3.94 (m, 1H, C_3H), 3.92 – 3.85 (m, 2H, C_9H, $C_{11}H$), 3.80 (s, 3H, PMB), 3.67 (s, 3H, MeO), 3.61 (dd, *J* = 9.3, 2.0 Hz, 1H, C_7H), 3.21 (d, *J* = 9.1 Hz, 1H, $C_{19}H$), 3.09 (dq, *J* = 10.8, 6.9 Hz, 1H, C_2H), 2.50 – 2.41 (m, 1H, $C_{22}H$), 2.35 – 2.27 (m, 1H, $C_{18}H$), 2.28 – 2.19 (m, 1H, $C_{10}H$), 2.03 – 1.90 (m, 3H, $C_{15}H_2$, C_8H), 1.89 – 1.80 (m, 1H, $C_{12}H$), 1.71 – 1.52 (m, 6H, C_4H_2, C_5H_a, C_6H, $C_{14}H_2$), 1.56 (d, *J* = 1.2 Hz, 3H, $C_{20}CH_3$), 1.31 – 1.20 (m, 5H, C_5H_b, $C_{23}H_2$, $C_{24}H_2$), 1.10 (d, *J* = 6.8 Hz, 3H, $C_{10}CH_3$), 1.05 (d, *J* = 6.9 Hz, 3H, C_2CH_3), 0.99 (d, *J* = 6.6 Hz, 3H, $C_{22}CH_3$), 0.93 (app. d, *J* = 7.1 Hz, 6H, C_8CH_3, $C_{12}CH_3$), 0.89 – 0.86 (m, 12H, TBS, $C_{25}H_3$), 0.81 (d, *J* = 6.4 Hz, 3H, C_6CH_3), 0.78 (d, *J* = 6.9 Hz, 3H, $C_{18}CH_3$), 0.09 (s, 3H, TBS), 0.08 (s, 3H, TBS); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1, 158.9, 150.9, 137.5, 134.4, 131.3, 131.2, 129.3, 128.6, 113.6, 89.1, 85.2, 84.2, 74.5, 74.0, 69.8, 69.0, 55.2, 51.6, 41.3, 39.8, 39.7, 38.8, 37.9, 35.2, 31.9, 31.5, 31.1,

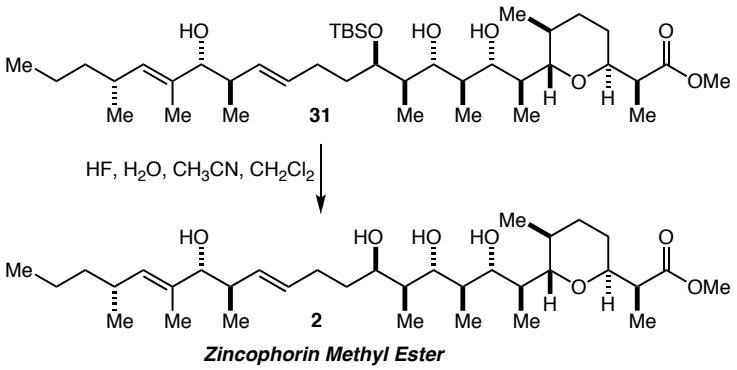
29.0, 27.0, 26.0, 24.9, 21.4, 20.7, 19.2, 18.1, 17.7, 17.3, 14.6, 14.2, 11.0, 9.3, 8.9, -4.0, -4.7; Exact mass (FAB+) calcd for $C_{49}H_{82}KO_9Si$ $[M+K]^+$: 881.5365; found 881.5323.



To a solution of PMB ether **28** (85 mg, 0.1 mmol, 1 equiv) in 10:1 CH_2Cl_2-pH 7 buffer (5 mL, 0.02 M) was added DDQ (92 mg, 0.4 mmol, 4 equiv) in four portions, separated by 15 min. After 2 h, the aqueous layer was separated and extracted with 20% EtOAc/Hex. The combined organic layers were washed with saturated aqueous $NaHCO_3$, saturated aqueous NaCl, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (2.5-20% EtOAc/Hex) to afford **30** (50 mg, 69% yield) as a colorless oil. TLC R_f = 0.4 (20% EtOAc/Hex); $[\alpha]^{23}_D$ +21.9 (*c* 1.00, $CHCl_3$); IR (thin film) 3509, 2955, 2928, 2857, 1740, 1460, 1379, 1258, 1212, 1171, 1085, 1021, 973, 837, 802, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.54 (dt, *J* = 15.3, 6.6 Hz, 1H, $C_{16}H$), 5.32 (dd, *J* = 15.3, 8.5 Hz, 1H, $C_{17}H$), 5.12 (dd, *J* = 9.4 Hz, 1.2 Hz, 1H, $C_{21}H$), 4.10 (app. t, *J* = 7.0 Hz, 1H, $C_{13}H$), 4.01 – 3.94 (m, 1H, C_3H), 3.92 – 3.82 (m, 2H, C_9H, $C_{11}H$), 3.67 (s, 3H, MeO), 3.61 (dd, *J* = 9.2, 2.1 Hz, 1H, C_7H), 3.54 (app. d, *J* = 9.0 Hz, 1H, $C_{19}H$), 3.09 (dq, *J* = 10.6, 6.9 Hz, 1H, C_2H), 2.45 – 2.36 (m, 1H, $C_{22}H$), 2.28 – 2.19 (m, 2H, $C_{10}H$, $C_{18}H$), 2.04 – 1.90 (m, 3H, $C_{15}H_2$, C_8H), 1.88 – 1.77 (m, 1H, $C_{12}H$), 1.72 – 1.51 (m, 6H, C_4H_2, C_5H_a, C_6H, $C_{14}H_2$), 1.59 (d, *J* = 1.2 Hz, 6H, $C_{20}CH_3$), 1.34 – 1.16 (m, 5H, C_5H_b, $C_{23}H_2$, $C_{24}H_2$), 1.09 (d, *J* = 6.8 Hz, 3H, $C_{10}CH_3$), 1.05 (d, *J* = 6.9 Hz, 3H, C_2CH_3), 0.94 (app. d, *J* = 6.8 Hz, 6H, C_8CH_3, $C_{22}CH_3$), 0.93 (d, *J* = 6.7 Hz, 3H, $C_{12}CH_3$), 0.89 – 0.86 (m, 12H, TBS, $C_{25}H_3$), 0.84 (app. t, *J* = 6.5 Hz, C_6CH_3, $C_{18}CH_3$), 0.08 (app. d, *J* = 2.0 Hz, 6H, TBS); ^{13}C NMR (100 MHz, CDCl3) δ 176.1, 151.0, 135.9, 133.5, 133.2, 131.8, 85.1, 84.3, 81.9, 74.4, 74.0, 69.5, 51.6, 41.4, 41.1, 39.9, 39.7, 37.8, 34.9, 31.8, 31.5, 31.1, 28.9, 27.0, 25.9, 24.8, 21.0, 20.7, 19.2, 18.1, 17.8, 17.3, 14.6, 14.2, 10.8, 9.3, 9.0, -4.0, -4.7; Exact mass (FAB+) calcd for $C_{41}H_{73}O_8Si$ $[M–H]^+$: 721.5075; found 721.5033.



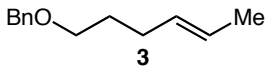
To a cooled (0 °C) solution of carbonate **30** (37 mg, 0.05 mmol) in 4:1 THF/MeOH (5 mL, 0.01 M) was added sodium methoxide (500 μL, 25% wt. MeOH). The mixture was allowed to warm to room temperature, and after 4 h, was recooled to 0 °C and quenched with saturated aqueous NH_4Cl. The aqueous layer was separated and extracted with 20% EtOAc/Hex. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (2-20% EtOAc/Hex) to afford **31** (32 mg, 90% yield). TLC R_f = 0.5 (20% EtOAc/Hex); $[\alpha]^{23}_D$ +23.1 (*c* 1.00, $CHCl_3$); IR (thin film) 3485, 2955, 2929, 2858, 1738, 1721, 1461, 1381, 1278, 1256, 1115, 1084, 1042, 1017, 970, 836, 774 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.57 (dt, *J* = 14.9, 6.6 Hz, 1H, $C_{16}H$), 5.33 (dd, *J* = 14.9, 8.0 Hz, 1H, $C_{17}H$), 5.13 (dd, *J* = 9.4, 1.2 Hz, 1H, $C_{21}H$), 4.18 (br s, 1H, OH), 4.05 – 3.99 (m, 1H, C_3H), 3.97 (app. t, *J* = 7.2 Hz, 1H, $C_{13}H$), 3.78 – 3.68 (m, 5H), 3.64 (d, *J* = 7.4 Hz, 1H, OH), 3.54 (app. d, *J* = 9.0 Hz, 1H, $C_{19}H$), 3.45 (dd, *J* = 12.6, 6.6 Hz, 1H), 3.09 (dq, *J* = 10.8, 6.9 Hz, 1H, C_2H), 2.48 – 2.35 (m, 1H, $C_{22}H$), 2.29 – 2.19 (m, 1H, $C_{18}H$), 2.19 – 2.06 (m, 1H, $C_{15}H_a$), 2.04 – 1.88 (m, 4H, C_8H, $C_{10}H$, $C_{12}H$, $C_{15}H_b$), 1.74 – 1.53 (m, 6H, C_4H_2, C_5H_a, C_6H, $C_{14}H_2$), 1.60 (d, *J* = 1.2 Hz, 3H, $C_{20}CH_3$), 1.35 – 1.15 (m, 5H, C_5H_b, $C_{23}H_2$, $C_{24}H_2$), 1.06 (d, *J* = 7.0 Hz, 3H, C_2CH_3), 0.98 – 0.93 (m, 9H), 0.92 – 0.88 (m, 12H), 0.88 – 0.83 (app. t, *J* = 7.1 H, $C_{18}CH_3$, $C_{25}H_3$), 0.81 (d, *J* = 6.4 Hz, 3H, C_6CH_3), 0.11 (s, 3H, TBS), 0.08 (s, 3H, TBS); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 135.9, 133.2, 133.1, 132.5, 81.9, 77.7, 77.2, 76.8, 75.6, 75.0, 74.7, 52.0, 41.2, 40.1, 39.9, 39.1, 36.0, 33.1, 31.8, 31.5, 29.5, 27.0, 25.9, 25.1, 21.0, 20.6, 18.1, 17.9, 17.3, 15.9, 14.4, 14.2, 12.3, 11.0, 10.9, -4.3, -4.3; Exact mass (FAB+) calcd for $C_{40}H_{77}O_7Si$ $[M+H]^+$: 697.5439; found 697.5413.



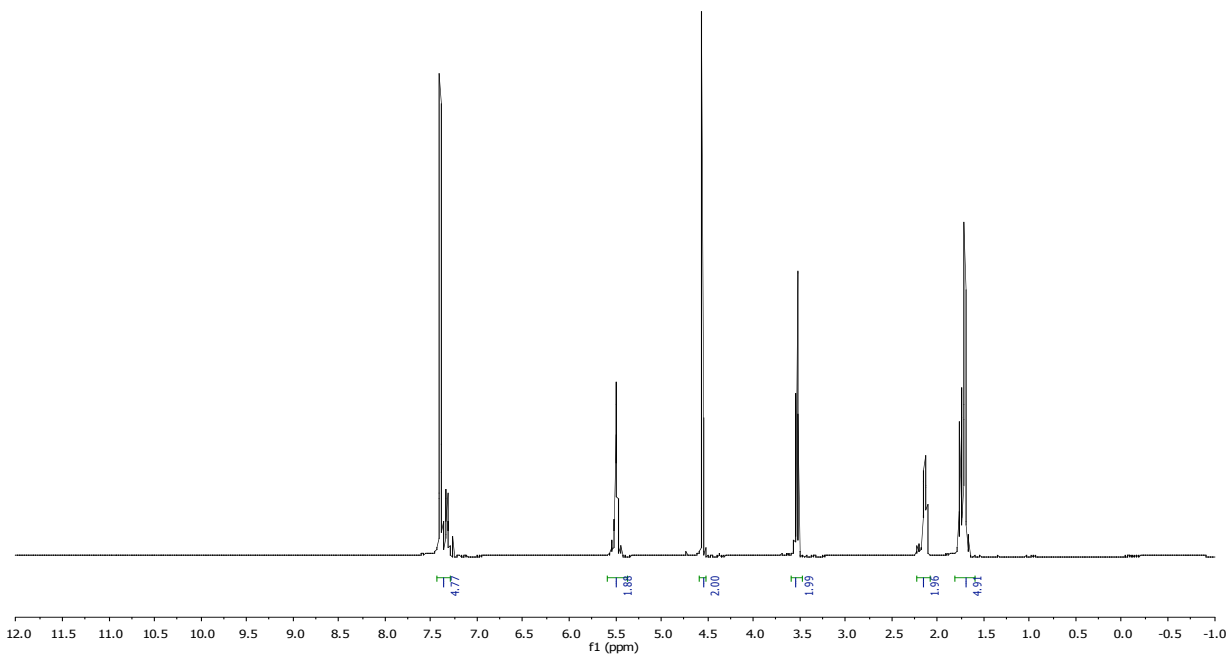
Zincophorin Methyl Ester

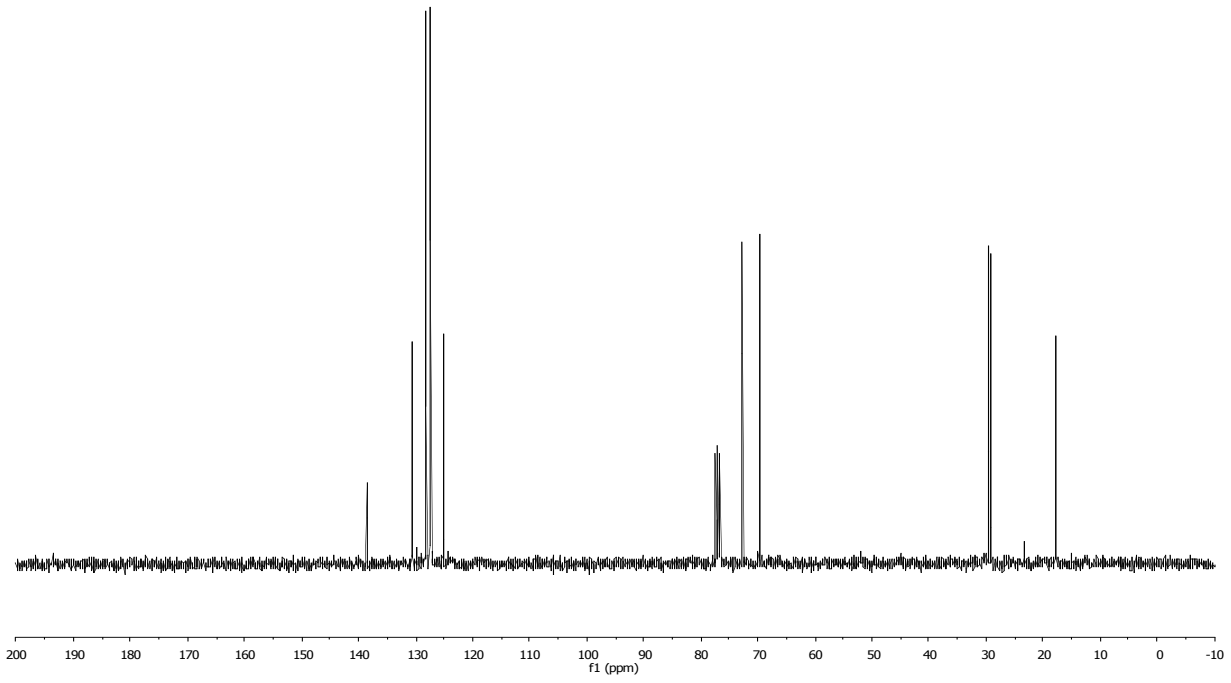
To a cooled (0 °C) solution of TBS ether **31** (10 mg, 0.01 mmol) in 1:1 acetonitrile:CH_2Cl_2 (2 mL) was added 500 μL of a freshly prepared HF solution (stock solution prepared from 500 μL 48% aqueous HF, 8.6 mL acetonitrile, and 900 μL H_2O). The mixture was allowed to warm to room temperature, and after 2 h was recooled to 0 °C and quenched with saturated aqueous $NaHCO_3$. The aqueous layer was separated and extracted with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel flash column chromatography (10-40% EtOAc/Hex) affording Zincophorin Methyl Ester **2** (8 mg, 96% yield). TLC R_f = 0.55 (40% EtOAc/Hex); $[\alpha]^{23}_D$ +24.6 (*c* 0.5, $CHCl_3$); IR (thin film) 3400, 3054, 2927, 2854, 1733, 1460, 1374, 1265, 1046, 896, 740, 705 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.91 (s, 1H), 5.63 (dt, *J* = 15.0, 6.7 Hz, 1H, $C_{16}H$), 5.34 (dd, *J* = 15.3, 9.0 Hz, 1H, $C_{17}H$), 5.11 (d, *J* = 9.5 Hz, 1H, $C_{21}H$), 4.42 (d, *J* = 8.1 Hz, 1H), 4.12 – 4.08 (m, 3H), 3.76 (d, *J* = 10.2 Hz, 1H), 3.72 (s, 3H, MeO), 3.63 (d, *J* = 8.7 Hz, 1H), 3.56 (d, *J* = 9.2 Hz, 1H), 3.43 (td, *J* = 8.8, 2.7 Hz, 1H), 3.22 (dq, *J* = 10.9, 7.0 Hz, 1H, C_2H), 2.46 – 2.37 (m, 1H), 2.29 – 2.18 (m, 3H), 2.11 (s, 1H), 2.03 – 1.94 (m, 2H), 1.77 – 1.62 (m, 4H), 1.60 (s, 3H, $C_{20}CH_3$), 1.46 – 1.15 (m, 6H), 1.10 (d, *J* = 7.7 Hz, 3H), 1.08 (d, *J* = 7.2 Hz, 3H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.90 – 0.86 (m, 5H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.2 Hz, 3H), 0.66 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 135.7, 133.4, 133.3, 133.2, 84.4, 84.0, 81.9, 76.1, 74.6, 69.0, 52.4, 41.8, 39.9, 39.7, 38.4, 37.4, 34.5, 34.0, 31.8, 31.6, 29.8, 26.3, 25.0, 21.0, 20.6, 17.7, 17.5, 14.8, 14.2, 13.3, 11.3, 11.2, 10.8; Exact mass (FAB+) calcd for $C_{34}H_{63}O_7$ $[M+H]^+$: 583.4574; found 583.4589.

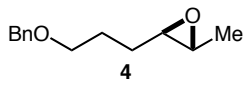
^{1}H and ^{13}C NMR Spectra:



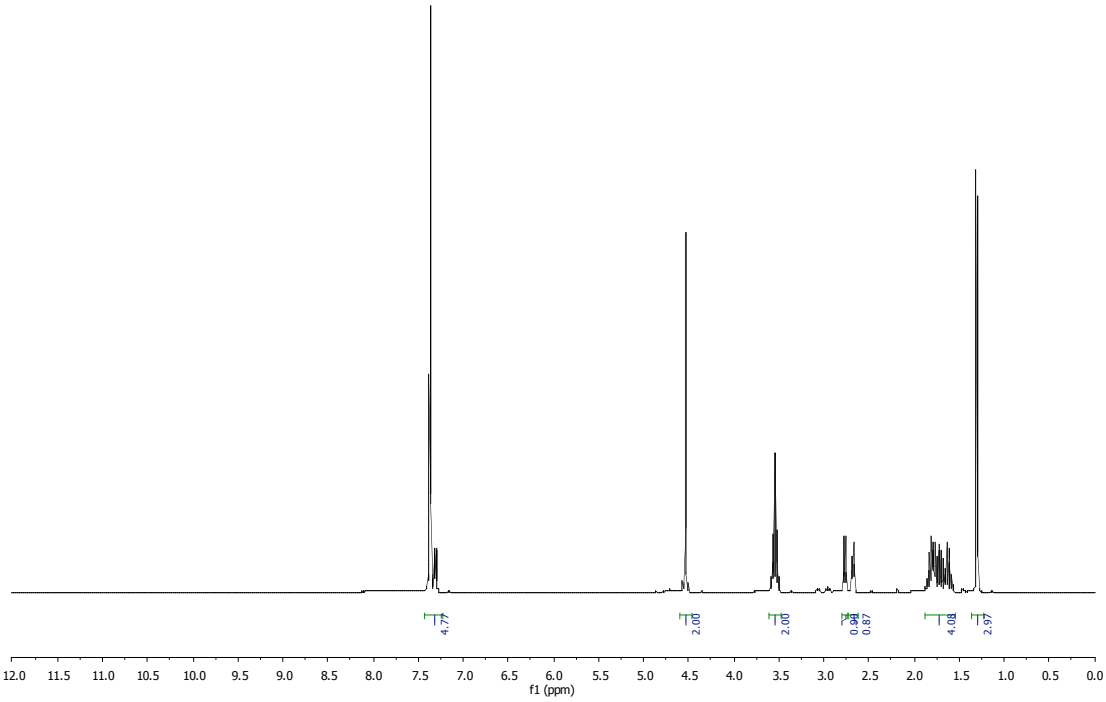
3

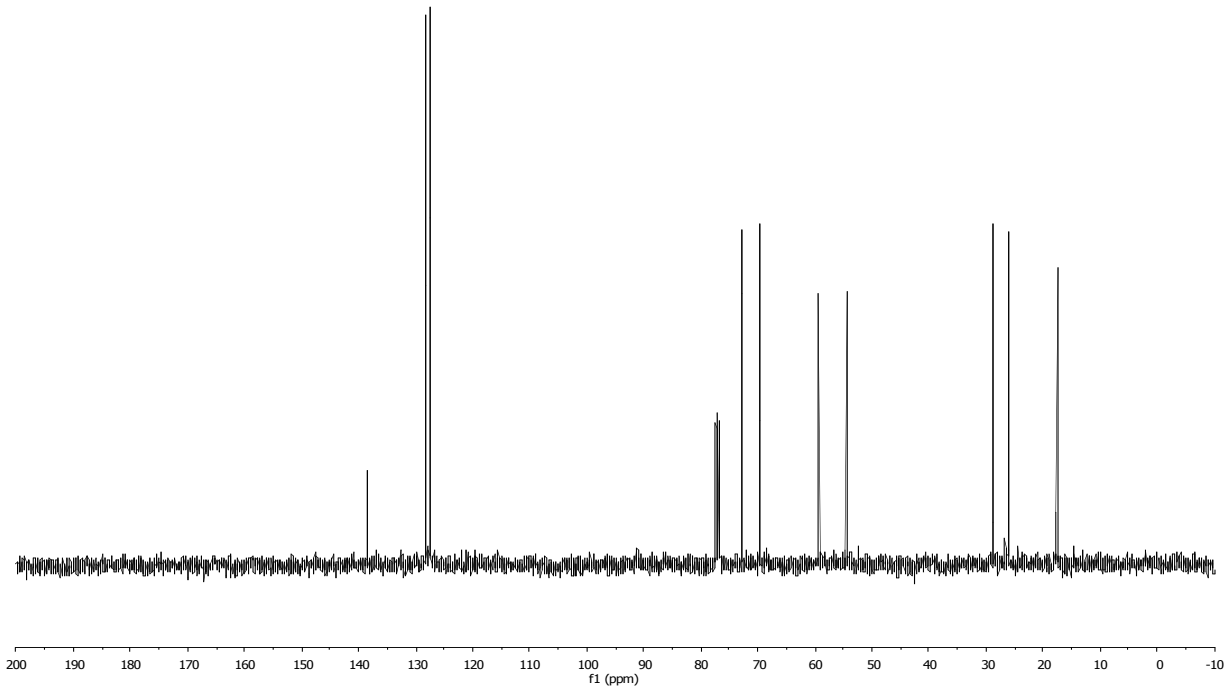





BnO
O
Me

4


4.77
2.00
2.00
0.94
0.87
4.08
2.97
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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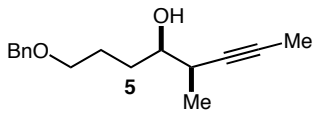
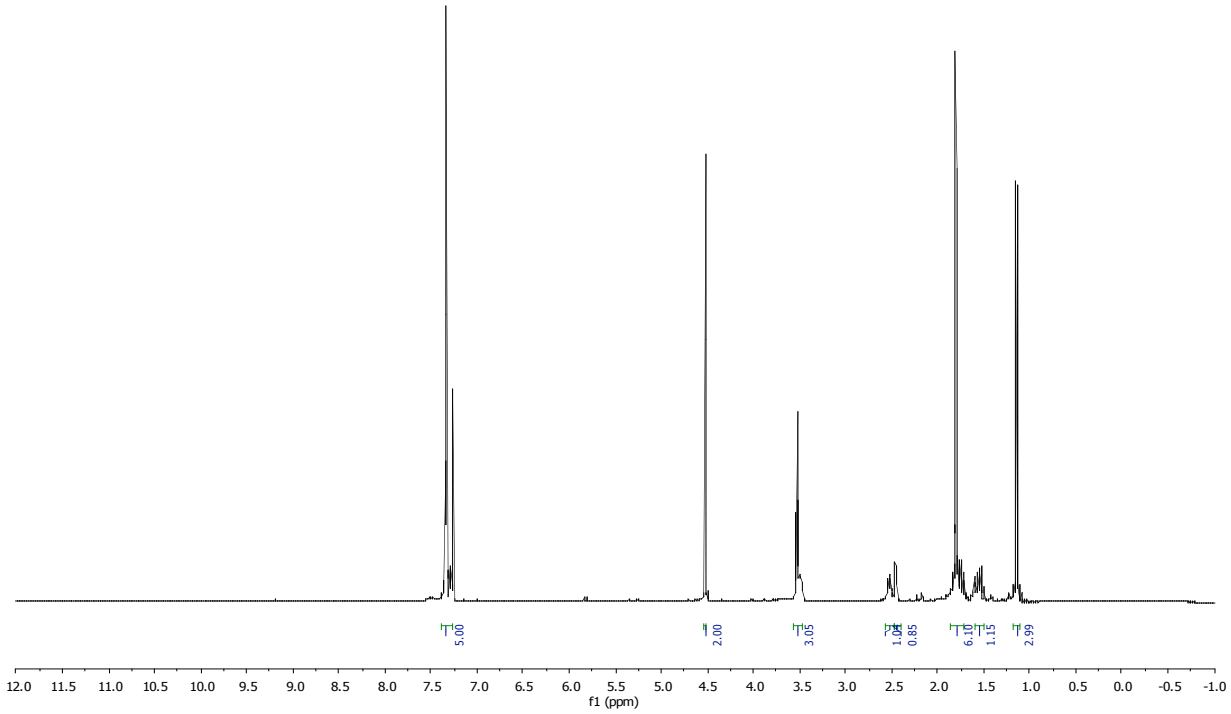
f1 (ppm)


OH
BnO
Me
5
Me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2.00
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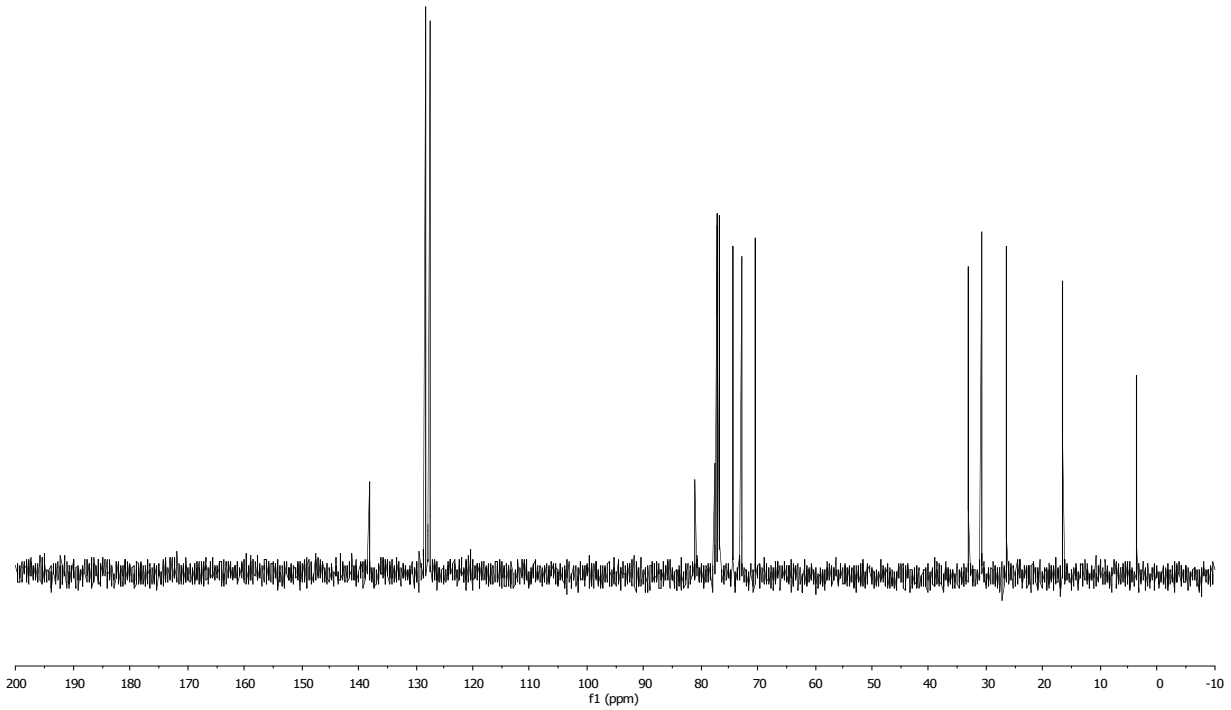
1.04
0.85
6.10
1.15
2.99
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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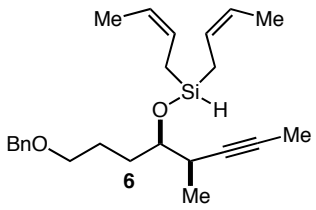
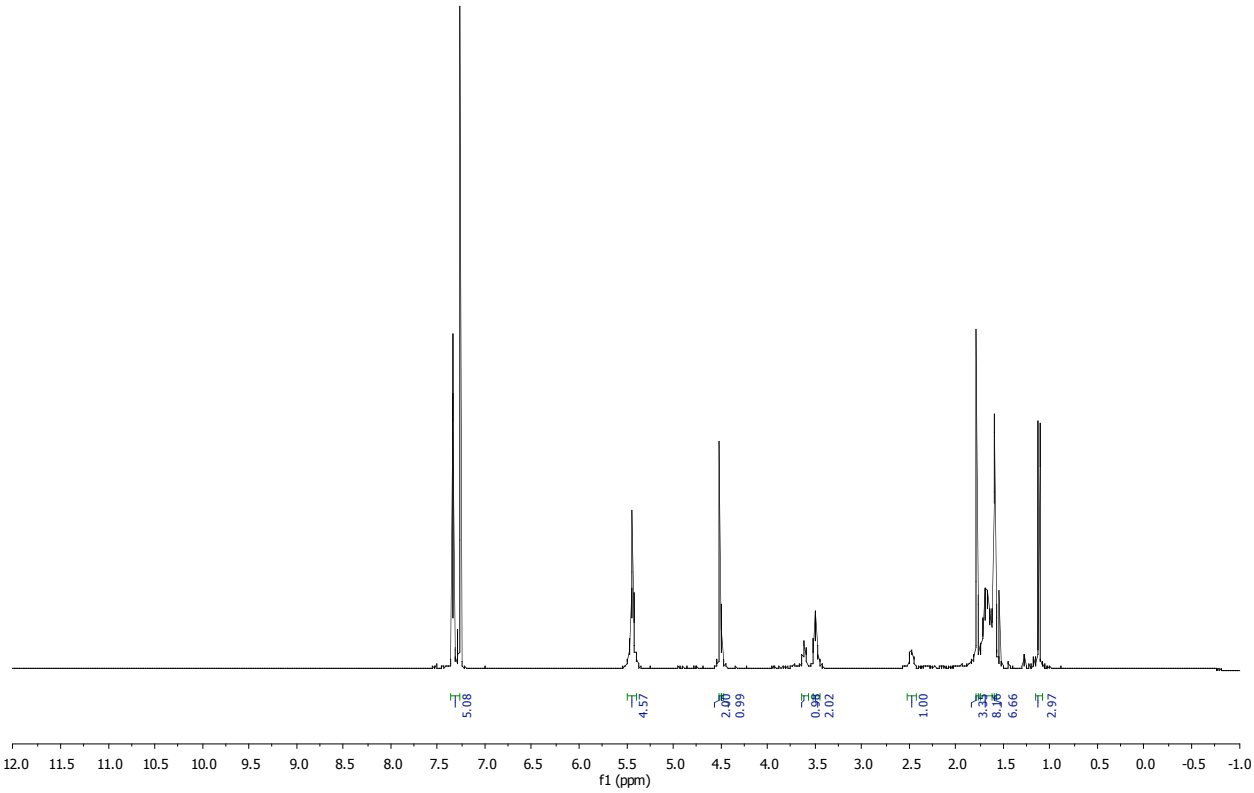
f1 (ppm)


Me
Me
Si
H
O
BnO
Me
6
Me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2.02
1.00
3.34
8.16
6.66
2.97
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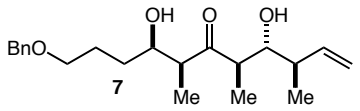
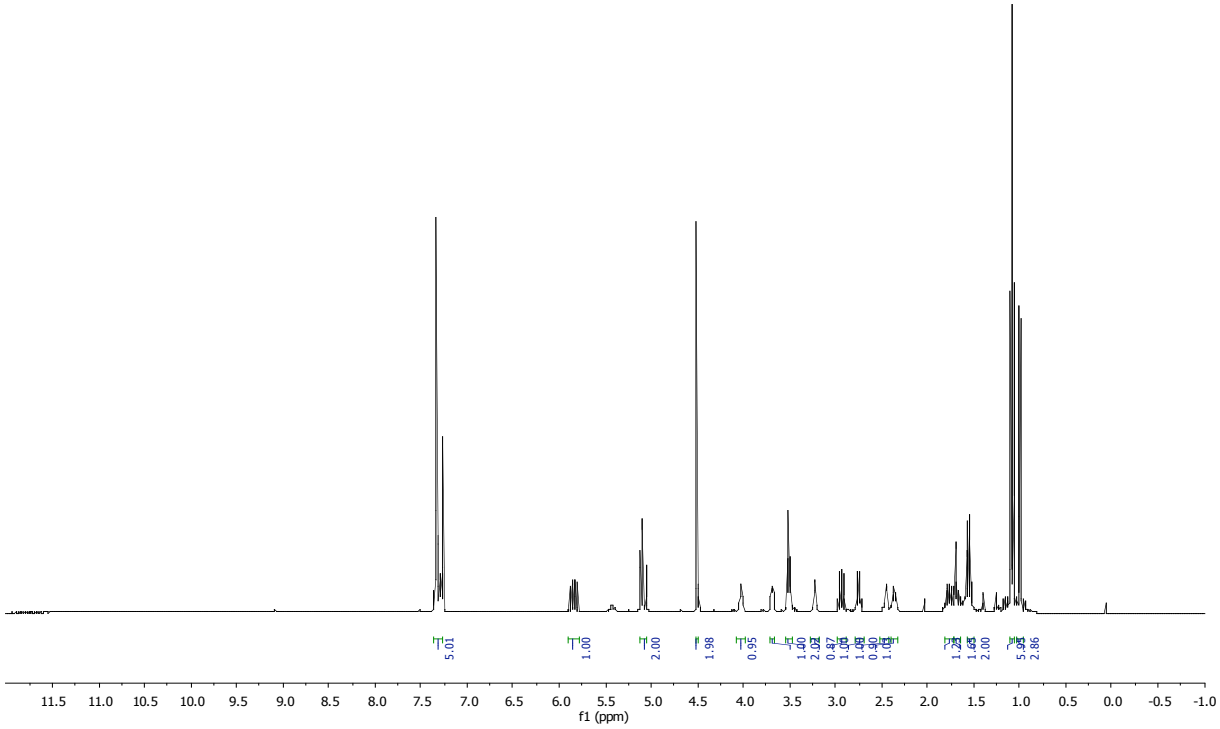
f1 (ppm)


OH
O
OH
BnO
7
Me
Me
Me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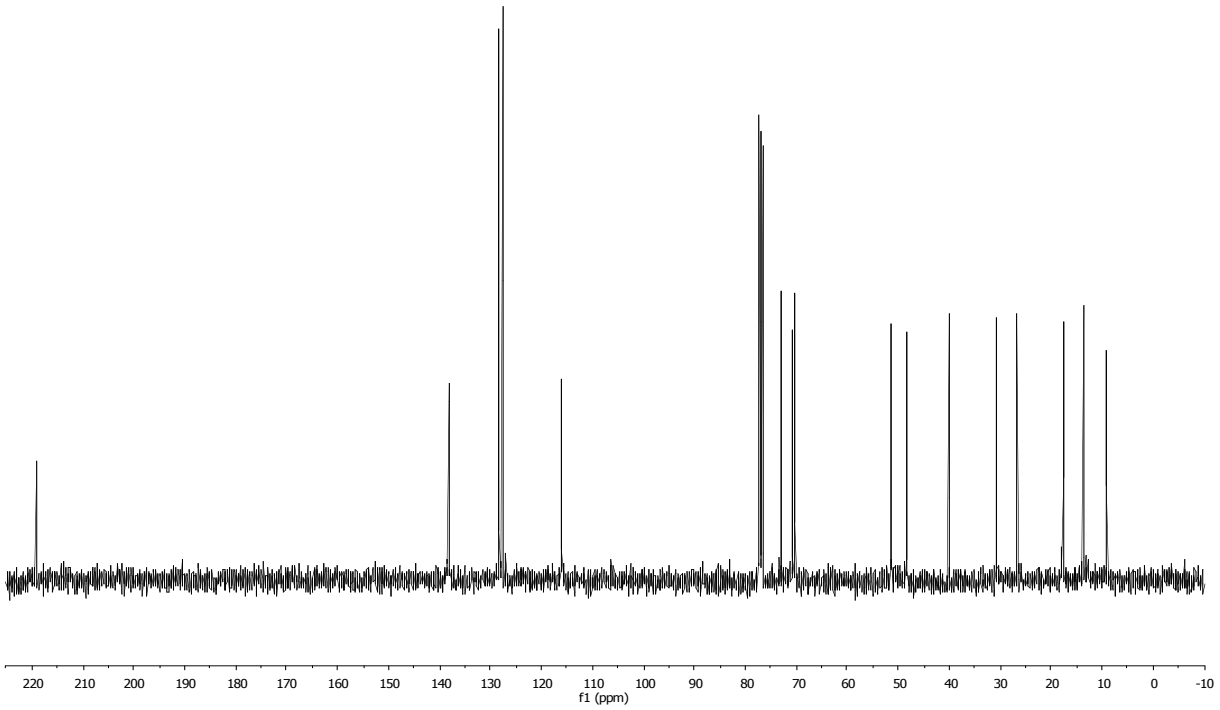
2.00
1.98
0.95
1.40
2.02
0.87
1.04
1.08
0.90
1.08
2.00
2.86
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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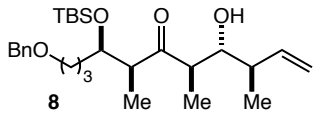
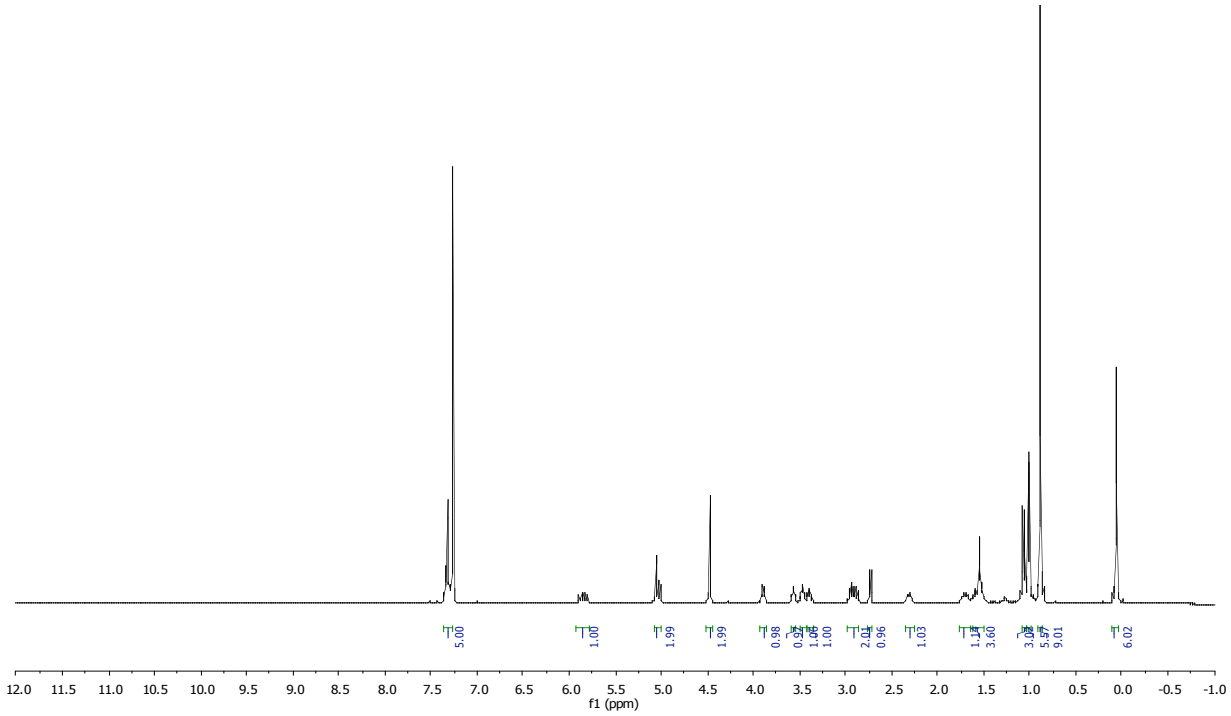
f1 (ppm)


TBSO
O
OH
BnO
3
Me
Me
Me

8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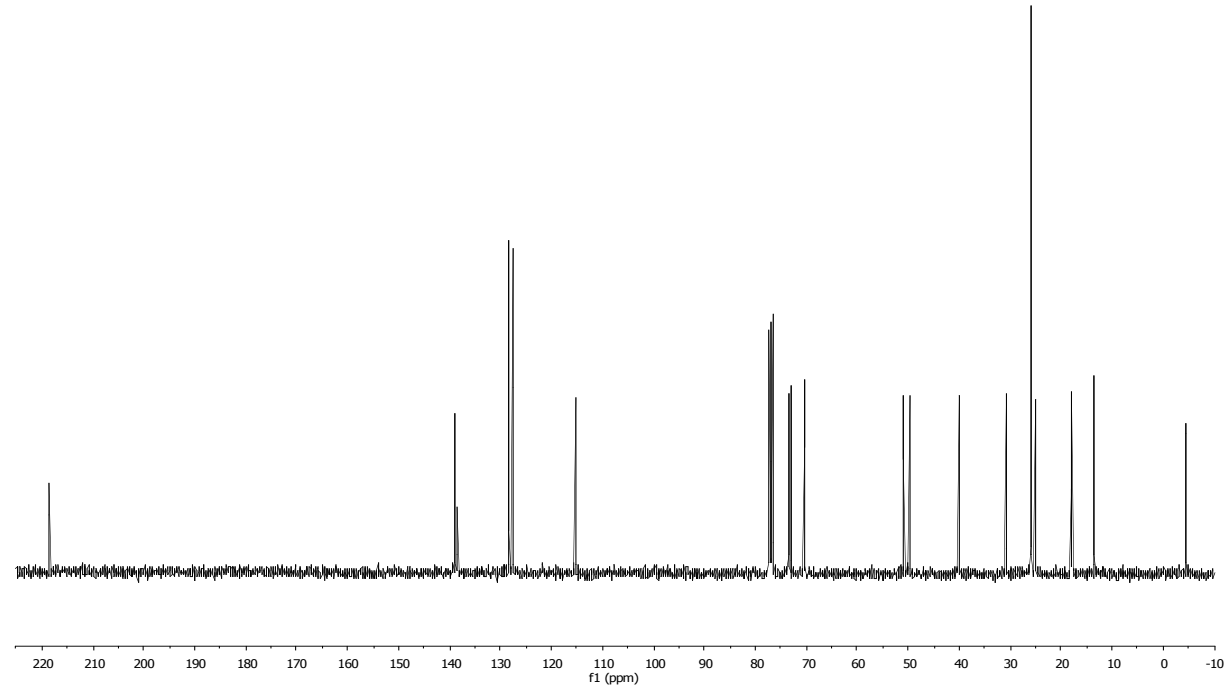
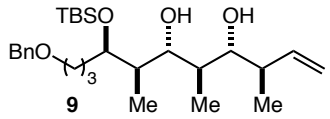
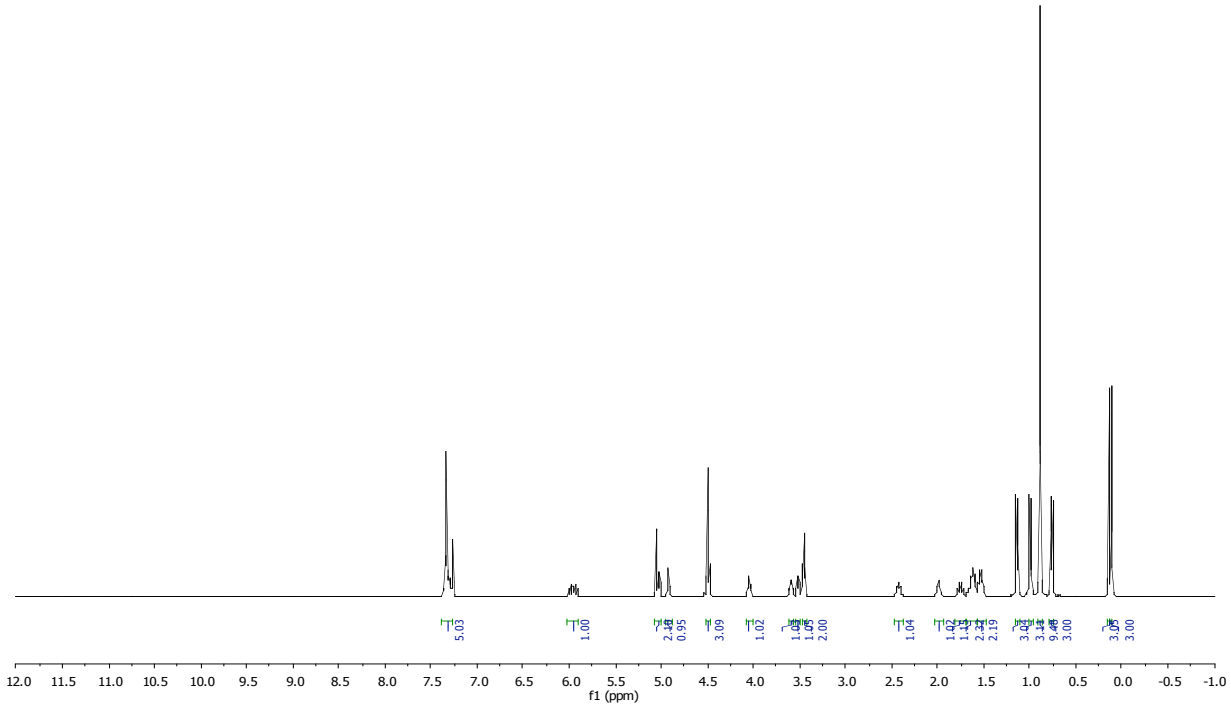
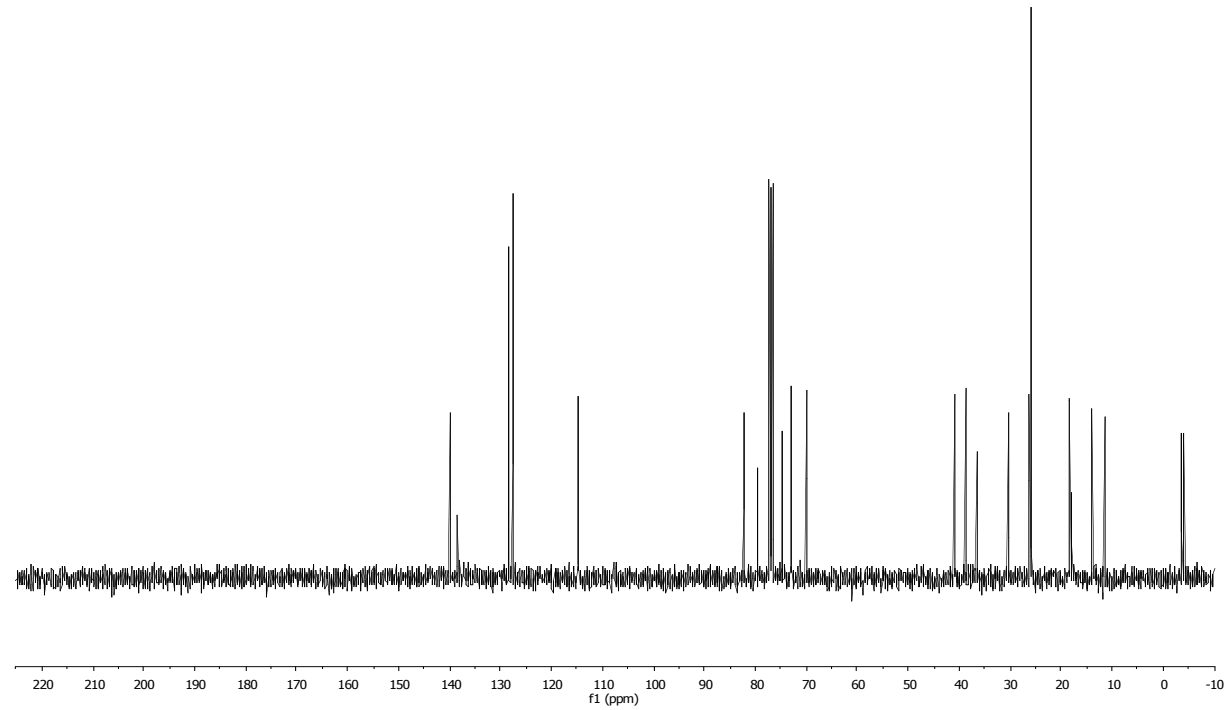
1.99
0.98
1.00
2.04
0.96
1.03
3.60
6.02
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

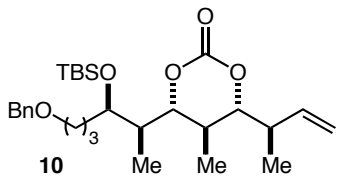

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

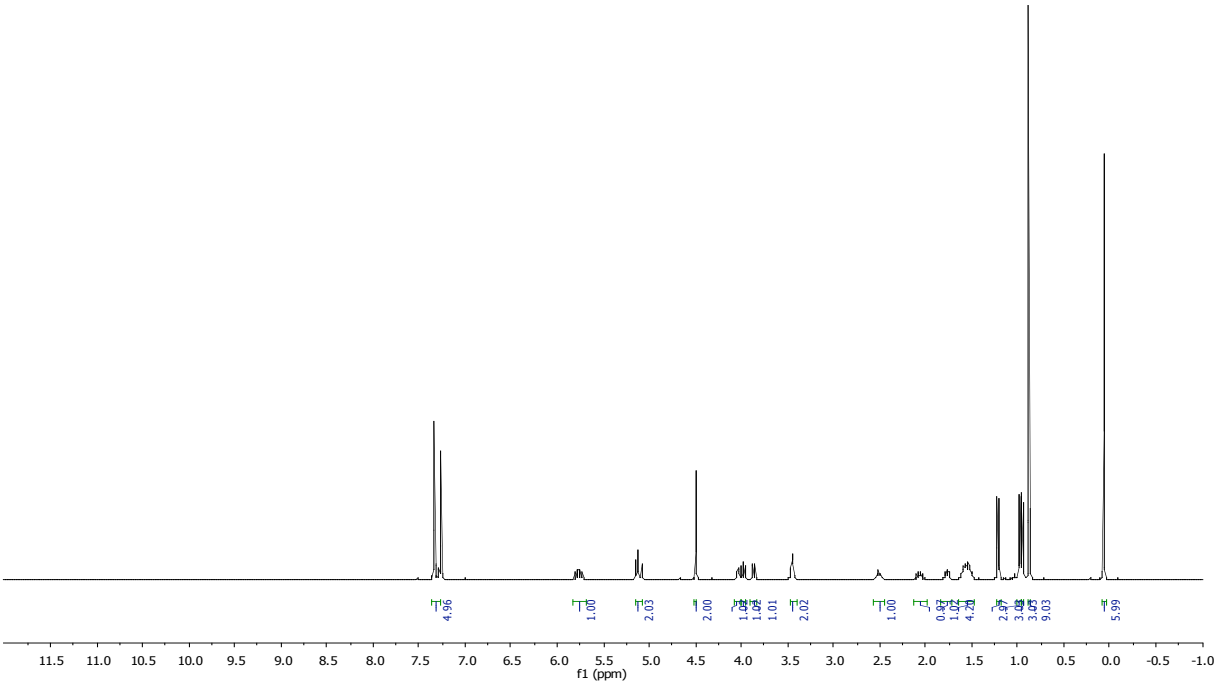

TBSO
OH
OH
BnO
3
Me
Me
Me

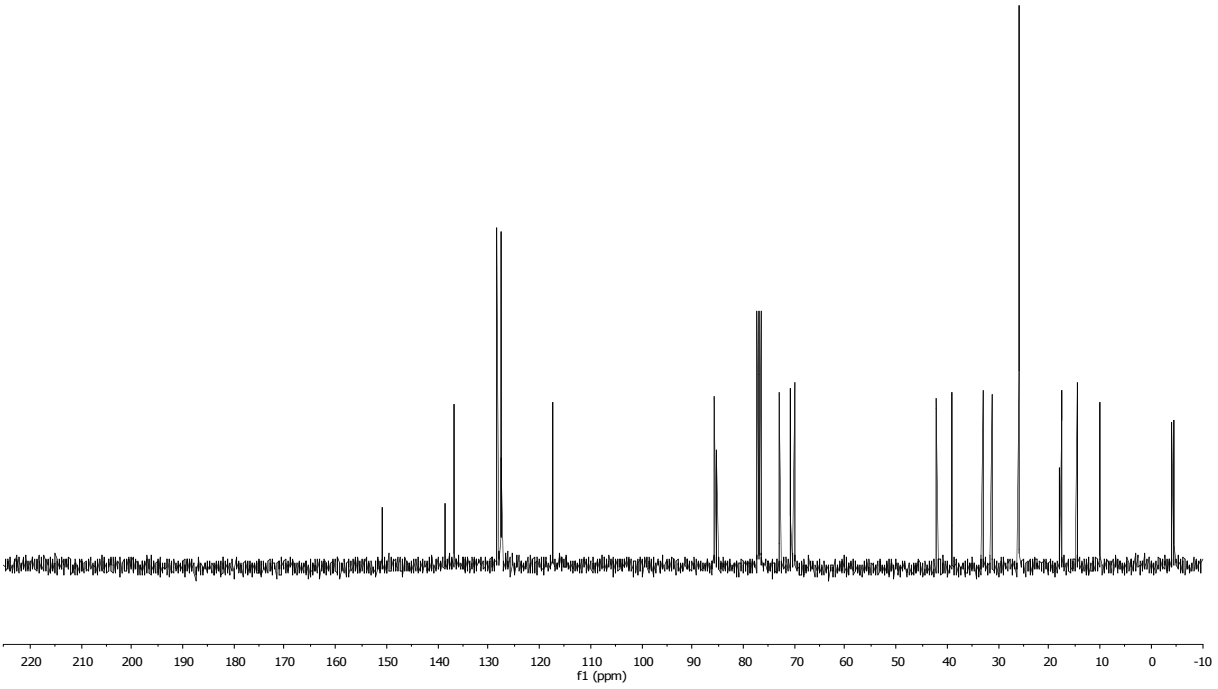
9

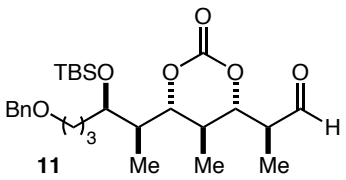

5.03
1.00
2.42
0.95
3.09
1.02
2.00
1.04
2.19
3.00
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

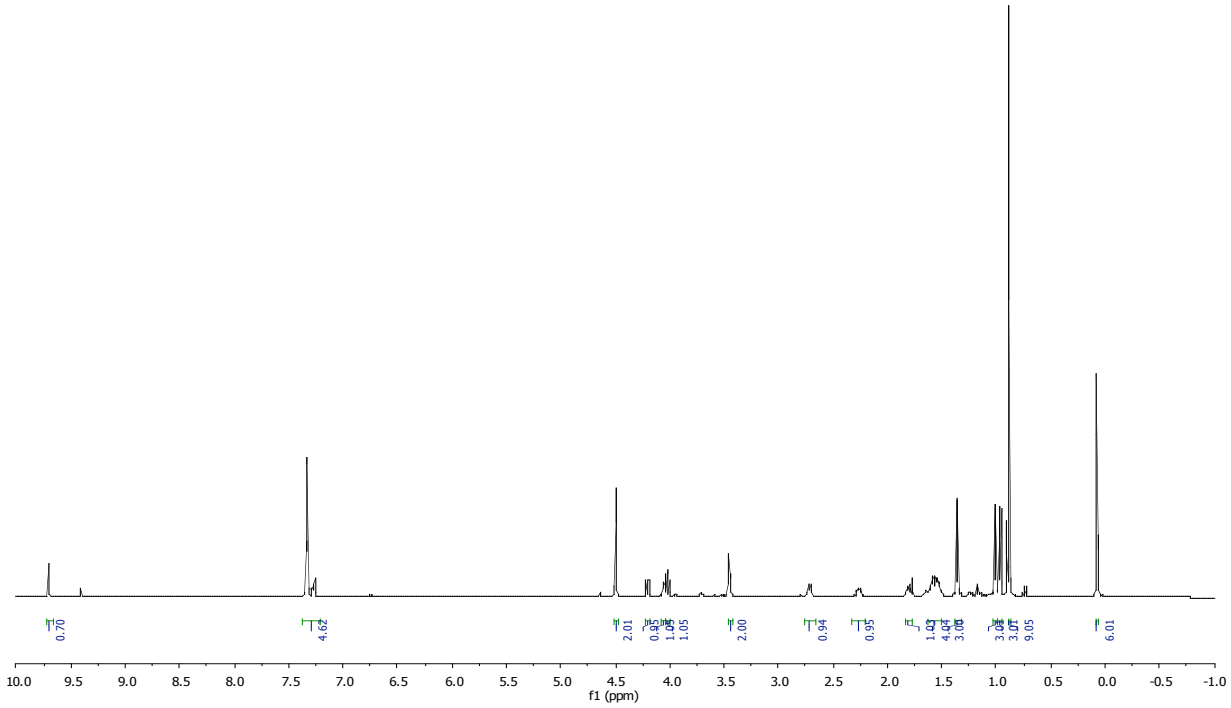

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

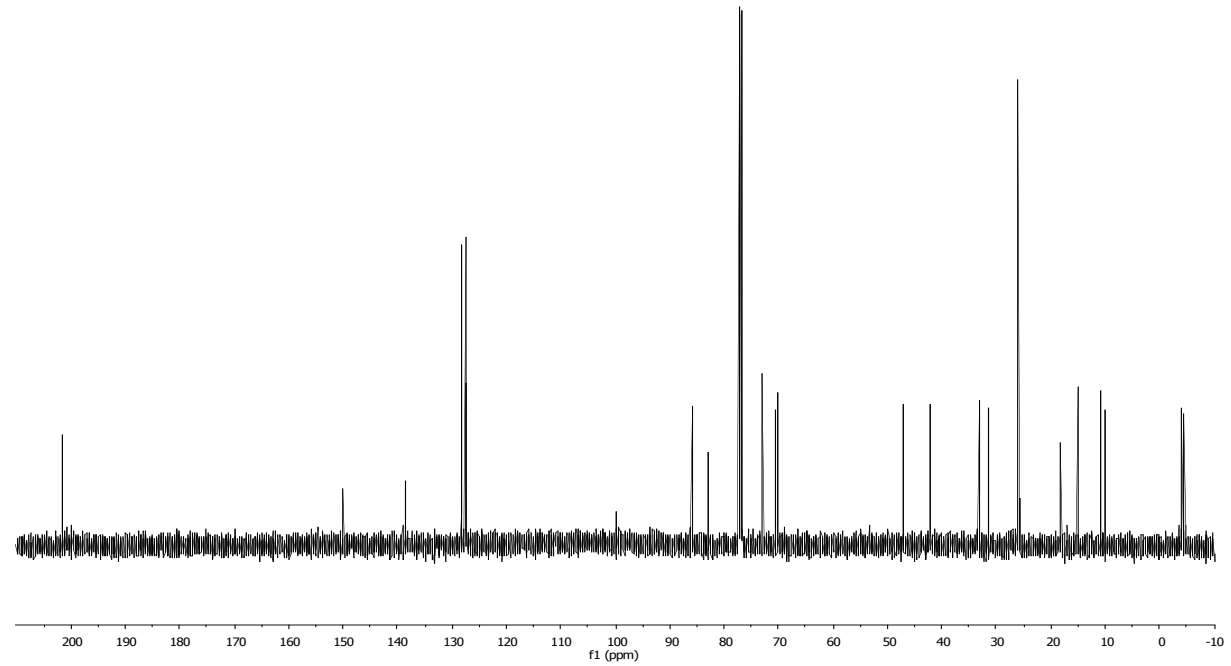

O
TBSO
O
O
BnO
3
10
Me
Me
Me

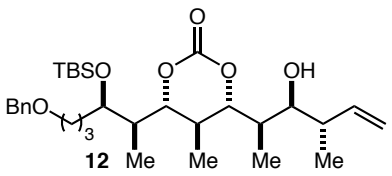

4.96
1.00
2.03
2.00
1.01
2.02
1.00
5.99
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

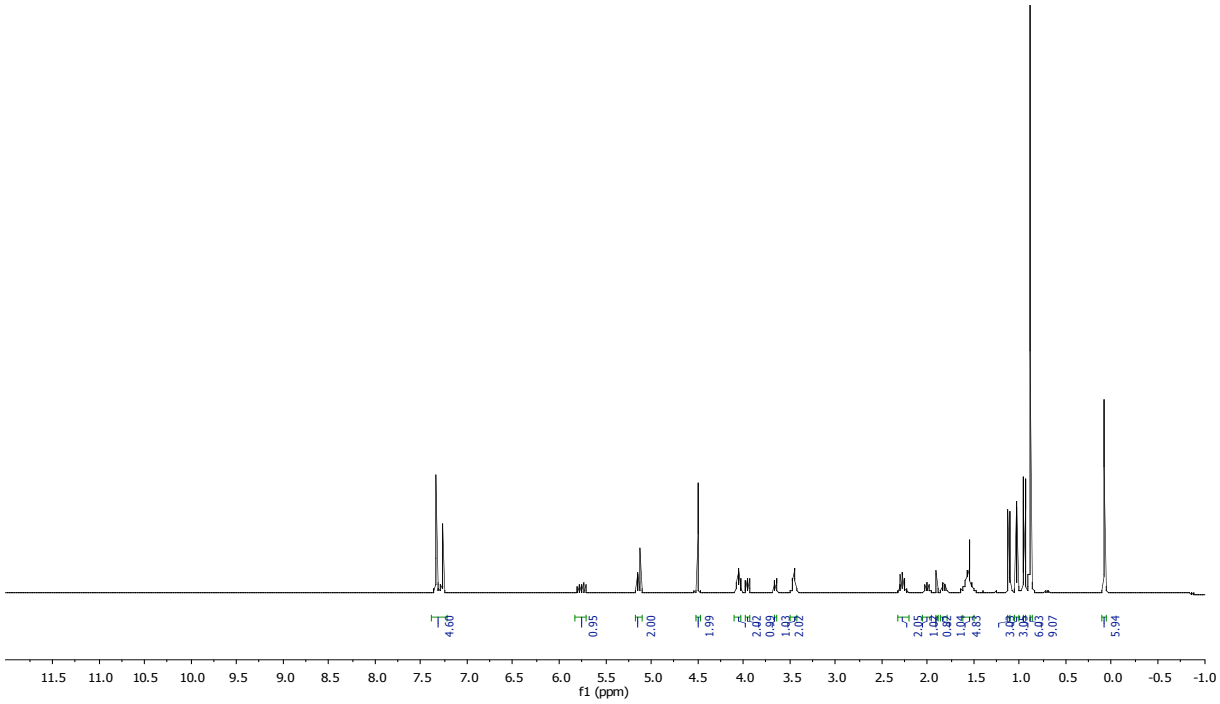

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

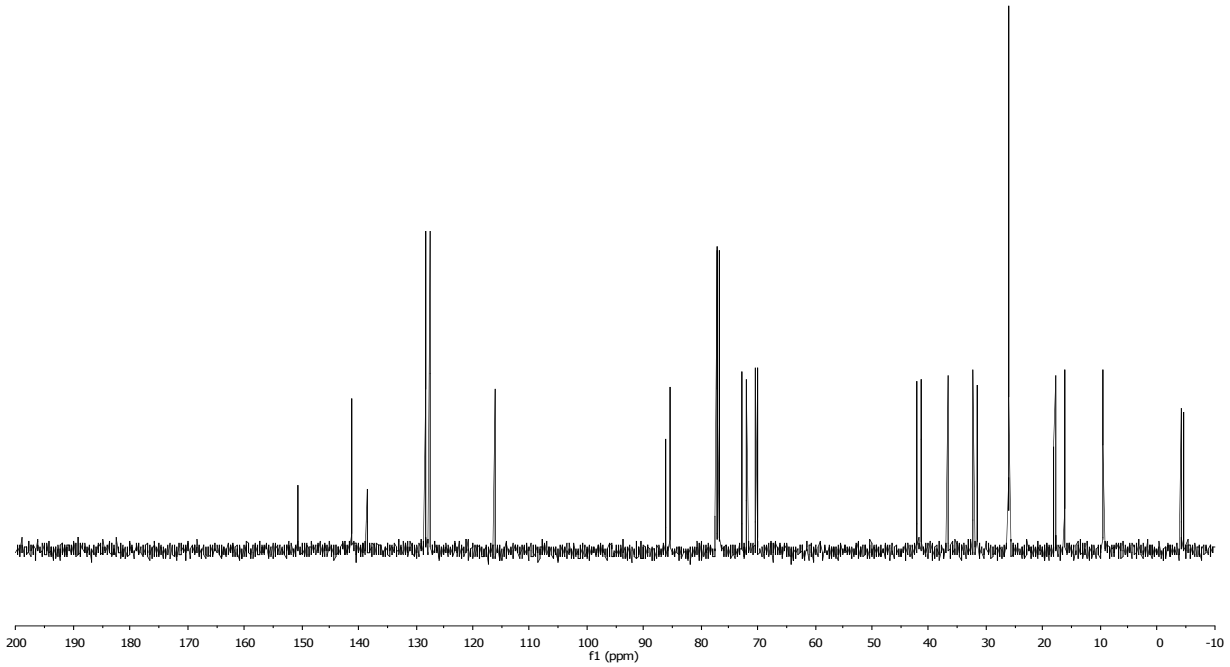

O
TBSO
O
O
O
BnO
3
H
11
Me
Me
Me

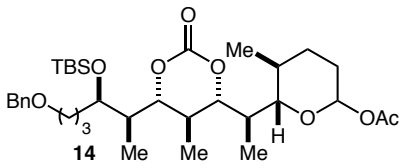

0.70
4.62
2.01
2.00
0.94
0.95
6.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

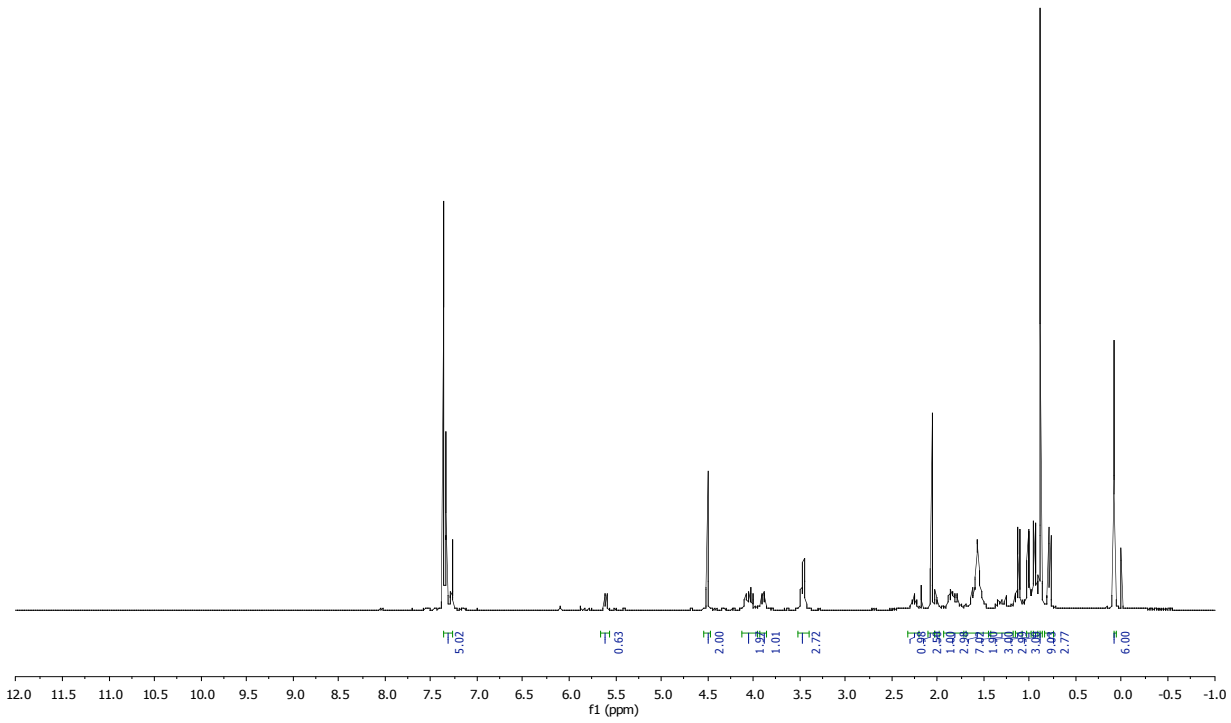

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

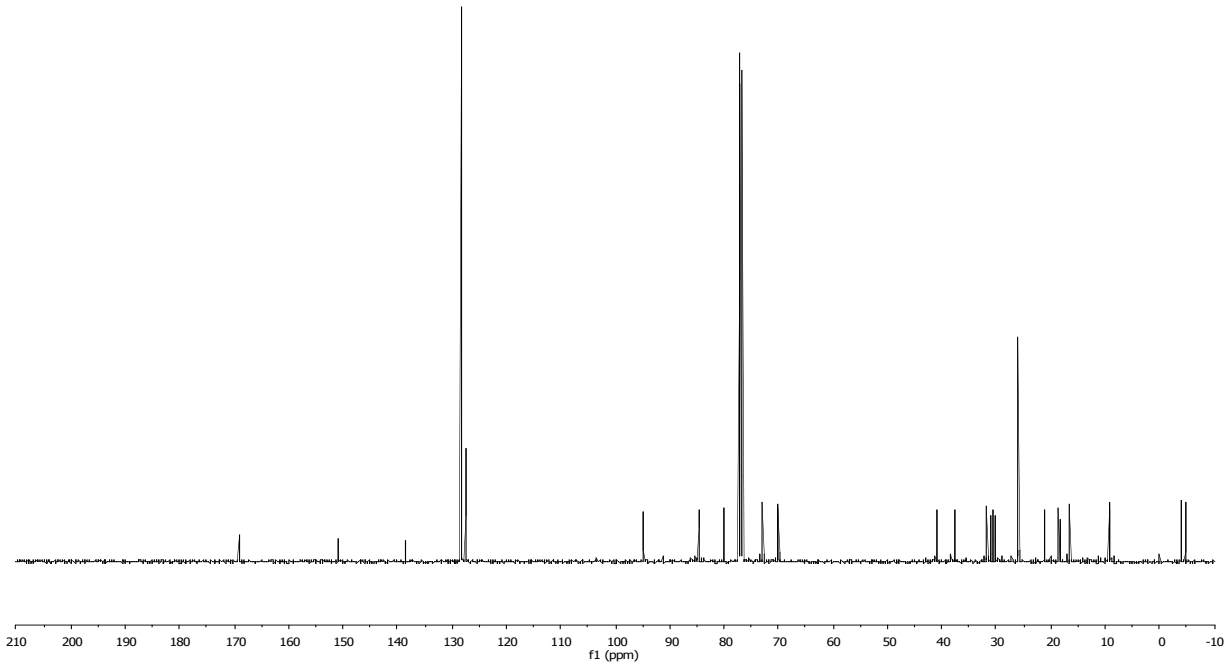

O
TBSO
O
O
OH
BnO
3
12
Me
Me
Me
Me

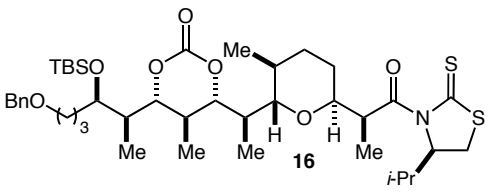

4.60
0.95
2.00
1.99
2.02
0.48
1.03
2.02
2.05
1.04
0.82
1.04
4.83
3.04
3.05
6.43
9.07
5.94
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

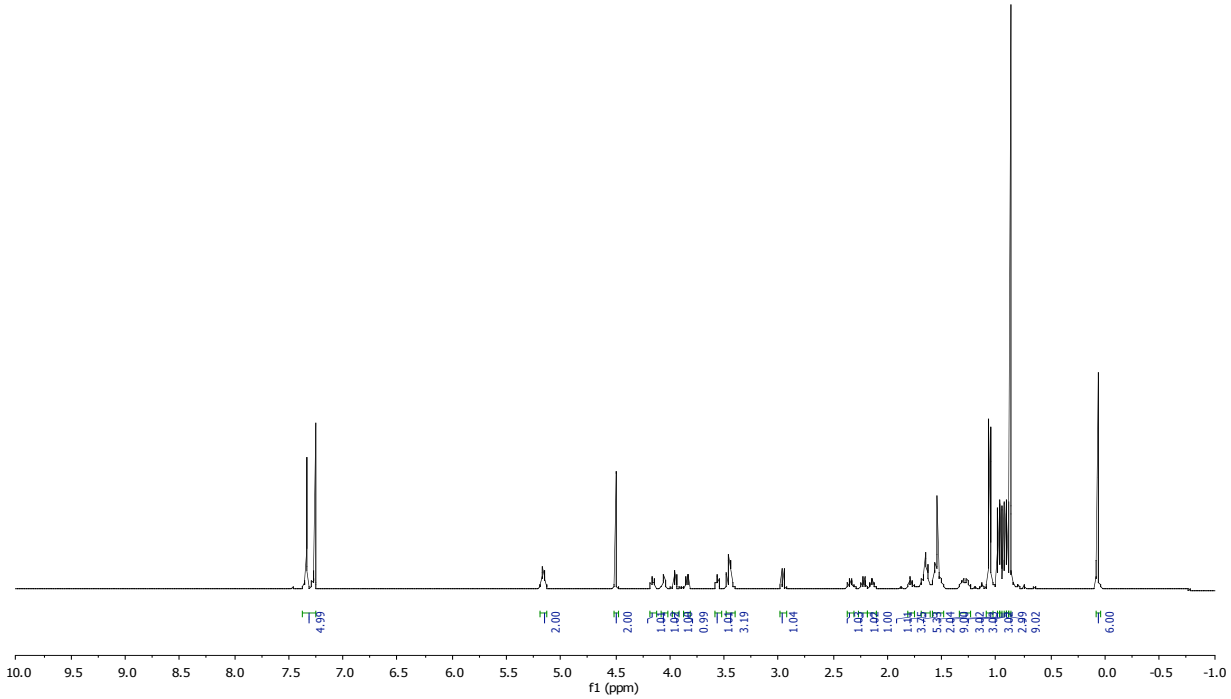

O
TBSO
O
O
Me
BnO
3
O
OAc
H
14
Me
Me
Me

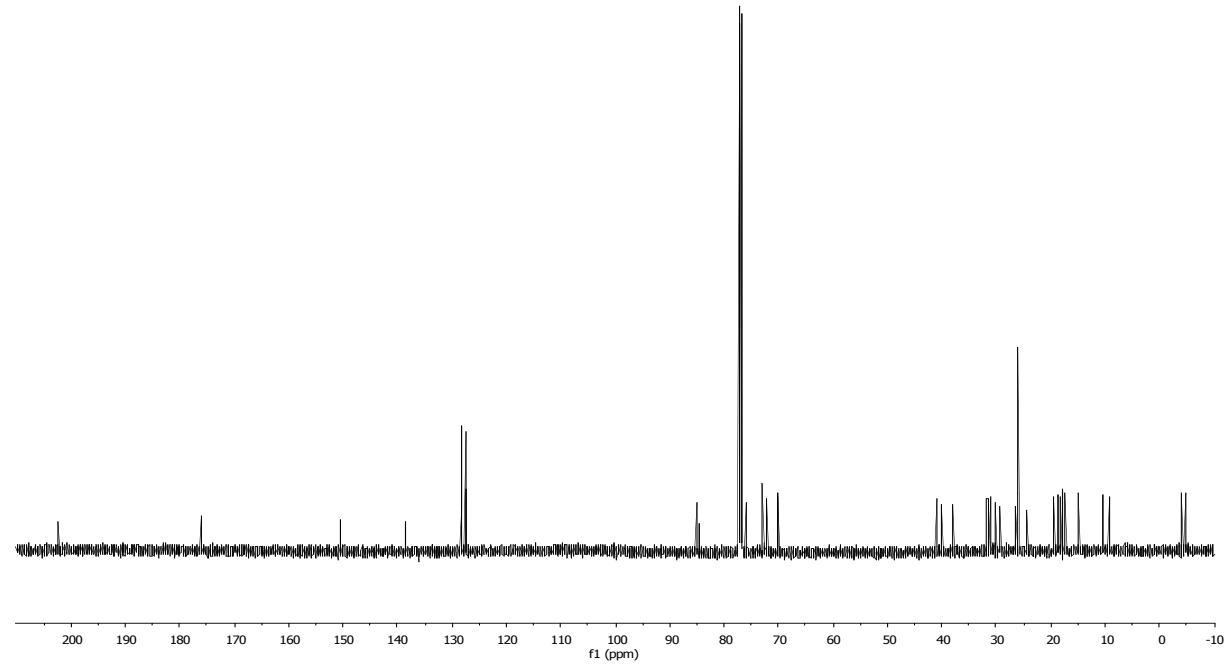

5.02
0.63
2.00
1.01
2.72
6.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

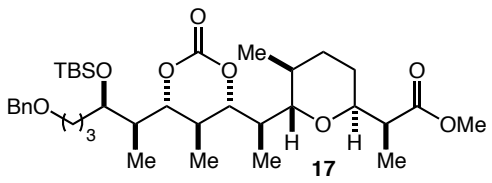

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


TBSO
BnO
3
O
O
O
Me
Me
Me
Me
H
O
H
O
N
S
S
Me
i-Pr

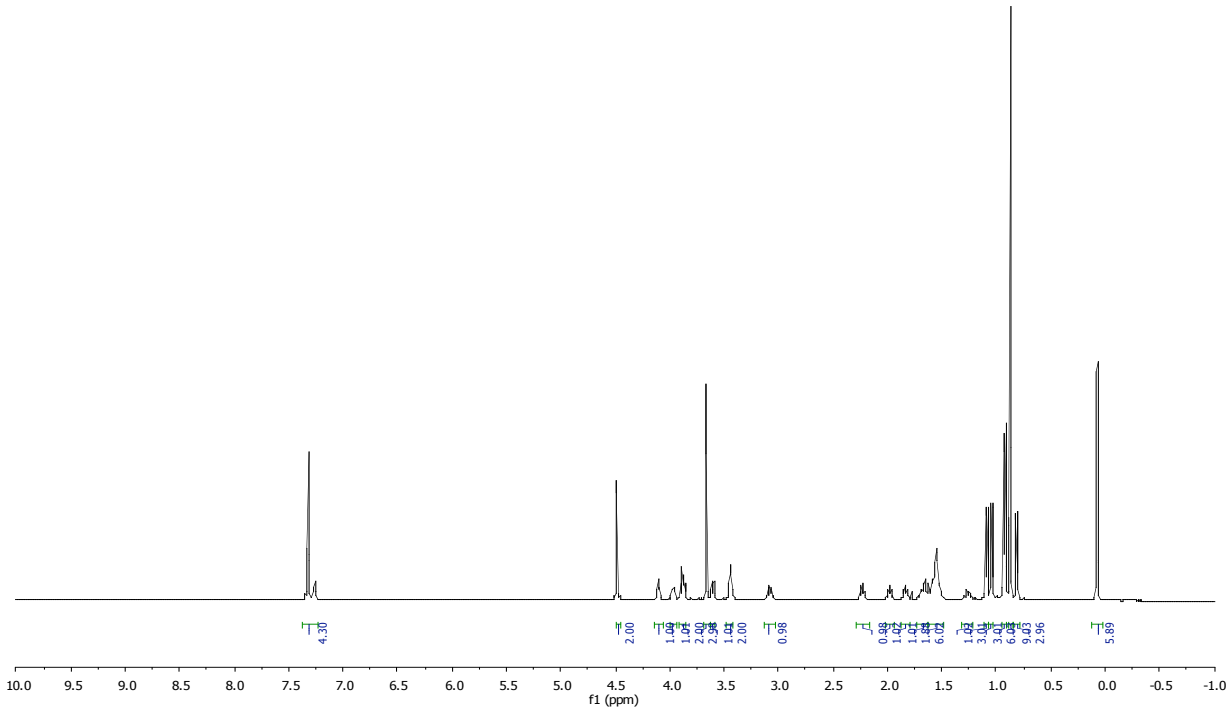
16

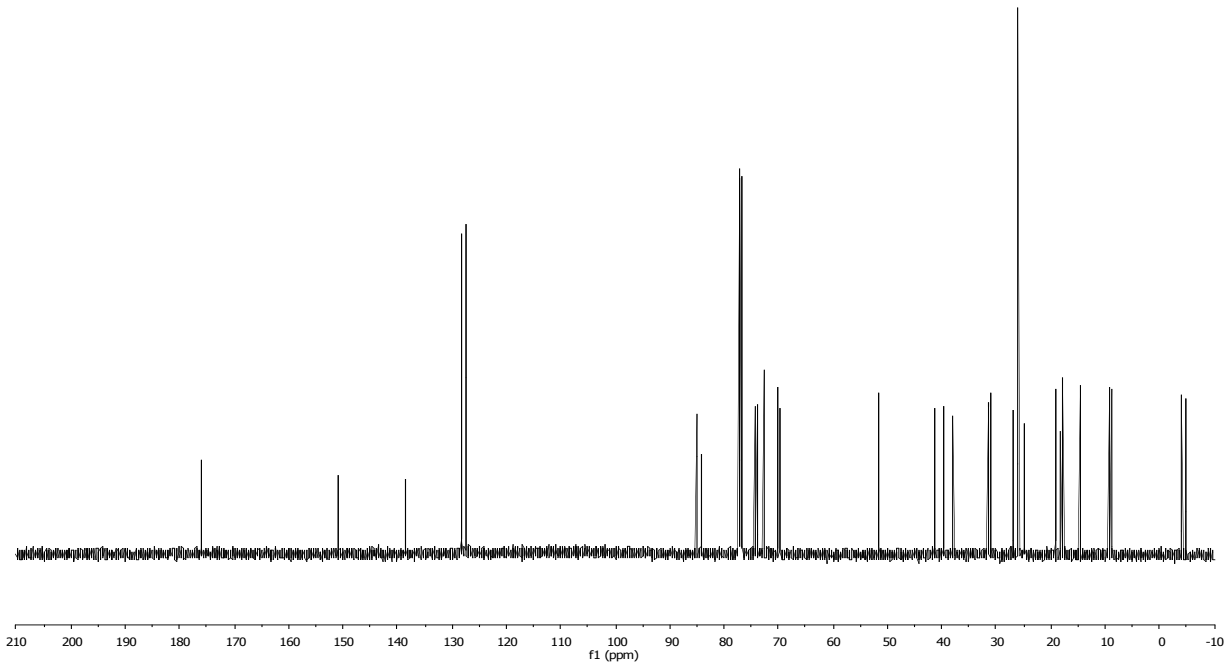

4.99
2.00
2.00
1.04
1.00
1.00
0.99
1.04
3.19
1.04
1.00
1.00
1.7
5.44
2.44
3.42
3.08
2.99
9.02
6.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

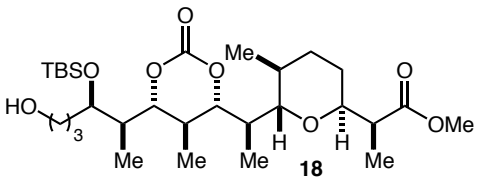

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O
TBSO
O
O
Me
O
BnO
3
O
OMe
H
H
Me
Me
Me
Me

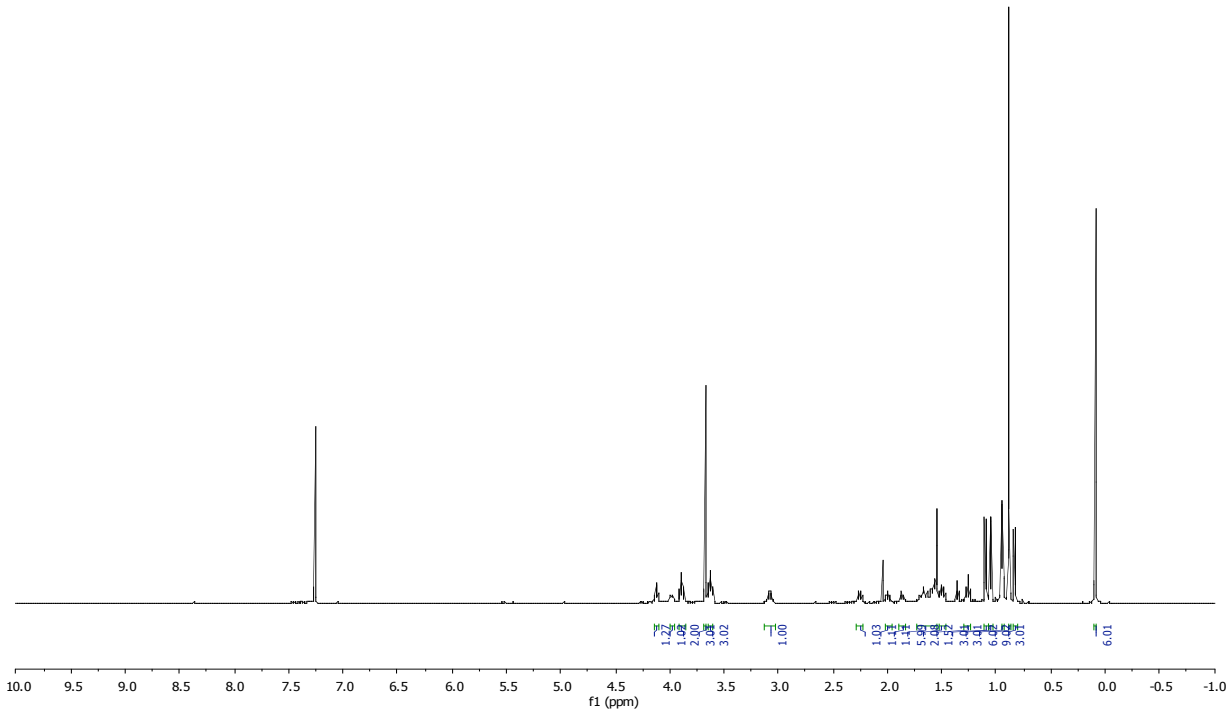
17

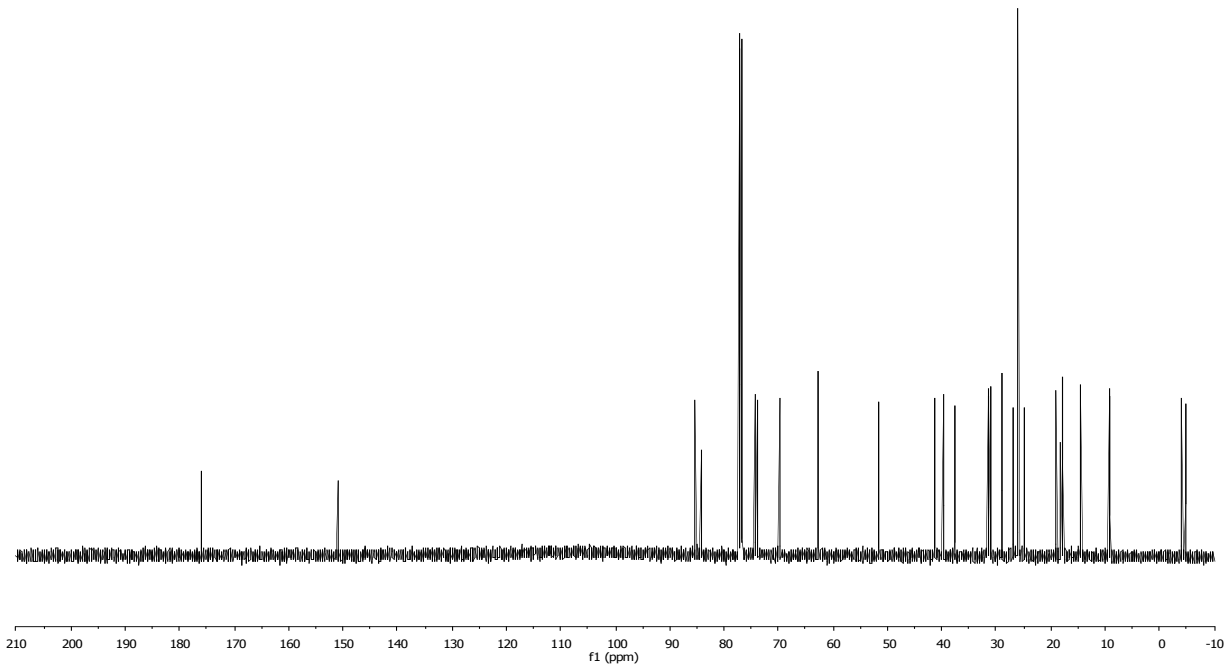

4.30
2.00
2.00
0.98
5.89
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

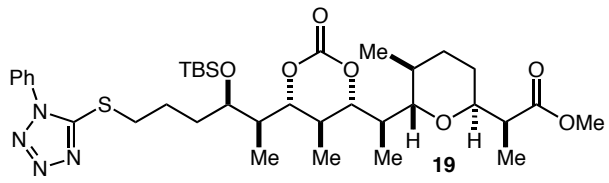

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
TBSO
O
O
Me
HO
3
O
OMe
H
O
H
Me
Me
Me
Me

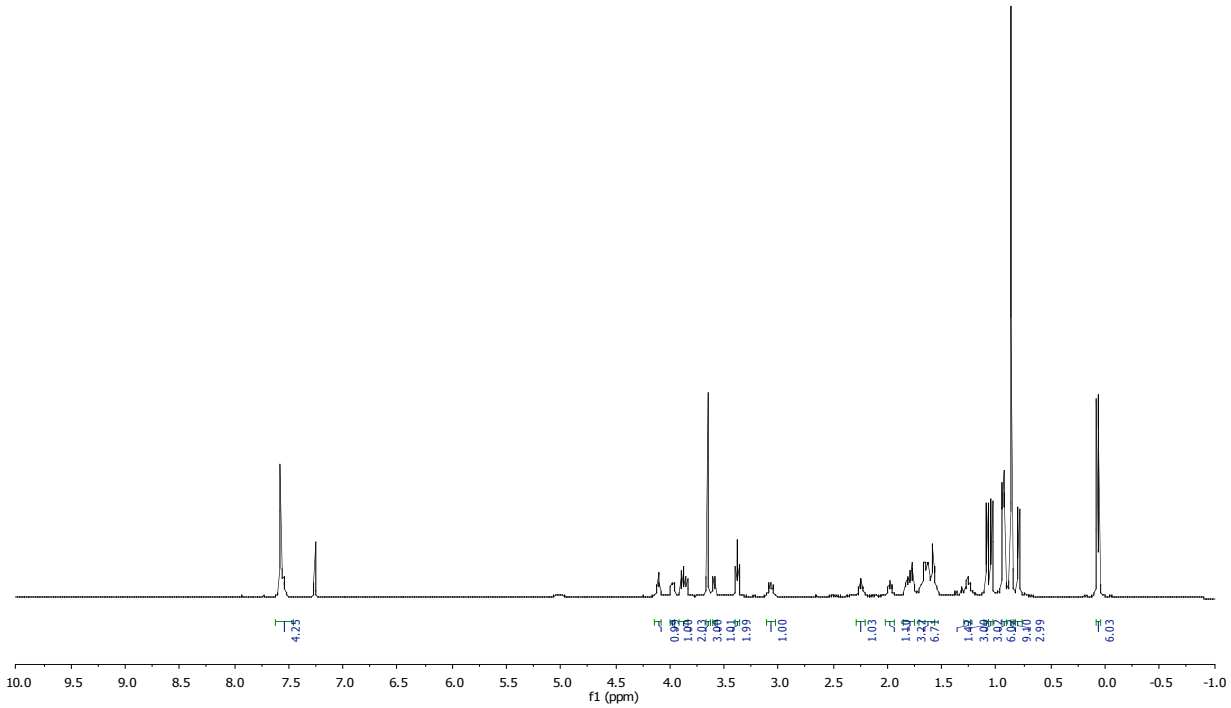
18

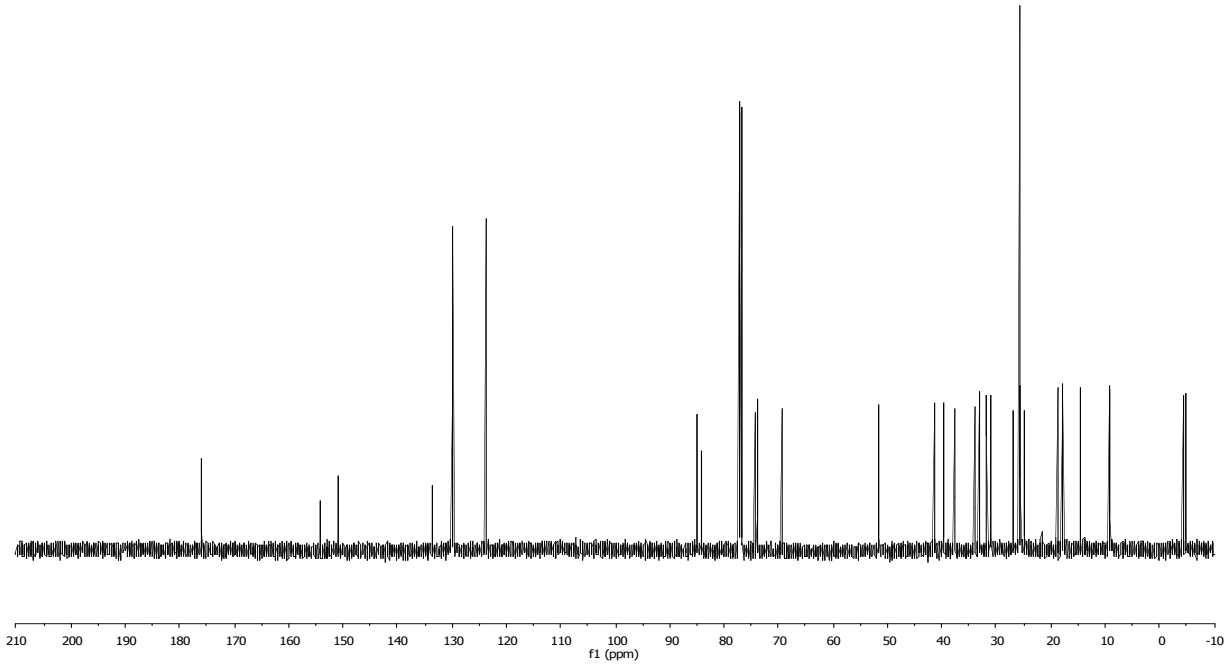

1.22
1.92
2.00
3.02
1.00
1.03
1.11
1.11
5.97
2.04
1.52
3.04
3.01
6.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

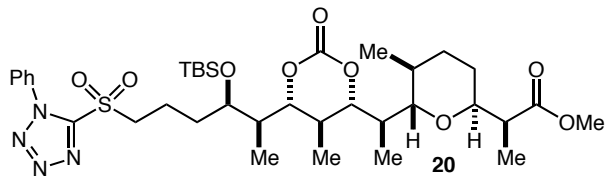

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

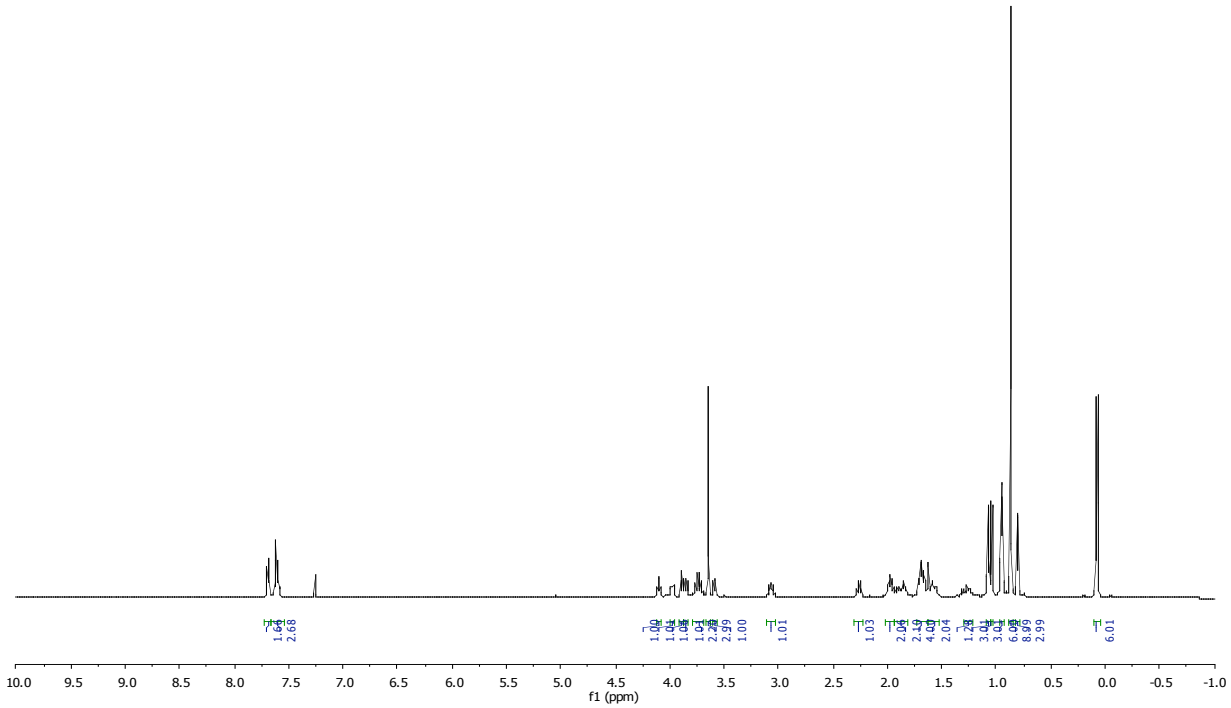

Ph
N
N
N
N
S
TBSO
O
O
O
Me
Me
Me
Me
H
O
H
O
OMe
Me

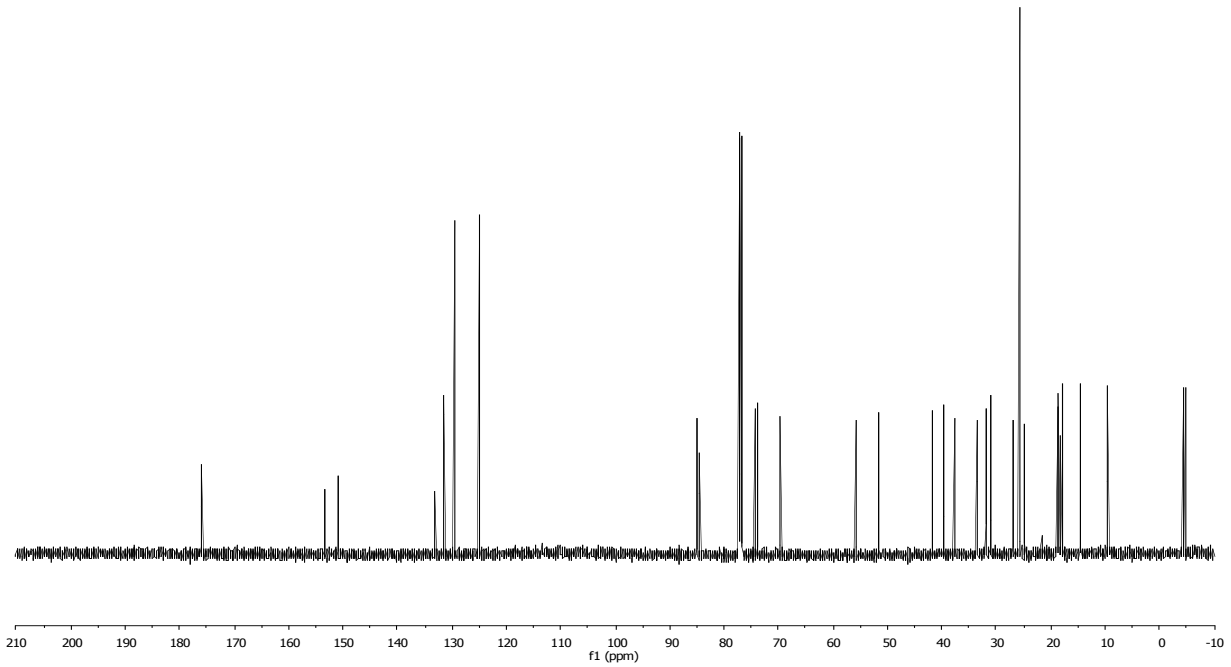
19

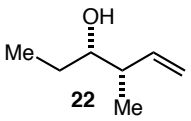

4.25
1.03
6.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

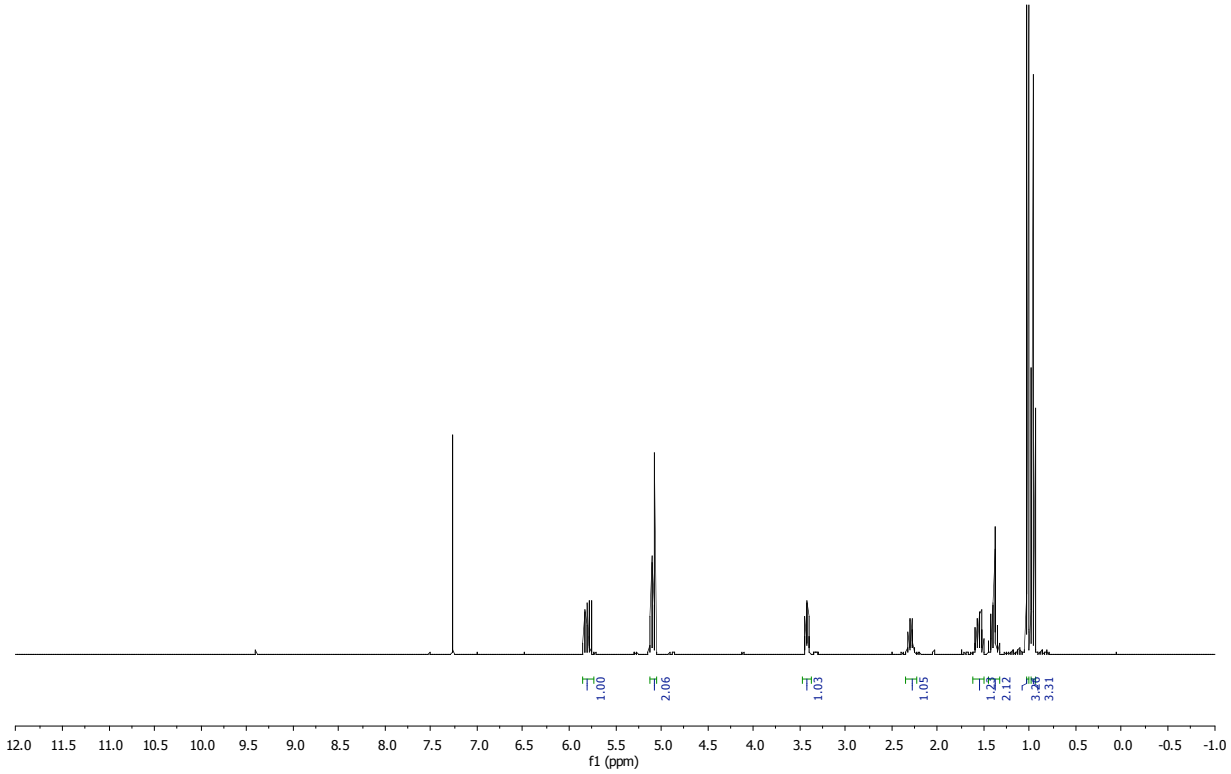

Ph
O
O
S
N
N
N
N
TBSO
O
O
O
Me
O
O
OMe
H
H
Me
Me
Me
Me
20

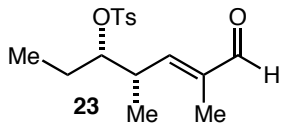

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

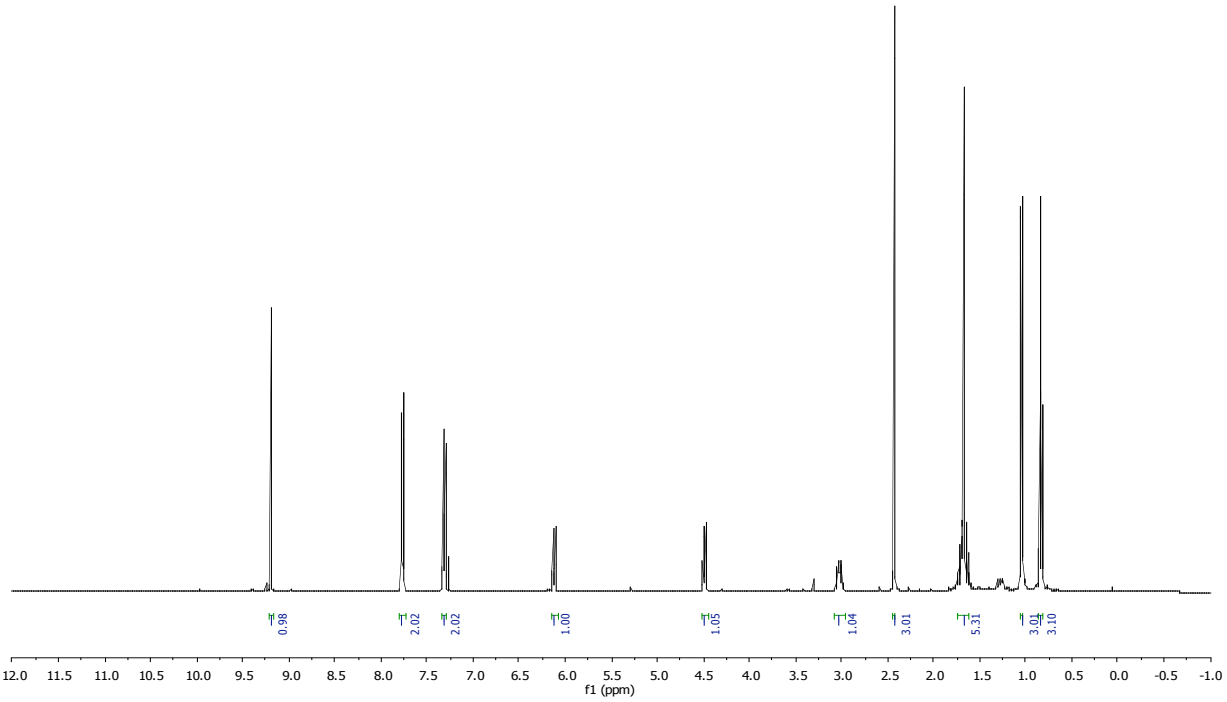

OH
Me
Me

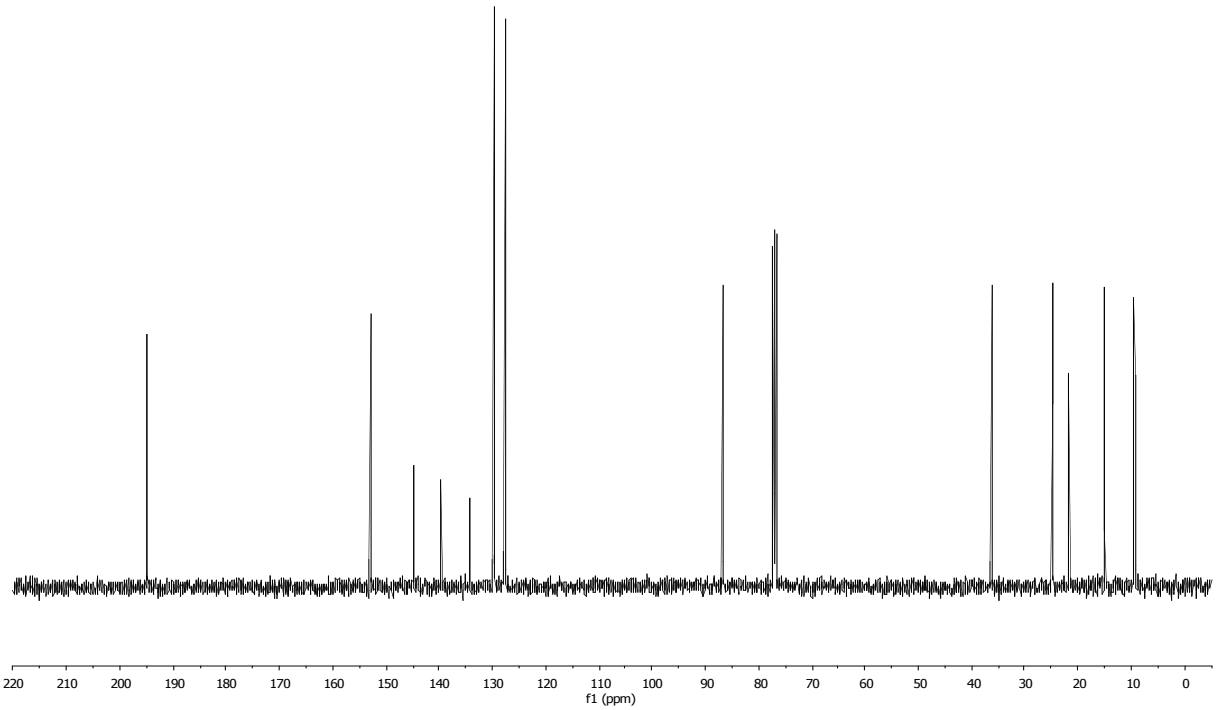
22

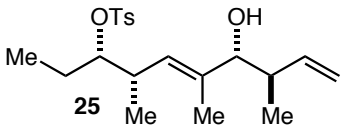

1.00
2.06
1.03
1.05
2.12
3.31
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

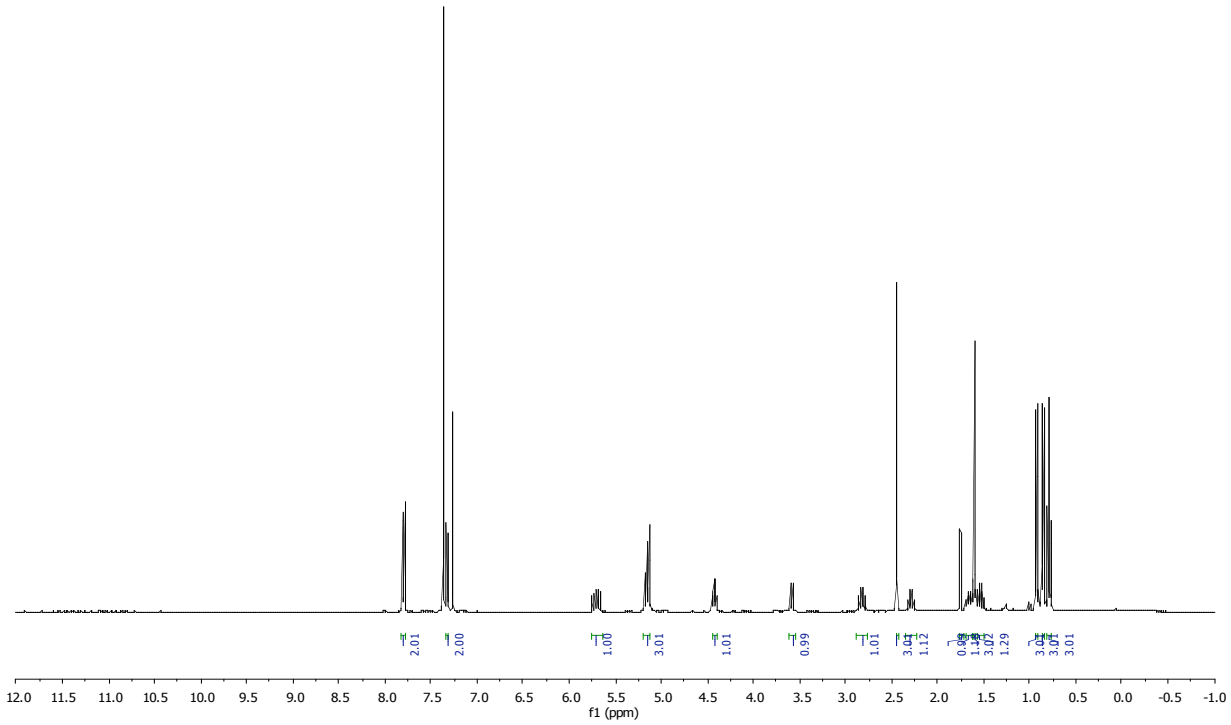

OTs
O
Me
H
Me
Me

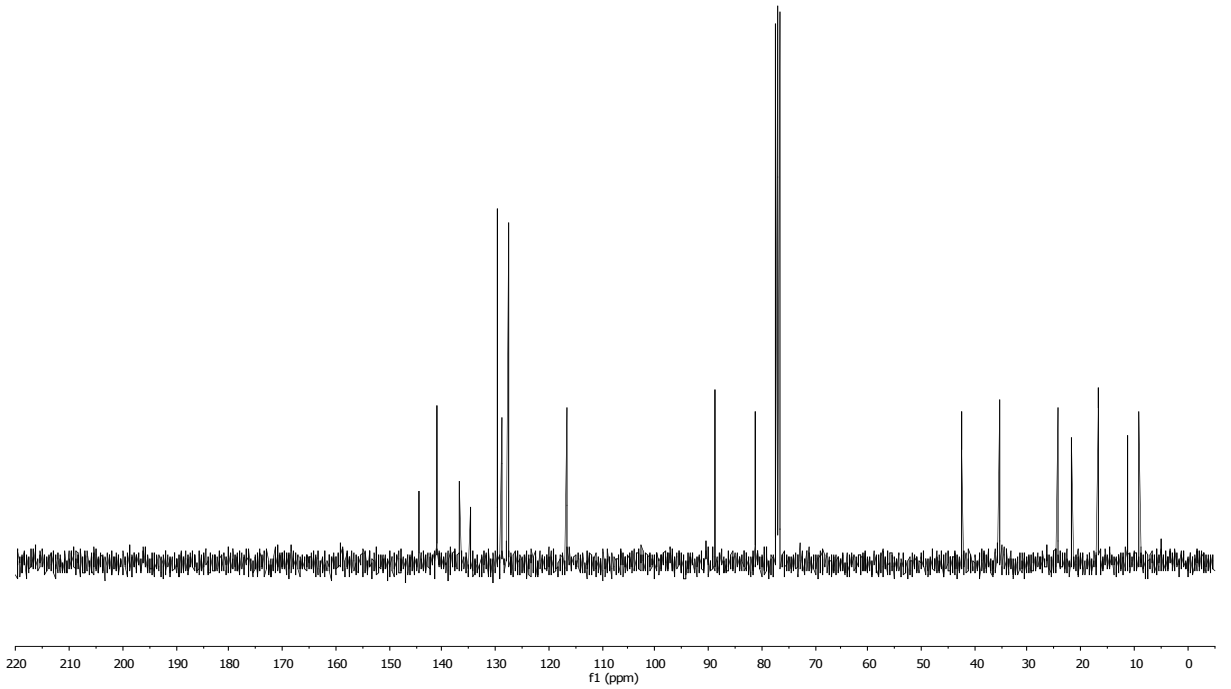
23

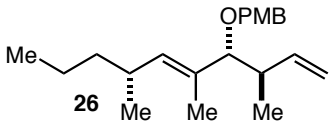

0.98
2.02
2.02
1.00
1.05
1.04
3.01
5.31
3.01
3.10
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

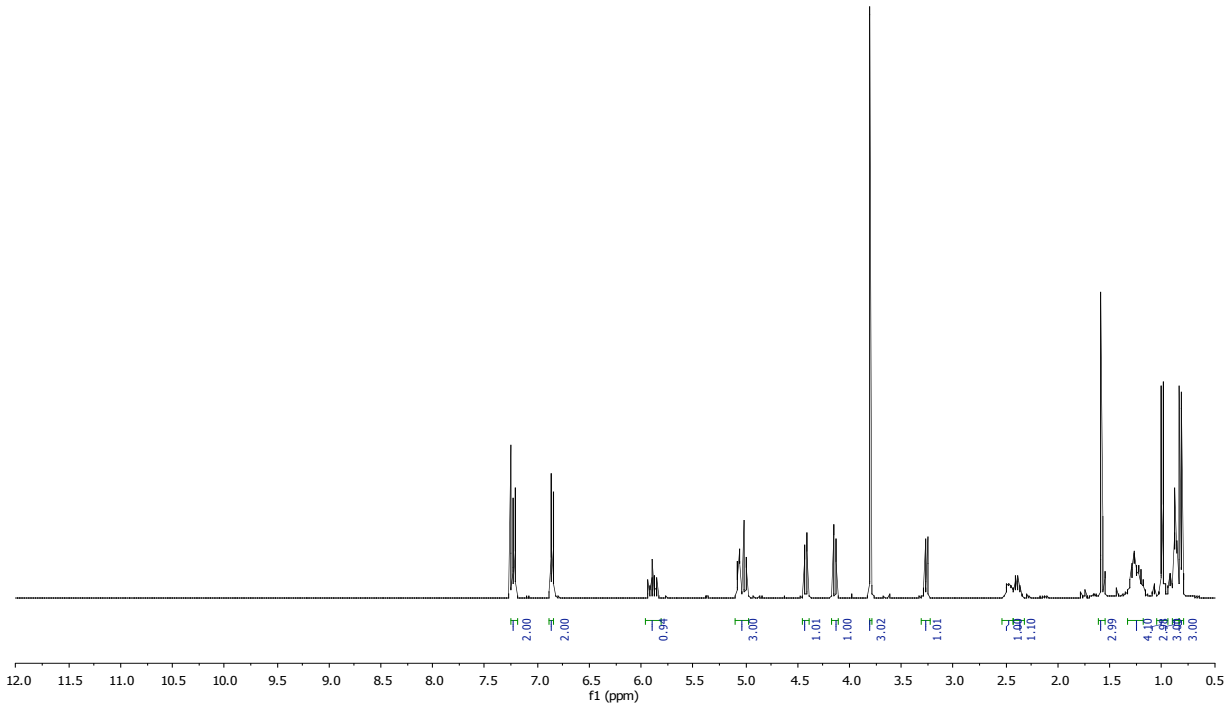

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

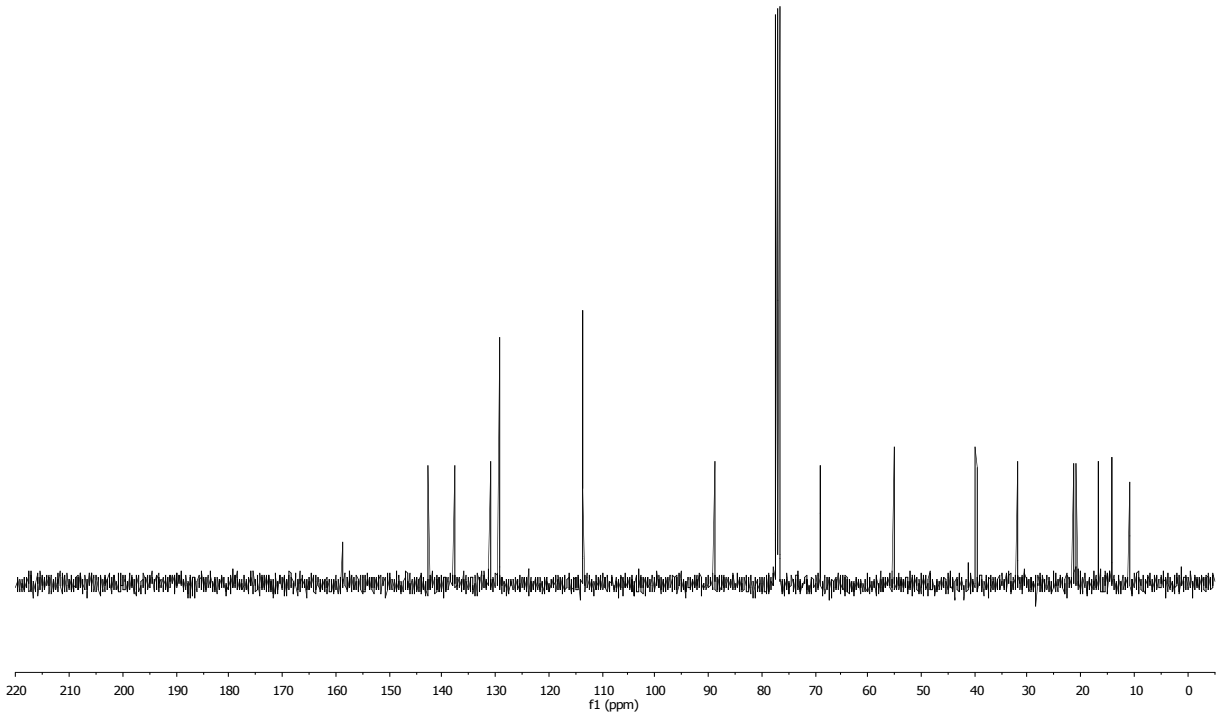

OTs
OH
Me
25
Me
Me
Me

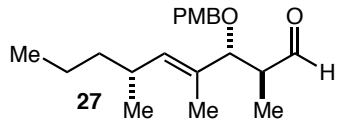

2.01
2.00
1.00
3.01
1.01
0.99
1.01
3.04
1.12
3.02
1.29
3.01
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

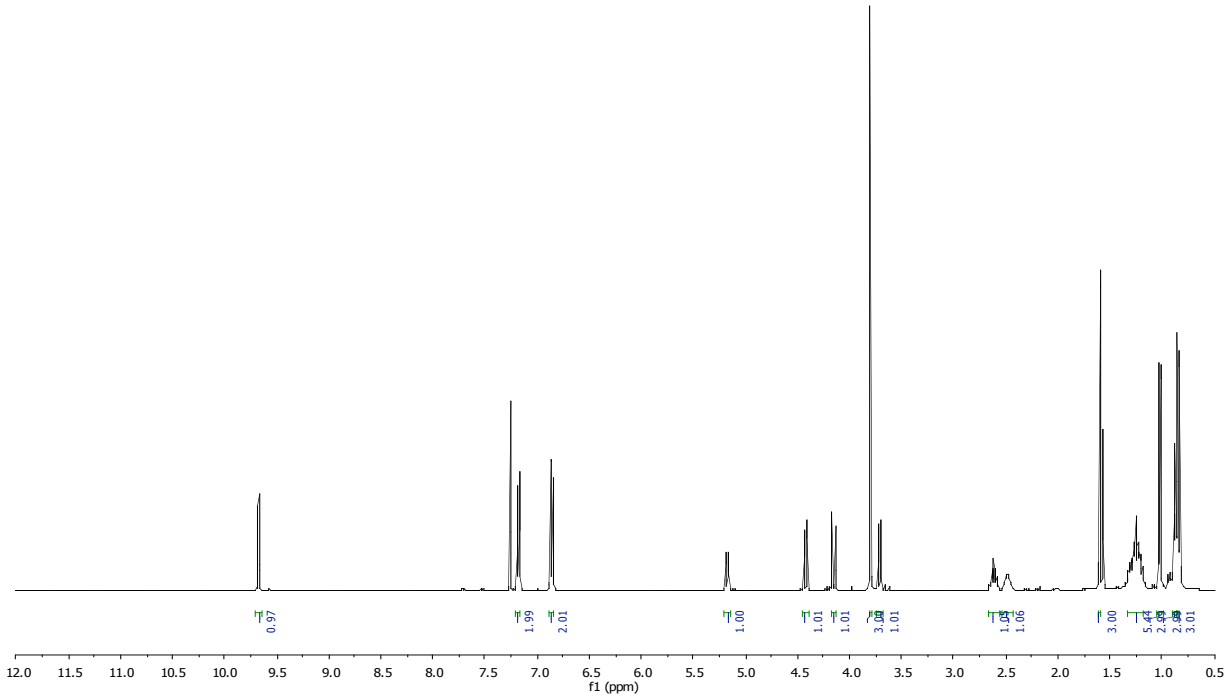

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

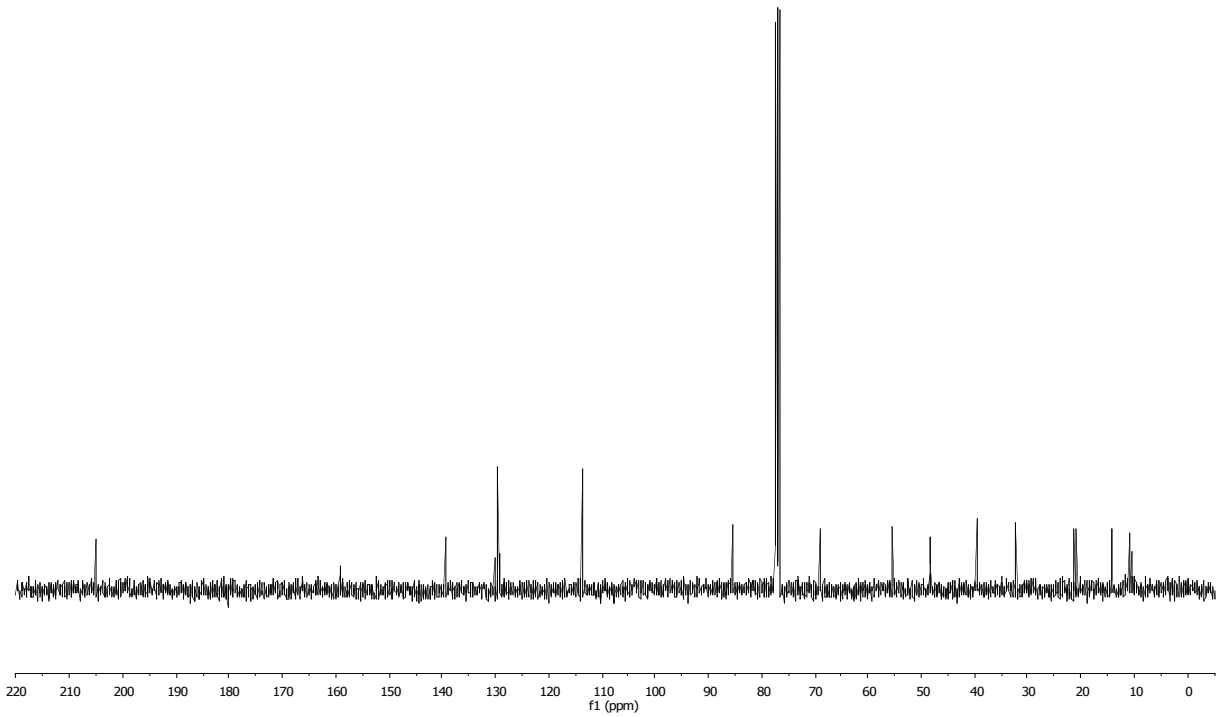

OPMB
Me
26
Me
Me
Me

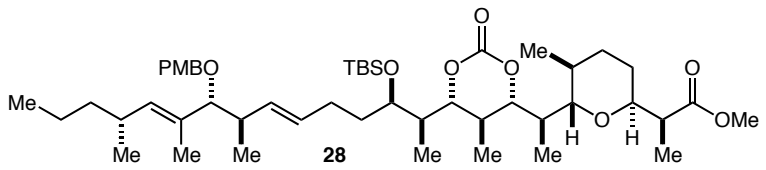

2.00
2.00
0.94
3.00
1.01
1.00
3.02
1.01
1.10
2.99
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

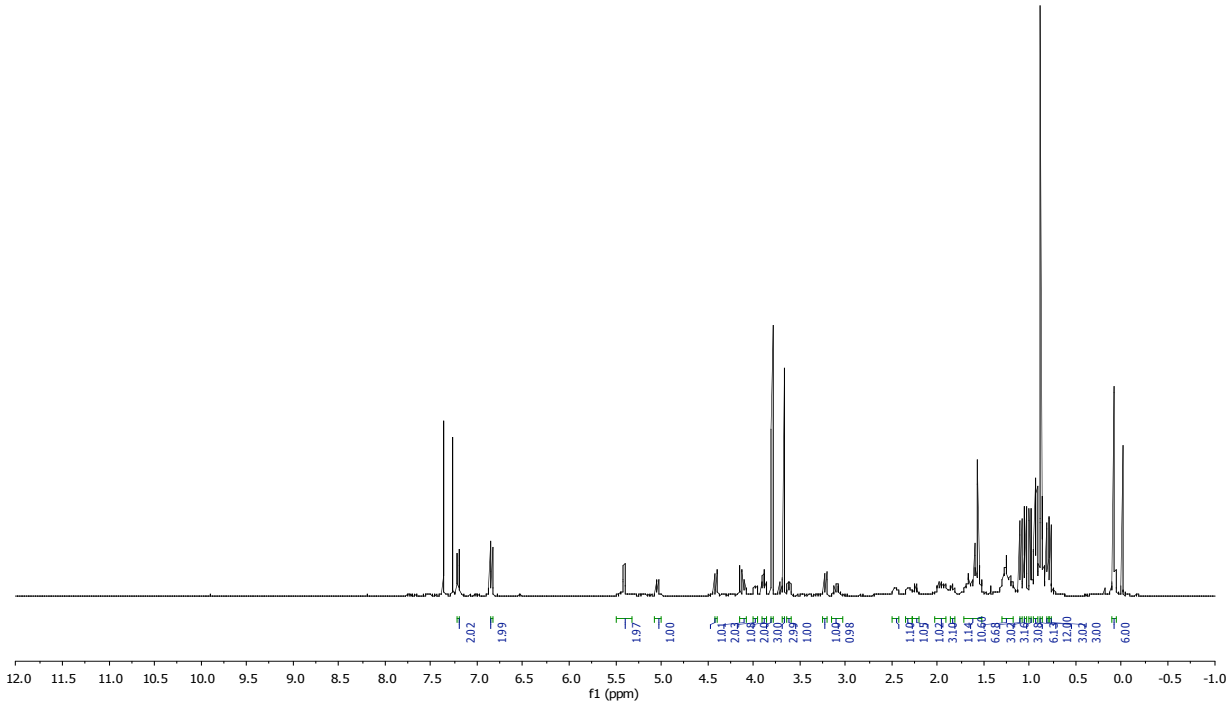

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

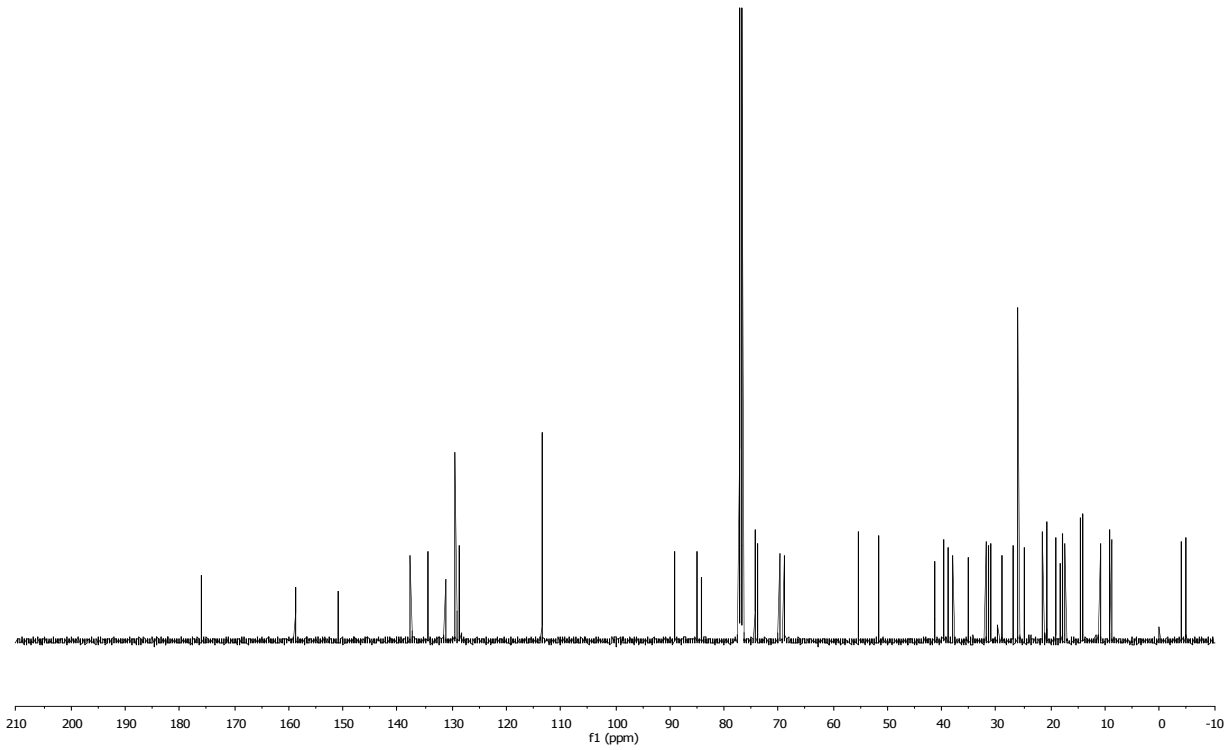

PMBO
O
Me
H
27
Me
Me
Me

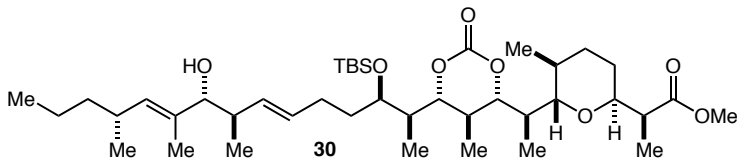

0.97
1.99
2.01
1.00
1.01
1.01
1.01
1.06
3.00
3.01
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

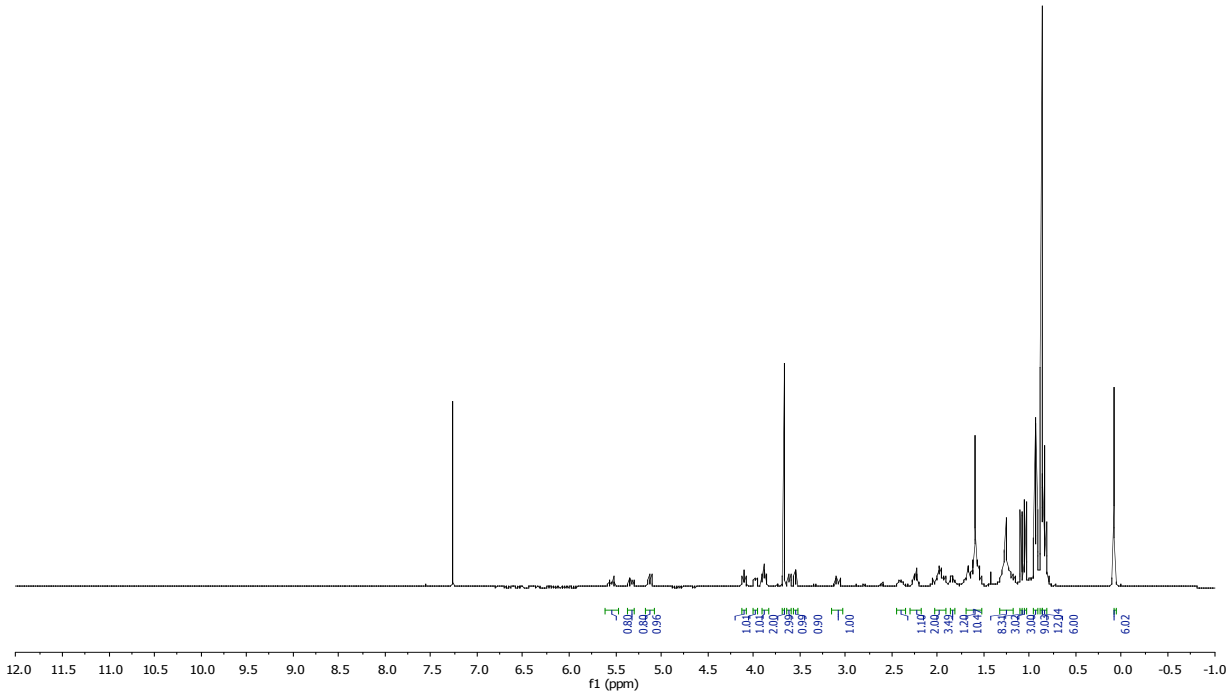

PMBO
TBSO
Me
Me
Me
Me
Me
Me
Me
Me
Me
Me
Me
O
O
O
O
O
O
H
H
OMe
28

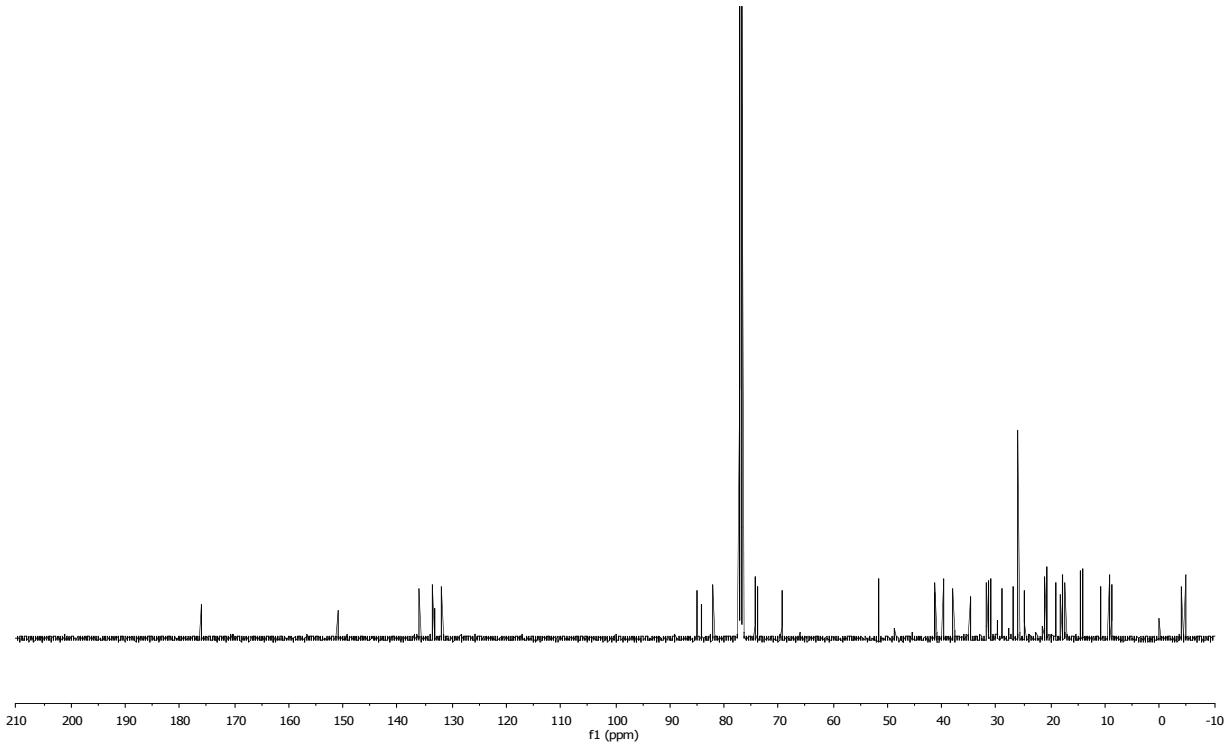

2.02
1.99
1.97
1.00
1.00
2.99
1.00
0.98
6.68
12.00
3.02
3.00
6.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

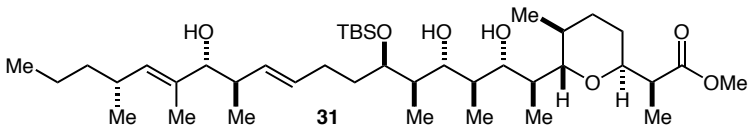

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

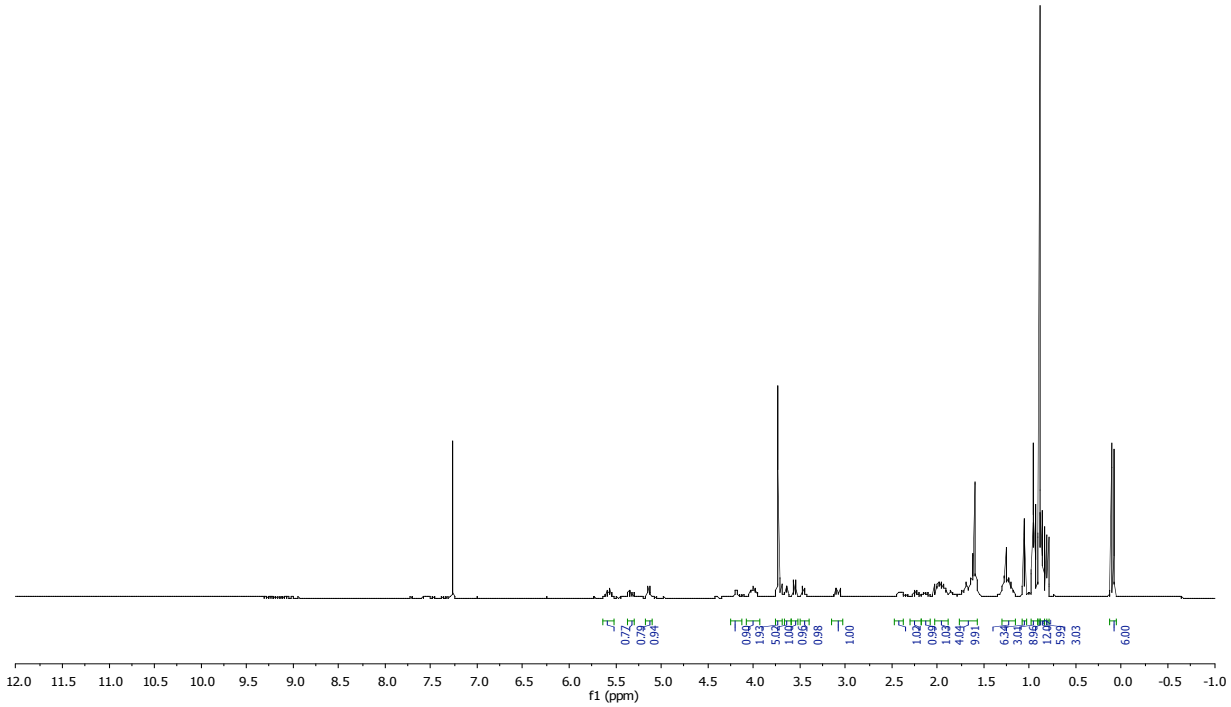

HO
TBSO
O
O
O
Me
Me
O
O
H
H
O
OMe
Me
Me
Me
Me
Me
Me
Me

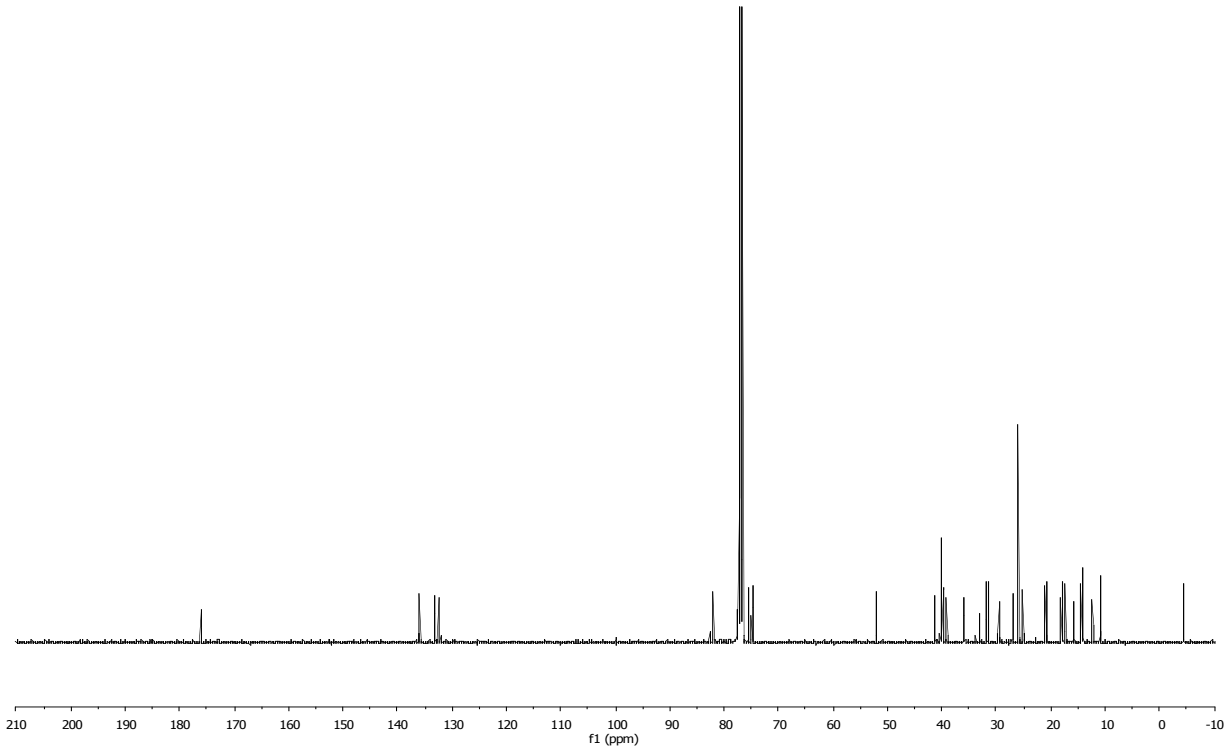
30

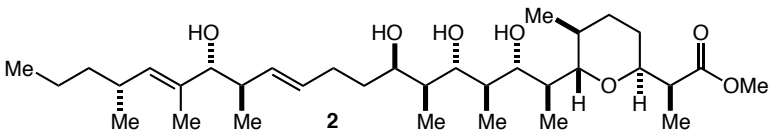

0.80
0.84
0.96
1.04
1.04
2.00
2.99
0.99
0.90
1.00
1.10
2.08
3.45
1.24
10.42
8.31
3.03
3.03
9.08
12.04
6.00
6.02
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Me
HO
TBSO
HO
HO
Me
O
OMe
Me
Me
Me
31
Me
Me
Me
H
O
H
Me

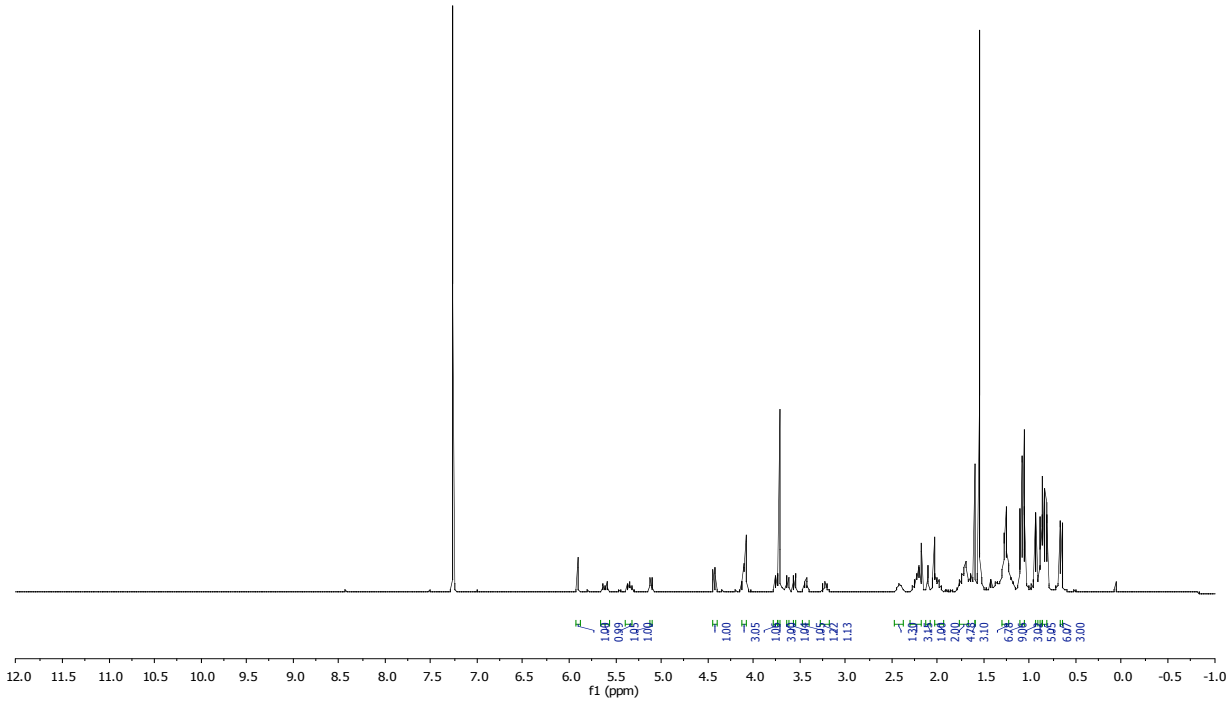

0.72
0.79
0.94
0.90
1.93
5.02
1.00
0.96
0.98
1.00
1.02
0.99
1.03
4.04
9.91
6.34
3.04
8.94
12.00
5.99
3.03
6.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

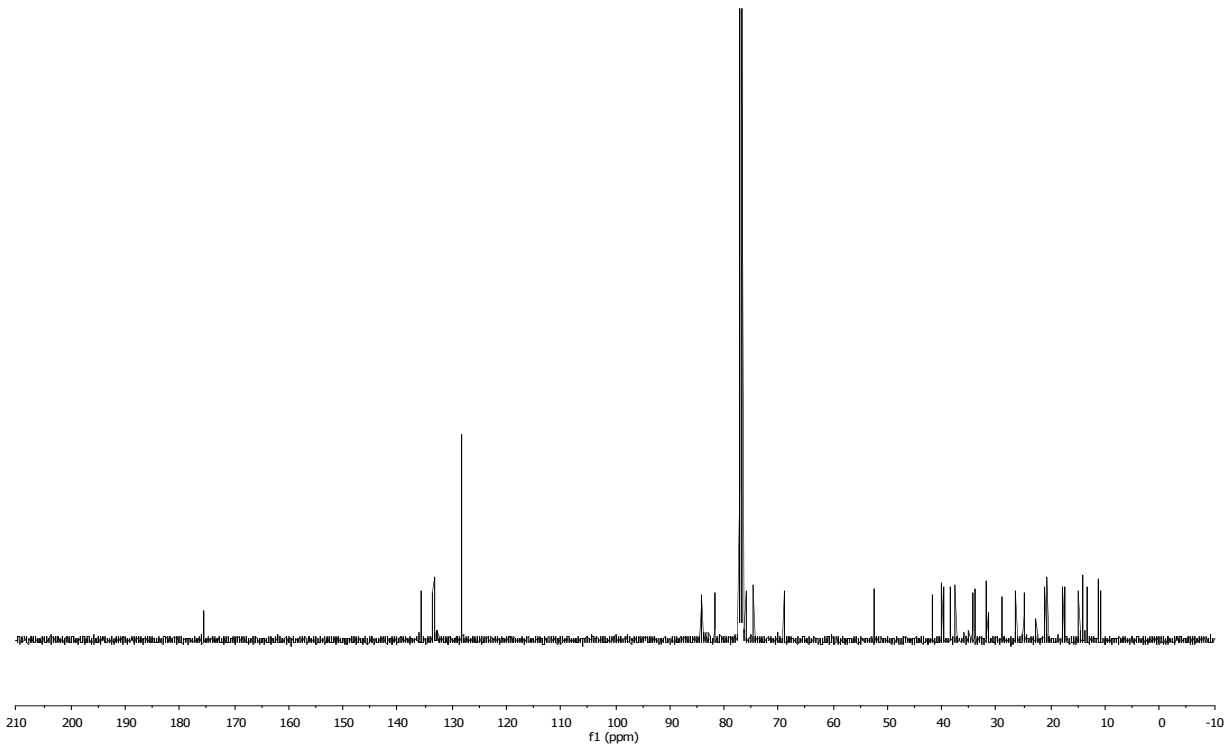

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



2

Zincophorin Methyl Ester





^{1}H and ^{13}C NMR spectra of Meyer's and Cossy's synthetic **2** (see: Defosseux, M.; Blanchard, N.; Meyer, C.; Cossy, J. *J. Org. Chem.* **2004**, *69*, 4626):